

2016

SCIENTIFIC REPORT



INCLIVA | VLC
Health Research Institute

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Fundación Investigación Hospital Clínico Universitario de Valencia

INCLIVA Health Research Institute

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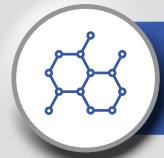
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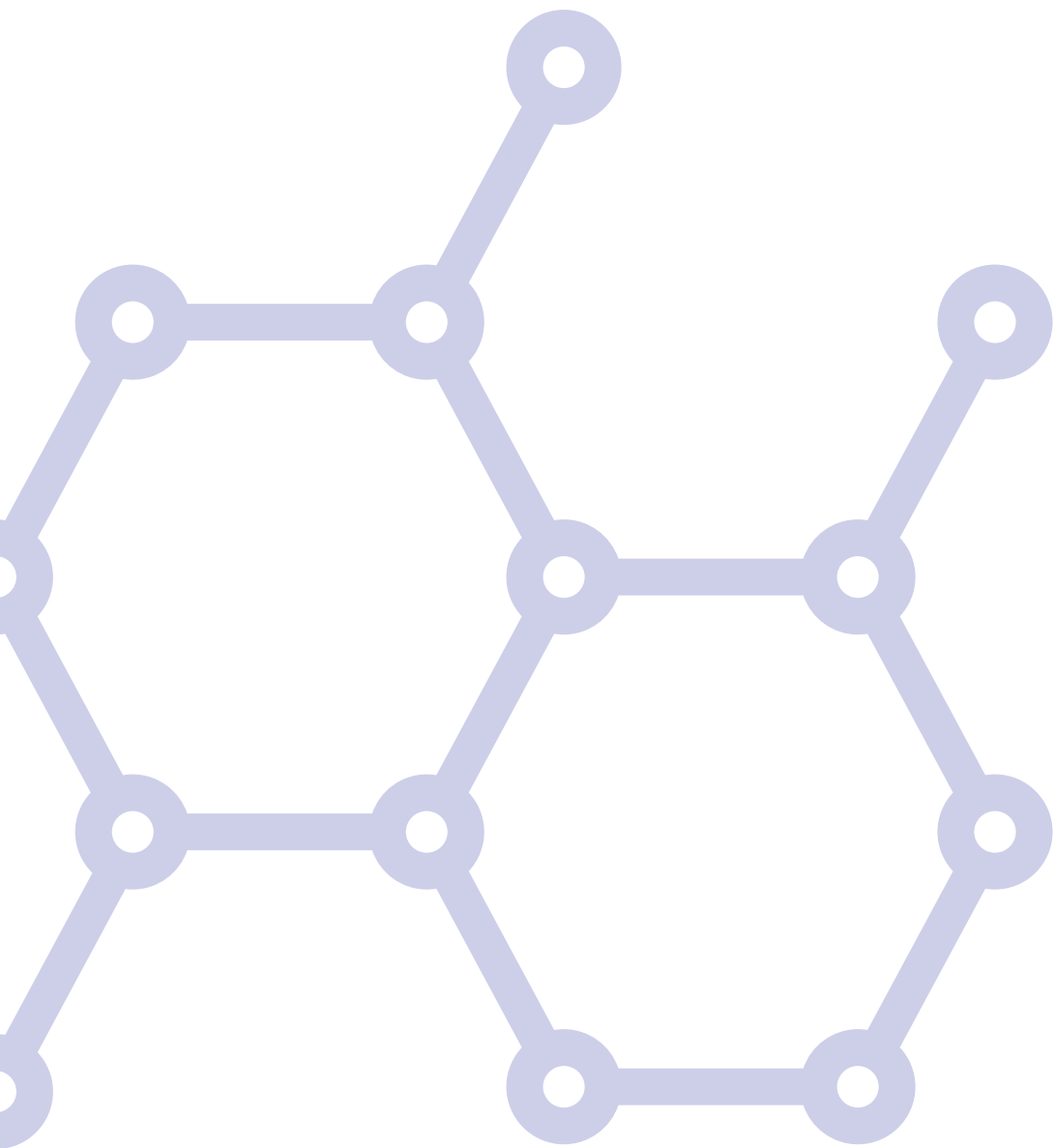
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Introduction





It's a pleasure for us to introduce once again INCLIVA's Annual Scientific Report 2016. As in previous years, this document provides an assessment of the scientific activities carried out during the year 2016 by INCLIVA's research groups from the *Hospital Clínico Universitario* of Valencia and its Department of Health, the University of Valencia and the *Instituto Universitario IVI*. The research activity of our Institute is, therefore, the result of the combined effort of our professionals, who have worked with great dedication during 2016. This report represents a unique chance to take stock of the activities and goals achieved and, therefore, to be able to face new challenges in the coming years. This year has represented a truly milestone for several reasons.

First, it is important to mention that in 2016 INCLIVA renewed its accreditation as Health Research Institute by the Carlos III Health Institute. After the visit of three auditors from the Carlos III Health Institute and a rigorous audit process in which over 700 documents were thoroughly reviewed, our efforts were rewarded with the accreditation of the institute, which will be in force for the next five years. The overall goal of the process was basically to verify compliance with the applicable regulations (Royal Decree, Ministerial Order and Evaluation Guide). Once the exam was accomplished, auditors transferred the main conclusions to INCLIVA's management team, highlighting its strengths and indicating a few opportunities for improvement. They expressed their satisfaction on the trajectory of the institute with a specific mention of the role that the management structure plays in the promotion and development of research.

Secondly, following the efforts in the area of quality management, INCLIVA's Innovation Unit obtained the certification UNE 166002:2014, a standard that guarantees that the R&D&I Management System deployed is committed to the systematization of the activities in order to plan, organize and control them. As a result a protocol for the interactions with other units and providing transparency and added value to the activity has been created. Furthermore, INCLIVA's genomics research platform was certified under ISO 9001:2015 standard, joining previously INCLIVA's ISO certified management systems (Biobank, ECCR, UCIM and scientific management). Together,

these awards reinforce the Institute's image of excellence and confirm its will to continually progress in order to give a day by day response that meets the expectations of both researchers and customers.

Moreover, the scientific and innovative culture promotion unit was accredited as a member of the Network of Units of Scientific Culture and Innovation (UCC+i) promoted by the Spanish Foundation for Science and Technology (FECYT). The unit received funds to join forces and resources around three areas: promoting innovation culture, increasing research activity among medical and nursing staff and establishing a dialogue between scientists and patients.

Additionally, the VLC-Bioclinic Program was continued together with the University of Valencia in order to enhance innovation and technology transfer through multidisciplinary collaboration among professionals from diverse fields. It is an ambitious initiative whose main goal is to promote translational research between researchers and physicians from both institutions. This year the program funded 5 innovative collaborative projects and 10 preparatory actions for cooperative research projects.

Regarding scientific output, during 2016 INCLIVA reached 649 papers and surpassed the impact factor barrier of 2.900, thus sustaining the upward trend of recent years. Likewise, the quality of scientific output in terms of publications was remarkable: articles published in journals within the first and second quartiles of their respective categories represented 60% and 18% of the total production, respectively.

In terms of scientific research projects, INCLIVA's groups competitively secured 20 new projects under the National R&D&I Plan (with special mention to the integrated excellence project funded by Carlos III Health Institute PIE15/00013), 2 international projects, 7 projects funded by the Valencian Government and 17 competitive grants from private funding entities. In total, during 2016 INCLIVA kept active over 140 competitive projects and 44 additional intramural research initiatives. Furthermore, INCLIVA's research groups were active in national competitive research networks (3 Platforms, 8 CIBER and 7 RETICS).



One of the priority goals of INCLIVA is to promote its scientific research and innovation at international level, collaborating with other top-notch research institutions all around Europe, as well as with SMEs, big companies and patient's organizations. Big efforts have been then put in place from the international area to gain recognition as leader in areas such as cardiovascular, personalized medicine, ageing, oncology, frailty or big data among others. In this regard, INCLIVA is involved as one of the main clinical leaders in the Big Data Value Association (BDVA), the European Infrastructure for Translational Medicine (EATRIS) or the Worldwide Initiative Networking in Personalized Cancer Medicine (WIN). Additionally, INCLIVA is member of several collaborative projects recently funded by the European Commission (MOTRICOLOR, INTRACOLOR or the ADVANTAGE initiative), the Innovative Medicines Initiative (BigData@Heart or Tripp) and COST Actions much more oriented to foster the thematic networking among researchers (EPICHEM, MuTaLig or MOUSEAGE).

In relation to clinical research, the main novelty of the year was the publication, on January 13th, of the new Royal Decree 1090/2015, which regulates clinical trials, Ethical Committees in Clinical Research and the Spanish Registry of Clinical Studies. Its most important change is that, since its publication, only one Committee ruling is needed in order to approve a given clinical

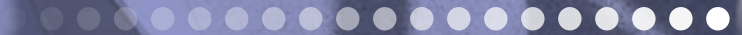
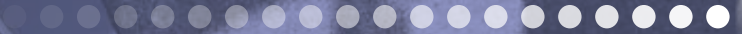
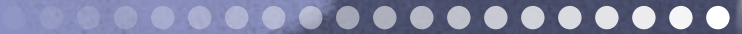
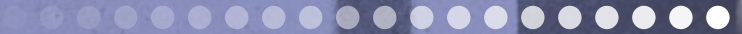
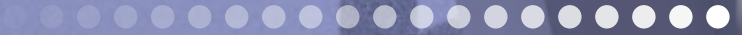
trial and issues a single and binding judgement for the entire national territory. As a consequence of this new regulation, *Hospital Clínico's* ECCR has processed only 15 studies in 2016. Nonetheless, INCLIVA managed 146 new clinical studies resulting in a total of 341 active clinical studies during the year.

Among the activities to promote the culture of research and training, during 2016 INCLIVA continued with its Training Plan by collaborating with the different hospital departments in the organization and management of 49 training initiatives, including 14 courses, 15 workshops and 5 seminars and 15 conferences. In addition, as every year, the Institute provided grants for research secondments in centers of excellence that allowed 18 INCLIVA's researchers to acquire new knowledge for clinical and research techniques. Finally, the involvement of university research groups has resulted in high participation in graduate programs, generating 90 doctoral thesis this year.

The present privileged position of INCLIVA has been possible thanks to the efforts of our nearly 600 researchers, 180 of which are directly hired by the Foundation. Nevertheless, we face the challenge of continuing to generate knowledge and guiding research excellence for the benefit of society.

Rafael Carmena Rodríguez
General Director

Josep Redón i Mas
Scientific Director







2

INCLIVA
Health
Research
Institute





2.1. History

The Foundation for the Research of the *Hospital Clínico Universitario* of Valencia was constituted in the year 2000 as the first valencian research foundation attached to a public hospital. Ten years later, some excellence groups in biomedical research from the University of Valencia and IUIVI (Valencian Infertility Institute) joined the Foundation through the establishment of specific agreements, so INCLIVA Health Research Institute was created.

The main aims of INCLIVA are both to manage the biomedical research carried out by the *Hospital Clínico Universitario* of Valencia and its Health Department and to encourage teaching

and scientific activities, thus improving patient treatment and knowledge sharing.

In 2011 INCLIVA was accredited as a Health Research Institute by the Ministry of Science and Innovation (*Ministerio de Ciencia e Innovación*) so it obtained preferential treatment by the Carlos III Health Institute (*Instituto de Salud Carlos III*), being recognized its excellent research.

During 2016 and after the visit of the auditors from the Institute of Carlos III Health Institute, INCLIVA received the official notification of renewal of its accreditation as Health Research Institute for the next five years.



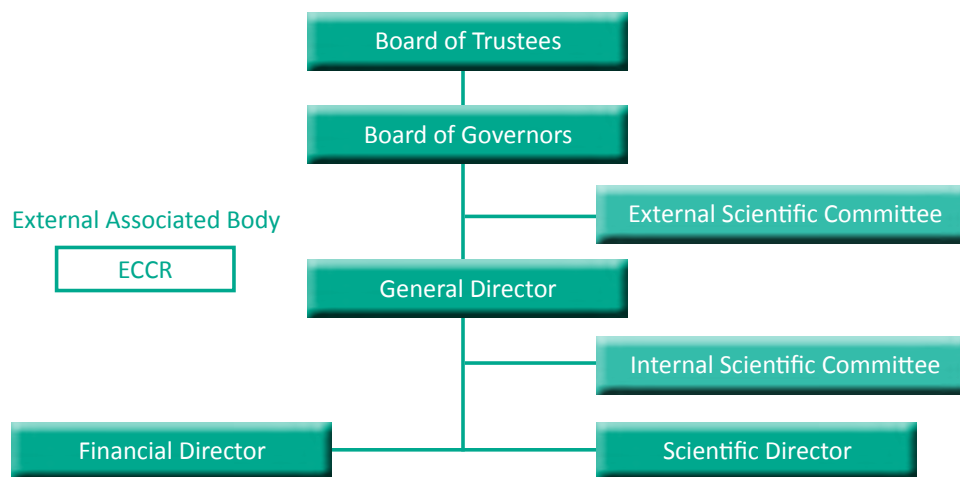


2.2. Organizational structure

2.2.1. Government structure

The highest government body in the Foundation, the Board of Trustees, is headed by the Regional Minister of Health of the Valencian Government. This body appoints a Board of Governors –headed by the Chief Executive Officer of the Health De-

partment– the General Director, the Scientific Director and the Financial Director. All of them count on the guidance of two Research Committees: the External Scientific Committee and the Internal Scientific Committee.



2.2.1.1 Board of Trustees

With a high representation from the valencian society, it is the highest collegiate body in the Institute and its function is to establish INCLIVA strategy and policies.

Dated December 31st 2016, its members are the following:

President:

- Ms. Carmen Montón, Regional Minister of Health of the Valencian Government.

Vice-president:

- Mr. Álvaro Bonet, Chief Executive Officer of the *Hospital Clínico Universitario* of Valencia and of the *Valencia's Clínico – Malvarrosa* Health Department.

Board members according to their positions:

- Mr. Esteban Morcillo, Most Illustrious Dean of the University of Valencia.
- Mr. Manuel Broseta, Social Council of the University of Valencia.

- Mr. Juan López-Trigo, Cañada Blanch Foundation.
- Mr. Rafael Alcón, Bancaja Foundation.
- Mr. José Noblejas, Valencia Chamber of Commerce.
- Mr. José Remohí, Scientific Director of the Valencian Infertility Institute.
- Ms. Ana María Ávila, General Director of Research, Innovation, Technology and Quality of the *Consellería de Sanidad Universal y Salud Pública* of the Valencian Government.
- Mr. Narcis Vázquez, Secretary of the *Consellería de Sanidad Universal y Salud Pública* of the Valencian Government.
- Mr. Martín Quirós, Valencian Council of Culture.
- Mr. Federico Pallardó, Most Illustrious Dean of the Faculty of Medicine.
- Mr. Jesús Fernández Crespo, Carlos III Institute of Health.
- Mr. Rafael Carmena, INCLIVA General Director.

**Board members in their own names:**

- Mr. Carlos Pascual
- Mr. Joaquín Ortega
- Mr. Tomás Trenor
- Mr. Manuel Montánchez

The Scientific Director and Financial Director attend the meetings with right to speak but without a vote.

2.2.1.2 Board of Governors

The Board of Governors executes and enforces the Board of Trustees agreements. Also it has other duties such as to prepare and pass the proposals of activities and research projects and to decide and allocate the budgetary means.

Dated December 31st 2016, its members are the following:

President:

- Dr. Álvaro Bonet, Chief Executive Officer, *Hospital Clínico Universitario* of Valencia.

Vice-president:

- Prof. Federico Pallardó, Most Illustrious Dean of the Faculty of Medicine.

Board members:

- Prof. Rafael Carmena, INCLIVA General Director.
- Dr. Ana María Ávila. General Director of Research, Innovation, Technology and Quality of the *Consellería de Sanidad Universitat y Salud Pública* of the Valencian Government.
- Prof. José Remohí, Scientific Director Instituto Universitario IVI.
- Prof. Josep Redón, INCLIVA Scientific Director.
- Dr. Jorge Navarro, Medical Director, *Hospital Clínico Universitario* of Valencia.
- Dr. Ana Sanmartin, Director of Primary Health Care, Health Service Department in Valencia *Clínico-Malvarrosa*.
- Prof. Salvador Lluch, Department of Physiology, University of Valencia.
- Dr. Antonio Peláez, President of the Ethical Committee in Clinical Research (ECCR), *Hospital Clínico Universitario* of Valencia.

- Dr. Manuel Alós, Head of the Pharmacy Department, *Hospital Clínico Universitario* of Valencia.
- Dr. Andrés Cervantes, Head of Oncology Department, *Hospital Clínico Universitario* of Valencia.
- Dr. Pascual Medina, Coordinator of Research Support Platform (UCIM), University of Valencia.

2.2.1.3 General Director

The highest person responsible for the execution of scientific, economic and administrative policies is the Foundation's General Director. The position has been held by Prof. Rafael Carmena Rodríguez since May 2012.



He graduated with Honors in Medicine from the Valencia's Faculty of Medicine in 1964, and he is Doctor "cum laude" from the *Universitat de València* in 1966. He is specialist in internal medicine and endocrinology. Professor of Pathology and Medical Clinics (Internal Medicine) at the universities of Valencia and Murcia, he has been Chief of the Internal Medicine Department of the *Ciudad Sanitaria Virgen de la Arrixaca* of Murcia (1974-1982), and Chief of both the Welfare Department, and the Endocrinology and Nutrition Department of the *Hospital Clínico Universitario* of Valencia for the last 28 years.

His research interest is focused on the lipid metabolism, the effects of dietary fats on cholesterolemia; conditions of resistance to insulin and its treatment; metabolic syndrome; genetics of hypercholesterolemia and treatment of diabetes dyslipidemia.

2.2.1.4 Scientific Director

The Scientific Director is appointed by government bodies. The scientific direction has been headed by Prof. Josep Redón since 2010. Prof. Redón is a specialist in Internal Medicine, Research Fellow in Hypertension in Northwestern University (Chica-



go), and Fellow of the Council for High Blood Pressure of the American Heart Association. He is currently Professor of Medicine, Head of the Internal Medicine Department and Coordinator of the Hypertension Unit of the *Hospital Clínico Universitario* of Valencia. Nowadays, he is member of the European Society of Hypertension, and he has authored many research works on hypertension and diabetes. He is also a member of the editorial committees of several international journals on the field of hypertension and cardiovascular risk.



2.2.1.5 External Scientific Committee

The External Scientific Committee assesses the collegiate government bodies regarding the research carried out and safeguards the quality of that research.

Their national and international members are appointed by the Board of Trustees that choose at least one expert in every INCLIVA priority area of research. It is constituted by well-known standing professionals among the scientific community.

The composition of the External Scientific Committee, dated December 31st 2016, is the following:

President:

- Prof. Javier Díez. Professor of Medicine, University of Navarra. Director of the Cardiovascular Sciences Area, Applied Medical Research Center (CIMA).

Members:

- Prof. José Baselga. Physician in Chief of the Memorial Sloan-Kettering of New York (U. S. A.). Professor of Medicine, Autonomous University of Barcelona.
- Prof. Nick S. Macklon. Professor in Obstetrics and Gynecology. Division of Developmental Origins of Adult Diseases (DOHaD).

University of Southampton. Princess Anne Hospital. Coxford Road, Southampton (United Kingdom).

- Prof. Antonio Vidal-Puig. Professor in Molecular Nutrition and Metabolism. University of Cambridge. Honorary Consultant in Metabolic Medicine. Metabolic research laboratories. Addenbrooke's Hospital, Cambridge (United Kingdom).
- Prof. Josep Tabernero. Chief of Medical Oncology Department. Vall d'Hebrón Hospital, Barcelona.
- Prof. José María Medina. Professor in Biochemistry and Molecular Biology. University of Salamanca. Castilla y León Neuroscience Institute (INCYL).
- Prof. Juan Carlos Lacal. Research Professor in Biomedical Research Institute (CSIC), Madrid.
- Prof. Manuel Tena-Sempere. Professor in Cell Biology, Physiology, and Immunology Department. University of Córdoba.
- Prof. Alberto Zanchetti. Professor Emeritus of Internal Medicine. Università di Milano. Director of the Istituto Auxologico Italiano (Italy). Consultant in WHO.

During 2016, the External Scientific Committee INCLIVA held two meetings: a meeting as teleconference held in May and a physical meeting of two days of duration held on November 5th and 6th.

Due to the new period of strategic planning, the committee activity focused on the analysis and evaluation of the new cross-research programs. Each program coordinator presented to the Committee members information about the SWOT analysis, the overall objectives of the programs, the different research lines and the related action plan. Committee members, in turn, provided specific feedback that greatly enriched the research programs.

Finally, as in previous years, INCLIVA's advisors evaluated the scientific and financial reports, and examined how the strategic, integration and training plans were put into practice.

2.2.1.6 Internal Scientific Committee

INCLIVA's Internal Scientific Committee acts as a counsellor to the General Director and the Scientific Director evaluating and supervising the scientific content of the research areas.

Dated December 31st 2016, the Committee composition is as follows:

**President:**

- Dr. Josep Redón i Mas

General Director:

- Dr. Rafael Carmena Rodríguez

Medical Director of the *Hospital Clínico Universitario* of Valencia:

- Dr. Jorge Navarro Pérez

Coordinators of the priority areas of research:

- Dr. Andrés Cervantes Ruipérez
- Dr. José Viña Ribes
- Dr. Carlos Simón Vallés
- Dr. Javier Chorro Gascó

Board members:

- Dr. Esteban Morcillo Sánchez
- Dr. Pilar Eroles Asensio
- Dr. Carlos Hermenegildo Caudevilla
- Dr. Ana Lluch Hernández
- Dr. Javier Chaves Martínez
- Dr. Eduardo Otero Coto
- Dr. Federico Pallardó Calatayud
- Dr. Gloria Ribas Despuig
- Dr. Irene Cervelló Alcaraz
- Dr. Felipe Vilella Mitjana
- Dr. Daniel Monleón Salvadó
- Dr. Fernando Martínez García
- Dr. Carlos Solano Vercet
- Dr. Rosa Zaragoza Colom
- Dr. Luis Sabater Ortí (invited member)
- Dr. Marina Soro Domingo (invited member)

2.2.1.7 Ethical Committee in Clinical Research

The Ethical Committee in Clinical Research (ECCR) of the *Hospital Clínico Universitario* of Valencia is the independent body whose task is to safeguard the protection of the rights, security

and welfare of the subjects taking part in a clinical trial or research project.

Among others tasks, this Committee assesses the protocol, the aptitude of the participating researchers, the adequacy of the center's facilities, and ensures the use and quality of the Fact Sheet for Patients in order to secure the informed consent.

The members of the ECCR in the *Hospital Clínico Universitario* of Valencia, dated December 31st 2016, are the following:

President:

- Dr. D. Antonio Peláez Hernández. Head of the Allergy Unit.

Vice-president:

- Dr. Marina Soro Domingo. Head of Section of the Anesthesiology and Reanimation Unit.

Secretary:

- Dr. Cristina Gomis Gozalbo. Specialist of the Gynecology Department.

Substitute Secretary:

- Ms. Begoña Hernández Genovés. Head of Supplies Service. Graduated in Law.

Members:

- Dr. Manuel Alós Almiñana. Head of the Pharmacy Department.
- Ms. M^a Ángeles Mora Pla. Outpatient Nursing Supervisor.
- Prof. Esteban Morcillo Sánchez. Dean of the University of Valencia. Professor of Pharmacology.
- Dr. José Luis Trillo Mata. Pharmaceutical Primary Care.
- Dr. M^a José Fabiá Valls. Specialist of the Internal Medicine Department.
- Ms. M^a José Tarín Blasco. Graduated in Law.
- Dr. Julio Palmero Da Cruz. Head of the Radiology Department.
- D. Carlos Pascual Vicens. Graduated in law.
- Dr. Francisco Tosca Flores. Specialist doctor in Obstetrics and Gynecology Department.
- Dr. José Álvaro Bonet Pla. Hospital Chief Executive Officer.
- Dr. Ricardo Ruiz Granell. Head of Section of Cardiostimulation Department.
- Dr. Diego V. Cano Blanquer. Primary Health Care Pharmaceutics.



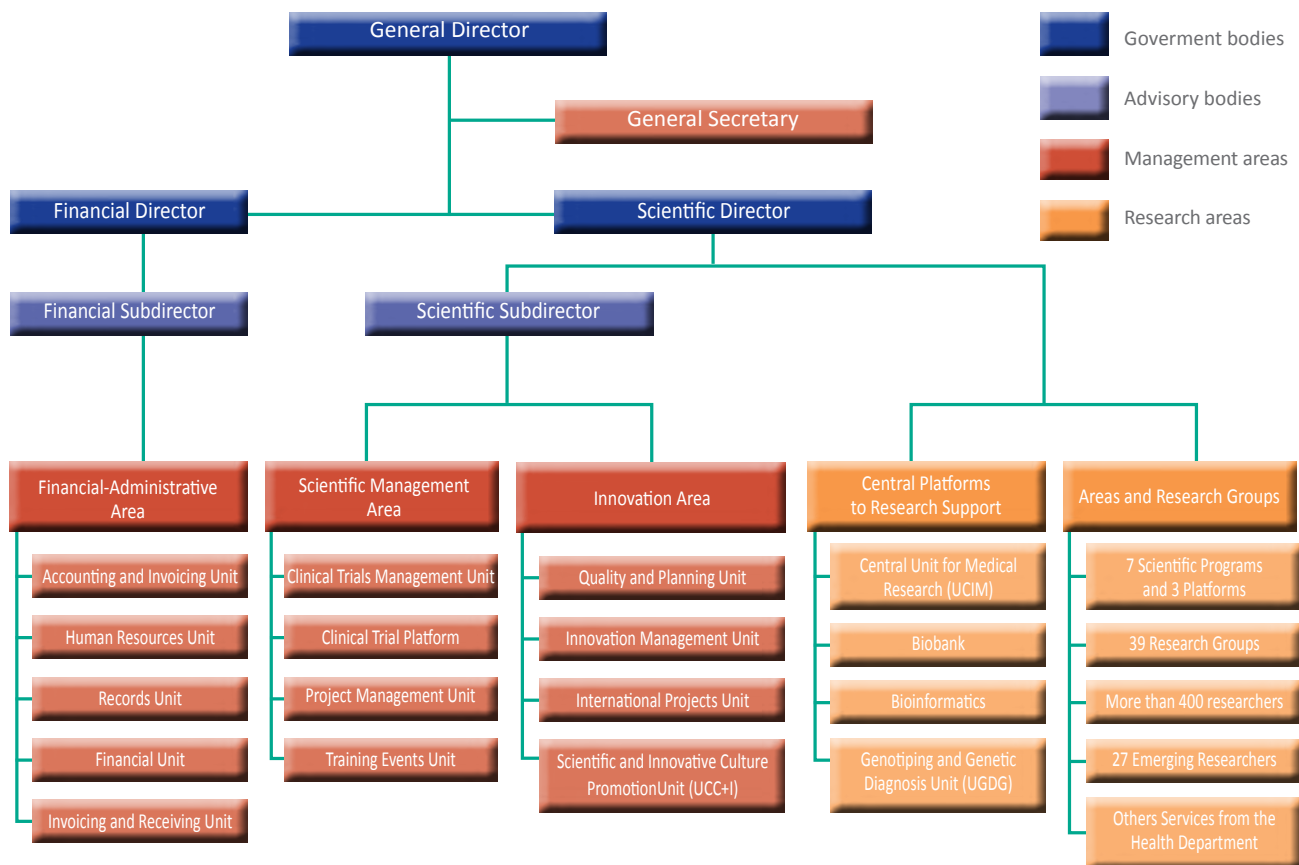
- Prof. Miguel Mínguez Pérez. Head of Section of Gastroenterology Department.
- Dr. Francisco Dasí Fernández. Stabilized Miguel Servet Researcher.
- Prof. Andrés Cervantes Ruipérez. Head of Hematology and Oncology Department.
- Prof. Joaquín Ortega Serrano. Head of the General Surgery Department.
- Dr. Luis González Luján. Specialist doctor in Primary Health Care.
- Dr. M^a Jesús Puchades Montesa. Specialist doctor in Nephrology Department.
- Dr. Rafael Fernández-Delgado. Head of Section of Pediatrics Department.
- Dr. Jorge Navarro Pérez. Medical Director of the *Hospital Clínico Universitario* of Valencia.
- Ms. Cristina Pérez Moreno. Lawyer.

2.2.2. Management structure

In 2013 organization chart is it comprised of two sub-directorates, economic and scientific, as well as a new area of innovation within the latter subdirectorate.

The first subdirectorate is in charge of the administrative area, which deals with the financial and administrative matters as well as with human resource management.

The second, in turn, is in charge of the scientific activity management and innovation. It is responsible for the integral scientific management that includes controlling and monitoring clinical trials and research projects, organizing courses, conferences and seminars, and several tasks related to general administration. Furthermore, it acts as an administrative support to the different attached scientific committees and to the Medical Research Central Unit. Finally, it comprises the new innovation area that is in charge of quality and planning, innovation management, international programs and scientific and innovative culture promotion (UCCI).



**Administrative Area:**

- Financial-Administrative Director: Mr. Vicente de Juan
- Financial-Administrative Subdirector: Ms. Consuelo López
- Accounting and Invoicing Unit: Ms. M^a José Rosalén
- Financial Unit: Ms. Consuelo López and Ms. Karen Iglesias
- Invoicing and Receiving Unit: Ms. Vera Marín
- Records Unit: Ms. Alicia Belenguer
- Purchasing Unit: Ms. Isabel Gomis
- Human Resources Unit: Ms. Ruth Cano , Ms. Vanessa Aznar and Ms. Anabel Gil
- Receptionists: Ms. Carmen Montagud and Mr. Julio Expósito

Scientific Management Area:

- Scientific Subdirector: Dr. Marta Peiró
- Projects Unit: Ms. Mayca Román and Ms. Noemí Hidalgo
- Clinical Trials Management Unit: Ms. Dolores Iglesias and Mr. Roberto Martínez

- Clinical Trials Platform: Ms. Ana Portolés, Ms. Laura Silla, Ms. Mireia Hernández, Mr. Bernat Navarro

Innovation Area:

- Coordination: Dr. Enrique Cremades
- Quality and Planning Unit: Mr. Rafael Barajas
- Innovation Management Unit: Dr. Pedro Fernández
- International projects: Ms. Ana Ferrer, Dr. Javier Gámez
- OPESVAL: Dr. Ana Levin
- Scientific and innovative culture promotion (UCCI): Ms. Clara Badenas, Mr. Justo Giner

General Secretary:

- Responsible: Ms. Maite Saenz
- Technician: Ms. Lorena Munuera





2.3 Core facilities

In 2004 INCLIVA and the Central Service for Experimental Research Support (SCIE) of the University of Valencia signed a collaboration agreement of which was to boost cooperation between both institutions, with special emphasis in the execution of research projects and collective research activities. It allows the access, stay and use of the Central Unit for Medical Research facilities to *Hospital Clínico Universitario* of Valencia research staff.

The Central Unit for Medical Research (UCIM) was created thanks to FEDER funds in 1990. From its inception, it has been granted with several infrastructure coming from both University of Valencia and INCLIVA funds, as well as from external funds (*Comisión Interministerial de Ciencia y Tecnología, Generalitat Valenciana* and *Fondo de Investigaciones Sanitarias*).

In addition to these support units, INCLIVA has four additional platforms: the Biobank, the Genotyping and genetic diagnosis unit, the Cytogenetics lab and the Bioinformatics Unit. The latter was created as such in 2013, through a Carlos III Health Institute (*Instituto de Salud Carlos III*) grant program to improve infrastructure, the so called PROMIIS grant.

These laboratories count on several research technicians and technical assistants who have been included in the organization structure thanks to diverse public grants or directly to the University's budget.

The research support platforms are:

- Cell culture unit
- Flow cytometric unit
- Multigenic analysis unit
- Confocal microscopy unit
- Sequenom platform
- Laboratory of molecular imaging and metabolomics
- Animal housing and experimental operating theaters unit
- Proteomics unit
- Small animals PET/CT camera and laboratory for radioactive isotopes
- Personal autonomy, dependence and severe mental disorders assessment unit

INCLIVA Platforms are:

- Biobank
- Bioinformatics unit
- Genotyping and genetic diagnosis unit
- Cytogenetics laboratory







3

INCLIVA
global
analysis





3.1 Scientific production global analysis

As in previous years, INCLIVA continued in 2016 with the upward trend in scientific output. Key indicators of research quality such as the publications of research results in international journals or the impact factor of these journals have improved. The number of indexed works in *Medline* database reached 649 in 2016.



To show this positive trend, the following figures depict the number and quality of the published manuscripts expressed in terms of total and average impact factor.

Indexed number of publications



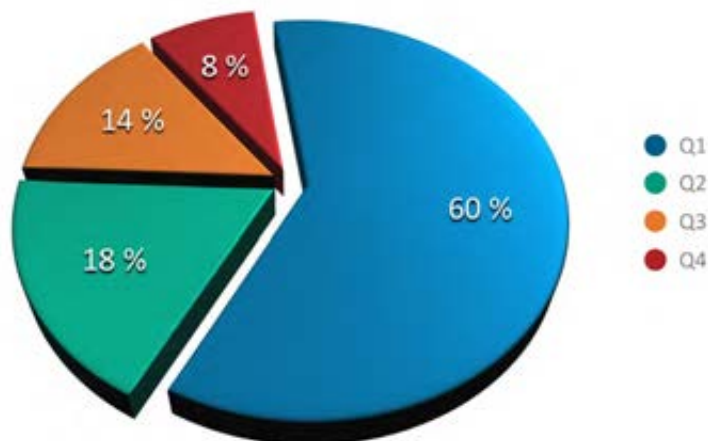
Cumulative impact factor





The distribution by quartiles within their thematic categories is shown below. In 2016, 78% of the papers that were published in indexed journals belong to the first and second quartiles of their corresponding thematic categories.

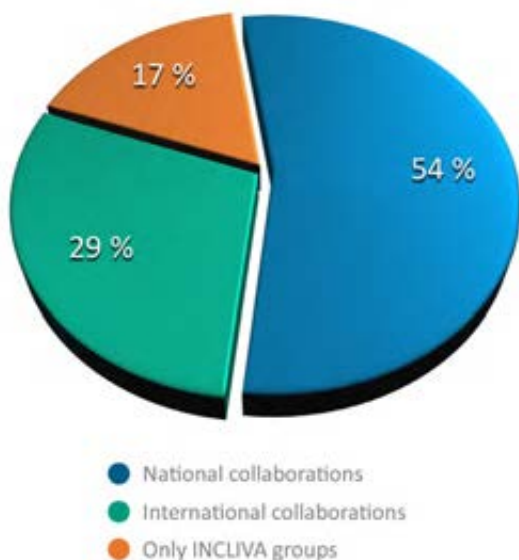
Quartile distribution



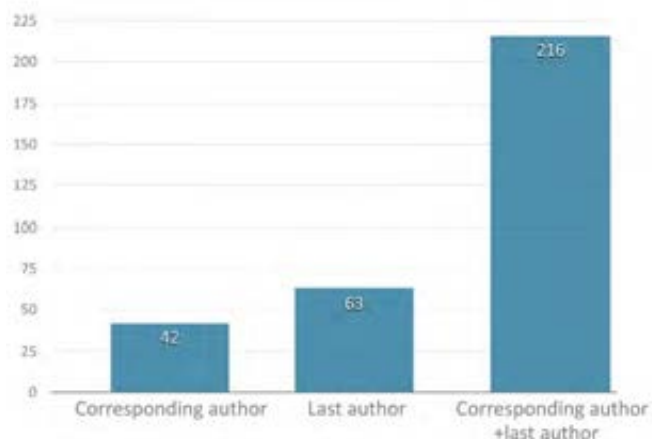
One of the main success factors for a biomedical research institution has to do with its potential to establish high level scientific collaborations. The percentage of national and international collaborations which led to scientific output in 2016 is listed below.

Another key performance indicator is the leadership role in scientific publications. The chart below shows the number of published articles in which INCLIVA researchers sign as last author, corresponding author or both at the same time.

Collaborations



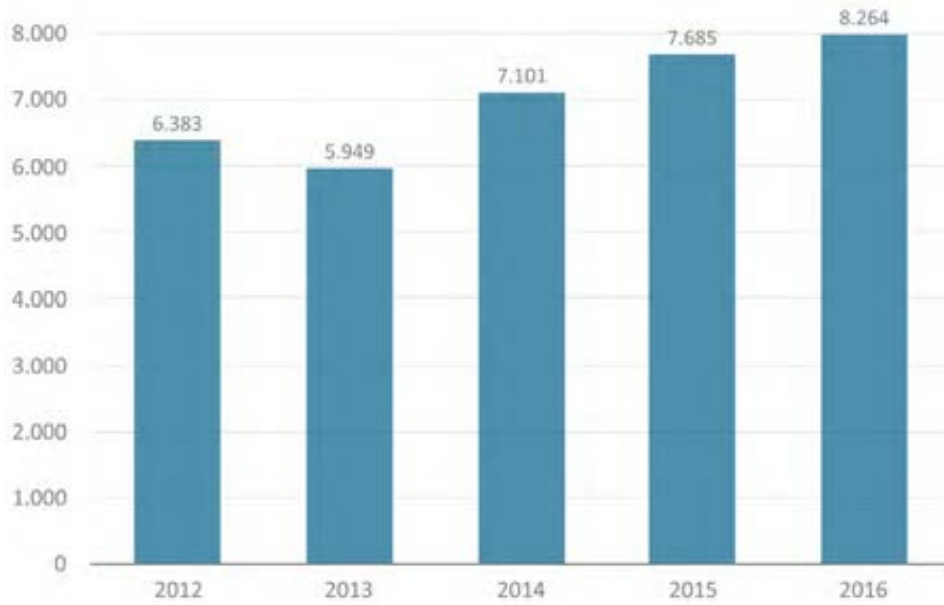
Leadership in scientific production





3.2. Financial resources

INCLIVA's funding during 2016 totaled 8.264.070€. The funds raised from competitive sources were still higher than the average of recent years.

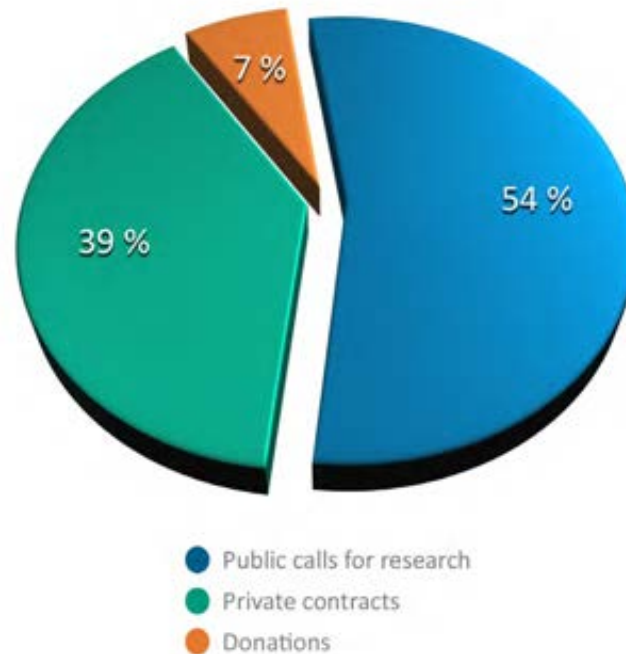


Funding source in the indicated period is shown below.





The remaining income corresponds to private sources of funding, clinical trial revenues and grants among others. The graph below shows this distribution of the year 2016.



3.3 Cooperative research networks








The Carlos III Health Institute (*Instituto de Salud Carlos III*) develops – through the General Subdirection of Networks and Centers for the Cooperative Research – the creation of stable research network structures such as *RETICS* (Thematic Networks of Cooperative Research) and *CIBER* (Network of Centres for Biomedical Research). INCLIVA participates in many of these research structures through its associated groups.

The following table shows the participation in scientific networks according to the prioritized research area, the center and its principal investigator.

**CIBER**

Research Area	INCLIVA PI	Scientific Network	Reference
Cardiovascular	Rafael Carmena Rodríguez	CIBERdem	 CB07/08/0018
	Empar Lurbe i Ferrer	CIBERobn	 CB06/03/0039
Metabolism and Organ Damage	Esteban Morcillo Sánchez	CIBERes	 CB06/06/0027
	Federico V. Pallardó Calatayud	CIBERer	 CB06/07/0073
	Julio Sanjuán Arias	CIBERsam	 CB07/09/006
	Juan Vicente Esplugues Mota	CIBERehd	 CB06/04/0071
	Guillermo Sáez Tormo	CIBERobn	 CB12/03/30016
	Rafael Tabarés Seisdedos	CIBERsam	 CB07/09/0021

RETIC

Research Area	INCLIVA PI	Scientific Network	Reference
Oncology	Samuel Navarro	RTICC	 RD12/0036/0020
	Ana Lluch Hernández	RTICC	 RD12/0036/0070
Cardiovascular	Francisco Javier Chorro Gascó	RIC	 RD12/0042/0048
	Juan Sanchis Forés	RIC	 RD12/0042/0010
	Carlos Hermenegildo Caudevilla	RIC	 RD12/0042/0052
Metabolism and Organ Damage	José Viña Ribes	RETICEF	 RD12/0043/0029
Others	Rafael Peris Bonet	RTICC	 RD12/0036/0053



In addition to research network structures, INCLIVA is member of three research platforms promoted by Carlos III Health Institute (*Instituto de Salud Carlos III*): biobank, clinical research and innovation platforms.

Reference: PT13/0010/0004

Title: Biobank Platform

Principal Investigator: Josep Redón I Mas

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2017

Total budget: 46.500€

Reference: PT13/0002/0031

Title: Clinical Research and Trials Platform

Principal Investigator: Andrés Cervantes Ruipérez

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2017

Total budget: 65.550€

Reference: PT13/0006/0023

Title: Innovation Platform

Principal Investigator: Josep Redón I Mas

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2017

Total budget: 38.985€

3.4 Knowledge transfer activities

INCLIVA Health Research Institute is fully committed to transfer the knowledge created both to the National Health System and to the industrial sector in order to fulfil its organizational mission.

3.4.1 Knowledge transfer to the National Health System

Clinical guidelines and consensus documents are one of the best indicators of knowledge transfer from research to clinical practice. The following table shows guidelines published in indexed journals in which authors attached to INCLIVA have been involved.

Clinical guidelines	IF
5	25,58

1. Basora M, Colomina MJ, Moral V, Asuero de Lis MS, Boix E, Jover JL, **Llau JV**, Rodrigo MP, Ripollés J, Calvo Vecino JM. Clinical practice guide for the choice of perioperative volume-restoring fluid in adult patients undergoing non-cardiac surgery. *Rev Esp Anestesiol Reanim.* 2016 Jan; 63(1):29-47. IF: 0
2. Klionsky DJ, Abdelmohsen K, Abe A, Abedin MJ, et al. Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). *Autophagy.* 2016; 12(1):1-222. IF: 11,753
3. **Lurbe I Ferrer E.** [2016 - European Society of Hypertension Guidelines for the management of high blood pressure in children and adolescents]. *An Pediatr (Barc).* 2016 Oct; 85(4):167-169. IF: 0,773
4. Smyth EC, Verheij M, Allum W, Cunningham D, **Cervantes A**, Arnold D, ESMO Guidelines Committee. Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2016 Sep; 27(suppl 5):v38-v49. IF: 9,269
5. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Capotano AL, Cooney MT, Corrà U, Cosyns B, Deaton C, Graham I, Hall MS, Richard Hobbs FD, Løchen ML, Löllgen H, Marques-Vidal P, Perk J, Prescott E, **Redon J**, Richter DJ, Sattar



N, Smulders Y, Tiberi M, Bart van der Worp H, van Dis I, Monique Verschuren WM. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. *Rev Esp Cardiol (Engl Ed)*. 2016 Oct; 69(10):939. IF: 3,792

Consensus documents	IF
8	22,81

1. **Llau JV**, Acosta FJ, Escolar G, Fernández-Mondéjar E, Guasch E, Marco P, Paniagua P, Páramo JA, Quintana M, Torrabadella P. Multidisciplinary consensus document on the management of massive haemorrhage (HEMOMAS document). *Rev Esp Anesthesiol Reanim*. 2016 Jan; 63(1):e1-e22. IF: 0
2. Masana L, **Ascaso JF**, Civeira F, Pedro-Botet J, Valdivielso P, Guijarro C, Mostaza J, López Miranda J, Pintó X, en nombre de la Sociedad Española de Arteriosclerosis. [Consensus document of the Spanish Society of Arteriosclerosis on indications of inhibitors of PCSK9]. *Clin Investig Arterioscler*. 2016 May-Jun; 28(3):164-5. IF: 0
3. Pedro-Botet J, Barrios V, Pascual V, **Ascaso JF**, Cases A, Millán J, Serrano A, Pintó X. [Delphi consensus on management of dyslipidaemia in patients with impaired glucose metabolism: Diana study]. *Clin Investig Arterioscler*. 2016 May-Jun; 28(3):132-40. IF: 0
4. Experts Panel from the Secretary of the National AIDS Plan (SPNS), Spanish Society of Psychiatry (SEP), **AIDS Study Group (GeSIDA)**, Spanish Society of Pediatric Infectious Diseases (SEIP). Executive summary of the consensus document on psychiatric and psychological aspects in adults and children with HIV infection. *Enferm Infecc Microbiol Clin*. 2016 Jan; 34(1):54-60. IF: 2,172
5. Besses C, **Hernández-Boluda JC**, Pérez Encinas M, Raya JM, Hernández-Rivas JM, Jiménez Velasco A, Martínez Lopez J, Vicente V, Burgaleta C, GEMFIN. Current opinion and consensus statement regarding the diagnosis, prognosis, and treatment of patients with essential thrombocythemia: a survey of the Spanish Group of Ph-negative Myeloproliferative Neoplasms (GEMFIN) using the Delphi method. *Ann Hematol*. 2016 Apr; 95(5):719-32. IF: 2,634
6. Van Cutsem E, **Cervantes A**, Adam R, Sobrero A, Van Krieken JH, Aderka D, Aranda Aguilar E, Bardelli A, Benson A, Bodoky G, Ciardiello F, D'Hoore A, Diaz-Rubio E, Douillard JY, Ducreux

M, Falcone A, Grothey A, Gruenberger T, Haustermans K, Heinemann V, Hoff P, Köhne CH, Labianca R, Laurent-Puig P, Ma B, Maughan T, Muro K, Normanno N, Österlund P, Oyen WJ, Papamichael D, Pentheroudakis G, Pfeiffer P, Price TJ, Punt C, Ricke J, Roth A, Salazar R, Scheithauer W, Schmoll HJ, Tabernero J, Taïeb J, Tejpar S, Wasan H, Yoshino T, Zaanán A, Arnold D. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. *Ann Oncol*. 2016 Aug; 27(8):1386-422. IF: 9,269

7. Vinuesa V, **Giménez E**, **Solano C**, Gimeno C, **Navarro D**, Spanish Society for Infectious Diseases and Clinical Microbiology Quality Control Study Group.. Would Kinetic Analyses of Plasma Cytomegalovirus DNA Load Help to Reach Consensus Criteria for Triggering the Initiation of Preemptive Antiviral Therapy in Transplant Recipients? *Clin Infect Dis*. 2016 Dec 1; 63(11):1533-1535. IF: 8,736
8. **Panel Europeo de Expertos**. Versión Española del Grupo de trabajo sobre Dislipemia Aterogénica. [Consensus for pharmacologic treatment of atherogenic dyslipidemia with statin-fenofibrate combined therapy]. *Clin Investig Arterioscler*. 2016 Mar-Apr; 28(2):87-93. IF: 0

Position statements	IF
6	14,87

1. Apostolo J, Holland C, O'Connell MD, Feeney J, Tabares-Seisdedos R, Tadros G, Campos E, Santos N, Robertson DA, Marcucci M, Varela-Nieto I, Crespo-Facorro B, Vieta E, Navarro-Pardo E, Selva-Vera G, Balanzá-Martínez V, **Cano A**. Mild cognitive decline. A position statement of the Cognitive Decline Group of the European Innovation Partnership for Active and Healthy Ageing (EIPAH). *Maturitas*. 2016 Jan; 83:83-93. IF: 2,942
2. Stergiou GS, Parati G, Vlachopoulos C, Achimastos A, Andreadis E, Asmar R, Avolio A, Benetos A, Bilo G, Boubouch-airiopolou N, Boutouyrie P, Castiglioni P, de la Sierra A, Dolan E, Head G, Imai Y, Kario K, Kollias A, Kotsis V, Manios E, McManus R, Mengden T, Mihailidou A, Myers M, Niiranen T, Ochoa JE, Ohkubo T, Omron S, Padfield P, Palatini P, Papaioannou T, Protogerou A, **Redon J**, Verdecchia P, Wang J, Zanchetti A, Mancia G, O'Brien E. Methodology and technology for peripheral and central blood pressure and blood pressure variability measurement: current status and future

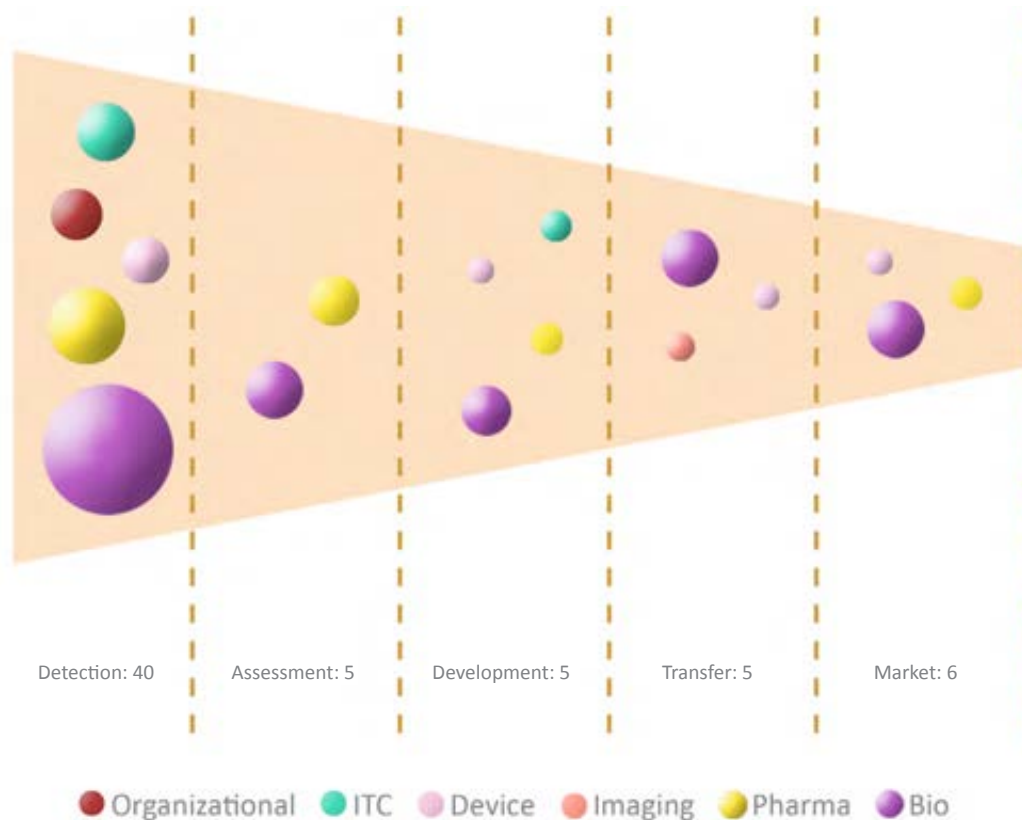


- directions - Position statement of the European Society of Hypertension Working Group on blood pressure monitoring and cardiovascular variability. *J Hypertens*. 2016 Sep; 34(9):1665-77. IF: 4,72
3. Ferreira-González I, Abu-Assi E, Arias MA, Gallego P, Sánchez-Recalde Á, Avanzas P, Bayes-Genis A, de Isla LP, **Sánchez J**. *Revista Española de Cardiología: Current Position and Future Directions*. *Rev Esp Cardiol (Engl Ed)*. 2016 Mar; 69(3):327-36. IF: 0
 4. Moss JG, Belli AM, Coca A, Lee M, Mancia G, Peregrin JH, **Redon J**, Reekers JA, Tsioufis C, Vorwerk D, Schmieder RE. Executive Summary of the Joint Position Paper on Renal Denervation of the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) and the European Society of Hypertension (ESH). *Cardiovasc Intervent Radiol*. 2016 Dec; 39(12):1681-1683. IF: 2,144
 5. Moss JG, Belli AM, Coca A, Lee M, Mancia G, Peregrin JH, **Redon J**, Reekers JA, Tsioufis C, Vorwerk D, Schmieder RE. Executive summary of the joint position paper on renal denervation of the Cardiovascular and Interventional Radiological Society of Europe and the European Society of Hypertension. *J Hypertens*. 2016 Dec; 34(12):2303-2304. IF: 5,062
 6. Lecube A, Monereo S, Rubio MÁ, Martínez-de-Icaya P, Martí A, Salvador J, Masmiquel L, Goday A, Bellido D, **Lurbe E**, García-Almeida JM, Tinahones FJ, García-Luna PP, Palacio E, Gargallo M, Bretón I, Morales-Conde S, Caixàs A, Menéndez E, Puig-Domingo M, Casanueva FF. Prevention, diagnosis, and treatment of obesity. 2016 position statement of the Spanish Society for the Study of Obesity. *Endocrinol Nutr*. 2016 Aug 16 ;. IF: 0

3.4.2 Knowledge transfer to industry

One of INCLIVA's foundational goals is the translation of the research carried out to the society. Giving a medical need, researchers and clinicians use their knowledge to make ideas that, through research and development may be taken into actual products or processes that overcome this existing problem.

The Innovation Unit of INCLIVA gives support in this process, detecting ideas, assessing them and paving the way for their transformation into products or services that can be transferred to society. This track is known as the innovation funnel because it starts with a broad range of ideas which are gradually refined, thus creating a handful of formal development projects that can be pushed to completion and transfer.





3.4.3 Patents

Knowledge protection is the first step to move scientific findings and ideas from researchers to the industry. The most common way to protect technologies that are new, inventive and have industrial application is through patents. Research institutions can exploit the patents they hold by licensing them to private companies. Currently, the following patent applications have been requested.

Title: Mass spectrometry-based methods for the detection of circulating histones h3 and h2b in plasma from sepsis or septic shock (ss) patients.

Inventors: José Luis García Giménez, Carlos Romá Mateo, Federico Pallardó Calatayud

Applicant: INCLIVA, CIBER, *Universidad de Valencia*

Publication number: EP16382509.4

Priority Date: 2016/11/10

Territory: Europe

Title: Non-invasive preimplantation genetic analysis and related methods.

Inventors: Carlos Simón Vallés

Applicant: IGENOMIX S. L.

Publication number: US 62/301.825

Priority Date: 2016/15/03

Territory: USA

Title: *Modulación de microRNAs contra la distrofia miotónica tipo 1 y antagonistas de microRNAs para ello.*

Inventors: Rubén Artero, Beatriz Llamusí, Estefanía Cerro, Juan M. Fernández

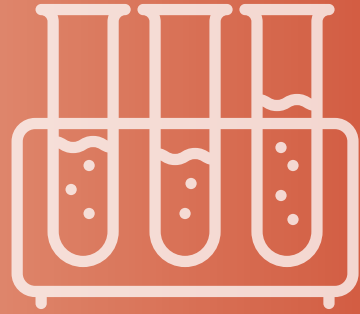
Applicant: *Universidad de Valencia*

Publication number: P201631216

Priority Date: 2016/19/09

Territory: Spain





4

Scientific
activity





4.1 Scientific structure

INCLIVA articulates its research in 4 areas of research, 7 scientific programs and 3 platforms.

Areas of research constitute the basis on which to articulate the scientific work of the groups:

- Research area in oncology.
- Research area in cardiovascular.
- Research area in metabolism and organ damage.
- Research area in reproductive medicine.



Scientific programs are aimed at specific diseases from a translational perspective:

- Program in overweight and cardiovascular and renal risk.
- Program in myocardial ischemic damage.
- Program in rare diseases.
- Program in neurological impairment.
- Program in translational oncology.
- Program in reproductive medicine.
- Program in aging and its associated diseases.



Platforms are based on the provision of research services to the whole institute:

- Inflammation platform.
- Metabolomics platform.
- Genomics, epigenomics and transcriptomics platform.





4.2 Scientific translational programs

4.2.1 Overweight and cardiovascular and renal risk

Obesity and overweight is a field in which new strategies are developed both for prevention and treatment with the use of traditional resources and the new technologies. The present program is focused on the study of pathology on the first stages of obesity (overweight with or without metabolic syndrome) integrating different clinical and experimental research studies.

Coordinators:

Juan F. Ascaso and Josep Redon

INCLIVA research groups involved

Clinical groups:

- Research Group on the Study of Cardiometabolic and Renal Risk (Dr. Redón)
- Research Group on Cardiometabolic Risk (Dr. Ascaso)
- Research Group on the Study of Cardiovascular Risk in Children and Adolescents (Dr. Lurbe)
- Translational Research Group on Nutrition and Metabolism (Dr. Hernández)
- Cardiometabolic Research Group on Primary Care (Dr. Navarro)

Experimental groups:

- Research Group of the Genotyping and Genetic Diagnosis Unit (UGDG) (Dr. Chaves)
- Research Group on Endothelial Cells (Dr. Hermenegildo)
- Research Group on Inflammation (Dr. Morcillo y Dr. Sanz)
- Research Group on Molecular Imaging and Metabolomics (Dr. Monleón)

Objectives

- To deepen in the early alterations, mechanisms and biomarkers that contribute to the development of obesity, vascular and renal alterations as a complication, from its fetal, biological, genetic and environmental origins.
- To know potential signaling pathways susceptible to be therapeutic targets.
- Early application of new technologies for the prevention and treatment of obesity and vascular and renal alterations in overweight subjects.

Research lines

- To identify early vascular and renal changes in overweight subjects and in animal models.
- To study the state, mechanisms of vascular inflammation and endothelial injury in overweight and animal models.
- To analyze the relationship of “-omic” markers (genomic, epigenetic and metabolomic) with obesity and vascular and renal alterations in overweight and animal models.
- Interaction of biomarkers (biological, genomic and metabolic) and intervention in progression to obesity and vascular and renal complications.



4.2.2 Myocardial ischemic damage

The program focuses on the study of the pathophysiological mechanisms involved in myocardial ischemic damage, on its structural, functional and electrophysiological repercussions on the evaluation of diagnostic tools and markers and prognoses and on the study of new therapeutic approaches that may help to prevent their adverse consequences.

It is a truly and translational research program that capitalizes the synergies between clinical and experimental research groups and also includes specialists in cardiac imaging techniques and technological development experts. The multidisciplinary approach extends the possibilities of collaboration between groups, strengthens those already existing and incorporates other groups into the activities of the program. Innovation through the development of analytical tools (imaging techniques such as cardiac magnetic resonance, cardiac electrical signals or cartographic techniques), allows the generalization of patents in the field of technological development.

Coordinator:

Francisco Javier Chorro Gascó

INCLIVA research groups involved

Clinical groups:

- Research Group on Clinical Cardiology (Dr. Sanchis, Dr. Nuñez)
- Group on Translational Research in Ischemic Heart Disease (Dr. Bodí)
- Research Group on Cardiac Experimental Electrophysiology (Dr. Chorro)

Experimental groups:

- Research Group on Aging and Physical Activity (Dr. José Viña)
- Research Group on Tissue Biochemistry (Dr. Juan Viña)
- Research Group on Inflammation (Dr. Morcillo and Dr. Anz)
- Research Group on Endothelial Cells (Dr. Hermenegildo)
- Research Group on Molecular Imaging and Metabolomics (Dr. Monleón)

Others groups involved

Universidad Politécnica de Valencia (Prof. D. Moratal, Prof. J. Millet), H. Clinic Barcelona (Dr. Ortiz), Heart Center Munich (Dr. Husser), ERESA (Dr. López), Universitat de Valencia, Fac. Físicas (Prof. J. Guerrero), Center for Arrhythmia Research (University of Michigan, Prof. Jalife), School of Engineering (Univ. of California, Prof. Escobar)

Objectives

- Study of the pathophysiological mechanisms involved in myocardial ischemic damage and its structural, functional and electrophysiological repercussions.
- Evaluation of diagnostic and prognostic tools and markers.
- Evaluation of new therapeutic approaches.
- Study of the role played by: a) oxidative stress and its modifications in post-infarction damage; b) the vascular endothelial growth factor VEGF-A165b in microvascular obstruction, the deterioration of systolic function in the neoangiogenesis.
- Development of new diagnostic tools in cardiac magnetic resonance (MRI) for the detection of damage associated with ischemia / reperfusion and fibrosis.



- Evaluation of new prognostic and functional biomarkers in myocardial infarction from MRI, maximal O₂ consumption, metabolomics and the combined use of CA125, galectin-1 and galectin 3.
- Development and analysis of preventive measures against the adverse consequences of postinfarction damage (remodeling, heart failure, arrhythmias).

Research lines

- Clinical research: acute coronary syndromes, interventional cardiology, ventricular remodeling and heart failure.
- Translational research: regulation of post-infarction fibrosis; development of innovative tools for their characterization by MR after an infarct and study of new therapeutic approaches.
- Experimental study of arrhythmogenesis in the context of ischemia and myocardial damage. Influence of the substrate and the modulating mechanisms.
- Microimaging using RM. Metabolomics.
- Research of textures using RM.
- Analysis, using molecular biology and biochemical techniques, of circulating metabolic factors associated with ischemic damage.
- Endothelial dysfunction.
- Microvascular obstruction.

4.2.3 Rare diseases

The main objectives of the program is to improve diagnosis and current treatments of rare diseases. To this end, we will proceed to identify and validate rare disease biomarkers for which we do not have effective diagnostic and / or prognostic indicators. On the other hand, new therapeutic strategies will be developed for the treatment of these diseases. Human and animal model samples will be used to understand the molecular basis of disease, to evaluate the activity of candidate drugs and to discover new biomarkers.

Basically, the program seeks to fill the gap between basic research and commercial development of diagnostic systems and treatments, so its aim is to transfer this knowledge to companies, in order to transform biomedical knowledge into products and services that improve the human health. With this objective contacts with biotechnology and pharmaceutical companies have been established. On the other hand, the program aims to disseminate its findings to society in order to get feedback about actual patients needs.

Coordinator:

Federico Pallardó and Francisco Dasí

INCLIVA research groups involved

Clinical groups:

- Research Group on Respiratory Problems in Neuromuscular Diseases (Dr. Servera)

Experimental groups:

- Research Group on Cellular and Organic Physiopathology of Oxidative Stress (Dr. Pallardó)
- Research Group on Molecular Imaging and Metabolomics (Dr. Monleón)
- Research Group on Neurological Impairment (Dr. Montoliu)



- Research Group on Translational Genomics (Dr. Artero)

Objectives

- To improve diagnosis and current treatment of rare diseases.
- Identification and validation of rare diseases biomarkers for which, nowadays, no effective diagnostic and / or prognostic indicators are available.
- Development of new therapeutic strategies.

Research lines

- Study of the oxidative profile in rare diseases.
- Pathophysiology of alpha-1 antitrypsin deficiency and Primary Ciliary Dyskinesia Syndrome.
- Gene therapy for the treatment of rare respiratory diseases.
- Design and testing of new biomarkers and experimental treatments in animal models.
- Study by exploratory and directed metabolomics of altered metabolic clusters in rare diseases.

4.2.4 Neurological impairment

Inflammation, which is associated with many chronic diseases (diabetes, liver cirrhosis, etc.), aging or major surgeries, leads to neuroinflammation and brain alterations that eventually lead to cognitive and functional impairment. This deterioration reduces the quality of life and increases the risk of accidents, falls, fractures and adverse consequences, which implies an increase in hospitalizations and the use of public resources.

Cognitive and functional impairment associated with aging and many chronic diseases is one of the most important challenges in order to improve the quality of life of the population and secure the sustainability of health systems. Early detection and treatment and prevention of cognitive and functional impairment would improve the quality of life of the elderly or with chronic diseases and reduce the demand for resources to the health system, improving its sustainability. Therefore, it is necessary to design new approaches to address these challenges, based on advances in knowledge on mechanisms, early diagnosis, prevention and treatment of cognitive and functional impairment.

Coordinator:

Carmina Montoliu and Vicente Felipo

INCLIVA research groups involved

Clinical groups:

- Research Group on the Study of Cardiometabolic and Renal Risk (Dr. Redón)
- Research Group on Cardiometabolic Risk (Dr. Ascaso)
- Research Group on Anesthesiology and Reanimation (Dr. Belda)

Experimental groups:

- Research Group on Neurological Impairment (Dr. Montoliu)
- Research Group on Inflammation (Dr. Morcillo and Dr. Sanz)
- Research Group on Aging and Physical Activity (Dr. José Viña)



- Research Group on Personal Autonomy, Dependence and Severe Mental Disorders (TMAP) (Dr. Tabarés)

Others groups involved

IPPC Neurobiology Research Group (Dr. Felipo), Cognitive Social Neuroscience Research Group from UV (Dr. Salvador), Hospital Neurorehabilitation Service NISA (Dr. Noe)

Objectives

- To characterize the alterations in inflammation, neuroinflammation, neurotransmission, brain function and structure associated with the appearance of cognitive and functional impairment.
- To characterize in detail the cognitive and functional alterations.
- To identify biomarkers for the early detection of cognitive and functional impairment.
- To identify the mechanisms by which: a) peripheral inflammation leads to neuroinflammation; b) neuroinflammation leads to functional, structural and neurotransmission alterations in the brain; c) changes in the brain lead to cognitive and functional impairment.
- To identify therapeutic targets to reverse or prevent cognitive and functional impairment.
- To design and test new therapeutic procedures to reverse or prevent cognitive and functional impairment.

Research lines

- Characterization of cognitive and functional alterations.
- Cognitive impairment in diabetes.
- Cognitive impairment for major surgeries and anesthesia.
- Alzheimer's and mild cognitive impairment.
- Cognitive and functional impairment in hyperammonemia and hepatic diseases.

4.2.5 Translational oncology

The translational oncology program called "Identification of oncogenic biomarkers: mechanisms and clinical implications, detection in non-invasive samples, omics analysis" tries to apply to the clinical practice the genomic screening in patients tumors. Its main objective is to evaluate the dynamics of the disease through non-invasive biopsies in order to detect minimal residual disease, early onset of markers after surgery and patient response to different treatments.

The high heterogeneity of cancer results in inefficiency of treatments, even when they are directed against specific molecular targets. The low availability of tumor specimens makes genomic studies difficult.

In this sense, the use of liquid biopsies would facilitate the serial collection of samples to carry out molecular analysis and would guarantee a minimum risk for the patient. Thus improving the follow-up and allowing a dynamic understanding of the evolution of the genomic parameters of the patient.

This point of view benefits the National Health System as a whole since it allows the application of more specific treatments to patients, thus avoiding those that would have been less effective, reducing hospitalization and improving life expectancy and quality thereof. It could also prevent generalized treatments, secondary toxicities and rapid treatment adequacy responses. Finally, it would improve the inclusion of patients in clinical trials which are stratified by molecular mutations.

**Coordinator:**

Andrés Cervantes

INCLIVA research groups involved

Clinical groups:

- Research Group on Colorectal Cancer and New Therapeutical Developments in Solid Tumours (Dr. Cervantes)
- Research Group on Breast Cancer Biology (Dr. Lluch)
- Translational Research Group on Pediatric Solid Tumours (Dr. Navarro)

Experimental groups:

- Research Group of the Genotyping and Genetic Diagnosis Unit (UGDG) (Dr. Chaves)
- Research Group on Cellular and Organic Physiopathology of Oxidative Stress (Dr. Pallardó)

Objectives

- To obtain a large database of genetic material (viable cells, DNA, RNA, serum / plasma) from tumors (solid and haematological). Implementing the clinical database for data management and data crossing. (Hospital, biobank, PROS-UPV).
- Molecular characterization of tumor biopsies using high throughput platforms (Sequenom, NGS).
- To improve inclusion of patients in clinical trials.
- To establish a routine for obtaining liquid biopsies in order to evaluate the detection of biomarkers as disease follow-up, minimal residual disease, early onset and response to treatment. (BIOBANK, BEAMing PCR, NGS).
- To develop functional assays (modified cell lines, patient cell lines, xenografts) to evaluate mechanisms of disease.
- Incorporation of molecular results into clinical decision making.

Research lines

- Development of new therapeutic agents through Phase I clinical trials (first-in-human).
- Development of non-invasive early diagnostic methods and monitoring of therapeutic effects.
- Application of methodologies for clinical and molecular characterization of solid tumors and response to treatment (analysis of gene expression profiles, microRNAs, methylation).
- Translational studies for the identification of mechanisms of resistance to targeted therapies.

4.2.6 Reproductive medicine

This program comprises two main lines:

1. Role of maternal miRNAs in the transmission of obesity and type 2 diabetes to the embryo:

Obesity and type 2 diabetes are increasingly important public health problems whose prevalence cannot be explained only by genetic and / or environmental factors, so the hypothesis of the program lies in the existence of an embryonic epigenetic regulation of maternal origin in these diseases. Preliminary data reveals that miRNAs secreted by the maternal endometrium to the endometrial fluid are internalized by the embryo, leading to a transcriptional and functional modification and increasing its adhesion to the endometrium during its implantation. In this sense, the program goal is to explore if this new epigenetic



mechanism of maternal origin could explain the origin of the development of certain adult-onset diseases such as obesity and type 2 diabetes.

2. Study of adult stem cells in human endometrium:

Use of autologous bone marrow stem cells by prior mobilization and collection of Peripheral Blood Progenitor Cells (PPSCs) and subsequent apheresis and transplantation of these cells in order to regenerate the endometrium de novo in patients undergoing assisted reproductive therapy (ART). The results of this study would allow a new therapeutic approach for the treatment of Asherman's Syndrome and endometrial atrophy, which currently lack of specific treatment.

Coordinator:

Carlos Simón

INCLIVA research groups involved

Clinical groups:

- Translational Research Group on Nutrition and Metabolism (Dr. Hernández)
- Research Group on Hematopoietic Transplantation (Dr. Solano)
- Research Group on Women Health (Dr. Cano)
- Research Group on the Study of Cardiovascular Risk in Children and Adolescents (Dr. Lurbe)

Experimental groups:

- Research Group on Stem Cells Applied to Reproduction, Embryo Viability and Endometrial Receptivity (Dr. Simón)
- Research Group on Male Infertility and Embryonic Stimulation (Dr. Remohí)

Objectives

- To advance in the understanding of the mechanisms that regulate maternal-fetal communication and that may be involved in the implantation of the embryo in the maternal uterus and to be able to understand the embryonic / fetal origin of adult diseases such as obesity and type II diabetes.
- To regenerate uterine function in patients suffering from endometrial atrophy and / or Asherman's Syndrome through cell therapy.
- The creation of an in vitro model to obtain germ cells by direct reprogramming of human somatic cells.

Research lines

- Role of maternal miRNAs in the transmission of obesity and type 2 diabetes to the embryo.
- Use of autologous bone marrow stem cells in order to regenerate the endometrium in patients with Asherman Syndrome and endometrial atrophy undergoing assisted reproductive therapy (ART).
- Identification of the main regulating genes of the development of the germinal line in humans, as well as of the experimental conditions that allow obtaining of germinal cells in vitro.



4.2.7 Aging and its associated diseases

This program has the priority of improving the quality of life of the elderly and promoting longevity as much as possible. Aging population it's a challenge for current health systems since the population over 65 years old contributes, in a very significant percentage, to health expenditure. As life expectancy increases, so do the diseases associated with aging.

In this context, the concept of "healthspan" (quality of life) has emerged. The program is formed by many researchers and health professionals who consider that efforts to extend life at the expense of causing a severe physical or psychic disability are undesirable and, on the contrary, they should focus on lengthening the part of life during which we are able to maintain autonomy, independence, productivity and well-being.

A central guiding idea in this program is that people who achieve exceptional longevity (i.e. centenarians) serve as a model of satisfactory aging. On the other hand, it is considered that the most problematic expression of the population aging is the clinical condition of the frailty since an important part of the collective of older people presents criteria of frailty. Approximately one-fourth of people over the age of 85 are estimated to be fragile. Frailty is a geriatric syndrome characterized by increased vulnerability to external aggressions as a result of an alteration in the physiological reserves of multiple systems, leading to difficulties in maintaining homeostasis. The program tries to identify specific molecular targets to be able to intervene in a concrete and rational way to improve the quality of life of the elderly.

For this, INCLIVA has an enormous advantage because of the great integration that exists, by proximity and interests, between the *Hospital Clínico Universitario de Valencia* and the Faculty of Medicine of the University of Valencia. This framework allows intense collaboration between basic research groups, that develop possible biomarkers associated with healthy aging, frailty or diseases associated with aging and clinical research groups that, on the one hand, provide samples of the subjects and, on the other hand, can transfer to the patient those results that have been interesting at the bench.

In addition to this, in INCLIVA has registered the first and only Spanish Group for the Study of Centenaries, which has research groups working in this field distributed in different Spanish communities.

Coordinator:

José Viña

INCLIVA research groups involved

Clinical groups:

- Research Group on the Study of Cardiometabolic and Renal Risk (Dr. Redón)
- Research Group on Oxidative Pathology (Dr. Sáez)
- Cardiometabolic Research Group on Primary Care (Dr. Navarro)
- Research Group on Clinical Cardiology (Dr. Sanchís)
- Research Group on Women Health (Dr. Cano)
- Group on Translational Research in Ischemic Heart Disease (Dr. Bodí)

Experimental groups:

- Research Group on Aging and Physical Activity (Dr. José Viña)
- Research Group on Inflammation (Dr. Morcillo and Dr. Sanz)
- Research Group on Genetics of Osteoporosis (Dr. García)
- Research Group on neurological impairment (Dr. Montoliu)



- Research Group on Endothelial Cells (Dr. Hermenegildo)
- Research Group on Cellular and Organic Physiopathology of Oxidative Stress (Dr. Pallardó)

Objectives

- Determination of parameters of oxidative stress and inflammation associated with healthy aging, frailty and diseases associated with healthy aging, frailty and others associated diseases (mainly cardiovascular and neurodegenerative).
- Determination of genetic biomarkers (microRNAs, mRNAs and SNPs) associated with healthy aging and frailty and others associated diseases (mainly cardiovascular and neurodegenerative).
- Determination of epigenetic biomarkers associated with healthy aging, frailty and others associated diseases (mainly cardiovascular and neurodegenerative).
- Determination of metabolic biomarkers associated with healthy aging, frailty and others associated diseases (mainly cardiovascular and neurodegenerative).
- Physical exercise protocols for the prevention of frailty and others associated diseases .
- Impairment of other biomarkers associated with healthy aging, frailty and others associated diseases.

Research lines

- Oxidative stress, associated inflammation and healthy aging.
- Genetics and healthy aging.
- Epigenetics and healthy aging.
- Metabolomics and healthy aging.
- Exercise and healthy aging.





4.3. Research areas

INCLIVA Health Research Institute has four research areas in order to organize its scientific activity. Despite their independence, they have a common objective: meeting health needs and improving R&D&i system.

Their main aim is to establish a common reference framework to promote collaboration between INCLIVA attached researchers. Each of the lines counts on the participation of one or several advisers from the External Scientific Committee. These lines are led by the following coordinators:

Cardiovascular Area

- Coordinator: Dr. Francisco Javier Chorro Gascó
- Mission: to contribute to the study of different aspects of cardiovascular disease (CVD) from its origins to its consequences.

Oncology Area

- Coordinator: Dr. Andrés Cervantes Ruipérez
- Mission: to contribute to the study of different aspects of oncological diseases, at the stage of diagnosis and molecular characterization and selection of specific molecular targets of therapeutic interest.

Metabolism and Organic Damage Area

- Coordinator: Dr. José Viña Ribes
- Mission: to contribute to the study of the etiology, pathophysiology and diagnosis mechanisms or treatment of various metabolic diseases; or those that generate organ damage as a fundamental link of its trigger action.

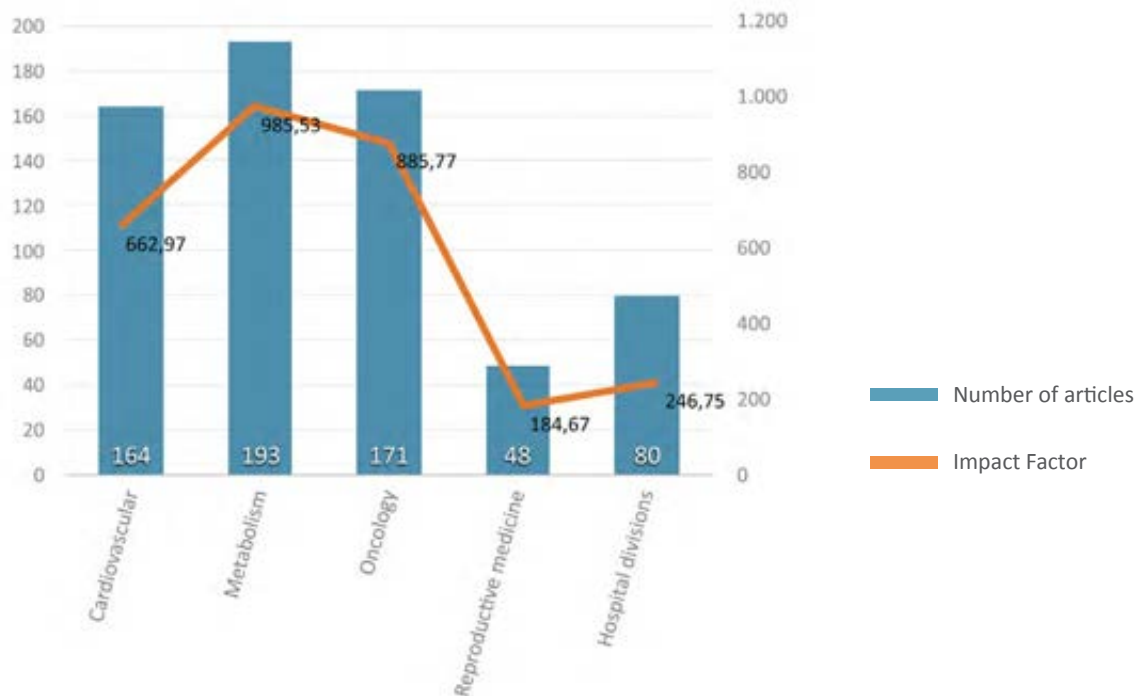
Reproductive Medicine Area

- Coordinator: Dr. Carlos Simón Vallés
- Mission: to advance in knowledge of human reproduction for translational application, improving the efficiency of assisted reproduction treatment and reducing adverse effects.



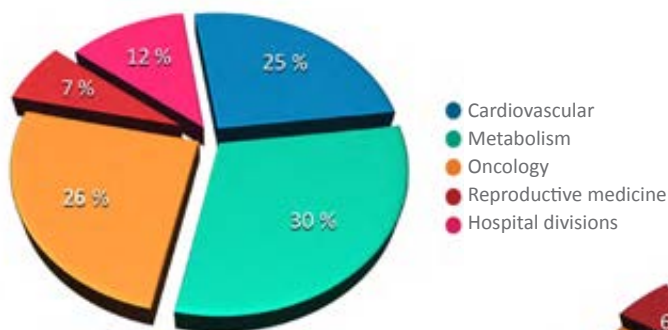
Scientific production analysis by research area

The following charts and figures summarize the main scientific activity indicators of the four areas of research and the other divisions from *Hospital Clínico de Valencia*.

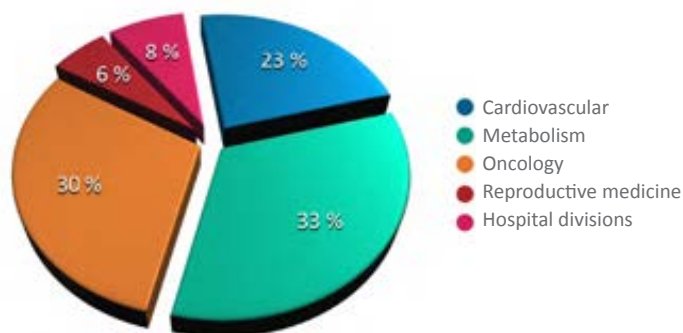


Since there are some scientific articles which are shared by two or more areas, it is worth mentioning that the sum of publications by area exceeds INCLIVA's total scientific output. Additionally, the next tables shows scientific publications distribution by area in terms of number of articles and impact factor.

Relative distribution of articles



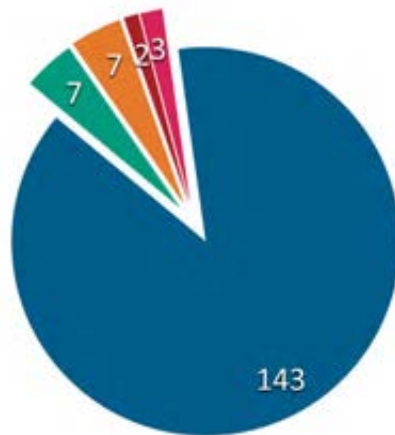
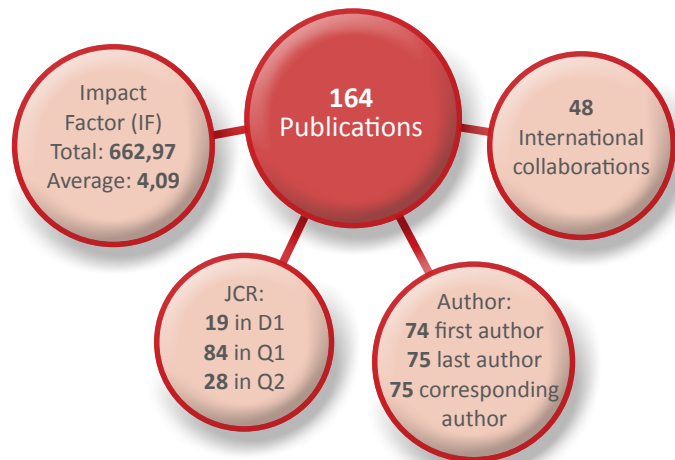
IF distribution





4.3.1 Cardiovascular Area

Research Group on Cardiometabolic Risk	50
Genotyping and Genetic Diagnosis Unit (UGDG)	55
Research Group on Cardiac Experimental Electrophysiology	58
Research Group on Endothelial Cells (LINCE)	63
Research Group on Clinical Cardiology	66
Research Group on the Study of Cardiovascular Risk in Children and Adolescents	72
Cardiometabolic Research Group on Primary Care	76
Research Group on the Study of Cardiometabolic and Renal Risk	78
Research Group on Vascular Function	86
Research Group on Pediatric Nutrition	88
Group on Translational Research in Ischemic Heart Disease	91



● Original articles ● Letters ● Editorial ● Clinical guidelines ● Review



Research Group on Cardiometabolic Risk Consolidated group



El doctor Ascaso, jefe del Servicio de Endocrinología y Nutrición del Clínico, ingresa en la Real Academia de Medicina de la Comunitat Valenciana. Diario Crónica. 25/05/2016

Team involved in



Group members

Principal investigator

Juan Francisco Ascaso Gimilio
Hospital. University
H Index: 26



Collaborating researchers

Rafael Carmena Rodríguez. University
José Tomás Real Collado. Hospital. University
José Francisco Martínez Valls. Hospital. University
Francisco Javier Ampudia Blasco. Hospital. University
M^a Antonia Priego Serrano. Hospital. University
Miguel Civera Andrés. Hospital
Marta Peiró Signes. INCLIVA. CIBERdem
Esther Benito Casado. Hospital. CIBERdem

PhD students

Griselda de Marco Solar. INCLIVA

Technicians

Cristina Pérez Soriano. INCLIVA
Ana Albert Viguer. INCLIVA

Emerging researchers

Sergio Martínez Hervás. Hospital. University
Ana Bárbara García García. CIBERdem



Strategic aims

- In terms of scientific activity of the research group during 2016 we wish to emphasize the continuity of three competitive and multidisciplinary research projects led by the Dr. Ascaso and Dr. Real. The Project led by Dr. Ascaso, entitled “Immunopharmacological modulation of the systemic inflammation associated to metabolic disorders. Search for new therapeutic targets and synthesis of novel drugs”, studies the role of shaft CCL11/CCR3 in systemic inflammation associated with Familial Hypercholesterolemia and its immune modulation by oral lipid overload, as well as the study of the role of the axis CXCL16/CXCR6 in Ang-II-induced Endothelial dysfunction in subjects with metabolic síndrome.
- On the other hand, the main objective the project “Study of new inflammatory and angiogenic mechanisms associated to severe morbid obesity: Role of CXCR3 axis and nuclear receptors RORs” led by Dr. Real, is to explore the CXCR3 axis and RORs receptors in patients with severe morbid obesity or without diabetes undergoing a gastric bypass.

Main lines of research

- Genetic diagnosis of primary hyperlipidemias and cardiovascular risk.
- Combination of primary hyperlipidemias with insulin resistance and diabetes mellitus.
- Postprandial lipidemia and atherosclerosis in states of insulin resistance.
- Insulin resistance, inflammation and oxidative stress.
- Diagnosis, prevention and treatment of diabetic foot.
- Genetic factors involved in the regulation of Body Mass Index and abdominal obesity.
- Sarcopenia and frailty in metabolic disease and diabetes.



Emerging researcher

Sergio Martínez Hervás

The line of research is based on cardiovascular risk, essentially on insulin resistance and diabetes, familial combined hyperlipidemia, inflammation, vitamin D, and atherosclerosis, just like new markers of cardiovascular risk.



Emerging researcher

Ana Bárbara García García

The research is mainly focused on DM2, one of the most frequent diseases of Western societies. On this subject, the work has several lines: an SREBF2 variant and its possible association with DM2, gene expression alterations in postprandial lipemia after an oral fat challenge in obese and diabetic populations, and identification of markers of β -cell destruction using circulating DNA.

On the other hand, other line of research is the identification of new genes responsible for abetalipoproteinemia using exome sequencing.

• PUBLICATIONS

Number of articles	IF	Average IF
24	56,37	2,34
National collaborations	International collaborations	Corresponding author
17	4	10

Original articles

1. Doblaz A, Roche E, **Ampudia-Blasco FJ**, Martínez-Corral M, Saavedra G, Garcia-Sucerquia J. Diabetes screening by tele-centric digital holographic microscopy. J Microsc. 2016 Mar; 261(3):285-90. IF: 2,331
2. de Pereda D, Romero-Vivo S, Ricarte B, Rossetti P, **Ampudia-Blasco FJ**, Bondia J. Real-time estimation of plasma insulin concentration from continuous glucose monitor measurements. Comput Methods Biomech Biomed Engin. 2016 Jul; 19(9):934-42. IF: 1,77



3. Basanta-Alario ML, Ferri J, **Civera M, Martínez-Hervás S, Ascaso JF, Real JT**. Differences in clinical and biological characteristics and prevalence of chronic complications related to aging in patients with type 2 diabetes. *Endocrinol Nutr*. 2016 Feb; 63(2):79-86. IF: 0
4. Müller-Wieland D, Assmann G, **Carmena R**, Davignon J, von Eckardstein A, Farinero E, Greten H, Olsson AG, Riesen WF, Shlyakhto E. Treat-to-target versus dose-adapted statin treatment of cholesterol to reduce cardiovascular risk. *Eur J Prev Cardiol*. 2016 Feb; 23(3):275-81. IF: 3,319
5. Amigó N, Mallol R, Heras M, **Martínez-Hervás S**, Blanco-Vaca F, Escolà-Gil JC, Plana N, Yanes Ó, Masana L, Correig X. Lipoprotein hydrophobic core lipids are partially extruded to surface in smaller HDL: "Herniated" HDL, a common feature in diabetes. *Sci Rep*. 2016 Jan 18; 6:19249. IF: 5,578
6. **Martínez-Hervás S**, Artero A, Martínez-Ibañez J, Tormos MC, Gonzalez-Navarro H, **Priego A, Martínez-Valls JF, Saez GT, Real JT, Carmena R, Ascaso JF**. Increased thioredoxin levels are related to insulin resistance in familial combined hyperlipidaemia. *Eur J Clin Invest*. 2016 Jul; 46(7):636-42. IF: 2,734
7. Andrés-Blasco I, Vinué Á, Herrero-Cervera A, **Martínez-Hervás S**, Nuñez L, Piqueras L, **Ascaso JF**, Sanz MJ, Burks DJ, González-Navarro H. Hepatic lipase inactivation decreases atherosclerosis in insulin resistance by reducing LIGHT/Lymphotoxin β -Receptor pathway. *Thromb Haemost*. 2016 May 12; 116(2). IF: 4,984
8. Ruiz-Saurí A, Valencia-Villa G, Romanenko A, **Pérez J**, García R, García H, Benavent J, Sancho-Tello M, Carda C, Llombart-Bosch A. Influence of Exposure to Chronic Persistent Low-Dose Ionizing Radiation on the Tumor Biology of Clear-Cell Renal-Cell Carcinoma. An Immunohistochemical and Morphometric Study of Angiogenesis and Vascular Related Factors. *Pathol Oncol Res*. 2016 Oct; 22(4):807-15. IF: 1,855
9. **Ascaso JF**. Inhibition of proprotein convertase subtilisin/kexin type 9 in the treatment of hypercholesterolemia. *Endocrinol Nutr*. 2016 Jun-Jul; 63(6):255-7. IF: 0
10. Cortes R, Ivorra C, **Martínez-Hervás S**, Pedro T, González-Albert V, Artero A, Adam V, **García-García AB, Ascaso JF, Real JT**, Chaves FJ. Postprandial Changes in Chemokines Related to Early Atherosclerotic Processes in Familial Hypercholesterolemic Subjects: A Preliminary Study. *Arch Med Res*. 2016 Jan; 47(1):33-9. IF: 2,645
11. Menéndez E, Delgado E, Fernández-Vega F, Prieto MA, Bordiú E, Calle A, **Carmena R**, Castaño L, Catalá M, Franch J, Gaztambide S, Gírbés J, Goday A, Gomis R, López-Alba A, Martínez-Larrad MT, Mora-Peces I, Ortega E, Rojo-Martínez G, Serrano-Ríos M, Urrutia I, Valdés S, Vázquez JA, Vendrell J, Soriguer F. Prevalence, Diagnosis, Treatment, and Control of Hypertension in Spain. Results of the Di@bet. Es Study. *Rev Esp Cardiol (Engl Ed)*. 2016 Jun; 69(6):572-8. IF: 4,596
12. Moriana M, Martínez-Ibañez J, Civera M, Martínez-Valls JF, **Ascaso JF**. Hyperammonemic encephalopathy after urinary diversion. *Diet therapy*. *Endocrinol Nutr*. 2016 Jun-Jul; 63(6):306-8. IF: 0
13. Masana L, **Ascaso JF**, Civeira F, Pedro-Botet J, Valdivielso P, Guijarro C, Mostaza J, López Miranda J, Pintó X, en nombre de la Sociedad Española de Arteriosclerosis.. [Consensus document of the Spanish Society of Arteriosclerosis on indications of inhibitors of PCSK9]. *Clin Investig Arterioscler*. 2016 May-Jun; 28(3):164-5. IF: 0
14. Pedro-Botet J, Barrios V, Pascual V, **Ascaso JF**, Cases A, Millán J, Serrano A, Pintó X. [Delphi consensus on management of dyslipidaemia in patients with impaired glucose metabolism: Diana study]. *Clin Investig Arterioscler*. 2016 May-Jun; 28(3):132-40. IF: 0
15. Millán-Núñez J, Mantilla-Morató T, Toro R, Millán-Pérez JJ, Mangas-Rojas A, **Scientific Committee of Hypertriglyceridemia Registry of Spanish Society of Arteriosclerosis (SEA)**. Cardiometabolic Risk Related to the Association of hypertriglyceridemia-Low HDLc. *Curr Pharm Des*. 2016; 22(3):365-71. IF: 3,452
16. **Real JT**, Folgado J, Molina Mendez M, **Martínez-Hervás S, Peiro M, Ascaso JF**. [Plasma homocysteine, Lp(a), and oxidative stress markers in peripheral macroangiopathy in patients with type 2 diabetes mellitus]. *Clin Investig Arterioscler*. 2016 Jul-Aug; 28(4):188-94. IF: 0
17. Brugnara L, Murillo S, Novials A, Rojo-Martínez G, Soriguer F, Goday A, Calle-Pascual A, Castaño L, Gaztambide S, Valdés S, Franch J, Castell C, Vendrell J, Casamitjana R, Bosch-Comas A, Bordiú E, **Carmena R**, Catalá M, Delgado E, Gírbés J, López-Alba A, Martínez-Larrad MT, Menéndez E, Mora-Peces I, Pascual-Manich G, Serrano-Ríos M, Gomis R, Ortega E. Low Physical Activity and Its Association with Diabetes and Other Cardiovascular Risk Factors: A Nationwide, Population-Based Study. *PLoS One*. 2016; 11(8):e0160959. IF: 3,057



18. Millán J, Hernández-Mijares A, **Ascaso JF**, Blasco M, Brea A, Díaz Á, González-Santos P, Mantilla T, Pedro-Botet J, Pintó X, Grupo de trabajo sobre Dislipemia Aterogénica. Sociedad Española de Arteriosclerosis. [The real measurement of non-HDL-cholesterol: Atherogenic cholesterol]. *Clin Investig Arterioscler*. 2016 Nov - Dec; 28(6):265-270. IF: 0
19. Brea A, Millán J, **Ascaso JF**, Blasco M, Díaz A, González-Santos P, Hernández-Mijares A, Mantilla T, Pedro-Botet JC, Pintó X, en nombre del Foro de la Dislipemia Aterogénica.. [Fibrates therapy: Rational use fenofibrate 2016. Executive summary]. *Clin Investig Arterioscler*. 2016 Nov - Dec; 28(6):295-301. IF: 0
20. Brea Á, Pintó X, **Ascaso JF**, Blasco M, Díaz Á, González-Santos P, Hernández Mijares A, Mantilla T, Millán J, Pedro-Botet J, Grupo de trabajo sobre Dislipemia Aterogénica. Sociedad Española de Arteriosclerosis. [Nonalcoholic fatty liver disease, association with cardiovascular disease and treatment. (I). Nonalcoholic fatty liver disease and its association with cardiovascular disease]. *Clin Investig Arterioscler*. 2016 Sep 27 ;. IF: 0
21. Brea Á, Pintó X, **Ascaso JF**, Blasco M, Díaz Á, González-Santos P, Hernández-Mijares A, Mantilla T, Millán J, Pedro-Botet J, Grupo de trabajo sobre Dislipemia Aterogénica, Sociedad Española de Arteriosclerosis.. [Nonalcoholic fatty liver disease, association with cardiovascular disease and treatment (II). The treatment of nonalcoholic fatty liver disease]. *Clin Investig Arterioscler*. 2016 Sep 27 ;. IF: 0
22. **Martinez-Hervas S**, Navarro I, **Real JT**, Artero A, **Peiro M**, Gonzalez-Navarro H, **Carmena R**, **Ascaso JF**. Unsaturated Oral Fat Load Test Improves Glycemia, Insulinemia and Oxidative Stress Status in Nondiabetic Subjects with Abdominal Obesity. *PLoS One*. 2016; 11(8):e0161400. IF: 3,057
23. Sánchez-Hernández RM, Civeira F, Stef M, Perez-Calahorra S, Almagro F, Plana N, Novoa FJ, Sáenz-Aranzúbia P, Mosquera D, Soler C, Fuentes FJ, Brito-Casillas Y, **Real JT**, Blanco-Vaca F, **Ascaso JF**, Pocoví M. Homozygous Familial Hypercholesterolemia in Spain: Prevalence and Phenotype-Genotype Relationship. *Circ Cardiovasc Genet*. 2016 Oct 26 ;. IF: 3,719

Review

24. Betteridge DJ, **Carmena R**. *The diabetogenic action of statins - mechanisms and clinical implications*. *Nat Rev Endocrinol*. 2016 Feb; 12(2):99-110. IF: 13,281

• THESIS

Thesis title: *Efecto de la sobrecarga oral con grasa insaturada en los marcadores de estrés oxidativo y expresión de ARN linfo-monocitos en sujeto con Diabetes Mellitus tipo 2.*

Doctoral candidate: Juan Caro Ibáñez

Director(s): Juan F. Ascaso Gimilio, José T. Real Collado

Date of the defense: 14-07-2016

Grade: *Sobresaliente "cum laude"*

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PROMETEOII/2014/002

Title: *Estudio de la relación del patrón de metilación del ADN de adipocitos con la diabetes y su remisión tras by-pass gástrico en sujetos con obesidad grave-mórbida.*

Principal Investigator: Rafael Carmena Rodríguez

Funding Body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2018

Total Budget: 48.000€

Reference: ISIC/2012/018

Title: *Instituto Superior de Investigaciones Científicas INCLIVA.*

Principal Investigator: Rafael Carmena Rodríguez

Funding Body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2018

Total budget: 35.550€

Reference: CB07/08/0018

Title: *CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERdem).*

Principal Investigator: Rafael Carmena Rodríguez

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2008-2016

Reference: SAF2014-57845-R

Title: *Modulación inmunofarmacológica de la inflamación sistémica asociada a desórdenes metabólicos. Búsqueda de nuevas dianas terapéuticas y síntesis de fármacos novedosos.*

Principal Investigator: Juan F. Ascaso Gimilio, M. J. Sanz



Funding Body: *Ministerio de Economía y Competitividad*
Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total budget: 302.500€

Reference: DATSIR

Title: *Desarrollo de sistemas de análisis y visualización de datos complejos en estudios de expresión génica con series temporales: estudio de ARN de linfomonocitos tras sobrecarga oral con grasa insaturada en pacientes con resistencia a la insulina y su implicación en aterosclerosis.*

Principal Investigator: Ana Bárbara García García

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2016

Total budget: 4.000€

Reference: PI15/00082

Title: *Estudio de nuevos mecanismos inflamatorios y angiogénicos asociados a la obesidad grave mórbida: Papel del eje CXCR3 y los receptores nucleares RORs.*

Principal Investigator: Laura Piqueras and José Tomás Real

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2018

Total budget: 154.577€

• AWARDS

In May 2016, Dr. Ascaso entered the *Real Academia de Medicina de la Comunitat Valenciana*.



