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It is a big pleasure to present the INCLIVA Annual Scientific Report 2015, which provides an assessment of the scientific activities carried out during the year 2015 by INCLIVA’s research groups. As the main novelty, the document presents this year two new chapters (highlights of the year and INCLIVA’s solidarity) and a new graphic design that we hope will contribute to show the information more attractively. INCLIVA Annual Scientific Report represents a unique opportunity 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 of all, in 2015 INCLIVA launched its new strategic plan which includes institutional goals and actions to be implemented during the next five years (2015-2019). Following External Scientific Committee specific recommendations, the plan organizes INCLIVA’s research activities around seven research programs – early cardiovascular risk in obese subjects; myocardial ischemic injury; biomarkers, rare diseases; translational oncology; endometrial receptivity and embryo viability; aging and associated diseases; and neurological impairment– and three scientific platforms – genetics and epigenetics, metabolomics and free radicals and inflammation–. These multidisciplinary disease-oriented initiatives will provide the basis for the institute’s scientific strategy of upcoming years.

Second, being aware that the processes of innovation and technology transfer require multidisciplinary collaboration among professionals from various fields, INCLIVA launched together with the University of Valencia the VLC-Bioclinic Program, an initiative whose main goal is to promote multidisciplinary translational research between researchers and practitioners from both institutions. The program funded both innovative collaborative projects and preparatory actions for cooperative research projects.

Moreover, following the efforts in the area of quality, INCLIVA was able to maintain its R&D management services and its Ethical Committee in Clinical Research (ECCR) ISO 9001:2008 certifications and expanded its quality management systems to INCLIVA’s Biobank, which was eventually certify on September. In addition, during the year the institute focused its attention to renew its accreditation as Health Research Institute by the Carlos III Health Institute since the external audit is expected to be held during the first quarter of 2016.

Scientific output during the year reached 635 papers, surpassed the barrier of 2500 impact factor at once for the very first time, and confirmed the steady tendency in recent years. It is worth noting that papers published in journals within the first and second quartiles of their respective categories have represented 53% and 20% of the total production, respectively.

Regarding scientific activities, INCLIVA’s research groups competitively secured and developed 179 research initiatives during the year, both internationally (9 projects within the 7th Framework Program and 3 non EU projects), as well as nationally (66 projects under the National R&D&I Plan) and regionally (17 projects funded by the Valencian Government). Additionally, 25 competitive grants from private funding entities were secured.

Furthermore, research groups were active in national research networks (3 Platforms, 8 CIBER and 7 RETICS). Finally, INCLIVA was able to secure a Carlos III Health Institute Excellent Integrated Project, which provided funding to develop an ambitious personalized medicine project in diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction.

Regarding clinical research activities, the Ethical Committee in Clinical Research (ECCR) has processed 120 additional trials. With the kick off of these studies, a total of 396 clinical trials and other studies were carried out during the year. In fact, 75% of these studies were clinical trials, while the remaining 25% were observational studies. It is worth noting the high relative weight of early stage clinical research, since the number of Phase I and
Phase II trials currently represent almost 31% of the studies developed at the Institute.

The present report also shows data reflecting the commitment of INCLIVA to training and transfer of biomedical research. The involvement of university research groups has resulted in high participation in graduate programmes, generating 45 doctoral theses this year. Regarding innovation and transfer activities it is noteworthy that INCLIVA joint the Patents Bank, a joint program of the Valencian Regional Government and public research organizations to promote meetings between entrepreneurs, businessmen and innovation knowledge centers, in order to facilitate technological transfer to business. Moreover, the institute was awarded by a grant for the first FIPSE call for feasibility studies of health innovation. Finally, INCLIVA’s innovation pipeline comprised, in 2015, 2 granted patents, 3 patent international extensions and 2 software records.

Among the activities to promote research culture, during 2015 INCLIVA continued with its Training Plan by collaborating with the different hospital departments in the organization and management of 62 training initiatives, including 15 courses, 8 workshops and 9 seminars and 30 conferences. In addition, as every year the Institute provided grants for research secondments in centers of excellence, that allowed 17 INCLIVA’s researchers to acquire new knowledge in clinical and research.

We cannot conclude without expressing our gratitude to all the professionals who enable INCLIVA to continue advancing. Thanks to the efforts of our over 500 researchers, 180 of which are directly hired by the Foundation, INCLIVA is able to maintain its present privileged position. However, all at INCLIVA face the challenge of continuing to generate scientific knowledge, guiding research excellence for the benefit of society and being an important part of solidarity initiatives.

Rafael Carmena Rodríguez
General Director

Josep Redón i Mas
Scientific Director
2.1. History

In the year 2000 the Foundation for the Research of the Hospital Clínico Universitario of Valencia was constituted, being 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 the INCLIVA Health Research Institute was created.

The main aims of INCLIVA are 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.
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 2015, its members are the following:

**President**
- Ms. Carmen Montón, Honorable Consellera de la Conselleria de Sanidad Universal y Salud Pública of the Valencian Government

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

**Board members according to their positions**
- Mr. Esteban Morcillo Sánchez, Most Illustrious Dean of the University of Valencia
- Mr. Federico Pallardó Calatayud, Most Illustrious Dean of the Faculty of Medicine
- Mr. José Noblejas Pérez, Valencia Chamber of Commerce
- Mr. Martín Quirós Palau, Valencian Council of Culture
- Mr. Manuel Broseta Duprè, Social Council of the University of Valencia
- Mr. Ángel Daniel Villanueva Pareja, Bancaja Foundation
- Mr. Rafael Alcón, Cañada Blanch Foundation
- Mr. Óscar Zurriaga, General Director of Research, Innovation, Technology and Quality of the Conselleria de Sanidad Universal y Salud Pública of the Valencian Government
- Ms. Dolores Salas, Secretary of the Conselleria de Sanidad Universal y Salud Pública of the Valencian Government
- Mr. Carlos Simón Vallés, Scientific Director of the Valencian Infertility Institute
- Mr. Carlos Segovia, Instituto de Salud Carlos III
- Mr. Rafael Carmena, INCLIVA General Director

**Board members in their names**
- Mr. Carlos Pascual de Miguel
- Mr. Joaquín Ortega Serrano
- Mr. Tomás Trenor Puig
- Mr. Manuel Montánchez Morera

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. They have other duties such as prepare and pass the proposals and research projects and decide and allocate the budgetary means.

Dated December 31st 2015, its members are the following:

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

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

Board members
- Prof. Rafael Carmena, INCLIVA General Director
- Prof. Josep Redón, INCLIVA Scientific Director
- Dr. Manuel Alós, Head of the Pharmacy Service, Hospital Clínic Universitario of Valencia
- Prof. Andrés Cervantes, Oncology Department, Hospital Clínico Universitario of Valencia
- Prof. Salvador Lluch, Department of Physiology, University of Valencia
- Dr. Jorge Navarro, Medical Director, Hospital Clínico Universitario of Valencia
- Prof. Salvador Lluch, Department of Physiology, University of Valencia
- Dr. Ana Sanmartín, Director of Primary Health Care, Health Service Department in Valencia Clínico-Malvarrosa
- Prof. Carlos Simón, Scientific Director, Instituto Universitario IVI
- Prof. Pascual Medina, Coordinator of Research Support Platform (UCIM), 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 appointed by the Board of Trustees 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 dyslipidaemia.

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 specialist in Internal Medicine, Research Fellow in Hypertension in Northwestern University (Chicago), 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. The Committee is constituted by well-known standing professionals among the scientific community.

The composition of the External Scientific Committee, dated December 31st 2015, is the following:

President:
• Dr. Javier Díez. Professor of Medicine, University of Navarra. Director of the Cardiovascular Sciences Area, Applied Medical Research Center (CIMA).

Members:
• Dr. José Baselga. Physician in Chief of the Memorial Sloan-Kettering of New York (U.S.A.). Professor of Medicine, Autonomous University of Barcelona. Director of the Vall d’Hebron Institute of Oncology, Barcelona.
• Dr. Juan Carlos Lacal. Research Professor in CSIC. Biomedical Research Institute, Madrid.
• Dr. Nick S. Macklon. Professor in Obstetrics and Gynecology. Division of Developmental Origins of Adult Diseases (DOHaD). University of Southampton. Princess Anne Hospital. Cuxford Road, Southampton (United Kingdom).
• Dr. José María Medina. Professor in Biochemistry and Molecular Biology. University of Salamanca. Castilla y León Neuroscience Institute (INCYL).
• Dr. Josép Tabernero. Chief of Medical Oncology Department. Vall d’Hebrón Hospital, Barcelona.
• Dr. Manuel Tena-Sempere. Professor in Cell Biology, Physiology, and Immunology Department. University of Córdoba.
• Dr. Antonio Vidal-Puig. Professor in Molecular Nutrition and Metabolism. University of Cambridge.
• Dr. Alberto Zanchetti. Professor Emeritus of Internal Medicine. Università di Milano. Director of the Istituto Auxologico Italiano (Italy). Consultant in WHO.

During 2015, the External Scientific Committee INCLIVA held two meetings: a 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 2015, 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. 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 2015, are the following:

President:
• Dr. Antonio Peláez Hernández. Head of the Allergy Unit

Vice-President:
• Dr. Marina Soro Domingo. Head of Section of the Anesthesiology and Reanimation Unit

Secretary:
• Dr. Cristina Gomis Gozalbo. Specialist of the Gynecology Department

Substitute Secretary:
• Ms. Begoña Hernández Genovés. Head of Supplies Service. Graduated in Law

Members:
• Dr. Manuel Alós Head of the Pharmacy Department
• Ms. Mª Ángeles Mora Pla. Outpatient Nursing Supervisor
• 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
• Prof. Esteban Morcillo Sánchez. Rector of the University of Valencia. Professor of Pharmacology
• Dr. Julio Palmero Da Cruz. Head of the Radiology Department
• Dr. Francisco Tosca Flores. Specialist doctor in Obstetrics and Gynecology Department
• Dr. José Álvaro Bonet Pla. Hospital Chief Executive Officer
• Ms. Cristina Pérez Moreno. Graduated in Law
• Dr. Ricardo Ruiz Granell. Head of Section of Cardiostimulation Department
• D. Diego V. Cano Blanquer. Primary Health Care Pharmaceutics. Graduated in Nursing
• Prof. Miguel Mínguez Pérez. Head of Section of Gastroenterology Department
• Dr. Francisco Dasí Fernández. Stabilized Miguel Servet Researcher
• Prof. Andrés Cervantes Ruipérez. Head of Hematology and Oncology Department
• Prof. Joaquín Ortega Serrano. Head of the General Surgery Department
• Dr. Luis González Luján. Specialist doctor in Primary Health Care
• Dr. 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

2.2.2. Management structure

In 2013 organization chart which it was approved two subdirectorates, economic and scientific, as well as a new area of innovation within the latter subdirectorate.

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

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

Administrative Area:
• Financial-Administrative Director: Mr. Juan Luis Huguet
• 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 and Ms. Vanessa Aznar
2.2.3. Scientific structure

2.2.3.1 Research areas, programs and platforms

INCLIVA articulates its research as it follows:

4 areas of research as a 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

7 scientific programs 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
• Translational oncology program
• Program in reproductive medicine
• Program in aging and its associated diseases

3 platforms based on the provision of services to the whole institute:

• Inflammation Platform
• Metabolomics Platform
• Genomics, Epigenomics and Transcriptomics Platform

2.2.3.2 Core facilities

In 2004 INCLIVA and the Central Service for Experimental Research Support (SCIE) at the University of Valencia signed a collaboration agreement. Whose aim is 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 three additional platforms: the Biobank, 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

• Biobank
• Bioinformatics unit
• Genotyping and genetic diagnosis unit
• Cytogenetics laboratory
INCLIVA
global analysis
3.1 Scientific production global analysis

INCLIVA Health Research Institute continue in 2015 with the gradual increase in the number of scientific publications produced every year. 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 635 in 2015.

The following figures show the trend in the last years, with the number and quality of the published manuscripts expressed in terms of total and cumulative impact factor.
This year the 73% of the papers published in indexed journals belong to the first and second quartiles of their corresponding thematic categories. The distribution by quartiles within their thematic categories is shown below:

One of the key factors of a biomedical research institution is the development of scientific collaborations. The number of national and international collaborations, which lead to scientific publications, it is listed below.

Another success factor is the leadership role in scientific publications. The graphic below shows the number of articles in which INCLIVA researcher signs as last author, corresponding author or both of them at the same time.
3.2. Financial resources

INCLIVA’s funding during 2015 totalled 7.685.591€. The funds raised from competitive sources in 2015 were higher than the average of recent years.

The found source in the indicated period is shown below.
Evolution of the last five periods is shown in the chart 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 2015.
### 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.

<table>
<thead>
<tr>
<th>Research Area</th>
<th>INCLIVA PI</th>
<th>Scientific Network</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>Carlos Hermenegildo Caudevilla</td>
<td>Red RIC</td>
<td>RD12/0042/0052</td>
</tr>
<tr>
<td></td>
<td>Rafael Carmena Rodríguez</td>
<td>CIBERdem</td>
<td>CB07/08/0018</td>
</tr>
<tr>
<td></td>
<td>Juan Sanchis Forés</td>
<td>Red RIC</td>
<td>RD12/0042/0010</td>
</tr>
<tr>
<td></td>
<td>Francisco Javier Chorro Gascó</td>
<td>Red RIC</td>
<td>RD12/0042/0048</td>
</tr>
<tr>
<td></td>
<td>Empar Lurbe i Ferrer</td>
<td>CIBERobn</td>
<td>CB06/03/0039</td>
</tr>
<tr>
<td><strong>Oncology</strong></td>
<td>Ana Lluch Hernández</td>
<td>RETICC</td>
<td>RD12/0036/0070</td>
</tr>
<tr>
<td></td>
<td>Samuel Navarro Fos</td>
<td>RETICC</td>
<td>RD12/0036/0020</td>
</tr>
<tr>
<td><strong>Metabolism and Organ Damage</strong></td>
<td>Esteban Morcillo Sánchez</td>
<td>CIBERes</td>
<td>CB06/06/0027</td>
</tr>
<tr>
<td></td>
<td>Federico V. Pallardó Catalayud</td>
<td>CIBERrer</td>
<td>CB06/07/0073</td>
</tr>
<tr>
<td></td>
<td>José Viña Ribes</td>
<td>Red RETICEF</td>
<td>RD12/0043/0029</td>
</tr>
<tr>
<td></td>
<td>Julio Sanjuán Arias</td>
<td>CIBERsam</td>
<td>CB07/09/006</td>
</tr>
<tr>
<td></td>
<td>Juan Vicente Esplugues Mota</td>
<td>CIBERehd</td>
<td>CB06/04/0071</td>
</tr>
<tr>
<td></td>
<td>Guillermo Sáez Tormo</td>
<td>CIBERobn</td>
<td>CB12/03/30016</td>
</tr>
<tr>
<td></td>
<td>Rafael Tabarés Seisdedos</td>
<td>CIBERsam</td>
<td>CB07/09/0021</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>Rafael Peris Bonet</td>
<td>RETICC</td>
<td>RD12/0036/0053</td>
</tr>
</tbody>
</table>
Besides research network structures, INCLIVA joined three additional research platforms promoted by Carlos III Health Institute which started their activities in 2014. These platforms are Biobank, Clinical research and trials and Innovation.

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 - 2016  
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 - 2016  
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 - 2016  
Total budget: 38.985€

3.4 Knowledge transfer to the National Health System

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

3.4.1 Knowledge transfer to the Health System

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

<table>
<thead>
<tr>
<th>Clinical guidelines</th>
<th>IF</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>117,67</td>
</tr>
</tbody>
</table>


**Committee.** Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2015 Sep;26 Suppl 5:v8-30. IF: 7,04


<table>
<thead>
<tr>
<th>Consensus documents</th>
<th>IF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>18,50</td>
</tr>
</tbody>
</table>


In addition to those published in indexed journals, INCLIVA has generated other guidelines promoted by different agencies. The following list collects these practice guidelines and the researcher involved in its preparation:


3.4.2 Knowledge transfer to industry

One of the foundational missions of INCLIVA 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 can be taken in products or processes that overcome this existing problem through research and development.

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

Plot of the INCLIVA innovation funnel in 2015 (please, note the attached plot is a suggestion)
3.4.3 Patents

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

**Granted patents**

- **Title:** Ex-vivo method for the early diagnosis of minimal hepatic encephalopathy by means of the determination of 3-nitrotyrosine in serum  
  **Inventors:** Vicente Felipo Orts; Omar Caulí; Carmina Montoliu Félix  
  **Applicants:** INCLIVA, CIPF  
  **Publication number:** EP20110806343  
  **Priority Date:** 2010/07/12  
  **Territory:** Europe (registered in Spain, United Kingdom, France, Germany and Italy).

- **Title:** Maxillomandibular prosthesis and production method  
  **Inventors:** M. Puche, V. Petrovic, JA. Gómez, JR. Blasco, L. Portolés, J. Ferrís, C. Atienza.  
  **Applicant:** INCLIVA, Instituto de Biomecánica de Valencia y Asociación de Investigación dela Industria Metal Mecánica, Afnies and Conexas.  
  **Publication number:** ES20130030734  
  **Priority Date:** 2013/05/21  
  **Territory:** Spain

**Patent application extensions**

- **Title:** Maxillomandibular prosthesis and method of manufacture  
  **Inventors:** M. Puche, V. Petrovic, JA. Gomez, JR. Blasco, L. Portolés, J. Ferrís, C. Atienza.  
  **Applicant:** INCLIVA, Instituto de Biomecánica de Valencia y Asociación de Investigación dela Industria Metal Mecánica, Afnies and Conexas.  
  **Application number:** EP14800737.0  
  **Priority Date:** 2013/05/21  
  **Territory:** Europe (EPC)

- **Title:** Compound for treatment of myotonic dystrophy type 2  
  **Inventors:** R. Artero, A. Bargiela, B. Llamusí, JM. Fernández Costa, M. Pérez  
  **Applicant:** Universidad de Valencia  
  **Application number:** PCT/EP2015/080508  
  **Priority Date:** 2014/12/18  
  **Territory:** PCT

- **Title:** Early detection of preeclampsia  
  **Inventors:** C. Simón C, T. Garrido, A. Pellicer  
  **Applicant:** IVI  
  **Application number:** WO2015166353  
  **Priority Date:** 2014/03/21  
  **Territory:** PCT

**Software**

- **Title:** HADA: diagnostic tool for angina pectoris.  
  **Authors:** Joan Vila Francés, Emilio Soria, Antonio Serrano López (Universitat de Valencia), Juan Sanchís Forés and Julio Núñez Víllota (INCLIVA).  
  **Register date:** 19/01/2015.

- **Title:** ANGIOPATHSW software for morphometric detection and characterization of blood and lymphatic vessels.  
  **Authors:** María Gloria Bueno García, D. Óscar Déniz Suárez (Universidad de Castilla la Mancha) Maria Rosa Noguera Salvá, Irene Tadeo Cervera (INCLIVA) and Marcial García Rojo (Servicio Andaluz de Salud)  
  **Register date:** 02/18/2015
Scientific activity
4.1. Research areas

INCLIVA Health Research Institute has four research areas to organize its scientific activity. Despite their independence, there 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 the attached researchers. Each of the lines counts on the participation of one or several advisers from the External Scientific Committee, and 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

To give an overview of the scientific production per area it shows several indicators.

The following figure shows the main key performance indicators of INCLIVA’s four research areas and other scientific contributions from the Hospital Clinico of Valencia.

Since there are some scientific articles which are shared by two or more areas, it is worth mentioning that the sum of the number of publications by area exceeds INCLIVA’s total scientific output.

Additionally, the next table shows scientific publications distribution by area in terms of number of articles and impact factor.
4.1.1 Cardiovascular Area

Research Group on Cardiometabolic Risk
Genotyping and Genetic Diagnosis Unit (UGDG)
Research Group on Cardiac Experimental Electrophysiology
Research Group on Endothelial Cells (LINCE)
Research Group on Clinical Cardiology
Research Group on the Study of Cardiovascular Risk in Children and Adolescents
Cardiometabolic Research Group on Primary Care
Research Group on the Study of Cardiometabolic and Renal Risk
Research Group on Vascular Function
Research Group on Pediatric Nutrition
Group on Translational Research in Ischemic Heart Disease
Research Group on Cardiometabolic Risk.
Consolidated group

“Tenemos mucho que hacer contra esta enfermedad y todos tenemos la posibilidad de cambiar hábitos de vida para prevenir el desarrollo de la diabetes”
Dr. Juan Ascaso. Elperiodico.com 13/11/2015

Team involved in

Group members
Principal investigator
Juan Francisco Ascaso Gimilio. Hospital. University
H Index: 25

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

PhD students
Griselda de Marco Solar. INCLIVA

Technicians
Cristina Pérez Soriano. INCLIVA
Ana Albert Viguera. INCLIVA

Emerging researchers
Sergio Martínez Hervás. Hospital. University
Ana Bárbara García García. CIBERdem
Strategic aims

- Study of autosomal dominant hypercholesterolemias and familial combined hyperlipidemia. An analysis of inflammation markers has been performed, as well as a comprehensive biochemical profile and a collection of clinical and genetic characteristics.
- Effect of postprandial lipidemia on cardiovascular system, mainly on lipid profile, inflammation markers and oxidative stress and the response of circulating cells to stress caused by lipidemia. Studies of oral lipid overload in obese diabetic patients have been carried out to study cell response to fatty acid delivery. Expression of all genes present in the lymphomonocytes of these patients has been examined comparing with control subjects and the results are currently being analyzed.
- Study of insulin resistance and diabetes. The aim is to early detect insulin-resistance, identifying early detection markers and risk and inflammatory factors linked to this condition.
- Diagnosis and treatment of diabetic foot. Confirmation of the connection between plasma homocysteine levels and risk for diabetic foot ulceration.
- Genetic factors involved in the regulation of Body Mass Index (BMI), waist circumference, obesity development and central obesity. Study of oxidative stress and other aspects of metabolism as factors able to modulate development of obesity. Levels of certain free radicals and oxidative stress regulate metabolism and energy homeostasis.

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.

