

# 2013

## Scientific Annual Report

**IMIBIC**  MAIMONIDES BIOMEDICAL  
RESEARCH INSTITUTE OF  
CORDOBA



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**IMIBIC**

Reina Sofía University Hospital

Avda. Menéndez Pidal s/n

Edificio Consultas Externas, Nivel-1

T (+34) 957 012 914 (corp. 512 914)

F (+34) 957 736 149 (corp. 580 149)

[www.imibic.org](http://www.imibic.org)

[info@imibic.org](mailto:info@imibic.org)



01  
**Introduction**



# 01 Introduction

## 1.1. PRESENTATION

It is now 5 years since Maimonides Institute for Biomedical Research of Córdoba (IMIBIC) was founded, based on a large tradition of collaborative research between professionals at the Reina Sofía University Hospital and the University of Córdoba. Over this time we have been accredited as health research institute by the Health Institute Carlos III. Moreover, we have pursued different strategies in order to sustain the growth achieved in knowledge generation and fundraising as well as infrastructure improvement and human resources recruitment.

In 2013, we strengthened our presence in cooperative structures, both the Andalusian Plan for Research, Development and Innovation and the Strategic Plans of Health Institute Carlos III, including CIBERs and RETICs. We also joined the Innovation Network ITEMAS, the Clinical Research and Trials Units Platform, the ProteoRed-ISCIII Network and the Biobanks Platform.

Throughout 2013, we continued our activity for knowledge generation. IMIBIC has published a total of 326 papers, of which 23% were generated in collaboration with foreign groups. 20% of them belong to journals of the first decile and 48% are papers of the first quartile. As a result, the total impact factor was 1,161.167 points. In addition, we have implemented 16 property patents, which implies an increase in annual activity.

Regarding fundraising, 46 new research projects have been secured, together with a total of 142 new clinical studies. We have also signed 47 cooperation agreements and contracts with companies from the national and international sphere. This has enabled us to triple the research personnel recruitment, with a focus on pre-doctoral and post-doctoral researchers as well as support technicians. One point especially noteworthy is that the construction of our new premises follows the planned schedule and they will be officially opened this year.

IMIBIC has followed its own program to encourage the mobility of researchers and reward those with the most outstanding results. In the field of Training, the PhD program in Biomedicine has retained the Mention towards Excellence with a total of 22 doctoral theses defended.



**Francisco Pérez Jiménez**  
*Scientific Director*





02

**Human, Technological  
and Economic  
Resources. Facilities**

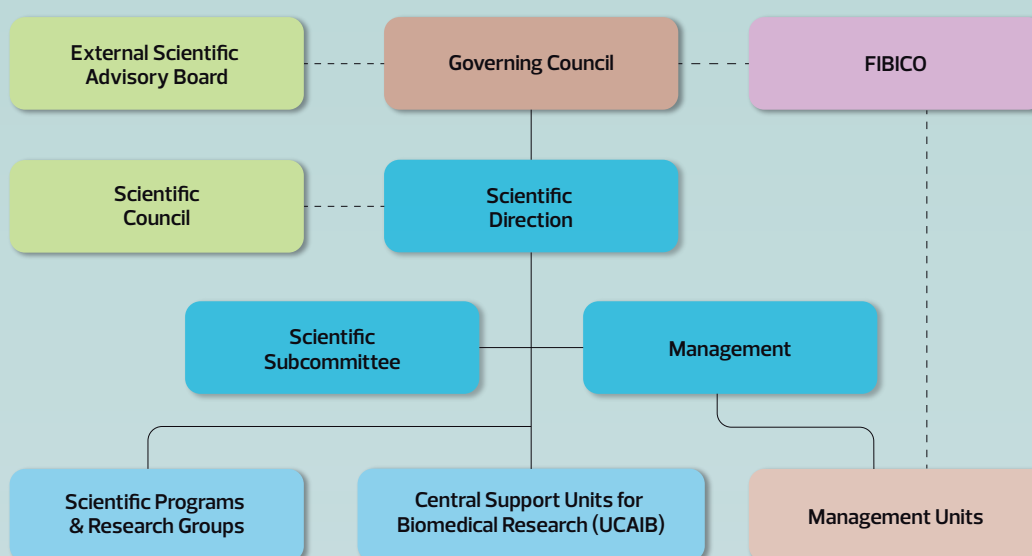


# 02

## Human, Technological and Economic Resources. Facilities

### 2.1.- Organization Chart

IMIBIC's governing and representative bodies are detailed below:



#### A. Collegiate Bodies

##### Governing Council

The Governing Council is the uppermost governing body of IMIBIC. The Governing Council is composed of the following members:

- Two representatives from the Regional Ministry of Health of the Andalusian Regional Government
  - Jerónimo Pachón Díaz.** General Director for Quality, Research, Development and Innovation. Chairman of the Governing Council.
  - José Manuel Aranda Lara.** Managing Director of the Reina Sofía University Hospital and President of FIBICO.
- Two representatives from the Regional Ministry of Economy, Innovation, Science and Employment
  - Eva María Vázquez Sánchez.** General Director for Research, Technology and Business.
  - José Ignacio Expósito Prats.** Provincial Delegate of Economy, Innovation, Science and Employment of Córdoba.
- Two representatives of the University of Córdoba
  - Justo P. Castaño Fuentes.** Vice-Chancellor of Scientific Policy and Campus of Excellence at the University of Córdoba.
  - José López Miranda.** Associate Dean for Hospital Affairs of the Faculty of Medicine.
- IMIBIC's Scientific Director
  - Francisco Pérez Jiménez.**
- One representative from the Progress and Health Foundation
  - Juan Jesús Bandera González.** Managing Director.

### Scientific Council

The Scientific Council is an advisory body to the Scientific Director. It is composed of the Scientific Director, the Deputy Scientific Director of IMIBIC, the Principal Investigators (PI), the Emerging Researchers (ER), the Associated Researchers (AR), a representative of the Reina Sofia University Hospital Board of Directors (RSUH), the IMIBIC's General Manager and representatives of the technical and management staff. It was established on July 9, 2009.

### External Scientific Advisory Board

The External Advisory Board is a body appointed by the Governing Council, whose mission is to assist the Scientific Director in the performance of his duties. It is an advisory body to the Scientific Direction but its decisions are not legally binding. It was established on July 9, 2009 under the name of External Advisory Board, and it was ratified by the Governing Council on December 21, 2009

## B. Individual Bodies

The Management Team is responsible for ensuring the correct performance, in order to increase the quality and impact of IMIBIC's research activity.

### Scientific Director

Francisco Pérez Jiménez, PhD. Professor of Medicine and Head of the Internal Medicine Service at Reina Sofía University Hospital. He was re-named scientific director of IMIBIC by the Governing Council at a meeting held on December 11, 2012.

### Deputy Scientific Director

Manuel Tena Sempere, PhD. Professor of Physiology at the Faculty of Medicine of the University of Córdoba. He was named Deputy Scientific Director by the Governing Council at a meeting held on June 21, 2012.

### General Manager

José Miguel Guzmán de Damas, PhD. He holds a BSc in Pharmacy and a BSc in Business Administration. He also holds a MsC in Health Economics and a Health Care Management and a Executive MBA from the IESE Business School. He was appointed General Manager of IMIBIC by the Governing Council at a meeting held on December 21, 2010.

## 2.2.- SCIENTIFIC STRUCTURE

The scientific structure of IMIBIC is based on its research groups, which cooperate in the development of the Scientific Programs approved by the Governing Council on July 12, 2013. These programs have been compiled following the recommendations of the Strategic Health Action Plan 2013-2016, which are oriented towards the European Union's "Horizon 2020" program. The aim of this structure is to define the horizon that should guide researchers towards translational and clinical research into human health. We aim to encourage interaction and cooperation through it, as well as foster participation to increase talent and critical mass and improve young people's training, which will make it easier for them to find a job. Our Scientific Programs are therefore a reflection of the strength of our research teams and show the unique specialization of IMIBIC. The programs are as follows:

### 1 - . Active aging and Fragility

This program is oriented towards understanding the molecular pathogenic basis of the aging process, its relation to quality of life and the search for new strategies for patient care assistance. It includes the following lines of research:

- Immunology and senescence
- Attention and care of the chronically ill
- Fragility and quality of life in the elderly

## 2 – . Nutrition and endocrine and metabolic diseases

This program is oriented towards studying diseases of the metabolism and the endocrine system, with particular interest in the role of nutrition in the prevention and management of these processes at different stages of life. It also focuses on the study of reproductive health and neuroendocrine tumors. It includes the following lines of research:

- Metabolic syndrome
- Reproductive Health
- Pediatric and perinatal diseases
- Neuroendocrine Tumors

## 3 – . Infectious and immunological diseases and organ transplants

This program focuses on the study of diseases by different infectious agents, with a special emphasis on the infections in immunocompromised patients. It includes the following lines of research:

- HIV + Hepatitis C Virus
- Transplants
- Multi-drug resistance

## 4 – . Cancer (Oncology and Oncohematology)

This program focuses on the study of neoplastic diseases, including both solid tumors and hematologic neoplasms. It includes the following lines of research:

- Lung Cancer
- Breast Cancer
- Hepatocellular carcinoma
- Leukemias and Lymphomas
- Digestive Tumors
- Other tumors

## 5 – . Chronic and Inflammatory Diseases

This program focuses on the study of a number of chronic diseases of modern society, with special emphasis on those of an inflammatory nature. This program includes both basic research and clinical studies, with the ultimate aim of promoting a better understanding of the basis of chronic/inflammatory diseases and the improvement of their therapies.

It includes the following lines of research:

- Cardiovascular diseases
- Diseases of the locomotor system and connective tissue
- Neurological diseases
- Mental health
- Kidney and urologic diseases
- Liver and digestive diseases
- Chronic inflammation and signaling

### RESEARCH GROUPS

CODE	TITLE	RESEARCHERS
GC1	T and NK immunosenescence. Antiviral immune response. PROGRAMS 1, 3, 5	Dr. Rafael Solana Lara (IR) Dr. José Peña Martínez (CO-IR)
GC2	Oxidative and nitrosative stress in acute and chronic liver disease. PROGRAMS 3, 4, 5	Dr. Manuel De La Mata García (IR) Dr. José Antonio Bãrcena Ruiz (CO-IR)

GC3	Infectious diseases. PROGRAMS 1, 3, 5	Dr. Julián De La Torre Cisneros (IR) Dr. Antonio Rivero Román (CO-IR)
GC4	Inflammation and cancer. PROGRAMS 2, 3, 4, 5	Dr. Eduardo Muñoz Blanco (IR) Dr. Marco A. Calzado (IE)
GC5	Systemic and chronic inflammatory autoimmune diseases of the locomotor system and connective tissue. PROGRAMS 2, 5	Dr. Rosario López Pedrera (IR) Dr. Eduardo Collantes Estévez (CO-IR)
GC6	New therapies in cancer. PROGRAM 4	Dr. Enrique Aranda Aguilar (IR) Dr. Antonio Rodríguez Ariza (CO-IR) Dr. Juan de la Haba Rodríguez (IE)
GC7	Nephrology. Cell damage in chronic inflammation. PROGRAMS 1.5	Dr. Pedro Aljama García (IR) Dr. Julia Carracedo Añón (CO-IR)
GC8	Hormones and cancer. PROGRAMS 2, 4	Dr. Justo P. Castaño Fuentes (IR) Dr. Francisco Gracia Navarro (CO-IR) Dr. Raúl Luque (CO-IR)
GC9	Nutrigenomics. Metabolic syndrome. PROGRAMS 1, 2, 4, 5	Dr. José López Miranda (IR) Dr. Francisco Pérez Jiménez (CO-IR)
GC10	Hormonal regulation of energy balance, puberty and reproduction. PROGRAMS 2, 4	Dr. Manuel Tena Sempere (IR)
GC11	Metabolism and adipocyte differentiation. Metabolic syndrome. PROGRAM 2	Dr. María del Mar Malagón Poyato (IR) Dr. Francisco Gracia Navarro (CO-IR)
GC12	Epidemiological Research in Primary Care. PROGRAMS 4, 5	Dr. Luis Ángel Pérula de Torres (IR)
GC13	Calcium metabolism. Vascular calcification PROGRAMS 2, 5	Dr. Mariano Rodríguez Portillo (IR)
GC14	Cell therapy. PROGRAM 5	Dr. I. Concepción Herrera Arroyo (IR)
GC15	Invasive cardiology and cell therapy. PROGRAM 5	Dr. José Suárez De Lezo Cruz-Conde (IR)
GC16	Cell biology in hematology. Hypercoagulability. PROGRAM 4	Dr. Joaquín Sánchez García (IR) Dr. Francisco Velasco Gimena (CO-IR)
GC17	Pathophysiology of the endocrine system of vitamin D. Biotechnology and aging. PROGRAMS 1, 2	Dr. José Manuel Quesada Gómez (IR)
GC18	Translational research in surgery of solid organ transplants. PROGRAMS 4, 5	Dr. Javier Briceño Delgado (IR)
GC19	Applications of machine vision. PROGRAM 5	Dr. Rafael Medina (IR)
GC20	Genetics and behavioural diseases. PROGRAM 5	Dr. Manuel Ruiz Rubio (IR)
GC21	Metabolomics. Identification of bioactive components. PROGRAMS 2, 4, 5	Dr. María Dolores Luque De Castro (IR) Dr. Feliciano Priego Capote (IE)
GC22	Epigenetics. PROGRAM 4	Dr. Teresa Roldán Arjona (IR)
GE1	Oxidative stress and nutrition. PROGRAMS 1, 2, 5	Dr. Isaac Túnez Fiñana (IE)
GE2	Infantile metabolism. PROGRAMS 2, 4	Dr. Mercedes Gil Campos (IE)
GA1	Lung transplantation. Thoracic malignancies. PROGRAM 4	Dr. Ángel Salvatierra Velázquez (IA)
GA2	Comprehensive care nurses - a multidisciplinary perspective. PROGRAMS 1, 5	Dr. María Aurora Rodríguez Borrego (IA)
GA3	Pneumology. PROGRAMS 2, 4, 5	Dr. Bernabé Jurado Gámez (IA)
GA4	Endocrinology and Nutrition. Insulin resistance, diabetes and metabolism. PROGRAM 2	Dr. Pedro Benito López (IA) Dr. Juan Antonio Paniagua González (IE)

GA5	Study of growth. Endocrinology and Child Nutrition. PROGRAM 2	Dr. Ramón Cañete Estrada (IA)
GA6	Clinical Analysis. PROGRAM 2	Dr. Cristóbal Aguilera Gámiz (IA) Dr. Fernando Rodríguez Cantalejo (IA) Dr. Javier Caballero Villarraso (IA)
GA7	Urology and sexual medicine PROGRAM 5	Dr. María José Requena Tapia (IA) Dr. Rafael Prieto Castro (IA)
GA8	Radiology PROGRAMS 2, 4, 5	Dr. Marina Álvarez Benito (IA)

GC – Established Groups

GA – Associated Groups

GE – Emerging Groups

## 2.3.- CENTRAL SUPPORT UNIT FOR BIOMEDICAL RESEARCH (UCAIB in Spanish)

The IMIBIC has undertaken a functional reorganization of its human and material resources in order to build a shared structure supporting research activities, known as Central Support Unit for Biomedical Research (UCAIB in Spanish). Its aim is to provide assistance to researchers interested in launching or consolidating biomedical research initiatives. At present, the UCAIB has a team of 12 advanced technicians providing support to research groups. These experts are listed below:

NOMBRE	Titulación académica
M <sup>a</sup> CARMEN MUÑOZ VILLANUEVA	PhD in Medicine
EDUARDO CHICANO GÁLVEZ	PhD in Biochemistry
DAVID OVELLEIRO FRAILE	MD in Biochemistry
ANA BELÉN POZO SALAS	Lab Technician
ANTONIA ARROYO SÁNCHEZ	Nuclear Medicine Technician
ESTHER PERALBO SANTAELLA	PhD in Biology
IGNACIO ORTEGA GARCÍA	PhD in Biochemistry
CARMEN PÉREZ CALLE	BD in Sciences
VIRGINIA RÚZ DE AZÚA	BD in Biology
ÁLVARO JIMÉNEZ VISTA	Lab Technician
MARÍA EUGENIA CARRILLO GIL	BD in Biology
ISABEL BEJERANO BLÁZQUEZ	MD in Biology and Clinical Trials

These staff members are embedded into the UCAIB's structure, which is described in the Research Facilities and Support Plan.

It includes:

### a.- Technological Processes Unit

- Proteomics Subunit: Eduardo Chicano Gálvez & Ignacio Ortea García.
- Bioinformatics Subunit: David Ovelleiro Fraile.
- Cytomics Subunit: Esther Peralbo Santaella.
- Animal Housing Subunit: Ana Belén Pozo Salas.
- Radioactive Isotopes Laboratory: Antonia Arroyo Sánchez.

### b.- Quality, Training and Methodological Support Unit

These two subunits are being developed by a highly qualified expert in Research Methodology and Biostatistics, with a Master in Quality: Maria del Carmen Muñoz Villanueva, PhD.

## C.ISCIII PLatforms

c.-ISCIII Platforms:

IMIBIC has become member of the new platforms to support research in health sciences and technologies of the Health Institute Carlos III.

PLATFORM	COORDINATORS and TECHNICIANS
<b>Medical Technology Innovation Platform (ITEMAS):</b>	Carlos González Navarro
<b>Biomolecular and Bioinformatics Resources Platform</b>	Eduardo Chicano Gálvez David Ovelleiro Fraile
<b>Clinical Research and Clinical Trials Units Platform –SCReN</b>	Isabel Bejerano Blázquez–Coordinator Francisco Pérez Jiménez–Director
<b>BiobanksPlatform</b> The Biobank of the Reina Sofia University Hospital collaborates with IMIBIC and is integrated into the network of Biobanks of the Health Institute Carlos III and the Andalusian Public Health System Biobank	Manuel Medina–Director Carmen Pérez Calle–Coordinator Virginia Rúz de Azúa Álvaro Jiménez Vista María Eugenia Carrillo Gil

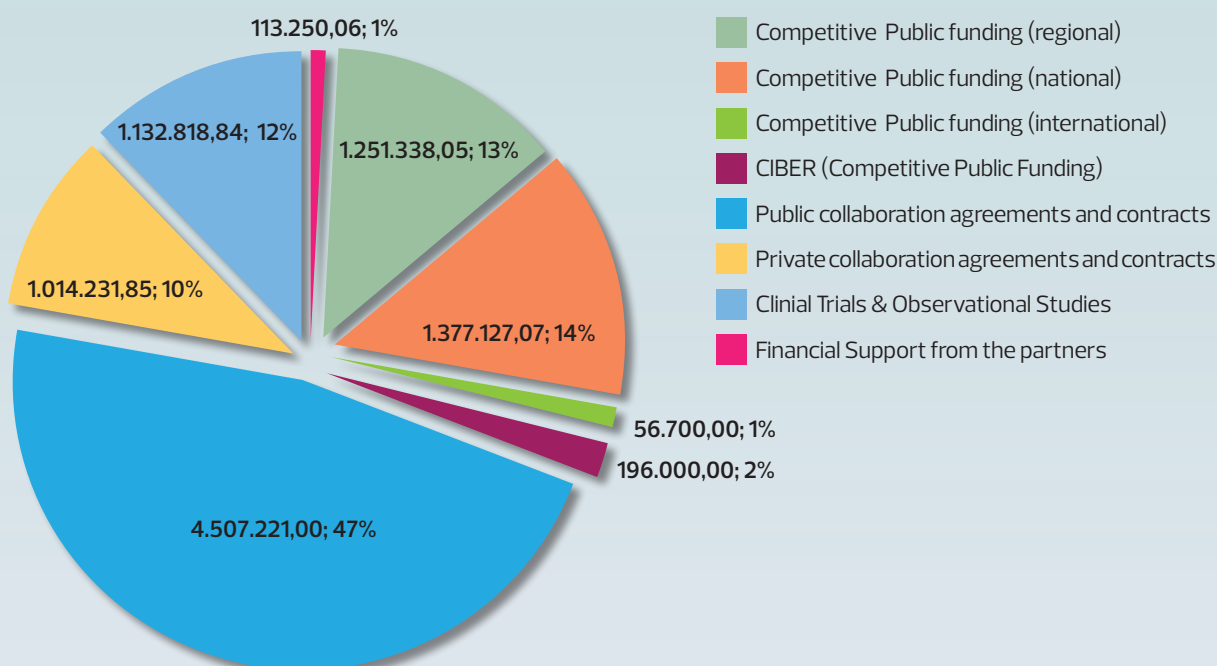
## d.- Other support units

–The IMIBIC has two animal housing units: one at the School of Medicine and another at the HURS. It also has the support of the Animal Housing Unit and the Veterinary Hospital, both located at the Campus de Rabanales of the University of Cordoba. By the date of publication of the annual report, the installation of the equipment for these areas at the new IMIBIC's facilities has been finished and it is expected to be functional by the second semester of 2014. It includes 8 stabling rooms, mainly for rat/mouse, 6 rooms of experimental laboratory of animals and an operating theater.

–The IMIBIC receives technical support from the SCAI (Central Support Services for Research) of the University of Córdoba.

## 2.4.– Economic Resources

The table below shows IMIBIC's sources of income for year 2013:





The incomes specified in the previous table have been obtained from the Profits and Loses Statement of IMIBIC in 2013. It should be noted that the incomes related to Infrastructures and Research Projects have increased considerably compared with the previous year. The increase of the Infrastructures is owing to the completion of the new premises of IMIBIC, and the increase of the Research projects are closely related to the Public Procurement Projects.

The incomes for the structure of IMIBIC got a total amount of 113.250,06€, and come from grants of the Regional Ministry of Equality, Health and Social Policies, the Regional Ministry of Economy, Innovation, Science and Employment and the University of Cordoba, all of them based on the Budget for 2014 which was approved in 2013. It has to be considered that this amount shows a decrease of 59% compared to the one of 2012.

IMIBIC has received a grant from the Regional Ministry of Economy, Innovation, Science and Employment of 1.999.000 €, in order to acquire scientific equipment. The is grant is expected to be executed during the year 2014.



03

**Goals achieved in 2013**



# 03 Goals Achieved in 2013

## **1. Developing a platform to provide a quality service aimed at attracting both commercial and non-commercial clinical trial assignments.**

During 2013, we have built a Phase I Unit which has strengthened our ability to carry out clinical trials.

## **2. Promoting the transfer of research results to clinical practice and to the socio-economic environment.**

We have joined the Clinical Research and Clinical Trials Units Platform as well as the Medical Technology Innovation Platform (ITEMAS). The number of registrations of industrial property titles increased to 16.

## **3. Intensifying IMIBIC's relationships with national and international research centres and corporations in order to improve cooperation in research.**

Our mobility policy has permitted a total of 17 researchers to conduct research stays abroad to enhance interaction. In addition, we have increased our involvement in European clinical trials.

## **4. Acquiring new equipment and facilities for the new IMIBIC headquarters.**

Here, we have followed the established plans, starting with the acquisition of property and equipment to give the IMIBIC building the latest equipment in the areas of UCAIB action (Proteomics) and then setting up and installing it (MALDI TOF -TOF, Triple TOF, etc.). In addition, the Animal Experimentation Service has acquired new racks and cages to house the animals; the Isotope Unit has acquired scintillation equipment for gamma and beta isotopes; and the Microscopy Unit has obtained a confocal microscopy set. It is understood that this process of general provision of equipment will continue in 2014 with the acquisition of laboratory furniture and other necessary equipment.

## **5. Promoting initiatives to increase private fundraising and sponsorship.**

Over the last year, we have launched an active policy of fundraising from donations and sponsors. In particular, we have collaborated with private entities such as Cajasur and obtained private donations, which are vital to extend the Institute's activity and increase society's awareness of the importance of research. In addition, relations with groups and associations have been encouraged. And, as a result of this effort, the first charity parade for Leukemia was held in Spring 2013.

## **6. Promoting communication and relationships between the IMIBIC and its researchers to progressively create a sense of belonging to this institution.**

During the last year, the communication plan was implemented, obtaining a total of 129 impacts, over 30% more than in 2012. The Institute's major communication landmarks were strengthened by turning them into major annual events (4th Conference Day for Young Researchers and 3rd Maimonides Commemorative Lecture). The communication plan has aimed at making the activity of the research groups widely known through external communication in the media and social networks. Finally, the website has been updated to suit the changing needs of the Institute.

## **7. Continuing the development of the Central Support Units for Biomedical Research, based on strategic interest and alignment with other platforms in Andalusia.**

In 2013, we joined the ProteoRed-ISCIII Network. In addition, we have increased our interaction with the Andalusian Biobank, developing joint strategies that have increased our volume of work in the collection and transfer of samples.

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**8. Intensifying fundraising –especially international funds– by the project management department through an individualized support policy aimed at IMIBIC research groups.**

Over the year, intense work has been going on to define our needs for international fundraising. A specialist in this area has been contracted to train researchers in preparing international proposals. As a result of this, one international project has been obtained and the number of proposals presented has increased, some of which were even led by our researchers.

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**9. Promoting the integration of research and technical personnel through competitive recruitment processes.**

We have continued our efforts to promote the Proteomics and the Technological Innovation Units, with the incorporation of specifically-trained technical staff.

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**10. Promoting the consolidation of emerging research groups and interactions between emerging groups, associated groups and collaborating groups at IMIBIC.**

In 2013, we have incorporated new emerging researchers and associate groups.

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04

**External Scientific  
Advisory Board**





# 04 External Scientific Advisory Board

The composition of the External Scientific Advisory Board was modified in 2013. The annual ordinary meeting took place in December 16, 2013. Its structure is as follows:

- Dr. **Lina Badimón**. Director of the Cardiovascular Research Centre (CSIC-ICCC) (Barcelona)
- Dr. **Carlos Diéguez**. Director of the Centre for Research in Molecular Medicine and Chronic Diseases (CIMUS) (Santiago de Compostela)
- Dr. **José María Ordovás**. Senior Scientist and Director for the Nutrition and Genomics Laboratory and Chair of the Functional Genomics Core of the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University (USA). Scientific Director of IMDEA Food (Madrid)
- Dr. **Francisco Sánchez Madrid**. Professor of Immunology at the Universidad Autónoma de Madrid and Scientific Director of La Princesa Research Institute (Madrid)
- Dr. **Carlos López-Otín**. Professor of Biochemistry and Molecular Biology at the University of Oviedo (Oviedo)
- D. **Jorge Barrero**. Deputy Chairman of the Spanish Association of Biotech Companies (ASEBIO) (Madrid)

According to the internal operation procedure, the main contents of the meeting were focused on mandatory matters. The members forwarded their opinions on the management of the Institute, such as the incorporation of new research groups, the implementation of strategic initiatives, the master plan to change the scientific structure and the approval of the budget for 2014.



From left to right: Manuel Tena Sempere, Carlos Diéguez, Francisco Sánchez, Lina Badimón, José María Ordovás and Francisco Pérez Jiménez



05

**Participation in  
Networks**



# 05 Participation in Networks

IMIBIC researchers are involved in a wide range of strategic initiatives coordinated by the Health Institute Carlos III and they participate in its National Research Networks program, through the Networks for Cooperative Research in Health (RETICs in Spanish) and the Biomedical Research Networking Centers (CIBERs in Spanish). In addition, during the financial year 2013, IMIBIC has joined its new platforms that support research in health sciences and technologies.

In fact, among the 32 groups integrated in the IMIBIC, 15 participate in partnership programs related to different ISCIII strategic initiatives. 10 groups are involved in 11 RETICs. Additionally, 3 groups are involved in 2 CIBERs and there are 24 groups involved in the Andalusian Plan for Research, Development & Innovation (PAIDI Program).

## CIBERs Program

Our researchers lead the following CIBERs' nodes:

CIBER	Group and Principal Investigator
CIBER on Obesity and Nutrition (CIBERobn)	José López Miranda (PI) GC9–Nutrigenomics. Metabolic Syndrome.
CIBER on Obesity and Nutrition (CIBERobn)	Manuel Tena–Sempere (PI) GC10–Hormonal regulation of energy balance, puberty and reproduction
CIBER on Liver and Digestive Diseases (CIBERehd)	Manuel de la Mata García (PI) GC2–Oxidative and nitrosative stress in acute and chronic liver disease

## Platforms

IMIBIC has become member of the new platforms that support research in health sciences and technologies of the Health Institute Carlos III:

- Medical Technology Innovation Platform (ITEMAS)
- Biomolecular and Bioinformatics Resources Platform
- Clinical Research and Clinical Trials Units Platform –SCReN
- Biobanks Platform

## RETICs Program

Some of our researchers lead the following network nodes:

Name of the Network	Principal Investigator
AIDS Research Network (RIS)	Eduardo Muñoz Blanco
Cooperative Research Thematic Network on Aging and Frailty (RETICEF)	José Manuel Quesada Gómez; Isaac Túnez Fiñana
Spanish Renal Research Network (REDinREN)	Pedro Aljama García

Spanish Network for Research into Infectious Pathologies (REIPI)	Julián de la Torre Cisneros
Network of Hospital Biobanks	Manuel Medina Pérez
Cooperative Research Thematic Network on Cancer (RETICC)	Enrique Aranda Aguilar

Other cooperative networks:

Name of the Network	Collaborating Researcher
AIDS Research Networks (RIS)	Antonio Rivero Román
AIDS Research Networks (RIS)	José Peña Martínez
Spanish Network for Research in Infectious Pathology (REIPI)	Rafael Solana Lara
Network for Research on Mother-Child Health (RedSAMID)	Mercedes Gil Campos
Research Network on Preventive and Health Promotion in Primary Care (RedIAPP)	Luis Ángel Pérula de Torres

Other research networks:

Name of the Network	Principal Investigator
Spanish Society for Rheumatology (REGISPONSER)	Eduardo Collantes Estévez
Spanish Myelodysplastic Syndrome Registry (RESMD)	Joaquín Sánchez García*
Observational Immune Tolerance Induction research program (OBSITI)	Francisco Velasco Gimena*

\*Members of the same group

## PAIDI Groups

Many IMIBIC researchers belong to or lead groups formed under the Andalusian Plan for Research, Development and Innovation (PAIDI, in Spanish).

- BIO-139. Principal investigator: Justo P. Castaño Fuentes
- BIO 208. Principal investigator: José Suárez de Lezo Cruz Conde
- BIO 216. Principal investigator: José Antonio Bárcena Ruiz
- BIO-272. Principal investigator: Manuel Ruiz Rubio
- BIO-301. Principal investigator: Rafael Rodríguez Ariza
- BIO-304. Principal investigator: Eduardo Muñoz Blanco
- BIO-310. Principal investigator: Manuel Tena Sempere
- CTS-179 Principal investigator: Escolástico Aguilera Tejero
- CTS 260 Principal investigator: Pedro Aljama García
- CTS-208. Principal investigator: José Peña Martínez
- CTS-212. Principal investigator: Francisco Pérez Jiménez
- CTS-234. Principal investigator: Enrique Aranda Aguilar
- CTS-273. Principal investigator: Manuel de la Mata García
- CTS-413. Principal investigator: José Manuel Quesada Gómez
- CTS-452. Principal investigator: Roger Ruiz Moral
- CTS-525. Principal investigator: José López Miranda
- CTS-651. Principal investigator: Juan Antonio Paniagua González
- CTS-620. Principal investigator: Francisco Velasco Gimena
- CTS-624. Principal investigator: Isaac Túnez Fiñana
- CTS-647. Principal investigator: Julián Carlos de la Torre Cisneros
- CTS-666. Principal investigator: Aurora Rodríguez Borrego
- CTS-639. Principal investigator: María Mercedes Gil Campos
- FQM-227. Principal investigator: María Dolores Luque de Castro
- TIC-161. Principal investigator: Rafael Medina Carnicer

06

**Training Activities**





# 06 Training Activities

## 6.1. INTRODUCTION

The Institute conceives training as a basic, crucial and institutional tool to achieve its scientific goals. Thus, it has designed a program aimed at promoting knowledge and reinforcing the current lines of research.

In the early part of 2013, the Training Coordinator was Dr. Eduardo Collantes Estévez but he handed it over to Dr. Rosario López Pedrera who is the current coordinator.

The IMIBIC leads a unique PhD Program in Biomedicine that has integrated the former PhD Program in Nutrition and the PhD Program in Research Methodology.

The new PhD Program in Biomedicine –coordinated by Dr. Francisco Gracia Navarro– has helped to obtain highly qualified researchers, promote teaching and favor professional qualification in the field of biomedical sciences.

## 6.2. TRAINING

The following sections list the research training activities, which took place in 2013.

### 6.2.1. PhD in Biomedicine

IMIBIC leads a unique PhD Program in Biomedicine. This new program, coordinated by Prof. Francisco Gracia Navarro, PhD, pretends to qualify human resources and stimulate professional qualification in the field of biomedical sciences. Website: <http://www.uco.es/idep/doctorado/programas/biomedicina>

### 6.2.2. MASTERS DEGREES AND PhDs

The three master's degrees are driven by academic directors who are members of the IMIBIC:

#### – Translational Biomedical Research

Academic Director: Prof. Dr. Francisco Gracia Navarro

Website: <http://www.uco.es/estudios/idep/masteres/investigacion-biomedica-traslacional>

#### – Metodology of Research in Health Sciences

Academic Director: Prof. Dr. Eduardo Collantes Estévez

Website: <http://www.uco.es/estudios/idep/masteres/metodologia-investigacion-ciencias-de-la-salud>

#### – Nutrition and Metabolism (with Quality Accreditation by ANECA)

Academic Director: Prof. Dr. Francisco Pérez Jiménez

Website: <http://www.uco.es/estudios/idep/masteres/nutricion-metabolismo>

### 6.2.3. COURSES and other training activities:

Specific courses in Research Methodology and other key research áreas at IMIBIC have been held during 2013.

### 6.2.3.1. COURSES

IMIBIC organized the following list of activities:

Type of Activity	Title	Duration*(h)
INSTITUTIONAL EVENT	3rd Maimonides Commemorative Lecture	4
INSTITUTIONAL EVENT	4th Conference of Young Researchers	10
SEMINAR	Sample size calculation in clinical research	3
COURSE	Basic Bioinformatics	40
COURSE	Research Methodology in Health Sciences: Developing a Protocol and Dissemination of Research	36

IMIBIC collaborated in the following list of activities:

Type of Activity	Title	Duration*(h)
INFORMATIVE SESSION	Informative Session on the new Horizon 2020 Programme	2
COURSE	Transcranial magnetic stimulation and neuromodulation: present and future in neuroscience	20
COURSE	Predictive models. Applications for optimizing clinical and health decisions.	20
WORKSHOP	Workshop for professional users of the voice: how to care for the voice and prevent voice disorders. Up-to-date diagnostic and therapeutic techniques.	4

### 6.2.3.2. IMIBIC Research Seminars

IMIBIC research seminars promote networking and contribute to the knowledge of the researchers.

The seminars organized by the Institute during the year 2013 were:

DATE	SPEAKER	INSTITUTION	TITLE
10/01/2013	Antonio Pineda Lucena	Príncipe Felipe Research Center.	New approaches applied to the discovery of anticancer drugs: from target identification to drug screening
17/01/2013	Mario Delgado	The Institute of Parasitology and Biomedicine "López-Neyra" (IPBLN)	Cortistatin as a pleiotropic agent
18/01/2013	Mónica Gandelha	Universidade Federal do Rio de Janeiro	Treatment of acromegaly: predictors of response to somatostatin analogues
24/01/2013	Agustin Valenzuela	University of La Laguna (Tenerife)	The Role of cytoskeleton and membrane dynamics in HIV fusion, entry and infection
31/01/2013	José Luis Martín Ventura	Jiménez Díaz Foundation (Madrid)	Identification of novel obesity and type 2 diabetes susceptibility
07/02/2013	Antonio Zorzano	Institute for Research in Biomedicine (Barcelona)	Identification of novel obesity and type 2 diabetes susceptibility genes
14/02/2013	Agnès Gruart I Masso	Pablo de Olavide University (Sevilla)	Mechanisms of Memory Formation and Memory Loss
21/02/2013	Oriol Casanovas	Bellvitge Biomedical Research Institute IDIBELL (Barcelona)	Angiogenesis in cancer: targeted therapies, promises, hopes and failures
27/02/2013	Albert Abad	Germans Trias I Pujol Hospital (Badalona)	Polymorphisms in Oncology. Basic features and clinical relevance
07/03/2013	M <sup>a</sup> Luisa Maestro de las Casas	San Carlos Clinical Hospital (Madrid)	Circulating tumor cells, basic and clinical features

13/03/2013	William G. Kerr	The State University of New York Upstate Medical University	Role of SHIP1 and LRBA in Bone Marrow Transplant and Cancer
14/03/2013	Ángel Gil	University of Granada	Biochemistry and Molecular Biology
21/03/2013	Juan Valcárcel	The Centre for Genomic Regulation (Barcelona)	Alternative splicing of mRNA in cancer
19/04/2013	Francisco Guarner	Vall d'Hebron University Hospital (Barcelona)	Genes and Functions of the Human Intestinal Microbiota
25/04/2013	Cintia Roodveldt	Andalusian Molecular Biology and Regenerative Medicine Centre CABIMER (Seville)	Alpha-synuclein and chaperones: their role in the immune response linked to Parkinson's Disease
02/05/2013	Francisco Tinahones	Clinical University Hospital of Málaga	Endocrinology and Nutrition
07/05/2013	Iván Quesada	Miguel Hernández University of Elche (Alicante)	Functional and structural adaptations to obesity of pancreatic alpha and beta cells
17/05/2013	Abel Santamaría	The National Institute of Neurology and Neurosurgery, 'Manuel Velasco Suárez' (México)	S-allyl cysteine, redox modulation and neuroprotection
25/09/2013	Manfredi Rizzo	University of Palermo (Italy)	Atherogenicity and clinical significance of LDL subclasses
26/09/2013	Manuel Santos Rosa	University of Coimbra (Portugal)	Immunity and sepsis
03/10/2013	Sergey Degtyare	SibEnzyme Ltd, Novosibirsk (Russia)	GLAD-PCR assay: a new epigenetic method for cancer diagnostics
07/11/2013	Alberto Muñoz Terol	Biomedical Research Institute 'Alberto Sols' (Madrid)	Pleiotropic actions of vitamin D
12/12/2013	Jesús Argente	Niño Jesús University Hospital (Madrid)	Obesity in children and adolescents: new concepts and new outlooks
19/12/2013	Marc Claret	August Pi i Sunyer Biomedical Research Institute IDIBAPS (Barcelona)	Mitofusin 2 in POMC neurons connects ER stress with leptin resistance and energy imbalance

### 6.2.3.3. INSTITUTIONAL EVENTS

## 4th Conference of Young Researchers

Date: 14th May

Organized by: IMIBIC, University of Cordoba and the Regional Government of Andalusia

### Program:

9.00–9.30. Registration and pinning up of posters.

9.30–10.00. Introduction and welcome

10.00–12.30. Session I. Cardiovascular Disease. Obesity and Metabolic Syndrome. Liver and digestive diseases. Kidney and nephrourological diseases.

10.00–10.15

Comparative effect of dietary fat in the expression of oxidative stress related genes in adipose tissue and peripheral blood mononuclear cells from metabolic syndrome patients.

**Patricia Judhit Peña Orihuela.**

10.15–10.30

Effects of parenteral nutrition formulas on plasma lipid profile in children with bone marrow transplantation.

**Mercedes Gil Campos.**

10.30–10.45

Obesity-induced hypogonadism in the male: premature reproductive senescence and contribution of Kiss1-mediated mechanisms.

**Miguel Ángel Sánchez-Garrido.**

10.45–11.00

The small GTPase Rab18 in the regulation of lipid droplet dynamics in adipocytes.

**Yoana Rabanal Ruiz.**

11.00–11.15

Magnesium increases osteogenic differentiation of rat mesenchymal stem cells through notch signaling activation.

**Juan Miguel Diaz Tocados.**

11.15–11.45. Coffee break. Poster session.

11.45–12.00

Neuroproteomic approaches to identify novel kisspeptin-regulated pathways in the hypothalamus: studies in Kiss1 ko mice.

**Antonio Romero-Ruiz.**

12.00–12.15

Effects of mediterranean diet supplemented with coenzyme q10 on metabolomic profile in elderly men and women.

**Lorena González de la Guardia.**

12.15–12.30

Proteomic profiling of adipose tissue subcutaneous in obese patients before and after bariatric surgery.

**Natalia Rocio Moreno Castellanos.**

12.30.12.45

Metabolic control of puberty: essential roles of alpha-msh signaling in mediating the permissive effects of leptin on puberty onset.

**María Manfredi Lozano.**

12.45–13.00

Calcium deficiency reduces circulating levels of fibroblast growth factor 23.

**María Encarnación Rodríguez Ortiz**

13.00–14.00. Plenary talk: Dr. Óscar Fernández Capetillo

14.00–16.00. Lunch

16.00–18.15. Session II. Oncology and Oncohematology. Chronic Inflammatory Diseases and Infectious Diseases. Senescence.

16.00–16.15

Role of carbamylated high density lipoprotein on EPCs selection in vitro.

**Carlos Luna Ruiz**

16.15–16.30

Combination of multitarget kinase inhibitor AEE788 and cyclooxygenase-2 inhibition for the treatment of colorectal cancer. a preclinical study.

**Araceli María Valverde Estepa**

16.30–16.45

Regulation of alternative splicing of ghrelin gene by the antisense strand gene GHRLOS.

**David Rincón Fernández-Pacheco**

16.45–17.00

AGTR-1 as a biomarker of response to treatment with the antiangiogenic drug bevacizumab in solid tumors.

**Francisco Manuel Conde Pérez**

#### 17.00–17.30. Poster session

17.30–17.45

The ubiquitin ligase SIAH2 as a prognostic and predictive marker in lung cancer.

**Paula Moreno Casado**

II.f 17.45–18.00

Recruitment of pluripotent "side population" cells in non-malignant reactive human lymph nodes.

**Vianihuini Figueroa**

II.g 18.00–18.15

Role of new components of somatostatin and ghrelin systems on the proliferation of pancreatic neuroendocrine tumor cell lines.