Research Group of the Genotyping and Genetic Diagnosis Unit (UGDG) Consolidated group



Group members

Principal investigator

Felipe Javier Chaves Martínez
INCLIVA
H Index: 20



Collaborating researchers

Alba Sanchís Juan. INCLIVA
Jesús Rodríguez Díaz. University
José Miguel Juanes Tébar. INCLIVA

PhD students

Pilar Rentero Garrido. INCLIVA
Daniel Pérez Gil. INCLIVA
Verónica Lendínez Tortajada. INCLIVA
Inmaculada Galán Chilet. INCLIVA

Technicians

Sebastián Blesa Lujan. INCLIVA
Verónica González Albert. INCLIVA
Victoria Adam Felici. INCLIVA
Azahara M^a Fuentes Trillo. INCLIVA



Strategic aims

- To identify genetic causes of complex diseases with high cardiovascular risk, especially of type 2 diabetes.
- To identify genetic causes of some rare diseases (Abeta, ATA and hereditary forms of hypercholesterolemias not caused by known genes).
- To identify alterations of methylation and hydroxymethylation in relation to the development of type 2 diabetes and its potential use as biomarkers.
- Study of environmental factors involved in the development of diseases of high cardiovascular risk, especially type 2 diabetes and associated organic damage.
- Support for genetic diagnosis in hereditary and oncological diseases.

Main lines of research

- Identification of genes involved in type 2 diabetes.
- Identification of genetic causes of rare diseases (not caused by genes known) as ATA, abeta or Hypercholesterolemia.
- Exome sequencing application for the detection of variants and genes involved in type 2 diabetes development.
- DNA methylation and hydroxymethylation as a biomarker for type 2 development risk and organ damage.
- DNA methylation as a biomarker for organ damage in obesity and type 2 diabetes.
- Identification, and characterization at population and functional levels of rare and functional genetic variants related to the development of type 2 diabetes.
- Identification of different genes and polymorphisms involved in the development of obesity through different metabolic and functional pathways.
- Identification of relationships between different genes, essential metals and pollutants in relation to diseases with high cardiovascular risk.

• PUBLICATIONS

Number of articles	IF	Average IF
9	32,03	3,55
National collaborations	International collaborations	Corresponding author
5	1	7

Original articles

1. Perez-Hernandez J, Olivares MD, Forner MJ, **Chaves FJ**, Cortes R, Redon J. Urinary dedifferentiated podocytes as a non-invasive biomarker of lupus nephritis. *Nephrol Dial Transplant*. 2016 May; 31(5):780-9. IF: 3,577
2. **Cortes R**, Ivorra C, Martínez-Hervás S, Pedro T, González-Albert V, Artero A, **Adam V**, García-García AB, Ascaso JF, Real JT, **Chaves FJ**. Postprandial Changes in Chemokines Related to Early Atherosclerotic Processes in Familial Hypercholesterolemic Subjects: A Preliminary Study. *Arch Med Res*. 2016 Jan; 47(1):33-9. IF: 2,645
3. Martorell PM, Huerta M, Quilis AC, Abellán M, **Blesa S**, **Chaves F**, Beltrán DD, Nascimento AF, Insa A. 8P EGFR, KRAS, BRAF, and PI3K mutations and ALK rearrangement in 327 consecutive Spanish non-squamous NSCLC patients. *J Thorac Oncol*. 2016 Apr; 11(4 Suppl):S60. IF: 5,282
4. Cuevas JM, Combe M, Torres-Puente M, Garijo R, Guix S, Buesa J, **Rodríguez-Díaz J**, Sanjuán R. Human norovirus hyper-mutation revealed by ultra-deep sequencing. *Infect Genet Evol*. 2016 Jul; 41:233-9. IF: 3,015
5. Carmona-Vicente N, Allen DJ, **Rodríguez-Díaz J**, Iturriza-Gómara M, Buesa J. Antibodies against Lewis antigens inhibit the binding of human norovirus GII.4 virus-like particles to saliva but not to intestinal Caco-2 cells. *Virology*. 2016 May 21; 13(1):82. IF: 2,181
6. Carmona-Vicente N, Fernández-Jiménez M, Vila-Vicent S, **Rodríguez-Díaz J**, Buesa J. Characterisation of a household norovirus outbreak occurred in Valencia (Spain). *BMC Infect Dis*. 2016 Mar 12; 16(1):124. IF: 2,613
7. Carmona-Vicente N, Vila-Vicent S, Allen D, Gozalbo-Rovira R, Iturriza-Gómara M, Buesa J, **Rodríguez-Díaz J**. Characterization of a Novel Conformational GII.4 Norovirus Epitope: Implications for Norovirus-Host Interactions. *J Virol*. 2016 Sep 1; 90(17):7703-14. IF: 4,606
8. Pichler G, Grau-Perez M, Martín-Escudero J, **Galan-Chilet**



I, Dominguez-Lucas A, **Chaves F**, Redon J, Tellez-Plaza M. [OP.2A.01] Urine cadmium levels and albuminuria in a general population from Spain: a gene-environment interaction population-based study. *J Hypertens*. 2016 Sep; 34 Suppl 2: e15. IF: 5,062

9. Marrachelli VG, **Rentero P**, Mansego ML, Morales JM, **Galan I**, Pardo-Tendero M, Martinez F, Martin-Escudero JC, Briongos L, **Chaves FJ**, Redon J, Monleon D. Genomic and Metabolomic Profile Associated to Clustering of Cardio-Metabolic Risk Factors. *PLoS One*. 2016; 11(9):e0160656. IF: 3,057

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI12/02615

Title: *Podocitos y sus componentes como biomarcadores de lesión en hipertensión arterial, diabetes y obesidad*

Principal Investigator: Josep Redón i Mas (Pablo Marin, Raquel Cortés, Verónica González and Pilar Rentero as collaborating researchers)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario Valencia*

Duration: 2013-2016

Total budget: 329.120€

Reference: PI14/00874

Title: Identification of exome sequence changes, methylation and hydroxymethylation associated in the development of type 2 diabetes principal.

Principal Investigator: Felipe Javier Chaves Martínez

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total budget: 162.000€

Reference: PIE14/00031

Title: Understanding obesity, metabolic syndrome type 2 diabetes and fatty liver diseases: A multidisciplinary approach.

Principal Investigator: Jose María Mato de la Paz (Felipe Javier Chaves Martínez as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: CIBERDEM

Duration: 2015-2017

Total budget: 660.000€

Reference: PROMETEO II/2014/002

Title: *Estudio de la relación del patrón de metilación del ADN de adipocitos con la diabetes y su remisión tras by-passgastrointestinal en sujetos con obesidad grave-mórbida.*

Principal Investigator: Rafael Carmena Rodríguez (Felipe Javier Chaves Martínez as collaborating researcher)

Funding Body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2018

Total budget: 48.000€ (this year)

• THESIS

Thesis title: *Identificación de variantes genéticas poco frecuentes y raras en diabetes mellitus tipo 2 mediante secuenciación de exoma.*

Doctoral candidate: Inmaculada Galán Chilet

Director(s): Felipe Javier Chaves Martínez

Date of the defense: 04/03/2016

Grade: *Sobresaliente "cum laude"*



Research Group on Cardiac Experimental Electrophysiology Consolidated group



Group members

Principal investigator

Francisco Javier Chorro Gascó
Hospital. University
H Index: 24



Team involved in



Collaborating researchers

Luis Such Belenguer. University
Antonio M. Alberola Aguilar. University
Luis Such Miquel. University
Isabel Trapero Gimeno. University
Joaquín Cánoves Femenía. Hospital
Laura López Bueno. Hospital. University
Manuel Zarzoso Muñoz. University
Óscar Julián Arias Mutis. INCLIVA

PhD students

Laia Brines Ferrando. INCLIVA
Irene del Canto Serrano. INCLIVA
Carlos Soler López. University
Patricia Genovés. INCLIVA



Strategic aims

- Publication of the results obtained on using the 1,4-benzothiazepine derivative JTV-519 to modify the proarrhythmic manifestations of mechanoelectric feedback and continuation of the programmed experimental series to analyze the effects of KN-93, carvedilol and analogues, late Na⁺ current inhibitors and the Nitric Oxide carrier S-nitrosoglutathione.
- Continuation of the analysis of the effects of modifications of the basic electrophysiological properties on the processes involved in the induction and maintenance of ventricular fibrillation.
- Analysis of the electrophysiological effects of chronic physical exercise and its protective effect against arrhythmias, the influence of the cardiac nervous system and mitochondrial oxidative stress and the involvement of the IKATP current.
- Development of instruments for recording, processing and analysing of cardiac electrophysiological signals obtained with mapping systems.
- Progressive development of the experimental series aimed to study the mechanisms involved in the deterioration of the systolic function, fibrosis and the inducibility of arrhythmias in a chronic model of infarction.
- Progressive development of an experimental model of metabolic syndrome to analyze the electrophysiological modifications and the inducibility of cardiac arrhythmias.

Main lines of research

- Myocardial stretching: analysis of electrophysiological changes induced by mechanical stretching. Autocrine/paracrine influences and study of protective actions by means of drugs.
- Clinical and basic research on heart failure: role of calcium homeostasis in arrhythmogenesis. Study on the effects of drugs acting on intracellular Ca²⁺ dynamics.
- Analysis of the effects of modifications in basic electrophysiological properties on the processes involved in induction and maintenance of ventricular fibrillation.
- Study of electrophysiological effects of chronic physical activity by: a) analysis of the protection against arrhythmias or scientific activity facilitation of its reversion; b) study of the influence of heart's nervous system and mitochondrial oxidative stress; and c) analysis of the effects on the elec-

trical instability induced by myocardial ischemia and the implication of IKATP current.

- Development and extension of tools for the registration, processing and analysis of cardiac electrophysiological signals based on multielectrodes and optical mapping systems able to analyze voltage and calcium signals.
- Study of mechanisms involved in the deterioration of the systolic function, fibrosis and the inducibility of arrhythmias in a chronic model of infarction.
- Study of electrophysiological modifications and inducibility of cardiac arrhythmias in an experimental model of metabolic syndrome.

• PUBLICATIONS

Number of articles	IF	Average IF
21	62,48	2,97
National collaborations	International collaborations	Corresponding author
14	3	16

Original articles

1. Núñez J, Mascarell B, Stubbe H, Ventura S, Bonanad C, Bodí V, Núñez E, Miñana G, Fácila L, Bayés-Genis A, **Chorro FJ**, Sanchis J. Bioelectrical impedance vector analysis and clinical outcomes in patients with acute heart failure. *J Cardiovasc Med (Hagerstown)*. 2016 Apr; 17(4):283-90. IF: 1,51
2. Hervas A, Ruiz-Sauri A, de Dios E, Forteza MJ, Minana G, Nunez J, Gomez C, Bonanad C, Perez-Sole N, Gavara J, **Chorro FJ**, Bodí V. Inhomogeneity of collagen organization within the fibrotic scar after myocardial infarction: results in a swine model and in human samples. *J Anat*. 2016 Jan; 228(1):47-58. IF: 2,097
3. Bodí V, Monmeneu JV, Ortiz-Perez JT, Lopez-Lereu MP, Bonanad C, Husser O, Minana G, Gomez C, Nunez J, Forteza MJ, Hervas A, de Dios E, Moratal D, Bosch X, **Chorro FJ**. Prediction of Reverse Remodeling at Cardiac MR Imaging Soon after First ST-Segment-Elevation Myocardial Infarction: Results of a Large Prospective Registry. *Radiology*. 2016 Jan; 278(1):54-63. IF: 6,867
4. Sanchis J, Abellán L, García-Blas S, **Mainar L**, Mollar A, Valero E, Consuegra-Sánchez L, Roqué M, Bertomeu-González V, **Chorro FJ**, Núñez E, Núñez J. Usefulness of delta troponin for diagnosis and prognosis assessment of non-ST-segment



- elevation acute chest pain. *Eur Heart J Acute Cardiovasc Care*. 2016 Sep; 5(5):399-406. IF: 0
5. Valero E, Bondanza L, **Mainar L**. Aborted sudden death in a cocaine consumer. *Rev Clin Esp*. 2016 May; 216(4):231-232. IF: 1,063
 6. Núñez J, Núñez E, Bayés-Genís A, Fonarow GC, Miñana G, Bodí V, Pascual-Figal D, Santas E, García-Blas S, **Chorro FJ**, Rizopoulos D, Sanchis J. Long-term serial kinetics of N-terminal pro B-type natriuretic peptide and carbohydrate antigen 125 for mortality risk prediction following acute heart failure. *Eur Heart J Acute Cardiovasc Care*. 2016 May 19 ;. IF: 0
 7. Núñez J, Comín-Colet J, Miñana G, Núñez E, Santas E, Mollar A, Valero E, García-Blas S, Cardells I, Bodí V, **Chorro FJ**, Sanchis J. Iron deficiency and risk of early readmission following a hospitalization for acute heart failure. *Eur J Heart Fail*. 2016 Jul; 18(7):798-802. IF: 6,526
 8. Núñez J, Domínguez E, Ramón JM, Núñez E, Sanchis J, Santas E, Heredia R, González J, Miñana G, López L, **Chorro FJ**, Palau P. Iron deficiency and functional capacity in patients with advanced heart failure with preserved ejection fraction. *Int J Cardiol*. 2016 Mar 15; 207:365-7. IF: 4,036
 9. Bonanad C, Monmeneu JV, Lopez-Lereu MP, Hervas A, de Dios E, Gavara J, Nunez J, Minana G, Husser O, Paya A, Racugno P, García-Blas S, **Chorro FJ**, Bodi V. Prediction of long-term major events soon after a first ST-segment elevation myocardial infarction by cardiovascular magnetic resonance. *Eur J Radiol*. 2016 Mar; 85(3):585-92. IF: 2,369
 10. Montesinos-Magraner L, **López-Bueno L**, Gómez-Garrido A, Gomis M, González LM, García-Massó X, Serra-Añó P. The influence of regular physical activity on lung function in paraplegic people. *Spinal Cord*. 2016 Oct; 54(10):861-865. IF: 1,804
 11. Willis BC, Pandit SV, Ponce-Balbuena D, **Zarzoso M**, Guerrero-Serna G, Limbu B, Deo M, Camors E, Ramirez RJ, Mironov S, Herron TJ, Valdivia HH, Jalife J. Constitutive Intracellular Na⁺ Excess in Purkinje Cells Promotes Arrhythmogenesis at Lower Levels of Stress Than Ventricular Myocytes From Mice With Catecholaminergic Polymorphic Ventricular Tachycardia. *Circulation*. 2016 Jun 14; 133(24):2348-59. IF: 15,073
 12. Herron TJ, Rocha AM, Campbell KF, Ponce-Balbuena D, Willis BC, Guerrero-Serna G, Liu Q, Klos M, Musa H, **Zarzoso M**, Bizy A, Furness J, Anumonwo J, Mironov S, Jalife J. Extracellular Matrix-Mediated Maturation of Human Pluripotent Stem Cell-Derived Cardiac Monolayer Structure and Electrophysiological Function. *Circ Arrhythm Electrophysiol*. 2016 Apr; 9(4). IF: 4,678
 13. Hervas A, Ruiz-Sauri A, Gavara J, Monmeneu JV, de Dios E, Rios-Navarro C, Perez-Sole N, Perez I, Monleon D, Morales JM, Minana G, Nunez J, Bonanad C, Diaz A, Vila JM, **Chorro FJ**, Bodi V. A Multidisciplinary Assessment of Remote Myocardial Fibrosis After Reperfused Myocardial Infarction in Swine and Patients. *J Cardiovasc Transl Res*. 2016 Aug; 9(4):321-33. IF: 3,017
 14. Palau P, Domínguez E, López L, Heredia R, González J, Ramón JM, Serra P, Santas E, Bodi V, Sanchis J, **Chorro FJ**, Núñez J. Inspiratory Muscle Training and Functional Electrical Stimulation for Treatment of Heart Failure With Preserved Ejection Fraction: Rationale and Study Design of a Prospective Randomized Controlled Trial. *Clin Cardiol*. 2016 Aug; 39(8):433-9. IF: 2,431
 15. García García MA, Rosero Arenas MA, Ruiz Granell R, **Chorro Gascó FJ**, Martínez Cornejo A. Usefulness of cardiac resynchronisation therapy devices and implantable cardioverter defibrillators in the treatment of heart failure due to severe systolic dysfunction: systematic review of clinical trials and network meta-analysis. *Heart Asia*. 2016; 8(1):8-15. IF: 0
 16. **Del Canto I**, **Such-Miquel L**, **Brines L**, **Soler C**, **Zarzoso M**, Calvo C, Parra G, Tormos Á, Alberola A, Millet J, **Such L**, **Chorro FJ**. Effects of JTV-519 on stretch-induced manifestations of mechanoelectric feedback. *Clin Exp Pharmacol Physiol*. 2016 Nov; 43(11):1062-1070. IF: 2,16
 17. Núñez J, Llàcer P, Bertomeu-González V, Bosch MJ, Merlos P, García-Blas S, Montagud V, Bodí V, Bertomeu-Martínez V, Pedrosa V, Mendizábal A, Cordero A, Gallego J, Palau P, Miñana G, Santas E, Morell S, Llàcer A, **Chorro FJ**, Sanchis J, Fácila L, CHANCE-HF Investigators.. Carbohydrate Antigen-125-Guided Therapy in Acute Heart Failure: CHANCE-HF: A Randomized Study. *JACC Heart Fail*. 2016 Nov; 4(11):833-843. IF: 7,218
 18. García-Blas S, **Mainar L**, Sanchis J, Núñez J. Complex left main coronary stent restenosis treated through radial approach using a sheathless catheter. *Rev Port Cardiol*. 2016 Oct; 35(10):543. E1-5. IF: 0,873
 19. Santas E, Valero E, Mollar A, García-Blas S, Palau P, Miñana G, Núñez E, Sanchis J, **Chorro FJ**, Núñez J. Burden of Recurrent Hospitalizations Following an Admission for Acute Heart



Failure: Preserved Versus Reduced Ejection Fraction. Rev Esp Cardiol (Engl Ed). 2016 Nov 2. IF: 0

20. Núñez J, Monmeneu JV, Mollar A, Núñez E, Bodí V, Miñana G, García-Blas S, Santas E, Agüero J, **Chorro FJ**, Sanchis J, López-Lereu MP. Left ventricular ejection fraction recovery in patients with heart failure treated with intravenous iron: a pilot study. ESC Heart Fail. 2016 Dec; 3(4):293-298. IF: 0
21. Escribano D, Santas E, Miñana G, Mollar A, García-Blas S, Valero E, Payá A, **Chorro FJ**, Sanchis J, Núñez J. High-sensitivity troponin T and the risk of recurrent readmissions after hospitalisation for acute heart failure. Rev Clin Esp. 2016 Nov 30. IF: 0,76

• THESIS

Thesis title: *Interés por la medicina de familia tras cursar una asignatura de atención primaria.*

Doctoral candidate: María Candelaria Ayuso Raya

Director(s): Francisco Javier Chorro Gascó, Francisco Jesús Escobar Rabadan

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Ensayo aleatorizado controlado sobre la terapia guiada por el antígeno carbohidrato 125 en pacientes dados de alta por insuficiencia cardiaca aguda: efecto sobre la mortalidad o reingreso por insuficiencia cardiaca aguda a 1 año.*

Doctoral candidate: Pau Llàcer Iborra

Director(s): Luis Such Belenguer, Julio Núñez

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio comparativo de los efectos electrofisiológicos miocárdicos intrínsecos de la apertura del canal katp y del ejercicio físico crónico, en situación de normoxia y tras isquemia regional aguda. Estudio experimental.*

Doctoral candidate: Catia Alves da Silva

Director(s): Luis Such Belenguer

Date of the defense: 21/01/2016

Grade: *Sobresaliente "cum laude"*

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: RD12/0042/0048

Title: *Red de Investigación Cardiovascular (RIC)*

Principal Investigator: Francisco Javier Chorro Gascó

Funding body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación del Hospital Clínico Universitario de Valencia*

Duration: 2013-2016

Total budget: 81.753€

Reference: PROMETEOII/2014/037

Title: *Estudio mediante técnicas cartográficas avanzadas de los mecanismos básicos implicados en las arritmias malignas y en su control.*

Principal Investigator: Francisco Javier Chorro Gascó

Funding body: *Generalitat Valenciana*

Beneficiary Institution: *Fundación Investigación del Hospital Clínico Universitario de Valencia*

Duration: 2014-2018

Total budget: 33.000€ (this year)

Reference: PIE15/00013

Title: *A multidisciplinary project to advance in basic mechanisms, diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction.*

Principal Investigator: Vicente Bodí Peris (Francisco Javier Chorro as collaborating Research)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2018

Total Budget: 589.050€

Reference: PI15/01408

Title: *Efectos de la inhibición de la desacetilación de las histonas en el remodelado post-infarto del sustrato arritmogénico.*

Principal Investigator: Francisco Javier Chorro Gascó

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2018

Total Budget: 93.170€



Reference: 09_TerGenInf-ALIÑO-MAINAR-2014-UV

Title: *Terapia génica del infarto agudo de miocardio mediante inyección hidrodinámica del gen humano IL-10 en el seno coronario del cerdo.*

Principal Investigator: Luis Mainar Latorre

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

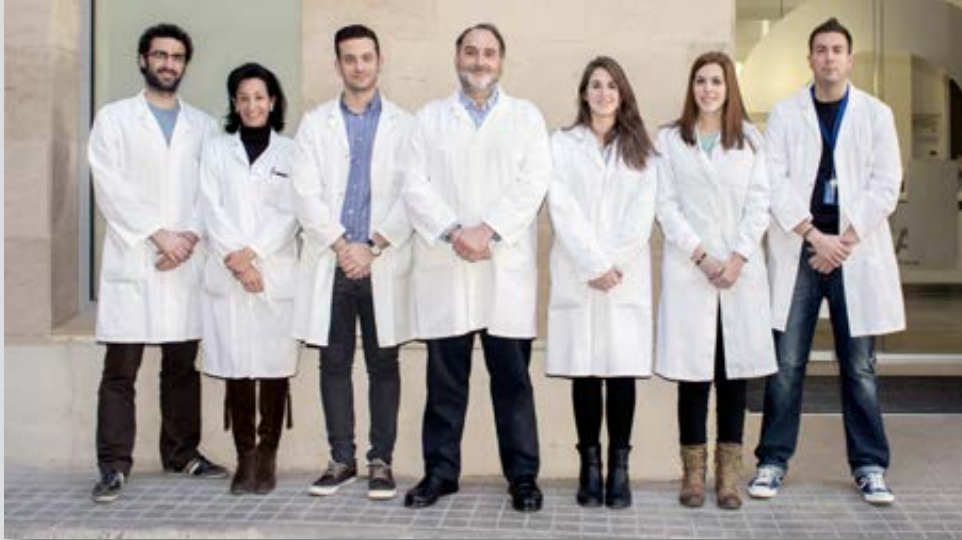
Beneficiary Institution: *Universidad de Valencia*

Duration: 2016

Total Budget: 44.250€



Research Group on Endothelial Cells (LINCE) Consolidated group

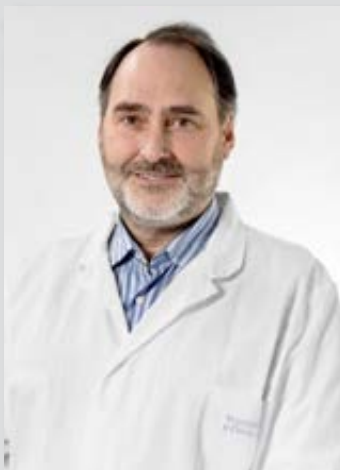


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Group members

Principal investigator

Carlos Hermenegildo Caudevilla
University
H Index: 27



Team involved in



Collaborating researchers

Elena Monsalve Villalba. University

PhD students

Daniel Bernardo Pérez Cremades. University
Xavier Vidal Gómez. INCLIVA
Ana Mompeón Campos. University

Emerging researcher

Susana Novella del Campo. University



Strategic aims

- To fulfill PI13/00617 research project objectives.
- To obtain and check the endothelial regulation of miRNA by estradiol and to analyze the role of estrogen receptors.
- To publish the endothelial effects induced by estradiol on angiotensin 1-7 production.
- To publish the role of cyclooxygenase in the decreased bioavailability of nitric oxide in aorta from ovariectomized and senescent mice.

Main lines of research

- Vascular effects of sex hormones.
- Identification of new hormone-regulated signalling pathways in endothelium.
- Identification and characterization of miRNA regulated by estradiol in endothelium.
- Interaction of sex hormones with pro-atherogenic factors.
- Determination of circulating endothelial progenitor cells and their link with hormone treatment.
- miRNA profile in vascular cells under estrogen exposure.



Emerging researcher

Susana Novella del Campo

Research is focused on the study of endothelial dysfunction associated with aging and lack of estrogen. During aging mechanical and functional alterations in the arterial wall are produced which lead to the occurrence of cardiovascular diseases. These alterations are conditioned by gender differences. Our main goal is to determine the mechanisms by which the main endothelial mediators, nitric oxide and prostanoids are affected during aging. We also studied the regulatory role of miRNAs associated with acute coronary syndrome and the estrogen-dependent vascular function and aging.

• PUBLICATIONS

Number of articles	IF	Average IF
9	36,73	4,08
National collaborations	International collaborations	Corresponding author
4	4	6

Original articles

1. **Mompeón A**, Lázaro-Franco M, Bueno-Betí C, **Pérez-Cremades D**, **Vidal-Gómez X**, **Monsalve E**, Gironacci MM, **Hermenegildo C**, **Novella S**. Estradiol, acting through ER?, induces endothelial non-classic renin-angiotensin system increasing angiotensin 1-7 production. *Mol Cell Endocrinol*. 2016 Feb 15; 422:1-8. IF: 4,405
2. **Vidal-Gómez X**, **Novella S**, Pérez-Monzó I, Garabito M, Dantas AP, Segarra G, **Hermenegildo C**, Medina P. Decreased bioavailability of nitric oxide in aorta from ovariectomized senescent mice. Role of cyclooxygenase. *Exp Gerontol*. 2016 Apr; 76:1-8. IF: 3,485
3. Atienzar-Aroca S, Flores-Bellver M, Serrano-Heras G, Martínez-Gil N, Barcia JM, Aparicio S, **Pérez-Cremades D**, García-Verdugo JM, Díaz-Llopis M, Romero FJ, Sancho-Pelluz J. Oxidative stress in retinal pigment epithelium cells increases exosome secretion and promotes angiogenesis in endothelial cells. *J Cell Mol Med*. 2016 Aug; 20(8):1457-66. IF: 4,753
4. Drechsler S, Lynch MA, **Novella S**, González-Navarro H, Hecimovic S, Barini E, Tucci V, Castro RE, Vandenbroucke RE, Osuchowski M, Potter PK. With mouse age comes wisdom: A review and suggestions of relevant mouse models for age-related conditions. *Mech Ageing Dev*. 2016 Jul 21 ; IF: 2,892
5. **Hermenegildo C**, **Mompeón A**, **Pérez-Cremades D**, Vidal-Gomez X, Gironacci MM, **Novella S**. [OP.6D.01] Estradiol increases endothelial angiotensin-(1-7) production through estrogen receptor alpha. *J Hypertens*. 2016 Sep; 34 Suppl 2:e75. IF: 5,062
6. **Novella S**, **Vidal-Gómez X**, **Mompeón A**, **Pérez-Cremades D**, Segarra G, Medina P, **Hermenegildo C**. [OP.3B.02] Ageing and lack of estrogens activates cyclooxygenases pathway increasing superoxide anion production in response to thromboxane A2. *J Hypertens*. 2016 Sep; 34 Suppl 2:e29. IF: 5,062
7. **Novella S**, **Vidal-Gómez X**, Pérez-Monzó I, **Mompeón A**, **Pérez-Cremades D**, Dantás AP, Segarra G, **Hermenegildo C**, Medina P. [OP.8C.02] Senescence increases vascular smooth muscle contractions through increased rho kinase activity in female mouse aorta. *J Hypertens*. 2016 Sep; 34 Suppl 2:e102. IF: 5,062
8. von Zglinicki T, Nieto IV, Brites D, Karagianni N, Ortolano S, Georgopoulos S, Cardoso AL, **Novella S**, Lepperdinger G, Trendelenburg AU, van Os R. Frailty in mouse ageing: A con-

ceptual approach. *Mech Ageing Dev.* 2016 Jul 18 ; IF: 2,892

- Segarra G, Cortina B, Mauricio MD, **Novella S**, Lluch P, Navarrete-Navarro J, Noguera I, Medina P. Effects of asymmetric dimethylarginine on renal arteries in portal hypertension and cirrhosis. *World J Gastroenterol.* 2016 Dec 28; 22(48):10545-10556. IF: 3,127

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: RD12/0042/0052

Title: *Nodo de la red de investigación cooperativa (RETIC) de Enfermedades Cardiovasculares.*

Principal Investigator: Carlos Hermenegildo Caudevilla

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación del Hospital Clínico Universitario de Valencia*

Duration: 2013-2016

Total budget: 110.977€

Reference: PI13/00617

Title: miRNA endothelial profile modification in response to estradiol and aging. Relationship to clinical course of coronary restenosis.

Principal Investigator: Carlos Hermenegildo Caudevilla

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación del Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total budget: 73.205€

Reference: COST Action BM1402

Title: Development of a European network for preclinical testing of interventions in mouse models of age and age-related diseases (MouseAGE).

Principal Investigator: Ilaria Bellantuono (Susana Novella as collaborating researcher)

Funding body: European Commission

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2018

• THESIS

Thesis title: *Aislamiento y función de células progenitoras endoteliales de sangre periférica durante la evolución clínica de pacientes con infarto agudo de miocardio. Efecto de las micropartículas shh+ en la función celular.*

Doctoral candidate: Carlos Bueno Betí

Director(s): Carlos Hermenegildo Caudevilla, Susana Novella del Campo

Date of the defense: 04/03/2016

Grade: *Sobresaliente "cum laude"*

• AWARDS

In June 2016, all the researchers of the group were awarded with the Premio Alberto Ferrari to the best communication in the form of a poster in the 26th European Meeting on Hypertension and Cardiovascular Protection for the scientific work "miRNA-regulated cardiovascular pathways in estradiol-treated human vein endothelial cells".

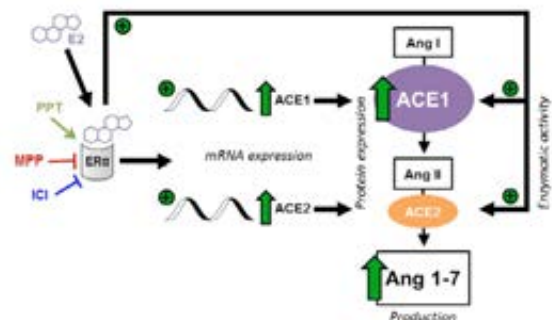


Fig. 1 Ang1-7 expression in cultured human endothelial cells

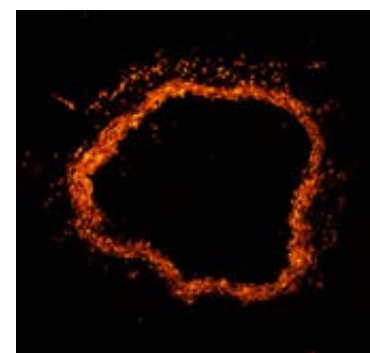


Fig 2: Superoxide production in murine arteries



Research Group on Clinical Cardiology Consolidated group



“Esta estrategia terapéutica, se asoció a una reducción significativa del riesgo de episodios adversos clínicos a un año, especialmente una reducción del cincuenta por ciento del riesgo de nuevos ingresos por insuficiencia cardiaca aguda “

Julio Núñez. ABC Salud. 01/09/2016

Group members

Principal investigator

Juan Sanchis Forés
Hospital. University
H Index: 30



Team involved in



Collaborating researchers

Vicente Ruiz Ros. Hospital. University
Sergio García Blas. Hospital. University
Ernesto Valero Picher. Hospital
Gemma Miñana Escrivá. Hospital

PhD students

Clara Sastre Arbona. INCLIVA
Anna Mollar Fernández. INCLIVA

Emerging researchers

Julio Núñez Villota. Hospital. University



Strategic aims

- Publication of manuscripts in high IF journals.
- CIBER Cardiovascular.
- Development of FIS projects.

Main lines of research

- Therapeutic and prognostic assessment of acute coronary syndromes and secondary prevention.
- Acute heart failure. New strategies for risk assessment and treatment and new control programs.



Emerging researcher

Julio Núñez Villota (Department of Cardiology - Hospital Clínico Universitario of Valencia)

Our research team has focused in the development of new clinical tools for improving diagnosis, risk stratification and treatment of patients with ischemic heart disease and heart failure. Along this line, we are conducting several clinical studies, many of them investigator-initiated clinical trials, aimed to evaluate: a) new therapies/strategies to improve prognosis, and, b) new biomarkers/devices useful for monitoring and guiding therapy after an episode of acute coronary and acute heart failure episode.

More specifically, we are focused on the potential utility of peritoneal dialysis for patients with refractory congestive heart failure, the development of new algorithms for monitoring patients, the efficacy of physical therapies in heart failure, the development of a multimarker and dynamic approach for risk stratification.

• PUBLICATIONS

Number of articles	IF	Average IF
45	136,32	3,02
National collaborations	International collaborations	Corresponding author
32	2	28

Original articles

1. **Núñez J**, Mascarell B, Stubbe H, Ventura S, Bonanad C, Bodí V, Núñez E, **Miñana G**, Fácila L, Bayés-Genis A, Chorro FJ, **Sanchis J**. Bioelectrical impedance vector analysis and clinical outcomes in patients with acute heart failure. *J Cardiovasc Med (Hagerstown)*. 2016 Apr; 17(4):283-90. IF: 1,51
2. Moreno-Arribas J, Bertomeu-González V, Anguita-Sanchez M, Cequier Á, Muñoz J, Castillo J, **Sanchis J**, Roldán I, Marín F, Bertomeu-Martínez V, investigators of the FANTASIA study. Choice of New Oral Anticoagulant Agents Versus Vitamin K Antagonists in Atrial Fibrillation: FANTASIA Study. *J Cardiovasc Pharmacol Ther*. 2016 Mar; 21(2):150-6. IF: 2,094
3. **Sanchis J**, Abellán L, **García-Blas S**, Mainar L, **Mollar A**, **Valero E**, Consuegra-Sánchez L, Roqué M, Bertomeu-González V, Chorro FJ, Núñez E, **Núñez J**. Usefulness of delta troponin for diagnosis and prognosis assessment of non-ST-segment elevation acute chest pain. *Eur Heart J Acute Cardiovasc Care*. 2016 Sep; 5(5):399-406. IF: 0
4. **Valero E**, Rumiz E, Pellicer M. Cardiac Involvement in Von Hippel-Lindau Disease. *Med Princ Pract*. 2016; 25(2):196-8. IF: 1,34
5. De La Torre Hernandez JM, Moreno R, Lee DH, Garcia Del Blanco B, Sanmartin JC, **Garcia Blas S**, Serra Garcia V, Gaviria K, Garcia I, Zueco J. The routine use of surgical exposure approach for trans-femoral implantation of the balloon expandable aortic prosthesis is associated to a low rate of vascular complications. *J Cardiovasc Surg (Torino)*. 2016 Aug; 57(4):615-9. IF: 1,461
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8. **Núñez J**, Comín-Colet J, **Miñana G**, Núñez E, Santas E, **Mollar A**, **Valero E**, **García-Blas S**, Cardells I, Bodí V, Chorro FJ, **Sanchis J**. Iron deficiency and risk of early readmission following a hospitalization for acute heart failure. *Eur J Heart Fail*. 2016 Jul; 18(7):798-802. IF: 6,526
 9. **Núñez J**, Domínguez E, Ramón JM, Núñez E, **Sanchis J**, Santas E, Heredia R, González J, **Miñana G**, López L, Chorro FJ, Palau P. Iron deficiency and functional capacity in patients with advanced heart failure with preserved ejection fraction. *Int J Cardiol*. 2016 Mar 15; 207:365-7. IF: 4,036
 10. **García-Blas S**, **Núñez J**, Carrillo P, Cordero A, **Miñana G**, Frutos A, **Valero E**, Cardells I, **Sanchis J**, López-Palop R. Usefulness of sheathless guide catheter for the percutaneous coronary intervention of left main disease by radial approach. *Int J Cardiol*. 2016 May 15; 211:49-52. IF: 4,036
 11. **Valero E**, Santas E, Machado F, **Núñez J**. Pseudoaneurysm with fistulization to the left atrium: A very rare late complication of previous aortic root surgery. *Int J Cardiol*. 2016 Jun 1; 212:145-7. IF: 4,036
 12. **Miñana G**, Rumiz E, Palau P, **Valero E**, Bodí V, Núñez E, **Sanchis J**, **Núñez J**. Plasma neutrophil gelatinase-associated lipocalin and long-term mortality in patients with acute heart failure and normal renal function. *Int J Cardiol*. 2016 Jul 1; 214:51-3. IF: 4,036
 13. Palau P, Domínguez E, López L, Heredia R, González J, Ramón JM, Serra P, Santas E, Bodí V, **Sanchis J**, Chorro FJ, **Núñez J**. Inspiratory Muscle Training and Functional Electrical Stimulation for Treatment of Heart Failure With Preserved Ejection Fraction: Rationale and Study Design of a Prospective Randomized Controlled Trial. *Clin Cardiol*. 2016 Aug; 39(8):433-9. IF: 2,431
 14. **Sanchis J**, Núñez E, Barrabés JA, Marín F, Consuegra-Sánchez L, Ventura S, **Valero E**, Roqué M, Bayés-Genís A, Del Blanco BG, Dégano I, **Núñez J**. Randomized comparison between the invasive and conservative strategies in comorbid elderly patients with non-ST elevation myocardial infarction. *Eur J Intern Med*. 2016 Nov; 35:89-94. IF: 2,591
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 16. Alegre O, Ariza-Solé A, Vidán MT, Formiga F, Martínez-Sellés M, Bueno H, **Sanchis J**, López-Palop R, Abu-Assi E, Cequier A. Impact of Frailty and Other Geriatric Syndromes on Clinical Management and Outcomes in Elderly Patients With Non-ST-Segment Elevation Acute Coronary Syndromes: Rationale and Design of the LONGEVO-SCA Registry. *Clin Cardiol*. 2016 Jul; 39(7):373-7. IF: 2,431
 17. **Núñez J**, Núñez E, **Miñana G**, Carratalá A, **Sanchis J**, Lupón J, Barallat J, Pastor MC, Pascual-Figal D, Bayés-Genís A. Serum neprilysin and recurrent hospitalizations after acute heart failure. *Int J Cardiol*. 2016 Jun 28; 220:742-744. IF: 4,638
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 19. **Núñez J**, Llàcer P, Bertomeu-González V, Bosch MJ, Merlos P, **García-Blas S**, Montagud V, Bodí V, Bertomeu-Martínez V, Pedrosa V, Mendizábal A, Cordero A, Gallego J, Palau P, **Miñana G**, Santas E, Morell S, Llàcer A, Chorro FJ, **Sanchis J**, Fácila L, CHANCE-HF Investigators.. Carbohydrate Antigen-125-Guided Therapy in Acute Heart Failure: CHANCE-HF: A Randomized Study. *JACC Heart Fail*. 2016 Nov; 4(11):833-843. IF: 7,218
 20. **Núñez J**, Teruel A, Quiñones-Torrel C, **García-Blas S**, Carratalá A, **Miñana G**, Santas E, Torregrosa I, Solano C, González M. Continuous ambulatory peritoneal dialysis as a promising therapy for light chain amyloidosis with congestive heart failure. *Int J Cardiol*. 2016 Aug 20; 223:807-809. IF: 4,638



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 22. **García-Blas S**, Mainar L, **Sanchis J**, **Núñez J**. Complex left main coronary stent restenosis treated through radial approach using a sheathless catheter. *Rev Port Cardiol*. 2016 Oct; 35(10):543. E1-5. IF: 0,873
 23. Vannini L, Muro A, **Sanchis J**, Ortiz-Pérez JT, Flores Umazor E, López-Lereu MP, Badimon L, Sabaté M, Brugaletta S. Can new generation P2Y12 inhibitors play a role in microvascular obstruction in STEMI? *Int J Cardiol*. 2016 Aug 8; 223:226-227. IF: 4,638
 24. **Sanchis J**, Núñez E, Ruiz V, **Núñez J**. Reply to Letter From Ganga and Jantz-Identifying Frailty in Elderly Patients With Acute Coronary Syndrome. *Can J Cardiol*. 2016 Oct; 32(10):1261. E17. IF: 3,112
 25. **Sanchis J**, **García-Blas S**, Carratalá A, **Valero E**, **Mollar A**, **Miñana G**, **Ruiz V**, Balaguer JV, Roqué M, Bosch X, **Núñez J**. Clinical Evaluation Versus Undetectable High-Sensitivity Troponin for Assessment of Patients With Acute Chest Pain. *Am J Cardiol*. 2016 Dec 1; 118(11):1631-1635. IF: 3,154
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 28. **Núñez J**, Monmeneu JV, **Mollar A**, Núñez E, Bodí V, **Miñana G**, **García-Blas S**, Santas E, Agüero J, Chorro FJ, **Sanchis J**, López-Lereu MP. Left ventricular ejection fraction recovery in patients with heart failure treated with intravenous iron: a pilot study. *ESC Heart Fail*. 2016 Dec; 3(4):293-298. IF: 0
 29. **Núñez J**, **Ruiz V**, Bonanad C, **Miñana G**, **García-Blas S**, **Valero E**, Núñez E, **Sanchis J**. Percutaneous coronary intervention and recurrent hospitalizations in elderly patients with non ST-segment acute coronary syndrome: The role of frailty. *Int J Cardiol*. 2016 Nov 10; 228:456-458. IF: 4,638
 30. Rumiz E, **Valero E**, Vilar JV, Santas E, Haba J. Infantile Aortic Coarctation in an Adult with Heart Failure. *Med Princ Pract*. 2016 Oct 31 ;. IF: 1,159
 31. Escribano D, Santas E, **Miñana G**, **Mollar A**, **García-Blas S**, **Valero E**, Payá A, Chorro FJ, **Sanchis J**, **Núñez J**. High-sensitivity troponin T and the risk of recurrent readmissions after hospitalisation for acute heart failure. *Rev Clin Esp*. 2016 Nov 30 ;. IF: 0,76
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32. **Núñez J**, Núñez E, **Sanchis J**. Spironolactone in patients with heart failure and preserved ejection fraction. *Rev Clin Esp*. 2016 Mar; 216(2):111. IF: 1,063
 33. **Núñez J**, Núñez E, **Miñana G**, Bayés-Genis A, **Sanchis J**. Worsening Renal Function in Acute Decompensated Heart Failure: The Puzzle is Still Incomplete. *JACC Heart Fail*. 2016 Mar; 4(3):232-3. IF: 0
 34. **Núñez J**, **Miñana G**, Consuegra-Sánchez L. Statins in Heart Failure. *Rev Esp Cardiol (Engl Ed)*. 2016 Feb; 69(2):232. IF: 4,596
 35. **Valero E**, Rodríguez JC, Moyano P, **Miñana G**, **Sanchis J**, **Núñez J**. Role of Neutrophil Gelatinase-associated Lipocalin in the Detection of Contrast-induced Nephropathy in Patients Undergoing a Coronary Angiography. *Rev Esp Cardiol (Engl Ed)*. 2016 May; 69(5):524-5. IF: 4,596
 36. **Sanchis J**, **Núñez J**. Immediate Invasive Strategy for Patients With Both New Ischemic Electrocardiographic Changes and Troponin Elevation. *JACC Cardiovasc Interv*. 2016 Apr 11; 9(7):753. IF: 7,345
 37. **Núñez J**, **García-Blas S**, Comín-Colet J. Iron deficiency and risk of early readmission following hospitalization for acute heart failure. Reply. *Eur J Heart Fail*. 2016 Jul; 18(7):881. IF: 5,135
 38. Cardells I, Payá A, Bondanza L, **Miñana G**, González M, **Núñez J**. Peritoneal Dialysis in Constrictive Pericarditis: A Report of Three Cases. *Rev Esp Cardiol (Engl Ed)*. 2016 Oct 31 ;. IF: 0



Editorial

39. **Núñez J**, Santas E. Cystatin C: One more component of the complex cardiorenal interaction in heart failure. *Rev Clin Esp*. 2016 Mar; 216(2):74-75. IF: 1,063
40. Ferreira-González I, Abu-Assi E, Arias MA, Gallego P, Sánchez-Recalde Á, Avanzas P, Bayes-Genis A, de Isla LP, **Sanchis J**. Revista Española de Cardiología: Current Position and Future Directions. *Rev Esp Cardiol (Engl Ed)*. 2016 Mar; 69(3):327-36. IF: 0
41. Subias PE, **SEC Working Group for ESC/ERS 2015 Guidelines for Diagnosis and Treatment of Pulmonary Hypertension**, Expert Reviewers for ESC/ERS 2015 Guidelines for Diagnosis and Treatment of Pulmonary Hypertension, SEC Guidelines Committee. Comments on the 2015 ESC/ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension. *Rev Esp Cardiol (Engl Ed)*. 2016 Feb; 69(2):102-8. IF: 0
42. Fernández-Lozano I, **SEC Working Group for 2015 ESC Guidelines for Management of Patients With Ventricular Arrhythmias and Prevention of Sudden Cardiac Death**, Expert Reviewers for 2015 ESC Guidelines for Management of Patients With Ventricular Arrhythmias and Prevention of Sudden Cardiac Death, SEC Guidelines Committee. Comments on the 2015 ESC Guidelines for the Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. *Rev Esp Cardiol (Engl Ed)*. 2016 Feb; 69(2):94-101. IF: 0
43. **SEC Working Group for the ESC 2015 Guidelines on the Management of Infective Endocarditis**, Expert Reviewers for the ESC 2015 Guidelines on the Management of Infective Endocarditis, SEC Guidelines Committee. Comments on the ESC 2015 Guidelines for the Management of Infective Endocarditis. *Rev Esp Cardiol (Engl Ed)*. 2016 Jan; 69(1):7-10. IF: 0
44. **Núñez J**. Blood urea nitrogen to creatinine ratio in acute heart failure: an old concept brought to reality? *Heart*. 2016 Oct 14 ; IF: 5,693

Review

45. Palau P, Núñez E, Domínguez E, **Sanchis J**, **Núñez J**. Physical therapy in heart failure with preserved ejection fraction: A systematic review. *Eur J Prev Cardiol*. 2016 Jan; 23(1):4-13. IF: 3,319

RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: RD12/0042/0010

Title: *Red de Investigación Cardiovascular (RIC)*.

Principal Investigator: Juan Sanchis Forés

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2013-2016

Total budget: 64.681€

Reference: PI13/01519

Title: Loop diuretics dosage in patients with acute heart failure and renal failure: conventional strategy versus strategy guided by CA125 plasma levels.

Principal Investigator: Julio Núñez Villota

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación del Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total budget: 67.034€

Reference: PI15/00837

Title: *Comparación aleatoria entre un estrategia de intervención sobre fragilidad frente a la estrategia habitual en pacientes frágiles después de un infarto agudo de miocardio.*

Principal Investigator: Juan Sanchis Forés

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2018

Total budget: 36.300€

Reference: HADA

Title: *Herramienta de ayuda al diagnóstico de angina.*

Principal Investigator: Juan Sanchis Forés

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2016

Total budget: 4.000€

Reference: PIE15/00013

Title: A multidisciplinary Project to advance in basic



mechanisms, diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction.

Principal Investigator: Vicente Bodí Peris (Juan Sanchis and Julio Núñez as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2018

Total Budget: 589.050€

- **THESIS**

Thesis title: *Impacto pronóstico de los síndromes geriátricos en el síndrome coronario agudo.*

Doctoral candidate: Clara Bonanad Lozano

Director(s): Juan Sanchis Forés, Vicente Ruiz Ros

Date of the defense: 01/02/2016

Grade: *Sobresaliente "cum laude"*



Research Group on the Study of Cardiovascular Risk in Children and Adolescents Consolidated group



CIBEROBN y la Sociedad Europea de Hipertensión recomiendan medir la presión arterial desde los 3 años.

Buenoparalasalud. Com. 24-08-2016

Group members

Principal investigator

Empar Lurbe i Ferrer
University
H Index: 26



Team involved in



Collaborating researchers

Isabel Torró Doménech. University
Julio Álvarez Pitti. University
Francisco Aguilar Bacallado. University
Consuelo García Vicent. University
Nuria García Carbonell. University
Pau Redón Lurbe. CIBERobn
Laura Cantero Milán. CIBERobn

Technician

Francisco Ponce Zanón. CIBERobn

Administrative assistant

Rachael Dix. CIBERobn
Christine Deutsch. CIBERobn



Strategic aims

- To work in UNIT PEDITEC which co-localizes in the daily work of health personnel with engineers who develop software for capturing signals via mobile devices. The study of physiological parameters that allow the therapeutic individualization has been a priority during 2015 and meant an advance in clinical practice in obese pediatric patients in the unit.
- To expand PAIDO personalized health care program that with the development of actions involving family, educators, nutritionist, physical education teachers and other social actors. The intervention on the pathology transcends the hospital space and involves also the environment and the individual sphere of children.
- To develop a prospective study in more than 200 children. The study collects information and material cord with epigenetic studies and metabolomics, and monitoring clinical parameters and cardiometabolic phenotype.
- To coordinate a new document of the European Guidelines on Hypertension in Children and Adolescents.

Main lines of research

- New technologies applied to the detection of congenital heart diseases and sepsis in asymptomatic newborn babies.
- Childhood obesity.
- New technologies applied to the treatment of obesity.
- Impact of intrauterine life in the development of cardiometabolic disease.
- Arterial hypertension in children.
- Cardiovascular and renal risk in diabetes.

• PUBLICATIONS

Number of articles	IF	Average IF
12	40,63	3,38
National collaborations	International collaborations	Corresponding author
6	2	7

Original articles

1. **Lurbe E**, Ingelfinger JR. Blood pressure in children and adolescents: current insights. *J Hypertens*. 2016 Feb; 34(2):176-83. IF: 4,72
2. **Lurbe E, Torro MI, Alvarez-Pitti J, Redon P**, Redon J. Central blood pressure and pulse wave amplification across the spectrum of peripheral blood pressure in overweight and obese youth. *J Hypertens*. 2016 Jul; 34(7):1389-95. IF: 4,72
3. **Lurbe E**, Redon J. Isolated Systolic Hypertension in Young People Is Not Spurious and Should Be Treated: Con Side of the Argument. *Hypertension*. 2016 Aug; 68(2):276-80. IF: 6,294
4. Urduguio RG, **Torró MI**, Bayón GF, Álvarez-Pitti J, Fernández AF, **Redon P**, Fraga MF, **Lurbe E**. Longitudinal study of DNA methylation during the first 5 years of life. *J Transl Med*. 2016 Jun 3; 14(1):160. IF: 3,694
5. **Lurbe I Ferrer E**. [2016 - European Society of Hypertension Guidelines for the management of high blood pressure in children and adolescents]. *An Pediatr (Barc)*. 2016 Oct; 85(4):167-169. IF: 0,773
6. **Lurbe E**, Redon J. Reply. *J Hypertens*. 2016 Oct; 34(10):2102. IF: 5,062
7. **Lurbe E, Torro MI, Alvarez-Pitti J, Redon P**, Redon J. [OP.6A.06] Vascular phenotypes by assessing peripheral and central blood pressure in obese youth. *J Hypertens*. 2016 Sep; 34 Suppl 2:e67-8. IF: 5,062
8. Villarrasa-Sapiña I, García-Massó X, Serra-Añó P, Garcia-Lucerga C, Gonzalez LM, **Lurbe E**. Differences in intermittent postural control between normal-weight and obese children. *Gait Posture*. 2016 Sep; 49:1-6. IF: 2,286
9. Lecube A, Monereo S, Rubio MÁ, Martínez-de-Icaya P, Martí A, Salvador J, Masmiquel L, Goday A, Bellido D, **Lurbe E**, García-Almeida JM, Tinahones FJ, García-Luna PP, Palacio E, Gargallo M, Bretón I, Morales-Conde S, Caixàs A, Menéndez



E, Puig-Domingo M, Casanueva FF. Prevention, diagnosis, and treatment of obesity. 2016 position statement of the Spanish Society for the Study of Obesity. *Endocrinol Nutr*. 2016 Aug 16 ;. IF: 0

10. **Lurbe i Ferrer E**, Manrique de Lara LA, Rodríguez Fernández LM, Solís Sánchez G. [Editors' corner: Anales de Pediatría annual report]. *An Pediatr (Barc)*. 2016 Jun; 84(6):301-3. IF: 0,773
11. Baños RM, Escobar P, Cebolla A, Guixeres J, **Alvarez Pitti J**, Lisón JF, Botella C. Using Virtual Reality to Distract Overweight Children from Bodily Sensations During Exercise. *Cyberpsychol Behav Soc Netw*. 2016 Feb; 19(2):115-9. IF: 2,188

Clinical guidelines

12. **Lurbe E**, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, Invitti C, Litwin M, Mancina G, Pall D, Rascher W, Redon J, Schaefer F, Seeman T, Sinha M, Stabouli S, Webb NJ, Wühl E, Zanchetti A. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. *J Hypertens*. 2016 Oct; 34(10):1887-920. IF: 5,062

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: CB06/03/0039

Title: *CIBER de la Obesidad y Nutrición (CIBERObn)*.

Principal Investigator: Empar Lurbe i Ferrer

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Consortio Hospital General Universitario de Valencia*

Duration: 2006-2016

Reference: PI14/01781

Title: *Impacto del peso al nacer y la ganancia ponderal postnatal en la disfunción endotelial e inflamación vascular.*

Principal Investigator: Empar Lurbe i Ferrer

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015 – 2017

Total budget: 93.500€

Reference: 120022/14

Title: *Desarrollo de un plan de transferencia de un prototipo de análisis de la capacidad cardiorrespiratoria y su aplicación en la prevención y el tratamiento de la obesidad infantil.*

Principal Investigator: Empar Lurbe i Ferrer

Funding Body: FIPSE

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015 - 2016

Total budget: 25.000€

Reference: ISIC/2011/005

Title: *ISITIC: Instituto Superior de Investigación, Traslación e Innovación Cooperativas Orientadas al Bienestar del Ser Humano*

Principal Investigator: Cristina Botella Arbona (Empar Lurbe as collaborating researcher)

Funding body: *Consellería de Educación, Formación y Ocupación*

Beneficiary institution: *Consortio Hospital General Universitario de Valencia*

Duration: 2012-2016

Total budget: 135.000€

Reference: EIT Health Bio TEI-LAB

Title: *Prototype analysis of cardiorespiratory capacity and its application in the prevention and treatment of Childhood Obesity.*

Principal Investigator: Pau Redón Lurbe

Funding body: *Universidad Politécnica de Madrid*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Reference: DEDIPAC KH

Title: *Determinants of diet and physical activity. Knowledge Hub to integrate and develop infrastructure for research across Europe.*

Principal Investigator: Empar Lurbe

Funding body: DEDIPAC

Beneficiary institution: CIBEROBN

Duration: 2013-2016

Total budget: 10.000€



- **THESIS**

Thesis title: *Intervención de ejercicio físico domiciliario en obesidad infantil. Ensayo controlado aleatorizado comparando modalidad tradicional versus plataforma web.*

Doctoral candidate: Alejandro Bruño Soler

Director(s): Empar Lurbe, Juan Francisco Lisón Parraga

Date of the defense: 20/07/2016

Grade: *Sobresaliente "cum laude"*

- **AWARDS**

In November 2016, Julio Álvarez was awarded with the *Premios Fundación Investigación Hospital General Universitario* for his project: *Innovando en el tratamiento de la obesidad infantil: desarrollo de una plataforma y su implantación en la clínica.*



Cardiometabolic Research Group on Primary Care Consolidated group



Group members

Principal investigator

Jorge Navarro Pérez
Clínico-Malvarrosa Health Department
H Index: 11



Collaborating researchers

Jose Vicente Lozano Vidal. Clínico-Malvarrosa Health Department
Alvaro Bonet Pla. Clínico-Malvarrosa Health Department
Victoria Gosalbes Soler. Clínico-Malvarrosa Health Department
Carlos Fluixá Carrascosa. Clínico-Malvarrosa Health Department
Nidia Ruiz Varea. Clínico-Malvarrosa Health Department
Pilar Roca Navarro. University. Clínico-Malvarrosa Health Department
Gaspar Sánchez Vela. Clínico-Malvarrosa Health Department
José Sanfélix-Genovés. Clínico-Malvarrosa Health Department
José Luis Trillo Mata. Clínico-Malvarrosa Health Department
Ruth Usó Talamantes. Clínico-Malvarrosa Health Department



Strategic aims

- Consolidation of various lines of cardiometabolic research.
- Consolidation of a network of partners in the area of primary care.

Main lines of research

- Epidemiological studies:
 - Valencian cardiometabolic study (ESCARVAL project).
- Intervention studies:
 - Euroaction Plus.
 - Secondary Prevention Program (PROPRESE program).
- Cost-effectiveness qualitative studies:
 - Antiaggregation.
- Systematic reviews of Cardiovascular Interventions.

• PUBLICATIONS

Number of articles	IF	Average IF
5	16,97	3,39

National collaborations	International collaborations	Corresponding author
4	1	-

Original articles

1. Arrieta F, Iglesias P, Pedro-Botet J, Tébar FJ, Ortega E, Nubiola A, Pardo JL, Maldonado GF, Obaya JC, Matute P, Petrecca R, Alonso N, Sarabia E, Sánchez-Margalet V, Alemán JJ, **Navarro J**, Becerra A, Duran S, Aguilar M, Escobar-Jiménez F, Grupo de Trabajo Diabetes y Enfermedad Cardiovascular de la Sociedad Española de Diabetes (SED). [Diabetes mellitus and cardiovascular risk: Working group recommendations of Diabetes and Cardiovascular Disease of the Spanish Society of Diabetes (SED, 2015)]. *Aten Primaria*. 2016 May; 48(5):325-36. IF: 0,953
2. Redon J, Tellez-Plaza M, Orozco-Beltran D, Gil-Guillen V, Pita-Fernandez S, **Navarro-Pérez J**, Pallares V, Valls F, Fernandez A, Perez-Navarro AM, Sanchis C, Dominguez-Lucas A, Sanz G, Martin-Moreno JM, ESCARVAL Study Group. Impact of hypertension on mortality and cardiovascular disease burden in patients with cardiovascular risk factors from a general practice setting: the ESCARVAL-risk study. *J Hypertens*. 2016 Jun; 34(6):1075-83. IF: 4,72
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5. Sancho-Mestre C, Vivas-Consuelo D, Alvis-Estrada L, Romero M, **Usó-Talamantes R**, Caballer-Tarazona V. Pharmaceutical cost and multimorbidity with type 2 diabetes mellitus using electronic health record data. *BMC Health Serv Res*. 2016 Aug 17; 16(1):394. IF: 1,606

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Title: CIBER de Epidemiología y Salud Pública (CIBERESP)

Principal Investigator: María Manuela Morales (Jorge Navarro Pérez as a Collaborating researcher).

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2007 – 2016

Reference: PI16/02130

Title: *Impacto de la auto-medición y el auto-ajuste de la medicación antihipertensiva en el control de la hipertensión arterial. Un ensayo clínico pragmático: estudio ADAMPA.*

Principal Investigator: José Sanfélix Genovés

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2019



Research Group on the Study of Cardiometabolic and Renal Risk Consolidated group



“Pertener a EATRIS es una oportunidad para mejorar la participación de nuestros investigadores en proyectos de excelencia a nivel europeo. Además la Red debe ser una herramienta importante para mejorar la prestación de atención médica y hará que el sector biofarmacéutico sea más competitivo y preparado para dar respuesta a las necesidades del sector de salud público.”

Josep Redon i Más. El Periodic. Com. 02/01/2016

Group members

Principal investigator

Josep Redón i Mas
Hospital. University
H Index: 50



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María Téllez Plaza. INCLIVA

Post-doctoral researchers

Raquel Cortés Vergaz. INCLIVA



Strategic aims

- To start-up the laboratory for the analysis of podocytes (identification, cultivation and phenotyping) and its derivatives: micro-RNA, exosomes.
- The integration of metabolomics and genomics in the study of factors related to the development of kidney damage.
- Development of studies for noninvasive hemodynamic characterization in vascular pathology.
- Analysis of morbidity and mortality linked to the presence of hypertension and renal injury.
- Development of *in vitro* studies of platelet and leukocyte adhesion in venous thromboembolism.
- Genetic studies related to obesity and overweight and venous thromboembolism.
- Development of phase III and IV clinical trials.

Main lines of research

- Mechanisms of development of renal damage associated with hypertension with special emphasis on the podocyte damage.
- Impact of cardiovascular risk factors and renal function in absolute morbidity and mortality in high-risk population and in the general population.
- Inflammation and oxidative stress in the development of cardiovascular disease.
- Genomics, proteomics and metabolomics of early cardiometabolic and renal disorders.
- Impact of environmental toxins (metals) in cardiometabolic risk.
- Identification of polymorphisms and related to the control of BMI and waist circumference and the risk of obesity genes.
- Venous thrombosis in young patients: factors associated with its development.
- The relationship between risk of venous thromboembolic disease and arteriosclerosis.



Emerging researcher

Fernando Martínez García

During the last year we have focused our research activity in those mechanisms, which are involved in the development of microalbuminuria and kidney damage in hypertensive patients. In this sense we have been studying the role of the podocytes in the regulation of urine albumin excretion not only in hypertension but also in obesity and diabetes.

We are also studying the role of new image techniques for the early diagnosis of atherosclerosis and the potential value of markers of vascular stiffness for risk prediction. Jointly with other research groups we are also performing some collaborative studies in metabolic syndrome and insulin resistance. Finally we are also taking advantage of the new Electronic Health Recordings system to analyse cardiovascular risk factors and events in real world.

All of our research is aimed to improve the prevention and the consequences of cardiovascular disease, especially those related with essential hypertension.



Emerging researcher

María Téllez Plaza

Dr. Tellez-Plaza's research interest is focused on the health consequences of widespread exposure to environmental toxicants. In recent years, her research has built expertise in population-based studies of the chronic cardiovascular effects of cadmium, arsenic and other toxic metals. Her current focus is on the use of DNA-methylation alterations as a tool for studying gene-environment interaction. The epigenetic epidemiology field is moving towards high-throughput platforms that allow genome-wide arrays and next-generation sequencing, and an important area of work involves the development of data analysis methods that can be applied to genome-wide DNA-methylation data in population-based studies. The simultaneous assessment of environmental exposures, genetic and epigenetic profiles and cardiovascular end-points can have important clinical and public health implications for cardiovascular disease prevention and control, while also developing novel research areas.



• PUBLICATIONS

Number of articles	IF	Average IF
50	335,54	6,71

National collaborations	International collaborations	Corresponding author
10	31	17

Original articles

1. **Pichler G, Martinez F, Vicente A, Solaz E, Calaforra O, Redon J.** Pulse pressure amplification and its determinants. *Blood Press.* 2016 Feb; 25(1):1-7. IF: 1,808
2. **Redon J.** The risk of visit-to-visit blood pressure variability in chronic kidney disease: cause or consequence. *J Hypertens.* 2016 Feb; 34(2):188-90. IF: 4,72
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- population. *J Hypertens*. 2016 Sep; 34 Suppl 2:e86. IF: 5,062
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Editorial

48. Bousquet J, Barbara C, Bateman E, Bel E, Bewick M, Chavannes NH, Cruz AA, Haahtela T, Hellings PW, Khaltaev N, Lodrup Carlsen K, Muraro A, Cordeiro CR, Rosado-Pinto J, Samolinski B, Strandberg T, Valiulis A, Yorgancioglu A, Zuberbier T, **AIRWAYS-ICPs working group**. AIRWAYS-ICPs (European Innovation Partnership on Active and Healthy Ageing) from concept to implementation. *Eur Respir J*. 2016 Apr; 47(4):1028-33. IF: 8,332

Guidelines

49. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney MT, Corrà U, Cosyns B, Deaton C, Graham I, Hall MS, Richard Hobbs FD, Løchen ML, Löllgen H, Marques-Vidal P, Perk J, Prescott E, **Redon J**, Richter DJ, Sattar N, Smulders Y, Tiberi M, Bart van der Worp H, van Dis I, Monique Verschuren WM. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. *Rev Esp Cardiol (Engl Ed)*. 2016 Oct; 69(10):939. IF: 0
50. Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, Invitti C, Litwin M, Mancina G, Pall D, Rascher W, **Redon J**, Schaefer F, Seeman T, Sinha M, Stabouli S, Webb NJ, Wühl E, Zanchetti A. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. *J Hypertens*. 2016 Oct; 34(10):1887-920. IF: 5,062



• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: HEALTH 2011.2.4.2-2

Title: Markers for Subclinical Cardiovascular Risk Assessment

Principal Investigator: Josep Redón i Mas

Funding body: European Commission

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2011-2016

Total budget: 370.000€

Reference: CB06/03/0039

Title: *CIBER de obesidad y trastornos de la nutrición*

Principal Investigator: Empar Lurbe i Ferrer (Josep Redón i Mas as collaborating research)

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital General Universitario de Valencia*

Duration: 2007-2016

Reference: PI15/00071

Title: *Metales y arteriosclerosis subclínica: papel de la variación genética y epigenética en genes candidatos*

Principal Investigator: María Téllez Plaza

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2018

Total budget: 195.415€

Reference: COST Action TD0905

Title: Epigenetics: Bench to Bedside

Principal Investigator: Arasu Ganesan (María Tellez as collaborating researcher)

Funding body: European Commission

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2010-2016

Reference: PT13/0010/0004

Title: Biobank Platform

Principal Investigator: Josep Redón i Mas

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2017

Total budget: 46.500€

Reference: PT13/0006/0023

Title: Innovation Platform

Principal Investigator: Josep Redón i Mas

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2017

Total budget: 38.985€

Reference: SIMBAD

Title: *Sistema basado en datos como ayuda a la decisión clínica*

Principal Investigator: Fernando Martínez García and María Téllez

Funding body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015 - 2016

Total budget: 4.000€

Reference: RTC-2016-4684-1 DeVaDip

Title: *Desarrollo de una nueva técnica de evaluación del tejido adiposo intramuscular mediante densitometría de doble energía.*

Principal Investigator: Josep Redon, Juan Sanchís

Funding Body: Ministerio de Economía y Competitividad

Beneficiary Institution: INCLIVA

Duration: 2016-2018

Total budget: 386.775€

Reference: PROMETEO/2016/084

Title: *Innovación tecnológica en la evaluación del sistema nervioso simpático en adolescentes y jóvenes obesos*

Principal Investigator: Josep Redón

Funding Body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2019

Total budget: 246.190€

Reference: APE/2016/03

Title: *Ayudas para la captación de proyectos europeos u otros programas de ámbito internacional*



Principal Investigator: Josep Redón

Funding Body: *Conselleria de Educación, Investigación, Cultura y Deporte*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

• THESIS

Thesis title: *Disfunción endotelial en territorio arterial en pacientes jóvenes con enfermedad tromboembólica venosa.*

Doctoral candidate: Elena Furió Rodríguez

Director(s): Laura Piqueras Ruiz, M^a José García Fuster, Fernando Martínez

Date of the defense: 09/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Automedicación en pacientes en urgencias de un centro de atención primaria.*

Doctoral candidate: Marwan Muhana Al nono

Director(s): M^a José Forner Giner

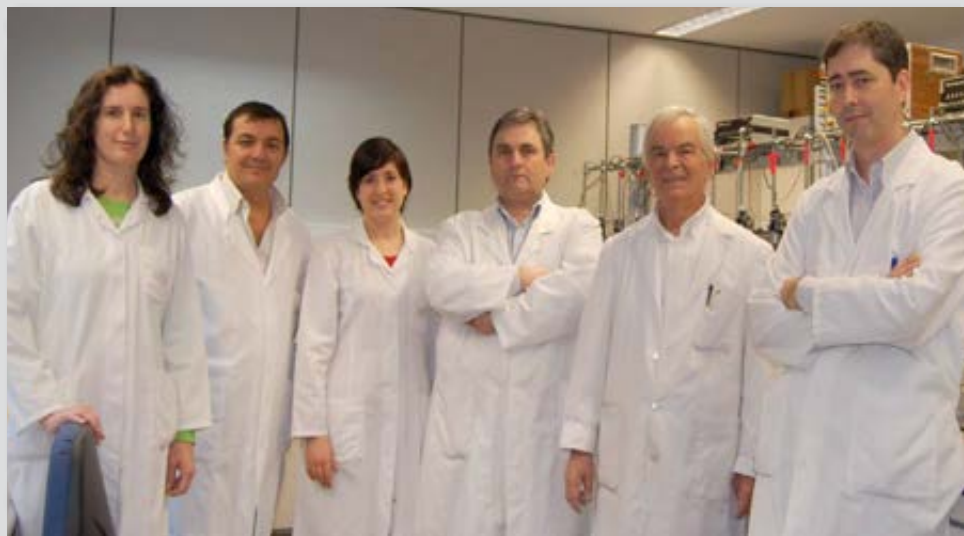
Date of the defense: 13/01/2016

Grade: *Sobresaliente "cum laude"*



Research Group on Vascular Function

Consolidated group



Group members

Principal investigator

José M^a Vila Salinas
University
H Index: 18

Collaborating researchers

Salvador Lluch López. University
Martín Aldasoro Celaya. University
Pascual Medina Besso. University
Gloria Segarra Irles. University
M^a Dolores Mauricio Aviñó. University





Strategic aims

- Vascular changes associated with experimental cirrhosis and portal hypertension.
- The involvement of VEGF in tumor growth.

Main lines of research

- Characterization of alterations in the control of vascular tone and endothelial function induced by aging.
- Alterations of ADMA-NO and EDHF system in obese patients with steatosis and steatohepatitis.
- The effects of exercise training on the vascular response.
- Vascular effects of ranolazine.
- Effects of ranolazine extravascular.

• PUBLICATIONS

Number of articles	IF	Average IF
6	22,98	3,83
National collaborations	International collaborations	Corresponding author
5	-	5

Original articles

1. Vidal-Gómez X, Novella S, Pérez-Monzó I, Garabito M, Dantas AP, Segarra G, Hermenegildo C, **Medina P**. Decreased bioavailability of nitric oxide in aorta from ovariectomized senescent mice. Role of cyclooxygenase. *Exp Gerontol*. 2016 Apr; 76:1-8. IF: 3,485
2. **Aldasoro M**, Guerra-Ojeda S, Aguirre-Rueda D, Mauricio MD, **Vila JM**, Marchio P, Iradi A, Aldasoro C, Jorda A, Obrador E, Valles SL. Effects of Ranolazine on Astrocytes and Neurons in Primary Culture. *PLoS One*. 2016; 11(3):e0150619. IF: 3,234
3. Hervas A, Ruiz-Sauri A, Gavara J, Monmeneu JV, de Dios E, Rios-Navarro C, Perez-Sole N, Perez I, Monleon D, Morales JM, Minana G, Nunez J, Bonanad C, Diaz A, **Vila JM**, Chorro FJ, Bodi V. A Multidisciplinary Assessment of Remote Myocardial Fibrosis After Reperfused Myocardial Infarction in Swine and Patients. *J Cardiovasc Transl Res*. 2016 Aug; 9(4):321-33. IF: 3,017
4. Novella S, Vidal-Gómez X, Mompeón A, Pérez-Cremades D, **Segarra G**, **Medina P**, Hermenegildo C. [OP.3B.02] Ageing and lack of estrogens activates cyclooxygenases pathway increasing superoxide anion production in response to thromboxane A2. *J Hypertens*. 2016 Sep; 34 Suppl 2:e29. IF: 5,062
5. Novella S, Vidal-Gómez X, Pérez-Monzó I, Mompeón A, Pérez-Cremades D, Dantás AP, **Segarra G**, Hermenegildo C, **Medina P**. [OP.8C.02] Senescence increases vascular smooth muscle contractions through increased rho kinase activity in female mouse aorta. *J Hypertens*. 2016 Sep; 34 Suppl 2:e102. IF: 5,062
6. **Segarra G**, Cortina B, **Mauricio MD**, Novella S, Lluch P, Navarrete-Navarro J, Noguera I, **Medina P**. Effects of asymmetric dimethylarginine on renal arteries in portal hypertension and cirrhosis. *World J Gastroenterol*. 2016 Dec 28; 22(48):10545-10556. IF: 3,127

• THESIS

Thesis title: *Efecto de la terapia fotodinámica como coadyuvante al raspado y alisado radicular en el tratamiento de la periodontitis crónica. Estudio clínico, microbiológico (real time-pcr) y bioquímico (il-1β, il-6, TNF-α, RANK-L/OPG).*

Doctoral candidate: Marta Segarra Vidal

Director(s): José M^a Vila Salinas, Francisco Alpiste Illueca, Francisco José Gil Loscos

Date of the defense: 22/04/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Efecto del entrenamiento físico sobre los factores endoteliales en el sistema arterial de conejo.*

Doctoral candidate: Patricia Marchio

Director(s): José M^a Vila Salinas, M^a Dolores Mauricio Aviñó

Date of the defense: 19/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Conciliación y formación farmacoterapéutica al paciente trasplantado renal en el ámbito hospitalario.*

Doctoral candidate: Mónica Montero Hernández

Director(s): Gloria Segarra Irlles, Isabel Font Noguera, José Luis Poveda Andrés

Date of the defense: 19/02/2016

Grade: *Sobresaliente "cum laude"*



Research Group on Pediatric Nutrition Consolidated group



Group members

Principal investigator

Cecilia Martínez Costa
Hospital. University
H Index: 13



Collaborating researchers

Francisco Núñez Gómez. Hospital. University
Javier Buesa Gómez. Hospital. University
Carmen Collado Amores. IATA-CSIC Valencia
M^a Ángeles Montal Navarro. Hospital. University
Pablo García Molina. Hospital. University
Evelin Balaguer López. Hospital. University
Elena Crehuá Gaudiza. Hospital
Bibiana Bertua Ríos. INCLIVA
Ana Paula Grattarola. OMS
Izaskun García-Mantrana. IATA-CSIC Valencia
Julia Sánchez Zahonero. Hospital
Inmaculada Tarazona Casany. Hospital
Javier Estañ Capell. Hospital. University
Laura Martínez Rodríguez. Hospital
Beatriz Padilla López. INCLIVA



Main lines of research

Cardiovascular area:

- Study of early markers of vascular damage in dyslipidemic obese children by Doppler ultrasonography to establish a correlation with insulin resistance and other metabolic markers.
- Monitoring exercise and energy consumption in obese schoolchildren and teenagers to adjust nutritional intervention.

Area of human milk:

- Analysis of defensive factors against norovirus infections and its relationship with histo-blood group antigens and FUT genotype.
- Analysis of mother-fetal microbiome and cold preservation methods.

Area of hospital malnutrition and artificial nutrition:

- Screening procedures for detecting the risk of malnutrition linked to chronic disease and pediatric hospitalization.
- Multicenter study of acceptance and quality of life in children treated with home enteral nutrition.

• PUBLICATIONS

Number of articles	IF	Average IF
15	48,19	3,21

National collaborations	International collaborations	Corresponding author
7	6	7

Original articles

1. de Onis M, Zeitlhuber J, **Martínez-Costa C**. Nutritional disorders in the proposed 11th revision of the International Classification of Diseases: feedback from a survey of stakeholders. *Public Health Nutr.* 2016 Dec; 19(17):3135-3141. IF: 2,433
2. Kunz C, Meyer C, **Collado MC**, Geiger L, **García-Mantrana I**, **Bertua-Ríos B**, **Martínez-Costa C**, Borsch C, Rudloff S. Influence of Gestational Age, Secretor and Lewis Blood Group Status on the Oligosaccharide Content of Human Milk. *J Pediatr Gastroenterol Nutr.* 2016 Sep 6 ;. IF: 2,4
3. Martínez-Rodríguez L, Estañ J, Bermudez JD, Molina A, Hortelano V, **Martínez-Costa C**. Influence of nutritional variables on the onset of necrotizing enterocolitis in preterm infants: A case-control study. *Early Hum Dev.* 2016 Oct 7; 103:193-198. IF: 1,913
4. **García-Molina P**. [Mitigating procedural pain during venipuncture in a pediatric population: A randomized factorial study]. *Enferm Clin.* 2016 Nov - Dec; 26(6):396-398. IF: 0
5. **García-Mantrana I**, **Collado MC**. Obesity and overweight: Impact on maternal and milk microbiome and their role for infant health and nutrition. *Mol Nutr Food Res.* 2016 Aug; 60(8):1865-75. IF: 4,603
6. **García-Mantrana I**, Yebra MJ, Haros M, Monedero V. Expression of bifidobacterial phytases in *Lactobacillus casei* and their application in a food model of whole-grain sourdough bread. *Int J Food Microbiol.* 2016 Jan 4; 216:18-24. IF: 3,082
7. Chenoll E, Casinos B, Bataller E, **Buesa J**, Ramón D, Genovés S, Fábrega J, Rivero Urgell M, Moreno Muñoz JA. Identification of a Peptide Produced by *Bifidobacterium longum* CECT 7210 with Antitroviral Activity. *Front Microbiol.* 2016; 7:655. IF: 3,989
8. Carmona-Vicente N, Vila-Vicent S, Allen D, Gozalbo-Rovira R, Iturriza-Gómara M, **Buesa J**, Rodríguez-Díaz J.



- Characterization of a Novel Conformational GII.4 Norovirus Epitope: Implications for Norovirus-Host Interactions. *J Virol*. 2016 Sep 1; 90(17):7703-14. IF: 4,606
9. Cabrera-Rubio R, Mira-Pascual L, Mira A, **Collado MC**. Impact of mode of delivery on the milk microbiota composition of healthy women. *J Dev Orig Health Dis*. 2016 Feb; 7(1):54-60. IF: 1,733
 10. **Collado MC**, Rautava S, Aakko J, Isolauri E, Salminen S. Human gut colonisation may be initiated in utero by distinct microbial communities in the placenta and amniotic fluid. *Sci Rep*. 2016 Mar 22; 6:23129. IF: 5,228
 11. Cernada M, Bäuerl C, Serna E, **Collado MC**, Martínez GP, Vento M. Sepsis in preterm infants causes alterations in mucosal gene expression and microbiota profiles compared to non-septic twins. *Sci Rep*. 2016 May 16; 6:25497. IF: 5,578
 12. Boix-Amorós A, **Collado MC**, Mira A. Relationship between Milk Microbiota, Bacterial Load, Macronutrients, and Human Cells during Lactation. *Front Microbiol*. 2016 Apr 20; 7:492. IF: 4,165
 13. Gomez-Gallego C, **García-Mantrana I**, Salminen S, **Collado MC**. The human milk microbiome and factors influencing its composition and activity. *Semin Fetal Neonatal Med*. 2016 Dec; 21(6):400-405. IF: 2,8
 14. Kumar H, du Toit E, Kulkarni A, Aakko J, Linderborg KM, Zhang Y, Nicol MP, Isolauri E, Yang B, **Collado MC**, Salminen S. Distinct Patterns in Human Milk Microbiota and Fatty Acid Profiles Across Specific Geographic Locations. *Front Microbiol*. 2016 Oct 13; 7:1619. IF: 4,165
 15. Wanden-Berghe Lozano C, Campos Martín C, Cuerda Compes C, Gómez Candela C, Burgos Peláez R, Moreno Villares JM, Pereira Cunill JL, Pérez de la Cruz A, Virgili Casas N, Martínez Faedo C, Álvarez Hernández J, Garde Orbaiz C, Penacho Lázaro MÁ, Sánchez Martos EÁ, Sanz Paris A, Gonzalo Marín M, Zugasti Murillo A, Matía Martín P, Martín Folgueras T, Carabaña Pérez F, Díaz Guardiola P, Tejera Pérez C, De Luis Román D, Luengo Pérez LM, Santacruz Carmona N, Apezetxea Celaya A, Ponce González MÁ, Urgeles Planella JR, Laborda González L, Martínez Olmos MÁ, Sánchez-Vilar Burdiel O, Joaquín Ortiz C, **Martínez Costa C**, Suárez Llanos JP, Calleja Fernández A, Leyes García P, Gil Martínez MC, Mauri Roca S, García Zafra MV, Carrera Santaliestra MJ, Nadya-Senpe G. Nutrición Parenteral Domiciliaria en España

durante 2015; informe del Grupo de Nutrición Artificial Domiciliaria y Ambulatoria NADYA. *Nutr Hosp*. 2016 Nov 29; 33(6):1487-1490. IF: 1,497

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: MAMI

Title: MAMI - The Power of Maternal Microbes on Infant Health

Principal Investigator: María Carmen Collado

Funding body: European Commission

Beneficiary institution: *Consejo Superior de Investigaciones Científicas*

Duration: 2015-2017

Total budget: 1.499.978,43€

Reference: I-LINK0679

Title: Impact of diet, nutrition and geographical location on host-microbe interactions.

Principal Investigator: María Carmen Collado

Funding body: ILINK-2013 CSIC

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2015

Total budget: 30.000€

• THESIS

Thesis title: *Influencia de un programa de intervención comunitaria sobre el estado de salud de una población semi-rural dominicana*

Doctoral candidate: Beatriz Tomás Aguirre

Director(s): Cecilia Martínez Costa, Francisco Núñez Gómez

Date of the defense: 02/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Dolor abdominal crónico en la edad pediátrica: implicación de factores clínicos, ambientales y psicosociales. Desarrollo de un programa informático específico.*

Doctoral candidate: Tatiana Salvador Pinto

Director(s): Cecilia Martínez Costa, Caterina Calderón Garrido

Date of the defense: 15/01/2016

Grade: *Sobresaliente "cum laude"*



Group on Translational Research in Ischemic Heart Disease Consolidated group



Group members

Principal investigator

Vicente Bodí Peris
Hospital. University
H Index: 24



Collaborating researchers

Clara Bonanad Lozano. INCLIVA. Hospital
Amparo Ruiz Saurí. University
Jose Vicente Monmeneu Menadas. Eresa
David Moratal Pérez. UPV
Paolo Racugno. Hospital
Ana Díaz Cuevas. University

PhD researchers

César Ríos Navarro. INCLIVA
José Gavara Doñate. INCLIVA

Technicians

Elena de Dios Lluch. INCLIVA
Nerea Pérez Solé. INCLIVA



Strategic aims

- From our research experience in the last years in the clinical and experimental field related to ischemic cardiopathy, our current goal is to focus into a translational approach.
- In 2016 we continued elucidating the physiological role of the immune dysregulation as well as the macroscopic, microscopic and molecular changes in the fibrotic process after a myocardial infarction by using a swine model. Moreover, we have started clarifying the implication of angiogenesis and new angiogenic biomarkers in the recovery of the microvasculature after a myocardial infarction in animal models and in patients.
- We have also developed new tools to study patients with ST-segment elevation myocardial infarction using cardiac magnetic resonance imaging.

Main lines of research

- Prospective registry of patients with first ST-segment elevation myocardial infarction studied with cardiac MRI.
- Multicenter registry of patients with myocardial ischemia studied with cardiac magnetic resonance imaging.
- Porcine and mice model of experimental myocardial ischemia and myocardial infarction. To achieve a better understanding of the pathophysiology of ischemia, necrosis, fibrosis, angiogenesis, and reperfusion injury and test new therapeutic avenues.
- Involvement in several large international multicenter clinical trials in the field of acute coronary syndromes.