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


• THESIS

Thesis title: Sobrecarga oral con grasa insaturada y estrés oxidativo en sujetos con obesidad abdominal
Doctoral candidate: María Inmaculada Navarro Hidalgo
Director(s): Sergio Martínez Hervás, Rafael Carmena Rodríguez
Date of the defense: 16/10/2015
Grade: Sobresaliente “cum laude”

Thesis title: Identificación de variantes exónicas en diabetes tipo 2
Doctoral candidate: Vanessa Martínez Barquero
Director(s): Juan F. Ascaso Gimilio, Mª Antonia Noguera Romero, Felipe Javier Gavés Martínez
Date of the defense: 05/06/2015
Grade: Sobresaliente “cum laude”

Thesis title: Análisis de la relación del genotipado y marcadores de estrés oxidativo con la presencia y grado de vasculopatía periférica en pacientes con diabetes tipo 2
Doctoral candidate: José Francisco Folgado Montesinos
Director(s): José Tomás Real Collado, Juan F. Ascaso Gimilio
Date of the defense: 14/04/2015
Grade: Sobresaliente “cum laude”

Thesis title: Estudio del estrés oxidativo en la polineuropatía diabética
Doctoral candidate: Mercedes Molina Méndez
Director(s): José Tomás Real Collado, Juan F. Ascaso Gimilio
Date of the defense: 14/04/2015
Grade: Sobresaliente “cum laude”
Thesis title: Efecto del género y parámetros antropométricos en marcadores de estrés oxidativo e inflamación en situación postprandial
Doctoral candidate: Jordi Ferri Císcar
Director(s): José Tomás Real Collado, Juan F. Ascaso Gimilio
Date of the defense: 28/04/2015
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 gastointestinal en sujetos con obesidad grave-mórbida
Principal Investigator: Rafael Carmena Rodríguez
Funding Body: Conselleria de Educación, Cultura y Deporte
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2014-2018
Total Budget: 48.000€

Reference: ISIC/2012/018
Title: Instituto Superior de Investigaciones Científicas INCLIVA
Principal Investigator: Rafael Carmena Rodríguez
Funding Body: Conselleria de Educación, Cultura y Deporte
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2014-2018
Total budget: 35.550€

Reference: CB07/08/0018
Title: CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERdem)
Principal Investigator: Rafael Carmena Rodríguez
Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2007-2016

Reference: PI12/01978
Title: Association of insulin resistance and oral fat load test with DNA methylation of adipocytes and hepatocytes in subjects with morbid obesity
Principal Investigator: José Tomás Real Collado
Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 121.000€

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

Group members

**Principal investigator**
Felipe Javier Chaves Martínez.
INCLIVA
H Index: 19

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

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

**Post-doctoral researchers**
Raquel Cortés Vergaz. INCLIVA

**Technicians**
Sebastián Blesa Lujan. INCLIVA
Verónica González Albert. INCLIVA
Victoria Adam Felici. INCLIVA
Azahara Mª Fuentes Trillo. INCLIVA
**Strategic aims**

- Detection of more polymorphisms with 250 functional and infrequent strong effect on the population potentially 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
- To determine the changes in gene expression in different groups of patients after oral lipid overload
- To determine the relationship between different genes, essential metals and pollutants in relation to diseases with high cardiovascular risk
- To determine the relationship between different polymorphisms in genes involved in the regulation of oxidative stress and the risk of breast cancer
- To improve methodology for different genetic studies
- To develop procedures for obtaining libraries

**Main lines of research**

- To detect genetic changes (mutations or polymorphisms) involved in the development of complex diseases with high cardiovascular risk, particularly related to oxidative stress, lipid metabolism, genes, etc.
- To study genetic variants in the exome in relation to the development of type 2 diabetes and its consequences
- To study the importance of environmental pollutants in the development of human diseases, mainly about heavy metals in relation to complex diseases with high cardiovascular risk

**PUBLICATIONS**

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**Original articles**


Review


• 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: PI12/01978
Title: Association of insulin resistance and oral fat load test with DNA methylation of adipocytes and hepatocytes in subjects with morbid obesity
Principal Investigator: José Tomás Real Collado (Verónica González and Victoria Adam as collaborating researchers)
Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 121.000€

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€

• THESIS

Thesis title: Identificación de variantes exómicas en diabetes tipo 2
Doctoral candidate: Vanessa Martínez Barquero
Director(s): Juan F. Ascaso Gimilio, Mª Antonia Noguera Romero, Felipe Javier Chaves Martínez
Date of the defense: 05/06/2015
Grade: Sobresaliente “cum laude”
Thesis title: Identificación de los perfiles de expresión en el adenocarcinoma ductal de páncreas. Implicaciones clínicas.

Doctoral candidate: María Del Carmen Gómez Mateo

Director(s): Felipe Javier Chaves Martínez, Antonio Ferrández Izquierdo, Luis Sabater Ortí

Date of the defense: 08/07/2015

Grade: Sobresaliente “cum laude”
Research Group on Cardiac Experimental Electrophysiology
Consolidated group

Group members
Principal investigator
Francisco Javier Chorro Gascó. Hospital, University
H Index: 22

Team involved in

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

PhD students
Laia Brines Ferrando. INCLIVA
Irene del Canto Serrano. INCLIVA
Carlos Soler López. University
Scientific activity

Strategic aims

- Publication of the results obtained by modifying the electrophysiological effects of myocardial stretching by EIPA, losartan, BQ-123, and ranolazine
- Continuation of the experimental series to analyze the effects of JTV519, KN-93, Carvedilol and analogues
- Continuation of the analysis of the effects of modifications of the basic electrophysiological properties on the processes involved in the initiation, perpetuation and the cessation of ventricular fibrillation
- It has continued the 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 analysis of cardiac electrophysiological signals obtained with mapping systems
- Home of the research 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 in rabbit hearts

Main lines of research

- Myocardial stress: 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 beginning, perpetuation and cessation 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 electrophysical signals based on multielectrodes and optical cartography systems able to analyze voltage and calcium signals

- Study the mechanisms involved in the deterioration of the systolic function, fibrosis and the inducibility of arrhythmias in a chronic model of infarction in rabbit hearts

PUBLICATIONS

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Original articles


**THESIS**

_Thesis title:_ Estudio de las modificaciones farmacológicas de los efectos electrofisiológicos producidos por el estiramiento local miocárdico a partir de técnicas dinámicas de cartografía eléctrica en un modelo experimental de corazón aislado de conejo.

_Doctoral candidate:_ Irene del Canto Serrano

_Doctor(s):_ Francisco J. Chorro Gascó, David Moratal

_Date of the defense:_ 29/01/2015

_Grade:_ Sobresaliente “cum laude”

_Thesis title:_ Diagnóstico precoz de la neumonía asociada al ventilador. Evaluación seriada de biomarcadores en minilavado broncoalveolar y monitorización microbiológica, complementada con condensado de aire exhalado y sangre.

_Doctoral candidate:_ Santiago Borrás Pallé

_Doctor(s):_ José Blanquer Olivas, Francisco Javier Chorro Gascó, Manuel Mata Roig

_Date of the defense:_ 24/04/2015

_Grade:_ Sobresaliente “cum laude”

_Thesis title:_ Beneficios de la terapia de resincronización cardíaca en pacientes con severa disfunción y dilatación ventricular izquierda en la insuficiencia cardíaca leve respecto a la avanzada.

_Doctoral candidate:_ Mónica Giménez Alcalá

_Doctor(s):_ Francisco Javier Chorro Gascó, Aurelio Quesada Dorador

_Date of the defense:_ 23/04/2015

_Grade:_ Sobresaliente “cum laude”

_Thesis title:_ Estudio de la posible participación de la corriente iKATP en las modificaciones que sobre estabilidad y heterogeneidad miocárdica produce el ejercicio físico crónico, en corazón aislado, normalmente oxigenado y tras isquemia regional aguda.

_Doctoral candidate:_ Manuel Koninckx Cañada

_Doctor(s):_ Luis Such Belenguer, Germán Parra Giraldo, Luis Such Miquel

_Date of the defense:_ 30/01/2015

_Grade:_ Sobresaliente “cum laude”

**RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

_Reference:_ PI12/00407

_Title:_ Utilidad de la estabilización de la homeostasis del calcio intracelular en el control de los procesos fibrilatorios

_Principal Investigator:_ Francisco Javier Chorro Gascó

_Funding body:_ Instituto de Salud Carlos III

_Beneficiary Institution:_ Fundación Investigación del Hospital Clínico Universitario de Valencia

_Duration:_ 2013-2015

_Total budget:_ 79.000€

_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:_ 2013-2015

_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
Clinico Universitario de Valencia
Duration: 2014-2018
Total budget: 33.000€ (this year)

Reference: UV-INV-PRECOMP14-206372
Title: Estudio del remodelado eléctrico cardíaco producido en un modelo experimental de síndrome metabólico y su implicación en la génesis de arritmias.
Principal Investigator: Manuel Zarzoso Muñoz
Funding body: Universitat de Valencia
Beneficiary Institution: Fundación Investigación del Hospital Clínico Universitario de Valencia
Duration: 2014-2015
Total budget: 10.913€
Research Group on Endothelial Cells (LINCE)
Consolidated group

Group members
Principal investigator
Carlos Hermenegildo Caudevilla.
University
H Index: 26

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

- The advance of the FIS PI13/00617 research project has solved the difficulty on the array analysis of miRNA profile in endothelial cells and the main results were checked. The recruitment of patients is ongoing and the follow up was enlarged up to one year
- To complete the effects induced by oxidized low density lipoprotein on endothelial transcriptomic profile and to publish
- To complete and to publish the first part of the Procell study in collaboration with 8 different groups of the Red de Investigación Cardiovascular on the time-course of mobilization of endothelial progenitor cells in acute cardiovascular events (acute myocardial infarction and stroke)
- In the murine model of senescence, we have demonstrated a decreased availability of nitric oxide in aorta from ovariectomized senescence mice involving cyclooxygenases (manuscript is in press)

Main lines of research

- Gender difference in cardiovascular area
- Vascular effects of sex hormones
- Identification of new hormone-regulated signalling pathways 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

The research is focused in the study of endothelial dysfunction associated with aging and lack of estrogen. During aging are produced mechanical and functional alterations in the arterial wall which leads 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

- **AWARDS**

The Investigator Carlos Hermenegildo was awarded “Alberto Ferrari prize” to the best poster in 25th European Meeting on Hypertension and Cardiovascular Protection celebrated in Milan in 2015.

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

Fig 2: Superoxide production in murine arteries
Research Group on Clinical Cardiology
Consolidated group

“Realizar un artículo supone un gran esfuerzo e implica dedicarle mucho tiempo. Desde luego, hace falta una gran capacidad de trabajo.”
Juan Sanchis, CardioTeca. 7-6-2015

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

Collaborating researchers
Vicente Ruiz Ros. Hospital. University
Sergio Garcia Blas. Hospital. University
Ernesto Valero Picher. Hospital
Gemma Miñana Escrivá. Hospital

PhD students
Estefanía Montalvo Torró. INCLIVA
Anna Mollar Fernández. INCLIVA

Emerging researchers
Julio Núñez Villota. Hospital. University

Team involved in


### Strategic aims

- To consolidate the research in acute coronary syndromes and heart failure

### 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**


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**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


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: 2013-2015
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€
Research Group on the Study of Cardiovascular Risk in Children and Adolescents
Consolidated group

Group members

Principal investigator
Empar Lurbe i Ferrer.
University
H Index: 24

Team involved in

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

Technician
Francisco Ponce Zanón. CIBERobn

Administrative assistant
Rachael Dix. CIBERobn
Scientific activity

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


Letter


Editorial

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: IPT-2011-0824-90000
Title: INNPACTO Plataforma IntegNeo
Principal Investigator: Empar Lurbe i Ferrer
Funding body: Ministerio de Ciencia e Innovación
Beneficiary institution: Consorcio Hospital General Universitario de Valencia
Duration: 2012-2014
Total budget: 99,689€

Reference: InTecMedic
Title: Investigación clínica y tecnología médica personalizada para prevención, diagnóstico y terapia
Principal Investigator: Empar Lurbe i Ferrer
Funding body: Microcluster
Beneficiary institution: Consorcio Hospital General Universitario de Valencia
Duration: 2011-2015

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: Conselleria de Educación, Formación y Ocupación
Beneficiary institution: Consorcio Hospital General Universitario de Valencia
Duration: 2012-2016
Total budget: 135,000€

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: Universidad de Valencia
Duration: 2012-2016
Total budget: 794,000€

Reference: 120022/14
Title: Desarrollo de un plan de transferencia de un prototipo de análisis de la capacidad cardiorrespiratoria y su aplicación en la prevención y el tratamiento de la obesidad infantil
Principal Investigator: Empar Lurbe i Ferrer
Funding Body: FIPSE
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2015 - 2016
Total budget: 25,000€

Reference: PI14/01781
Title: Impacto del peso al nacer y la ganancia ponderal postnatal en la disfunción endotelial e inflamación vascular
Principal Investigator: Empar Lurbe i Ferrer
Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2015 - 2017
Total budget: 113,135€

• AWARDS

In 2015 Empar Lurbe received the Pronokal award to support the research to prevent childhood obesity. Another member of the group, Francisco Aguilar, was awarded with the López Trigo Prize.
Cardiometabolic Research Group on Primary Care
Consolidated group

Group members

Principal investigator
Jorge Navarro Pérez.
Clínico-Malvarrosa Health Department
H Index: 24

Collaborating researchers
Jose Vicente Lozano Vidal. Clínico-Malvarrosa Health Department
Alvaro Bonet Pla. Clínico-Malvarrosa Health Department
Victoria Gosalbes Soler. Clínico-Malvarrosa Health Department
Carlos Fluixá Carrascosa. Clínico-Malvarrosa Health Department
Nidia Ruiz Varea. Clínico-Malvarrosa Health Department
Pilar Roca Navarro. University. Clínico-Malvarrosa Health Department
Gaspar Sánchez Vela. Clínico-Malvarrosa Health Department
José Sanfélix-Genovés. Clínico-Malvarrosa Health Department
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 – 2015
Research Group on the Study of Cardiometabolic and Renal Risk
Consolidated group

“Hacer investigación y desarrollar tratamientos que curan o, cuando menos, que mejoran la calidad de vida de estos enfermos es el principal objetivo de nuestros investigadores.”

Josep Redon i Más. Bioval.org, 21-02-2015

http://www.bioval.org/2015/02/24/incliva-y-la-universitat-de-valencia-crean-el-primer-centro-de-enfermedades-raras-de-ambito-autonomico-2/

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
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. Téllez-Plaza's research interest is in 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**


Review


Letter


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: 2011-2015
Total budget: 370.000€

Reference: CB06/03/0039
Title: CIBER de obesidad y trastornos de la nutrición
Principal Investigator: Empar Lurbe i Ferrer (Josep Redón i Mas as collaborating research)
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Fundación Investigación Hospital General Universitario de Valencia
Duration: 2007-2016

Reference: PI12/02615
Title: Podocitos y sus componentes como biomarcadores de lesión en hipertensión arterial, diabetes y obesidad
Principal Investigator: Josep Redón i Mas
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2016
Total budget: 270.000€

Reference: CP12/03080
Título: DNA Methylation and Hydroxymethylation, Metal Exposure and Cardiovascular Risk: an Epidemiologic Study
Principal Investigator: María Téllez Plaza
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Fundación Investigación del Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 60.750€

Reference: COST Action TD0905
Title: Epigenetics: Epigenetics: Bench to Bedside
Principal Investigator: Arasu Ganesan (María Téllez as collaborating researcher)
Funding body: European Commission
Beneficiary institution: University of East Anglia, Norwich Research Park (UK)
Duration: 2010-2015

Reference: AFI
Title: Desarrollo de la Unidad de Gestión de Proyectos Internacionales
Principal Investigator: Josep Redón i Mas
Funding Body: Conselleria de Sanidad
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2014-2015

Title: Estudio metabolómico de lípidos intra-miocelulares en preobesidad.
Principal Investigator: Fernando Martínez García
Funding Body: Fundación ERESA
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2014-2015
Total budget: 16.000€

Title: Deterioro neurocognitivo (DNC) en mujeres VIH positivo. (Parte II)
Principal Investigator: Mª José Galindo Puerto
Funding Body: Janssen - Cilag S.A.
Program: Research Fellowship Program
Fellow: Ramón Ferrando Vilalta
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2014 - 2015
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
**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**


**Review**

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
Elena Martínez Arias. Hospital
Virtudes Molina Sevilla. Hospital
Javier Estañ Capell. Hospital. University
Laura Martínez Rodríguez. Hospital
Strategic aims

• To measure the vascular changes by Doppler ultrasound and its correlation with the metabolic alterations in cardiovascular risk children
• To quantify norovirus-specific antibodies and their blocking activity on the binding of norovirus-like particles of Caco-2 and / or saliva cells. To relate it with the results with the ABO blood group, the secretory phenotype mother and Lewis antigen. To analyze the composition of the microbiota in human milk longitudinal samples in term and preterm infants
• To analyze the nutritional response of home support and to apply validated systems to measure their impact on the quality of life of patients and their caregivers

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. Wanden-Berghe C, Pereira Cunill JL, Cuerda Compes C, Moreno Villares JM, Pérez de la Cruz A, Burgos Peláez R, Gómez Candela C, Virgili Casas N, Penacho Lázaro MA,


**RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: SAF2012-38368
Title: Especificidad de receptores y antigenicidad de variantes epidérmicas de norovirus genotipo GII.4 causantes de gastroenteritis aguda
Principal Investigator: Javier Buesa Gómez (Cecilia Martínez Costa as collaborating researcher)
Funding body: Ministerio de Economía y Competitividad
Beneficiary institution: Universidad de Valencia
Duration: 2013-2015
Total budget: 42.000€

Title: Búsqueda de las bases genéticas no descritas hasta el momento en la abetalipoproteinemia mediante secuenciación de exoma
Principal Investigator: Ana Bárbara García García (Cecilia Martínez Costa as collaborating researcher)
Funding body: Fundación Mutua Madrileña
Beneficiary institution: CIBERdem
Duration: 2013-2015
Total budget: 14.700€

**THESIS**

Thesis title: Análisis de los factores epidemiológicos y clínicos implicados en el desarrollo de la enterocolitis necrosante
Doctoral candidate: Laura Martínez Rodríguez
Director(s): Cecilia Martínez Costa, Javier Estañ Capell, Juan Brines
Date of the defense: 17/11/2015
Grade: Sobresaliente “cum laude”

Thesis title: Adaptación cultural y validación de la escala de valoración de riesgo de desarrollar úlceras por presión en neonatos hospitalizados (Neonatal Skin Risk Assessment Scale).
Doctoral candidate: Pablo García Molina
Director(s): José Verdú Soriano, Francisco Pedro García-Fernández.
Date of the defense: 23/10/2015
Grade: Sobresaliente “cum laude”
Group on Translational Research in Ischemic Heart Disease
Consolidated group

Group members

Principal investigator
Vicente Bodí Peris.
Hospital. University
H Index: 24

Collaborating researchers
Clara Bonanad Lozano. INCLIVA. Hospital
Amparo Ruiz Saurí. University
Jose Vicente Monmeneu Menadas. Eresa
Eva Rumiz Gómez. Hospital
David Moratal Pérez. UPV
José Gavara Doñate. INCLIVA
Nerea Pérez Solé. INCLIVA

Predoctoral researchers
Arantxa Hervás Lorente. INCLIVA

Technicians
Ana Díaz Cuevas. University
Elena de Dios Lluc. INCLIVA
Scientific activity

Strategic aims

• To focus into a translational approach
• To continue dilucidating the physiological role of the immune dysregulation. Indeed we have deeply elucidated the macroscopic, microscopic and molecular changes in the fibrotic process after a myocardial infarction by using a swine model
• To develop new tools to study patients with myocardial infarction using magnetic resonance imaging
• To advance in basic mechanisms, diagnosis, prediction and prevention of cardiac damage in reperfused acute myocardial infarction

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 stress cardiac MRI
• Porcine model of experimental myocardial ischemia and myocardial infarction. To achieve a better understanding of the pathophysiology of ischemia, necrosis, fibrosis and reperfusion injury and test novel
• Involvement in several large international multicenter clinical trials in the field of acute coronary syndromes

• PUBLICATIONS

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Original articles


Letter


• 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: PIE15/00013
Title: Estudio prospectivo para el análisis de la fibrosis cardíaca mediante resonancia magnética cardíaca usando la secuencia T1 mapping
Principal Investigator: Vicente Bodí Peris
Funding Body: Instituto de Salud Carlos III Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2015 - 2018
Total Budget: 589.050€

Reference: FPU12/01140
Title: Diagnóstico y pronóstico de enfermedades cardiovascular 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€

• THESIS

Thesis title: Estudio de la afectación del ventrículo derecho en el infarto anterior reperfundido.
Doctoral candidate: Eva Rumiz González
Director(s): Vicente Bodí Peris
Date of the defense: 21/12/2015
Grade: Sobresaliente “cum laude”
• AWARDS

On 2015, Vicente Bodí was awarded by the Cardiac Imaging Section of the Valencian Society of Cardiology for his work “Predicción de eventos cardíacos mayores a largo plazo mediante resonancia magnética cardíaca tras un infarto agudo de miocardio con elevación del segmento ST”. Moreover, he was also awarded by the Real Academia de Medicina de la Comunidad Valenciana for the scientific work “Proof-of-concept methodology for studying the effect of ischemic-reperfusion injury on microvascular obstruction in myocardial samples of an in vivo model of myocardial infarction”.

Fig 1: The group led by Dr. Bodí 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, you can study the inflammatory process and the degree of fibrosis at different levels: macroscopic, microscopic, cell, gene expression and protein and through magnetic resonance microimage.
### 4.1.2 Oncology Area

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**Impact Factor (IF)**
- Total: **1,019.80**
- Average: **6.18**

**JCR:**
- 61 in D1
- 93 in Q1
- 31 in Q2

**Author:**
- 34 first author
- 48 last author
- 41 corresponding author

**165 Publications**

**69 International collaborations**

**Pie Chart**
- Original articles: 133
- Letters: 18
- Editorial: 7
- Clinical guidelines: 5
- Review: 2
Research Group on Histopathology and Tissue Engineering
Consolidated group

Group members

Principal investigator
Carmen Carda Batalla
University
H Index: 20

Collaborating researchers
Amando Peydró Olaya. Hospital. University
Amparo Ruiz Sauri. University
María Sancho-Tello Valls. University
José Javier Martín de Llano. University
Manuel Mata Roig. University
Lara Milian Medina. INCLIVA
Teresa Sagrado Vives. University
Miguel Armengot Carceller. University
Carlos Tejerina Botella. Hospital
Miguel Puche Torres. Hospital
Mari Fe Miguez Rey. Hospital
Genaro Galán Gil. Hospital
Antonio Silvestre Muñoz. Hospital
Francisco Forriol Brocal. University
Antonio Fons Font. University
Rosa María Cibrian Ortiz de Anda. University
Santiago Peydró Tomas. University

PhD students
Esperanza Núñez Benito. University
María Oliver Ferrándiz. University
Javier Alcácer Fernández-Coronado. University
Strategic aims

- In relation to the line of Tissue Engineering we have secured funding to continue working on regeneration techniques cartilage and bone
- A project in relation to micro-cluster of Dentistry was also secured in order to investigate possible modifications of titanium as a biomaterial in different dental therapies
- We provide publications, theses and attending conferences of which are derived that guarantee the trajectory in this annuity

Main lines of research

Regenerative medicine:

- Study of cartilage regeneration
- Study of bone regeneration
- Study of 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 tumours
- Study of ciliary pathology
- Study of endometriosis

PUBLICATIONS

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Original articles


modulated by Ole e 1-derived peptides. Mol Immunol. 2015 Apr;64(2):252-61. IF: 2,973


**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:** Redes Excelencia
**Title:** Red de investigación para el desarrollo de implantes de titanio funcionalizados, BIOIMPLANT
**Principal Investigator:** José Luis Gómez Ribelles (Carmen Carda as collaborating researcher)
**Funding Body:** Ministerio de Economía y Competitividad
**Beneficiary Institution:** Universidad de Valencia
**Duration:** 2014-2015

**Reference:** Intramural BBN
**Title:** Biofunctionalization of titanium implant surfaces: protein conformation, osseointegration and antimicrobial activity (BIO-SURFACES)
**Principal Investigator:** José Luis Gómez Ribelles (Carmen Carda as collaborating researcher)
**Funding Body:** CIBERBbn
**Beneficiary Institution:** Universidad de Valencia
**Duration:** 2014-2015

**Reference:** 07_EQ-BIO-2015
**Title:** Diseño de una plataforma experimental basada en la microbalanza electroquímica de cristal de cuarzo (EQCM) para el desarrollo y ensayo in-vivo de nuevas aleaciones biomédicas

**Principal Investigator:** Carmen Carda Batalla
**Funding Body:** Ministerio de Educación, Cultura y Deporte
**Beneficiary Institution:** Universidad de Valencia
**Duration:** 2015

**Reference:** Programa VLC-BIOCLINIC Subprograma A
**Title:** Soportes tridimensionales biodegradables basados en micropartículas 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

**AWARDS**

On December, Carmen Carda Batalla received the “Premio Real Academia de Medicina de Andalucía Oriental”.