**Alicia Villa Osaba**

#### 18.15–19.00. Prize giving and closing ceremony.

## 3rd Maimonides Commemorative Lecture and IMIBIC prize-giving 2013

Date: 16th December

Organized by: IMIBIC, UCO and the Regional Government of Andalusia

### Program:

#### 11.00. Opening Ceremony

#### 11.10. IMIBIC Awards

– "Enrique Aguilar Benítez de Lugo" prize for the most relevant publication

**Francisco Javier Ruíz Pino.** "Role of Neurokinin B in the control of female puberty and its modulation by metabolic status"

– Prize for the most relevant scientific publication in collaboration with international groups

**María Encarnación Rodríguez Ortiz.** "Calcium Deficiency Reduces Circulating Levels of FGF23"

– Prizes for the most relevant research results

**Javier Delgado Lista.** "PadMed, software for health professionals"

– **Carlos Pérez Sánchez.** "Mitochondrial dysfunction in antiphospholipid syndrome: implications in the pathogenesis of the disease and effects of coenzyme Q10 treatment"

– Award for the best master's degree thesis

– **Juan Miguel Díaz Togados.** "The role of magnesium in the regulation of osteogenesis and the mineralization of mesenchymal stem cells"

– Award for the journalistic news report most valuable to IMIBIC

**Lourdes Chaparro Ruiz.** "El Día de Córdoba" newspaper.

#### 12.00. Conference – Tribute to Maimonides

**Dr. Jose Alvarez Kindelán**

#### 12.15. Maimonides Lecture

**Dr. Lina Badimón**

#### 13.00. Prize-giving and closing ceremony

## 6.3 . RESULTS OF TRAINING ACTIVITIES

### 6.3.1. DOCTORAL THESES

The training dedication of the IMIBIC is also reflected by the large number of doctoral theses that are directed and supported by the IMIBIC members. A list is provided below of the 22 doctoral theses directed by researchers from the Centre during 2013:

Thesis Author	Title	Thesis Director
Mario Frias Casas	Effect of a therapeutic vaccine based on dendritic cells on the innate immune response in HIV infection	José Peña Martínez
Antonio Rivero Juárez*	Predictive response values to treatment of hepatitis C virus in patients coinfecting with HIV	José Peña Martínez
Rafael José Ortí Rodríguez	Usefulness of artificial neural networks in donor-recipient allocation in liver transplantation	Manuel de la Mata García
Elena Schiotis Ruxandra	Relationship of pharmacological treatment and genetic polymorphisms with clinical and structural severity in ankylosing spondylitis	Eduardo Collantes Estévez
Cosmina Filipescu Iliana	The monitoring of the evolution, clinical and paraclinical correlations in rheumatoid arthritis treated with anti-tnfalpha agents	Eduardo Collantes Estévez
Fernando Sánchez López	Role of oxidative stress and neurotrophic factors in Huntington's disease: its possible use as a biomarker	Isaac Túnez Fiñana
Farid Almabouada	Molecular mechanisms of action of GTPase RAB18 in intracellular trafficking and cell physiology	María del Mar Malagón Poyato
Carmen Herencia Bellido	Role of bone marrow stem cells in hepatology: in vivo and in vitro studies.	Juan Rafael Muñoz Castañeda
Francisco Javier Toledano Delgado	Degree of late neointimal coverage in coronary segments treated by implantation of drug-eluting stents: study of optical coherence.	Manuel Pan Álvarez-Ossorio
Antonio Luis Gámez López	Effects on mortality and hospital readmission of three different intervention programmes in patients hospitalized for heart failure.	José Suárez de Lezo Cruz-Conde
Juan Luis Bonilla Palomas	Prognostic influence of nutritional status in patients with heart failure	José Suárez de Lezo Cruz-Conde
Manuel Crespín Crespín	Implantation of percutaneous aortic valve prosthesis: short-term results. Effects of phenolic compounds on gene expression and endothelial dysfunction in patients with high cardiovascular risk	José Suárez de Lezo Cruz-Conde
Daniel García Fuentes	Evaluation of the anatomy of the interatrial septum in patients referred for percutaneous closure of interauricular communication	Manuel Pan Álvarez-Ossorio
María Cristina López Ibáñez*	Effectiveness and safety in clinical practice of oral anticoagulation in patients of 80 years old or over with chronic non-valvular atrial fibrillation	Martín Ruiz Ortiz
Marcelino González Padilla	Impact of respiratory colonization and asymptomatic bacteriuria on the risk of infection in candidates for liver and heart transplantation	Julián de la Torre Cisneros
Francisco Javier Ariza Fuentes	High convective transport improves microinflammation parameters and endothelial dysfunction, regardless of the technique used.	Alejandro Martín Malo
Mirian Moreno Conde	Effect of the amount and type of dietary fat on the regulatory function of the endothelium during the postprandial state in patients with metabolic syndrome.	Jose Lopez Miranda
Cristina Cruz Teno	Influence of the quality and quantity of dietary fat on the degree of inflammatory response in patients with metabolic syndrome	Jose Lopez Miranda
José García Quintana	Effect of type of dietary fat on oxidative stress parameters during the postprandial state in patients with metabolic syndrome	Jose Lopez Miranda
Miguel Ángel Sánchez-Garrido Noguerras	Characterization of metabolic and reproductive abnormalities in models of nutritional and gonadal manipulation applied at various stages of development: impact of obesity on the reproductive axis	Manuel Tena Sempere

Francisco Jesús Llorente Cantarero*	Evaluating metabolic, inflammatory and oxidative stress plasma markers in healthy children according to fitness	Juan de Dios Benítez de Sillero
Belén Chancón García	Role of somatostatin, cortistatin and ghrelin in cellular and molecular dysregulation of the endocrine pancreas in normal and extreme metabolic conditions such as obesity and diabetes	Francisco Gracia Navarro

\*Theses with International Mention

### 6.3.2. PROFILE OF STUDENTS ENROLLED FOR MASTER'S DEGREES

MASTER'S DEGREE IN	TOTAL STUDENTS ENROLLED	Nº
TRANSLATIONAL BIOMEDICAL RESEARCH	43	PCS = 0 NS = 4 R = 18 O = 21
RESEARCH METHODOLOGY IN HEALTH SCIENCES	52	PCS = 0 NS = 6 R = 36 O = 10
NUTRITION AND METABOLISM	35	PCS = 0 NS = 5 R = 17 O = 13

PCS = Primary Care Staff; NS = Nursing Staff; R = Residents, O = Other categories.

### 6.4. RESEARCH STAYS

Throughout the year 2013, 17 researchers IMIBIC completed a research stay in national and international centers. This number reflects clear research dedication and it is orientated towards the creation of networks.

The Institute has launched a support program to help its researchers to complete research stays in well-known centers to share knowledge and consolidate alliances all over the world.

The information gathered from the research groups is set out in the table below:

Professional Category	Type of Internship	National Internship	International Internship
Researchers	Public scheme		N:2 Total duration: 14 months
	Others		
	Internal scheme	N:1 Total duration: 1½ months	N: 2 Total duration: 4½ months
Pre-doctoral Researchers	Public scheme	N: 1 Total duration: 7 months	N: 1 Total duration: 7 months
	Others		
	Internal scheme		N:2 Total duration: 6½ months
Post-doctoral Researchers	Public scheme	N: 1 Total duration: 3 months	N: 1 Total duration: 3 months
	Others	N: 1 Total duration: 3 months	N: 1 Total duration: 3 months
	Internal scheme	N: 1 Total duration: 3 months	N: 3 Total duration: 6 1/2 months

\* Internal Scheme: The IMIBIC Program of incentives for strategic activities is a comprehensive development plan aimed at professionals who carry out research in the Institute.

\* Public Scheme: Internship grants awarded by public organizations.

\* Other: Individual internships made by a member of the research groups.





07

**Acquisition of  
Scientific Equipment**



# 07 Acquisition of Scientific Equipment

Over the year 2013, several pieces of equipment were acquired in order to facilitate the work of our researchers. Specifically, the Regional Ministry of Equality, Health and Social Policies provided with a €135,000 grant for the formation of a Phase I Trial Unit aimed at dynamizing and enhancing clinical research at our institute.



IMBIC's new facilities

This grant was used to build a day hospital in the premises of the institute with capacity for seven patients (hospital chairs, monitor screens, gaz dispensers, etc) and a complete two-bed hospitalization room with a monitoring system and patient-nurse communication system, monitor screens, etc.). Additionally, the grant allowed to build four medical offices, a cooling equipment room, a small laboratory, two data managing rooms, a waiting room and an archive.

Moreover, €201,521-worth equipment has been acquired for the different research groups.

Finally, the following equipment was acquired with FEDER funds obtained by the University of Cordoba:

- Isotope Unit:
  - 1 scintillation Beta counter;
  - 1 MicroBeta luminiscence counter;
  - 2 gamma isotope counters;
- Proteomics Unit:
  - 1 MALDI TOF-TOF
  - 1 Triple TOF
  - 1 Sprayer
- Microscopy / cytometry Unit: 1 High-performance confocal microscope
- General Equipment:
  - 1 gel photo documentation and image analysis system for chemiluminescence, fluorescence and colorimetry.
  - Complete electrophysiology composed of:
    - 1 Fluorescence microscope
    - 1 Vibratome unit

- 1 cryostat unit
- 1 microelectrode amplifier
- 1 digitizer unit
- 1 microscope translation system fitted with a micromanipulation system
- 1 micropipette puller
- 1 automated perfusion system
- 1 open-profile perfusion chamber
- 1 set of antivibration table and a Faraday cage
- 1 personal protective equipment for radiation hazard

Regarding the acquisition of the equipment covered by the rest of aid granted through FEDER resources (laboratory furniture, equipment in rooms of cultivation, etc) its execution is expected to take place in the next financial year 2014, since the corresponding call for tenders will be launched this year.

08

Scientific Production



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# GC1

## T and NK cell Immunosenescence Antiviral Immune Response

### Team Leaders

#### Principal Investigator (PI)

Rafael Solana Lara

[rsolana@uco.es](mailto:rsolana@uco.es)

Spanish Network for Research in Infectious Pathology (REIPI) (Collaborator)

#### Co-Principal Investigator (Co-PI)

José Peña Martínez

AIDS Research Network (RIS)(Collaborator)

PAIDI CTS-208 scientific Group

#### Senior Researcher

Rafael González Fernández

#### Post-doctoral Researchers

Bárbara Martín Manzanares

Laura Castro Orgaz

Alejandra Pera Rojas

#### Pre-doctoral Researchers

Rocío Aguado Álvarez

Orlando Estévez Cordero

Juan Eduardo Molina Alcaide

Ana M<sup>a</sup> Navas Romo

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)

Corona Alonso Díaz

Carmen Campos Fernández

M<sup>a</sup> Luisa Velarde Martínez



## Scientific Activity

The process of senescence of the immune system in different models: chronological aging, cancer, inflammatory diseases, viral infection and other situations of chronic activation of the immune system. In particular, we analyze the receptors involved in the regulation of cytotoxicity in T (CTL) and NK cells

and their ligands in these models, and the role of CMV. We also analyze the immunopathogenesis of HIV infection and the impact that different therapeutic situations have on it as well as the innate immune response in HIV-1 + patients treated with "ex vivo" autologous dendritic cells as part of the protocol of developing a preventive vaccine.

## Keywords

AIDS, HIV-1, HAART, preventive vaccine. Immunosenescence, aging, melanoma, NK cells, NKT cells, NK receptors, CMV, cytotoxic T lymphocytes (CTL).

## Publications

### Originals Publications

Estevez OA, Ortega C, Tejero A, Fernandez S, Aguado R, Arostegui JI, Gonzalez-Roca E, Pena J, Santamaria M. A novel phenotype variant of severe congenital neutropenia caused by G6PC3 deficiency. *Pediatr Blood Cancer*. 2013, 60(7):E29-31. IF: 2,353

Cantisán S, Torre-Cisneros J, Lara R, Zarraga S, Montejo M, Solana R. Impact of Cytomegalovirus on Early Immunosenescence of CD8+ T Lymphocytes After Solid Organ Transplantation. *J Gerontol Ser A-BiolSci Med Sci*. 2013, 68(1):1-5. IF: 4,314

Ortega C, Estevez OA, Fernandez S, Aguado R, Rumbao JM, Gonzalez T, Perez-Navero JL, Santamaria M. Interleukin-21 Overexpression Dominates T Cell Response to Epstein-Barr Virus in a Fatal Case of X-Linked Lymphoproliferative Syndrome Type 1. *Clin Vaccine Immunol*. 2013, 20(5):765-771. IF: 2,598

Gayoso I, Cantisán S, Cerrato C, Sanchez-García J, Martín C, Solana R, Torres-Gomez A, Torre-Cisneros J. Clinical Factors Influencing Phenotype of HCMV-Specific CD8+ T Cells and HCMV-Induced Interferon-Gamma Production after Allogeneic Stem Cells Transplantation. *Clin Dev Immunol*. 2013, n° art 347213. IF: 3,064

### Joint Publications

Ortega C, Fernández S, Estévez OA, Aguado R, Molina JJ, Santamaria M. IL-17 Producing T Cells in Celiac Disease: Angels or Devils?. *Int Rev Immunol*. 2013, 2(5-6):534-43. IF: 5,73

Cantisán S, Lara R, Montejo M, Redel J, Rodríguez-Benot A, Gutiérrez-Aroca J, González-Padilla M, Bueno L, Rivero A, Solana R, Torre-Cisneros J. Pretransplant Interferon- Secretion by CMV-Specific CD8+ T Cells Informs the Risk of CMV Replication After Transplantation. *Am J Transplant*. 2013, 13:738-745. IF: 6,192

Sanchez-Correa B, Bergua JM, Campos C, Gayoso I, Arcos MJ, Banas H, Morgado S, Casado JG, Solana R, Tarazona R. Cytokine profiles in acute myeloid leukemia patients at diagnosis: Survival is inversely correlated with IL-6 and directly correlated with IL-10 levels. *Cytokine*. 2013, 61(3):885-891. IF: 2,518

Ferrando-Martinez S, Romero-Sanchez MC, Solana R, Delgado J, de la Rosa R, Muñoz-Fernandez MA, Ruiz-Mateos E, Leal M. Thymic function failure and C-reactive protein levels are independent predictors of all-cause mortality in healthy elderly humans. *Age*. 2013, 35(1):251-259. IF: 4,084

Rivero-Juarez A, Gonzalez R, Camacho A, Manzanares-Martin B, Caruz A, Martinez-Peinado A, Torre-Cisneros J, Pineda JA, Pena J, Rivero A. Natural Killer KIR3DS1 Is Closely Associated with HCV Viral Clearance and Sustained Virological Response in HIV/HCV Patients. *Plos One*. 2013, 8(4):e61992. IF: 3,73

Rivero-Juarez A, Camacho A, Merchante N, Pérez-Camacho I, Macías J, Ortiz-García C, Cifuentes C, Torre-Cisneros J, Peña J, Pineda JA, Rivero A. Grupo para el estudio de las hepatitis víricas (HEPAVIR) de la Sociedad Andaluza de Enfermedades Infecciosas (SAEI). Incidence of liver damage of uncertain origin in HIV patients not co-infected with HCV/HBV. *PLoS One*. 2013, 8(7):e68953. IF: 3,73

### Research Projects

Peña Martínez, J. Influence of genotype combinations of NK receptors (KIR) and HLA molecules in the progression of HIV-1 infection in different clinical and therapeutic situations. Sponsored by: Institute Carlos III Health (ISCIII). Reference: 09/0424

Solana Lara, R. Effect of age and CMV infection on the multifunctionality of NK cell, invariant NKT cells, NKT-like lymphocytes and CMV specific lymphocytes. Sponsored by: Carlos III Health (ISCIII). Referencia: 09/0723

Rafael Solana, L. Allogeneic use of ASCs for the systemic treatment of inflammatory diseases:

clinical approach to rheumatoid arthritis. Sponsored by: Ministry of Economy and Competitiveness (MINECO) Reference: IPT-010000-2010-40

Solana Lara, R. Micro-RNA expression (miRNA) in NK cell subpopulations. Role of age- and CMV-associated changes. Sponsored by: Institute Carlos III Health (ISCIII). Reference: PI13/02691 \*2014 Annuity

### Collaboration Agreements

Peña Martínez, J. Collaboration agreement with Oxoid. Influence of genotype combinations of nk receptors (KIR) and HLA molecules in the progression of HIV-1 infection in different clinical and therapeutic situations. Sponsored by: Roche Farma, S.A. Reference: CCB.0009

Peña Martínez, J. Agreement with Innogenetics Diagnostica Iberia SL. Sponsored by: Fujirebio Iberia S.L. Reference: CCB.0036

Peña Martínez, J. Agreement with Innogenetics Diagnostica Iberia SL. Sponsored by: Fujirebio Iberia S.L. Reference: CCB.0057

## GC2

# Oxidative and Nitrosative Stress in Acute and Chronic Liver Disease

### Team Leaders

#### Principal Investigator (PI)

Manuel de la Mata García

[hepatoh2hrs.sspa@juntadeandalucia.es](mailto:hepatoh2hrs.sspa@juntadeandalucia.es)

CIBER on Liver and Digestive Diseases (CIBERehd)

PAIDI CTS-273 scientific group

#### Co-Principal Investigator (Co-PI)

Jose Antonio Bárcena Ruiz

PAIDI BIO-216 scientific group

### Senior Researchers

Patricia Aguilar Melero

Guadalupe Costán Rodero

Gustavo Ferrín Sánchez

Enrique Fragas Rivas

Valle Garcia Sanchez

Federico Gomez Camacho

Emilia Martínez Galisteo

Jose Luis Montero Álvarez

Alicia Padilla Peña

Jose Peinado Peinado

Antonio Poyato González

### Post-doctoral Researchers

Raúl González Ojeda

Brian Mcdonagh Null

### Pre-doctoral Researchers

Sandra Gonzalez Rubio

Juan Jurado Garcia

Clara Linares Luna

### Other members of the Group

(Other researchers, Technical, and Administrative Staff)

Pilar Barrera Baena

Luis Vida Pérez



## Scientific Activity

The members of the research team are divided into the BIO-216 and the CTS-273 scientific group –within the Andalusian Research Plan– and the CIBER for liver and digestive diseases (CIBERehd) in the context of a mixed group consisting of a healthcare team made up of hepatologists, surgeons and a biomedical research team of the HURS Research Unit and Department of Biochemistry and Molecular Biology of the UCO with associated teaching activity. Our biomedical research focuses on acute and chronic hepatocellular injury, hepatocarcinoma and liver transplants, with special emphasis on post-translational modifications of the proteome as a consequence of oxidative stress (reactive oxygen species, ROS) and nitrosative stress (reactive nitrogen species, RNS) in eukaryotic cells (hepatocytes and yeasts). The intracellular cytoprotection signal for molecules of various antioxidants (N-

acetylcysteine,  $\alpha$ -tocopherol) or cellular redox state regulators (redoxins) have been characterized in models of cellular injury. The mitochondrial dysfunction caused by redox imbalance is at the root of a large number of pathologies. The group of proteins from the family of cellular and mitochondrial redoxinas plays a major part in antioxidant defence, the maintenance of thiol systems and the interaction between reduced glutathione, ROS and RNS. For this purpose, normal and chimeric mutants and recombinant proteins are produced using techniques of molecular biology and in vitro characterization; and (second generation) targeted proteomics are carried out using biochemical analysis techniques.

The group's proven experience in the analysis of post-translational modifications is employed in the identification of biomarkers for hepatocellular carcinoma detection and diagnosis using proteomic analysis tools. In the area of liver transplants, we have

identified the cytoprotection mechanisms mediated by cardiotrophin-1 in the preservation injury in liver transplantation developed in experimental animals (rats and "mini-pigs"). In addition, the clinical group is involved in the development of a large number of phase II, III and IV clinical trials in the areas of viral hepatitis (boceprevir), hepatocellular carcinoma (sorafenib), liver cirrhosis (sativaptan), acute liver failure (bioartificial liver, MARS) and liver transplantation (immunosuppression strategies).

## Keywords

Reactive oxygen species, nitric oxide, antioxidants, redoxins, proteomics, apoptosis, necrosis, hepatocytes, yeast, mitochondria, liver cancer, biomarkers, liver transplantation, cirrhosis, viral hepatitis, acute and chronic liver failure.

## Publications

### Originals Publications

Rodríguez-Perálvarez M, Germani G, Papastergiou V, Tsochatzis E, Thalassinou E, Luong TV, Rolando N, Dhillion AP, Patch D, O'Beirne J, Thorburn D, Burroughs AK. Early tacrolimus exposure after liver transplantation: Relationship with moderate/severe acute rejection and long-term outcome. *J Hepatol*. 2013, 58(2):262-270. IF:9,858

Jimenez-Perez M, Garcia DM, Grande RG, Daga JAP, Pulido LB, Aguilar MDME, Bravo MAG, Lopez JMR, Garcia MMD. Analysis of the Recurrence of Hepatitis C Virus After Liver Transplantation: Results of the Andalusian Liver Registry. *Transplant Proc*. 2013, 45(1):276-278. IF:0,952

Aguilar-Melero P, Luque A, Machuca MM, de Obanos MPP, Navarrete R, Rodríguez-García IC, Briceño J, Iniguez M, Ruiz J, Prieto J, de la Mata M, Gomez-Villamandos RJ, Muntane J, Lopez-Cillero P. Cardiotrophin-1 reduces ischemia / reperfusion injury during liver transplant. *J Surg Res*. 2013, 181(2):e83-91. IF: 2,018

Briceño J, Ciria R, de la Mata M. Donor-recipient matching: Myths and realities. *J Hepatol*. 2013, 58(4):811-820. IF:9,858

Senent SG, Barreiro-de Acosta M, Garcia-Sanchez V. Enterocutaneous fistulas and Crohns disease: Clinical characteristics and response to treatment. *Rev Esp Enferm Dig*. 2013, 105(1):3-6. IF:1,652

Aguilar-Melero P, Prieto-Alamo MJ, Jurado J, Holmgren A, Pueyo C. Proteomics in HepG2 hepatocarcinoma cells with stably silenced expression of PRDX1. *J Proteomics*. 2013, 79:161-171. IF:4,088

Rodríguez-Perálvarez M, Tsochatzis E, Naveas MC, Pieri G, García-Caparrós C, O'Beirne J, Poyato-González A, Ferrín-Sánchez G, Montero-Alvarez JL, Patch D, Thorburn D, Briceño J, De la Mata M, Burroughs AK. Reduced exposure to calcineurin inhibitors early after liver transplantation prevents recurrence of hepatocellular carcinoma. *J Hepatol*. 2013, 59(6):1193-1199. IF: 9,858

Gonzalez R, Ferrin G, Aguilar-Melero P, Ranchal I, Linares CI, Bello RI, de la Mata M, Gogvadze V, Barcena JA, Alamo JM, Orrenius S, Padillo FJ, Zhivotovsky B, Muntané J. Targeting hepatoma using nitric oxide donor strategies. *Antioxid Redox Signal*. 2013, 18(5):491-506. IF:7,189

McDonagh B, Pedrajas JR, Padilla CA, Bârcena JA. Thiol redox sensitivity of two key enzymes of heme biosynthesis and pentose phosphate pathways: uroporphyrinogen decarboxylase and transketolase. *Oxid Med Cell Longev*. 2013, 2013:

n° art UNSP 932472. IF:3,393

Ruiz Cuesta P, Hervás Molina AJ, Muñoz García-Borrueal M, Jurado García J, García Sánchez V, Pleguezuelo Navarro M, Casás Juanena LL, Naranjo Rodríguez A. Endoscopic retrograde cholangiopancreatography in patients with anatomic abnormalities of the stomach due to surgery. *Gastroenterol Hepatol*. 2013, 36(10):609-15. IF:0,567

Cruz-Ramírez M, Hervas-Martinez C, Gutierrez PA, Perez-Ortiz M, Briceño J, de la Mata M. Memetic Pareto differential evolutionary neural network used to solve an unbalanced liver transplantation problem. *Soft Computing*. 2013, 17(2):275-284. IF:1,124

Ferrin G, Ranchal I, Llamaza C, Rodríguez-Perálvarez ML, Romero-Ruiz A, Aguilar-Melero P, López-Cillero P, Briceño J, Muntané J, Montero-Alvarez JL, De la Mata M. Identification of candidate biomarkers for hepatocellular carcinoma in plasma of HCV-infected cirrhotic patients by 2-D DIGE. *Liver Int*. 2013, 34(3):438-446. IF:3,870

Cruz-Ramírez M, Hervas-Martinez C, Fernandez JC, Briceño J, de la Mata M. Predicting patient survival after liver transplantation using evolutionary multi-objective artificial neural networks. *Artif Intell Med*. 2013, 58(1):37-49. IF:1,355

de Lerma NL, Peinado J, Peinado RA. In vitro and in vivo antioxidant activity of musts and skin extracts from off-vine dried *Vitis vinifera* CV. "Tempranillo" grapes. *J Funct Foods*. 2013, 5(2): 914–922.  
IF: 2,632

Rodríguez-Perálvarez M, Luong TV, Andreana L, Meyer T, Dhillon AP, Burroughs AK. A systematic review of microvascular invasion in hepatocellular carcinoma: diagnostic and prognostic variability. *Ann Surg Oncol*. 2013; 20(1): 325–39.  
IF: 4,120

Rodríguez-Perálvarez M, Germani G, Darius T, Lerut J, Tsochatzis E, Burroughs AK. Reducing early exposure to calcineurin inhibitors: the key factor for a successful renal sparing strategy. *Am J Transplant*. 2013; 13(1):239.  
IF: 6,192

Jurado García J, Ruiz Cuesta P, Hervás Molina AJ, Rodríguez Perálvarez ML, García Sánchez V. Endoscopic extraction of a foreign body in the sigmoid colon. *Gastroenterol Hepatol*. 2013, 36(10):647–648.  
IF: 0,567

Rodríguez-Perálvarez M, Germani G, Darius T, Lerut J, Tsochatzis E, De la Mata M, Burroughs AK. Tacrolimus exposure after liver transplantation in randomized controlled trials: too much for too long. *Am J Transplant*. 2013, 13(5):1371–2.  
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Vida Pérez L. The paradox of fatty diet on protease inhibitors against C hepatitis. *Gastroenterol Hepatol*. 2013, 36(8):549–550.  
IF: 0,567

Vida Pérez L, Martínez Rivas F. Intraabdominal desmoid tumors. *Med Clin (Barc)*. 2013, 141:314–319.  
IF: 1,399

## Joint Publications

Fernandez-Banares F, de Sousa MR, Salas A, Beltran B, Piqueras M, Iglesias E, Gisbert JP, Lobo B, Puig-Divi V, García-Planella E, Ordas I, Andreu M, Calvo M, Montoro M, Esteve M, Viver JM. Epidemiological Risk Factors in Microscopic Colitis: A Prospective Case-Control Study. *Inflamm Bowel Dis*. 2013, 19(2):411–417.  
IF: 5,119

Gallach M, Calvet X, Lanas A, Feu F, Ponce J, Gisbert JP, Brullet E, Pinera P, Castro M, Martín De Argila C, Domínguez Muñoz E, Almela P, Villanueva C, González Galilea A, Pérez Aisa A, García-Iglesias P, Gene E, Villoria A, Barkun A. Clinical practice guidelines for managing nonvariceal upper gastrointestinal bleeding. *Emergencias*. 2013, 25(6):472–481.  
IF: 2,578

Fernandez-Banares F, de Sousa MR, Salas A, Beltran B, Piqueras M, Iglesias E, Gisbert JP, Lobo B, Puig-Divi V, García-Planella E, Ordas I, Andreu M, Calvo M, Montoro M, Esteve M, Viver JM. Im-

pact of Current Smoking on the Clinical Course of Microscopic Colitis. *Inflamm Bowel Dis*. 2013, 19(7):1470–1476.  
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Mearin F, Barreiro-de Acosta M, Gonzalez-Galilea A, Gisbert JP, Cucala M, Ponce J. Prevalence and characteristics of anemia and iron deficiency in patients hospitalized for gastrointestinal diseases in Spain. *Gastroenterol Hepatol*. 2013, 36(8):499–507.  
IF: 0,567

Moreno D, Balasiddaiah A, Lamas O, Duret C, Neri L, Guembe L, Galarraga M, Larrea E, Daujat-Chavanieu M, Muntane J, Maurel P, Riezu JJ, Prieto J, Aldabe R. Usage of Adenovirus Expressing Thymidine Kinase Mediated Hepatocellular Damage for Enabling Mouse Liver Repopulation with Allogenic or Xenogenic Hepatocytes. *PLoS One*. 2013, 8(9): n° art e74948.  
IF: 3,73

Nunes T, Etchevers MJ, Merino O, Gallego S, García-Sánchez V, Marin-Jimenez I, Menchen L, Barreiro-de Acosta M, Bastida G, García S, Gento E, Ginard D, Gomollon F, Arroyo M, Monfort D, García-Planella E, Gonzalez B, Loras C, Agusti C, Figueroa C, Sans M. Tobacco-Eneida Study Grp GETECCU. Does Smoking Influence Crohns Disease in the Biologic Era? The TABACROHN Study. *Inflamm Bowel Dis*. 2013, 19(1):23–29.  
IF: 5,119

Sangro B, Gomez-Martin C, de la Mata M, Inarrairaegui M, Garralda E, Barrera P, Riezu-Boj JJ, Larrea E, Alfaro C, Sarobe P, Lasarte JJ, Perez-Gracia JL, Melero I, Prieto J. A clinical trial of CTLA-4 blockade with tremelimumab in patients with hepatocellular carcinoma and chronic hepatitis C. *J Hepatol*. 2013, 59(1):81–88.  
IF: 9,858

Banares R, Nevens F, Larsen FS, Jalan R, Albillos A, Dollinger M, Saliba F, Sauerbruch T, Klammt S, Ockenga J, Pares A, Wendon J, Brunner T, Kramer L, Mathurin P, de la Mata M, Gasbarrini A, Mullhaupt B, Wilmer A, Laleman W, Eefsen M, Sen S, Zipprich A, Tenorio T, Pavesi M, Schmidt HHJ, Mitzner S, Williams R, Arroyo V. RELIEF Study Grp. Extracorporeal albumin dialysis with the molecular adsorbent recirculating system in acute-on-chronic liver failure: The RELIEF trial. *Hepatology*. 2013, 57(3):1153–1162.  
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Nunes T, Etchevers MJ, Merino O, Gallego S, García-Sánchez V, Marin-Jimenez I, Menchen L, Barreiro-de Acosta M, Bastida G, García S, Gento E, Ginard D, Martí E, Gomollon F, Arroyo M, Monfort D, García-Planella E, Gonzalez B, Loras C, Agusti C, Figueroa C, Sans M. TABACROHN Study Group of GETECCU. High smoking cessation rate in Crohns disease patients after physician advice – The TABACROHN Study. *J Crohns Colitis*. 2013, 7(3):202–207.  
IF: 3,385

Berenguer M, Roche B, Aguilera V, Duclos-Vallee JC, Navarro L, Rubin A, Pons JA, de la Mata M,

Prieto M, Samuel D. Efficacy of the retreatment of hepatitis C virus infections after liver transplantation: role of an aggressive approach. *Liver Transplantation*. 2013, 19(1):69–77.  
IF: 3,944

Nunes T, Etchevers MJ, Domenech E, García-Sánchez V, Ber Y, Penalva M, Merino O, Nos, P, García-Planella E, Casbas AG, Esteve M, Samsó CT, Huguet MM, Gisbert JP, Arranz MDM, García-Sepulcre MF, Barreiro-de Acosta M, Beltran B, Suarez NA, Tobacco-Eneida Study Group of GETECCU. Smoking does influence disease behaviour and impacts the need for therapy in Crohns disease in the biologic era. *Aliment Pharmacol Ther*. 2013, 38(7):752–760.  
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Torrejón A, Oltra L, Hernández-Sampelayo P, Marin L, García-Sánchez V, Casellas F, Alfaro N, Lázaro P, Vera MI. Development of quality standards in inflammatory bowel disease management and design of an evaluation tool of nursing care. *Rev Esp Enferm Dig*. 2013, 105(5):262–271.  
IF: 1,652

Chaparro M, Ordás I, Cabré E, García-Sánchez V, Bastida G, Peñalva M, Gomollón F, García-Planella E, Merino O, Gutiérrez A, Esteve M, Márquez L, García-Sepulcre M, Hinojosa J, Vera I, Muñoz F, Mendoza JL, Cabriada JL, Montoro MA, Barreiro-de Acosta M, Ceña G, Saro C, Aldeguez X, Barrío J, Maté J, Gisbert JP. Safety of thiopurine therapy in inflammatory bowel disease: long-term follow-up study of 3931 patients. *Inflamm Bowel Dis*. 2013, 19(7):1404–1410.  
IF: 5,119

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IF: 0,836

Panés J, López-Sanromán A, Bermejo F, García-Sánchez V, Esteve M, Torres Y, Domènech E, Piqueras M, Gomez-García M, Gutiérrez A, Taxonera C, Sans M, AZTEC Study Group. Early azathioprine therapy is no more effective than placebo for newly diagnosed Crohn's disease. *Gastroenterology*. 2013, 145(4):766–774.  
IF: 12,821

Argüelles-Arias F, Castro-Laria L, Lobatón T, Aguas-Peris M, Rojas-Feria M, Barreiro-de Acosta M, Soto-Escribano P, Calvo-Moya M, Ginard-Vicens D, Chaparro-Sánchez M, Hernández-Durán M, Castro-Senosaián B, Fernández-Villaverde A, García-Sánchez V, Domínguez-Muñoz E, Caunedo-Álvarez A, Herrerías-Gutiérrez JM. Characteristics and treatment of pyoderma gangrenosum in inflammatory bowel disease. *Dig Dis Sci*. 2013; 58(10):2949-2954. IF:2,26

García-Bosch O, Gisbert JP, Canas-Ventura A, Merino O, Cabriada JL, García-Sánchez V, Gutiérrez A, Nos P, Penalva M, Hinojosa J, García-Planella E, Muñoz F, Calvet X, Panes J. Observational study on the efficacy of adalimumab for the treatment of ulcerative colitis and predictors of outcome. *J Crohns Colitis*. 2013; 7(9):717-722. IF:3,385

Haad CR, Rodríguez-Benot A, Martínez-Vaquera S, Navarro-Cabello MD, Agüera-Morales ML, Ruiz de Mier MV, Montero-Alvarez JL, Mata-García M, Briceño-Delgado J, Ajlaja-García P. Combined Liver-Kidney Transplantation: Survey of a Single Center in Spain. *Transplant Proc*. 2013; 45(10):3640-3643. IF:0,951

Ruiz Cuesta P, Hervás Molina AJ, Jurado García J, Pleguezuelo Navarro M, García Sánchez V, Casáis Juanena LL, Gálvez Calderón C, NaranjoRodríguez A. Pneumatic dilation in the treatment of achalasia. *Gastroenterol Hepatol*. 2013; 36(8):508-12. IF:0,567

Julia A, Domenech E, Ricart E, Tortosa R, García-Sánchez V, Gisbert JP, Mateu PN, Gutierrez A, Gommollon F, Mendoza JL, García-Planella E, Barreiro-de Acosta M, Muñoz F, Vera M, Saro C, Esteve M, Andreu M, Alonso A, Lopez-Lasanta M, Codo L, Gelpi JL, García-Montero AC, Bertranpetit J, Absher D, Panes J, Marsal S. A genome-wide association study on a southern European population identifies a new Crohn's disease susceptibility locus at RFX1-EP300. *Gut*. 2013; 62(10):1440-1445. IF:10,732

Cantero JMB, García JJ, Cuesta PR, Galilea AG, García-Borrueal MM, Sanchez VG, Calderon CG. Early evaluation of anaemia in patients with acute gastrointestinal bleeding: venous blood gas analysis compared to conventional laboratory. *Med Clin (Barc)*. 2013; 141(8):332-337. IF:1,399

Koretz RL, Pleguezuelo M, Arvaniti V, Baena PB, Ciria R, Gurusamy KS, Davidson BR, Burroughs AK. Interferon for interferon nonresponding and relapsing patients with chronic hepatitis C. *Cochrane DB Syst Rev*. 2013; 1:CD003617. IF:5,703

Ayllón-Terán MD, Torres-Lorite M, Benítez-Cantero JM, Sánchez-Hidalgo JM, Díaz-Iglesias C, Rufián-Peña S. An uncommon cause of high blood pressure in young people: retroperitoneal paraganglioma with vascular invasion. *Nefrología*. 2013; 33(3): 435-437. IF: 1,274

Moreau R, Jalan R, Gines P, Pavesi M, Angeli P, Cor-doba J, Durand F, Gustot T, Saliba F, Domenicali M, Gerbes A, Wendon J, Alessandria C, Laleman W, Zeuzem S, Trebicka J, Bernardi M, Arroyo V; CA-NONIC Study Investigators of the EASL-CLIF Consortium(De la Mata). Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. *Gastroenterology*. 2013; 144(7):1426-37. IF:12,821

Tsochatzis E, Garcovich M, Marelli L, Papastergiou V, Fatourou E, Rodríguez-Peralvarez ML, Germani G, Davies N, Yu D, Luong TV, Dhillon AP, Thorburn D, Patch D, O'Beirne J, Meyer T, Burroughs AK. Transarterial embolization as neo-adjuvant therapy pretransplantation in patients with hepatocellular carcinoma. *Liver Int*. 2013; 33(6): 944-9. IF: 3,87

## Research Projects

De la Mata García, M. Inhibition of the mTOR pathway in liver transplantation for hepatocellular carcinoma and its impact on disease recurrence. Sponsored by: Institute Carlos III Health (ISCIII). Reference: PI11-02867

Montero Álvarez, J.L.A multicenter, randomized, placebo-controlled, double-blinded phase IV study to assess the efficacy and safety of sorafenib in patients with advanced liver cell cancer with radiological progression. Sponsored by: Spanish Ministry of Health, Social Services and Equality Reference: EC11-185

García Sánchez, MV.Functional validation of SNP rs6105269 in Crohn disease Sponsored by: Carlos III Health Institute (ISCIII). Reference: PI12/02091

García Sánchez, MV.Functional validation of SNP rs6105269 in Crohn disease Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: Reference: PI-0485-2012

Bárcena Ruiz, A.Modulation of the Thiol proteome by redoxins: mechanisms and implications in iron metabolism, mitochondrial function and apoptosis. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO) Reference: BFU2012-32056

Aguilar Melero, P. Proteomic biomarkers for prediction of response to Anti-Tnf drugs in patients with Crohn disease. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CIS-PS). Reference: Reference: PI-0199-2013.