• PUBLICATIONS

Number of articles	IF	Average IF
18	48,78	2,76

National collaborations	International collaborations	Corresponding author
13	3	14

Original articles

1. Núñez J, Mascarell B, Stubbe H, Ventura S, **Bonanad C, Bodí V**, Núñez E, Miñana G, Fácila L, Bayés-Genis A, Chorro FJ, Sanchis J. Bioelectrical impedance vector analysis and clinical outcomes in patients with acute heart failure. *J Cardiovasc Med (Hagerstown)*. 2016 Apr; 17(4):283-90. IF: 1,51
2. Núñez-Gil IJ, Almendro-Delia M, Andrés M, Sionis A, Martín A, Bastante T, Córdoba-Soriano JG, Linares JA, González Sucarrats S, Sánchez-Grande-Flecha A, Fabregat-Andrés O, Pérez B, Escudier-Villa JM, Martín-Reyes R, Pérez-Castellanos A, Rueda Sobella F, Cambeiro C, Piqueras-Flores J, Vidal-Perez R, **Bodí V**, García de la Villa B, Corbí-Pascua M, Biagioni C, Mejía-Rentería HD, Feltes G, Barrabés J, RETAKO investigators. Secondary forms of Takotsubo cardiomyopathy: A whole different prognosis. *Eur Heart J Acute Cardiovasc Care*. 2016 Aug; 5(4):308-16. IF: 0
3. Hervas A, **Ruiz-Sauri A, de Dios E**, Forteza MJ, Minana G, Nunez J, Gomez C, **Bonanad C, Perez-Sole N, Gavara J**, Chorro FJ, **Bodí V**. Inhomogeneity of collagen organization within the fibrotic scar after myocardial infarction: results in a swine model and in human samples. *J Anat*. 2016 Jan; 228(1):47-58. IF: 2,097
4. **Bodí V, Monmeneu JV**, Ortiz-Perez JT, Lopez-Lereu MP, **Bonanad C**, Husser O, Minana G, Gomez C, Nunez J, Forteza MJ, Hervas A, **de Dios E**, Moratal D, Bosch X, Chorro FJ. Prediction of Reverse Remodeling at Cardiac MR Imaging Soon after First ST-Segment-Elevation Myocardial Infarction: Results of a Large Prospective Registry. *Radiology*. 2016 Jan; 278(1):54-63. IF: 6,867
5. Valero E, Martín J, **Monmeneu JV**. Aborted sudden death during a marathon race. *Med Intensiva*. 2016 Jun-Jul; 40(5):316-9. IF: 1,336
6. Núñez J, Núñez E, Bayés-Genís A, Fonarow GC, Miñana G, **Bodí V**, Pascual-Figal D, Santas E, García-Blas S, Chorro FJ, Rizopoulos D, Sanchis J. Long-term serial kinetics of N-terminal pro B-type natriuretic peptide and carbohydrate antigen 125 for mortality risk prediction following acute heart failure. *Eur Heart J Acute Cardiovasc Care*. 2016 May 19 ;. IF: 0
7. Núñez J, Comín-Colet J, Miñana G, Núñez E, Santas E, Mollar A, Valero E, García-Blas S, Cardells I, **Bodí V**, Chorro FJ, Sanchis J. Iron deficiency and risk of early readmission following a hospitalization for acute heart failure. *Eur J Heart Fail*. 2016 Jul; 18(7):798-802. IF: 6,526
8. **Bonanad C, Monmeneu JV**, Lopez-Lereu MP, Hervas A, **de Dios E, Gavara J**, Nunez J, Minana G, Husser O, Paya A, **Racugno P**, García-Blas S, Chorro FJ, **Bodí V**. Prediction of long-term major events soon after a first ST-segment elevation myocardial infarction by cardiovascular magnetic resonance. *Eur J Radiol*. 2016 Mar; 85(3):585-92. IF: 2,369



9. Miñana G, Rumiz E, Palau P, Valero E, **Bodí V**, Núñez E, Sanchis J, Núñez J. Plasma neutrophil gelatinase-associated lipocalin and long-term mortality in patients with acute heart failure and normal renal function. *Int J Cardiol.* 2016 Jul 1; 214:51-3. IF: 4,036
 10. Hervas A, **Ruiz-Sauri A**, **Gavara J**, **Monmeneu JV**, **de Dios E**, **Rios-Navarro C**, **Perez-Sole N**, Perez I, Monleon D, Morales JM, Minana G, Nunez J, **Bonanad C**, Diaz A, Vila JM, Chorro FJ, **Bodí V**. A Multidisciplinary Assessment of Remote Myocardial Fibrosis After Reperfused Myocardial Infarction in Swine and Patients. *J Cardiovasc Transl Res.* 2016 Aug; 9(4):321-33. IF: 3,017
 11. Palau P, Domínguez E, López L, Heredia R, González J, Ramón JM, Serra P, Santas E, **Bodí V**, Sanchis J, Chorro FJ, Núñez J. Inspiratory Muscle Training and Functional Electrical Stimulation for Treatment of Heart Failure With Preserved Ejection Fraction: Rationale and Study Design of a Prospective Randomized Controlled Trial. *Clin Cardiol.* 2016 Aug; 39(8):433-9. IF: 2,431
 12. Agra RM, Al-Daghri NM, Badimon L, **Bodí V**, Carbone F, Chen M, Cubedo J, Dullaart RP, Eiras S, García-Monzón C, Gary T, Gnoni A, González-Rodríguez Á, Gremmel T, Hafner F, Hakala T, Huang B, Ickmans K, Irace C, Kholová I, Kimer N, Kytö V, März W, Miazgowski T, Møller S, Montecucco F, Niccoli G, Nijs J, Ozben S, Ozben T, Papassotiriou I, Papastamataki M, Reina-Couto M, **Rios-Navarro C**, Ritsch A, Sabico S, Seetho IW, Severino A, Sipilä J, Sousa T, Taszarek A, Taurino F, Tietge UJ, Tripolino C, Verloop W, Voskuil M, Wilding JP. Research update for articles published in EJCI in 2014. *Eur J Clin Invest.* 2016 Oct; 46(10):880-94. IF: 2,687
 13. Husser O, Núñez J, Burgdorf C, Holzamer A, Templin C, Kessler T, **Bodí V**, Sanchis J, Pellegrini C, Luchner A, Maier LS, Schmid C, Lüscher TF, Schunkert H, Kastrati A, Hilker M, Hengstenberg C. Improvement in Risk Stratification in Transcatheter Aortic Valve Implantation Using a Combination of the Tumor Marker CA125 and the Logistic EuroSCORE. *Rev Esp Cardiol (Engl Ed).* 2016 Sep 9 ; IF: 4,485
 14. Núñez J, **Monmeneu JV**, Mollar A, Núñez E, **Bodí V**, Miñana G, García-Blas S, Santas E, Agüero J, Chorro FJ, Sanchis J, López-Lereu MP. Left ventricular ejection fraction recovery in patients with heart failure treated with intravenous iron: a pilot study. *ESC Heart Fail.* 2016 Dec; 3(4):293-298. IF: 0
 15. Núñez J, Ruiz V, **Bonanad C**, Miñana G, García-Blas S, Valero E, Núñez E, Sanchis J. Percutaneous coronary intervention and recurrent hospitalizations in elderly patients with non ST-segment acute coronary syndrome: The role of frailty. *Int J Cardiol.* 2016 Nov 10; 228:456-458. IF: 4,638
 16. González-Parra E, Daudén E, Carrascosa JM, Oliveira A, Botella R, **Bonanad C**, Rivera R, en representación del Grupo de Trabajo en Inflamación Sistémica en Psoriasis. Kidney Disease and Psoriasis. A New Comorbidity? *Actas Dermosifiliogr.* 2016 Dec; 107(10):823-829. IF: 0
 17. Cosa A, Moreno A, Pacheco-Torres J, Ciccocioppo R, Hyytiä P, Sommer WH, **Moratal D**, Canals S. Multi-modal MRI classifiers identify excessive alcohol consumption and treatment effects in the brain. *Addict Biol.* 2016 Jun 8 ; IF: 4,547
 18. Pérez-Ramírez Ú, Arana E, **Moratal D**. Brain metastases detection on MR by means of three-dimensional tumor-appearance template matching. *J Magn Reson Imaging.* 2016 Sep; 44(3):642-52. IF: 3,25
- **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**
- Reference:** PROMETEO/2013/007
Title: *Inmunidad y metabolismo: exploración de nuevas vías fisiopatológicas y oportunidades terapéuticas en el infarto agudo de miocardio.*
Principal Investigator: Vicente Bodí Peris
Funding Body: *Conselleria de Educació, Cultura y Deporte*
Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*
Duration: 2013-2016
Total budget: 60.100€
- Reference:** PI14/00271
Title: *Fibrosis miocárdica tras un infarto de miocardio. Estudio traslacional para la innovación diagnóstica con resonancia magnética y para el entendimiento de los mecanismos reguladores.*
Principal Investigator: Vicente Bodí Peris
Funding Body: *Instituto de Salud Carlos III*
Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*
Duration: 2015-2017
Total budget: 101.500€



Reference: PIE15/00013

Title: A multidisciplinary project to advance in basic mechanisms, diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction.

Principal Investigator: Vicente Bodí Peris

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016 - 2018

Total Budget: 589.050€

Reference: FPU12/01140

Title: Diagnóstico y pronóstico de enfermedades cardiovasculares mediante el análisis de la señal de espectroscopia por resonancia magnética nuclear de suero sanguíneo y su determinación metabólica.

Principal Investigator: Vicente Bodí Peris

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Universidad de Valencia

Duration: 2013-2016

Total Budget: 55.560€

• AWARDS

In 2016 Dr. Bodí was awarded with the prize to the best poster in angiogenesis area on the European Society Congress of Cardiology 2016 for the scientific communication "Serum-induced neoangiogenesis parallels the dynamics of MVO after reperfused MI in an in vivo model".

Furthermore he won the Award of the Section of Ischemic Cardiopathy and Cardiovascular Acute Care to the best article published in *Revista Española de Cardiología* for the scientific article "Pronóstico y manejo del síndrome coronario agudo en España en 2012: estudio DIOCLE".

Also the *Sociedad Valenciana de Cardiología* awarded two of his communications: award for the best communication about ischemic heart disease in 2016 for the work "La comparación de la FEVI calculada por ecocardiografía y por resonancia para estratificación de riesgo y valorar implante de DAI tras un IAMEST" and for the best communication about experimental cardiology and basic research in 2016 for "La neoangiogenesis inducida por suero es paralela a la dinámica de la obstrucción microvascular tras un infarto de miocardio reperfundido".

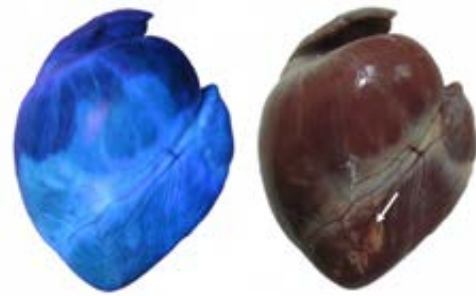


Fig 1: The group has developed a model of acute myocardial infarction in which a transient occlusion of the left anterior descending artery is induced. With these samples, you can simulate events that occur in the pathophysiology of myocardial regeneration after myocardial

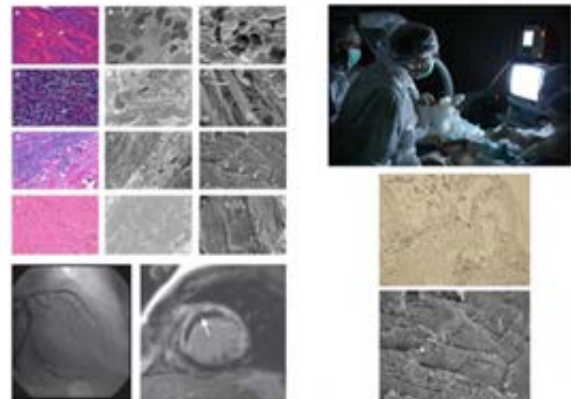
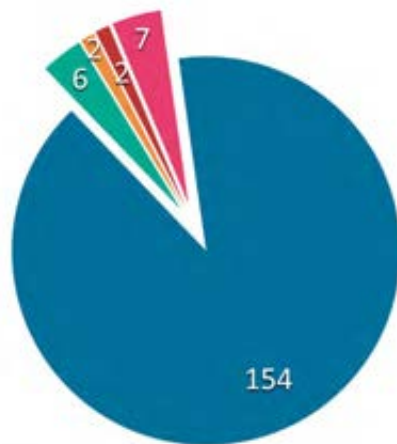
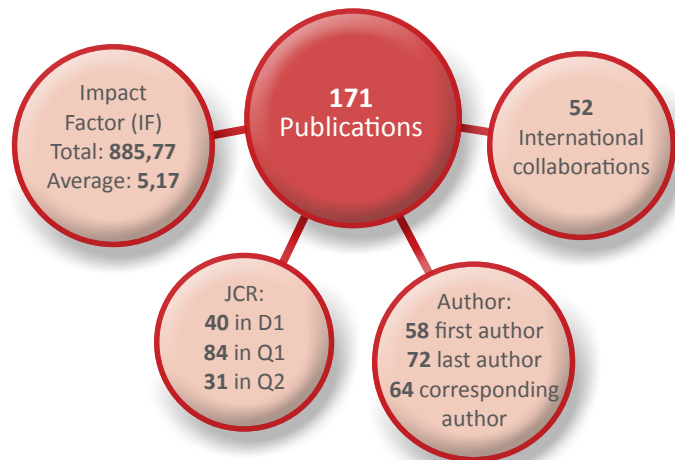


Fig.2: In samples obtained in patients with acute myocardial infarction and in an in vivo myocardial infarction model, can be studied the inflammatory process and the degree of fibrosis at different levels: macroscopic, microscopic, cell, gene expression and protein and through by magnetic resonance microimage



4.3.2 Oncology Area

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● Original articles ● Letters ● Editorial ● Clinical guidelines ● Review



Research Group on Histopathology and Tissue Engineering

Consolidated group



Group members

Principal investigator

Carmen Carda Batalla
University
H Index: 20



Collaborating researchers

Amando Peydró Olaya. Hospital. University
Amparo Ruiz Sauri. University

María Sancho-Tello Valls. University
José Javier Martín de Llano. University
Manuel Mata Roig. University
Lara Milian Medina. INCLIVA
Teresa Sagrado Vives. University
Miguel Armengot Carceller. University
Carlos Tejerina Botella. Hospital
Miguel Puche Torres. Hospital
Mari Fe Minguez Rey. Hospital
Genaro Galán Gil. Hospital
Antonio Silvestre Muñoz. Hospital
Francisco Forriol Brocal. University
Antonio Fons Font. University
Rosa María Cibrian Ortiz de Anda. University
Santiago Peydró Tomas. University
Javier Zurriaga Carda. Hospital
Ignacio Peregrín Nevado. Hospital
Giovanna Foschini Martínez. Hospital

PhD students

Esperanza Núñez Benito. University
María Oliver Ferrándiz. University
Javier Alcácer Fernández-Coronado. University
Rubén Salvador Clavell. University



Strategic aims

- Contributing in terms of publications, thesis and attendance to congresses.
- In specific relation with the line of Tissue Engineering we have obtained funding to continue working on the regeneration techniques of cartilage and bone (*Proyecto Ministerio*) as well as in the application to tracheal pathology.

Main lines of research

Regenerative medicine:

- Study of cartilage regeneration
- Study of bone regeneration
- Study and use of pulpal precursors in regenerative therapies
- Study of regeneration of dental and periodontal tissues
- Study of corneal induction and regeneration
- Study of tracheal regeneration

Histopathology:

- Study of recurrent myocardial infarction and its determinants
- Study of vascularization in renal tumors
- Study of ciliary pathology

• PUBLICATIONS

Number of articles	IF	Average IF
22	59,94	2,72

National collaborations	International collaborations	Corresponding author
15	2	9

Original articles

- Jovani-Sancho MD, Sheth CC, Marqués-Mateo M, **Puche-Torres M**. Platelet-Rich Plasma: A Study of the Variables that May Influence Its Effect on Bone Regeneration. *Clin Implant Dent Relat Res*. 2016 Oct; 18(5):1051-1064. IF: 3,589
- Hervas A, **Ruiz-Sauri A**, de Dios E, Forteza MJ, Minana G, Nunez J, Gomez C, Bonanad C, Perez-Sole N, Gavara J, Chorro FJ, Bodi V. Inhomogeneity of collagen organization within the fibrotic scar after myocardial infarction: results in a swine model and in human samples. *J Anat*. 2016 Jan; 228(1):47-58. IF: 2,097
- Franco J, Llopis E, **Galán G**. Hemothorax After Endobronchial Ultrasound-guided Transbronchial Needle Aspiration. *J Bronchology Interv Pulmonol*. 2016 Oct; 23(4):328-330. IF: 0
- García-de-la-Asunción J, García-Del-Olmo E, **Galan G**, Guijarro R, Martí F, Badenes R, Perez-Griera J, Duca A, Delgado C, Carbonell J, Belda J. Glutathione oxidation correlates with one-lung ventilation time and PO2/FiO2 ratio during pulmonary lobectomy. *Redox Rep*. 2016 Sep; 21(5):219-26. IF: 1,522
- Assaf AT, Hillerup S, Rostgaard J, **Puche M**, Blessmann M, Kohlmeier C, Pohlenz P, Klatt JC, Heiland M, Caparso A, Papay F. Technical and surgical aspects of the sphenopalatine ganglion (SPG) microstimulator insertion procedure. *Int J Oral Maxillofac Surg*. 2016 Feb; 45(2):245-54. IF: 1,565
- Ruiz-Saurí A**, Valencia-Villa G, Romanenko A, Pérez J, García R, García H, Benavent J, **Sancho-Tello M**, **Carda C**, Llombart-Bosch A. Influence of Exposure to Chronic Persistent Low-Dose Ionizing Radiation on the Tumor Biology of Clear-Cell Renal-Cell Carcinoma. An Immunohistochemical and Morphometric Study of Angiogenesis and Vascular Related Factors. *Pathol Oncol Res*. 2016 Oct; 22(4):807-15. IF: 1,855
- Vikingsson L, Sancho-Tello M, **Ruiz-Saurí A**, Martínez Díaz S, Gómez-Tejedor JA, Gallego Ferrer G, **Carda C**, Monllau JC, Gómez Ribelles JL. Implantation of a polycaprolactone scaffold with subchondral bone anchoring ameliorates nodules formation and other tissue alterations. *Int J Artif Organs*. 2016 Feb 8; 38(12):659-66. IF: 0,962
- Martin JM, **Ruiz-Saurí A**, San-Miguel T, Jorda E, Monteagudo C. Telomeric length heterogeneity influences spontaneous regression of malignant melanoma. *J Eur Acad Dermatol Venereol*. 2016 Dec; 30(12):e223-e224. IF: 2,826
- Bagan J, **Peydró A**, Calvo J, Leopoldo M, Jiménez Y, Bagan L. Medication-related osteonecrosis of the jaw associated with bisphosphonates and denosumab in osteoporosis. *Oral Dis*. 2016 May; 22(4):324-9. IF: 2,427
- Hervas A, **Ruiz-Sauri A**, Gavara J, Monmeneu JV, de Dios E, Rios-Navarro C, Perez-Sole N, Perez I, Monleon D, Morales JM, Minana G, Nunez J, Bonanad C, Diaz A, Vila JM, Chorro FJ, Bodi V. A Multidisciplinary Assessment of Remote Myocardial Fibrosis After Reperfused Myocardial Infarction in Swine and Patients. *J Cardiovasc Transl Res*. 2016 Aug; 9(4):321-33. IF: 3,017



11. Clavell RS, **de Llano JJ**, **Carda C**, Ribelles JL, Vallés-Lluch A. In vitro assessment of the biological response of Ti6Al4V implants coated with hydroxyapatite microdomains. *J Biomed Mater Res A*. 2016 Nov; 104(11):2723-9. IF: 3,263
12. Fabregat G, García-de-la-Asunción J, Sarriá B, **Mata M**, Cortijo J, de Andrés J, Gallego L, Belda FJ. Expression of aquaporins 1 and 5 in a model of ventilator-induced lung injury and its relation to tidal volume. *Exp Physiol*. 2016 Nov 1; 101(11):1418-1431. IF: 2,818
13. Milara J, Morell A, Ballester B, **Armengot M**, Morcillo EJ, Cortijo J. MUC4 impairs the anti-inflammatory effects of corticosteroids in chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol*. 2016 Sep 14 ;. IF: 12,485
14. Ortiz JL, Ortiz A, Milara J, **Armengot M**, Sanz C, Compañ D, Morcillo E, Cortijo J. Evaluation of Mucociliary Clearance by Three Dimension Micro-CT-SPECT in Guinea Pig: Role of Bitter Taste Agonists. *PLoS One*. 2016 Oct 10; 11(10):e0164399. IF: 3,057
15. Almenar-Medina S, Palomar-De Lucas B, Guerrero-Albors E, **Ruiz-Sauri A**. Morphometric characterization of the human portal and hepatic venous trees: A quantitative support to the liver micro-anatomic models free of subunits. *Histol Histopathol*. 2016 Sep 23 ;:11823. IF: 1,875
16. Marqués-Mateo M, **Puche-Torres M**, Iglesias-Gimilio ME. Temporomandibular chronic dislocation: The long-standing condition. *Med Oral Patol Oral Cir Bucal*. 2016 Nov 1; 21(6):e776-e783. IF: 0
17. Pino-Almero L, **Mínguez-Rey MF**, Sentamans-Segarra S, Salvador-Palmer MR, Anda RM, La O JL. Quantification of topographic changes in the surface of back of young patients monitored for idiopathic scoliosis: correlation with radiographic variables. *J Biomed Opt*. 2016 Nov 1; 21(11):116001. IF: 2,556
18. Priego Quesada JI, Pérez-Soriano P, Lucas-Cuevas AG, Salvador Palmer R, **Cibrián Ortiz de Anda RM**. Effect of bike-fit in the perception of comfort, fatigue and pain. *J Sports Sci*. 2016 Aug 4 ;:1-7. IF: 2,142
19. Priego Quesada JI, Carpes FP, Salvador Palmer R, Pérez-Soriano P, **Cibrián Ortiz de Anda RM**. Effect of saddle height on skin temperature measured in different days of cycling. *Springerplus*. 2016 Feb 27; 5:205. IF: 0,982
20. González-Sanz R, **Mata M**, Bermejo-Martín J, Álvarez A, Cortijo J, Melero JA, Martínez I. ISG15 Is Upregulated in Respiratory Syncytial Virus Infection and Reduces Virus Growth through Protein ISGylation. *J Virol*. 2016 Jan 13; 90(7):3428-38. IF: 4,606
21. Martínez N, Psikuta A, Kuklane K, Quesada JI, **de Anda RM**, Soriano PP, Palmer RS, Corberán JM, Rossi RM, Annaheim S. Validation of the thermophysiological model by Fiala for prediction of local skin temperatures. *Int J Biometeorol*. 2016 Dec; 60(12):1969-1982. IF: 2,309
22. Mir-Palomo S, Náchér A, Díez-Sales O, Ofelia Vila Busó MA, Caddeo C, Manca ML, Manconi M, Fadda AM, **Saurí AR**. Inhibition of skin inflammation by baicalin ultradeformable vesicles. *Int J Pharm*. 2016 Sep 10; 511(1):23-9. IF: 3,994

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: MAT2013-46467-C4-4-R.

Title: *Estimulación mecánica local de células mesenquimales de cara a su diferenciación osteogénica y condrogénica en medicina regenerativa*

Principal Investigator: Carmen Carda Batalla and María Sancho-Tello Valls

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2014-2016

Total Budget: 73.469€

Reference: Programa VLC-BIOCLINIC Subprograma A

Title: *Soportes tridimensionales biodegradables basados en microparticulas para la regeneración del cartílago articular.*

Principal Investigator: Carmen Carda Batalla

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015 – 2016

Total Budget: 4.000€

Reference: TEHACOS

Title: *Sustitutos electrohilados celularizados para el tratamiento de la osteonecrosis por bisfosfonatos.*

Principal Investigator: José Javier Martín de Llano

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary institution: *Fundación Investigación Hospital*



Clínico Universitario de Valencia

Duration: 2016

Total budget: 3.000€

Reference: IMPORTOX

Title: *Investigación sobre la toxicidad de implantes porosos fabricados en Ti6Al4V por la tecnología EBM y varios métodos de limpieza.*

Principal Investigator: Miguel Puche Torres

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total budget: 2.000€

Reference: MAT2014-52905-REDIT

Title: *Red de investigación para el desarrollo de implantes de titanio funcionalizados.*

Principal Investigator: José Luis Gómez Ribelles (Carmen Carda as collaborating researcher)

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *University of Valencia*

Duration: 2015-2016

Total budget: 10.000€

Reference: FIPSE Fase I. Expediente 06-00001182-15

Title: *Innovación en Prótesis Personalizadas para Reconstrucción Maxilofacial.*

Principal Investigator: Miguel Puche Torres

Funding Body: FIPSE

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total budget: 35.000€

Reference: Thermobike_COST TU 1101

Title: *Evaluar la exactitud de la proyección de imagen de infrarrojos para detectar el calentamiento en la carga de ejercicio.*

Principal Investigator: Rosa Maria Cibrián Ortiz De Anda

Funding Body: *EMPA Swiss Federal Laboratories for Materials Science and Technology*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2013 - 2016

Reference: 10-TERMOPIE-CIBRIAN-BLASCO-2016-A

Title: *TERMOPIE. Diagnóstico y seguimiento del pie diabético mediante termografía infrarroja.*

Principal Investigator: Carmen Blasco Molla (Rosa Cibrián as collaborating researcher)

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2016 - 2017

Total Budget: 4.000€

• THESIS

Thesis title: *Estudio "in vitro" de la resistencia a la fractura tras la fatiga de coronas cementadas sobre pilares de circona.*

Doctoral candidate: Ana Roig Vanaclocha

Director(s): Antonio Fons Font, M^a Fernanda Solá Ruiz, Rubén Agustín Panadero

Date of the defense: 04/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Eficacia y cambios anatómicos inducidos por los dispositivos de avance mandibular en pacientes con síndrome de apnea-hipopnea del sueño (SAHS).*

Doctoral candidate: Rocío Marco Pitarch

Director(s): Antonio Fons Font, Enrique Fernández Julián, Francisco Javier Puertas Cuesta

Date of the defense: 15/04/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio 'in vitro' del láser de Nd:YAG sobre la superficie del esmalte: Efectos estructurales, cambios morfológicos y térmicos.*

Doctoral candidate: Vicente Manuel Torres Celda

Director(s): José Gandía Franco, Rosa Cibrián Ortiz de Anda, Vicente Torres Zaragoza

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Patrón de las alteraciones dentales asociadas a la impactación del canino maxilar por palatino.*

Doctoral candidate: Esther Olivera Aguilar

Director(s): José Gandía Franco, Rosa Cibrián Ortiz de Anda, Vanessa Paredes Gallardo

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*



Thesis title: *La acústica virtual como herramienta arqueológica. Historia y sonido en el Teatro Principal de Valencia.*

Doctoral candidate: Arturo Barba Sevillano

Director(s): Rosa Cibrián Ortiz de Anda, Francesc de Paula Daumal Domènech, Alicia Giménez Pérez

Date of the defense: 01/02/2016

Grade: *Sobresaliente "cum laude"*

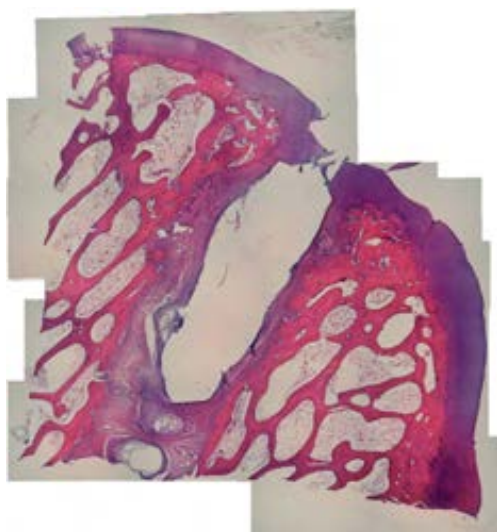
Thesis title: *Predicción de la inclusión de caninos superiores en una población infantil.*

Doctoral candidate: Jordi Gascón Pellicer

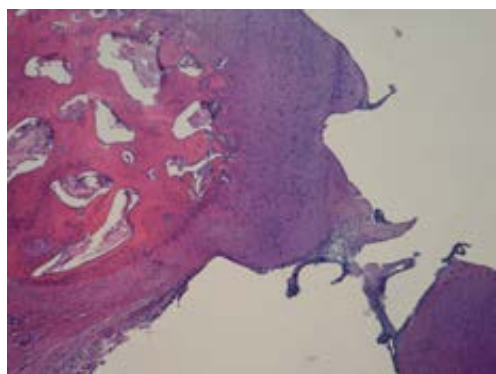
Director(s): José Gandía Franco, Rosa Cibrián Ortiz de Anda, Vanessa Paredes Gallardo

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*



(A) Panoramic view of a sample, 4.5 months after implantation in the articular cartilage of a polycaprolactone disc attached to an anchoring nail to the subchondral bone.



(B) Detail of the new-tissue that has grown in the articular surface, which presents characteristics of hyaline cartilage. Samples stained with hematoxylin-eosin.



Research Group on Central Nervous System Tumours Consolidated group



Group members

Principal investigator

Miguel Cerdá Nicolás
Hospital. University
H Index: 24



Collaborating researchers

Rosario Gil Benso. University
Concepción López Ginés. University
Teresa San Miguel Díez. University
José Manuel Almerich Silla. University
Robert Callaghan Pitlik. University
M. Aurelia Gregori Romero. University
Pablo Cerdá Durán. University
Pedro Roldán Badía. Hospital. University
Javier Megías Vericat. University

PhD students

Lisandra Muñoz Hidalgo. INCLIVA

Technicians

Ana María Clari Pérez. University
Lara Navarro Cerveró. University



Strategic aims

- Clinical-pathological study of 40 patients affected by primary glioblastoma according to established protocol. Sample collection (formaldehyde, freezing, collection in culture medium) was performed, tissue matrices of the 40 tumors and neuropathological, immunohistochemical and FISH analysis of the matrices were performed according to established methodology.
 - Short-cell cultures and their viability analysis have been performed. Analysis by FISH of EGFR status and freezing of the different passes according to established methodology.
 - The study of the proteomic analysis of the 40 tumors (frozen samples) by Western Blott according to established methodology has been completed.
 - A cell line has been established from a primary culture of glioblastoma. Morphological, genetic and behavioral analysis in vitro (generation of neurospheres, functional migration profiles) have been completed.
- Experimental study.
 - Spheres (neurospheres) have been elaborated from different cell lines and cell cultures of glioblastoma, characterizing and analyzing their behavior.
 - Analysis of cultures subjected to silencing and overexpression by transfection of miRNAs by the lipofection method.
 - Analysis of cell cultures in hypoxia situation, analyzing their characteristics and behavior before silencing and overexpression by transfection of selected miRNAs in hypoxia situation and in the different amplification status of the EGFR.
 - The pilot study of viability and effectiveness of xenotransplantation in nude mice has been completed with the achievement of neoplasias under study.

Main lines of research

- Primary GBM. Amplification status of EGFR and angiogenic/infiltrative phenotype. Molecular networks responsible for tumor modulation and reprogramming processes.
- Role of microRNA in the regulation of EGFR-dependent signalling pathways in high-grade astrocytic gliomas.
- Development of a model for analyzing the modulation of microRNA gene activity in cell cultures of primary GBM and GBM cell lines.

- Development of a model of population analysis and spatial distribution of these neoplasias.
- Metabolomics and microvascular environment characterization of aggressive human glioma by DCE-MRI and genetic study of biopsies.

• PUBLICATIONS

Number of articles	IF	Average IF
17	28,56	1,68
National collaborations	International collaborations	Corresponding author
13	2	8

Original articles

1. Serra-Torres S, Bellot-Arcís C, Montiel-Company JM, Marco-Algarra J, **Almerich-Silla JM**. Effectiveness of mandibular advancement appliances in treating obstructive sleep apnea syndrome: A systematic review. *Laryngoscope*. 2016 Feb; 126(2):507-14. IF: 2,144
2. Giner E, Recio MC, Ríos JL, **Cerdá-Nicolás JM**, Giner RM. Chemopreventive effect of oleuropein in colitis-associated colorectal cancer in c57bl/6 mice. *Mol Nutr Food Res*. 2016 Feb; 60(2):242-55. IF: 4,603
3. Bermell-Baviera A, Bellot-Arcís C, Montiel-Company JM, **Almerich-Silla JM**. Effects of mandibular advancement surgery on the temporomandibular joint and muscular and articular adaptive changes-a systematic review. *Int J Oral Maxillofac Surg*. 2016 May; 45(5):545-52. IF: 1,565
4. Real-Peña L, Talamantes Escribá F, Quilis-Quesada V, **González-Darder JM**. [Prognostic variability in atypical meningioma with complete resection. Proposed treatment algorithm]. *Neurocirugía (Astur)*. 2016 Jan-Feb; 27(1):15-23. IF: 0,293
5. Boronat-Catalá M, Bellot-Arcís C, Montiel-Company JM, Catalá-Pizarro M, **Almerich-Silla JM**. Orthodontic treatment need of 9, 12 and 15 year-old children according to the Index of Orthodontic Treatment Need and the Dental Aesthetic Index. *J Orthod*. 2016 Jun; 43(2):130-6. IF: 0
6. Machado I, **Navarro L**, Pellin A, Navarro S, Agaimy A, Tardío JC, Karseladze A, Petrov S, Scotlandi K, Picci P, Llombart-Bosch A. Defining Ewing and Ewing-like small round cell tumors (SRCT): The need for molecular techniques in their



- categorization and differential diagnosis. A study of 200 cases. *Ann Diagn Pathol*. 2016 Jun; 22:25-32. IF: 1,117
7. Llorca-Cardesa MJ, Fleitas T, Ibarrola-Villava M, Peña-Chilet M, Mongort C, Martínez-Ciarpaglini C, **Navarro L**, Gambardella V, Castillo J, Roselló S, Navarro S, Ribas G, Cervantes A. Epigenetic changes in localized gastric cancer: the role of RUNX3 in tumor progression and the immune microenvironment. *Oncotarget*. 2016 Sep 27; 7(39):63424-63436. IF: 5,008
 8. Ivorra-Carbonell L, Montiel-Company JM, **Almerich-Silla JM**, Paredes-Gallardo V, Bellot-Arcís C. Impact of functional mandibular advancement appliances on the temporomandibular joint - a systematic review. *Med Oral Patol Oral Cir Bucal*. 2016 Sep 1; 21(5):e565-72. IF: 0
 9. Negre-Barber A, Montiel-Company JM, Boronat-Catalá M, Catalá-Pizarro M, **Almerich-Silla JM**. Hypomineralized Second Primary Molars as Predictor of Molar Incisor Hypomineralization. *Sci Rep*. 2016 Aug 25; 6:31929. IF: 5,228
 10. Puig-Silla M, Montiel-Company JM, Dasí-Fernández F, **Almerich-Silla JM**. Prevalence of periodontal pathogens as predictor of the evolution of periodontal status. *Odontology*. 2016 Nov 25 ;. IF: 1,538
 11. Almerich-Torres T, Montiel-Company JM, Bellot-Arcís C, **Almerich-Silla JM**. Relationship between caries, body mass index and social class in Spanish children. *Gac Sanit*. 2016 Nov 22 ;. IF: 1,509
 12. Montiel-Company JM, Subirats-Roig C, Flores-Martí P, Bellot-Arcís C, **Almerich-Silla JM**. Validation of the Maslach Burnout Inventory-Human Services Survey for Estimating Burnout in Dental Students. *J Dent Educ*. 2016 Nov; 80(11):1368-1375. IF: 0,83
 13. Fernández-Ferrer L, Montiel-Company JM, Candel-Martí E, **Almerich-Silla JM**, Peñarrocha-Diogo M, Bellot-Arcís C. Corticotomies as a surgical procedure to accelerate tooth movement during orthodontic treatment: A systematic review. *Med Oral Patol Oral Cir Bucal*. 2016 Nov 1; 21(6):e703-e712. IF: 0
 14. **Megías J**, Martínez A, Yáñez A, Goodridge HS, Gozalbo D, Gil ML. TLR2, TLR4 and Dectin-1 signalling in hematopoietic stem and progenitor cells determines the antifungal phenotype of the macrophages they produce. *Microbes Infect*. 2016 May; 18(5):354-63. IF: 2,291
 15. Narváez-Martínez Y, García S, **Roldán P**, Torales J, Rumià J. [Stereoencephalography by using O-Arm® and Vertek® passive articulated arm: Technical note and experience of an epilepsy referral centre]. *Neurocirugia (Astur)*. 2016 Nov - Dec; 27(6):277-284. IF: 0,41
 16. **Roldán P**, García S, González J, Reyes LA, Torales J, Valero R, Oleaga L, Enseñat J. [Low field intra-operative magnetic resonance imaging for brain tumour surgery: preliminary experience]. *Neurocirugia (Astur)*. 2016 Oct 14 ;. IF: 0,41
 17. Jiménez P, Brell M, Sarriá-Echegaray P, **Roldán P**, Tomás-Barberán M, Ibáñez J. "Intrasellar Balloon Technique" in intraoperative MRI guided transsphenoidal endoscopic surgery for sellar region tumors. Usefulness on image interpretation and extent of resection evaluation. Technical note. *Acta Neurochir (Wien)*. 2016 Mar; 158(3):445-9. IF: 1,617
- **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**
- Reference:** PI14/01669
- Title:** *Interacción de miRNA-200 y miRNA-138 en la infiltración y perfiles de MGMT del Glioblastoma Multiforme primario. Utilidad como biomarcadores en el diagnóstico, pronóstico y terapéutico.*
- Principal Investigator:** Miguel Cerdá Nicolás
- Funding Body:** *Instituto de Salud Carlos III*
- Beneficiary Institution:** *Fundación Investigación Hospital Clínico Universitario de Valencia*
- Duration:** 2015-2017
- Total Budget:** 50.000€
- Reference:** PROMETEO II/2015/007
- Title:** *Papel de los microRNA en la regulación de las vías de señalización dependientes de EGFR en "gliomas astrocitarios de alto grado". Desarrollo de un modelo poblacional de análisis poblacional y de distribución espacial de estas neoplasias.*
- Principal Investigator:** Miguel Cerdá Nicolás
- Funding Body:** *Conselleria de Educación, Cultura y Deporte*
- Beneficiary Institution:** *Fundación Investigación Hospital Clínico Universitario de Valencia*
- Duration:** 2015-2018
- Total Budget:** 50.500€



Reference: TLR-GBM

Title: *Estudio de las consecuencias de la activación de receptores TLR en cultivos celulares de glioblastoma*

Principal Investigator: Miguel Cerdá Nicolás

Funding Body: *Universidad de Valencia*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2015-2016

Total Budget: 4.000€.

- **THESIS**

Thesis title: *Estudio de la implicación de los receptores de quimiocinas cxcr3-a y cxcr7 y sus ligandos en la progresión del melanoma cutáneo humano.*

Doctoral candidate: Ana Pellín Carcelén

Director(s): Rosario Gil Benso, Carlos Monteagudo, David Ramos Soler

Date of the defense: 28/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio de la expresión de marcadores de transición epitelio-mesenquimal y de célula madre cancerosa en el melanoma cutáneo, y su asociación con la progresión tumoral.*

Doctoral candidate: Liria Terrádez Más

Director(s): Rosario Gil Benso, Carlos Monteagudo

Date of the defense: 20/01/2016

Grade: *Sobresaliente "cum laude"*



Research Group of Innovative Diagnostic and Therapeutic Developments in Solid Tumours - InDeST Consolidated group

Group members

Principal investigator

Andrés Cervantes Ruipérez
Hospital. University
H Index: 40



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<http://indest.uv.es>

Un valenciano, primer español que dirige el Congreso Europeo de Oncología. El Mundo. 05/10/201

Technicians

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Emerging researchers

Gloria Ribas Despuig. INCLIVA

Nurses

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Emerging researcher

Gloria Ribas Despuig

My scientific interests are based on both the study of genetic susceptibility to complex diseases, mainly Melanoma, as well as the understanding of genomic deregulation in solid tumors.

First, we published two studies on Melanoma, one related to sex-specific genetic effects associated with pigmentation, sun-sensitivity and variants on MC1R another on vitamin D levels. In addition, my participation in the M-SKIP Consortium (Melanoma - SKIn cancer and Phenotypic characteristics" formed by members of 11 countries) can be seen in several past publications being the last a meta-analysis on the association of MC1R variants with pigmentary traits in humans. We have several ongoing studies.

As for the genomic deregulation in solid tumors, I am interested in the identification and characterization of the genetic distinctiveness of breast cancer in very young women (35 years or younger). In order to do so, we carried several studies with global microRNA and gene expression, methylation, copy number, together with IHQ staining and qPCR validation on selected genes. The main objective is to find out whether new markers could be more suitable to treat these patients and would improve their response to therapy. We have contributed to the field with two publications so far, and several posters in four different international meetings. Three manuscripts are nearly submitted to peer review. I am also implicated in the characterization of genetic and epigenetic alterations that play a role in gastric cancer, specifically in Instability and Epstein Bar virus positive subgroups. We published one work already studying the role of RUNX3 in tumor progression and the immune microenvironment.

In collaboration with Dr. A Cervantes we set up the analysis of the mutational screening of solid tumors in 25 oncogenes (287 hotspot mutations) using the Mass Array-Sequenom platform located at the Faculty of Medicine UCIM. Up to now, we have screened more than 300 tumors from several oncologic pathologies: colorectal, breast, ovarian, gastric, melanoma, etc, results can be seen in two publications and one review. In this context, we recently upgraded the screening up to Next Generation Sequencing using customized panels (Illumina) to work both with tumor FFPE and liquid biopsy samples.

Strategic aims

- Our group aims is to improve the patient survival and quality of life through the development of new diagnostic and therapeutic methods.
- In addition to this main goal, we intend to implement strategies to facilitate the development of precision medicine in solid tumors with innovative therapeutic approaches such as molecular classification, genomic and epigenomic sequencing, the use of predictive biomarkers and/or new experimental models.

Main lines of research

- To develop first-in-human Phase I trials of antineoplastic agents with innovative designs.
- To develop liquid biopsies (ctDNA, microRNAs) for early diagnosis, monitoring and the prediction of therapeutic effects in patients with gastro-intestinal malignancies.
- To study the role of acetylated nuclear ribonucleoproteins in predicting resistance to anti-EGFR antibodies.

• PUBLICATIONS

Number of articles	IF	Average IF
40	167,80	4,19
National collaborations	International collaborations	Corresponding author
13	16	18

Original articles

1. Brotto L, Brundage M, Hoskins P, Vergote I, **Cervantes A**, Casado HA, Poveda A, Eisenhauer E, Tu D, Gynecologic Cancer Intergroup Study of the NCIC Clinical Trials Group (NCIC CTG), the European Organization for Research and Treatment of Cancer—Gynecologic Cancer Group (EORTC-GCG) and the Grupo de Investigación de Cáncer de Ovario (GEICO). Randomized study of sequential cisplatin-topotecan/carboplatin-paclitaxel versus carboplatin-paclitaxel: effects on quality of life. *Support Care Cancer*. 2016 Mar; 24(3):1241-9. IF: 2,364
2. Meulendijks D, Jacob W, Martinez-Garcia M, Taus A, Lolkema MP, Voest EE, Langenberg MH, **Fleitas Kanonnikoff T**, **Cervantes A**, De Jonge MJ, Sleijfer S, Soerensen MM,



- Thomas M, Ceppi M, Meneses-Lorente G, James I, Adessi C, Michielin F, Abiraj K, Bossenmaier B, Schellens JH, Weisser M, Lassen UN. First-in-Human Phase I Study of Lumretuzumab, a Glycoengineered Humanized Anti-HER3 Monoclonal Antibody, in Patients with Metastatic or Advanced HER3-Positive Solid Tumors. *Clin Cancer Res*. 2016 Feb 15; 22(4):877-85. IF: 8,722
3. Marinello FG, Bagueña G, Lucas E, Frasson M, Hervás D, Flor-Lorente B, Esclapez P, **Espí A**, García-Granero E. Anastomotic leakage after colon cancer resection: does the individual surgeon matter? *Colorectal Dis*. 2016 Jun; 18(6):562-9. IF: 2,351
 4. Elez E, Hendlisz A, Delaunoy T, Sastre J, **Cervantes A**, Varea R, Chao G, Wallin J, Tabernero J. Phase II study of necitumumab plus modified FOLFOX6 as first-line treatment in patients with locally advanced or metastatic colorectal cancer. *Br J Cancer*. 2016 Feb 16; 114(4):372-80. IF: 4,836
 5. Frasson M, Granero-Castro P, Ramos Rodríguez JL, Flor-Lorente B, Braithwaite M, Martí Martínez E, Álvarez Pérez JA, Codina Cazador A, **Espí A**, Garcia-Granero E, ANACO Study Group. Risk factors for anastomotic leak and postoperative morbidity and mortality after elective right colectomy for cancer: results from a prospective, multicentric study of 1102 patients. *Int J Colorectal Dis*. 2016 Jan; 31(1):105-14. IF: 2,449
 6. Reynés G, Martínez-Sales V, Vila V, Balañá C, Pérez-Segura P, Vaz MA, Benavides M, Gallego O, Palomero I, Gil-Gil M, **Fleitas T**, Reche E. Phase II trial of irinotecan and metronomic temozolomide in patients with recurrent glioblastoma. *Anticancer Drugs*. 2016 Feb; 27(2):133-7. IF: 1,784
 7. **Roselló S, Cervantes A**. Non-surgical treatment of localized rectal cancer is an experimental option. *Cir Esp*. 2016 Jun-Jul; 94(6):311-2. IF: 0,743
 8. **Gambardella V, Tarazona N, Cejalvo JM, Roselló S, Cervantes A**. Clinical pharmacokinetics and pharmacodynamics of ramucirumab in the treatment of colorectal cancer. *Expert Opin Drug Metab Toxicol*. 2016 Apr; 12(4):449-56. IF: 2,831
 9. Sclafani F, Brown G, Cunningham D, Wotherspoon A, Tait D, Peckitt C, Evans J, Yu S, Sena Teixeira Mendes L, Tabernero J, Glimelius B, **Cervantes A**, Thomas J, Begum R, Oates J, Chau I. PAN-EX: a pooled analysis of two trials of neoadjuvant chemotherapy followed by chemoradiotherapy in MRI-defined, locally advanced rectal cancer. *Ann Oncol*. 2016 Aug; 27(8):1557-65. IF: 7,04
 10. **Ibarrola-Villava M, Fleitas T, Llorca-Cardenosa MJ, Mongort C**, Alonso E, Navarro S, Burgues O, Vivancos A, Cejalvo JM, Perez-Fidalgo JA, **Roselló S, Ribas G, Cervantes A**. Determination of somatic oncogenic mutations linked to target-based therapies using MassARRAY technology. *Oncotarget*. 2016 Apr 19; 7(16):22543-55. IF: 6,359
 11. Hernando B, **Ibarrola-Villava M**, Fernandez LP, Peña-Chilet M, Llorca-Cardenosa M, **Oltra SS**, Alonso S, Boyano MD, Martinez-Cadenas C, **Ribas G**. Sex-specific genetic effects associated with pigmentation, sensitivity to sunlight, and melanoma in a population of Spanish origin. *Biol Sex Differ*. 2016; 7:17. IF: 4,837
 12. **Gil A**, López JI, Pulido R. Assessing PTEN Subcellular Localization. *Methods Mol Biol*. 2016; 1388:169-86. IF: 0
 13. Martorell PM, Huerta M, Quilis AC, Abellán M, Blesa S, Chaves F, Beltrán DD, Nascimento AF, **Insa A**. 8P EGFR, KRAS, BRAF, and PI3K mutations and ALK rearrangement in 327 consecutive Spanish non-squamous NSCLC patients. *J Thorac Oncol*. 2016 Apr; 11(4 Suppl):S60. IF: 5,282
 14. Smyth EC, **Tarazona N**, Peckitt C, Armstrong E, Mansukhani S, Cunningham D, Chau I. Exclusion of Gastrointestinal Cancer Patients With Prior Cancer From Clinical Trials: Is This Justified? *Clin Colorectal Cancer*. 2016 Jun; 15(2):e53-9. IF: 2,813
 15. Pearson A, Smyth E, Babina IS, Herrera-Abreu MT, **Tarazona N**, Peckitt C, Kilgour E, Smith NR, Geh C, Rooney C, Cutts R, Campbell J, Ning J, Fenwick K, Swain A, Brown G, Chua S, Thomas A, Johnston SR, Ajaz M, Sumpter K, Gillbanks A, Watkins D, Chau I, Popat S, Cunningham D, Turner NC. High-Level Clonal FGFR Amplification and Response to FGFR Inhibition in a Translational Clinical Trial. *Cancer Discov*. 2016 Aug; 6(8):838-51. IF: 19,453
 16. **Tarazona N**, Smyth EC, Peckitt C, Chau I, Watkins D, Rao S, Starling N, Cunningham D. Efficacy and toxicity of salvage weekly paclitaxel chemotherapy in non-Asian patients with advanced oesophagogastric adenocarcinoma. *Ther Adv Med Oncol*. 2016 Mar; 8(2):104-12. IF: 2,827
 17. **Martínez-Ciarpaglini C**, Monteagudo C. Pigmented desmoplastic trichilemmoma. *J Cutan Pathol*. 2016 Jun; 43(6):535-537. IF: 1,582
 18. Breugom AJ, Bastiaannet E, Boelens PG, Iversen LH, Martling A, Johansson R, Evans T, Lawton S, O'Brien KM, Van Eycken E, Janciauskiene R, Liefers GJ, **Cervantes A**, Lemmens VE, van de Velde CJ. Adjuvant chemotherapy and relative survival of



- patients with stage II colon cancer - A EURECCA international comparison between the Netherlands, Denmark, Sweden, England, Ireland, Belgium, and Lithuania. *Eur J Cancer*. 2016 Jun 11; 63:110-117. IF: 6,163
19. Tagliabue E, Gandini S, García-Borrón JC, Maisonneuve P, Newton-Bishop J, Polsky D, Lazovich D, Kumar R, Ghiorzo P, Ferrucci L, Gruis NA, Puig S, Kanetsky PA, Motokawa T, **Ribas G**, Landi MT, Fagnoli MC, Wong TH, Stratigos A, Helsing P, Guida G, Autier P, Han J, Little J, Sera F, Raimondi S, M-SKIP Study group.. Association of Melanocortin-1 Receptor Variants with Pigmentary Traits in Humans: A Pooled Analysis from the M-Skip Project. *J Invest Dermatol*. 2016 Sep; 136(9):1914-7. IF: 6,915
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 21. Sclafani F, Chau I, Cunningham D, Lampis A, Hahne JC, Ghidini M, Lote H, Zito D, Tabernero J, Glimelius B, **Cervantes A**, Begum R, De Castro DG, Wilson SH, Peckitt C, Eltahir Z, Wotherspoon A, Tait D, Brown G, Oates J, Braconi C, Valeri N. Sequence variation in mature microRNA-608 and benefit from neo-adjuvant treatment in locally advanced rectal cancer patients. *Carcinogenesis*. 2016 Sep; 37(9):852-7. IF: 4,874
 22. Gruenberger T, Beets G, Van Laethem JL, Rougier P, **Cervantes A**, Douillard JY, Figueras J, Gruenberger B, Haller DG, Labianca R, Maleux G, Roth A, Ducreux M, Schmiegel W, Seufferlein T, Van Cutsem E. Treatment sequence of synchronously (liver) metastasized colon cancer. *Dig Liver Dis*. 2016 Oct; 48(10):1119-23. IF: 2,719
 23. Garcés-Albir M, García-Botello SA, **Espi A**, Pla-Martí V, Martín-Arevalo J, Moro-Valdezate D, Ortega J. Three-dimensional endoanal ultrasound for diagnosis of perianal fistulas: Reliable and objective technique. *World J Gastrointest Surg*. 2016 Jul 27; 8(7):513-20. IF: 0
 24. Llorca-Cardenosa MJ, **Fleitas T**, **Ibarrola-Villava M**, Peña-Chilet M, **Mongort C**, **Martínez-Ciarpaglini C**, Navarro L, **Gambardella V**, Castillo J, **Roselló S**, Navarro S, **Ribas G**, **Cervantes A**. Epigenetic changes in localized gastric cancer: the role of RUNX3 in tumor progression and the immune microenvironment. *Oncotarget*. 2016 Sep 27; 7(39):63424-63436. IF: 5,008
 25. Van Laethem JL, Carneiro F, Ducreux M, Messman H, Lordick F, Ilson DH, Allum WH, Haustermans K, Lepage C, Matsiyak-Budnik T, Cats A, Schmiegel W, **Cervantes A**, Van Cutsem E, Rougier P, Seufferlein T. The multidisciplinary management of gastro-oesophageal junction tumours: European Society of Digestive Oncology (ESDO): Expert discussion and report from the 16th ESMO World Congress on Gastrointestinal Cancer, Barcelona. *Dig Liver Dis*. 2016 Nov; 48(11):1283-1289. IF: 2,719
 26. **Roselló S**, **Cervantes A**. Erratum to «Non-surgical treatment of localized rectal cancer is an experimental option». *Cir Esp*. 2016 Dec; 94(10):617. IF: 1
 27. Cejalvo JM, Pérez-Fidalgo JA, **Ribas G**, Burgués O, **Mongort C**, Alonso E, **Ibarrola-Villava M**, Bermejo B, Martínez MT, **Cervantes A**, Lluch A. Clinical implications of routine genomic mutation sequencing in PIK3CA/AKT1 and KRAS/NRAS/BRAF in metastatic breast cancer. *Breast Cancer Res Treat*. 2016 Nov; 160(1):69-77. IF: 4,085
 28. Hernando B, **Ibarrola-Villava M**, Peña-Chilet M, Alonso S, **Ribas G**, Martínez-Cadenas C. Sex and MC1R variants in human pigmentation: Differences in tanning ability and sensitivity to sunlight between sexes. *J Dermatol Sci*. 2016 Dec; 84(3):346-348. IF: 3,739
 29. Riffo-Campos ÁL, Castillo J, Vallet-Sánchez A, Ayala G, **Cervantes A**, López-Rodas G, Franco L. In silico RNA-seq and experimental analyses reveal the differential expression and splicing of EPDR1 and ZNF518B genes in relation to KRAS mutations in colorectal cancer cells. *Oncol Rep*. 2016 Dec; 36(6):3627-3634. IF: 2,486
 30. **Cervantes A**. In the literature: May 2016. *ESMO Open*. 2016 May 25; 1(3):e000071. IF: 0
 31. **Cervantes A**. In the literature: March 2016. *ESMO Open*. 2016 Mar 16; 1(2):e000046. IF: 0
 32. Hernández-Ostiz S, Pérez-Ramada MD, Ortiz B, Requena C, **Ribas G**, Aznar E, Nagore E. 25-Hydroxyvitamin D in Patients With Melanoma and Factors Associated With Inadequate Levels. *Actas Dermosifiliogr*. 2016 Nov; 107(9):758-764. IF: 0



Letter

33. Cherny NI, Kloke M, **Cervantes A**, Pentheroudakis G, ESMO Guidelines Committee. Reply to the letter to the editor 'How much evidence isn't in evidence-based guidelines?' by Johnson et al. *Ann Oncol*. 2016 Mar; 27(3):550-1. IF: 7,04

Editorials

34. Dittrich C, Kosty M, Jezdic S, Pyle D, Berardi R, Bergh J, El Saghir N, Lotz JP, Österlund P, Pavlidis N, Purkalne G, **ESMO/ASCO Global Curriculum Working Group**. ESMO/ASCO recommendations for a Global Curriculum (GC) in medical oncology-edition 2016. *Ann Oncol*. 2016 Aug; 27(8):1378-81. IF: 9,269
35. **Cervantes A**. In the literature: October 2016. *ESMO Open*. 2016 Oct 18; 1(5):e000103. IF: 0

Clinical guidelines

36. Smyth EC, Verheij M, Allum W, Cunningham D, **Cervantes A**, Arnold D, ESMO Guidelines Committee. Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2016 Sep; 27(suppl 5):v38-v49. IF: 9,269
37. González-Flores E, Losa F, Pericay C, Polo E, **Roselló S**, Safont MJ, Vera R, Aparicio J, Cano MT, Fernández-Martos C. SEOM Clinical Guideline of localized rectal cancer (2016). *Clin Transl Oncol*. 2016 Dec; 18(12):1163-1171. IF: 2,075

Reviews

38. Martínez MT, **Pérez-Fidalgo JA**, Martín-Martorell P, Cejalvo JM, Pons V, Bermejo B, Martín M, Albanell J, Lluch A. Treatment of HER2 positive advanced breast cancer with T-DM1: A review of the literature. *Crit Rev Oncol Hematol*. 2016 Jan; 97:96-106. IF: 4,027
39. Tarazona N, **Gambardella V**, Huerta M, **Roselló S**, **Cervantes A**. Personalised Treatment in Gastric Cancer: Myth or Reality? *Curr Oncol Rep*. 2016 Jul; 18(7):41. IF: 2,891
40. **Fleitas T**, **Ibarrola-Villava M**, **Ribas G**, **Cervantes A**. MassARRAY determination of somatic oncogenic mutations in solid tumors: Moving forward to personalized medicine. *Cancer Treat Rev*. 2016 Jul 29; 49:57-64. IF: 7,983

• THESIS

Thesis Title: *Estudio de acetilación de proteínas en líneas celulares humanas de cáncer colorrectal KRAS mutado o salvaje.*

Doctoral candidate: Desamparados Roda Pérez

Director(s): Andrés Cervantes, Rosa Zaragoza Colom, Elena Ruiz García-Trevijano

Date of the defense: 08/02/2016

Grade: *Apto "cum laude"*

Thesis Title: *Análisis de polimorfismos en genes que codifican para enzimas que regulan el estrés oxidativo y su relación con la respuesta al tratamiento y la supervivencia en pacientes con cáncer de pulmón.*

Doctoral candidate: Amelia Insa Mollá

Director(s): Ana Lluch Hernández, José Franco Serrano

Date of the defense: 08/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis Title: *Factores pronósticos en el cáncer de recto localmente avanzado tratado con quimiorradioterapia neoadyuvante seguida de cirugía. Valor pronóstico del neoadjuvant rectal score y del nomograma de Valentini.*

Doctoral candidate: Susana Roselló Keranen

Director(s): Andrés Cervantes Ruipérez, Eduardo García-Granero Ximénez, Matteo Frasson

Date of the defense: 05/09/2016

Grade: *Sobresaliente "cum laude"*

Thesis Title: *Evaluación del perfil genómico de la plataforma de investigación basada en PAM50 y miRNAs en el cáncer de mama de mujeres muy jóvenes (≤ 35 años): Correlación con parámetros clínicos.*

Doctoral candidate: María Teresa Martínez Martínez

Director(s): Gloria Ribas Despuig, Ana Lluch Hernández

Date of the defense: 02/02/2016

Grade: *Sobresaliente "cum laude"*

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PROMETEO/2013/005

Title: *Estudio traslacional sobre la hiperacetilación de proteínas como vía final de resistencia a fármacos anti-EGFR en cánceres de alta incidencia clínica.*

Principal Investigator: Andrés Cervantes Ruipérez



Funding body: *Conselleria de Educaci3n, Cultura y Deporte*

Beneficiary institution: *Fundaci3n Investigaci3n Hospital Cl3nico Universitario de Valencia*

Duration: 2013-2016

Total budget: 54.535€

Reference: PT13/0002/0031

Title: Clinical Research and Trials Platform.

Principal Investigator: Andr3s Cervantes Ruip3rez

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundaci3n Investigaci3n Hospital Cl3nico Universitario de Valencia*

Duration: 2014 - 2017

Total budget: 65.550€

Reference: PI15/02180

Title: *Enfermedad m3nima residual en c3nceres colorrectales de alto riesgo resecaados. Valor de las biopsias l3quidas en el seguimiento y an3lisis de la heterogeneidad tumoral.*

Principal Investigator: Andr3s Cervantes Ruip3rez

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundaci3n Investigaci3n Hospital Cl3nico Universitario de Valencia*

Duration: 2016-2018

Total budget: 80.465€

Title: *Hiperacetilaci3n de riboproteinas heter3neas nucleares (hnRNPs) como v3a final de resistencia a f3rmacos anti-EGFR en c3ncer de pr3stata.*

Principal Investigator: Ana Isabel Gil

Funding Body: *Fundaci3n de la Asociaci3n Espa3ola contra el C3ncer*

Beneficiary Institution: *Fundaci3n Investigaci3n Hospital Cl3nico Universitario de Valencia*

Duration: 2014-2015

Reference: 635342 - MoTriColor

Title: Molecularly guided trials with specific treatment strategies in patients with advanced newly molecular defined subtypes of colorectal cancer (MoTriColor).

Principal Investigator: Dr. Josep Tabernero (Andr3s Cervantes as collaborating researcher)

Funding Body: *European Commission*

Beneficiary Institution: *Fundaci3n Investigaci3n Hospital Cl3nico Universitario de Valencia, entre otras*

Duration: 2015-2019

Total budget: 5.996.992€

Reference: IntraColor

Title: INTRACOLOR - Translational research on human tumour heterogeneity to overcome recurrence and resistance to therapy

Principal Investigator: Andr3s Cervantes

Funding Body: *European Commission through ISCIII (TRANSCAN)*

Beneficiary institution: *Fundaci3n Investigaci3n Hospital Cl3nico Universitario de Valencia*

Duration: 2016-2018

Total Budget: 1.026.927,5€

Reference: PI13/00606

Title: Transcriptional deregulation in tumoral tissue from very young women with breast cancer and functional Implications.

Principal Investigator: Gloria Ribas Despuig

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundaci3n Investigaci3n Hospital Cl3nico Universitario de Valencia*

Duration: 2014-2016

Total budget: 68.365€

Reference: 04-CAPABLE-NOGUERA-CERVANTES-2016B

Title: *Heterogeneidad clonal en c3ncer: biopsia l3quida como tecnolog3a de alto rendimiento.*

Principal Investigator: Andr3s Cervantes, Rosa Noguera

Funding Body: *Fundaci3n Investigaci3n Hospital Cl3nico Universitario de Valencia*

Beneficiary Institution: *Fundaci3n Investigaci3n Hospital Cl3nico Universitario de Valencia*

Duration: 2016-2017

Total budget: 6.000€

• AWARDS:

In November 2016, Dr. Andr3s Cervantes was awarded with the prize "Valencianos en la Onda" in the scientific field. This is a recognition that the radio station makes to the most extraordinary valencians of the year.



Image 1: Ibarrola-Villava M et al. *Oncotarget*. 2016

A) Genomic mutations found across the different solid tumor types enrolled in the study. Selected genes are mutated in at least one tumor sample. Samples with mutations are shown in black. The histogram represents the percentage of gene mutation across the different tumor types. Colorectal cancer and breast cancer are represented with dots and with lines, respectively, while all other tumors are represented together in black.

B) Genomic co-occurrence mutations found across those tumor samples with two or more mutations. The length of the arc corresponds to the frequency of mutations in the first gene, and the width of the ribbon corresponds to the percentage of patients who also had a mutation in the second gene.

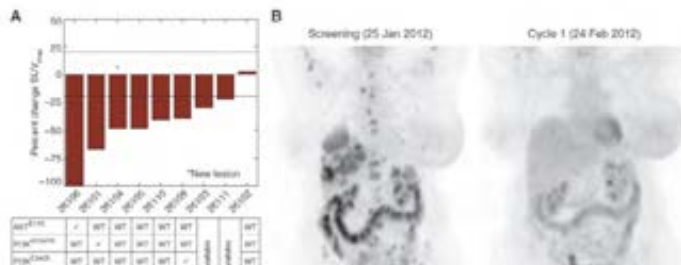
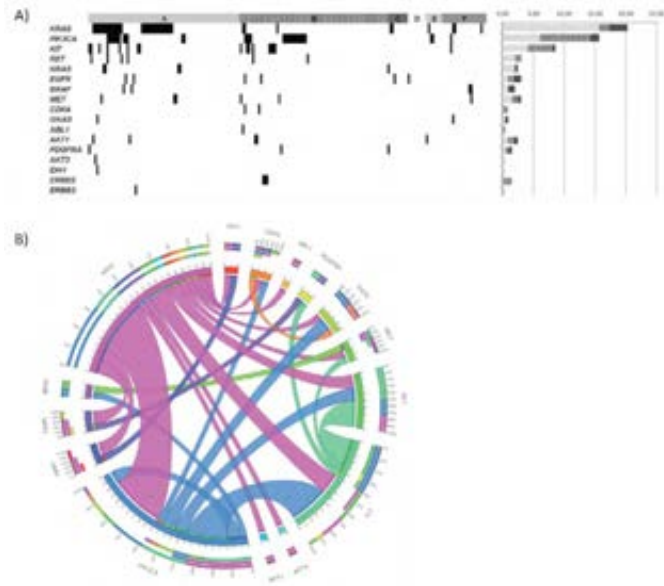


Image 2: Saura C et al. *Cancer Discovery*. 2016

Patients with MBC with tumors having *PTEN* loss and/or *PIK3CA*/*AKT* mutations showed target lesion metabolic responses by [18 F] FDG-PET following ipatasertib. A, Nine patients with MBC, with archival tumors having activation of the *PI3K*/*AKT* pathway as determined by the investigator, were dosed with ipatasertib 600 mg and had [18 F]FDG-PET scans done at screening and in cycle 1 after two weeks. The maximum percentage change in SUV between the on-treatment and pretreatment PET scans (SUV max) in target lesions was then graphed for each patient, ranked by order of response. Eight of the nine evaluable patients (89%) had a metabolic PET response, as defined by an SUV max decrease $\geq 20\%$ in the target lesions. One patient (ID# 26102) did not have a PET response, but this patient also stopped the study drug in cycle 1 at the time of the PET scan. Most of the patients with metabolic PET responses also had archival tumors with activation of the *PI3K*/*AKT* pathway, including decreased *PTEN* expression ($n = 6$), *PIK3CA* mutations ($n = 3$), and an *AKT1* mutation ($n = 1$), as determined centrally. WT, wild-type. B, One patient with MBC (HER2-negative) harboring an *AKT1* E17K mutation in the archival tumor sample exhibited a complete metabolic response at cycles 1 and 2. All FDG-avid target lesions identified at baseline were indistinguishable from background on the on-treatment PET scans (% SUV max decrease set to 100%).



Research Group on Breast Cancer Biology

Consolidated group



"Mis pacientes me han enseñado a vivir."

Ana Lluch. Levante. 21.12.2015.

Group members

Principal investigator

Ana Lluch Hernández
Hospital. University
H Index: 41

Team involved in



Collaborating researchers

Begoña Bermejo De Las Heras. Hospital
Octavio Burgues Gasión. Hospital
Antonio Caballero Garate. Hospital
Angel Martínez Agullo. Hospital
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Isabel Catoira Domenech. INCLIVA
Patricia Martínez Belenguer. INCLIVA
Antonio Millet Serrano. Hospital. University
Vicenta Garcés Honrubia. Hospital
Begoña Pineda Merlo. INCLIVA
María Peña Chilet. INCLIVA

Emerging researchers

Isabel Chirivella González. Hospital
Pilar Eroles Asensio. INCLIVA
Joan Climent Bataller. INCLIVA

PhD students

Eduardo Tormo Martín. INCLIVA
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Technicians

Elisa Alonso Yuste. INCLIVA

Administrative assistant

Yolanda De La Cruz Robles. INCLIVA



Strategic aims

- Study of TDM1 and trastuzumab resistance in HER2+ by the generation and characterization of preclinical Trastuzumab-Resistant HER2+ Breast Cancer Models.
- Implication of miRNAs in breast cancer: miR-26a and the relation with metformin treatment.
- Determination of a PAM50-based Chemo-Endocrine Score for Hormone Receptor-Positive Breast Cancer.
- Clinical implications of routine genomic mutation sequencing in PIK3CA/AKT1 and KRAS/NRAS/BRAF in metastatic breast cancer and determination of somatic oncogenic mutations using MassARRAY technology.
- Determination of High Proliferation as predictor of Pathological Complete Response to Neoadjuvant Chemotherapy in Early Breast Cancer.
- Determination of the resistance to taxanes and anthracyclines by c-Jun N-Terminal Kinase Inactivation by Mitogen-Activated Protein Kinase Phosphatase 1.
- Prediction of outcome in borderline oestrogen receptor positive breast carcinoma by Non-canonical NF- κ B pathway activation.
- Involvement of FoxA and LIPG endothelial lipase in control the uptake of extracellular lipids for breast cancer growth.

Clinical trials to evaluate:

- Neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere).
- Nab-Paclitaxel in Metastatic Breast Cancer -Hormone Receptor-Positive Breast Cancer Receiving Adjuvant Triptorelin Plus Exemestane or Tamoxifen in the Suppression of Ovarian Function Trial (SOFT): The SOFT-EST Substudy.
- Pooled analysis of prospective European studies assessing the impact of using the 21-gene Recurrence Score assay on clinical decision making in women with oestrogen receptor-positive, human epidermal growth factor receptor 2-negative early-stage breast cancer.

Main lines of research

- Study of methylation as a prognostic and predictive factor of neoadjuvant treatment in triple negative breast cancer.
- Evaluation of microRNAs and mRNAs differentially expressed after chemotherapy treatment.
- Involvement of miRNAs in breast cancer processes.
- Role of tumor heterogeneity and dynamic reprogramming of tumor cell resistance to anti-HER2 therapy.
- Evaluation of the involvement of stem cells and epithelial mesenchymal transition in the mechanisms of resistance to treatment in HER2 + breast cancer.
- Primary and secondary resistance in HER2 + breast cancer: search for new treatments.
- Interaction between estrogen receptors, tumor angiogenesis and breast cancer metabolism.
- Molecular and clinical characterization of breast tumors from very young women.



Emerging researcher

Isabel Chirivella González

The research line suggests a possible relation between mammographic density, as a genetic susceptibility marker and the risk to suffer breast cancer in women with a mutation in BRCA (hereditary breast cancer). Women with a mutation in genes BRCA1 or BRCA2 have a higher risk of developing breast cancer (40-70%) and the risk could possibly be modified by genetic variations related to mammographic density.

We also have a project to evaluate a set of endometrial cancer risk markers in Lynch syndrome patients. The study will prospectively analyze these markers and the progression to endometrial cancer in a series of endometrial biopsies taken from a prominent cohort of Lynch syndrome carriers during the follow-up period. The ultimate goal of this research is to achieve the minimum required clinical evidence to use these markers to improve the medical decision process towards a customized recommendation on the management options (surveillance vs. prophylactic hysterectomy) in these patients.



Emerging researcher

Pilar Eroles Asensio

The lines of research aim at deepening the knowledge of some of the molecular subtypes of breast cancer, especially HER2+ and triple negative, through studies of expression and epigenetic changes (microRNAs, methylation) to decipher the possible mechanisms of resistance to current treatments. We intend to develop new strategies for diagnostic and therapeutic intervention to reverse the identified resistance, based on combinations with other biologic agents and the use of predictive biomarkers of resistance.



Emerging researcher

Joan Climent Bataller

The research area of Dr. Climent lab is focused in exploiting "Systems" approaches to the understanding of susceptibility to cancer and its related sub-phenotypes, and to apply this knowledge to the problems posed by the increasing human cancer burden. The main expertise is focused in breast cancer research and it covers the use of novel mathematical tools for comprehensive analysis of genetic and gene expression data, with the purpose of optimizing predictive responses to targeted drug treatment.

These algorithms are based on mathematical methods of network analysis for determining not whether single specific genes are deregulated in tumors, but for identifying the combinations of the many possible gene expression changes that are most commonly associated with a particular outcome. Outcomes can be either patient or cell line responses to a particular treatment, levels of expression or polymorphic variants from specific genes.

Advances in technology have allowed us to construct a global view of tissue architecture, filtered through the lens of genetic control of gene expression and now could be used to generate copy-number profiles based on breast cancer patients response to chemotherapy treatments. Novel network analysis tools can be used to identify critical signaling hubs that may reflect underlying susceptibility of different individuals to cancer development, progression or therapeutic responses. The same signaling hubs may also be targets for chemoprevention or therapeutic intervention, in addition to informing basic questions in cancer biology.

• PUBLICATIONS

Number of articles	IF	Average IF
27	197,63	7,31
National collaborations	International collaborations	Corresponding author
16	8	10

Original articles

1. **Eroles P, Tormo E, Pineda B**, Espin E, **Lluch A**. MicroRNAs in Breast Cancer: One More Turn in Regulation. *Curr Drug Targets*. 2016; 17(9):1083-100. IF: 3,021
2. González-Martín A, Alba E, Ciruelos E, Cortés J, Llombart A, **Lluch A**, Andrés R, Álvarez I, Aramendía JM, de la Peña FA, Barnadas A, Batista N, Calvo L, Galve E, García-Palomo A, García-Sáenz JÁ, de la Haba J, López R, López-Vivanco G, Martínez-Jáñez N, de Dueñas EM, Plazaola A, Rodríguez-Lescure Á, Ruiz M, Sánchez-Rovira P, Santaballa A, Seguí MÁ, Tusquets I, Zamora P, Martín M. Nab-Paclitaxel in Metastatic Breast Cancer: Defining the Best Patient Profile. *Curr Cancer Drug Targets*. 2016; 16(5):415-28. IF: 3,522
3. Panach L, **Pineda B**, Mifsut D, Tarín JJ, Cano A, García-Pérez MÁ. The role of CD40 and CD40L in bone mineral density and in osteoporosis risk: A genetic and functional study. *Bone*. 2016 Feb; 83:94-103. IF: 3,973
4. Bellet M, Gray KP, Francis PA, Láng I, Ciruelos E, **Lluch A**, Climent MA, Catalán G, Avella A, Bohn U, González-Martin A, Ferrer R, Catalán R, Azaro A, Rajasekaran A, Morales J, Vázquez J, Fleming GF, Price KN, Regan MM. Twelve-Month Estrogen Levels in Premenopausal Women With Hormone Receptor-Positive Breast Cancer Receiving Adjuvant Triptorelin Plus Exemestane or Tamoxifen in the Suppression of Ovarian Function Trial (SOFT): The SOFT-EST Substudy. *J Clin Oncol*. 2016 May 10; 34(14):1584-93. IF: 18,428
5. Alba E, **Lluch A**, Ribelles N, Anton-Torres A, Sanchez-Rovira P, Albanell J, Calvo L, García-Asenjo JA, Palacios J, Chacon JI, Ruiz A, De la Haba-Rodriguez J, Segui-Palmer MA, Cirauqui B, Margeli M, Plazaola A, Barnadas A, Casas M, Caballero R, Carrasco E, Rojo F. High Proliferation Predicts Pathological Complete Response to Neoadjuvant Chemotherapy in Early Breast Cancer. *Oncologist*. 2016 Feb; 21(2):150-5. IF: 4,865
6. Gianni L, Pienkowski T, Im YH, Tseng LM, Liu MC, **Lluch A**, Starosawska E, de la Haba-Rodriguez J, Im SA, Pedrini JL, Poirier B, Morandi P, Semiglazov V, Srimuninnimit V, Bianchi



- GV, Magazzù D, McNally V, Douthwaite H, Ross G, Valagussa P. 5-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 2 randomised trial. *Lancet Oncol.* 2016 Jun; 17(6):791-800. IF: 24,69
7. Ribi K, Luo W, Bernhard J, Francis PA, Burstein HJ, Ciruelos E, Bellet M, Pavesi L, **Lluch A**, Visini M, Parmar V, Tondini C, Kerbrat P, Perelló A, Neven P, Torres R, Lombardi D, Puglisi F, Karlsson P, Ruhstaller T, Colleoni M, Coates AS, Goldhirsch A, Price KN, Gelber RD, Regan MM, Fleming GF. Adjuvant Tamoxifen Plus Ovarian Function Suppression Versus Tamoxifen Alone in Premenopausal Women With Early Breast Cancer: Patient-Reported Outcomes in the Suppression of Ovarian Function Trial. *J Clin Oncol.* 2016 May 10; 34(14):1601-10. IF: 18,443
 8. Ibarrola-Villava M, Fleitas T, Llorca-Cardenosa MJ, Mongort C, **Alonso E**, Navarro S, Burgues O, Vivancos A, Cejalvo JM, Perez-Fidalgo JA, Roselló S, Ribas G, Cervantes A. Determination of somatic oncogenic mutations linked to target-based therapies using MassARRAY technology. *Oncotarget.* 2016 Apr 19; 7(16):22543-55. IF: 6,359
 9. Hernando B, Ibarrola-Villava M, Fernandez LP, **Peña-Chilet M**, Llorca-Cardenosa M, Oltra SS, Alonso S, Boyano MD, Martinez-Cadenas C, Ribas G. Sex-specific genetic effects associated with pigmentation, sensitivity to sunlight, and melanoma in a population of Spanish origin. *Biol Sex Differ.* 2016; 7:17. IF: 4,837
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 11. Slebe F, Rojo F, Vinaixa M, García-Rocha M, Testoni G, Guiu M, Planet E, Samino S, Arenas EJ, Beltran A, Rovira A, **Lluch A**, Salvatella X, Yanes O, Albanell J, Guinovart JJ, Gomis RR. FoxA and LIPG endothelial lipase control the uptake of extracellular lipids for breast cancer growth. *Nat Commun.* 2016 Apr 5; 7:11199. IF: 11,47
 12. Lainez N, García-Donas J, Esteban E, Puente J, Sáez MI, Gallardo E, Pinto-Marín Á, Vázquez-Estévez S, León L, García-Carbonero I, Suárez-Rodríguez C, Molins C, Climent-Duran MA, Lázaro-Quintela M, González Del Alba A, Méndez-Vidal MJ, **Chirivella I**, Afonso FJ, López-Brea M, Sala-González N, Domenech M, Basterretxea L, Santander-Lobera C, Gil-Arnáiz I, Fernández O, Caballero-Díaz C, Mellado B, Marrupe D, García-Sánchez J, Sánchez-Escribano R, Fernández Parra E, Villa Guzmán JC, Martínez-Ortega E, Belén González M, Morán M, Suarez-Paniagua B, Lecumberri MJ, Castellano D. Impact on clinical practice of the implementation of guidelines for the toxicity management of targeted therapies in kidney cancer. The protect-2 study. *BMC Cancer.* 2016 Feb 22; 16(1):135. IF: 3,362
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 14. Robles EF, Mena-Varas M, Barrio L, Merino-Cortes SV, Balogh P, Du MQ, Akasaka T, Parker A, Roa S, Panizo C, Martin-Guerrero I, Siebert R, Segura V, Agirre X, Macri-Pellizeri L, Aldaz B, Vilas-Zornoza A, Zhang S, Moody S, Calasanz MJ, Tousseyn T, Broccardo C, Brousset P, Campos-Sanchez E, Cobaleda C, Sanchez-Garcia I, Fernandez-Luna JL, Garcia-Muñoz R, Pena E, Bellosillo B, Salar A, Baptista MJ, Hernandez-Rivas JM, Gonzalez M, Terol MJ, **Climent J**, Ferrandez A, Sagaert X, Melnick AM, Prosper F, Oscier DG, Carrasco YR, Dyer MJ, Martinez-Climent JA. Homeobox NKX2-3 promotes marginal-zone lymphomagenesis by activating B-cell receptor signalling and shaping lymphocyte dynamics. *Nat Commun.* 2016 Jun 14; 7:11889. IF: 11,329
 15. Rojo F, González-Pérez A, Furriol J, Nicolau MJ, Ferrer J, **Burgués O**, Sabbaghi M, González-Navarrete I, Cristobal I, Serrano L, Zazo S, Madoz J, Servitja S, Tusquets I, Albanell J, **Lluch A**, Rovira A, **Eroles P**. Non-canonical NF- κ B pathway activation predicts outcome in borderline oestrogen receptor positive breast carcinoma. *Br J Cancer.* 2016 Jul 26; 115(3):322-31. IF: 5,569
 16. Albanell J, Svedman C, Gligorov J, Holt SD, Bertelli G, Blohmer JU, Rouzier R, **Lluch A**, Eiermann W. Pooled analysis of prospective European studies assessing the impact of using the 21-gene Recurrence Score assay on clinical decision making in women with oestrogen receptor-positive, human epidermal growth factor receptor 2-negative early-stage breast cancer. *Eur J Cancer.* 2016 Aug 18; 66:104-113. IF: 6,163



17. Cabello P, **Pineda B, Tormo E, Lluch A, Eroles P**. The Antitumor Effect of Metformin Is Mediated by miR-26a in Breast Cancer. *Int J Mol Sci*. 2016 Aug 10; 17(8). IF: 3,257
18. Llorca-Cardena MJ, Fleitas T, Ibarrola-Villava M, **Peña-Chilet M**, Mongort C, Martinez-Ciarpaglini C, Navarro L, Gambardella V, Castillo J, Roselló S, Navarro S, Ribas G, Cervantes A. Epigenetic changes in localized gastric cancer: the role of RUNX3 in tumor progression and the immune microenvironment. *Oncotarget*. 2016 Sep 27; 7(39):63424-63436. IF: 5,008
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21. Cejalvo JM, Pérez-Fidalgo JA, Ribas G, **Burgués O**, Mongort C, **Alonso E**, Ibarrola-Villava M, **Bermejo B**, Martínez MT, Cervantes A, **Lluch A**. Clinical implications of routine genomic mutation sequencing in PIK3CA/AKT1 and KRAS/NRAS/BRAF in metastatic breast cancer. *Breast Cancer Res Treat*. 2016 Nov; 160(1):69-77. IF: 4,085
22. Hernando B, Ibarrola-Villava M, **Peña-Chilet M**, Alonso S, Ribas G, Martínez-Cadenas C. Sex and MC1R variants in human pigmentation: Differences in tanning ability and sensitivity to sunlight between sexes. *J Dermatol Sci*. 2016 Dec; 84(3):346-348. IF: 3,739
23. Prat A, **Lluch A**, Turnbull AK, Dunbier AK, Calvo L, Albanell J, de la Haba-Rodríguez J, Arcusa A, Chacón I, Sánchez-Rovira P, Plazaola A, Muñoz M, Paré L, Parker JS, Ribelles N, Jimenez B, Bin Aiderus AA, Caballero R, Adamo B, Dowsett M, Carrasco EM, Martín M, Dixon JM, Perou CM, Alba E. A PAM50-based Chemo-Endocrine Score for Hormone Receptor-Positive Breast Cancer with an Intermediate Risk of Relapse. *Clin Cancer Res*. 2016 Nov 30 ;. IF: 8,738
24. Zazo S, González-Alonso P, Martín-Aparicio E, Chamizo C, Cristóbal I, Arpí O, Rovira A, Albanell J, **Eroles P, Lluch A**, Madoz-Gúrpide J, Rojo F. Generation, characterization, and maintenance of trastuzumab-resistant HER2+ breast cancer cell lines. *Am J Cancer Res*. 2016 Nov 1; 6(11):2661-2678. IF: 3,425
25. González-Alonso P, Cristóbal I, Zazo S, Martín-Aparicio E, Chamizo C, Madoz-Gúrpide J, Rovira A, **Eroles P, Lluch A**, Albanell J, Rojo F. Recent Insights into the Development of Preclinical Trastuzumab-Resistant HER2+ Breast Cancer Models. *Curr Med Chem*. 2016 Dec 16 ;. IF: 3,455

Review

26. Martínez MT, Pérez-Fidalgo JA, Martín-Martorell P, Cejalvo JM, Pons V, Bermejo B, Martín M, Albanell J, **Lluch A**. Treatment of HER2 positive advanced breast cancer with T-DM1: A review of the literature. *Crit Rev Oncol Hematol*. 2016 Jan; 97:96-106. IF: 4,027
27. Alba E, **Lluch A**, Ribelles N, Anton-Torres A, Sanchez-Rovira P, Albanell J, Calvo L, García-Asenjo JA, Palacios J, Chacon JI, Ruiz A, De la Haba-Rodríguez J, Seguí-Palmer MA, Cirauqui B, Margeli M, Plazaola A, Barnadas A, Casas M, Caballero R, Carrasco E, Rojo F. High Proliferation Predicts Pathological Complete Response to Neoadjuvant Chemotherapy in Early Breast Cancer. *Oncologist*. 2016 Jun; 21(6):778. IF: 4,789

• THESIS

Thesis title: *Análisis de polimorfismos en genes que codifican para enzimas que regulan el estrés oxidativo y su relación con la respuesta al tratamiento y la supervivencia en pacientes con cáncer de pulmón.*

Doctoral candidate: Amelia Insa Mollá

Director(s): Ana Lluch Hernández, José Franco Serrano

Date of the defense: 08/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Recaída locorregional en mujeres con cáncer de mama portadoras de mutación BRCA tratadas mediante cirugía conservadora.*

Doctoral candidate: María José Juan Fita

Director(s): Ana Lluch Hernández, José Antonio López Guerrero, Amparo Ruiz Simón



Date of the defense: 08/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Utilidad de los informes estructurados basados en una plataforma web para el diagnóstico por imagen en patología mamaria.*

Doctoral candidate: Rosana Medina García

Director(s): Ana Lluch Hernández, José Damián Segrelles Quilis, Luis Marti Bonmati

Date of the defense: 26/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio de la densidad mamográfica como modificador de riesgo de cáncer de mama en mujeres con mutación BRCA1/2.*

Doctoral candidate: Luisa Fernanda Tamayo Orjuela

Director(s): Ana Lluch Hernández

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Evaluación del perfil genómico de la plataforma de investigación basada en pam50 y mirnas en el cáncer de mama en mujeres jóvenes (< 35 años): correlación con parámetros clínicos.*

Doctoral candidate: María Teresa Martínez Martínez

Director(s): Ana Lluch Hernández, Gloria Ribas

Date of the defense: 02/02/2016

Grade: *Sobresaliente "cum laude"*

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI13/01887

Title: *Genomic architecture of triple negative breast cancer. A systems genetics analysis of cancer risk progression and therapeutic response.*

Principal Investigator: Joan Climent Bataller

Funding Body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total Budget: 89.540€

Reference: PI15/01617

Title: *Papel de la heterogeneidad tumoral y la reprogramación dinámica de la célula tumoral en la resistencia a anticuerpos*

antiHER2 en cáncer de mama HER2 positivo.

Principal Investigator: Ana Lluch Hernández

Funding Body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2018

Total Budget: 182.407€

Reference: RD12/0036/0070

Title: *Red Temática de Investigación Cooperativa en Cáncer (RTICC)*

Principal Investigator: Ana Lluch Hernández

Funding Body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2013-2016

Total Budget: 85.728€

Reference: Program VLC-Bioclinic

Title: *Nuevas estrategias dirigidas a pacientes con cáncer de mama con tumores triples negativos.*

Principal Investigator: Ana Lluch Hernández

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015 - 2016

Total Budget: 44.250€

• AWARDS:

In April 2016 Dr. Ana Lluch received the medal of the *Consell Valencià de Cultura (CVC)*, for her contribution and her research in the fight against breast cancer. She received the prize from the President of the *Generalitat*, Ximo Puig, and the president of the CVC, Santiago Grisolia.

Also Dr. Ana Lluch, in representation of INCLIVA, received the R & D prize in Oncology during the gala of delivery of the XI edition of the Best in Class awards, from the Regional Minister of Health of the Valencian Government, Carmen Montón.



Research Group on Skin Cancer Consolidated group



Group members

Principal investigator

José Carlos Monteagudo Castro
Hospital. University
H Index: 23



Collaborating researchers

Antonio Pellín Pérez. University
Esperanza Jordá Cuevas. Hospital. University
David Ramos Soler. Hospital (La Fe). University
José M^a Martín Hernández. Hospital. University
Miguel Martínez Rodríguez. Telemark Hospital, Skien, Noruega
Ana Pellín Carcelén. European University of Valencia
Liria Terrádez Más. Hospital
Verónica López Castillo. Quirón Hospital
Inés Escandell González. Hospital

PhD researchers

Beatriz Sánchez Sendra. INCLIVA
José Francisco González Muñoz. INCLIVA



Strategic aims

- Nuclear CD34 expression by immunohistochemistry is present in primary melanomas which subsequently develop distant metastasis and have a shorter distant-metastasis-free survival. Nuclear location was confirmed in melanoma four cell lines by westernblot.
- After modification of miR-205 expression levels in A375 melanoma cell line, the transcriptomic study revealed 271 genes differentially expressed (FDR<0.05).
- The study of circulating miRNAs as biomarkers in patients with melanoma by NGS of serum RNA revealed that hsa-miR-425-5p is downregulated in serum in melanoma patients which further developed metastasis compared with those who remained nonmetastatic.

Main lines of research

- Expression of epithelial–mesenchymal transition markers and tumor initiating cells (tumorstem cells) in tumor progression of human skin melanoma and in xenotransplantation in immunodeficient mice.
- Epidemiology and genetics of Birt-Hogg-Dubé familial cancer syndrome.
- Implication of certain microRNAs in tumor progression of melanoma.

• PUBLICATIONS

Number of articles	IF	Average IF
15	15,16	1,01

National collaborations	International collaborations	Corresponding author
1	2	13

Original articles

1. **Escandell I**, Cabezas M, **Martín JM**, **Terradez L**, Pinazo MI. Effective treatment with Dabrafenib and Trametinib for a BRAF-mutated metastatic dedifferentiated malignant spindle cell neoplasm. *J Eur Acad Dermatol Venereol*. 2016 Jul; 30(7):1224-6. IF: 2,826
2. Ayala D, Ramón MD, Cabezas M, **Jordá E**. Primary Cutaneous CD4+ Small/Medium-Sized Pleomorphic T-Cell Lymphoma With Expression of Follicular T-Helper Cell Markers and Spontaneous Remission. *Actas Dermosifiliogr*. 2016 May; 107(4):357-359. IF: 0
3. Ayala D, Ramón MD, **Martín JM**, **Jordá E**. Atypical Phacomatosis Pigmentokeratotic as the Expression of a Mosaic RASopathy With the BRAF-Glu586Lys Mutation. *Actas Dermosifiliogr*. 2016 May; 107(4):344-346. IF: 0
4. **Martín JM**, Ruiz-Saurí A, San-Miguel T, **Jorda E**, **Monteagudo C**. Telomeric length heterogeneity influences spontaneous regression of malignant melanoma. *J Eur Acad Dermatol Venereol*. 2016 Dec; 30(12):e223-e224. IF: 2,826
5. Martínez-Ciarpaglini C, **Monteagudo C**. Pigmented desmoplastic trichilemmoma. *J Cutan Pathol*. 2016 Jun; 43(6):535-537. IF: 1,582
6. Cleary IA, Reinhard SM, Lazzell AL, **Monteagudo C**, Thomas DP, Lopez-Ribot JL, Saville SP. Examination of the pathogenic potential of *Candida albicans* filamentous cells in an animal model of haematogenously disseminated candidiasis. *FEMS Yeast Res*. 2016 Mar; 16(2):fow011. IF: 2,818
7. Machado I, **Navarro L**, **Pellin A**, Navarro S, Agaimy A, Tardío JC, Karseladze A, Petrov S, Scotlandi K, Picci P, Lombart-Bosch A. Defining Ewing and Ewing-like small round cell tumors (SRCT): The need for molecular techniques in their categorization and differential diagnosis. A study of 200 cases. *Ann Diagn Pathol*. 2016 Jun; 22:25-32. IF: 1,117
8. Torres C, Revert Á, **Terrádez L**, **Jordá E**. Linear Dermatofibroma. *Actas Dermosifiliogr*. 2016 Nov; 107(9):787-789. IF: 0
9. **Martín JM**, **Escandell I**, Ayala D, **Jordá E**. Spontaneous Remission of Recalcitrant Warts in Girls After Human Papillomavirus Vaccination. *Actas Dermosifiliogr*. 2016 Jul-Aug; 107(6):533-5. IF: 0
10. Ayala D, Ramón MD, Cabezas M, **Jordá E**. Nevus Spilus Associated with Agminated Blue Nevus: A Rare Combination. *Actas Dermosifiliogr*. 2016 Sep; 107(7):614-6. IF: 0
11. **Martín JM**, **Jordá E**, Martín-Gorgojo A, Beteta G, **Monteagudo C**. Histiocytosis with mixed cell populations. *J Cutan Pathol*. 2016 May; 43(5):456-460. IF: 1,582
12. **Martín JM**, Mateo E, **Jordá E**. Azithromycin for the Treatment of Ciclosporin-Induced Gingival Hyperplasia. *Actas Dermosifiliogr*. 2016 Nov; 107(9):780. IF: 0
13. Ayala D, Puglia V, **Jordá E**. Hyperkeratotic Subungual Tumor. *Actas Dermosifiliogr*. 2016 Jul 16 ;. IF: 0



14. Fernandez-Flores A, **Monteagudo C.** Immunoexpression of p53 in cutaneous and subcutaneous leiomyosarcomas. *Ann Diagn Pathol.* 2016 Oct; 24:25-9. IF: 1,022

Letter

15. Martínez-Ciarpaglini C, **Monteagudo C.** Is It a Metastatic Disease: A Case Report and New Understanding of Rosai-Dorfman Disease? *Am J Dermatopathol.* 2016 Nov 23 ; IF: 1,396

• THESIS

Thesis title: *Estudio de la prevalencia de mutaciones en línea germinal (síndrome de birt-hogg-dubé) y somáticas del gen *f1cn* en pacientes con fibrofoliomas o tricodiscomas cutáneos y/o neumotórax recidivantes y/o bilaterales.*

Doctoral candidate: Verónica López Castillo

Director(s): Carlos Monteagudo Castro, Esperanza Jordá Cuevas

Date of the defense: 08/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio de la implicación de los receptores de quimiocinas CXCR3-A y CXCR7 y sus ligandos en la progresión del melanoma cutáneo humano.*

Doctoral candidate: Ana Pellín Carcelén

Director(s): Carlos Monteagudo Castro, Rosario Gil Benso, David Ramos Soler

Date of the defense: 28/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio de la expresión de marcadores de transición epitelio-mesenquimal y de célula madre cancerosa en el melanoma cutáneo, y su asociación con la progresión tumoral.*

Doctoral candidate: Liria Terrádez Más

Director(s): Carlos Monteagudo Castro, Rosario Gil Benso

Date of the defense: 20/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estado mutacional del oncogen N-RAS en melanoma cutáneo como factor pronóstico. Estudio clínico-patológico.*

Doctoral candidate: Paola Fernanda Lara Valencia

Director(s): Carlos Monteagudo Castro

Date of the defense: 10/02/2016

Grade: *Sobresaliente "cum laude"*

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI13/02786

Title: Implication of selected miRNAs in tumor progression of cutaneous malignant melanoma, and their value as prognostic and therapeutic biomarkers.

Principal Investigator: José Carlos Monteagudo Castro

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total Budget: 59.592€

Reference: 16-MELANOMA-MONTEAGUDO-MARTIN-2016-A

Title: *Estudio de la respuesta inmune circulante frente a antígenos de diferenciación melanocítica y su correlación con el estadio clínico en pacientes con melanoma cutáneo.*

Principal Investigator: Carlos Monteagudo Castro, José María Martín Hernández

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2016

Total Budget: 4.000€

Reference: PROMETEO II 2015/009

Title: *Análisis transcriptómico y proteómico de los cambios condicionados por miRNAs en el melanoma cutáneo: identificación de nuevos biomarcadores proteicos con significación pronóstica.*

Principal Investigator: José Carlos Monteagudo Castro

Funding body: *Generalitat Valenciana*

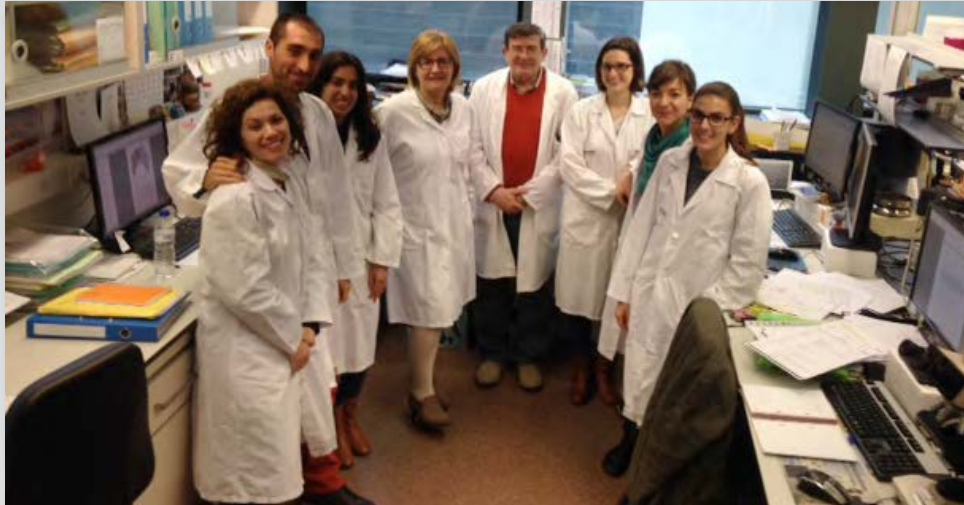
Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2018

Total Budget: 51.100€ (this year)



Translational Research Group on Pediatric Solid Tumours Consolidated group



Los estibadores donan 20.000 euros para investigar tumores infantiles.