VLC- Bioclinic Project: articcular cartilage regeneration using biodegradable microparticles
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

- Clinicopathological study of 20 patients with primary GBM. To collect samples (formol, freezing, crop pickup means). To conduct tissue arrays of 20 tumors; neuropathological, immunohistoquimic and FISH study matrix according to established methodology
- To realize tissue cultures of short duration and feasibility analysis; FISH analysis of EGFR status and freezing of the different countries according to established methodology
- To study molecular genomic analysis of the 20 tumours (frozen samples) MLPA techniques, sequencing and RT-qPCR analysis of gene alterations and mRNA expression and miRNAs is performed according to established methodology
- To do proteomic analysis of 20 tumors (frozen samples) by Western blot methodology
- To start an experimental study. Analysis of situations

### Main lines of research

- Primary GBM. Amplification status of EGFR and angiogenic/infiltrative phenotype. Molecular networks responsible for tumour 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

### Original articles


• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PROMETEO/2011/083
Title: Papel del 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 Valencia
Duration: 2011-2015
Total budget: 42,100€

Reference: PI13/02786
Title: Implicación de los microRNAs 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: Instituto de Salud Carlos III
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2014-2016
Total Budget: 59,592€

Reference: PI14/01669
Title: Interacción de miRNA en la infiltración y perfiles de MMPI 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€

• AWARDS

Lisandra Muñoz Hidalgo had received the Innovation Award Genetics, an award given each year for the Cátedra Universitat de Valencia/Fundación Sistemas Genómicos. L. Muñoz: “This prize gives me strength to continue investigating.”
Research Group on Colorectal Cancer and New Therapeutical Developments in Solid Tumours
Consolidated group


Group members

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

PhD students
Marta Llorca Cardeñosa. INCLIVA
Sara Oltra Sanchís. INCLIVA

Collaborating researchers
Jose. A. Pérez Fidalgo. Hospital
Amelia Insa Mollá. Hospital
Susana Roselló Keranen. Hospital
Desamparados Roda Pérez. INCLIVA
Inma Blasco Blasco. INCLIVA
Estefania García Botello. Hospital
Alejandro Espí Macías. Hospital. University
Maider Ibarrola Villava. INCLIVA
Josefa Castillo Aliaga. INCLIVA
Ana Isabel Gil Tébar. INCLIVA
Marcelino Telechea Fernández. INCLIVA
Marisol Huerta Álvaro. Hospital
Noelia Tarazona Llavero. Hospital
Gema Bruixola Campos. Hospital
María Carolina Martínez Ciarpaglini. INCLIVA

Emerging researchers
Gloria Ribas Despuig. INCLIVA

Technicians
Cristina Mongort Sanchís. INCLIVA

Administrative assistant
Gabriela Perez Garity. INCLIVA
Emerging researcher

Gloria Ribas Despuig

My scientific interests are based both on the study of the genetic susceptibility to complex diseases as well as on the study of genomics deregulation in solid tumours.

In relation to genetic susceptibility, we have unravelled new variants associated to sporadic melanoma susceptibility. The group has contributed to the study of variants in pathways related to pigmentation, DNA repair after UV irradiation and oxidative stress. Some of the more relevant results are the study of the genetic variation of MC1R (melanocortin receptor 1, the most important gene predisposing to susceptibility to sporadic melanoma) and the identification of new genes associated to this disease, the most important has been SLC45A2.

During 2015 we have investigated the role of genetic variation in TERT related genes and their association to telomerase length and to melanoma. We have several ongoing studies in collaboration with international groups and the consortium M-SKIP.

As for the genomic deregulation in solid tumours, 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 out several studies with microRNA expression, methylation, IHQ staining and bioinformatics analysis to validate our data. 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.

In collaboration with Dr. Cervantes we have set up the mutational screening of solid tumours in 25 oncogenes (287 hotspots) with the Mass Array-Sequenom platform at the Faculty of Medicine. Up to now we have screened more than 150 tumours from several oncologic pathologies: colorectal, breast, ovarian, gastric, melanoma, etc.

### Strategic aims

- To implement strategies in order to facilitate precision medicine development in solid tumours with innovative therapeutic approaches
- To provide knowledge on how to approach precision medicine in colorectal and gastric cancer: molecular classification, predictive biomarkers and innovative therapeutic approaches

### 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

### PUBLICATIONS

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**Original articles**


Letter


Editorial


**Clinical guidelines**


**THESIS**

**Thesis Title:** Resonancia magnética pélvica dinámica versus videodefecografía en el estudio del síndrome de defecación obstrutiva.

**Doctoral candidate:** Gonzalo Martín Martín
Director(s): Alejandro Espí Macías, José Vicente Roig Vila, Juan García Armengol
Date of the defense: 13/10/2015
Grade: Sobresaliente “cum laude”

Thesis Title: Cirugía del cáncer de colon. Análisis de los resultados en una unidad especializada.
Doctoral candidate: Gloria Gema Báguena Requena
Director(s): Eduardo García Granero Ximenez, Alejandro Espí Macías, Andrés Cervantes Ruipérez
Date of the defense: 21/09/2015
Grade: Sobresaliente “cum laude”

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI12/02767
Title: Hyperacetylation of heterogeneous nuclear riboproteins (hnRNPs) as a final pathway to resistance to antiEGFR agents in colorectal cancer
Principal Investigator: Andrés Cervantes Ruipérez
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 74.415€

Reference: PROMETEO/2013/005
Title: Estudio traslacional sobre la hiperacetilación de proteínas como vía final de resistencia a fármacos anti-EGFR en cánceres de alta incidencia clínica
Principal Investigator: Andrés Cervantes Ruipérez
Funding body: Conselleria de 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: Molecularly guided trials with specific treatment strategies in patients with advanced newly molecular defined subtypes of colorectal cancer (MoTriColor)
Principal Investigator: Dr. Josep Tabernero
Funding Body: Comisión Europea
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia.
Duration: 2015-2019
Total budget: 5.996.992€

• AWARDS:
The oncologist Andrés Cervantes received several awards during 2015. He entered the Royal Academy of Medicine of Valencia. He was appointed honorary member of the European Society for Therapeutic Radiology and Oncology and received a Recognition of Service for its special contribution to the success of the program “ESMO Fellowship Programme”.

Title: Hiperacetilación de riboproteínas heterogéneas nucleares (hnRNPs) como vía final de resistencia a fármacos anti-EGFR en cáncer de próstata
Principal Investigator: Ana Isabel Gil
Funding Body: Fundación de la Asociación Española contra el Cáncer
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2014-2015
Reference: 635342 - MoTriColor
Title: Molecularly guided trials with specific treatment strategies in patients with advanced newly molecular defined subtypes of colorectal cancer (MoTriColor)
Principal Investigator: Dr. Josep Tabernero
Funding Body: Comisión Europea
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia.
Duration: 2015-2019
Total budget: 5.996.992€
Research Group on Breast Cancer Biology
Consolidated group

“Mis pacientes me han enseñado a vivir.”

Group members

Principal investigator
Ana Lluch Hernández
Hospital. University
H Index: 41

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 Garcés Honrubia. Hospital
Begoña Pineda Merlo. INCLIVA

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

PhD students
Eduardo Tormo Martín. INCLIVA
María Peña Chilet. INCLIVA

Technicians
Elisa Alonso Yuste. INCLIVA

Administrative assistant
Yolanda De La Cruz Robles. INCLIVA
Strategic aims

- Identification of methylated areas in DNA (triple negative breast cancer pts) that differentiate responders and non-responders to treatment
- Pattern of miRNAs and mRNAs: modification of expression by chemotherapy
- Evaluation of the role of miR-26a and miR-30b in the development of resistance in HER2+ breast cancer
- Assessment of the PI3K/Akt pathway in resistance to anti-HER2 + therapies
- Determination of the association PP2A inhibition and poor outcome and doxorubicin resistance in early breast cancer
- Validation of a differential microRNA expression of breast cancer in very young women using METABRIC and TCGA public databases in addition to our own data. We have also characterized cell lines from young women and identified two as good models for functional studies.

Main lines of research

- Study of methylation as a prognostic and predictive factor of treatment response in triple negative breast cancer
- Evaluation of microRNAs and mRNAs differentially expressed after chemotherapy treatment
- Involvement of miRNAs in cancer processes in breast cancer
- Role of tumor heterogeneity and dynamic reprogramming of tumor cell resistance to anti-HER2
- 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 po-
4. Scientific activity

...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 tumours, 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


20. Bianchini G, Pusztai L, Pienkowski T, Im YH, Bianchi GV,


Letter


Editorial


Review

Scientific activity


Clinical guidelines


• THESIS

Thesis Title: Expresión diferencial de microRNAs en tumores de mujeres jóvenes con cáncer de mama: Cribado de dianas moleculares
Doctoral candidate: María del Carmen Peña Chilet
Director(s): Ana Lluch Hernández, Gloria Ribas Despuig
Date of the defense: 18/12/2015
Grade: Sobresaliente “cum laude”

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI12/01421
Title: Identificación de mecanismos de resistencia a nuevos anticuerpos anti-HER2 en cáncer de mama
Principal Investigator: Ana Lluch Hernández
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 105.270€

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: 2013-2015
Total Budget: 85.728€

Reference: Convocatoria 2012 de ayudas intramurales para grupos emergentes
Title: Papel del reloj molecular circadiano en la progresión y tratamiento del cáncer de mama
Principal Investigator: Joan Bataller Climent
Funding body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 8.000€

Reference: PI13/00606
Title: Transcriptional deregulation in tumoral tissue from very young women with breast cancer and functional Implications
Principal Investigator: Gloria Ribas Despuig
Funding body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2014-2016
Total Budget: 68.365€

Reference: Convocatoria 2012 de ayudas intramurales para grupos emergentes
Title: ¿Tiene el cáncer de mama en mujeres jóvenes una entidad genética diferente? Análisis de tejido tumoral de mujeres jóvenes mediante el estudio de la expresión de miRNAs
Principal Investigator: Gloria Ribas Despuig
Funding body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 6.800€
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: Convocatoria 2014 de ayudas intramurales para grupos emergentes
Title: Mecanismos de resistencia al tratamieneto en cancer de mama triple negativo
Principal Investigator: Pilar Eroles Asensio
Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2015
Total Budget: 3.500€

Reference: Programa 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, Fundación CETIR
Duration: 9 months
Total Budget: 44.250€

• AWARDS:
The oncologist Ana Lluch was awarded with several awards during 2015. The “Premio ABC Salud 2015”, the “Premio Valencianos para el Siglo XXI” and the “Premio Clara Campoamor”. 
Research Group on Skin Cancer
Consolidated group

Group members

Principal investigator
José Carlos Monteagudo Castro
Hospital. University
H Index: 23

Collaborating researchers
Antonio Pellín Pérez. University
Esperanza Jordá Cuevas. Hospital. University
David Ramos Soler. Hospital (La Fe). University
José 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
Lara Navarro Cerveró. INCLIVA
Strategic aims

• PhD thesis on spontaneous regression of melanocytic neoplasms. Main results: 1) demonstration that an increase in telomere length variation (TLV) correlates with spontaneous regression in cutaneous melanomas. 2) A prediction equation including lamellar fibrosis, melanophage, blood vessel and granzyme B+ lymphocyte density, as well as the age of the patient can correctly identify malignancy in 87% of melanocytic lesions with partial regression. Completion of 4 additional PhD theses at the end of 2015

• Modification of endogenous levels of miRNA-205 in melanoma cell lines A375 and SKMEL147 by lentiviral vectors. Transcriptomic study of the differential gene expression between cells with low and high miRNA-205 expression, and experimental xenograft study in immunodeficient mice of both types of cells

• First demonstration that CD34 nuclear immunexpression, as well as CD133, SPARC and ABCG2 expression in melanoma correlates with the development of distant metastases (paper under review)

Main lines of research

• Expression of epithelial–mesenchymal transition markers and tumor initiating cells (tumour stem cells) in tumour 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


11. 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. 2015 Dec 15 ;: IF: 0

**Letter**


**THESIS**

**Thesis title:** Determinación de parámetros clínico-patológicos y moleculares implicados en la regresión espontánea de neoplasias melanocíticas cutáneas.

**Doctoral candidate:** José María Martín Hernández

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

**Date of the defense:** 13/02/2015

**Grade:** Sobresaliente “cum laude”

**Thesis title:** Carcinoma epidermoide cutáneo: relación con los trastornos respiratorios del sueño y definición de la variante alto riesgo

**Doctoral candidate:** Tania Díaz Corpas

**Director(s):** Esperanza Jordá Cuevas, María Manuela Morales Suárez-Varela, Estrella Fernández Fabrellas

**Date of the defense:** 11/06/2015

**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:** Programa VLC-BIOCLINIC

**Title:** Biosensor molecular para la detección espaciotemporal de miRNAs

**Principal Investigator:** Carlos Monteagudo Castro

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

**Beneficiary Institution:** Universidad de Valencia

**Duration:** 2015

**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:** Carlos Monteagudo Castro

**Funding body:** Generalitat Valenciana

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

**Duration:** 2015-2018

**Total Budget:** 167.010€ (2015: 51.100€)

**AWARDS**

José María Martín, Esperanza Jordá and Carlos Monteagudo received the grant “Premio Campaña Euromelanoma” awarded by the Spanish Academy of Dermatology and Venereology for the scientific work: The heterogeneity of telomere length influences the spontaneous regression of melanoma.

In addition they received the prize “Pierre Fabre Dermatology about Acne” in the category: care process, organized by the Spanish Academy of Dermatology and Venereology and sponsored by Pierre Fabre Dermatology Laboratory for the work entitled “Differences in treatment efficacy and quality of life patients with moderate and severe acne comparing different doses of isotretinoin”.

José María Martín, Esperanza Jordá and Carlos Monteagudo received the grant “Premio Campaña Euromelanoma” awarded by the Spanish Academy of Dermatology and Venereology for the scientific work: The heterogeneity of telomere length influences the spontaneous regression of melanoma.

In addition they received the prize “Pierre Fabre Dermatology about Acne” in the category: care process, organized by the Spanish Academy of Dermatology and Venereology and sponsored by Pierre Fabre Dermatology Laboratory for the work entitled “Differences in treatment efficacy and quality of life patients with moderate and severe acne comparing different doses of isotretinoin”.
Translational Research Group on Pediatric Solid Tumours
Consolidated group

“Micromecenazgo para lograr imágenes en 3D para el diagnóstico de tumores infantiles”.

Rosa Noguera. Levante. 10.11.2015
https://www.aecc.es/RedSocial/Blogs%20investigadores/Paginas/RosaNoguera.aspx

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
Maite Blanquer Maceiras. INCLIVA

PhD students
Susana Martín Vañó. University
Víctor Zúñiga Zaragoza. University

Technicians
Alejo Miguel Sempere Crespo. University
Rebeca Brugos Panadero. INCLIVA
Strategic aims

- Genetic analyses of neuroblastoma. At a European level, the group is participating in the establishment of a standardized nomenclature, a standard operating procedure and studies of quality validation, critical tools to maintain high quality in FISH, MLPA and SNPs results used in therapeutic stratification.
- Identification of new genetic factors with prognostic value in malignant pediatric neuroblastic and skeletogenic tumours.
- Obtention and characterization of cell lines from fresh pediatric skeletogenic tumours.
- Establishment and characterization of in vivo models of malignant skeletogenic tumours.
- Expression studies of markers in colorectal carcinoma and pediatric solid tumours.
- To analyze histopathologic and genetic studies in uterine mesenchymal tumours.
- To study genetic and immunohistochemical characterization of renal clear cell carcinoma.

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 tumours, soft-tissue sarcomas, skeletogenic tumours and gynecologic mesenchymal tumours.
- ALK as a prognostic factor in NB.
- Identification and isolation of stem cells in NB.
- Establishment and characterization of in vitro and in vivo models of malignant skeletogenic tumours. Cell line extraction in these tumours.
- Expression study of immunohistochemistry and Western blot markers in these tumours in order to identify possible therapeutic targets.
- Study of NB hyperstructure.

PUBLICATIONS

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Original articles


15. Machado I, Cruz J, Lavernia J, Llombart-Bosch A. Solitary, multiple, benign, atypical, or malignant: the “Granular Cell Tumor” puzzle. Virchows Arch. 2015 Dec 5 ;:IF: 2,651

Clinical guidelines


• THESIS

Thesis title: Estudio clínico, histopatológico, inmunohistoquímico y citogenético de los tumores mesenquimales uterinos de musculo liso. Búsqueda de dianas terapéuticas.

Doctoral candidate: Nuria Santonja López

Director(s): Samuel Navarro Fos, José Juan Santonja Lucas, Rosa Noguera Salvá

Date of the defense: 01/12/2015

Grade: Sobresaliente “cum laude”
Thesis title: Integración de la genómica en la modelización de los tumores neuroblásticos
Doctoral candidate: Ana Pilar Berbegall Beltrán
Director(s): Samuel Navarro Fos, Rosa Noguera Salvá
Date of the defense: 10/07/2015
Grade: Sobresaliente “cum laude”

Thesis title: Estudio del armazón arquitectónico y del sistema vascular de los tumores neuroblásticos
Doctoral candidate: Irene Tadeo Cervera
Director(s): Samuel Navarro Fos, Rosa Noguera Salvá
Date of the defense: 16/01/2015
Grade: Sobresaliente “cum laude”

**RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: 261474
Title: European network for cancer in children and adolescent (ENCCA)
Principal Investigator: Ruth Landenstein (Rosa Noguera as collaborating researcher)
Funding body: European Commission
Beneficiary institution: Universitat de València
Duration: 2011-2015
Total budget: 11,997,958€

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: Universitat de València
Duration: 2013-2016
Total budget: 73,000€/year

Title: Prospective Validation of alterations in 1q and 16q as Biomarkers in Ewing Sarcoma
Principal Investigator: Enrique de Álava Casado (Rosa Noguera and Samuel Navarro as collaborating researchers)
Funding body: Fundación CRIS-FISEVI
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2016
Total budget: 67,500€

Reference: FAECC2015
Title: Búsqueda de dianas terapéuticas en los puntos de contacto de la célula tumoral en el neuroblastoma infantil con su matriz extracelular
Principal Investigator: Rosa Noguera
Funding body: AECC-Asociación Española Contra el Cáncer
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2015-2018
Total budget: 150,000€

Reference: 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€

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
Julia Peláez González. INCLIVA
Joana Hernández Martín. INCLIVA
Paula Amat Martínez. Hospital
Estela Giménez Quiles. Hospital
Strategic aims

- To advance in translational research in biology and treatment of graft versus host disease after allogeneic hematopoietic progenitor cells
- To study the Infection and immune reconstitution after hematopoietic transplantation
- To investigate in biology implant in hematopoietic transplantation
- To research cell therapy with adult stem cells in the context of hematopoietic transplantation

Main lines of research

- Biology of hematopoietic implant
- Cell therapy with adult stem cells in relation with hematopoietic transplantation
- Translational research on complications of allogeneic hematopoietic transplantation: graft-versus-host disease
- Infection and immune reconstitution after hematopoietic transplantation

• PUBLICATIONS

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Original articles


D. Functional patterns of cytomegalovirus (CMV) pp65 and immediate early-1-specific CD8+ T cells that are associated with protection from and control of CMV DNAemia after allogeneic stem cell transplantation. Transpl Infect Dis. 2015 Jun;17(3):361-70. IF: 2.064


Review


Letters


• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI12/01466
Title: Estudio integral de biomarcadores de la enfermedad inyerto contra huésped (EICH) en el trasplante alogénico de células hematopoyéticas (TPH-ALO)
Principal Investigator: Carlos Solano Vercet
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 96,800€

Reference: PI12/01992
Title: Infección activa por el citomegalovirus (CMV) en el trasplante alogénico de precursores hematopoyéticos: investigación de nuevos factores biológicos para la estimación del riesgo y análisis integral de los mecanismos inmunitarios que previenen y controlan
Principal Investigator: David Navarro Ortega
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 85,305€

• AWARDS

Carlos Solano received the Van Bekkum Award 2015, award for best paper presented at the 41st Congress of the European Society of Transplant Blood and Marrow Transplant (EBMT).
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
Scientific activity

Strategic aims

• VEGF/VEGF-R increases migration of B-CLL cells through an increased in expression and functional activation of CXCR-4/CCR7 pathway. Increment in expression and migration correlates with adverse clinical features such as CD38/ZAP-70 expression, advanced Binet/RAi stage
• The 936T allele at SNP rs3025039 of the VEGF gene is associated with a lower risk of B-CLL while variant genotype T/- SNP rs1449683 in the bFGF gene contributes to disease initiation and progression, showing a reduction in survival
• Haplotype CGAC +/- of the SNPs rs3025039, rs1109324, rs1547651 y rs833052 VEGF gene, associates with a lowe survival of CLL patients compared with the rest. This is especially relevant in the CD38/ZAP-70 positive Group
• Both therapeutic approaches based on VMP and Rd, in an alternating or sequential schedules are associated with high efficacy and acceptable toxicity profile with no differences between them

Main lines of research

• Analysis of the interactions of CLL cells with their cellular microenvironment: further study of the intracellular mechanisms triggered by VEGF. Analysis of the possible correlation with CXCR4/CCR7 cytokines pathway. Transactivation mechanisms of the aforementioned receptors
• Development of new ex-vivo co-culture models of the cells of CLL with bone marrow stroma and dendritic cells for the efficacy analysis of new kinase inhibitor drugs. Drug resistance effect mediated by microcellular environment
• Identification and analysis of VEGF polymorphisms in CLL progression: study of samples from CLL patients obtained at diagnosis and controlled at the institution
• Study of polymorphisms in folate pathway genes (MTHFR, DHFR, TS) and predisposition to develop lymphomas. Correlation with the clinical and biological characteristics of the disease, response to treatment, toxicity and survival
• Study of polymorphisms of circadian rhythm-regulating genes in follicular lymphomas: correlation with the clinical and biological characteristics of the disease, response to treatment, toxicity and survival
• New therapeutic options for CLL/MM patients who are resistant to chemoimmunotherapy

PUBLICATIONS

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Original articles


cells to arsenic trioxide involves Mcl-1 upregulation and is overcome by inhibiting the PI3K? or PKC? Signaling pathways. Oncotarget. 2015 Dec 29 ;6(42):44832-48. IF: 6,359

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI14/01781
Title: Papel de la vía de señalización NOTCH1/FBXW7/PI3K/ PTEN/AKT en la progresión de la Leucemia Linfocticá 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€
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
Vicente Martín Guillem Primo. INCLIVA
Blanca Navarro Cubells. Hospital
Marisa Calabuig Muñoz. Hospital
Montserrat Gómez Calafaz. Hospital

Emerging researcher
Juan Carlos Hernández Boluda. Hospital
Strategic aims

- To study the involvement of VEGF / VEGFR pathway in AML and their relation to different clinical, cytogenetic and molecular variables with established prognostic value
- To study the role of complex RUNX1 / CBF-beta / p300 / HIPK2 in leukemic progression of chronic myeloproliferative neoplasms
- To study the influence of SNPs involved in the synthesis and repair of DNA in toxicity and survival (SRV) patients diagnosed with LAL treated with therapeutic regimens containing MTX

Main lines of research

- Studies of new biological prognostic factors in acute myelogenous leukemia
- Study of mechanisms of the leukemic chronic myeloproliferative neoplasms progression
- Clinical guidelines for diagnosis, prognosis and treatment of myelodysplastic syndromes
- Study the influence of SNPs involved in the synthesis and repair of DNA in toxicity and survival patients diagnosed with LAL treated with therapeutic regimens containing MTX
- Clinical guidelines for assessment of response in chronic myeloid leukemia
- Studies inside of CETLAM registry
- Studies inside of PETHEMA registry
- Studies inside of Spanish registry of myelofibrosis
- Spanish inside of registry of Myelodysplastic syndromes

PUBLICATIONS

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Original articles


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.