\*2014 Annuity

## Third Party Services

García Sánchez, MV.Sample collection service for the Innacto project.Sponsored by: Fundació Institut de Recerca Hospital Universitari Vall D'hebron. Referencia:PSS.0021

De La Mata García, M. Molecular predictors of response to sorafenib as adjuvant Therapy A

after resection in Hepatocellular Carcinoma (Bio-Storm). Sponsored by:Bayer Pharma AG. Reference:PSS.0036

## Collaboration Agreements

De la Mata García, M. Collaboration Agreement between Ciberehd and institution. Sponsored by: Centro de Investigación Biomédica en Red en el Área Temática de Enfermedades Hepáticas y Digestivas (CIBER on Liver and Digestive Diseases (CIBERehd)). Reference: MCI.CIBERehd

De La Mata García, M. Participation and support for collaborators at the Digestive Tract Unit of the Reina Sofia University Hospital of Cordoba. Sponsored by: Merck Sharp & Dohme SA. Reference: CCB.0015

García Sánchez, MV.Funding for collaborators at the Digestive Tract Unit of the Reina Sofia University Hospital of Cordoba. Sponsored by: Merck Sharp & Dohme SA. Referencia:CCB.0037

De la Mata García, M. Funding for collaborators at the Digestive Tract Unit of the Reina Sofia University Hospital of Cordoba. Sponsored by: Merck Sharp & Dohme SA. Referencia:CCB.0038

De La Mata García, M. Supopr agreement for collaborators at the Digestive Tract Unit of the Reina Sofia University Hospital of Cordoba. Sponsored by: Merck Sharp & Dohme SA. Reference: CCB.0051

## Clinical Trials

0198/07: Open, multicenter, randomized study of the efficacy and safety of prednisone with Ada column® versus prednisone alone in the treatment of patients with active mild to moderate steroid-dependent ulcerative colitis. PI: Dr/a García Sánchez, Valle

0103/08: A randomized, double-blind, placebo-controlled phase III study of sorafenib as adjuvant treatment for liver cell carcinoma after surgical resection or local ablation. PI: Dr/a De La Mata García, Manuel

0020/08/EPA: Long-term non-interventionist registration to assess the safety and effectiveness of HUMIRA® (adalimumab) in patients with active mild to moderate Crohn disease (CD). PI: Dr/a García Sánchez, Valle

0027/09: Phase III, multicenter, randomized, double-blind study on the effectiveness of brivanib against sorafenib as first-line treatment in patients with advanced hepatocellular carcinoma. (BRISK FL study) PI: Dr/a De La Mata García, Manuel

0009/10: Long-term follow-up of participants in a phase II or III SCG 503034 trial for the treatment of chronic hepatitis C. PI: Dr/a De La Mata García, Manuel

0120/10: A multicenter, randomized, placebo-

controlled, double-blind phase III study to assess the efficacy and safety of everolimus (RAD001) in adult patients with advanced liver cell cancer after failure of treatment with sorafeniv.  
PI: Dr/a Montero Alvarez, Jose Luis

0026/10/EPA-SP: Validation of a treatment adherence questionnaire in patients with hepatitis B. HABIT study.  
PI: Dr/a Fraga Rivas, Enrique

0041/11: A multicenter, prospective, randomized, comparative trial to assess the effectiveness of two vaccines against the hepatitis B virus in patients with inflammatory bowel disease.  
PI: Dr/a Iglesias Flores, Eva

0066/11: Simplification trial with tenofovir in patients with chronic hepatitis B resistant to lamivudina and undetectable viral load in treatment with lamivudina in combination with adefovir dipivoxil (Tenosimp-B study).  
PI: Dr/a Fraga Rivas, Enrique

0192/11: An Open-Label multicenter study to evaluate the impact of Adalimumab on quality of life, health care utilization and costs of ulcerative colitis subjects in the usual clinical practice setting.  
PI: Dr/a Iglesias Flores, Eva

0232/11: A multicenter, randomized, double-blind parallel-group trial to assess the effectiveness of Adalimumab versus Azathioprine in the prevention of postsurgical recurrence of Crohn disease after 52 weeks.  
PI: Dr/a García Sánchez, Valle

0215/11: High-sensitivity calprotectin and C-reactive protein as markers of a new diagnostic-therapeutic strategy that evaluates mucosa activity to individualize treatments and improve the prognosis of patients with Crohn disease.  
PI: Dr/a García Sánchez, Valle

0068/11: Trial of tenofovir in the profilaxis of hematological anti-HBc positive and AgHBs-negative patients on treatment with rituximab. PREBLIN study.  
PI: Dr/a Fraga Rivas, Enrique

0015/12: A multicenter, randomized, placebo-controlled, double-blind phase IV study to assess the efficacy and safety of sorafenib in patients with advanced liver cell cancer with radiological progression.  
PI: Dr/a Montero Alvarez, Jose Luis

0304/12: A phase 3, randomized, double-blind study of tivantinib (ARQ 197) in subjects with metastatic high inoperable hepatocellular carcinoma (HCC) treated with one prior systemic therapy  
PI: Dr/a Montero Alvarez, Jose Luis

0039/13: Randomized, double-blind, placebo-controlled, multicenter phase III study of regorafenib in patients with hepatocellular carcinoma (HCC) after sorafenib.  
PI: Dr/a Barrera Baena, Pilar

0113/13: Multicentric, randomized, open-label, controlled study, of 12 months of follow-up to assess the effect in renal function of an immunosuppressive treatment based on tacrolimus minimization in combination with everolimus in patients with novo liver transplantation.  
PI: Dr/a De La Mata Garcia, Manuel

0201/13: Albumin administration in the prevention of hepatorenal syndrome and death in patients with cirrhosis, bacterial infections other than spontaneous bacterial peritonitis and high risk of hospital mortality  
PI: Dr/a Montero Alvarez, Jose Luis

0329/13: A randomized, open-label, multicenter, controlled study to assess safety and efficacy of elad in subjects with acute alcoholic hepatitis (AAH) who have failed steroid therapy  
PI: Dr/a Montero Alvarez, Jose Luis

0162/13: A randomized, open-label, multicenter, controlled study to assess safety and efficacy of elad in subjects with alcohol-induced liver decompensation (AILD).  
PI: Dr/a Montero Alvarez, Jose Luis

0014/07/EPA1: Recurrence rates and predictive factors in the treatment of Hepatitis C in real clinical practice in Spanish hospitals (FAST-4 Study).  
PI: Dr/a Fraga Rivas, Enrique

1835: A multicenter, observational, retrospective study to assess elective liver retransplantation in Spain  
PI: Dr/a Poyato González, Antonio

1875: Use of Everolimus in liver transplantation  
PI: Dr/a De La Mata Garcia, Manuel

1312: Study of co-morbidity and clinical expression of immunologically-mediated inflammatory diseases (psoriasis, Spondyloarthropathy and inflammatory bowel disease).  
PI: Dr/a Gómez Camacho, Federico

1970: A study to assess patients' preferences concerning therapies for Crohn's disease treatments.  
PI: Dr/a Iglesias Flores, Eva

2017: A study of the renal tubular function and bone remodeling markers during prolonged treatment with entecavir and tenofovir in patients with chronic infection with hepatitis B virus.  
PI: Dr/a Fraga Rivas, Enrique

2057: Cost, effectiveness, usefulness and efficacy of adalimumab in the management of Crohn's disease.  
PI: Dr/a García Sánchez, Valle

2058: Improving the safety of biologic-agent-based treatments in patients with inflammatory bowel disease through early detection of latent tuberculosis.  
PI: Dr/a García Sánchez, Valle

2061: Predicting short-term response to anti-TNF treatment in patients with Crohn's disease.  
PI: Dr/a García Sánchez, Valle

2072: Enterourinary fistulas in Crohn's disease: prevalence and clinical characteristics.  
PI: Dr/a Iglesias Flores, Eva

2171: Chronic-UC: Assessing the diagnostic capacity of Walmsley's questionnaire available on an online application (online completion by patients) versus the same questionnaire delivered by the physician to patients with ulcerative colitis.  
PI: Dr/a Iglesias Flores, Eva

2342: Registry of Telaprevir and Boceprevir in regular clinical practice.  
PI: Dr/a De La Mata Garcia, Manuel

2366: A retrospective study of clinical practice in patients with Crohn's disease and ileocolic surgery in Spain.  
PI: Dr/a García Sánchez, Valle

2395: An observational study of the effect of minimizing immunosuppression in liver recipients.  
PI: Dr/a De La Mata Garcia, Manuel

# GC3

## Infectious Diseases

### Team Leaders

#### Principal Investigator (PI)

Julián de la Torre Cisneros

[julian.torre.sspa@juntadeandalucia.es](mailto:julian.torre.sspa@juntadeandalucia.es)

Spanish Network for Research in Infectious Pathology (REIPI)

PAIDI CTS-647 scientific group

#### Co-Principal Investigator (Co-PI)

Antonio Rivero Roman

AIDS Research Network (RIS) (Collaborator)

#### Senior Researchers

Ángela Camacho Espejo

Milagros García Lázaro

Ana Gordon Bermúdez-Coronel

Irene Gracia Ahufinger

Rafael Jurado Jimenez

Jose M<sup>o</sup> Kindelan Jaquotot

Clara Natera Kindelan

Jose Rumbao Aguirre

Elisa Vidal Verdu

#### Post-doctoral Researchers

Sara Cantisán Bohórquez

Antonio Rivero Juárez

Casas

#### Pre-doctoral Researchers

Cristina Arenas Muñoz

Marcelino Gonzalez Padilla

Emilio Guirao Arrabal

Loreto Martínez-Dueñas

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)

M<sup>o</sup> Teresa Añon Gámez

Daniel Camacho Perez

Rosario Lara Contreras

Laura Ruiz Torres

Aurora Paez Vega

Ismael Zafra Soto





## Scientific Activity

Our group studies infectious diseases from two approaches:

- Clinical-epidemiological studies (which include clinical trials). In these studies, our objective is to differentiate risk factors, clinical features and efficacy/safety of new treatments, thus aiming to improve the prognosis of infectious diseases.
- Studies on pathogenesis from which specific clinical strategies are planned. The most relevant are our studies on

immunopathology (in collaboration with the Immunology group) and mitochondrial toxicity (in collaboration with the Clinical Analysis Service).

All our studies start with the identification of a clinical problem that we try to solve using an experimental approach. Our aim is our scientific findings to have an impact on healthcare solutions and improve disease prognosis (translational research).

In particular, our lines of research are as follows:

- Immunopathology, pathogenesis

and treatment of HIV infection.

- Pathogenesis and treatment of HIV / HCV co-infection.
- Clinical and epidemiological characterization of infection in transplant patients
- Immunopathology of cytomegalovirus infection.

## Keywords

HIV, CMV, HCV, Immunopathology, Transplant, Antiretroviral therapy. Mitochondrial toxicity.

## Publications

### Originals Publications

Gracia-Ahufinger I, Gutierrez-Aroca J, Cordero E, Vidal E, Cantisan S, del Castillo D, Martin-Gandul C, Rivero A, Torre-Cisneros J. Use of High-Dose Ganciclovir for the Treatment of Cytomegalovirus Replication in Solid Organ Transplant Patients With Ganciclovir Resistance-Inducing Mutations. *Transplantation*. 2013, 95(8):1015-1020. IF:3,781

Rivero-Juarez A, Mira JA, Santos-Gil I, Lopez-Cortes LF, Giron-Gonzalez JA, Marquez M, Merino D, Tellez F, Caruz A, Pineda JA, Rivero A. Atazanavir-Based Therapy Is Associated with Higher Hepatitis C Viral Load in HIV Type 1-Infected Subjects with Untreated Hepatitis C. *AIDS Res Hum Retrovir*. 2013, 29(2):223-225. IF:2,705

Rivero-Juarez A, Mira JA, Camacho A, Neukam K, Perez-Camacho I, Caruz A, Macias J, Torre-Cisneros J, Pineda JA, Rivero A. Baseline risk factors for relapse in HIV/HCV co-infected patients treated with PEG-IFN/RBV. *Infection*. 2013, 41(1):21-26. IF:2,44

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González-Padilla M, Castón JJ, Vidal E, Arizón JM, Segura C, Montejo M, Rivero A, Torre-Cisneros J. Epidemiology and clinical impact of infection in patients awaiting heart transplantation. *Int J Infect Dis*. 2013, 17(9):681-685. IF:2,357

Cantisan S, Torre-Cisneros J, Lara R, Zarraga S, Montejo M, Solana R. Impact of Cytomegalovirus on Early Immunosenescence of CD8+ T Lympho-

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Rivero-Juarez A, Camacho A, Merchante N, Pérez-Camacho I, Macias J, Ortiz-Garcia C, Cifuentes C, Torre-Cisneros J, Peña J, Pineda JA, Rivero A. Grupo para el estudio de las hepatitis víricas (HEPAVIR) de la Sociedad Andaluza de Enfermedades Infecciosas (SAEI). Incidence of liver damage of uncertain origin in HIV patients not co-infected with HCV/HBV. *PLoS One*. 2013, 8(7):e68953. IF: 3,73

Rivero A, Pulido F, Caylá J, Iribarren JA, Miró JM, Moreno S, Pérez-Camacho I, por el Grupo de Estudio de Sida (GESIDA). The Spanish AIDS Study Group and Spanish National AIDS Plan (GESIDA/Secretaría del Plan Nacional sobre el Sida) recommendations for the treatment of tuberculosis in HIV-infected individuals (Updated January 2013). *Enferm Infecc Microbiol Clin*. 2013, 31(10):672-684. IF:1,478

Rivero-Juarez A, Lopez-Cortes LF, Camacho A, Caruz A, Torres-Cornejo A, Martinez-Dueñas L, Ruiz-Valderas R, Torre-Cisneros J, Gutierrez-Valencia A, Rivero A. The IL28B effect on hepatitis C virus kinetics among HIV patients after the first weeks of pegylated-interferon/ribavirin treatment varies according to hepatitis C virus-1 subtype. *AIDS*. 2013, 27(12):1941-1947. IF:6,407

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### Joint Publications

Viasus D, Marinescu C, Villoslada A, Cordero E, Gálvez-Acebal J, Fariñas MC, Gracia-Ahufinger I, Fernández-Navarro A, Niubó J, Ortega L, Muñoz-Rubio E, Romero-Gómez MP, Carratalà J. The Influenza A (H1N1) Study Group of the Spanish Network for Research in Infectious Diseases (REIPI). Community-acquired pneumonia during the first post-pandemic influenza season: A prospective, multicentre cohort study. *J Infect*. 2013, 67(3):185-193. IF:4,073

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Mandorfer M, Neukam K, Reiberger T, Payer BA, Rivero A, Puoti M, Boesecke C, Baumgarten A, Grzeszczuk A, Zangerle R, Meyer-Olson D, Rockstroh JK, Trauner M, Pineda JA, Peck-Radosavljevic M. The impact of interleukin 28B rs12979860 single nucleotide polymorphism and liver fibrosis stage on response-guided therapy in HIV/HCV-coinfected patients. *AIDS*. 2013;27(17):2707-2714. IF:6,407

Sulkowski M, Pol S, Mallolas J, Fainboim H, Cooper C, Slim J, Rivero A, Mak C, Thompson S, Howe AYM, Wenning L, Sklar P, Wahl J, Greaves W. Boceprevir versus placebo with pegylated interferon alfa-2b and ribavirin for treatment of hepatitis (virus genotype 1 in patients with HIV: a randomised, double-blind, controlled phase 2 trial. *Lancet Infect Dis*. 2013;13(7):597-605. IF:19,966

Di Lello FA, Caruz A, Rallon NI, Rivero-Juarez A, Neukam K, Barreiro P, Camacho A, Garcia-Rey S, Rivero A, Soriano V, Cifuentes C, Macias J, Pineda JA. Effects of the genetic pattern defined by low-density lipoprotein receptor and IL28B genotypes on the outcome of hepatitis C virus infection. *Eur J Clin Microbiol Infect Dis*. 2013;32(11):1427-1435. IF:3,024

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cohort study. *BMC Infect Dis*. 2013;13:nº art 344. IF:3,025

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REIPI/SAB group. Impact of an Evidence-Based Bundle Intervention in the Quality-of-Care Management and Outcome of *Staphylococcus aureus* Bacteremia. *Clin Infect Dis*. 2013;57(9):1225-1233. IF:9,374

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## Research Projects

Camacho Espejo, A. Evaluation of occult hepatitis C virus infection in peripheral blood mononuclear cells and liver tissue in HIV-infected patients with spontaneous clearance of viremia. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0036-2010.

De la Torre Cisneros, J. Study of the kinetics of CMV infection in CMV-Seronegative patients receiving an organ from a seropositive donor and its potential association with early immune senescence. Sponsored by: Institute Carlos III Health (ISCIII). Reference: PI11/02091.

Rivero Román, A. Predictive value of immediate VHC viral kinetics on the sustained viral

response in patients co-infected with the VIH/VHC. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0036-2010.

De la Torre Cisneros, J. Spanish Network for Research on Infectious Diseases (REIP). Sponsored by: Institute Carlos III Health (ISCIII). Reference: RD12/0015/0002.

Cantisán Bohórquez, S.A translational study to assess the clinical usefulness of determining the IFN $\gamma$  secreted by specific T CD8+ CMV cells to guide the prevention of CMV infection in low-risk solid organ-transplanted patients. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0004-2012.

Rivero Román, A. Influence of inhibitory natural killer cell receptors (KIRs) on response to treatment for VHC in HIV/HCV co-infected patients. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0430-2012

De la Torre Cisneros, J (nodo). A randomised, double-blind, dose-ranging, multicentre Phase IIb study to evaluate safety, tolerability, and efficacy of GSK1322322 compared to levofloxacin in hospitalized adult subjects with community acquired bacterial pneumonia'. COMBACTE Project. Innovative Medicines Initiatives program. EoINumber 115523. Sponsored by: European Commission. Reference: IMI Call IMI-IU-6-12

Camacho Espejo, A. Assessing persistence of hepatitis C virus in HIV co-infected patients achieving a sustained viral response. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0187-2013

Rivero Román, A (node). Partners of people on Antiretrovirals (ART) New Evaluation of Risk (The PARTNER Study). Sponsored by: National Institute for Health Research in the UK (NIHR)

## Clinical Trials

0122/08: An open, randomized phase IV comparative study to assess the effectiveness of lopinavir/ritonavir alone versus abacavir/lamivudine and lopinavir/ritonavir/peripheral for peripheral (or limb) fat recovery. KRETA study. PI: Dr/a Rivero Román, Antonio

0045/09: Effectiveness of high doses of Pegylated interferon- $\alpha$ -2a and Ribavirin in the treatment of HIV co-infected patients with C virus-induced cirrhosis (genotypes 1'0 4) not responding to previous therapy with standard pegylated interferon and Ribavirin doses. PI: Dr/a Rivero Román, Antonio

0184/09: Phase 2b study to assess the safety and effectiveness of Boceprevir in patients co-infected with HIV and Hepatitis C PI: Dr/a Rivero Román, Antonio

0011/10: A comparative clinical trial of two therapeutic decision-making strategies in the

study of tuberculosis contacts: standard strategy based on the tuberculin sensitivity test (PT) versus PT in combination with QuantiFERON-TB Gold In Tube.

PI: Dr/a Kindelan Jaquotot, Jose M<sup>o</sup>

0199/10: A randomized, double-blind, phase III study to assess the safety and effectiveness of GSK1349572 50 mg once a day versus Raltegravir 400 mg twice a day both administered as a double combination at a fixed dose of nucleoside-analog reverse-transcriptase inhibitors for a 96-week period in adult patients VIH-1 co-infected patients who have not received previous antiretroviral treatment.

PI: Dr/a Rivero Román, Antonio

0273/10: A prospective, randomized, comparative trial to assess the effectiveness and safety of Levofloxacin versus Isoniazid in the treatment of latent tuberculosis infection of liver transplant. PI: Dr/a De La Torre Cisneros, Julian Carlos

0334/10: A pilot, phase III clinical trial to assess antiviral activity of pegylated interferon + ribavirin + nitazoxanide in chronic patients with genotype-4 HCV and HIV.

PI: Dr/a Rivero Román, Antonio

0044/11: A multicenter, randomized, blinded, placebo-controlled study to assess the safety of Maraviroc in combination with other antiretrovirals in subjects infected with HIV-1 and hepatitis C and/or B.

PI: Dr/a Rivero Román, Antonio

0088/11: An open, randomized, noninferiority trial and 96 week-follow-up study to assess the effectiveness of azatanavir/ritonavir + lamivudine as maintenance treatment in patients with viral load suppression.

PI: Dr/a Rivero Román, Antonio

0079/11: A randomized, open, controlled, 48-week clinical trial to assess the activity and tolerability of a combination therapy of lopinavir/ritonavir and 3TC replacing a triple therapy of lopinavir/ritonavir and 3TC or FTC in patients with HIV and viral suppression.

PI: Dr/a Rivero Román, Antonio

0177/11: A randomized, prospective, comparative trial assessing the effectiveness and safety of a seasonal vaccine dose versus two vaccine doses for the prevention of influenza in solid organ recipients.

PI: Dr/a De La Torre Cisneros, Julian Carlos

0121/11: A randomized, controlled, partially-blind Phase IIb trial to assess the safety, effectiveness and dose-response relation of BMS-663068 in the treatment of HIV-1 patients previously treated followed by an open regime period with the recommended dose.

PI: Dr/a Rivero Román, Antonio

0255/11: A randomized, double-blind, placebo-controlled, phase III study of the effectiveness, safety and tolerability of a single infusion of MK 3415 (human monoclonal antibody versus Clostridium difficile toxin A) and MK 3415A (human

monoclonal antibody versus Clostridium difficile toxins A and B) in patients undergoing antibiotic treatment for Clostridium difficile infection. (MODIFY I).

PI: Dr/a De La Torre Cisneros, Julian Carlos

0197/11: Protease (DRV/RTV) inhibitor in monotherapy or triple therapy in patients with HIV-1 suppression.

PI: Dr/a Rivero Román, Antonio

0201/11: A multicenter, randomized, double blind, comparative study of maraviroc + danunavir/ritonavir versus emtricitabin/tenofovir + darunavir/ritonavir for the treatment of patients with HIV-1 CCR5 tropism not previously treated with antiretrovirals.

PI: Dr/a Rivero Román, Antonio

0246/11: An open study of retreatment with pegylated interferon alpha-2a ribavirin and BMS-79003067-30 with or without BMS-650032 in patients with chronic hepatitis C.

PI: Dr/a Rivero Román, Antonio

0258/11: An open, randomized, phase 3B, 48-week comparative study of antiviral effectiveness and safety of ATV/RTV + 3TC versus ATV7RTV plus TDF7FTC in naive HIV-1 patients followed by a 48-week period on ATV7RTV plus 3TC.

PI: Dr/a Rivero Román, Antonio

0283/11: A multicenter, randomized, blind, parallel-group, non-inferiority comparative trial of the effectiveness and safety of an immunotherapy versus a viremia-guided approach in the prophylaxis of cytomegalovirus infection in seropositive renal recipients.

PI: Dr/a De La Torre Cisneros, Julian Carlos

0016/12: An open, phase IIb study to assess the effectiveness and safety of Telaprevir, Pegylated interferon- $\alpha$ -2a and ribavirin in chronic genotype 1 hepatitis C and HIV-1 co-infected patients with or without previous treatment for hepatitis C.

PI: Dr/a Rivero Román, Antonio

0072/12: An open study to assess the safety, antiviral activity and pharmacokinetics of direct acting antivirals (DAAs) in combination with peginterferon alpha-2a and ribavirin (pegIFN/RBV) in chronic HCV patients presenting virological failure in a previous study of Abbvie or Abbott in combination with DAAs.

PI: Dr/a Rivero Román, Antonio

0308/12: A randomized, double-blind, placebo-controlled study to assess the efficacy and safety of ABT450/ritonavir/ABT-267 (ABT-450/r/abt-267) and ABT-333 administered in combination with ribavirin (RBV) in previously treated chronic HCV-1 adult patients (SAPPHIRE-III).

PI: Dr/a Rivero Román, Antonio

0040/13: Efficacy of a sequential short therapy vs standards intravenous treatment in patients with uncomplicated catheter-related bacteremia using S. Aureus Meticillin-Sensible.

PI: Dr/a Natera Kindelan, Clara

28/13: A randomized, open, controlled, single-pattern, phase III study with active product of bi 207127 in combination with faldaprevir and ribavirin versus telaprevir in combination with pegylated alpha interferon plus ribavirin for the treatment of chronic genotype-1b HCV infection in naive patients.

PI: Dr/a Rivero Román, Antonio

0138/13: Changes in liver steatosis after replacing efavirenz with raltegravir in HIV/HCV co-infected patients treated with two nucleoside analogs plus efavirenza: Sternal study.

PI: Dr/a Rivero Román, Antonio

0152/13: Follow-up study to assess the resistance and durability of response to treatment with AbbVie direct-acting antivirals in patients who participated in phase II/III studies for the treatment of chronic HCV infection.

PI: Dr/a Rivero Román, Antonio

0032/08/EPA: An international, multicenter, observational, prospective study on the safety of Maraviroc in combination with an optimized background therapy in previously treated HIV-1 patients.

PI: Dr/a Rivero Román, Antonio

0009/10/2: Long-term follow-up of participants in a phase II or III SCH 503034 trial for the treatment of chronic Hepatitis C.

PI: Dr/a Rivero Román, Antonio

0004: Survival of HIV patients receiving renal replacement therapy or renal transplantation in Spain.

PI: Dr/a García Lazaro, Milagros

1431: A multicenter, retrospective study to identify the incidence of severe hepatotoxicity in patients co-infected with hepatitis B or C and HIV-1 who previously received treatment with Maraviroc: (LIVERMAC study).

PI: Dr/a Rivero Román, Antonio

1714: Influence of nevirapin on hepatitis C viral load levels in patients co-infected with VIH/VHC. HELICON study.

PI: Dr/a Rivero Roman, Antonio

1716: An observational study to determine the clinical management of in-hospital patients with community acquired pneumonia or complex skin and soft tissue infections: REACH Study.

PI: Dr/a Gracia Ahufinger, Irene

1764: Bacterial infection with Staphylococcus aureus: impact of an intervention program on the improvement of the clinical management and study of its clinical and molecular epidemiology.

PI: Dr/a Natera Kindelan, Clara

1893: A study of risk factors of nosocomial pneumonia due to infection with methicillin-resistant staphylococcus aureus. A case and control study.

PI: Dr/a Natera Kindelan, Clara

1854: Bridging the gap between antiretroviral treatment guidelines and regular clinical practice. Studying the barriers to the initiation of HAART in patients with indication of HAART.

PI: Dr/a Rivero Román, Antonio

1928: Effectiveness and tolerability of patterns including abacavir/3tc with Darunavir/Ritonavir.

PI: Dr/a Camacho Espejo, Angela

1973: A multicenter observational retrospective study of the effectiveness and tolerability of the antiretroviral treatments that include MARAVIROC (MVC) in clinical practice.

PI: Dr/a Rivero Román, Antonio

2302: Impact of genetic variations of TLR2, 4 and 9 on the risk of cytomegalovirus infection after transplantation and its usefulness in prevention.

PI: Dr/a Cantisán Bohorquez, Sara

# GC4

## Inflammation and Cancer

### Team Leaders

#### Principal Investigator (PI)

Eduardo Muñoz Blanco

[fi1muble@uco.es](mailto:fi1muble@uco.es)

AIDS Research Network (RIS)

PAIDI BIO-304 scientific group

#### Emerging Researcher

Marco Antonio Calzado Canale

#### Senior Researcher

Eugenio Jiménez Millán

#### Post-doctoral Researchers

Irene Cantarero Carmona

Carmen García Limones

Paula Moreno Casado (I)

Moises Pérez Aguilera

#### Pre-doctoral Researchers

Victor García González

M<sup>o</sup> Isabel Lara Chica

Rafael Soler Torronteras

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)

Juan A. Collado Rojas

Rosario Molina Morán

Lourdes Santaella Ruiz

(I) Contract Rio Hortega



## Scientific Activity

The Group's main areas of research over recent years are the identification of the molecular signaling pathways that regulate inflammation processes and tumorigenesis, and the latency of HIV-1. The identification of the molecular targets that regulate these processes helps us identify new natural compounds and derivatives (drugs and nutraceuticals) in-

hibiting the activity of these targets. Our research studies have allowed us to establish sophisticated models of biological activity screening in molecules with therapeutic potential and collaborate with many leading international research groups in the field of pharmaceutical Chemistry. We recently established a new research area focused on the study of the inflammatory processes that occur in skin ulcers, to develop new formula-

tions based on biopharmaceuticals and natural products favouring tissue regeneration.

## Keywords

Inflammation, cancer, tissue regeneration, HIV-1 latency, Pharmacology and Nutraceuticals.

## Publications

### Joint Publications

Villagomez R, Rodrigo GC, Collado IG, Calzado MA, Muñoz E, Akesson B, Sterner O, Almanza GR, Duan RD. Multiple Anticancer Effects of Damsin and Coronopilin Isolated from *Ambrosia arborescens* on Cell Cultures. *Anticancer Research*. 2013, 33(9):3799-3805.

IF: 1,713

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IF: 4,178

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### Research Projects

Muñoz Blanco, E. Red de investigación en SIDA (RIS). Sponsored by: Institute Carlos III Health (ISCI). Reference: RD06/0006/0028RIS

Muñoz Blanco, E. A study of dyrk2 regulation mechanisms in response to hiposis and oncogenic stress. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: P09-CTS-4973

Calzado Canale, M.A. A study of the dyrk2 kynase regulation and expression as a prognostic factor in lung cancer. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: 0650/2010

Calzado Canale, M. A. Siah-2-mediated chk2 modulation mechanisms in response to oncogenic stress. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: SAF2010-17122

Muñoz Blanco, E. A study of hif-1alpha factor regulation mechanisms using endocannabinoids. Implications for neuroprotection. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: SAF2010-19292

Muñoz Blanco, E. Pre-clinical development of new cannabinoid derivatives for the treatment of neuro-inflammatory diseases. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: IPT-2011-0861-900000

Calzado Canale, M A. Analysis of the metabolic footprint of lung cancer. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0246-2013

### Collaboration Agreements

Muñoz Blanco, E. Biological activity of natural biomedical products. Sponsored by: Beros Consulting S.L. Reference: CCB.UCO.0040

Muñoz Blanco, E. Integration of technological platforms for the development of drugs for the treatment of central neural system diseases. Sponsored by: GMV Soluciones Globales Internet S.A. Reference: CCB.UCO.0041

Muñoz Blanco, E. Integration of technological platforms for the development of drugs for the treatment of central neural system diseases. Sponsored by: Vivacell Biotechnology España, S.L. Reference: CCB.UCO.0049

Muñoz Blanco, E. Project for the production and research on hemp and derivatives. Sponsored by: Phytoplant Research S.L. Reference: CCB.UCO.0057

Muñoz Blanco, E. Isolation, purification and characterization of the biological activity of active plant ingredients. Sponsored by: Phytoplant Research S.L. Reference: CCB.UCO.0060

Muñoz Blanco, E. Outsourcing within the ININTERCONECTA project: ATENA -"Olive oil and other healthy fats. Technological applications for the transformation of olive oil fats into high value added products". Sponsored by: Phytoplant Research S.L. Reference: CCB.UCO.0062

## GC5

# Systemic Autoimmune and Chronic Inflammatory Diseases of the Musculoskeletal System and Connective Tissue

### Team Leaders

#### Principal Investigator (PI)

Rosario López Pedrera  
rosario.lopez.exts@juntadeandalucia.es  
Nicolás Monardes Contract

#### Co-Principal Investigator (Co-PI)

Eduardo Collantes Estevez  
Professor at University of Cordoba.  
Head of the Clinical Management Unit of Rheumatology

#### Senior Researchers

M<sup>a</sup> Ángeles Aguirre Zamorano  
Pilar Font Ugalde  
Inmaculada Gómez Gracia  
Verónica Pérez Guijo

#### Post-doctoral Researcher

Nuria Barbarroja Puerto

#### Pre-doctoral Researchers

Carlos Pérez Sánchez  
Patricia Ruiz Limón  
Rafaela Ortega Castro

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)  
Miguel Ángel Caracuel Ruiz  
Rosario M<sup>a</sup> Carretero Prieto  
M<sup>a</sup> Carmen Castro Villegas  
Alejandro Escudero Contreras  
Carmen López Montilla  
Desiree Ruiz Vilchez



Rafael A. Butelo

## Scientific Activity

Our research team uses synergistic clinical-therapeutic, molecular and cellular approaches. Its main objectives are as follows:

1) To analyze the cellular and molecular mechanisms regulating the effect of statins and other drugs on development (biological therapy) in preventing thrombosis and atherothrombosis in systemic autoimmune diseases (SAD), such as Primary Antiphospholipid Syndrome (APS), Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA). We also conduct studies on mitochondrial dysfunction and oxidative stress in atherothrombosis associated with SAD; in addition, we perform pro-

teomic analyses aimed at identifying new genes/proteins whose expression in patients with APS, SLE or RA and atherosclerosis is altered, and determining the variations in expression patterns as a result of different treatments.

2) To register, describe and analyze the clinical, epidemiological, demographic, genetic and radiographic characteristics of the physiological and therapeutic response in patients with ankylosing spondylitis in Spain and compare them with data from Latin American patients.

The most interesting point will be to ascertain whether the possible differences in clinical expression are due to the genetic load we assume comes from the same genotype (in terms of

HLA-B27) and its relationship with the interaction with the environment. Moreover, in this same area: to design, develop and validate a new mobility measurement system (the most important expression of structural damage) in these patients.

## Keywords

Systemic autoimmune diseases (Primary Antiphospholipid Syndrome, Systemic Lupus Erythematosus, Rheumatoid Arthritis), oxidative stress, inflammation, cardiovascular disease, new therapies, spondyloarthropathies, epidemiology, diagnostic criteria, structural damage.

## Publications

### Originals Publications

Vander Cruyssen B, Vastesaeger N, Collantes-Estevez E. Hip disease in ankylosing spondylitis. *Curr Opin Rheumatol*. 2013, 25(4):448-454.

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Rodríguez-Lozano C, Juanola X, Cruz-Martínez J, Peña-Arrébola A, Mulero J, Gratacós J, Collantes E. Outcome of an education and home-based exercise program for patients with ankylosing spondylitis: a nationwide randomized study. *Clin Exp Rheumatol*. 2013, 31(5):739-748.

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Collantes-Estevez E. New paradigms in the diagnosis and classification of the spondylarthritis. *Reumatol Clin*. 2013, 9(4):199-200.

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### Joint Publications

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## Research Projects

Lopez Pedrera, R. Endothelial microparticles regulating vascular damage/repair balance. A study using the accelerated atherosclerosis model of chronic kidney disease. Sponsored by: Institute Carlos III Health (ISCIII). Reference: 09/1809

Collantes Estevez, E. Monitoring therapeutic response in patients with ankylosing spondylitis using a new metrological index basing on the analysis of movement. Sponsored by: Institute Carlos III Health (ISCIII). Reference: 10/01524

Pérez Guijo, V. Performing a biomechanical analysis of movement and balance to assess the effectiveness of intraarticular treatments in patients with osteoarthritis in the knee. Sponsored by: Andalusian Progress and Health Foundation. Reference: PI-0049-2011

Escudero Contreras, A. A study of molecular targets involved in the inflammation and apposition of fibrous and bone tissue in ankylosing spondylitis. Alternative therapies. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0314-2012

Lopez Pedrera, R. Mechanisms of atherosclerosis and cardiovascular disease. Sponsored by: Institute Carlos III Health (ISCIII). Reference: PI12/01511

Font Ugalde, P. Clinical applicability of a standardized dose-reduction protocol in patients in persistent clinical remission diagnosed with rheumatoid arthritis and treated with TNF antagonists. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0182-2013

Barbarroja Puerto, N. Role of joint inflammation in the development of rheumatoid arthritis-associated insulin resistance and atherosclerosis. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0191-2013

Lopez Pedrera, R. Cellular and molecular mechanisms of atherothrombosis in systemic autoimmune diseases: An epigenetic study. Assessment of response to new therapies.

Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: CTS-7940

Collantes Estevez, E. PRECISESADS > Evidence of the ability to carry out the clinical trials foreseen. Sponsored by: European Commission Reference: IMI/0002

## Third Party Services

Collantes Estevez, E. CLEIA Project: Online health care system for the individualized treatment of low back pain. Sponsored by: Spanish Ministry of Industry, Energy and Tourism. Reference: AVANZA.001

Collantes Estevez, E. CLEIA Project: Online health care system for the individualized treatment of low back pain. Sponsored by: Hispafuentes S.L. Reference: AVANZA.0001

Collantes Estevez, E. Service provided by Dr. Collantes Programa Esperanza. Sponsored by: Fundación Española de Reumatología (Spanish Rheumatology Foundation). Reference: PSS.0008

Collantes Estevez, E. Monitoring therapeutic response in patients with ankylosing spondylitis using a new metrological index basing on the analysis of movement. Sponsored by: Fundación Española de Reumatología (Spanish Rheumatology Foundation). Reference: PSS.0019

Collantes Estevez, E. Movement as a support tool for clinical decision in rheumatology patients. Sponsored by: MT Global (Specials Events). Reference: PSS.0023

Collantes Estevez, E. Asas Comospa. Sponsored by: Association de Recherche Clinique en Rheumatologie. Reference: PSS.0024

## Collaboration Agreements

Collantes Estevez, E. UCB Pharma- Dr. Collantes- Diagnosis and treatment of rheumatoid arthritis. Sponsored by: UCB Pharma, S.A. Referencia: CCB.0019

Pérez Sanchez, C. Agreement between the Clinical Management Unit of Rheumatology and UCB Pharma. Sponsored by: UCB Pharma, S.A. Reference: CCB.0033

Collantes Estevez, E. A study of new molecular targets involved in the inflammation and apposition of fibrous and bone tissue in ankylosing spondylitis. Sponsored by: Roche Farma, S.A. Reference: CCB.0035

Escudero Contreras, A. A study of the development and control mechanisms of atherothrombosis in systemic autoimmune diseases. New therapeutic approaches. Sponsored by: Fundación Española de Reumatología (Spanish Rheumatology Foundation). Reference: CCB.0045

López Pedrera, R. Sponsored Research Agreement KANEKA. Sponsored by: Kaneka Corporation. Reference: CCB.0054

Collantes Estevez, E. Agreement between MSD and the UGC of Rheumatology. Sponsored by: Merck Sharp & Dohme de España SA. Reference: CCB.0042

## Clinical Trials

0201/08: A randomized, placebo-controlled, phase III study to assess the effectiveness and safety of odanacatib (MK-0822) to reduce fracture risk in postmenopausal women with osteoporosis treated with Vitamin D and calcium. PI: Dr/a Escudero Contreras, Alejandro

0128/09: A multicenter study of the effectiveness and safety of the human monoclonal anti-TNF Adalimumab in patients with axial spondylitis. PI: Dr/a Collantes Estevez, Eduardo

0196/09: A multicenter, randomized, double-blind, parallel-group study to assess the safety, disease remission and prevention of articular structural damage in patients with early, moderate to severe rheumatoid arthritis on tocilizumab monotherapy. PI: Dr/a Escudero Contreras, Alejandro

0284/09: Assessing response to etoricoxib in patients with ankylosing spondylitis and inadequate response to > 2 AINES. PI: Dr/a Collantes Estevez, Eduardo

0027/10: A multicenter, double-blind, parallel-group, phase III to assess the effectiveness and safety of certolizumab pegol in adult patients with active, progressive psoriatic arthritis. PI: Dr/a Collantes Estevez, Eduardo

0028/10: A multicenter, double-blind, parallel-group, placebo-controlled phase III to assess the effectiveness and safety of certolizumab pegol in adult patients with active, progressive psoriatic arthritis. PI: Dr/a Collantes Estevez, Eduardo

0191/10: A multicenter, pilot, randomized, parallel-group, placebo-controlled study to assess the effectiveness and safety of three different Adant(r) dosing regimens in patients with knee osteoarthritis. PI: Dr/a Escudero Contreras, Alejandro

0219/10: A randomized, double-blind, parallel-group, placebo-controlled study to assess the safety and reduction of signs and symptoms during treatment with tocilizumab versus placebo in ankylosing spondylitis patients showing inadequate response to previous treatment with a TNF antagonist. PI: Dr/a Collantes Estevez, Eduardo

0220/10: A randomized, double-blind, parallel-group, placebo-controlled study to assess the

safety and reduction of signs and symptoms during treatment with tocilizumab versus placebo in ankylosing spondylitis patients showing unadequate response to previous treatment with a TNF antagonist.

PI: Dr/a Collantes Estevez, Eduardo

0246/10: Diagnosis-escalation, single-blind, phase IB/IIA trial to assess the safety of intravenous administration of expanded allogeneic mesenchymal stem cells derived from adipose tissue to patients with refractory rheumatoid arthritis.

PI: Dr/a Collantes Estevez, Eduardo

0261/10: A multicenter, randomized, double-blinded, placebo-controlled, 12-week duration study of etanercept with a base NSAIDs in the treatment of adult subjects with axial ankylosing spondylitis without radiographic signs, with an open extension of 92 weeks.

PI: Dr/a Collantes Estevez, Eduardo

0057/11: A non-inferiority trial to assess the effectiveness and safety of Chondroitin sulfate + Glucosamine hydrochloride versus Celecoxib in patients with osteoarthritis in the knee.

PI: Dr/a Caracuel Ruiz, Miguel Ángel

0100/11: A multicenter, double-blind, randomized trial to assess the safety and effectiveness of tocilizumab (TCZ) plus methotrexate (MTX) versus changing to TCZ (placebo-controlled) in patients with active rheumatoid arthritis showing unadequate response to previous treatment with MTX and having attained a low activity of the disease (DAS 28 &#8804; 3.2) with TCZ in combination with MTX.

PI: Dr/a Escudero Contreras, Alejandro

0220/11: A multicenter, randomized, placebo-controlled, double-blind phase III study to assess the efficacy, safety, tolerability and pharmacokinetics of BMS-817399 in adult patients with active moderate to severe rheumatoid arthritis and inadequate response to methotrexate.

PI: Dr/a Escudero Contreras, Alejandro

0113/12: Assessment of the clinical utility of a standardized dose reduction protocol in patients with axial spondyloarthritis in persistent clinical remission on treatment with TNF antagonists: An open, multicenter, controlled, randomized study.

PI: Dr/a Collantes Estevez, Eduardo

0125/12: A multicenter, randomized, placebo-controlled, double-blind, parallel-group phase III study to assess the efficacy and safety of Apremilast (CC-10004) in the treatment of active ankylosing spondylitis.

PI: Dr/a Collantes Estevez, Eduardo

0291/12: A randomized, double-blind, placebo-controlled study to assess the safety, tolerability, pharmacokinetics, pharmacodynamic and clinical effectiveness of multiple subcutaneous doses of BI655064 in healthy subjects and patients with rheumatoid arthritis showing not

satisfactory response to a previous treatment with methotrexate.

PI: Dr/a Escudero Contreras, Alejandro

0320/12: A randomized, double-blind, placebo-controlled, 52-week duration study to assess adverse events of special interest in adults with systemic antibody positive lupus erythematosus receiving belimumab.

PI: Dr/a Aguirre Zamorano, M<sup>a</sup> Ángeles

0015/13: A randomized, placebo-controlled study of sarilumab and methotrexate vs etanercept in combination with MTX in patients with rheumatoid arthritis showing unadequate response after four months of treatment with adalimumab and MTX.

PI: Dr/a Collantes Estevez, Eduardo

0034/13: A randomized, double-blind, multicenter, placebo-controlled, 24-week duration study to assess the long-term efficacy and safety of Ixekizumab (LY2439821) in patients with active psoriatic arthritis that have not received disease-modifying anti-rheumatic drugs.

PI: Dr/a López Montilla, M<sup>a</sup> Dolores

0079/13: A randomized, double-blind, placebo-controlled, phase II, dose-finding study to assess the efficacy and safety of tofacitinib in patients with active ankylosing spondylitis.

PI: Dr/a Collantes Estevez, Eduardo

0105/13: A multicenter, randomized, double-blind, placebo-controlled, phase IIB, dose-finding study of GLPG0634 administered for 24 weeks in combination with methotrexate to patients with active moderate to severe rheumatoid arthritis with unadequate response to methotrexate alone.

PI: Dr/a Escudero Contreras, Alejandro

0139/13: A phase IIIb study to assess the efficacy, safety and tolerability of subcutaneous Tocilizumab (TCZ) administered alone or in combination with methotrexate (MTX) and other non-biological DMARDs in patients with rheumatoid arthritis.

PI: Dr/a Escudero Contreras, Alejandro

0248/13: A multicenter, randomized, double-blind, placebo-controlled phase III study to demonstrate the efficacy of Secukinumab after 16 weeks of treatment and assess its long-term safety, tolerability and efficacy in a period of three years in patients with active ankylosing spondylitis.

PI: Dr/a Collantes Estevez, Eduardo

0000/10: A multicenter study of the effectiveness and safety of the human monoclonal anti-TNF Adalimumab in patients with peripheral spondylitis.

PI: Dr/a Collantes Estevez, Eduardo

1644: Clinical value of the ASDAS index in Spanish patients with ankylosing spondylitis. AXIS study.

PI: Dr/a Collantes Estevez, Eduardo

1695: Predictive value of FRAX of fracture risk in patients seen in Rheumatology Units in Spain.

