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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
2.1. 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 Department— 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. Narcís Vázquez, Secretary of the Consellería de Sanidad Universal y Salud Pública of the Valencian Government.
- Mr. Martín Quirós, Valencia 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 Carmona, 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 *Conselleria de Sanidad Universitaria 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 Sanmartín, 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.

**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).
- 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.

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 Zaragozá 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 Ginecology Department.

Substitute Secretary:

Members:
• Dr. Manuel Alós Almiñana. Head of the Pharmacy Department.
• Ms. Mª 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. Mª José Fabiá Valls. Specialist of the Internal Medicine Department.
• Ms. Mª 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 Pharmaceuticals.
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 sub-directorate.

The first sub-directorate 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).

- Prof. Miguel Mínguez Pérez. Head of Section of Gastroenterology Department.
- Dr. Francisco Dasi 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. Mª 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.
Administrative Area:
- Financial-Administrative Director: Mr. Vicente de Juan
- Financial-Administrative Subdirector: Ms. Consuelo López
- Accounting and Invoicing Unit: Ms. Mª 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
- Recepcionists: 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

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
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.
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.

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.
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

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

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

<table>
<thead>
<tr>
<th>Clinical guidelines</th>
<th>IF</th>
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<tbody>
<tr>
<td>5</td>
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Consensus documents

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</table>


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 generalize 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 Tissular 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 O\textsubscript{2} 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 functionally modification and increasing its adhesion to the endometrium during its implantation. In this sense, the program goal is to explore if this new epigenetic...
A 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 Embriornary Stimulation (Dr. Remohi)

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 is 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, 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 INCLÍVA’s total scientific output. Additionally, the next tables shows scientific publications distribution by area in terms of number of articles and impact factor.
4.3.1 Cardiovascular Area

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<td>Group on Translational Research in Ischemic Heart Disease</td>
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164 Publications

- Impact Factor (IF)
  - Total: 662.97
  - Average: 4.09

- JCR:
  - 19 in D1
  - 84 in Q1
  - 28 in Q2

- Author:
  - 74 first author
  - 75 last author
  - 75 corresponding author

48 International collaborations

143

- 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

ciberdem

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
Mª 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 Bábara García García. CIBERdem
Scientific activity

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 sínndrome.

• 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

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Original articles


Review


• THESIS

Thesis title: Efecto de la sobrecarga oral con grasa insaturada en los marcadores de estrés oxidativo y expresión de ARN linfomonocitos 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 gastrointestinal en sujetos con obesidad grave-mórbida.
Principal Investigator: Rafael Carmen 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 Carmen 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 Carmen 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 Mª 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

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Original articles


5. Carmona-Vicente N, Allen DJ, Rodríguez-Díaz J, Iturriaza-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. Virol J. 2016 May 21; 13(1):82. IF: 2,181


**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

• **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 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 Femenia. 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 proarrhythogenic 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 Ca\(^2+\) 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 electrical 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**

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Original articles


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


**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€

**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 Rabada  
**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”
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

http://www.uv.es/lince/SP/index.html

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 ovarietomized 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

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Original articles


**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

**THESS**

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](image1)

![Fig 2: Superoxide production in murine arteries](image2)
Research Group on Clinical Cardiology
Consolidated group

“This strategy therapeutic was associated with a significant reduction in the risk of adverse clinical episodes within a year, especially a reduction of fifty percent in the risk of new admissions for acute heart failure”
Julio Núñez. ABC Salud. 01/09/2016

Group members

Principal investigator
Juan Sanchis Forés
Hospital. University
H Index: 30

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
Scientific activity

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.

PUBLICATIONS

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Original articles


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.


Letters


Editorial


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


• 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 una 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 Sanchís 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 Clinico Universitario de Valencia

**Duration:** 2016 - 2018

**Total Budget:** 589,050€

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**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

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

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Original articles


### Clinical guidelines


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### 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:** Consorcio 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 Clinico 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 Clinico 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:** Consorcio 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 Clinico 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

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
Clinico-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 Fluxá 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
Scientific activity

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

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Original articles


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

"Pertenecer 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

**Collaborating researchers**

Mª José García-Fuster González-Alegre. Hospital
Mª José Galindo Puerto. Hospital. University
Mª José Forner Giner. Hospital. University
Gernot Helmut Pichler. INCLIVA
María José Fabiá Valls. Hospital
Elena Solaz Moreno. Hospital
Carlos Sánchez Sánchez. INCLIVA

**PhD students**

Óscar Calaforra Juan. CIBERobn
Javier Pérez Hernández. INCLIVA

**Emerging researchers**

Fernando Martínez García. Hospital. University
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

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Original articles


population. J Hypertens. 2016 Sep; 34 Suppl 2:e86. IF: 5,062


34. **NCD Risk Factor Collaboration (NCD-RisC).** A century of trends in adult human height. Elife. 2016 Jul 26; 5. IF: 8,303