• 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: 2014-2016
Total Budget: 79,860€
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

Technician
Josefa Castillo Aliaga. INCLIVA

http://www.bioeticaweb.com/byline/luis-franco-vera/
Scientific activity

Strategic aims

- We have finished and published the analysis of the changes in structure and epigenetic regulation of the murine Egr1 gene during the induction-repression cycle at a mononucleosomal resolution.
- The influence of liver transfection with Gas1 gene in mice bearing hepatocellular carcinoma has been published. The results show a significant decrease in the size of tumours and metastasis and a reversal of the expression of genes which are altered in tumours.
- We have gone on analysing the consequences of KRAS G13D mutation in gene splicing and expression in colorectal cancer cells, to find that ZNF518B and EPDR1 genes show a clear differential behavior. The results were incorporated in a Ph. D. Thesis, as it was the influence of that mutation in the alternative splicing of the KRAS gene itself.
- A collaboration of Prof. López Rodas with other groups working on epigenetics of multiple sclerosis has also given rise to several papers published.

Main lines of research

- Involvement of chromatin in the regulation of Egr1. Study of chromatin changes associated with Egr1 expression during phorbol esters-induced proliferation in a cell line and in vivo mouse liver after partial hepatectomy.
- Gas1 overexpression effects in reducing the size of liver tumours. Study of the effects of overexpression of Gas1 in mice bearing HCC in reducing the size of tumours and their metastatic potential and normalization of the expression levels of genes involved in cell proliferation.
- Analysis of differential expression and splicing of genes in relation with KRAS mutational activation in colorectal cancer (CRC). The study is specially centred in ZNF518B and EPDR1 genes and it covers as well the consequences of knocking down these genes on the malignant properties of CRC cells. We are also studying the differential isoform expression of these genes in CRC patients.
- Regulation of the ZNF518B expression at a chromatin level.
- Study of the alternative splicing of KRAS in CRC cells at a chromatin level. The research covers the nucleosomal organization and epigenetic modifications in the regions involved in alternative splicing.

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 colorectal
Principal Investigator: Gerardo López Rodas
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Universitat de València
Duration: 2013-2015
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€

• THESIS

Thesis title: Chromatin regulatory mechanisms of gene expression at mononucleosomal level: nucleosome occupancy and epigenetic modifications
Doctoral candidate: Angela Leticia Rifo Campos
Director(s): Luis Franco Vera, Gerardo López Rodas, Josefa Castillo Aliaga
Date of the defense: 28/09/2015
Grade: Sobresaliente “cum laude”

Fig. 1. Model of the structural changes and histone modifications during the activation and repression of the Egr1 gene. The position of nucleosomes -2, -1, and +1 is given at four different times after TPA addition. The partial eviction of nucleosomes is symbolized by increasing the transparency of the ovals. The location of transcription factors serum-response factor, ELK1, SP1, and CREB and the phosphorylation of the latter is based on previous results (78). The tentative positions of the BRM-containing remodeler and the preinitiation complex (PIC) are also shown. The transcriptional rate is symbolized by placing more or less arrows over the RNA pol II molecule. The relative level of histone modifications is given according to the color code depicted at the top.

Fig. 2. Differential expression of KRAS isoforms in two human colorectal cancer cell lines.
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
Remedios Segura Sabater. University
Antonio Pellín Carcelén. University
Mercedes Pardo Tendero. INCLIVA

Technician
José Manuel Morales Tatay. University
Strategic aims

- Development of new diagnostic tools, prognostic and predictive based on NMR metabolomic profiles for patient stratification in cardiometabolic disease
- Development of new diagnostic tools, prognostic and predictive based on NMR metabolomic profiles for patient stratification in glioblastoma multiforme
- Development of new diagnostic tools, prognostic and predictive based on NMR metabolomic profiles for patient stratification in sepsis

Main lines of research

- Study of intestinal microbiota metabolic interaction-host in cardiometabolic disease
- Identification of new markers of cardiometabolic risk by metabolomic profiles in blood and urine
- Study of the interaction between tumor metabolism, angiogenesis, hypoxia and estrogen receptors in breast cancer
- Study of the interaction between tumor metabolism, hypoxia and invasion in glioblastoma multiforme

PUBLICATIONS

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Original articles


RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: HEALTH 2011.2.4.2-2
Title: Markers for Subclinical Cardiovascular Risk Assessment (EU MASCARA)
Principal Investigator: Josep Redón i Mas (Daniel Monleón, Vannina González and José Manuel Morales as a collaborating researchers)
Funding Body: European Commission
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2011-2015
Total budget: 370.000€
**Scientific activity**

Reference: SAF2014-52875R
Title: Estudio metabolómico de la interacción huésped-microbiota intestinal en la enfermedad cardiométabólica. 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: Convocatoria 2014 de ayudas intramurales para grupos emergentes
Title: Interacción entre receptores de estrógenos, hipoxia, angiogénesis y metabolismo tumoral en células de cáncer de mama
Principal Investigator: Daniel Monleón Salvadó
Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 10.200€
4.1.3 Metabolism and organic damage area

- Research Group on Genetics of Osteoporosis: 128
- Translational Research Group on Nutrition and Metabolism: 131
- Research Group on Neurological Impairment: 135
- Research Group on Inflammation: 139
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- Research Group on Anesthesiology and Reanimation: 166
- Research Group on Translational Genomics: 171
- Research Group on General and Digestive Surgery: 174
- Research Group on Personal Autonomy, Dependence and Severe Mental Disorders (TMAP): 177

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**Impact Factor (IF)**
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- Average: 4.04

**JCR**
- 30 in D1
- 81 in Q1
- 42 in Q2

**Author**
- 59 first author
- 79 last author
- 65 corresponding author

**International collaborations**: 52
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 students
Layla Panach González. INCLIVA
**Scientific activity**

### PUBLICATIONS

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#### International collaborations

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#### Corresponding author

- 5

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#### Original articles


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#### Review


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### RESEARCH PROJECTS AND GRANTS FOR RESEARCH

**Reference:** P112/02582

**Title:** Identificación de polimorfismos y genes asociados a la osteoporosis posmenopáusica: análisis genético y funcional

**Principal Investigator:** Miguel Ángel García Pérez

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

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

**Duration:** 2013-2015

**Total budget:** 98.978€

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**Strategic aims**

- To continue with the studies of genetic association between candidate genes and bone phenotypes
- Characterization of the association CD40 / CD40L in bone mass by genetic and epigenetic techniques
- To study the profile of miRNAs and cytokines in osteoporotic hip fracture. Also the analysis of SNPs in genes of miRNAs precursors and bone phenotypes in a collaborative study
- To analyze the role of B lymphocytes in bone loss associated with estrogen deficiency by microarray studies and association studies to bone phenotypes
- To analyze the state of the transcriptome in osteoporotic bone fracture to detect and identify candidate genes for population studies
- To do collaborations in areas related to bone metabolism during pregnancy and fertility related issues

**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
- 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
Reference: FOCUS
Title: Frailty management Optimisation through EIP AHA Commitments and Utilisation of Stakeholders input
Principal Investigator: Antonio Cano Sánchez (Juan José Tarín and Miguel Ángel García Pérez as collaborating researchers)
Funding body: Comisión Europea- DG SANCO
Beneficiary institution: Universidad de Valencia
Duration: 2015-2018
Total budget: 2.379.633€

Research on genetics of human postmenopausal osteoporosis through a translational approach from animal models. To do this, initially its identified genes differentially expressed in B lymphocyte of mouse bone marrow ovariectomized (OVX, red) and compared to control animals (SHAM, blue). A) Analysis of Principal Component (PCA mapping) of microarray both types of mice and B) Hierarchical Clustering of differentially expressed genes. C) Analysis of functional pathways KEGG overrepresented in OVX B lymphocytes has shown that osteoclast differentiation pathway is one of the most affected (19 genes, p = 3.5x10^-8). Later it was studied the genetic association to bone phenotypes of SNPs selected candidate genes after genotyping in human cohort studies. Microarray experiments were performed in the facilities of INCLIVA.
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. FISABIO
Víctor Manuel Víctor González. University
Juan Vicente Esplugues Mota. University
Carlos Morillas Ariño. University
Eva Solá Izquierdo. University
Celia Bañuls Morant. University
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

http://www.farmacologiavalencia.es/index.php/inv-ppales/victor-gonzalez-victor-m-phd
**Strategic aims**
- To determine the implication of the stress of endoplasmic reticulum (RE), mitochondrial and endothelial dysfunction in the underlying mechanisms associated with insulin resistance in diseases such as type 2 diabetes, obesity and polycystic ovary syndrome, and its relationship with the risk of cardiovascular disease. In addition, we evaluated possible therapeutic targets that could help to understand the mechanism and source of stress of RE in different cell models.
- To develop various projects that focus on the efficacy of functional foods with properties of health, for the reduction of risks of chronic diseases.

**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**
11. Víctor VM, Rovira-Llopis S, Bañuls C, Díaz-Morales N,


Review


• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI12/01984
Title: Implicación del estrés de retículo endoplasmático en la fisiopatología del síndrome de ovario poliquístico: Posibles aplicaciones terapéuticas de los sensibilizadores de la insulina
Principal Investigator: Antonio Hernández Mijares
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Fundación para la Investigación Hospital Dr. Peset
Duration: 2013-2015
Total budget: 62.315€

Reference: PI13/00073
Title: Efecto de la pérdida de peso sobre marcadores de estrés de retículo endoplasmático en la obesidad mórbida: Implicaciones fisiopatológicas y nuevas dianas terapéuticas
Principal Investigator: Milagros Rocha Barajas
Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO)
Duration: 2014-2016
Total Budget: 82.280€

Reference: PI13/01025
Title: Disfunción endotelial-mitocondrial, estrés de retículo y autofagia en la diabetes tipo 2: Implicaciones fisiopatológicas, clínicas y terapéuticas
Principal Investigator: Víctor Manuel Víctor González
Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO)
Duration: 2014-2016
Total Budget: 116.170€

Reference: PI11/00327
Title: Caracterización de nuevos mecanismos celulares de hepatoxicidad por antiretrovirales
Principal Investigator: Juan Vicente Esplugues Mota
Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO)
Duration: 2012-2014
Total budget: 217.800€
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: Universidade de Valencia
Duration: 2007-2014

Thesis title: Alteraciones metabólicas de la Hiperlipemia Familiar Combinada y su asociación con la obesidad abdominal y la inflamación de bajo grado.
Doctoral candidate: María Díaz Ruiz
Director(s): Antonio Hernández Mijares
Date of the defense: 02/07/2015
Grade: Sobresaliente “cum laude”

Reference: UGP14-095
Title: Disfunción endotelial-mitocondrial, estrés de retículo y autofagia en la diabetes tipo 2: implicaciones fisiopatológicas, clínicas y terapéuticas
Principal Investigator: Víctor Manuel Víctor González
Funding Body: 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: 2015
Total budget: 12.500€

Thesis title: Estudio de los mecanismos moleculares de estrés oxidativo, disfunción mitocondrial, estrés de retículo endoplasmático y autogamia en leucocitos de pacientes con diabetes tipo 2.
Doctoral candidate: Susana Rovira Llopis
Director(s): Antonio Hernández Mijares
Date of the defense: 19/10/2015
Grade: Sobresaliente “cum laude”

Reference: UGP14-093
Title: Efecto de la pérdida de peso sobre marcadores de estrés de retículo endoplasmático en la obesidad mórbida: Implicaciones fisiopatológicas y nuevas dianas terapéuticas
Principal Investigator: Milagros Rocha Barajas
Funding Body: 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: 2015
Total budget: 12.500€

THESIS

Thesis title: Estudio clínico de la correlación de los niveles de glucosa en sangre y saliva; y la importancia de las citocinas proinflamatorias en la enfermedad periodontal de los pacientes diabéticos.
Doctoral candidate: Esther Carramolino Cuéllar
Director(s): Antonio Hernández Mijares
Date of the defense: 20/02/2015
Grade: Sobresaliente “cum laude”
Research Group on neurological impairment
Consolidated group

Group members

Principal investigator
Carmina Montoliu Félix. INCLIVA. University
H Index: 30

Collaborating researchers
Ana Agustí Feliu. INCLIVA
Miguel Ángel Serra Desfilis. Hospital. University
Amparo Escudero García. Hospital. University
María Luisa García Torres. Hospital
Paloma Lluch García. Hospital
Joan Tosca Cuquerella. Hospital
José Ballester Fayos. Hospital

PhD students
Alba Mangas Losada. INCLIVA
Isidro Torregrosa. Hospital

Technicians
Remedios González Ballesteros. Hospital
Laura Puchades. INCLIVA

http://www.neurocipf.es/web/montoliu.car/pagina-personal
Strategic aims

- 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

- Minimal Hepatic encephalopathy (MHE), clinical and biochemical diagnostics
- Detection of the presence of MHE in cirrhotic patients. Comparison of psychometric tests and critical flicker frequency. Study of peripheral parameters related with cGMP homeostasis and inflammation as possible indicators of the presence of MHE
- Identification of metabolites to be use in the diagnosis of MHE
- 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 MHE
- 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
- Minimal Hepatic Encephalopathy and Critical Flicker Frequency are Associated With Survival of Patients With Cirrhosis
- Rats with Mild Bile Duct Ligation Show Hepatic Encephalopathy with Cognitive and Motor Impairment in the Absence of Cirrhosis: Effects of Alcohol Ingestion
- Modulation of GABAA receptors by neurosteroids. A new concept to improve cognitive and motor alterations in hepatic encephalopathy
- Real-time cytometric assay of nitric oxide and superoxide interaction in peripheral blood monocytes: A no-wash, no-lyse kinetic method
- 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
- Valor de NGAL, KIM-1, I-FABP e Interleukina-18 como marcadores precoces de insuficiencia renal aguda en pacientes críticos y tras cirugía y cateterismo cardíacos.
- ELISA-measured urinary Klotho as an early biomarker of acute kidney failure in patients undergoing heart surgery or coronary angiography.

• PUBLICATIONS

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Original articles


Review


• THESIS

Thesis title: Biomarcadores precoces de fracaso renal agudo tras angiografía coronaria o cirugía cardíaca en pacientes con síndrome coronario o falla cardiaca agudo

Doctoral candidate: Isidro Antonio Torregrosa Maicas

Director(s): Juan Alfonso Miguel Carrasco, Guillermo Sáez Tormo y Carmina Montoliu Felix

Date of the defense: 23/07/2015

Grade: Sobresaliente “cum laude”
**RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

**Reference:** PI12/00884
**Title:** Caracterización de las alteraciones neurológicas 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 Clínic Universitario de Valencia
**Duration:** 2013-2015
**Total budget:** 123,420€

**Reference:** Proyect Number 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:** 2011-2015

**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 Felix
**Funding Body:** Fundación ERESA
**Beneficiary institution:** Fundación Investigación Hospital Clínico Universitario de Valencia
**Duration:** 2014-2015
**Total budget:** 20,000€

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**Figure.** Hyperammonemia and inflammation act synergistically to induce neurological alterations in chronic liver disease. Chronic liver failure induces both hyperammonemia and peripheral inflammation, leading to microglial activation and neuroinflammation, which alters neurotransmission, leading to cognitive and motor impairment.
Research Group on Inflammation
Consolidated group

“La Universidad de Valencia crea ciudadanía crítica, es lengua y patrimonio, es plural y abierta, y genera riqueza y cohesión social”  Esteban Morcillo. El País. 1-5-2015
http://ccaa.elpais.com/ccaa/2015/04/30/valencia/143099293_013729.html

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

PhD students
Aida Collado Sánchez. INCLIVA
Patrice Gomes Marques. University

Technicians
Ángela Vinué Visús. INCLIVA
Strategic aims

- Study of the anti-inflammatory and anti-angiogenic activity of combinations of sub-optimal doses of rosvastatin and bexarotene in atherosclerosis and abdominal aortic aneurysm
- Study of Roflumilast on corticosteroid resistance in COPD bronchial epithelial cells stimulated with toll like receptor 3 agonist and its metabolic Effects of Bleomycin-Induced fibrosis in vivo
- Molecular mechanisms of neutrophil extracellular traps (NET) formation and degradation in the liver vasculature in infection with methicillin-resistant Staphylococcus aureus
- Synthesis of hexahydrocyclopenta isoquinolines, new potential drugs in the control of dopaminergic disorders
- Study of the effect of increased expression of the INK4/ARF locus on hepatic steatosis and inflammation associated with the glucose metabolism derangement
- Study of the impact of the hepatic lipase in the development of insulin resistance and hepatic steatosis

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 SuperInk4/Arf locus and hepatic lipase in age-associated insulin resistance and atherosclerosis

Emerging researcher

**Herminia González Navarro**

Molecular Physiopathology of the diabetes and atherosclerosis.

Our research is focused in the study of the molecular mechanisms of the diabetes mellitus (DM) and its effect on atherosclerosis development which is one of the main causes of cardiovascular diseases. To this end, we perform studies in genetically-modified mice that develop metabolic alterations such as diabetes, insulin resistance, fatty liver disease 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 by promoting the death of vascular smooth muscle cells present in the atheroma plaques which favours plaque rupture and acute events such as myocardial infarction. We have also identified some of the inflammatory mediators that participate in these processes in the mouse models and in human patients.

In another line of research we are studying the role of the CDK-N2A and 2B genes, contained in the Ink4/Arf locus, in the development of diabetes. We have found that increased expression of these genes, in mice with impaired IRS2-mediated signalling, protects the mice from developing glucose intolerance, insulin resistance and fatty liver disease. Currently, we are studying whether these genes are relevant for the human pathology by analysing the expression and functionality of these genes in human samples.

**Laura Piqueras Ruiz**

Abdominal aortic aneurysm (AAA) is a degenerative disease of the aorta that mainly affects elderly population over the age of 65. Given the high mortality rate associated with AAA, it is important to find new pharmacological approaches to prevent its progression. Our work focuses on the study of molecular mechanism associated to AAA develop-
ment and to investigate new pharmacological approaches to halt its progression.

In recent years, 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.