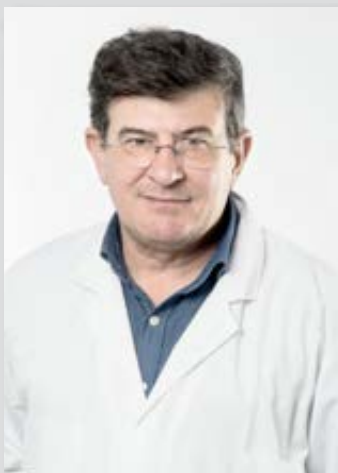
El Levante. 12.04.2016

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Group members

Principal investigator

Samuel Navarro Fos
Hospital. University
H Index: 26



Team involved in



Collaborating researchers

Rosa Noguera Salvá. University
Antonio Llombart Bosch. University
Ana Pilar Berbegall Beltrán. University
Irene Tadeo Cervera. INCLIVA

PhD students

Susana Martín Vañó. University
Víctor Zúñiga Zaragoza. University
Maite Blanquer Maceiras. INCLIVA

Technicians

Alejo Miguel Sempere Crespo. University
Rebeca Brugos Panadero. INCLIVA



Strategic aims

- Heterogeneity in the genomics of neuroblastoma (NB) especially heterogeneous MYCN amplification.
- Value of epigenetics as prognostic factor in NB.
- Xenograft models of NB.
- Relevance of the extracellular matrix and vascularization in NB.
- Morphologic and molecular analysis of rare bone and soft tissue tumors.

Main lines of research

- Analysis of histopathological and genetic prognostic factors in neuroblastoma (NB).
- Development of high-throughput pan-genomic techniques in NB and sarcomas.
- Study of apoptosis, proliferation, angiogenesis and hypoxia in pediatric tumors, soft-tissue sarcomas, skeletogenic tumors and gynecologic mesenchymal tumors.
- ALK as a prognostic factor in NB.
- Identification and isolation of stem cells in NB.
- Establishment and characterization of in vitro and in vivo models of malignant skeletogenic tumors. Cell line extraction in these tumors.
- Expression study of immunohistochemistry and Western blot markers in these tumors in order to identify possible therapeutic targets.
- Study of NB hyperstructure.

• PUBLICATIONS

Number of articles	IF	Average IF
23	92,18	4

National collaborations	International collaborations	Corresponding author
11	11	12

Original articles

1. **Berbegall AP**, Villamón E, Piqueras M, **Tadeo I**, Djos A, Ambros PF, Martinsson T, Ambros IM, Cañete A, Castel V, **Navarro S**, **Noguera R**. Comparative genetic study of intratumoral heterogenous MYCN amplified neuroblastoma versus aggressive genetic profile neuroblastic tumors. *Oncogene*. 2016 Mar 17; 35(11):1423-32. IF: 8,459
2. Decock A, Ongenaert M, Cannoodt R, Verniers K, De Wilde B, Laureys G, Van Roy N, **Berbegall AP**, Bienertova-Vasku J, Bown N, Clément N, Combaret V, Haber M, Hoyoux C, Murray J, **Noguera R**, Pierron G, Schleiermacher G, Schulte JH, Stallings RL, Tweddle DA, Children's Cancer and Leukaemia Group (CCLG), De Preter K, Speleman F, Vandesompele J. Methyl-CpG-binding domain sequencing reveals a prognostic methylation signature in neuroblastoma. *Oncotarget*. 2016 Jan 12; 7(2):1960-72. IF: 6,359
3. Machado I, Chong A, Serrano A, Naranjo Ugalde AM, Pineda D, Savón L, Olivera E, **Llombart-Bosch A**. Epithelioid Heman-gioma (Angiolymphoid Hyperplasia With Eosinophilia) of the Heart With Peripheral Eosinophilia and Nephrotic Syndrome. *Int J Surg Pathol*. 2016 Feb; 24(1):59-65. IF: 0,953
4. Machado I, Cruz J, Lavernia J, **Llombart-Bosch A**. Solitary, multiple, benign, atypical, or malignant: the "Granular Cell Tumor" puzzle. *Virchows Arch*. 2016 May; 468(5):527-38. IF: 2,651
5. Bogen D, Brunner C, Walder D, Ziegler A, Abbasi R, Ladenstein RL, **Noguera R**, Martinsson T, Amann G, Schilling FH, Ussowicz M, Benesch M, Ambros PF, Ambros IM. The genetic tumor background is an important determinant for heterogeneous MYCN-amplified neuroblastoma. *Int J Cancer*. 2016 Jul 1; 139(1):153-63. IF: 5,085
6. Braekeveldt N, Wigerup C, **Tadeo I**, Beckman S, Sandén C, Jönsson J, Erjefält JS, **Berbegall AP**, Börjesson A, Backman T, Øra I, **Navarro S**, **Noguera R**, Gisselsson D, Pålman S, Bexell D. Neuroblastoma patient-derived orthotopic xenografts reflect the microenvironmental hallmarks of aggressive patient tumours. *Cancer Lett*. 2016 Jun 1; 375(2):384-9. IF: 5,621
7. **Berbegall AP**, López-Almaraz R, **Navarro S**, **Noguera R**. Genetic features of neuroblastic tumors associated with opso-clonus-myoclonus syndrome opens up the possibility for detection in peripheral blood. *Expert Rev Neurother*. 2016 May; 16(5):465-7. IF: 2,783
8. Ruiz-Saurí A, Valencia-Villa G, Romanenko A, Pérez J, García R, García H, Benavent J, Sancho-Tello M, Carda C, **Llombart-Bosch A**. Influence of Exposure to Chronic Persistent Low-Dose Ionizing Radiation on the Tumor Biology of Clear-Cell Renal-Cell Carcinoma. *An Immunohistochemical and*



- Morphometric Study of Angiogenesis and Vascular Related Factors. *Pathol Oncol Res.* 2016 Oct; 22(4):807-15. IF: 1,855
9. Ibarrola-Villava M, Fleitas T, Llorca-Cardeñosa MJ, Mongort C, Alonso E, **Navarro S**, Burgues O, Vivancos A, Cejalvo JM, Perez-Fidalgo JA, Roselló S, Ribas G, Cervantes A. Determination of somatic oncogenic mutations linked to target-based therapies using MassARRAY technology. *Oncotarget.* 2016 Apr 19; 7(16):22543-55. IF: 6,359
 10. **Tadeo I**, Bueno G, **Berbegall AP**, Fernández-Carrobles MM, Castel V, García-Rojo M, **Navarro S**, **Noguera R**. Vascular patterns provide therapeutic targets in aggressive neuroblastic tumors. *Oncotarget.* 2016 Apr 12; 7(15):19935-47. IF: 6,359
 11. Machado I, Navarro L, Pellin A, **Navarro S**, Agaimy A, Tardío JC, Karseladze A, Petrov S, Scotlandi K, Picci P, **Llombart-Bosch A**. Defining Ewing and Ewing-like small round cell tumors (SRCT): The need for molecular techniques in their categorization and differential diagnosis. A study of 200 cases. *Ann Diagn Pathol.* 2016 Jun; 22:25-32. IF: 1,117
 12. Jubierre L, Soriano A, Planells-Ferrer L, París-Coderch L, Tenbaum SP, Romero OA, Moubarak RS, Almazán-Moga A, Molist C, Roma J, **Navarro S**, **Noguera R**, Sánchez-Céspedes M, Comella JX, Palmer HG, Sánchez de Toledo J, Gallego S, Segura MF. BRG1/SMARCA4 is essential for neuroblastoma cell viability through modulation of cell death and survival pathways. *Oncogene.* 2016 Sep 29; 35(39):5179-90. IF: 8,459
 13. Berlanga P, Muñoz L, Piqueras M, Sierrol JA, Sánchez-Izquierdo MD, Hervás D, Hernández M, Llavador M, Machado I, **Llombart-Bosch A**, Cañete A, Castel V, Font de Mora J. miR-200c and phospho-AKT as prognostic factors and mediators of osteosarcoma progression and lung metastasis. *Mol Oncol.* 2016 Aug; 10(7):1043-53. IF: 5,331
 14. Machado I, Arana E, Cruz J, Brotons S, Vendrell J, Escriba I, Chust ML, Martínez-Banaclocha N, Lavernia J, **Llombart-Bosch A**. Malignant Peripheral Nerve Sheath Tumor With Osseous Heterologous Differentiation in Uncommon Locations (Heart and Retropharynx). *Int J Surg Pathol.* 2016 Aug; 24(5):456-62. IF: 0,953
 15. **Tadeo I**, **Berbegall AP**, Castel V, García-Miguel P, Callaghan R, Pählman S, **Navarro S**, **Noguera R**. Extracellular matrix composition defines an ultra-high-risk group of neuroblastoma within the high-risk patient cohort. *Br J Cancer.* 2016 Aug 9; 115(4):480-9. IF: 5,569
 16. **Berbegall AP**, **Navarro S**, **Noguera R**. Diagnostic implications of intrapatient genetic tumor heterogeneity. *Mol Cell Oncol.* 2016 Mar; 3(2):e1079671. IF: 0
 17. Llorca-Cardeñosa MJ, Fleitas T, Ibarrola-Villava M, Peña-Chilet M, Mongort C, Martínez-Ciarpaglini C, Navarro L, Gambardella V, Castillo J, Roselló S, **Navarro S**, Ribas G, Cervantes A. Epigenetic changes in localized gastric cancer: the role of RUNX3 in tumor progression and the immune microenvironment. *Oncotarget.* 2016 Sep 27; 7(39):63424-63436. IF: 5,008
 18. Decock A, Ongenaert M, De Wilde B, Brichard B, **Noguera R**, Speleman F, Vandesompele J. Stage 4S neuroblastoma tumors show a characteristic DNA methylation portrait. *Epigenetics.* 2016 Sep 6 ;0. IF: 4,774
 19. Machado I, **Navarro S**, Picci P, **Llombart-Bosch A**. The utility of SATB2 immunohistochemical expression in distinguishing between osteosarcomas and their malignant bone tumor mimickers, such as Ewing sarcomas and chondrosarcomas. *Pathol Res Pract.* 2016 Sep; 212(9):811-6. IF: 1,388
 20. Machado I, López-Soto MV, Pérez-López AS, Domínguez-Álvarez C, **Llombart-Bosch A**. Hyaline globules and papillary fragments in cytologic smears from two intra-abdominal tumors (ovarian and hepatic) in female patients: A diagnostic pitfall with histologic correlation. *Diagn Cytopathol.* 2016 Nov; 44(11):935-943. IF: 0,98
 21. Gronchi A, Stacchiotti S, Verderio P, Ferrari S, Martin Broto J, Lopez-Pousa A, **Llombart-Bosch A**, Dei Tos AP, Collini P, Jurado JC, De Paoli A, Donati DM, Poveda A, Quagliuolo V, Comandone A, Grignani G, Morosi C, Messina A, De Sanctis R, Bottelli S, Palassini E, Casali PG, Picci P. Short, full-dose adjuvant chemotherapy (CT) in high-risk adult soft tissue sarcomas (STS): long-term follow-up of a randomized clinical trial from the Italian Sarcoma Group and the Spanish Sarcoma Group. *Ann Oncol.* 2016 Dec; 27(12):2283-2288. IF: 9,269
- Letter**
22. Machado I, Lavernia J, Illueca C, Salazar C, Mengual JL, **Llombart-Bosch A**. Histologic transformation to diffuse large B cell lymphoma with profuse signet-ring cell change in bone marrow and lymph node biopsies in a patient with marginal zone lymphoma. A cytologic-histologic correlation. *Diagn Cytopathol.* 2016 Oct; 44(10):860-3. IF: 0,98



Review

23. Machado I, Navarro S, Lombart-Bosch A. Ewing sarcoma and the new emerging Ewing-like sarcomas: (CIC and BCOR-rearranged-sarcomas). A systematic review. *Histol Histopathol.* 2016 Nov; 31(11):1169-81. IF: 1,875

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: RD12/0036/0020

Title: Red temática de investigación cooperativa en cáncer (RTICC).

Principal Investigator: Samuel Navarro Fos

Funding body: Instituto de Salud Carlos III

Beneficiary institution: Universidad de Valencia

Duration: 2013-2016

Total budget: 73.000€

Title: Prospective Validation of alterations in 1q and 16q as Biomarkers in Ewing Sarcoma.

Principal Investigator: Enrique de Álava Casado (Rosa Noguera and Samuel Navarro as collaborating researchers)

Funding body: Fundación CRIS-FISEVI

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2013-2016

Total budget: 67.500€

Reference: PI14/01008

Title: Estudio de la biotensegridad en los tumores neuroblásticos.

Principal Investigator: Rosa Noguera

Funding body: Ministerio de Economía y Competitividad

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2015-2017

Total budget: 122.815€

Reference: 261474

Title: European network for cancer in children and adolescent (ENCCA).

Principal Investigator: Rosa Noguera

Funding Body: European Commission

Beneficiary Institution: Universidad de Valencia

Duration: 2011-2016

Total budget: 11.997.958€

Reference: FAECC2015.

Title: Búsqueda de dianas terapéuticas en los puntos de contacto de la célula tumoral en el neuroblastoma infantil con su matriz extracelular.

Principal Investigator: Rosa Noguera

Funding Body: AECC-Asociación Española Contra el Cáncer

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2015-2018

Total budget: 150.000€

Reference: VLC-Biomed A/HetMNA (2015/0760)

Title: Detection of circulating tumor DNA in child patients with MYCN oncogene amplification heterogeneous in their neuroblastic tumors (2016-2016).

Principal Investigator: Rosa Noguera, Adela Cañete

Funding Body: Fundación de Investigación Sanitaria La Fe

Beneficiary Institution: Universidad de Valencia/ Fundación de Investigación Sanitaria La Fe

Duration: 2016

Total budget: 4.000€

Reference: 04-CAPABLE-NOGUERA-CERVANTES-2016B

Title: Heterogeneidad clonal en cáncer: biopsia líquida como tecnología de alto rendimiento.

Principal Investigator: Andrés Cervantes, Rosa Noguera

Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2017

Total budget: 6.000€

Reference: PRECIPITA 2016

Title: Mejora del diagnóstico de tumores infantiles por bioimagen.

Principal Investigator: Rosa Noguera

Funding body: Fundación Española para la Ciencia y Tecnología (FECYT)

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia / Universidad de Valencia

Duration: 2016 - 2017

Total budget: 33.070€



Reference: Asociación NEN 2016

Title: *Análisis mediante la técnica de aSNP de las modificaciones del DNA en los tumores neuroblásticos.*

Principal Investigator: Rosa Noguera

Funding body: *Asociación NEN 2016*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia / Universidad de Valencia*

Duration: 2016

Total budget: 13.700€

Reference: INCLIVA, Lab. Molecular.34

Title: Molecular Laboratory Research Unit.

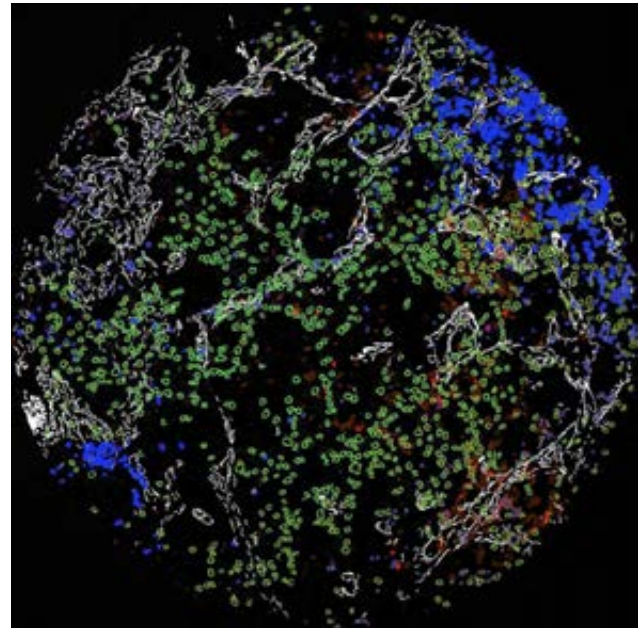
Principal Investigator: Rosa Noguera

Funding body: *Teaming - Un granito de arena*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia/ Universidad de Valencia*

Duration: 2016

Total budget: 700€



Overlapping images obtained after staining a tumor sample of neuroblastoma with different histochemical and immunohistochemical markers, in order to perform topological studies. Legend: CD163 + (green), CD45 + (blue), CD11c + (purple), CD8 + (red) and reticulin fibers of the matrix (white) Cells.



Research Group on Hematopoietic Transplantation

Consolidated group



Group members

Principal investigator

Carlos Solano Vercet
Hospital. University
H Index: 26

Collaborating researchers

Cristina Arbona Castaño. Hospital
María José Remigia Pellicer. Hospital
Rosa Goterris Vicedo. Hospital
David Navarro Ortega. Hospital. University
Joana Hernández Martín. INCLIVA
Paula Amat Martínez. Hospital
Estela Giménez Quiles. Hospital
Marc Poch Martell. Hospital
Ariadna Pérez Martínez. Hospital
Ana Isabel Usero Ruiz. INCLIVA



Strategic aims

- Translational research of biology and treatment of graft versus host disease after allogeneic transplantation of hematopoietic progenitor cells.
- Infection and immune reconstitution after hematopoietic transplantation.
- Investigation of alloreactivity in new forms of allogeneic transplantation from compatible and incompatible alternative donors (haploidentical).

Main lines of research

- Translational research on complications of allogeneic hematopoietic transplantation: graft-versus-host disease.
- Infection and immune reconstitution after hematopoietic transplantation.
- Translational research of alloreactivity in the context of new modalities of allogeneic transplantation from compatible and incompatible alternative donors (haploidentical transplant).

• PUBLICATIONS

Number of articles	IF	Average IF
26	250,92	9,65
National collaborations	International collaborations	Corresponding author
10	6	14

Original articles

1. Piñana JL, Sanz J, Esquirol A, Martino R, Picardi A, Barba P, Parody R, Gayoso J, Montesinos P, Guidi S, Terol MJ, Moscardó F, **Solano C**, Arcese W, Sanz MA, Sierra J, Sanz G, GETH GITMO groups. Umbilical cord blood transplantation in adults with advanced Hodgkin's disease: high incidence of post-transplant lymphoproliferative disease. *Eur J Haematol*. 2016 Feb; 96(2):128-35. IF: 2,066
2. González-Gascón Y Marín I, Hernández-Sánchez M, Rodríguez-Vicente AE, Sanzo C, Aventín A, Puiggros A, Collado R, Heras C, Muñoz C, Delgado J, Ortega M, González MT, Marugán I, de la Fuente I, Recio I, Bosch F, Espinet B, González M, Hernández-Rivas JM, Hernández JÁ, Grupo Español de Leucemia Linfática Crónica (GELLC), Grupo Cooperativo Español de Citogenética Hematológica (**GCECGH**). A high proportion of cells carrying trisomy 12 is associated with a worse outcome in patients with chronic lymphocytic leukemia. *Hematol Oncol*. 2016 Jun; 34(2):84-92. IF: 3,084
3. Piñana JL, Serra MÁ, Hernández-Boluda JC, **Navarro D**, Calabuig M, **Solano C**. Successful treatment of hepatitis C virus infection with sofosbuvir and simeprevir in the early phase of an allogeneic stem cell transplant. *Transpl Infect Dis*. 2016 Feb; 18(1):89-92. IF: 2,064
4. Kröger N, **Solano C**, Wolschke C, Bandini G, Patriarca F, Pini M, Nagler A, Selleri C, Risitano A, Messina G, Bethge W, Pérez de Oteiza J, Duarte R, Carella AM, Cimminiello M, Guidi S, Finke J, Mordini N, Ferra C, Sierra J, Russo D, Petrini M, Milone G, Benedetti F, Heinzelmann M, Pastore D, Jurado M, Terruzzi E, Narni F, Völp A, Ayuk F, Ruutu T, Bonifazi F. Antilymphocyte Globulin for Prevention of Chronic Graft-versus-Host Disease. *N Engl J Med*. 2016 Jan 7; 374(1):43-53. IF: 55,873
5. **Solano C**, **Giménez E**, Piñana JL, Vinuesa V, Poujois S, Zaragoza S, Calabuig M, **Navarro D**. Preemptive antiviral therapy for CMV infection in allogeneic stem cell transplant recipients guided by the viral doubling time in the blood. *Bone Marrow Transplant*. 2016 May; 51(5):718-21. IF: 3,57
6. Orti G, Sanz J, Bermudez A, Caballero D, Martínez C, Sierra J, Cabrera Marin JR, Espigado I, **Solano C**, Ferrà C, García-Noblejas A, Jimenez S, Sampol A, Yañez L, García-Gutiérrez V, Pascual MJ, Jurado M, Moraleda JM, Valcarcel D, Sanz MA, Carreras E, Duarte RF. Outcome of Second Allogeneic Hematopoietic Cell Transplantation after Relapse of Myeloid Malignancies following Allogeneic Hematopoietic Cell Transplantation: A Retrospective Cohort on Behalf of the Grupo Español de Trasplante Hematopoyetico. *Biol Blood Marrow Transplant*. 2016 Mar; 22(3):584-8. IF: 3,404
7. Vinuesa V, **Navarro D**, Poujois S, Zaragoza S, Borrás R. Performance characteristics of the new Abbott Real Time MTB assay for detection of Mycobacterium tuberculosis complex in respiratory specimens. *Diagn Microbiol Infect Dis*. 2016 Mar; 84(3):212-4. IF: 2,457
8. Di Minno G, Perno CF, Tiede A, **Navarro D**, Canaro M, Güertler L, Ironside JW. Current concepts in the prevention of pathogen transmission via blood/plasma-derived products for bleeding disorders. *Blood Rev*. 2016 Jan; 30(1):35-48. IF: 5,565



9. Falcón R, Martínez A, Albert E, Madrid S, Oltra R, **Giménez E**, Soriano M, Vinuesa V, Gozalbo D, Gil ML, **Navarro D**. High vancomycin MICs within the susceptible range in *Staphylococcus aureus* bacteraemia isolates are associated with increased cell wall thickness and reduced intracellular killing by human phagocytes. *Int J Antimicrob Agents*. 2016 May; 47(5):343-50. IF: 4,296
10. Santamaria X, Cabanillas S, Cervelló I, **Arbona C**, Raga F, Ferro J, Palmero J, Remohí J, Pellicer A, Simón C. Autologous cell therapy with CD133+ bone marrow-derived stem cells for refractory Asherman's syndrome and endometrial atrophy: a pilot cohort study. *Hum Reprod*. 2016 May; 31(5):1087-96. IF: 4,569
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14. **Navarro D**, **Amat P**, de la Cámara R, López J, Vázquez L, Serrano D, Nieto J, Rovira M, Piñana JL, **Giménez E**, **Solano C**. Efficacy and Safety of a Preemptive Antiviral Therapy Strategy Based on Combined Virological and Immunological Monitoring for Active Cytomegalovirus Infection in Allogeneic Stem Cell Transplant Recipients. *Open Forum Infect Dis*. 2016 Apr; 3(2):ofw107. IF: 0
15. Kekre N, Marquez-Malaver FJ, Cabrero M, Piñana J, Esquirol A, Soiffer RJ, Caballero D, Terol MJ, Martino R, Antin JH, Lopez-Corral L, **Solano C**, Armand P, Pérez-Simon JA. Fludarabine/Busulfan versus Fludarabine/Melphalan Conditioning in Patients Undergoing Reduced-Intensity Conditioning Hematopoietic Stem Cell Transplantation for Lymphoma. *Biol Blood Marrow Transplant*. 2016 Oct; 22(10):1808-15. IF: 3,98
16. Vinuesa V, **Solano C**, **Giménez E**, Piñana JL, Boluda JC, **Amat P**, **Navarro D**. Lack of evidence for a reciprocal interaction between bacterial and cytomegalovirus infection in the allogeneic stem cell transplantation setting. *Transpl Int*. 2016 Nov; 29(11):1196-1204. IF: 2,835
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19. Peyvandi F, Scully M, Kremer Hovinga JA, Cataland S, Knöbl P, Wu H, Artoni A, Westwood JP, Mansouri Taleghani M, Jilma B, Callewaert F, Ulrichs H, DUBY C, Tersago D, **TITAN Investigators**. Caplacizumab for Acquired Thrombotic Thrombocytopenic Purpura. *N Engl J Med*. 2016 Feb 11; 374(6):511-22. IF: 59,558
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Study Group. Contribution of Candida biomarkers and DNA detection for the diagnosis of invasive candidiasis in ICU patients with severe abdominal conditions. *Crit Care*. 2016 May 16; 20(1):149. IF: 0

Review

22. **Navarro D.** Expanding role of cytomegalovirus as a human pathogen. *J Med Virol*. 2016 Jul; 88(7):1103-12. IF: 2,347
23. Blanco-Lobo P, Bulnes-Ramos Á, McConnell MJ, **Navarro D**, Pérez-Romero P. Applying lessons learned from cytomegalovirus infection in transplant patients to vaccine design. *Drug Discov Today*. 2016 Apr; 21(4):674-81. IF: 6,691

Letters

24. **Giménez E**, **Solano C**, Piñana JL, **Amat P**, Vinuesa V, **Navarro D.** Re-examining the relationship between active cytomegalovirus (CMV) infection and acute graft-versus-host disease in allogeneic stem cell transplant recipients in the era of real-time PCR CMV assays. *Transpl Int*. 2016 Jan; 29(1):126-8. IF: 2,599
25. Aguilar G, Ferriols R, Carbonell JA, Ezquer C, Alonso JM, Villena A, Puig J, **Navarro D**, Alós M, Belda FJ. Pharmacokinetics of anidulafungin during venovenous extracorporeal membrane oxygenation. *Crit Care*. 2016 Oct 17; 20(1):325. IF: 0
26. Kröger N, **Solano C**, Bonifazi F. Antilymphocyte Globulin for Chronic Graft-versus-Host Disease. *N Engl J Med*. 2016 May 12; 374(19):1894-5. IF: 59,558

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI15/00090

Title: *Inmunobiología de la infección por el citomegalovirus en el trasplante alogénico de precursores hematopoyéticos haploideéntico asociado al uso de ciclofosfamida postrasplante.*

Principal Investigator: David Navarro Ortega

Funding body: Instituto de Salud Carlos III

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016 - 2018

Total budget: 98.615€

Reference: PI15/01396

Title: *Inmunobiología de la aloreactividad NK en el trasplante de progenitores hematopoyéticos haploideénticos asociado al uso de ciclofosfamida post-trasplante.*

Principal Investigator: Carlos Solano Vercet

Funding body: Instituto de Salud Carlos III

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016 - 2018

Total budget: 116.765€

• THESIS

Thesis title: *Infección por el citomegalovirus (CMV) en el paciente trasplantado de progenitores hematopoyéticos: investigación de nuevos factores biológicos para la estimación del riesgo y análisis integral de los mecanismos inmunitarios que previenen y controlan.*

Doctoral candidate: Estela Berenice Giménez Quiles

Director(s): David Navarro

Date of the defense: 09/03/2016

Grade: Sobresaliente "cum laude"

Thesis title: *Influencia de los polimorfismos genéticos en la leucemia mieloide crónica.*

Doctoral candidate: Paula Amat Martínez

Director(s): Carlos Solano, Juan Carlos Hernández, Vicente Martín

Date of the defense: 26/01/2016

Grade: Sobresaliente "cum laude"

Thesis title: *Factores predictores de respuesta a los tratamientos de inmunotolerancia en pacientes hemofílicos a con inhibidores.*

Doctoral candidate: Saturnino Haya Guaita

Director(s): Carlos Solano

Date of the defense: 09/02/2016

Grade: Sobresaliente "cum laude"

Thesis title: *Fracaso renal agudo en el trasplante de progenitores hematopoyéticos: análisis de la incidencia, factores de riesgo e implicaciones pronósticas, valor pronóstico y en el diagnóstico precoz de la cistacina C plasmática.*

Doctoral candidate: Miguel Angel Solís Salguero

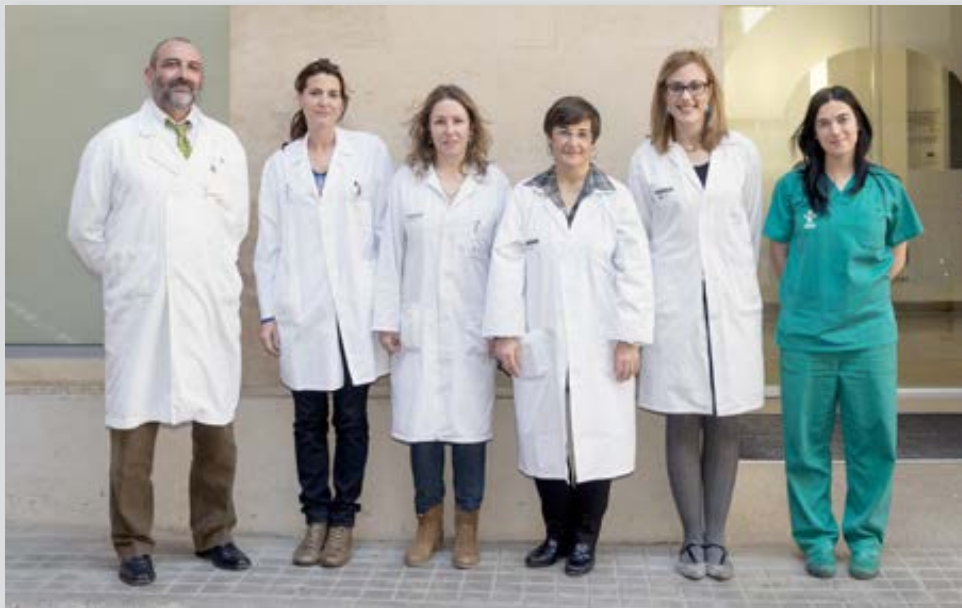
Director(s): Carlos Solano, Juan Carlos Hernández, Isidro Torregrosa

Date of the defense: 08/02/2016

Grade: Sobresaliente "cum laude"



Research Group on Lymphoproliferative Disorders Consolidated group



Group members

Principal investigator

Mª José Terol Casterá
Hospital. University
H Index: 26

Collaborating researchers

Antonio Ferrández Izquierdo. Hospital. University
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Lucía Brines Sirerol. INCLIVA
Blanca Ferrer Loes. INCLIVA
Ariadna Pérez Martínez. Hospital
Alicia Serrano. INCLIVA
Estefanía Martínez Albert. UV
Marta Melia Prades. UPV



Strategic aims

- During the year 2016, we were able to deepen the knowledge of the role of the NOTCH1 / FBXW7 / PI3K / PTEN / AKT signaling pathway in the progression of Chronic Lymphocytic Leukemia B (CLL-B) to advanced forms. Thus, in the cell lines and in the patient's primary cells, we observed a variation in the number of gene copies by both FISH and PCRq in the NOTCH1, FBXW7 and PTEN genes, with an inverse relationship between NOTCH1 and FBXW7 / PTEN.
- A second objective has been to analyze the clinical significance of the rearrangements of myc, bcl-2 and bcl-6 in diffuse large cell lymphoma. We have been able to verify that patients with concomitant c-myc and bcl-2 protein expression present a worse prognosis in terms of SLP and Sg than the rest.
- Thirdly, during 2016, the study of the mutational status of IgVH in CLL and its prognostic impact in a wide series of patients has been implemented. New molecular markers (mutations TP53, BIRC3, MYD88, NOTCH1 and SF3B1) have also been studied in CLL by new generation sequencing techniques. In addition, we have continued the collaboration in the GENOMA CLL sequencing project, with a clinical-evolutionary update.
- Finally, we have expanded our participation in clinical research projects in CLL, refractory lymphomas and multiple myeloma, both with the incorporation of new drugs and in the design and development of new therapeutic options.

Main lines of research

- Analysis of the interactions of CLL cells with their cellular microenvironment: further study of the intracellular mechanisms triggered by VEGF. Analysis of the possible correlation with CXCR4/CCR7 cytokines pathway. Transactivation mechanisms of the aforementioned receptors.
- Role of the NOTCH1 / FBXW7 / PI3K / PTEN / AKT signaling pathway in the progression of Chronic Lymphocytic Leukemia B (CLL-B) to advanced forms: pathway molecular profile analysis in 100 patients with CLL-B of primary cells obtained at diagnosis and at the time of the progression, analyzing for this, the presence of mutations and number of copies of DNA, gene expression, FISH and (RT-PCR).

- Study of the rearrangements of bcl-2, bcl-6 and myc in diffuse large cell lymphoma: clinical significance and correlation with immunohistochemical expression using FISH and IHQ techniques.
- Study of new molecular markers (mutations of IgVH, TP53, BIRC3, MYD88, NOTCH1 and SF3B1) in CLL: conventional versus NGS techniques. Implication in clonal evolution associated with tumor progression.
- New therapeutic options for CLL/MM patients who are resistant to chemoimmunotherapy.

• PUBLICATIONS

Number of articles	IF	Average IF
11	77,07	7
National collaborations	International collaborations	Corresponding author
7	2	2

Original articles

1. Piñana JL, Sanz J, Esquirol A, Martino R, Picardi A, Barba P, Parody R, Gayoso J, Montesinos P, Guidi S, **Terol MJ**, Moscardó F, Solano C, Arcese W, Sanz MA, Sierra J, Sanz G, GETH GITMO groups. Umbilical cord blood transplantation in adults with advanced hodgkin's disease: high incidence of post-transplant lymphoproliferative disease. *Eur J Haematol.* 2016 Feb; 96(2):128-35. IF: 2,066
2. Mateos MV, Martínez-López J, Hernández MT, Ocio EM, Rosiñol L, Martínez R, **Teruel AI**, Gutiérrez NC, Martín Ramos ML, Oriol A, Bargay J, Bengoechea E, González Y, Pérez de Oteyza J, Gironella M, Encinas C, Martín J, Cabrera C, Paiva B, Cedena MT, Puig N, Bladé J, Lahuerta JJ, San-Miguel J. Sequential vs alternating administration of VMP and Rd in elderly patients with newly diagnosed MM. *Blood.* 2016 Jan 28; 127(4):420-5. IF: 10,452
3. Paiva B, Mateos MV, Sanchez-Abarca LI, Puig N, Vidriales MB, López-Corral L, Corchete LA, Hernandez MT, Bargay J, de Arriba F, de la Rubia J, **Teruel AI**, Giraldo P, Rosiñol L, Prosper F, Oriol A, Hernández J, Esteves G, Lahuerta JJ, Bladé J, Perez-Simon JA, San Miguel JF, Grupo Español de Mieloma/Programa de Estudio y Tratamiento de las Hemopatías Malignas cooperative study groups. Immune status of high-risk smoldering multiple myeloma patients and its therapeutic modulation under LenDex: a longitudinal



- analysis. *Blood*. 2016 Mar 3; 127(9):1151-62. IF: 10,452
4. Montesinos P, Cabrero M, Valcárcel D, Rovira M, García-Marco JA, Loscertales J, Moreno C, Duarte R, **Terol MJ**, Villamor N, Abrisqueta P, Caballero D, Sanz J, Delgado J. The addition of ofatumumab to the conditioning regimen does not improve the outcome of patients with high-risk CLL undergoing reduced intensity allogeneic haematopoietic cell transplantation: a pilot trial from the GETH and GELLC (CLL4 trial). *Bone Marrow Transplant*. 2016 Oct; 51(10):1404-1407. IF: 3,57
 5. Martínez C, Díaz-López A, Rodríguez-Calvillo M, García-Sanz R, **Terol MJ**, Pérez-Ceballos E, Jiménez MJ, Cantalapiedra A, Domingo-Domenech E, Rodríguez MJ, Sampol A, Espeso M, López FJ, Briones J, García JF, Sureda A, Hodgkin Lymphoma Subcommittee of Spanish Group of Lymphoma Bone Marrow Transplantation (GELTAMO). Phase II trial of ofatumumab plus ESHAP (O-ESHAP) as salvage treatment for patients with relapsed or refractory classical Hodgkin lymphoma after first-line chemotherapy. *Br J Haematol*. 2016 Sep; 174(6):859-67. IF: 4,971
 6. Nadeu F, Delgado J, Royo C, Baumann T, Stankovic T, Pinyol M, Jares P, Navarro A, Martín-García D, Beà S, Salaverria I, Oldreive C, Aymerich M, Suárez-Cisneros H, Rozman M, Villamor N, Colomer D, López-Guillermo A, González M, Alcoceba M, **Terol MJ**, Colado E, Puente XS, López-Otín C, Enjuanes A, Campo E. Clinical impact of clonal and subclonal TP53, SF3B1, BIRC3, NOTCH1, and ATM mutations in chronic lymphocytic leukemia. *Blood*. 2016 Apr 28; 127(17):2122-30. IF: 10,452
 7. Paiva B, Cedena MT, Puig N, Arana P, Vidriales MB, Cordon L, Flores-Montero J, Gutierrez NC, Martín-Ramos ML, Martínez-Lopez J, Ocio EM, Hernandez MT, **Teruel AI**, Rosiñol L, Echeveste MA, Martínez R, Gironella M, Oriol A, Cabrera C, Martín J, Bargay J, Encinas C, Gonzalez Y, Van Dongen JJ, Orfao A, Bladé J, Mateos MV, Lahuerta JJ, San Miguel JF, Grupo Español de Mieloma/Programa para el Estudio de la Terapéutica en Hemopatías Malignas (GEM/PETHEMA) Cooperative Study Groups. Minimal residual disease monitoring and immune profiling in multiple myeloma in elderly patients. *Blood*. 2016 Jun 23; 127(25):3165-74. IF: 10,452
 8. Robles EF, Mena-Varas M, Barrio L, Merino-Cortes SV, Balogh P, Du MQ, Akasaka T, Parker A, Roa S, Panizo C, Martín-Guerrero I, Siebert R, Segura V, Agirre X, Macri-Pellizeri L, Aldaz B, Vilas-Zornoza A, Zhang S, Moody S, Calasanz MJ, Tousseyn T, Broccardo C, Brousset P, Campos-Sanchez E, Cobaleda C, Sanchez-Garcia I, Fernandez-Luna JL, Garcia-Muñoz R, Pena E, Bellosillo B, Salar A, Baptista MJ, Hernandez-Rivas JM, Gonzalez M, **Terol MJ**, Climent J, Ferrandez A, Sagaert X, Melnick AM, Prosper F, Oscier DG, Carrasco YR, Dyer MJ, Martinez-Climent JA. Homeobox NKX2-3 promotes marginal-zone lymphomagenesis by activating B-cell receptor signalling and shaping lymphocyte dynamics. *Nat Commun*. 2016 Jun 14; 7:11889. IF: 11,329
 9. Kekre N, Marquez-Malaver FJ, Cabrero M, Piñana J, Esquirol A, Soiffer RJ, Caballero D, **Terol MJ**, Martino R, Antin JH, Lopez-Corral L, Solano C, Armand P, Pérez-Simon JA. Fludarabine/Busulfan versus Fludarabine/Melphalan Conditioning in Patients Undergoing Reduced-Intensity Conditioning Hematopoietic Stem Cell Transplantation for Lymphoma. *Biol Blood Marrow Transplant*. 2016 Oct; 22(10):1808-15. IF: 3,98
 10. Núñez J, **Teruel A**, Quiñones-Torrel C, García-Blas S, Carratalá A, Miñana G, Santas E, Torregrosa I, Solano C, González M. Continuous ambulatory peritoneal dialysis as a promising therapy for light chain amyloidosis with congestive heart failure. *Int J Cardiol*. 2016 Aug 20; 223:807-809. IF: 4,638
- Letter**
11. Ocio EM, Oriol A, Bladé J, **Teruel AI**, Martín J, de la Rubia J, Gutiérrez NC, Rodríguez Díaz-Pavón J, Martínez González S, Coronado C, Fernández-García EM, Sigüero Gómez M, Fernández-Teruel C, San Miguel J. Phase I/II study of weekly PM00104 (Zalypsis®) in patients with relapsed/refractory multiple myeloma. *Br J Haematol*. 2016 Feb; 172(4):625-8. IF: 4,711

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI14/01781

Title: *Papel de la vía de señalización NOTCH1/FBXW7/PI3K/P TEN/AKT en la progresión de la Leucemia Linfocítica Crónica B (LLC-B) a formas avanzadas.*

Principal Investigator: M^º José Terol Casterá

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total Budget: 67.000€



Title: *Estudio de nuevos marcadores moleculares (mutaciones IgVH, TP53, BIRC3, MYD88, NOTCH1 y SF3B1) en la Leucemia Linfática Crónica-B (LLC-B): técnicas convencionales versus NGS (Next Generation Sequencing). Implicación en la evolución clonal asociada a la progresión tumoral.*

Principal Investigator: Blanca Ferrer Lores

Funding Body: *Sociedad Española de Hematología y Hemoterapia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2018

• THESIS

Thesis title: *Papel de los receptores angiogénicos del VEGF en la apoptosis y migración celular de la leucemia linfática crónica-b. Correlación con los receptores de quimiocinas CXCR4, CCR7 Y CD49d y las características clínicas de los pacientes.*

Doctoral candidate: Sandra Ballester García

Director(s): M^a José Terol, Pilar Eroles, Antonio Ferrández

Date of the defense: 03/02/2016

Grade: *Sobresaliente "cum laude"*



Research Group on Myeloid Neoplasms Consolidated group



<http://www.Esmo.Org/Profiles/Juan-Carlos-Hernandez-Boluda>

Group members

Principal investigator

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Collaborating researchers

Blanca Navarro Cubells. Hospital
Marisa Calabuig Muñoz. Hospital
Montserrat Gómez Calafaz. Hospital
Eva Villamon Ribate. INCLIVA
Elena Fernández Pons. Hospital

PhD researchers

Iván Martín Castillo. INCLIVA

Emerging researcher

Juan Carlos Hernández Boluda. Hospital





Strategic aims

- We have studied the expression of VEGF-C gene in bone marrow samples of adult acute myeloid leukemia “de novo” patients and its relationship with several clinical, cytogenetic and molecular variables with established prognostic value, as well as the rate of complete remission (CR), overall survival (OS) and event free survival (EFS). We also study expression of 84 genes involved in VEGF signaling in AML patients, through microarray technology. The results have been submitted to a scientific journal for publication.
- We have studied the role of the RUNX1 / CBF-beta / p300 / HIPK2 complex in the leukemic progression of chronic myeloproliferative malignancies.
- We are assessing the predictive value of DNMT3A and IDH1 / IDH2 mutations in the azacytidine response in a number of patients with myeloid neoplasms. Preliminary results will be presented at the next international meeting of myelodysplastic syndromes in May of 2017.

Main lines of research

- Studies of new biological prognostic factors in acute myelogenous leukemia.
- Studies of mutations of DNA methylation genes as biomarkers for response of hypomethylating agent used to treat high-risk myelodysplastic syndromes and acute myeloid leukemia in patients who are not eligible for intensive strategies.
- Study of factors influencing the risk of thrombosis in Philadelphia-negative myeloproliferative disorders.
- Study of mechanisms involved in the leukemic progression of chronic myeloproliferative neoplasms.
- Clinical guidelines for diagnosis, prognosis and treatment of myelodysplastic syndromes.
- Clinical guidelines for assessment of response in chronic myeloid leukemia.
- Studies within the CETLAM registry.
- Studies within the PETHEMA registry.
- Studies within the Spanish Registry of Myelofibrosis.
- Spanish within the registry of Myelodysplastic syndromes.



Emerging researcher

Juan Carlos Hernández Boluda

The research is focused on the molecular mechanisms involved in the progression of the chronic myeloproliferative neoplasms from the chronic phase to the leukemic phase.

• PUBLICATIONS

Number of articles	IF	Average IF
25	112,56	4,50

National collaborations	International collaborations	Corresponding author
16	6	9

Original articles

1. **Gómez M**, Guillem V, Pereira A, Ferrer-Marín F, Álvarez-Larrán A, Kerguelen A, Estrada N, Martínez-López J, Angona A, Amat P, **Navarro B**, Besses C, **Hernández-Boluda JC**. Risk factors for non-melanoma skin cancer in patients with essential thrombocythemia and polycythemia vera. *Eur J Haematol*. 2016 Mar; 96(3):285-90. IF: 2,066
2. Berbegall AP, **Villamón E**, Piqueras M, Tadeo I, Djos A, Ambros PF, Martinsson T, Ambros IM, Cañete A, Castel V, Navarro S, Noguera R. Comparative genetic study of intratumoral heterogenous MYCN amplified neuroblastoma versus aggressive genetic profile neuroblastic tumors. *Oncogene*. 2016 Mar 17; 35(11):1423-32. IF: 8,459
3. **Hernández-Boluda JC**, Martínez-Trillos A, García-Gutiérrez V, Ferrer-Marín F, Xicoy B, Alvarez-Larrán A, Kerguelen A, Barba P, Gómez M, Herrera JC, Correa JG, Cervantes F. Long-term results of prednisone treatment for the anemia of myelofibrosis. *Leuk Lymphoma*. 2016 Jan; 57(1):120-4. IF: 2,891
4. Piñana JL, Serra MÁ, **Hernández-Boluda JC**, Navarro D, **Calabuig M**, Solano C. Successful treatment of hepatitis C virus infection with sofosbuvir and simeprevir in the early phase of an allogeneic stem cell transplant. *Transpl Infect Dis*. 2016 Feb; 18(1):89-92. IF: 2,064
5. Solano C, Giménez E, Piñana JL, Vinuesa V, Poujois S, Zaragoza S, **Calabuig M**, Navarro D. Preemptive antiviral therapy for CMV infection in allogeneic stem cell transplant recipients guided by the viral doubling time in the blood. *Bone Marrow Transplant*. 2016 May; 51(5):718-21. IF: 3,57



6. Ramos F, Pedro C, **Tormo M**, de Paz R, Font P, Luño E, Caballero M, Solano F, Almagro M, Xicoy B, Jiménez M. Impact of anaemia on health-related quality of life and cardiac remodelling in patients with lower risk myelodysplastic syndromes. Results of GlobQoL study. *Eur J Cancer Care (Engl)*. 2016 Jan 4 ;. IF: 1,564
7. Ribera JM, García O, Oriol A, Gil C, Montesinos P, Bernal T, González-Campos J, Lavilla E, Ribera J, Brunet S, Martínez MP, **Tormo M**, Genescà E, Barba P, Sarrà J, Monteserín MC, Soria B, Colorado M, Cladera A, García-Guiñón A, Calbacho M, Serrano A, Ortín X, Pedreño M, Amigo ML, Escoda L, Feliu E, PETHEMA Group, Spanish Society of Hematology. Feasibility and results of subtype-oriented protocols in older adults and fit elderly patients with acute lymphoblastic leukemia: Results of three prospective parallel trials from the PETHEMA group. *Leuk Res*. 2016 Feb; 41:12-20. IF: 2,351
8. Forero-Castro M, Robledo C, Lumbreras E, Benito R, Hernández-Sánchez JM, Hernández-Sánchez M, García JL, Corchete-Sánchez LA, **Tormo M**, Barba P, Menárguez J, Ribera J, Grande C, Escoda L, Olivier C, Carrillo E, García de Coca A, Ribera JM, Hernández-Rivas JM. The presence of genomic imbalances is associated with poor outcome in patients with burkitt lymphoma treated with dose-intensive chemotherapy including rituximab. *Br J Haematol*. 2016 Feb; 172(3):428-38. IF: 4,711
9. Xicoy B, Germing U, Jimenez MJ, Garcia O, Garcia R, Schemenau J, Pedro C, Luño E, Bernal T, González B, Strupp C, Ardanaz M, Kuendgen A, Cedená MT, Neukirchen J, **Calabuig M**, Brunet S, Medina A, Amigo ML, Ramos F, Callejas M, Díez-Campelo M, Bailén A, Collado R, Vicente A, Arnán M, Valcarcel D, Arilla MJ, Zamora L, Benlloch L, Sanz G. Response to erythropoietic-stimulating agents in patients with chronic myelomonocytic leukemia. *Eur J Haematol*. 2016 Jul; 97(1):33-8. IF: 2,066
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11. Cervantes F, Correa JG, **Hernandez-Boluda JC**. Alleviating anemia and thrombocytopenia in myelofibrosis patients. *Expert Rev Hematol*. 2016 May; 9(5):489-96. IF: 2,07
12. Ramos F, Robledo C, Izquierdo-García FM, Suárez-Vilela D, Benito R, Fuertes M, Insunza A, Barragán E, Del Rey M, García-Ruiz de Morales JM, **Tormo M**, Salido E, Zamora L, Pedro C, Sánchez-Del-Real J, Díez-Campelo M, Del Cañizo C, Sanz GF, Hernández-Rivas JM, Spanish Group for Myelodysplastic Syndromes (GESMD).. Bone marrow fibrosis in myelodysplastic syndromes: a prospective evaluation including mutational analysis. *Oncotarget*. 2016 May 24; 7(21):30492-503. IF: 6,359
13. De Stefano V, Ruggeri M, Cervantes F, Alvarez-Larrán A, Iurlo A, Randi ML, Elli E, Finazzi MC, Finazzi G, Zetterberg E, Vianelli N, Gaidano G, Rossi E, Betti S, Nichele I, Cattaneo D, Palova M, Ellis MH, Cacciola R, Tieghi A, **Hernandez-Boluda JC**, Pungolino E, Specchia G, Rapezzi D, Forcina A, Musolino C, Carobbio A, Griesshammer M, Sant'Antonio E, Vannucchi AM, Barbui T. High rate of recurrent venous thromboembolism in patients with myeloproliferative neoplasms and effect of prophylaxis with vitamin K antagonists. *Leukemia*. 2016 Oct; 30(10):2032-2038. IF: 10,431
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15. Besses C, **Hernández-Boluda JC**, Pérez Encinas M, Raya JM, Hernández-Rivas JM, Jiménez Velasco A, Martínez Lopez J, Vicente V, Burgaleta C, GEMFIN. Current opinion and consensus statement regarding the diagnosis, prognosis, and treatment of patients with essential thrombocythemia: a survey of the Spanish Group of Ph-negative Myeloproliferative Neoplasms (GEMFIN) using the Delphi method. *Ann Hematol*. 2016 Apr; 95(5):719-32. IF: 2,634
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- hydroxycarbamide in 890 patients with polycythaemia vera. *Br J Haematol.* 2016 Mar; 172(5):786-93. IF: 4,971
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 20. Vinuesa V, Solano C, Giménez E, Piñana JL, **Boluda JC**, Amat P, Navarro D. Lack of evidence for a reciprocal interaction between bacterial and cytomegalovirus infection in the allogeneic stem cell transplantation setting. *Transpl Int.* 2016 Nov; 29(11):1196-1204. IF: 2,835
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 22. **Hernández-Boluda JC**, Correa JG, García-Delgado R, Martínez-López J, Alvarez-Larrán A, Fox ML, García-Gutiérrez V, Pérez-Encinas M, Ferrer-Marín F, Mata-Vázquez MI, Raya JM, Estrada N, García S, Kerguelen A, Durán MA, Albors M, Cervantes F. Predictive factors for anemia response to erythropoiesis stimulating agents in myelofibrosis. *Eur J Haematol.* 2016 Dec 23 ; IF: 2,544
 23. **Martín I**, Such E, **Navarro B**, Vicente A, López-Pavía M, Ibáñez M, **Tormo M**, **Villamón E**, Gómez-Seguí I, Luna I, Oltra S, Pedrola L, Sanz MA, Cervera J, Sanz G. Negative impact on clinical outcome of the mutational co-occurrence of SF3B1 and DNMT3A in refractory anemia with ring sideroblasts (RARS). *Leuk Lymphoma.* 2016 Oct 24 ;:1-8. IF: 3,093
 24. De Stefano V, Vannucchi AM, Ruggeri M, Cervantes F, Alvarez-Larrán A, Iurlo A, Randi ML, Pieri L, Rossi E, Guglielmelli P, Betti S, Elli E, Finazzi MC, Finazzi G, Zetterberg E, Vianelli N, Gaidano G, Nichele I, Cattaneo D, Palova M, Ellis MH, Cacciola E, Tieghi A, **Hernandez-Boluda JC**, Pungolino E, Specchia G, Rapezzi D, Forcina A, Musolino C, Carobbio A, Griesshammer M, Barbui T. Splanchnic vein thrombosis in myeloproliferative neoplasms: risk factors for recurrences in a cohort of 181 patients. *Blood Cancer J.* 2016 Nov 4; 6(11):e493. IF: 4,411
 25. Ibáñez M, Carbonell-Caballero J, García-Alonso L, Such E, Jiménez-Almazán J, Vidal E, Barragán E, López-Pavía M, Llop M, **Martín I**, Gómez-Seguí I, Montesinos P, Sanz MA, Dopazo J, Cervera J. The Mutational Landscape of Acute Promyelocytic Leukemia Reveals an Interacting Network of Co-Occurrences and Recurrent Mutations. *PLoS One.* 2016 Feb 17; 11(2):e0148346. IF: 3,057
- **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**
 - Reference:** PI13/00636
 - Title:** Role of the RUNX1/CBF-beta/p300/HIPK2 complex in the leukemic progression of the chronic myeloproliferative neoplasms.
 - Principal Investigator:** Juan Carlos Hernández Boluda
 - Funding Body:** *Instituto de Salud Carlos III*
 - Beneficiary Institution:** *Fundación Investigación Hospital Clínico Universitario de Valencia*
 - Duration:** 2014-2018
 - Total Budget:** 79.860€
 - **THESIS**
 - Thesis title:** *Influencia de los polimorfismos genéticos en la leucemia mieloide crónica.*
 - Doctoral candidate:** Paula Amat Martínez
 - Director(s):** Carlos Solano, Juan Carlos Hernández, Vicente Martín
 - Date of the defense:** 26/01/2016
 - Grade:** *Sobresaliente "cum laude"*

 - Thesis title:** *Fracaso renal agudo en el trasplante de progenitores hematopoyéticos: análisis de la incidencia, factores de riesgo e implicaciones pronósticas, valor pronóstico y en el diagnóstico precoz de la cistacina C plasmática.*
 - Doctoral candidate:** Miguel Angel Solís Salguero
 - Director(s):** Carlos Solano, Juan Carlos Hernández, Isidro Torregrosa
 - Date of the defense:** 08/02/2016
 - Grade:** *Sobresaliente "cum laude"*



Research Group on Epigenetics and Chromatin Consolidated group



[http://www. Bioeticaweb. Com/byline/luis-franco-vera/](http://www.Bioeticaweb.Com/byline/luis-franco-vera/)



Group members

Principal investigator

Luis Franco Vera
University
H Index: 19

Collaborating researchers

Gerardo López Rodas. University
Josefa Castillo Aliaga. INCLIVA



Strategic aims

- The expression of two genes EPDR1 and ZNF518B, which was negligible in the CRC cell lines Caco2, RKO and SW48 (wt KRAS), was observed in the HCT116, DLD1 and D-Mut1 cell lines, (G13D KRAS). The ratio of alternative splicing isoforms also depends on KRAS mutations. This opens a novel possibility to study the mechanisms of the KRAS mutation-dependent resistance of CRC.
- The upregulation of early and late inflammatory genes rely on histone acetylation associated with recruitment of histone acetyltransferase CBP in severe acute pancreatitis. The promoter of early genes showed a rapid, transient increase in H3K14ac, H3K27ac, and H4K5ac and a chromatin-remodelling complex containing BRG-1 was recruited. Therefore epigenetic changes are important in the control of the inflammatory cascade.

Main lines of research

- Exploring the role of ZNF518B and EPDR1 genes in human colorectal cancer: A translational approach. We intend to compare the expression of these genes and of their isoforms in tumour and normal mucosa from CRC patients. The role of these genes in cell proliferation and invasivity will also be studied.
- Epigenetic changes in acute pancreatitis. The study was aimed at the detection of epigenetic marks in histones in relation to the expression of early and late inflammatory genes.
- Epigenetic changes in gastric cancer. The study focus on the changes in RUNX3 gene.

• PUBLICATIONS

Number of articles	IF	Average IF
3	12,47	4,15
National collaborations	International collaborations	Corresponding author
3	-	2

Original articles

1. Llorca-Cardesa MJ, Fleitas T, Ibarrola-Villava M, Peña-Chilet M, Mongort C, Martínez-Ciarpaglini C, Navarro L, Gambardella V, **Castillo J**, Roselló S, Navarro S, Ribas G, Cervantes A. Epigenetic changes in localized gastric cancer: the role of RUNX3 in tumor progression and the immune microenvironment. *Oncotarget*. 2016 Sep 27; 7(39):63424-63436. IF: 5,008
2. Riffo-Campos ÁL, **Castillo J**, Vallet-Sánchez A, Ayala G, Cervantes A, **López-Rodas G**, **Franco L**. In silico RNA-seq and experimental analyses reveal the differential expression and splicing of EPDR1 and ZNF518B genes in relation to KRAS mutations in colorectal cancer cells. *Oncol Rep*. 2016 Dec; 36(6):3627-3634. IF: 2,486
3. Sandoval J, Pereda J, Pérez S, Finamor I, Vallet-Sánchez A, Rodríguez JL, **Franco L**, Sastre J, **López-Rodas G**. Epigenetic Regulation of Early- and Late-Response Genes in Acute Pancreatitis. *J Immunol*. 2016 Nov 15; 197(10):4137-4150. IF: 4,985

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI12/02110

Title: *Acetilación de hnRNP-L y modificaciones epigenéticas de la cromatina: hacia una aplicación traslacional en cáncer colorrectal*

Principal Investigator: Gerardo López Rodas

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Universidad de Valencia*

Duration: 2013-2016

Total budget: 96.195€



Reference: PROMETEO/2013/005

Title: *Estudio traslacional sobre la hiperacetilación de proteínas como vía final de resistencia a fármacos anti-EGFR en cánceres de alta incidencia clínica.*

Principal Investigator: Andrés Cervantes Ruipérez (Gerardo López-Rodas and Luis Franco as collaborating researchers)

Funding body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario Valencia*

Duration: 2013-2016

Total budget: 54.535€

Reference: SAF2015-71208-R

Title: *Papel de la señalización redox, beta-arrestina 2 y nucleosomas extracelulares en la pancreatitis aguda.*

Principal Investigator: Juan Sastre (Luis Franco as collaborating researcher)

Funding body: *Ministerio de Economía y Competitividad*

Beneficiary institution: *Universidad de Valencia*

Duration: 2016-2019

Total budget: 254.100€

• THESIS

Thesis title: Chromatin regulatory mechanisms of gene expression at mononucleosomal level: nucleosome occupancy and epigenetic modifications.

Doctoral candidate: Angela Leticia Riffo Campos

Director(s): Luis Franco Vera, Gerardo López Rodas, Josefa Castillo Aliaga

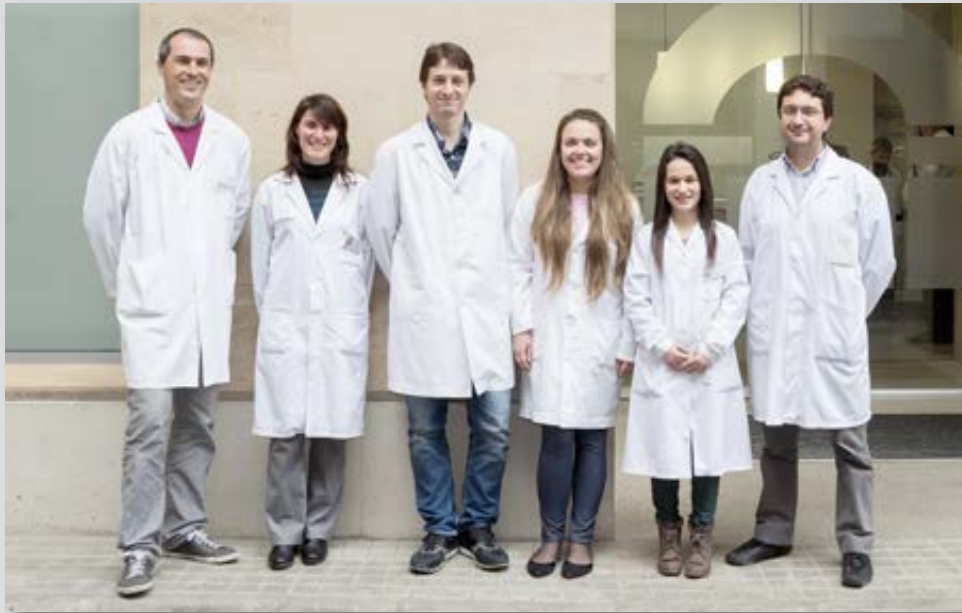
Date of the defense: 28/09/2015

Grade: *Sobresaliente "cum laude"*



Research Group on Molecular Imaging and Metabolomics

Emerging group



Group members



Principal investigator

Daniel Monleón Salvadó
INCLIVA
H Index: 21

Collaborating researchers

Vannina González Marrachelli. INCLIVA
Antonio Pellín Carcelén. University
Mercedes Pardo Tendero. INCLIVA
Itziar Pérez Terol. INCLIVA

Technician

José Manuel Morales Tatay. University



Strategic aims

- Identify new metabolomic markers of tumor aggressiveness in breast cancer.
- Identify new markers of myocardial infarction.
- Identify new metabolomic cardiovascular risk markers based on the microbiota-host interaction.

Main lines of research

- Tumor metabolism through metabolic profiles in biopsies, biofluids and cells (breast cancer, glioblastoma multiforme, prostate, bladder).
- Metabolic profiles in the progression of cardiometabolic risk modulated by the microbiota-host interaction.
- Metabolic profiles of healthy aging vs frailty.
- MRI microimaging study of porcine cardiac tissue samples to develop new detection methods.

• PUBLICATIONS

Number of articles	IF	Average IF
6	30,10	5,01
National collaborations	International collaborations	Corresponding author
3	3	3

Original articles

1. Zhang ZY, **Marrachelli VG**, Thijs L, Yang WY, Wei FF, **Monleon D**, Jacobs L, Nawrot T, Verhamme P, Voigt JU, Kuznetsova T, Redón J, Staessen JA. Diastolic Left Ventricular Function in Relation to Circulating Metabolic Biomarkers in a General Population. *J Am Heart Assoc.* 2016 Mar 29; 4(3):e002681. IF: 4,306
2. Duparc T, Plovier H, **Marrachelli VG**, Van Hul M, Essaghir A, Ståhlman M, Matamoros S, Geurts L, **Pardo-Tendero MM**, Druart C, Delzenne NM, Demoulin JB, van der Merwe SW, van Pelt J, Bäckhed F, **Monleon D**, Everard A, Cani PD. Hepatocyte MyD88 affects bile acids, gut microbiota and metabolome contributing to regulate glucose and lipid metabolism. *Gut.* 2016 May 5 ; IF: 14,66
3. Haukaas TH, Moestue SA, Vettukattil R, Sitter B, Lamichhane S, **Segura R**, Giskeødegård GF, Bathen TF. Impact of Freezing Delay Time on Tissue Samples for Metabolomic Studies. *Front Oncol.* 2016; 6:17. IF: 0
4. Hervas A, Ruiz-Sauri A, Gavara J, Monmeneu JV, de Dios E, Rios-Navarro C, Perez-Sole N, Perez I, **Monleon D**, Morales JM, Minana G, Nunez J, Bonanad C, Diaz A, Vila JM, Chorro FJ, Bodi V. A Multidisciplinary Assessment of Remote Myocardial Fibrosis After Reperfused Myocardial Infarction in Swine and Patients. *J Cardiovasc Transl Res.* 2016 Aug; 9(4):321-33. IF: 3,017
5. **Marrachelli V**, **Monleon D**, **Morales JM**, Martínez F, Martín-Escudero JC, Redon J. [OP.7B.03] Blood pressure and obesity metabolomic stratified analysis of a spanish general population. *J Hypertens.* 2016 Sep; 34 Suppl 2:e86. IF: 5,062
6. **Marrachelli VG**, Rentero P, Mansego ML, **Morales JM**, Galan I, **Pardo-Tendero M**, Martínez F, Martín-Escudero JC, Briongos L, Chaves FJ, Redon J, **Monleon D**. Genomic and Metabolomic Profile Associated to Clustering of Cardio-Metabolic Risk Factors. *PLoS One.* 2016; 11(9):e0160656. IF: 3,057

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: SAF2014-52875R

Title: *Estudio metabolómico de la interacción huésped-microbiota intestinal en la enfermedad cardiometabólica. Detección temprana, prevención y tratamiento.*

Principal Investigator: Daniel Monleón Salvadó

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total budget: 160.000€

Reference: 01_METABOPTO-MONTES-MONLEON-2014-UV

Title: *Marcadores metabolómicos del crecimiento ocular axial humano*

Principal Investigator: Daniel Monleón Salvadó

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary institution: *Universidad de Valencia*

Duration: 2015-2016

Total budget: 44.250€



Reference: PIE15/00013

Title: A multidisciplinary Project to advance in basic mechanisms, diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction.

Principal Investigator: Vicente Bodí Peris (Daniel Monleón as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2018

Total Budget: 589.050€

• THESIS

Thesis title: *Desarrollo de una estrategia diagnóstica por resonancia magnética multimodal para tumores cerebrales.*

Doctoral candidate: José Luis León Guijarro

Director(s): Daniel Monleón, Joaquín Gil, Bernardo Celda

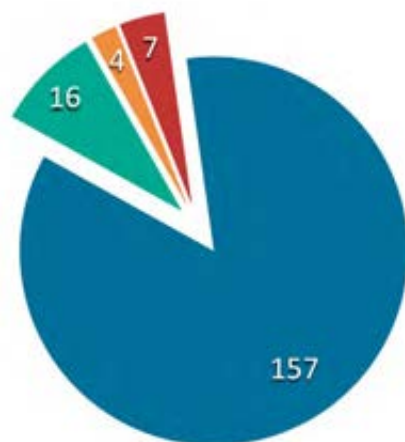
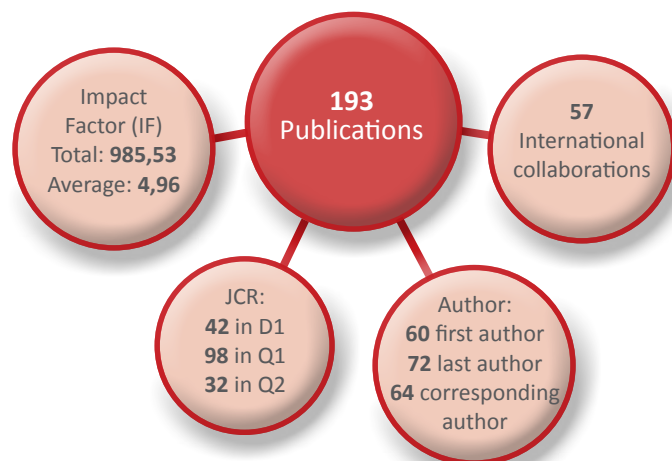
Date of the defense: 20/01/2016

Grade: *Sobresaliente "cum laude"*



4.3.3 Metabolism and organic damage area

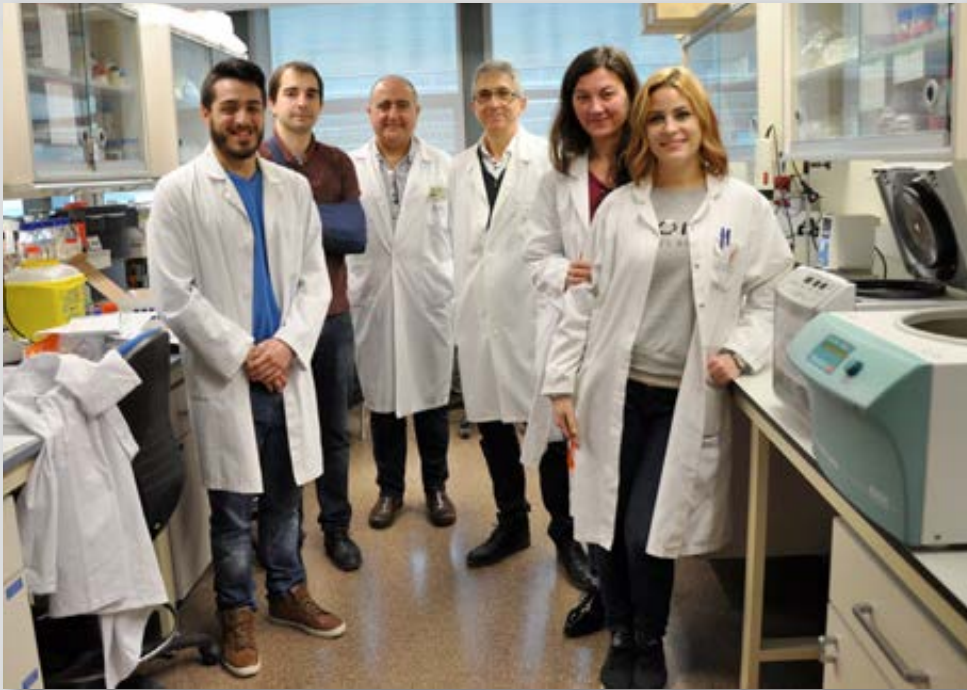
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● Original articles
 ● Letters
 ● Clinical guidelines
 ● Reviews



Research Group on Genetics of Osteoporosis Consolidated group



Group members

Principal investigator

Miguel Ángel García Pérez
University
H Index: 16

Collaborating researchers:

Rosa María Aliaga Corachán. University
Damian Mifsut Miedes. Hospital. University

PhD researches

Layla Panach González. INCLIVA
Álvaro Acebrón Fabregat. Hospital



Strategic aims

- This year we have continued our genetic association studies between candidate genes and bone phenotypes.
- We continued the analysis on the role of B lymphocytes in bone loss associated with estrogen deficiency by microarray studies and studies of association with bone phenotypes.
- This year, we have characterized the transcriptome in the osteoporotic bone fracture to detect and identify candidate genes for population studies. At the moment we are studying the association of 5 genes with bone phenotypes.
- We continued the study of miRNAs involved in bone phenotypes in a national collaborative study.
- We have performed the usual collaborations on aspects related to bone metabolism during pregnancy and on aspects related to fertility.

Main lines of research

- Research and analysis of polymorphisms in estrogen-regulated, the immune system of the Wnt / beta-catenin pathway and B-cell associated with postmenopausal osteoporosis genes.
- Identification of new genes regulated by estrogen via microarray in murine models of accelerated bone loss.
- Analysis of miRNAs profile and circulating cytokines in osteoporotic hip fracture.
- Identification of genes differentially expressed in osteoblasts after an osteoporotic fracture.
- Role of B cell and CD40 / CD40L system in postmenopausal bone loss.
- The role of B cells in the production of osteoprotegerin in the bone marrow.
- Functional characterization via genetic and epigenetic variants associated with bone phenotypes techniques.

• PUBLICATIONS

Number of articles	IF	Average IF
3	8,25	2,75

National collaborations	International collaborations	Corresponding author
3	-	1

Original articles

1. **Panach L**, Pineda B, **Mifsut D**, Tarín JJ, Cano A, **García-Pérez MA**. The role of CD40 and CD40L in bone mineral density and in osteoporosis risk: A genetic and functional study. *Bone*. 2016 Feb; 83:94-103. IF: 3,973
2. Tarín JJ, **García-Pérez MA**, Cano A. Obstetric and offspring risks of women's morbid conditions linked to prior anticancer treatments. *Reprod Biol Endocrinol*. 2016 Jul 7; 14(1):37. IF: 2,147
3. Tarín JJ, **García-Pérez MA**, Cano A. Potential risks to offspring of intrauterine exposure to maternal age-related obstetric complications. *Reprod Fertil Dev*. 2016 Aug 10. IF: 2,135

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: FOCUS

Title: Frailty management Optimisation through EIP AHA Commitments and Utilisation of Stakeholders input.

Principal Investigator: Antonio Cano Sánchez (Miguel Ángel García Pérez as collaborating researchers)

Funding body: European Commission - DG SANTE

Beneficiary institution: *Universidad de Valencia*

Duration: 2015-2018

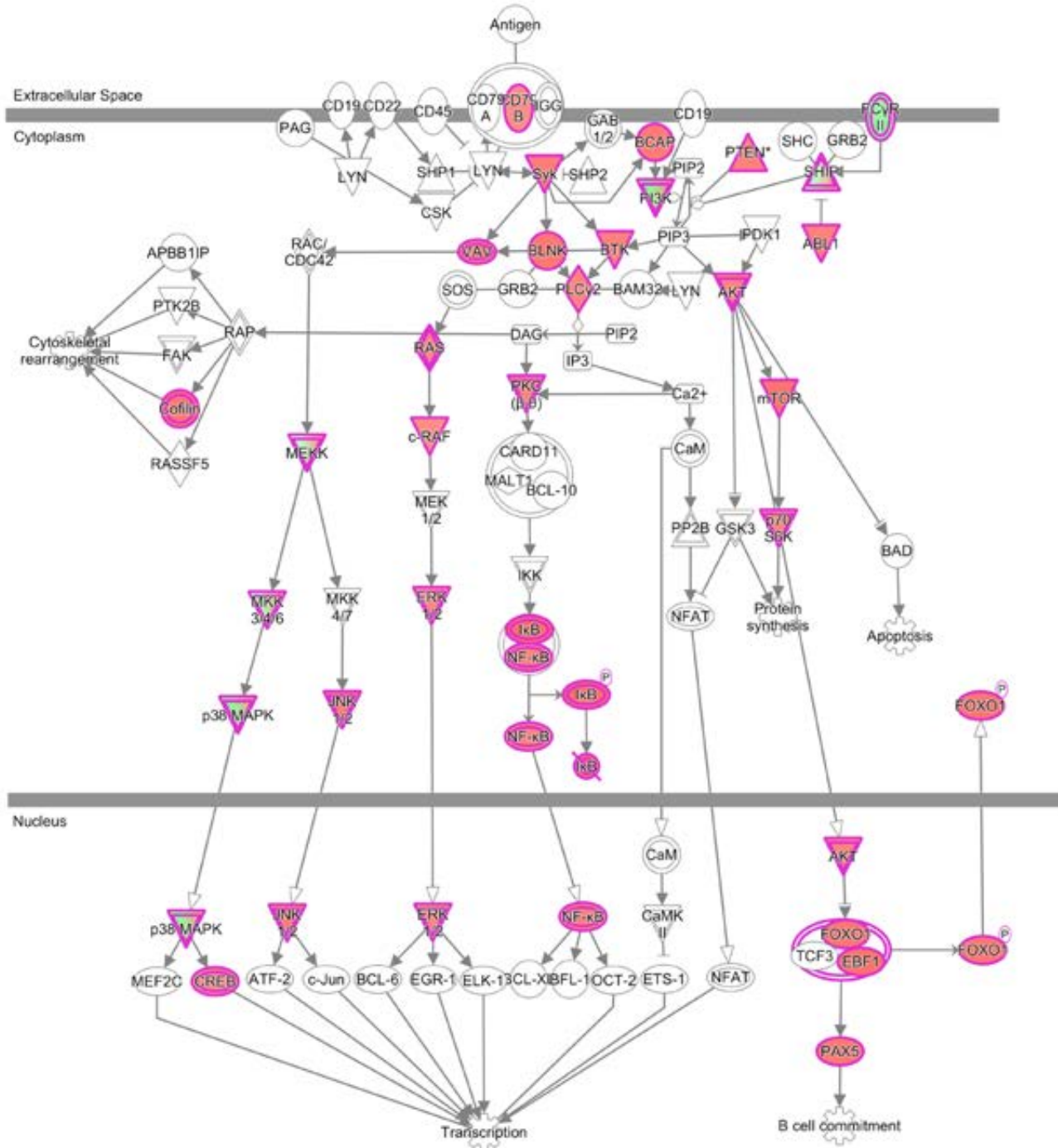
Total budget: 2.379.633€

• AWARDS

Dr. Miguel Angel García Pérez on behalf of its collaborators received the Award Certificate for Publishing Excellence from Calcified Tissue Int., an award granted for being one of the 10 most cited articles of the magazine in the years 2015-16 for its publication: *Panach L, Mifsut D, Tarín JJ, Cano A, and García-Pérez MA (2015). Serum Circulating MicroRNAs as Biomarkers of Osteoporotic Fracture. Calcif Tissue Int 97 (5): 495-505.* They were informed of the award in 2016 although it will be delivered in 2017.



B Cell Receptor Signaling



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Genes altered in the signaling pathway of the B cell receptor after ovariectomy. The image represents the pathway of the B cell receptor indicating genes that have undergone an increase in gene expression (in red) and those that have suffered a decrease in expression (in green). Gene expression was determined in bone marrow B cells obtained from ovariectomized mice versus control mice. The analysis was performed using Ingenuity Pathway Analysis (IPA) software.



Translational Research Group on Nutrition and Metabolism Consolidated group



Team involved in

ciberehd

Group members

Principal investigator

Antonio Hernández Mijares
University
H Index: 20



Collaborating researchers:

Milagros Rocha Barajas. Hospital Dr. Peset - FISABIO
 Víctor Manuel Víctor González. University
 Juan Vicente Esplugues Mota. University
 Carlos Morillas Ariño. University
 Eva Solá Izquierdo. University
 Celia Bañuls Morant. Hospital Dr. Peset - FISABIO
 Ana Jover Fernández. Hospital Dr. Peset
 Marcelino Gómez Balaguer. Hospital Dr. Peset
 Nadezda Apostolova Atanasovska. CIBERehd
 Silvia Veses Martín. Hospital Dr. Peset
 Susana Rovira Llopis. Hospital Dr. Peset - FISABIO



Strategic aims

- To evaluate mitochondrial function and mitochondrial dynamics in leukocytes of T2D (Type 2 diabetes) patients, considering the degree of glycemic control and comparing it to that in control subjects.
- To evaluate the beneficial effect of MitoQ on oxidative stress parameters and leukocyte-endothelium interactions in leukocytes of T2D patients.
- To assess the effects of an inositol-enriched beverage on blood glucose levels and inflammation status in subjects with an impaired fasting glucose (IFG) state according to body mass index (BMI).
- To assess the effects of inositols on glycaemic control in fasting and postprandial states and evaluated lipoprotein profile and LDL particle size in healthy population.
- To evaluate the relationship between myeloperoxidase and leukocyte activation in PCOS patients according to homeostatic model assessment of IR, and explore a possible correlation between these factors and endocrine and inflammatory parameters.
- To investigate the effect of simvastatin and ezetimibe on mitochondrial function and leukocyte endothelium interactions in polymorphonuclear cells of hyperlipidemic patients.
- To evaluate the short- and long-term effects of weight loss on lipid and hydrocarbonated metabolism parameters, systemic inflammatory markers, and hepatic enzymes in morbidly obese patients after a gastric bypass.
- To evaluate the acute effects of clinically relevant concentrations of the most widely used NRTIs, alone or combined with acetaminophen, on mitochondrial function and cellular viability.

Main lines of research

- Diabetes mellitus and cardiovascular risk.
- Obesity, inflammation and endothelial dysfunction.
- Polycystic ovary syndrome and insulin resistance.
- Dyslipidemia and residual cardiovascular risk.
- Functional foods and their influence on cardiovascular risk factors.
- Endoplasmic reticulum stress, mitochondrial dysfunction and oxidative stress.
- Characterization of new cellular mechanisms of anti-retroviral hepatotoxicity.

• PUBLICATIONS

Number of articles	IF	Average IF
33	125,09	3,79
National collaborations	International collaborations	Corresponding author
27	4	9

Original articles

1. Vayá A, Alis R, Suescún M, Rivera L, Murado J, Romagnoli M, **Solá E, Hernández-Mijares A**. Association of erythrocyte deformability with red blood cell distribution width in metabolic diseases and thalassemia trait. *Clin Hemorheol Microcirc.* 2016 Jan 4; 61(3):407-15. IF: 2,242
2. **Bañuls C, Rovira-Llopis S, Falcón R, Veses S, Monzó N, Víctor VM, Rocha M, Hernández-Mijares A**. Chronic consumption of an inositol-enriched carob extract improves postprandial glycaemia and insulin sensitivity in healthy subjects: A randomized controlled trial. *Clin Nutr.* 2016 Jun; 35(3):600-7. IF: 4,476
3. Cosín-Roger J, Ortiz-Masiá D, Calatayud S, Hernández C, **Esplugues JV, Barrachina MD**. The activation of Wnt signaling by a STAT6-dependent macrophage phenotype promotes mucosal repair in murine IBD. *Mucosal Immunol.* 2016 Jul; 9(4):986-98. IF: 7,374
4. Hernández C, Barrachina MD, Vallecillo-Hernández J, Álvarez Á, Ortiz-Masiá D, Cosín-Roger J, **Esplugues JV, Calatayud S**. Aspirin-induced gastrointestinal damage is associated with an inhibition of epithelial cell autophagy. *J Gastroenterol.* 2016 Jul; 51(7):691-701. IF: 4,523
5. Blas-García A, Martí-Rodrigo A, **Víctor VM, Polo M, Alegre F, Funes HA, Apostolova N, Esplugues JV**. The purine analogues abacavir and didanosine increase acetaminophen-induced hepatotoxicity by enhancing mitochondrial dysfunction. *J Antimicrob Chemother.* 2016 Apr; 71(4):916-26. IF: 5,313
6. Gómez-Abril SÁ, **Morillas-Ariño C, Ponce-Marco JL, Torres-Sánchez T, Delgado-Gomis F, Hernández-Mijares A, Rocha M**. Short- and Long-Term Effects of Weight Loss on the Complement Component C3 After Laparoscopic Gastric Bypass in Obese Patients. *Obes Surg.* 2016 Nov; 26(11):2756-2763. IF: 3,747
7. Díaz-Morales N, **Rovira-Llopis S, Bañuls C, Escribano-Lopez I, de Marañon AM, Lopez-Domenech S, Orden S, Roldan-**



- Torres I, Alvarez A, **Veses S, Jover A, Rocha M, Hernández-Mijares A, Víctor VM**. Are Mitochondrial Fusion and Fission Impaired in Leukocytes of Type 2 Diabetic Patients? *Antioxid Redox Signal*. 2016 Jul 10; 25(2):108-15. IF: 7,407
8. **Hernández-Mijares A, Bañuls C, Rovira-Llopis S**, Diaz-Morales N, Escribano-Lopez I, de Pablo C, Alvarez A, **Veses S, Rocha M, Víctor VM**. Effects of simvastatin, ezetimibe and simvastatin/ezetimibe on mitochondrial function and leukocyte/endothelial cell interactions in patients with hypercholesterolemia. *Atherosclerosis*. 2016 Apr; 247:40-7. IF: 3,994
 9. **Víctor VM, Rovira-Llopis S, Bañuls C**, Diaz-Morales N, Martínez de Marañón A, Rios-Navarro C, Alvarez A, Gomez M, **Rocha M, Hernández-Mijares A**. Insulin Resistance in PCOS Patients Enhances Oxidative Stress and Leukocyte Adhesion: Role of Myeloperoxidase. *PLoS One*. 2016; 11(3):e0151960. IF: 3,234
 10. Rubio-Puchol O, Garzón-Pastor S, Salom-Vendrell C, **Hernández-Mijares A**. [Primary hyperaldosteronism due to unilateral adrenal hyperplasia with surgical resolution]. *Hipertens Riesgo Vasc*. 2016 Oct - Dec; 33(4):155-158. IF: 0
 11. Pedro-Botet J, Mantilla-Morató T, Díaz-Rodríguez Á, Brea-Hernando Á, González-Santos P, **Hernández-Mijares A**, Pintó X, Millán Núñez-Cortés J. [The role of atherogenic dyslipidaemia in clinical practice guidelines]. *Clin Investig Arterioscler*. 2016 Mar-Apr; 28(2):65-70. IF: 0
 12. Diaz-Morales N, **Rovira-Llopis S**, Escribano-Lopez I, **Bañuls C**, Lopez-Domenech S, Falcón R, de Marañón AM, **Sola E, Jover A**, Roldan I, Díez JL, **Rocha M, Hernández-Mijares A, Víctor VM**. Role of Oxidative Stress and Mitochondrial Dysfunction in Skeletal Muscle in Type 2 Diabetic Patients. *Curr Pharm Des*. 2016; 22(18):2650-6. IF: 3,452
 13. **Rocha M**, Diaz-Morales N, **Rovira-Llopis S**, Escribano-Lopez I, **Bañuls C, Hernández-Mijares A**, Diamanti-Kandarakis E, **Víctor VM**. Mitochondrial Dysfunction and Endoplasmic Reticulum Stress in Diabetes. *Curr Pharm Des*. 2016; 22(18):2640-9. IF: 3,452
 14. **Esplugues JV**, De Pablo C, Collado-Díaz V, Hernández C, Orden S, Álvarez Á. Interference with purinergic signalling: an explanation for the cardiovascular effect of abacavir? *AIDS*. 2016 Jun 1; 30(9):1341-51. IF: 5,554
 15. Ortiz-Masiá D, Cosín-Roger J, Calatayud S, Hernández C, Alós R, Hinojosa J, **Esplugues JV**, Barrachina MD. M1 Macrophages Activate Notch Signalling in Epithelial Cells: Relevance in Crohn's Disease. *J Crohns Colitis*. 2016 May; 10(5):582-92. IF: 6,234
 16. Macias-Ceja DC, Cosín-Roger J, Ortiz-Masiá D, Salvador P, Hernández C, Calatayud S, **Esplugues JV**, Barrachina MD. The flesh ethanolic extract of *Hylocereus polyrhizus* exerts anti-inflammatory effects and prevents murine colitis. *Clin Nutr*. 2016 Dec; 35(6):1333-1339. IF: 4,476
 17. Blas-García A, **Apostolova N**, Valls-Bellés V, **Esplugues JV**. Endoplasmic Reticulum and Mitochondria: Independent Roles and Crosstalk in Fatty Liver Diseases and Hepatic Inflammation. *Curr Pharm Des*. 2016; 22(18):2607-18. IF: 3,452
 18. Miova B, Dimitrovska M, Dinevska-Kjovkarovska S, **Esplugues JV, Apostolova N**. The Heat Stress Response and Diabetes: More Room for Mitochondrial Implication. *Curr Pharm Des*. 2016; 22(18):2619-39. IF: 3,452
 19. Millán J, **Hernández-Mijares A**, Ascaso JF, Blasco M, Brea A, Díaz Á, González-Santos P, Mantilla T, Pedro-Botet J, Pintó X, Grupo de trabajo sobre Dislipemia Aterogénica. Sociedad Española de Arteriosclerosis.. [The real measurement of non-HDL-cholesterol: Atherogenic cholesterol]. *Clin Investig Arterioscler*. 2016 Nov - Dec; 28(6):265-270. IF: 0
 20. Brea A, Millán J, Ascaso JF, Blasco M, Díaz A, González-Santos P, **Hernández-Mijares A**, Mantilla T, Pedro-Botet JC, Pintó X, en nombre del Foro de la Dislipemia Aterogénica.. [Fibrates therapy: Rational use fenofibrate 2016. Executive summary]. *Clin Investig Arterioscler*. 2016 Nov - Dec; 28(6):295-301. IF: 0
 21. **Bañuls C, Rovira-Llopis S**, López-Doménech S, **Veses S, Víctor VM, Rocha M, Hernández-Mijares A**. Effect of consumption of a carob pod inositol-enriched beverage on insulin sensitivity and inflammation in middle-aged prediabetic subjects. *Food Funct*. 2016 Oct 12; 7(10):4379-4387. IF: 2,686
 22. Brea Á, Pintó X, Ascaso JF, Blasco M, Díaz Á, González-Santos P, **Hernández-Mijares A**, Mantilla T, Millán J, Pedro-Botet J, Grupo de trabajo sobre Dislipemia Aterogénica, Sociedad Española de Arteriosclerosis.. [Nonalcoholic fatty liver disease, association with cardiovascular disease and treatment (II). The treatment of nonalcoholic fatty liver disease]. *Clin Investig Arterioscler*. 2016 Sep 27 ;. IF: 0
 23. **Panel Europeo de Expertos**. Versión Española del Grupo de trabajo sobre Dislipemia Aterogénica.. [Consensus for pharmacologic treatment of atherogenic dyslipidemia with statin-fenofibrate combined therapy]. *Clin Investig Arterioscler*. 2016 Mar-Apr; 28(2):87-93. IF: 0



24. **Victor VM.** Proteinase-3 and Type 1 Diabetes: A New Target for Treatment? Crit Care Med. 2016 Sep; 44(9):1802-3. IF: 7,422
25. Papalou O, **Victor VM**, Diamanti-Kandarakis E. Oxidative Stress in Polycystic Ovary Syndrome. Curr Pharm Des. 2016; 22(18):2709-22. IF: 3,052
26. Escribano-Lopez I, Diaz-Morales N, **Rovira-Llopis S**, de Marañon AM, Orden S, Alvarez A, **Bañuls C**, **Rocha M**, Murphy MP, **Hernandez-Mijares A**, **Victor VM**. The mitochondria-targeted antioxidant MitoQ modulates oxidative stress, inflammation and leukocyte-endothelium interactions in leukocytes isolated from type 2 diabetic patients. Redox Biol. 2016 Oct 27; 10:200-205. IF: 6,235
27. Chueca E, Apostolova N, **Esplugues JV**, García-González MA, Lanás Á, Piazzuelo E. Proton Pump Inhibitors Display Antitumor Effects in Barrett's Adenocarcinoma Cells. Front Pharmacol. 2016 Nov 25; 7:452. IF: 4,418
28. Chico A, Herranz L, Corcoy R, Ramírez O, Goya MM, Bellart J, González-Romero S, Codina M, Sánchez P, Cortázar A, Acosta D, Picón MJ, Rubio JA, Megía A, Sancho MA, Balsells M, **Solá E**, González NL, López-López J, GEDE (Group of Diabetes and Pregnancy of the Spanish Diabetes Association).. Glycemic control and maternal and fetal outcomes in pregnant women with type 1 diabetes according to the type of basal insulin. Eur J Obstet Gynecol Reprod Biol. 2016 Nov; 206:84-91. IF: 1,662
29. Escalada J, Orozco-Beltran D, **Morillas C**, Alvarez-Guisasola F, Gomez-Peralta F, Mata-Cases M, Palomares R, Iglesias R, Carratalá-Munuera C. Attitudes towards insulin initiation in type 2 diabetes patients among healthcare providers: A survey research. Diabetes Res Clin Pract. 2016 Dec; 122:46-53. IF: 3,045

Reviews

30. **Victor VM.** Editorial: Endoplasmic Reticulum Stress and Mitochondrial Dysfunction in Diseases: Molecular Targets. Curr Pharm Des. 2016; 22(18):2605-6. IF: 3,452
31. Di Meo S, Reed TT, Venditti P, **Victor VM.** Role of ROS and RNS Sources in Physiological and Pathological Conditions. Oxid Med Cell Longev. 2016; 2016:1245049. IF: 4,492

Editorial

32. Di Meo S, Reed TT, Venditti P, **Victor VM.** Harmful and Beneficial Role of ROS. Oxid Med Cell Longev. 2016; 2016:7909186. IF: 4,492

Clinical guidelines

33. Klionsky DJ, Abdelmohsen K, Abe A, (et al). Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). Autophagy. 2016; 12(1):1-222. IF: 11,753

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI13/01025

Title: *Disfunción endotelial-mitocondrial, estrés de retículo y autofagia en la diabetes tipo 2: Implicaciones fisiopatológicas, clínicas y terapéuticas*

Principal Investigator: Víctor Manuel Víctor González

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO)

Duration: 2014-2016

Total Budget: 116.170€

Reference: PI13/00073

Title: *Efecto de la pérdida de peso sobre marcadores de estrés de retículo endoplasmático en la obesidad mórbida: Implicaciones fisiopatológicas y nuevas dianas terapéuticas*

Principal Investigator: Milagros Rocha Barajas

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO)

Duration: 2014-2016

Total Budget: 82.280€

Reference: PI14/00312

Title: *Papel de los fármacos anti-VIH en la aparición y/o progresión de la enfermedad de hígado graso no alcohólico.*

Principal Investigator: Juan Vicente Esplugues Mota / Nadezda Apostolova Atanasovska

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO)

Duration: 2015-2017

Total budget: 98.615€



Reference: PI15/01424

Title: *Prevalencia de desnutrición en el medio hospitalario y ambulatorio. Mecanismos moleculares asociados a la desnutrición: estrés oxidativo, inflamación y estrés de retículo endoplasmático.*

Principal Investigator: Antonio Hernández Mijares

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2018

Total budget: 86.515€

Reference: GV/2016/169

Title: *Evaluación de parámetros de estrés oxidativo y análisis de biomarcadores (miRNAs y actividad telomérica) en obesos metabólicamente sanos vs no sanos.*

Principal Investigator: Celia Bañuls Morant

Funding Body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2017

Total Budget: 16.000€

Reference: UGP-15-193

Title: *Efecto de los antioxidantes con diana en la mitocondria SS31 y MitoQ sobre la disfunción mitocondrial, la autofagia y el estrés de retículo endoplasmático en la diabetes tipo 2: Implicaciones fisiopatológicas, clínicas y terapéuticas.*

Principal Investigator: Víctor M. Víctor González

Funding Body: *Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO)*

Beneficiary Institution: *Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO)*

Duration: 2016 - 2017

Total budget: 25.500€

Reference: CB06/04/0071

Title: *CIBER de Enfermedades Hepáticas y Digestivas (CIBERehd)*

Principal Investigator: Juan Vicente Esplugues Mota

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2007-2016

• THESIS

Thesis title: *Relación entre disfunción eréctil e isquemia miocárdica silente en varones con diabetes mellitus tipo 2*

Doctoral candidate: Katerinne Eloise García Malpartida

Director(s): Antonio Hernández, Víctor Manuel Víctor

Date of the defense: 26/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio de prevalencia de desnutrición en atención primaria del departamento Valencia Dr Peset.*

Doctoral candidate: Juana Cantero Llorca

Director(s): Antonio Hernández, José Luis Alfonso

Date of the defense: 10/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Polimorfismos implicados en la hiperlipemia familiar combinada*

Doctoral candidate: Antonio López Ruiz

Director(s): Antonio Hernández, Marta Casado, María Teresa Martínez

Date of the defense: 04/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio comparativo del efecto de diferentes fármacos antirretrovirales sobre la interacción leucocito-endotelio*

Doctoral candidate: Samuel Orden Ruiz

Director(s): Juan Vicente Esplugues, Ángeles Álvarez

Date of the defense: 15/07/2016

Grade: *Sobresaliente "cum laude"*

• AWARDS

The Dr. Susana Rovira Llopis was awarded with the *Premio-Medalla García Blanco* on April 2016 for recognition of her scientific career of young researchers under 30 years old.