Editorial


Guidelines


**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  
**Total budget:** 38.985€

**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 Téllez as collaborating researcher)  
**Funding body:** European Commission  
**Beneficiary institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2010-2016  
**Total budget:** 386.775€

**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  
**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 Redón, 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, Mª 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):** Mª 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 Mª Vila Salinas
University
H Index: 18

Collaborating researchers
Salvador Lluch López. University
Martín Aldasoro Celaya. University
Pascual Medina Besso. University
Gloria Segarra Irles. University
Mª Dolores Mauricio Aviñó. University
Scientific activity

**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**

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**Original articles**


**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 Mª 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 Mª Vila Salinas, Mª 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 Irles, 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
Mª 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

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Original articles


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


• 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**

**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 dilucidating 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

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Original articles


• 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 Educación, 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 Clínic 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 metabolómica.
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 DIOCLES”.
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 resonanancia para estratificación de riesgo y valorar implante de DAI tras un IAMES” 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 infarction.

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

- Research Group on Histopathology and Tissue Engineering 96
- Research Group on Central Nervous System Tumours 101
- Research Group of Innovative Diagnostic and Therapeutical Developments in Solid Tumours - InDeST 105
- Research Group on Breast Cancer Biology 112
- Research Group on Skin Cancer 118
- Translational Research Group on Pediatric Solid Tumours 121
- Research Group on Hematopoietic Transplantation 126
- Research Group on Lymphoproliferative Disorders 130
- Research Group on Myeloid Neoplasms 134
- Research Group on Epigenetics and Chromatin 138
- Research Group on Molecular Imaging and Metabolomics 141

- Impact Factor (IF)
  - Total: \(885,77\)
  - Average: \(5,17\)

- JCR:
  - 40 in D1
  - 84 in Q1
  - 31 in Q2

- Author:
  - 58 first author
  - 72 last author
  - 64 corresponding author

- 171 Publications

- 52 International collaborations

- Original articles
- Letters
- Editorial
- Clinical guidelines
- Review

154
Research Group on Histopathology and Tissue Engineering
Consolidated group

Group members

Principal investigator
Carmen Carda Batalla
University
H Index: 20

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 Miguez Rey. Hospital
Genaro Galán Gil. Hospital
Antonio Silvestre Muñoz. Hospital
Francisco Forriol Brocal. University
Antonio Fons Font. University
Rosa María Cibrían 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

Collaborating researchers

Amando Peydró Olaya. Hospital. University
Amparo Ruiz Sauri. 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

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Original articles


19. Priego Quesada JJ, 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


**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*
**Scientific activity**

**Clínico Universitario de Valencia**

**Duration:** 2016
**Total budget:** 3.000€

**Reference:** IMPORTOYX

**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:** Thermobilke_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€

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**THESIS**

**Thesis title:** Estudio “in vitro” de la resistencia a la fractura tras la fatiga de coroas cementadas sobre pilares de circona.

**Doctoral candidate:** Ana Roig Vanaclocha

**Director(s):** Antonio Fons Font, Mª 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 Zaragozá

**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”

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(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**

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**Original articles**


**RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: PI14/01669
Title: Interacción de miRNA-200 y miRNA-138 en la infiltración y perfiles de MMMI 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 an Therapeutical Developments in Solid Tumours - InDeST
Consolidated group

Group members

Principal investigator
Andrés Cervantes Ruipérez
Hospital. University
H Index: 40

Collaborating researchers
Susana Roselló Keranen. Hospital Desamparados Roda Pérez. INCLIVA
Tania Fleitas. INCLIVA
Maider Ibarrola Villava. INCLIVA
Josefa Castillo Aliaga. INCLIVA
Ana Isabel Gil Tébar. INCLIVA
María Peña Chilet. INCLIVA
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Alejandro Espí Macías. Hospital. University
Estefanía García Botello. Hospital

PhD researchers
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Noelia Tarazona Llavero. Hospital
Gema Bruixola Campos. Hospital
Maria Carolina Martínez Ciarpaglini. INCLIVA
Valentina Gambardella. INCLIVA
Sara Oltra. INCLIVA
Marta Llorca Cardeñosa. INCLIVA
Marcelino Telechea Fernández. INCLIVA

Technicians
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Emerging researchers
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Nurses
Inma Blasco Blasco. INCLIVA
Celia Martínez. INCLIVA
Luna Porta. INCLIVA

Administrative assistant
Gabriela Perez Garity. INCLIVA
Jessica Fraile. INCLIVA
Elena Jiménez. INCLIVA
Julia Peláez. INCLIVA

http://indest.Uv.Es

Un valenciano, primer español que dirige el Congreso Europeo de Oncología. El Mundo. 05/10/2011
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.