PI: Dr/a Caracuel Ruiz, Miguel Ángel

1729: A national, multicenter, observational, retrospective follow-up study of the patients who took part in the loadet trial "loadet study".

PI: Dr/a Collantes Estevez, Eduardo

1789: Assessing cardiovascular risk and its determinants in patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis.

PI: Dr/a Collantes Estevez, Eduardo

1794: National Lupus Register of the Spanish Society of Rheumatology.

PI: Dr/a Aguirre Zamorano, M<sup>a</sup> Ángeles

1811: SCORE: Follow-up and control in rheumatology-nursing.

PI: Dr/a Collantes Estevez, Eduardo

1815: Prevalence of axial and peripheral spondyloarthritis in first-degree relatives in patients with ankylosing spondylitis.

PI: Dr/a Collantes Estevez, Eduardo

2031: Immunogenicity in anti-TNF therapies in patients with rheumatic diseases.

PI: Dr/a Castro Villegas, M<sup>a</sup> Carmen

2035: Pain assessment in Rheumatology.

PI: Dr/a Collantes Estevez, Eduardo

2139: A cross-over, observational study of the functional limitation and limitations of work and daily activities in patients with systemic sclerosis with or without digital ulcers.

PI: Dr/a Escudero Contreras, Alejandro

2148: Rheumatologists and patients preferences regarding the biological agents used to treat rheumatic diseases in Spain.

PI: Dr/a Collantes Estevez, Eduardo

2219: Beneficial effects of coenzyme Q10 treatment on the mitochondrial dysfunction and oxidative stress associated to atherothrombosis development in antiphospholipid syndrome patients.

PI: Dr/a López Pedrera, Rosario

2273: Spanish registry of patients with axial ankylosing spondylitis treated with anti-TNF.

PI: Dr/a Collantes Estevez, Eduardo

2276: A retrospective study of patients with rheumatic diseases initiating treatment with biological therapies (SE-BIO Study).

PI: Dr/a Castro Villegas, M<sup>a</sup> Carmen

2457: Multi-Country Registry of clinical characteristics, including radiographic progression, and burden of disease over 5 years in real-life setting) PROOF.

PI: Dr/a Collantes Estevez, Eduardo

# GC6

## New Cancer Therapies

### Team Leaders

#### Principal Investigator (PI)

Enrique Aranda Aguilar  
earandaa@seom.org  
Cooperative Research Thematic Network on Cancer (RETICC)

#### Co-Principal Investigator (Co-PI)

Antonio Rodríguez Ariza  
Nicolás Monardes Contract

#### Emerging Researcher

Juan Rafael de la Haba Rodríguez

#### Senior Researchers

Isidoro Barneto Aranda  
M<sup>a</sup> Carmen Cañabate Arias  
Francisco Manuel Conde Perez  
M<sup>a</sup> Auxiliadora Gomez España  
Antonio Martínez Peinado  
M<sup>a</sup> José Méndez Vidal  
M<sup>a</sup> Jesús Rubio Pérez  
Carlos Villar Pastor  
Ruth Zarate Romero

#### Post-doctoral Researchers

Laura M<sup>a</sup> López Sánchez  
Jon Peñarando Sáez  
Araceli Valverde Estepa

#### Pre-doctoral Researchers

Amanda Cañas Rodríguez  
Nuria Galera

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)

M<sup>a</sup> Eugenia Carrillo Gil  
M<sup>a</sup> Ángeles Diaz Diaz  
Inmaculada Diéguez Cantueso  
Jesús Garcia Foncillas  
Vanesa Hernández Nieto  
Isabel Jaraba Mezquina  
Amalia Leña Barranco  
Maria Lopez Garcia  
Jacinta Marin Serrano  
M<sup>a</sup> Jose Marin Serrano  
Rosario Miranda Garcia  
Sonia Rodriguez de Julian



## Scientific Activity

Our research group conducts its scientific activities in several areas of both clinical and experimental research. The first area is related to the identification of clinical or molecular factors useful in predicting clinical evolution, response or toxicity in cancer treatment.

In this area we have published clinical evolutionary models for predicting colon and breast cancer; in addition, we have conducted studies on polymorphisms such as UGT1A1, GSTT1 and CYP2D6, and neoplasms in relation to both their toxicity and response. We participate very actively in the development of new therapeutic strategies using drugs aimed at specific targets. To achieve this, we are cur-

rently carrying out research studies to develop response markers to this type of (mostly anti-angiogenic) therapies. The development of these markers will optimize the use of new therapies in cancer patients. Another research area looks into the role of nitrosative stress and the regulation of nitrosothiol homeostasis in different experimental models and diseases. Our research is aimed at exploring pathogenic mechanisms and identifying new therapeutic options and targets. Using the latest proteomic approaches to identify posttranslational nitrosative modifications, notably the S-nitrosylation of proteins, we analyse the importance of maintaining the homeostasis of nitrosothiols and the formation of S-nitrosoproteins. Our research has focused so far on differ-

ent models of hepatocellular injury. However, given the importance of inflammation and nitric oxide production in cancer, we are also conducting studies in experimental models of colon and breast cancer and in clinical samples of patients with this type of neoplasm undergoing different antitumoural treatments.

## Keywords

Colon Cancer, Breast Cancer, Polymorphisms, Gene Expression, Pharmacogenomics, Predictive Models, Angiogenesis, Angiotensins, anti Her-2 therapies, anti-EGFR Therapy, Clinical Trial, Nitric Oxide, Nitrosative Stress, S-nitrosylation, Proteomics, Genomics.

## Publications

### Originals Publications

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### Joint Publications

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## Research Projects

Aranda Aguilar, E. A study of genetic polymorphisms in the renin angiotensin and the Vegf & Vegfr-1 system in colon and breast cancer as predictors of response to antiangiogenic therapy. Sponsored by: Regional Ministry of Equality, Health and Social Policy (CISPS). Reference:0009/2010

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Rodríguez Ariza, A. ONCOVER: Detection system of volatile compounds for early diagnosis of lung and colon cancer. Sponsored by: University of Córdoba. Reference:CCB.030PM

De la Haba Rodríguez, J R. Analysis of polymorphisms related to hypertension as a predictor of response to antiangiogenic treatment in cancer. Sponsored by: Institute Carlos III Health (ISCIII). Reference:PI12/02017

Aranda Aguilar, E. Genetic variations associated with hypertension and thrombosis as predictors of response to antiangiogenic therapy in patients with colon cancer. Sponsored by: Institute Carlos III Health (ISCIII). Reference:PI13/00951

Rodríguez Ariza, A. Role of nitric oxide and nitrosothiols homeostasis in the generation and maintenance of tumor stem cells: new approaches to colon and breast cancer. Sponsored by: Institute Carlos III Health (ISCIII). Reference:PI13/00553

## Third Party Services

Aranda Aguilar, E. VISNU project. Sponsored by: Treatment of digestive tumours (TTD Group). Reference:PSS.0022

Aranda Aguilar, E. Interconecta Oncoexpert biotechnology for the diagnosis and treatment of cancer. Sponsored by: Oncoexpert. Reference: INTER.0003

## Collaboration Agreements

De la Haba Rodríguez, JR. Analytical assays for the evaluation of AGTR1 expression in tumors as a possible predictor of response to angiogenic therapy in connection with the clinical development of bevacizumab. Sponsored by: Roche Farma, S.A. Reference:CCB.0028

## Clinical Trials

0012/04: A multicenter, randomized, phase III comparative study of epirubicin. PI: Dr/a Aranda Aguilar, Enrique

0099/04: A randomized, phase III comparative study of exemestane versus placebo in postmenopausal women at increased risk of developing breast cancer. PI: Dr/a De la Haba Rodríguez, Juan Rafael

0215/04: An open, multicenter, randomized trial to assess the effectiveness of zoledronic acid in preventing bone loss associated with cancer treatment in postmenopausal women with RE+ breast cancer. PI: Dr/a Aranda Aguilar, Enrique

0198/05: An open, multicenter, randomized phase IV–III study to assess the effectiveness of maintenance treatment with capecitabine (X) after standard adjuvant chemotherapy in patients with operable breast cancer who have hormone-receptor- and HER2neu-negative tumors. PI: Dr/a De la Haba Rodríguez, Juan Rafael

0109/06: A multicenter, open, pilot, non-controlled, phase II study to assess the efficacy and safety of cetuximab combined with chemotherapy (docetaxel, cisplatin, 5-fluorouracil) as neoadjuvant treatment followed by concomitant chemoradiotherapy (cisplatin) combined with cetuximab in patients with locoregional esophageal cancer. PI: Dr/a Aranda Aguilar, Enrique

0254/06: A phase III trial to assess ovarian function suppression and Exemestane as adjuvant treatments for premenopausal women with endocrine-sensitive breast cancer – Tamoxifen versus ovarian function suppression + Exemestane. PI: Dr/a De la Haba Rodríguez, Juan Rafael

0090/07: An open, multicenter, randomized, phase III study of lapatinib, trastuzumab sequentially administered or administered in com-

ination as adjuvant treatment in a patient with HER2/ERBB2-positive breast cancer. PI: Dr/a De la Haba Rodríguez, Juan Rafael

0106/07: A randomized study of adjuvant chemotherapy individualized according to BRCA1 ARNm levels in patients with non-small cell lung cancer. PI: Dr/a Barneto Aranda, Isidoro

0148/07: A multicenter, randomized study to assess the effectiveness and safety of bevacizumab in combination with letrozol alone in postmenopausal women with locally recurrent or metastatic breast cancer with indication of hormone therapy as first-line treatment. PI: Dr/a De la Haba Rodríguez, Juan Rafael

0165/07: An open, multicenter, randomized, parallel-group, phase III trial to compare the effectiveness and tolerability of administering Fulvestrant (FASLO-DEX®) for three years in combination with Anastrozol (ARIMIDEX®) for five years versus Anastrozol for five years as adjuvant hormone treatment in postmenopausal women with early hormone-receptor positive breast cancer. PI: Dr/a De la Haba Rodríguez, Juan Rafael

0179/07: A multicenter, international, randomized phase II study of trastuzumab and docetaxel versus trastuzumab, docetaxel and pertuzumab versus trastuzumab and pertuzumab in patients with locally advanced inflammatory or early breast cancer. PI: Dr/a Aranda Aguilar, Enrique

0002/08: A randomized, phase II study of continuous treatment vs. standard treatment with capecitabine in patients with metastatic breast cancer. PI: Dr/a De la Haba Rodríguez, Juan Rafael

0040/08: A multicenter, randomized, double-blind, phase III study with multiple doses of Alpharadin in the treatment of patients with hormone-refractory prostate cancer and bone metastases. PI: Dr/a Aranda Aguilar, Enrique

0144/08: A randomized, phase II clinical study of radiotherapy, hormone therapy and chemotherapy with docetaxel versus radiotherapy and hormone therapy in patients with high-risk localized prostate cancer (Stage III and IV). PI: Dr/a Aranda Aguilar, Enrique

0133/08: A multicenter, randomized, phase II study of treatment with epirubicin and cyclophosphamide followed by treatment with docetaxel and trastuzumab versus epirubicin and cyclophosphamide followed by docetaxel and lapatinib in women with resectable primary or locally-advanced HER2-positive breast cancer. PI: Dr/a De la Haba Rodríguez, Juan Rafael

0253/08: An open, multicenter, randomized, exploratory study to assess the effectiveness and safety of panitumumab in combination with

FOLFOX 4 chemotherapy or panitumumab with FOLFIRI chemotherapy in subjects with colorectal cancer with non-mutated KR.

PI: Dr/a Aranda Aguilar, Enrique

0260/08: A randomized, open, two-group, phase IIIb study to assess the safety of 3-hour intraperitoneal administration of catumaxomab with and without premedication with prednisolone in patients with malign ascites caused by an epithelial cancer.

PI: Dr/a Aranda Aguilar, Enrique

0265/08: Topotecan plus carboplatin vs standard treatment (paclitaxel plus carboplatin or gemcitabine + carboplatin) in the treatment of patients with recurrent platinum-sensitive peritoneal carcinoma, fallopian tube carcinoma or epithelial ovarian carcinoma.

PI: Dr/a Rubio Pérez, María Jesús

0046/09: An open, multicenter, phase II study to assess the safety and effectiveness of panitumumab in combination with irinotecan in patients with metastatic colorectal cancer with non-mutated KRAS refractory to irinotecan-based chemotherapy.

PI: Dr/a Aranda Aguilar, Enrique

0048/09: A randomized, phase II study of citabine+Bevacizumab+external radiotherapy versus Capecitabine+external radiotherapy as preoperative treatment in patients with resectable locally advanced rectal cancer.

PI: Dr/a Aranda Aguilar, Enrique

0076/09: A randomized, double-blind, multicenter, phase II study to assess the efficacy of AZD2281 in the treatment of patients with platinum-sensitive serous ovarian cancer after treatment with two or more platinum regimens.

PI: Dr/a Rubio Pérez, M<sup>a</sup> Jesús

0081/09: A randomized, double-blind, placebo-controlled, phase III study to assess the efficacy and safety of farletuzumab (MORAb-003) administered weekly in combination with carboplatin and taxane in patients with platinum-sensitive ovarian cancer in first relapse.

PI: Dr/a Rubio Pérez, M<sup>a</sup> Jesús

0131/09: Selective treatment in colorectal cancer: selection of capecitabine or 5-fluorouracil based on TS-3'UTR and ERCC1-118 polymorphisms for combination with oxaliplatin or irinotecan as chemotherapy in combination with first-line bevacizumab in advanced colon cancer.

PI: Dr/a Aranda Aguilar, Enrique

0139/09: A multicenter, open, randomized, two-arm, phase III study of bevacizumab plus chemotherapy vs chemotherapy alone for the treatment of patients with platinum-resistant primary peritoneal carcinoma, fallopian tube carcinoma or epithelial ovarian carcinoma.

PI: Dr/a Rubio Pérez, M<sup>a</sup> Jesús

0181/09: A randomized, double-blind, placebo-controlled trial with neratinib (HKI-272) after trastuzumab in women with initial stage breast

cancer with overexposure/amplification of HER2/neu.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0226/09: A multicenter, multinational, randomized, phase II study to assess pertuzumab in combination with trastuzumab administered concomitantly or sequentially to a regular anthracycline-based chemotherapy or concomitantly to a non-anthracycline chemotherapy as neoadjuvant treatment in patients with breast cancer.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0250/09: A phase II study of panitumumab as a first-line single agent in fragile elderly patients with advanced colorectal cancer with non-mutated KRAS.

PI: Dr/a Aranda Aguilar, Enrique

0260/09: A multicenter, randomized, double-blind, placebo-controlled phase III study of everolimus daily administered in combination with trastuzumab and vinorelbine in women previously treated with metastatic or locally advanced breast cancer with HER2/neu overexpression.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0002/10: A phase II study of capecitabine-trastuzumab (xelox-trastuzumab) as perioperative treatment in patients with nonresectable gastric or gastroesophageal junction adenocarcinoma.

PI: Dr/a Aranda Aguilar, Enrique

0013/10: A multicenter, randomized, phase II, pilot study to assess the safety and efficacy of a treatment with mFOLFOX-6 plus cetuximab versus an initial treatment with mFOLFOX-6 plus cetuximab (8 cycles) followed by exclusive maintenance treatment with cetuximab as first-line treatment in patients with metastatic colorectal cancer and KRAS tumors.

PI: Dr/a Aranda Aguilar, Enrique

0082/10: An open, randomized, phase II study to assess the effectiveness and safety of paclitaxel administered weekly as a single agent and two different administration regimens of SAR240550 (BSI-201), a PARP-1 inhibitor, in combination with paclitaxel administered weekly as neoadjuvant therapy in patients with stage II-IIIa triple-negative breast cancer.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0194/10: A multicenter, randomized, placebo-controlled, double-blinded phase III study to assess the efficacy and safety of pazopanib as adjuvant treatment in patients with localized or locally advanced kidney cell carcinoma after nephrectomy.

PI: Dr/a Rubio Pérez, M<sup>a</sup> Jesús

0215/10: A randomized, double-blind, phase III trial of paclitaxel administered weekly plus MAG386 or placebo in women with recurrent partially platinum-sensitive or platinum-resistant peritoneal carcinoma, fallopian tube carcinoma or epithelial ovarian carcinoma.

PI: Dr/a Rubio Pérez, M<sup>a</sup> Jesús

0227/10: A randomized, phase III study to assess the effectiveness and safety of continuous and reinduction treatment with bevacizumab in combination with chemotherapy in locally recurrent or metastatic breast cancer patients after first-line treatment with chemotherapy and bevacizumab.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0229/10: A global study to assess the addition of bevacizumab to carboplatin and paclitaxel as first-line treatment of primary peritoneal carcinoma, fallopian tube carcinoma or epithelial ovarian carcinoma.

PI: Dr/a Rubio Pérez, M<sup>a</sup> Jesús

0243/10: A randomized, phase IIb trial to assess the effectiveness of gemcitabine-erlotinib-capecitabine in patients with metastatic pancreatic cancer. GECA.

PI: Dr/a Aranda Aguilar, Enrique

00259/10: A randomized, open, phase II study of lapatinib plus chemotherapy vs trastuzumab plus chemotherapy as first-line treatment in women with metastatic, HER2-positive and p95HER2-positive.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0268/10: A randomized, phase II trial of docetaxel-carboplatin in combination with Iniparib (BSI-201) and docetaxel-carboplatin as neoadjuvant treatment of patients with early stage and triple-negative phenotype breast cancer.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0270/10: An open, multicenter, randomized, phase III study to assess the safety and effectiveness of TKI258 versus sorafenib in patients with metastatic renal cell cancer after therapy failure (mTOR inhibitor VEGF-targeted).

PI: Dr/a Aranda Aguilar, Enrique

0284/10: A randomized, phase III trial of cisplatin plus paclitaxel with and without bevacizumab vs non-platinum doublet, topotecan plus paclitaxel, with or without bevacizumab in recurrent or persistent IVB stage cervical carcinoma.

PI: Dr/a Rubio Pérez, M<sup>a</sup> Jesús

0294/10: An open, multicenter, one-group trial to provide access to cabazitaxel prior to its commercialization to patients with metastatic hormone-resistant prostate cancer previously treated with a docetaxel-containing regimen and assess its safety in this type of patients.

PI: Dr/a Méndez Vidal, María José

0318/10: A multicenter, placebo-controlled, phase II study to assess the safety and effectiveness of the cream ATH008 in patients with Palmar Plantar Erythrodysesthesia Syndrome (SEPP) secondary to capecitabine monotherapy.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0327/10: An open, multicenter, expanded access study of RO5185426 in patients with metastatic melanoma.

PI: Dr/a Aranda Aguilar, Enrique

0019/11: An open study of abiraterone acetate in patients with castration-resistant metastatic prostate cancer with progression after chemotherapy with taxanes.

PI: Dr/a Méndez Vidal, María Jose

0024/11: A phase II trial of cetuximab in refractory colorectal cancer with mutated K-RAS and favorable FcyRIIIa genotypes.

PI: Dr/a Aranda Aguilar, Enrique

0054/11: A multicenter, controlled, double-blind trial by the Gynaecologic Cancer Intergroup of Cediranib (AZD 2171) in combination with platinum-based chemotherapy and as a single agent in maintenance therapy in women with relapsing ovarian cancer six months after completion of first-line platinum-based treatment.

PI: Dr/a Rubio Pérez, María Jesús

0129/11: A phase II study of Axitinib as maintenance treatment in patients with metastatic colorectal carcinoma.

PI: Dr/a Aranda Aguilar, Enrique

0133/11: A randomized, phase III study of ABI-007 plus Gemcitabine versus Gemcitabine alone weekly administered in patients with metastatic pancreatic adenocarcinoma.

PI: Dr/a Aranda Aguilar, Enrique

0138/11: Anamorelin HCl in the treatment of cachexy associated with non-small lung cancer: An extension study.

PI: Dr/a Barneto Aranda, Isidoro

0143/11: A randomized, double-blind, phase III study to assess the effectiveness and safety of PF-00299804 versus erlotinib in the treatment of advanced non-small cell lung cancer after progression for at least a previous chemotherapy or in case of intolerance.

PI: Dr/a Barneto Aranda, Isidoro

0198/11: A multicenter, randomized, double-blind, placebo-controlled study to compare chemotherapy plus trastuzumab and placebo versus chemotherapy plus trastuzumab and pertuzumab as adjuvant treatment in HER-2 positive primary breast cancer patients.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0226/11: A phase II open label study of cabazitaxel in patients with advanced or metastatic transitional cell carcinoma of the urothelium who have progressed 12 months after a previous platinum-based chemotherapy.

PI: Dr/a Méndez Vidal, María Jose

0231/11: An open, multicenter, randomized, parallel-group phase II clinical study to assess the effectiveness and safety of pertuzumab administered in combination with trastuzumab and an aromatase inhibitor for first-line treatment.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0240/11: An open, multicenter, phase II study of E7080 alone or in combination with Everolimus in patients with nonresectable or metastatic renal cell cancer after a targeted anti-VEGF therapy.

PI: Dr/a Méndez Vidal, María Jose

0017/12: A randomized, open, phase II study of MM-121 controlled with paclitaxel vs paclitaxel alone in patients with platinum resistant or refractory ovarian cancer.

PI: Dr/a Rubio Pérez, María Jesus

0071/12: A randomized, phase II clinical trial to explore the impact of BRAF and PI3K state on the effectiveness of FOLFIRI + Bevacizumab or Cetuximab as first-line treatment of patients with metastatic colorectal cancer with native KRAS and less than three circulating tumor cells.

PI: Dr/a Aranda Aguilar, Enrique

0073/12: A randomized, phase III clinical trial to assess the effectiveness of FOLFOX + bevacizumab versus FOLFOXIRI + bevacizumab as first-line treatment in naive patients with metastatic colorectal cancer with three or more circulating tumor cells.

PI: Dr/a Aranda Aguilar, Enrique

0075/12: A phase IIIb study of regorafenib in patients with metastatic colorectal cancer with progression to conventional treatments.

PI: Dr/a Aranda Aguilar, Enrique

0081/12: An open, multicenter, single-arm, non-randomized, phase II study to assess the effectiveness of oral TKI258 as second-line therapy in patients with advanced and/or metastatic endometrial cancer with mutated or wild-type FGFR2.

PI: Dr/a Rubio Pérez, María Jesús

0086/12: LUX-Breast 3: A randomized, phase II study of afatinib alone or in combination with vinorebin versus the researcher's treatment of choice in HER2-positive breast cancer patients with progressive cerebral metastasis after a trastuzumab- and/or lapatinib-based therapy.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0098/12: An open, exploratory, pharmacogenomic, single-group phase II study of eribulin (HALAVEN®) monotherapy as neoadjuvant treatment for operable I-II stage breast cancer without HER2 overexpression.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0104/12: An expanded access study for postmenopausal women with estrogen receptor positive locally advanced or metastatic breast cancer who have progressed following prior endocrine therapy, investigating the treatment of everolimus (RAD001) in combination with exemestane.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0123/12: Radium-223 chloride (Alpharadin) in patients with castration-resistant (hormone-resistant) prostate cancer with bone metastasis.

PI: Dr/a Méndez Vidal, María Jose

0127/12: An open, phase II study of ketoconazole as CYP17 inhibitor in locally advanced or disseminated ovarian granulosa cell cancer.

PI: Dr/a Rubio Pérez, María Jesús

0146/12: A randomized, double-blind, placebo-controlled, phase II study of BKM120 plus paclitaxel in patients with inoperable, HER2-negative,

metastatic or locally-advanced breast cancer with or without PI3K signalling pathway activation.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0156/12: An open, multicenter, single-arm clinical trial to assess the safety and health-related quality of life of aflibercept in metastatic colorectal cancer patients.

PI: Dr/a Aranda Aguilar, Enrique

0160/12: A randomized, multicenter, double-blind, two-part, phase II study to assess the efficacy and safety of pertuzumab in combination with standard chemotherapy vs placebo plus standard chemotherapy in women with epithelial cancer.

PI: Dr/a Rubio Pérez, María Jesús

0171/12: A randomized, double-blind, placebo-controlled, phase III study of BKM120 in combination with fulvestrant in postmenopausal women with locally advanced or metastatic hormone-receptor positive and HER2-negative breast cancer with progression after a treatment with an aromatase inhibitor.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0174/12: A randomized, double-blind, placebo-controlled, phase II/III study of first-line immunotherapy with or without TF4010 in patients with IV-stage non-small cell lung cancer (NSCLC).

PI: Dr/a Barneto Aranda, Isidoro

0229/12: A multicenter, single-arm study of trastuzumab emtansine (TDM1) in patients with metastatic or locally advanced, HER2-positive breast cancer patients previously treated with an anti-HER2 agent-based treatment plus chemotherapy.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0233/12: A randomized, phase I/II trial of neoadjuvant paclitaxel vs. BIBF112 priming followed by BIBF112 plus caplitaxel in HER-2 negative cancer with correlative proteomic and dynamic-image studies.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0235/12: A randomized, double-blind, phase III trial of PROSTVAC-V/F ± FEC-GM in patients with asymptomatic or minimally symptomatic castration-resistant prostate cancer.

PI: Dr/a Méndez Vidal, María Jose

0312/12: A multicenter, randomized, double-blind, placebo-controlled, phase III trial to assess the efficacy and safety of pertuzumab in combination with to assess the efficacy of trastuzumab and chemotherapy in patients with HER2-positive gastric and gastroesophageal junction cancer.

PI: Dr/a Aranda Aguilar, Enrique

0347/12: An open, randomized, multicenter, phase II trial to assess the toxicity and efficacy or pre-surgical chemotherapy with or without Bevacizumab in patients with advanced ovarian cancer.

PI: Dr/a Rubio Pérez, María Jesús

0363/12: An open, randomized, phase III trial of cisplatin and 5-FU with or without panitumumab for patients with nonresectable advanced or metastatic esophageal squamous cell cancer.

PI: Dr/a Aranda Aguilar, Enrique

0020/13: ARCHER 1050: A randomized, open, phase III study of the efficacy and safety of Dacomitinib (PF-00299804) vs. Gefitinib in first-line treatment of locally advanced or metastatic non-small cell lung cancer in patients with activating mutation(s) of the epidermal growth factor (EGF) receptor.

PI: Dr/a Barneto Aranda, Isidoro

0049/13: A randomized, double-blind, phase III study to assess the efficacy and safety of Gemcitabine in combination with TH-302 vs. Gemcitabine plus placebo in patients with locally advanced nonresectable pancreas adenocarcinoma.

PI: Dr/a Aranda Aguilar, Enrique

0059/13: A phase II study of regorafenib as single agent for first-line treatment of fragile patients with metastatic colorectal cancer and/or not candidates for polychemotherapy.

PI: Dr/a Aranda Aguilar, Enrique

65/13: Neoadjuvant chemotherapy with nab-paclitaxel in patients with high-risk her2-negative breast cancer.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

82/13: An open study of afatinib in naive patients (first-line) or patients previously treated with chemotherapy with locally advanced or metastatic non-small cell lung cancer and EGFR mutations.

PI: Dr/a Barneto Aranda, Isidoro

91/13: A randomized, double-blind, phase III study of Vintafolide (EC 145) in combination with pegylated liposomal doxorubicin (DLP/Doxil®/Caelyx®) vs. DLP in patients with platinum-resistant ovarian cancer.

PI: Dr/a Rubio Pérez, María José

0132/13: A multicenter, randomized, double-blind, placebo-controlled, phase III study of maintenance therapy with Olaparib alone in patients with BRCA-positive ovarian cancer or with platinum-sensitive relapsed ovarian cancer with complete response, or patients with EGFR activating mutations.

PI: Dr/a Rubio Pérez, María José

0136/13: A multicenter, randomized, double-blind, placebo-controlled, phase III study of maintenance therapy with Olaparib alone in patients with FIGO stage IIb-IV ovarian cancer with complete or partial response after platinum-based first-line chemotherapy.

PI: Dr/a Rubio Pérez, M<sup>a</sup> Jesús

0144/13: A randomized, multicenter, open, phase II/III study of nab<sup>®</sup>-paclitaxel administered weekly in combination with gemcitabine or carboplatin vs gemcitabine/carboplatin as first-line treatment in patients with RE-, RPg- and HER2-negative metastatic breast cancer (triple negative).

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0230/13: A randomized, double-blind, placebo-controlled, phase III study of adjuvant regorafenib vs. placebo in patients with IV stage colorectal cancer after curative treatment of liver metastasis.

PI: Dr/a Aranda Aguilar, Enrique

0252/13: An open, single-arm, pilot study to assess the association of the hormone resistance biomarkers and mTOR pathway with the clinical efficacy of everolimus plus letrozol in first-line treatment of postmenopausal women with nonresectable metastatic or locally advanced hormone-receptor positive breast cancer.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

0246/13: Abiraterona acetate maintenance in combination with docetaxel after disease progression to abiraterona acetate in metastatic castration resistant prostate cancer. Randomized phase II study.

PI: Dr/a Méndez Vidal, María Jose

0281/13: A study of the safety of repeating treatment with Radium-233 chloride in patients with castration-resistant prostate cancer with bone metastasis receiving an initial cycle with six 50 kBq/kg doses of Radium-233 chloride.

PI: Dr/a Méndez Vidal, María Jose

0012/09/EPA-SP: A prospective study to assess the prognostic and predictive value of response to drug treatment of focal adhesion kinase and other biomarkers in patients with advanced or metastatic renal cell carcinoma treated with sunitinib in first-line.

PI: Dr/a Méndez Vidal, María Jose

1134: Lifestyle and breast cancer risk in Spain.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

1759: A retrospective study of cases of patients with renal cell carcinoma or mantle cell lymphoma treated with Tamsinolimus.

PI: Dr/a Méndez Vidal, María José

1760: A prospective, observational study to determine circulating endothelial cell levels in patients with advanced clear-cell renal-cell carcinoma without radiological progression after three months of first-line treatment according to regular clinical practice.

PI: Dr/a Méndez Vidal, María José

1834: Assessing the usefulness of targeted drug management guides in renal cancer in clinical practice.

PI: Dr/a Méndez Vidal, María José

1894: A post-authorisation, observational study to assess the tolerability of Raltitrexed and the profile of patients treated with Raltitrexed alone or in combination with oxaliplatin (TOMOX) to treat advanced colorectal cancer following regular clinical practice.

PI: Dr/a Gómez España, María Auxiliadora

1988: A combined analysis of the genome wide association study and the microarray study (miarrn) for the identification of predictors of effectiveness of therapy with bevacizumab in patients with metastatic breast cancer.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

2030: Assessing rapid in situ mRNA (RISH<sup>TM</sup>) hybridization as a technique for detecting HER2 overexpression in breast cancer.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

2059: A study to assess arterial hypertension as a predictor of effectiveness of bevacizumab (BV) associated with chemotherapy in metastatic colorectal cancer and metastatic breast cancer.

PI: Dr/a Aranda Aguilar, Enrique

2081: Analysing the epidemiological characteristics of patients with metastatic renal cancer with long progression-free survival after receiving treatment with sunitinib.

PI: Dr/a Méndez Vidal, María Jose

2149: An observational, prospective study to assess the impact of determining the intrinsic subtypes of breast cancer with PAM50 using nanostring technology to use adjuvant chemotherapy in patients with hormone-receptor positive, node-negative breast cancer.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

2107: A retrospective study of the management of patients with metastatic colorectal cancer resistant to first-line oxaliplatin-based therapy.

PI: Dr/a Aranda Aguilar, Enrique

2172: An observational, retrospective, multicenter study to assess the clinical benefit of lapatinib in combination with trastuzumab in patients with HER2-positive metastatic breast cancer previously treated with trastuzumab and/or lapatinib in Spain.

PI: Dr/a De la Haba Rodríguez, Juan Rafael

2177: A retrospective, observational study to describe the management of patients with advanced or metastatic non-small cell lung cancer with EGFR mutations in Spain.

PI: Dr/a Barneto Aranda, Isidoro

2178: A post-authorisation, observational, prospective study to assess progression patterns of advanced EGFR-positive non-small cell lung cancer treated with erlotinib.

PI: Dr/a Barneto Aranda, Isidoro

2274: Circulating markers in patients with advanced or metastatic renal carcinoma on first-line treatment.

PI: Dr/a Méndez Vidal, María Jose

2235: An observational, prospective study to identify the management of patients with castration-resistant metastatic prostate cancer on second-line treatment after docetaxel in regular clinical practice.

PI: Dr/a Méndez Vidal, María Jose

2348: Register of rare sarcomas: A tool to assess the number of cases registered for each subtype and the therapeutic approach used by the Grupo Español de Investigación en Sarcomas (GEIS).

PI: Dr/a Barneto Aranda, Isidoro



# GC7

## Nephrology

### Cell Damage in Chronic Inflammation

#### Team Leaders

##### Principal Investigator (PI)

Pedro Aljama García  
[pedro.aljama.sspa@juntadeandalucia.es](mailto:pedro.aljama.sspa@juntadeandalucia.es)  
Renal Research Network (REINREN)  
PAIDI CTS-260 scientific group

##### Co-Principal Investigator (Co-PI)

Julia Carracedo Añón  
Nicolás Monardes Contract

##### Senior Researchers

M<sup>ª</sup> Luisa Agüera Morales  
M<sup>ª</sup> Antonia Álvarez de Lara Sánchez  
Mario Espinosa Hernández  
Alejandro Martín Malo  
Ana M<sup>ª</sup> Merino Rodríguez  
Alberto Rodríguez Benot  
Rafael Santamaría Olmo  
Sagrario Soriano Cabrera

##### Other members of the Group

(Other researchers, Technical, and Administrative Staff)  
F<sup>º</sup> Javier Ariza Fuentes  
Andrés Carmona Carpio  
Rodolfo Crespo Montero  
María López Andreu  
M<sup>ª</sup> José Jiménez Moral  
M<sup>ª</sup> Dolores Navarro Cabello  
M<sup>ª</sup> Rosa Moyano García

##### Post-doctoral Researcher

Paula Buendía Bello

##### Pre-doctoral Researcher

Carlos Luna Ruiz



## Scientific Activity

1.-The latest technological advances in the treatment of chronic kidney disease have helped minimize the inflammation associated with the disease and improve our patients' survival rates and quality of life. However, in these patients a microinflammatory state persists accompanied by a high percentage of activated cells that are capable of producing a sustained inflammatory response and can pro-

duce pathological complications when combined with other low-intensity stimuli. Our team assesses the effectiveness of pharmacological therapies, hemodialysis and kidney transplantation in improving this chronic microinflammatory state associated with kidney disease.

2.-Mechanisms of cell damage and repair conditioning the response to stress caused by chronic inflammation. The working model focuses on

immunocompetent cells and vascular wall cells. In addition, we analyze the mechanisms regulating the stress response in circulating progenitor cells in peripheral blood.

## Keywords

Cell activation, chronic renal failure, microinflammation, cell therapy, renal transplantation. Inflammation, cellular stress, genomic damage, endothelium.

## Publications

### Originals Publications

Martin-Malo A, Papadimitriou M, Cruz J, Bustamante J, Verbeelen D, Nony A, Vanholder R, Jacobson SH, Montenegro J, Hannedouche T, Wizemann V, Locatelli F, Outcome Mpo Study Group, For The Membrane Permeability. Geographical variability of patient characteristics and treatment patterns affect outcomes for incident hemodialysis patients. *Journal of Nephrology*. 2013, 26(1):119-128.  
IF: 2,015

Carracedo, J, Buendia, P, Merino, A, Soriano, S, Esquivias, E, Martin-Malo, A, Aljama, P, Ramirez, R. Cellular senescence determines endothelial cell damage induced by uremia. *Exp. Gerontol*. 2013, 48:766-773.  
IF: 3,911

Ariza, F, Merino, A, Carracedo, J, de Lara, MAA, Crespo, R, Ramirez, R, Martin-Malo, A, Aljama, P. Post-Dilution High Convective Transport Improves Microinflammation and Endothelial Dysfunction Independently of the Technique. *KARGER*. 2013, 35:270-278.  
IF: 2,062

Martinez-Vaquera S, Navarro Cabello MD, López-Andreu M, Jurado JM, Haad CR, Salas RO, Benot AR, Hernández JP, Arista JC, Aljama P. Outcomes in renal transplantation with expanded-criteria donors. *Transplant Proc*. 2013, 45:3595-3598.  
IF: 0,952

Haad CR, Rodríguez-Benot A, Martínez-Vaquera S, Navarro-Cabello MD, Agüera-Morales ML, Ruiz de Mier MV, Montero-Alvarez JL, Mata-García Mde L, Briceño-Delgado J, Aljama-García P. Combined Liver-Kidney Transplantation: Survey of a Single Center in Spain. *Transplant Proc*. 2013, 45:3640-3643.  
IF: 0,952

Gracia-Ahufinger I, Gutierrez-Aroca J, Cordero E, Vidal E, Cantisan S, del Castillo D, Martín-Gandul C, Rivero A, Torre-Cisneros J. Use of High-Dose Ganciclovir for the Treatment of Cytomegalovi-

rus Replication in Solid Organ Transplant Patients With Ganciclovir Resistance-Inducing Mutations. *Transplantation*. 2013, 95(8):1015-1020.  
IF: 3,781

Soriano S, Ojeda R, Rodríguez ME, Almadén Y, Martín-Malo A, Aljama P. The effect of phosphate binders, calcium and lanthanum carbonate on FGF23 levels in chronic kidney disease patients. *Clin Nephrol*. 2013, 80:17-22.  
IF: 1,288

Álvarez-Lara MA, Martín-Malo A, Aljama-García P. New alternatives in the treatment of myeloma. *Nefrología*. 2013, 33(4):443-7.kidney. PMID: 23897175.  
IF: 1,274.