Research Group on Neurological Impairment Consolidated group



La frecuencia de parpadeo permite diagnosticar la encefalopatía hepática.

La Vanguardia CVA – Salud e Investigación. 25/03/2016

Group members

Principal investigator

Carmina Montoliu Félix
INCLIVA. University
H Index: 32



Collaborating researchers

Miguel Ángel Serra Desfilis. Hospital. University
Amparo Urios. INCLIVA
Amparo Escudero García. Hospital. University
María Luisa García Torres. Hospital
Paloma Lluch García. Hospital
Joan Tosca Cuquerella. Hospital
José Ballester Fayos. Hospital
Cristina Montón. Hospital

PhD researchers

Alba Mangas Losada. INCLIVA
Raquel García. INCLIVA



Strategic aims

- To better characterize the neuropsychological alterations in attention, coordination, perception, and spatial intelligence in patients with minimal hepatic encephalopathy (MHE).
- To characterize the alterations in sleep in patients with and without MHE.
- To analyze the contribution of oxidative and nitrosative stress and of inflammation to MHE and to specific neuropsychological alterations.
- To study by fMRI:
 - The pattern of activation of brain areas while performing tests of attention and “mismatch negativity”.
 - The neuronal connectivity of the default mode network.
 - The cerebral mechanisms of alterations in cognitive and motor tasks in patients with MHE.

Main lines of research

- Hepatic encephalopathy. Clinical and biochemical diagnostics.
- Detection of the presence of MHE in cirrhotic patients. Comparison of psychometric tests and critical flicker frequency. Study of peripheral parameters related with cGMP homeostasis and inflammation as possible indicators of the presence of MHE.
- MHE biomarkers. Identification of metabolites to be use in the diagnosis of minimal hepatic encephalopathy.
- Study of brain disorders using magnetic resonance imaging (including edema, cerebral atrophy, abnormal neural tracts) in patients with liver cirrhosis. Useful in the diagnosis of minimal hepatic encephalopathy.
- Study of alterations in attention, quality and sleep patterns in patients with liver cirrhosis with or without minimal hepatic encephalopathy.
- Study of impaired driving ability in patients with liver cirrhosis. Correlation with the presence of MHE.
- Analysis of synergistic effect between hyperammonemia and inflammation in the induction of MHE cognitive impairment.
- About the hepatitis, to study the epidemiological and therapeutic aspects of immunoprophylaxis.
- Development and characterization of an animal model of alcohol-induced hepatic encephalopathy.
- Molecular and cellular mechanisms of liver injury in

obesity: pathogenic, diagnostic and therapeutic implications.

• PUBLICATIONS

Number of articles	IF	Average IF
6	21,44	3,57

National collaborations	International collaborations	Corresponding author
6	-	2

Original articles

1. **Agusti A**, Llansola M, Hernández-Rabaza V, Cabrera-Pastor A, **Montoliu C**, Felipo V. Modulation of GABAA receptors by neurosteroids. A new concept to improve cognitive and motor alterations in hepatic encephalopathy. *J Steroid Biochem Mol Biol*. 2016 Jun; 160:88-93. IF: 3,628
2. Belghiti M, **Agusti A**, Hernandez-Rabaza V, Cabrera-Pastor A, Llansola M, Felipo V. Sildenafil Treatment Eliminates Pruritogenesis and Thermal Hyperalgesia in Rats with Portacaval Shunts. *Neurochem Res*. 2016 Jun 20 ;. IF: 2,472
3. **Montoliu C**, Felipo V. Current state of knowledge of hepatic encephalopathy (part II): changes in brain white matter tracts integrity are associated with cognitive deficits in minimal hepatic encephalopathy. *Metab Brain Dis*. 2016 Dec; 31(6):1359-1360. IF: 2,603
4. Dadsetan S, Balzano T, Forteza J, Cabrera-Pastor A, Taoro-Gonzalez L, Hernandez-Rabaza V, Gil-Perotín S, Cubas-Núñez L, García-Verdugo JM, **Agusti A**, Llansola M, Felipo V. Reducing Peripheral Inflammation with Infliximab Reduces Neuroinflammation and Improves Cognition in Rats with Hepatic Encephalopathy. *Front Mol Neurosci*. 2016 Nov 2; 9:106. IF: 5,154
5. **Urios A**, **Mangas-Losada A**, Gimenez-Garzó C, González-López O, Giner-Durán R, **Serra MA**, Noe E, Felipo V, **Montoliu C**. Altered postural control and stability in cirrhotic patients with minimal hepatic encephalopathy correlate with cognitive deficits. *Liver Int*. 2016 Dec 18 ;. IF: 4,47
6. Segarra G, Cortina B, Mauricio MD, Novella S, **Lluch P**, Navarrete-Navarro J, Noguera I, Medina P. Effects of asymmetric dimethylarginine on renal arteries in portal hypertension and cirrhosis. *World J Gastroenterol*. 2016 Dec 28; 22(48):10545-10556. IF: 3,127



• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI15/00035

Title: *Caracterización de las alteraciones neurológicas en pacientes con encefalopatía hepática mínima y de las alteraciones cerebrales responsables. Contribución del estrés oxidativo y la inflamación.*

Principal Investigator: Carmina Montoliu Félix

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2018

Total budget: 159.115€

Reference: EHM-DIAG

Title: *Desarrollo de una herramienta para el diagnóstico temprano, monitorización y seguimiento, por imagen cerebral, del deterioro cognitivo leve (encefalopatía hepática mínima) en pacientes cirróticos.*

Principal Investigator: Carmina Montoliu Félix

Funding Body: *PROGRAMA VLC-BIOCLINIC*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015 - 2016

Total Budget: 4.000€

Reference: EHM-DIAG

Title: *Desarrollo de una herramienta para el diagnóstico temprano, monitorización y seguimiento, por imagen cerebral, del deterioro cognitivo leve (encefalopatía hepática mínima) en pacientes cirróticos.*

Principal Investigator: Carmina Montoliu Félix

Funding Body: *PROGRAMA VLC-BIOCLINIC*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2017

Total Budget: 9.000€

Reference: BF13007

Title: *Caracterización de las alteraciones en resonancia magnética funcional en pacientes cirróticos con encefalopatía hepática mínima. Correlación con los déficits de atención y con otras alteraciones neurológicas. Posibles implicaciones diagnósticas.*

Principal Investigator: Carmina Montoliu Félix

Funding Body: *ERESA*

Beneficiary Institution: *Fundación Investigación Hospital*

Clínico Universitario de Valencia

Duration: 2014 - 2016

Total Budget: 20.000€

Reference: 282957

Title: *DENAMIC—Developmental neurotoxicity assessment of mixtures in children* Call (part) identifier: FP7-ENV-2011

Principal Investigator: Vicente Felipo Orts (Carmina Montoliu as collaborating researcher)

Funding Body: *European Commission*

Beneficiary Institution: *Centro de Investigación Príncipe Felipe*

Duration: 2011 - 2016

Reference: *FONDOS FEDER PARA EQUIPAMIENTO CIENTIFICO*

Title: *Estrategia de la Comunidad Valenciana para la detección temprana y prevención del deterioro cognitivo y funcional.*

Principal Investigator: Carmina Montoliu and Vicente Felipo

Funding Body: *Conselleria de Educación, Investigación, Cultura y Deporte*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 534.820€

• THESIS

Thesis title: *Evaluación de los efectos del tratamiento con tadalafilo sobre las funciones cerebrales, neurológicas y bioquímicas en pacientes con hiperplasia benigna de próstata y disfunción eréctil*

Doctoral candidate: Felipe Ordoño Domínguez

Director(s): Carmina Montoliu, Felipe Ordoño, Cristina Doménech

Date of the defense: 26/01/2016

Grade: *Sobresaliente “cum laude”*

Thesis title: *Alteraciones del ritmo del sueño en modelos animales de encefalopatía hepática*

Doctoral candidate: Nicolás Peñaranda Sarmiento

Director(s): Carmina Montoliu, Vicente Felipo, M^a Ángeles Lloret

Date of the defense: 23/12/2016

Grade: *Sobresaliente “cum laude”*



Figure 1. A process by which chronic diseases may induce cognitive and functional decline



Research Group on Inflammation Consolidated group



Group members

Principal investigator

Esteban Morcillo Sánchez
University. Hospital
H Index: 31



María Jesús Sanz Ferrando
University
H Index: 31



Team involved in

ciberes

Emerging researchers

Laura Piqueras Ruiz. INCLIVA
Herminia González Navarro. INCLIVA

Collaborating researchers

Nuria Cabedo Escrig. INCLIVA
Luisa Hueso Soler. INCLIVA
Andrea Herrero Cervera. INCLIVA

PhD researchers

Aida Collado Sánchez. INCLIVA
Patrice Gomes Marques. University

Technicians

Ángela Vinué Visús. INCLIVA
Francisca Selles Sorli. INCLIVA
Gonzalo Boigues López. INCLIVA
Laura Vila Dasí. INCLIVA



Strategic aims

- Study of the novel molecular, biochemical, cellular and genetic mechanisms involved in the etiopathogenesis of chronic obstructive pulmonary disease (COPD).
- Study of the role of CXCL16/CXCR6 axis in the cardiovascular disease associated to COPD, metabolic syndrome and abdominal aortic aneurysm (AAA).
- Study of the beneficial effect of Vitamin D in AAA development.
- Study of the impact of the hepatic lipase on the development of atherosclerosis and hepatic steatosis in insulin resistance states.
- Synthesis of new dopaminergic isoquinolines with D₂ agonist activity.

Main lines of research

- Study of the novel molecular, biochemical, cellular and genetic mechanisms involved in the etiopathogenesis of chronic obstructive pulmonary disease (COPD). Lung and systemic effects.
- Study of the vascular inflammation induced by different risk factors of atherosclerosis: angiotensin-II, menopause, cigarette smoke, metabolic syndrome, insulin resistance or familial hypercholesterolemia.
- Study of the role of retinoid X receptors (RXR) in inflammation angiogenesis.
- Study of the role of CXCR3 axis and nuclear ROR receptors in human obesity.
- Study of new anti-angiogenic mediators in acute myocardial infarct.
- Study of the CDKN2A/B genes and the LIGHT cytokine in the atherosclerosis associated with insulin resistance.
- Synthesis of new dopaminergic isoquinolines as anti-Parkinson drugs.
- Synthesis of new dual PPAR α / γ agonists to be used in cardiometabolic disorders.



Emerging researcher

Herminia González Navarro

Our research is focused in the study of the molecular mechanisms of the diabetes mellitus (DM) and its effect on atherosclerosis the most frequent cause of cardiovascular disease. To this end, we perform studies in genetically-modified mice that develop metabolic alterations such as diabetes, insulin resistance and atherosclerosis. To translate our findings into the human pathology we also perform investigations in human subjects and in human cell cultures. Recent studies in our laboratory have shown that insulin resistance aggravates atherosclerosis in mice by increasing inflammatory mediators which promote changes in proliferation and apoptosis within lesions. Thus, we have shown that the decrease in atherosclerosis upon hepatic lipase gene inactivation in insulin-resistant mice is associated with decreased macrophage proliferation and LIGHT cytokine expression. We are also focused in another consequence of DM and insulin resistance, the fatty liver disease. In this sense, we have recently started a project to investigate the role LIGHT cytokine, a main inflammatory mediator with a main role in T cell maturation, in the development of fatty liver disease in DM by strategies of gain and loss of function in mice.

In another line of research, we investigate the potential role of the CDKN2A/2B genes in the development of DM and coronary artery disease in humans. We have found that subjects with these pathologies have decreased expression of these genes which is consistent with previous studies by us indicating a protective role of the CDKN2A/2B in insulin resistance and hepatic steatosis. Currently, we are studying whether changes in these genes correlate with changes in inflammatory cells and mediators.



Emerging researcher

Laura Piqueras Ruiz

Abdominal aortic aneurysm (AAA), the progressive weakening and dilation of the aortic wall, is a common, age-related vascular disease. Preclinical research that focuses on understanding the molecular and cellular mechanisms underlying aneurysm development and progression is vital



to the design of effective pharmacological therapies with which to slow or reverse aneurysm progression. Recently, angiogenesis and inflammation in aortic aneurysmal disease has been related with the risk of rupture and complications. In this regard, emerging evidence indicates that a single drug may not be sufficient to combat the wide array of proangiogenic and proinflammatory factors produced during AAA. Thus, we are currently testing potential alternative approach with the use of combinations of already available clinical drugs that exhibit anti-angiogenic and anti-inflammatory activity and whose long-term safety has been proven. To carry out our research we are using a model of AAA induced by angiotensin-II- in apolipoprotein E deficient mice. This experimental model shares many characteristic features of the human disease, including chemokine and protease generation, leukocyte infiltration and neovascularization. Currently, we are also exploring the effect of several nuclear receptors; retinoid X receptor (RXR), peroxisome proliferator activating receptors (PPAR) and Vitamin D receptor (VDR) ligands on the AAA development. We are also interested in characterizing new molecular mechanism associated to aneurysm formation in animal models and human samples.

Additionally, metabolic disorders contribute to a disproportionate burden of illness and economic cost to the National Health System and the World Health Organization has estimated that by 2020 the associate cardiovascular diseases will be the main sanitary problem and socio-economic problem world wide. Numerous evidences indicate that there is a low-grade systemic inflammation in obesity. Indeed, we are focus on the characterization on different inflammatory axis and its ligands in morbid obesity and diabetes. We will use different approaches, in vitro studies-cell cultures- and in vivo, in obese patients and animal models. Our main interest is carry out a translational research to improve the clinical outcomes.

• PUBLICATIONS

Number of articles	IF	Average IF
11	53,35	4,85
National collaborations	International collaborations	Corresponding author
8	3	4

Original articles

- Martinez-Hervas S, Artero A, Martinez-Ibañez J, Tormos MC, **Gonzalez-Navarro H**, Priego A, Martinez-Valls JF, Saez GT, Real JT, Carmena R, Ascaso JF. Increased thioredoxin levels are related to insulin resistance in familial combined hyperlipidaemia. *Eur J Clin Invest.* 2016 Jul; 46(7):636-42. IF: 2,734
- Andrés-Blasco I, **Vinué Á**, Herrero-Cervera A, Martínez-Hervás S, Nuñez L, **Piqueras L**, Ascaso JF, **Sanz MJ**, Burks DJ, **González-Navarro H**. Hepatic lipase inactivation decreases atherosclerosis in insulin resistance by reducing LIGHT/Lymphotoxin β -Receptor pathway. *Thromb Haemost.* 2016 May 12; 116(2). IF: 4,984
- Milara J, Escrivá J, Ortiz JL, Juan G, Artigues E, **Morcillo E**, Cortijo J. Vascular effects of sildenafil in patients with pulmonary fibrosis and pulmonary hypertension: an ex vivo/ in vitro study. *Eur Respir J.* 2016 Jun; 47(6):1737-49. IF: 7,636
- Martorell S, **Hueso L**, **Gonzalez-Navarro H**, **Collado A**, **Sanz MJ**, **Piqueras L**. Vitamin D Receptor Activation Reduces Angiotensin-II-Induced Dissecting Abdominal Aortic Aneurysm in Apolipoprotein E-Knockout Mice. *Arterioscler Thromb Vasc Biol.* 2016 Aug; 36(8):1587-97. IF: 5,969
- Drechsler S, Lynch MA, Novella S, **González-Navarro H**, Hecimovic S, Barini E, Tucci V, Castro RE, Vandenbroucke RE, Osuchowski M, Potter PK. With mouse age comes wisdom: A review and suggestions of relevant mouse models for age-related conditions. *Mech Ageing Dev.* 2016 Dec; 160:54-68. IF: 2,892
- Párraga J, Andujar SA, Rojas S, Gutierrez LJ, El Aouad N, **Sanz MJ**, Enriz RD, **Cabedo N**, Cortes D. Dopaminergic isoquinolines with hexahydrocyclopenta[ij]-isoquinolines as D2-like selective ligands. *Eur J Med Chem.* 2016 Jun 10; 122:27-42. IF: 3,902
- Milara J, Morell A, Ballester B, Armengot M, **Morcillo EJ**, Cortijo J. MUC4 impairs the anti-inflammatory effects of corticosteroids in chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol.* 2016 Sep 14 ;. IF: 12,485
- Köks S, Dogan S, Tuna BG, **González-Navarro H**, Potter P, Vandenbroucke RE. Mouse models of ageing and their relevance to disease. *Mech Ageing Dev.* 2016 Dec; 160:41-53. IF: 2,892
- Martinez-Hervas S, Navarro I, Real JT, Artero A, Peiro M, **Gonzalez-Navarro H**, Carmena R, Ascaso JF. Unsaturated Oral Fat Load Test Improves Glycemia, Insulinemia and Oxidative Stress Status in Nondiabetic Subjects with Abdominal Obesity. *PLoS One.* 2016; 11(8):e0161400. IF: 3,057



10. Ortiz JL, Ortiz A, Milara J, Armengot M, Sanz C, Compañ D, **Morcillo E**, Cortijo J. Evaluation of Mucociliary Clearance by Three Dimension Micro-CT-SPECT in Guinea Pig: Role of Bitter Taste Agonists. PLoS One. 2016 Oct 10; 11(10):e0164399. IF: 3,057
11. Milara J, Cervera A, de Diego A, Sanz C, Juan G, Gavaldà A, Miralpeix M, **Morcillo E**, Cortijo J. Non-neuronal cholinergic system contributes to corticosteroid resistance in chronic obstructive pulmonary disease patients. Respir Res. 2016 Nov 8; 17(1):145. IF: 3.751

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PROMETEO II/2013/ 014

Title: *Nuevas dianas farmacológicas para el tratamiento de la EPOC y sus comorbilidades vasculares.*

Principal Investigator: Esteban Morcillo Sánchez

Funding body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2013-2016

Total budget: 400.000€

Reference: CB06/06/0027

Title: *CIBER Enfermedades Respiratorias.*

Principal Investigator: Esteban Morcillo Sánchez

Fundingbody: *Instituto de Salud Carlos III*

Beneficiary institution: *Universidad de Valencia*

Duration: 2007-2015

Reference: SAF2014-57845-R

Title: *Modulación Inmunofarmacológica de la Inflamación Sistémica asociada a Desordenes Metabólicos. Búsqueda de nuevas dianas terapéuticas y síntesis de fármacos novedosos.*

Principal Investigator: María Jesús Sanz Ferrando, Juan Francisco Ascaso Gimilio

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total Budget: 302.500€

Reference: COST Action BM0907

Title: European Network for Translational Immunology Research and Education (ENTIRE): From immunomonitoring to

personalized immunotherapy.

Principal Investigator: Dominique Baeten (María Jesús Sanz Ferrando as collaborating researcher)

Funding body: European Commission

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia/ Universidad de Valencia*

Duration: 2009-2016

Title: *The William Harvey International Translational Research Academy (WHRI-ACADEMY).*

Principal Investigator: Márta Korbonits (Maria Jesús Sanz Ferrando as collaborating research)

Funding Body: *FP7 Marie Curie Actions*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Title: *Efecto del cigarrillo electrónico (propilenglicol, dietilenglicol y nicotina) sobre la función pulmonar y la inflamación sistémica: estudios de toxicidad y activación leucocitaria en diferentes subpoblaciones de células circulantes inmunitarias. Medida de citocinas y quimiocinas plasmáticas.*

Principal Investigator: Cruz González Villaescusa (María Jesús Sanz and Emilio Servera as collaborating researcher)

Funding Body: *Sociedad Valenciana de Neumología/ Fundación de Neumología de la Comunidad Valenciana.*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015 - 2017

Total budget: 6.000€

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: Study of new molecular and inflammatory mechanisms involved in abdominal aortic aneurysm.

Principal Investigator: Laura Piqueras Ruiz

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total Budget: 4.917€



Reference: PI13/00834

Title: Study of the molecular mechanisms of Diabetes Mellitus and its role on atherosclerosis.

Principal Investigator: Herminia González Navarro

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2014-2016

Total Budget: 89.298€

Reference: PIE15/00013

Title: A multidisciplinary Project to advance in basic mechanisms, diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction.

Principal Investigator: Vicente Bodí Peris (Laura Piqueras as collaborating researcher)

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016 - 2018

Total Budget: 589.050€

Reference: COST Action BM1402

Title: Development of a European network for preclinical testing of interventions in mouse models of age and age-related diseases (MouseAGE).

Principal Investigator: Prof. Ilaria Bellantuono (Herminia González as collaborating researcher)

Funding Body: European Union

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2015-2019

Reference: COST Action BM1402

Title: Development of a European network for preclinical testing of interventions in mouse models of age and age-related diseases (MouseAGE).

Principal Investigator: Prof. Ilaria Bellantuono (Laura Piqueras as collaborating researcher)

Funding Body: European Union

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2015-2019

Reference: Proyecto Paula

Title: Estudio del papel del locus *Ink4/Arf* en la funcionalidad de las células β en un modelo murino de diabetes.

Principal Investigator: Herminia González Navarro

Funding Body: Proyecto Paula

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2013 - 2017

Total Budget: 108.472,03€

Reference: EFSD/Novo Nordisk Programme 2016 Programme for Diabetes Research in Europe

Title: Role of the cytokine LIGHT(TNFSF14) in the development of insulin resistance and fatty liver disease.

Principal Investigator: Herminia González Navarro

Funding Body: European Foundation for the Study of Diabetes

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016 - 2018

Total budget: 70.000€

Reference: SAF2015-65368-R

Title: Modulación farmacológica de la señalización inflamación-remodelado por inhibidores isoforma-selectivos de PDE4 y comparadores en modelos humanos in vitro relevantes en EPOC.

Principal Investigator: Esteban Morcillo Sánchez

Funding body: Ministerio de Economía y Competitividad

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2018

Total budget: 181.500€

Reference: CP15/00150

Title: Synthesis and pharmacological evaluation of new dual PPARalpha/gamma agonists as new therapeutic tools in the control of cardiometabolic disorders.

Principal Investigator: Nuria Cabedo Escrig

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2018

Total budget: 121.000€

Reference: COST Action CA15135

Title: Multi-target paradigm for innovative ligand identification in the drug discovery process (MuTaLig).

Principal Investigator: Stefano Alcaro (Nuria Cabedo as Management Committee substitute)

Funding Body: European Commission



Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2020

• THESIS

Thesis title: Effect of RXR/PPAR interaction in Angiotensin II-induced vascular inflammation and angiogenesis. Role of CXCL16/CXCR6 axis in angiotensin II cigarette smoke-induced vascular inflammation.

Doctoral candidate: Paula Escudero Díaz

Director(s): M^a Jesús Sanz Ferrando, Laura Piqueras Ruiz

Date of the defense: 04/07/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Disfunción endotelial en el territorio arterial en pacientes jóvenes con enfermedad tromboembólica.*

Doctoral candidate: Elena Furió Rodríguez

Director(s): Laura Piqueras Ruiz, M^a José García Fuster, Fernando Martínez

Date of the defense: 09/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Síntesis de nuevas isoquinoleinas 1-sustituidas con actividad antibacteriana y antifúngica o dopaminérgica.*

Doctoral candidate: Abraham Galán Morant

Director(s): M^a Jesús Sanz Ferrando, Diego M. Cortes Martínez, Nuria Cabedo Escrig

Date of the defense: 19/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Papel de la lipasa hepática y de los genes *cdkn2a/2b* en la aterosclerosis y la diabetes.*

Doctoral candidate: Irene Andrés Blasco

Director(s): Nuria Cabedo Escrig

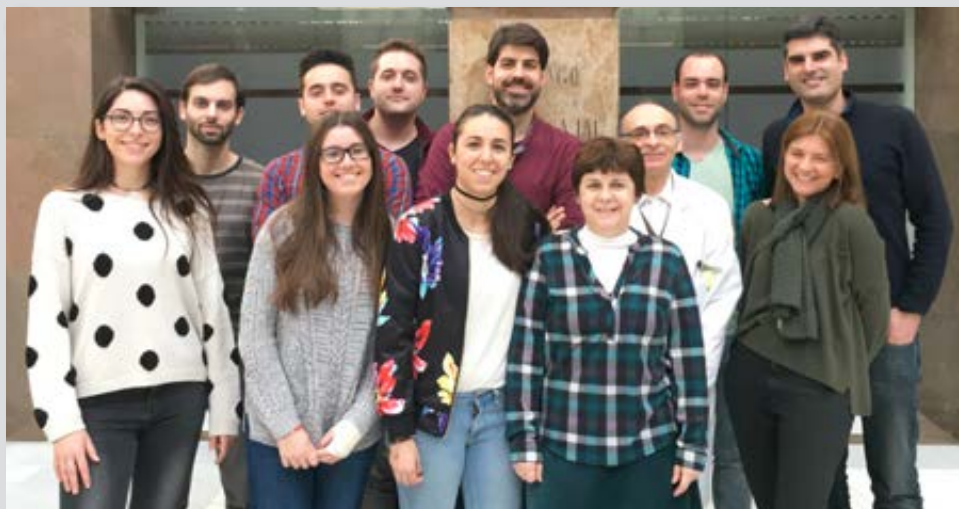
Date of the defense: 11/03/2016

Grade: *Sobresaliente "cum laude"*



Research Group on Cellular and Organic Physiopathology of Oxidative Stress

Consolidated group



Group members

Principal investigator

Federico V. Pallardó Calatayud
University
H Index: 44

Emerging researchers

Francisco Dasí Fernández. University. INCLIVA
José Luis García Giménez. CIBERer



Team involved in



Collaborating researchers

Amparo Gimeno Monrós. University
Carlos Romá Mateo. University
Pilar González Cabo. CIBERer
Carla Giménez Garzó. INCLIVA
Esther Berenguer Pascual. EPIFrailty
Eva M^a García López. University
Giselle Pérez Machado. University
M^a Mercedes Navarro García. University

PhD researchers

José Santiago Ibáñez Cabellos. University
Marta Seco Cervera. INCLIVA
Sara Pastor Puente. INCLIVA
Ana Reula Martín. INCLIVA
Lucía Bañuls Soto. INCLIVA
Diana Carolina Muñoz Lasso. University

Technicians

Isabel Esmoris Méndez. INCLIVA



Strategic aims

- Among the scientific activity of the research group, remarkable achievements are the European patent “Mass spectrometry-based methods for the detection of circulating histones H3 and H2B in plasma from sepsis or septic shock (ss) patients (EP 16 382 509.4)”, and the extension to PCT phase (PCT/EP2016/063935) and transference to the CIBER-INCLIVA spin-off EpiDisease, S. L., of the patent “Kit and method for the diagnosis/prognosis of idiopathic scoliosis”.
- In reference to acquisition of budget and resources, funding from the following programs and grants has been obtained: VLC-Bioclinic (1 project, 2016), *Grupo Español de Estudio del Raquis* (1 project, 2016-2017), *Plan Nacional I+D+i del Mineco* (1 project, 2016-2019), AES 2016 (2 projects, 2017-2019), *Fundación Ramón Areces* (1 project, 2017-2019).
- Regarding teaching and outreach activities, the group has maintained the teaching of the subject “*Enfermedades raras*”, in Medicine’s study plan at the University of Valencia and also in the “*Máster de enfermedades raras*”, directed by Dr. Pallardó, at the same University. Besides, it was organized, in collaboration with the *Escuela Valenciana de Estudios de la Salud* and the CIBERER, the 1st edition of the on-line course “*Introducción a las EE. RR. investigación y atención clínica*” addressed to residents of medical specialties from the Valencian public health system. In the context of scientific outreach activities, Dr. Romá-Mateo has published the book “*¿Qué sabemos de? La epigenética*” (ISBN: 978-84-00-10073-5).
- Within the framework of the Alliance for translational research in rare diseases of the Comunitat Valenciana, Dr. Pallardó has coordinated the joint application for FEDER funding for acquisition of research infrastructure. Recently, the Conselleria de Sanitat has confirmed availability of those funds (3.000.000 €) for 2017. Accordingly, the conference “*I Congreso de Investigación Traslacional en EE. RR. de la CV*” was held at the Faculty of Medicine and Dentistry, University of Valencia, on February 25th-26th 2016.

Main lines of research

- Pathophysiology of Friedreich’s ataxia and other neuromuscular diseases.
- Study of oxidative stress and mechanisms of DNA repair in different progeroid syndromes and genodermatosis.
- Epigenetic regulation in the pathophysiology of rare diseases.
- Rare respiratory diseases: Alpha-1 antitrypsin deficiency and Primary Ciliary Dyskinesia.



Emerging researcher

José Luis García Giménez

We are interested in understanding the role of epigenetics in the physiopathology of rare diseases (e. g. Friedreich ataxia, dyskeratosis congenita and adolescent idiopathic scoliosis). Our goal is to identify epigenetic marks and mechanisms underlying the natural history of disease. Therefore, one of our challenge is the identification of epigenetic biomarkers based on DNA methylation, histone variants and post-translational modifications and non-coding RNAs (e. g., microRNAs) which provide us of new tools for diagnostic and prognostic of disease. Furthermore, we are investigating the redox-related mechanisms controlling the sophisticated epigenetic regulation. In this regard, we are interested in the impact of several novel histone redox-related PTMs on cell physiology and gene regulation.



Emerging researcher

Francisco Dasí Hernández

Research is mainly devoted to the study alpha-1 antitrypsin deficiency (AATD). Research in other pulmonary rare diseases such as primary ciliary dyskinesia is currently under development.

The scientific interests of the group are:

- To characterize the molecular mechanisms (especially those aspects related to the REDOX signalling) involved in the development of liver and/or lung disease in patients with AATD, in order to understand why some patients develop serious liver and/or lung disease, while other patients bearing the same of alpha-1



antitrypsin (AAT) phenotype, are perfectly healthy.

- To assess cell-free circulating nucleic acids for the diagnosis and prognosis of AATD.
- To develop new therapeutic strategies based on gene therapy.
- To generate social awareness of pulmonary rare diseases, through scientific disclosure of biomedical advances and social and health policies to improve the quality of life of patients with pulmonary rare diseases.

• PUBLICATIONS

Number of articles	IF	Average IF
5	26,59	5,31

National collaborations	International collaborations	Corresponding author
3	2	2

Original articles

1. Mollá B, Riveiro F, Bolinches-Amorós A, Muñoz-Lasso DC, Palau F, **González-Cabo P**. Two different pathogenic mechanisms, dying-back axonal neuropathy and pancreatic senescence, are present in the YG8R mouse model of Friedreich's ataxia. *Dis Model Mech*. 2016 Jun 1; 9(6):647-57. IF: 4,973
2. Escribano A, Pastor S, Reula A, Castillo S, Vicente S, Sanz F, Casas F, Torres M, Fernández-Fabrellas E, Codoñer-Franch P, **Dasí F**. Accelerated telomere attrition in children and teenagers with α 1-antitrypsin deficiency. *Eur Respir J*. 2016 Aug; 48(2):350-8. IF: 8,332
3. **Romá-Mateo C**, Raththagala M, Gentry MS, Sanz P. Assessing the Biological Activity of the Glucan Phosphatase Laforin. *Methods Mol Biol*. 2016; 1447:107-19. IF: 0
4. Puig-Silla M, Montiel-Company JM, **Dasí-Fernández F**, Almerich-Silla JM. Prevalence of periodontal pathogens as predictor of the evolution of periodontal status. *Odontology*. 2016 Nov 25 ;. IF: 1,538

Clinical guidelines

5. Klionsky DJ, Abdelmohsen K, Abe A, (et al). Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). *Autophagy*. 2016; 12(1):1-222. IF: 11,753

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: HIST-BIRTH

Title: HIST-BIRTH: Innovative and rapid point-of-care histone test strips for early diagnosis of sepsis in pregnancy and childbirth.

Principal Investigator: Federico V. Pallardó

Funding body: USAID. USA Agency for Innovation and Development Saving Lives at Birth Development Change

Beneficiary institution: *Universidad de Valencia*

Duration: 2013-2016

Total budget: 186.712€

Reference: CB06/07/0073

Title: *CIBER de Enfermedades Raras (CIBERer)*.

Principal Investigator: Federico Vicente Pallardó Calatayud

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Universidad de Valencia*

Duration: 2007-2015

Reference: 03_LDmiRNA-2015

Title: *Análisis de microARNs como biomarcadores de monitorización farmacológica en modelos de enfermedad de Lafora*.

Principal Investigator: Carlos Roma Mateo

Funding Body: Ministerio de Educación, Cultura y Deporte

Beneficiary institution: Universidad de Valencia

Duration: 2015 – 2016

Total budget: 13.050€

Reference: PI14/02162

Title: *Análisis de parámetros de estrés oxidativo, función mitocondrial, longitud de telómeros y perfil de miRNAs circulantes en pacientes con déficit de alfa-1 antitripsina. Implicaciones pronósticas*.

Principal Investigator: Francisco Dasí Fernández

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total budget: 76.500€

Reference: CLEVERMIRNA

Title: *Análisis de los perfiles de expresión de microRNAs utilizando mapas auto organizados para el diagnóstico y pronóstico de individuos con déficit de alfa-1 antitripsina*.



Principal Investigator: Francisco Dasí Fernández

Funding Body: Universidad de Valencia

Beneficiary Institution: Universidad de Valencia

Duration: 2015 - 2016

Total budget: 9.000€

Reference: EPIFRILITY

Title: *Regulación epigenética de la esclerostina y la ruta wnt/b-catenina para la identificación de biomarcadores de fragilidad ósea.*

Principal Investigator: Federico Pallardó Calatayud

Funding body: IIS La Fe

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total budget: 4.000€

Reference: Beca GEER

Title: *Regulación epigenética de la esclerostina y de la ruta wnt/b-catenina en osteoporosis. Identificación de biomarcadores basados en la metilación del ADN y los microarns de fragilidad ósea.*

Principal Investigator: Teresa Bas Hermida (José Luis García-Giménez as collaborating researcher)

Funding body: *Sociedad Española de Enfermedades del Raquis*

Beneficiary institution: IIS La Fe

Duration: 2016

Total budget: 4.000€

Reference: PROMETEO II/2014/056

Title: *Señalización por radicales libres de oxígeno en células madre: importancia en medicina regenerativa.*

Principal Investigator: José Viña Ribes (Federico Pallardó Calatayud and José Luis García-Giménez as collaborating researcher)

Funding Body: *Consellería de Educación, Cultura y Deporte*

Beneficiary Institution: University of Valencia

Duration: 2014-2018

Total budget: 240.000€

Reference: PI14/00894

Title: *Identificación y validación de biomarcadores periféricos para el déficit neurocognitivo en el trastorno bipolar, depresión, esquizofrenia y diabetes.*

Principal Investigator: Rafael Tabares Seisdedos (Carlos Romá as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total budget: 82.000€

Reference: SAF 2015-66625-R

Title: *El paisaje de la biología axonal y las membranas asociadas a mitocondria en las enfermedades neurogenéticas.*

Principal Investigator: Pilar González Cabo

Funding body: *Ministerio de Economía y Competitividad.*

Beneficiary institution: *CIBER de Enfermedades Raras; Fundación Sant Joan de Deu*

Duration: 2016-2019

Total budget: 411.400€

Title: *Diseño y desarrollo de un método basado en CRISPR/Cas9 para la reparación del gen de la alfa-1-antitripsina.*

Principal Investigator: Amparo Escribano (Francisco Dasí as collaborating researcher)

Funding body: *Sociedad Valenciana de Neumología*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2018

Total budget: 12.000€

Title: *Estudio del perfil de miRNAs circulantes en pacientes con déficit de alfa-1 antitripsina (DAAT). Implicaciones diagnósticas, pronósticas y terapéuticas.*

Principal Investigator: Amparo Escribano (Francisco Dasí as collaborating researcher)

Funding body: *Asociación Española de Pediatría*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2017

Total budget: 30.000€

Title: *Caracterización del perfil oxidativo en células epiteliales nasales de pacientes con Discinesia Ciliar Primaria.*

Principal Investigator: Amparo Escribano (Francisco Dasí as collaborating researcher)

Funding body: *Sociedad Española de Neumología Pediátrica*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015 – 2017

Total budget: 10.000€



• THESIS

Thesis title: *Fenotipo celular de las neuronas sensitivas afectadas en la ataxia de Friedreich.*

Doctoral candidate: Belén Mollá Moliner

Director(s): Pilar González Cabo; Francesc Palau, José Enrique O' Connor Blasco

Date of the defense: 11/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio de la población anciana ambulatoria con cáncer de pulmón no microcítico: análisis clínico y factores pronósticos inflamatorios.*

Doctoral candidate: María Martín Ureste

Director(s): Federico Vicente Pallardó Calatayud, Inmaculada Maeztu Maiques, Vicente Giner Bosch

Date of the defense: 08/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio de la utilidad clínica del perfil de estrés oxidativo en pacientes con déficit de alfa-1 antitripsina.*

Doctoral candidate: Silvia Castillo Corullón

Director(s): Francisco Dasí Fernández, Amparo Escribano Montaner

Date of the defense: 06/10/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estrés oxidativo y su valor pronóstico en osteonecrosis idiopática de cabeza femoral.*

Doctoral candidate: María Carmen Blasco Mollá

Director(s): Francisco Dasí Fernández

Date of the defense: 03/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Conocimiento del déficit de alfa1-antitripsina y de la discinesia ciliar primaria por estudiantes de medicina y profesionales sanitarios.*

Doctoral candidate: M^a Ángeles Requena Fernández

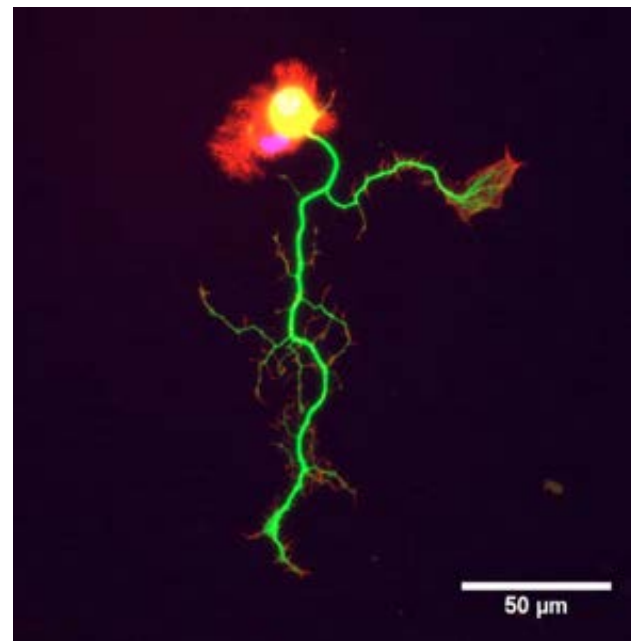
Director(s): Francisco Dasí Fernández, Amparo Escribano Montaner

Date of the defense: 29/01/2016

Grade: *Sobresaliente "cum laude"*

• AWARDS

In February 2016, the researcher Ana Reula was awarded with the Best Communication in Primary Ciliary Discinesia Award in the *I Congreso Internacional de Enfermedades Raras Respiratorias*.



Sensitive unidirectional neuron of a primary dorsal ganglion culture of a 3-month Y47R mouse. Immunofluorescence for β -tub-III (green, AF488), active filamentous (red, Phalloidin-TRITC) and nuclei (blue, DAPI Fluoromount-G[®]). At the distal end of each of the axons is observed the growth cone, a motile and oval shaped structure specialized in guiding axon growth. The growth cone is enriched in filamentous (red) and microtubule (green) actin.



Research Group on Oxidative Pathology Consolidated group



Team involved in

ciberobn

Group members

Principal investigator

Guillermo Sáez Tormo
University
H Index: 30



Collaborating researchers

Antonio Iradi Casal. University
Concha Cerdá Micó. University
Carmen Tormos Muñoz. University
Leticia Bagán Debón. University
Benjamín Climent Díaz. University
Antonio Vázquez Prado. Hospital General Universitario de Valencia
Ana Bediaga Collado. University
Amaya Hernando Espinilla. Hospital Universitario Dr. Peset
Delia Acevedo Leon. Hospital Universitario Dr. Peset

Technicians

Lidia Monzó Beltrán. University
Paula García Pérez. University



Strategic aims

- To study the role of Mediterranean diet and the individual effect of olive oil and dietary polyphenols on hemodynamics, endothelial function, abdominal adiposity and gene expression in patients at high cardiovascular risk has been studied.
- To investigate the systemic levels of inflammatory mediators and oxidative stress in verrucous leukoplakia in patients with acute renal failure.
- To monitor the morbidly obese patients in terms of anthropometric changes, metabolic and oxidative stress markers before and after dietary intervention, exercise and bariatric surgery.
- To analyze in gastric carcinoma patients the role of DNA damage and different markers of oxidative stress in order to validate the modified base 8-oxo-dG as a possible tumor marker at high cardiovascular risk.

Main lines of research

- Study of the role of Oxidative Stress (OS) as a physiological mechanism of cardiovascular diseases.
- Study p53-dependent signaling routes in patients with cardiovascular evolution pathologies, in order to identify differences between grades of expression in different genes, especially those in control of repairing the genetic material.
- Study of OS role in the pathology of neoplastic diseases, as well as the possible validation of their molecular oxidative products as clinical markers.

• PUBLICATIONS

Number of articles	IF	Average IF
14	36.91	2,63
National collaborations	International collaborations	Corresponding author
12	1	3

Original articles

1. **Bagan L, Sáez GT, Tormos MC**, Labaig-Rueda C, Murillo-Cortes J, Bagan JV. Salivary and serum interleukin-6 levels in proliferative verrucous leukoplakia. *Clin Oral Investig*. 2016 May; 20(4):737-43. IF: 2,352
2. Benlloch M, Obrador E, Valles SL, Rodriguez ML, Siererol JA, Alcácer J, Pellicer JA, Salvador R, **Cerdá C, Sáez GT**, Estrela JM. Pterostilbene Decreases the Antioxidant Defenses of Aggressive Cancer Cells In Vivo: A Physiological Glucocorticoids- and Nrf2-Dependent Mechanism. *Antioxid Redox Signal*. 2016 Jun 10; 24(17):974-90. IF: 7,407
3. Bagan JV, **Bagan L**, Poveda R, Scully C. Mitoxantrone as a contributing factor in medication-related osteonecrosis of the jaws. *Int J Oral Maxillofac Surg*. 2016 Mar; 45(3):377-9. IF: 1,565
4. Martinez-Hervas S, Artero A, Martinez-Ibañez J, **Tormos MC**, Gonzalez-Navarro H, Priego A, Martinez-Valls JF, **Saez GT**, Real JT, Carmena R, Ascaso JF. Increased thioredoxin levels are related to insulin resistance in familial combined hyperlipidaemia. *Eur J Clin Invest*. 2016 Jul; 46(7):636-42. IF: 2,734
5. Rangel-Zuñiga OA, Haro C, **Tormos C**, Perez-Martinez P, Delgado-Lista J, Marin C, Quintana-Navarro GM, Cerdá C, **Sáez GT**, Lopez-Segura F, Lopez-Miranda J, Perez-Jimenez F, Camargo A. Frying oils with high natural or added antioxidants content, which protect against postprandial oxidative stress, also protect against DNA oxidation damage. *Eur J Nutr*. 2016 Mar 25 ;. IF: 3,467
6. Aldasoro M, Guerra-Ojeda S, Aguirre-Rueda D, Mauricio MD, Vila JM, Marchio P, **Iradi A**, Aldasoro C, Jorda A, Obrador E, Valles SL. Effects of Ranolazine on Astrocytes and Neurons in Primary Culture. *PLoS One*. 2016; 11(3):e0150619. IF: 3,234
7. Viña J, **Saez GT**, Gambini J, Gomez-Cabrera MC, Borrás C. Role of NAD(+)/NADH redox ratio in cell metabolism: A tribute to Helmut Sies and Theodor Bücher and Hans A. Krebs. *Arch Biochem Biophys*. 2016 Apr 1; 595:176-80. IF: 3,017
8. Pellicer-Chover H, Cervera-Ballester J, Peñarrocha-Oltra D, **Bagán L**, Peñarrocha-Diago MA, Peñarrocha-Diago M. Influence of the prosthetic arm length (palatal position) of zygomatic implants upon patient satisfaction. *Med Oral Patol Oral Cir Bucal*. 2016 May 1; 21(3):e380-4. IF: 0
9. Silvestre FJ, Silvestre-Rangil J, **Bagán L**, Bagán JV. Effect of nonsurgical periodontal treatment in patients with periodontitis and rheumatoid arthritis: A systematic review. *Med Oral Patol Oral Cir Bucal*. 2016 May 1; 21(3):e349-54. IF: 0
10. Bagan J, Peydró A, Calvo J, Leopoldo M, Jiménez Y, **Bagan L**. Medication-related osteonecrosis of the jaw associated with bisphosphonates and denosumab in osteoporosis. *Oral Dis*. 2016 May; 22(4):324-9. IF: 2,427



11. **Bagan L**, Ocete-Monchon MD, Leopoldo-Rodado M, Muri-Ilo-Cortes J, Díaz-Fernández JM, Medina-Gonzalez R, Gimeno-Cardona C, Bagan J. Prevalence of salivary Epstein-Barr virus in potentially malignant oral disorders and oral squamous cell carcinoma. *Med Oral Patol Oral Cir Bucal*. 2016 Mar 1; 21(2):e157-60. IF: 0
12. Silvestre-Rangil J, **Bagán L**, Silvestre FJ, Bagán JV. Oral manifestations of rheumatoid arthritis. A cross-sectional study of 73 patients. *Clin Oral Investig*. 2016 Dec; 20(9):2575-2580. IF: 2,352
13. Sala-Vila A, Guasch-Ferré M, Hu FB, Sánchez-Tainta A, Bulló M, Serra-Mir M, López-Sabater C, Sorlí JV, Arós F, Fiol M, Muñoz MA, Serra-Majem L, Martínez JA, Corella D, Fitó M, Salas-Salvadó J, Martínez-González MA, Estruch R, Ros E, **PREDIMED Investigators**. B. Dietary ω -3 Fatty Acids, and Mortality in a Population With High Fish Consumption: Findings From the PREvención con Dieta MEDiterránea (PREDIMED) Study. *J Am Heart Assoc*. 2016 Jan 26; 5(1). IF: 5,117
14. Sánchez-Tainta A, Zazpe I, Bes-Rastrollo M, Salas-Salvadó J, Bullo M, Sorlí JV, Corella D, Covas MI, Arós F, Gutierrez-Bedmar M, Fiol M, de la Corte FG, Serra-Majem L, Pinto X, Schröder H, Ros E, López-Sabater MC, Estruch R, Martínez-González MA, **PREDIMED study investigators**. Nutritional adequacy according to carbohydrates and fat quality. *Eur J Nutr*. 2016 Feb; 55(1):93-106. IF: 3,239

• THESIS

Thesis title: *Valoración del estado nutricional en los diferentes estadios de la enfermedad renal crónica y su relación con el estrés oxidativo y la inflamación.*

Doctoral candidate: Patricia Tomás Simó

Director(s): Guillermo Sáez Tormo, Juan Alfonso Miguel Carrasco, María Jesús Puchades Montesa

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Daño oxidativo en la leucemia linfática crónica y la linfocitosis b monoclonal. Asociación con alteraciones cromosómicas.*

Doctoral candidate: María Isabel Oliver Domínguez

Director(s): Guillermo Sáez Tormo, Félix Carbonell, Rosa María Collado Nieto

Date of the defense: 10/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Opciones terapéuticas en la sinovitis en pacientes afectos de hemofilia: sinoviortesis.*

Doctoral candidate: María Magdalena Querol Giner

Director(s): Antonio Iradi Casal, Felipe Querol Fuentes, Sofía Pérez Alenda

Date of the defense: 30/09/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estrés oxidativo y lesión del material genético en la obesidad mórbida.*

Doctoral candidate: Antonio Vázquez Tarragón

Director(s): Guillermo Sáez Tormo, Antonio Vázquez Prado

Date of the defense: 25/11/2016

Grade: *Sobresaliente "cum laude"*

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI13/01848

Title: *Factores genéticos y metabólicos en la obesidad mórbida y su modulación tras intervención dietética, ejercicio físico y cirugía bariátrica. Estudio especial de P53, SIRT1 y sistemas de reparación del ADN en la patogenia de sus complicaciones neoplásicas.*

Principal Investigator: Guillermo Sáez Tormo

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2014-2016

Total budget: 134.915€

Reference: CB12/03/30016

Title: *CIBER de la Obesidad y Nutrición (CIBERObn)*

Principal Investigator: Guillermo Sáez Tormo

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2012-2017

Reference: PLASEPCOLOREC

Title: *Ensayo plasmático de espermia en orina como biomarcador de cáncer colorrectal.*

Principal Investigator: Guillermo Sáez Tormo

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2016

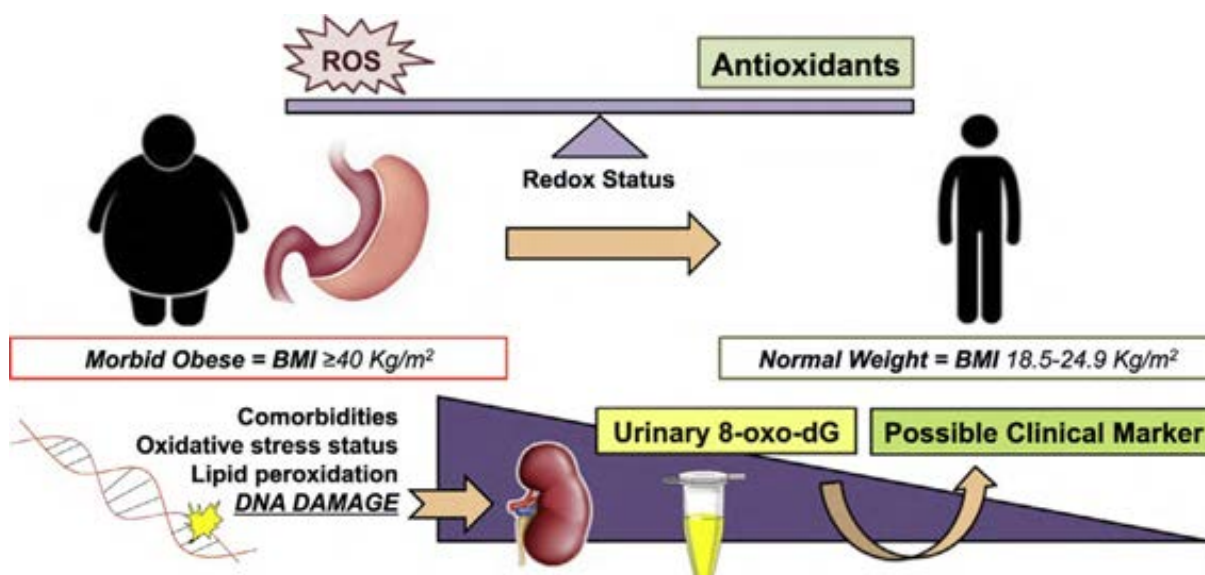
Total budget: 4.000€



• AWARDS

In March 2016 Dr. Sáez was awarded with the “*Medalla Conmemorativa del 50 Aniversario del Instituto de Ciencias Médicas y Preclínicas Victoria de Girón de la Habana*” for his dedication and collaboration in the formation of Cuban scientifics.

Oxidative Stress and Morbid Obesity





Research Group on Psychiatry and Neurodegenerative Diseases Consolidated group



Group members

Principal investigator

Julio Sanjuán Arias
Hospital. University
H Index: 19



Team involved in



Collaborating researchers

José Carlos González Piqueras. Hospital. University
Eduardo Jesús Aguilar García-Iturrospe. Hospital. University
Esther Lorente Rovira. Hospital
María José Escarti Fabra. Hospital
María Dolores Moltó Ruiz. University
Marien Gadea Domenech. University
Gracián García Martí. CIBERSAM
Manuel Jover Martínez. Hospital
José Luis Ivorra Martínez. CIBERSAM
Javier Gilabert Juan. University
Juan Nácher Roselló. University
Francisco Olucha Bordonau. University



Strategic aims

- Elaboration of a mobile application associated to the Clinical Records to improve adherence to the treatment of patients with first episode psychosis.
- Extension of common database for multicentric studies within CIBERSAM.
- Application of new EEG-fMRI techniques for the identification of hallucinations in psychosis.
- Development of new techniques-patents for the measurement in cerebral morphometry.
- Development of animal models in severe mental disorder and neurodegenerative diseases.
- Evaluation of brain changes after cognitive therapy in persistent hallucinations in psychosis.
- Prediction and treatment models in first psychotic episodes.

Main lines of research

- Identifying risk polymorphisms in psychosis and affective disorders.
- Epigenetic studies (functional expression) of candidate genes in psychosis and mental illness.
- Study of serious mental illness in animal models.
- Generating models of neurodegenerative diseases (Friedreich ataxia) on invertebrate animals (*Drosophila*).
- Study of mutations in monogenic neurodegenerative diseases.
- Identifying genetic and environmental risk factors in affective and psychotic disorders.
- Identifying abnormal patterns in neuroimage (morphometry, functional, spectroscopy) in psychotic patients.
- Design and coordination of clinical, genetic and neuroimage data bases oriented to performing multicenter projects.
- Development of interactive systems for improving therapeutic adherence.
- Study on the genetic and environmental factors in childhood emotional development.
- Study on the efficiency of psycho-social intervention techniques in serious mental illness.

• PUBLICATIONS

Number of articles	IF	Average IF
14	52,56	3,75
National collaborations	International collaborations	Corresponding author
9	5	4

Original articles

1. Tzanoulinou S, García-Mompó C, Riccio O, Grosse J, Zanoletti O, Dedousis P, **Nacher J**, Sandi C. Neuroigin-2 Expression in the Prefrontal Cortex is Involved in Attention Deficits Induced by Peripubertal Stress. *Neuropsychopharmacology*. 2016 Feb; 41(3):751-61. IF: 7,048
2. Bioque M, Llerena A, Cabrera B, Mezquida G, Lobo A, González-Pinto A, Díaz-Caneja CM, Corripio I, **Aguilar EJ**, Bulbena A, Castro-Fornieles J, Vieta E, Lafuente A, Mas S, Parellada M, Saiz-Ruiz J, Cuesta MJ, Bernardo M, PEPs GROUP. A Pharmacovigilance Study in First Episode of Psychosis: Psychopharmacological Interventions and Safety Profiles in the PEPs Project. *Int J Neuropsychopharmacol*. 2016 Apr; 19(4). IF: 4,009
3. Rubio A, Belles M, Belenguer G, Vidueira S, Fariñas I, **Nacher J**. Characterization and isolation of immature neurons of the adult mouse piriform cortex. *Dev Neurobiol*. 2016 Jul; 76(7):748-63. IF: 3,37
4. Pina-Camacho L, Del Rey-Mejías Á, Janssen J, Bioque M, González-Pinto A, Arango C, Lobo A, Sarró S, Desco M, **Sanjuan J**, Lacalle-Aurioles M, Cuesta MJ, Saiz-Ruiz J, Bernardo M, Parellada M, PEPs Group. Age at First Episode Modulates Diagnosis-Related Structural Brain Abnormalities in Psychosis. *Schizophr Bull*. 2016 Mar; 42(2):344-57. IF: 8,45
5. Gutiérrez-Zotes A, Labad J, Martín-Santos R, García-Esteve L, Gelabert E, Jover M, Guillamat R, Mayoral F, Gornemann I, Canellas F, Gratacós M, Guitart M, Roca M, Costas J, Ivorra JL, Navinés R, de Diego-Otero Y, Vilella E, **Sanjuan J**. Coping strategies for postpartum depression: a multi-centric study of 1626 women. *Arch Womens Ment Health*. 2016 Jun; 19(3):455-61. IF: 2,164
6. **Gadea M**, Aliño M, Garijo E, Espert R, Salvador A. Testing the Benefits of Neurofeedback on Selective Attention Measured Through Dichotic Listening. *Appl Psychophysiol Biofeedback*. 2016 Jun; 41(2):157-64. IF: 1,847



7. Carceller H, Rovira-Esteban L, **Nacher J**, Castrén E, Guirado R. Neurochemical Phenotype of Reelin Immunoreactive Cells in the Piriform Cortex Layer II. *Front Cell Neurosci.* 2016; 10:65. IF: 4,289
8. Guirado R, La Terra D, Bourguignon M, Carceller H, Umemori J, Sipilä P, **Nacher J**, Castrén E. Effects of PSA Removal from NCAM on the Critical Period Plasticity Triggered by the Antidepressant Fluoxetine in the Visual Cortex. *Front Cell Neurosci.* 2016; 10:22. IF: 4,289
9. Castillo-Gómez E, Varea E, Blasco-Ibáñez JM, Crespo C, **Nacher J**. Effects of Chronic Dopamine D2R Agonist Treatment and Polysialic Acid Depletion on Dendritic Spine Density and Excitatory Neurotransmission in the mPFC of Adult Rats. *Neural Plast.* 2016; 2016:1615363. IF: 3,582
10. Soriano S, Calap-Quintana P, Llorens JV, Al-Ramahi I, Gutiérrez L, Martínez-Sebastián MJ, Botas J, **Moltó MD**. Metal Homeostasis Regulators Suppress FRDA Phenotypes in a Drosophila Model of the Disease. *PLoS One.* 2016; 11(7):e0159209. IF: 3,057
11. Mas S, Gassó P, Lafuente A, Bioque M, Lobo A, González-Pinto A, Olmeda MS, Corripio I, Llerena A, Cabrera B, Saiz-Ruiz J, Bernardo M, **PEPs GROUP**. Pharmacogenetic study of antipsychotic induced acute extrapyramidal symptoms in a first episode psychosis cohort: role of dopamine, serotonin and glutamate candidate genes. *Pharmacogenomics J.* 2016 Oct; 16(5):439-45. IF: 3,784
12. Castillo-Gómez E, Pérez-Rando M, Vidueira S, **Nacher J**. Polysialic Acid Acute Depletion Induces Structural Plasticity in Interneurons and Impairs the Excitation/Inhibition Balance in Medial Prefrontal Cortex Organotypic Cultures. *Front Cell Neurosci.* 2016 Jun 29; 10:170. IF: 4,609
13. López-Hidalgo R, Ballestín R, Vega J, Blasco-Ibáñez JM, Crespo C, Gilabert-Juan J, **Nacher J**, Varea E. Hypocellularity in the Murine Model for Down Syndrome Ts65Dn Is Not Affected by Adult Neurogenesis. *Front Neurosci.* 2016 Mar 2; 10:75. IF: 0

Letter

14. Domenech J, Marti-Bonmati L, Alberich-Bayarri A, **Garcia-Martí G**. Letter to the editor concerning "A new approach to corpus callosum anomalies in idiopathic scoliosis using diffusion tensor magnetic resonance imaging" by Joly O et al. (2014) *Eur Spine J* 23:2643-9. *Eur Spine J.* 2016 Apr; 25(4):1289-90. IF: 2,066

RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI13/00447

Title: Neuroimaging and genetic markers for language disorders in psychosis

Principal Investigator: Julio Sanjuán Arias

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total Budget: 116.160€

Reference: PROMETEO/2016/082

Title: *Investigación de marcadores biológicos y nuevas estrategias terapéuticas en la Psicosis*

Principal Investigator: Julio Sanjuán Arias

Funding Body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2019

Total budget: 179.940€

Reference: CB07/09/0006

Title: *CIBER de Enfermedades Mentales (CIBERSam)*

Principal Investigator: Julio Sanjuán Arias

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Universidad de Valencia*

Duration: 2008-2016

Reference: SAF 2015-68436-R

Title: Plasticity of perisomatic inhibition on pyramidal neurons of the prefrontal cortex: impact of peripubertal stress and implication in psychiatric disorder

Principal Investigator: Juan Salvador Nacher Roselló

Funding body: *Ministerio de Economía y Competitividad*

Beneficiary institution: *Universitat de Valencia*

Duration: 2016-2019

Total budget: 160.000€

Title: Identification of genetic factors involved on FXN transcriptional silencing mediated by the GAA repeat expansion.

Principal Investigator: M^a Dolores Moltó Ruiz

Funding body: *Friedreich's Ataxia Research Alliance (FARA)*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2017



Reference: PI14/00044

Title: *Eficacia del entrenamiento metacognitivo individualizado (EMC+) en personas con psicosis de reciente evolución.*

Principal Investigator: Susana Ochoa (Esther Lorente and Ana Luengo as collaborating researcher)

Funding body: *Ministerio de Ciencia e innovación*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2018

Total budget: 92.565€

Reference: PROMETEO/2013/069

Title: *Plasticidad estructural de circuitos inhibitorios. Implicación en esquizofrenia*

Principal Investigator: Juan Salvador Nácher Roselló

Funding body: *Generalitat Valenciana*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2013-2016

Total budget: 160.000€

Reference: PROMETEOII/2014/067

Title: *Utilización de Drosophila como organismo modelo en investigación biomédica*

Principal Investigator: Nuria Paricio Ortiz

Funding body: *Generalitat Valenciana*

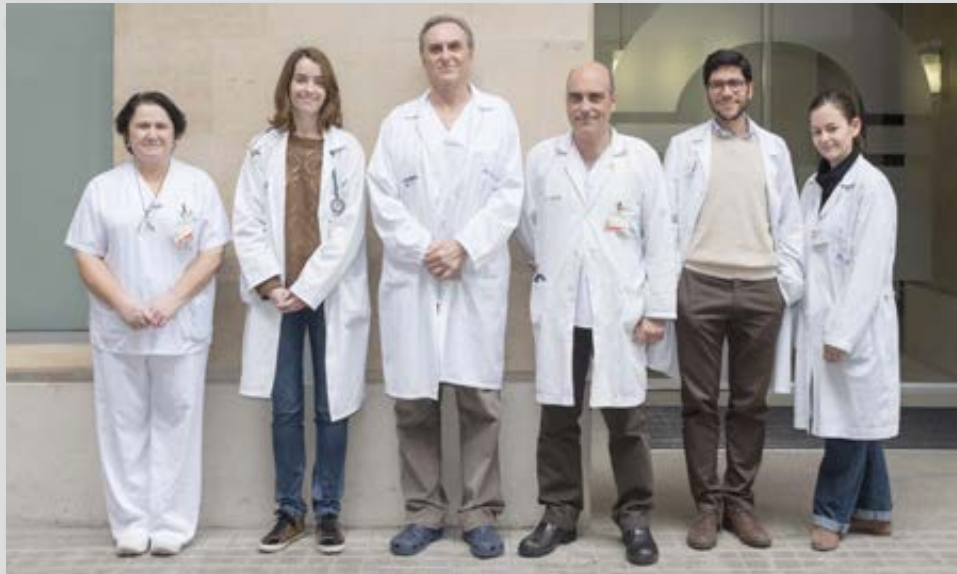
Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total budget: 73.665€



Research Group on Respiratory Problems of Neuromuscular Diseases and Lung Damage Consolidated group



Group members

Principal investigator

Emilio Servera Pieras
Hospital. University
H Index: 15



Collaborating researchers

Jesús Sancho Chinesta. Hospital
María Pilar Barreto Martín. University
José Luís Díaz Cordobés. Hospital
Pilar Bañuls Polo. Hospital
Manuela Marín González. Hospital
M^a Luisa Briones Urtiaga. Hospital
M^a Jesús Zafra Pirés. University
María Belén Safont Muñoz. Hospital
M^a Cruz González Villaescusa. Hospital
José Vicente Ferreres Franco. Hospital
Enric Burés Sales. INCLIVA
Jaime Signes-Costa Miñana. Hospital
Helena Mondragón Ilorca. INCLIVA
Heidi Mora Bastida. Hospital



Strategic aims

- The utility of non invasive ventilation in the weaning process of patients with chronic critical disorders and those with prolonged mechanical ventilation in Respiratory Care Units.
- The analysis of cough physiology in patients with amyotrophic lateral sclerosis (ALS) during mechanically assisted cough, with high frequency oscillations.
- The effect of bulbar type of ALS over the efficacy of coughing, mechanically assisted with in-exhuflation, through high frequency oscillations in ALS patients.
- The identification of predictive factors for complicated grief in relatives of severe respiratory patients.
- The search of affected areas through neuro-psychological exams in a high percentage of patients with neuromuscular disorders to identify a deficit in cognitive behavioral tasks.
- Signal genetic variability analysis mediated by TLRs/IL-1R in respiratory diseases: Community acquired pneumonia (CAP).
- Signal genetic variability analysis mediated by TLRs/IL-1R in the prognosis of CAP and pneumococcal CAP.
- To identify the role of conjugated anti pneumococcal vaccine (V-13) to prevent respiratory problems in pneumococcal CAP with bacteremia.

Main lines of research

- Study of long term utility of mechanically assisted cough with in-exhuflation, through high frequency oscillations, in ALS patients.
- Study of the efficacy of mechanically assisted cough with in-exhuflation, through high frequency oscillations, during acute respiratory infections, in ALS patients.
- Study of long term utility of mechanically assisted cough with in-exhuflation, through high frequency oscillations, in ALS patients and mechanical ventilation trough tracheotomy.
- Study of physio-pathology of assisted cough with in-exhuflation, through high frequency oscillations, in ALS patients.
- Study of the effect of bulbar alteration in survival of ALS patients and non invasive mechanical ventilation.
- Study of the physio-pathology in the failure of non invasive mechanical ventilation in ALS patients.

- Study of treatment with quinidine/dextromethorphan in the delay of failure of non invasive management of respiratory problems in ALS patients.
- To improve knowledge in the staging of patients with neuromuscular diseases to anticipate decisions and to adjust respiratory therapeutic measures.
- To improve knowledge in technical assistance and replacement of the respiratory muscles in neuromuscular diseases, particularly to the life-prolonging without adding suffering.
- To improve knowledge in the management of the psycho-emotional needs in neuromuscular patients with COPD and incapacitating dyspnea and their caregivers.
- To improve knowledge about the role of genetic polymorphisms in the predisposition, severity and susceptibility to bacteremia in community-acquired pneumonia.
- To evaluate the efficiency of the management of dyspnea.
- To assess cognitive / behavioral signs associated with neuromuscular dementia patients and their involvement in the decision-making process.
- To evaluate the prevalence of stressful life events, different styles of attachment and the proportion of adaptive and problem duels present in relatives of patients at the end of life.
- Cardiac morphological changes in patients with sleep respiratory disorders and ischemic heart disease: response to CPAP treatment.
- Effects of e-liquids (propylene glycol (PG), diethylene glycol (DG), and nicotine) from electronic cigarettes in human cell cultures: Human umbilical vein endothelial cells (HUVEC) and adenocarcinomic human alveolar basal epithelial cells (A549).
- Efficacy of a tobacco treatment program about severe exacerbation in smokers with a moderate or severe COPD.
- Evaluation of CPAP on kidney function in patients with early-stage renal disease and sleep apnea syndrome (RENAS study).
- Characterization of asthmatic patients: new bio-markers (periostine and protein CC16) and their relationship with the severity of bronchial asthma.
- Study of genetic variability in the susceptibility and severity of pneumonia.
- Efficiency of an integrated program for COPD patients with frequent hospital admissions.



- Open label multicentric study of RCP1063 oral in recurrent multiple sclerosis (MS).
- Randomized, double-blind, multicentric, parallel groups, controlled with placebo and variable duration, to evaluate efficacy and safety of Sponimod (BAF312) in patients with secondary MS, followed by an open extension treatment of BAF312.

• PUBLICATIONS

Number of articles	IF	Average IF
14	25,82	1,84

National collaborations	International collaborations	Corresponding author
11	-	3

Original articles

- Rudilla D, Galiana L, Oliver A, **Barreto P**. Demoralization Scale in Spanish-Speaking Palliative Care Patients. *J Pain Symptom Manage*. 2016 Apr; 51(4):769-775. E1. IF: 2,795
- Rudilla D, Galiana L, Oliver A, **Barreto P**. Comparing counseling and dignity therapies in home care patients: A pilot study. *Palliat Support Care*. 2016 Aug; 14(4):321-9. IF: 1,525
- Fombuena M, Galiana L, **Barreto P**, Oliver A, Pascual A, Soto-Rubio A. Spirituality in patients with advanced illness: The role of symptom control, resilience and social network. *J Health Psychol*. 2016 Dec; 21(12):2765-2774. IF: 1,748
- Rudilla D, Oliver A, Galiana L, **Barreto P**. A new measure of home care patients' dignity at the end of life: The Palliative Patients' Dignity Scale (PPDS). *Palliat Support Care*. 2016 Apr; 14(2):99-108. IF: 1,525
- Sancho J, Bures E**, de La Asunción S, **Servera E**. Effect of High-Frequency Oscillations on Cough Peak Flows Generated by Mechanical In-Exsufflation in Medically Stable Subjects With Amyotrophic Lateral Sclerosis. *Respir Care*. 2016 Aug; 61(8):1051-8. IF: 1,838
- Sanz-Herrero F, Gimeno-Cardona C, Tormo-Palop N, Fernández-Fabrellas E, **Briones ML**, Cervera-Juan Á, **Blanquer-Olivas J**. The potential role of 13-valent pneumococcal conjugate vaccine in preventing respiratory complications in bacteraemic pneumococcal community-acquired pneumonia. *Vaccine*. 2016 Apr 4; 34(15):1847-52. IF: 3,624
- Lorente L, Martín MM, **Ferreres J**, Solé-Violán J, Labarta L, Díaz C, Jiménez A, Borreguero-León JM. Serum caspase 3 levels are associated with early mortality in severe septic patients. *J Crit Care*. 2016 Aug; 34:103-6. IF: 2,445
- Álvarez-Lerma F, Marín-Corral J, Vila C, Masclans JR, González de Molina FJ, Martín Loeches I, Barbadillo S, Rodríguez A, **H1N1 GETGAG/SEMICYUC Study Group**. Delay in diagnosis of influenza A (H1N1) pdm09 virus infection in critically ill patients and impact on clinical outcome. *Crit Care*. 2016 Oct 23; 20(1):337. IF: 0
- Lorente L, Martín MM, López-Gallardo E, **Ferreres J**, Solé-Violán J, Labarta L, Díaz C, Jiménez A, Montoya J, Ruiz-Pesini E. Septic patients with mitochondrial DNA haplogroup JT have higher respiratory complex IV activity and survival rate. *J Crit Care*. 2016 Jun; 33:95-9. IF: 2,445
- Lorente L, Martín MM, Pérez-Cejas A, Barrios Y, Solé-Violán J, **Ferreres J**, Labarta L, Díaz C, Jiménez A. Association between Interleukin-6 Promoter Polymorphism (-174 G/C), Serum Interleukin-6 Levels and Mortality in Severe Septic Patients. *Int J Mol Sci*. 2016 Nov 8; 17(11). IF: 3,257
- Sancho J, Servera E**, Jara-Palomares L, Barrot E, Sanchez-Oro-Gómez R, Gómez de Terreros FJ, Martín-Vicente MJ, Utrabo I, Núñez MB, Binimelis A, Sala E, Zamora E, Segrelles G, Ortega-Gonzalez A, Masa F. Noninvasive ventilation during the weaning process in chronically critically ill patients. *ERJ Open Res*. 2016 Oct 28; 2(4). IF: 0
- López-Rodríguez M, Herrera-Ramos E, Solé-Violán J, Ruíz-Hernández JJ, Borderías L, Horcajada JP, Lerma-Chippirraz E, Rajas O, **Briones M**, Pérez-González MC, García-Bello MA, López-Granados E, Rodríguez de Castro F, Rodríguez-Gallego C. IFITM3 and severe influenza virus infection. No evidence of genetic association. *Eur J Clin Microbiol Infect Dis*. 2016 Nov; 35(11):1811-1817. IF: 2,857
- Esteban Ronda V, Franco Serrano J, **Briones Urriaga ML**. Pulmonary *Strongyloides stercoralis* infection. *Arch Bronconeumol*. 2016 Aug; 52(8):442-3. IF: 1,771

Letter

- Franco Serrano J, **Burés Sales E**. The Contribution of Cell Blocks in the Diagnosis of Mediastinal Masses and Hilar Adenopathy Samples from Echobronchoscopy. *Arch Bronconeumol*. 2016 Feb; 52(2):107. IF: 1,823



• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PROMETEO II/2013/014

Title: *Nuevas dianas farmacológicas para el tratamiento de la EPOC y sus comorbilidades vasculares.*

Principal Investigator: Esteban Morcillo Sánchez (Emilio Servera and Maria Cruz González as collaborating researchers)

Funding body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary institution: *Universidad de Valencia*

Duration: 2013-2016

Title: Physiological and clinical effectiveness of mechanically assisted coughing techniques using cough assist with oscillations in amyotrophic lateral sclerosis patients.

Principal Investigator: Emilio Servera Pieras.

Funding body: *Philips Respironics*

Beneficiary institution: *Universidad de Valencia*

Duration: 2015-2017

Total budget: 80.000€

Reference: PSI2014-51962R

Title: *Apego, acontecimientos vitales estresantes y duelo.*

Principal Investigator: Pilar Barreto

Funding body: *Ministerio de Ciencia e Innovación*

Beneficiary institution: *Universidad de Valencia*

Duration: 2015-2017

Total budget: 72.600€

Title: *Efecto de los líquidos del cigarro electrónico (propilenglicol, dietilenglicol y nicotina) sobre los cultivos celulares humanos: células epiteliales pulmonares y células endoteliales.*

Principal Investigator: Jaime Signes-Costa Mañana

Funding body: *Sociedad Valenciana de Neumología/ Fundación de neumología de la Comunidad Valenciana.*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total budget: 6.000€

Title: *Valoración de la demencia frontotemporal y su repercusión en el proceso de toma de decisiones terapéuticas en pacientes con esclerosis lateral amiotrófica.*

Principal Investigator: Emilio Servera

Funding Body: *Sociedad Valenciana de Neumología/ Fundación de Neumología De La Comunidad Valenciana.*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2018

Total budget: 12.000€

Title: *Eficacia de un programa intensivo de tratamiento del tabaquismo sobre las exacerbaciones graves de pacientes fumadores con epoc moderada-severa.*

Principal Investigator: Jaime Signes-Costa

Funding Body: *Sociedad Española de Neumología y Cirugía Torácica*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2018

Total budget: 12.000€



Research Group on Tissular Biochemistry Consolidated group



Group members

Principal investigator

Juan R. Viña
University
H Index: 27



Collaborating researchers

Luis Torres Asensi. University
Elena Ruiz García-Trevijano. University
Vicente Miralles Fernández. University
Teresa Barber Ballester. University

PhD researchers

Lucía Rodríguez Fernández. University

Technicians

Concha García de Mier. University

Emerging researcher

Rosa Zaragoza Colom. University



Strategic aims

- Calpains, activated in the mammary gland during involution, cleave several proteins located in cell membrane, lysosomes, mitochondria and nuclei favoring cell death. Calpains can be implicated in cell anchoring loss. The isoform-specific function of CAPN1 and -2 was explored in two models of cell-adhesion disruption: mice mammary gland during involution and breast cancer cell lines. Both CAPNs were able to cleave adhesion proteins from lactating mammary gland in vitro. CAPN2/E-cadherin in vivo interaction was dramatically increased during involution. Calpain inhibitor administration prevented the cytosolic accumulation of truncated E-cadherin cleaved by CAPN2. In breast cancer cells, CAPN2 was restricted to the nuclear compartment, CAPN1 and CAPN2 knock-down cells showed that cleavage of adhesion proteins and cell migration was mediated by CAPN1 independently of the breast-cancer subtype.

Main lines of research

- The mammary gland as a physiological model for the study of programmed cell death.
- Mammalian tissues metabolism and its regulation
- Epigenomic and protein acetylation studies in K-ras mutated. Colon cancer cell lines.



Emerging researcher

Rosa Zaragoza Colom

Research has been focused on the pathways that regulate mammary gland involution after the pregnancy/lactation cycle and how these pathways become deregulated in breast cancer. Recently, our group has demonstrated a dual role for calpains in mammary tissue controlling programmed cell death and adipocyte redifferentiation. Moreover, these calcium-dependent proteases seem to play also a role in cell migration in breast tumors.

• PUBLICATIONS

Number of articles	IF	Average IF
7	25,62	3,66
National collaborations	International collaborations	Corresponding author
4	3	2

Original articles

1. Cernada M, Bäuerl C, **Serna E**, Collado MC, Martínez GP, Vento M. Sepsis in preterm infants causes alterations in mucosal gene expression and microbiota profiles compared to non-septic twins. *Sci Rep*. 2016 May 16; 6:25497. IF: 5,578
2. **Rodríguez-Fernández L**, Ferrer-Vicens I, García C, Oltra SS, **Zaragoza R**, **Viña JR**, **García-Trevijano ER**. Isoform-specific function of calpains in cell adhesion disruption: studies in postlactational mammary gland and breast cancer. *Biochem J*. 2016 Sep 15; 473(18):2893-909. IF: 3,562
3. Prieto J, León M, Ponsoda X, García-García F, Bort R, **Serna E**, Barneo-Muñoz M, Palau F, Dopazo J, López-García C, Torres J. Dysfunctional mitochondrial fission impairs cell reprogramming. *Cell Cycle*. 2016 Dec; 15(23):3240-3250. IF: 3,952
4. Jordán-Pla A, Miguel A, **Serna E**, Pelechano V, Pérez-Ortín JE. Biotin-Genomic Run-On (Bio-GRO): A High-Resolution Method for the Analysis of Nascent Transcription in Yeast. *Methods Mol Biol*. 2016; 1361:125-39. IF: 0
5. Borrás C, Abdelaziz KM, Gambini J, **Serna E**, Inglés M, de la Fuente M, García I, Matheu A, Sanchís P, Belenguer A, Errigo A, Avellana JA, Baretino A, Lloret-Fernández C, Flames N, Pes G, Rodríguez-Mañas L, Viña J. Human exceptional longevity: transcriptome from centenarians is distinct from septuagenarians and reveals a role of Bcl-xL in successful aging. *Aging (Albany NY)*. 2016 Oct 28; 8(12):3185-3208. IF: 3,979
6. Ferreyra Solari NE, Belforte FS, Canedo L, Videla-Richardson GA, Espinosa JM, Rossi M, **Serna E**, Riudavets MA, Martinetto H, Sevlever G, Perez-Castro C. The NSL Chromatin-Modifying Complex Subunit KANSL2 Regulates Cancer Stem-like Properties in Glioblastoma That Contribute to Tumorigenesis. *Cancer Res*. 2016 Sep 15; 76(18):5383-94. IF: 8,556



Review

- Hawkins RA, **Viña JR**. How Glutamate Is Managed by the Blood-Brain Barrier. *Biology (Basel)*. 2016 Oct 8; 5(4). IF: 0

• THESIS

Thesis Title: *Estudio de acetilación de proteínas en líneas celulares humanas de cáncer colorrectal KRAS mutado o salvaje.*

Doctoral candidate: Desamparados Roda Pérez

Director(s): Andrés Cervantes, Rosa Zaragoza Colom, Elena Ruiz García-Trevijano

Date of the defense: 08/02/2016

Grade: *Apto "cum laude"*

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: BFU2013-46434P

Title: *Papel dual de las calpaínas en la involución de la glándula mamaria murina tras la lactancia: Implicaciones en el desarrollo tumoral post-gestacional*

Principal Investigator: Juan R. Viña and Rosa Zaragoza Colom

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total Budget: €96.800

Reference: PROMETEOII/2014/055

Title: *Vías de señalización que controlan la involución de la glándula mamaria e importancia en el cáncer de mama post-gestacional: estudio en modelos murinos y en líneas celulares humanas*

Principal Investigator: Juan Viña Ribes

Funding Body: *Consellería de Educación, Cultura y Deporte*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2014-2018

Total Budget: €25.000 (this year)

• AWARDS

Since 1995 Dr. Viña is appointed Research Professor in the Chicago Medical School of the Rosalind Franklin University of Medicine and Science.



Research Group on Aging and Physical Activity

Consolidated group



Group members

Principal investigator

José Viña Ribes

University

H Index: 60

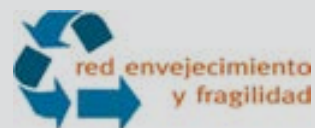
Emerging researcher

Consuelo Borrás Blasco. University

M^a Carmen Gómez Cabrera. University



Team involved in



Collaborating researchers

Ana Lloret Alcañíz. University

Juan Gambini Buchón. University

Gloria Olaso González. University

José Viña Almunia. University

Marta Inglés de la Torre. University

Aitor Carretero. INCLIVA

Consolación García Lucerga. University

Eva Serna García. University

PhD researchers

Cristina Mas Bagues. University

Andrea Salvador Pascual. University

Helena Cabo Plaza. University

Paloma Monllor Taltavull. University

Tanja Fuchsberger. University

Coralie Arc-Chagnaud. University

Mar Dromant. University

Lucia Gimeno. University



Strategic aims

- Prevented of neuronal death in Alzheimer's by Glutaminase Inhibition Pr.
- Identification of exercise training as a drug to treat age associated frailty.
- Testing that G6PD protects from oxidative damage and improves healthspan in mice.
- Reductive stress: a new concept in Alzheimer's disease.

Main lines of research

- Aging: identification of genes associated with aging, particularly genes that are specific in centenary people. Implication of the estrogens and phytoestrogens in the prevention of age-related damage.
- Physical activity: identification of the molecular mechanisms by which physical activity is good for health. Identification of the mechanisms by which physical activity and antioxidant supplements help preventing primary and secondary sarcopenia in both human and animal studies. Identification of the best exercise intervention to delay and to treat frailty in humans.
- Physiopathology of the Alzheimer's disease: identification of the mechanisms by which free radicals, originators of the oxidative stress are used to unleash cell signals that lead to cell death in Alzheimer disease.



Emerging researcher

Consuelo Borrás Blasco

Research is focused on stem cells and oxygen concentration in regenerative medicine. We are studying the role of oxygen concentration when culturing stem cells. High rates

of stem cell proliferation are an important tool in regenerative medicine. Ambient oxygen tensions (21% O₂) are normally used for *in vitro* culture, but physiological levels in vivo range between 3-6% O₂. Our aim is to compare different parameters such as proliferation, pluripotency, senescence or apoptosis culturing human Dental Pulp Stem Cells (hDPSC) under physiological or environmental oxygen concentrations. The results will be determinant to obtain enough cells and with good quality for applying them in regenerative medicine.



Emerging researcher

María Carmen Gómez Cabrera

The main aim of this research is to study the beneficial effects of physical activity in prevention and treatment of several pathologies and more specifically on Alzheimer's disease, senile sarcopenia and frailty. We are also interested in the study of the molecular bases of skeletal muscle atrophy during periods of immobilization, as well as in its prevention.

• PUBLICATIONS

Number of articles	IF	Average IF
27	164,91	6,34
National collaborations	International collaborations	Corresponding author
14	10	14

Original articles

1. Erusalimsky JD, Grillari J, Grune T, Jansen-Duerr P, Lippi G, Sinclair AJ, Tegnér J, **Viña J**, Durrance-Bagale A, Miñambres R, Viegas M, Rodríguez-Mañas L, FRAILOMIC Consortium. In Search of 'Omics'-Based Biomarkers to Predict Risk of Frailty and Its Consequences in Older Individuals: The FRAILOMIC Initiative. *Gerontology*. 2016; 62(2):182-90. IF: 3,059
2. **Lloret A**, **Fuchsberger T**, Giraldo E, **Vina J**. Reductive Stress: A New Concept in Alzheimer's Disease. *Curr Alzheimer Res*. 2016; 13(2):206-11. IF: 3,889
3. **Gambini J**, Gimeno-Mallench L, **Inglés M**, **Olaso G**, Abdelaziz KM, Avellana JA, Belenguer Á, Cruz R, **Mas-Bargues C**, **Borras C**, **Viña J**. [Identification of single nucleotide polymorphisms in centenarians]. *Rev Esp Geriatr Gerontol*. 2016 May-Jun; 51(3):146-9. IF: 0
4. Di Domenico F, Pupo G, Giraldo E, **Lloret A**, Badia MC, Schinina ME, Giorgi A, Butterfield DA, **Vina J**, Perluigi M. Autoantibodies Profile in Matching CSF and Serum from AD and aMCI patients: Potential Pathogenic Role and Link to Oxidative Damage. *Curr Alzheimer Res*. 2016; 13(2):112-22. IF: 3,889
5. Di Domenico F, Pupo G, Giraldo E, Badia MC, Monllor P, **Lloret A**, Schininà ME, Giorgi A, Cini C, Tramutola A, Butterfield



- DA, **Viña J**, Perluigi M. Oxidative signature of cerebrospinal fluid from mild cognitive impairment and Alzheimer disease patients. *Free Radic Biol Med*. 2016 Feb; 91:1-9. IF: 5,736
6. Traylor M, Zhang CR, Adib-Samii P, Devan WJ, Parsons OE, Lanfranconi S, Gregory S, Cloonan L, Falcone GJ, Radmanesh F, Fitzpatrick K, Kanakis A, Barrick TR, Moynihan B, Lewis CM, Boncoraglio GB, Lemmens R, Thijs V, Sudlow C, Wardlaw J, Rothwell PM, Meschia JF, Worrall BB, Levi C, Bevan S, Furie KL, Dichgans M, Rosand J, Markus HS, Rost N, **International Stroke Genetics Consortium**. Genome-wide meta-analysis of cerebral white matter hyperintensities in patients with stroke. *Neurology*. 2016 Jan 12; 86(2):146-53. IF: 8,286
 7. Llana-Belloch S, Priego Quesada JI, Pérez-Soriano P, Lucas-Cuevas ÁG, **Salvador-Pascual A**, **Olaso-González G**, Moliner-Martinez Y, Verdú-Andres J, Campins-Falco P, **Gómez-Cabrera MC**. Disinfection by-products effect on swimmers oxidative stress and respiratory damage. *Eur J Sport Sci*. 2016 Aug; 16(5):609-17. IF: 1,55
 8. Tarazona-Santabalbina FJ, **Gómez-Cabrera MC**, Pérez-Ros P, Martínez-Arnau FM, **Cabo H**, Tsaparas K, **Salvador-Pascual A**, Rodríguez-Mañas L, **Viña J**. A Multicomponent Exercise Intervention that Reverses Frailty and Improves Cognition, Emotion, and Social Networking in the Community-Dwelling Frail Elderly: A Randomized Clinical Trial. *J Am Med Dir Assoc*. 2016 May 1; 17(5):426-33. IF: 4,939
 9. Brodaty H, Woolf C, Andersen S, Barzilai N, Brayne C, Cheung KS, Corrada MM, Crawford JD, Daly C, Gondo Y, Hagberg B, Hirose N, Holstege H, Kawas C, Kaye J, Kochan NA, Lau BH, Lucca U, Marcon G, Martin P, Poon LW, Richmond R, Robine JM, Skoog I, Slavin MJ, Szewieczek J, Tettamanti M, **Viña J**, Perls T, Sachdev PS. ICC-dementia (International Centenarian Consortium - dementia): an international consortium to determine the prevalence and incidence of dementia in centenarians across diverse ethnorracial and sociocultural groups. *BMC Neurol*. 2016 Apr 21; 16:52. IF: 2,04
 10. **Viña J**, Rodríguez-Mañas L, **Salvador-Pascual A**, Tarazona-Santabalbina FJ, **Gomez-Cabrera MC**. Exercise: the lifelong supplement for healthy ageing and slowing down the onset of frailty. *J Physiol*. 2016 Apr 15; 594(8):1989-99. IF: 5,037
 11. **Viña J**, Tarazona-Santabalbina FJ, Pérez-Ros P, Martínez-Arnau FM, **Borras C**, **Olaso-Gonzalez G**, **Salvador-Pascual A**, **Gomez-Cabrera MC**. Biology of frailty: Modulation of ageing genes and its importance to prevent age-associated loss of function. *Mol Aspects Med*. 2016 Aug; 50:88-108. IF: 10,238
 12. **Viña J**, **Salvador-Pascual A**, Tarazona-Santabalbina FJ, Rodríguez-Mañas L, **Gomez-Cabrera MC**. Exercise training as a drug to treat age associated frailty. *Free Radic Biol Med*. 2016 Sep; 98:159-64. IF: 5,736
 13. Nóbrega-Pereira S, Fernandez-Marcos PJ, Brioché T, **Gomez-Cabrera MC**, **Salvador-Pascual A**, Flores JM, **Viña J**, Serrano M. G6PD protects from oxidative damage and improves healthspan in mice. *Nat Commun*. 2016 Mar 15; 7:10894. IF: 11,47
 14. **Inglés M**, Serra-Añó P, **Gambini J**, Abu-Sharif F, Dromant M, Garcia-Valles R, Pareja-Galeano H, Garcia-Lucerga C, **Gomez-Cabrera MC**. Active paraplegics are protected against exercise-induced oxidative damage through the induction of antioxidant enzymes. *Spinal Cord*. 2016 Oct; 54(10):830-837. IF: 1,804
 15. Bonet-Costa V, Herranz-Pérez V, Blanco-Gandía M, **Mas-Bargues C**, **Inglés M**, Garcia-Tarraga P, Rodríguez-Arias M, Miñarro J, **Borras C**, Garcia-Verdugo JM, **Viña J**. Clearing Amyloid- β through PPAR γ /ApoE Activation by Genistein is a Treatment of Experimental Alzheimer's Disease. *J Alzheimers Dis*. 2016 Feb 10; 51(3):701-11. IF: 4,151
 16. **Viña-Almunia J**, **Borras C**, **Gambini J**, El Alamy M, Peñarrocha M, **Viña J**. Influence of different types of pulp treatment during isolation in the obtention of human dental pulp stem cells. *Med Oral Patol Oral Cir Bucal*. 2016 May 1; 21(3):e374-9. IF: 0
 17. **Viña J**, Saez GT, Gambini J, **Gomez-Cabrera MC**, **Borrás C**. Role of NAD(+)/NADH redox ratio in cell metabolism: A tribute to Helmut Sies and Theodor Bücher and Hans A. Krebs. *Arch Biochem Biophys*. 2016 Apr 1; 595:176-80. IF: 3,017
 18. Knafo S, Sánchez-Puelles C, Palomer E, Delgado I, Draffin JE, Mingo J, Wahle T, Kaleka K, Mou L, Pereda-Perez I, Klosi E, Faber EB, Chapman HM, Lozano-Montes L, Ortega-Molina A, Ordóñez-Gutiérrez L, Wandosell F, **Viña J**, Dotti CG, Hall RA, Pulido R, Gerges NZ, Chan AM, Spaller MR, Serrano M, Venero C, Esteban JA. PTEN recruitment controls synaptic and cognitive function in Alzheimer's models. *Nat Neurosci*. 2016 Mar; 19(3):443-53. IF: 16,095
 19. **Inglés M**, **Gambini J**, **Mas-Bargues C**, García-García FJ, **Viña J**, **Borrás C**. Brain-Derived Neurotrophic Factor as a Marker of Cognitive Frailty. *J Gerontol A Biol Sci Med Sci*. 2016 Jul 22 ;. IF: 5,476



20. **Viña J, Gomez-Cabrera MC**, Jackson M. Special Issue "Human performance and redox signaling in health and disease". *Free Radic Biol Med*. 2016 Sep; 98:1. IF: 5,784
21. **Fuchsberger T**, Martínez-Bellver S, Giraldo E, Teruel-Martí V, **Lloret A, Viña J**. A? Induces Excitotoxicity Mediated by APC/C-Cdh1 Depletion That Can Be Prevented by Glutaminase Inhibition Promoting Neuronal Survival. *Sci Rep*. 2016 Aug 12; 6:31158. IF: 5,228
22. **GBD 2015 Risk Factors Collaborators**. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016 Oct 8; 388(10053):1659-1724. IF: 44,002
23. **Borras C**, Abdelaziz KM, **Gambini J, Serna E, Inglés M**, de la Fuente M, Garcia I, Matheu A, Sanchís P, Belenguer A, Errigo A, Avellana JA, Baretino A, Lloret-Fernández C, Flames N, Pes G, Rodriguez-Mañas L, **Viña J**. Human exceptional longevity: transcriptome from centenarians is distinct from septuagenarians and reveals a role of Bcl-xL in successful aging. *Aging (Albany NY)*. 2016 Oct 28; 8(12):3185-3208. IF: 3,979
24. Guadalupe-Grau A, Carnicero JA, Losa-Reyna J, Tresguerres J, **Gómez-Cabrera MD**, Castillo C, Alfaro-Acha A, Rosado-Artalejo C, Rodriguez-Mañas L, García-García FJ. Endocrinology of Aging From a Muscle Function Point of View: Results From the Toledo Study for Healthy Aging. *J Am Med Dir Assoc*. 2016 Oct 21 ; IF: 6,616
25. **Gomez-Cabrera MC, Viña J**, Ji LL. Role of Redox Signaling and Inflammation in Skeletal Muscle Adaptations to Training. *Antioxidants (Basel)*. 2016 Dec 13; 5(4). IF: 0
26. Olivieri F, Capri M, Bonafè M, Morsiani C, Jung HJ, Spazzafumo L, **Viña J**, Suh Y. Circulating miRNAs and miRNA shuttles as biomarkers: Perspective trajectories of healthy and unhealthy aging. *Mech Ageing Dev*. 2016 Dec 13. IF: 2,892

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: FRAILOMIC

Title: Utility ofOMIC-Based biomarkers in characterizing older individuals at risk for frailty, its progression to disability and general consequences to health and well-being - THE FRAILOMIC INITIATIVE (FRAILOMIC)

Principal Investigator: José Viña Ribes

Funding body: European Commission

Beneficiary institution: *Universidad de Valencia*

Duration: 2013-2018

Total budget: 596.520€

Reference: PROMETEOII/2014/056

Title: *Señalización por radicales libres de oxígeno en células madre: importancia en medicina regenerativa*

Principal Investigator: José Viña Ribes

Funding Body: *Consellería de Educación, Cultura y Deporte*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2014-2018

Total Budget: 240.000€

Reference: SAF 2013-44663-R

Title: *Identificación de biomarcadores de fragilidad y de estrategias para su prevención y tratamiento. Centenarios como un modelo de envejecimiento saludable*

Principal Investigator: Jose Viña Ribes

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2014-2016

Total Budget: €217.800

Reference: CB16/10/00435

Title: CIBER de Fragilidad y envejecimiento

Principal Investigator: José Viña Ribes

Funding Body: CIBER

Beneficiary institution: *Universitat de València*

Duration: 2016-2017

Reference: RD12/0043/0029

Title: *Red Temática de Investigación Cooperativa en Envejecimiento y Fragilidad (RETICEF)*

Principal Investigator: José Viña Ribes

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Universidad de Valencia*

Duration: 2013-2016

Total budget: €56.016

Reference: AICO/2016/067

Title: *Efecto de la administración de genisteína y/o bexaroteno para el tratamiento de la enfermedad de Alzheimer en el modelo de ratón transgénico APP/PS1.*

Principal Investigator: Consuelo Borrás Blasco

Funding Body: *Conselleria de Educación, Cultura y Deporte*



Beneficiary institution: *Universidad de Valencia*

Duration: 2016 - 2018

Total Budget: 39.900€

Reference: AICO/2016/076

Title: *Estudio del papel de la enzima xantina oxidoreductasa en la pérdida de masa muscular en modelos animales y humanos. Implicaciones en el tratamiento de la sarcopenia primaria y secundaria.*

Principal Investigator: Mari Carmen Gomez-Cabrera

Funding Body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary institution: *Universidad de Valencia*

Duration: 2016 - 2018

Total Budget: 37.800€

Reference: AICO/2016/078

Title: *Papel de APC-C/Cdh1 en la Enfermedad de Alzheimer: bases moleculares y búsqueda de nuevos biomarcadores.*

Principal Investigator: Ana Lloret Alcañiz

Funding Body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary institution: *Universidad de Valencia*

Duration: 2016 - 2018

Total Budget: 40.000€

Reference: PIE15/00013

Title: A multidisciplinary Project to advance in basic mechanisms, diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction.