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**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, cmicroRNAs) 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-EFGR antibodies.

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**PUBLICATIONS**

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**Original articles**


Scientific activity

Letter


Editorials


Clinical guidelines


Reviews


• 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 Zaragozá 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
Scientific activity

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

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

**Duration:** 2013-2016

**Total budget:** 54.535€

**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:** PI15/02180

**Title:** Enfermedad mínima residual en cánceres colorrectales de alto riesgo resecados. Valor de las biopsias líquidas en el seguimiento y análisis de la heterogeneidad tumoral.

**Principal Investigator:** Andrés Cervantes Ruipérez

**Funding Body:** Instituto de Salud Carlos III

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

**Duration:** 2016-2018

**Total budget:** 80.465€

**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€

**• AWARDS:**

In November 2016, Dr. Andrés 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.

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.


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 ≥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

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 Gasion. Hospital
Antonio Caballero Garate. Hospital
Angel Martínez Agullo. Hospital
Estela Contel Martín. INCLIVA
Isabel Catoira Domenech. INCLIVA
Patricia Martínez Belenguer. INCLIVA
Antonio Millet Serrano. Hospital. University
Vicenta García 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
Paula Cabello Navarro. INCLIVA
Anna Adam-Artigues. INCLIVA
Iris Garrido Cano. INCLIVA
Birlipta Pattanayak. INCLIVA

Technicians
Elisa Alonso Yuste. INCLIVA

Administrative assistant
Yolanda De La Cruz Robles. INCLIVA

“Mis pacientes me han enseñado a vivir.”
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-κB 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).
- 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 tumours 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

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Original articles


Review


• 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 Martí Bonmatí

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: Maríà Teresa Martínez Martínez
Director(s): Ana Lluch Hernández

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 Grisolía.

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 Monteaudo 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 Mª 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 western blot.

• 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 (tumor stem 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

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Original articles


3. Ayala D, Ramón MD, Martín JM, Jordá E. Atypical Phacomatosis Pigmentokeratotica as the Expression of a Mosaic RASopathy With the BRAF-Glu586Lys Mutation. Actas Dermosifiliogr. 2016 May; 107(4):344-346. IF: 0


**Letter**


**THESIS**

**Thesis title:** Estudio de la prevalencia de mutaciones en línea germinal (síndrome de birt-hogg-dubé) y somáticas del gen flicn en pacientes con fibrofoliculomas o tricoideosomas 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.

**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, skeletal 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 skeletal 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**

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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


Letter


**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€

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€

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€
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 Viciedo. 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
Scientific activity

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 donates (haploidentic).

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

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Original articles


Review


Letters


• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI15/00090
Title: Inmunobiología de la infección por el citomegalovirus en el trasplante alógénico de precursores hematopoyéticos haploidentifico asociado al uso de ciclofosfamida posttrasplante.
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 haploidenticos asociado al uso de ciclofosfamida post-trasplante.
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
Ana Isabel Teruel Casaús. Hospital
Sandra Ballester García. INCLIVA
Lucía Brines Sirerol. INCLIVA
Blanca Ferrer Lores. 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 cytokine 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

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Original articles


Letter


• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI14/01781
Title: Papel de la vía de señalización NOTCH1/FBXW7/P13K/PTEN/AKT en la progresión de la Leucemia Linfocítica Crónica B (LLC-B) a formas avanzadas.
Principal Investigator: Mª 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

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**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):** Mª 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
Mar Tormo Díaz
Hospital. University
H Index: 27

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

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Original articles


• 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


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 mutatons. 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 invasitivity 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

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Original articles


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 Ríffo 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
Scientific activity

**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**

<table>
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<tr>
<th>Number of articles</th>
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Original articles


**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

<table>
<thead>
<tr>
<th>Research Group</th>
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<td>Research Group on Genetics of Osteoporosis</td>
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<tr>
<td>Translational Research Group on Nutrition and Metabolism</td>
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<tr>
<td>Research Group on Neurological Impairment</td>
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<td>Research Group on Inflammation</td>
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<td>Research Group on Cellular and Organic Physiopathology of Oxidative Stress</td>
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**Impact Factor (IF)**
- Total: 985.53
- Average: 4.96

**JCR:**
- 42 in D1
- 98 in Q1
- 32 in Q2

**Author:**
- 60 first author
- 72 last author
- 64 corresponding author

**193 Publications**

**57 International collaborations**
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

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Original articles


• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: FOCUS
Title: Frailty management Optimisation though 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.
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

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 inositol 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 antiretroviral hepatotoxicity.