García-Rubio JH, García JR, Hernández PC, López JM, Curado FA, Vallejo ML, López JC, Gómez EG, Aljama P, Tapia MJ. Correlation between dual kidney biopsy in expanded-criteria donors and transplant survival. *Transplant Proc*. 2013, 45(10):3606-3608.  
IF: 0,952

Pendón-Ruiz de Mier MV, Álvarez-Lara MA, Ojeda-López R, Martín-Malo A, Carracedo J, Caballero-Villarraso J, Alonso C, Aljama P. Effectiveness of haemodiafiltration with ultrafiltrate regeneration in the reduction of light chains in multiple myeloma with renal failure. *Nefrología*. 2013, 33:788-796.  
IF: 1,274

### Joint Publications

Gómez EG, Hernández JP, López FJ, García JR, Montemayor VG, Curado FA, Vallejo ML, López JC, Cabello MD, Aljama P, Tapia MJ. Long-term Allograft Survival After Kidney Transplantation. *Transplant Proc*. 2013, 45(10):3599-3602.  
IF: 0,952

Cantisán S, Lara R, Montejo M, Redel J, Rodríguez-Benot A, Gutiérrez-Aroca J, González-Padilla M, Bueno L, Rivero A, Solana R, Torre-Cisneros J. Pretransplant Interferon- Secretion by CMV-Specific CD8+T Cells Informs the Risk of CMV

Replication After Transplantation. *Am J Transplant*. 2013, 13:738-745.  
IF: 6,192

Praga, M, Merello, JI, Palomares, I, Bayh, I, Marcelli, D, Aljama, P, Luno, J. Type of Vascular Access and Survival among Very Elderly Hemodialysis Patients. *Nephron Clin Pract*. 2013, 124:47-53.  
IF: 1,651

Campistol JM, Arias M, Ariceta G, Blasco M, Espinosa M, Grinyo JM, Praga M, Torra R, Vilalta R, de Córdoba SR. An update for atypical haemolytic uraemic syndrome: diagnosis and treatment. A consensus document. *Nefrología*. 2013, 33(1):27-45.  
IF: 1,274

Alfaro AG, Hernández PC, Gómez EG, García JR, Carazo JL, López FM, Curado FJ, Vallejo ML, López JC, Aljama P, Tapia MJ. Variations in initial renal transplant function by type of organ retrieval. *Transplant Proc*. 2013, 45(10):3603-3605.  
IF: 0,952

Mazuecos, A, Fernandez, A, Zarraga, S, Andres, A, Rodríguez-Benot, A, Jimenez, C, Gomez, E, Paul, J, Jimeno, L, Fernandez, C, Burgos, D, Sanchez-Fructuoso, A, Guirado, L. High incidence of delayed graft function in HIV-infected kidney transplant recipients. *Transpl Int*. 2013, 26:893-902.  
IF: 3,155

Locatelli, F, Hannedouche, T, Martin-Malo, A, Jacobson, SH, Vanholder, R, Ronco, C, La Milia, V, Gomez, JML, Stefoni, S, Maheut, H, Klinger, M, Krummel, T, Dhondt, A, Berdud, I, Gauly, A. The Relationship of NT-proBNP and Dialysis Parameters with Outcome of Incident Haemodialysis Patients: Results from the Membrane Permeability Outcome Study. *Blood Purif*. 2013, 35:216-223.  
IF: 2,061

Palomares I, Ramos R, Martín-Malo A, Merello JI, Praga M, Luño J, de Francisco AL. ORD group. Compliance with Mineral Metabolism Targets in Haemodialysis Patients: Moving Backwards?. *Blood Purif*. 2013, 36(2):122-131.  
IF: 2,061

Maduell F, Ramos R, Palomares I, Martín-Malo A, Molina M, Bustamante J, Pérez-García R, Grassmann A, Merello JI, ORD group. Impact of targeting Kt instead of Kt/V. *Nephrol Dial Transplant*. 2013, 28:2595-2603. IF: 3,371

Herrero JA, López-Gómez JM, Maduell F, Martín-de Francisco AL, Martín-Malo A, Martínez-Castelao A, Navarro-González JF, Pérez-Fontán M, Pérez J, Selgas R, Solozabal C. Activation of vitamin D receptors in the optimization of hyperparathyroidism secondary to dialysis. *Nefrología*. 2013, 33:571-584. IF: 1,274

Campistol JM, Carreno A, Morales JM, Pallardo L., Franco A, Navarro D, Grinyo JM, Montenegro J, Fructuoso AIS, Romero R, Guirado L, Arias M. Once-Monthly Pegylated Epoetin Beta Versus Darbepoetin Alfa Every Two Weeks in Renal Transplant Recipients: A Randomized Trial. *Transplantation*. 2013, 95(2); E6-E10 IF: 4,003

## Research Projects

Martin Malo, A. Effect of the purification efficiency of different dialysis modalities on inflammation and endothelial damage. Sponsored body: Institute Carlos III Health (ISCIII). Reference: 10/00960

Aljama García, P. Endothelial damage in patients with chronic renal failure: cellular therapy. Sponsored body: Regional Ministry of Economy, Innovation, Science and Employment (CEICE) Reference: P08-CTS-03797

Carracedo Añón, J. Modulating role of endothelial microparticles in the development of endothelial damage, Arteriosclerosis and vascular calcification. Sponsored body: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: CTS-7352

Carracedo Añón, J. Inflammation and calcifying vascular disease in uremia. Sponsored body: Institute Carlos III Health (ISCIII). Reference: PI12/01489

Santamaria Olmo, R. Modulation of endothelial damage and repair mediators through the inhibition of xanthine oxidase in patients with chronic kidney disease. A cross-over, double-blind, placebo-controlled study. Sponsored body: Institute Carlos III Health (ISCIII). Reference: PI12/01866

Aljama García, P. Red de Investigación Renal (Renal Research Network (REINREN)). Sponsored body: Institute Carlos III Health (ISCIII). Reference: RD12/0021/0011

## Clinical Trials

0113/06: An open, multicenter, randomized, 2-year follow-up study to assess the effect of suppressing calcineurin inhibitors and introducing

everolimus early in renal transplant recipients. PI: Dr/a Aljama García, Pedro

0155/06: Assessing treatment with Cinacalcet HCl to reduce cardiovascular events PI: Dr/a Martín Malo, Alejandro

0097/07: Utility of rapamycin for secondary prevention of skin tumors in renal transplant recipients with recurrent squamous cell carcinoma. PI: Dr/a Navarro Cabello, M<sup>a</sup> Dolores

0242/10: An open, multicenter, trial of eculizumab in adult patients with atypical hemolytic uremic syndrome. PI: Dr/a Espinosa Hernández, Mario

0256/10: An open, multicenter, randomized, two-arm trial to investigate de novo diabetes mellitus in renal transplant recipients receiving an advagraf-based immunosuppressive regime with or without corticosteroids. ADVANCE. PI: Dr/a Rodríguez Benot, Alberto

0209/11: Effect of Paricalcitol on albuminuria, inflammation and fibrosis in patients with chronic proteinuric renal disease: A randomized controlled trial. PI: Dr/a Soriano Cabrera, Sagrario

0083/13: A randomized, prospective, open, parallel-group, multicenter study with masked assessment of evaluation criteria (PROBE1 Design) to compare the efficacy of administering enalapril 20 mg plus lercanidipine. PI: Dr/a Santamaria Olmo, Rafael

0096/13: A randomized, cross-over, double-blind, placebo-controlled study. Modulation of endothelial damage and repair mediators through the inhibition of xanthine oxidase in patients with chronic kidney disease. PI: Dr/a Santamaria Olmo, Rafael

0102/13: Efficacy and safety of paricalcitol in reducing secondary hyperparathyroidism after kidney transplantation. PI: Dr/a Rodríguez Benot, Alberto

0190/13: An international, multicenter, randomized, double-blind, parallel-group, placebo-controlled study of the effect of atrasentan on kidney outcomes in subjects with diabetes type 2 and nephropathy. SONAR: trial of diabetic nephropathy. PI: Dr/a Santamaria Olmo, Rafael

0219/13: A randomized, multicenter, parallel-group, active-controlled, dose-ranging, phase 2B study to assess the dose-response relation of GSK1278863 within the first four weeks of treatment, and assess the safety and efficacy of GSK1278863 for 24 weeks in patients with anaemia associated with chronic kidney disease requiring hemodialysis receiving recombinant human erythropoietin. PI: Dr/a Álvarez de Lara Sánchez, M<sup>a</sup> Antonia

0221/13: A randomized, multicenter, parallel-group, active-controlled, phase 2B, 24-week

duration study to assess the safety and efficacy of GSK1278863 in patients with anaemia associated with chronic kidney disease not receiving dialysis. PI: Dr/a Sagrario Soriano, María

0263/13: An observer-blind study to assess the immunogenicity and safety of GSK Biologicals' subunit GSK1437173A vaccine against Herpes Zoster (HZ/su) in kidney transplantation recipients aged >18. PI: Dr/a Agüera Morales, M<sup>a</sup> Luisa

1643: An observational, multicenter, retrospective study to assess the impact of nephrectomy in the evolution of the second kidney transplantation. PI: Dr/a Rodríguez Benot, Alberto

1734: An observational, retrospective review of medical records to analyze changes in calcium levels after the administration of cinacalcet in patients with persistent secondary hyperparathyroidism after renal transplantation. PI: Dr/a Rodríguez Benot, Alberto

1747: Impact of screening, monitorization and reduction of immunosuppression on viral replication and incidence of VBK-associated nephropathy. PI: Dr/a Rodríguez Benot, Alberto

1757: A post-commercialization observation study to monitor the clinical use of Renvela® in hyperphosphatemic adult patients with chronic renal failure not receiving dialysis with serum phosphorus concentrations > 1.78 mmol / l. PI: Dr/a Soriano Cabrera, Sagrario

1761: A multicenter, epidemiological, prospective, observational study to assess the incidence of cytomegalovirus-induced disease and associated risk factors in Receptor + renal transplant recipients. PI: Dr/a Navarro Cabello, M<sup>a</sup> Dolores

1762: National Registry of Humoral Rejection: An epidemiological, multicenter, observational, prospective study to assess the clinical, serological and histological characteristics and five-year evolution of humoral rejection after renal transplantation in Spain. PI: Dr/a Agüera Morales, M<sup>a</sup> Luisa

1855: A multicenter, prospective, observational study to analyze progression factors in chronic renal disease in diabetic patients vs non-diabetic patients. PI: Dr/a Santamaria Olmo, Rafael

1971: A multicenter, retrospective, observational study to assess long-term renal function in renal transplant recipients converted from a tacrolimus-based immunosuppressive treatment of immediate release (Prograf) to tacrolimus. PI: Dr/a Rodríguez Benot, Alberto

# GC8

## Hormones and Cancer

### Team Leaders

#### Principal Investigator (PI)

Justo P. Castaño Fuentes

[justo@uco.es](mailto:justo@uco.es)

CIBER on Obesity and Nutrition (CIBERObn) (Collaborator)

#### Co-Principal Investigator (Co-PI) 1

Francisco Gracia Navarro

PAIDI BIO-139 scientific group

#### Co-Principal Investigator (Co-PI) 2

Raúl M. Luque Huertas

#### Senior Researcher

Antonio Jesús Martínez Fuentes

#### Post-doctoral Researchers

Jose Córdoba Chacón

Antonio Moreno Herrera

#### Pre-doctoral Researchers

M<sup>º</sup> Carmen Vázquez Borrego

Daniel Hormaechea Agulla

Alejandro Ibáñez Costa

David Rincón Fernández-Pacheco

Alicia Villa Osaba

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)

Esther Rivero Cortes

M<sup>º</sup> Amparo Gomez Elices



## Scientific Activity

Our group investigates the cellular and molecular principles underlying the natural processes of neuroendocrinometabolic regulation and their dysfunctions in tumour diseases and cancer, paying special attention to the role played by some neuropeptide systems such as somatostatin, cortistatin, ghrelin, kisspeptins and their receptors. Starting from the study of pituitary somatotropes producing the growth hormone (GH), our group has developed a Research Area focused on the analysis of extracellular signals (somatostatin, cortistatin, GHRH, ghrelin, Kisspeptins, etc.), receptors (sst1-5, GHRH-R, GHS-R, Kiss1r) and signalling pathways involved in the regulation of this cell

type, as well as other endocrine cell types (eg corticotropes, gonadotropes, pancreatic beta cells) and the global role of these molecules in metabolic homeostasis and the development of tumour pathologies.

To achieve this, we use a wide range of techniques, including primary cultures of normal and tumour cells, cell lines, genetically modified animals, hormone secretion measurements, second messengers and gene expression, dynamics association/dissociation studies and membrane protein trafficking using FRET, confocal microscopy in living cells, and so on. Our studies have led to the discovery and characterization of new receptors, functions and mechanisms of action for different neuroendocrinometabolic signals and drugs

involved in the control of hormone secretion, tumorigenesis, or cell survival and death in various normal and pathological cell types (eg, pituitary tumours, breast cancer, diabetes, obesity), with the ultimate aim of contributing to the future design of innovative therapeutic strategies.

### Keywords

Cellular and Molecular Endocrinology. Hypothalamic-hypophysis. Somatostatin, cortistatin, ghrelin, GHRH and Kisspeptins and their receptors. Expression and secretion of hormones (GH, LH) and intracellular signalling systems. Regulation of the somatotropic and gonadotropic-reproductive axes. Hypophysary tumours. Breast cancer.

## Publications

### Originals Publications

Luque RM, Ibáñez-Costa A, López-Sánchez L, Jiménez-Reina L, Venegas-Moreno E, Gálvez M, Villa-Osaba A, Madrazo-Atutxa A, Japon M, de la Riva A, Cano D, Benito-López P, Soto-Moreno A, Gahete M, Leal-Cerro A, Castaño J. A Cellular and Molecular Basis for the Selective Desmopressin-Induced ACTH Release in Cushing Disease Patients: Key Role of AVPR1b Receptor and Potential Therapeutic Implications. *J Clin Endocrinol Metab.* 2013, 98(10):4160-4169. IF:6,429

Chanclon B, Luque RM, Córdoba-Chacon J, Gahete MD, Pozo-Salas AI, Castaño JP, Gracia-Navarro F, Martínez-Fuentes AJ. Role of Endogenous Cortistatin in the Regulation of Ghrelin System Expression at Pancreatic Level under Normal and Obese Conditions. *PLoS One.* 2013, 8(2):e57834-. IF:3,73

Córdoba-Chacon J, Gahete MD, Pozo-Salas AI, Castaño JP, Kineman RD, Luque RM. Endogenous Somatostatin Is Critical in Regulating the Acute Effects of L-Arginine on Growth Hormone and Insulin Release in Mice. *Endocrinology.* 2013, 154(7):2393-2398. IF:4,717

### Joint Publications

Gahete MD, Córdoba-Chacon J, Luque RM, Kineman RD. The Rise in Growth Hormone during Starvation Does Not Serve to Maintain Glucose Levels or Lean Mass but Is Required for Appropriate Adipose Tissue Response in Female Mice.

*Endocrinology.* 2013, 154(1):263-269. IF:4,717

Gahete MD, Córdoba-Chacón J, Lin Q, Brüning JC, Kahn CR, Castaño JP, Christian H, Luque RM, Kineman RD. Insulin and IGF-I inhibit GH synthesis and release in vitro and in vivo by separate mechanisms. *Endocrinology.* 2013, 154(7):2410-2420. IF:4,717

García-Arnes JA, Gonzalez-Molero I, Oriola J, Mazoncos N, Luque R, Castano J, Arraez MA. Familial Isolated Pituitary Adenoma Caused by a Aip Gene Mutation not Described Before in a Family Context. *Endocr Pathol.* 2013, 24(4):234-238. IF:1,600

Duran-Prado M, Morell M, Delgado-Maroto V, Castaño JP, Aneiros-Fernandez J, de Lecea L, Culler MD, Hernandez-Cortes P, O'Valle F, Delgado M. Cortistatin Inhibits Migration and Proliferation of Human Vascular Smooth Muscle Cells and Decreases Neointimal Formation on Carotid Artery Ligation. *Circulation Res.* 2013, 112(11):1444-+. IF:11,861

Lubbers ER, List EO, Jara A, Sackman-Sala L, Córdoba-Chacon J, Gahete MD, Kineman RD, Boparai R, Bartke A, Kopchick JJ, Berryman DE. Adiponectin in mice with altered GH action: links to insulin sensitivity and longevity?. *J Endocrinol.* 2013, 152(12):4800-4812. IF:4,057

Pulido MR, Rabanal-Ruiz Y, Almabouada F, Diaz-Ruiz A, Burrell MA, Vazquez MJ, Castaño JP, Kineman RD, Luque RM, Dieguez C, Vázquez-Martínez R, Malagón MM. Nutritional, hormonal, and depot-dependent regulation of the expression of the small GTPase Rab18 in rodent adipose tis-

sue. *J Mol Endocrinol.* 2013, 50(1):19-29. IF:3,577

Souza-Moreira L, Morell M, Delgado-Maroto V, Pedreno M, Martínez-Escudero L, Caro M, O Valle F, Luque R, Gallo M, de Lecea L, Castaño JP, Gonzalez-Rey E. Paradoxical Effect of Cortistatin Treatment and Its Deficiency on Experimental Autoimmune Encephalomyelitis. *J Immunol.* 2013, 191(5):2144-2154. IF:5,520

Díaz-Ruiz A, Rabanal-Ruiz Y, Trávez A, Gracia-Navarro F, Cruz-García D, Montero-Hadjadje M, Anouar Y, Gasman S, Vitale N, Vázquez-Martínez R, Malagón MM. The Long Coiled-Coil Protein NECC2 Is Associated to Caveolae and MODULATES NGF/TrkA Signaling IN PC12 CELLS. *PLoS One.* 2013, 8(9):e73668. IF:3,73

Oberg K, Casanovas O, Castaño JP, Chung D, Delle Fave G, Deneffe P, Harris P, Khan MS, Kulke MH, Scarpa A, Tang LH, Wiedenmann B. Molecular Pathogenesis of Neuroendocrine Tumors: Implications for Current and Future Therapeutic Approaches. *Clin Cancer Res.* 2013, 19:2842-2849. IF:7,837

### Research Projects

Castaño Fuentes JP. Role of Somatostatin, cortistanina and ghrelin in the pathological interaction between obesity and breast cancer. Sponsored by: Ministry of Economy and Competitiveness (MINECO). Reference: BFU2010-19300

Luque Huertas RM. Functional role and therapeutic potential of aberrant splicing variants of the ghrelin system (in1-ghrelin/ghs-r1b) and of

the somatostatin receptor 5 (sst5tmd4 / 5) in pituitary tumors and in breast and prostate cancer. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS).Reference: PI-0639-2012

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Luque Huertas RM. Identifying new molecular targets of the regulatory systems of somatostatin, ghrelin and its receptors in human pituitary pathologies: Presence, role and functional potential. Sponsored by: Merck Serono Research Grants. Reference: CCB.0052

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Gracia Navarro F. Grants: Cellular and Molecular Endocrinology scientific Group (BIO-139). Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE).

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### Third Party Services

Castaño Fuentes JP; Luque Huertas RM. Truncated sst5TMD4/5 receptors in neuroendocrine tumors, prostate cancer and Cushing disease: functional role and potential therapeutic value. Sponsored by: IPSEN-SCRAS S.A.S.

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Castaño Fuentes JP; Luque Huertas RM. In1-ghrelin, a novel aberrantly spliced ghrelin variant, GOAT and GHSR1a and GHSR1b in neuroendocrine tumors, prostate cancer and Cushing disease: presence, function and therapeutic potential. Sponsored by: IPSEN-SCRAS S.A.S.

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### Collaboration Agreements

Castaño Fuentes JP; Martínez Fuentes, J. Characterization of gene expression in gastroenteropancreatic neuroendocrine tumors and its correlation with clinical aspects and behavior of the tumor. Sponsored by: Grupo Español de Tumores Neuroendocrinos (Getne).Reference: CCB.UCO0053

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# GC9

## Nutrigenomics. Metabolic Syndrome

### Team Leaders

#### Principal Investigator (PI)

José López Miranda  
jlopezmir@gmail.com  
CIBER on Obesity and Nutrition (CIBERObn)  
PAIDI CTS-525 scientific Group

#### Co-Principal Investigator (Co-PI)

Francisco Pérez Jiménez.  
IMIBIC's Scientific Director  
PAIDI CTS-212 scientific group

#### Senior Researchers

M<sup>o</sup> Ángeles Blanco Molina  
Francisco Javier Delgado Lista  
Rafael Á. Fernández de la Puebla  
Francisco Fuentes Jimenez  
Francisco Gomez Delgado  
Luciano Lopez Jimenez  
Manuel Montero Perez-Barquero  
Anabel Perez Caballero  
Pablo Perez Martinez  
Oriol Alberto Rangel Zuñiga  
Esther Sanchez Garcia  
Elena Yubero Serrano  
Yolanda Almaden Peña

#### Post-doctoral Researchers

Antonio Camargo García  
Juan Criado García

Cristina Cruz Teno  
Nieves Delgado Casado  
Manuel David Gahete Ortiz<sup>(I)</sup>  
M<sup>o</sup> de Mar Gámez del Estal  
Antonio García Ríos  
Purificación Gómez Luna  
Anabel Jiménez Morales  
Carmen Marín Hinojosa<sup>(II)</sup>

#### Pre-doctoral Researchers

J. Francisco Alcalá Díaz  
Andreaa Corina Baba  
Francisco Gómez Delgado  
Sonia García Carpintero  
Lorena González de la Guardia<sup>(IV)</sup>  
Carmen M<sup>o</sup> Haro Mariscal<sup>(III)</sup>  
Luis Mateo Pino López

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)  
Rosario Carreras Calero  
Luciano López Jiménez  
Vanesa Navarro Martos  
Gracia M<sup>o</sup> Quintana Navarro  
Carmen Ruiz Valencia  
Amalia Torres Roldan  
Rosa Jimenez Lucena  
Magdalena Romero Jiménez

(I) Contract Sara Borrel. (II) Contract Miguel Servet. (III) Contract PFIS. (IV) Contract FPI



## Scientific Activity

Our group studies the effect of dietary components on cardiovascular risk from a dual approach: nutrigenetics and their biological action on factors and mechanisms related to the development of atherosclerosis, preferably in patients with metabolic syndrome. Through nutrigenetics, we investigate how common genetic variants modulate the influence of diet on markers

such as postprandial metabolism, endothelial function, obesity or glucose metabolism. While investigating their biological effects, we analyze the action of nutrients on atherogenic mechanisms such as oxidative stress, inflammation, endothelial function, hemostasis, cellular signalling mechanisms and the activation of genes involved in atherogenesis.

## Keywords

Atherosclerosis, metabolic syndrome, Mediterranean diet, endothelium, inflammation, oxidative stress, cholesterol, polyphenols, gene expression, proteomics, nutrigenetics, nutrigenomics.

## Publications

### Originals Publications

Peña-Orihuela P, Camargo A, Rangel-Zuñiga OA, Perez-Martinez P, Cruz-Teno C, Delgado-Lista J, Yubero-Serrano EM, Paniagua JA, Tinahones FJ, Malagón MM, Roche HM, Perez-Jimenez F, López-Miranda J. Antioxidant system response is modified by dietary fat in adipose tissue of metabolic syndrome patients. *J Biomech Nutri.* 2013, 24 (10):1717-1723.  
IF: 4,552

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## Joint Publications

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## Research Projects

Pérez Jiménez, F. Formalization of Economic Compensation Agreement. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO) Reference MCL.CIBEROBN

Pérez Jiménez, F. Biomodulatory effects of olive oil on the molecular mechanisms of inflammation and oxidative stress in patients with metabolic syndrome. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference P09-CTS-5015

Pérez Martínez, P. Characterization of the genetic architecture of metabolic syndrome related to the inflammatory response and interaction with the Mediterranean diet. Sponsored by: Regional Ministry of Health and Social Policy (CISPS). Reference:0058/2010

Pérez Martínez, P. Nutrigenetics in lipid and inflammatory response in patients with metabolic syndrome. Comparative effect of a Mediterranean diet rich in olive oil versus a low fat diet: Cordioprev study. Sponsored by: Institute Carlos III Health (ISCIII). Reference:10/01041

Pérez Jiménez, F. Influence of the bacterial population of the digestive system (microbiota) in the degree of endotoxemia, inflammation and insulin resistance in patients with metabolic syndrome after two healthy diet models: a low fat and a Mediterranean diet. Sponsored by: Institute Carlos III Health (ISCIII). Reference 10/02412

Marín Hinojosa, C. Nutrigenomics and new biomarkers involved in endothelial dysfunction associated with cellular aging and risk of cardiovascular disease, according to dietary. Sponsored by: Institute Carlos III Health (ISCIII). Reference:CP11/00185

López Miranda, J. Effect of a Mediterranean diet rich in virgin olive oil on the risk and incidence of Type 2 Diabetes Mellitus: Cordioprev-diab. study. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO). Reference:AGL2012-39615

López Miranda, J. Nutrigenomic Analysis of the effect of a Mediterranean diet rich in virgin olive oil on endothelial damage and regenerative capacity and its predictive value in cardiovascular risk. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference CVI-7450

Fuentes Jiménez, F. Evaluation and Characterization of Coronary Atherosclerosis. Sponsored by: Institute Carlos III Health (ISCIII). Reference:PI12/01461

López Miranda, J. Application of new technologies and tools to nutrition research—the example of phenotypic flexibility. NUTRITECH. Sponsored by: European Union 7th Framework Program. Reference FP7-KBBE-2011-5

Almadén Peña, Y. Role of angiotensin II (All) and system PDGF / PDGFR in vascular calcification associated with renal failure. Sponsored by: Institute Carlos III Health (ISCIII). Reference 10/01311

Delgado Lista, FJ. Glucogene project: developing a clinical tool for the identification, staging and individualized non-pharmacological treatment of coronary patients with high genetic risk of developing alterations in the metabolism of carbohydrates. Sponsored by: Institute Carlos III Health (ISCIII). Reference:PI13/00023

Pérez Martínez, P. Developing a technological platform to evaluate the ageing level and establish an individualized treatment regime based on the clinical, biological and genetic profile of the patient. Sponsored by: Institute Carlos III Health (ISCIII). Reference:PI13/00185 2014 Annuity

García Ríos, A. Influence of clock-genes and diet in the ethiopathogeny of the metabolic syndrome: New clinical approach. Sponsored by: Regional Ministry of Health and Social Policy (CISPS). Reference:PI-0206-2013 2014 Annuity

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Pérez Jiménez, F. Identifying the bowel microbiota pattern to predict the development of the metabolic syndrome and diet-based modulation. Sponsored by: Institute Carlos III Health (ISCIII). Reference:PI13/00619 2014 Annuity

## Third Party Services

Pérez Jiménez, F. R & D contract between the Andalusian Design Technology Center and the Foundation for Biomedical Research of Cordoba for conducting a research project. Sponsored by: Foundation Center Design Andalusian Technology. Reference:PSS.0001

Pérez Martínez, P. Merck Serono research grant to the study: Characterization of the genetic architecture of metabolic syndrome related to the inflammatory response and interaction with the Mediterranean diet. Sponsored by: Fundación Salud 2000. Reference:PSS.0004

Pérez Jiménez, F. Nutritional Intervention Study to assess the evolution of health benefits de-

rived from the consumption of hake in populations at high cardiovascular risk. PESCANOVA project. Sponsored by: Centro de Investigación Biomédica en Red de la Fisiopatología de la Obesidad y Nutrición (CIBER on Obesity and Nutrition (CIBERObn)). Reference:PSS.0011

López Miranda, J. Services Agreement TNO-FIBICO. Sponsored by: Tno Earth, Environmental and L.S. Reference:PSS.0014

## Collaboration Agreements

López Miranda, J. Astrazeneca agreement. Sponsored by: Astrazeneca Farmaceutica Spain S.A. Reference:CCB.0046

López Miranda, J. Study based on effects on health about a good healthy confectionery. Sponsored by: Astrazeneca Farmaceutica Spain S.A. Reference:CCB.UCO0052

## Clinical Trials

0021/08: Two-year extension of a global, multicenter, randomized, placebo-controlled, 76-week study to assess the tolerability and effectiveness of anacetrapib added to an ongoing statin-based treatment in patients with heart disease or equivalent risk of developing a heart disease. Extension of the reversibility period from 12 weeks to one year.

PI: Dr/a Pérez Jiménez, Francisco

0117/10: A multicenter, randomized, double-blind, placebo-controlled phase II trial to investigate the effectiveness and safety of liposomal aerosolized cyclosporine 10 and 20 mg daily (L-CsA) versus aerosolized placebo in the prevention of obliterant bronchiolitis syndrome in lung recipients.

PI: Dr/a Vaquero Barrios, Jose Manuel

0094/11: A long-term, randomized, parallel-group, double-blind, placebo-controlled phase III assay to assess the safety and effectiveness of eprotromb 50 mg and 100 mg / day in patients with heterozygous familial hypercholesterolemia on adequate standard treatment.

PI: Dr/a Pérez Jiménez, Francisco

0114/11: A multicenter, placebo-controlled, randomized, double-blind study to assess tolerability and effectiveness AMG 145 in LDL cholesterol in patients with heterozygous familial hypercholesterolemia.

PI: Dr/a López Miranda, Jose

0159/11: Open label extension (OLE), controlled, multicenter study to assess the safety and long-term efficacy of AMG 145.

PI: Dr/a López Miranda, Jose

0267/11: A global, multicenter, double-blind, randomized, parallel-group, placebo-controlled, one-year study to assess the effectiveness and tolerability of Anacetrapib added to an ongoing statin-based treatment, combined or not with

other lipid modifying agents in patients with heterozygous familial hypercholesterolemia.  
PI: Dr/a López Miranda, Jose

0014/12: Long-term safety and tolerability profile of REGN727/SAR236553 in patients at high cardiovascular risk with inadequately controlled hypercholesterolemia with a lipid-modifying therapy: A randomized, double-blind, controlled study.  
PI: Dr/a Pérez Jiménez, Francisco

0136/12: A multicenter, randomized, double-blind study to assess the safety and efficacy of AMG 145, compared with ezetimibe in hypercholesterolemic subjects intolerant to an effective dose of an HMG-CoA reductase inhibitor.  
PI: Dr/a López Miranda, Jose

0139/12: Multicenter, randomized, double-blind, placebo-controlled study to assess the safety, tolerability and efficacy of AMG 145 in LDL cholesterol in subjects with heterozygous familial hypercholesterolemia.  
PI: Dr/a López Miranda, Jose

0166/12: A multicenter, randomized, double-blind, placebo-controlled study to assess the effect of a further reduction of LDL cholesterol in major cardiovascular events when AMG 145 is used in combination with statins in patients with clinically evident heart disease.  
PI: Dr/a López Miranda, Jose

0183/12: A multicenter, double-blind, placebo-controlled, parallel-group study to assess the effectiveness and safety of SAR236553/REGN727 in patients with heterozygous familial hypercholesterolemia that is not adequately controlled with their treatment.  
PI: Dr/a Pérez Jiménez, Francisco

0231/12: Evaluation of the clinical effects of cholesteryl ester transfer protein inhibition induced with evacetrapib in patients at a high cardiovascular risk.  
PI: Dr/a Pérez Jiménez, Francisco

0346/12: A multicenter, randomized, double-blind, double-simulation, parallel-group, active-control, 52-week study of the effect of QVA149 versus salmeterol/fluticasone.  
PI: Dr/a Delgado Lista, Javier

0032/13: A multicenter, open study to assess the safety, tolerability and long-term efficacy of AMG 145 in C-LDL cholesterol in subjects with severe heterozygous familial hypercholesterolemia.  
PI: Dr/a Fuentes Jiménez, Francisco

0033/13: A two-part, phase2/3 study to assess the safety, tolerability and long-term efficacy of AMG 145 in subjects with heterozygous familial hypercholesterolemia.  
PI: Dr/a Fuentes Jiménez, Francisco

0086/13: An open label extension (OLE), controlled, multicenter study to assess the safety and long-term efficacy of AMG 145.  
PI: Dr/a López Miranda, Jose

0223/13: A multicenter, double-blind, placebo-controlled, parallel-group study to assess the effectiveness and safety of Alirocumab in statin-naive patients with primary heterozygous familial hypercholesterolemia.  
PI: Dr/a Fuentes Jiménez, Francisco

0282/13: A randomized, double-blind, double-blind, placebo-controlled, parallel-group, 52-week study to assess the efficacy, safety and tolerability of PF-04950615 in patients with heterozygous familial hypercholesterolemia.  
PI: Dr/a Pérez Martínez, Pablo

0295/13: A randomized, multicenter, double-blind, double-blind, placebo-controlled, parallel-group study to assess the efficacy, safety and tolerability of PF-04950615 in reducing the number of severe cardiovascular events in high-risk patients.  
PI: Dr/a Pérez Martínez, Pablo

0296/13: A randomized, multicenter, double-blind, double-blind, placebo-controlled, parallel-group study to assess the efficacy, safety and tolerability of PF-04950615 in reducing the number of severe cardiovascular events in high-risk patients.  
PI: Dr/a Pérez Martínez, Pablo

0314/13: A randomized, multicenter, double-blind, placebo-controlled, parallel-group study of the effects of Canagliflozin in renal events in adult subjects with Diabetes Mellitus Type 2.  
PI: Dr/a Fuentes Jiménez, Francisco

0001: Pulmonary hypertension-associated risk factors (PHI study).  
PI: Dr/a Vaquero Barrios, Jose Manuel

1972: An epidemiological study on the current status of patients with type I Gaucher disease in Spain, as assessed by the Therapeutic Goals MAP (Monitor, Action and Progress) Tool ©.  
PI: Dr/a Fernández De la Puebla Giménez, Rafael Angel

2053: Xalixa-Xarelto ® for initial long-term anticoagulation in venous thromboembolism (VTE).  
PI: Dr/a Blanco Molina, M<sup>a</sup> Angeles

2239: Prevention of thromboembolia episodes/ European Registry of venous thromboembolia. ESTUDIO PREFER study of VTE.  
PI: Dr/a López Jiménez, Luciano

2239/0: Prevention of thromboembolia episodes/ European Registry of venous thromboembolia. ESTUDIO PREFER study of VTE.  
PI: Dr/a Blanco Molina, M<sup>a</sup> Angeles

# GC10

## Hormonal Regulation of Energy Balance, Puberty and Reproduction

### Team Leader

#### Principal Investigator (PI)

M. Tena-Sempere

[fi1tesem@uco.es](mailto:fi1tesem@uco.es)

IMIBIC'S Deputy Scientific Director

CIBER on Obesity and Nutrition (CIBERObn)

PAIDI BIO-310 scientific group

#### Senior Researchers

Leonor Pinilla, Francisco Gaytan

#### Post-doctoral Researchers

Juan Castellano

David Garcia-Galiano

Juan Roa Rivas

Maria Jesús Vazquez Villar

Antonio Romero Ruiz

Rafael Pineda Reyes

#### Pre-doctoral Researchers

Miguel A. Sanchez-Garrido

Maria Manfredi Lozano

Silvia Leon Tellez

Alexia Barroso Romero

Violeta Heras Hernandez

Francisco Ruiz Pino

Inmaculada Velasco

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)

Maria Jesús Sanchez Tapia

Rocio Onieva

Ana Belen Rodríguez Sanchez

Ana Belen Pedraza Casado

Aurora Zamora Perez



Rafael A. Butelo

## Scientific Activity

Our research group studies the neuroendocrine mechanisms responsible for the integrated control of food intake, body weight, puberty and reproductive function. By using various analytical methods and animal models, in recent years our group has identified new neuropeptides and hormones involved in the joint regulation of metabolic status and reproduction. Thus, we have made substantial contributions to the characterization of the physiological role, mechanisms of action, and patho-

physiological and therapeutic implications of kisspeptins in the control of puberty, ovulation and the secretion of gonadotropins. In addition, we have characterized the actions of different gastrointestinal hormones (ghrelin, PYY) and adipose tissue (leptin, resistin, adiponectin), as well as the control of food intake and reproductive function. Additionally, we have defined the role in the reproductive axis of the different neuropeptides (GALP, neuropeptides, 26/43RFa, VGF) primarily involved in the control of food intake. Even when our research activity is basic in nature, this has allowed us to

identify mechanisms of action and pharmacological effects of practical interest for a broad group of neuroendocrine factors with the potential translational results in the context of increasingly prevalent diseases such as obesity and other body weight disorders, changes of puberty and various forms of infertility.

## Keywords

Body weight, obesity, puberty, fertility, kisspeptins, GPR54, gonadotropins, GnRH, leptin, ghrelin, adipokines, neuropeptides.

## Publications

### Originals Publications

Sangiao-Alvarellos S, Manfredi-Lozano M, Ruiz-Pino F, Navarro VM, Sanchez-Garrido MA, Leon S, Dieguez C, Cordido F, Matagne V, Dissen GA, Ojeda SR, Pinilla L, Tena-Sempere M. Changes in Hypothalamic Expression of the Lin28/let-7 System and Related MicroRNAs During Postnatal Maturation and After Experimental Manipulations of Puberty. *Endocrinology*. 2013, 154(2):942-955. IF:4,717

Aguilar E, Pineda R, Gaytan F, Sanchez-Garrido MA, Romero M, Romero-Ruiz A, Ruiz-Pino F, Tena-Sempere M, Pinilla L. Characterization of the Reproductive Effects of the Vgf-Derived Peptide TLQP-21 in Female Rats: In vivo and in vitro Studies. *Neuroendocrinology*. 2013, 98:38-50. IF:3,537

Gaytan F, Sangiao-Alvarellos S, Manfredi-Lozano M, Garcia-Galiano D, Ruiz-Pino F, Romero-Ruiz A, Leon S, Morales C, Cordido F, Pinilla L, Tena-Sempere M. Distinct Expression Patterns Predict Differential Roles of the miRNA-Binding Proteins, Lin28 and Lin28b, in the Mouse Testis: Studies During Postnatal Development and in a Model of Hypogonadotropic Hypogonadism. *Endocrinology*. 2013, 154(3):1321-1336. IF:4,717

Sanchez-Garrido MA, Castellano JM, Ruiz-Pino F, Garcia-Galiano D, Manfredi-Lozano M, Leon S, Romero-Ruiz A, Dieguez C, Pinilla L, Tena-Sempere M. Metabolic programming of puberty: Sexually dimorphic responses to early nutritional challenges. *Endocrinology*. 2013, 9:3387-3400. IF:4,717

Roa, J. Role of GnRH Neurons and Their Neuronal Afferents as Key Integrators between Food Intake Regulatory Signals and the Control of Reproduction. *Int J Endocrinol*. 2013, n° art 518046. IF:2,518

Sanchez-Garrido MA, Tena-Sempere M. Metabolic control of puberty: Roles of leptin and kisspeptins. *Horm Behav*. 2013, 64:187-194-. IF: 3,735

Tena-Sempere M. Keeping puberty on time: novel signals and mechanisms involved. *Curr Top Dev Biol*. 2013, 105:299-329. IF: 6,912

Garcia-Galiano D, Tena-Sempere M. Emerging Roles of NUCB2/Nesfatin-1 in the Metabolic Control of Reproduction. *Curr Pharm Des*. 2013, 19(39):6966-6972. IF: 3,311

Witchel SF, Tena-Sempere M. The Kiss1 system and polycystic ovary syndrome: lessons from physiology and putative pathophysiological implications. *Fertil Steril*. 2013, 100(1):12-22. IF:4,174

Tena-Sempere M. Interaction Between Energy Homeostasis and Reproduction: Central Effects of Leptin and Ghrelin on the Reproductive Axis. *Horm Metab Res*. 2013, 45(13):919-927. IF:2,145

Castellano, JM, Tena-Sempere, M. Metabolic regulation of kisspeptin. *Advances in experimental. Medicine and Biology*. 2013. 784 363 - 383 IF: 1,093

Lecumberri Santamaria B, Fernández-Aranda F, Tena-Sempere M. Creating a European consortium to study GnRH deficiency (COST Action BM1105). *Endocrinol Nutr*. 2013, 60(8):485-486.

### Joint Publications

Alvarez-Crespo M, Martínez-Sánchez N, Ruiz-Pino F, García-Lavandeira M, Alvarez CV, Tena-Sempere M, Nogueiras R, Dieguez C, López M. The orexigenic effect of orexin-a revisited: dependence of an intact growth hormone axis. *Endocrinology*. 2013, 154:3589-3598. IF: 4,717

Overgaard A, Tena-Sempere M, Franceschini I, Desroziers E, Simonneaux V, Mikkelsen JD. Comparative analysis of kisspeptin-immunoreactivity reveals genuine differences in the hypothalamic Kiss1 systems between rats and mice. *Peptides*. 2013, 45:85-90. IF:2,522

Moreno-Navarrete JM, Ortega F, Sanchez-Garrido MA, Sabater M, Ricart W, Zorzano A, Tena-Sempere M, Fernandez-Real JM. Phosphorylated S6K1 (Thr389) is a molecular adipose tissue marker of altered glucose tolerance. *Journal of Nutritional Biochemistry*. 2013, 24(1):32-38. IF:4,552

Pulido MR, Rabanal-Ruiz Y, Almabouada F, Diaz-Ruiz A, Burrell MA, Vazquez MJ, Castaño JP, Kineman RD, Luque RM, Dieguez C, Vázquez-Martínez R, Malagón MM. Nutritional, hormonal, and depot-dependent regulation of the expression of the small GTPase Rab18 in rodent adipose tissue. *Journal of Molecular Endocrinology*. 2013, 50(1):19-29. IF: 3,577

Sirotkin AV, Pavlova S, Tena-Sempere M, Grossmann R, Jimenez MR, Rodríguez JMC, Valenzuela F. Food restriction, ghrelin, its antagonist and obestatin control expression of ghrelin and its receptor in chicken hypothalamus and ovary. *Comparative Biochemistry Physiology A-Molecular Integrative Physiology*. 2013, 164(1):141-153. IF:2,167

Tello JA, Kohout T, Pineda R, Maki RA, Scott Struthers R, Millar RP. Reproductive physiology of a humanized GnRH receptor mouse model: application in evaluation of human-specific analogs. *Am J Physiol Endocrinol Metab*. 2013, 305(1):E66-E67. IF:4,514

Imbernon M, Beiroa D, Vazquez MJ, Morgan DA, Veyrat-Durebex C, Porteiro B, Diaz-Arteaga A, Senra A, Busquets S, Velásquez DA, Al-Massadi O, Varela L, Gándara M, López-Soriano FJ, Gallego R, Seoane LM, Argiles JM, López M, Davis

RJ, Sabio G, Rohner-Jeanraud F, Rahmouni K, Dieguez C, Nogueiras R. Central melanin-concentrating hormone influences liver and adipose metabolism via specific hypothalamic nuclei and efferent autonomic/JNK1 pathways. *Gastroenterology*. 2013, 144(3):636-649.  
IF: 12,821

Romero-Picó A, Vazquez MJ, González-Touceda D, Folgueira C, Skibicka KP, Alvarez-Crespo M, Van Gestel MA, Velásquez DA, Schwarzer C, Herzog H, López M, Adan RA, Dickson SL, Diéguez C, Nogueiras R. Hypothalamic kappa-Opioid Receptor Modulates the Orexigenic Effect of Ghrelin. *Neuropsychopharmacology*. 2013, 38(7):1296-1307.  
IF: 8,678

Gore AC, Balthazart J, Bikle D, Carpenter DO, Crews D, Czernichow P, Diamanti-Kandarakis E, Soares RM, Grattan D, Hof PR, Hollenberg AN, Lange C, Lee AV, Levine JE, Millar RP, Nelson RJ, Porta M, Poth M, Power DM, Prins GS, Ridgway EC, Rissman EF, Romijn JA, Sawchenko PE, Sly PD, Söder O, Taylor HS, Tena-Sempere M, Vaudry H, Wallen K, Wang Z, Wartofsky L, Watson CS. Policy decisions on endocrine disruptors should be based on science across disciplines: a response to Dietrich et al. *Andrology*. 2013, 169(6):E1-E4.  
IF: 4,717

Gore AC, Balthazart J, Bikle D, Carpenter DO, Crews D, Czernichow P, Diamanti-Kandarakis E, Soares RM, Grattan D, Hof PR, Hollenberg AN, Lange C, Lee AV, Levine JE, Millar RP, Nelson RJ, Porta M, Poth M, Power DM, Prins GS, Ridgway EC, Rissman EF, Romijn JA, Sawchenko PE, Sly PD, Söder O, Taylor HS, Tena-Sempere M, Vaudry H, Wallen K, Wang Z, Wartofsky L, Watson CS. Policy decisions on endocrine disruptors should be based on science across disciplines: a response to Dietrich et al. *Horm Res Paediatr*. 2013, 80(5):305-308.  
IF: 1,553

George JT, Veldhuis JD, Tena-Sempere M, Millar RP, Anderson RA. Exploring the pathophysiology of hypogonadism in men with type 2 diabetes: Kisspeptin-10 stimulates serum testosterone and LH secretion in men with type 2 diabetes and mild biochemical hypogonadism. *ClinEndocrinol*. 2013; 79(1):100-104  
IF: 3,396

Meza-Herrera CA, Vargas-Beltran F, Tena-Sempere M, Gonzalez-Bulnes A, Macias-Cruz U, Veliz-Deras FG. Short-term beta-carotene-supplementation positively affects ovarian activity and serum insulin concentrations in a goat model. *J Endocrinol Invest*. 2013, 36(3):185-189  
IF: 1,654

Lomiczi A, Loche A, Castellano JM, Ronnekleiv OK, Bosch M, Kaidar G, Knoll JG, Wright H, Pfeifer GP, Ojeda SR. Epigenetic control of female puberty. *Nat Neurosci*. 2013, 16:281-289.  
IF: 15,251

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fertility on kisspeptin-Gpr54 signaling at the GnRH neuron. *Nat Commun*. 2013, 4:2492.  
IF: 10,015

Lomiczi A, Wright H, Castellano JM, Sonmez K, Ojeda SR. A system biology approach to identify regulatory pathways underlying the neuroendocrine control of female puberty in rats and nonhuman primates. *Horm Behav*. 2013, 64(2):175-86.  
IF: 3,735

## Research Projects

Tena Sempere, M. Translational research in puberty and infertility: analysis of the kiss-system 1 / GPR54. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: P08-CVI-03788

Tena Sempere, M. Epi-puberty-metabolic control of puberty: role of epigenetic regulatory mechanisms. Sponsored by: European Commission. Reference: P10F-GA-2010-273034

Tena Sempere, M. Puberty: new microRNAs and neuropeptide regulating systems and their interaction with obesity and metabolic signals. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO) Reference: BFU2011-25021

Tena Sempere, M. MicroRNAs and reproductive health: Mechanistic and Translational studies. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: FQM1943.  
2014 Annuity

## Collaboration Agreements

Tena Sempere, M. Optimization of protocols for functional manipulation of Let-7 miRNA levels in the hypothalamus in vivo using nasal delivery in suitable preclinical models. LET 7A Hypothalamus. Sponsored by: Life, S.L. Reference: CCB. UCO0054

Tena Sempere, M. Proof-of-principle studies for the validation of Gpr54 agonists as therapeutic tool in preclinical (rodent) models of functional hypogonadotropichypogonadism and ovulatory dysfunction. GPR54-PCOS. Sponsored by: London Research Institute. Reference: CCB. UCO0061

# GC11

## Metabolism and Adipocyte Differentiation Metabolic Syndrome

### Team Leaders

#### Principal Investigator (PI)

M<sup>º</sup> del Mar Malagón Poyato  
bc1mapom@uco.es  
CIBER on Obesity and Nutrition (CIBERobn) (Collaborator)

#### Co-Principal Investigator (Co-PI)

Francisco Gracia Navarro  
PAIDI BIO-139 scientific group

#### Senior Researchers

Socorro García Navarro  
Rafael Vázquez Martínez

#### Post-doctoral Researcher

Rocío Guzmán Ruiz

#### Pre-doctoral Researchers

Farid Almabouada  
Yoana Rabanal Ruiz  
Andrés Trávez García  
Andreia Cristina Sá Gomes

#### Other members of the Group

(Other researchers, Technical, and  
Administrative Staff)  
M<sup>º</sup> Amparo Gómez Élices  
Laura Molero Murillo  
Natalia Rocío Moreno Castellanos  
Karen Gwendolyne Crespo



## Scientific Activity

This research group investigates the cellular and molecular mechanisms that control adipose tissue activity. Thus, this group is focused on the central role of adipose tissue in lipid metabolism regulation and in body response to insulin, as well as on its role as an endocrine organ producing a number of signalling molecules. Specifically, this group analyzes the different components of adipose tissue, mature adipocytes and stromal vascular fraction, including the study of pre-adipocytes and adipogenesis. Additionally, this group is interested in other fundamental processes in adipocyte dysfunction, such as intracellu-

lar lipid and organelle traffic and their relationship with the cytoskeleton, oxidative stress, inflammation, etc. These studies are performed in the context of disorders associated with adipose-tissue dysfunction, obesity and lipodystrophy that result in the development of metabolic disease. Finally, this group also investigates the interventions that best improve the metabolic profile (bariatric surgery, diet). To address these studies, this group uses multiple experimental approaches such as the application of comparative proteomics to the adipose tissue under different experimental conditions or to other tissues related to the control of metabolism. In addition, gene expression, protein

interaction, confocal microscopy, real-time videomicroscopy for the localization of proteins and functional studies of gene overexpression or silencing using primary or cell line cultures are also performed.