Principal Investigator: Vicente Bodí Peris (José Viña as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2018

Total Budget: 589.050€

• THESIS

Thesis title: *Estudio de los valores de referencia para los parámetros de estrés oxidativo: malondialdehído y glutatión medidos por cromatografía líquida de alta eficacia, en humanos y animales de experimentación.*

Doctoral candidate: Consuelo Escrivá López

Director(s): José Viña Ribes, M^a Carmen Gómez Cabrera, Consuelo Borrás Blasco

Date of the defense: 15/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: The role of APC/Cdh1 in Alzheimer's disease.

Doctoral candidate: Tanja Fuchsberger

Director(s): José Viña Ribes, Ana Lloret Alcañiz

Date of the defense: 30/11/2016

Grade: *Sobresaliente "cum laude"*

• AWARDS

In November 2016, Dr. José Viña was awarded with the Albert Struyvenberg Medal of the European Society for Clinical Investigation, a recognition granted annually by this society to a scientist for his outstanding achievements in the field of clinical research. In December 2016, he was appointed President of the Society for Free Radical Research Europe (SFRR Europe).



Research Group on Anesthesiology and Reanimation Consolidated group



<http://www.Anestesiainclinicovalencia.Org>

Group members

Principal investigator

Francisco Javier Belda Nácher
Hospital. University
H Index: 18

Collaborating researchers

Marina Soro Domingo. Hospital. University
Gerardo Aguilar Aguilar. Hospital
Carlos Ferrando Ortola. Hospital
José García de la Asunción. Hospital
Beatriz Garrigues Olivé. Hospital



Juan Vicente Llau Pitarch. Hospital. University
Rafael Badenes Quiles. Hospital
Armando Maruenda Paulino. Hospital. University
María Luisa García Pérez. Hospital
Carlos Tornero Tornero. Hospital. University
Benigno Escamilla Cañete. Hospital
María Luisa Laredo Alcázar. Hospital
Arturo Carratalá Calvo. Hospital
Jaime Pérez-Griera. Hospital
José Miguel Alonso Iñigo. Hospital
Blanca Arocas Chicote. Hospital
José Antonio Carbonell López. Hospital
Pedro Charco Mora. Hospital
Mario de Fez Barberá. Hospital
Mar Garzando Civera. Hospital
Andrea Gutiérrez Valcárcel. Hospital
Irene León Carsi. Hospital
M^a José Parra González. Hospital
Ernesto Pastor Martínez. Hospital
Jaume Puig Bernabéu. Hospital
Ana Mugarra Llopis. Hospital
Laura Reviriego Agudo. Hospital
Estefania Gracia Ferrandiz. Hospital

Emerging researcher

Carlos Ferrando Ortola. Hospital



Strategic aims

- The effects of advanced monitoring on hemodynamic management in critically ill patients.
- Open lung approach for the acute respiratory distress syndrome.
- Stratification and outcome of acute respiratory distress syndrome.
- Recommendations on invasive candidiasis in patients with complicated intra-abdominal infection and surgical patients with ICU extended stay.
- Pharmacokinetics of anidulafungin during venovenous extracorporeal membrane oxygenation.

Main lines of research

- Studying gases used in anesthesia: halogenated agents, xenon and oxygen; and the effects of anesthetics; oxidative stress and protection of organs in ischemia-reperfusion surgery.
- Study of hyperglycemia and aldose reductase-mediated mitochondrial dysfunction and apoptosis in platelets in critical patients.
- Ventilatory and pharmacological strategies to decrease organ damage in the lungs associated with mechanical ventilation in healthy and injured lungs.
- To study safety and potential benefit in terms of protection of halogenated agents during prolonged sedation.
- Development of hemodynamic monitoring and its application in the field of patients undergoing surgery or admitted to critical care units.
- Study and development of instruments and drugs to quantify or involved in different pathways of hemostasis in two ways: prevention of thrombotic complications and bleeding prevention in the perioperative period.
- Study and development of methods of detection of infections, especially fungal and virological, and how to prevent them.
- Development of neurological monitoring and study measures to protect brain damage.
- Development of new strategies and drugs for pain treatment.



Emerging researcher

Carlos Ferrando Ortola

Some of the ongoing research lines in our group that I am leading are:

1. Role of anaesthetics in the inflammatory response in anaesthesia and critical care patients.

2. Strategies to optimize and individualize intraoperative ventilatory management (precision medicine)

3. Role of the perioperative ventilatory strategies in postoperative complications. Protocol published in *Trials* (Ferrando et al. *Trials* 2015). This multicenter randomized controlled trial was performed in 20 Spanish Hospitals and enrolled 1012 patients. Currently we are drafting the manuscript for a high IF Journal.

4. Role of perioperative supplemental oxygen in postoperative complications. We are going to start a multicentre randomized controlled trial with a sample size of 756 patients in 26 Spanish Hospitals to investigate whether an individualized perioperative approach with High versus Conventional FIO₂ prevents postoperative SSI (Clinicaltrials. Gov NCT02776046. PI: Carlos Ferrando).

• PUBLICATIONS

Number of articles	IF	Average IF
20	58,38	2,91
National collaborations	International collaborations	Corresponding author
10	8	4

Original articles

1. Perel A, Saugel B, Teboul JL, Malbrain ML, **Belda FJ**, Fernández-Mondéjar E, Kirov M, Wendon J, Lussmann R, Maggiorini M. The effects of advanced monitoring on hemodynamic management in critically ill patients: a pre and post questionnaire study. *J Clin Monit Comput.* 2016 Oct; 30(5):511-8. IF: 1,985
2. **Llau JV**, Acosta FJ, Escolar G, Fernández-Mondéjar E, Guasch E, Marco P, Paniagua P, Páramo JA, Quintana M, Torrabadella P. Multidisciplinary consensus document on the management of massive haemorrhage (HEMOMAS document). *Rev Esp Anestesiología Reanim.* 2016 Jan; 63(1):e1-e22. IF: 0



3. Kacmarek RM, Villar J, Sulemanji D, Montiel R, **Ferrando C**, Blanco J, Koh Y, Soler JA, Martínez D, Hernández M, Tucci M, Borges JB, Lubillo S, Santos A, Araujo JB, Amato MB, Suárez-Sipmann F, Open Lung Approach Network. Open Lung Approach for the Acute Respiratory Distress Syndrome: A Pilot, Randomized Controlled Trial. *Crit Care Med*. 2016 Jan; 44(1):32-42. IF: 6,312
4. **García-de-la-Asunción J**, García-Del-Olmo E, **Galan G**, Guisjarro R, Martí F, **Badenes R**, **Perez-Griera J**, Duca A, Delgado C, Carbonell J, **Belda J**. Glutathione oxidation correlates with one-lung ventilation time and PO₂/FiO₂ ratio during pulmonary lobectomy. *Redox Rep*. 2016 Sep; 21(5):219-26. IF: 1,522
5. Planells Roig M, Arnal Bertomeu C, Garcia Espinosa R, Cervera Delgado M, **Carrau Giner M**. Ambulatory laparoscopic cholecystectomy by minilaparoscopy versus traditional multiport ambulatory laparoscopic cholecystectomy. Prospective randomized trial. *Cir Esp*. 2016 Feb; 94(2):86-92. IF: 0,743
6. Meier J, Filipescu D, Kozek-Langenecker S, **Llau Pitarch J**, Mallett S, Martus P, Matot I, ETPOS collaborators. Intraoperative transfusion practices in Europe. *Br J Anaesth*. 2016 Feb; 116(2):255-61. IF: 4,853
7. Sakr Y, Ferrer R, Reinhart K, Beale R, Rhodes A, Moreno R, Timsit JF, Brochard L, Thompson BT, Rezende E, Chiche JD, IC-GLOSSARI Investigators, **ESICM Trials Group**. The Intensive Care Global Study on Severe Acute Respiratory Infection (IC-GLOSSARI): a multicenter, multinational, 14-day inception cohort study. *Intensive Care Med*. 2016 May; 42(5):817-28. IF: 7,214
8. Villar J, Ambrós A, Soler JA, Martínez D, **Ferrando C**, Solano R, Mosteiro F, Blanco J, Martín-Rodríguez C, Fernández MM, López J, Díaz-Domínguez FJ, Andaluz-Ojeda D, Merayo E, Pérez-Méndez L, Fernández RL, Kacmarek RM, Stratification and Outcome of Acute Respiratory Distress Syndrome (STANDARDS) Network.. Age, PaO₂/FIO₂, and Plateau Pressure Score: A Proposal for a Simple Outcome Score in Patients With the Acute Respiratory Distress Syndrome. *Crit Care Med*. 2016 Jul; 44(7):1361-9. IF: 6,312
9. Montero A, Mulero JF, **Tornero C**, Guitart J, Serrano M. Pain, disability and health-related quality of life in osteoarthritis-joint matters: an observational, multi-specialty trans-national follow-up study. *Clin Rheumatol*. 2016 Sep; 35(9):2293-305. IF: 1,696
10. Villar J, **Belda J**, Añón JM, Blanco J, Pérez-Méndez L, **Ferrando C**, Martínez D, Soler JA, Ambrós A, Muñoz T, Rivas R, Corpas R, Díaz-Domínguez FJ, **Soro M**, García-Bello MA, Fernández RL, Kacmarek RM, DEXA-ARDS Network. Evaluating the efficacy of dexamethasone in the treatment of patients with persistent acute respiratory distress syndrome: study protocol for a randomized controlled trial. *Trials*. 2016 Jul 22; 17:342. IF: 1,859
11. Fabregat G, **García-de-la-Asunción J**, Sarriá B, Mata M, Cortijo J, de Andrés J, Gallego L, **Belda FJ**. Expression of aquaporins 1 and 5 in a model of ventilator-induced lung injury and its relation to tidal volume. *Exp Physiol*. 2016 Nov 1; 101(11):1418-1431. IF: 2,818
12. Maseda E, Rodríguez AH, **Aguilar G**, Pemán J, Zaragoza R, Ferrer R, Llinares P, Grau S, EPICO Project Group. EPICO 3.0. Recommendations on invasive candidiasis in patients with complicated intra-abdominal infection and surgical patients with ICU extended stay. *Rev Iberoam Micol*. 2016 Oct - Dec; 33(4):196-205. IF: 1,444
13. **Alonso-Iñigo JM**, Escribá FJ, Carrasco JI, Fas MJ, Argente P, Galvis JM, Llopis JE. Measuring cardiac output in children undergoing cardiac catheterization: comparison between the Fick method and PRAM (pressure recording analytical method). *Paediatr Anaesth*. 2016 Nov; 26(11):1097-1105. IF: 2,082
14. Villar J, **Belda J**, Blanco J, Suarez-Sipmann F, Añón JM, Pérez-Méndez L, **Ferrando C**, Parrilla D, Montiel R, Corpas R, González-Higueras E, Pestaña D, Martínez D, Fernández L, **Soro M**, García-Bello MA, Fernández RL, Kacmarek RM, NAVA In Acute respiraTORy failure (NAVIATOR) Network.. Neurally adjusted ventilatory assist in patients with acute respiratory failure: study protocol for a randomized controlled trial. *Trials*. 2016 Oct 13; 17(1):500. IF: 1,859
15. León C, Ruiz-Santana S, Saavedra P, Castro C, Loza A, Zakariya I, Úbeda A, Parra M, Macías D, Tomás JI, Rezusta A, Rodríguez A, Gómez F, Martín-Mazuelos E, **Cava Trem Study Group**. Contribution of Candida biomarkers and DNA detection for the diagnosis of invasive candidiasis in ICU patients with severe abdominal conditions. *Crit Care*. 2016 May 16; 20(1):149. IF: 0
16. **International Surgical Outcomes Study group**. Global patient outcomes after elective surgery: prospective cohort study in 27 low-, middle- and high-income countries. *Br J Anaesth*. 2016 Nov; 117(5):601-609. IF: 5,616



Letters

17. **Badenes R**, Bilotta F. Inhaled sedation in acute brain injury patients. *Br J Anaesth*. 2016 Jun; 116(6):883-4. IF: 4,853
18. **Aguilar G**, Ferriols R, Carbonell JA, Ezquer C, Alonso JM, Villena A, Puig J, Navarro D, Alós M, **Belda FJ**. Pharmacokinetics of anidulafungin during venovenous extracorporeal membrane oxygenation. *Crit Care*. 2016 Oct 17; 20(1):325. IF: 0

Review

19. Vincent JL, Shehabi Y, Walsh TS, Pandharipande PP, Ball JA, Spronk P, Longrois D, Strøm T, Conti G, Funk GC, **Badenes R**, Mantz J, Spies C, Takala J. Comfort and patient-centred care without excessive sedation: the eCASH concept. *Intensive Care Med*. 2016 Jun; 42(6):962-71. IF: 7,214

Clinical guidelines

20. Basora M, Colomina MJ, Moral V, Asuero de Lis MS, Boix E, Jover JL, **Llau JV**, Rodrigo MP, Ripollés J, Calvo Vecino JM. Clinical practice guide for the choice of perioperative volume-restoring fluid in adult patients undergoing non-cardiac surgery. *Rev Esp Anestesiología Reanimación*. 2016 Jan; 63(1):29-47. IF: 0

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: EC10-318

Title: *Tratamiento anticipado con ganciclovir de la infección activa por el citomegalovirus (CMV) en el paciente crítico en ventilación mecánica con sepsis grave o shock séptico*

Principal Investigator: Gerardo Aguilar Aguilar

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2012-2016

Total budget: 38.500€

Reference: PI13/02742

Title: Prospective observational study of the direct oral anticoagulants perioperative management

Principal Investigator: Raquel Ferrandis Comes

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total Budget: 53.845€

Reference: PI13/00119

Title: *Reducción de las asincronías y de la duración de la ventilación mecánica mediante la Ventilación Asistida Ajustada Neuralmente (NAVA) en pacientes con insuficiencia respiratoria aguda*

Principal Investigator: Jesús Villar Hernández (Francisco Javier Belda as collaborating researcher)

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Canaria de Investigación y Salud (FUNCIS)*

Duración: 2014-2016

Total budget: 55.418€

Reference: PI14/00829

Title: *Reducción de las complicaciones postoperatorias y de la estancia hospitalaria con una estrategia perioperatoria individualizada de ventilación de protección pulmonar. Estudio comparativo, prospectivo.*

Principal Investigator: Carlos Ferrando Ortolá

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duración: 2015-2017

Total budget: 108.250€

Title: *Reducción de las complicaciones postoperatorias y de la estancia hospitalaria con una estrategia perioperatoria individualizada de ventilación de protección pulmonar.*

Principal Investigator: Carlos Ferrando Ortolá and Marina Soro

Funding Body: European Society of Anaesthesiology (ESA)

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015 - 2017

Total budget: 30.000€

• THESIS

Thesis title: *Expresión de aquaporinas 1 y 5 en el pulmón de ratas sometidas a ventilación mecánica: efectos del volumen corriente y el tiempo de ventilación*

Doctoral candidate: Gustavo Fabregat Cid

Director(s): Antonio M Alberola Aguilar, José García de la Asunción, Benjamín Sarriá

Date of the defense: 08/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Preacondicionamiento remoto por isquemia-reperusión en la lobectomía pulmonar. Un estudio sobre la prevención del estrés oxidativo*

Doctoral candidate: Laura Bruno Carlos

Director(s): José García de la Asunción, Genaro Galán Gil

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Descripción de una metodología docente para el aprendizaje de la fibroscopia flexible en el control de la vía aérea*

Doctoral candidate: Pedro Charco Mora

Director(s): Francisco Javier Belda Nácher, Marina Soro

Date of the defense: 27/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Efecto de la duloxetina sobre la expresión de fos en el tronco del encéfalo y en la médula espinal de la rata en modelos de dolor persistente*

Doctoral candidate: Carlos Tornero Tornero

Director(s): Francisco Javier Belda Nácher, Alfonso A. Valverde Navarro, Francisco Martínez Soriano

Date of the defense: 21/01/2016

Grade: *Sobresaliente "cum laude"*

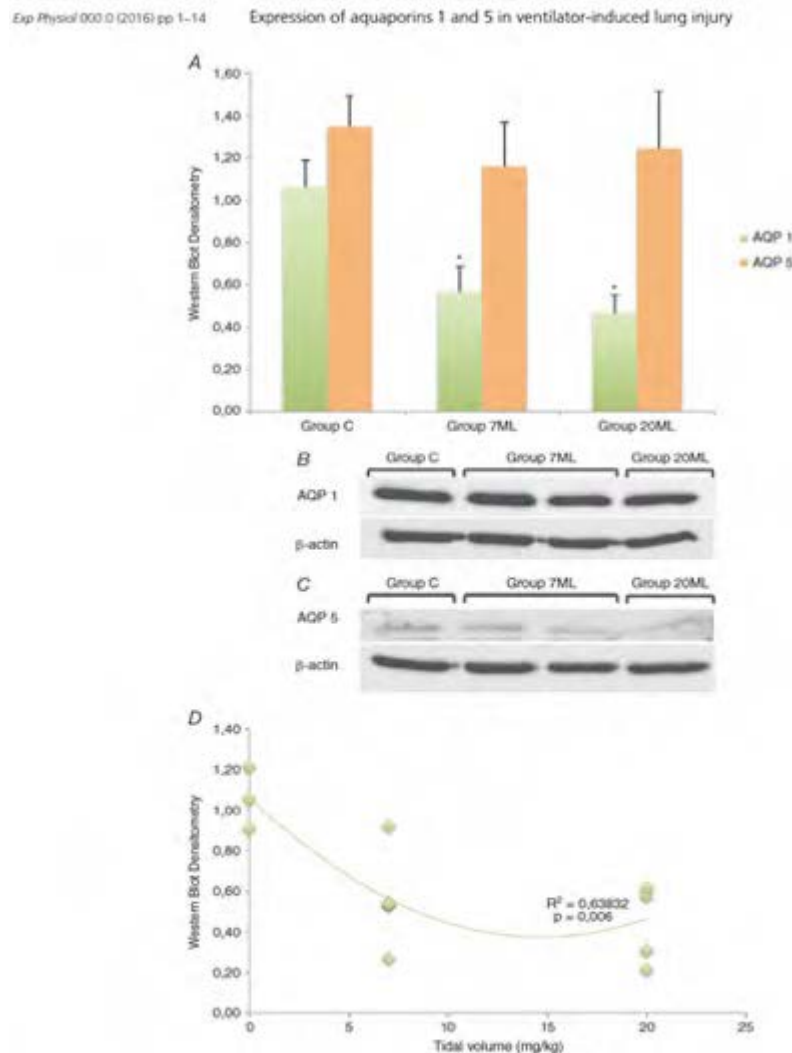


Figure 6. Expression of aquaporins measured by Western Blot. **A**, bar chart showing Western blot mean densitometry values. Error bars represent SEM. Abbreviations: AQP1, aquaporin 1; and AQP5, aquaporin 5. * $P < 0.05$ versus group C. **B**, Western blot for AQP1. Data presented are representative of 13 experiments. **C**, Western blot for AQP5. Data presented are representative of 13 experiments. **D**, dispersion chart and regression lines of Western blot densitometry values of AQP1 in relation to tidal volume. The dispersion coefficient R^2 and the degree of significance are presented. Group C, $n = 3$; group 7ML, $n = 5$; and group 20ML, $n = 5$.



Research Group on Translational Genomics Consolidated group



<http://medicina-genomica.blogspot.com.es/> <https://twitter.com/MPAlonso> <http://www.uv.es/gt/>
 “Genetistas de la Universidad de Valencia avanza hacia la cura de nuestra Distrofia Muscular”
<http://www.conquistandoescalones.org>

Group members

Principal investigator

Rubén D. Artero Allepuz
 University
 H Index: 16



Collaborating researchers

Manuel Pérez Alonso. University
 M^a Beatriz Llamusí Troisi. University
 Juan M. Fernandez Costa. University
 Ariadna Bargiela Schönbrunn. University

PhD students

Estefanía Cerro Herreros. University
 Piotr Konieczny. University
 Mouli Chakraborty. University
 Anna Serafina Rapisarda. University
 Estela Selma Soriano. University
 María Sabater Arcis. University



Strategic aims

- We have reached several important scientific objectives during 2016. First, we have published proof-of-concept that boosting endogenous expression of Muscleblind by blocking specific inhibitory miRNAs was able to suppress several Myotonic Dystrophy-like phenotypes in a Drosophila model of disease. This proved that miRNA-based drugs constitute a new potential therapeutic strategy for the disease.
- We have completed previous work towards the identification of a miRNA-based Myotonic Dystrophy serum biomarker.
- We have started scientific collaborations that confirm our laboratory as a national reference in the characterization of Drosophila heart phenotypes.

Main lines of research

- Using miRNAs as therapeutic targets in myotonic dystrophy (DM).
- Discovery, development, and repurposing of drugs for the treatment of DM.
- Study of the molecular causes of muscle atrophy, heart dysfunction, and CNS degeneration in DM.
- Study of the molecular mechanisms associated with spinal muscular atrophy and search for potential therapies.
- Understanding human podocyte function through Drosophila nephrocytes.
- Development of a LGMD1F Drosophila model.

• PUBLICATIONS

Number of articles	IF	Average IF
3	11,66	3,88

National collaborations	International collaborations	Corresponding author
1	1	2

Original articles

1. Iyer J, Wang Q, Le T, Pizzo L, Grönke S, Ambegaokar SS, Imai Y, Srivastava A, **Troisí BL**, Mardon G, **Artero R**, Jackson GR, Isaacs AM, Partridge L, Lu B, Kumar JP, Girirajan S. Quantitative Assessment of Eye Phenotypes for Functional Genetic Studies Using Drosophila melanogaster. G3 (Bethesda). 2016 May 3; 6(5):1427-37. IF: 3,198
 2. **Fernandez-Costa JM**, **Llamusi B**, **Bargiela A**, Zulaica M, Alvarez-Abril MC, **Perez-Alonso M**, Lopez de Munain A, Lopez-Castel A, **Artero R**. Six Serum miRNAs Fail to Validate as Myotonic Dystrophy Type 1 Biomarkers. PLoS One. 2016; 11(2):e0150501. IF: 3,234
 3. **Cerro-Herreros E**, **Fernandez-Costa JM**, **Sabater-Arcis M**, **Llamusi B**, **Artero R**. Derepressing muscleblind expression by miRNA sponges ameliorates myotonic dystrophy-like phenotypes in Drosophila. Sci Rep. 2016 Nov 2; 6:36230. IF: 5,228
- **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**
- Reference:** ISIC/2013/004
Title: Instituto Superior de Investigación Cooperativa de Biotecnología y Biomedicina (ISIC BIOTECMED).
Principal Investigator: Juan Ferre Manzanero (Rubén Darío Artero as collaborating researcher)
Funding body: Conselleria de Educación, Cultura y Deporte
Beneficiary institution: Universidad de Valencia
Duration: 2013-2016
Total budget: 50.000€ (this year)
- Reference:** PROMETEO II/2014/067
Title: Aproximaciones genéticas para el estudio de patologías humanas y del desarrollo en Drosophila.
Principal Investigator: Nuria Paricio Ortiz (Rubén Artero as collaborating researcher)
Funding Body: Conselleria de Educación Cultura y Deporte
Beneficiary Institution: University of Valencia
Duration: 2014-2018
- Reference:** BLOCK-DM
Title: Desarrollo de fármacos bloqueadores de la toxicidad de expansiones CUG responsables de la distrofia miotónica.
Principal Investigator: Rubén Artero Allepuz
Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2015 - 2016
Total budget: 4.000€
- Title:** A Spinal Muscular Atrophy Drosophila model for in vivo drug discovery
Principal Investigator: Rubén Artero Allepuz



Funding Body: SMA Europe

Beneficiary Institution: *Universidad de Valencia*

Duration: 2016 - 2018

Total budget: 121.500€

Reference: SAF 2015-64500-R

Title: *Modulación terapéutica de la expresión de genes patogénicos en Distrofia Miotónica: prueba de concepto.*

Principal Investigator: Rubén Artero Allepuz

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *University of Valencia*

Duration: 2016-2018

Total budget: 145.000€

Reference: PI13/00386

Title: *Development of pharmacological therapies for myotonic dystrophy*

Principal Investigator: Manuel Pérez Alonso

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total Budget: 86.515€

Reference: 73

Title: *Analysis of the structure-activity relationships of anti-myotonic dystrophy hexapeptides*

Principal Investigator: M^a Beatriz Llamusi Troisi

Funding Body: *Telemaratón RTVE Todos somos raros, todos somos únicos*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total budget: 99.990€

Reference: 2014/063

Title: *Characterization of novel suppressors of neurodegeneration in myotonic dystrophy type1*

Principal Investigator: Manuel Pérez Alonso

Funding body: *Fundación La Marató de TV3*

Beneficiary institution: *INCLIVA*

Duration: 2015-2017

Total budget: 125.125€

Reference: 18-IMRTZH2C-ARTERO-EROLES-2016-A

Title: *Implicación de la familia de proteínas MBNL en cáncer de mama HER2+ y su posible relación con la respuesta/resistencia al tratamiento con trastuzumab.*

Principal Investigator: Rubén Artero, Pilar Eroles

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total budget: 4.000€

• THESIS

Thesis title: *Caracterización de la actividad biológica y farmacológica del alcaloide boldina en la distrofia miotónica de tipo 1*

Doctoral candidate: M^a Carmen Álvarez Abril

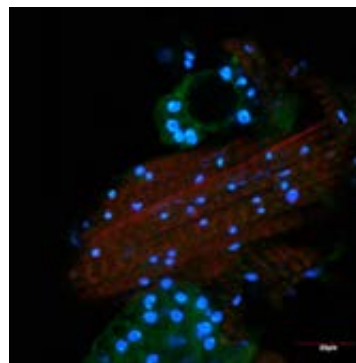
Director(s): Rubén Artero Allepuz, Arturo López Castel, Manuel Pérez Alonso

Date of the defense: 15/01/2016

Grade: *Sobresaliente "cum laude"*

• AWARDS

In November 2016, Dr. Manuel Pérez Alonso was awarded with the "2016 plaque of honor to the Entrepreneurship" merit granted by the Spanish Association of Scientists.



Drosophila heart stained with DAPI (blue stained nuclei), Muscledblind (green) and phalloidin (red). The heart itself is the fibers marked in red.



Research Group on General and Digestive Surgery Consolidated group



Group members

Principal investigator

Joaquín Ortega Serrano
Hospital
H Index: 12



Collaborating researchers

Bruno Camps Vilata. Hospital
Luis Sabater Ortí. Hospital
Elena Muñoz Forner. Hospital
Francisco Morera Ocón. Hospital
José Martín Arévalo. Hospital
David Moro Valdezate. Hospital
Vicente Pla Martín. Hospital
Norberto Cassinello Fernández. Hospital
Consuelo Sebastián Pastor. Hospital
Fernando López Mozos. Hospital
Roberto Martí Obiol. Hospital
Julio Calvete Chornet. Hospital
Elena Martí Cuñat. Hospital
Marina Garcés Albir. Hospital
Raquel Alfonso Ballester. Hospital
Dimitri Dorcaratto. Hospital



Strategic aims

- Incorporation of the retroperitoneoscopy as a new surgical technique for the department, as a treatment of adrenal tumors.
- Development of the clinical pathway for thyroidectomy.
- International edition of a book on esophageal cancer: "Esophageal cancer: symptoms, management and prognosis".
- Completion of the national multicenter trial on the differences between the pancreato-gastrostomy and pancreato-jejunostomy in cephalic pancreaticoduodenectomy technique.

Main lines of research

- Coloproctological surgery: study of the quality standards for coloproctology 3D endorectal ultrasound, sacral neuromodulation and perianal fistula surgery.
- Hepatobiliary and pancreatic surgery: acute pancreatitis, gene transfection, pancreaticoduodenectomy.
- Endocrine surgery: laparoscopic adrenal tumors, recurrences study in thyroid surgery, parathyroid adenomas intraoperative localization.
- Metabolic and bariatric surgery: pathophysiology of postoperative changes.
- Breast surgery: utility of fibrin sealants in postoperative seroma.
- Gastroesophageal surgery: mutations in GIST tumors, overexpression of HER2 and HER3 in gastric tumors, perioperative QT in advanced gastric cancer.

• PUBLICATIONS

Number of articles	IF	Average IF
14	32,16	2,29

National collaborations	International collaborations	Corresponding author
7	1	7

Original articles

1. Ferro O, Soria J, Garcés M, Guijarro J, Gámez JM, **Sabater L**. [Pseudoaneurysm of the superior mesenteric artery after pancreatoduodenectomy]. *Gastroenterol Hepatol*. 2016 Jun-Jul; 39(6):400-2. IF: 0,838
2. Bennasar Remolar MÁ, Martínez Ramos D, **Ortega Serrano J**, Salvador Sanchís JL. Nutritional alterations after very low-calorie diet before bariatric surgery. *Cir Esp*. 2016 Mar; 94(3):159-164. IF: 0,743
3. Marinello FG, Baguena G, Lucas E, Frasson M, Hervás D, Flor-Lorente B, Esclapez P, **Espí A**, García-Granero E. Anastomotic leakage after colon cancer resection: does the individual surgeon matter? *Colorectal Dis*. 2016 Jun; 18(6):562-9. IF: 2,351
4. Mora F, **Cassinello N**, Mora M, Bosca M, Minguez M, **Ortega J**. Esophageal abnormalities in morbidly obese adult patients. *Surg Obes Relat Dis*. 2016 Mar-Apr; 12(3):622-8. IF: 4,066
5. Frasson M, Granero-Castro P, Ramos Rodríguez JL, Flor-Lorente B, Braithwaite M, Martí Martínez E, Álvarez Pérez JA, Codina Cazador A, **Espí A**, García-Granero E, ANACO Study Group. Risk factors for anastomotic leak and postoperative morbidity and mortality after elective right colectomy for cancer: results from a prospective, multicentric study of 1102 patients. *Int J Colorectal Dis*. 2016 Jan; 31(1):105-14. IF: 2,449
6. **Garcés-Albir M**, García-Botello SA, Espi A, **Pla-Martí V**, **Martín-Arevalo J**, **Moro-Valdezate D**, **Ortega J**. Three-dimensional endoanal ultrasound for diagnosis of perianal fistulas: Reliable and objective technique. *World J Gastrointest Surg*. 2016 Jul 27; 8(7):513-20. IF: 0
7. **Sabater L**, Ausania F, Bakker OJ, Boadas J, Domínguez-Muñoz JE, Falconi M, Fernández-Cruz L, Frulloni L, González-Sánchez V, Lariño-Noia J, Lindkvist B, Lluís F, **Morera-Ocón F**, Martín-Pérez E, Marra-López C, Moya-Herraiz Á, Neoptolemos JP, Pascual I, Pérez-Aisa Á, Pezzilli R, Ramia JM, Sánchez B, Molero X, Ruiz-Montesinos I, Vaquero EC, de-Madaria E. Evidence-based Guidelines for the Management of Exocrine Pancreatic Insufficiency After Pancreatic Surgery. *Ann Surg*. 2016 Dec; 264(6):949-958. IF: 8,569
8. Martín-Richard M, Ginès A, Ayuso JR, **Sabater L**, Fabregat J, Mendez R, Fernández-Esparrach G, Molero X, Vaquero EC, Cuatrecasas M, Ferrández A, Maurel J, Comité multidisciplinar para la actualización de las recomendaciones para el manejo de las lesiones pre-malignas y el adenocarcinoma de páncreas.. [Recommendations for the diagnosis, staging and treatment of pre-malignant lesions and pancreatic adenocarcinoma]. *Med Clin (Barc)*. 2016 Nov 18; 147(10):465. E1-465. E8. IF: 1,267



9. León-Espinoza C, López-Mozos F, Martí-Obiol R, Garcés-Albir M, Ortega-Serrano J. "Magic" of our gastric cancer results on perioperative chemotherapy. *World J Gastrointest Pathophysiol.* 2016 Aug 15; 7(3):283-7. IF: 0
10. Villar-Del-Moral J, Capela-Costa J, Jiménez-García A, Sitges-Serra A, Casanova-Rituerto D, Rocha J, Martos-Martínez JM, de la Quintana-Basarrate A, Rosa-Santos J, Guirao-Garriga X, Bravo-de-Lifante JM, Vidal-Pérez Ó, Moral-Duarte A, Polónia J, **Iberpara Study Group**.. Compliance with recommendations on surgery for primary hyperparathyroidism-from guidelines to real practice: results from an Iberian survey. *Langenbecks Arch Surg.* 2016 Nov; 401(7):953-963. IF: 2,149
11. Díaz-Tobarra M, **Cassinello Fernández N**, Jordá Gómez P, Nofal MN, Alfonso Ballester R, **Ortega Serrano J**. One-Stage vs Two-Stage Laparoscopic Roux-en-Y Gastric Bypass in Obese Patients with Body Mass Index >55 Kg/m²; 5-YEAR FOLLOW UP. *Obes Surg.* 2016 Oct 9 ;. IF: 3,346

Letters

12. Cholvi Calduch R, Fernández Moreno MC, Díaz-Tobarra M, **Calvete Chornet J**. Hemoperitoneum secondary to perforated inflammatory myofibroblastic tumor: A case report of an unusual complication. *Rev Esp Enferm Dig.* 2016 Jan; 108(1):51-2. IF: 1,414
13. Gámez-del-Castillo JM, **Garcés-Albir M**, Fernández-Moreno MC, **Morera-Ocón FJ**, Villagrasa R, **Sabater-Ortí L**. Disconnected pancreatic duct syndrome: complete pancreas transection secondary to acute pancreatitis. *Rev Esp Enferm Dig.* 2016 Mar; 108(3):165-6. IF: 1,455

Review

14. Cascales-Campos PA, López-López V, Muñoz-Casares FC, Feliciangeli E, Torres Melero J, Barrios P, Morales R, Ramos I, Ortega G, **Camps B**, González-Bayón L, Bretcha-Boix P, Farré-Alegre J, González-Moreno S, Gil J. Morbidity and mortality outcomes after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in patients aged 75 years and over: Spanish group of peritoneal cancer surgery (GECOP) multicenter study. *Surg Oncol.* 2016 Jun; 25(2):111-6. IF: 3,514

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI15/00076

Title: *Duodenopancreatectomía cefálica en tumores de páncreas y periampulares: abordaje inicial de la arteria mesentérica superior versus abordaje clásico. Estudio prospectivo, aleatorizado y multicéntrico.*

Principal Investigator: Luis Sabater Ortí

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2018

Total budget: 56.265€

Reference: PI15/02180

Title: *Enfermedad mínima residual en cánceres colorrectales de alto riesgo resecaados. Valor de las biopsias líquidas en el seguimiento y análisis de la heterogeneidad tumoral.*

Principal Investigator: Andrés Cervantes Ruipérez (Alejandro Espí as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2018

Total budget: 80.465€

• THESIS

Thesis title: *Bypass distal de miembros inferiores: análisis de resultados en un servicio de cirugía cardiovascular de la Comunidad Valenciana.*

Doctoral candidate: Iván Martín González

Director(s): Luis Sabater Ortí

Date of the defense: 13/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Una nueva técnica de remodelación de la punta nasal en rinoplastia, para casos extremadamente difíciles, mediante la resección total de los cartílagos alares.*

Doctoral candidate: Salvador Rodríguez-Camps Devís

Director(s): Alejandro Espí Macías

Date of the defense: 26/02/2016

Grade: *Sobresaliente "cum laude"*



- **AWARDS**

On 2016 Dr. Vicente Plá and collaborators won the Award to the Best Movie in the Women's Health Area, on the XX International Medical Film, Health and Telemedicine Competition VIDEOMED 2016 with the video: *Transvaginal repair with biological mesh of symptomatic rectocele*. Dr. Luis Sabater and collaborators won the Best Surgery Film on the XX International Medical Film, Health and Telemedicine Competition VIDEOMED 2016 with the video: *Corporocaudal pancreatectomy with resection of hepatic artery and celiac trunk: modified Appleby's intervention*.

Also Dr. Bruno Camps won the National Champion (Spain) on the Peritoneal Surface Oncology Group International - PSOGI 2016 in New York.



Research Group on Personal Autonomy, Dependence and Severe Mental Disorders (TMAP)

Consolidated group



Group members

Principal investigator

Rafael Tabarés Seisdedos
University
H Index: 26

Collaborating researchers

Gabriel Selva Vera. University. Hospital
Manuel Gómez Beneyto. University
Patricia Correa Ghisays. University
Inmaculada Fuentes Durá. University
Cristina Amézcuca García. CIBERSAM
Ferrán Catalá López. University



Strategic aims

- The development of a guide / consensus with “Asociación European Psychiatric Association (EPA) - Working Group on Mental Health Consequences of Economic Crises of the EPA Council of National Psychiatric Associations EPA guidance on mental health and economic crises in Europe”.
- Project on “Comorbidity between Cancer and Central Nervous System Disorders”, which aims to synthesize epidemiological evidence and assess the validity of associations between central nervous system disorders and the risk of developing or dying from cancer. It is a collaborative meta-analysis in 5 countries (Spain, Canada, Australia, United Kingdom and the United States) coordinated by the University of Valencia/CIBERSAM (Dr. Catalá-López, Prof. Tabarés-Seisdedos). The study has been prospectively registered in PROSPERO and the protocol article is currently under review.
- “The Global Burden of Disease Study” is the largest international collaborative project on the epidemiology of diseases, injuries and risk factors at the global, national and regional levels. During this year, results corresponding to the 2013 (Dr. Catalá-López) and 2015 iterations (Dr. Catalá-López, Prof. Tabarés-Seisdedos) have been published in prestigious journals such as The Lancet and JAMA.
- Projects in advanced methods of systematic reviews and meta-analyses, including the publication of two papers in PLoS Medicine (PLoS Med. 2016;13(5):e1002028 and PLoS Med. 2016;13(3):e1001971).
- Dr. Balanzá has co-authored several papers published in high IF journals and given several international conferences about three major lines of research: neurocognition in BD, nutritional psychiatry, and the microbiota-gut-brain axis. Moreover, he participates as PI of this group in the Cohortes CIBERSAM project, an innovative, nation-wide cohort of cohorts of first episode psychoses
- Various papers and editorials have been published on methodological quality, biases and conflicts of interest in mental health research, public health and health economics.

Main lines of research

- Study of neurocognitive endophenotypes in schizophrenia and bipolar disorder.
- Study of pharmacological strategies for improving cognitive function in bipolar disorder.
- Epidemiology and disability associated with SMI.
- Identification of biomarkers in SMI.
- Study of the direct and reverse comorbidity in SMI in relation to cancer and diabetes.
- Development and efficacy study of psychoeducation and neurocognitive therapy and functional rehabilitation for people with SMI.
- Establishment of a clinical staging system (ClinicalStaging) applied to bipolar disorder by the combination of biomarkers, neurocognitive and functional performance.
- Nutritional psychiatry.

• PUBLICATIONS

Number of articles	IF	Average IF
31	331,89	10,70
National collaborations	International collaborations	Corresponding author
10	21	9

Original articles

1. Medel-Herrero A, **Gómez-Beneyto M**, Saz-Parkinson Z, Bravo-Ortiz MF, Amate JM. Discordance between two national health statistics sources (EMH and EESCRI, 1990-2009). Analysis of psychiatric morbidity. Rev Psiquiatr Salud Ment. 2016 Jan-Mar; 9(1):22-30. IF: 1,622
2. Bonnin CM, Reinares M, Martínez-Arán A, **Balanzá-Martínez V**, Sole B, Torrent C, **Tabarés-Seisdedos R**, García-Portilla MP, Ibáñez A, Amann BL, Arango C, Ayuso-Mateos JL, Crespo JM, González-Pinto A, Colom F, Vieta E, CIBERSAM Functional Remediation Group. Effects of functional remediation on neurocognitively impaired bipolar patients: enhancement of verbal memory. Psychol Med. 2016 Jan; 46(2):291-301. IF: 5,938
3. Bonnin CM, Torrent C, Arango C, Amann BL, Solé B, González-Pinto A, Crespo JM, **Tabarés-Seisdedos R**, Reinares M, Ayuso-Mateos JL, García-Portilla MP, Ibáñez Á, Salmero



- M, Vieta E, Martínez-Aran A, CIBERSAM Functional Remediation Group. Functional remediation in bipolar disorder: 1-year follow-up of neurocognitive and functional outcome. *Br J Psychiatry*. 2016 Jan; 208(1):87-93. IF: 7,991
4. Anaya C, Torrent C, Caballero FF, Vieta E, Bonnin Cdel M, Ayuso-Mateos JL, **CIBERSAM Functional Remediation Group**. Cognitive reserve in bipolar disorder: relation to cognition, psychosocial functioning and quality of life. *Acta Psychiatr Scand*. 2016 May; 133(5):386-98. IF: 5,605
 5. Page MJ, Shamseer L, Altman DG, Tetzlaff J, Sampson M, Tricco AC, **Catalá-López F**, Li L, Reid EK, Sarkis-Onofre R, Moher D. Epidemiology and Reporting Characteristics of Systematic Reviews of Biomedical Research: A Cross-Sectional Study. *PLoS Med*. 2016 May; 13(5):e1002028. IF: 0
 6. Hutton B, **Catalá-López F**, Moher D. [The PRISMA statement extension for systematic reviews incorporating network meta-analysis: PRISMA-NMA]. *Med Clin (Barc)*. 2016 Sep 16; 147(6):262-6. IF: 1,417
 7. **Catalá-López F**, Macías Saint-Gerons D, González-Bermejo D, Rosano GM, Davis BR, Ridao M, Zaragoza A, Montero-Corominas D, Tobías A, de la Fuente-Honrubia C, **Tabarés-Seisdedos R**, Hutton B. Cardiovascular and Renal Outcomes of Renin-Angiotensin System Blockade in Adult Patients with Diabetes Mellitus: A Systematic Review with Network Meta-Analyses. *PLoS Med*. 2016 Mar; 13(3):e1001971. IF: 0
 8. **Catalá-López F**, Ridao M, Alonso-Arroyo A, García-Altés A, Cameron C, González-Bermejo D, Aleixandre-Benavent R, Bernal-Delgado E, Peiró S, **Tabarés-Seisdedos R**, Hutton B. The quality of reporting methods and results of cost-effectiveness analyses in Spain: a methodological systematic review. *Syst Rev*. 2016 Jan 7; 5:6. IF: 0
 9. **Catalá-López F**, Moher D, Tabarés-Seisdedos R. Improving transparency of scientific reporting to increase value and reduce waste in mental health research. *Rev Psiquiatr Salud Ment*. 2016 Jan-Mar; 9(1):1-3. IF: 1,622
 10. Ayesa-Arriola R, Rodríguez-Sánchez JM, Suero ES, Reeves LE, **Tabarés-Seisdedos R**, Crespo-Facorro B. Diagnosis and neurocognitive profiles in first-episode non-affective psychosis patients. *Eur Arch Psychiatry Clin Neurosci*. 2016 Oct; 266(7):619-28. IF: 3,525
 11. Ridao M, **Catalá-López F**. Quality of Methods and Results Reporting in Cost-effectiveness Analyses of Cardiovascular Interventions. *Rev Esp Cardiol (Engl Ed)*. 2016 Sep; 69(9):876-7. IF: 4,596
 12. **GBD 2015 Maternal Mortality Collaborators**. Global, regional, and national levels of maternal mortality, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016 Oct 8; 388(10053):1775-1812. IF: 44,002
 13. **GBD 2015 Child Mortality Collaborators**. Global, regional, national, and selected subnational levels of stillbirths, neonatal, infant, and under-5 mortality, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016 Oct 8; 388(10053):1725-1774. IF: 44,002
 14. **GBD 2015 DALYs and HALE Collaborators**. Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016 Oct 8; 388(10053):1603-1658. IF: 44,002
 15. **GBD 2015 Disease and Injury Incidence and Prevalence Collaborators**. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016 Oct 8; 388(10053):1545-1602. IF: 44,002
 16. **GBD 2015 Mortality and Causes of Death Collaborators**. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016 Oct 8; 388(10053):1459-1544. IF: 44,002
 17. **GBD 2015 SDG Collaborators**. Measuring the health-related Sustainable Development Goals in 188 countries: a baseline analysis from the Global Burden of Disease Study 2015. *Lancet*. 2016 Oct 8; 388(10053):1813-1850. IF: 44,002
 18. Li L, **Catalá-López F**, Alonso-Arroyo A, Tian J, Aleixandre-Benavent R, Pieper D, Ge L, Yao L, Wang Q, Yang K. The Global Research Collaboration of Network Meta-Analysis: A Social Network Analysis. *PLoS One*. 2016 Sep 29; 11(9):e0163239. IF: 3,057
 19. **GBD 2015 HIV Collaborators**, et al. Estimates of global, regional, and national incidence, prevalence, and mortality of HIV, 1980-2015: the Global Burden of Disease Study 2015. *Lancet HIV*. 2016 Aug; 3(8):e361-87. IF: 0
 20. **Global Burden of Disease Pediatrics Collaboration et al**. Global and National Burden of Diseases and Injuries Among



- Children and Adolescents Between 1990 and 2013: Findings From the Global Burden of Disease 2013 Study. *JAMA Pediatr.* 2016 Mar; 170(3):267-87. IF: 9,528
21. Haagsma JA, Graetz N, Bolliger I, (et al). The global burden of injury: incidence, mortality, disability-adjusted life years and time trends from the Global Burden of Disease study 2013. *Inj Prev.* 2016 Feb; 22(1):3-18. IF: 1,693
 22. Pelayo-Terán JM, Gajardo Galán VG, de la Ortiz-García de la Foz V, Martínez-García O, **Tabarés-Seisdedos R**, Crespo-Facorro B, Ayesa-Arriola R. Rates and predictors of relapse in first-episode non-affective psychosis: a 3-year longitudinal study in a specialized intervention program (PAFIP). *Eur Arch Psychiatry Clin Neurosci.* 2016 Oct 28 ;. IF: 4,113
 23. **Global Burden of Disease Cancer Collaboration.**, (et al). Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study. *JAMA Oncol.* 2016 Dec 3 ;. IF: 0
 24. Macías Saint-Gerons D, de la Fuente Honrubia C, de Andrés Trelles F, **Catalá-López FC**. [Future Perspective of Pharmacoepidemiology in the “Big Data Era” and the Growth of Information Sources]. *Rev Esp Salud Publica.* 2016 Dec 1; 90:e1-e7. IF: 0,606
 25. Bueno C, **Tabares-Seisdedos R**, Moraleda JM, Martinez S. Rett Syndrome Mutant Neural Cells Lacks MeCP2 Immunoreactive Bands. *PLoS One.* 2016 Apr 11; 11(4):e0153262. IF: 3,057
 26. Martin-Carrasco M, Evans-Lacko S, Dom G, Christodoulou NG, Samochowiec J, González-Fraile E, Bienkowski P, **Gómez-Beneyto M**, Dos Santos MJ, Wasserman D. EPA guidance on mental health and economic crises in Europe. *Eur Arch Psychiatry Clin Neurosci.* 2016 Mar; 266(2):89-124. IF: 4,113
 29. **Tabarés-Seisdedos R**, Baudot A. Editorial: Direct and Inverse Comorbidities Between Complex Disorders. *Front Physiol.* 2016; 7:117. IF: 3,534
 30. **Catalá López F**, Pérez Andrés C. [The GATHER Statement for Accurate and Transparent Health Estimates Reporting from Multiple Populations and Multiple Information Sources]. *Rev Esp Salud Publica.* 2016 Aug 22; 90:e1-3. IF: 0,606
 31. Apostolo J, Holland C, O’Connell MD, Feeney J, **Tabares-Seisdedos R**, Tadros G, Campos E, Santos N, Robertson DA, Marcucci M, Varela-Nieto I, Crespo-Facorro B, Vieta E, Navarro-Pardo E, **Selva-Vera G**, **Balanzá-Martínez V**, Cano A. Mild cognitive decline. A position statement of the Cognitive Decline Group of the European Innovation Partnership for Active and Healthy Ageing (EIPAH). *Maturitas.* 2016 Jan; 83:83-93. IF: 2,942

Reviews

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI14/00894

Title: *Identificación y validación de biomarcadores periféricos para el déficit neurocognitivo en el trastorno bipolar, depresión, esquizofrenia y diabetes.*

Principal Investigator: Rafael Tabares Seisdedos

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total budget: 82.000€

Reference: PI14/00031

Title: Understanding obesity, metabolic syndrome, type 2 diabetes and fatty liver disease: a multidisciplinary approach.

Principal Investigator: José María Mato de la Paz (Rafael Tabarés as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: CIBERSAM

Duration: 2015-2017

Total budget: 606.000€

Reference: PROMETEOII /2015/021

Title: INverse and direct CANCER comorbidity in people with Central Nervous System disorders: from drug repurposing to

Letter

27. **Catalá-López F**, Hutton B, Page MJ, Vieta E, **Tabarés-Seisdedos R**, Moher D. Declaration of transparency: A step towards complete reporting of research articles. *Rev Psiquiatr Salud Ment.* 2016 Jan-Mar; 9(1):63-64. IF: 1,622

Editorials

28. **Catalá López F**, Ridao M. [Improving the transparency and credibility of cost-effectiveness analysis of healthcare interventions]. *Rev Esp Salud Publica.* 2016 Mar 23; 90:E1. IF: 0,693



effective strategies for cancer prevention (INCANCER/CNSd).

Principal Investigator: Rafael Tabarés Seisedos

Funding Body: *Conselleria de Educación Cultura y Deporte*

Beneficiary Institution: *Universitat de Valencia*

Duration: 2015-2018

Total budget: 212.400€

Reference: Intramural CIBER

Title: INverse and direct CANCER comorbidity in people with Central Nervous System disorders: from drug repurposing to effective strategies for cancer prevention (INCANCER/CNSd).

Principal Investigator: Rafael Tabarés Seisedos

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: CIBER

Duration: 2015-2017

Total budget: 35.000€

Reference: CB07/09/0021

Title: *CIBER de Enfermedades Mentales (CIBERSAM).*

Principal Investigator: Rafael Tabarés Seisedos

Funding Body: CIBER

Beneficiary institution: CIBERSAM

Duration: 2015-2017

Total budget: 35.000€

Reference: 10_APDTMG-2015

Title: *Autonomía Personal, Dependencia y Trastornos Mentales Graves.*

Principal Investigator: Rafael Tabarés Seisedos

Funding Body: *Ministerio de Educación, Cultura y Deporte*

Beneficiary institution: *Universidad de Valencia*

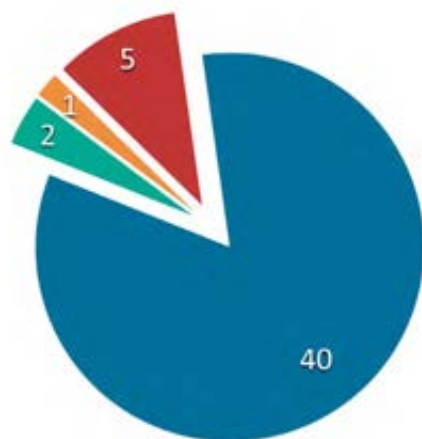
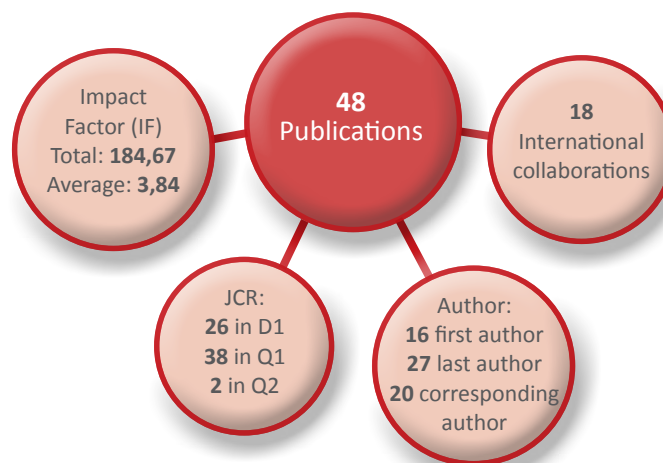
Duration: 2015-2016

Total budget: 10.000€



4.3.4 Reproductive medicine area

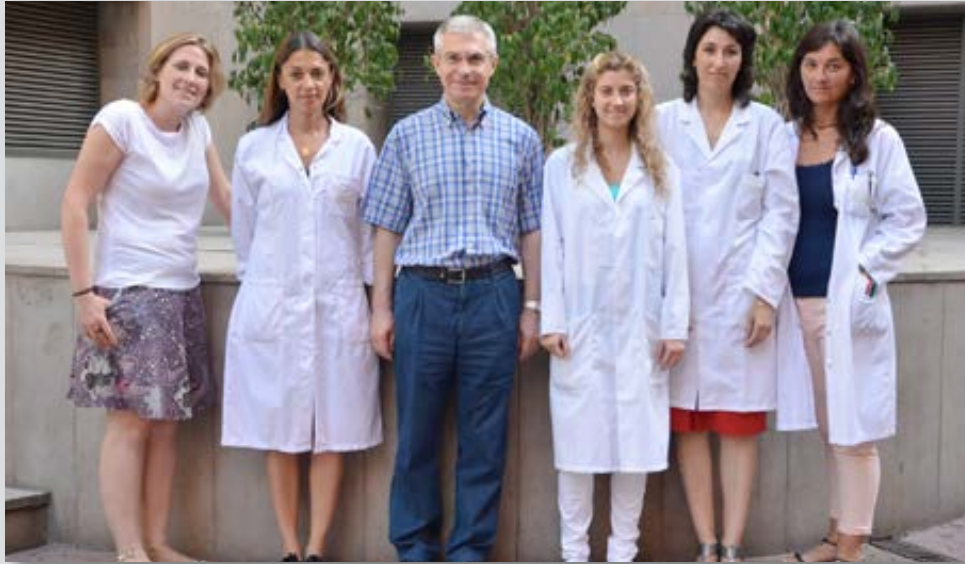
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Research Group on Male Infertility and Embrionary Stimulation	215



● Original articles ● Letters ● Editorial ● Reviews



Research Group on Women Health Consolidated group



“El envejecimiento saludable pasa por reducir al máximo las deficiencias de distintos sistemas, y uno de los más importantes es la capacidad cognitiva”

Antonio Cano. Levante-EMV. 04.08.2016.

Group members

Principal investigator

Antonio Cano Sánchez
University
H Index: 26

Collaborating researchers

Juan José Tarín Folgado. University
Esperanza Navarro. University

Emerging researcher

Raúl Gómez Gallego. INCLIVA





Strategic aims

- We have positioned our group in the field of healthy ageing, with special interest in frailty, where we have collaborated in the support of INCLIVA in the project ADVANTAGE.
- We have collaborated to position the reference site of the Valencia Region within EIPAHA, the partnership of the European Commission. Moreover, we have participated in the application to different European projects with groups from different European countries, including an application to the Marie Curie grants.
- Finally, we continue being coordinators of the FOCUS European project.

Main lines of research

- In healthy ageing in the female we are continuing our interest on osteoporosis but we have also added frailty and functional decline. We are consolidating the CARMEN cohort on EIP on AHA.
- With regard to endometriosis:
 - To analyze the role of microRNA and vascularization regulators and pain mechanisms. Role of the TNF cytokine family.
 - To analyze the initial atherogenesis and selective estrogen receptor modulators.



Emerging researcher

Raúl Gómez Gallego

Dr. Gomez's lines of research are focused on dissecting how deregulation of the angiogenic component is related to the onset and maintenance of gynecological disorders such as endometriosis, ovarian hyperstimulation syndrome, recurrent miscarriage or preeclampsia. We routinely employ animal models to mimic human disorders in which the effects of drugs are non-invasively assessed by monitorization of signal emitted by fluorescently or bioluminescently labeled xenografted pathological tissue. We are also interested in developing test for the early non-invasive diagnosis of endometriosis through combined analysis of multiple biomarkers simultaneously.

• PUBLICATIONS

Number of articles	IF	Average IF
12	30,39	2,53

National collaborations	International collaborations	Corresponding author
4	3	8

Original articles

1. González Ricarte M, Castro Pérez Ad, **Tarín JJ, Cano A**. Progestogens and risk of breast cancer: a link between bone and breast? *Gynecol Endocrinol*. 2016 Jan; 32(1):6-8. IF: 1,333
2. García-Pascual CM, Ferrero H, Juárez I, Martínez J, Villanueva A, Pozuelo-Rubio M, Soengas M, Tormo D, Simón C, **Gómez R**, Pellicer A. Evaluation of the antiproliferative, proapoptotic, and antiangiogenic effects of a double-stranded RNA mimic complexed with polycations in an experimental mouse model of leiomyoma. *Fertil Steril*. 2016 Feb; 105(2):529-38. IF: 4,59
3. Panach L, Pineda B, Mifsut D, **Tarín JJ, Cano A**, García-Pérez MÁ. The role of CD40 and CD40L in bone mineral density and in osteoporosis risk: A genetic and functional study. *Bone*. 2016 Feb; 83:94-103. IF: 3,973
4. Apostolo J, Cooke R, Bobrowicz-Campos E, Santana S, Marcucci M, **Cano A**, Vollenbroek M, Holland C. Predicting risk and outcomes for frail older adults: a protocol for an umbrella review of available frailty screening tools. *JBI Database System Rev Implement Rep*. 2016 Jan 15; 13(12):14-24. IF: 0
5. **Cano A**, Baró F, Fernández C, Inaraja V, García-Domínguez CA. Evaluation of the risk factors of asymptomatic vertebral fractures in postmenopausal women with osteopenia at the femoral neck. *Maturitas*. 2016 May; 87:95-101. IF: 2,942
6. Apóstolo J, Cooke R, Bobrowicz-Campos E, Santana S, Marcucci M, **Cano A**, Vollenbroek M, Holland C. Effectiveness of the interventions in preventing the progression of pre-frailty and frailty in older adults: a systematic review protocol. *JBI Database System Rev Implement Rep*. 2016 Feb 12; 14(1):4-19. IF: 0
7. **Tarín JJ**, García-Pérez MA, **Cano A**. Obstetric and offspring risks of women's morbid conditions linked to prior anti-cancer treatments. *Reprod Biol Endocrinol*. 2016 Jul 7; 14(1):37. IF: 2,147



8. **Tarín JJ**, García-Pérez MA, **Cano A**. Potential risks to offspring of intrauterine exposure to maternal age-related obstetric complications. *Reprod Fertil Dev*. 2016 Aug 10 ; IF: 2,135
9. Mendoza N, De Teresa C, **Cano A**, Godoy D, Hita-Contreras F, Lapotka M, Llana P, Manonelles P, Martínez-Amat A, Ocón O, Rodríguez-Alcalá L, Vélez M, Sánchez-Borrego R. Benefits of physical exercise in postmenopausal women. *Maturitas*. 2016 Nov; 93:83-88. IF: 3,12

Letters

10. Raga F, Llinares C, Cholvi S, Bonilla F, Pascual C, **Cano A**. HD-live imaging of cystic uterine leiomyoma degeneration. *Ultrasound Obstet Gynecol*. 2016 May; 47(5):655-6. IF: 3,853
11. **Cano A**. Physical activity and healthy aging. *Menopause*. 2016 May; 23(5):477-8. IF: 3,361

Review

12. Apostolo J, Holland C, O'Connell MD, Feeney J, Tabares-Seisdedos R, Tadros G, Campos E, Santos N, Robertson DA, Marcucci M, Varela-Nieto I, Crespo-Facorro B, Vieta E, Navarro-Pardo E, Selva-Vera G, Balanzá-Martínez V, **Cano A**. Mild cognitive decline. A position statement of the Cognitive Decline Group of the European Innovation Partnership for Active and Healthy Ageing (EIPAH). *Maturitas*. 2016 Jan; 83:83-93. IF: 2,942

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI14/00547

Title: *Efectos de la inactivación de CD276 y activación de CD137 sobre el tamaño de las lesiones y el dolor en la endometriosis.*

Principal Investigator: Raúl Gómez Gallego

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total budget: 98.500€

Reference: FOCUS

Title: *Frailty management Optimisation through EIP AHA Commitments and Utilisation of Stakeholders input.*

Principal Investigator: Antonio Cano Sánchez (Juan José Tarín

and Miguel Ángel García Pérez as collaborating researchers)

Funding body: European Commission - DG SANCO

Beneficiary institution: *Universidad de Valencia*

Duration: 2015-2018

Total budget: 2.379.633€

Reference: CP13/00038

Title: *Global multivariant analysis of putative biomarkers identified through combined multi-technical approach for the non-invasive detection of endometriosis.*

Principal Investigator: Raúl Gómez Gallego

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total budget: 121.380€

• THESIS

Thesis title: *Papel del grosor íntima-media en carótida y del tc de coronarias en la detección temprana de aterosclerosis en la mujer y posible modulación por polimorfismos relacionados con la acción estrogénica.*

Doctoral candidate: Antonio Jorge Cano Marquina

Director(s): Antonio Cano Sánchez, Alicia M. Maceira González, Juan Cosín Sales

Date of the defense: 07/10/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Efectos del ejercicio físico con banda elástica en mujeres mayores de 65 años durante 12 meses. Estudio comparativo sobre densidad ósea, componentes sanguíneos, estabilidad, antropometría y dolor.*

Doctoral candidate: M^a Cinta Gómez Tomás

Director(s): Antonio Cano Sánchez, Yasser Alakhdar Mohmara, José Luis Martínez Gil

Date of the defense: 17/06/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Papel de la vitamina d en la postmenopausia. Influencia de la suplementación en el metabolismo óseo y otras dianas.*

Doctoral candidate: Gemma Arribas Ferriol

Director(s): Antonio Cano Sánchez

Date of the defense: 01/02/2016

Grade: *Sobresaliente "cum laude"*



Thesis title: *Efectos del ibandronato sobre el metabolismo óseo y el perfil de riesgo cardiovascular en mujeres con osteoporosis postmenopáusica tratadas previamente con raloxifeno.*

Doctoral candidate: Marta Ferrer Piquer

Director(s): Antonio Cano Sánchez

Date of the defense: 19/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Valoración de la afectación de la reserva ovárica tras criopreservación de tejido ovárico y tratamiento oncológico: papel destacado de la hormona antimulleriana.*

Doctoral candidate: Ester Ortiz Murillo

Director(s): Antonio Cano Sánchez

Date of the defense: 19/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Evaluación del papel terapéutico de la inhibición del PAI en el tratamiento de la endometriosis en un modelo animal murino homólogo.*

Doctoral candidate: Ana Moreno Collado

Director(s): Raúl Gómez Gallego

Date of the defense: 27/01/2016

Grade: *Sobresaliente "cum laude"*



Research Group on Stem Cells Applied to Reproduction, Embryo Viability and Endometrial Receptivity

Consolidated group



Carlos Simón, premiado por la Sociedad Americana de Medicina Reproductiva.

EFE. 18-10-2016

Group members

Principal investigator

Carlos Simón Vallés
IVI. University
H Index: 68



Collaborating researchers

Amparo Mercader Bayarri. IVI
Ana Cristina Cerveró Sanz. IVI
María José de los Santos Molina. IVI
Tamara Garrido Gómez. IVI
Alicia Quiñonero Villora. IVI
Xavier Santamaría Costa. IVI
Hortensia Ferrero Cháfer. INCLIVA
Diana Valbuena Perilla. IVI
Pilar Alamá Faubel. IVI
Marta Gonzalo Moja. IVI
M^a Amparo Faus Esteve. IVI
José Bellver Pradas. IVI
Ernesto Bosch Aparicio. IVI
David Blesa Jarque. IVI
Patricia Díaz Gimeno. IVI
Elena Labarta Demur. IVI
Antonio Díez Juan. IVI

Emerging researcher

Francisco Domínguez Hernández. INCLIVA
Irene Cervelló Alcaraz. IVI
Felip Vilella Mitjana. INCLIVA

PhD researchers

Nuria Balaguer Cuenca. University
José Manuel Mínguez Forján. University
Anna Buigues Monfort. University
Stefania Salsano. INCLIVA
Alessia Grasso. INCLIVA
Hannes Marcus Campo. IVI
Silvia Pérez Deben. University
Nuria López Pérez. University
Iolanda García Grau. University
Irene Corachán García. INCLIVA

Technician

María Herrero Baena. INCLIVA



Strategic aims

- To advance in the understanding of the mechanisms that regulate maternal-fetal communication and that may be involved in the implantation of the embryo in the maternal uterus and to be able to understand the embryonic / fetal origin of adult diseases such as obesity and type II diabetes.
- Regenerate the reproductive function of women suffering from endometrial atrophy and / or Asherman's Syndrome through a new therapeutic approach.
- Creation of an in vitro model to obtain germ cells by direct reprogramming of human somatic cells.

Main lines of research

- Adult stem cells in the human endometrium: the ability to regenerate endometrial tissue, which occurs monthly under hormonal influence, makes it a candidate for research on its population of stem cells not yet described.
- Study of endometrial proteomics and embryonic viability: this line of research aims to accurately determine the protein profile of the human endometrial response. On the other hand, at the present time the selection of the most viable embryo is based only on morphological parameters, which do not guarantee a genetically normal embryo, for which reason several molecular techniques are investigated.
- Study of endometrial receptivity: study of the molecular mechanisms that regulate the receptive state of the endometrium.



Emerging researcher

Irene Cervelló Alcaraz

Research is based on the identification, characterization and isolation of Somatic Stem Cells in the endometrium. Endometrial Stem Cells have been identified in human and murine models, the regenerative potential of these cells has been proven and there is an ongoing research on the existence of Lgr5 marker in the endometrial tissue.

Moreover, the work is also focused on essential processes based on the regenerative medicine related with the porcine and human uterus.



Emerging researcher

Felip Vilella Mitjana

The research line of Endometrial Receptivity is based on the study of endometrial secretions, specifically the endometrial fluid.

We use secretomic and genomic approach so we can describe new molecules that can be correlated with the days of the menstrual cycle and may be involved in obtaining the window of implantation period, opening a new field of study for the analysis of the changes in the endometrium during the menstrual cycle and the cross-talk between the embryo and the endometrium.

We have demonstrated that human endometrial epithelium secretes specific microRNAs (miRNAs) during the time frame when the embryo enters the uterine cavity and initiates its adhesion to the uterine wall. Maternal miRNAs are secreted to the endometrial fluid, transported through exosomes or bound to proteins, and are uptaken by the preimplantation embryo, before implantation occurs, suffering thus transcriptomic modifications that induce profound molecular and functional changes.



Emerging researcher

Francisco Domínguez Hernández

Francisco Dominguez, Ph. D is principal investigator in the Reproductive Medicine group at INCLIVA. He was doctorate in 2003 at Valencia University at Carlos Simon's lab focusing its research career in the molecular biology of implantation and the search of biomarkers of endometrial receptivity. He is reviewer of several leading journals in reproductive medicine and has more than 35 peer reviewed papers and 15 book chapters specialized in the reproductive medicine. He has also been the Chief Scientific Officer of Embryomics, a technology-based company devoted to the development of non-invasive diagnostics of chromosome abnormalities in the pre-implantation embryo using metabolomic techniques and he is actually acting as associate editor of the Human Reproduction journal, the first original article journal specialized in reproductive medicine.



• PUBLICATIONS

Number of articles	IF	Average IF
24	99,75	4,15
National collaborations	International collaborations	Corresponding author
10	12	11

Original articles

- Sanchez-Delgado M, Court F, Vidal E, Medrano J, Monteagudo-Sánchez A, Martín-Trujillo A, Tayama C, Iglesias-Platas I, Kondova I, Bontrop R, Poo-Llanillo ME, Marques-Bonet T, Nakabayashi K, **Simón C**, Monk D. Human Oocyte-Derived Methylation Differences Persist in the Placenta Revealing Widespread Transient Imprinting. *PLoS Genet.* 2016 Nov 11; 12(11):e1006427. IF: 7,528
 - Medrano JV, Martínez-Arroyo AM, Míguez JM, Moreno I, Martínez S, **Quiñonero A**, Díaz-Gimeno P, Marqués-Marí AI, Pellicer A, Remohí J, **Simón C**. Human somatic cells subjected to genetic induction with six germ line-related factors display meiotic germ cell-like features. *Sci Rep.* 2016 Apr 26; 6:24956. IF: 5,578
 - Moreno I, Codoñer FM, **Vilella F**, **Valbuena D**, Martínez-Blanch JF, Jiménez-Almazán J, Alonso R, **Alamá P**, Remohí J, Pellicer A, Ramon D, **Simon C**. Evidence that the endometrial microbiota has an effect on implantation success or failure. *Am J Obstet Gynecol.* 2016 Dec; 215(6):684-703. IF: 4,681
 - Strug MR, Su R, Young JE, Dodds WG, Shavell VI, Díaz-Gimeno P, Ruíz-Alonso M, **Simón C**, Lessey BA, Leach RE, Fazleabas AT. Intrauterine human chorionic gonadotropin infusion in oocyte donors promotes endometrial synchrony and induction of early decidual markers for stromal survival: a randomized clinical trial. *Hum Reprod.* 2016 Jul; 31(7):1552-61. IF: 4,569
 - Santamaria X**, Cabanillas S, **Cervelló I**, Arbona C, Raga F, Ferro J, Palmero J, Remohí J, Pellicer A, **Simón C**. Autologous cell therapy with CD133+ bone marrow-derived stem cells for refractory Asherman's syndrome and endometrial atrophy: a pilot cohort study. *Hum Reprod.* 2016 May; 31(5):1087-96. IF: 4,569
- Most popular article from 2016 in Human Reproduction**
- Medrano JV, Rombaut C, **Simon C**, Pellicer A, Goossens E. Human spermatogonial stem cells display limited proliferation in vitro under mouse spermatogonial stem cell culture conditions. *Fertil Steril.* 2016 Nov; 106(6):1539-1549. E8. IF: 4,426
 - Vera-Rodríguez M, Michel CE, **Mercader A**, Bladon AJ, Rodrigo L, Kokocinski F, Mateu E, Al-Asmar N, Blesa D, **Simón C**, Rubio C. Distribution patterns of segmental aneuploidies in human blastocysts identified by next-generation sequencing. *Fertil Steril.* 2016 Apr; 105(4):1047-1055. E2. IF: 4,59
 - García-Pascual CM, **Ferrero H**, Juárez I, Martínez J, Villanueva A, Pozuelo-Rubio M, Soengas M, Tormo D, **Simón C**, Gómez R, Pellicer A. Evaluation of the antiproliferative, proapoptotic, and antiangiogenic effects of a double-stranded RNA mimic complexed with polycations in an experimental mouse model of leiomyoma. *Fertil Steril.* 2016 Feb; 105(2):529-38. IF: 4,59
 - Sermon K, Capalbo A, Cohen J, Coonen E, De Rycke M, De Vos A, Delhanty J, Fiorentino F, Gleicher N, Griesinger G, Grifo J, Handyside A, Harper J, Kokkali G, Mastenbroek S, Meldrum D, Meseguer M, Montag M, Munné S, Rienzi L, Rubio C, Scott K, Scott R, **Simon C**, Swain J, Treff N, Ubaldi F, Vassena R, Vermeesch JR, Verpoest W, Wells D, Geraedts J. The why, the how and the when of PGS 2.0: current practices and expert opinions of fertility specialists, molecular biologists, and embryologists. *Mol Hum Reprod.* 2016 Aug; 22(8):845-57. IF: 3,943
 - Rancan L, **Simón C**, Marchal-Duval E, Casanova J, Paredes SD, Calvo A, García C, Rincón D, Turrero A, Garutti I, Vara E. Lidocaine Administration Controls MicroRNAs Alterations Observed After Lung Ischemia-Reperfusion Injury. *Anesth Analg.* 2016 Dec; 123(6):1437-1447. IF: 3,827
 - Campo H, **Cervelló I**, **Simón C**. Bioengineering the Uterus: An Overview of Recent Advances and Future Perspectives in Reproductive Medicine. *Ann Biomed Eng.* 2016 Dec 27 ;. IF: 2,887
 - Santamaria X**, Katzorke N, **Simón C**. Endometrial 'scratching': what the data show. *Curr Opin Obstet Gynecol.* 2016 Aug; 28(4):242-9. IF: 2,134
 - Mir P, Mateu E, **Mercader A**, Herrer R, Rodrigo L, Vera M, Peinado V, Milán-Sánchez M, Campos-Galindo I, García-Herrero S, **Simón C**, Rubio C. Confirmation rates of array-CGH in day-3 embryo and blastocyst biopsies for preimplantation genetic screening. *J Assist Reprod Genet.* 2016 Jan; 33(1):59-66. IF: 1,718



14. Galán A, **Simón C**. Monitoring Stemness in Long-Term hESC Cultures by Real-Time PCR. *Methods Mol Biol*. 2016; 1307:89-104. IF: 0
15. Garcia NA, Moncayo-Arlandi J, Sepulveda P, **Diez-Juan A**. Cardiomyocyte exosomes regulate glycolytic flux in endothelium by direct transfer of GLUT transporters and glycolytic enzymes. *Cardiovasc Res*. 2016 Mar 1; 109(3):397-408. IF: 5,94
16. Motato Y, **de Los Santos MJ**, Escriba MJ, Ruiz BA, Remohí J, Meseguer M. Morphokinetic analysis and embryonic prediction for blastocyst formation through an integrated time-lapse system. *Fertil Steril*. 2016 Feb; 105(2):376-384. E9. IF: 4,59
17. Moncayo-Arlandi J, Guasch E, Sanz-de la Garza M, Casado M, Garcia NA, Mont L, Sitges M, Knöll R, Buyandelger B, Campuzano O, **Diez-Juan A**, Brugada R. Molecular disturbance underlies to arrhythmogenic cardiomyopathy induced by transgene content, age and exercise in a truncated PKP2 mouse model. *Hum Mol Genet*. 2016 Sep 1; 25(17):3676-3688. IF: 5,985
18. Genbacev O, Larocque N, Ona K, Prakobphol A, **Garrido-Gomez T**, Kapidzic M, Bárcena A, Gormley M, Fisher SJ. Integrin $\alpha 4$ -positive human trophoblast progenitors: functional characterization and transcriptional regulation. *Hum Reprod*. 2016 Jun; 31(6):1300-14. IF: 4,621
19. Garin-Muga A, Odriozola L, Martínez-Val A, Del Toro N, Martínez R, Molina M, Cantero L, Rivera R, Garrido N, **Dominguez F**, Sanchez Del Pino MM, Vizcaíno JA, Corrales FJ, Segura V. Detection of Missing Proteins Using the PRIDE Database as a Source of Mass Spectrometry Evidence. *J Proteome Res*. 2016 Nov 4; 15(11):4101-4115. IF: 4,173
20. Garcia-Herrero S, **Cervero A**, Mateu E, Mir P, Póo ME, Rodrigo L, Vera M, Rubio C. Genetic Analysis of Human Preimplantation Embryos. *Curr Top Dev Biol*. 2016; 120:421-47. IF: 4,677
21. ESHRE Guideline Group on Good Practice in IVF Labs, **De los Santos MJ**, Apter S, Cotichio G, Debrock S, Lundin K, Plancha CE, Prados F, Rienzi L, Verheyen G, Woodward B, Vermeulen N. Revised guidelines for good practice in IVF laboratories (2015). *Hum Reprod*. 2016 Apr; 31(4):685-6. IF: 4,621
22. Franasiak JM, Ruiz-Alonso M, Scott RT, **Simón C**. Both slowly developing embryos and a variable pace of luteal endometrial progression may conspire to prevent normal birth in spite of a capable embryo. *Fertil Steril*. 2016 Apr; 105(4):861-6. IF: 4,59
23. Meldrum DR, Casper RF, **Diez-Juan A**, **Simon C**, Domar AD, Frydman R. Aging and the environment affect gamete and embryo potential: can we intervene? *Fertil Steril*. 2016 Mar; 105(3):548-59. IF: 4,59
24. Katzorke N, **Vilella F**, Ruiz M, Krüssel JS, **Simón C**. Diagnosis of Endometrial-Factor Infertility: Current Approaches and New Avenues for Research. *Geburtshilfe Frauenheilkd*. 2016 Jun; 76(6):699-703. IF: 0,931

• THESIS

Thesis title: *Nuevas posibilidades terapéuticas en el fallo de implantación.*

Doctoral candidate: Sevkiye Tugce Pehlivan Budak

Director(s): Carlos Simón Vallés, Carmen Rubio Lluesa

Date of the defense: 26/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio prospectivo y randomizado sobre la utilidad de los Arrays de CGH para el estudio de aneuploidias embrionarias en factor masculino severo.*

Doctoral candidate: Gemma Castellón Cortés

Director(s): Carlos Simón Vallés, Carmen Rubio Lluesa, Inmaculada Sánchez Ribas

Date of the defense:

Grade: *Sobresaliente "cum laude"*

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: BFU2015-72131-EXP

Title: *Criptocromos, la inexplicable presencia de sensores de luz en la oscuridad que conectan el embrión temprano con el cosmos.*

Principal Investigator: Carlos Simón Vallés

Funding Body: *Ministerio de Economía, Industria y Competitividad*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2017

Total budget: 60.000€

Review

22. Franasiak JM, Ruiz-Alonso M, Scott RT, **Simón C**. Both



Reference: SAF2015-67154-R

Title: *Regulación transcriptómica materna del embrión pre-implantario. Nuevo mecanismo para el estudio del origen de enfermedades complejas del adulto: obesidad y/o exposición tabaco*

Principal Investigator: Carlos Simón Vallés

Funding Body: *Ministerio de Economía, Industria y Competitividad*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016-2018

Total budget: 169.400€

Reference: Grant for Fertility Innovation

Title: Analysis of miRNAs in endometrial fluid as a tool for noninvasive diagnosis of endometrial receptivity.

Principal Investigator: Carlos Simón Vallés

Funding Body: EMD Serono Research Institute, Inc.

Beneficiary institution: *Fundación IVI*

Duration: 2013-2015

Total budget: 239.600€

Title: Bone morphogenic protein signaling pathways in uterine biology

Principal Investigator: Carlos Simón Vallés (Principal Investigator Sub-Project 2)

Funding body: National Institute of Health, USA.

Beneficiary institution: Baylor College of Medicine

Duration: 2015- 2016

Total budget: 328.888 USD

Reference: SARM 324509 (Marie Curie Program)

Title: Endometrial and Embryonic Genomics, Searching for Biomarkers in Assisted Reproduction.

Funding Body: European Commission (Marie Curie Program)

Principal Investigator: Carlos Simón Vallés

Beneficiary institution: Igenomix

Duration: 2013- 2016

Total budget: 668.759€

Reference: PROMETEO II/2013/018

Title: Isolation and characterization of endometrial somatic stem cells in endometriosis. Pathogenic and therapeutic implications. Identification of Endometrial Stem Cell Markers. From Animal Models to Human Endometrial Stem Cell Therapy

Principal Investigator: Carlos Simón Vallés

Funding body: *Conselleria de Educació, Cultura y Deporte*

Beneficiary institution: *Universidad de Valencia*

Duration: 2013-2016

Total budget: 287.000€

Reference: CP13/00075

Title: *Desarrollo de una herramienta diagnóstica de fallo de implantación. Descripción del perfil proteómico y definición del interactoma del fallo de implantación.*

Principal Investigator: Francisco Domínguez Hernández

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2013-2019

Total budget: 121.450€

Reference: PI14/00545

Title: *Estudio de los miRNAs secretados al líquido endometrial y su papel en la regulación del embrión en los primeros estadios de desarrollo.*

Principal Investigator: Felipe Vilella Mitjana

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total budget: 81.500€

Reference: CP13/00038

Title: Diagnostic tool to predict obesity and T2D in offspring. Role of maternal miRNAs on the transmission of obesity and type 2 diabetes to the embryo.

Principal Investigator: Felipe Vilella Mitjana

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2017

Total budget: 324.000€

Reference: GV/2016/33

Title: *Herramienta para el Diagnóstico Precoz de Preeclampsia basado en el fallo de decidualización endometrial que se manifiesta en el embarazo de mujeres.*

Principal Investigator: Tamara Garrido

Funding Body: *Conselleria de Educació, Cultura y Deporte*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016 - 2018

Total Budget: 16.000€



- **PATENTS**

Inventors: Carlos Simon Vallés

Research group: *Receptividad Endometrial*

Title: Non-invasive preimplantation genetic analysis and related methods.

Application number: US 62/301.825

Priority country: USA

Priority date: 15/03/2016

Applicant: Igenomix SL

- **AWARDS:**

In October 2016 Dr. Carlos Simón was awarded with the Distinguished Research Award by the American Society for Reproductive Medicine. Also the Society for Reproductive Endocrinology and Infertility (SREI) awarded him with the Paper Prize.

Moreover the Society for Reproductive Investigation (SRI) awarded with the Pfizer-SRI President's Presenter's Award two scientific works on the 63rd Annual Scientific Meeting of the Society for Reproductive Investigation in Montreal. The articles were:

- Simon B, Moreno I, Bolumar D, Vilella F, Simón C. Trophoctoderm cells of embryos secrete extracellular vesicles to the conditioned media.
- Balaguer N, Moreno I, Herrero M, Simón C, Vilella F. Maternal endometrial HSA-MIR-30d is internalized and secreted in exosomes by binding with hnRNPC1.



Research Group on Male Infertility and Embryonic Stimulation Consolidated group



“Cuatro ginecólogos del IVI entre los mejores en Biología Reproductiva”.
La Estrella. Com. 15/01/2016

Group members

Principal investigator

José Remohí Giménez
IVI. University
H Index: 60



Collaborating researchers

Amparo Ruiz Jorro. IVI
Carmen Rubio Lluesa. IVI
Jaime Ferro Camargo. IVI
Jose Antonio Martínez Conejero. IVI
Rocío Rivera Egea. INCLIVA
Lorena Rodrigo Vivó. IVI
Inmaculada Campos Galindo. IVI
José María de los Santos Molina. IVI
Tamara Viloria Samochín. IVI
M^a del Carmen Vidal Martínez. IVI
Juan Giles Jiménez. IVI

Emerging researcher

Marcos Meseguer Escrivá. IVI
Nicolás Garrido Puchalt. IVI



Strategic aims

- Human male somatic cells can be directly converted into induced germ cell-like cells (iGS-LCs), through regulation exerted by DAZL and DDX4 on the pool of transcripts induced by PRDM1 and PRDM14, also up-regulated by LIN28A, while SYCP3 induction resulted essential for meiosis initiation. These iGC-LCs recapitulate all the transcriptomic and epigenetic features of human germ cells, can overcome meiosis to produce haploid cells and colonize the testicular niche in a xenograft model. However, the direct conversion from somatic to iGC-LCs is highly inefficient, so future investigation is essential to optimize this technology.
- TCL (thermochemiluminescence) is an oxidative stress (OS) determination technique of biological samples, based on heat oxidation induction. Embryos were cultured in independent well slides (Embryoslides) in the Embryoscope Incubator (Vitrolife, Denmark).
- TCL device could analyzed 368 samples of the 400 obtained. The oxidative parameters recorded were: TCL amplitude after 50 seconds (H1), 100 seconds (H2) and 280 seconds (H3). The Embryos cultured in less oxidized environment (those that present highest oxidation potential) showed higher implantation than the rest of cohort's embryos.

Main lines of research

- Artificial gamete creation through germ line reprogramming from human somatic cells.
- Use of oxidative stress as a biomarker for embryo viability in human IVF and its use as an additional marker to the existing morphokinetic algorithms provided by time-lapse.



Emerging researcher

Nicolás Garrido Puchalt
(IVI University Institute)

In this research line about male fertility, factors related to sperm physiology are intended to be discovered, and sperm selection techniques in order to improve reproductive results are being evaluated. Using assisted reproduction techniques and several instrumental tools, the gene-

tic, proteomic and metabolomic profiles, together with DNA integrity are being scrutinized in order to determine the relevance of these parameters and improve the diagnosis and the design of new optimal sperm selection techniques to achieve parenthood.



Emerging researcher

Marcos Meseguer Escrivá
(IVI University Institute)

Traditionally, embryo incubation and assessment daily has been under a light microscope, these observations are inevitably restricted to specific times and considering that the development of the embryo is a dynamic process, several critical stages in between observations may go unnoticed. For this reason, the new technologies, time lapse monitoring; have focused on the research for additional markers of viability to supplement current criteria for embryo selection and thus, achieve a reduction in the number of embryos transferred and so multiple pregnancies, making the selection procedure even easier for the embryologist. Our group is pioneer in the introduction and development of time-lapse technology, being a reference in the scientific community. Time-lapse allows embryo analysis without using an invasive technique.

The processes in our laboratory have changed, since it is not needed to take out the embryos from the incubator to be observed, and we have more information of each embryo. Time-lapse incubators take continuous pictures of development that allows selecting those that have major implantation rate according to its morphokinetic patterns. In this way we also achieved a much more stable incubation.

Capturing images is done in multiple focal planes and pre-programmed time intervals. The sum of each embryo frame generates a recording that displays the embryonic development continuously. It represents a major conceptual advance in the quality assessment by measuring embryonic developmental processes against embryo stages. Control randomized studies have demonstrated an increase up to 20% in the chance of success of assisted reproductive technology. Parallel projects with new hardware time-lapse technologies as Auxogyn-Eeva and Geri-Genea are being performed validating and improving the existing tool for the embryology lab.

New software is being tested to improve current algorithms for embryo selection. New projects underway are combining time-lapse technology with non-invasive analysis of surrounding



embryo culture media. Our research is focused in oxygen consumption, oxidative profile and embryo protein secretions. Special interest is done in the use of TCL analyzer, a biochemical measurement that examines the oxidative profile, also connected to signal transduction which is based on free radicals activity and the metabolism of the embryo with the culture media where it grows.