### PUBLICATIONS

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Original articles


7. Díaz-Morales N, Rovira-Llopis S, Bañuls C, Escribano-Lopez I, de Marañón AM, Lopez-Domenech S, Orden S, Roldan-


Reviews


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Clinical guidelines


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Editorial

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, Àngeles 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

- 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 used 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


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


**RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: P15/00035  
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: 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: 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: PROGRAMA VLC-BIOCLINIC  
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: 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: 2016 - 2017  
Total Budget: 9,000€

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: 2016 - 2017  
Total Budget: 9,000€

Reference: BF13007  
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Principal Investigator: Carmina Montoliu Félix  
Funding Body: ERESA  
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia  
Duration: 2016 - 2017  
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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: 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: 2016 - 2017  
Total Budget: 9,000€

**THESIS**

Thesis title: Evaluación de los efectos del tratamiento con tadalafil 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, Mª 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

Maria Jesús Sanz Ferrando
University
H Index: 31

Team involved in
Emerging researchers
Laura Piqueras Ruiz. INCLIVA
Herminia González Navarro. INCLIVA

Collaborating researchers
Nuria Cabejo 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
Scientific activity

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

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 activit.

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 PPARα/γ agonists to be used in cardiometabolic disorders.
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**

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**Original articles**


• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PROMETEO II/2013/014
Title: Nuevas dianas farmacológicas para el tratamiento de la EPOC y sus comorbididades 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
Funding body: 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 (María 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: Proyecto Paula
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013 - 2017
Total Budget: 108.472,03€

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: 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: Ministerio de Economía y Competitividad
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

Doctoral candidate: Paula Escudero Díaz
Director(s): Mª 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, Mª 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): Mª 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 Dasi Fernández. University. INCLIVA
José Luis García Giménez. CIBERer

Collaborating researchers
Amparo Gimeno Monró. University
Carlos Romá Mateo. University
Pilar González Cabo. CIBERer
Carla Giménez Garzó. INCLIVA
Esther Berenguer Pascual. EPIFrailty
Eva Mª García López. University
Giselle Pérez Machado. University
Mª 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, a 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 specialities 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 Trasacional 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 genodermatoses.
- 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 Dasi 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**

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**Original articles**


**Clinical guidelines**


**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: P114/02162
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 Dasi Fernández  
**Funding Body:** Universidad de Valencia  
**Beneficiary Institution:** Universidad de Valencia  
**Duration:** 2015-2016  
**Total budget:** 9.000€

**Reference:** EPIFRAILTY  
**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 Clínic Universitario de Valencia  
**Duration:** 2016  
**Total budget:** 4.000€

**Reference:** Becas 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:** Conselleria 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 Clínic 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€

**Reference:** Beca GEER  
**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 Clínic Universitario de Valencia  
**Duration:** 2016 – 2018  
**Total budget:** 12.000€

**Reference:** PROMETEO II/2014/056  
**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 Clínic Universitario de Valencia  
**Duration:** 2016 - 2018  
**Total budget:** 12.000€

**Reference:** PI14/00894  
**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 Enfermedades del Raquis  
**Beneficiary institution:** IIS La Fe  
**Duration:** 2016  
**Total budget:** 4.000€

**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 Clínic 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:** Mª 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.**

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**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

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 physiopathological 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

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Original articles


**THESIS**

Thesis title: Valoração 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”

**RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: PI13/01848
Title: Factores genéticos y metabolómicos en la obesidad mórbida y su modulación tras intervención dietética, ejercicio físico y cirugía bariátrica. Estudio especial de PS3, 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: PLASESPCOLOREC
Title: Ensayo plasmódico de esperma en orina como biomarcador de cáncer correctal.
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 Gilbert 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.

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Letter


**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: 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: Mª 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
Mª Luisa Briones Urtiaga. Hospital
Mª Jesús Zafra Pirés. University
María Belén Safont Muñoz. Hospital
Mª 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**

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**Original articles**


**Letter**

• **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

**Reference:** PROMETEO II/2013/014

**Title:** *Nuevas dianas farmacológicas para el tratamiento de la EPOC y sus comorbididades 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, detinenglicol 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 Zaragozá 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 Zaragozá 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

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Original articles


Review


**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 Zaragozá 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 calpainas 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 Zaragozá 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
Mª 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 Bargues. 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
Scientific activity

**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.

**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.

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**Emerging researcher**

**Maria Carmen Góme zam 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.

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**PUBLICATIONS**

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**Original articles**


**RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: FRAILOMIC

Title: Utility of OMIC-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 Investigador: 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 Frágilidad y envejecimiento

Principal Investigador: 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 Investigador: 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 Investigador: Consuelo Borras 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, Mª 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

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 Arccas 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 Carri. Hospital
Mª José Parra González. Hospital
Ernesto Pastor Martínez. Hospital
Jaume Puig Bernabéu. Hospital
Ana Mugarza Llopis. Hospital
Laura Reviriego Agudo. Hospital
Estefanía Gracia Ferrandiz. Hospital

Emerging researcher
Carlos Ferrando Ortolá. 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 Ortolá