## Keywords

Adipose tissue, adipocyte, lipid metabolism, adipogenesis, proteomics, intracellular trafficking, intracellular signaling, adipokines, receptors, obesity, lipodystrophy, insulin resistance, metabolic syndrome.

## Publications

### Originals Publications

Almabouada F, Díaz-Ruiz A, Rabanal-Ruiz Y, Peinado JR, Vázquez-Martínez R, Malagón MM. Adiponectin Receptors Form Homomers and Heteromers Exhibiting Distinct Ligand Binding and Intracellular Signaling Properties. *J Biol Chem.* 2013, 288(5):3112-3125. IF:4,651

Malagón MM, Díaz-Ruiz A, Guzmán-Ruiz R, Jiménez-Gómez Y, Moreno NR, García-Navarro S, Vázquez-Martínez R, Peinado JR. Adipobiology for Novel Therapeutic Approaches in Metabolic Syndrome. *Curr Vasc Pharmacol.* 2013, 11(6):954-967. IF:2,821

Malagón MM, Vaudry H. Hypothalamic control of energy homeostasis. *Horm Metab Res.* 2013, 45(13):917-918. IF:2,145

Díaz-Ruiz A, Rabanal-Ruiz Y, Trávez A, Gracia-Navarro F, Cruz-García D, Montero-Hadjadje M, Anouar Y, Gasman S, Vitale N, Vázquez-Martínez R, Malagón MM. The Long Coiled-Coil Protein NECC2 Is Associated to Caveolae and MODULATES NGF/TrkA Signaling IN PC12 CELLS. *PLoS One.* 2013, 8(9):e73668-. IF:3,73

### Joint Publications

Peña-Orihuela P, Camargo A, Rangel-Zuñiga OA, Perez-Martínez P, Cruz-Teno C, Delgado-Lista J, Yubero-Serrano EM, Paniagua JA, Tinahones FJ, Malagón MM, Roche HM, Perez-Jimenez F,

Lopez-Miranda J. Antioxidant system response is modified by dietary fat in adipose tissue of metabolic syndrome patients. *J Nutr Biochem.* 2013, 24(10):1717-1723. IF:4,552

Camargo A, Rangel-Zuñiga OA, Pena-Orihuela P, Marín C, Perez-Martínez P, Delgado-Lista J, Gutierrez-Mariscal FM, Malagón MM, Roche HM, Tinahones FJ, Perez-Jimenez F, Lopez-Miranda J. Postprandial changes in the proteome are modulated by dietary fat in patients with metabolic syndrome. *J Nutr Biochem.* 2013, 24(1):318-324. IF: 4,552

Camargo A, Meneses ME, Rangel-Zuñiga OA, Perez-Martínez P, Marín C, Delgado-Lista J, Paniagua JA, Tinahones FJ, Roche H, Malagón MM, Perez-Jimenez F, Lopez-Miranda J. Endoplasmic reticulum stress in adipose tissue determines postprandial lipoprotein metabolism in metabolic syndrome patients. *Mol Nutr Food Res.* 2013, 57(12):2166-2176. IF:4,310

Perez-Caballero AI, Alcalá-Díaz JF, Perez-Martínez P, García-Ríos A, Delgado-Casado N, Marín C, Yubero-Serrano E, Camargo A, Caballero J, Malagón MM, Tinahones FJ, Perez-Jimenez F, Lopez-Miranda J, Delgado-Lista J. Lipid metabolism after an oral fat test meal is affected by age-associated features of metabolic syndrome. *Atherosclerosis.* 2013, 226(1):258-262. IF:3,706

Jimenez-Gomez Y, Mattison JA, Pearson KJ, Martin-Montalvo A, Palacios HH, Sossong AM, Ward TM, Younts CM, Lewis K, Allard JS, Longo DL, Belman JP, Malagón MM, Navas P, Sanghvi M, Moaddel R, Tilmont EM, Herbert RL, Morrell CH, Egan JM, Baur JA, Ferrucci L, Bogan JS, Bernier M, de Cabo R. Resveratrol Improves Adipose

Insulin Signaling and Reduces the Inflammatory Response in Adipose Tissue of Rhesus Monkeys on High-Fat, High-Sugar Diet. *Cell Metab.* 2013, 18(4):533-545. IF:14,619

Chanclon B, Luque RM, Córdoba-Chacon J, Gahete MD, Pozo-Salas AI, Castaño JP, Gracia-Navarro F, Martínez-Fuentes AJ. Role of Endogenous Cortistatin in the Regulation of Ghrelin System Expression at Pancreatic Level under Normal and Obese Conditions. *PLoS One.* 2013, 8(2):e57834-. IF:3,73

Porteiro B, Díaz-Ruiz A, Martínez G, Senra A, Vidal A, Serrano M, Guallillo O, López M, Malagón MM, Diéguez C, Nogueiras R. Ghrelin requires p53 to stimulate lipid storage in fat and liver. *Endocrinology.* 2013, 154(10):3671-3679. IF:4,717

Pulido MR, Rabanal-Ruiz Y, Almabouada F, Díaz-Ruiz A, Burrell MA, Vazquez MJ, Castaño JP, Kinnamon RD, Luque RM, Dieguez C, Vázquez-Martínez R, Malagón MM. Nutritional, hormonal, and depot-dependent regulation of the expression of the small GTPase Rab18 in rodent adipose tissue. *J Mol Endocrinol.* 2013, 50(1):19-29. IF:3,577

Rodríguez-Pacheco F, Novelle MG, Vazquez MJ, García-Escobar E, Sorriquer F, Rojo-Martínez G, García-Fuentes E, Malagón MM, Dieguez C. Resistin Regulates Pituitary Lipid Metabolism and Inflammation In Vivo and In Vitro. *Mediat Inflamm.* 2013, n° art 479739. IF:3,882

Tinahones FJ, Araguez LC, Murri M, Olivera WO, Torres MDM, Barbarroja N, Huelgas RG, Malagón MM, El Bekay R. Caspase Induction and BCL2



Inhibition in Human Adipose Tissue A potential relationship with insulin signaling alteration. Diabetes Care. 2013, 36(3):513-521.  
IF:7,735

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## Research Projects

Malagón, MM. Identifying markers for Adipose Tissue Dysfunction in Insulin Resistance Conditions. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0200-2013

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Malagón, MM. Characterization of new markers regulating adipose tissue function. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: BFU2010-17116

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Malagón, MM. High-performance proteomic approaches to identify markers of adipose tissue obesity. Adipocyte phosphoproteome disorders resulting from insulin resistance. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: P10-CTS-6606

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## GC12

# Epidemiological Research in Primary Care

### Team Leader

#### Principal Investigator (PI)

Luis Angel Pérula de Torres.

[langel.perula.sspa@juntadeandalucia.es](mailto:langel.perula.sspa@juntadeandalucia.es)

Research Network on preventive actions and health promotion in primary care (RedIAPP)  
PAIDI CTS-452 scientific group

#### Senior Researchers

Maria Jose Acosta Garcia

Cristina Aguado Taberne

Antonio Blanco Hungría

Miguel Angel Fernández Fernández

Jose Ángel Fernández Garcia

Jesús Gonzalez Lama

Jose Antonio Prados Castillejo

Antonio Ranchal Sanchez

Juana Redondo Sanchez

Roger Ruiz Moral

Joaquin Ruiz De Castroviejo Del Campo

Antonio Valero Martin

#### Other members of the Group

(Other researchers, Technical, and  
Administrative Staff)

Maria Antonia Alba Dios

Celia Jimenez Garcia

Antonio Manuel Jodral Segado

Inmaculada Olaya Caro

Juan Manuel Parras Rejano

Carlos Perula de Torres

Francisco Jose Varas Fabra

#### Post-doctoral Researcher

Enrique Martín Rioboo

#### Pre-doctoral Researcher

Carlos Ortega Millán



## Scientific Activity

Preventive activities, promotion and protection of health in Primary Health Care (PHC). Validation of measuring instruments in PHC. Patient Safety

(rational drug use). Communication in health care, clinical interviews. Medical education.

## Keywords

Epidemiology, Preventive Medicine and Public Health, Primary Health Care.

## Publications

### Originals Publications

Pérula de Torres LA, Pulido Ortega L, Pérula de Torres C, González Lama J, Olaya Caro I, Ruiz Moral R, Grupo corporativo Estudio ATEM-AP. Efficacy of motivational interviewing for reducing medication errors in chronic patients over 65 years with polypharmacy: Results of a cluster randomized trial. *Med Clin (Barc)*. 2013, S0025-7753(13)00784-7.  
IF: 1,399

their actions in real clinical scenarios. Sponsored by: Institute Carlos III Health (ISCIII). Reference:PI11-00771

### Joint Publications

Bóveda Fontán J, Pérula de Torres LA, Campiñez Navarro M, Bosch Fontcuberta JM, Barragán Brun N, Prados Castillejo JA, en representación del Grupo Colaborativo Estudio Dislip-EM. Current evidence on the motivational interview in the approach to health care problems in primary care. *Aten Primaria*. 2013, 45(9):486-495.  
IF: 0,957

Carratalá-Munuera MC, Gil-Guillen VF, Orozco-Beltran D, Navarro-Pérez J, Caballero-Martínez F, Alvarez-Guisasola F, Garcia-Soldán J, Fluixá-Carrascosa C, Franch-Nadal J, Martín-Rioboó E, Carrillo-Fernández L, Artola-Menéndez S. Integrated Management of Type 2 Diabetes Mellitus. Research Group. Barriers associated with poor control in Spanish diabetic patients. A consensus study. *Int J Clin Pract*. 2013, 67(9):888-894.  
IF: 2,427

Dios Guerra, C, Alba Dios, MA, Ruiz Moral, Roger, Jiménez García, Celia, Pérula de Torres, L, Rodríguez Borrego, M. Evaluation of user satisfaction of nursing consultation in health centers based on quality and technical communication indicators. *Enfermería Global*. 2013.12(31).162-176  
IF: 0

## Research Projects

Pérula de Torres, LA. Effectiveness of opportunistic detection of atrial fibrillation in people aged 65 years or more in primary care. Dofa-Ap. Project. Sponsored by: Andalusian Progress and Health Foundation. Reference:PI-0117-2011

Ruiz Moral, R. Preferences of physicians and patients concerning their participation in the decision-making process and coherence of

# GC13

## Calcium Metabolism Vascular Calcification

### Team Leader

#### Principal Investigator (PI)

Mariano Rodríguez Portillo  
juanm.rodriguez.sspa@juntadeandalucia.es

#### Senior Researchers

Escolástico Tejero Aguilera\*  
Antonio L. Canalejo Raya  
Jose C. Estepa Nieto  
Ignacio López Villalba  
Juan R. Muñoz Castañeda

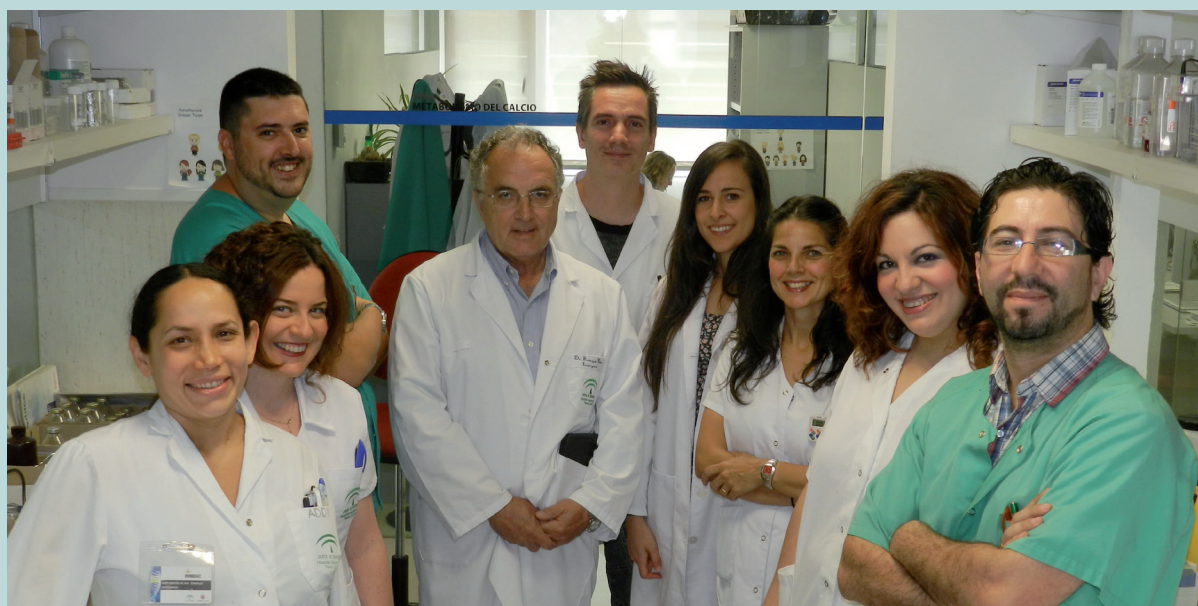
#### Post-doctoral Researchers

Fátima Guerrero Pavón  
Carmen Herencia Bellido  
Addy Montes de Oca González  
M<sup>ª</sup> Encarnación Rodríguez Ortiz

#### Pre-doctoral Researchers

Julio M. Martínez Moreno  
Jose A. Morales Martínez  
Juan M. Tocados Díaz

\*Member of PAIDI CTS-179 scientific group



## Scientific Activity

This group is focused on different aspects of calcium metabolism and vascular calcification. Our primary area of research is centred on the study of the pathogenetic mechanisms of secondary hyperparathyroidism associated with renal failure. In this sense, this group investigates the parathyroid function, both at cellular and molecular level (PTH synthesis and secretion and cell proliferation) of normal and hyperplastic parathyroid glands.

More recently, this group has incorporated into its research activity both in vivo (experimental models with rats) and in vitro studies (vascular smooth muscle cells) of the mechanisms underlying the development of vascular calcification in chronic kidney disease. Thus, in the context of vascular calci-

fication this group is centred on analyzing the role of different diets (with different contents of phosphorus, calcitriol, micronutrients such as magnesium or calcium, calorie diets ...) in FGF23 regulation and in cardiovascular disease progression.

This group has opened a new line of research centred on the study of the involvement of bone marrow mesenchymal stem cells in vascular calcification. Basing on a stem cell-based approach, this group analyzes the signalling pathways by which vascular calcification progresses. Mesenchymal stem cells are also used to investigate how the chronic kidney disease or its treatments may affect bone regarding the formation of new osteoblasts. From this line also derives the study of the regulation of bone production of FGF23. The lines of research group listed above involve the

study of gene expression of vitamin D, calcium or FGF23 receptors, and the analysis of different intracellular signaling pathways as Wnt/b-catenin, Nocth, Erk, epigenetic modifications, measuring of parameters indicative of osteogenic transdifferentiation, inflammation.

Research derived from each of these lines can lead to the proposal and use of new therapeutic targets for preventing and reversing vascular calcification and associated complications.

## Keywords

Calcium, phosphorus, metabolism, parathyroid, calcification, uremia. Mineral metabolism, parathyroid hormone, HPTH<sup>2</sup>, vascular calcification, renal failure, VDR, CaR. Mesenchymal stem cells, Wnt / beta-catenin.

## Publications

### Originals Publications

Rodríguez M, Urena-Torres P, Petavy F, Cooper K, Farouk M, Goodman WG. Calcium-Mediated Parathyroid Hormone Suppression to Assess Progression of Secondary Hyperparathyroidism During Treatment Among Incident Dialysis Patients. *J Clin Endocrinol Metab.* 2013, 98(2):618-625. IF:6,429

Pineda C, Aguilera-Tejero E, Guerrero F, Raya AI, Rodríguez M, Lopez I. Mineral metabolism in growing cats: changes in the values of blood parameters with age. *J Feline Med Surg.* 2013, 15(10):866-871. IF:1,08

de Francisco, ALM, Rodríguez, M. Magnesium - its role in CKD. *Nephro.* 2013, 33:389-399. IF:1,274

Mendoza FJ, Perez-Ecija RA, Toribio RE, Estepa JC. Thyroid hormone concentrations differ between donkeys and horses. *Equine Vet J.* 2013, 45(2):214-218. IF:2,286

Pineda C, Aguilera-Tejero E, Raya AI, Guerrero F, Rodríguez M, Lopez I. Assessment of calcitonin response to experimentally induced hypercalcemia in cats. *Am J Vet Res.* 2013, 74:1514-1521. IF:1,348

Peralta-Ramírez A, Montes de Oca A, Raya AI, Pineda C, López I, Guerrero F, Diez E, Muñoz-

Castañeda JR, Martínez J, Almaden Y, Rodríguez M, Aguilera-Tejero E. Vitamin E protection of obesity-enhanced vascular calcification in uremic rats. *Am J Physiol Renal Physiol.* 2014 15;306(4):F422-9. IF:3,61

Rodríguez M, Muñoz-Castañeda JR, Almaden Y. Therapeutic Use Of Calcitriol. *Curr Vasc Pharmacol.* 2013 May 16. IF:2,82

### Joint Publications

Gracia-Iguacel C, Gonzalez-Parra E, Rodríguez-Osorio L, Sanz AB, Almaden Y, de la Piedra C, Egido J, Rodríguez M, Ortiz A. Correction of hypocalcemia allows optimal recruitment of FGF-23-dependent phosphaturic mechanisms in acute hyperphosphatemia post-phosphate enema. *J Bone Miner Metab.* 2013, 31(6):703-707. IF:2,219

Urena-Torres, P, Bridges, I, Christiano, C, Cournoyer, SH, Cooper, K, Farouk, M, Kopyt, NP, Rodríguez, M, Zehnder, D, Covic, A. Efficacy of cinacalcet with low-dose vitamin D in incident haemodialysis subjects with secondary hyperparathyroidism. *Nephrol Dial Transplant.* 2013, 28:1241-1254. IF:3,371

Arenas MD, de la Fuente V, Delgado P, Gil MT, Gutierrez P, Ribero J, Rodríguez M, Almaden Y. Pharmacodynamics of cinacalcet over 48 hours in patients with controlled secondary hyperparathyroidism: useful data in clinical practice. *J Clin*

*Endocrinol Metab.* 2013, 98(4):1718-1725. IF:6,429

Soriano S, Ojeda R, Rodríguez ME, Almaden Y, Martín-Malo A, Aljama P. The effect of phosphate binders, calcium and lanthanum carbonate on FGF23 levels in chronic kidney disease patients. *Clin Nephrol.* 2013, 80:17-22. IF:1,288

Vizueté G, Diez E, Galisteo J, Agüera E, Aguilera-Tejero E, Perez-Marin CC. Comparison of different treatments for oestrous induction in seasonally anovulatory mares. *Reprod Domest Anim.* 2013, 48(3):463-469. IF:1,392

Duranton F, Rodríguez-Ortiz ME, Duny Y, Rodríguez M, Dures JP, Argiles A. Vitamin D treatment and mortality in chronic kidney disease: a systematic review and meta-analysis. *Am J Nephrol.* 2013, 37(3):239-248. IF:2,623

Felsenfeld A, Rodríguez M, Levine B. New insights in regulation of calcium homeostasis. *Curr Opin Nephrol Hypertens.* 2013, 22(4):371-376. IF:3,964

de Francisco ALM, Rodríguez M. Response to the comment on "Magnesium and chronic kidney disease. *Nefrología.* 2013, 33(6):850-851. IF:1,274

## Research Projects

Rodríguez Portillo, JM. Role of adult stem cells and vascular smooth muscle in damage induced by vascular calcification. Relationship between phosphorus wnt / beta-catenin and osteogenesis. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: P09-CTS-5205

Rodríguez Portillo, JM. (SYSKID). Systems biology towards novel chronic kidney disease diagnosis and treatment. Sponsored by: European Commission Reference: FP7-241544

Aguilera Tejero, E. Vascular calcification, epigenetics and oxidative stress. Sponsored by: Institute Carlos III Health (ISCIII). Reference: P111/00098

Rodríguez Portillo, JM. Vascular calcification. Regulation of osteogenic gene expression in vascular smooth muscle cells and smooth muscle mesenchymal progenitor cells via wnt / beta-catenin and smad. Sponsored by: Institute Carlos III Health (ISCIII). Reference: P111-02055

Rodríguez Portillo, JM. Effect of phosphorus on epigenetic modifications and wnt/b- catenin and tgf / bmp pathways in mesenchymal stem cells differentiated into vascular smooth muscle cells. Sponsored by: Andalusian Health Service (SAS). Reference: 10/0132

Muñoz Castañeda, JR. In vivo and in vitro studies of oxidative stress, inflammation and vascular calcification in chronic kidney disease: application of mesenchymal stem cells to the search for new therapeutic targets. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: CVI-7925

Rodríguez Portillo, J M. I+D+i project funding- Senefro Foundation. Sponsored by: Fundacion Senefro. Reference: PFS.001

## Third Party Services

Rodríguez Portillo, JM. Research support services. Sponsored by: University of Cordoba. Reference: PSS.0009

Rodríguez Portillo, JM. Effect of paricalcitol on vascular smooth muscle cells. Sponsored by: AbbVie Farmaceutica S.L.U. Reference: PSS.0015

Rodríguez Portillo, JM. Research Program Agreement for measuring AMG 416 activity against isolated rat PTG. Sponsored by: Amgen Inc. S.A. Reference: PSS.0020

## Collaboration Agreements

Rodríguez Portillo, JM. New therapeutic strategies for treatment and prevention of secondary hyperparathyroidism and vascular calcifications (calcimimetics, interleukin antagonists and cell

cycle inhibitors) (Extend). Sponsored by: Amgen Inc. S.A. Reference: CCB.UCO0001

Rodríguez Portillo, JM. Research Collaboration, License and Option Agreement with Amgen, para la ejecución de investigación para el consorcio SYSKID (Extend). Sponsored by: Amgen Inc. S.A. Reference: CCB.UCO0008

## Clinical Trials

0348/12: A multicenter, randomized, placebo-controlled, double-blind phase III study to assess the efficacy and safety of AMG 416 in the treatment of secondary hyperparathyroidism in patients with chronic renal failure undergoing hemodialysis.

PI: Dr/a Rodríguez Portillo, J. Mariano

0002/13: A multicenter, extension, one-arm study to assess the long-term efficacy and safety of AMG 416 in the treatment of secondary hyperparathyroidism in patients with chronic renal failure undergoing hemodialysis.

PI: Dr/a Rodríguez Portillo, J. Mariano

0114/13: A multicenter, multiple-dose, two-arm, active-controlled, double-blind, double-masked study to assess the efficacy and safety of oral cinacalcet HCl doses vs. intravenous AMG 416 doses.

PI: Dr/a Rodríguez Portillo, J. Mariano

0260/13: A randomized, multicenter, placebo-controlled, double-blind, parallel-group study to assess the efficacy and safety of five fixed doses of BAY 85 3934 administered orally to correct anaemia prior to dialysis in patients from European and the Asian Pacific with chronic nephropathy who have never received a erythropoiesis-stimulating drug.

PI: Dr/a Rodríguez Portillo, J. Mariano

0265/13: A multicenter, controlled, extension, parallel-group, open study to assess the efficacy and safety of BAY 85 3934 administered orally vs. darbepoetin alfa in long-term treatment of anaemia prior to dialysis in patients with chronic nephropathy from Europe and the Asian Pacific.

PI: Dr/a Rodríguez Portillo, J. Mariano

# GC14

## Cell Therapy

### Team Leader

#### Principal Investigator (PI)

Inmaculada C. Herrera Arroyo

[inmaculada.herrera.sspa@juntadeandalucia.es](mailto:inmaculada.herrera.sspa@juntadeandalucia.es)

#### Senior Researchers

M<sup>a</sup> Sagrario Cañadillas López

Antonio Chacón Quevedo

José García-Revillo García

Vanesa Martín Palanco

Sonia Nogueras Martín <sup>(i)</sup>

#### Post-doctoral Researchers

Rosario Jiménez Moreno

Vanesa Martín Palanco

#### Pre-doctoral Researchers

M<sup>a</sup> Dolores Carmona Luque

María Muñoz Calero

Luis M. Paco Meza

Laura López Gálvez

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)

Miguel Canis López

M<sup>a</sup> Luisa Castilla Rodríguez

Rosario Gutiérrez Fernández

María Luque Zafra

Teresa Muñoz Liñan

Noelia Romero Mata

(i) Contract ISCIII



## Scientific Activity

The Cell Therapy Unit centres its main activity on clinical research in this area by carrying out different clinical trials. This Unit is currently conducting clinical trials with adult stem cells in autologous bone marrow in acute myocardial infarction, chronic ischemic heart disease, idiopathic dilated cardiomyopathy and chronic

critical ischemia of the lower limbs. From 2011, we will be in a position to produce mesenchyme cells in GMP conditions for the initiation of new clinical trials with these cells.

At the same time, we are carrying out several translational studies both in vitro and with animal models, particularly in therapeutic angiogenesis of mononuclear bone marrow cells.

## Keywords

Stem cells, cell therapy, regenerative medicine, myocardial regeneration, chronic ischemia, therapeutic angiogenesis.

## Publications

### Joint Publications

de Lezo JS, Herrera C, Romero M, Pan M, de Lezo JS, Carmona MD, Jimenez R, Segura J, Nogueras S, Mesa D, Pavlovic D, Ojeda S, Mazuelos F, Delgado M, Ruiz M, Castilla ML, Torres A. Functional Improvement in Patients With Dilated Cardiomyopathy After the Intracoronary Infusion of Autologous Bone Marrow Mononuclear Cells. *Rev Esp Cardiol.* 2013, 66:450–457. IF: 3,204

Cuende N, Herrera C, Keating A. When the best is the enemy of the good: the case of bone-marrow mononuclear cells to treat ischemic syndromes. *Hematologica.* 2013, 98(3):323–324. IF: 5,935

### Research Projects

Nogueras Martín, S. A comparative study of myocardial regeneration capacity of bone marrow mononuclear cells (MNC-mo), versus mesenchymal cells from bone marrow (MSCS-mo) and adipose tissue (MSCS-ta) in an in vivo model of dilated cardiomyopathy. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: 0191/2010

Herrera Arroyo, Inmaculada C. Cell preservation system project. Sponsored by: University of Córdoba. Reference: CCB.031PM

Herrera Arroyo, Inmaculada C. Phase I study of intraarterial injection of VEGF producing MSC for the treatment of critical limb ischemia. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: CIRM

Cañadillas López, MS. Combination therapy with mesenchymal stem cells and erythropoietin in the treatment of chronic renal failure in an experimental study in rats. Sponsored by: Andalusian Progress and Health Foundation. Reference: PI-0141-2011

Martín Palanco, V. Genomic and functional analysis of mo-mscs and mo-mscs-derived exosomes in diabetic patients with peripheral arterial ischemia. Implications for cell therapy.

Implications for cellular therapy. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0551-2012

Pan Álvarez-Ossorio, M. Revascularization and Myocardial regeneration in Patients With Chronic Coronary Occlusion and Ventricular Dysfunction. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0315-2012

In collaboration

### Clinical Trials

0291/10: A multicenter, randomized, semi-crossover, double-blind, phase I/II clinical trial to assess the safety and feasibility of systemic therapy with mesenchymal cells derived from autologous bone marrow in patients with multiple sclerosis.

PI: Dr/a Herrera Arroyo, Inmaculada C. National coordinator of the international multicenter trial

0197/09: An open, randomized, phase II trial of intraarterial infusion of mononuclear cells from autologous bone marrow in non-diabetic patients with lower limb critical chronic ischemia.

PI: Dr/a Herrera Arroyo, Inmaculada C. National coordinator of the international multicenter trial

### In collaboration with others IMIBIC groups:

0287/09: A phase II clinical trial on the effect of intracoronary infusion of bone marrow mononuclear cells on functional recovery in patients with previous chronic myocardial and severely depressed left ventricular function

PI: Dr/a Romero Moreno, Miguel Ángel

0063/13: An open, single-center, randomized, controlled, phase III clinical trial of intra-arterial infusion of autologous bone marrow mononuclear cells in patients with previously revascularized chronic coronary occlusion and ventricular dysfunction.

PI: Dr/a Pan Álvarez-Ossorio, Manuel

0150/13: A multicenter, randomized, double-blind, placebo-controlled, phase III trial to assess the efficacy of intra-arterial infusion of adult

unexpanded autologous bone marrow mononuclear cells on the functional recovery of patients with dilated cardiomyopathy and heart failure.

PI: Dr/a Suárez de Lezo Cruz-Conde, José M<sup>a</sup>



# GC15

## Invasive Cardiology and Cell Therapy

### Team Leader

#### Principal Investigator (PI)

José Suárez de Lezo Cruz-Conde  
[jose.suarezlezo.sspa@juntadeandalucia.es](mailto:jose.suarezlezo.sspa@juntadeandalucia.es)  
PAIDI BIO-208 scientific group

#### Senior Researchers

Francisco Mazuelos Bellido  
Soledad Ojeda Pineda  
Manuel Pan Álvarez-Ossorio  
Djordje Pavlovic Djurovic  
Miguel A. Romero Moreno  
Jose M<sup>a</sup> Segura Saint-Gerons  
Javier Suárez de Lezo Cruz-Conde



## Scientific Activity

Our group studies the effect of cell therapy in myocardial regeneration. We mainly deal with patients with 2 types of heart pathologies: those with ventricular dysfunction secondary to myocardial infarction, both in acute and in chronic phases, and those with dilated cardiomyopathy of non-ischemic origin.

There are two well-defined lines of study: first, the recovery of ventricular function and its clinical impact: here, we study global and regional contractility, potentiation, diastolic function and coronary reserve. The other line looks at the influence of biological parameters (cell lines, migration, distribution, nesting capabilities, etc.) in functional improvement. All the patients enrolled in the various

studies are followed up periodically from the clinical, ultrasonic, ergometric and angiographic viewpoints.

## Keywords

Ventricular dysfunction, cell therapy, stem cells, acute myocardial infarction and dilated cardiomyopathy.

## Publications

### Originals Publications

de Lezo JS, Herrera C, Romero M, Pan M, de Lezo JS, Carmona MD, Jimenez R, Segura J, Noguera S, Mesa D, Pavlovic D, Ojeda S, Mazuelos F, Delgado M, Ruiz M, Castilla ML, Torres A. Functional Improvement in Patients With Dilated Cardiomyopathy After the Intracoronary Infusion of Autologous Bone Marrow Mononuclear Cells. *Rev Esp Cardiol.* 2013, 66(6):450-457. IF:3,204

Ortiz MR, Ogayar C, Romo E, Mesa D, Delgado M, Anguita M, Castillo JC, Arizon JM, de Lezo JS. Long-term survival in elderly patients with stable coronary disease. *Eur J Clin. Invest.* 2013, 43(8):774-782. IF:3,365

Mesa D, Castillo F, Ruiz Ortiz M, Puentes M, Suarez de Lezo J. Impact of transcatheter aortic valve implantation or surgical aortic valve replacement on right ventricular function. *Heart.* 2013, 99:286-286. IF:5,014

Santisteban M, Pan M, Romero M, Casares J (H), Gómez E, Suárez de Lezo J. Fenestration Closure After Fontan Surgery. *Contributions of Percutaneous Interventionism.* *Rev Esp Cardiol.* 2013, 66(11):909-911. IF:3,204

### Joint Publications

Stankovic G, Lefevre T, Chieffo A, Hildick-Smith D, Lassen JF, Pan M, Darremont O, Albiero R, Ferenc M, Finet G, Adriaenssens T, Koo BK, Burzotta F, Louvard Y. Consensus from the 7th European Bifurcation Club meeting. *EuroIntervention.* 2013, 9(1):36-45. IF:3,173

Delgado M, Ruiz, M, Mesa D, de Lezo JS, Pan M, Lopez J, Villanueva E, Cejudo L. Early Improvement of the Regional and Global Ventricle Function Estimated by Two-Dimensional Speckle Tracking Echocardiography After Percutaneous Aortic Valve Implantation Speckle Tracking After CoreValve Implantation Reply. *Echocardiogra-*

*phy-J Cardiovasc Ultrasound Allied Tech.* 2013, 30(7):859-859. IF:1.261

## Research Projects

Pan Álvarez-Ossorio, M. Use of the "jailed guide-wire" technique in the percutaneous treatment of coronary bifurcation stenting: A randomized study of stereoscopic microscopy. Sponsored by: Institute Carlos III Health (ISCIII). Reference: PI12/00440

Pan Álvarez-Ossorio, M. Revascularization and Myocardial regeneration in Patients With Chronic Coronary Occlusion and Ventricular Dysfunction. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0315-2012

## Clinical Trials

0170/09: A clinical trial of the feasibility, safety and efficacy of cardiac resynchronization therapy and mononuclear bone marrow stem cell intracoronary transplantation in patients with acute myocardial infarction. PI: Dr/a Suárez de Lezo Cruz-Conde, José M<sup>a</sup>

0287/09: A phase II clinical trial on the effect of intracoronary infusion of bone marrow mononuclear cells on functional recovery in patients with previous chronic myocardial and severely depressed left ventricular function PI: Dr/a Miguel Angel Romero Moreno

0063/13: An open, single-center, randomized, controlled, phase III clinical trial of intra-arterial infusion of autologous bone marrow mononuclear cells in patients with chronic coronary occlusion and ventricular dysfunction. PI: Dr/a Pan Álvarez-Ossorio, Manuel

0150/13: A multicenter, randomized, double-blind, placebo-controlled, phase III trial to assess the efficacy of intra-arterial infusion of adult unexpanded autologous bone marrow mononuclear cells on the functional recovery of patients with dilated cardiomyopathy and heart failure. PI: Dr/a Suárez de Lezo Cruz-Conde, José M<sup>a</sup>

1309: Post-commercialization surveillance study of VPT Melody™. PI: Dr/a Suárez de Lezo Cruz-Conde, José M<sup>a</sup>

1756: An observational register of stable patients undergoing a scheduled electrical (or pharmacological) cardioversion in Spain and 12-month evolution. *CARDIOVERSE Study* PI: Dr/a Segura Saint-Gerons, José M<sup>a</sup>

1681: European study of coronary bifurcations: a randomized study to compare the provisional stenting strategy vs the systematic implantation of two stents in true bifurcation lesions located in large vessels. PI: Dr/a Pan Álvarez-Ossorio, Manuel

# GC16

## Cell Biology in Haematology Hypercoagulability

### Team Leaders

#### Principal Investigator (PI)

Joaquín Sánchez García

[Joaquin.sanchez@cheerful.com](mailto:Joaquin.sanchez@cheerful.com)

Spanish Myelodysplastic Syndrome Registry (Resmd) (Collaborator)

#### Co-Principal Investigator (Co-PI)

Francisco Velasco Gimena

Observational Immune Tolerance Induction research program (ObsIT) (Collaborator)

PAIDI CTS-620 scientific group

#### Senior Researchers

Carmen Martín Calvo

Jose R. Molina Hurtado

Rafael Rojas Contreras

Josefina Serrano López

#### Pre-doctoral Researcher

Vianihuini Figueroa Vázquez

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)

Miguel A. Álvarez Rivas

Victor Arqueros Martínez

Javier Casaño Sánchez

Pedro Gómez García

#### PhD Researcher Collaborator

Antonio Torres Gómez



## Scientific Activity

Our cell biology group in Hematology works in two areas:

1. The immunological mechanisms of the phenomena of graft versus host disease and graft versus leukemia occurring after hematopoietic transplantation for hematologic malignancies. This study covers antigen presenting cells, lymphocyte effectors and regulatory populations in quantitative and functional studies.

2. In addition, the group studies the mechanisms of leukemogenesis through the study of normal and leukemic primitive quiescent precursors (G0, Side population). The main methods used are cell culture, multiparameter flow cytometry with cell sorting and complete Western blot proteomics for intracellular signalling proteins.

The group also studies the mechanisms of hypercoagulability associated with oncohematologic process-

es. Its members participate in groups of the region (GASMD, GALA, GNL), of the country (PETHEMA, SEHOP, GETH, RESMD) and in the international group focused on transplantation (EBMT) for the study and treatment of hemopathies in children and adults.

## Keywords

Immunology of hematopoietic transplantation. Cell biology of acute leukemias.