• PUBLICATIONS

Number of articles	IF	Average IF
23	101,59	4,41
National collaborations	International collaborations	Corresponding author
16	5	9

Original articles

- Gruhn JR, Al-Asmar N, Fasnacht R, Maylor-Hagen H, Peinado V, **Rubio C**, Broman KW, Hunt PA, Hassold T. Correlations between Synaptic Initiation and Meiotic Recombination: A Study of Humans and Mice. *Am J Hum Genet.* 2016 Jan 7; 98(1):102-15. IF: 10,931
- Mir P, Mateu E, Mercader A, Herrer R, **Rodrigo L**, Vera M, Peinado V, Milán-Sánchez M, Campos-Galindo I, García-Herrero S, Simón C, **Rubio C**. Confirmation rates of array-CGH in day-3 embryo and blastocyst biopsies for preimplantation genetic screening. *J Assist Reprod Genet.* 2016 Jan; 33(1):59-66. IF: 1,718
- Costa-Borges N, Bellés M, **Meseguer M**, Galliano D, Ballesteros A, Calderón G. Blastocyst development in single medium with or without renewal on day 3: a prospective cohort study on sibling donor oocytes in a time-lapse incubator. *Fertil Steril.* 2016 Mar; 105(3):707-13. IF: 4,59
- Motato Y, **de Los Santos MJ**, Escriba MJ, Ruiz BA, **Remohí J**, **Meseguer M**. Morphokinetic analysis and embryonic prediction for blastocyst formation through an integrated time-lapse system. *Fertil Steril.* 2016 Feb; 105(2):376-384. E9. IF: 4,59
- Gianza M, Muñoa-Hoyos I, Urizar-Arenaza I, Larreategui Z, Quintana F, **Garrido N**, Subirán N, Irazusta J. Angiotensin II type 2 receptor is expressed in human sperm cells and is involved in sperm motility. *Fertil Steril.* 2016 Mar; 105(3):608-16. IF: 4,59
- Coello A, Campos P, **Remohí J**, **Meseguer M**, Cobo A. A combination of hydroxypropyl cellulose and trehalose as supplementation for vitrification of human oocytes: a retrospective cohort study. *J Assist Reprod Genet.* 2016 Mar; 33(3):413-21. IF: 1,718
- Cobo A, García-Velasco JA, Coello A, Domingo J, Pellicer A, **Remohí J**. Oocyte vitrification as an efficient option for elective fertility preservation. *Fertil Steril.* 2016 Mar; 105(3):755-764. E8. IF: 4,59
- Santamaria X, Cabanillas S, Cervelló I, Arbona C, Raga F, **Ferro J**, Palmero J, **Remohí J**, Pellicer A, Simón C. Autologous cell therapy with CD133+ bone marrow-derived stem cells for refractory Asherman's syndrome and endometrial atrophy: a pilot cohort study. *Hum Reprod.* 2016 May; 31(5):1087-96. IF: 4,569
- Medrano JV, Martínez-Arroyo AM, Míguez JM, Moreno I, Martínez S, Quiñonero A, Díaz-Gimeno P, Marqués-Marí AI, Pellicer A, **Remohí J**, Simón C. Human somatic cells subjected to genetic induction with six germ line-related factors display meiotic germ cell-like features. *Sci Rep.* 2016 Apr 26; 6:24956. IF: 5,578
- Vera-Rodríguez M, Michel CE, Mercader A, Bladon AJ, **Rodrigo L**, Kokocinski F, Mateu E, Al-Asmar N, Blesa D, Simón C, **Rubio C**. Distribution patterns of segmental aneuploidies in human blastocysts identified by next-generation sequencing. *Fertil Steril.* 2016 Apr; 105(4):1047-1055. E2. IF: 4,59
- Tejera A, Castelló D, **de Los Santos JM**, Pellicer A, **Remohí J**, **Meseguer M**. Combination of metabolism measurement and a time-lapse system provides an embryo selection method based on oxygen uptake and chronology of cytokinesis timing. *Fertil Steril.* 2016 Jul; 106(1):119-126. E2. IF: 4,59
- Aguilar J, Rubio I, Muñoz E, Pellicer A, **Meseguer M**. Study of nucleation status in the second cell cycle of human embryo and its impact on implantation rate. *Fertil Steril.* 2016 Aug; 106(2):291-299. E2. IF: 4,59
- Sermon K, Capalbo A, Cohen J, Coonen E, De Rycke M, De Vos A, Delhanty J, Fiorentino F, Gleicher N, Griesinger G, Grifo J, Handyside A, Harper J, Kokkali G, Mastenbroek S, Meldrum D, **Meseguer M**, Montag M, Munné S, Rienzi L, **Rubio C**, Scott K, Scott R, Simon C, Swain J, Treff N, Ubaldi F, Vassena R, Vermeesch JR, Verpoest W, Wells D, Geraedts J. The why, the how and the when of PGS 2.0: current practices and expert opinions of fertility specialists, molecular biologists,



- and embryologists. *Mol Hum Reprod*. 2016 Aug; 22(8):845-57. IF: 3,943
14. Nohales-Córcoles M, Sevillano-Almerich G, Di Emidio G, Tatone C, Cobo AC, Dumollard R, **De Los Santos Molina MJ**. Impact of vitrification on the mitochondrial activity and redox homeostasis of human oocyte. *Hum Reprod*. 2016 Aug; 31(8):1850-8. IF: 4,621
 15. Aparicio-Ruiz B, Basile N, Pérez Albalá S, Bronet F, **Remohí J, Meseguer M**. Automatic time-lapse instrument is superior to single-point morphology observation for selecting viable embryos: retrospective study in oocyte donation. *Fertil Steril*. 2016 Nov; 106(6):1379-1385. E10. IF: 4,426
 16. Garin-Muga A, Odriozola L, Martínez-Val A, Del Toro N, Martínez R, Molina M, Cantero L, **Rivera R, Garrido N**, Dominguez F, Sanchez Del Pino MM, Vizcaíno JA, Corrales FJ, Segura V. Detection of Missing Proteins Using the PRIDE Database as a Source of Mass Spectrometry Evidence. *J Proteome Res*. 2016 Nov 4; 15(11):4101-4115. IF: 4,173
 17. Castelló D, Motato Y, Basile N, **Remohí J, Espejo-Catena M, Meseguer M**. How much have we learned from time-lapse in clinical IVF? *Mol Hum Reprod*. 2016 Oct; 22(10):719-727. IF: 3,943
 18. Garcia-Herrero S, Cervero A, Mateu E, Mir P, Póo ME, **Rodrigo L, Vera M, Rubio C**. Genetic Analysis of Human Preimplantation Embryos. *Curr Top Dev Biol*. 2016; 120:421-47. IF: 4,677
 19. Salas-Huetos A, Blanco J, Vidal F, Grossmann M, Pons MC, **Garrido N**, Anton E. Spermatozoa from normozoospermic fertile and infertile individuals convey a distinct miRNA cargo. *Andrology*. 2016 Nov; 4(6):1028-1036. IF: 2,515
 20. Camprubí C, Salas-Huetos A, Aiese-Cigliano R, Godo A, Pons MC, Castellano G, Grossmann M, Sanseverino W, Martin-Subero JJ, **Garrido N**, Blanco J. Spermatozoa from infertile patients exhibit differences of DNA methylation associated with spermatogenesis-related processes: an array-based analysis. *Reprod Biomed Online*. 2016 Dec; 33(6):709-719. IF: 2,796
 21. Moreno I, Codoñer FM, Vilella F, Valbuena D, Martínez-Blanch JF, Jimenez-Almazán J, Alonso R, Alamá P, **Remohí J, Pellicer A, Ramon D, Simon C**. Evidence that the endometrial microbiota has an effect on implantation success or failure. *Am J Obstet Gynecol*. 2016 Dec; 215(6):684-703. IF: 4,681

Review

22. Swain JE, Carrell D, Cobo A, **Meseguer M, Rubio C**, Smith GD. Optimizing the culture environment and embryo manipulation to help maintain embryo developmental potential. *Fertil Steril*. 2016 Mar; 105(3):571-87. IF: 4,59

Editorial

23. **Meseguer M**. Time-lapse: the remaining questions to be answered. *Fertil Steril*. 2016 Feb; 105(2):295-6. IF: 4,59

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI13/00546

Title: Artificial gamete creation through germ line reprogramming from human somatic cells.

Principal Investigator: José Remohí Giménez

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total Budget: 45.980€

Reference: PI14/00523

Title: *Estudio clínico del estrés oxidativo como biomarcador adicional de viabilidad embrionaria en fecundación in vitro combinado con la selección por morfocinética.*

Principal Investigator: Nicolás Garrido Puchalt, Marcos Meseguer Escrivá

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total Budget: 108.925€

Reference: PROMETEOII/2013/018

Title: Isolation and characterization of endometrial somatic stem cells in endometriosis. Pathogenic and therapeutic implications. Identification of endometrial stem cell markers. From animal models to human endometrial stem cell therapy.

Principal Investigator: Carlos Simón Vallés (José Remohí as collaborating researcher)

Funding Body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2013-2016

Total budget: 70.000€ (this year)



Reference: PROMETEOII/2014/045

Title: Development of new safety methods for fertility preservation in oncologic patients.

Principal Investigator: Antonio Pellicer Martínez (José Remohí as collaborating researcher)

Funding Body: *Conselleria de Educación, Cultura y Deporte*

Beneficiary Institution: *Universitat de Valencia*

Duration: 2014-2017

Total budget: 111.255€

• THESIS

Thesis title: *Tasa acumulada de recién nacido vivo en donación de ovocitos.*

Doctoral candidate: Víctor Hugo Gómez Hernández

Director(s): José Remohí Giménez, Ana Cristina Cobo Cabal

Date of the defense: 06/05/2017

Grade: *Sobresaliente "cum laude"*

Thesis title: *Producción de blastocistos diploides, heteroparentales a partir de pre-embriones tripronucleares humanos procedentes de FIV e ICSI.*

Doctoral candidate: Noelia Grau Grau

Director(s): José Alejandro Remohí Jiménez, María José Escribá Pérez

Date of the defense: 29/01/2017

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio de anomalías meióticas y aneuploidías en pacientes con azoospermia secretora.*

Doctoral candidate: Vanessa Peinado Cervera

Director(s): Carmen Rubio Lluesa, Manuel Gil Salom, José Remohí Giménez

Date of the defense: 21/01/2016

Grade: *Sobresaliente "cum laude"*

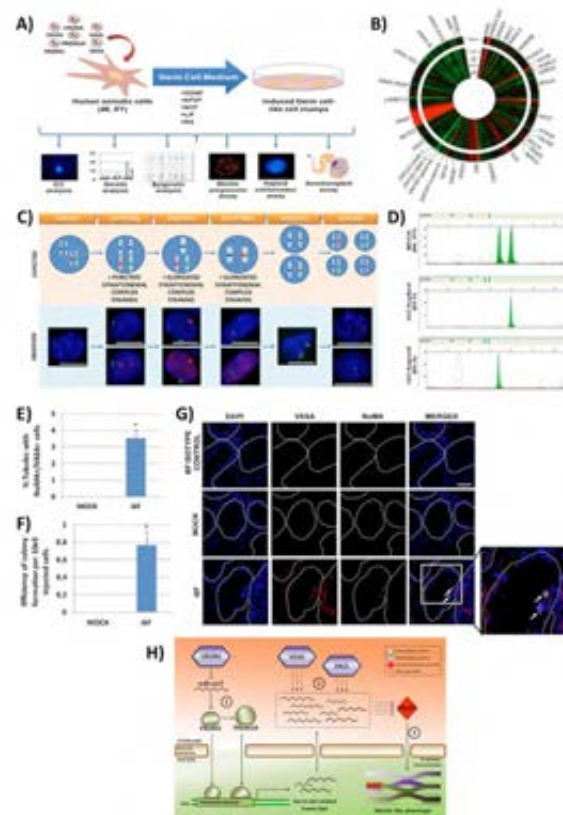
Thesis title: *Estudio cinematográfico de parámetros morfológicos del pre-embrión humano.*

Doctoral candidate: Raquel Herrer Saura

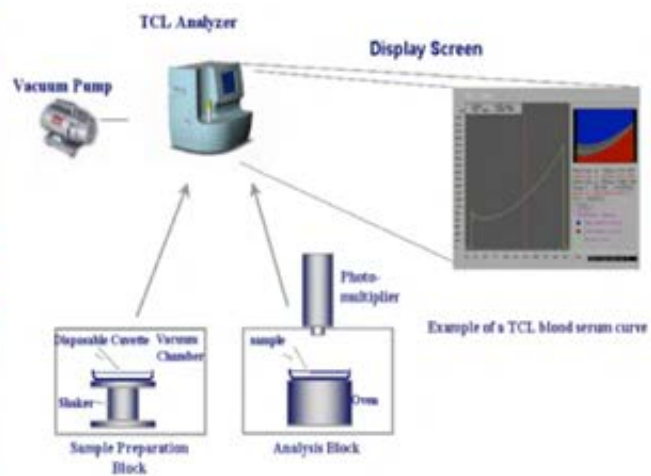
Director(s): Marcos Meseguer Escrivá, Juan Antonio García Velasco

Date of the defense: 02/02/2016

Grade: *Sobresaliente "cum laude"*



A) Schematic diagram of the experimental setup of the study. B) Epigenetic characterization of the *in vitro* iGC-LCs from induced from fibroblasts showing circular heat map presentation of the methylation for 37 annotated human imprinted loci. C) Combined SYCP3 staining and FISH analysis reveals that meiotic-like cells recapitulate all the stages of the meiosis. D) Molecular assessment of the ploidy in iGC-LCs single cells by PCR products of the Amelogenin gene results in a peak of 118pb for the copy in X and a 124pb peak for the copy in Y. E) Percentage of tubules containing NuMA+/VASA+ iGC-LCs in xenotransplanted testis. F) Efficiency of colonization per 10e5 injected iGC-LCs in mouse transplanted testis. G) Illustrative pictures showing iGC-LCs xenotransplant results with NuMA+/VASA+ co-localization on the basal layer of germ cell depleted seminiferous tubules in MOCK and i6F transplanted testis. H) Proposed model for the germ line conversion and meiotic induction by direct conversion of somatic cells into iGC-LCs by



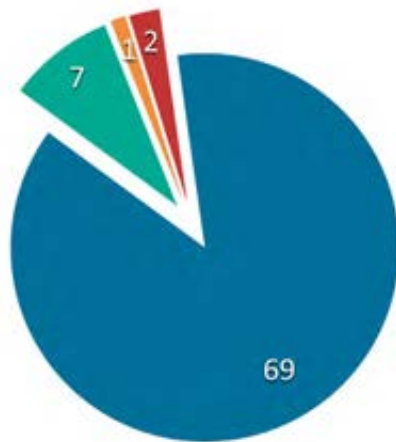
The diagram shows the main components of the TCL Analyzer. (Schnizer et al., 2003)



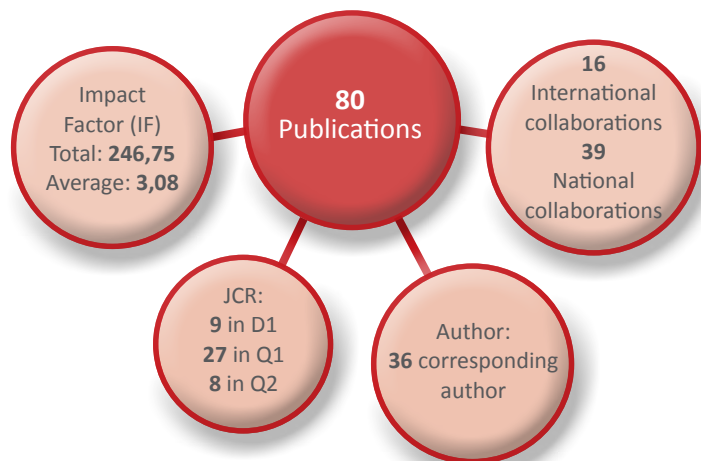
4.4 Hospital divisions research area

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● Original articles ● Letters ● Editorial ● Reviews





4.4 Other scientific contributions from the Hospital Divisions and the *Valencia Clínico-Malvarrosa* Health Department

Department of Admission and Clinical Documentation

Main lines of research

- National Registry of Childhood Cancer.
- Epidemiology of childhood cancer: incidence and survival of childhood cancer in Spain, geographic, temporal, national and international variations, epidemiology of the biological characteristics that have a clinical relevance in childhood cancer.

Team involved in



• PUBLICATIONS

Number of articles	IF	Average IF
1	3,271	3,271

National collaborations	International collaborations	Corresponding author
-	-	-

Original articles

1. Larrañaga N, Sanchez MJ, Ardanaz E, Felipe S, Marcos-Gragera R, Ramos M, Carulla M, Chirlaque MD, Argüelles MV, Martos C, Mateo A, **Peris-Bonet R**. Incidence Patterns and Trends of non-Central Nervous System Solid Tumours in Children and Adolescents. A Collaborative Study of the Spanish Population Based Cancer Registries. *J Cancer*. 2016; 7(3):335-43. IF: 3,271

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: RD12/0036/0053

Title: *Red temática de investigación cooperativa de cáncer (RTICC).*

Principal Investigator: Rafael Peris-Bonet

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Universidad de Valencia*

Duration: 2013-2016

Total budget: 219.000€

Allergology Unit

Main lines of research

- Relationship between allergenic profiles of patients and the efficacy of mite immunotherapy.
- Application of the basophil activation test to the diagnosis of respiratory allergy.

Cardiac Stimulation Unit

Strategic aims

- The study FIRE & ICE in which the group participated has been published in *New England Journal of Medicine*.
- During 2016 the group has been involved in leading a multicenter randomized study on dosification in cryoablation of the pulmonary veins. The study is expected to be concluded in 2017 1st quarter and thereafter ready to submit for publication.

Main lines of research

- Atrial fibrillation (AF):
 - Cryoballoon ablation (dose, time to isolation and their influence on results; silent cerebral damage during procedures).
 - Detection of AF in cardiac devices: participation in the international multicentre trial ARTESIA on new anti-coagulants in silent, device detected, self limited AF.
- Atrial flutter: zero radiology during ablation, ablation guided by electrogram voltage.
- Ventricular tachycardia: epicardial and endocardial approach in the same procedure of ablation.



- Cardiac Resynchronization therapy: value of radionuclide imaging in the study of the response to therapy.

• PUBLICATIONS

Number of articles	IF	Average IF
2	59,55	29,77

National collaborations	International collaborations	Corresponding author
1	1	-

Original articles

1. García García MA, Rosero Arenas MA, **Ruiz Granell R**, Chorro Gascó FJ, Martínez Cornejo A. Usefulness of cardiac resynchronisation therapy devices and implantable cardioverter defibrillators in the treatment of heart failure due to severe systolic dysfunction: systematic review of clinical trials and network meta-analysis. *Heart Asia*. 2016; 8(1):8-15. IF: 0
2. Kuck KH, Brugada J, Fürnkranz A, Metzner A, Ouyang F, Chun KR, Elvan A, Arentz T, Bestehorn K, Pocock SJ, Albenque JP, Tondo C, **FIRE AND ICE Investigators**. *Cryoballoon* or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation. *N Engl J Med*. 2016 Jun 9; 374(23):2235-45. IF: 59,558

Department of Thoracic Surgery

Main lines of research

- Viability study of decellularized human tracheas as a tracheal substitute. This is one of the priority research lines of Thoracic Surgery.
- Epithelized tracheal substitutes generated by tissue engineering.
- SpainRDR. Carlos III Health Institute. National Register of Rare Diseases, in the section of Tracheal Stenosis, framed in the context of Centers for Biomedical Research in Network (CIBER).
- Impact of the surgical approach on postoperative morbidity and mortality and oncologic prognosis in patients submitted to anatomic pulmonary resection. 2015. VATS-SECT Working Group.

- Diagnostic profitability and prognostic value of pleural lavage pre- and post-resection of the lungs in NSCLC. Collaborative researcher (Multicenter prospective study). Start date 11/15/2015. Endorsed by SECT.

• PUBLICATIONS

Number of articles	IF	Average IF
5	17,61	3,52

National collaborations	International collaborations	Corresponding author
3	1	2

Original articles

1. Marron MC, Lora D, Gamez P, Rivas JJ, Embun R, Molins L, de la Cruz J, **GECMP-CCR-SEPAR Spanish Colorectal Metastasectomy Registry**. Agreement Between Computed Tomography and Pathologic Nodule Counts in Colorectal Lung Metastases. *Ann Thorac Surg*. 2016 Jan; 101(1):259-65. IF: 3,849
2. Franco J, Llopis E, **Galán G**. Hemothorax After Endobronchial Ultrasound-guided Transbronchial Needle Aspiration. *J Bronchology Interv Pulmonol*. 2016 Oct; 23(4):328-330. IF: 0
3. García-de-la-Asunción J, García-Del-Olmo E, **Galan G**, Guijarro R, Martí F, Badenes R, Perez-Griera J, Duca A, Delgado C, Carbonell J, Belda J. Glutathione oxidation correlates with one-lung ventilation time and PO₂/FiO₂ ratio during pulmonary lobectomy. *Redox Rep*. 2016 Sep; 21(5):219-26. IF: 1,522
4. Hernández J, Molins L, Fibla JJ, Heras F, Embún R, Rivas JJ, Grupo Español de Metástasis Pulmonares de Carcinoma Colo-Rectal (GECMP-CCR) de la Sociedad Española de Neumología y Cirugía Torácica (**SEPAR**). Role of major resection in pulmonary metastasectomy for colorectal cancer in the Spanish prospective multicenter study (GECMP-CCR). *Ann Oncol*. 2016 May; 27(5):850-5. IF: 9,269
5. Embun R, Rivas de Andrés JJ, Call S, de Olaiz Navarro B, Freixinet JL, Bolufer S, Jarabo JR, Pajuelo N, Molins L, Spanish Group of Lung Metastases of Colo-Rectal Cancer (GECMP-CCR) of the Spanish Society of Pneumology and Thoracic Surgery (**SEPAR**). Causal Model of Survival After Pulmonary Metastasectomy of Colorectal Cancer: A Nationwide Prospective Registry. *Ann Thorac Surg*. 2016 May; 101(5):1883-90. IF: 2,975



Department of Cardiovascular Surgery

• PUBLICATIONS

Number of articles	IF	Average IF
3	8,34	2,78

National collaborations	International collaborations	Corresponding author
1	-	-

Original articles

1. **Garcia-Valentin A, Mestres CA, Bernabeu E, Bahamonde JA, Martín I, Rueda C, Domenech A, Valencia J, Fletcher D, Machado F, Amores J.** Validation and quality measurements for EuroSCORE and EuroSCORE II in the Spanish cardiac surgical population: a prospective, multicentre study. *Eur J Cardiothorac Surg.* 2016 Feb; 49(2):399-405. IF: 3,304
2. Valero E, Santas E, **Machado F**, Núñez J. Pseudoaneurysm with fistulization to the left atrium: A very rare late complication of previous aortic root surgery. *Int J Cardiol.* 2016 Jun 1; 212:145-7. IF: 4,036
3. **Fletcher Sanfeliu D, Rueda Muñoz C, Martín-González I, Bahamonde Romano JÁ.** Juxtarenal aortoiliac occlusive disease in a patient with left sided inferior vena cava. *Cir Esp.* 2016 Dec 8 ;. IF: 1

Department of Plastic Surgery



Strategic aims

- Increase of microsurgery.
- Development of news investigation lines as doctoral studies.

Main lines of research

- Opening of 6 doctoral thesis that will be defended in the near future, based on the following lines: breast reconstruction and VAC therapy.

Department of Dermatology

Strategic aims

- To continue making a biobank of melanoma patients.

Main lines of research

- About melanoma: to study cytokines involved in the regression of melanocytic lesions.
- Psoriasis: to study the application of new molecules for the treatment of patients with severe psoriasis.

• PUBLICATIONS

Number of articles	IF	Average IF
10	8,90	0,89

National collaborations	International collaborations	Corresponding author
2	-	9

Original articles

1. **Escandell I, Cabezas M, Martín JM, Terradez L, Pinazo MI.** Effective treatment with Dabrafenib and Trametinib for a BRAF-mutated metastatic dedifferentiated malignant spindle cell neoplasm. *J Eur Acad Dermatol Venereol.* 2016 Jul; 30(7):1224-6. IF: 2,826
2. **Ayala D, Ramón MD, Cabezas M, Jordá E.** Primary Cutaneous



CD4+ Small/Medium-Sized Pleomorphic T-Cell Lymphoma With Expression of Follicular T-Helper Cell Markers and Spontaneous Remission. *Actas Dermosifiliogr.* 2016 May; 107(4):357-359. IF: 0

3. **Ayala D, Ramón MD, Martín JM, Jordá E.** Atypical Phacomatosis Pigmentokeratolica as the Expression of a Mosaic RASopathy With the BRAF-Glu586Lys Mutation. *Actas Dermosifiliogr.* 2016 May; 107(4):344-346. IF: 0
4. Torres C, Revert Á, Terrádez L, **Jordá E.** Linear Dermatofibroma. *Actas Dermosifiliogr.* 2016 Nov; 107(9):787-789. IF: 0
5. **Martín JM, Escandell I, Ayala D, Jordá E.** Spontaneous Remission of Recalcitrant Warts in Girls After Human Papillomavirus Vaccination. *Actas Dermosifiliogr.* 2016 Jul-Aug; 107(6):533-5. IF: 0
6. **Ayala D, Ramón MD,** Cabezas M, **Jordá E.** Nevus Spilus Associated with Agminated Blue Nevus: A Rare Combination. *Actas Dermosifiliogr.* 2016 Sep; 107(7):614-6. IF: 0
7. **Martín JM, Jordá E,** Martín-Gorgojo A, Beteta G, Monteagudo C. Histiocytosis with mixed cell populations. *J Cutan Pathol.* 2016 May; 43(5):456-460. IF: 1,582
8. **Martín JM,** Mateo E, **Jordá E.** Azithromycin for the Treatment of Ciclosporin-Induced Gingival Hyperplasia. *Actas Dermosifiliogr.* 2016 Nov; 107(9):780. IF: 0
9. **Ayala D,** Puglia V, **Jordá E.** Hyperkeratotic Subungual Tumor. *Actas Dermosifiliogr.* 2016 Jul 16 ;. IF: 0
10. **Jordá E,** Domingo C, Alcalá MD, Ciafre A, Beltran DD, Albiach EF. Economic Impact of Palliative Radiation Therapy of Bone Metastases With a Single Fraction Dose: A One-Institution Experience. *Int J Radiat Oncol Biol Phys.* 2016 Oct 1; 96(2S):E519-E520. IF: 4,495

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI13/02786

Title: Implication of selected miRNAs in tumor progression of cutaneous malignant melanoma, and their value as prognostic and therapeutic biomarkers.

Principal Investigator: José Carlos Monteagudo Castro (Esperanza Jordá as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital*

Clínico Universitario de Valencia

Duration: 2014-2016

Total Budget: 59.592€

Department of Pharmacy

Strategic aims

- Implementation of a new therapeutical drug monitoring system in a clinical analytical laboratory for pharmacokinetic control of antibiotic (meropenem, piperacillin, ceftazidime) and antifungals (voriconazole) in the hospitalized patient, with the aim of optimal and rational use of antimicrobials.
- Study of pharmacokinetics of caspofungin in patients under hemodiafiltration.

Main lines of research

- Pharmacokinetics/pharmacodynamics of anidulafungin in plasma and intraperitoneal fluid in the critical patient with secondary peritonitis and suspected/evidenced candida spp infection. Efficacy Study.
- Observational study of population pharmacokinetic model of voriconazole in allogeneic stem cell transplantation.
- Implementation of a new therapeutical drug monitoring system in a clinical analytical laboratory for pharmacokinetic control of antineoplastics in the oncological patient, with the aim of optimal and rational use of oncological medication.
- Cost effectiveness analysis of direct-acting antiviral therapy for treatment-of patients with chronic HCV infection.

• PUBLICATIONS

Number of articles	IF	Average IF
5	15,87	3,17

National collaborations	International collaborations	Corresponding author
3	-	2



Original articles

1. Ezquer-Garin C, Escuder-Gilabert L, Martín-Biosca Y, Lisart RF, Sagrado S, Medina-Hernández MJ. Fit-for-purpose chromatographic method for the determination of amikacin in human plasma for the dosage control of patients. *Talanta*. 2016 Apr 1; 150:510-5. IF: 3,545
2. Pérez-Pitarch A, Guglieri-López B, Ferriols-Lisart R, Merino-Sanjuán M. A model-based meta-analysis of sofosbuvir-based treatments in chronic hepatitis C patients. *Int J Antimicrob Agents*. 2016 Mar; 47(3):184-94. IF: 4,296
3. Guglieri-López B, Pérez-Pitarch A, Porta Oltra B, Ferriols-Lisart F, Royo-Peiró Á, Climente-Martí M. Effectiveness, toxicity, and economic evaluation of ipilimumab for the treatment of patients with metastatic melanoma in the Spanish outpatient setting. *Anticancer Drugs*. 2016 Aug; 27(7):679-84. IF: 2,268
4. Guglieri-López B, Pérez-Pitarch A, Martínez-Gómez MA, Porta-Oltra B, Climente-Martí M, Merino-Sanjuán M. A Wide Linearity Range Method for the Determination of Lenalidomide in Plasma by High-Performance Liquid Chromatography: Application to Pharmacokinetic Studies. *J Lab Autom*. 2016 Dec; 21(6):806-810. IF: 1,297

Letter

5. Aguilar G, Ferriols R, Carbonell JA, Ezquer C, Alonso JM, Villena A, Puig J, Navarro D, Alós M, Belda FJ. Pharmacokinetics of anidulafungin during venovenous extracorporeal membrane oxygenation. *Crit Care*. 2016 Oct 17; 20(1):325. IF: 4,476

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: EC10-318

Title: *Tratamiento anticipado con ganciclovir de la infección activa por el citomegalovirus (CMV) en el paciente crítico en ventilación mecánica con sepsis grave o shock séptico*

Principal Investigator: Gerardo Aguilar Aguilar (Teresa Torrecilla as collaborating researcher)

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2012-2016

Total budget: 38.500€

Department of Biochemistry and Clinical Analysis



Strategic aims

- Obtaining reference values for lipids, lipoproteins, insulin resistance and folic acid.
- Document strategies of laboratory test requesting appropriateness and patient safety.

Main lines of research

- Demand management for laboratory testing and patient safety.
- The research contribution is also performed in collaboration with the clinical research groups: Cardiometabolic Risk and Diabetes (lipid metabolism and insulin resistance) Clinical Hematology (myeloma), Gastroenterology (inflammatory bowel disease), Hepatology (prevalence of HCV infection), Anesthesia (oxidative stress), Internal Medicine and Rheumatology (autoimmune diseases), Otorhinolaryngology (inflammatory mediators in mandibular implant), Public Health (Colorectal Cancer Screening Program).

• PUBLICATIONS

Number of articles	IF	Average IF
10	37,82	3,78
National collaborations	International collaborations	Corresponding author
5	1	8



Original articles

1. **Quiñones-Torrel C, Villanueva-Gil MP, Rodríguez-Muñoz A, Abellán-Tejada L, Aparici-Ibáñez M, Carratalá-Calvo A.** When an Analytical Interference Is a Useful Diagnostic Tool: Finding Monoclonal Gammopathies in Routine Analysis. *J Clin Lab Anal.* 2016 Mar; 30(2):140-4. IF: 1,038
2. Togo A, Espadas Maciá D, Blanes Segura S, Sivó Díaz N, **Villalba Martínez C.** [Is there vitamin D deficiency in children in a sunny Mediterranean city?]. *An Pediatr (Barc).* 2016 Mar; 84(3):163-9. IF: 0,833
3. García-de-la-Asunción J, García-Del-Olmo E, Galan G, Guijarro R, Martí F, Badenes R, **Perez-Griera J, Duca A, Delgado C, Carbonell J, Belda J.** Glutathione oxidation correlates with one-lung ventilation time and PO₂/FiO₂ ratio during pulmonary lobectomy. *Redox Rep.* 2016 Sep; 21(5):219-26. IF: 1,522
4. **Rodríguez-Borja E, Villalba-Martínez C, Barba-Serrano E, Carratala-Calvo A.** Failure to review STAT clinical laboratory requests and its economical impact. *Biochem Med (Zagreb).* 2016; 26(1):61-7. IF: 2,667
5. Salinas M, López-Garrigós M, Pomares FJ, Flores E, Uris J, Leiva-Salinas C, en nombre del resto de autores del Grupo piloto para la adecuación de la demanda de pruebas de laboratorio (**REDCONLAB**). Request of thyroid function tests from Primary Care in Spain. *Endocrinol Nutr.* 2016 Jan; 63(1):19-26. IF: 0
6. Núñez J, Núñez E, Miñana G, **Carratalá A, Sanchis J, Lupón J, Barallat J, Pastor MC, Pascual-Figal D, Bayés-Genís A.** Serum neprilysin and recurrent hospitalizations after acute heart failure. *Int J Cardiol.* 2016 Jun 28; 220:742-744. IF: 4,638
7. Núñez J, Teruel A, **Quiñones-Torrel C, García-Blas S, Carratalá A, Miñana G, Santas E, Torregrosa I, Solano C, González M.** Continuous ambulatory peritoneal dialysis as a promising therapy for light chain amyloidosis with congestive heart failure. *Int J Cardiol.* 2016 Aug 20; 223:807-809. IF: 4,638
8. Sanchis J, García-Blas S, **Carratalá A, Valero E, Mollar A, Miñana G, Ruiz V, Balaguer JV, Roqué M, Bosch X, Núñez J.** Clinical Evaluation Versus Undetectable High-Sensitivity Troponin for Assessment of Patients With Acute Chest Pain. *Am J Cardiol.* 2016 Dec 1; 118(11):1631-1635. IF: 3,154
9. **Rodríguez-Borja E, Barba-Serrano E, Alfayate-Guerra R, Martínez-Camarasa C.** The unfinished story of interference in thyroid hormones with Roche immunoassays: when prewashing procedures matter. *Clin Chem Lab Med.* 2016 Dec 17 ;. IF: 3,017
10. Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, Fitó M, Chiva-Blanch G, Fiol M, Gómez-Gracia E, Arós F, Lapetra J, Serra-Majem L, Pintó X, Buil-Cosiales P, Sorlí JV, Muñoz MA, Basora-Gallisá J, Lamuela-Raventós RM, Serra-Mir M, Ros E, **PREDIMED Study Investigators.** Effect of a high-fat Mediterranean diet on bodyweight and waist circumference: a prespecified secondary outcomes analysis of the PREDIMED randomised controlled trial. *Lancet Diabetes Endocrinol.* 2016 Aug; 4(8):666-76. IF: 16,32

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI14/02018

Title: *Papel de la vía de señalización NOTCH1/FBXW7/PI3K/PTEN/AKT en la progresión de la Leucemia Linfocítica Crónica B (LLC-B) a formas avanzadas.*

Principal Investigator: M^a José Terol Casterá (Ana Cuesta Peredo as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2015-2017

Total budget: 67.000€

Reference: PI13/01519

Title: Loop diuretics dosage in patients with acute heart failure and renal failure: conventional strategy versus strategy guided by CA125 plasma levels.

Principal Investigator: Julio Núñez Villota (Juana María Vaquer as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014-2016

Total Budget: 67.034€

Reference: PI14/00959

Title: *Comparación aleatoria entre un estrategia de intervención sobre fragilidad frente a la estrategia habitual en pacientes frágiles después de un infarto agudo de miocardio.*

Principal Investigator: Juan Sanchis Forés (Enrique Rodríguez Borja as collaborating researcher)



Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2015-2018
Total budget: 36.300€

Title: Validación de microdeleciones microduplicaciones y mosaicismos. Diagnóstico prenatal no invasivo en DNA fetal circulante.

Principal Investigator: Sonia Santillán (Ana Cuesta Peredo as collaborating researcher)

Funding Body: Sistemas Genómicos S. L
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2016

Reference: 48 Unidad de Investigación del Servicio de Laboratorio

Title: Implantación y gestión del registro de los resultados de las gasometrías que se realizan en distintos Servicios del Hospital Clínico en el Sistema Informático del Laboratorio (SIL).

Principal Investigator: Arturo Carratalá Calvo
Funding Body: Radiometer
Beneficiary Institution: Hospital Clínico Universitario de Valencia
Duration: 2016
Total budget: 15.000€

Reference: 48 Unidad de Investigación del Servicio de Laboratorio

Title: Apoyo de laboratorio a proyectos de investigación del Hospital Clínico Universitario de Valencia.

Principal Investigator: Arturo Carratalá Calvo
Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary Institution: Hospital Clínico Universitario de Valencia
Duration: 2016
Total budget: 27.000€

Reference: 48 Unidad de Investigación del Servicio de Laboratorio

Title: Aplicación de la técnica de hibridación genómica comparada mediante arrays (array-CGH) al estudio de retraso mental, reordenamientos cromosómicos en cáncer, diagnóstico prenatal y preimplantacional.

Principal Investigator: Ana Cuesta Peredo

Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia

Beneficiary Institution: Hospital Clínico Universitario de Valencia

Duration: 2016

Total budget: 15.000€

Department of Maxillofacial surgery

Strategic aims

- FIPSE project: Innovation in personalised prosthesis for maxillofacial reconstruction.
- Translational research project for the development of implants with high added value through additive manufacturing.

Main lines of research

- Cost-effectiveness analysis of the management of oral surgery processes in patients with severe dependence and / or plurypathological chronicles with comorbidities. Proposal for a new organizational model of care.
- Evaluation of surgical implantation technique of the sphenopalatine ganglion neurostimulator to treat chronic cluster headache and disabling chronic migraine.
- Radiological evaluation of predictive factors of access to pterygopalatine fossa. Research surgical approach for the installation of a neuromodulator in the sphenopalatine ganglion to treat of certain chronic headaches.
- Research on materials involved in bone regeneration.

• PUBLICATIONS

Number of articles	IF	Average IF
3	6,32	2,10
National collaborations	International collaborations	Corresponding author
1	1	1

Original articles

1. Jovani-Sancho MD, Sheth CC, Marqués-Mateo M, Puche-To-



- rres M. Platelet-Rich Plasma: A Study of the Variables that May Influence Its Effect on Bone Regeneration. *Clin Implant Dent Relat Res.* 2016 Oct; 18(5):1051-1064. IF: 3,589
- Assaf AT, Hillerup S, Rostgaard J, **Puche M**, Blessmann M, Kohlmeier C, Pohlenz P, Klatt JC, Heiland M, Caparso A, Papay F. Technical and surgical aspects of the sphenopalatine ganglion (SPG) microstimulator insertion procedure. *Int J Oral Maxillofac Surg.* 2016 Feb; 45(2):245-54. IF: 1,565
 - Marqués-Mateo M, Puche-Torres M, Iglesias-Gimilio ME.** Temporomandibular chronic dislocation: The long-standing condition. *Med Oral Patol Oral Cir Bucal.* 2016 Nov 1; 21(6):e776-e783. IF: 1.171

Department of Gastroenterology and Hepatology

Strategic aims

- Update of protocols and clinical guidelines of the Department.
- It has been possible to consolidate the relationship of the Unit of Inflammatory Bowel Disease of our Department with the network of National Units, through collaborative studies that have been published in international journals of category Q1 and Q3. The group has also consolidated motility and pancreas research in the national and international area through consensus guides that have been published in journals with categories Q1-Q4.

Main lines of research

- On the section of gastroenterology, to continue the studies on digestive hemorrhage, acute pancreatitis, inflammatory bowel disease, motion sickness and digestive benign anorectal pathology.
- On the hepatology division to continue the analysis of hepatic encephalopathy, the nonalcoholic, epidemiological, therapeutic and immunoprophylaxis on Hepatitis Virus steatohepatitis. Also hepatocellular damage and nitric oxide and liver tumors.
- About endoscopy division: study on the therapeutic dilatation, the ecoendoscopy diagnostics and therapeutics, ampulectomia, diverticulotomy of Zencker and digestive prostheses.

• PUBLICATIONS

Number of articles	IF	Average IF
18	61,15	3,39
National collaborations	International collaborations	Corresponding author
11	1	9

Original articles

- Piñana JL, **Serra MÁ**, Hernández-Boluda JC, Navarro D, Calabuig M, Solano C. Successful treatment of hepatitis C virus infection with sofosbuvir and simeprevir in the early phase of an allogeneic stem cell transplant. *Transpl Infect Dis.* 2016 Feb; 18(1):89-92. IF: 2,064
- Mora F**, Cassinello N, Mora M, **Bosca M, Minguez M**, Ortega J. Esophageal abnormalities in morbidly obese adult patients. *Surg Obes Relat Dis.* 2016 Mar-Apr; 12(3):622-8. IF: 4,066
- Boscá Watts MM**, Marco Marqués A, Savall-Núñez E, Artero-Fullana A, Lanza Reynolds B, Andrade Gamarra V, Puglia Santos V, Burgués Gasió O, **Mora Miguel F.** IBD or strongyloidiasis? *Rev Esp Enferm Dig.* 2016 Aug; 108(8):516-20. IF: 1,414
- Gisbert JP, Barreiro-de Acosta M, Esteve M, García-Sánchez V, Gomollón F, Guardiola J, Hinojosa J, Martín Arranz MD, **Minguez M**, Taxonera C, Vera I. Physician Perspectives on Unresolved Issues in the Management of Ulcerative Colitis: The UC Horizons Project. *Inflamm Bowel Dis.* 2016 Mar; 22(3):583-98. IF: 4,464
- Moreno Primera O, Barreda Matta L, **Mas Mercader P.** A Rare Cause of Persistent Rectal Bleeding. *Clin Gastroenterol Hepatol.* 2016 May; 14(5):A25-6. IF: 7,896
- Guerra I, Pérez-Jeldres T, Iborra M, Algaba A, Monfort D, Calvet X, Chaparro M, Mañosa M, Hinojosa E, **Minguez M**, Ortiz de Zarate J, Márquez L, Prieto V, García-Sánchez V, Guardiola J, Rodríguez GE, Martín-Arranz MD, García-Tercero I, Sicilia B, Masedo Á, Lorente R, Rivero M, Fernández-Salazar L, Gutiérrez A, Van Domselaar M, López-SanRomán A, Ber Y, García-Sepulcre M, Ramos L, Bermejo F, Gisbert JP, Spanish GETECCU group (ENEIDA project). Incidence, Clinical Characteristics, and Management of Psoriasis Induced by Anti-TNF Therapy in Patients with Inflammatory Bowel Disease: A Nationwide Cohort Study. *Inflamm Bowel Dis.* 2016 Apr; 22(4):894-901. IF: 4,464



7. Iborra M, Pérez-Gisbert J, **Bosca-Watts MM**, López-García A, García-Sánchez V, López-Sanromán A, Hinojosa E, Márquez L, García-López S, Chaparro M, Aceituno M, Calafat M, Guardiola J, Belloc B, Ber Y, Bujanda L, Beltrán B, Rodríguez-Gutiérrez C, Barrio J, Cabriada JL, Rivero M, Camargo R, van Domselaar M, Villoria A, Schuterman HS, Hervás D, Nos P, Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU).. Effectiveness of adalimumab for the treatment of ulcerative colitis in clinical practice: comparison between anti-tumour necrosis factor-naïve and non-naïve patients. *J Gastroenterol*. 2016 Oct 8 ; IF: 4,414
 8. Iborra M, Gisbert JP, **Bosca-Watts MM**, López-García A, García-Sánchez V, López-Sanromán A, Hinojosa E, Márquez L, García-López S, Chaparro M, Aceituno M, Calafat M, Guardiola J, Belloc B, Ber Y, Bujanda L, Beltrán B, Rodríguez-Gutiérrez C, Barrio J, Cabriada JL, Rivero M, Camargo R, van Domselaar M, Villoria A, Schuterman HS, Hervás D, Nos P, Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU).. Erratum to: Effectiveness of adalimumab for the treatment of ulcerative colitis in clinical practice: comparison between anti-tumour necrosis factor-naïve and non-naïve patients. *J Gastroenterol*. 2016 Nov 24 ; IF: 4,414
 9. Ruiz de León San Juan A, Ciriza de Los Ríos C, Pérez de la Serna Bueno J, Canga Rodríguez-Valcárcel F, Estremera Arévalo F, García Sánchez R, Huamán Ríos JW, Pérez Fernández MT, Santander Vaquero C, Serra Pueyo J, Sevilla Mantilla C, Barba Orozco E, Bosque López MJ, Casabona Francés S, Carrión Bolorino S, Castillo Grau P, Delgado Aros S, Domínguez Carbajo AB, Fernández Orcajo P, García-Lledó J, Gigantó Tomé F, Iglesias Picazo R, Lacima Vidal G, López López P, Llabrés Rosselló M, **Mas Mercader P**, Mego Silva M, Mendarte Barrenetxea MU, Miliani Molina C, Oreja Arrayago M, Sánchez Ceballos F, Sánchez Prudencio S. Practical aspects of high resolution esophageal manometry. *Rev Esp Enferm Dig*. 2016 Dec 19; 109. IF: 1,455
 10. Fiorino G, Cortes PN, Ellul P, Felice C, Karatzas P, Silva M, Lakatos PL, Bossa F, Ungar B, Sebastian S, Furfaro F, Karmiris K, Katsanos KH, Muscat M, Christodoulou DK, Maconi G, Kopylov U, Magro F, Mantzaris GJ, Armuzzi A, **Boscà-Watts MM**, Ben-Horin S, Bonovas S, Danese S. Discontinuation of Infliximab in Patients With Ulcerative Colitis Is Associated With Increased Risk of Relapse: A Multinational Retrospective Cohort Study. *Clin Gastroenterol Hepatol*. 2016 Oct; 14(10):1426-1432. E1. IF: 7,68
 11. Khodayar-Pardo P, **Peña Aldea A**, Ramírez González A, Meseguer Carrascosa A, Calabuig Bayo C. Very Early Presentation of Extrahepatic Portal Vein Obstruction Causing Portal Hypertension in an Infant: Uncertainties in the Management and Therapeutic Limitations. *Case Rep Gastroenterol*. 2016 Jul 19; 10(2):360-5. IF: 0
 12. **Mínguez M**, López Higuera A, Júdez J. Use of polyethylene glycol in functional constipation and fecal impaction. *Rev Esp Enferm Dig*. 2016 Dec; 108(12):790-806. IF: 1,455
 13. López-Serrano A, Crespo J, **Pascual I**, Salord S, Bolado F, Del-Pozo-García AJ, Ilzarbe L, de-Madaria E, Moreno-Osset E, Members of the Autoimmune Pancreatitis in Spain Study Group.. Diagnosis, treatment and long-term outcomes of autoimmune pancreatitis in Spain based on the International Consensus Diagnostic Criteria: A multi-centre study. *Pancreatol*. 2016 May-Jun; 16(3):382-90. IF: 2,406
 14. **Bosca-Watts MM**, Cortes X, Iborra M, Huguet JM, Sempere L, Garcia G, Gil R, Garcia M, Muñoz M, Almela P, Maroto N, Paredes JM. Short-term effectiveness of golimumab for ulcerative colitis: Observational multicenter study. *World J Gastroenterol*. 2016 Dec 21; 22(47):10432-10439. IF: 2,787
 15. R-Grau Mdel C, Chaparro M, Mesonero F, Barreiro-de Acosta M, Castro L, Castro M, Domènech E, Mancenido N, Pérez-Calle JL, Taxonera C, Barrio J, De Francisco R, Fernández-Salgado E, Luzón L, Merino O, Oltra L, Saro C, Bermejo F, García-Sánchez V, Ginard D, Gutiérrez A, Vera I, **Antón R**, Ber Y, Calvet X, Gisbert JP. Effectiveness of anti-TNF? drugs in patients with Crohn's disease who do not achieve remission with their first anti-TNF? agent. *Dig Liver Dis*. 2016 Jun; 48(6):613-9. IF: 2,719
- Letter**
16. Gámez-del-Castillo JM, Garcés-Albir M, Fernández-Moreno MC, Morera-Ocón FJ, **Villagrasa R**, Sabater-Ortí L. Disconnected pancreatic duct syndrome: complete pancreas transection secondary to acute pancreatitis. *Rev Esp Enferm Dig*. 2016 Mar; 108(3):165-6. IF: 1,455
- Guideline**
17. Mearin F, Ciriza C, **Mínguez M**, Rey E, Mascort JJ, Peña E, Cañones P, Júdez J. Clinical Practice Guideline: Irritable bowel syndrome with constipation and functional constipation in the adult. *Rev Esp Enferm Dig*. 2016 May 27; 108. IF: 1,414



Review

18. **Tosca Cuquerella J, Bosca-Watts MM**, Anton Ausejo R, Tejedor Alonso S, **Mora De Miguel F, Minguez Perez M**. Amyloidosis in Inflammatory Bowel Disease: A Systematic Review of Epidemiology, Clinical Features, and Treatment. *J Crohns Colitis*. 2016 Oct; 10(10):1245-53. IF: 6,585

Department of Intensive Medicine

Main lines of research

- Histones.
- UCI Epidemiology. BMR.
- Serious flu.
- Genetics in severe NAC.

• PUBLICATIONS

Number of articles	IF	Average IF
7	31,63	3,95
National collaborations	International collaborations	Corresponding author
6	1	-

Original articles

1. Sakr Y, Ferrer R, Reinhart K, Beale R, Rhodes A, Moreno R, Timsit JF, Brochard L, Thompson BT, Rezende E, Chiche JD, **IC-GLOSSARI Investigators**, ESICM Trials Group. The Intensive Care Global Study on Severe Acute Respiratory Infection (IC-GLOSSARI): a multicenter, multinational, 14-day inception cohort study. *Intensive Care Med*. 2016 May; 42(5):817-28. IF: 7,214
2. Lorente L, Martín MM, **Ferreres J**, Solé-Violán J, Labarta L, Díaz C, Jiménez A, Borreguero-León JM. Serum caspase 3 levels are associated with early mortality in severe septic patients. *J Crit Care*. 2016 Aug; 34:103-6. IF: 2,445
3. Rodríguez AH, Avilés-Jurado FX, Díaz E, Schuetz P, Trefler SI, Solé-Violán J, Cordero L, Vidaur L, Estella Á, Pozo Laderas JC, Socias L, Vergara JC, Zaragoza R, Bonastre J, Guerrero JE, Suberviola B, Cilloniz C, Restrepo MI, Martín-Loeches I, **SEMI-**

CYUC/GETGAG Working Group. Procalcitonin (PCT) levels for ruling-out bacterial coinfection in ICU patients with influenza: A CHAID decision-tree analysis. *J Infect*. 2016 Feb; 72(2):143-51. IF: 4,382

4. Álvarez-Lerma F, Marín-Corral J, Vila C, Masclans JR, González de Molina FJ, Martín Loeches I, Barbadillo S, Rodríguez A, **H1N1 GETGAG/SEMICYUC Study Group**. Delay in diagnosis of influenza A (H1N1) pdm09 virus infection in critically ill patients and impact on clinical outcome. *Crit Care*. 2016 Oct 23; 20(1):337. IF: 4,476
5. Lorente L, Martín MM, López-Gallardo E, **Ferreres J**, Solé-Violán J, Labarta L, Díaz C, Jiménez A, Montoya J, Ruiz-Pesini E. Septic patients with mitochondrial DNA haplogroup JT have higher respiratory complex IV activity and survival rate. *J Crit Care*. 2016 Jun; 33:95-9. IF: 2,445
6. Lorente L, Martín MM, Pérez-Cejas A, Barrios Y, Solé-Violán J, **Ferreres J**, Labarta L, Díaz C, Jiménez A. Association between Interleukin-6 Promoter Polymorphism (-174 G/C), Serum Interleukin-6 Levels and Mortality in Severe Septic Patients. *Int J Mol Sci*. 2016 Nov 8; 17(11). IF: 3,257
7. Zubia-Olaskoaga F, Maraví-Poma E, Urreta-Barallobre I, Ramírez-Puerta MR, Mourelo-Fariña M, Marcos-Neira MP, **Epidemiology of Acute Pancreatitis in Intensive Care Medicine Study Group**. Comparison Between Revised Atlanta Classification and Determinant-Based Classification for Acute Pancreatitis in Intensive Care Medicine. Why Do Not Use a Modified Determinant-Based Classification? *Crit Care Med*. 2016 May; 44(5):910-7. IF: 7,422

Department of Nuclear Medicine

Strategic aims

- Dosimetric assessment in patients with hyperthyroidism treated with 131-Iodine.
- Cardiac sympathetic nerve activity by 123I-MIBG scintigraphy in heart failure patients.
- Evaluation of left ventricular dyssynchrony by Gated SPECT myocardial perfusion in the evaluation of cardiac resynchronization therapy.
- Radioguided surgery by intraoperative scintigraphy with portable gamma camera in patients with primary hyper-



parathyroidism and not conclusive pre-surgical scintigraphy.

- Sentinel node detection in breast cancer after neoadjuvant chemotherapy.

Main lines of research

- Radioembolization of hepatocarcinoma by resin microspheres labeled with 90-Yttrium.
- Assessment of cardiac sympathetic nerve activity by 123I-MIBG scintigraphy in heart failure patients.
- Evaluation of left ventricular dyssynchrony by Gated SPECT myocardial perfusion in patients with cardiac resynchronization therapy.
- Sentinel lymph node detection in breast cancer in patients with previous mammary surgery.
- Evaluation of screws loosening and other complications after lumbar spinal fusion surgery by bone SPECT.
- Diagnosis and follow-up of hyperplasia of the mandibular condyles by bone SPECT.

• PUBLICATIONS

Number of articles	IF	Average IF
1	1,054	1,05
National collaborations	International collaborations	Corresponding author
1	-	-

Original articles

1. Díaz-Expósito R, Martí-Bonmatí L, Burgués O, **Casáns-Tormo I**, Bermejo-de Las Heras B, Julve-Parreño A, Caballero-Garate A. Selective sentinel node biopsy after intratumour administration of radiotracer in breast cancer patients treated with neoadjuvant chemotherapy in relation to the level of tumour response. *Rev Esp Med Nucl Imagen Mol.* 2016 Nov - Dec; 35(6):358-364. IF: 1,054

Department of Preventive Medicine

• PUBLICATIONS

Number of articles	IF	Average IF
1	0,833	0,833
National collaborations	International collaborations	Corresponding author
1	-	1

Original articles

1. **Boone AL, Besó-Delgado M**, Alguacil-Ramos AM, Pastor-Villalba E, Portero-Alonso A. [More is not always better. Individual guideline or systematic vaccination against pneumococcus]. *An Pediatr (Barc).* 2016 Dec; 85(6):320-321. IF: 0,833

Department of Microbiology

Strategic aims

- Production of virus-like particles (VLPs) and P particles representative of diverse genotypes norovirus.
- Characterization of a new conformational epitope in the GII.4 norovirus capsid protein identified by a neutralizing monoclonal antibody.
- Epidemiological surveillance of circulating strains of rotavirus and norovirus in Valencia and different geographical areas of Spain (Valladolid, Zaragoza, Barcelona, Murcia).

Main lines of research

- Molecular epidemiology of rotavirus (EuroRotaNet Project).
- Characterization of norovirus genotypes causing outbreaks and sporadic cases of acute gastroenteritis.
- Study of the interaction between norovirus VLPs and P particles and receptors in saliva and intestinal cells (MINECO SAF2012-38368 Project).
- Phylogenetic analysis of rotavirus G12 strains isolated in different Spanish regions.
- Analysis of the relationship between histo-blood group



antigens (HBGAs) and rotaviruses.

- Analysis by site-directed mutagenesis of a conformational epitope in the norovirus capsid protein recognized by a monoclonal antibody (MINECO SAF2012-38368 Project).

• PUBLICATIONS

Number of articles	IF	Average IF
7	28,11	4,01

National collaborations	International collaborations	Corresponding author
4	-	7

Original articles

- Rodríguez de la Pinta ML, Castro Lareo MI, Ramon Torrell JM, **García de Lomas J**, Devadiga R, Reyes J, McCoig C, Tafalla M, García-Corbeira P. Seroprevalence of pertussis amongst healthcare professionals in Spain. *Vaccine*. 2016 Feb 17; 34(8):1109-14. IF: 3,624
- Solano C, **Giménez E**, Piñana JL, **Vinuesa V**, **Poujois S**, **Zaragoza S**, Calabuig M, **Navarro D**. Preemptive antiviral therapy for CMV infection in allogeneic stem cell transplant recipients guided by the viral doubling time in the blood. *Bone Marrow Transplant*. 2016 May; 51(5):718-21. IF: 3,57
- Vinuesa V**, **Navarro D**, **Poujois S**, **Zaragoza S**, Borrás R. Performance characteristics of the new Abbott Real Time MTB assay for detection of Mycobacterium tuberculosis complex in respiratory specimens. *Diagn Microbiol Infect Dis*. 2016 Mar; 84(3):212-4. IF: 2,457
- Falcón R, Martínez A, Albert E, Madrid S, Oltra R, **Giménez E**, Soriano M, **Vinuesa V**, Gozalbo D, Gil ML, **Navarro D**. High vancomycin MICs within the susceptible range in Staphylococcus aureus bacteraemia isolates are associated with increased cell wall thickness and reduced intracellular killing by human phagocytes. *Int J Antimicrob Agents*. 2016 May; 47(5):343-50. IF: 4,296
- Vinuesa V**, Solano C, Giménez E, Piñana JL, Boluda JC, Amat P, **Navarro D**. Lack of evidence for a reciprocal interaction between bacterial and cytomegalovirus infection in the allogeneic stem cell transplantation setting. *Transpl Int*. 2016 Nov; 29(11):1196-1204. IF: 2,835
- Vinuesa V**, **Giménez E**, Solano C, Gimeno C, **Navarro D**, Spanish Society for Infectious Diseases and Clinical Microbiology Quality Control Study Group. Would Kinetic Analyses of Plasma Cytomegalovirus DNA Load Help to Reach Consensus Criteria for Triggering the Initiation of Preemptive Antiviral Therapy in Transplant Recipients? *Clin Infect Dis*. 2016 Dec 1; 63(11):1533-1535. IF: 8,736

Letter

- Giménez E**, Solano C, **Piñana JL**, Amat P, **Vinuesa V**, **Navarro D**. Re-examining the relationship between active cytomegalovirus (CMV) infection and acute graft-versus-host disease in allogeneic stem cell transplant recipients in the era of real-time PCR CMV assays. *Transpl Int*. 2016 Jan; 29(1):126-8. IF: 2,599

Department of Nephrology

Strategic aims

- To start two new investigation lines of research: Kidney damage in hematopoietic stem cell transplantation and myeloma kidney treatment by chemotherapy and dialysis filters PMMA.

Main lines of research

- Study of oxidative stress, nutrition and inflammation in patients with chronic kidney disease in stages 3, 4 and 5.
- Implications of hepcidin on iron metabolism in dialysis patients.
- Treatment of cardio-renal syndrome by peritoneal dialysis.
- Biomarkers of acute renal failure.
- Kidney damage in hematopoietic stem cell transplantation.
- Myeloma kidney treatment by chemotherapy and dialysis filters PMMA.



• PUBLICATIONS

Number of articles	IF	Average IF
3	11,22	3,74
National collaborations	International collaborations	Corresponding author
2	-	-

Original articles

- Núñez J, Teruel A, Quiñones-Torrel C, García-Blas S, Carratalá A, Miñana G, Santos E, **Torregrosa I**, Solano C, **González M**. Continuous ambulatory peritoneal dialysis as a promising therapy for light chain amyloidosis with congestive heart failure. *Int J Cardiol*. 2016 Aug 20; 223:807-809. IF: 4,638
- Cardells I, Payá A, Bondanza L, Miñana G, **González M**, Núñez J. Peritoneal Dialysis in Constrictive Pericarditis: A Report of Three Cases. *Rev Esp Cardiol (Engl Ed)*. 2016 Oct 31. IF: 3,792
- Tosca Cuquerella J, Bosca-Watts MM, Anton Ausejo R, **Tejedor Alonso S**, Mora De Miguel F, Minguez Perez M. Amyloidosis in Inflammatory Bowel Disease: A Systematic Review of Epidemiology, Clinical Features, and Treatment. *J Crohns Colitis*. 2016 Oct; 10(10): 1245-53. IF: 6,585

• THESIS

Thesis title: *Fracaso renal agudo en el trasplante de progenitores hematopoyéticos: análisis de la incidencia, factores de riesgo e implicaciones pronósticas, valor pronóstico y en el diagnóstico precoz de la cistatina C plasmática.*

Doctoral candidate: Miguel Angel Solís Salguero

Director(s): Carlos Solano, Juan Carlos Hernández Boluda, Isidro Torregrosa

Date of the defense: 08/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Valoración del estado nutricional en los diferentes estadios de la enfermedad renal crónica y su relación con el estrés oxidativo y la inflamación.*

Doctoral candidate: Patricia Tomás Simó

Director(s): Alfonso Miguel Carrasco, Guillermo Sáez Tormo, María Jesús Puchades Montesa

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: BCM-PD-02-INT

Title: *Iniciativa sobre la evolución de los pacientes con Diálisis-DP.*

Principal Investigator: Alfonso Miguel Carrasco (Miguel González Rico, M^a Jesús Puchades Montesa as collaborating researchers)

Funding Body: Fresenius medical care

Beneficiary Institution: *Hospital Clínico Universitario de Valencia*

Duration: 2015-2021

Total Budget: 2.940€

Reference: PrEFiNe

Title: *Estudio de prevalencia de la enfermedad de Fabry en pacientes en diálisis.*

Principal Investigator: M^a Jesús Puchades

Funding Body: SHIRE

Beneficiary Institution: *Hospital Clínico Universitario de Valencia*

Duration: 2015-2016

Total Budget: 0€

• AWARDS

In February 2016, Juan José Guzmán was awarded with the award to the best clinical case at the *Segunda Reunión de Residentes de Nefrología de la Comunidad Valenciana* for the communication "*Fracaso renal agudo en paciente con Toxoplasmosis cerebral asociada a VIH/SIDA*".

Department of Pneumology

• PUBLICATIONS

Number of articles	IF	Average IF
11	23,51	2,13
National collaborations	International collaborations	Corresponding author
4	1	6

**Original articles**

1. **Franco J**, Llopis E, Galán G. Hemothorax After Endobronchial Ultrasound-guided Transbronchial Needle Aspiration. *J Bronchology Interv Pulmonol*. 2016 Oct; 23(4):328-330. IF: 0
2. Sanz-Herrero F, Gimeno-Cardona C, Tormo-Palop N, Fernández-Fabrellas E, **Briones ML**, Cervera-Juan Á, Blanquer-Olivas J. The potential role of 13-valent pneumococcal conjugate vaccine in preventing respiratory complications in bacteraemic pneumococcal community-acquired pneumonia. *Vaccine*. 2016 Apr 4 ; 34(15): 1847-52. IF: 3,624
3. **Esteban Ronda V**, **Franco Serrano J**, **Briones Urtiaga ML**. Pulmonary Strongyloides stercoralis infection. *Arch Bronconeumol*. 2016 Aug; 52(8): 442-3. IF: 1,771
4. Lopez-Campos JL, Soriano JB, Calle M, **3E Project**. Determinants of use of the bronchodilator test in primary and secondary care: results of a national survey in Spain. *Clin Respir J*. 2016 Mar; 10(2): 217-22. IF: 2,147
5. Martínez-González D, **Franco J**, Navarro-Ortega D, Muñoz C, Martí-Obiol R, Borrás-Salvador R. Achalasia and mycobacterium goodii pulmonary infection. *Pediatr Infect Dis J*. 2011 May; 30(5): 447-8. IF: 3,569
6. **Llopis Pastor E**, Pérez Guzmán E, Ávila Martínez R, Villena Garrido MV, Sobradillo Ecenarro P. Provision of care by medical residents and the impact on quality. *Arch Bronconeumol*. 2015 Oct; 51(10): 515-9. IF: 1,823
7. Sanz F, Dean N, Dickerson J, Jones B, Knox D, Fernández-Fabrellas E, Chiner E, **Briones ML**, Cervera Á, Aguar MC, Blanquer J. Accuracy of PaO₂ /FiO₂ calculated from SpO₂ for severity assessment in ED patients with pneumonia. *Respirology*. 2015 Jul; 20(5): 813-8. IF: 3,345
8. Jiménez Ruiz CA, de Granda Orive JI, Solano Reina S, Riesco Miranda JA, de Higes Martínez E, Pascual Lledó JF, García Rueda M, Lorza Blasco JJ, **Signes Costa-Miñana J**, Valencia Azcona B, Villar Laguna C, Cristóbal Fernández M. Guidelines for the Treatment of Smoking in Hospitalized Patients. *Arch Bronconeumol*. 2016 Dec 22;. IF: 1,771

Letters

9. **Franco Serrano J**, **Burés Sales E**. The Contribution of Cell Blocks in the Diagnosis of Mediastinal Masses and Hilar Adenopathy Samples from Echobronchoscopy. *Arch Bronconeumol*. 2016 Feb; 52(2):107. IF: 1,823
10. Lizarzábal Suárez PC, Núñez Savall E, **Carrión Valero F**. Li-

pid pneumonia due to accidental aspiration of paraffin in a "fire-eater". *Arch Bronconeumol*. 2015 Oct; 51(10): 530-1. IF: 1,823

11. Rosario Martín C, Navarro Cubells B, **Carrión Valero F**. Immune-mediated leukopenia due to Chlamydomydia pneumoniae pneumonia. *Arch Bronconeumol*. 2015 Dec; 51(12): 663-664. IF: 1,823

Department of Neurosurgery**• PUBLICATIONS**

Number of articles	IF	Average IF
3	4,26	1,42
National collaborations	International collaborations	Corresponding author
-	1	2

Original articles

1. **Real-Peña L**, **Talamantes Escribá F**, **Quilis-Quesada V**, **González-Darder JM**. [Prognostic variability in atypical meningioma with complete resection. Proposed treatment algorithm]. *Neurocirugia (Astur)*. 2016 Jan-Feb; 27(1):15-23. IF: 0,41
2. Wang J, Yoshioka F, Joo W, Komune N, **Quilis-Quesada V**, Rhoton AL Jr. The cochlea in skull base surgery: an anatomy study. *J Neurosurg*. 2016 Nov; 125(5):1094-1104. IF: 3,443
3. **González-Darder JM**. [History of the craniotomy]. *Neurocirugia (Astur)*. 2016 Sep-Oct; 27(5):245-57. IF: 0,41

Department of Neurology**• PUBLICATIONS**

Number of articles	IF	Average IF
4	15,15	3,03
National collaborations	International collaborations	Corresponding author
-	4	-



Original articles

1. Lampl C, Thomas H, Tassorelli C, Katsarava Z, **Lainez JM**, Lantéri-Minet M, Rastenyte D, Ruiz de la Torre E, Stovner LJ, Andrée C, Steiner TJ. Headache, depression and anxiety: associations in the Eurolight project. *J Headache Pain*. 2016 Dec; 17(1):59. IF: 2,801
2. Lampl C, Thomas H, Stovner LJ, Tassorelli C, Katsarava Z, **Lainez JM**, Lantéri-Minet M, Rastenyte D, Ruiz de la Torre E, Andrée C, Steiner TJ. Interictal burden attributable to episodic headache: findings from the Eurolight project. *J Headache Pain*. 2016 Dec; 17(1):9. IF: 2,801
3. Barloese MC, Jürgens TP, May A, **Lainez JM**, Schoenen J, Gaul C, Goodman AM, Caparso A, Jensen RH. Cluster headache attack remission with sphenopalatine ganglion stimulation: experiences in chronic cluster headache patients through 24 months. *J Headache Pain*. 2016 Dec; 17(1):67. IF: 3,497
4. Jürgens TP, Barloese M, May A, **Lainez JM**, Schoenen J, Gaul C, Goodman AM, Caparso A, Jensen RH. Long-term effectiveness of sphenopalatine ganglion stimulation for cluster headache. *Cephalalgia*. 2016 May 9. IF: 6,052

Department of Neurophysiology

Main lines of research

- Role of magnetic resonance imaging (MRI) and electromyography (EMG) in the diagnosis of cervical and lumbosacral radiculopathy. Situation: data collection continues for further statistical analysis. Currently we have 353 patients with lumbosacral radiculopathy, and 54 with cervical radiculopathy. We continue to collect cases to increase the size of the sample. We collaborate with Dr. José Luis León and Dr. Iciar Puchades (Magnetic Resonance, ERESA).
- Definitive diagnosis of sleep disorders after clinical and polysomnographic evaluation in patients with clinical suspicion of sleep apnea-hyponeal syndrome and normal or inconclusive respiratory polygraphy. Situation: data collection continues for further statistical analysis. We have 82 patients collected. We continue to collect cases to increase the size of the sample.

• THESIS

Thesis title: *Alteraciones del ritmo del sueño en modelos animales de encefalopatía hepática.*

Doctoral candidate: Nicolás Peñaranda Sarmiento

Director(s): Carmina Montoliu, Vicente Felipo, M^a Ángeles Lloret

Date of the defense: 23/12/2016

Grade: *Sobresaliente "cum laude"*

Department of Otorhinolaryngology

Strategic aims

- The multi-center CBAS project sponsored and funded by Cochlear Co. (Göteborg, Sweden) has been completed in 2016 and has last for 3 years. Two types of osteointegrated implants with and without hydroxyapatite have been studied, being the only Spanish hospital participant with centers in Sweden, Holland and France. They participated with 30 patients. At the moment, three articles have been sent for publication, two of them in a very advanced position to be published.
- The study of cochlear implants has been started in cases of unilateral deafness and normal or near-normal hearing in the contralateral ear. This project is sponsored by Oticon Medical (Copenhagen, Denmark). They have recruited 7 patients who are undergoing very precise studies of sound localization and understanding with background noise in different experimental situations.

Main lines of research

- Cochlear implants in unilateral deafness.
- Simultaneous bilateral cochlear implants in children.
- Location of sound and hearing loss in different experimental situations.
- Situation of vestibular system.



• PUBLICATIONS

Number of articles	IF	Average IF
8	2,14	0,26
National collaborations	International collaborations	Corresponding author
5	-	6

Original articles

1. **García Callejo FJ, Rincón Piedrahita I, Monzó Gandía R, Sánchez Valenzuela O, Martínez Beneyto MP, Marzo Sanz M.** Factors related to post-tonsillectomy pain in adults. *Acta Otorrinolaringol Esp.* 2016 Jan-Feb; 67(1):23-32. IF: 0
2. Serra-Torres S, Bellot-Arcís C, Montiel-Company JM, **Marco Algarra J**, Almerich-Silla JM. Effectiveness of mandibular advancement appliances in treating obstructive sleep apnea syndrome: A systematic review. *Laryngoscope.* 2016 Feb; 126(2):507-14. IF: 2,144
3. Escorihuela García V, **Pitarch Ribas MI**, Llópez Carratalá I, Latorre Monteagudo E, Morant Ventura A, **Marco Algarra J.** Comparative study between unilateral and bilateral cochlear implantation in children of 1 and 2 years of age. *Acta Otorrinolaringol Esp.* 2016 May-Jun; 67(3):148-155. IF: 0
4. Redondo-Martínez J, Bécares-Martínez C, Orts-Alborch M, García-Callejo FJ, Pérez-Carbonell T, **Marco-Algarra J.** Relationship between video head impulse test (vHIT) and caloric test in patients with vestibular neuritis. *Acta Otorrinolaringol Esp.* 2016 May-Jun; 67(3):156-161. IF: 0
5. Canals P, **Pérez Del Valle B**, Lopez F, Marco A. The efficacy of individual treatment of subjective tinnitus with cognitive behavioural therapy. *Acta Otorrinolaringol Esp.* 2016 Jul-Aug; 67(4):187-92. IF: 0
6. **García Callejo FJ**, Redondo Martínez J, Andrade Gamarra V, Pérez Carbonell T. Osteoblastoma of the thyroid cartilage. *Acta Otorrinolaringol Esp.* 2016 Nov - Dec; 67(6):e37-e39. IF: 0
7. Redondo-Martínez J, Morant-Ventura A, Robledo-Aguayo D, Ayas-Montero A, Mencheta-Benet E, **Marco-Algarra J.** Extra-tympanic electrocochleography in a normal population. A descriptive study. *Acta Otorrinolaringol Esp.* 2016 Sep-Oct; 67(5):254-60. IF: 0
8. **García Callejo FJ**, Redondo Martínez J, Pérez Carbonell T, Monzó Gandía R, **Martínez Beneyto MP**, Rincón Piedrahita I. Hiccups. Attitude in Otorhinolaryngology Towards

Consulting Patients. A Diagnostic and Therapeutic Approach. *Acta Otorrinolaringol Esp.* 2016 Aug 16 ; IF: 0

• THESIS

Thesis title: *Análisis perceptivo de los dispositivos auditivos osteointegrados percutáneos*

Doctoral candidate: Ignacio Pla Gil

Director(s): María de la Paz Martínez Beneyto, Jaime Marco Algarra

Date of the defense: 13/05/2016

Grade: *Sobresaliente "cum laude"*

Department of Ophthalmology

Strategic aims

- To finish the epidemiological, prospective, multicentric and open study that evaluates characteristics and frequency of adenoviral conjunctivitis diagnosed by the AdenoPlus test in patients with acute conjunctivitis.

Main lines of research

- Measurement of the efficacy of glaucoma filtering surgeries using the SENSIMED TRIGGERFISH® monitoring system.
- Quantitative analysis of the retinal ganglion cell layer by OCT in patients with multiple sclerosis: correlation with the degree of disability and brain atrophy in MR.





• PUBLICATIONS

Number of articles	IF	Average IF
7	1,381	1,381
National collaborations	International collaborations	Corresponding author
1	-	6

Original articles

1. Barreiro-González A, **Barreiro-Rego A**. An ophthalmologist Pope. Arch Soc Esp Oftalmol. 2016 Oct; 91(10):e85-6. IF: 0
2. **Pérez-Torregrosa VT, Olate-Pérez Á, Cerdà-Ibáñez M, Gargallo-Benedicto A, Osorio-Alayo V, Barreiro-Rego A, Duch-Samper A**. Combined phacoemulsification and XEN45 surgery from a temporal approach and 2 incisions. Arch Soc Esp Oftalmol. 2016 Sep; 91(9):415-21. IF: 0
3. **Gargallo-Benedicto A, Hernández Pérez D, Olate-Pérez Á, Betancur-Delgado E, Cerdà-Ibáñez M, Duch-Samper A**. Large pterygium surgery: When coverage of the scleral bed justifies graft rotation. Arch Soc Esp Oftalmol. 2016 Oct; 91(10):469-74. IF: 0
4. **Gargallo-Benedicto A, Cerdà-Ibáñez M, Olate-Pérez Á, Clemente-Tomás R, Almor Palacios I, Hervás Hernandis JM, Duch-Samper A**. Papillophlebitis versus paediatric venous thrombosis. A case with 46C/T polymorphism in the F12 coagulation gene. Arch Soc Esp Oftalmol. 2016 Oct 20 ;. IF: 0
5. **Cerdà-Ibáñez M, Bayo-Calduch P, Manfreda-Domínguez L, Duch-Samper A**. Acute vision loss as the only sign of leukemia relapse. Retin Cases Brief Rep. 2016 Aug 23 ;. IF: 0
6. **Cerdà-Ibáñez M, Gargallo-Benedicto A, Almor Palacios I, Ruiz Del Río N, Hervás Herrandis JM, Duch-Samper A**. Combined hamartoma of the retina and retinal pigment epithelium. Arch Soc Esp Oftalmol. 2016 Dec 19 ;. IF: 0

Letter

7. **Arciniegas-Perasso CA, Díaz-Cespedes RA, Manfreda-Domínguez L, Toro-Giraldo D**. Preganglionic or postganglionic efferent pupillary defect? Clinical versus neuroimaging diagnosis. Neurologia. 2016 Jan-Feb; 31(1):66-68. IF: 1,381

Department of Pediatrics

• PUBLICATIONS

Number of articles	IF	Average IF
7	25,53	3,64
National collaborations	International collaborations	Corresponding author
2	3	3

Original articles

1. Rauch D, Wetzke M, Reu S, Wesselak W, Schams A, Hengst M, Kammer B, Ley-Zaporozhan J, Kappler M, Proesmans M, Lange J, Escribano A, Kerem E, Ahrens F, Brasch F, Schwerk N, Griese M, **PTI (Persistent Tachypnea of Infancy) Study Group of the Kids Lung Register**. Persistent Tachypnea of Infancy. Usual and Aberrant. Am J Respir Crit Care Med. 2016 Feb 15; 193(4):438-47. IF: 12,996
2. Griese M, Lorenz E, Hengst M, Schams A, Wesselak T, Rauch D, Wittmann T, Kirchberger V, **Escribano A**, Schaible T, Baden W, Schulze J, Krude H, Aslanidis C, Schwerk N, Kappler M, Hartl D, Lohse P, Zarbock R. Surfactant proteins in pediatric interstitial lung disease. Pediatr Res. 2016 Jan; 79(1-1):34-41. IF: 2,314
3. de Dios Caballero J, Del Campo R, Royuela A, Solé A, Máiz L, Oliveira C, Quintana-Gallego E, de Gracia J, Cobo M, de la Pedrosa EG, Oliver A, Cantón R, **GEIFQ (Grupo Español para el Estudio de la Colonización/Infección Broncopulmonar en Fibrosis Quística)**. Bronchopulmonary infection-colonization patterns in Spanish cystic fibrosis patients: Results from a national multicenter study. J Cyst Fibros. 2016 May; 15(3):357-65. IF: 3,475
4. **Fernández-Delgado R**. [Paediatric oncology: Past, present and future]. An Pediatr (Barc). 2016 Aug; 85(2):59-60. IF: 0,773
5. **Martínez-Rodríguez L, Estañ J, Bermudez JD, Molina A, Hortelano V**, Martínez-Costa C. Influence of nutritional variables on the onset of necrotizing enterocolitis in preterm infants: A case-control study. Early Hum Dev. 2016 Oct 7; 103:193-198. IF: 1,913

Letters

6. Lara Gallego B, **Castillo Carullón S**, Martínez Martínez MT, García Reymundo M, Miravittles M. [Profiles of cases included in the Spanish registry of patients with alpha-1



antitrypsin deficiency]. *An Pediatr (Barc)*. 2016 Apr; 84(4):233-4. IF: 0,833

7. **Espadas D, Castillo S, Moreno M, Escribano A.** Lack of effect of azithromycin on QT interval in children: a cohort study. *Arch Dis Child*. 2016 Aug 11 ;. IF: 3,231

Department of Psychiatry

• PUBLICATIONS

Number of articles	IF	Average IF
1	5,491	5,491

National collaborations	International collaborations	Corresponding author
-	1	-

Original articles

1. Ochoa S, López-Carrilero R, Barrigón ML, Pousa E, Barajas A, **Lorente-Rovira E**, González-Higueras F, Grasa E, Ruiz-Delgado I, Cid J, Birulés I, Esteban-Pinos I, Casañas R, **Luengo A**, Torres-Hernández P, Corripio I, Montes-Gámez M, Beltran M, De Apraiz A, Domínguez-Sánchez L, Sánchez E, Llacer B, Pélaez T, Bogas JL, Moritz S, Spanish Metacognition Study Group. Randomized control trial to assess the efficacy of metacognitive training compared with a psycho-educational group in people with a recent-onset psychosis. *Psychol Med*. 2017 Feb 7:1-12. IF: 5,491

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI14/00044

Title: *Eficacia del entrenamiento metacognitivo individualizado (EMC+) en personas con psicosis de reciente evolución*

Principal Investigator: Susana Ochoa (Ester Lorente and Ana Luengo as collaborating researcher)

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación para la investigación y docencia Sant Joan de Deu*

Duration: 2015-2018

Total budget: 92.565€

Department of Radiologic Diagnosis

Main lines of research

- To participate in clinical trials with Hematology and Oncology Departments by performing CT and / or biopsies to check inclusion of patients in new chemotherapy treatments.
- To evaluate cerebral reperfusion syndrome after treatment of carotid stenosis by stent.
- To study gastric pre-oesophagectomy conditioning to reduce the incidence of dehiscence of sutured anastomoses.

• PUBLICATIONS

Number of articles	IF	Average IF
3	5,40	1,80

National collaborations	International collaborations	Corresponding author
1	-	2

Original articles

1. Ferro O, Soria J, Garcés M, **Guijarro J**, Gámez JM, Sabater L. [Pseudoaneurysm of the superior mesenteric artery after pancreatoduodenectomy]. *Gastroenterol Hepatol*. 2016 Jun-Jul; 39(6):400-2. IF: 0,838
2. Sánchez-Oro R, **Sanchís-García JM**, Saravia M, Bértolo-Domínguez M. Intravascular papillary endothelial hyperplasia: Sonographic and magnetic resonance imaging appearance with histopathologic correlation. *Reumatol Clin*. 2016 May-Jun; 12(3):167-168. IF: 0
3. Santamaria X, Cabanillas S, Cervelló I, Arbona C, Raga F, Ferro J, **Palmero J**, Remohí J, Pellicer A, Simón C. Autologous cell therapy with CD133+ bone marrow-derived stem cells for refractory Asherman's syndrome and endometrial atrophy: a pilot cohort study. *Hum Reprod*. 2016 May; 31(5):1087-96. IF: 4,569



Department of Traumatology and Orthopedic Surgery

Strategic aims

- To study the determination of oxidative stress, getting results on the degree of oxidation and its correlation with the diagnosis / prognosis of the disease.
- To describe the specific oxidation mechanism of the pathology.

Main lines of research

- Cellular oxidative stress and its relation with idiopathic femoral osteonecrosis.
- Cellular regulatory mechanisms of the inflammatory response in chronic inflammatory diseases.
- Protection strategies against osteoarticular degradative processes.
- Robotics as a precision procedure in reconstructive orthopedic surgery.
- Role of microRNA as risk factors responsible for the pathogenesis of osteoarthritis and as a potential target for new biological therapies for osteoarthritis.
- Rehabilitation as an improvement process in results after total knee arthroplasty. Randomized prospective study.
- Local mechanical stimulation of mesenchymal cells towards their chondrogenic and osteogenic differentiation in regenerative medicine.

• PUBLICATIONS

Number of articles	IF	Average IF
4	15,98	3,99
National collaborations	International collaborations	Corresponding author
4	-	2

Original articles

1. Panach L, Pineda B, **Mifsut D**, Tarín JJ, Cano A, García-Pérez MÁ. The role of CD40 and CD40L in bone mineral density and in osteoporosis risk: A genetic and functional study. *Bone*. 2016 Feb; 83:94-103. IF: 3,973
2. Platas J, Guillén MI, Pérez Del Caz MD, **Gomar F**, Castejón MA, Mirabet V, Alcaraz MJ. Paracrine effects of human adipose-derived mesenchymal stem cells in inflammatory stress-induced senescence features of osteoarthritic chondrocytes. *Aging (Albany NY)*. 2016 Aug; 8(8):1703-17. IF: 3,979
3. Platas J, Guillén MI, **Gomar F**, Castejón MA, Esbrit P, Alcaraz MJ. Anti-senescence and Anti-inflammatory Effects of the C-terminal Moiety of PTHrP Peptides in OA Osteoblasts. *J Gerontol A Biol Sci Med Sci*. 2016 Jun 6 ;. IF: 5,476
4. **Pino-Almero L**, **Mínguez-Rey MF**, Sentamans-Segarra S, Salvador-Palmer MR, Anda RM, La O JL. Quantification of topographic changes in the surface of back of young patients monitored for idiopathic scoliosis: correlation with radiographic variables. *J Biomed Opt*. 2016 Nov 1; 21(11):116001. IF: 2,556

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: SAF2013-48724R

Title: *Mecanismos celulares reguladores de la respuesta inflamatoria en patologías inflamatorias crónicas*

Principal Investigator: M^a José Alcaraz Tormo (Francisco Gomar as collaborating researcher)

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2014-2016

Total Budget: 163.350€

Reference: MAT2013-46467-C4-4-R

Title: *Estimulación mecánica local de células mesenquimales de cara a su diferenciación osteogénica y condrogénica en medicina regenerativa*

Principal Investigator: María Fe Mínguez Rey (Carmen Carda Batalla and María Sancho Tello as collaborating researcher)

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2014-2016

Total Budget: 73.469€

Reference: 10-TERMOPIE-CIBRIAN-BLASCO-2016-A

Title: *TERMOPIE. Diagnóstico y seguimiento del pie diabético mediante termografía infrarroja.*

Principal Investigator: Carmen Blasco Molla

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Universidad de Valencia*



Duration: 2016 - 2017

Total Budget: 4.000€

Reference: 21-SECOMDEP-BENÍTEZ-SILVESTRE-2016-A

Title: *SECOMDEP. Secuencialidad de la contracción muscular: importancia en la detección precoz de disfunciones lumbopélvicas, cervicales y de la cintura escapular.*

Principal Investigator: Antonio Silvestre Muñoz

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2016 - 2017

Total Budget: 4.000€

• THESIS

Thesis title: *Estrés oxidativo y su valor pronóstico en osteonecrosis idiopática de cabeza femoral*

Doctoral candidate: María Carmen Blasco Mollá

Director(s): Francisco Gomar Sancho; Antonio Silvestre Muñoz; Francisco Dasí Fernández

Date of the defense: 3/02/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Efectos de la hormona paratiroidea PTH (1-84) en la consolidación de las fracturas*

Doctoral candidate: José Enrique Arova Navarro

Director(s): Francisco Gomar Sancho, José Luis Peris Serra

Date of the defense: 12/01/2016

Grade: *Sobresaliente "cum laude"*

Thesis title: *Manejo de la osteoporosis en un servicio de rehabilitación: impacto de la puesta en marcha de un protocolo*

Doctoral candidate: Carmen Candel Romero

Director(s): Francisco Gomar Sancho, Inmaculada Pereiró Berenguer, Ángeles Forner Cordero

Date of the defense: 03/02/2016

Grade: *Sobresaliente "cum laude"*

Quality Central Unit

• PUBLICATIONS

Number of articles	IF	Average IF
4	19,68	4,92

National collaborations	International collaborations	Corresponding author
1	3	1

Original articles

1. Woitha K, Carrasco JM, Clark D, Lynch T, Garralda E, **Martin-Moreno JM**, Centeno C. Policy on palliative care in the WHO European region: an overview of progress since the Council of Europe's (2003) recommendation 24. *Eur J Public Health*. 2016 Apr; 26(2):230-5. IF: 2,591
2. Woitha K, Garralda E, **Martin-Moreno JM**, Clark D, Centeno C. Ranking of Palliative Care Development in the Countries of the European Union. *J Pain Symptom Manage*. 2016 Sep; 52(3):370-7. IF: 2,649
3. Lana A, Struijk E, Guallar-Castillón P, **Martín-Moreno JM**, Rodríguez Artalejo F, Lopez-Garcia E. Leptin concentration and risk of impaired physical function in older adults: the Seniors-ENRICA cohort. *Age Ageing*. 2016 Nov; 45(6):819-826. IF: 4,201
4. **Martin-Moreno JM**, Harris M, Jakubowski E, Kluge H. Defining and Assessing Public Health Functions: A Global Analysis. *Annu Rev Public Health*. 2016; 37:335-55. IF: 10,24

Department of Medical Emergency

• PUBLICATIONS

Number of articles	IF	Average IF
2	4,42	2,21

National collaborations	International collaborations	Corresponding author
1	3	1



Original articles

1. **Brasó Aznar JV, Greco C.** [Acute angioedema in Emergency Department]. *Med Clin (Barc)*. 2016 Sep 16; 147(6):267-73. IF: 1,267
2. Sanchis J, García-Blas S, Carratalá A, Valero E, Mollar A, Miñana G, Ruiz V, **Balaguer JV**, Roqué M, Bosch X, Núñez J. Clinical Evaluation Versus Undetectable High-Sensitivity Troponin for Assessment of Patients With Acute Chest Pain. *Am J Cardiol*. 2016 Dec 1; 118(11):1631-1635. IF: 3,154

Department of Urology

Strategic aims

- To consolidate the line of research related to metabolomics in prostate cancer.
- Open a new research line in relation to metabolomics in bladder cancer.
- Open a new research line in relation to oxidative stress and prostate cancer.

Main lines of research

- Usefulness of microRNAs in blood and urine in the diagnosis and prognosis of bladder cancer.
- Testosterone deficiency syndrome in the aging male and its relation to erectile dysfunction.
- Metabolic analysis of urine in patients with prostate cancer.

• PUBLICATIONS

Number of articles	IF	Average IF
8	6,01	0,75
National collaborations	International collaborations	Corresponding author
4	-	7

Original articles

1. **Panach-Navarrete J, García-Morata F, Valls-González L, Martínez-Jabaloyas JM.** Use of individual containers for

prostate biopsy samples: Do we gain diagnostic performance? *Actas Urol Esp*. 2016 May; 40(4):224-228. IF: 1,022

2. **Panach-Navarrete J, Morales-Giraldo A, March-Villalba JA, Sales-Maicas MA, Martínez-Jabaloyas JM.** [Paratesticular sarcoma: An infrequent genitourinary tumor]. *Arch Esp Urol*. 2016 Jun; 69(5):234-8. IF: 0,307
3. **Martínez-Jabaloyas JM, Castelló-Porcar A, González-Baena AC, Cózar-Olmo JM, Miñana-López B, Gómez-Veiga F, Rodríguez-Antolín A, Grupo Español de Cáncer de Próstata.** Influence of demographic and tumour variables on prostate cancer treatment with curative intent in Spain. Results of the 2010 national prostate cancer registry. *Actas Urol Esp*. 2016 Oct; 40(8):485-91. IF: 0,964
4. **Panach-Navarrete J, Gironés-Montagud A, Sánchez-Cano E, Doménech-Pérez C, Martínez-Jabaloyas JM.** [Use of prostatic specific antigen in primary care (PSA)]. *Semergen*. 2016 Jun 22 ;. IF: 0
5. **Panach-Navarrete J, Morales-Giraldo A, Ferrandis-Cortés C, García-Morata F, Pastor-Lence JC, Martínez-Jabaloyas JM.** Satisfaction and treatment adherence in erectile dysfunction in the medium and long term. *Actas Urol Esp*. 2016 Nov 16 ;. IF: 0,964
6. Castelló-Porcar AM, **Martínez-Jabaloyas JM.** Testosterone/estradiol ratio, is it useful in the diagnosis of erectile dysfunction and low sexual desire? *Aging Male*. 2016 Dec; 19(4):254-258. IF: 1,493
7. Palmero-Martí JL, **Panach-Navarrete J, Valls-González L, Ganau-Ituren A, Miralles-Aguado J, Benedicto-Redón A.** Comparative study between thulium laser (Tm: YAG) 150W and greenlight laser (LBO:ND-YAG) 120W for the treatment of benign prostatic hyperplasia: Short-term efficacy and security. *Actas Urol Esp*. 2016 Nov 25 ;. IF: 0,964

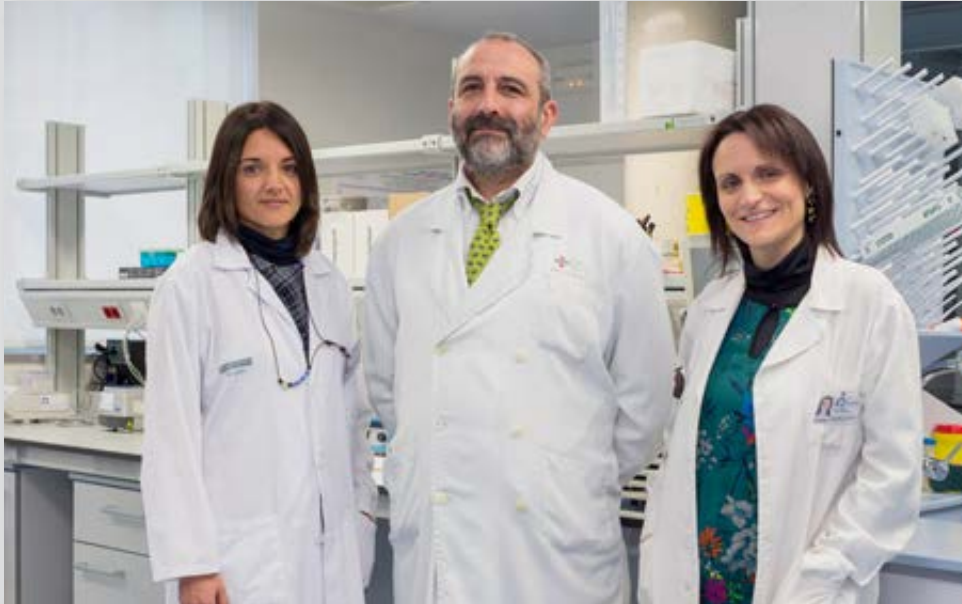
Letter

8. **Panach-Navarrete J, Palmero Martí JL, Ganau Ituren A, Pastor Lence JC, Benedicto Redón A.** [Renal hemorrhage after ESWL: From small hematoma to renal blowout]. *Arch Esp Urol*. 2016 Apr; 69(3):143-6. IF: 0,307



4.5 Other scientific contributions from scientific platforms

4.5.1 Biobank



biobanco@incliva.es



Team

Principal Investigator

Dr. Antonio Ferrández Izquierdo
Hospital. University

Collaborating researchers:

Dr. Lorena Peiró Chova. INCLIVA

Technicians

Olga Bahamonde Ponce. INCLIVA
Marta Belda Moscardó. INCLIVA



ACTIVITIES DEVELOPED

Incorporation of samples in pre-existing collections:

Oncological Node:

- Collection of solid tumors (Tumor Bank): around 142 new cases.
- Collection of peripheral blood and derivative products in patients suffering from breast cancer (CM-S [Blood-Breast Cancer]): around 940 new sample donations.
- Collections of peripheral blood and derivative products in patients suffering from lung cancer (CP-S [Blood-Lung Cancer]): around 198 new sample donations.
- Collection of peripheral blood and derivative products in patients suffering from melanoma (MM-S [Blood-Melanoma]): around 28 new cases.
- Collection of peripheral blood and derivative products in patients suffering from gastrointestinal (GAS-S [Blood-Gastrointestinal]): around 323 new sample donations.

Immunological Diseases Node:

- Collection of peripheral blood and derivative products in patients suffering from Systemic Lupus Erythematosus (LES-S

[Blood-Systemic Lupus Erythematosus]) or other autoimmune diseases: around 19 new cases.

Cardiovascular Node:

- Collections from the cardiovascular node: around 7 new cases.

Other collections:

- Collection of sepsis gravis and septic shock (SGSS): around 80 new sample donations.
- Collection of peripheral blood and derivative products in patients suffering from Multiple Esclerosis: around 27 new cases.
- Collection of peripheral blood and derivative products in standard population: around 49 new cases.

In summary, 1813 new sample donations have been received and 5458 samples have been processed in 2016 at INCLIVA Biobank facilities.

In addition, the Biobank has surplus diagnostic samples from the Hospital Pathology and Hematology Departments that may be used in research provided they have the corresponding Biobank Informed Consent.