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

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Original articles


Letters


Review


Clinical guidelines


• 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 Ferrandíez 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 la complicaciones postoperatorias y de la estancia hospitalaria con una estrategia perioperatoria individualizada de ventilación de protección pulmonar. Estudio comparativo, prospeccivo.
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€

• 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-reperfusión en la lobectomia 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”
Research Group on Translational Genomics
Consolidated group


“Genetistas de la Universidad de Valencia avanzan hacia la cura de nuestra Distrofia Muscular”
http://www.conquistandoescaones.org

Group members

Principal investigator
Rubén D. Artero Allepuz
University
H Index: 16

Collaborating researchers
Manuel Pérez Alonso. University
Mª 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

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Original articles


• 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
Scientific activity

**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**: Mª Beatriz Llamusí 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**: Mª 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.
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.
- 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.
- Endoscopic 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**

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Original articles


Letters


Review


• 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€

• 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 Devis
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 Amézcuá García. CIBERSAM
Ferrán Catalá López. University
Scientific activity

PUBLICATIONS

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Original articles


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.

Strategic aims

- The development of a guide / consensus with “Association 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.
- 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.

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Letter


Editorials


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
effective strategies for cancer prevention (INCANCER/CNSd).

**Principal Investigator:** Rafael Tabarés Seisdedos  
**Funding Body:** Conselleria de Educación Cultura y Deporte  
**Beneficiary Institution:** Universitat de València  
**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 Seisdedos  
**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 Seisdedos  
**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 Seisdedos  
**Funding Body:** Ministerio de Educación, Cultura y Deporte  
**Beneficiary Institution:** Universidade de València  
**Duration:** 2015-2016  
**Total budget:** 10,000€
4.3.4 Reproductive medicine area

| Research Group on Women Health | 205  |
| Research Group on Stem Cells Applied to Reproduction, Embryo Viability and Endometrial Receptivity | 209  |
| Research Group on Male Infertility and Embryonic Stimulation | 215  |
“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 CAR-MEN 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 monitoring 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**

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**Original articles**


Letters


Review


**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 though 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 multivariate 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: Mª 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

Group members

Principal investigator
Carlos Simón Vallés
IVI. University
H Index: 68

Collaborating researchers
Amparo Merceder 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
Mª 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

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 Domínguez, 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

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**Original articles**


**Most popular article from 2016 in Human Reproduction**


Review


• 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 Castillón Cortés
Director(s): Carlos Simón Vallés, Carmen Rubio Lluesa, Inmaculada Sánchez Ribas
Date of the defense: 26/01/2016
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 Economia, Industria y Competitividad
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2016-2017
Total budget: 60.000€
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
Principal Investigator: Carlos Simón Vallés
Funding body: Conselleria de Educación, Cultura y Deporte
Beneficiary institution: Universitat de València
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. Trophoectoderm 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
Mª 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

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**

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**Original articles**


Review


Editorial


**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: Universitat de València
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”

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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**80 Publications**
- Impact Factor (IF)
  - Total: 246,75
  - Average: 3,08

**JCR:**
- 9 in D1
- 27 in Q1
- 8 in Q2

**Author:**
- 36 corresponding author

**International collaborations:**
- 16

**National collaborations:**
- 39
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

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Original articles


• 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):
  - Crioballoon 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 anticoagulants in silent, device detected, self limited AF.
- Atrial flutter: zero radioscopy during ablation, ablation guided by electrogram voltaje.
- 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**

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**Original articles**


**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).

- 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.

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**Original articles**


Department of Cardiovascular Surgery

**Strategic aims**
- Increase of microsurgery.
- Development of new 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.

**PUBLICATIONS**

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Original articles


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.

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Original articles


2. Ayala D, Ramón MD, Cabezas M, Jordá E. Primary Cutaneous
**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.

**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

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Original articles


Letter


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).

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**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: Mª 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 una 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)
**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**
- 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**

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**Original articles**

1. Jovani-Sancho MD, Sheth CC, Marqués-Mateo M, Puche-To-...
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 ecoendoscopia diagnostics and therapeutics, ampulectomia, diverticulotomy of Zencker and digestive prostheses.

- PUBLICATIONS

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Original articles


**Department of Intensive Medicine**

**Main lines of research**
- Histones.
- UCI Epidemiology. BMR.
- Serious flu.
- Genetics in severe NAC.

**PUBLICATIONS**

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**Original articles**


**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 dysynchrony 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-Ytrium.
• 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

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Original articles

Department of Preventive Medicine

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Original articles

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**

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Original articles


Letter


**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

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**Original articles**


• 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 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

**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, Mª 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:** Mª 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

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Original articles


Letters


Department of Neurosurgery

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Department of Neurology

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Original articles


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. Icíar Puchades (Magnetic Resonance, ERESA).
- Definitive diagnosis of sleep disorders after clinical and polysomnographic evaluation in patients with clinical suspicion of sleep apnea-hypopnea 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.