• PUBLICATIONS

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Original articles


12. Andrés-Blasco I, Herrero-Cervera A, Vinué Á, Martínez-

- **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

**Reference:** PI12/01271  
**Title:** Estudio de nuevos marcadores inflamatorios en la disfunción endotelial: Papel de los ligandos de PPAR y RXR  
**Principal Investigator:** Laura Piqueras Ruiz  
**Funding body:** Instituto de Salud Carlos III  
**Beneficiary institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2013-2015  
**Total budget:** 36.300€

**Reference:** PROMETEO II/2013/ 014  
**Title:** Nuevas dianas farmacológicas para el tratamiento de la EPOC y sus comorbilidades vasculares  
**Principal Investigator:** Esteban Morcillo Sánchez  
**Funding body:** Conselleria de Educación, Cultura y Deporte  
**Beneficiary institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2013-2016  
**Total budget:** 400.000€

**Reference:** 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  
**Duration:** 2009-2015  
**Total budget:** 6.500.000€

**Reference:** SAF2012-31042  
**Title:** Modulación farmacológica de la señalización de receptores toll-like por inhibidores de fosfodiesterasa 4 (PDE4) y esteroides en modelos experimentales relevantes en EPOC  
**Principal Investigator:** Esteban Morcillo Sánchez  
**Funding Body:** Ministerio de Ciencia e Innovación  
**Beneficiary Institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2012-2015  
**Total budget:** 125.000€

**Referencia:** CB06/06/0027  
**Título:** CIBER Enfermedades Respiratorias  
**Investigador principal:** Esteban Morcillo Sánchez  
**Fundingbody:** Instituto de Salud Carlos III  
**Beneficiary institution:** Universidad de Valencia  
**Duración:** 2007-2015

**Reference:** PI13/00834  
**Title:** Study of the molecular mechanisms of Diabetes Mellitus and its role on atherosclerosis  
**Principal Investigator:** Herminia González Navarro  
**Funding Body:** Instituto de Salud Carlos III  
**Beneficiary Institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2014-2016  
**Total Budget:** 89.298€

**Reference:** PRV00052  
**Title:** Estudio del papel del locus Ink4/Arf en la funcionalidad de las células β en un modelo murino de diabetes  
**Principal Investigator:** Herminia González Navarro  
**Funding Body:** Proyecto Paula  
**Beneficiary Institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2013 - 2016  
**Total Budget:** 45.000€

**Reference:** SAF2012-31042  
**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  
**Duration:** 2009-2015  
**Total budget:** 6.500.000€

**Reference:** Convocatoria 2012 de ayudas intramurales para grupos emergentes  
**Title:** Estudio de nuevos marcadores inflamatorios en la disfunción endotelial: papel modulador de ligandos de PPAR y RXR
**Principal Investigator:** Laura Piqueras Ruiz  
**Funding Body:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Beneficiary Institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2013-2015  
**Total Budget:** 8.000€  

**Reference:** SAF 2011-23777  
**Title:** Estudio de los mecanismos moleculares y celulares en la disfunción endotelial asociada a enfermedades con inflamación sistémica que podrían inducir desórdenes cardiovasculares  
**Principal Investigator:** María Jesús Sanz Ferrando  
**Funding Body:** Ministerio de Ciencia e Innovación  
**Beneficiary institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2012-2015  
**Total Budget:** 217.800€

**Reference:** Convocatoria 2014 de ayudas intramurales para grupos emergentes  
**Title:** Estudio del papel de la lipasa hepática en la dislipemia de la diabetes y síndrome metabólico en el desarrollo de la enfermedad cardiovascular  
**Principal Investigator:** Herminia González Navarro  
**Funding Body:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Beneficiary Institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2013 - 2015  
**Total Budget:** 3.500€  

**Reference:** CB07/08/0043  
**Title:** CIBER de Diabetes y Enfermedades Metabólicas Asociadas  
**Principal Investigator:** Deborah J Burks (Herminia González as collaborating researcher)  
**Funding Body:** Instituto de Salud Carlos III  
**Beneficiary institution:** CIPF  
**Duration:** 2013-2016  

**Reference:** COST Action BM1402  
**Title:** Sistema de inclusión en parafina y microtomo.  
**Principal Investigator:** Herminia González Navarro  
**Funding Body:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Beneficiary Institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2015  
**Total Budget:** 12.000€

**Reference:** 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 Navarro)  
**Funding Body:** European Union  
**Beneficiary Institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2015-2019
Research Group on Cellular and Organic Physiopathology of Oxidative Stress
Consolidated group

“Lo que se pretende actualmente es dar vida a los años y no años a la vida”
http://revistageneticamedica.com/2015/02/05/entrevista-federico-pallardo/

Group members

Principal investigator
Federico V. Pallardó Calatayud
University
H Index: 44

Team involved in

Collaborating researchers
Amparo Gimeno Monrós. University
Carlos Romá Mateo. University
Pilar González Cabo. CIBERer
Carla Giménez Garzón. INCLIVA

PhD students
José Santiago Ibáñez Cabellos. University
Marta Seco Cervera. INCLIVA

Technicians
Isabel Esmoris Méndez. INCLIVA

Emerging researchers
Francisco Dasí Fernández. University. INCLIVA
José Luis García Giménez. CIBERer
Strategic aims

- A European patent for the method and kit of diagnosis for idiopathic scoliosis by miRNAs (EP15382319.0) was approved. New projects are the following: “Identifying circulating histones by mass spectrometry methods in plasma of patients with severe sepsis and septic shock” by INCLIVA, and “Analysis of microRNAs as biomarkers of drug monitoring for Lafora disease models”, by the micro-cluster of ER (MCI-FER) of VLC / Campus and CIBERER’s spin-off (EpiDisease), other projects initiated in 2013 and 2014, where founded by an international consortium (USAID,UKAID, Melinda and Bill Gates Foundation, Grand Challenges Canada, Government of Norway).
- Approval of an optional teaching subject “Rare Diseases” (RD) in the curricula of the medical degree being the first course in the country. Awarded by FEDER as the best initiative to increase the quality of life of people with rare diseases.
- Official agreement for the establishment of the Alliance in translational research in Rare Diseases of the Valencian Community (DOCV 7654, 10/11/15) was signed between the Generalitat Valenciana, CIBERER, FEDER and other valencian universities and research institutes to develop a common research strategy in Rare Diseases. Dr. Pallardó was appointed as president of the scientific committee of the Alliance.
- To analyze the pathophysiological mechanisms of KINDLER syndrome and WERNER syndrome, two progerias that help to understand the process of organic aging
- To build up a new animal model of CHARCOT-MARIE-TOOTH disease and contribute to better understand the relationship between oxidative stress and the mechanisms of gene regulation modulated by epigenetic factors
- To study the DOWN syndrome from the perspective of change in the processes of cell turnover, helping to elucidate its pathophysiology
- To describe the presence of oxidative stress and lack of antioxidant defense in Lafora disease

Main lines of research

- Epigenetic regulation of cell proliferation by nuclear glutathione

Emerging researcher

José Luis García Giménez

We are interested in understanding the role of epigenetics in the physiological pathologies 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 on the impact of several novel histone redox-related PTMs on cell physiology and gene regulation.

Francisco Dasí Hernández

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

The scientific interests of the group are:

- To characterize the molecular mechanisms (especially those aspects related to the REDOX signalling) involved in the development of liver and/or lung disease in patients with AATD, in order to understand why some patients develop serious liver and/or lung disease, while other patients bearing the same of alpha-1 antitrypsin (AAT) phenotype, are perfectly healthy.
- To assess cell-free circulating nucleic acids for the diagnosis and prognosis of AATD.
• To develop new therapeutic strategies based on gene therapy.
• To generate social awareness of pulmonary rare diseases, through scientific disclosure of biomedical advances and social and health policies to improve the quality of life of patients with pulmonary rare diseases.

• PUBLICATIONS

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Original articles


Letter


• THESIS

Thesis title: Perfiles de expresión genómica: nuevo enfoque diagnóstico para la sepsis en recién nacidos menores de 1500 gramos

Doctoral candidate: María Cernada Badía

Date of the defense: 19/10/2015

Grade: Sobresaliente “cum laude”

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI12/02263

Title: Estudio de miRNAs en pacientes de ataxia de Friedreich. Implicaciones diagnósticas y terapéuticas

Principal Investigator: Federico V Pallardó Calatayud

Funding body: Instituto de Salud Carlos III

Beneficiary institution: Fundación Investigación del Hospital Clínico Universitario de Valencia

Duration: 2013-2015

Total budget: 92.565€

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
Scientific activity

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: Fundación Investigación del Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 5.000€

AWARDS

Federico Pallardó was received the FEDER award to the best regional initiative to increase the quality of life to people with rare diseases. On the other hand, Francisco Dasí Fernández was awarded for the paper presented at the International Congress of Respiratory Diseases celebrated in Amsterdam by the European Respiratory Society-ERS.

Reference: TREAT-CMT
Title: Translational Research, Experimental Medicine and Therapeutics on Charcot-Marie-Tooth Disease (TREAT-CMT)
Principal Investigator: Francesc Palau (Federico V. Pallardó, José Luis García-Giménez, Amparo Gimeno and Jelena Markovic as collaborating researchers)
Funding body: Instituto de Salud Carlos III
Beneficiary institution: CIBERER
Duration: 2011-2015
Total budget: 3.065.198€

Reference: HIST-BIRTH
Title: Bases Fisiopatológicas de la Enfermedad de Lafora
Principal Investigator: Federico Vicente Pallardó Calatayud
Funding body: I USAID. USA Agency for Innovation and Development Saving Lives at Birth Development Change
Beneficiary institution: Universitat de Valencia
Duration: 2013-2015
Total budget: 186.712€

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

Reference: Convocatoria 2012 de ayudas intramurales para grupos emergentes
Title: Evaluación de la función mitochondrial en leucocitos de pacientes con déficit de alfa-1 antitripsina
Principal Investigator: Francisco Dasí Fernández
Funding body: Fundación Investigación del Hospital Clínico Universitario de Valencia
Research Group on Oxidative Pathology
Consolidated group

Team involved in
ciberobn

Group members

Principal investigator
Guillermo Sáez Tormo
University
H Index: 30

Collaborating researchers
Antonio Iradi Casal. University
Carmen Tormos Muñoz. University
Benjamín Climent Díaz. University

Technicians
Lidia Monzó Beltrán. 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 morbidity 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

Main lines of research

- Study of the role of 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


• 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 P53, SIRT1 y sistemas de reparación del ADN en la patogenia de sus complicaciones neoplásicas
Principal Investigator: Guillermo Sáez Tormo
Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Universidad de Valencia
Duration: 2014-2016
Total budget: 134.915€

Reference: CB12/03/30016
Title: CIBER de la Obesidad y Nutrición (CIBEROBN)
Principal Investigator: Guillermo Sáez Tormo
Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Universidad de Valencia
Duration: 2012-2015

• THESIS

Thesis title: Biomarcadores precoces de fracaso renal agudo tras angiografía coronaria o cirugía cardíaca en pacientes con síndrome coronario o fallo cardíaco agudo
Doctoral candidate: Isidro Antonio Torregrosa Maicas
Director(s): Juan Alfonso Miguel Carrasco, Guillermo Sáez Tormo, Carmina Montoliu Felix
Date of the defense: 23/07/2015
Grade: Sobresaliente “cum laude”
Research Group on Psychiatry and Neurodegenerative Diseases
Consolidated group

"Una app para ayudar a los pacientes con psicosis".
Europa Press. 25/11/2015

Group members

Principal investigator
Julio Sanjuán Arias
Hospital. University
H Index: 19

Team involved in

Collaborating researchers
José Carlos González Piqueras. Hospital. University
Eduardo Jesús Aguilar García-Iturrospe. Hospital. University
Esther Lorente Rovira. Hospital
María José Escarti Fabra. Hospital
María Dolores Moltó Ruiz. University
Marien Gadea Domenech. University
Gracián García Martí. CIBERSAM
Manuel Jover Martínez. Hospital
José Luis Ivorra Martínez. CIBERSAM
Javier Gilabert Juan. University
Juan Nácher Roselló. University
Francisco Olucha Bordona. University
### Strategic aims

- To develop a mobile application associated with the Health Record to improve adherence for treatment of patients with first psychotic episodes
- To enlarge the common data base for multicenter studies (CIBERSAM)
- To apply of EEG-fMRI new techniques for identifying hallucinations in psychosis
- To develop of new patents measurement techniques for brain morphometry
- To develop of animal models in severe mental disorder and neurodegenerative diseases
- Evaluation of brain changes after cognitive therapy in persistent hallucinations in psychosis
- Prediction models and treatment in first psychotic episodes

### Main lines of research

- Differential expression of candidate genes in the brains of patients with psychosis
- Animal models for mental illness and degenerative diseases
- Study of mutations in degenerative diseases monoclonal gene
- Identification of the interactions between environmental and genetic factors in the risk of early psychotic episodes
- Identification of abnormal patterns of activation in fMRI psychosis
- Database Design for multicenter studies in genetics and neuroimaging of psychosis
- Prototyping of mobile applications to improve adherence in first psychotic episodes

### PUBLICATIONS

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• 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/2012/025
Title: Desarrollo de marcadores biológicos y estrategias terapéuticas en el trastorno mental grave
Principal Investigator: Julio Sanjuán Arias
Funding Body: Conselleria de Sanitat. Generalitat Valenciana
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2012-2015
Total Budget: 217.935€
Scientific activity

Reference: CB07/09/0006
Title: CIBER de Enfermedades Mentales (CIBERsam)
Principal Investigator: Julio Sanjuán Arias
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Universidad de Valencia
Duration: 2008-2015

Title: European brain imaging network for psychosis (EBINP)
Principal Investigator: Julio Sanjuán Arias
Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2014
Total budget: 4.000€

Reference: EU-GEI 241909
Title: Gene-Environment Interactions (EU-GEI)
Investigator Principal: Celso Arango López (Julio Sanjuán as collaborating researcher)
Entidad Financiadora: European Commission
Beneficiary institution: Universidad de Valencia
Duration: 2010-2015
Total budget: 347.330€

Reference: 520785
Title: Effects of juvenile and chronic stress on the structure and connectivity of neural circuits
Principal Investigator: Juan Salvador Nácher Roselló
Funding body: École Polytechnique Fédérale de Lausanne (Suiza)
Beneficiary institution: Universidad de Valencia
Duration: 2011-2014
Total budget: 50.000€

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:

Reference: BFU2012-32512
Title: Plasticidad estructural de interneuronas en el cerebro adulto. Implicaciones en esquizofrenia.
Principal Investigator: Juan Salvador Nácher Roselló
Funding body: Ministerio de Ciencia e innovación
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 125.000€

Reference: PROMETEO/2013/069
Title: Plasticidad estructural de circuitos inhibitoryos. 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€

• AWARDS

The Investigator Eduardo Aguilar and its collaborators were awarded for the scientific work “normalization of limbic hyperactivity trough cognitive behaviour therapy for auditory hallucinations assessed using an emotional fmr auditory paradigm” by the Reial Acadèmia de Medicina de la Comunitat Valenciana.
Research Group on Respiratory Problems in Neuromuscular Diseases
Consolidated group

“Neumología del Clínico ofrece el primer curso en España para cuidadores de pacientes neuromusculares con problemas respiratorios”.
24/11/2015 | elperiodic.com

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
Strategic aims

• To identify predictive factors for the failure of non-invasive ventilation in patients with amyotrophic lateral sclerosis who are suffering from a respiratory infection
• To identify predictive factors for the tolerance of volume-cycled non-invasive ventilation in subjects with amyotrophic lateral sclerosis
• To identify, in clinically stable patients with amyotrophic lateral sclerosis, predictors for the need for non-invasive mechanical ventilation during an acute respiratory infection
• We have found that a considerable percentage of ALS patients suffer from frontal impairment, especially with regard to executive function, and that FrSBe is a tool which enables the identification of these behavioural changes
• To identify the biological, psychological and social factors which impact upon the perception of dyspnoea and we have established a interdisciplinary action plan which can alleviate this symptom
• We are aware of the variables at play in the generation of complicated grief in relatives of patients suffering from respiratory diseases and we have established an action plan which can facilitate the adaptation process for these people

Main lines of research

• 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

PUBLICATIONS

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Original articles


**RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

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€

Reference: PROMETEO II/2013/014
Title: Nuevas dianas farmacológicas para el tratamiento de la EPOC y sus comorbilidades vasculares
Principal Investigator: Esteban Morcillo Sánchez (Emilio Servera and María Cruz González as collaborating researchers)
Funding body: Conselleria de Educación, Cultura y Deporte
Beneficiary institution: Universidad de Valencia
Duration: 2013-2016

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: 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€
Research Group on Tissular Biochemistry
Consolidated group

Group members

Principal investigator
Juan R. Viña
University
H Index: 26

Collaborating researchers
Luis Torres Asensi. University
Elena Ruiz García-Trevijano. University
Vicente Miralles Fernández. University
Teresa Barber Ballester. University

PhD student
Lucía Rodríguez Fernández. University

Technicians
Eva Serna García. University
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

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**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 tumours.

**PUBLICATIONS**

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**Original articles**


**THESIS**

**Thesis title:** NF-KB e ID2 como nodos de regulación de redes transcripcionales en diferentes modelos biológicos

**Doctoral candidate:** Iván Ferrer Vicens

**Director(s):** Elena Ruiz García-Trevijano, Juan Viña Ribes

**Date of the defense:** 16/01/2015

**Grade:** Sobresaliente “cum laude”

**Thesis title:** Perfiles de expresión genómica: nuevo enfoque diagnóstico para la sepsis en recién nacidos menores de 1500 gramos

**Doctoral candidate:** María Cernada Badía

**Director(s):** Eva Serna García, Federico Pallardó Calatayud

**Date of the defense:** 19/10/2015

**Grade:** Sobresaliente “cum laude”
• **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

**Reference:** P112/02394  
**Title:** Papel de las metilaciones y acetilaciones en las vías de señalización desencadenadas por mutaciones en KRas como mecanismo de resistencia a fármacos en cáncer colo-rectal  
**Principal Investigator:** Elena Ruiz García-Trevijano  
**Funding body:** Instituto de Salud Carlos III  
**Beneficiary institution:** Universidad de Valencia  
**Duration:** 2013-2015  
**Total budget:** 74.415€

**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)
Research Group on Aging and Physical Activity
Consolidated group

Group members

Principal investigator
José Viña Ribes
University
H Index: 60

Team involved in

Collaborating researchers
Ana Lloret Alcañíz. University
Juan Gambini Buchón. University
Gloria Olaso González. University
José Viña Almunia. University
Esther Giraldo Reboloso. INCLIVA
Marta Inglés de la Torre. University

PhD students
Cristina Mas Bargues. University
Andrea Salvador Pascual. University

Emerging researcher
Consuelo Borrás Blasco. University
Mª Carmen Gómez Cabrera. University
**Strategic aims**

- To identify a multicomponent exercise intervention to reverse frailty (JAMDA, 2016). One of our major aims is to prove that exercise can be considered as a drug (we published in the Journal of Pharmacology, 2012) and more recently considered as a supplement to reach healthy ageing and retard frailty. (J Physiol., 2016)
- Concerning Alzheimer’s disease, during 2015 we identified that PTEN is a major protein in controlling synapsis and cognitive function in Alzheimer’s (Nature Neuroscience, 2016). We also identified, using redox proteomics, an oxidative signature in cerebrospinal fluid to mark changes from cognitive impairment to dementia in Alzheimer’s (Free Radical Biology and Medicine, 2016). Moreover, we performed extensive studies that led us to determine that genistein is a treatment for experimental Alzheimer’s disease. (Journal of Alzheimer’s disease, 2016)
- We have been part of the Frailomics initiative (funded by the EU) and to identify biomarkers that predict the risk of frailty in older individuals (Gerontology, 2016)
- We have kept our work on centenarians and have recently identified that single nucleotide polymorphism, which is associated with exceptional longevity and it was published in the Revista de Geriatria y Gerontologia, 2015

**Main lines of research**

- Aging: identification of genes associated with aging, especially genes that are specific in centenary people. Implication of estrogen and phytoestrogens in the prevention of age-related damage
- Physical activity: identification of the mechanisms by which physical activity is good for health. Identification of the mechanisms by which physical activity helps preventing senile sarcopenia. Identification of the possible doping agents in professional practice of physical activity
- Physiopathology of the Alzheimer’s disease: identification of the mechanisms by which free radicals, originators of the oxidative stress are used to unleash cell signals that lead to cell death in Alzheimer disease

**Emerging researcher**

**Consuelo Borrás Blasco**

Research is focused on stem cells and oxygen concentration in regenerative medicine. We are studying the role of oxygen concentration when culturing stem cells. High rates of stem cell proliferation are an important tool in regenerative medicine. Ambient oxygen tensions (21% O$_2$) are normally used for in vitro culture, but physiological levels in vivo range between 3-6% O$_2$. Our aim is to compare different parameters such as proliferation, pluripotency, senescence or apoptosis culturing human Dental Pulp Stem Cells (hDPSC) under physiological or environmental oxygen concentrations. The results will be determinant to obtain enough cells and with good quality for applying them in regenerative medicine

**Emerging researcher**

**María Carmen Gómez Cabrera**

The main aim of this research is to study the beneficial effects of physical activity in prevention and treatment of several pathologies and more specifically on Alzheimer’s disease, senile sarcopenia and frailty. We are also interested in the study of the molecular bases of skeletal muscle atrophy during periods of immobilization, as well as in its prevention.

**PUBLICATIONS**

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**Original articles**


Letter


Review


Reference: SAF2013-44663-R
Title: Identificación de biomarcadores de fragilidad y de estrategias para su prevención y tratamiento. Centenarios como un modelo de envejecimiento saludable
Principal Investigator: Jose Viña Ribes
Funding Body: Ministerio de Economía y Competitividad
Beneficiary Institution: Universidad de Valencia
Duration: 2014-2016
Total Budget: 217.800€

Reference: Convocatoria 2014 de ayudas para la internacionalización de grupos INCLIVA
Title: Applied Nanotechnologies for AGEING related clinical decisions (ANAGEING)
Principal Investigator: Jose Viña Ribes
Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2014-2015
Total budget: 4.000€

Reference: Convocatoria 2012 de ayudas intramurales para grupos emergentes
Title: Efecto de la administración de genisteína y/o bexaroteno para el tratamiento de la enfermedad de Alzheimer en el modelo de ratón transgénico APP/PS1
Principal Investigator: Consuelo Borrás Blasco
Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2014 - 2015
Total budget: 3.500€

Reference: Convocatoria 2012 de ayudas intramurales para grupos emergentes
Title: Estudio de parámetros de longevidad en mujeres con tratamiento de estrógenos y progestágenos tras una menopausia inducida con GnRH
Principal Investigator: Consuelo Borrás Blasco
Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: RD12/0043/0029
Title: Red Temática de Investigación Cooperativa en Envejecimiento y Fragilidad (RETICEF)
Principal Investigator: José Viña Ribes
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Universidad de Valencia
Duration: 2013-2015
Total budget: 56.016€

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: Convocatoria 2014 de ayudas intramurales para grupos emergentes

Title: Ejercicio físico controlado como intervención en el tratamiento de la fragilidad en el anciano y en la prevención de la dependencia. Bases moleculares.

Principal Investigator: Mari Carmen Gómez Cabrera

Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2014 - 2015

Total budget: 3.500€
Research Group on Anesthesiology and Reanimation

Consolidated group

"El Hospital Clínico presenta un protocolo de la organización asistencial en el manejo del paciente politraumatizado". Rafael Badenes. 26/11/2015 | elperiodic.com
http://www.anestesiaclinicovalencia.org

Group members

Principal investigator
Francisco Javier Belda Nácher
Hospital. University
H Index: 14

Collaborating researchers
Marina Soro Domingo. Hospital. University
Gerardo Aguilar Aguilar. Hospital
José García de la Asunción. Hospital
Francisco Martí Canoves. Hospital
Beatriz Garrigues Olivé. Hospital
Juán Vicente Llau Pitarch. Hospital. University
Rafael Badenes Quiles. Hospital
Armando Maruenda Paulino. Hospital. University
María Luisa García Pérez. Hospital
Carlos Tornero Tornero. Hospital
Benigno Escamilla Cañete. Hospital
María Luisa Laredo Alcázar. Hospital
Arturo Carratalá Calvo. Hospital
Jaime Pérez-Griera. Hospital
José Miguel Alonso Íñigo. Hospital
Blanca Arocas Chicote. Hospital
José Antonio Carbonell López. Hospital
Pedro Charco Mora. Hospital
Mario De Fez Barberá. Hospital
Mar Garzando Civera. Hospital
Andrea Gutiérrez Valcárcel. Hospital
Irene León Carsi. Hospital
Mª Jesús Montero Hernández. Hospital
Mª José Parra González. Hospital
Ernesto Pastor Martínez. Hospital
Jaume Puig Bernabéu. Hospital
Ana Mugarra Llopis. Hospital
Laura Reviriego Agudo. Hospital

Emerging researcher
Carlos Ferrando Ortolá. Hospital
Scientific activity

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 individualized 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. We are currently drafting the manuscript for the NEJM.

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).