Transfer of samples

Project	Ref./Agency	Principal Researcher/ Institution	Samples
<i>Estudio de la desregulación de microRNAs diana en suero de pacientes con cáncer de mama y cáncer gástrico.</i>		Dra. Maider Ibarrola, INCLIVA	Breast cancer and Gastrointestinal tumors: serum
<i>Enfermedad mínima residual en cánceres colorrectales de alto riesgo resecaados. Valor de las biopsias líquidas en el seguimiento y análisis de la heterogeneidad tumoral.</i>	PI15/02180, ISCIII, Ministerio de Economía y Competitividad	Dr. Andrés Cervantes, HCUV/INCLIVA	Gastrointestinal tumors: plasma and tissue
<i>Biomarcadores de respuesta a los inhibidores de tirosina quinasa mediante fenotipado metabólico de biopsias líquidas de pacientes con adenocarcinoma pulmonar con mutaciones de EGFR.</i>	2015/0345	Dr. Oscar Juan Vidal, IISLaFe	Lung cancer and standard population: serum



<i>Caracterización de la trombocitemia esencial JAK2V617F y MPL negativa mediante secuenciación de exoma.</i>	P113/00393, ISCIII, Ministerio de Economía y Competitividad	Dra. Beatriz Bellosillo, Hospital del Mar	Haemathological samples: DNA
<i>Desarrollo de kits de hematología con marcado CE.</i>	IMEGEN S. L.	Dr. Carlos Ruiz Lafora, IMEGEN S. L.	Haemathological samples: DNA and RNA
<i>Avanzar en el diagnóstico, la prognosis y la terapia de enfermedades neurodegenerativas raras.</i>	P115/00187, ISCIII, Ministerio de Economía y Competitividad	Dra. Carmen Espinós, CIPF	Standard population: plasma
<i>Búsqueda de marcadores discriminatorios del deterioro cognitivo leve.</i>	13/703, Corporación Tecnológica de Andalucía	Dr. Javier Santos Burgos Muñoz, Neuron Bio S. A	Standard population: serum
<i>Optimización de muestras de tejido para el desarrollo y la validación de biomarcadores de enfermedad: proyecto OPTIMARK.</i>	P116/01500, ISCIII, Ministerio de Economía y Competitividad	Dra. Lorena Peiró, INCLIVA	Solid tumors: OCT and FFPE
<i>MicroARNs como biomarcadores de invasión en cáncer de mama. Aplicación y nuevo uso de los excedentes de la determinación de ganglio centinela.</i>	GV/2016/029, Generalitat Valenciana. Conselleria d'Educació, Investigació, Cultura i Esport	Dra. Lorena Peiró, INCLIVA	Breast cancer: plasma and tissue
<i>Relación entre los biomarcadores de fibrosis cardíaca y la función de los grandes vasos en una población hipertensa con miocardiopatía hipertensiva.</i>	Fondos privados (ERESA) y CDTI	Dr. Fernando Martínez, HCUV/INCLIVA	Cardiovascular node: plasma and serum
<i>Desarrollo de un test epigenético predictivo en pacientes con cáncer de mama precoz en el contexto neoadyuvante.</i>	FAB-118, Ferrer Internacional S. A.	Dr. Manel Esteller, IDIBELL (Ferrer Internacional S. A.)	Solid tumors: FFPE

In summary, 769 aliquots have been provided in 2016 to respond to these sample requests.

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PT13/0010/0004

Title: Biobank network

Principal Investigator: Dr. Josep Redón i Mas

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2014-2017

Total Budget: 44.478€

Reference: GV/2016/029

Title: *MicroARNs como biomarcadores de invasión en cáncer de mama. Aplicación y nuevo uso de los excedentes de la determinación de ganglio centinela.*

Principal Investigator: Dra. Lorena Peiró Chova

Funding Body: Generalitat Valenciana, Conselleria d'Educació, Investigació, Cultura i Esport.

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2017

Total Budget: 16.000€



• PUBLICATIONS

Note that this are 2016 scientific articles derived from the use of samples or services provided by the biobank.

Original articles

1. Matamala N. et al. MicroRNA deregulation in triple negative breast cancer reveals a role of miR-498 in regulating BRCA1 expression. *Oncotarget* 2016, Apr 12;7(15):20068-79.
2. Gimenez JLG. et al. Epigenetics as the driving force in long-term immunosuppression. *J Clin Epigenet.* 2016, 2:2.
3. Rojo F. et al. Non-canonical NF-κB pathway activation predicts outcome in borderline estrogen receptor positive breast carcinoma. *Br J Cancer.* 2016 Jul 12.
4. Moran S. et al. Epigenetic profiling to classify cancer of unknown primary: a multicentre, retrospective analysis. *Lancet Oncol.* 2016 Oct;17(10):1386-1395

4.5.2 Oncology Phase I Clinical Trials Unit

INCLIVA is the only hospital in Valencia performing Phase I cancer clinical trials, and one of the few in Spain. Phase I trials are those in which a substance or product is tested in humans for the first time.

INCLIVA is conducting, through the Oncology and Hematology Department, 189 clinical trials, 99 of them related to treatment in the early stages of testing (33 phase I or “first in human” and 66 phase II). INCLIVA’s new facilities provide a full floor and a half specifically dedicated to host the unit.

The unit aims to develop and select new drugs through clinical trials and performing studies related to the pathogenesis, prognosis and new experimental therapies in solid tumors.

FUNCTIONS:

The unit implements early clinical trials and to perform studies with experimental agents in the field of Oncology.

EQUIPMENTS:

- -80° C Freezer
- -20° C Freezer
- Refrigerated desktop centrifuge
- Scientific refrigerator
- Conventional fridge
- Defibrillator
- Electrocardiographic equipment
- 7 monitors (blood pressure, heart rate and O² saturation)
- 7 double medication infusion pumps
- 7 heads gases (oxygen and vacuum)

LOCATION:

The following facilities are located on the second floor:

- Reception and waiting room
- 2 Consulting rooms
- Staff room
- Meeting room
- Therapy room

The third floor hosts the following facilities

- Clinical trials office
- Monitoring room
- Clinical trials archives

PERSON IN CHARGE:

Head of Unit: Prof. Andres Cervantes Ruipérez

E-mail: Andres. Cervantes@uv. Es

Contact phone: +34 961973528

HUMAN RESOURCES

Medical doctors

Dr. Alejandro Pérez Fidalgo

Dr. Susana Roselló Keränen

Dr. Cristina Herrando Meliá

Dr. Marisol Huerta Lázaro

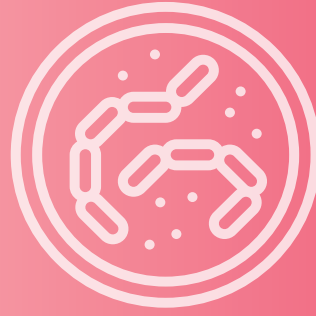
Dr. Gema Bruixola Campos

Nurses

Inmaculada Blasco Blasco

Celia Martínez Ridaura





5

Clinical trials
and other
studies





5.1. Activity of the Ethical Committee in Clinical Research (ECCR)

On January 13th 2016, the new Royal Decree 1090/2015, which regulates clinical trials with drugs, the Committees of Ethics of Research with medicines and the Spanish Registry of Clinical Studies was published. This new regulatory framework has introduced important changes in the management and evaluation of clinical trials in humans at the national level. Since its publication, only one Committee of the national territory evaluates the Clinical Trial and issues a single and binding judgement for the entire country.

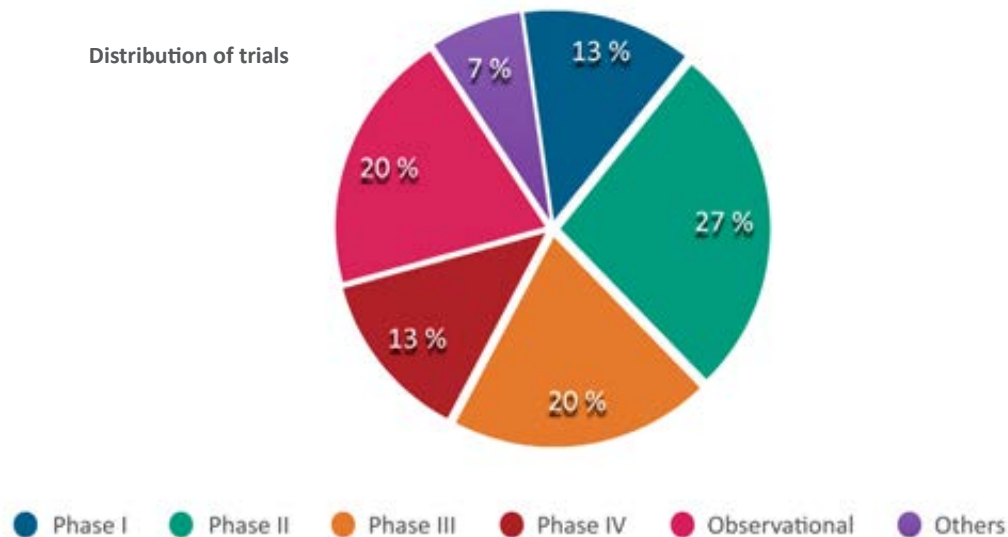
In this context, the Clinical Research Ethics Committee of the *Hospital Clínico Universitario de Valencia* obtained the recertifi-

cation of the ISO 9001 standard. This recognition guarantees the quality of the assessment performed by the ECCR, whose main goal is to ensure respect for the rights and safety of participants in clinical studies and other research initiatives.

As a result of its activity along 2016, the ECCR has processed a total of 15 studies (clinical trials and observational studies): 13 positively valued, 1 denied and 1 is pending of approval.

The distribution of these trials by phase is: Phase I: 2; Phase II: 4; Phase III: 3; Phase IV: 2; Observational studies: 3; others: 1. The following table shows the number of clinical trials and other studies according to their typology.

Distribution of trials



Distribution of the clinical studies depending on the department where they are performed is the following:

Department	Number
Anesthesia and Reanimation	2
Cardiology	1
Haematology	3
Psychiatry	1
Oncology	3
Otorhinolaryngology	1
Dermatology	1
Pneumology	1
Traumatology	1
Tutelage of other centers	1
Total	15



5.2. Clinical research activity performed by the *Valencia Clínico-Malvarrosa* Health Department

5.2.1. Activity during 2016

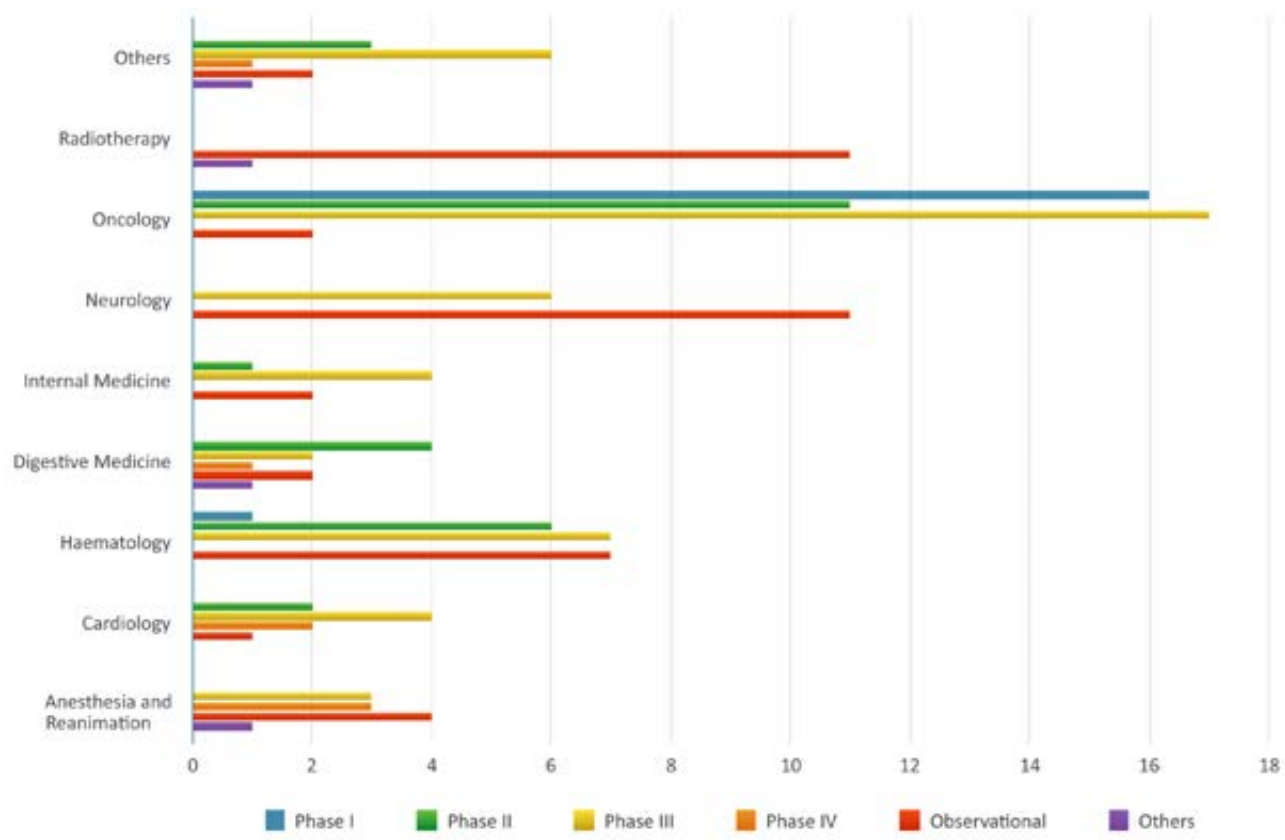
INCLIVA Health Research Institute manages clinical research (trials, observational studies, and research projects) carried out by the *Hospital Clínico Universitario* and the *Valencia Clínico-Malvarrosa* Health Department researchers.

As a result of its activity along 2016, INCLIVA has processed a total of 146 studies (clinical trials and observational studies).

The distribution of these trials by phase is: Phase I: 17; Phase II: 27; Phase III: 49; Phase IV: 7; Observational studies: 42; others: 4. The following table shows the number of clinical trials and other studies according to their phase and department.

Department	Phase I	Phase II	Phase III	Phase IV	Others	Observational	TOTAL
Anesthesia and Reanimation			3	3	1	2	9
Cardiology		2	4	2		4	12
Haematology	1	6	7			1	15
Digestive Medicine		4	2	1	1	7	15
Internal Medicine		1	4			2	7
Neurology			6			2	8
Oncology	16	11	17			11	55
Radiotherapy					1	2	3
Others		3	6	1	1	11	22
TOTAL	17	27	49	7	4	42	146





The Department of Medical Oncology leads the number of trials processed by INCLIVA. It is followed by the departments of Haematology, Digestive Medicine and Cardiology. These four departments make over 79% of the total processed trials.

Department	Number	%
Anesthesia and Reanimation	9	6
Cardiology	12	8
Haematology	15	10
Digestive Medicine	15	10
Internal Medicine	7	5
Neurology	8	5
Oncology	55	38
Radiotherapy	3	2
Others	22	15



In turn, Principal Investigator (PI) distribution shown below indicates the Departments of Medical Oncology, Haematology and Digestive Medicine count on 5 PI who are involved in clinical research. They are followed by the Departments of Cardiology and Anesthesia and Reanimation.

Department	Number of PI's	%
Medical Oncology	5	10
Haematology	5	10
Digestive Medicine	5	10
Anesthesia and Reanimation	4	8
Cardiology	4	8
Neurology	3	6
Endocrinology	2	4
Neumology	2	4
Pediatrics	2	4
Psychiatry	2	4
Traumatology	2	4
Primary Health Care	2	4
Others	11	22
Total	49	100

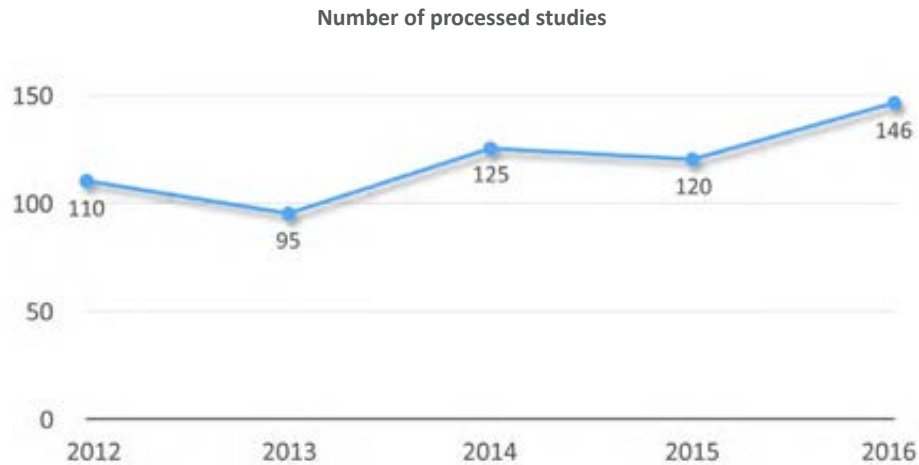
Regarding the distribution of studies per sponsor, 34 trials are considered Independent Clinical Research (trials from associations, groups, foundations, and private individuals), and the rest of them have been sponsored by the pharmaceutical industry.

Sponsor	Nº
INDEPENDENT CLINICAL RESEARCH	34
JANSSEN-CILAG	8
GILEAD SCIENCES	7
NOVARTIS FARMACÉUTICA S. A.	6
BOEHRINGER INGELHEIM ESPAÑA S. A.	5
MERCK	5
PFIZER	5
ROCHE FARMA S. A.	4
TAKEDA FARMACÉUTICA	4
ABBVIE SPAIN, S. L. U.	3
ELI LILLY AND COMPANY LIMITED UK	3
F. HOFFMANN-LA ROCHE LTD	3
MILLENNIUM	3
ABBOTT LABORATORIES, S. A.	2
AMGEN INC	2
B. BRAUN MEDICAL S. A.	2
CELGENE INTERNATIONAL SARL	2
CONATUS PHARMACEUTICALS INC	2
GENENTECH INC	2
MEDIMMUNE LLC,	2
SANOFI-AVENTIS	2
SHIRE VIROPHARMA, INCORPORATED	2
OTHER INDUSTRIAL PROMOTORS	38



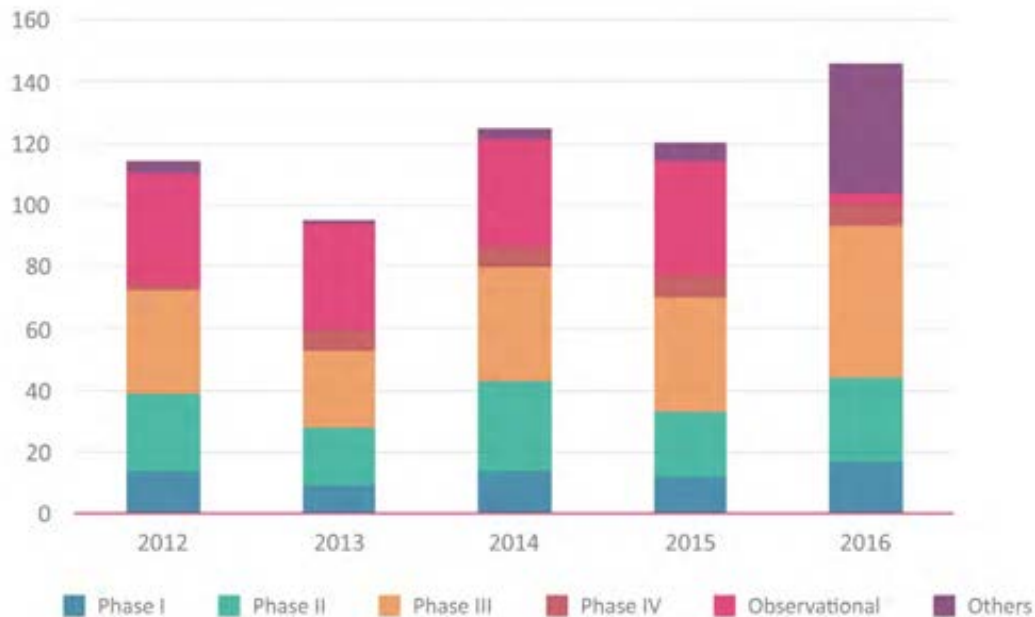
5.2.2 Assessment activity during last 5 years

The table below confirms the importance of the Committee's activity during the last five years. The number of studies processed yearly remains close over a hundred.



One of INCLIVA's main goals is to develop clinical research at its early stages, thus contributing to translational research that moves scientific knowledge from bench to bedside. With this regard, during the period 2012-2016, Phase I and Phase II trials are prioritized and its number remains stable as shown in the graph below.

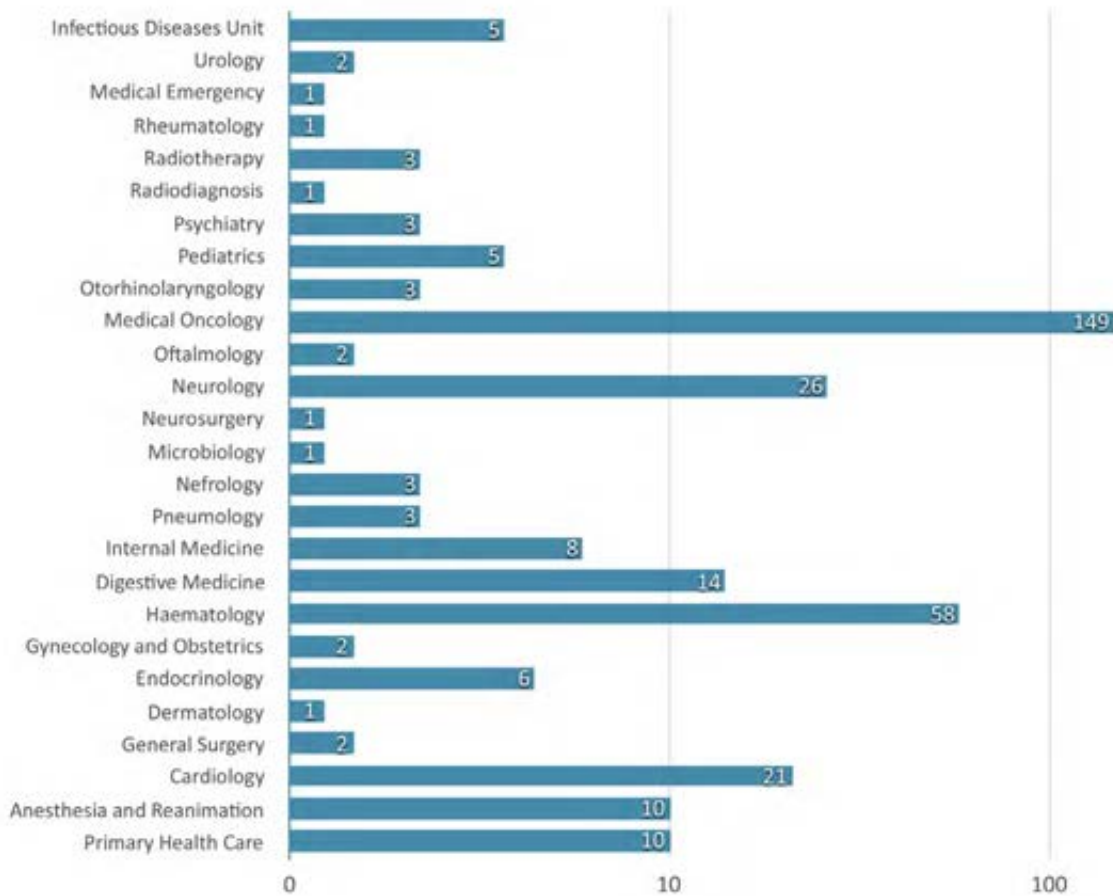
Evolution of clinical trial distribution by phase



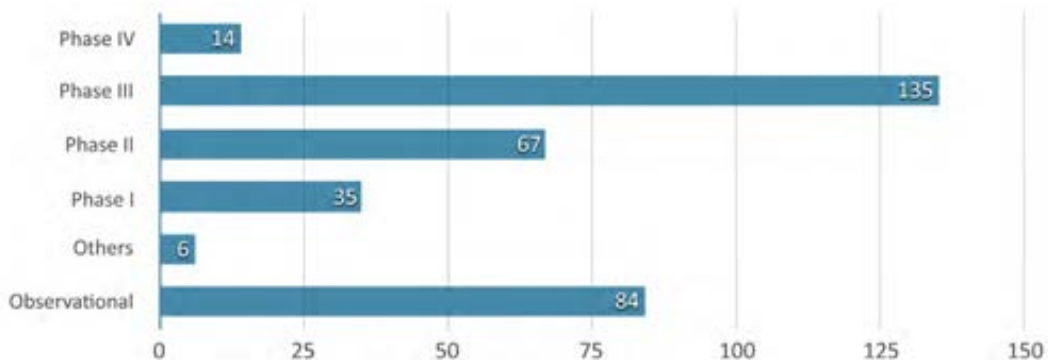


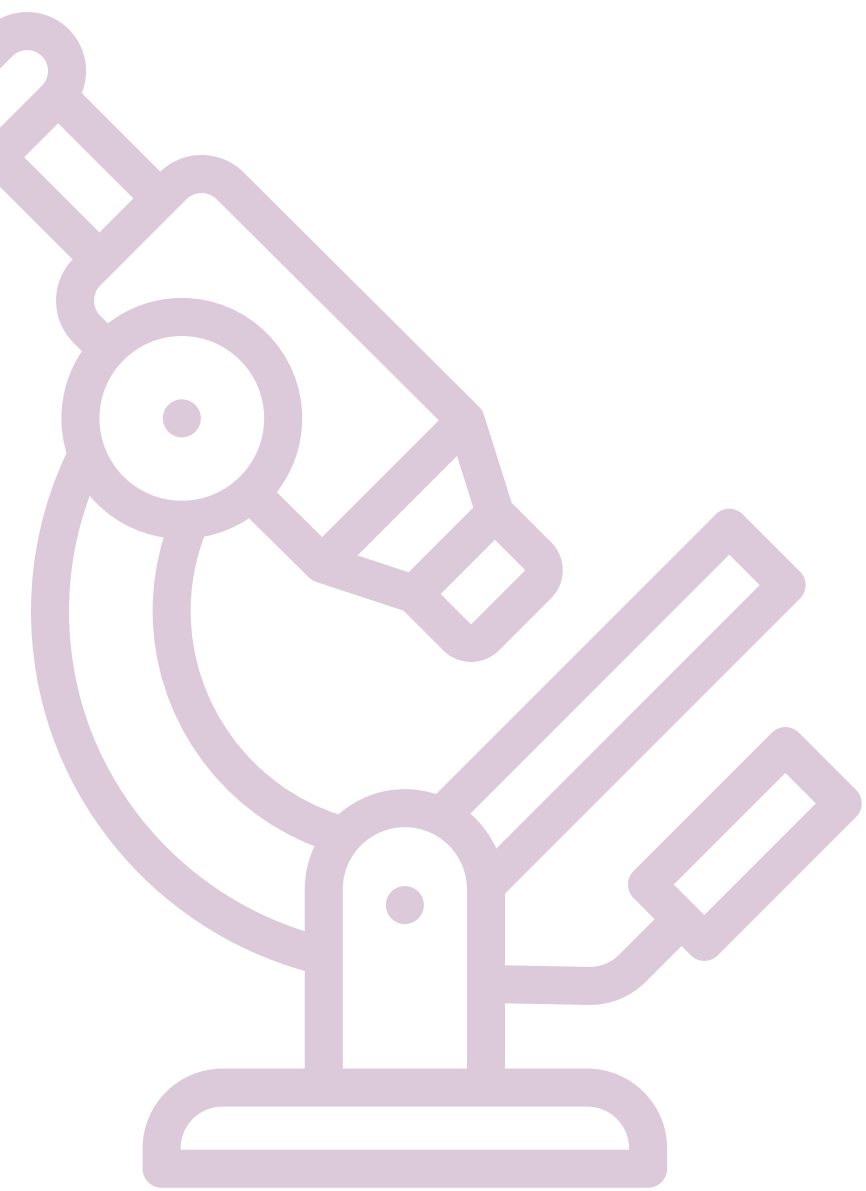
5.2.3. Ongoing studies in the Valencia Clínico-Malvarrosa Health Department

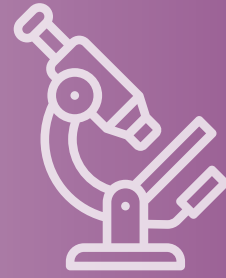
During 2016, 396 studies have been active. The distribution of clinical trials per department analysed below uses a semilogarithmic scale due to the great difference between the Departments of Medical Oncology and Haematology and the rest of the Departments.



The distribution of ongoing trials and other studies according to their typology is the following:







6

Initiatives for research promotion





6.1. VLC - Bioclinic research grants

The main aim of VLC-Bioclinic program is to promote the cooperation in research, technological development and innovation in health, in order to generate synergies and partnerships among researchers and professionals and strengthen translational research with innovative results that benefit patients.

Being aware that the processes of innovation and knowledge transfer require multidisciplinary collaboration among professionals from various fields, both the University of Valencia, is interested in establishing concrete partnerships with hospital foundations which are related to the area of specialization in health and INCLIVA, whose general objective is to promote, encourage, favour and implement the scientific and technical research, launched together in 2015 the VLC-Bioclinic Program.

After the excellent reception of this initiative, these are the projects funded in 2016.

VLC- BIOCLINIC Subprogram A

Title: *Diseño y prueba de concepto de una cinta rodante con tecnología inmersiva para valorar y reeducar la marcha en pacientes con secuelas de ictus.*

Principal Investigator: Alejandro Ponz de Tienda, M^a Arántzazu Ruescas Nicolau

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 4.000€

Title: *Análisis proteómico de biopsias líquidas para personalizar las terapias dirigidas contra el adenocarcinoma pulmonar.*

Principal Investigator: Amelia Insa Mollá, Julián Carretero Asunción

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 4.000€

Title: *Estudio de la viabilidad de técnicas de aprendizaje automático para discernir la presencia de endometriosis sin*

necesidad de cirugía (ENDOMETriosis assessed by Machine Learning).

Principal Investigator: Raúl Gómez Gallego, José David Martín Guerrero

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 4.000€

Title: *Secuencialidad de la contracción muscular: importancia en la detección precoz de disfunciones lumbopélvicas, cervicales y de la cintura escapular.*

Principal Investigator: Antonio Silvestre Muñoz, Josep Carles Benítez Martínez

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 4.000€

Title: *Diagnóstico y seguimiento del pie diabético mediante termografía infrarroja.*

Principal Investigator: Carmen Blasco Molla, Rosa María Cibrián Ortiz de Anda

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 4.000€

Title: *Estudio de la respuesta inmune circulante frente a antígenos de diferenciación melanocitaria y su correlación con el estadio clínico en pacientes con melanoma cutáneo.*

Principal Investigator: José María Martín Hernández, Carlos Monteagudo Castro

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 4.000€



Title: *Efectos cognitivos de la cirugía cardiovascular mediante circulación extracorpórea (CEC).*

Principal Investigator: José Ángel Bahamonde Romano, Raúl Espert Tortajada

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 4.000€

Title: *Implicación de la familia de proteínas MBNL en cáncer de mama HER2+ y su posible relación con la respuesta/resistencia al tratamiento con trastuzumab.*

Principal Investigator: Pilar Eroles Asensio, Rubén Artero Allepuz

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 4.000€

Title: *Análisis de datos avanzado como ayuda a la decisión en clínica.*

Principal Investigator: María Téllez Plaza, Joan Vila Francés

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 4.000€

VLC- BIOCLINIC Subprogram B

Title: *Análisis de los perfiles de expresión de miRNAs utilizando mapas auto-organizados para el pronóstico de pacientes con déficit de alfa-1 tripsina.*

Principal Investigator: Francisco Dasí, Marcelino Martínez

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 9.000€

Title: *Desarrollo de una herramienta para el diagnóstico temprano, monitorización y seguimiento por imagen cerebral, del deterioro cognitivo leve (encefalopatía hepática mínima) en pacientes cirróticos.*

Principal Investigator: Carmina Montoliu, Jesús Malo

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 9.000€

Title: *Validación del estudio traslacional de un ensayo plasmónico de espermina en orina como biomarcador de cáncer colorrectal.*

Principal Investigator: Guillermo Sáez, Julia Pérez

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 9.000€

Title: *Nueva diana farmacológica en la prevención del riesgo cardiometabólico.*

Principal Investigator: José Tomás Real, Pilar D'Ocón

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 6.000€

Title: *Heterogeneidad clonal en cáncer: Biopsia líquida como tecnología de alto rendimiento.*

Principal Investigator: Andrés Cervantes, Rosa Noguera

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2016

Total Budget: 6.000€



6.2 Grants for intramural projects by emerging researchers

As in previous years, with the aim of improving the quality of their projects and promoting publishing in high impact journals, INCLIVA launched an intramural call for research projects available exclusively to their emerging researchers.

During 2016 the 14 projects granted in 2014 were extended.

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Reconstrucción del endometrio humano a través de xenotrasplante de células madre (LGR5+) en el modelo de ratón NOD-SCID*

Principal Investigator: Irene Cervelló Alcaraz

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: 2.000€

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Expresión, localización y estudio funcional de la proteína PGRMC1 (Progesterone Receptor Membrane Component 1) en el endometrio*

Principal Investigator: Francisco Domínguez

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €3.500

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Identificación de miRNAs secretados al líquido endometrial en pacientes con obesidad y diabetes tipo 2.*

Principal Investigator: Felipe Vilella Mitjana

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €3.500

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Arquitectura genómica del cáncer de mama triple negativo. Análisis mediante genética de sistemas del riesgo a la progresión tumoral y respuesta terapéutica*

Principal Investigator: Joan Bataller Climent

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €4.917

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Papel del complejo RUNX1/CBF-beta/p300/HIPK2 en la progresión leucémica de las neoplasias*

Principal Investigator: Juan Carlos Hernández Boluda

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €6.146

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Study of new molecular and inflammatory mechanisms involved in abdominal aortic aneurysm*

Principal Investigator: Laura Piqueras Ruiz

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €4.917

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Análisis de parámetros de estrés oxidativo, función mitocondrial, longitud de telómeros y perfil de miRNAs circulantes en pacientes con déficit de alfa-1-antitripsina*

Principal Investigator: Francisco Dasí Fernández

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*



Duration: 2014 - 2016

Total budget: €4.917

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Papel de la calcineurina y de su regulador RCAN en la respuesta cerebral al estrés oxidativo y la apoptosis: estudio en ratones RCAM-/-*

Principal Investigator: Ana Lloret

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €3.500

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Efecto de la administración de genisteína y/o bexaroteno para el tratamiento de la enfermedad de Alzheimer en el modelo de ratón transgénico APP/PS1*

Principal Investigator: Consuelo Borrás Blasco

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €3.500

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Identificación de Histonas circulantes en plasmas de pacientes con sepsis y sepsis grave*

Principal Investigator: José Luis García Giménez

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €3.688

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Mecanismos de resistencia al tratamiento en cáncer de mama triple negativo*

Principal Investigator: Pilar Eroles

Funding Body: *Fundación Investigación Hospital Clínico*

Universitario de Valencia

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €3.500

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Evaluación del papel terapéutico de la inhibición del PAI-1 sobre la endometriosis humana en un modelo murino heterólogo*

Principal Investigator: Raúl Gómez

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €3.500

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *ADN circulante y daño orgánico en individuos con Diabetes Mellitus tipo 2*

Principal Investigator: Ana Bárbara García

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €3.500

Reference: *Convocatoria 2014 de ayudas intramurales para grupos emergentes*

Title: *Ejercicio físico controlado como intervención en el tratamiento de la fragilidad en el anciano y en la prevención de la dependencia. Bases moleculares*

Principal Investigator: M^a Carmen Gómez

Funding Body: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2014 - 2016

Total budget: €3.500



6.3 Grants for secondments in centers of excellence

To allow researchers to acquire new knowledge for clinical and research techniques, INCLIVA promotes every year its Grants for research secondments in centers of excellence.

Since the establishment of this scholarship program, over 100 professionals have visited national and foreign centers. In 2016 the average number of awards was 18, 14 of them to international centers and 4 to national ones.

The awarded researchers and the assigned training centers in 2016 are shown in the following table:

Beatriz Alarcón Torres	Hospital Royal Marsden
Sara Cholvi Camarasa	Chu Estaing - Chu Clermont-Ferrand
María del Pilar Cordero Romero	Hôpital Saint Louis de Paris
Carolina Domingo Boluda	Universitair Medisch Centrum Groningen
Beatriz García Parreño	Hospital de la Sta Creu i Sant Pau
M ^a Beatriz Llamusí Troisi	Instituto de Genética y Biología Molecular y Celular (IGBMC)
Alba Mangas Losada	Vu University Medical Center
Alejandro Pérez Pitarch	Netherlands Cancer Institute
Javier Pérez Hernández	Paris-Cardiovascular Research Center (Parcc)
Ignacio Pla Gil	Hospital General Universitario Gregorio Marañón
Anna Ramos Pachón	Mount Sinai Hospital

Ana Reula Martin	University of Southampton
Lucía Rodríguez Fernández	Manchester Cancer Research Centre
Marta Seco Cervera	Children's Hospital, Harvard University
Cristina Tormo Martín	Hospital Universitario Virgen de las Nieves
Xavier Vidal Gómez	Institut de Biologie Santé (Inserm)
Regis Villegas	University Institute of Mental Health
Víctor Zúñiga Zaragoza	Hospital de Tortosa Verge de la Cinta

6.4 Training and Teaching Activities

INCLIVA and its researchers play an important role in the training of researchers and of health sciences degree and master students, which come from of Valencian universities and other national and international regions.

The number of internal secondments in 2016 was 6 which represent an aggregate of 19 months of training during the period. A total of 15 stays outside of INCLIVA were carried out.

The Institute has kept on developing, along the year, its annual training program. The courses, seminars and educational conferences that have been developed during the year 2016 are the following:

Courses (14)

- *Curso de Buenas Prácticas Clínicas para investigadores 2016*
- *1 Curso sobre elaboración de proyectos de investigación en Enfermería*



- *Curso de Bioestadística III: Análisis estadístico de Ensayos Clínicos (2016)*
- *Curso de Bioestadística II: Comparación de grupos (2016)*
- *Curso de Bioestadística I: Análisis exploratorio de datos (2016).*
- *Curso “Comunicación de los resultados de investigación”*
- *Curso “Estructurar y elaborar un proyecto de investigación clínica”*
- *II Workshop Internacional de Ecografía y Resonancia Anorrectal*
- *Curso de anatomía quirúrgica aplicada hepato-bilio-pancreática. 5ª Edición*
- *Curso “H2020: de la idea al proyecto”*
- *Curso de patología infecciosa 2016*
- *Curso “Introducción a la Implantación de Dispositivos de Resincronización”*
- *I Curso de formación continuada en enfermedades hepáticas para médicos de atención primaria del Departamento de Salud Clínico - Malvarrosa*
- *Programa de “Sesiones de actualización, formación e investigación clínica en reumatología”*

INCLIVA Seminars (5)

- *Seminario INCLIVA - M. Pegtel*
- *Seminario INCLIVA - Antoni Bayes-Genis*
- *Seminario INCLIVA - Fernando Suárez Sipmann*
- *Seminario INCLIVA - Anthony Newman*
- *Seminario INCLIVA - Pedro Baptista*

Workshops (15)

- *1ª jornada científica de residentes del Hospital Clínico Universitario De Valencia*
- *I Jornada de investigación en prediabetes, diabetes y enfermedad cardiovascular*
- *I Jornada de genética clínica y enfermedades raras para Atención Primaria*
- *VIII Jornadas de insulización en Atención Primaria*
- *Jornada sobre Enfermedad de Fabry*
- *Jornada “La metabolómica por RMN en el entorno clínico. Aplicaciones en la investigación biomédica y el diagnóstico clínico”*
- *Jornada sobre el control de la vía aérea: I+D+D*
- *Jornada sobre investigación en Dolor: I+D+D*

- *Instituto de Enfermedades Minoritarias*
- *I Jornada INCLIVA - HCUV sobre insuficiencia cardíaca*
- *I Jornada de atención integral al paciente crónico complejo*
- *II Jornada de atención integral al paciente crónico complejo*
- *8ª Jornada Valenciana “Tabaquismo y Respiración” - Tabaquismo y EPOC*
- *Jornada de cooperación INCLIVA - REDIT*
- *La Red Precipita en INCLIVA*

Conferences (15)

- *Tiziano Balzano, Papel de la neuroinflamación en la encefalopatía hepática. implicaciones terapéuticas.*
- *Dr. Felip Vilella, “The dialogue between the maternal endometrium and the embryo. Potential impact on the onset of adult diseases”*
- *Dra. Rosa Oltra, Comisión de Infecciones.*
- *Dra. Blanca Navarro, Anticoagulación. Indicaciones y opciones terapéuticas disponibles.*
- *Sesión HematoIncliva: “Situación actual del tratamiento de las hepatitis víricas”*
- *I Congreso Internacional de Enfermedades Raras Respiratorias*
- *I Congreso de Investigación Traslacional de Enfermedades Raras de la Comunidad Valenciana*
- *I Foro sobre investigación básico-clínica en Diabetes*
- *X SIMPOSIO 2016: Avances y resultados en investigación en cánceres de mama y colon*
- *Aspectos prácticos en el manejo del paciente con déficit de hierro en IC*
- *Charla Investigadora Invitada: Mousumi Mutsuddi*
- *Foro: La innovación sanitaria, una fuente de recursos*
- *Seminario Isaac García Murillas*
- *Laparoscopic Collorrectal Minifellowship*
- *III Workshop Cirugía laparoscópica colorrectal avanzada*

Other activities in which INCLIVA participates (3)

- *Debate interactivo ginecología obstetricia 2016 DIGO*
- *I Congress on Coordination and Management of EU-funded Health Research Projects*
- *Curso de bienvenida de residentes 2016*



Doctoral Thesis

Within INCLIVA research groups, a total of 91 doctoral thesis have been defended during the course of 2016:

Thesis title: *Bypass distal de miembros inferiores: análisis de resultados en un servicio de cirugía cardiovascular de la Comunidad Valenciana.*

Doctoral candidate: Iván Martín González

Director(s): Luis Sabater Ortí

Date of the defense: 13/01/2016

Group: Research Group on General and Digestive Surgery

Thesis title: *Caracterización de la actividad biológica y farmacológica del alcaloide boldina en la distrofia miotónica de tipo 1.*

Doctoral candidate: M^a Carmen Álvarez Abril

Director(s): Rubén Artero Allepuz, Arturo López Castel, Manuel Pérez Alonso

Date of the defense: 15/01/2016

Group: Research Group on Translational Genomics

Thesis title: *Expresión de aquaporinas 1 y 5 en el pulmón de ratas sometidas a ventilación mecánica: efectos del volumen corriente y el tiempo de ventilación.*

Doctoral candidate: Gustavo Fabregat Cid

Director(s): Antonio M Alberola Aguilar, José García de la Asunción, Benjamín Sarriá

Date of the defense: 08/02/2016

Group: Research Group on Anesthesiology and Reanimation

Thesis title: *Preacondicionamiento remoto por isquemia-reperusión en la lobectomía pulmonar. Un estudio sobre la prevención del estrés oxidativo.*

Doctoral candidate: Laura Bruno Carlos

Director(s): José García de la Asunción, Genaro Galán Gil

Date of the defense: 05/02/2016

Group: Research Group on Anesthesiology and Reanimation, Research Group on Histopathology and Tissue Engineering

Thesis title: *Descripción de una metodología docente para el aprendizaje de la fibroscopia flexible en el control de la vía aérea.*

Doctoral candidate: Pedro Charco Mora

Director(s): Francisco Javier Belda Náchter, Marina Soro

Date of the defense: 27/01/2016

Group: Research Group on Anesthesiology and Reanimation

Thesis title: *Efecto de la duloxetina sobre la expresión de fos en el tronco del encéfalo y en la médula espinal de la rata en modelos de dolor persistente.*

Doctoral candidate: Carlos Tornero Tornero

Director(s): Francisco Javier Belda Náchter, Alfonso A. Valverde Navarro, Francisco Martínez Soriano

Date of the defense: 21/01/2016

Group: Research Group on Anesthesiology and Reanimation

Thesis title: *Fenotipo celular de las neuronas sensitivas afectadas en la ataxia de Friedreich.*

Doctoral candidate: Belén Mollá Moliner

Director(s): Pilar González Cabo; Francesc Palau, José Enrique O' Connor Blasco

Date of the defense: 11/01/2016

Group: Research Group on Cellular and Organic Physiopathology of Oxidative Stress

Thesis title: *Estudio de la población anciana ambulatoria con cáncer de pulmón no microcítico: análisis clínico y factores pronósticos inflamatorios.*

Doctoral candidate: María Martín Ureste

Director(s): Federico Vicente Pallardó Calatayud, Inmaculada Maeztu Maiques, Vicente Giner Bosch

Date of the defense: 08/02/2016

Group: Research Group on Cellular and Organic Physiopathology of Oxidative Stress

Thesis title: *Estudio de la utilidad clínica del perfil de estrés oxidativo en pacientes con déficit de alfa-1 antitripsina.*

Doctoral candidate: Silvia Castillo Corullón

Director(s): Francisco Dasí Fernández, Amparo Escribano Montaner

Date of the defense: 06/10/2016

Group: Research Group on Cellular and Organic Physiopathology of Oxidative Stress

Thesis title: *Estrés oxidativo y su valor pronóstico en osteonecrosis idiopática de cabeza femoral.*

Doctoral candidate: María Carmen Blasco Mollá

Director(s): Francisco Dasí Fernández

Date of the defense: 03/02/2016



Group: Research Group on Cellular and Organic Physiopathology of Oxidative Stress

Thesis title: *Conocimiento del déficit de alfa1-antitripsina y de la discinesia ciliar primaria por estudiantes de medicina y profesionales sanitarios.*

Doctoral candidate: M^a Ángeles Requena Fernández

Director(s): Francisco Dasí Fernández, Amparo Escribano Montaner

Date of the defense: 29/01/2016

Group: Research Group on Cellular and Organic Physiopathology of Oxidative Stress

Thesis title: *Papel de los receptores angiogénicos del VEGF en la apoptosis y migración celular de la leucemia linfática crónica-b. Correlación con los receptores de quimiocinas CXCR4, CCR7 Y CD49d y las características clínicas de los pacientes.*

Doctoral candidate: Sandra Ballester García

Director(s): M^a José Terol Casterá, Pilar Eroles, Antonio Ferrández

Date of the defense: 03/02/2016

Group: Research Group on Lymphoproliferative Disorders

Thesis title: *Influencia de los polimorfismos genéticos en la leucemia mieloide crónica.*

Doctoral candidate: Paula Amat Martínez

Director(s): Carlos Solano, Juan Carlos Hernández, Vicente Martín Guillem

Date of the defense: 26/01/2016

Group: Research Group on Myeloid Neoplasms, Research Group on Hematopoietic Transplantation

Thesis title: *Fracaso renal agudo en el trasplante de progenitores hematopoyéticos: análisis de la incidencia, factores de riesgo e implicaciones pronósticas, valor pronóstico y en el diagnóstico precoz de la cistacina C plasmática.*

Doctoral candidate: Miguel Angel Solís Salguero

Director(s): Carlos Solano, Juan Carlos Hernández Boluda, Isidro Torregrosa

Date of the defense: 08/02/2016

Group: Research Group on Myeloid Neoplasms, Research Group on Hematopoietic Transplantation, Department of Nephrology

Thesis title: *Infección por el citomegalovirus (CMV) en el paciente trasplantado de progenitores hematopoyéticos: investigación de nuevos factores biológicos para la estimación del riesgo y análisis integral de los mecanismos inmunitarios que previenen y controlan.*

Doctoral candidate: Estela Berenice Giménez Quiles

Director(s): David Navarro

Date of the defense: 09/03/2016

Group: Research Group on Hematopoietic Transplantation

Thesis title: *Factores predictores de respuesta a los tratamientos de inmunotolerancia en pacientes hemofílicos a con inhibidores.*

Doctoral candidate: Saturnino Haya Guaita

Director(s): Carlos Solano

Date of the defense: 09/02/2016

Group: Research Group on Hematopoietic Transplantation

Thesis title: *Estudio metabolómico en pacientes diagnosticados de sepsis grave y shock séptico en la unidad de cuidados intensivos.*

Doctoral candidate: Mónica García Simón

Director(s): José Blanquer Olivas

Date of the defense: 09/02/2016

Group: Department of Intensive Medicine

Thesis title: *Función plaquetaria y síndrome coronario agudo: Valor predictivo de los test de agregabilidad.*

Doctoral candidate: Mónica García Simón

Director(s): José Blanquer Olivas

Date of the defense: 09/02/2016

Group: Department of Intensive Medicine

Thesis title: *Disfunción endotelial en territorio arterial en pacientes jóvenes con enfermedad tromboembólica venosa.*

Doctoral candidate: Elena Furió Rodríguez

Director(s): M^a José García Fuster González-Alegre, Laura Piqueras Ruiz, Fernando Martínez

Date of the defense: 09/02/2016

Group: Research Group on the Study of Cardiometabolic and Renal Risk, Research Group on Inflammation

Thesis title: *Estudio de acetilación de proteínas en líneas celulares humanas de cáncer colorrectal KRAS mutado o salvaje.*

Doctoral candidate: Desamparados Roda Pérez

Director(s): Andrés Cervantes, Rosa Zaragoza Colom, Elena



Ruiz García-Trevijano

Date of the defense: 08/02/2016

Group: Research Group on Colorectal Cancer and New Therapeutical Developments in Solid Tumors

Thesis title: *Análisis de polimorfismos en genes que codifican para enzimas que regulan el estrés oxidativo y su relación con la respuesta al tratamiento y la supervivencia en pacientes con cáncer de pulmón.*

Doctoral candidate: Amelia Insa Mollá

Director(s): Ana Lluch Hernández, José Franco Serrano

Date of the defense: 08/02/2016

Group: Research Group on Colorectal Cancer and New Therapeutical Developments in Solid Tumors

Thesis title: *Factores pronósticos en el cáncer de recto localmente avanzado tratado con quimioradioterapia neoadyuvante seguida de cirugía. Valor pronóstico del neoadjuvant rectal score y del nomograma de Valentini.*

Doctoral candidate: Susana Roselló Keranen

Director(s): Andrés Cervantes Ruipérez, Eduardo García-Granero Ximénez, Matteo Frasson

Date of the defense: 05/09/2016

Group: Research Group on Colorectal Cancer and New Therapeutical Developments in Solid Tumors

Thesis title: *Evaluación del perfil genómico de la plataforma de investigación basada en PAM50 y miRNAs en el cáncer de mama de mujeres muy jóvenes (≤ 35 años): Correlación con parámetros clínicos.*

Doctoral candidate: María Teresa Martínez Martínez

Director(s): Gloria Ribas Despuig, Ana Lluch Hernández

Date of the defense: 02/02/2016

Group: Research Group on Colorectal Cancer and New Therapeutical Developments in Solid Tumors, Research Group on Breast Cancer Biology

Thesis title: *Estudio de la prevalencia de mutaciones en línea germinal (síndrome de birt-hogg-dubé) y somáticas del gen *flcn* en pacientes con fibrofolliculomas o tricodiscosomas cutáneos y/o neumotórax recidivantes y/o bilaterales.*

Doctoral candidate: Verónica López Castillo

Director(s): Carlos Monteagudo Castro, Esperanza Jordá Cuevas

Date of the defense: 08/02/2016

Group: Research Group on Skin Cancer

Thesis title: *Estudio de la implicación de los receptores de quimiocinas CXCR3-A y CXCR7 y sus ligandos en la progresión del melanoma cutáneo humano.*

Doctoral candidate: Ana Pellín Carcelén

Director(s): Carlos Monteagudo Castro, Rosario Gil Benso, David Ramos Soler

Date of the defense: 28/01/2016

Group: Research Group on Skin Cancer, Research Group on Central Nervous System Tumors

Thesis title: *Estudio de la expresión de marcadores de transición epitelio-mesenquimal y de célula madre cancerosa en el melanoma cutáneo, y su asociación con la progresión tumoral.*

Doctoral candidate: Liria Terrádez Más

Director(s): Carlos Monteagudo Castro, Rosario Gil Benso

Date of the defense: 20/01/2016

Group: Research Group on Skin Cancer, Research Group on Central Nervous System Tumors

Thesis title: *Estado mutacional del oncogen N-RAS en melanoma cutáneo como factor pronóstico. Estudio clínico-patológico.*

Doctoral candidate: Paola Fernanda Lara Valencia

Director(s): Carlos Monteagudo Castro

Date of the defense: 10/02/2016

Group: Research Group on Skin Cancer

Thesis title: *Recaída locorregional en mujeres con cáncer de mama portadoras de mutación BRCA tratadas mediante cirugía conservadora.*

Doctoral candidate: María José Juan Fita

Director(s): Ana Lluch Hernández, José Antonio López Guerrero, Amparo Ruiz Simón

Date of the defense: 08/02/2016

Group: Research Group on Breast Cancer Biology

Thesis title: *Utilidad de los informes estructurados basados en una plataforma web para el diagnóstico por imagen en patología mamaria.*

Doctoral candidate: Rosana Medina García

Director(s): Ana Lluch Hernández, José Damián Segrelles Quilis, Luis Martí Bonmati

Date of the defense: 26/01/2016

Group: Research Group on Breast Cancer Biology



Thesis title: *Estudio de la densidad mamográfica como modificador de riesgo de cáncer de mama en mujeres con mutación BRCA1/2.*

Doctoral candidate: Luisa Fernanda Tamayo Orjuela

Director(s): Ana Lluch Hernández

Date of the defense: 05/02/2016

Group: Research Group on Breast Cancer Biology

Thesis title: *Estudi clínic, neuropsicològic i de r. M. de l'esclerosi múltiple primària progressiva.*

Doctoral candidate: Nuria Martín Ibáñez

Director(s): Francisco Coret Ferrer, Bonaventura Casanova Estruch

Date of the defense: 05/02/2016

Group: Department of Neurology

Thesis title: *Estudio de la afectación medular en la esclerosis múltiple. Establecimiento de patrones de lesión en neuroimagen y su relación con la discapacidad.*

Doctoral candidate: Aránzazu Navarré Gimeno

Director(s): Francisco Coret Ferrer, Bonaventura Casanova Estruch

Date of the defense: 02/02/2016

Group: Department of Neurology

Thesis title: *Interés por la medicina de familia tras cursar una asignatura de atención primaria.*

Doctoral candidate: María Candelaria Ayuso Raya

Director(s): Francisco Javier Chorro Gascó, Francisco Jesús Escobar Rabadan

Date of the defense: 05/02/2016

Group: Research Group on Cardiac Experimental Electrophysiology

Thesis title: *Ensayo aleatorizado controlado sobre la terapia guiada por el antígeno carbohidrato 125 en pacientes dados de alta por insuficiencia cardíaca aguda: efecto sobre la mortalidad o reingreso por insuficiencia cardíaca aguda a 1 año.*

Doctoral candidate: Pau Llàcer Iborra

Director(s): Luis Such Belenguer, Julio Núñez

Date of the defense: 05/02/2016

Group: Research Group on Cardiac Experimental Electrophysiology

Thesis title: *Estudio comparativo de los efectos electrofisiológicos miocárdicos intrínsecos de la apertura*

del canal KATP y del ejercicio físico crónico, en situación de normoxia y tras isquemia regional aguda. Estudio experimental.

Doctoral candidate: Catia Alves da Silva

Director(s): Luis Such Belenguer

Date of the defense: 21/01/2016

Group: Research Group on Cardiac Experimental Electrophysiology

Thesis title: *Valoración del estado nutricional en los diferentes estadios de la enfermedad renal crónica y su relación con el estrés oxidativo y la inflamación.*

Doctoral candidate: Catia Alves da Silva

Director(s): Guillermo Sáez Tormo, Juan Alfonso Miguel Carrasco, María Jesús Puchades Montesa

Date of the defense: 05/02/2016

Group: Research Group on Oxidative Pathology

Thesis title: *Importancia del fallo orgánico de inicio en la evolución de la pancreatitis aguda.*

Doctoral candidate: Francisco Javier Lizarraga Purroy

Director(s): Miguel Mínguez Pérez

Date of the defense: 05/02/2016

Group: Research Group on Digestive Motility

Thesis title: *Efecto de una intervención de educación para la salud sobre los hábitos y la calidad de vida tras la realización de colonoscopia en una población con riesgo medio de padecer cáncer colorrectal.*

Doctoral candidate: Olga Forero Rincón

Director(s): Rafael Ortí Lucas

Date of the defense: 07/03/2016

Group: Research Group on Digestive Motility

Thesis title: *Relevancia clínica de la sensibilización a polen de morera y estudio de su reactividad cruzada con otros polenes.*

Doctoral candidate: Francisco David El-Qutob López

Director(s): Amparo Mir Gisbert

Date of the defense: 27/01/2016

Group: Research Group on Digestive Motility

Thesis title: *Relación entre disfunción eréctil e isquemia miocárdica silente en varones con diabetes mellitus tipo 2.*

Doctoral candidate: Katerinne Eloise García Malpartida

Director(s): Antonio Hernández Mijares, Víctor Manuel Víctor González

Date of the defense: 26/01/2016



Group: Translational Research Group on Nutrition and Metabolism

Thesis title: *Estudio de prevalencia de desnutrición en atención primaria del departamento Valencia Dr Peset.*

Doctoral candidate: Juana Cantero Llorca

Director(s): Antonio Hernández Mijares, José Luis Alfonso Sánchez

Date of the defense: 10/02/2016

Group: Translational Research Group on Nutrition and Metabolism

Thesis title: *Polimorfismos implicados en la hiperlipemia familiar combinada.*

Doctoral candidate: Antonio López Ruiz

Director(s): Antonio Hernández Mijares, Marta Casado Pinna, María Teresa Martínez Triguero

Date of the defense: 04/02/2016

Group: Translational Research Group on Nutrition and Metabolism

Thesis title: *Estudio comparativo del efecto de diferentes fármacos antirretrovirales sobre la interacción leucocito-endotelio.*

Doctoral candidate: Samuel Orden Ruiz

Director(s): Juan Vicente Esplugues Mota, Ángeles Álvarez Ribelles

Date of the defense: 15/07/2016

Group: Translational Research Group on Nutrition and Metabolism

Thesis title: *Desarrollo de una estrategia diagnóstica por resonancia magnética multimodal para tumores cerebrales.*

Doctoral candidate: José Luis León Guijarro

Director(s): Daniel Monleón, Joaquín Gil Romero, Bernardo Celda Muñoz

Date of the defense: 20/01/2016

Group: Research Group on Molecular Imaging and Metabolomics

Thesis title: *Automedicación en pacientes en urgencias de un centro de atención primaria.*

Doctoral candidate: Marwan Muhana Al nono

Director(s): M^a José Forner Giner

Date of the defense: 13/01/2016

Group: Research Group on the Study of Cardiometabolic and Renal

Thesis title: *Impacto pronóstico de los síndromes geriátricos en el síndrome coronario agudo.*

Doctoral candidate: Clara Bonanad Lozano

Director(s): Juan Sanchis Forés, Vicente Ruiz Ros

Date of the defense: 01/02/2016

Group: Research Group on Clinical Cardiology

Thesis title: *Tasa acumulada de recién nacido vivo en donación de ovocitos.*

Doctoral candidate: Víctor Hugo Gómez Hernández

Director(s): José Remohí Giménez, Ana Cristina Cobo Cabal

Date of the defense: 06/05/2017

Group: Research Group on Male Infertility and Embryonic Stimulation

Thesis title: *Producción de blastocistos diploides, heteroparentales a partir de pre-embiones tripnucleares humanos procedentes de FIV e ICSI.*

Doctoral candidate: Noelia Grau Grau

Director(s): José Alejandro Remohí Jiménez, María José Escribá Pérez

Date of the defense: 29/01/2017

Group: Research Group on Male Infertility and Embryonic Stimulation

Thesis title: *Estudio de anomalías meióticas y aneuploidías en pacientes con azoospermia secretora.*

Doctoral candidate: Vanessa Peinado Cervera

Director(s): Carmen Rubio Lluosa, Manuel Gil Salom, José Remohí Giménez

Date of the defense: 21/01/2016

Group: Research Group on Male Infertility and Embryonic Stimulation

Thesis title: *Estudio cinematográfico de parámetros morfológicos del pre-embrión humano.*

Doctoral candidate: Raquel Herrer Saura

Director(s): Marcos Meseguer Escrivá, Juan Antonio García Velasco

Date of the defense: 02/02/2016

Group: Research Group on Male Infertility and Embryonic Stimulation

Thesis title: *Papel del grosor íntima-media en carótida y del TC de coronarias en la detección temprana de aterosclerosis en la mujer y posible modulación por polimorfismos relacionados con la acción estrogénica.*



Doctoral candidate: Antonio Jorge Cano Marquina
Director(s): Antonio Cano Sánchez, Alicia M. Maceira González, Juan Cosín Sales
Date of the defense: 07/10/2016
Group: Research Group on Women Health

Thesis title: *Efectos del ejercicio físico con banda elástica en mujeres mayores de 65 años durante 12 meses. Estudio comparativo sobre densidad ósea, componentes sanguíneos, estabilidad, antropometría y dolor.*

Doctoral candidate: M^a Cinta Gómez Tomás
Director(s): Antonio Cano Sánchez, Yasser Alakhdar Mohmara, José Luis Martínez Gil
Date of the defense: 17/06/2016
Group: Research Group on Women Health

Thesis title: *Papel de la vitamina D en la postmenopausia. Influencia de la suplementación en el metabolismo óseo y otras dianas.*

Doctoral candidate: Gemma Arribas Ferriol
Director(s): Antonio Cano Sánchez
Date of the defense: 01/02/2016
Group: Research Group on Women Health

Thesis title: *Efectos del ibandronato sobre el metabolismo óseo y el perfil de riesgo cardiovascular en mujeres con osteoporosis postmenopáusica tratadas previamente con raloxifeno.*

Doctoral candidate: Marta Ferrer Piquer
Director(s): Antonio Cano Sánchez
Date of the defense: 19/01/2016
Group: Research Group on Women Health

Thesis title: *Valoración de la afectación de la reserva ovárica tras criopreservación de tejido ovárico y tratamiento oncológico: papel destacado de la hormona antimülleriana.*

Doctoral candidate: Ester Ortiz Murillo
Director(s): Antonio Cano Sánchez
Date of the defense: 19/01/2016
Group: Research Group on Women Health

Thesis title: *Evaluación del papel terapéutico de la inhibición del PAI en el tratamiento de la endometriosis en un modelo animal murino homólogo.*

Doctoral candidate: Ana Moreno Collado
Director(s): Raúl Gómez Gallego

Date of the defense: 27/01/2016
Group: Research Group on Women Health

Thesis title: *Nuevas posibilidades terapéuticas en el fallo de implantación.*

Doctoral candidate: Sevkiye Tugce Pehlivan Budak
Director(s): Carlos Simón Vallés, Carmen Rubio Lluesa
Date of the defense: 26/01/2016
Group: Research Group on Stem Cells Applied to Reproduction, Embryo Viability and Endometrial Receptivity

Thesis title: *Identificación de variantes genéticas poco frecuentes y raras en diabetes mellitus tipo 2 mediante secuenciación de exoma.*

Doctoral candidate: Inmaculada Galán Chilel
Director(s): Felipe Javier Chaves Martínez
Date of the defense: 04/03/2015
Group: Research Group of the Genotyping and Genetic Diagnosis Unit (UGDG)

Thesis title: *Aislamiento y función de células progenitoras endoteliales de sangre periférica durante la evolución clínica de pacientes con infarto agudo de miocardio. Efecto de las micropartículas shh+ en la función celular.*

Doctoral candidate: Carlos Bueno Betí
Director(s): Carlos Hermenegildo Caudevilla, Susana Novella del Campo
Date of the defense: 04/03/2016
Group: Research Group on Endothelial Cells (LINCE)

Thesis title: *Intervención de ejercicio físico domiciliario en obesidad infantil. Ensayo controlado aleatorizado comparando modalidad tradicional versus plataforma web.*

Doctoral candidate: Alejandro Bruño Soler
Director(s): Empar Lurbe, Juan Francisco Lisón Parraga
Date of the defense: 20/07/2016
Group: Research Group on the Study of Cardiovascular Risk in Children and Adolescents

Thesis title: *Efecto de la terapia fotodinámica como coadyuvante al raspado y alisado radicular en el tratamiento de la periodontitis crónica. Estudio clínico, microbiológico (real time-PCR) y bioquímico (IL-1 β , il-6, TNF- α , RANK-L/OPG).*

Doctoral candidate: Marta Segarra Vidal
Director(s): José M^a Vila Salinas, Francisco Alpiste Illueca, Francisco José Gil Loscos



Date of the defense: 22/04/2016

Group: Research Group on Vascular Function

Thesis title: *Efecto del entrenamiento físico sobre los factores endoteliales en el sistema arterial de conejo.*

Doctoral candidate: Patricia Marchio

Director(s): José M^a Vila Salinas, M^a Dolores Mauricio Aviñó

Date of the defense: 19/02/2016

Group: Research Group on Vascular Function

Thesis title: *Conciliación y formación farmacoterapéutica al paciente trasplantado renal en el ámbito hospitalario.*

Doctoral candidate: Mónica Montero Hernández

Director(s): Gloria Segarra Irlés, Isabel Font Noguera, José Luis Poveda Andrés

Date of the defense: 19/02/2016

Group: Research Group on Vascular Function

Thesis title: *Influencia de un programa de intervención comunitaria sobre el estado de salud de una población semi-rural dominicana.*

Doctoral candidate: Beatriz Tomás Aguirre

Director(s): Cecilia Martínez Costa, Francisco Núñez Gómez

Date of the defense: 02/02/2016

Group: Research Group on Pediatric Nutrition

Thesis title: *Dolor abdominal crónico en la edad pediátrica: implicación de factores clínicos, ambientales y psicosociales. Desarrollo de un programa informático específico.*

Doctoral candidate: Tatiana Salvador Pinto

Director(s): Cecilia Martínez Costa, Caterina Calderón Garrido

Date of the defense: 15/01/2016

Group: Research Group on Pediatric Nutrition

Thesis title: *Estudio de los valores de referencia para los parámetros de estrés oxidativo: malondialdehído y glutatión medidos por cromatografía líquida de alta eficacia, en humanos y animales de experimentación.*

Doctoral candidate: Consuelo Escrivá López

Director(s): José Viña Ribes, M^a Carmen Gómez Cabrera, Consuelo Borrás Blasco

Date of the defense: 15/01/2016

Group: Research Group on Aging and Physical Activity

Thesis title: The role of APC/Cdh1 in Alzheimer's disease.

Doctoral candidate: Tanja Fuchsberger

Director(s): José Viña Ribes, Ana Lloret Alcañiz

Date of the defense: 30/11/2016

Group: Research Group on Aging and Physical Activity

Thesis title: *Evaluación de los efectos del tratamiento con tadalafilo sobre las funciones cerebrales, neurológicas y bioquímicas en pacientes con hiperplasia benigna de próstata y disfunción eréctil.*

Doctoral candidate: Felipe Ordoño Domínguez

Director(s): Carmina Montoliu, Felipe Ordoño, Cristina Doménech

Date of the defense: 26/01/2016

Group: Research Group on neurological impairment

Thesis title: *Alteraciones del ritmo del sueño en modelos animales de encefalopatía hepática.*

Doctoral candidate: Nicolás Peñaranda Sarmiento

Director(s): Carmina Montoliu, Vicente Felipo, M^a Ángeles Lloret

Date of the defense: 23/12/2016

Group: Research Group on Inflammation

Thesis title: Effect of RXR/PPAR interaction in Angiotensin II-induced vascular inflammation and angiogenesis. Role of CXCL16/CXCR6 axis in angiotensin II cigarette smoke-induced vascular inflammation.

Doctoral candidate: Paula Escudero Díaz

Director(s): M^a Jesús Sanz Ferrando, Laura Piqueras Ruiz

Date of the defense: 04/07/2016

Group: Research Group on Inflammation

Thesis title: *Síntesis de nuevas isoquinoleinas 1-sustituidas con actividad antibacteriana y antifúngica o dopaminérgica.*

Doctoral candidate: Abraham Galán Morant

Director(s): M^a Jesús Sanz Ferrando, Diego M. Cortes Martínez, Nuria Cabedo Escrig

Date of the defense: 19/02/2016

Group: Research Group on Inflammation

Thesis title: *Papel de la lipasa hepática y de los genes cdkn2a/2b en la aterosclerosis y la diabetes.*

Doctoral candidate: Irene Andrés Blasco

Director(s): Nuria Cabedo Escrig

Date of the defense: 11/03/2016

Group: Research Group on Inflammation



Thesis title: *Daño oxidativo en la leucemia linfática crónica y la linfocitosis b monoclonal. Asociación con alteraciones cromosómicas.*

Doctoral candidate: María Isabel Oliver Domínguez

Director(s): Guillermo Sáez Tormo, Félix Carbonell, Rosa María Collado Nieto

Date of the defense: 05/02/2016

Group: Research Group on Oxidative Pathology

Thesis title: *Opciones terapéuticas en la sinovitis en pacientes afectos de hemofilia: sinoviortesis.*

Doctoral candidate: María Magdalena Querol Giner

Director(s): Antonio Iradi Casal, Felipe Querol Fuentes, Sofía Pérez Alenda

Date of the defense: 30/09/2016

Group: Research Group on Oxidative Pathology

Thesis title: *Análisis perceptivo de los dispositivos auditivos osteointegrados percutáneos.*

Doctoral candidate: Ignacio Pla Gil

Director(s): Jaime Marco Algarra

Date of the defense: 13/05/2016

Group: Department of Otolaryngology

Thesis title: *Valor pronóstico del gen de fusión Tmprss2-ERG. Metilación de PITX2 y marcadores inmunohistoquímicos en el cáncer de próstata.*

Doctoral candidate: Cristina Ferrandis Cortés

Director(s): David Ramos Soler, José M. Martínez Jabaloyas

Date of the defense: 25/01/2016

Group: Department of Urology

Thesis title: *Caracterización genética mediante mpla (multiplex ligation-dependent probe amplification) e inmunohistoquímica del carcinoma renal de células claras y su correlación pronóstica.*

Doctoral candidate: Nelson Díez Calzadilla

Director(s): Rosa Noguera Salvá, José M Martínez Jabaloyas, Maria Pilar Soriano Sarrió

Date of the defense: 12/01/2016

Group: Department of Urology, Research Group on Pediatric Solid Tumors

Thesis title: Defective carbohydrate metabolism in Multiple Sclerosis.

Doctoral candidate: Deepali Mathur

Director(s): Gerardo López-Rodas, María Burgal, Buenaventura Casanova

Date of the defense: 28/01/2016

Group: Research Group on Epigenetics and Chromatin

Thesis title: *Una nueva técnica de remodelación de la punta nasal en rinoplastia, para casos extremadamente difíciles, mediante la resección total de los cartílagos alares.*

Doctoral candidate: Salvador Rodríguez-Camps Devís

Director(s): Alejandro Espí Macías

Date of the defense: 26/02/2016

Group: Research Group on Colorectal Cancer and New Therapeutical

Thesis title: *Efectos de la hormona paratiroidea PTH (1-84) en la consolidación de las fracturas.*

Doctoral candidate: José Enrique Arova Navarro

Director(s): Francisco Gomar Sancho, José Luis Peris Serra

Date of the defense: 12/01/2016

Group: Department of Traumatology and Orthopedic Surgery

Thesis title: *Manejo de la osteoporosis en un servicio de rehabilitación: impacto de la puesta en marcha de un protocolo.*

Doctoral candidate: Carmen Candel Romero

Director(s): Francisco Gomar Sancho, Inmaculada Pereiró Berenguer, Ángeles Forner Cordero

Date of the defense: 03/02/2016

Group: Department of Traumatology and Orthopedic Surgery

Thesis title: *Estudio "in vitro" de la resistencia a la fractura tras la fatiga de coronas cementadas sobre pilares de circona.*

Doctoral candidate: Ana Roig Vanaclocha

Director(s): Antonio Fons Font, M^a Fernanda Solá Ruiz, Rubén Agustín Panadero

Date of the defense: 04/02/2016

Grade: *Sobresaliente "cum laude"*

Group: Research Group on Histopathology and Tissue Engineering

Thesis title: *Eficacia y cambios anatómicos inducidos por los dispositivos de avance mandibular en pacientes con síndrome de apnea-hipopnea del sueño (SAHS).*

Doctoral candidate: Rocío Marco Pitarch

Director(s): Antonio Fons Font, Enrique Fernández Julián, Francisco Javier Puertas Cuesta



Date of the defense: 15/04/2016

Grade: *Sobresaliente "cum laude"*

Group: Research Group on Histopathology and Tissue Engineering

Thesis title: *Estudio 'in vitro' del láser de Nd:YAG sobre la superficie del esmalte: Efectos estructurales, cambios morfológicos y térmicos.*

Doctoral candidate: Vicente Manuel Torres Celda

Director(s): José Gandía Franco, Rosa Cibrián Ortiz de Anda, Vicente Torres Zaragoza

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*

Group: Research Group on Histopathology and Tissue Engineering

Thesis title: *Patrón de las alteraciones dentales asociadas a la impactación del canino maxilar por palatino.*

Doctoral candidate: Esther Olivera Aguilar

Director(s): José Gandía Franco, Rosa Cibrián Ortiz de Anda, Vanessa Paredes Gallardo

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*

Group: Research Group on Histopathology and Tissue Engineering

Thesis title: *La acústica virtual como herramienta arqueológica. Historia y sonido en el Teatro Principal de Valencia.*

Doctoral candidate: Arturo Barba Sevillano

Director(s): Rosa Cibrián Ortiz de Anda, Francesc de Paula Daumal Domènech, Alicia Giménez Pérez

Date of the defense: 01/02/2016

Grade: *Sobresaliente "cum laude"*

Group: Research Group on Histopathology and Tissue Engineering

Thesis title: *Predicción de la inclusión de caninos superiores en una población infantil.*

Doctoral candidate: Jordi Gascón Pellicer

Director(s): José Gandía Franco, Rosa Cibrián Ortiz de Anda, Vanessa Paredes Gallardo

Date of the defense: 05/02/2016

Grade: *Sobresaliente "cum laude"*

Group: Research Group on Histopathology and Tissue Engineering

Thesis title: *Factores de riesgo de la fibrilación auricular tras la cirugía torácica.*

Doctoral candidate: Amparo Oliva Gimeno

Director(s): Genaro Galán Gil, M^a Luisa Blasco Cortés

Date of the defense: 01/12/2016

Grade: *Sobresaliente "cum laude"*

Group: Department of Intensive Medicine





7

Highlights





INCLIVA joins EATRIS network.

INCLIVA will approach the research of acute myocardial infarction in an integrated way.

INCLIVA and Universidad de Valencia analyze the cardiac alterations of Myotonic dystrophy using the vinegar fly.

The First Project of INCLIVA in Precipita, funding record.

INCLIVA, LABORATORIOS RUBIÓ and BIOSFER TESLAB will collaborate to develop biomedical research based on a metabolomic approach.

JANUARY

The Coloproctology Unit of Hospital Clínico de Valencia trains specialists in sonography and resonance of anorectal pathologies.

INCLIVA leads a clinical trial to evaluate two surgical techniques used in pancreatic cancer.

INCLIVA will analyze the viability of manufacturing a personalized maxillomandibular prosthesis.

More than 150 professionals meet at the First International Congress of Rare Respiratory Diseases organized by INCLIVA.

Eight Researchers from INCLIVA among best researchers from Valencia.

INCLIVA and the UV present the latest research on rare diseases.

FEBRUARY

Researcher from INCLIVA and the IUIVI develop a new therapy to reduce endometriotic lesions.

An international team led by INCLIVA publishes a study comparing the most used antihypertensive treatments in diabetics.

Cardiologists from INCLIVA and the Hospital Clinico demonstrate that cardiac resonance predicts the evolution of stroke patients.

INCLIVA researchers conclude that the blink frequency may be useful to diagnose the minimal hepatic encephalopathy disease.

MARCH

A team of INCLIVA-UV in collaboration with CNIO finds new evidence in favor of the role of oxidation in aging.

The hypertension risk factor in metabolic syndrome with greater impact.

APRIL

INCLIVA hosts the 10th Symposium "Advances and results in research on breast and colon cancers" from the AECC Scientific Foundation.

Researchers from INCLIVA and the UV conclude that a protein could influence the maturation of neurons of the adult brain.

Success on the first day on the management model of heart failure organized by INCLIVA and the Hospital Clinico.

Researchers from INCLIVA show that changes in podocytes predict kidney damage in patients with lupus.

Iron deficiency determines the possibility of an admission for acute heart failure.

Unbeatable reception of Dr. Newman's INCLIVA seminar.

Dr. Ascaso enters in the RAMCV as a number academic.

MAY

INCLIVA and IVI will investigate the influence of the obese and / or smoker mother on the genetic profile of their baby during gestation.

Nobel Prize Zur Hausen visited INCLIVA.

INCLIVA in SCReN journey "Challenges and opportunities for the independent clinical research".

INCLIVA starts its Equality Plan.

I Research Day on Prediabetes, Diabetes and Cardiovascular Disease.

INCLIVA and CIPF create the Mixed Unit of Rare Diseases of the Comunidad Valenciana.

Talk about sensitization in Emergencies on Gender Violence.

Good Clinical Practices Course for researchers 2016.

Dr. Aguilar, psychiatrist, awarded by the RAMCV.

I Journey of cooperation REDIT-INCLIVA.

JUNE

Metabolomics by NMR in the Clinical Environment. Applications in Biomedical Research and Clinical Diagnostics.

Design a user-friendly system to predict the prognosis of patients with severe lung injury.

The length of telomeres, a possible biomarker for disease prognosis.

Andrés Cervantes directs the International Course ESMO-ESO on oncology medicine.

JULY





JULY

INCLIVA and the Consellería de Economía Sostenible collaborate in the promotion of innovation.

Men have a higher risk of developing skin cancer.

An INCLIVA researcher coordinates the European clinical consensus guidelines for the diagnosis and treatment of patients with colorectal cancer .

INCLIVA Health Research Institute, from Valencia, and the IDIBGI from Girona, find an explanation for sudden cardiac death.

AGOST

INCLIVA researchers lead European consensus on cognitive impairment.

INCLIVA determines that the treatment of acute infarction achieves healing of the infarcted area and prevents unnecessary fibrosis of the healthy myocardium.

The organization of reticulin fibers influences the aggressiveness of neuroblastoma tumors.

The European Foundation for the Study of Diabetes provides financing for a valencian research project of INCLIVA.

A recent clinical study concludes that physiological changes in the left ventricle of the heart following a heart attack can predict the patient's subsequent course.

Advance application of calls for predoctoral contracts and aids to predoctoral mobility.

Associate the activation of a genetic pathway to the survival rate in one of the types of breast cancer.

SEPTEMBER

Valencian cardiologists propose a pioneering therapy guided by carbohydrate 125 antigen levels following admission for acute heart failure.

The Clinical Trials Unit Phase I of INCLIVA has 21 trials with experimental oncological drugs.

Oncology specialists from Colombia visit INCLIVA to learn about the latest advances and treatments in breast cancer.

INCLIVA and Hospital Clínico de Valencia host a conference about Fabry's disease.

OCTOBER

The valencian oncologist Andrés Cervantes, the first Spanish scientific director to lead The European Congress of Oncology.

INCLIVA researchers are participating in a study published in The Lancet that assesses health progress in 188 countries.

Unsaturated fats found in olive oil and nuts lower triglycerides levels and reduce insulin resistance.

Satisfaction with the results of the call for research projects FIS of the AES 2016.

Resolved the 2016 call for the VLC Bioclinic program.

Carlos Simón, first European to be awarded by the American Society of Reproductive Medicine for his research trajectory.

Tribute in Gandia to Ana Lluch.

INCLIVA and the Hospital Clinic address the attention of Rare Diseases in Primary Care.

Pediatric nurses at the Hospital Clínico de Valencia investigate factors to improve the safety and quality of care for hospitalized children.

NOVEMBER

The spin off Epidisease, receives the First prize of entrepreneurship of the Generalitat Valenciana.

Companies, researchers and managers participate in the first congress of coordination and management of european projects in health.

Researchers from the *Universidad de Valencia* and INCLIVA validate a genetic method to treat myotonic dystrophy type 1.

The hypertension is the number one cause of death in the world.

BIC Awards recognize as the best R&D in Oncology to Dr. Ana Lluch.

INCLIVA and the Universidad de Valencia investigate how to combine cells and materials to regenerate the cartilage of the joints.

Andrés Cervantes, among the winners of the awards "Valencianos en la Onda".

INCLIVA adheres to the local innovation pact.

Researchers discover which proteins are involved in the conversion of adult cells into pluripotent stem cells.

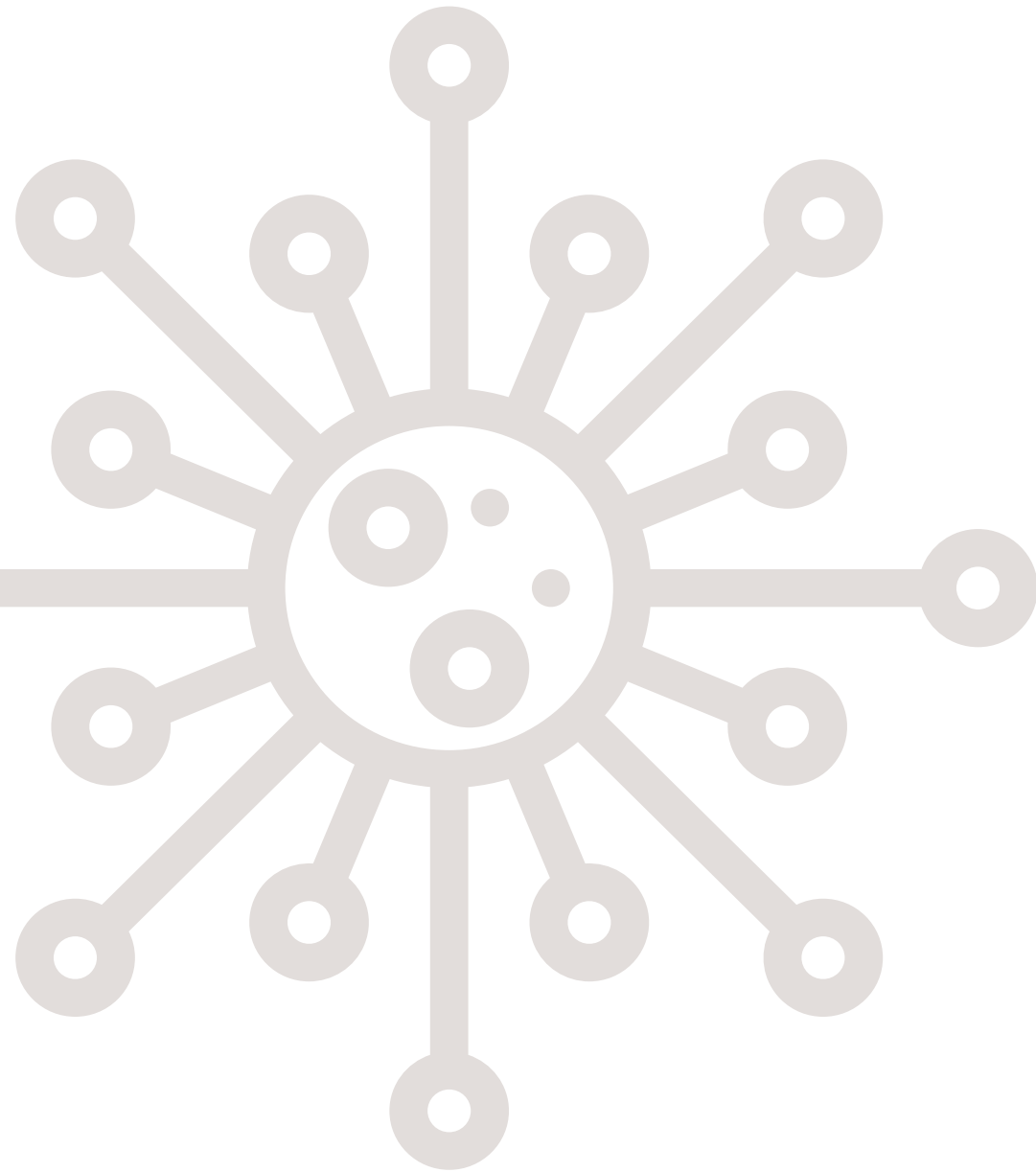
INCLIVA signs an agreement with Bankia and the rest of Sanitary Research Centers of the Comunidad Valenciana to grant scholarships to 26 students.

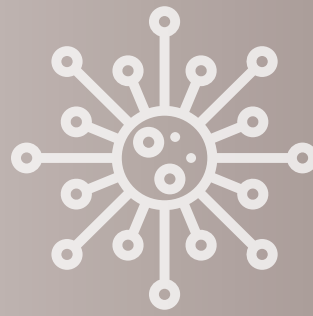
INCLIVA participates in a project that recognizes the Valencian Community as a European model of active and healthy aging.

DECEMBER

A scientific study relates for the first time the low presence of lactobacilli in the uterus with a worse reproductive prognosis.

Lung, colorectal and breast, the most lethal cancers in Spain.





8

INCLIVA
Solidary





INCLIVA's mission is "to contribute to improve the health and quality of life of citizens", therefore, in addition to our own research projects, the institute is also involved and committed to initiatives promoted by individuals who live near some illness.

INCLIVA is currently working on four joint initiatives: *Proyecto Mama*, *Proyecto Paula*, *Fundacion Le Cadó* and *Nico contra el Cancer*. One of the fundamental premises of the institute is the maximum transparency in the management of the contributions received.

These donations provide tax benefits under the Article 66 of the Law 30/1994 of 24 November on Foundations and Tax to private participation in activities of general interest incentives.

8.1 Solidary Projects

PROYECTO PAULA

This project was born in 2011 from the hand of Cristina Ponce, when her 8 years old daughter, Paula, was diagnosed with type 1 diabetes mellitus, a disease that completely destroyed her insulin-producing cells.

Proyecto Paula focuses its work in raising funds and resources, both public and private, to investigate the diabetes and to find a cure for Paula and other people with this illness.

INCLIVA has several groups dedicated to research in diabetes and belongs to the Biomedical Research Centre in Diabetes and Associated Metabolic Diseases (CIBERDEM), a public consortium led by Spain's research effort of excellence in diabetes and related metabolic diseases, as well as the translation of research results into clinical practice.

Since its inception, *Proyecto Paula* has contributed with more than 93.000€.



PROYECTO MAMA

Proyecto Mama started in September 2012 promoted by Pedro Alarcon after the death of his mother as a result of breast cancer. The purpose of this initiative is to get public and private funds to investigate this disease.

Breast cancer is the most common tumor in women, begins to appear around age 30, gradually increasing its impact, affecting up to 9% of the female population at 70 years of age.



FUNDACION LE CADÓ

Fundación Le Cado was created in 2010 under the leadership of its president Elvira Monferrer Daudi. This initiative seeks to unite efforts and resources in supporting this kind of tumor research, which is currently the fourth leading cause of death of women.

Fundación Le Cado collaborates with INCLIVA funding the research project "Study of breast cancer in young women under 35 years," conducted by Dr. Gloria Ribas. It also involves other researchers such as Dr. Isabel Chirivella (a genetic diagnosis specialist physician) and Ms. Carmen Peña Chilet, all this team led by the oncologist Dr. Ana Lluch.

Almost 30.000€ has been donated for the project so far.



NICO CONTRA EL CANCER

The movement “*Nico contra el cancer*” was formed in November 2015 in Ourense, after Nicolas Rodriguez Leal came back from his surgery intervention at the *Hospital La Paz* in Madrid.

The movement is led by his mother and aunts as a dependent activity of the *Asociación NEN*, whose main objective is to finance research projects against childhood cancer, and more specifically solid tumors.



8.2 Solidary news

The first project of INCLIVA in Precipita, a funding record

The project “Improving the diagnosis of childhood tumors by bioimaging” by the researcher Rosa Noguera was the first project to be presented INCLIVA in the Precipita Network, the public micro-patronage platform, under the Ministry of Economy and Competitiveness.

The Research Group of INCLIVA and the *Universitat de Valencia*, led by Dr. Noguera is specialized in oncopediatrics and specifically in the study of morphological and genetic techniques of the causes, development and new therapies of childhood bone tumors and soft tissues.

The project focuses on studying and relating forms, sizes, locations and connections between tumor cells and cells incorporated into the tumor mass, as well as the textures of intercellular elements in microscopic images reconstructed in 3D and their implementation in a web which is accessible to all researchers, expanding the global network of collaborative research in pediatric cancer.

The project had as a goal to reach 25.000€ in ninety days and has finally surpassed it, reaching 32.950€, thus placing at the head of the projects that have received the most funding. According to Dr. Noguera, “any donation even the smallest is appreciated and in our case, we are very excited about the support shown. We have far exceeded our expectations. It is good that society is involved in supporting research because in the end we all benefit.”

With the contributions received, two researchers will be hired in digital pathology that will enhance the analysis of microscopic tumor images and test the design of prototype patterns of the different neuroblast tumor tissues in relation to the risk of relapse or a poor response to therapy that will include in a website accessible to other researchers.

The direction of INCLIVA and the Research Group of Dr. Noguera, want to thank the collaboration of the Precipita platform in the diffusion of the project, to all those who have made a contribution to the project, and in particular, to the port stibers of SEVASA-puerto de Valencia for giving up its Christmas basket, to the company ALSA for its voluntary donations campaign from its website and to the company Surus Inversa and its platform of auctions Escrapalia.

8.3 Private solidary donations and acknowledgments

On behalf of INCLIVA, we want to thank the support and solidarity to all the people who have helped research through with their donations. For us, these collaboration means much more than an economic contribution. It is the encouragement we need to keep investigating and working for research.

Private donations

Esteban Borreda Bolinches, Francisco Botella Aparicio, Rafael Caballer Molina, Guillermo Pascual Caballero De Lujan, Nicolás Carrión Domínguez, Joaquín Casado Catalina, Lucía Cases Ferreres, María Luisa Ebri Méndez, Natalia Font Ferrando, Nuria Gelonch Soler, Empar Lurbe Ferrer, Blas Macías Camero, Emilia Marco Estellers, Alicia Martínez Espinosa, Jesús Picó López, Cristina Ponce Costa, Josep Redón Más, Remedios Sánchez Hernández, Rosalía Sánchez Rilla, Ana Sanz Moliner, Antonia Serrano Monedero, María Inmaculada Serrano Monedero.



Corporative donations

Abbott Laboratories S. A., Abbvie Spain, S. L. U., Acreedores varios, Actelion Pharmaceutical España SL, AMGEN S. A., Associació de Jovens de Cabanes, Associació Familiars i Amics Pacients amb Neuroblastoma, Asociación de Afectados de Cáncer, Asociación de Mujeres Afectadas por Cáncer de Mama de Elche y Comarca, Asociación de Mujeres y Hombres Afectados de Cáncer de Mama, Asociación Garmitxa, Asociación la Virgen de los Dolores, Asociación Tiradas Contra el Cáncer Memorial Vicente Estellés, Ayuntamiento de Benirredrà, Ayuntamiento de Puzol, BIOMED Central LTD, Springer Healthcare LTD, Canals contra el Cáncer, CEM Biotronik S. A, Chiesi España S. A, Covidien Spain S. L., Frasquet, Fundación Bancaria Caixa d'estalvis i pensions de Barcelona, Fundación Española para la Ciencia y la Tecnología, Fundación IVI, Fundación LeCadó, Fundación Patrimonio Benéfico Marqués de Dos Aguas, Fundación Senefro, Fundación Sociedad Arteriosclerosis, GE Healthcare Biosciences S. A., Global Asesores Jurídicos y Economistas S. L., Grupo Gasmedi S. L. U., Helados y Postres S. A., Humana Spain S. L., IGENOMIX S. L., Industria Restauración Colectiva S. L., Italfarmaco S. A., Junta Local Contra el Cáncer Montesa, Laboratorios Farmacéuticos Rovi S. A., Laboratorios Gebro Pharma S. A., Medtronic Ibérica S. A., Pfizer Gep S. L. U. Pfizer S. L. U., Pindaro Sports S. L., Prosmédica Valencia S. L., Quilmedic S. L., Radiometer Ibérica S. L., Sanlúcar Fruit S. L., Santa Lucía, Seguros El Corte Inglés Vida, Pensiones y Reaseguros S. A., Sociedad Amigos Internacionales de Pedralba, Sofpromed Investigación Clínica S. L. U., St. Jude Medical España S. A.,

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