Department of Otorhinolaryngology

Strategic aims

- The multi-center CBAS project sponsored and funded by Cochlear Co. (Goteborg, 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 participating 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 cofosis 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 cofosis.
- Simultaneous bilateral cochlear implants in children.
- Location of sound and hearing loss in different experimental situations.
- Situation of vestibular system.
• PUBLICATIONS

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**Original articles**


**THESES**

**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.
**Department of Pediatrics**

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**Original articles**


**Letters**

6. Lara Gallego B, Castillo Carullón S, Martínez Martínez MT, García Reymundo M, Miravitlles M. Profiles of cases included in the Spanish registry of patients with alpha-1...


**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.

**Department of Psychiatry**

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**Original articles**


**RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: P14/00044
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 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

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Original articles


- RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: SAF2013-48724R
Title: Mecanismos celulares reguladores de la respuesta inflamatoria en patologías inflamatorias crónicas
Principal Investigator: Mª 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-TERMPIE-CIBRIAN-BLASCO-2016-A
Title: TERMPIE. 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
Quality Central Unit

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Original articles


Department of Medical Emergency

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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”
Original articles


**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**

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**Original articles**


**Letter**

4.5 Other scientific contributions from scientific platforms

4.5.1 Biobank

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

biobanco@incliva.es
**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.

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**Transfer of samples**

<table>
<thead>
<tr>
<th>Project</th>
<th>Ref./Agency</th>
<th>Principal Researcher/Institution</th>
<th>Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Estudio de la desregulación de microRNAs diana en suero de pacientes con cáncer de mama y cáncer gástrico.</em></td>
<td></td>
<td>Dra. Maider Ibarrola, INCLIVA</td>
<td>Breast cancer and Gastrointestinal tumors: serum</td>
</tr>
<tr>
<td><em>Enfermedad mínima residual en cánceres colorrectales de alto riesgo resecados. Valor de las biopsias líquidas en el seguimiento y análisis de la heterogeneidad tumoral.</em></td>
<td>PI15/02180, ISCIII, Ministerio de Economía y Competitividad</td>
<td>Dr. Andrés Cervantes, HCUV/INCLIVA</td>
<td>Gastrointestinal tumors: plasma and tissue</td>
</tr>
<tr>
<td><em>Biomarcadores de respuesta a los inhibidores de tirosina quinasa mediante fenotipado metabolómico de biopsias líquidas de pacientes con adenocarcinoma pulmonar con mutaciones de EGFR.</em></td>
<td>2015/0345</td>
<td>Dr. Oscar Juan Vidal, IISLaFe</td>
<td>Lung cancer and standard population: serum</td>
</tr>
</tbody>
</table>
### 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€

In summary, 769 aliquots have been provided in 2016 to respond to these sample requests.

| Caracterización de la trombocitemia esencial JAK2V617F y MPL negativa mediante secuenciación de exoma. | PI13/00393, ISCIII, Ministerio de Economía y Competitividad | Dra. Beatriz Bellosillo, Hospital del Mar | Haemathological samples: DNA |
| Desarrollo de kits de hematology con marcado CE. | IMEGEN S. L. | Dr. Carlos Ruiz Lafora, IMEGEN S. L. | Haemathological samples: DNA and RNA |
| Avanzar en el diagnóstico, la prognosis y la terapia de enfermedades neurodegenerativas raras. | PI15/00187, ISCIII, Ministerio de Economía y Competitividad | Dra. Carmen Espínós, CIPF | Standard population: plasma |
| Búsqueda de marcadores discriminatorios del deterioro cognitivo leve. | 13/703, Corporación Tecnológica de Andalucía | Dr. Javier Santos Burgos Muñoz, Neuron Bio S. A | Standard population: serum |
| Optimización de muestras de tejido para el desarrollo y la validación de biomarcadores de enfermedad: proyecto OPTIMARK. | PI16/01500, ISCIII, Ministerio de Economía y Competitividad | Dra. Lorena Peiró, INCLIVA | Solid tumors: OCT and FFPE |
| MicroARNs como biomarcadores de invasión en cáncer de mama. Aplicación y nuevo uso de los excedentes de la determinación de ganglio centinela. | GV/2016/029, Generalitat Valenciana, Conselleria d’Educació, Investigació, Cultura i Esport | Dra. Lorena Peiró, INCLIVA | Breast cancer: plasma and tissue |
| Relación entre los biomarcadores de fibrosis cardíaca y la función de los grandes vasos en una población hipertensa con miocardiopatía hipertensiva. | Fondos privados (ERESA) y CDTI | Dr. Fernando Martínez, HCUV/INCLIVA | Cardiovascular node: plasma and serum |
| Desarrollo de un test epigenético predictivo en pacientes con cáncer de mama precoz en el contexto neoadyuvante. | FAB-118, Ferrer Internacional S. A. | Dr. Manel Esteller, IDIBELL (Ferrer Internacional S. A.) | Solid tumors: FFPE |

**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


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:
• -80º C Freezer
• -20º 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
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 recertification 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.