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 oxidative stress biomarkers in exhaled lung water
• 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 government bodies 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

PUBLICATIONS

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Original articles


**Scientific activity**


4 Scientific activity


Letters


Review


Editorial


38. European Society of Anaesthesiology task force reports on place of aprotinin in clinical anaesthesia. Aprotinin: is it time to reconsider?Eur J Anaesthesiol. 2015 Sep ;32(9):591-5.IF: 2,942

• THESIS

Thesis title: Continuous cardiac index trending (proaqt) via a radial arterial line versus standard care in general surgical patients

Doctoral candidate: Jaume Puig Bernabeu

Director(s): Francisco Javier Belda Nácher, Daniel Arnulf Reuter

Date of the defense: 29/06/2015

Grade: Sobresaliente “cum laude”

Thesis title: Efecto de las diferentes ondas de flujo y de la pausa teleinspiratoria sobre la oxigenación y ventilación en modelo animal

Doctoral candidate: María Luisa García Perez

Director(s): Rafael Badenes Quiles, Carlos Ferrando Ortolá, Marina Soro Domingo

Date of the defense: 29/06/2015

Grade: Sobresaliente “cum laude”

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: EC10-318

Title: Tratamiento anticipado con ganciclovir de la infección activa por el citomegalovirus (CMV) en el paciente crítico en ventilación mecánica con sepsis grave o shock séptico

Principal Investigator: Gerardo Aguilar Aguilar

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2012-2016

Total budget: 38.500€

Reference: PI13/02742

Title: Prospective observational study of the direct oral anticoagulants perioperative management

Principal Investigator: Raquel Ferrandis Comes

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2014-2016

Total Budget: 53.845€

Reference: PI13/00119

Title: Reducción de las asincronías y de la duración de la ventilación mecánica mediante la Ventilación Asistida Ajustada Neuralmente (NAVA) en pacientes con insuficiencia respiratoria aguda

Principal Investigator: Jesús Villar Hernández (Francisco Javier Belda as collaborating researcher)

Funding body: Instituto de Salud Carlos III

Beneficiary institution: Fundación Canaria de Investigación y Salud (FUNCIS)

Duración: 2014-2016

Total budget: 55.418€
Reference: PI14/00829
Title: Reducción de las complicaciones postoperatorias y de la estancia hospitalaria con una estrategia perioperatoria individualizada de ventilación de protección pulmonar. Estudio comparativo, prospektivo.
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€

• AWARDS

Carlos Ferrando Ortolá was awarded with the Young Investigator Start-Up Grant 2015 by the European Society of Anaesthesiology (ESA).
Research Group on Translational Genomics
Consolidated group

“No descarto promover la creación de más empresas y aportar mi modesta contribución al panorama de la Biotecnología en España”

Manuel Pérez Alonso. Genetic Insider. 5-5-2015

Group members

Principal investigator
Rubén D. Artero Alepuz
University
H Index: 13

Collaborating researchers
Manuel Pérez Alonso. University
Mª Beatriz Llamusí Troísi. University
Ariadna Bargiela Schönbrunn. University
Juan M. Fernandez Costa. 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
Eleni Foteinou. University
Strategic aims

- To describe that increased autophagy and apoptosis contribute to muscle atrophy in a Myotonic Dystrophy type 1 Drosophila model, which also suggest new therapeutic strategies for the disease
- To show that pentamidine rescues heart contractility and rhythmicity in the same model of Myotonic Dystrophy in Drosophila making use of a quite unique equipment and know-how

Main lines of research

- Using miRNAs as therapeutic targets in myotonic dystrophy (DM)
- Drug discovery and development in DM
- Study of the causes of cardiac alterations in DM
- Study of the molecular causes of muscle and CNS degeneration in DM
- Study of the molecular mechanisms associated with spinal muscular atrophy and search for potential therapies
- Development of a model in Drosophila for the discovery of inhibitors of protein-protein interactions
- Understanding human podocyte function through Drosophila nephrocytes

• PUBLICATIONS

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Original articles


• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: SAF2012-36854
Title: Utilización de microRNAs como dianas terapéuticas y biomarcadores de progresión en Distrofia Miotónica
Principal Investigator: Rubén Artero Allepuz
Funding body: Ministerio de Economía y Competitividad
Beneficiary institution: Universidad de Valencia
Duration: 2013-2016
Total budget: 150.000€

Reference: FPA/2015/085
Title: Utilización de microRNAs como dianas terapéuticas y biomarcadores de progresión en distrofia miotónica
Principal Investigator: Rubén Artero Allepuz
Funding body: Conselleria d’Educació, Cultura i Esport
Beneficiary institution: Universidad de Valencia
Duration: 2015
Total budget: 9.300€

Reference: PI12/03106
Title: Estudio de las causas de los defectos cardiacos en las Distrofias Miotónicas
Principal Investigator: Mª Beatriz Llamusí Troisi
Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2013-2015
Total budget: 54.450€

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: 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
Thesis title: Regulación transcripcional de muscleblind y nuevos mecanismos de patogénesis en un modelo de Distrofia Miotónica en Drosophila
Doctoral candidate: Ariadna Bargiela Schönbrunn
Director(s): Rubén Artero, Beatriz Llamusi
Date of the defense: 29/05/2015
Grade: Sobresaliente “cum laude”

Thesis title: Implicación de miRNAs en la toxicidad mediada por expansiones de repeticiones CTG en Distrofia Miotónica
Doctoral candidate: Juan M. Fernández Costa
Director(s): Rubén Artero Allepuz
Date of the defense: 18/12/2015
Grade: Sobresaliente “cum laude”

• AWARDS

Manuel Pérez Alonso was awarded with the Premio a la Innovación Sanitaria given annually by the Instituto de Investigación y Desarrollo Social de Enfermedades Poco Frecuentes (INDEPF).

In the upper panels two images of muscles of Drosophila in which cell nuclei in blue and activation process of autophagy in red are detected when the charge of myotonic dystrophy (CTG expansions) mutation is expressed. In the two lower images show something similar but in human myoblasts, in which there is abnormal activation of autophagy (absence of red signal in the lower left panel), but if patient myoblasts (lower right panel).
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
Vicente Martí Martí. 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
Strategic aims

• Incorporation of the retroperitoneoscopy as a new surgical technique for the department, as a treatment of adrenal tumours
• Development of the clinical pathway for thyroidectomy
• Completion of the national multicenter trial on the differences between the pancreatico-gastrostomy and pancrato-jejunosotony in cephalic pancreaticoduodenectomy technique

Main lines of research

• About coloproctological surgery: study of the quality standards for coloproctology 3D endorectal ultrasound, sacral neuromodulation and perianal fistula surgery
• About hepatobiliary and pancreatic surgery: acute pancreatitis, gene transfection, pancreaticoduodenectomy
• About endocrine surgery: laparoscopic adrenal tumours, recurrences study in thyroid surgery, parathyroid adenomas intraoperative localization
• About metabolic and bariatric surgery: pathophysiology of postoperative changes
• About breast surgery: utility of fibrin sealants in postoperative seroma
• About gastroesophageal surgery: mutations in GIST tumours, overexpression of HER2 and HER3 in gastric tumours, perioperative QT in advanced gastric cancer

Original articles


**PUBLICATIONS**

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**Letter**


**Review**


**Thesis**

**Thesis title:** Efectos de un programa de fisioterapia respiratoria preoperatoria sobre la oxigenación y la función respiratoria perioperatoria en pacientes obesos mórbidos sometidos a cirugía bariátrica laparoscópica.

**Doctoral candidate:** Lucas Rovira Soriano

**Director(s):** Joaquín Ortega Serrano, Julio Llorens Herrerías

**Date of the defense:** 13/03/2015

**Grade:** Sobresaliente “cum laude”

**Thesis title:** Impacto del tratamiento neoadyuvante en los resultados de la cirugía del cáncer de recto localmente avanzado

**Doctoral candidate:** Rafael Estevan Estevan

**Director(s):** Luis Sabater Ortí, Rafael Alos Company

**Date of the defense:** 17/12/2015

**Grade:** Sobresaliente “cum laude”

**Thesis title:** Identificación de los perfiles de expresión en el adenocarcinoma ductal de páncreas. Implicaciones clínicas.

**Doctoral candidate:** María del Carmen Gómez Mateo

**Director(s):** Felipe Javier Chaves Martínez, Antonio Ferrández Izquierdo, Luis Sabater Ortí

**Date of the defense:** 08/07/2015

**Grade:** Sobresaliente “cum laude”

**AWARDS**

The Investigator Luis Sabater had received in 2015 the National Surgery award.
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 Amézcu García. CIBERSAM
Ferrán Catalá López. University
Scientific activity

Strategic aims
• To participated in the publication of the Global Burden of Disease study 2013 in The Lancet (2015 Nov 28;386(10009):2145-91). Among the most relevant findings of this study is the epidemiologic transition, on a global level, from infectious diseases to chronic non-communicable diseases during the period 1990-2013
• To edit a Research Topic in Frontiers entitled “Direct and Inverse comorbidities between complex disorders” with the aim of helping to understand unexpected associations between apparently different diseases/illnesses. We have also published 7 original articles, with diverse perspectives ranging from epidemiology to bioinformatics, about diseases such as malaria, bipolar disorder, dementia (e.g. Alzheimer’s), Down’s syndrome, glioblastoma and lung cancer
• To play an active role in defining a clinically useful position regarding Mild Cognitive Decline as members of the Cognitive Decline Group of the European Innovation Partnership for Active and Healthy Ageing (EIPAPA)

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 TMG
• Identification of biomarkers in TMG
• Study of the direct and reverse comorbidity in TMG 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

Original articles

PUBLICATIONS

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Letters

24. Catalá-López F, Tabarés-Seisdedos R. Alzheimer’s disease and cancer: the need of putting research into context with...
previous published systematic reviews. J Cancer Res Clin Oncol. 2015 Mar;141(3):569-70. IF: 3.081


Editorial


Review


• 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 Tabarés 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 (ob), metabolic syndrome (mets), type 2 diabetes (t2dm) and fatty liver disease (fl): a multidisciplinary approach.
Principal Investigator: José María Mato De La Paz (as collaborating researcher Rafael Tabarés Seisdedos)
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: IntraCIBER2015
Title: CANCER comorbidity in people with Central Nervous System disorders
Principal Investigator: Rafael Tabarés Seisdedos
Funding Body: CIBER
Beneficiary Institution: CIBERSAM
Duration: 2015-2017
Total budget: 35.000€
4.1.4 Reproductive medicine area

Research Group on Women Health 181
Research Group on Stem Cells Applied to Reproduction, Embryo Viability and Endometrial Receptivity 184
Research Group on Male Infertility and Embryonic Stimulation 191
Research Group on Women Health.
Consolidated group

“Nuestro objetivo es crear mecanismos para que podamos avanzar en la reducción de la vulnerabilidad frente a la enfermedad o, incluso, a la muerte”
Antonio Cano. Valencia Económica. 11/05/2015

Group members

Principal investigator
Antonio Cano Sánchez
University
H Index: 26

Collaborating researchers
Juan José Tarín Folgado. University

Emerging researcher
Raúl Gómez Gallego. INCLIVA

Technician
Rosa Aliaga Corachán. University
Strategic aims

- Vitamin D in women’s health. We have continued with the inclusion of the cohort, which has already reached 1200 participants. To extend the study of bone metabolism during pregnancy
- Postmenopausal osteoporosis: role of the calcium sensor receptor in bone formation and osteoclastogenesis. Intervention with calcium sensor receptor has been discarded in its actions on bone bone-forming cells
- Initial aterogenesis and gonadal steroids. Experiences have been completed in ApoE mutated mice. To publish a systematic review on bone metabolism in pregnancy
- Gonadal protection in pre-menopausal women treated with chemotherapy. Progress has been made in the cohort inclusion process, which is now close to 100 members. To include endocrine studies in a database

Main lines of research

- In the postmenopausal osteoporosis field, to analyze the role of calcium sensing receptor in bone formation and osteoclastogenesis and to study calcium and vitamin D supplementation and its impact on bone metabolism
- 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
  - To study the role of vitamin D in women’s health
  - To determine the general and cognitive frailty on women

Emerging researcher

Raúl Gómez Gallego

Raúl Gómez’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 bioluminiscently 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


Letter


Review


Editorial


• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI12/02775
Title: Activación del receptor sensor del calcio por sales de calcio y vitamina D. Estudio básico y clínico
Principal investigator: Antonio Cano Sánchez
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Universidad de Valencia
Duration: 2013-2015
Total budget: 98,615€

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: CP13/00038
Title: Global multivariant analysis of putative biomarkers identified through combined multi-technical approach for the non-invasive detection of endometriosis

• THESIS

Doctoral candidate: Lorena Sabonet Morente
Director(s): Antonio Cano Sánchez, Juan José Tarín Folgado, María Reyes Balanza Chancosa
Date of the defense: 13/07/2015
Grade: Sobresaliente “cum laude”

Thesis title: Efectos del tratamiento con agonistas dopaminérgicos sobre las lesiones endometriosis
Doctoral candidate: Silvia Tamarit Bordes
Director(s): Antonio Pellicer Martínez, Raúl Gómez Gallego, José Bellver Pradas
Date of the defense: 14/01/2015
Grade: Sobresaliente “cum laude”
Research Group on Stem Cells Applied to Reproduction, Embryo Viability and Endometrial Receptivity
Consolidated group

“No se trata de disponer de bebés a la carta, este tema no es trivial, estamos hablando de poder corregir enfermedades que causan sufrimiento y muerte”.

Carlos Simón. Encuentros de Excelencia de VLC/Campus. 1-7-2015.
http://www.carlos-simon.com/es/

Group members
Principal investigator
Carlos Simón Vallés
IVI. University
H Index: 61

Collaborating researchers
Amparo Mercader Bayarri. IVI
Ana Cristina Cerveró Sanz. IVI
María José de los Santos Molina. IVI
Tamara Garrido Gómez. IVI
Alicia Quiñonero Villora. IVI
Xavier Santamaría Costa. IVI
Hortensia Ferrero Cháfer. INCLIVA
Diana Valbuena Perilla. IVI
Pilar Alamá Faubel. IVI
Marta Gonzalo Moja. IVI
Mª Amparo Faus Esteve. IVI
José Bellver Pradas. IVI
Ernesto Bosch Aparicio. IVI
David Blesa Jarque. IVI
Inmaculada Moreno Gimeno. IVI
Patricia Díaz Gimeno. IVI
Elena Labarta Demur. IVI
Antonio Díez Juan. IVI
to the difficulty of collecting endometrial fluid from the patients suffering obesity. Regardless of this setback and with the aim to identify a miRNA profile intrinsically linked to the transfer of obesity from mothers to offspring, two approximations in the “in silico” analyses of the raw data obtained were done. We are recruiting more patients.

Main lines of research

- Adult stem cells in the human endometrium
- Study of endometrial proteomics and embryo viability
- Study of endometrial receptivity

Strategic aims

- Our research was focused on two main objectives: (1) The identification of specific SSCs markers described in the human endometrium in the last ten years (W5C5, ICAM, PDGF, CD146, CD133 and Side Population) by in vitro and in vivo experiments; and (2) to investigate cell therapies using stem cells derived from bone marrow as well as their secreted paracrine factors to regenerate the endometrium in endometrial pathologies
- We have performed a comparative proteomic analysis using I-TRAQ technique to determine the protein expression profile of receptive endometria coming from fertile donors, with refractory endometrium coming from patients with and IUD and finally patients with Recurrent Implantation Failure (RIF). Thus proteomic comparative will allow us to design and develop and interactome of the endometrial receptivity, knowing the most important proteins for the acquisition of this vital ability of the endometrium to achieve a correct implantation
- We currently start to analyze by arrays the first set of samples collected 8 control patients (8 samples obtained in the phase of the cycle LH+2 and 8 samples in LH+7) and 6 obese patients. The disparity in the number of samples within each study group is associated

Emerging researcher

Francisco Domínguez Hernández. INCLIVA
Irene Cervelló Alcaraz. IVI
Felip Vilella Mitjana. INCLIVA

PhD students

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

Technician

María Herrero Baena. INCLIVA

Emerging researcher

Irene Cervelló Alcaraz

Research is based on the identification, characterization and isolation of Somatic Stem Cells in the endometrium. Endometrial Stem Cells have been identified in human and murine models, the regenerative potential of these cells has been proven and there is an ongoing research on the existence of Lgr5 marker in the endometrial tissue.

Moreover, the work is also focused on essential processes based on the regenerative medicine related with the porcine and human uterus.

Emerging researcher

Felip Vilella Mitjana

The research line of Endometrial Receptivity is based on the study of endometrial secretions, specifically the endometrial fluid.

We use secretomic and genomic approach so we can describe new molecules that can be correlated with the days of the menstrual cycle and may be involved in obtaining the window of implantation period, opening a new field of study for the analysis of the changes in the endometrium during the menstrual cycle and the cross-talk between the embryo and the endometrium.

We have demonstrated that human endometrial epithelium secretes specific microRNAs (miRNAs) during the time frame when the embryo enters the uterine cavity and initiates its ad-
hesion 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 Simón’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**


21. Bosch E. High responders and patients with a good prognosis are not immune to the negative impact on live birth rate of elevated P on the day of triggering. Fertil Steril. 2015 Jun;103(6):1423. IF: 4.59


Editorial


Review


• THESIS

Thesis title: Patrón de decidualización en mujeres con pre-eclampsia mediante la aplicación de métodos de transcriptómica y proteómica

Doctoral candidate: Pablo Padilla Iserte

Director(s): Alfredo Perales Marín, Carlos Simón Vallés

Date of the defense: 13/01/2015

Grade: Sobresaliente “cum laude”

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: SARM 324509

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 - 2015

Total budget: 668.759€

Reference: E6478-NOTED

Title: Non-invasive Tests for Endometrial Dysfunction – Novel Clinical Perspectives for Infertility and Endometriosis Diagnostics

Funding body: European Comission (Eurostars-Eureka Programme)

Principal Investigator: Carlos Simón Vallés

Beneficiary institution: Igenomix

Duration: 2013 - 2015

Total budget: 159.082€

Reference: PROMETEO II/2013/018


Principal Investigator: Carlos Simón Vallés

Funding body: Conselleria de Educación, Cultura y Deporte

Beneficiary institution: Universidad de Valencia

Duration: 2013-2016

Total budget: 217.000€
Reference: SAF 2012/31017
Title: Demostración de que Leucine-rich repeat-containing G-protein coupled receptor S(Lgr5) es un marcador de células madre endometriales. Desde los modelos animales hasta su contribución en terapia celular e ingeniería tisular
Principal Investigator: Carlos Simón Vallés
Funding Body: Ministerio de Sanidad, Servicios Sociales e Igualdad
Beneficiary Institution: Fundación Investigación Hospital Clínico Universidad de Valencia
Duration: 2013-2015
Total budget: 91.707€

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€

Reference: PI12/00450
Title: Descripción del perfil proteómico endometrial del Fallo de Implantación recurrente. Creación del interactoma del fallo de implantación
Principal Investigator: Francisco Domínguez Hernández
Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Fundación Investigación Hospital Clínico Universidad de Valencia
Duration: 2014-2015
Total budget: 3.500€

Reference: GV/2013/136
Title: Expresión, localización y estudio funcional de la proteína PGRMC1 (Progesterone Receptor Membrane Component 1) en el endometrio
Principal Investigator: Francisco Domínguez Hernández
Funding Body: Fundación Investigación Hospital Clínico Universidad de Valencia
Beneficiary Institution: Fundación Investigación Hospital Clínico Universidad de Valencia
Duration: 2013-2015
Total budget: 404.000€

Reference: EMD Serono Research Institute, Inc.
Title: Análisis de miRNAs en fluido endometrial como diagnóstico no invasivo de receptividad endometrial
Principal Investigator: Felipe Vilella Mitjana
Funding Body: Generalitat Valenciana
Beneficiary Institution: Fundación Investigación Hospital Clínico Universidad de Valencia
Duration: 2013-2015
Total budget: 239.600€
**Clinico Universitario de Valencia**

**Duration:** 2014-2015  
**Total budget:** 12,000€

**Reference:** Convocatoria 2014 de ayudas intramurales para grupos emergentes  
**Title:** Reconstrucción del endometrio humano a través de xenotrasplante de células madre (LG5+) 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:** 2014-2015  
**Total budget:** 2,000€

**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:** 2014-2015  
**Total budget:** 3,500€

**AWARDS:**

In 2015 Felipe Vilella was awarded with the New Investigator Plenary Session Award by the Society for Reproductive Investigation (SRI) in the 62nd Annual Meeting in San Francisco (USA). Moreover Aymara Más received the Best New Investigator Poster Award by Society for Reproductive Investigation (SRI) in the 62nd Annual Meeting in San Francisco (USA).
Research Group on Male Infertility and Embryonic Stimulation
Consolidated group

“Congela tu tiempo, preserva tu futuro y conserva tus sueños”.
José Remohí. Posted by Official Press Date: 16 junio, 2015

Group members

Principal investigator
José Remohí Giménez
IVI. University
H Index: 57

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**

- Our results obtained by inducing the exogenous expression of a combination of selected key germ cell developmental factors over human somatic cells demonstrate the ability of human male somatic cells to directly convert into a meiotic germ-like phenotype. Nevertheless, our study must be considered an initial attempt to create an in vitro model for the direct conversion of somatic cells from patients with gamete-alterations production into germ cells in vitro, opening the field to discover new cell therapies to treat them in the future.
- Based on a pilot study that we carried out with 17 infertile couples of oocyte donation program, we have settled down an initial model with potential diagnostic which combines embryo oxidative profile and time-lapse morphokinetic. Through a logistic regression analyses we have been able to identify two parameters: cell cycle duration (cc2) (morphokinetic parameter) and the presence/absence of interleukin 6 (IL-6). Regarding these two factors, it has been established four embryo categories to develop a hierarchical selection model of embryos. It was observed a positive correlation between embryo categories and implantation rate.

**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**

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**


15. Cobo A, **Garrido N**, Pellicer A, Remohí J. Six years’ experience in ovum donation using vitrified oocytes: report of cumulative outcomes, impact of storage time, and...
Scientific activity


Editorial


• THESIS

Thesis title: La adición de LH a la estimulación ovárica no produce más maduración endometrial prematura ni diferente patrón de expresión génica endometrial que la estimulación con solo fsh. Un estudio comparativo en donantes de ovocitos
Doctoral candidate: Elkin Albeiro Muñoz Muñoz
Director(s): José Remohí Giménez
Date of the defense: 17/07/2015
Grade: Sobresaliente “cum laude”

Thesis title: Cuantificación de la calidad embrionaria mediante el consumo de oxígeno durante el proceso rutinario de incubación y desarrollo in vitro
Doctoral candidate: Alberto Tejera Pastor
Director(s): Marcos Meseguer Escrivá, Mª José De Los Santos Molina, Nicolás Garrido Puchalt
Date of the defense: 18/02/2015
Grade: Sobresaliente “cum laude”

• 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 y 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 investigator researcher)
Funding Body: Conselleria de Educación, Cultura y Deporte
Beneficiary Institution: Universidad de Valencia
Duration: 2013-2016
Total budget: 70.000€ (this year)

Sequential culture media recruitment and storage.
### Hospital divisions areas

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4.2 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

Allergology Unit

Main lines of research

- Application of the basophil activation test (Basotest) for the diagnosis of respiratory and medication allergies
- Relationship between patient’s allergenic profiles and the efficiency of the immunotherapy with mites
- Use of the anti-IgE (omalizumab) in the treatment for the cutaneous allergic pathology

PUBLICATIONS

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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€

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Original articles

Scientific activity


Department of Otolaryngology

Un médico valenciano, elegido Presidente de la Sociedad Española de ORL y Cirugía de Cabeza y Cuello.