## Publications

### Originals Publications

Serrano-Lopez J, Serrano J, Figueroa V, Torres-Gomez A, Tabares S, Casaño J, Fernandez-Escallada N, Sanchez-Garcia J. Cytoplasmic localization of wild-type survivin is associated with constitutive activation of the PI3K/Akt signaling pathway and represents a favorable prognostic factor in patients with acute myeloid leukemia. *Haematologica*. 2013, 98(12):1877-1885. IF: 5,935

Sanchez-Garcia J, Serrano J, Serrano-Lopez J, Gomez-Garcia P, Martinez F, Garcia-Castellano JM, Rojas R, Martin C, Rodriguez-Villa A, Molina-Hurtado JR, Alvarez MA, Casano J, Torres-Gomez A. Quantification of minimal residual disease levels by flow cytometry at time of transplant predicts outcome after myeloablative allogeneic transplantation in ALL. *Bone Marrow Transplantation*. 2013, 48(3):396-402. IF: 3,541

Martinez-Losada C, Alhambra-Exposito MR, Sanchez-Sanchez R, Casaño J, Tenorio-Jimenez C, Sanchez-Garcia J. Dysplastic extramedullary haematopoiesis with ringed sideroblasts mimicking adrenal adenoma. *Histopathology*. 2013, 63(5):738-739. IF: 2,857

Martinez-Losada C, Martin C, Cuenca T, Torres A. Duodenal leishmaniasis after allogeneic hematopoietic SCT. *Bone Marrow Transplant*. 2013, 48:614-615. IF: 3,541

### Joint Publications

Gayoso I, Cantisan S, Cerrato C, Sanchez-Garcia J, Martin C, Solana R, Torres-Gomez A, Torre-Cisneros J. Clinical Factors Influencing Phenotype of HCMV-Specific CD8+ T Cells and HCMV-Induced Interferon-Gamma Production after Allogeneic Stem Cells Transplantation. *Clin Dev Immunol*. 2013, n° art 347213. IF: 3,064

Guillem V, Hernandez-Boluda JC, Gallardo D, Buño I, Bosch A, Martinez-Laperche C, de la Cámara R, Brunet S, Martin C, Nieto JB, Martinez C, Pérez A, Montoro J, Garcia-Noblejas A, Solano C. Spanish Hematopoietic Stem Cell Transplantation and Cell Therapy Group (GETH). A polymorphism in the TYMP gene is associated with the outcome of HLA-identical sibling allogeneic stem cell transplantation. *Am J Hematol*. 2013, 88(10):883-889. IF: 4,138

Costa D, Munoz C, Carrio A, Nomdedeu M, Calvo X, Sole F, Luno E, Cervera J, Vallespi T, Berneaga D, Gomez C, Arias A, Such E, Sanz G, Grau J, Insunza A, Calasanz MJ, Ardanaz MT, Hernandez JM, Azaceta G, Alvarez S, Sanchez J, Martin ML, Bargay J, Gomez V, Cervero CJ, Allegue MJ, Colado R, Campo E, Nomdedeu B. Spanish Group of Myelodysplastic Syndromes (GESMD). Reciprocal translocations in myelodysplastic syndromes and chronic myelomonocytic leukemias: Review of 5,654 patients with an evaluable karyotype. *Genes Chromosomes Cancer*. 2013, 52(8):753-763. IF: 3,546

Sanz J, Picardi A, Boluda JCH, Martin C, Ferra C, Nozzoli C, Gonzalez-Vicent M, Rambaldi A, Valcarcel D, Verdeguer A, Serrano D, de Heredia CD, Pascual MJ, de Paz R, Montesinos P, Bartolozzi B, Algarotti A, Sanz MA, Arcese W, Sanz GF. Impact of Graft-versus-Host Disease Prophylaxis on Outcomes after Myeloablative Single-Unit Umbilical Cord Blood Transplantation. *Biol Blood Marrow Transplant*. 2013, 19(9):1387-1392. IF: 3,94

De la Serna J, Jarque I, Lopez-Jimenez J, Fernandez-Navarro JM, Gomez V, Jurado M, Pascual A, Serrano J, Romero M, Vallejo C. Treatment of invasive fungal infections in high risk hematological patients. The outcome with liposomal amphotericin B is not negatively affected by prior administration of mold-active azoles. *Rev Esp Quimioter*. 2013, 26(1):64-69. IF: 0,836

Rives S, Camos M, Estella J, Gomez P, Moreno MJ, Vivanco JL, Melo M, Fernandez-Delgado R, Verdeguer A, Fernandez-Teijeiro A, Lendinez

F, Lopez-Almaraz R, Uriz JJ, Badell I. Longer follow-up confirms major improvement in outcome in children and adolescents with Philadelphia chromosome acute lymphoblastic leukaemia treated with continuous imatinib and haematopoietic stem cell transplantation. Results from the Spanish Cooperati. 2013, *Br J Hematol* 162(3):419-421. IF: 4,942

## Research Projects

Velasco Gimena, F°. Analysis of the cellular and molecular mechanisms regulating the effect of fluvastatin and new antioxidant drugs in the prevention of thrombosis and syndrome-associated atherothrombosis. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: P08-CVI-04234

## Third Party Services

Sánchez García, J. Collaboration agreement with Janssen. Identifying markers and new cellular therapeutic targets of Graft-Versus-Host-Disease (GVHD) using T lymphocytes gene expression arrays for T-cell activation. Sponsored by: Janssen-Cilag, S.A. Reference: PSS.0039

## Clinical Trials

0290/09: A multicenter, randomized, double-blind, placebo-controlled, phase III study of panobinostat in combination with bortezomib and dexamethasone in patients with relapsed multiple myeloma. PI: Dr/a Alvarez Rivas, Miguel Ángel

0167/09: A multicenter, randomized, double-blind, phase III study of Revlimid (lenalidomida) versus placebo in patients with low-risk myelodysplastic syndrome (low and intermediate-1 IPSS) with impaired 5q-and anemia without transfusion requirements. PI: Dr/a Sánchez García, Joaquín

0112/10: A multicenter, randomized, open-label, phase II study of Vidaza (Azacitidine) versus supportive therapy in patients with low-risk MDS (low and intermediate-1IPSS) without 5q-deletion and anemia requiring transfusion.

PI: Dr/a Sánchez García, Joaquín

0299/10: Maintenance treatment with 5-Azacitidine in patients with acute myelogenous leukemia ineligible for intensive treatment with partial or complete response to induction chemotherapy.

PI: Dr/a Serrano López, Josefina

0070/11: A multicenter, prospective, open-label, single-arm, phase I-II clinical trial to analyze the induction treatment with a combination of fludarabine, idarubicin, cytarabine, G-CSF and plerixafor for the treatment of young patients with recurrent or resistant LM.

PI: Dr/a Serrano López, Josefina

0020/12: Ofatumumab as part of the reduced intensity conditioning system (RIC) in patients at high risk of developing non-Hodgkin's lymphoma B receiving allogeneic hematopoietic stem cell transplantation.

PI: Dr/a Martín Calvo, M<sup>a</sup> Carmen

0293/12: A randomized, double-blind, placebo-controlled, phase 3 study of the efficacy and safety of oral azacitidine plus the best supportive treatment vs. the best supportive treatment as maintenance therapy in patients with acute myelogenous leukemia in complete remission.

PI: Dr/a Serrano López, Josefina

0202/13: A randomized, double-blind, phase 3 study to assess the efficacy and safety of rituximab plus lenalidomide (CC-5013) vs. rituximab plus placebo in subjects with indolent relapsed / resistant lymphoma.

PI: Dr/a Sánchez García, Joaquín

0008/13: An open, randomized, prospective, two-arm, phase III study to assess the treatment-free remission rate in patients with Ph-positive chronic myeloid leukemia (CML) after two treatments of different durations.

PI: Dr/a Molina Hurtado, José Ramón

0165/13: An open, phase IIIb trial to assess the safety of changing intravenous rituximab to subcutaneous rituximab in the course of first-line treatment of CD20+ Follicular and Diffuse Non-Hodgkin's Large B-Cell Lymphoma.

PI: Dr/a Sánchez García, Joaquín

1657: Effectiveness and safety of liposomal amphotericin B in combination with voriconazole in the treatment of invasive fungal infection caused by filamentous fungi in immunocompromised paediatric patients.

PI: Dr/a Gómez García, Pedro

1790: Study of the correlation between ex vivo response to anticancer drugs and their effectiveness in treating acute myeloid leukemia.

PI: Dr/a Serrano López, Josefina

1959: Hematopoietic stem cell transplantation from haploidentical donors with in vitro selective depletion of allo-reactive lymphocytes in patients with high-risk hematological malignancies.

PI: Dr/a Martín Calvo, M<sup>a</sup> Carmen

1949: An observational, multicenter study of the guidelines for recombinant factor IX treatment in patients with hemophilia B in Spain. Observation period: 1 year

PI: Dr/a Velasco Gimena, Francisco

2109: An observational, post-authorization study to assess the evolution in regular clinical practice of patients newly diagnosed with myelodysplastic syndrome (MDS) or myelomonocytic leukemia (MML) according to the time of treatment initiation.

PI: Dr/a Sánchez García, Joaquín

2224: A multicenter, retrospective study to describe the effectiveness and safety of clofarabine as compassionate use treatment in adult patients with relapsed/refractory acute leukemia prior to hematopoietic stem cell transplantation.

PI: Dr/a Serrano López, Josefina

2277: Modelling treatment and disease burden of chronic lymphocytic leukemia to determine the treatment of choice in the United Kingdom, Italy and Spain.

PI: Dr/a Molina Hurtado, José Ramón

2257: A study to validate an ex vivo individualized test for acute lymphoblastic leukemia.

PI: Dr/a Serrano López, Josefina

2365: A retrospective study to evaluate the subcutaneous administration of bortezomib in the first-line treatment of patients with multiple myeloma (MM) who are not candidates for autologous hematopoietic stem cell transplantation (VERSA STUDY).

PI: Dr/a Álvarez Rivas, Miguel Ángel

## GC17

# Physiopathology of Endocrine Vitamin D System Biotechnology and Aging

### Team Leader

#### Principal Investigator (PI)

José Manuel Quesada Gómez

[md1qugoj@uco.es](mailto:md1qugoj@uco.es)

Thematic Network of Research Partnerships on Aging–Frailty (RETICEF)

PAIDI CTS–413 scientific group

### Senior Researchers

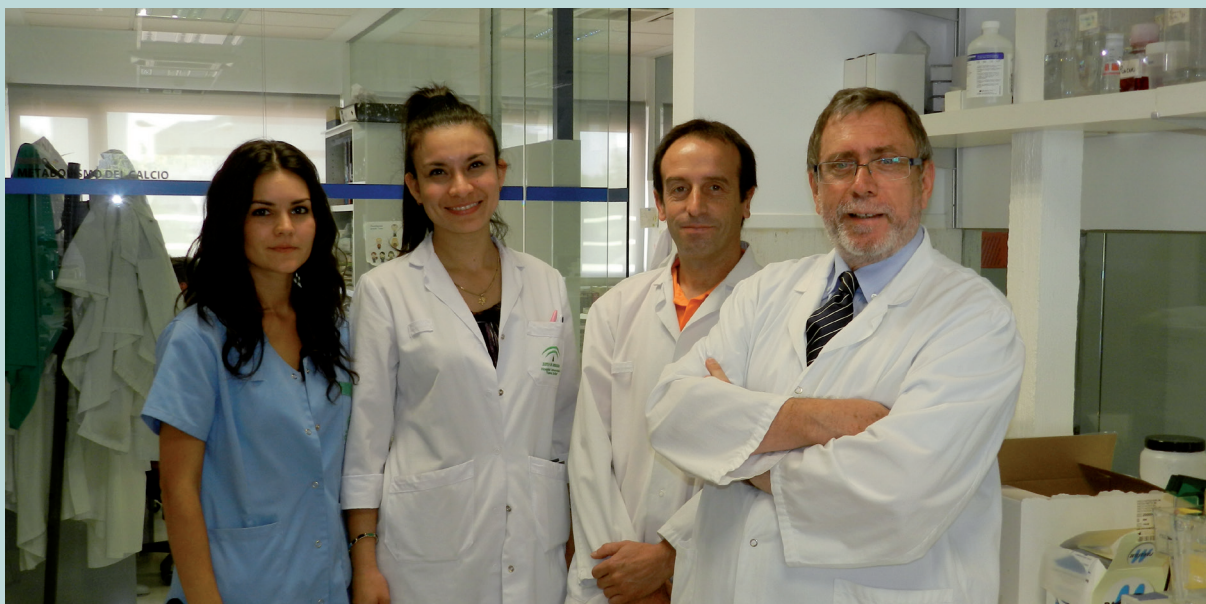
Antonio Casado Diaz

Rafael Cuenca Acevedo

Jose M<sup>a</sup> Mata Granados

Raquel Santiago Mora

Ignacio Serrano Alférez



## Scientific Activity

Our group studies:

1. Osteoporosis: related risk factors, genetics and epidemiology. Endocrine system of vitamin D, other liposoluble vitamins, carotenoids, fatty acids related to osteoporosis and aging.

2. Differentiation of mesenchymal stem cells into osteoblasts, adipocytes or vessels. Study of genes and related factors. Its application in human clinical medicine.

a) Evaluation of compounds that may influence the differentiation of mesenchymal stem cells to osteoblasts and adipocytes. By following this line,

we intend to evaluate the differentiation capacity of mesenchymal stem cells into adipocytes and osteoblasts in drugs and natural compounds in order to determine what may favour or hinder the formation of new bone. The results obtained in this area may open up new therapeutic strategies to prevent and counter osteoporosis.

b) Studies of gene expression of genes related to osteogenesis and adipogenesis.

The aim of this research is to identify human stem cells, which are genes involved in the differentiation into osteoblasts and adipocytes, and associated with osteoporosis. To achieve this,

we hope to carry out functional genomics studies to compare gene expression profiles between stem cells originating from both osteoporotic and non-osteoporotic women.

## Keywords

Osteoporosis, vitamin D, carotenoids, fatty acids, human mesenchymal stem cells (MStC) of adult adipocytes, osteoblasts, polyphenols, gene expression, proteomics, nutrigenetics, and nutrigenomics.

## Publications

### Originals Publications

Casado-Díaz A, Santiago-Mora R, Dorado G, Quesada-Gómez JM. Risedronate Positively Affects Osteogenic Differentiation of Human Mesenchymal Stromal Cells. *Arch Med Res.* 2013, 44(5):325-334.  
IF:2,079

Casado-Díaz A, Santiago-Mora R, Dorado G, Quesada-Gómez JM. The omega-6 arachidonic fatty acid, but not the omega-3 fatty acids, inhibits osteoblastogenesis and induces adipogenesis of human mesenchymal stem cells: potential implication in osteoporosis. *Osteoporosis Int.* 2013, 24(5):1647-1661.  
IF:4,039

Mata-Granados JM, Cuenca-Acebedo R, Luque de Castro MD, Quesada Gómez JM. Lower vitamin E serum levels are associated with osteoporosis in early postmenopausal women: a cross-sectional study. *J Bone Miner Metab.* 2013, 31(4):455-460.  
IF:2,219

Quesada-Gomez JM, Diaz-Curiel M, Sosa-Henriquez M, Malouf-Sierra J, Nogues-Solan X, Gomez-Alonso C, Rodriguez-Manas L, Neyro-Bilbao JL, Cortes X, Delgadillo J. Low calcium intake and inadequate vitamin D status in postmenopausal osteoporotic women. *J Steroid Biochem Mol Biol.* 2013, 136(Nº especial SI):175-177.  
IF:3,984

Casado-Díaz A, Cuenca-Acebedo R, Navarro-Valverde C, Diaz-Molina C, Caballero-Villarraso J, Santiago-Mora R, Dorado G, Quesada-Gomez JM. Vitamin D status and the Cdx-2 polymorphism of the vitamin D receptor gene are determining factors of bone mineral density in young healthy postmenopausal women. *J Steroid Biochem Mol Biol.* 2013, 136(Nº especial SI):187-189.  
IF: 3,984

### Joint Publications

Guerri-Fernandez RC, Nogues X, Gomez JMQ, del Pliego ET, Puig L, Garcia-Giralt N, Yoskovitz G, Mellibovsky L, Hansma PK, Diez-Perez A. Microindentation for In Vivo Measurement of Bone Tissue Material Properties in Atypical Femoral Fracture Patients and Controls. *J Bone Min Res.* 2013, 28(1):162-168.  
IF:6,128

### Research Projects

Quesada Gómez, JM. Study of the effect of Oleuropein on fibroblasts. Implications in the treatment of diabetic foot. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0335-2012

Quesada Gómez, JM. Evaluation of the healing effect in an in vivo model. Sponsored by: Carlos III Health Institute (ISCIII). Reference: PI12/02315

Quesada Gómez, JM. RETICEF. Sponsored by: Carlos III Health Institute (ISCIII). Reference: RD12/0043/0028

# GC18

## Translational Research in Surgery of Solid Organ Transplantation

### Team Leader

#### Principal Investigator (PI)

Francisco Javier Briceño Delgado  
javibriceno@hotmail.com

#### Senior Researchers

Rubén Ciria Bru  
Manuel Leva Vallejo  
Pedro López Cillero  
María Pleguezuelo Navarro  
Juan Carlos Pozo Laderas  
Juan Carlos Regueiro López  
Juan Carlos Robles Ariza  
Sebastián Rufián Peña  
Juan Ruiz Rabelo

#### Other members of the Group

(Other researchers, Technical, and  
Administrative Staff)  
Álvaro Arjona Sánchez  
Juan Pablo Campos Hernández  
Jesús Jiménez Gómez  
Francisco Cristóbal Muñoz Casares  
Diana Valencia Núñez





## Scientific Activity

Our group studies aspects related to the increase in the donor pool and technical innovations in solid organ transplants. It also aims to establish guidelines to improve the use of expanded criteria donors, and to devel-

op and implement improvements in surgical techniques and technological innovations in the transplant of solid organs.

## Keywords

Liver transplant, pancreas transplant, kidney transplant, lung transplant, heart transplant, living donor transplantation, pediatric transplantation, split transplantation, expanded criteria donors.

## Publications

### Originals Publications

Arjona-Sanchez A, Muñoz-Casares FC, Casado-Adam A, Sanchez-Hidalgo JM, Teran MDA, Orti-Rodríguez R, Padial-Aguado AC, Medina-Fernandez J, Ortega-Salas R, Pulido-Cortijo G, Gomez-España A, Rufian-Pena S. Outcome of patients with aggressive pseudomyxoma peritonei treated by cytoreductive surgery and intraperitoneal chemotherapy. *World J Surg.* 2013, 37(6):1263-1270. IF:2,228

Briceño J, Ciria R, de la Mata M. Donor-recipient matching: Myths and realities. *J Hepatol.* 2013, 58(4):811-820. IF:9,858

Fernandez FJM, Teran MDA, Galera MSL, Torres PR, Estudillo GB, Pena SR. Resection margins in conservative breast cancer surgery. *Cir Esp.* 2013, 91(7):404-412. IF:0,871

Aguilar-Melero P, Luque A, Machuca MM, de Obanos MPP, Navarrete R, Rodríguez-García IC, Briceño J, Iniguez M, Ruiz J, Prieto J, de la Mata M, Gomez-Villamandos RJ, Muntane J, Lopez-Cillero P. Cardiotrophin-1 reduces ischemia/reperfusion injury during liver transplant. *J Surg Res.* 2013, 181(2):e83-91. IF:2,018

Ayllon-Teran MD, Torres-Lorite M, Benitez-Cantero JM, Sanchez-Hidalgo JM, Diaz-Iglesias C, Rufian-Pena S. An uncommon cause of high blood pressure in young people: retroperitoneal paraganglioma with vascular invasion. *Neurologia.* 2013, 33(3):435-6. IF:1,274

Valencia Nuñez DM1, Merino Cejas C, Alados Arboledas P, Muñoz Carvajal I. Heart transplantation in a patient with recurrent early extensive endocarditis. *Interact Cardiovasc Thorac Surg.* 2013;17(2):423-5. IF: 1,112

### Joint Publications

Grau S, Salavert M, Laderas JCP, Vargas MG, Barrueta JA, Mir N. Cost-effectiveness of anidulafungin in confirmed candidaemia and other in-

vasive Candida infections in Spain. *J Mycol Med.* 2013, 23(3):5-163. IF:0,740

Gomez-Bravo MA, Salcedo M, Fondevila C, Suarez F, Castellote J, Rufian S, Pons JA, Alamo JM, Millan O, Brunet M. Impact of Donor and Recipient CYP3A5 and ABCB1 Genetic Polymorphisms on Tacrolimus Dosage Requirements and Rejection in Caucasian Spanish Liver Transplant Patients. *J Clin Pharmacol.* 2013, 53(11):1146-54. IF:2,963

Cruz-Ramirez M, Hervás-Martínez C, Fernandez JC, Briceño J, de la Mata M. Predicting patient survival after liver transplantation using evolutionary multi-objective artificial neural networks. *Artif Intell Med.* 2013, 58(1):37-49. IF:1,355

Ruiz Cuesta P, Hervás Molina AJ, Jurado García J, Pleguezuelo Navarro M, García Sánchez V, Casáis Juanena LL, Gálvez Calderón C, Naranjo Rodríguez A. Pneumatic dilation in the treatment of achalasia. *Gastroenterol Hepatol.* 2013, 36:508-12. IF:0,567

Cruz-Ramirez M, Hervás-Martínez C, Gutierrez PA, Perez-Ortiz M, Briceño J, de la Mata M. Memetic Pareto differential evolutionary neural network used to solve an unbalanced liver transplantation problem. *Soft Computing.* 2013, 17(2):275-284. IF:1,124

Rodríguez-Perálvarez M, Tsochatzis E, Naveas MC, Pieri G, García-Caparrós C, O'Beirne J, Poyato-González A, Ferrín-Sánchez G, Montero-Alvarez JL, Patch D, Thorburn D, Briceño J, De la Mata M, Burroughs AK. Reduced exposure to calcineurin inhibitors early after liver transplantation prevents recurrence of hepatocellular carcinoma. *J Hepatol.* 2013, 59(6):1193-1199. IF:9,858

Ferrín G, Ranchal I, Llamaza C, Rodríguez-Perálvarez ML, Romero-Ruiz A, Aguilar-Melero P, López-Cillero P, Briceño J, Muntané J, Montero-Alvarez JL, De la Mata M. Identification of candidate biomarkers for hepatocellular carcinoma in plasma of HCV-infected cirrhotic patients by 2-D DIGE. *Liver Int.* 2013, 34(3):438-446. IF:3,870

Haad CR, Rodríguez-Benot A, Martínez-Vaquera S, Navarro-Cabello MD, Agüera-Morales ML, Ruiz de Mier MV, Montero-Alvarez JL, Mata-Gar-

cia Mde L, Briceño-Delgado J, Aljama-García P. Combined Liver-Kidney Transplantation: Survey of a Single Center in Spain. *Transplant Proc.* 2013, 45(10):3640-3643. IF:0,952

García-Rubio JH, García JR, Hernández PC, López JM, Curado FA, Vallejo ML, López JC, Gómez EG, Aljama P, Tapia MJ. Correlation between dual kidney biopsy in expanded-criteria donors and transplant survival. *Transplant Proc.* 2013, 45(10):3606-3608. IF:0,952

Ruiz Cuesta P, Hervás Molina AJ, Muñoz García-Borrueal M, Jurado García J, García Sánchez V, Pleguezuelo Navarro M, Casáis Juanena LL, Naranjo Rodríguez A. Endoscopic retrograde cholangiopancreatography in patients with anatomic abnormalities of the stomach due to surgery. *Gastroenterol Hepatol.* 2013, 36(10):609-15. IF:0,567

Koretz RL, Pleguezuelo M, Arvaniti V, Baena PB, Ciria R, Gurusamy KS, Davidson BR, Burroughs AK. Interferon for interferon nonresponding and relapsing patients with chronic hepatitis C. *Cochrane Database Syst Rev.* 2013, n°1:n° de art CD003617. IF:5,703

### Research Projects

Rufián Peña, S. Role of intraoperative intraperitoneal chemotherapy with paclitaxel in radical surgical treatment of peritoneal carcinomatosis of ovarian origin: hyperthermia versus normothermia. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: 0678/2010

Ciria Bru, R. The biliary tract in liver transplantation: A global study measuring O2 tissue microvoltage, microflowmetry and histology of the factors involved in its viability. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0543-2012

Muñoz Casares, FC. Efficacy and safety of early postoperative intraperitoneal chemotherapy with paclitaxel in radical surgical treatment of ovarian peritoneal carcinomatosis. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0327-2013

Ruiz Rabelo, JF. Sequential preclinical study to improve and validate a standard port for single-incision laparoscopic and thoracoscopic surgery. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0327-2013

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## Third Party Services

Briceño Delgado, FJ. Stand in course on advanced liver surgery. Sponsored by: Covidien Spain, S.L. Reference: PSS.0041

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## Clinical Trials

0026/07/EPA: A prospective study to assess the prevalence and clinical relevance of polymorphisms in genes encoding biotransformation enzymes and tacrolimus and mycophenolate mofetil carrier proteins in primary transplant patients. Pharmacogenetics and immunosuppression in liver tx. LIVERGEN study.  
PI: Dr/a Rufián Peña, Sebastián

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0286/09: An open, multicenter, randomized, phase III trial on the therapeutic use of intraportal infusion of autologous bone marrow mononuclear cells as liver regeneration enhancer prior to liver resection.  
PI: Dr/a Rufián Peña, Sebastián

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0239/11: Role of intraoperative intraperitoneal paclitaxel chemotherapy in radical surgical treatment of ovarian-origin peritoneal carcinomatosis: hyperthermia versus normotemia.  
PI: Dr/a Rufián Peña, Sebastián

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1707: A study to assess the feasibility, validity and reliability of the three-day voiding diary in women attending functional urology and urodynamics units. DM.3D Study  
PI: Dr/a Leva Vallejo, Manuel

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# GC19

## Applications of Artificial Vision

### Team Leader

#### Principal Investigator (PI)

Rafael Medina Carnicer

[rmedina@uco.es](mailto:rmedina@uco.es)

PAIDI TIC-161 scientific group

### Senior Researchers

Ángel Carmona Poyato

Nicolás L. Fernández García

Juan L. Garrido Castro

Fº José Madrid Cuevas

Manuel J. Marín Jiménez

Rafael Muñoz Salinas

Enrique Yeguas Bolívar

### Pre-doctoral Researchers

Eusebio J. Aguilera Aguilera

Sergio Garrido Jurado

David López Fernández

Manuel I. López Quintero

Victor M. Mondejar Guerra



## Scientific Activity

The main line of research of this group is focused on fundamental problems in artificial vision, which supports all the technology developed in the lines applied.

The activity of this group is centred on some basic topics and results in the publication of papers in impact reviews. The topics are as follows: Unsupervised segmentation of scenes, Tracking, unsupervised recognition of

objects in a scene, Volumetric Reconstruction.

This group develops practical lines of research related to 2D and 3D Vision Systems Design for specific applications in biomedical or industrial environments. The latest activities of the Group were centred on unsupervised evaluation of human mobility, automatic calculation of the geometry of irregular objects for an optimal waste storage, fall risk prediction in the elderly and the development of

automated X-ray analysis systems supporting the diagnosis of any type disease.

## Keywords

Unsupervised Segmentation, Edge detection, Histogram Thresholding, Hystéresis, Tracking, Points Dominant. 3D-Vision.

## Publications

### Originals Publications

Marin-Jimenez MJ, Yeguas E, de la Blanca NP. Exploring STIP-based models for recognizing human interactions in TV videos. *Pattern Recognit Lett.* 2013, 34(15):1819-1828.

IF: 1,266

### Research Projects

Garrido Castro, J L. Three-dimensional kinematic analysis of shot in volleyball: comparing senior female players vs young players as a tool for improving players' training and performance. Sponsored by: Spanish National Sports Council. Reference: 024/SAL10/12

Medina Carciner, R. Svsmem: 3D Vision system without markers for unsupervised assessment of mobility. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO) Reference: TIN2012-32952

### Collaboration Agreements

Medina Carciner, R. Implementing a 3D vision system (SVCS) for determining irregular object geometries in CN. Jose Cabrera. Sponsored by: Enresa

# GC20

## Genetics and Behavior Diseases

### Team Leader

#### Principal Investigator (PI)

Manuel Ruiz Rubio  
[ge1rurum@uco.es](mailto:ge1rurum@uco.es)  
PAIDI BIO-272 scientific group

#### Senior Researchers

Encarna Alejandre Durán  
Rafael Burgos Marín  
Vicente Sánchez Vázquez

#### Post-doctoral Researcher

M<sup>a</sup> del Mar Gámez del Estal

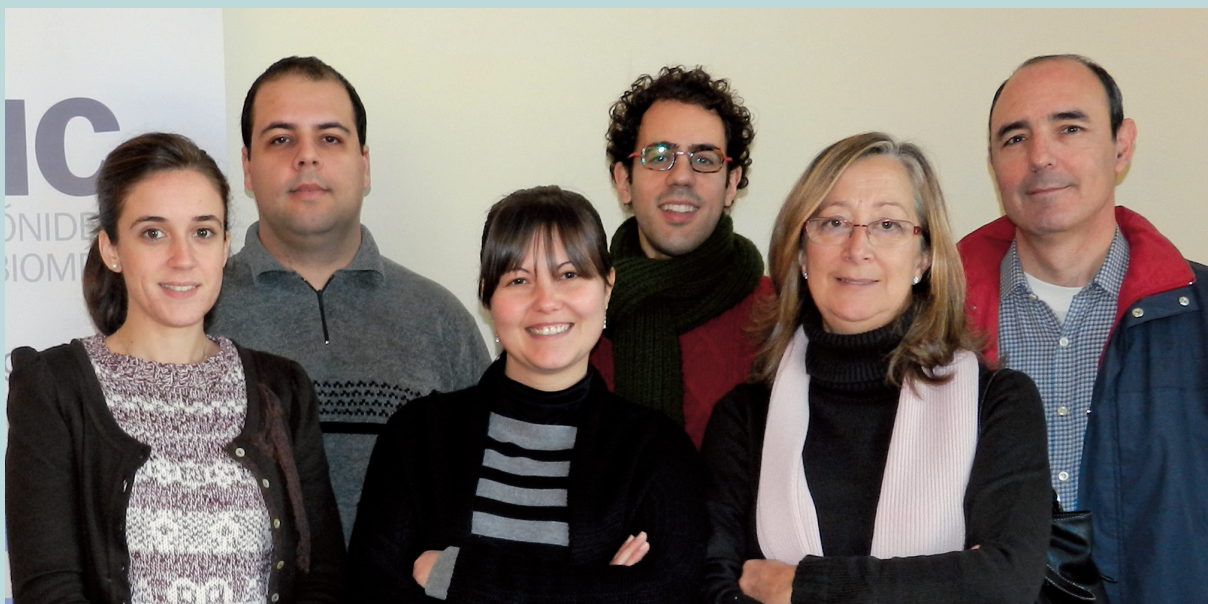
#### Pre-doctoral Researcher

Jaime Osuna Luque

#### Other members of the Group

(Other researchers, Technical, and  
Administrative Staff)

Teresa Gujarro Granados  
Pilar Martín Borreguero  
M<sup>a</sup> Auxiliadora Romero Balsera  
M<sup>a</sup> Araceli Sánchez Raya



## Scientific Activity

Significant progress is being made nowadays in our understanding of the genetic basis of autism. Many of the genes involved encode proteins which are involved in synaptic function. *Caenorhabditis elegans* is an organism which constitutes an ideal model for studying synapse interactions because it only has about 300 neurons, and these are well characterized. In *C. elegans* there are genes which are orthologous to the human genes involved in autism, which encode proteins involved in the synapse. We have characterized mutants in

some of these genes by observing changes in behaviour, as well as in response to chemical compounds that interfere with neurotransmitters, such as gamma-aminobutyric acid (GABA) or acetylcholine. The use of *C. elegans* as a model organism allows us to create an experimental setting that facilitates the genetic study of synaptic components. With the results obtained, our long term aim is to extrapolate them to humans and be able to explain the neurobiological mechanisms involved in the etiology of autism and other developmental diseases.

On the other hand, the members

of the Unit for Child and Adolescent Mental Health (USMI-J) are conducting a detailed phenotypic analysis of a sample of patients diagnosed with autism in order to establish distinctive features and to determine whether autism can be associated in the future with specific genetic or environmental alterations.

## Keywords

Autism, pervasive developmental disorders, neuronal synapses, postsynaptic density, *C. elegans* as a model organism in synaptic function.

## Publications

### Originals Publications

Izquierdo PG, Calahorro F, Ruiz-Rubio M. Neurotrophin modulates the locomotory dopaminergic and serotonergic neuronal pathways of *C. elegans*. *Neurogenetics*. 2013, 14(3-4):233-242  
IF: 3,575

Calahorro, F, Ruiz-Rubio, M. Human alpha- and beta-NRXN1 isoforms rescue behavioral impairments of *Caenorhabditis elegans* neurexin-deficient mutants. *Genes, Brain and Behavior*. 2013, 12(4):453-464.  
IF: 3,597

### Third Party Services

Ruiz Rubio, M. *Caenorhabditis elegans* as models of neurological diseases. Sponsored body: Canvax Biotech S.L. Reference:INTER.0002

# GC 21

## Metabolomics. Identification of Bioactive Components

### Team Leaders

#### Principal Investigator (PI)

M<sup>o</sup> Dolores Luque de Castro

qa1lucam@uco.es

PAIDI FQM-227 scientific group

#### Emerging Researcher

Feliciano Priego Capote

### Senior Researchers

Beatriz Álvarez Sánchez

Carlos Ferreiro Vera

José Gonzalez Rodriguez

Rafael Japón Luján

José Luis Luque García

José María Mata Granados

Salomé Morales Muñoz

Pedro Pérez Juan

José Antonio Pérez Serradilla

María Isabel Orozco Solano

Jose Ruiz Jimenez

### Pre-doctoral Researchers

Miguel Alcaide Molina

Mónica Calderón Santiago

María Pilar Delgado De La Torre

María Auxiliadora Fernández Peralbo

Antonio Mena Bravo

M<sup>o</sup> del Mar Delgado Povedano

Mónica Molina Calle

Carlos Augusto Escobar Ledesma

Asunción López Bascón

Francisco Sánchez Borrego

Angela Peralbo Molina

Verónica Sanchez De Medina Baena



## Scientific Activity

This group deals mainly with the development of analytical methods in which the preparation stage of the sample, as required, is fully or partially automated with the help of dynamic systems and is accelerated by auxiliary energies such as microwaves, ultrasound or pressure+ temperature (overheated liquids). In the analysis stage, the very latest equipment is used (GC-MS/MS, Quad-triple HPLC, HPLC-Q-TOF) to achieve maximum

sensitivity, selectivity and precision. The group carries out research in the area of metabolomics and to a lesser extent, in proteomics. In the former, most of its contributions have been aimed at lipidomics, nutrimentalomics and the search for biomarkers of bone metabolism. One research line linked to this is the utilization of agricultural residues and feeding industries to obtain high value-added products for the production of nutraceuticals, food supplements and natural dyes.

Another area of interest for the group is the study of the degradation pathways of toxic compounds using auxiliary energy.

## Keywords

Metabolomics, proteomics, metabolites, biomarkers, analytical platforms, nutraceuticals, food supplements, preparation of samples, degradation assisted by auxiliary energy.

## Publications

### Originals Publications

De La Torre MPD, Ferreiro-Vera C, Priego-Capote F, Luque de Castro MD. Anthocyanidins, proanthocyanidins, and anthocyanins profiling in wine lees by solid-phase extraction-liquid chromatography coupled to electrospray ionization tandem mass spectrometry with data-dependent methods. *J Agric Food Chem.* 2013, 61(51), 12539-12548  
IF:2,906

de Medina, VS, Priego-Capote, F, Luque de Castro MD. Comparison of saponification methods for characterization of the nonsaponifiable fraction of virgin olive oil. *Eur J Lipid Sci Technol.* 2013, 115(11):1325-1333.  
IF:2,266

Fernández Peralbo MA, Priego-Capote F, Galache-Osuna JG, Luque de Castro MD. Targeted analysis of omega-6-derived eicosanoids in human serum by SPE-LC-MS/MS for evaluation of coronary artery disease. *Electrophoresis.* 2013, 34(19):2901-2909.  
IF:3,261

Calderón-Santiago M, Priego-Capote F, Galache-Osuna JG, Luque de Castro MD. Metabolomic discrimination between patients with stable angina, non-ST elevation myocardial infarction, and acute myocardial infarct. *Electrophoresis.* 2013, 34(19), 2827-2835.  
IF:3,261

de Medina VS, El Riachy M, Priego-Capote F, Luque de Castro MD. Mass spectrometry to evaluate the effect of the ripening process on phenols of virgin olive oils. *Eur J Lipid Sci Technol.* 2013, 115(9):1053-1061.  
IF:2,266

Alvarez-Sanchez B, Priego-Capote F, García-Olmo J, Ortiz-Fernandez MC, Sarabia-Peinador LA, Luque Castro MD. Near-infrared spectroscopy and partial least squares-class modeling (PLS-CM) for metabolomics fingerprinting discrimina-

tion of intervention breakfasts ingested by obese individuals. *J Chemometr.* 2013, 27(9):221-232.  
IF:1,937

Orozco-Solano MI, Priego-Capote F, Luque de Castro MD. Analysis of esterified and nonesterified fatty acids in serum from obese individuals after intake of breakfasts prepared with oils heated at frying temperature. *Anal Bioanal Chem.* 2013, 405(18):6117-6129.  
IF:3,659

Ferreiro-Vera C, Priego-Capote F, Calderón-Santiago M, Luque de Castro MD. Global metabolomic profiling of human serum from obese individuals by liquid chromatography-time-of-flight/mass spectrometry to evaluate the intake of breakfasts prepared with heated edible oils. *Food Chem.* 2013, 141(3):1722-1731.  
IF:3,334

Peralbo-Molina A, Priego-Capote F, Luque de Castro MD. Characterization of grape seed residues from the ethanol-distillation industry. *Anal Methods.* 2013, 5(8):1922-1929.  
IF:1,855

Ferreiro-Vera C, Priego-Capote F, Luque de Castro MD. An approach for quantitative analysis of vitamins D and B-9 and their metabolites in human biofluids by on-line orthogonal sample preparation and sequential mass spectrometry detection. *Analyst.* 2013, 138(7):2146-2155.  
IF:3,969

Ferreiro-Vera C, Priego-Capote F, Luque de Castro MD. Integrated identification / confirmatory and targeted analysis of epoxyeicosatrienoic acids in human serum by LC-TOF MS and automated on-line SPE-LC-QqQ MS/MS. *Talanta.* 2013, 106:440-447.  
IF:3,498

Orozco-Solano MI, Priego-Capote F, Luque de Castro MD. Ultrasound-assisted hydrolysis and chemical derivatization combined to lab-on-valve solid-phase extraction for the determination of sialic acids in human biofluids by mu-liquid chromatography-laser induced fluorescence.

*Anal Chim Acta.* 2013, 766:69-76.  
IF:4,387

Calderón-Santiago M, Priego-Capote F, Galache-Osuna JG, Luque de Castro MD. Method based on GC-MS to study the influence of tricarboxylic acid cycle metabolites on cardiovascular risk factors. *J Pharm Biomed Anal.* 2013, 74:178-185.  
IF:2,947

Ferreiro-Vera C, Priego-Capote F, Luque de Castro MD. Short-term comparative study of the influence of fried edible oils intake on the metabolism of essential fatty acids in obese individuals. *Food Chem.* 2013, 136(2):576-584.  
IF:3,334

Alcaide-Molina M, Priego-Capote F, Luque de Castro MD. Sequential determination of metabolites involved in the biosynthesis of aromatic amino acids after ultrasound-assisted extraction from plants and reverse LC separation. *Talanta.* 2013, 105:429-434.  
IF:3,498

Delgado-Povedano MM, Luque de Castro MD. Ultrasound-assisted analytical emulsification-extraction. *Trac-Trends Anal Chem* 2013, 45:1-13.  
IF:6,351

Delgado-Povedano MM, Luque de Castro MD. Ultrasound-assisted extraction and in situ derivatization. *J Chromatogr A.* 2013, 1296(Nº especial SI):226-234.  
IF:4,612

Peralbo-Molina A, Luque de Castro MD. Potential of residues from the Mediterranean agriculture and agrifood industry. *Trends Food Sci Technol.* 2013, 32(1):16-24.  
IF:4,135

### Joint Publications

Villatoro-Pulido M, Priego-Capote F, Alvarez-Sánchez B, Saha S, Philo M, Obregón-Cano S, De Haro-Bailón A, Font R, Del Río-Celestino M. An approach to the phytochemical profiling of rocket



[*Eruca sativa* (Mill.) Thell]. *J Sci Food Agric*. 2013, 93(15):3809–3819.  
IF:1,759

Rojano-Delgado AM, Priego-Capote F, Barro F, Luque de Castro MD, De Prado R. Liquid chromatography–diode array detection to study the metabolism of glufosinate in *Triticum aestivum* T-590 and influence of the genetic modification on its resistance. *Phytochemistry*. 2013, 96:117–122.  
IF:3,051

Mata-Granados JM, Cuenca-Acebedo R, Luque de Castro MD, Quesada Gómez JM. Lower vitamin E serum levels are associated with osteoporosis in early postmenopausal women: a cross-sectional study. *J Bone Miner Metab*. 2013, 31(4):455–460.  
IF:2,219

Perez-Herrera A, Rangel-Zuñiga OA, Delgado-Lista J, Marin C, Perez-Martinez P, Tasset I, Tunez I, Quintana-Navarro GM, Lopez-Segura F, Luque de Castro MD, Lopez-Miranda J, Camargo A, Perez-Jimenez F. The antioxidants in oils heated at frying temperature, whether natural or added, could protect against postprandial oxidative stress in obese people. *Food Chem*. 2013, 138(4):2250–2259.  
IF:3,334

## Research Projects

Luque de Castro MD. Development of analytical metabolomic platforms to identify cardiac biomarkers and contribute to the design of individualized diets. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: CTQ2009-07430

Priego Capote, F. Development of analytical platforms for the identification of biomarkers of glycosylated proteins: Application to diabetic patients. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: P10-FQM-6420

Luque de Castro MD. Study of the relevance of ultrasound frequency in improving sample preparation stages in proteomics, metabolomics and degradation processes. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: CTQ2012-37428

Luque de Castro, MD. Optimizing and applying metabolomic platforms for non-invasive analysis of biofluids to determine markers for early diagnosis of lung cancer. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: FQM1602-2012

## Collaboration Agreements

Luque de Castro, MD. Completing the development of active plant compound extraction methods for their identification and quantification. Sponsored by: Phytoplant Research, S. L.

Luque de Castro, MD. Extraction of stevia plants: identifying the components of the extract and optimizing the extraction and purification of the compounds of interest. Sponsored by: Consortium with "Campus de Excelencia Internacional en Agroalimentación (ceiA3)" (Agrifood Campus of International Excellence)

# GC22

## Epigenetics

### Team Leader

#### Principal Investigator (PI)

Teresa Roldán Arjona  
ge2roarm@uco.es

#### Senior Researcher

Rafael Rodríguez Ariza

#### Post-doctoral Researchers

M<sup>º</sup> Dolores Córdoba Cañero  
M<sup>º</sup> Victoria García Ortiz  
M<sup>º</sup> Isabel Martínez Macías  
M<sup>º</sup> Teresa Morales Ruiz

#### Pre-doctoral Researchers

Jara T. Parilla Doblaz  
Ángel Ramiro Merina  
Casimiro Barbado García-Gil  
Iván Devesa Guerra



## Scientific Activity

Our scientific activity is focused on the study of the mechanisms involved in maintaining genome and epigenome stability. Our group has found genetic and biochemical evidence for the existence of a mechanism for active demethylation of DNA in plants. We have identified a family of proteins, whose prototype is ROS1 and DME, which exhibit methylcytosine 5-DNA glycosylase activity, and initiate the deletion of 5-mec by a mech-

anism analogous to the Base Excision Repair (BER). Using genetic and molecular approaches, we have characterized in detail the biochemical activity of this new family of enzymes. In addition we have identified other proteins involved in this mechanism of epigenetic reprogramming. We are currently investigating the relevance of the base repair system in the maintenance and control of genetic and epigenetic information. In addition, we intend to analyze the relationship between this new route for demeth-

ylation of DNA and different modifications in the structure of chromatin. Finally, we are exploring the feasibility of using ROS1 and DME to initiate a controlled demethylation of DNA in human cells.

## Keywords

Genetics, Epigenetics, Mutagenesis, DNA repair, DNA methylation, gene regulation.