<table>
<thead>
<tr>
<th>Department</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesia and Reanimation</td>
<td>2</td>
</tr>
<tr>
<td>Cardiology</td>
<td>1</td>
</tr>
<tr>
<td>Haematology</td>
<td>3</td>
</tr>
<tr>
<td>Psychiatry</td>
<td>1</td>
</tr>
<tr>
<td>Oncology</td>
<td>3</td>
</tr>
<tr>
<td>Otorhinolaryngology</td>
<td>1</td>
</tr>
<tr>
<td>Dermatology</td>
<td>1</td>
</tr>
<tr>
<td>Pneumology</td>
<td>1</td>
</tr>
<tr>
<td>Traumatology</td>
<td>1</td>
</tr>
<tr>
<td>Tutelage of other centers</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>15</strong></td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>Department</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Phase IV</th>
<th>Others</th>
<th>Observational</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesia and Reanimation</td>
<td>0</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Cardiology</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td></td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Haematology</td>
<td>1</td>
<td>6</td>
<td>7</td>
<td>1</td>
<td></td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Digestive Medicine</td>
<td></td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>Internal Medicine</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Neurology</td>
<td></td>
<td></td>
<td></td>
<td>6</td>
<td>2</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Oncology</td>
<td>16</td>
<td>11</td>
<td>17</td>
<td>11</td>
<td></td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>Radiotherapy</td>
<td></td>
<td>1</td>
<td></td>
<td>2</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>11</td>
<td>22</td>
</tr>
<tr>
<td>TOTAL</td>
<td>17</td>
<td>27</td>
<td>49</td>
<td>7</td>
<td>4</td>
<td>42</td>
<td>146</td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>Department</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesia and Reanimation</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Cardiology</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Haematology</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Digestive Medicine</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Internal Medicine</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Neurology</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Oncology</td>
<td>55</td>
<td>38</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Others</td>
<td>22</td>
<td>15</td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>Sponsor</th>
<th>Nº</th>
</tr>
</thead>
<tbody>
<tr>
<td>INDEPENDENT CLINICAL RESEARCH</td>
<td>34</td>
</tr>
<tr>
<td>JANSSEN-CILAG</td>
<td>8</td>
</tr>
<tr>
<td>GILEAD SCIENCES</td>
<td>7</td>
</tr>
<tr>
<td>NOVARTIS FARMACÉUTICA S. A.</td>
<td>6</td>
</tr>
<tr>
<td>BOEHRINGER INGELHEIM ESPAÑA S. A.</td>
<td>5</td>
</tr>
<tr>
<td>MERCK</td>
<td>5</td>
</tr>
<tr>
<td>PFIZER</td>
<td>5</td>
</tr>
<tr>
<td>ROCHE FARMA S. A.</td>
<td>4</td>
</tr>
<tr>
<td>TAKEDA FARMACÉUTICA</td>
<td>4</td>
</tr>
<tr>
<td>ABBVIE SPAIN, S. L. U.</td>
<td>3</td>
</tr>
<tr>
<td>ELI LILLY AND COMPANY LIMITED UK</td>
<td>3</td>
</tr>
<tr>
<td>F. HOFFMANN-LA ROCHE LTD</td>
<td>3</td>
</tr>
<tr>
<td>MILLENNIUM</td>
<td>3</td>
</tr>
<tr>
<td>ABBOTT LABORATORIES, S. A.</td>
<td>2</td>
</tr>
<tr>
<td>AMGEN INC</td>
<td>2</td>
</tr>
<tr>
<td>B. BRAUN MEDICAL S. A.</td>
<td>2</td>
</tr>
<tr>
<td>CELGENE INTERNATIONAL SARL</td>
<td>2</td>
</tr>
<tr>
<td>CONATUS PHARMACEUTICALS INC</td>
<td>2</td>
</tr>
<tr>
<td>GENENTECH INC</td>
<td>2</td>
</tr>
<tr>
<td>MEDIMMUNE LLC,</td>
<td>2</td>
</tr>
<tr>
<td>SANOFI-AVENTIS</td>
<td>2</td>
</tr>
<tr>
<td>SHIRE VIROPHARMA, INCORPORATED</td>
<td>2</td>
</tr>
<tr>
<td>OTHER INDUSTRIAL PROMOTORS</td>
<td>38</td>
</tr>
</tbody>
</table>

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.
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.
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:
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, Mª 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:** 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:** 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:** 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€