El Levante. 19-12-2015.

El Dr. Jaime Marco Algarra nombrado Presidente de la Sociedad Española de ORL y Cirugía de Cabeza y Cuello.

Elperiodic.com 19/12/2015

- PUBLICATIONS

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Original articles


Letters

3. Morales-Piga AA, García Callejo FJ, González Herranz P, ...

Department of Maxillofacial Surgery

Strategic aims

- Translational phase of the 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 installation neuromodulator in the sphenopalatine ganglion treatment of certain chronic headaches
- Research on materials involved in bone regeneration
- Evaluation of platelet factors (PRP) and fibrin rich plasma in the treatment of osteonecrosis associated with drugs intake (bisphosphonates)

- PUBLICATIONS

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Original articles

**Department of Pharmacy**

**Strategic aims**

- Implementation of a new therapeutical drug monitoring system in a clinical analytical laboratory for pharmacokinetic control of antibiotic (meropenem, piperacillin, ceftazidime) and antifungals (voriconazole) in the hospitalized patient, with the aim of optimal and rational use of antimicrobials
- Study of pharmacokinetics of caspofungin in patients under hemodiafiltration

**Main lines of research**

- Pharmacokinetics/Pharmacodynamics of anidulafungin in plasma and intraperitoneal fluid in the critical patient with secondary peritonitis and suspected/evidenced candida spp. Infection. Efficacy Study
- Observational Study of population pharmacokinetic model of voriconazole in allogeneic stem cell transplantation
- Implementation of a new therapeutical drug monitoring system in a clinical analytical laboratory for pharmacokinetic control of antineoplastics in the oncological patient, with the aim of optimal and rational use of oncological medication
- Cost effectiveness analysis of direct-acting antiviral therapy for treatment-of patients with chronic HCV infection

**PUBLICATIONS**

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**Original articles**


**Review**


**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 Thoracic Surgery**

**Main lines of research**
- Tracheal surgery in benign lesions, trauma and malignancies
- Implementation of VATS surgery
- Surgical rescue in advanced lung cancer

**PUBLICATIONS**

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**Original articles**


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**Department of Radiologic Diagnosis**

**Main lines of research**
- To participate in several clinical trials of Hematology and Oncology Service 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 Biochemistry and Clinical Analysis**

**Strategic aims**
• To adequate the analytical demand through electronic request laboratory information system GestLab
• Implementation of immunoassays against monoclonal light-chain isotypes in the diagnosis and monitoring of diseases chain gammopathy

**Main lines of research**
• To collaborate with others investigation groups: Cardiology Clinic (ischemic heart disease and heart failure), cardiometabolic risk and Diabetes (lipid metabolism and insulin resistance) and Women’s Health (bone metabolism in postmenopausal osteoporosis, genetic diagnosis prenatal noninvasive and biochemical evaluation of the role of ovarian function in Assisted reproduction)

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**Original articles**


**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:** PI14/00959  
**Title:** Comparación aleatoria entre un estrategia de intervención sobre fragilidad frente a la estrategia habitual en pacientes frágiles después de un infarto agudo de miocardio.  
**Principal Investigator:** Juan Sanchís Forés (Enrique Rodríguez Borja as collaborating researcher)  
**Funding Body:** Instituto de Salud Carlos III  
**Beneficiary Institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2015-2018  
**Total budget:** 36.300€

**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:** 2013-2015  
**Total budget:** 98.615€
Main lines of research

- Study of oxidative stress, nutrition and inflammation in patients with chronic kidney disease in stages 3a, 3b, 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**: Biomarcadores precoces de fracaso renal agudo tras angiografía coronaria o cirugía cardíaca en pacientes con síndrome coronario o fallo cardíaco agudo

**Doctoral candidate**: Isidro Antonio Torregrosa Maicas

**Director(s)**: Juan Alfonso Miguel Carrasco, Guillermo Sáez Tormo, Carmina Montoliu Félix

**Date of the defense**: 23/07/2015

**Grade**: Sobresaliente “cum laude”
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


Letters


Thesis

**Thesis title:** Determinación de parámetros clínico-patológicos y moleculares implicados en la regresión espontánea de neoplasias melanocíticas cutáneas.

**Doctoral candidate:** José María Martín Hernández

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

**Date of the defense:** 13/02/2015

**Grade:** Sobresaliente “cum laude”

**Thesis title:** Carcinoma epidermoide cutáneo: relación con los trastornos respiratorios del sueño y definición de la variante alto riesgo

**Doctoral candidate:** Tania Díaz Corpas

**Director(s):** Esperanza Jordá Cuevas, María Manuela Morales Suárez-Varela, Estrella Fernández Fabrellas

**Date of the defense:** 11/06/2015

**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 (Esperanza Jordá as collaborating researcher)

**Funding Body:** Instituto de Salud Carlos III
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2014-2016
Total Budget: 59,592€

Department of Gastroenterology and Hepatology

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 continue the analysis of hepatic encephalopathy, the nonalcoholic, epidemiological, therapeutic and immunoprophylaxis on Hepatitis Virus steatohepatitis. Also hepatocellular damage and nitric oxide and liver tumours
• About endoscopy division: study on the therapeutic dilatation, the ecoendoscopia diagnostics and therapeutics, ampulectomy, diverticulotomy of Zencker and digestive prostheses

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Original articles


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


THESIS

Thesis title: Enfermedad hepática grasa no alcohólica en la obesidad mórbida: Implicaciones patogénicas y diagnósticas
Doctoral candidate: María Luisa García Torres, José Manuel Rodrigo Gómez.
Director(s): Desamparados Escudero García
Date of the defense: 21/09/2015
Grade: Sobresaliente “cum laude”

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

THESIS

Thesis title: Papel del nf-K946 y MiRNA-34A en la patogénesis de la osteoartritis y como posible diana de las nuevas terapias biológicas
Doctoral candidate: Francisco Argüelles Linares
Director(s): Antonio Silvestre Muñoz, José Miguel Cerdá Nicolás
• 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

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 Minguez 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€

Department of Intensive Medicine

Main lines of research
• Bleeding acute spontaneous intraparenchymal (HIP)
• Study of Biomarkers of brain injury (BNP, D-dimer, neuron-specific enolase (NSE) and S-100B) and inflammatory markers as prognostic and related mortality and quality of life in the short and medium term in patients with HIP factors
• Study of the ratio of the volume of the hematoma and other prognostic factors in relation to mortality and quality of life in the short and medium term in patients with HIP
• Sepsis: biomarkers study, metabolic pathways and oxidative stress critic septic patient
• Modes of Mechanical Ventilation and therapeutic strategies for ARDS
  • Hyperglycemia and variability in critically ill patients
  • Test of Platelet Aggregation

• PUBLICATIONS

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Original articles

6. Lorente L, Martín MM, Abreu-González P, de la Cruz T,
Date of the defense: 24/04/2015
Grade: Sobresaliente “cum laude”

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)

THESIS

Thesis title: Diagnóstico precoz de la neumonía asociada al ventilador. Evaluación seriada de biomarcadores en minilavado broncoalveolar y monitorización microbiológica, complementada con condensado de aire exhalado y sangre.

Doctoral candidate: Santiago Borrás Pallé

Director(s): José Blanquer Olivas, Francisco Javier Chorro Gas-có, Manuel Mata Roig

Dialogues

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Scientific activity

• THESIS

Thesis title: Patrón infeccioso de la población extranjera. Periodo 2006-2010
Doctoral candidate: Elena Navarro Calderón
Director(s): Rafael Borras Salvador and Juan José Camarena Miñana
Date of the defense: 02/19/2014
Grade: Sobresaliente “cum laude”

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: SAF2012-38368
Title: Especificidad de receptores y antigenicidad de variantes epidémicas de norovirus genotipo gII.4 causantes de gastroenteritis aguda
Principal Investigator: Francisco Javier Buesa Gómez
Funding body: Ministerio de Economía y Competitividad
Beneficiary Institution: Universitat de València
Duration: 2013-2015
Total budget: 42.000€

Title: Rotavirus surveillance in Europe: Determining the diversity of cocirculating rotavirus strains in consecutive rotavirus seasons.
Investigator Principal: Miren Iturriza Gómara (Jesús Rodríguez Díaz as collaborating Research)
Funding Body: Sanofi Pasteur y Glaxo Smith Kline Biologicals, coordinado por University of Liverpool, auspiciado por la Organización Mundial de la Salud.
Beneficiary Institution: Universitat de València
Duration: 2006 - 2016.

Letters


Cardiac Stimulation Unit

Strategic aims

• Accreditation courses on Cryoballoon ablation have started successfully, with participants from Europe (Great Britain, Italy, Portugal) and from other countries (Russia, Lebanon, Iran...)
• The series on endoepicardial approach in VT ablation has been published in Circulation Arrhythmias and Electrophysiology
• Fire&Ice trial was finished
**Main lines of research**

- Cryoballoon ablation: dose of cryoenergy based on time to effect
- VT ablation
- Silent brain damage (biomarkers) in ablation procedures
- CTI ablation with zero x-ray exposition and guided by electrogarm amplitude
- Ventricular activation modelling (collaborative project with UPV, CICYT grant)
- Heart innervation and multipoint left ventricular pacing
- Characterization of atrial signal in the beginning of paroxysmal atrial fibrillation episodes
- Physiologic signals monitoring during driving (collaborative with UPV, CICYT grant)
- ARTESIA study: NOAC in silent episodes of atrial tachyarrhythmias detected by implanted devices

**PUBLICATIONS**

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**Original articles**


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**Department of Urology**

**Strategic aims**

- To complete the projects:
  - TMPRSS2-ERG gene fusión AND DNA metilation in prostate cancer
  - Immunohistochemical analysis of tissue microarrays in non musculoinvasive bladder cancer
  - Genetic analysis of renal cancer using Multiplex ligation dependent probe amplification
  - To Start the Project: Metabolomic profile in prostate cancer
  - To advance in the Project: Clinical utility of serum and urine MicroRNAs expression as bladder cancer biomarker

**Main lines of research**

- Nuclear Magnetic Resonance spectroscopy-based metabolomic profiling of prostate cancer
- MicroRNAs expression in bladder cancer
- Prognosis value of Immunohistochemical markers in bladder cancer
- Multiplex ligation dependent probe amplification (MLPA) in renal cancer
- TMPRSS2-ERG gene fusion AND DNA metilation in prostate cancer

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**Original articles**

Department of Neurophysiology

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Letter

1. de Entrambasaguas M, Ponz A, Sánchez-Monzó P, Peñaranda N. [Fasciculations, cramps, and statins]. Rev Neurol. 2015 Apr 16;60(8):380-1. IF: 0.83

Department of Neurology

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Original articles


THESIS


Doctoral candidate: José Antonio March Villalba

Director(s): José M. Martínez Jabaloyas, David Ramos Soler, Cristina Domenech Pérez

Date of the defense: 18/12/2015

Grade: Sobresaliente “cum laude”


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**Department of Pediatrics**

- **PUBLICATIONS**

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Department of Radiotherapy

- **PUBLICATIONS**

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Department of Nuclear Medicine

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Department of Rheumatology

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Original articles


Department of Pneumology

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**Original articles**


2. Lizarzábal Suárez PC, Núñez Savall E, **Carrión Valero F**. Lipoid pneumonia due to accidental aspiration of paraffin in a “fire-eater”. Arch Bronconeumol. 2015 Oct ;51(10):530-1. IF: 1,823


Quality Central Unit

- PUBLICATIONS

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**Original articles**


4.3 Other scientific contributions from scientific platforms

4.3.1 Biobank resources

Biobank members

Principal Investigator
Dr. Antonio Ferrández Izquierdo
Hospital. University

Collaborating researchers:
Dr. Lorena Peiró Chova. INCLIVA

Technicians
Olga Bahamonde Ponce. INCLIVA
Marta Belda Moscardó. INCLIVA
**ACTIVITIES DEVELOPED**

**Incorporation of samples in pre-existing collections:**

**Oncological Node:**
- Collection of solid tumours (Tumor Bank): around 53 new cases (98 aliquots).
- Collection of peripheral blood and derivative products in patients suffering from breast cancer (CM-S [Blood-Breast Cancer]): around 267 new cases (3912 aliquots).
- Collections of peripheral blood and derivative products in patients suffering from lung cancer (CP-S [Blood-Lung Cancer]): around 183 new cases (2750 aliquots).
- Collection of peripheral blood and derivative products in patients suffering from melanoma (MM-S [Blood-Melanoma]): around 14 new cases (119 aliquots).
- Collection of peripheral blood and derivative products in patients suffering from gastrointestinal (GAS-S [Blood-Gastrointestinal]): around 37 new cases (609 aliquots).

**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 18 new cases (313 aliquots).

**Cardiovascular Node:**
- Collections from the cardiovascular node: around 17 new cases (264 aliquots).

**Other collections:**
- Collection sepsis gravis and septic shock (SGSS): around 54 new sample donations (629 aliquots).
- Collection of peripheral blood and derivative products in patients suffering from Multiple Esclerosis: around 37 new cases (442 aliquots).

**2015 new collections:**
- Collection of peripheral blood and derivative products in standard population: around 21 cases (263 aliquots).

In summary, 701 new cases have been received, 2172 samples have been processed and 9399 aliquots have been stored in 2015 at INCLIVA Biobank facilities.

**Transfer of samples**

<table>
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<th>Principal Researcher/Institution</th>
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<tr>
<td><em>Posible implicación de la bacteria Helicobacter Pylori en enfermedad tiroidea autoinmune.</em></td>
<td>UGP-14-459, FISABIO</td>
<td>Dr. Alejandro Mira Obrador FISABIO</td>
<td>Solid tumours: FFPE</td>
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<td><em>Exosomas urinarios en el Lupus Eritematoso Sistémico: potenciales biomarcadores y mediadores de señalización intrarrenal.</em></td>
<td>X</td>
<td>Dr. Raquel Cortés Vergaz INCLIVA</td>
<td>Blood-Systemic Lupus Erythematosus: DNA and plasma</td>
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<td><em>Identificación de mecanismos de resistencia a nuevos anticuerpos anti-HER2 en cáncer de mama.</em></td>
<td>PI12-01421, ISCIII, Ministerio de Economía y Competitividad</td>
<td>Dr. Ana Lluch Hernández HCUV/INCLIVA</td>
<td>Breast cancer: DNA, RNA, FFPE</td>
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<tr>
<td><em>Nuevas estrategias dirigidas a pacientes de cáncer de mama con tumores triples negativos. Targeting TNBC.</em></td>
<td>VLC-Bioclínica. INCLIVA9, HCUV/INCLIVA</td>
<td>Dr. Ana Lluch Hernández HCUV/INCLIVA</td>
<td>Breast cancer: DNA, tissue</td>
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### Projects supported by sepsis gravis and septic shock (SGSS) collection.

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<td>Estudio de la especificidad y sensibilidad de un método basado en la detección de histonas circulantes como biomarcadores de sepsis grave y shock séptico.</td>
<td>Emergente GV2014, Generalitat Valenciana</td>
<td>Dr. García-Giménez (CIBERER/UV/INCLIVA)</td>
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<tr>
<td>Identificación de histonas circulantes mediante procedimientos de espectrometría de masas en plasmas de pacientes con sepsis grave y shock séptico.</td>
<td>Emergente INCLIVA</td>
<td>Dr. García-Giménez (CIBERER/UV/INCLIVA)</td>
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### 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€

### PUBLICATIONS

**Original articles**


In summary, 533 aliquots have been provided in 2015 to respond to these 8 sample requests.
4.3.2 Oncology Phase I Clinical Trials Unit

INCLIVA is the only hospital of 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 (34 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 tumours.

FUNCTIONS:
The unit implements early clinical trials 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. Ethical Committee in Clinical Research (ECCR) Activity

INCLIVA Health Research Institute –through its Ethical Committee in Clinical Research (ECCR) – manages the clinical studies (trials, observational studies, and research projects) carried out by the Hospital Clínico Universitario and the Valencia Clínico-Malvarrosa Health Department.

The ECCR of the Hospital Clínico was awarded in 2013 with the ISO 9001 certification, a well-known international quality 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 2015, the ECCR has processed a total of 120 studies (clinical trials and observational studies): 115 assessed, all positively valued.

The distribution of these trials by phase is: Phase I: 11, Phase II: 21, Phase III: 37, Phase IV: 7, Observational studies: 37, others: 6. The following table shows the number of clinical trials and other studies according to their typology.

<table>
<thead>
<tr>
<th>Service</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Oncology and Haematology</td>
<td>52</td>
<td>43.3</td>
</tr>
<tr>
<td>Neurology</td>
<td>14</td>
<td>11.7</td>
</tr>
<tr>
<td>Cardiology</td>
<td>12</td>
<td>10.0</td>
</tr>
<tr>
<td>Internal Medicine</td>
<td>7</td>
<td>5.8</td>
</tr>
<tr>
<td>Endocrinology</td>
<td>6</td>
<td>5.0</td>
</tr>
<tr>
<td>Anesthesia and Reanimation</td>
<td>4</td>
<td>3.3</td>
</tr>
<tr>
<td>Digestive Medicine</td>
<td>4</td>
<td>3.3</td>
</tr>
<tr>
<td>Ginecology</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>Neumology</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>Unit of Infectious Diseases</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>Others</td>
<td>12</td>
<td>10.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>120</td>
<td>100</td>
</tr>
</tbody>
</table>

Once again, the Department of Medical Oncology and Haematology leads the number of trials presented to the ECCR. It is followed by the departments of Neurology, Cardiology, Internal Medicine and Endocrinology. These five departments make over 75% of the total processed trials. The following table shows the number of trials presented per departments and its percentage.
In turn, the Principal Investigator (PI) distribution shown below indicates that 9 PI involved in clinical trial development belong to the Department of Medical Oncology and Haematology. They are followed by the Departments of Cardiology and Endocrinology with 6 and 5 PI respectively.

<table>
<thead>
<tr>
<th>Service</th>
<th>Number of PI's</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Oncology and Haematology</td>
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<td>17.6</td>
</tr>
<tr>
<td>Cardiology</td>
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<td>11.8</td>
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<tr>
<td>Endocrinology</td>
<td>5</td>
<td>9.8</td>
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<tr>
<td>Anesthesia and Reanimation</td>
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<td>7.8</td>
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<tr>
<td>Internal Medicine</td>
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<td>3.9</td>
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<tr>
<td>Ginecology</td>
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<td>3.9</td>
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<tr>
<td>Nephrology</td>
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<tr>
<td>Neumology</td>
<td>2</td>
<td>3.9</td>
</tr>
<tr>
<td>Psychiatry</td>
<td>2</td>
<td>3.9</td>
</tr>
<tr>
<td>Radiology</td>
<td>2</td>
<td>3.9</td>
</tr>
<tr>
<td>Others</td>
<td>7</td>
<td>13.7</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>100</td>
</tr>
</tbody>
</table>
Regarding the distribution of studies per promoter, 24 trials are considered Independent Clinical Research (trials from associations, groups, foundations, and private individuals), and the rest of them have been promoted by the pharmaceutical industry.

<table>
<thead>
<tr>
<th>PROMOTOR</th>
<th>Nº</th>
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</thead>
<tbody>
<tr>
<td>AbbVie Deutschland GmbH and Co.</td>
<td>1</td>
</tr>
<tr>
<td>Ablynx</td>
<td>1</td>
</tr>
<tr>
<td>Amgen Inc</td>
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</tr>
<tr>
<td>Ariad Pharmaceuticals, Inc</td>
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</tr>
<tr>
<td>Astellas Pharma S.A</td>
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</tr>
<tr>
<td>AstraZeneca AB</td>
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</tr>
<tr>
<td>AVEO Pharmaceuticals, Inc.</td>
<td>1</td>
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<tr>
<td>Bayer Healthcare AG</td>
<td>9</td>
</tr>
<tr>
<td>Biogen Idec Ibeica</td>
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<tr>
<td>Biotronik SE&amp;CO.KG</td>
<td>1</td>
</tr>
<tr>
<td>Boehringer Ingelheim España S.A.</td>
<td>2</td>
</tr>
<tr>
<td>Bristol-Myers Squibb International Corp.</td>
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</tr>
<tr>
<td>Campofrío Food Group</td>
<td>1</td>
</tr>
<tr>
<td>Celldex Therapeutics, Inc.</td>
<td>1</td>
</tr>
<tr>
<td>Codman Neuro</td>
<td>1</td>
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<tr>
<td>Coretherapix SLU</td>
<td>1</td>
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<tr>
<td>Daiichi Sankyo Development Limited</td>
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<tr>
<td>ElectroCore, LLC</td>
<td>1</td>
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<tr>
<td>Eli Lilly and Company Limited UK</td>
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</tr>
<tr>
<td>F. Hoffmann-La Roche Ltd.</td>
<td>4</td>
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<tr>
<td>Ferrer Internacional S.A.</td>
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<tr>
<td>Fresenius Medical Care España S.A.</td>
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</tr>
<tr>
<td>GE Healthcare Ltd. And its affiliates</td>
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<tr>
<td>Genentech, Inc.</td>
<td>5</td>
</tr>
<tr>
<td>Genzyme Corporation</td>
<td>1</td>
</tr>
<tr>
<td>Gilead Sciences, Inc</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>PROMOTOR</th>
<th>Nº</th>
</tr>
</thead>
<tbody>
<tr>
<td>GlaxoSmithkline S.A.</td>
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<td>Hamilton Health Sciences Corporation</td>
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<tr>
<td>Hanmi Pharmaceutical Co., Ltd.</td>
<td>1</td>
</tr>
<tr>
<td>Hospira UK Ltd.</td>
<td>1</td>
</tr>
<tr>
<td>Independent Clinical Research</td>
<td>24</td>
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<tr>
<td>Janssen-Cilag</td>
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<tr>
<td>Janssen Sciences Ireland UC</td>
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<tr>
<td>Lilly S.A.</td>
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<td>MacroGenics, Inc</td>
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<td>Merck Sharp &amp; Dohme Corp</td>
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<tr>
<td>Merrimack Pharmaceuticals Inc.</td>
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<tr>
<td>Mirati Therapeutics, Inc.</td>
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</tr>
<tr>
<td>Novartis Farmacéutica S.A.</td>
<td>7</td>
</tr>
<tr>
<td>Orion Pharma SL</td>
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</tr>
<tr>
<td>Pfizer INC</td>
<td>1</td>
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<td>Pharma Mar S.A.</td>
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<tr>
<td>Portóla Pharmaceuticals, Inc.</td>
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<tr>
<td>ProNAi Therapeutics, Inc.</td>
<td>1</td>
</tr>
<tr>
<td>Receptos, Inc.</td>
<td>1</td>
</tr>
<tr>
<td>Roche Farma S.A.</td>
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</tr>
<tr>
<td>Sanofi-aventis S.A</td>
<td>4</td>
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<tr>
<td>Shire Human Genetic Therapies, Inc.</td>
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<tr>
<td>Synageva BioPharma Corp.</td>
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</tr>
<tr>
<td>Sysmex Inostics GmbH</td>
<td>1</td>
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<tr>
<td>Thermo Fisher Scientific/BRAHMS GmbH</td>
<td>1</td>
</tr>
<tr>
<td>UCB Biopharma SPRL.</td>
<td>2</td>
</tr>
</tbody>
</table>
5.2. 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 to a hundred.