**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:** 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: 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
Initiatives for research promotion

**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 genisteina 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
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:

<table>
<thead>
<tr>
<th>Name</th>
<th>Training Center</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beatriz Alarcón Torres</td>
<td>Hospital Royal Marsden</td>
</tr>
<tr>
<td>Sara Cholvi Camarasa</td>
<td>Chu Estaing - Chu Clermont-Ferrand</td>
</tr>
<tr>
<td>María del Pilar Cordero Romero</td>
<td>Hôpital Saint Louis de Paris</td>
</tr>
<tr>
<td>Carolina Domingo Boluda</td>
<td>Universitair Medisch Centrum Groningen</td>
</tr>
<tr>
<td>Beatriz García Parreño</td>
<td>Hospital de la Sta Creu i Sant Pau</td>
</tr>
<tr>
<td>Mª Beatriz Llamusí Troisi</td>
<td>Instituto de Genética y Biología Molecular y Celular (IGBMC)</td>
</tr>
<tr>
<td>Alba Mangas Losada</td>
<td>Vu University Medical Center</td>
</tr>
<tr>
<td>Alejandro Pérez Pitarch</td>
<td>Netherlands Cancer Institute</td>
</tr>
<tr>
<td>Javier Pérez Hernández</td>
<td>Paris-Cardiovascular Research Center (Parcc)</td>
</tr>
<tr>
<td>Ignacio Pla Gil</td>
<td>Hospital General Universitario Gregorio Marañón</td>
</tr>
<tr>
<td>Anna Ramos Pachón</td>
<td>Mount Sinai Hospital</td>
</tr>
</tbody>
</table>

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
- I 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 “H2O20: 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 insulinización 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.
• Sesión HematolIncliva: “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 Colorrectal 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:** Mª 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-reperfusión 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 Nácher, 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 Nácher, 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: Mª 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): Mª 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 Ángel 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 metabólico 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): Mª José García Fuster González-Alegre, Laura Piquer Instituto, 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 Ruípérez, 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 fibrofoliculomas 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  
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  
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 Skin Cancer  
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

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 Rabada
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: 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
Initiatives for research promotion

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-endootelio.
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: Translational Research Group on Nutrition and Metabolism

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 Embryonary Stimulation

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

Group: Research Group on Male Infertility and Embryonary Stimulation

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

Group: Research Group on Male Infertility and Embryonary 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 Embryonary 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 sanguíneas, estabilidad, antropometría y dolor.

Doctoral candidate: Mª 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 postmenopáusicas 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 antimulleriana.

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 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 Chilet
Director(s): Felipe Javier Chaves Martínez
Date of the defense: 04/03/20156
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 Hermanegildo Caudevilla, Susana Novella del Campo
Date of the defense: 04/03/2016
Group: Research Group on Endothelial Cells (LINCE)

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-1β, IL-6, TNF-α, RANK-L/OPG).

Doctoral candidate: Marta Segarra Vidal
Director(s): José Mª 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 Mª Vila Salinas, Mª 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 Irles, 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 Pedriatric 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 Pedriatric 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, Mª Carmen Gómez Cabrera, Consuelo Borràs 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 Alcàñiz
Date of the defense: 30/11/2016
Group: Research Group on Aging and Physical Activity

Thesis title: Evaluación de los efectos del tratamiento con tadalafil 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, Mª Ángeles Lloret
Date of the defense: 23/12/2016
Group: Research Group on Inflammation

Doctoral candidate: Paula Escudero Díaz
Director(s): Mª 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): Mª 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

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 mlpa (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 cartilagios 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, 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, Mª 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  

Doctoral candidate: Vicente Manuel Torres Celda  
Director(s): José Gandía Franco, Rosa Cibrián Ortiz de Anda, Vicente Torres Zaragozá  
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, Mª Luisa Blasco Cortés  
Date of the defense: 01/12/2016  
Grade: Sobresaliente “cum laude”  
Group: Department of Intensive Medicine
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.

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.

Researcher from INCLIVA and the IUIVI develop a new therapy to reduce endometriosic lesions.
An international team led by INCLIVA publishes a study comparing the most used antihypertensive treatments in diabetics.
Cardiologists from INCLIVA and the Hospital Clínico 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.

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.

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 Clínico.
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.

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.

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.
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.

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.

Valencian cardiology 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 oncolgical drugs.

Oncology specialists from Colombia visit INCLIVA to learn about the latest advances and treatments in breast cancer.

INCLIVA and Hospital Clínic de Valencia host a conference about Fabry’s disease.

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 Clínic de Valencia investigate factors to improve the safety and quality of care for hospitalized children.

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.

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.
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, Fundación 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 Pon-ce, 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 then 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 CADO

Fundación Le Cadó 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 Cadó 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.
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.

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

Incliva Solidary

Corporate donations

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Health Research Institute

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