![Graph showing number of processed studies from 2011 to 2015]

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 2011-2015, Phase I and Phase II trials are prioritized and its number remains stable as shown in the graph below.

![Graph showing evolution of clinical trial distribution by phase from 2011 to 2015]
## 5.3. Ongoing studies in the Valencia Clínico-Malvarrosa Health Department

During 2015, 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 Department 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 grants

Being aware that the processes of innovation and knowledge transfer require multidisciplinary collaboration among professionals from various fields, the University of Valencia, is interested in establishing concrete partnerships with hospital foundations which are related to the area of specialization in health and IN-CLIVA, whose general objective is to promote, encourage, favour and implement the scientific and technical research, launched in 2015 VLC-Bioclinic Program.

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 between researchers and professionals in the field of health and strengthen translational research with innovative results that benefit patients.

In 2015 the following projects were funded.

VLC- BIOCLINIC Subprogram A

Title: Soportes tridimensionales biodegradables basados en macropartículas 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
Total Budget: 44.250€

Title: Nuevas estrategias dirigidas a pacientes con cáncer de mama con tumores triples negativos
Principal Investigator: Ana Lluch
Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia, – Fundación CETIR
Duration: 2015
Total Budget: 44.250€

Title: Marcadores metabolómicos del crecimiento ocular axial humano
Principal Investigator: Daniel Monleón Salvado
Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary Institution: Universidad de Valencia
6.2 Grants for intramural projects by emerging researchers

Like previous years, INCLIVA launched an intramural call for research projects with the aim of improving the quality of their projects and promoting publishing in high impact journals, available exclusively to their emerging researchers. During 2015 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 - 2015
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 Dasi Fernández
Funding Body: Universidad de Valencia
Beneficiary Institution: Universidad de Valencia
Duration: 2015
Total budget: 4.000€
**Go to page 6**

**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 - 2015  
**Total budget:** 4.917€

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

**Title:** Papel del complejo RUNX1/CBF-beta/p300/HIPK2 en la progresión leucémica de las neoplasias  
**Principal Investigator:** Juan Carlos Hernández Boluda  
**Funding Body:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Beneficiary Institution:** Fundación Investigación Hospital Clínico Universitario de Valencia  
**Duration:** 2014 - 2015  
**Total budget:** 6.146€

**Reference:** Convocatoria 2014 de ayudas intramurales para grupos emergentes
Initiatives for research promotion

Clínico Universitario de Valencia

Duration: 2014 - 2015
Total budget: 3.500€

Reference: Convocatoria 2014 de ayudas intramurales para grupos emergentes
Title: Ejercicio físico controlado como intervención en el tratamiento de la fragilidad en el anciano y en la prevención de la dependencia. Bases moleculares
Principal Investigator: Mª Carmen Gómez
Funding Body: Fundación Investigación Hospital Clínico Universitario de Valencia
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

6.3 Grants for secondments in centers of excellence

As every year, the Institute has announced its Grants for research secondments in centers of excellence, to allow the staff to acquire new knowledge for clinical and research techniques.

Since the establishment of this scholarship program, over 100 professionals have visited national and foreign centers. In 2015 the average number of awards was a total of 17 scholarships, 12 of them to international centers and 5 to national ones.

The awarded researchers and the assigned training centers in 2015 are shown in the following table:

<table>
<thead>
<tr>
<th>Laura Álvarez Bravos</th>
<th>Institut balear de Salut mental de la infància i l’adolescència (IBSMIA), Hospital Universitario Son Espases, Palma de Mallorca</th>
</tr>
</thead>
<tbody>
<tr>
<td>Julio Calvete Chornet</td>
<td>Divisione di Senologia dell’Instituto Europeo di Oncologia, Milano</td>
</tr>
<tr>
<td>Irene del Canto Serrano</td>
<td>Laboratorio de órganos y matrices bioartificiales, Instituto De Investigación Sanitaria Gregorio Marañón, Madrid</td>
</tr>
</tbody>
</table>
6.4 Training and Teaching Activities

INCLIVA and its researchers play an important role in the training of researchers and health sciences degree and master students, which come from Valencian universities and other national and international regions.

Thus, the number of internal secondments in 2015 was 5, an aggregate of 10 months of training during the period. Moreover INCLIVA has hosted over 55 students throughout the year, from the University of Valencia, Polytechnic University and the University of Lleida, an aggregate of 2.178 months of training during the period.

The Institute has kept on developing, along the year, the Training Program with seminars and courses. The courses, seminars and educational conferences that have been developed during the year 2015 have been the following:

### Courses

- **Curso de formación en investigación biomédica: Como estructurar y presentar un proyecto de investigación clínica.**
- **Curso de formación en investigación biomédica: Bioestadística I. Análisis exploratorio de datos.**
- **Curso de formación en investigación biomédica: Bioestadística II. Comparación de grupos.**
- **Curso de formación en investigación biomédica: Bioestadística III. Análisis estadístico de ensayos clínicos.**
- **Curso de formación en interpretación de HER2 en cáncer de mama.**
- **Curso de formación en investigación biomédica: Búsquedas bibliográficas.**
- **VIII Curso de ventilación mecánica pediátrica (asistencia inicial y transporte).**
- **Fundamental Critical Care Support Course. Dirigido a titulados en enfermería.**
• Fundamental Critical Care Support Course. Dirigido a médicos.
• Fundamental Critical Care Support Course. Dirigido a titulados en enfermería.
• Fundamental Critical Care Support Course. Dirigido a médicos.
• Enfermedades Infecciosas VIH. Curso para Residentes.
• Curso de actualización sobre el uso de antiagregantes orales en la cardiopatía isquémica.
• I Workshop Internacional de Ecografía y Resonancia Anorrectal.
• Curso de Anatomía Quirúrgica Aplicada Hepatobilipancreática.

INCLIVA Seminars

• Eliseo Guallar, MD: “Estudios epidemiológicos basados en exámenes rutinarios de salud – Experiencia en el Kangbuk Samsung Health Study”.
• Damián Tormo: “Nuevos inhibidores orales del receptor de linfocitos para el tratamiento de enfermedades autoinmunes”.
• Prof. Dr. Patrice D. Cani: “Obesity and diabetes: when adipose tissue talks to the gut microbes...”.
• Dr. Rubén Artero: “Drosophila como herramienta para el descubrimiento de fármacos”.
• Dr. Fco. Javier Puertas: “Consecuencias metabólicas y cardiovasculares de los trastornos del sueño”.
• Dr. Esteban Ballestar: “Perspectivas de la Epigenómica en enfermedades del sistema inmune: Aplicaciones clínicas en procesos neoplásicos”.
• Dr. Jaume Marrugat: “Evolución de la incidencia de cardiopatía isquémica en Europa 1980-2010 y proyecciones hasta 2049”.
• Fernando Macián: “Mecanismos moleculares que regulan la tolerancia en los linfocitos T. Relevancia para el desarrollo de inmunoterapia”.
• Dr. Joaquín Dopazo. Seminario INCLIVA noviembre.

Workshops

• Jornada de meta-análisis en anestesiología.
• Jornada de investigación en neurociencia.
• Jornada de situación de la investigación en tratamiento del dolor.
• Jornada “Síndrome de Discinesia Ciliar Primaria: Perspectiva biomédicas y aspectos sociales”.
• Jornadas sobre comunicación con el paciente y la sociedad.
• I Jornada de enfermería pediátrica.
• 7ª Jornada Valenciana “Tobaco y Respiración”: Tabaco y Pulmón.
• Jornada Actualización de Patología Prostática.

Conferences

• Dra. Vannina González: “Perfil genómico y metabolómico asociado a la Microalbuminuria”.
• Dra. Tania Romacho: “Inter-organ crosstalk: tejido adiposo en el centro de la diana”.
• Dr. Carlos Romá: “Enfermedad de Lafora, ayer y hoy”.
• Daniel Pérez Cremades: “Alteraciones de las células endoteliales en respuesta a histonas extracelulares”.
• Dra. Irene del Canto: “Metodología experimental para el abordaje electrofisiológico de los parámetros ligados al desencadenamiento de las arritmias cardiacas”.
• Lucía Rodríguez: “Papel de las calpainas en la pérdida de los anclajes celulares en la glándula mamaria: estudio en modelos fisiológicos y patológicos”.
• Sara Martorell: “Estudio del receptor nuclear VDR como posible diana terapéutica para el tratamiento del aneurisma aortico abdominal”.
• Taller de Meta-análisis en anestesiología.
• Avances en carcinoma de ovario y en carcinoma de mama hormonosensible.
• Conferencia Jose Luis Ribelles: “Soportes sintéticos para el cultivo y trasplante en células en Ingeniería Tisular”.
• INCLIVA Biomedical Research Institute & Turkish Society of Hypertension and Renal Diseases: “Hypertension Treatment: From Past to Future”.
• Proyecto ESCARVAL de formación y mejora en práctica clínica sobre anticoagulación y antiagregación en atención primaria.
• Formación de médicos residentes y adjuntos sobre calidad asistencial en unidades de salud mental.
• Preceptorship en cáncer de mama avanzado.
• UniBS Agreement seminar
• Seminario “Investigación y divulgación: una carretera de doble sentido”.
• Actualización en el tratamiento de la insuficiencia cardíaca.
• Curso de terapia de resincronización cardíaca.
• **Formación de médicos residentes y adjuntos sobre la calidad asistencial en las unidades de salud mental del área clínico.**
• Lunch Seminar: “La investigación básica y la medicina actual”.
• Lunch Seminar: “ELISA, quimioluminiscencia y otras”.
• Lunch Seminar: “Citometría de flujo”.
• Lunch Seminar: “Geles de proteínas y de ácidos nucleicos - Interacción genómica –clínica. Aspectos prácticos”.
• Lunch Seminar: “Bases genéticas de las enfermedades.

**Other activities in which INCLIVA participates**

• “Máster oficial en bioinformática”, October 2014-June 2015. Organized by Universitat de València, INCLIVA and CIPF.
<table>
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<th>TITLE</th>
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<td>Pablo Padilla Iserte</td>
<td>Patrón de decidualización en mujeres con preeclampsia mediante la aplicación de métodos de transcriptómica y proteómica</td>
<td>13/01/2015</td>
<td>Alfredo Perales Marín, Carlos Simón</td>
<td>Carlos Simón</td>
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<td>Silvia Tamarit Bordes</td>
<td>Efectos del tratamiento con agonistas dopaminérgicos sobre las lesiones endometriósicas</td>
<td>14/01/2015</td>
<td>Raúl Gómez Gallego</td>
<td>Carlos Simón</td>
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<td>Iván Ferrer Vicens</td>
<td>NF-KB E ID2 como nodos de regulación de redes transcripcionales en diferentes modelos biológicos</td>
<td>16/01/2015</td>
<td>Juan Viña Ribes</td>
<td>Juan Viña</td>
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<tr>
<td>Irene Tadeo Cervera</td>
<td>Estudio del armazón arquitectónico y del sistema vascular de los tumores neuroblásticos</td>
<td>16/01/2015</td>
<td>Samuel Navarro Fos</td>
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A research advances in reducing lung injury caused by mechanical ventilation. INCLIVA is visited by Eliseo Guallar, an epidemiologist at Johns Hopkins University.

INCLIVA and the University of Valencia created the first Regional Center for Rare Diseases.

The Minister of Health recognizes the research of Dr. Pallardó, Dr. Cervantes and Dr. Sanfélix. Chromosome 21 involved in Down Syndrome protective agent against cancer. INCLIVA presents its research to the Southwestern University of Dallas.

The cardiologist Vicente Bodí, Prize of the Valencian Royal Academy of Medicine. Molecules generating resistance in breast cancer tumors have been identified. INCLIVA adscribes the Patent Bank’s of Generalitat Valenciana. A mechanism responsible of oxidation of fats in adipose tissue it is presented in INCLIVA.

INCLIVA researcher, Maider Ibarrola receives the García-Blanco medal, in its 35th edition. A study in which Hospital Clínico de Valencia participates, confirms that the combined use of two antibodies slows colon cancer. The Race Dona at Gandia donated over 24,000€ to investigate breast cancer. A research on rare diseases by INCLIVA is doubly awarded by the Valencian Society of Pneumology.

A joint investigation by INCLIVA and UV is awarded by the Spanish Society of Geriatrics and Gerontology. Eighth edition of the Paediatric Mechanical Ventilation Course. Success in ALIMARA show for the benefit of cancer research. Researchers from INCLIVA and IVI awarded at the XXIV edition of the Merck Serono Research Grants. RUBIÓ LABORATORIES and INCLIVA sign an agreement to promote research. Success in INCLIVA colloquium with the Nobel Prize Erwin Neher, Ferid Murad and Richard J. Roberts.
INCLIVA and Lanzadera sign a cooperation agreement.

INCLIVA joins to the first Spanish company in epigenetics.

INCLIVA’s Biobank receives the ISO 9001 quality certificate. Investigators show that genetic variants in a gene are related to the severity of the myeloid leukaemia. Maite Girau, Councillor for Health and Sports Valencia visits INCLIVA.

The European Respiratory Society awards Dr. Francisco Dasí. INCLIVA researchers discover a protein that protects against diabetes. The VLC Health Ecosystem initiative is presented in the Botanic. Andrés Cervantes, awarded by the European Society for Therapeutic Radiology and Oncology (ESTRO).

MoTriColor: pan-European project for the development of new therapies in patients with advanced colorectal cancer. A new application to facilitate monitoring and improving adherence to treatment of patients with psychosis has been designed. Blood marker which indicate the mild neurological impairment in patients with minimal hepatic encephalopathy has been identified. The European Society for Medical Oncology recognizes INCLIVA and the Clinical Hospital of Valencia for the excellence of their training. The Obra Social “la Caixa” collaborates with the Paula Project led by INCLIVA with 6,000 euros for research on diabetes. The association between extracellular vesicles and the degree of renal involvement in lupus is demonstrated. A new antibody could be effective against solid tumours.

Resolution of the announcement of the Strategic Action in Health with a result of support to fund 12 research projects with 1.762.145€ and 9 research contracts funded with 745.560€. Highlighting the Integrated Project Excellence of Dr. Vicente Bodí. INCLIVA and REDIT signed a collaboration agreement to boost biomedical innovation. Dr. Cervantes gets into the Royal Academy of Medicine of Valencia. INCLIVA and REDIT signed a collaboration agreement to boost biomedical innovation.
INCLIVA’s mission is “to contribute to improving the health and quality of life of citizens”, therefore, in addition to our own research projects, it is also involved and committed to initiatives promoted by individuals who live near some illness.

INCLIVA is currently working on four joint initiatives: Proyecto Mama, Proyecto Paula, Fundacion Le Cadó and Nico contra el Cancer. One of the fundamental premises of the institute is the maximum transparency in the management of the contributions received.

These donations provide tax benefits under the Article 66 of the Law 30/1994 of 24 November on Foundations and Tax to private participation in activities of general interest incentives.

8.1 Solidary Projects

PROYECTO PAULA

This project was born in 2011 from the hand of Cristina Ponce, when her 8 years old daughter, Paula, was diagnosed with type 1 diabetes mellitus, a disease that completely destroyed their insulin-producing cells.

Proyecto Paula focuses its work in raising the necessary funds and resources, both public and private, to investigate the Diabetes and in the future to find a cure for Paula and other people with this illness.

INCLIVA has several groups dedicated to research in diabetes and belongs to the Biomedical Research Centre in Diabetes and Associated Metabolic Diseases (CIBERDEM), a public consortium led by Spain’s research effort of excellence in diabetes and related metabolic diseases, as well as the translation of research results into clinical practice.

Since its inception, Proyecto Paula has contributed with more than 93.000€.

PROYECTO MAMA

Proyecto Mama started in September 2012 promoted by Pedro Alarcon after the death of his mother as a result of breast cancer. The purpose of this initiative is to get public and private funds to investigate this disease.

Breast cancer is the most common tumor in women, begins to appear around age 30, gradually increasing its impact, affecting up to 9% of the female population at 70 years of age.

FUNDACION LE CADO

Fundación Le Cado was created in 2010 under the leadership of its president Elvira Monferrer Daudi. This initiative seeks to unite efforts and resources in supporting this kind of tumor research, which is currently the fourth leading cause of death of women.

Fundación Le Cado collaborates with the 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), Dr. Jaime Ferrer Lozano (a pathologist) and Ms. Carmen Peña Chilet, all this team led by the oncologist Dr. Ana Lluch.

Almost 30.000€ have been donated for the Project so far.
**NICO CONTRA EL CANCER**

The movement “Nico contra el cancer” was formed in November 2015 in Ourense, after Nicolas Rodriguez Leal came back from his surgery intervention at the Hospital La Paz in Madrid.

The movement is led by his mother and aunts as a dependent activity of the Asociación NEN, whose main objective is to finance research projects against childhood cancer, and more specifically solid tumours.

**8.2 Solidary news**

*The Obra Social “la Caixa” collaborates with Paula Project INCLIVA with 6,000 euros for research on diabetes.*

Coinciding with the World Diabetes Day, which was held last Saturday, this morning, INCLIVA, received from the hands of representatives of the Obra Social “la Caixa” a contribution of six thousand euros to support the Paula Project and diabetes research.

The Director General of INCLIVA, Rafael Carmena, CFO Juan Luis Huguet, Medical Director of the Clinical Hospital, Jorge Navarro, Cristina Ponce and Paula Botella from the Paula Project and researcher Herminia González from Research Group Inflammation participated in the event.

According to Professor Carmena “Patronage is a pending subject in our society, we cannot expect it to be the state that will meet the Spanish investigation as a whole; civil society must also contribute. But to do this, we must have a similar law to other neighboring countries, to encourage donations from businesses and individuals that may deduct contributions in full and not a small percentage “.

In turn, Jorge Navarro stated that “INCLIVA Research Groups are the representation of health excellence in the Valencian health, and at the Hospital Clínico in particular.” He also thanked the contribution of “la Caixa” as an example of public-private partnership that should be encouraged in our society.

Meanwhile researcher Herminia González presented the research being done on genetic polymorphisms of diabetes, particularly those that predispose or protect people who have them, and new markers of inflammation associated with diabetes and thus new therapeutic pathways that act on these pathways. “In this way we hope to be able to improve the treatment and outcome of complications of diabetes.” She stated that “without the support of Paula Project we had not be able to prove that a protein, CdK5a / 2b is a protective agent in insulin resistance and fatty liver, as we published this past October.”

*A show from INCLIVA’s benefit to investigate in cancer.*

The Palau de la Música in Valencia hosts this Saturday June 20 at 19:30 pm a charity event for research against breast cancer.

The dance group ALIMARA represent his show “El Somni”, a journey through the different shows that Alimara has done throughout its 40 years of existence.

The event is organized by the Fundación Le Cado and all proceeds will go to the study of breast cancer in young women which is carried out in INCLIVA.

Tickets can be purchased at the ticket office in Palau de la Música.

*La Carrera de la Dona de Gandia donated over 24,000€ to investigate breast cancer.*

The Management of Club Atletisme la Safor and the Director General of Delizia, its sponsor, have been received today by the Research Institute INCLIVA, the Managing Director of the Clinical Hospital, Luis Martí, the oncologist Ana Lluch, and his research group in breast cancer biology, after the solidarity race celebra-
During the interventions, the Director General of the Institute, Rafael Carmena, thanked the work of the club and the sponsor, not only by the collected amount (24,747€) but for their solidarity and work. “The 100% of the proceeds will go to research.”

“Acts like the one held in Gandia show us that we are not alone and that citizens value the work of professionals and researchers in public health,” said Dr. Martí.

Dr. Lluch presented the research project that the funds raised will be dedicated to: “Analyzing the biological differences of breast cancer in women under 35 years old. We want to know why in young women the tumours are more aggressive, larger and less responsive to treatment” she says. In this sense the researcher sincerely thanked the support of the Club Atletisme La Safor.

The Club Atletisme La Safor explained that the race has become a big event in Gandia in which the whole city is involved. Vicent Mengual, from the Board, expressed its intention to continue working with INCLIVA and research in breast cancer in future editions of the Carrera de la Dona.

Success in “III Tirada contra el Cáncer” in favor of INCLIVA

For second consecutive year, the courts of the range of the Lideronero in Cheste, hosted on Saturday a competition skeet in favor of cancer research at the Institute of Health Research INCLIVA, the “III Tirada contra el Cáncer”, Estelles Vicente Memorial and Tribute to Juan Ruiz Pedrosa.

The facilities that runs the Valencian world champion, Christopher Jimenez, welcomed more than 120 shooters from different categories, from veterans to hunter’s sharpshooters in a festive gathering. Some of the national champions of their own categories where among there participants.

The Dr. Joan Climent, from the research Group on Breast Cancer Biology, came on behalf of INCLIVA.

At the end of the day, during the awards ceremony, 3,516€ were donated to INCLIVA which will go to breast cancer research.

From INCLIVA we want to recognize the commitment and solidarity of the entire organization with the initiative and participants in the event.

In particular, INCLIVA wants to thank Enrique Alhambra, Antonio Torre, Cesar Navarro and Cristobal Jimenez very sincerely for their work and their solidarity with biomedical research in the Valencian Community.

April 19th Cursa de la Dona in Gandia in favor of INCLIVA

Next Sunday, April 19th is going to celebrate the eighth edition of the “Cursa de la Dona de Gandia” for INCLIVA, the Institute of Health Research of the Clinical Hospital of Valencia.

The organization is in charge of Club Atletisme Safor. Around seven thousand inscriptions are overcome and the organization encourages register to exceed the number of brokerages previous editions.

Following the example of previous years, the Club Atletisme Safor allocate each one euro entry to the research project “Breast cancer in women under 35 years," Research Group Biology of breast cancer led by Dr. Ana Lluch in INCLIVA.

The route of the race will pass through the old town of Gandia and the expected distance is 5.700 meters.

Inscriptions on the race can be made through the network on the page, www.cursadeladona.gandia.com or in person at various establishments of Gandia, Alcoy, Javea, Denia, Cocentaina, Xàtiva, Onteniente, Sueca, Tavernes and Oliva.

In addition, the organization has also initiated a parallel action selling a solidarity bracelets, which can be purchased in the same establishments where enrolment to benefit fully from INCLIVA research project is carried out.

8.3 Solidary private donations and acknowledgment

On behalf of INCLIVA we want to thank the support and solidarity to all the people who help with their donations. For us, your collaboration means much more than an economic contribution, is the encouragement we need to keep investigating and working for research.

Private donations

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