## Publications

### Originals publications

Parrilla-Doblas JT, Ponferrada-Marín MI, Roldán-Arjona T, Ariza RR. Early steps of active DNA demethylation initiated by ROS1 glycosylase require three putative helix-invading residues. *Nucleic Acids Res.* 2013, 41(18):8654-8664. IF: 8,278

Martínez-Merina A, Ariza RR, Roldán-Arjona T. Molecular characterization of a putative plant homolog of MBD4 DNA glycosylase. *DNA Repair.* 2013, 12(11):890-898. IF: 4,274

Martínez-Macias MI, Córdoba-Canero D, Ariza RR, Roldán-Arjona T. The DNA repair Protein XRCC1 Functions in the Plant DNA Demethylation Pathway by Stimulating Cytosine Methylation (5-mec) Excision, Gap Tailoring, and DNA Ligation. *J Biol Chem.* 2013, 288(8):5496-5505. IF: 4,651

### Joint Publications

Martin MJ, García-Ortiz MV, Gomez-Bedoya A, Esteban V, Guerra S, Blanco L. A specific N-terminal extension of the 8 kDa domain is required for DNA end-bridging by human Polmu and Pol lambda. *Nucleic Acids Res.* 2013;41(19):9105-9116. IF: 8,278

Martin MJ, García-Ortiz MV, Esteban V, Blanco L. Ribonucleotides and manganese ions improve non-homologous end joining by human Pol mu. *Nucleic Acids Res.* 2013, 41:2428-2436. IF: 8,278

### Research Projects

Roldán Arjona, M<sup>a</sup> T. DNA demethylation: basic molecular mechanisms and their relevance to the reversal of epigenetic silencing. Sponsored by: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: BFU2010-18838

Roldán Arjona, M<sup>a</sup> T. Molecular mechanisms of DNA demethylation and implications in epigenome reprogramming. Sponsored by: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: CVI-7576

### Third Party Services

Roldán Arjona, M<sup>a</sup> T. Services provided by M<sup>a</sup> Teresa Roldán a Canvax' research group to Canvax. Sponsored by: Canvax Biotech S.L. Reference: PSS.0032

# GE1

## Oxidative Stress and Nutrition

### Team Leader

#### Emerging Researcher

Isaac Túnez Fiñana

[fm2tufi@uco.es](mailto:fm2tufi@uco.es)

PAIDI CTS-624 scientific group

#### Senior Researchers

Félix Gascón Luna

Evelio Luque Carabot

José Peña Amaro

M<sup>ª</sup> Concepción Ruiz Villen

Manuel Salcedo Espinosa

Ignacio Jimena Medina

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)

Eduardo Agüera Morales

Ana Isabel Giraldo Polo

Manuel de la Torre Luque

Fernando Sánchez López

#### Pre-doctoral Researchers

Natacha R. Núñez Paiva

Danilo Avelar Sampaio Ferreira



## Scientific Activity

Our group studies the effect of different antioxidant agents, as well as transcranial magnetic stimulation on neuroplasticity (neurogenesis and synaptogenesis), cell death, oxidative stress and behavioural phenotype in models of neurodegeneration induced by neurotoxins and neuropsychiatric models induced by olfactory bulbectomy. Through these models, we analyze the role played by reactive

oxygen and nitrogen species in the abovementioned phenomena, as well as the possibility of using the properties of the different agents used as new therapeutic strategies.

Recently, the scope of the study has covered the analysis of transcription factors and vitagenes involved in the antioxidant response.

Additionally, the group is currently studying the role of nitrate and oxidative status, as well as and inflammation in vitagene activation in patients

with different neurodegenerative diseases. Finally, the group is involved in intense horizontal research in partnership with other groups in the assessment, analysis and interpretation of oxidative status in different study models and processes.

## Keywords

Oxidative stress, inflammation, mitochondria, cell death, neuroplasticity, antioxidant systems, vitagenes, Nrf2.

## Publications

### Originals Publications

Medina FJ, Túnez I. Mechanisms and pathways underlying the therapeutic effect of transcranial magnetic stimulation. *Rev Neurosci*. 2013; 24(5):507–525  
IF:3,260

Tasset I, Bahamonde C, Agüera E, Conde C, Cruz AH, Pérez-Herrera A, Gascón F, Giraldo AI, Ruiz MC, Lillo R, Sánchez-López F, Túnez I. Effect of natalizumab on oxidative damage biomarkers in relapsing-remitting multiple sclerosis. *Pharmacol Rep*. 2013;65(3):624–31.  
IF:1,965

Tasset I, Pérez-Herrera A, Medina FJ, Arias-Carrión O, Drucker-Colin R, Túnez I. Extremely low-frequency electromagnetic fields activate the antioxidant pathway Nrf2 in a Huntington's disease-like rat model. *Brain Stimul*. 2013; 6(1):84–6.  
IF:4,538

### Joint Publications

Pérez-Herrera A, Rangel-Zuñiga OA, Delgado-Lista J, Marín C, Perez-Martinez P, Tasset I, Túnez I, Quintana-Navarro GM, Lopez-Segura F, de Castro MDL, Lopez-Miranda J, Camargo A, Perez-Jimenez F. The antioxidants in oils heated at frying temperature, whether natural or added, could protect against postprandial oxidative stress in obese people. *Food chemistry*. 2013; 138(4):2250–2259.  
IF:3,334

Yubero-Serrano EM, Delgado-Lista J, Peña-Orihuela P, Perez-Martinez P, Fuentes F, Marín C, Túnez I, Tinahones FJ, Perez-Jimenez F, Roche HM, Lopez-Miranda J. Oxidative stress is associated with the number of components of metabolic syndrome: LIPGENE study. *Exp Mol Med*. 2013; 45:e28–.  
IF:2,573

Yubero-Serrano EM, Gonzalez-Guardia L, Rangel-Zuñiga O, Delgado-Casado N, Delgado-Lista J, Perez-Martinez P, Garcia-Rios A, Caballero J, Marín C, Gutierrez-Mariscal FM, Tinahones FJ, Villalba JM, Túnez I, Perez-Jimenez F, Lopez-Miranda J. Postprandial antioxidant gene expression is modified by Mediterranean diet supplemented with coenzyme Q(10) in elderly men and women. *Age*. 2013; 35(1):159–170.  
IF:4,084

Munoz-Guillen NM, Leon-Lopez R, Túnez-Finana I, Cano-Sanchez A. From vasospasm to early brain injury: new frontiers in subarachnoid haemorrhage research. *Neurologia*. 2013; 28(5):309–316.  
IF:1,322

### Third Party Services

Túnez Fiñana, I. Development of in vitro CNS disease models and trial of the activity of active compounds identified using FRIDA. Sponsored body: Canvax Biotech S.L. Reference: INTER.001

### Collaboration Agreements

Sánchez López, F. Collaboration agreement with the Sociedad Española de Neurología. Sponsored body: Sociedad Andaluza de Neurología (Spanish Association of Neurology). Reference: CCB.0005

### Clinical Trials

0080/09: A randomized, double-blind, placebo-controlled, multicenter, phase III trial of oral cladribine in patients with a first high-risk clinical episode of conversion into multiple sclerosis.  
PI: Dr/a Sánchez López, Fernando

0132/09: A multicenter, randomized, double-blind, parallel-group, placebo-controlled study to evaluate the efficacy and safety of pegylated interferon beta-1a (biib017) in subjects with relapsing multiple sclerosis  
PI: Dr/a Sánchez López, Fernando

0133/09: A multicenter, extension, blind-dose study to determine the safety and efficacy of long-term monotherapy dose of BG00012 in patients with relapsing-remitting multiple sclerosis  
PI: Dr/a Sánchez López, Fernando

0056/10: A multicenter, double-blind, randomized, parallel-group, active-controlled, monotherapy study to determine the effectiveness and safety of daclizumab obtained through a high performance process (DAC HYP) versus Avonex.  
PI: Dr/a Sánchez López, Fernando

0291/10: A multicenter, randomized, semi-crossover, double-blind, phase I/II clinical trial to assess the safety and feasibility of systemic therapy with mesenchymal cells derived from autologous bone marrow in patients with multiple sclerosis.  
PI: Dr/a Sánchez López, Fernando

0329/10: A multicenter, double-blind, placebo-controlled, parallel-group study to assess the effectiveness and safety of Teriflunomid in patients with recurrent multiple sclerosis on treatment with interferon-beta  
PI: Dr/a Sánchez López, Fernando

0103/11: An open, multicenter, non-randomized, parallel-group study evaluating the efficacy of fingolimod in de novo patients vs. fingolimod in patients previously treated with interferon or glatiramer acetate as assessed by measuring the number of bouts in patients with relapsing-remitting multiple sclerosis.  
PI: Dr/a Agüera Morales, Eduardo

0106/11: A long-term, prospective, observational safety study of patients with multiple sclerosis who participated in clinical trials with cladribine  
PI: Dr/a Sánchez López, Fernando

0145/11: A multicenter, extension, dose-blind frequency study to determine the safety and efficacy of long-term pegylated interferon beta-1a (BIB017) therapy in patients with relapsing multiple sclerosis  
PI: Dr/a Sánchez López, Fernando

0196/11: A randomized, double-blind, placebo-controlled, parallel group study to investigate on MRI scans the efficacy and safety of atumumab administered for a period of six months to patients with relapsing-MS

PI: Dr/a Sánchez López, Fernando

0295/11: A multicenter, randomized, placebo-controlled, triple-blind phase I / II clinical trial to assess the safety, feasibility and effectiveness of intravenous therapy with three doses of autologous mesenchymal cells of adipose tissue in patients with moderate to severe Amyotrophic Lateral Sclerosis.

PI: Dr/a Agüera Morales, Eduardo

0221/12: A multicenter, double-blind, parallel-group, placebo-controlled study to assess the efficacy, safety, tolerability and pharmacokinetics of BIIB033 in patients with a first episode of acute optic neuritis.

PI: Dr/a Sánchez López, Fernando

0362/12: A randomized, double-blind, parallel-group, placebo-controlled, 12-week trial of leuco methylthionium bis (hydromethanesulfonate) in patients with mild-to-moderate Alzheimer's disease.

PI: Dr/a Agüera Morales, Eduardo

0031/13: An open, multicenter, extension study to assess the long-term efficacy and safety of BIIB019, Daclizumab obtained using a high-yield process (DAC HYP) in monotherapy in patients with multiple sclerosis who have completed the 205MS301 study.

PI: Dr/a Sánchez López, Fernando

92/13: A randomized, double-blind, placebo-controlled, parallel group, dose-finding study to assess the efficacy, safety, tolerability and pharmacokinetics of biib033 in patients with relapsing multiple sclerosis when used in combination with avonex.

PI: Dr/a Sánchez López, Fernando

0243/13: A multicenter, randomized, parallel-group, observer-blind, phase II study to assess the efficacy, safety and tolerability of plovamer acetate 0.5, 3, 10 and 20 mg vs Copaxone in patients with relapsing-remitting multiple sclerosis.

PI: Dr/a Sánchez López, Fernando

1011: A global, observational study to assess adherence to disease-modifying drugs in patients with relapsing-remitting multiple sclerosis.

PI: Dr/a Sánchez López, Fernando

1634: An epidemiological study to assess the diagnosis and follow-up of patients with a first demyelinating episode suggestive of multiple sclerosis.

PI: Dr/a Agüera Morales, Eduardo

1738: A validation study of questionnaires used to predict and assess adherence to treatments for neurological syndrome and multiple sclerosis in Spain (SAVE)

PI: Dr/a Agüera Morales, Eduardo

1782: Study of quality of life in patients with spasticity due to multiple sclerosis. CANDLE study.

PI: Dr/a Sánchez López, Fernando

1816: Evaluation of functionality of patients with multiple sclerosis in Spain and its impact on their quality of life

PI: Dr/a Sánchez López, Fernando

1873: Validating the Spanish version of the Relevant Outcome Scale for Alzheimer's disease (ROSA).

PI: Dr/a Agüera Morales, Eduardo

1969: A study of biomarkers in CSF for the diagnosis of prodromal Alzheimer's disease in patients with mild cognitive impairment.

PI: Dr/a Agüera Morales, Eduardo

1989: Long-term effectiveness of Copaxone in regular clinical practice. Observational study (XPERIENCIA-5)

PI: Dr/a Agüera Morales, Eduardo

2085: A prospective, observational study to assess the influence of anti-JC antibodies test on risk perception in treatments with natalizumab (Tysabri®) in patients with multiple sclerosis and their attending neurologists.

PI: Dr/a Sánchez López, Fernando

2238: An observational, retrospective, cross-over study to assess suboptimal treatment adherence in patients with relapsing-remitting multiple sclerosis with a bout after treatment.

PI: Dr/a Sánchez López, Fernando

# GE2

## Child Metabolism

### Team Leader

#### Emerging Researcher

Mercedes Gil Campos

[mercedes\\_gil\\_campos@yahoo.es](mailto:mercedes_gil_campos@yahoo.es)

Research Network on Maternal and Child Health (RedSAMID)

PAIDI CTS-639 scientific group

#### Senior Researchers

Montserrat Antón Gamero

M<sup>º</sup> José de la Torre Aguilar

José Fernando Fernández Gutiérrez

Ignacio Ibarra de la Rosa

Eduardo López Laso

M<sup>º</sup> Elena Mateos González

Juan Luis Pérez Navero

M<sup>º</sup> Ester Ulloa Santamaría

M<sup>º</sup> Jose Velasco Jabalquinto

#### Post-doctoral Researchers

Francisco Jesús Llorente Cantarero

Katherine Ubina Flores Rojas

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)

M<sup>º</sup> José Arroyo Marín

Susana Jaraba Caballero



## Scientific Activity

Our group has initiated work in various sub-areas within Pediatrics to form a research group. Previously with other groups, and now with the group we have created, the research is based on understanding the role of metabolism in various pediatric diseases. Basically, this group works on nutritional aspects, as well as in

the study of hormonal factors, inflammation and oxidative stress. In recent years we have focused on the study of childhood obesity and the metabolic syndrome currently associated with other pediatric illnesses too, such as prematurity or intra and extra-uterine growth retardation. In addition, the group also carries out research into the genetics of obesity. In future research, we expect to ad-

dress neuropediatrics, and particular, the inborn errors of metabolism.

## Keywords

Obesity, metabolic syndrome, arteriosclerosis, inflammation, oxidative stress, gene expression, proteomics, nutrigenetics, nutrigenomics.

## PUBLICATIONS

### Originals Publications

Fernandez-Ramos JA, Lopez-Laso E, Ordonez-Diaz MD, Camino-Leon R, Ibarra-de la Rosa I, Frias-Perez MA, Gilbert-Perez JJ, Perez-Navero JL. Neurological complications in patients receiving solid organ transplants. *An Pediatr*. 2013, 78(3):149-156.  
IF:0,867

Ortiz-Espejo M, Perez-Navero JL, Munoz-Villanueva MC, Mercedes GC. Nutritional assessment in neonatal and prepubertal children with a history of extrauterine growth restriction. *Early Hum Dev*. 2013, 89(9):763-768.  
IF:2,02

Llorente-Cantarero FJ, Gil-Campos M, Benitez-Sillero JD, Munoz-Villanueva MC, Tasset I, Perez-Navero JL. Profile of oxidant and antioxidant activity in prepubertal children related to age, gender, exercise, and fitness. *Appl Physiol Nutr Metab*. 2013, 38(4):421-426.  
IF:2,009

Mateos ME, Beyer K, Lopez-Laso E, Siles JL, Perez-Navero JL, Pena MJ, Guzman J, Matas J. Simpson-golabi-behmel syndrome type 1 and hepatoblastoma in a patient with a novel exon 2-4 duplication of the GPC3 gene. *Am J Med Genet. A*. 2013, 161(5):1091-1095.  
IF:2,303

Ortiz-Espejo M, Pérez-Navero JL, Olza J, Muñoz-Villanueva MC, Aguilera CM, Gil-Campos M. Changes in plasma adipokines in prepubertal children with a history of extrauterine growth restriction. *Nutrition*. 2013, 29(11-12):1321-1325.  
IF:2,859

Baena-Gómez MA, de la Torre Aguilar MJ, Mesa MD, Llorente-Cantarero FJ, Pérez Navero JL, Gil-Campos M. Effects of Parenteral Nutrition Formulas on Plasma Lipid Profile in Children with Bone Marrow Transplantation. *Ann Nutr Metab*. 2013, 63(1-2):103-110.  
IF:1,661

### Joint Publications

Ortega C, Estevez OA, Fernandez S, Aguado R, Rumbao JM, Gonzalez T, Perez-Navero JL, Santamaria M. Interleukin-21 Overexpression Dominates T Cell Response to Epstein-Barr Virus in a Fatal Case of X-Linked Lymphoproliferative Syndrome Type 1. *Clin Vaccine Immunol*. 2013, 20(5):765-771.  
IF:2,598

Rupérez AI, López-Guarnido O, Gil F, Olza J, Gil-Campos M, Leis R, Tojo R, Cañete R, Gil A, Aguilera CM. Paraoxonase 1 activities and genetic variation in childhood obesity. *Br J Nutr*. 2013, 110(9):1639-1647.  
IF:3,302

Rupérez AI, Olza J, Gil-Campos M, Leis R, Mesa MD, Tojo R, Cañete R, Gil A, Aguilera CM. Are Catalase -844A/G Polymorphism and Activity Associated with Childhood Obesity?. *Antioxid Redox Signal*. 2013, 19(16):1970-1975.  
IF:7,189

Claverie-Martin F, Garcia-Nieto V, Loris C, Ariceta G, Nadal I, Espinosa L, Fernandez-Maseda A, Anton-Gamero M, Avila A, Madrid A, Gonzalez-Acosta H, Córdoba-Lanus E, Santos F, Gil-Calvo M, Espino M, Garcia-Martinez E, Sanchez A, Muley R. Claudin-19 Mutations and Clinical Phenotype in Spanish Patients with Familial Hypomagnesemia with Hypercalciuria and Nephrocalcinosis. *Plos One*. 2013, 8(1):e53151-.  
IF:3,73

Article. Olza, J; Gil-Campos M, Leis R, Ruperez AI, Tojo R, Canete R, Gil A, Aguilera CM. Influence of variants in the NPY gene on obesity and metabolic syndrome features in Spanish children. *Pepptides*. 2013, 45:22-27.  
IF:2,521

Olza J, Ruperez AI, Gil-Campos M, Leis R, Fernandez-Orth D, Tojo R, Cañete R, Gil A, Aguilera CM. Influence of FTO variants on obesity, inflammation and cardiovascular disease risk biomarkers in Spanish children: a case--control multicentre study. *BMC Med Genet*. 2013, 14: n° art 123.  
IF:2,536

Fernandez-Ramos JA, Lopez-Laso E, Simon-De Las Heras R, Camino-Leon R, Guerra-Garcia P,

Camacho-Salas A, Aguilar-Quintero M, Nunez-Enamorado N. Aicardi syndrome: retrospective study of a series of seven case reports. *Rev Neurol*. 2013, 57(11):481-488.  
IF:1,179

### Research Projects

Mateos González, ME. An integral comprehensive proteomic study of liver cancer in children: identification of diagnostic and prognostic factors, key signaling pathways and new therapeutic targets. Sponsored body: Institute Carlos III Health (ISCIII). Reference: PI10/02082

Gil Campos, M. Search for cardiovascular risk biomarkers and antioxidant defense system in prepubertal children with a history of extrauterine growth retardation (biorica). Sponsored body: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0480-2012

Gil Campos, M. Search for cardiovascular risk biomarkers and antioxidant defense system in prepubertal children with a history of extrauterine growth retardation (biorica). Sponsored body: Institute Carlos III Health (ISCIII). Reference: PI13/01245  
2014 Annuity

### Collaboration Agreements

Gil Campos, M. Usefulness of new biomarkers of cardiac function: mr-proadreno-medulin, copeptin and nt-1 proendothelin heart failure after cardiopulmonary bypass surgery in children with congenital heart disease.

Gil Campos, M. Functional assessment of two start infant formulas supplemented with probiotic isolates from breast milk. Sponsored by: Puleva Biotech. Reference: Puleva Biotech

### Clinical Trials

0018/09: A randomized, open, multicenter, phase III trial to assess the efficacy of sodium thiosulfate in reducing ototoxicity in patients receiving chemotherapy with cisplatin for stan-



ard risk hepatoblastoma.

PI: Dr/a Mateos Gonzalez, María Elena

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0010/10: Efficacy and safety of levosimendan in critically ill children with severe acute heart failure

PI: Dr/a Ulloa Santamaria, María Esther

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0061/11: European Neuroblastoma Treatment Protocol for low or intermediate risk / European Low and Intermediate Risk Neuroblastoma

PI: Dr/a Mateos Gonzalez, María Elena

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0106/12: A prospective, multicenter, randomized, double-blind, placebo-controlled phase 3 study to assess the pharmacokinetics, safety and efficacy of paricalcitol capsules in reducing intact Parathyroid hormone levels in serum in children and adolescents aged 10 to 16 years with chronic moderate-to-severe nephropathy.

PI: Dr/a Anton Gamero, Montserrat

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1783: Register of patients with type C Nleemann-Pick.

PI: Dr/a López Laso, Eduardo

# GA1

## Lung Transplants Thoracic Neoplasms

### Team Leader

#### Associated Researcher

Ángel Salvatierra Velázquez  
[angel.salvatierra.sspa@juntadeandalucia.es](mailto:angel.salvatierra.sspa@juntadeandalucia.es)

#### Senior Researchers

F° Javier Algar Algar  
Antonio Álvarez Kindelan

#### Other members of the Group

(Other researchers, Technical, and  
Administrative Staff)  
Jose Ayala Montoro  
Carlos Baamonde Laborda  
Dionisio Espinosa Jimenez



## Scientific Activity

Our research activity is focused on the effect of different molecules on lung preservation for transplantation. Additionally, we study the mechanism of chronic lung rejection and its effect on the regulation of different molecules.

## Publications

### Originals Publications

Tomas EA, Madueno FC, Velazquez AS. Bronchiectasis due to pulmonary artery aneurysm. *Interact Cardiovasc Thorac Surg.* 2013, 17(1):176-178.  
IF: 1,112

Madueno FC, Tomas EA, Velazquez AS. Lung transplant in Jehovahs Witness patient. *J Thorac CardiovascSurg.* 2013, 145:e65-e67.  
IF: 3,526

Arango Tomás E, Baamonde Laborda C, Algar Algar J, Salvatierra Velázquez A. Chest wall reconstruction with methacrylate prosthesis in Poland syndrome. *Arch Bronconeumol.* 2013, 49(10):450-452.  
IF: 1,372

Arango-Tomás E, Algar-Algar FJ, Salvatierra Velázquez A. Deciduoid pleural mesothelioma in an adolescent. *Arch Bronconeumol.* 2013, 49:218-219.  
IF: 1,372

Arango Tomás E, Algar Algar FJ, Salvatierra Velázquez A. Subcarinal gastrointestinal stromal tumor. *Cir Esp.* 2013, 91(10):677-678.  
IF: 0,871

Moreno P, Alvarez A, Illana J, Espinosa D, Baamonde C, Cerezo F, Algar FJ, Salvatierra A. Early lung retrieval from traumatic brain-dead donors does not compromise outcomes following lung transplantation. *Eur J Cardiothorac Surg.* 2013, 43(6):e190-197.  
IF: 2,674

Alvarez A, Moreno P, Illana J, Espinosa D, Baamonde C, Arango E, Algar FJ, Salvatierra A. Influence of donor-recipient gender mismatch on graft function and survival following lung transplantation. *Interact CardiovascThorac Surg.* 2013, 16(4):426-435.  
IF: 1,112

Arango Tomás E, Quero Ríos MI, Robles Arista JC, Algar Algar FJ, Wolf JI, Alvarez Kindelan A, Cerezo Madueño F, Baamonde Laborda C, Guerrero Pabon R, Salvatierra Velazquez A. Postoperative complications in the intensive care unit following lung transplantation in adults: results in Univer-

In our studies on lung preservation and chronic lung rejection we investigate the biological effects of different molecules especially serine-protease inhibitors on oxidative stress, inflammation, the endothelial function and cell signaling mechanisms.

## Keywords

Lung preservation, chronic rejection, bronchiolitis obliterans, endothelium, inflammation, oxidative stress, proteomics, genomics.

sity Hospital Reina Sofia. *Transplant Proc.* 2013, 44(9):2663-2665.  
IF: 0,952

### Joint Publications

Alvarez MA, Ruano J, Gomez FJ, Casas E, Baamonde C, Salvatierra A, Moreno JC. Differences between objective efficacy and perceived efficacy in patients with palmar hyperhidrosis treated with either botulinum toxin or endoscopic thoracic sympathectomy. *J Eur Acad Dermatol Venerol.* 2013, 27(3):e282-e288.  
IF: 2,694

de Pablo A, Santos F, Sole A, Borro JM, Cifrian JM, Laporta R, Monforte V, Roman A, de la Torre M, Ussetti P, Zurbano F. Recommendations on the use of everolimus in lung transplantation. *Transplant Rev.* 2013, 27(1):9-16.  
IF: 2,675

Anglada-Curado FJ, Campos-Hernandez P, Carrasco-Vallente J, Anaya-Henares F, Carazo-Carazo JL, Alvarez-Kindelan J, Regueiro-Lopez JC, Requena-Tapia MJ. Extracorporeal shock wave lithotripsy for distal ureteral calculi: Improved efficacy using low frequency. *Int J Urol.* 2013, 20(2):214-219.  
IF: 1,734

Coll E, Santos F, Ussetti P, Canela M, Borro JM, De La Torre M, Varela A, Zurbano F, Mons R, Morales P, Pastor J, Salvatierra A, de Pablo A, Gomez P, Moreno A, Sole J, Roman A. The Spanish Lung Transplant Registry: First Report of Results (2006-2010). *Arch Bronconeumol.* 2013, 49(2):70-78.  
IF: 1,372

## Research Projects

Álvarez Kindelán, A. Neumosur Grant No. 3/2010. Sponsored by: Asociación de Neumología y cirugía torácica del sur. Reference: Project Neumosur

Álvarez Kindelán, A. Neumosur Grant No. 14/2010. Sponsored by: Asociación de Neumología y cirugía torácica del sur. Reference: Project Neumosur 2

Álvarez Kindelán, A. Neumosur Grant No. 20/2010. Sponsored by: Asociación de Neu-

mología y cirugía torácica del sur. Reference: Project Neumosur 2

Third Party Services

Baamonde Laborda, C. Sponsorship and MIR course on minimally invasive thoracic surgery. Sponsored by: Covidien Spain, S.L. Reference: PSS.0028

Salvatierra Velazquez, A. 20 years of lung transplantation in Andalusia. Sponsored by: Novartis farmaceutica, S.A. Reference: PSS.0033

# GA2

## Comprehensive Nursing Care Multidisciplinary Perspective

### Team Leader

#### Associated Researcher

M<sup>º</sup> Aurora Rodríguez Borrego  
[en1robom@uco.es](mailto:en1robom@uco.es)  
PAIDI CTS-666 scientific group

#### Senior Researchers

Joaquin Alanis Lopezosa  
M<sup>º</sup> Jesús Delgado Márquez  
Manuel García Montero  
Rosane Gonçalves Nitschke  
Luis Peñas Maldonado  
M<sup>º</sup> José de la Torre Barbero  
África Ruiz Gándara  
Manuel Vaquero Abellán

#### Pre-doctoral Researchers

Caridad Dios Guerra  
Dolores Guerra Martín  
Vicente Fernández Rodríguez  
Pedro Hidalgo Lopezosa  
Rosa Miñarro del Moral  
Clara Inés Flórez Alomnacid  
Juan Manuel Carmona Torres  
Pablo Jesús López Soto

#### Other members of the Group

(Other researchers, Technical, and Administrative Staff)  
Susana Arce Rodríguez  
Francisca Cuevas Pareja  
Carmen de Frutos Delgado  
Magdalena de Miguel Fernández  
Juana Marín Sánchez  
M<sup>º</sup> José Medina Valverde  
Beatriz Méndez Serrano  
M<sup>º</sup> del Pilar Moros Molina  
Adoración Muñoz Alonso  
Julia Parra Perea  
Rosa Redondo Pedraza  
Antonio Jesús Luna Martín



## Scientific Activity

The scientific activity of this research group is based on four basic principles that allow flexibility in the composition of and topics addressed by this group. The four basic principles are:

1. To promote research activity among nursing professionals to foster evidence-based nursing care practice. This Group is a vehicle for nursing professionals interested in research.

2. To promote the professional development of nursing professionals by generating knowledge that serves as a guideline for nursing care practice.

3. To make a commitment to provide scientific training for future nursing professionals

4. To adopt a comprehensive and integral approach to how the human being experiences health and disease.

## Keywords

Integral nursing care, nursing care philosophy, professional development of nursing professionals, assessment of training methods in Higher Education, nursing service management, evidence-based nursing care, health and disease, disease experience, health communication, integral human being, female nurses, healthcare in old age, aging-life quality, fragility.

## Publications

### Originals Publications

Hidalgo-Lopezosa P, Rodríguez-Borrego MA, Muñoz-Villanueva MC. Are Birth Plans Associated with Improved Maternal or Neonatal Outcomes? *MCN-Am J Matern-ChildNurs.* 2013, 38(3):150-156.  
IF: 0.897

Alcántara Luque R, Rodríguez Borrego MA, González Galán CM, Clapes Roldán C. Risk perception in nursing students. *Enfermería Global.* 2013.12(29).341-351

Dios Guerra, C, Alba Dios, MA, Ruiz Moral, Roger, Jiménez García, Celia, Pérula de Torres, L, Rodríguez Borrego, M. Evaluation of user satisfaction of nursing consultation in health centers based on quality and technical communication indicators. *Enfermería Global.* 2013.12(31).162-176

### Research Projects

Rodríguez Borrego, M<sup>a</sup> A. Violence in couples formed by health professionals working at the Spanish National Health System. Sponsored by: Institute Carlos III Health (ISCIII). Reference: PI13/01253

Rodríguez Borrego, M<sup>a</sup> A. Study focus on vulnerable older people's influence the family and community environment. Association with Foundation "Hombres Nuevos". Sponsored by: University of Cordoba.

Rodríguez Borrego, M<sup>a</sup> A. Feed forward: tutoring and evaluating learning in cooperative groups. Sponsored by: University of Cordoba. Project to improve teaching quality. 1st Call of the Educational Innovation Plan. Reference: 123078

# GA3

## Pneumology

### Team Leader

#### Associated Researcher

Bernabé Jurado Gámez  
bjg01co@hotmail.com

#### Senior Researchers

Marisol Arenas de Larriva  
Laura Caballeros Ballesteros  
Luis M Entrenas Costa  
Luis Muñoz Cabrera  
Francisco Santos Luna  
Antonio Pablo Arenas Vacas

#### Post- doctoral Researcher

M<sup>º</sup> Carmen Fernández Marín

#### Pre- doctoral Researchers

Inmaculada Garcia Porcuna  
Montserrat Castillo Jurado

#### Other members of the Group

(Other researchers, Technical, and  
Administrative Staff)

Nuria Feu Collado  
Rafael Lama Martínez  
Francisco Luis Gil García  
Natalia Pascual Martínez



## Scientific Activity

Our line of research is focused on three key points, the effect of hypoxemia on metabolism and lung cancer, early diagnosis of lung cancer and the effect of new drugs and respiratory therapies basing on new technologies (TICs).

Objectives:

1. The effect of hypoxemia, chronic or intermittent on metabolism and vascular impact.
2. Search for markers basing on new technologies (metabolomics, proteomics, epigenetics) for early diagnosis of lung cancer.
3. Application of metabolomics in the development of new drugs in chronic

respiratory diseases (EPOC, asthma, HPP, FQ).

4. Application of TICs in the diagnosis and control of respiratory disease.

In addition, our research team collaborates in the investigation on the effect of intermittent hypoxemia with the research group of Dr. José López Miranda (Internal Medicine) in patients with vascular risk factors to determine the impact of hypoxemia on the effect of Mediterranean diet and vascular risk.

With the research group of Dr. Teresa Roldán Arjona (epigenetics), Dr. Antonio Rodríguez Ariza (oncology, Coordinator of the Oncover group) and Dr. M<sup>a</sup> Dolores Luque de Castro (metabolomics and proteomics) in the identification and quantification of

compounds useful in the diagnosis of lung cancer in exhaled breath condensate. In this line, this group also collaborates with the research group of Dr M. Dolores Luque de Castro in the performance of metabolomic studies for the identification of clinical phenotypes in exhaled breath condensate, and in the search for new lung cancer markers in different biological fluids.

## Keywords

Cancer, hypoxemia, cell damage, chronic respiratory disease, epigenetics, metabolomics, proteomics, telecare, telemedicine, respiratory therapies.

## Publications

### Originals Publications

Jurado Gámez B, Feu Collado N, Jurado García JC, García Gil F, Muñoz Gomariz E, Jiménez Murillo L, Muñoz Cabrera L. Home intervention and predictor variables for rehospitalization in chronic obstructive pulmonary disease exacerbations. *Arch Bronconeumol.* 2013, 49(1):10-14.  
IF:1,372

### Joint Publications

Miravittles M, Soriano JB, Ancochea J, Muñoz L, Duran-Tauleria E, Sanchez G, Sobradillo V, García-Río F. Characterisation of the overlap COPD-asthma phenotype. Focus on physical activity and health status. *Respir Med.* 2013, 107(7):1053-1060.  
IF:2,585

Tordera MP, Río FG, Gutierrez FJA, Serrano CC, Torrero LC, Costa LME, Moreno CM, Nieto MJR, Fernandez AT. Guidelines for the Study of Non-specific Bronchial Hyperresponsiveness in Asthma. *Arch Bronconeumol.* 2013, 49(10):432-446.  
IF:1,372

Guglielmi O, Gomez AIS, Jurado-Gomez B, Buela-Casal G. Obstructive Sleep Apnea Syndrome Effects on Quality of Life and Daytime Sleepiness. *UnivPsicol.* 2013, 12(2):601-611.  
IF: 0,544

Ancochea J, Miravittles M, García-Río F, Muñoz L, Sanchez G, Sobradillo V Duran-Tauleria E, Soriano JB. Underdiagnosis of Chronic Obstructive Pulmonary Disease in Women: Quantification of the Problem, Determinants and Proposed Ac-

tions. *Arch Bronconeumol.* 2013, 49(6):223-229.  
IF:1,372

García-Río F, Soriano JB, Miravittles M, Muñoz L, Duran-Tauleria E, Sanchez G, Sobradillo V, Ancochea J. Frequency of Multi-dimensional COPD Indices and Relation with Disease Activity Markers. *COPD-J Chronic ObstrPulm Dis.* 2013, 10(4):436-443.  
IF:2,31

de Pablo A, Santos F, Sole A, Borro JM, Cifrian JM, Laporta R, Monforte V, Roman A, de la Torre M, Ussetti P, Zurbano F. Recommendations on the use of everolimus in lung transplantation. *Transplant Rev.* 2013, 27(1):9-16.  
IF: 2,675

Coll E, Santos F, Ussetti P, Canela M, Borro JM, De La Torre M, Varela A, Zurbano F, Mons R, Morales P, Pastor J, Salvatierra A, de Pablo A, Gámez P, Moreno A, Sole J, Roman A. The Spanish Lung Transplant Registry: First Report of Results (2006-2010). *Arch Bronconeumol.* 2013, 49(2):70-78.  
IF:1,372

## Research Projects

Jurado Gámez, B. 12/2011 Neumosur Grant. Sponsored by: Asociación de Neumología y cirugía torácica del sur (Spanish Pneumology Association). Reference: Project Neumosur 3

Arenas de Larriva, MS. 03/2011 Neumosur Grant. Sponsored by: Asociación de Neumología y cirugía torácica del sur (Spanish Pneumology Association). Reference: Project Neumosur 5

Muñoz Cabrera, L. Neumosur Grant: Contribution of metabolomics to the study of exhaled breath

condensate for the differentiation and establishment of physiopathological bases in obstructive chronic lung disease phenotypes. Sponsored by: Asociación de Neumología y cirugía torácica del sur (Spanish Pneumology Association). Reference: 12/2013.

Jurado Gámez, B. Neumosur Grant: Relationship between the 6-minute walk test and desaturation during regular physical activity in patients with chronic obstructive lung disease. Sponsored by: Asociación de Neumología y cirugía torácica del sur (Spanish Pneumology Association). Reference: 2/2013.

## Collaboration Agreements

Jurado Gámez, B. A study of the effect of an exercise program on the severity of SAHS and the modification of vascular risk factors. Sponsored by: Linde Medicinal

Entrenas Costa, LM. Novartis collaboration agreement. De novo or not followed up asthma patients attending the emergency unit with symptoms of bronchospasm. Sponsored by: Novartis farmaceutica, S.A. Reference: CCB.0060

## Clinical Trials

0013/08: Post-marketing observational surveillance program of Ambrisentan. VOLT study. PI: Dr/a Santos Luna, Francisco

0114/10: A multicenter, randomized study of first-line treatment combined with ambrisentan and tadalafil in subjects with pulmonary hypertension. PI: Dr/a Santos Luna, Francisco

0019/12. An open, parallel/group trial to assess the safety of roflumilast administered once a day on alternate days for two weeks vs. standard administration patterns (once a day).

PI: Dr/a Muñoz Cabrera, Luis

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1641. Perception of renal dysfunction perception in maintenance lung transplant patients.

PI: Dr/a Santos Luna, Francisco

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1706: A comparative study of four COPD-specific health-related quality of life surveys (AQ20, COPDSS, CAT y CCQ) as instruments for predicting COPD exacerbation, version 2.0.

PI: Dr/a Muñoz Cabrera, Luis

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1950: Use of Omalizumab in real clinical practice in Spain after a 5-year experience.

PI: Dr/a Entrenas Costa, Luis Manuel

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2045: longitudinal and cross-evaluation of asthma control.

PI: Dr/a Entrenas Costa, Luis Manuel

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2054: Assessing utilities in patients with chronic obstructive lung disease in Spain.

PI: Dr/a Muñoz Cabrera, Luis

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2392: A multicenter, prospective, observational study to assess specific immune response to the cytomegalovirus (CMV) as assessed by Quantiferon, and overall immune response as measured by Immuknow in lung transplant patients with positive CMV serology prior to transplantation (R+) and their involvement in the development of CMV infection. REIVI study.

PI: Dr/a Muñoz Cabrera, Luis

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# GA4

## Endocrinology and Nutrition

### Insulin Resistance, Diabetes and Metabolism

#### Team Leaders

##### Associated Researcher

Juan Antonio Paniagua González  
japaniguag@yahoo.es  
PAIDI CTS-651 scientific group

##### Other associated Researcher

Pedro Benito López

##### Senior Researchers

Alfonso Calañas Continente  
M<sup>a</sup> Ángeles Gálvez Moreno  
Magdalena Romero Jimenez  
Remedios Vigara Madueño

##### Pre-doctoral Researchers

Juan Manuel Escandell Morales  
Zahira Noemi Fernández Bedmar

##### Other members of the Group

(Other researchers, Technical, and  
Administrative Staff)  
Enrique Bellido Muñoz  
M<sup>a</sup> Sierra Corpas Jiménez  
Carmen Gutiérrez Alcántara  
M<sup>a</sup> Jose Molina Puertas  
Rafael Palomares Ortega  
M<sup>a</sup> Rosario Torres Roldán



## Scientific Activity

This research group investigates the effect of different nutrients on insulin resistance and body fat distribution in patients with metabolic syndrome from two points of view:

1.- Line of research of Endocrinology and Nutrition, on which several groups work:

Along with Dr. Justo Castaño Fuentes' group, we investigate the expression of different hormone receptors and intracellular mediators in the onset and development of pituitary tumors. In line with transactional research principles, this group applies the findings of its research to real clinical practice using inhibitors or stimulators in order to inhibit hormone production and / or reduce their size when surgery is not fully successful.

Also, this group collaborates with Dr. Quesada Gómez's group in the investigation of osteoporosis, particularly, vitamin D and bone stem cells.

This group also collaborates with Dr. Soriguier in the performance of epidemiological studies of diabetes mellitus type 2 and in the prevention of diabetes through a behaviour modification program which is being implemented in a village in southern Cordoba. This group also collaborates with Dr. Caballero in the study of bone metabolism in pregnant women with diabetes.

2.- Line of research: insuline resistance, diabetes and metabolism. This group studies the effect of diet components and pharmacologic interventions on the insuline resistance syndrome and the risk of developing diabetes in patients with "prediabetes". For such purpose, this group characterizes the specific effect of macronutrients on the release of digestive tract incretins and the subsequent signalling. In addition, this group also investigates the effect of diets with different macronutrient contents on body composition and body fat re-

distribution, and its relationship with insulin sensitivity and secretion. This group studies the role of adipose tissue expansion as a pathogenic factor of insulin resistance, beta-cell failure and diabetes. Finally, this group examines the transcription of metabolic, inflammatory and adipokine pathways in peripheral adipose tissue into diet models, macronutrients and different pharmacologic agents.

## Keywords

Insulin resistance,  $\beta$ -pancreatic dysfunction, prediabetes, metabolic syndrome, and adipotoxicidad adipose tissue, inflammation, oxidative stress, gene expression, metabolomics. Pituitary Adenoma. Somatostatin receptors, Vitamin D, Metabolic Syndrome, Prevalence of Diabetes Mellitus Type 2, Diabetes Mellitus and Pregnancy

## PUBLICATIONS

### Originals Publications

Tenorio Jiménez C, Manzano García G, Prior Sánchez I, Corpas Jiménez MS, Molina Puerta MJ, Benito López P. Bariatric surgery in inflammatory bowel disease; case report and review of the literature. *Nutr Hosp*. 2013, 28(3):958-960.  
IF: 1,305

### Joint Publications

Luque RM, Ibáñez-Costa A, López-Sánchez L, Jiménez-Reina L, Venegas-Moreno E, Gálvez M, Villa-Osaba A, Madrazo-Atutxa A, Japón M, de la Riva A, Cano D, Benito-López P, Soto-Moreno A, Gahete M, Leal-Cerro A, Castaño J. A Cellular and Molecular Basis for the Selective Desmopressin-Induced ACTH Release in Cushing Disease Patients: Key Role of AVPR1b Receptor and Potential Therapeutic Implications. *J Clin Endocrinol Metab*. 2013, 98(10):4160-4169.  
IF: 6,429

Martin-Rodríguez JF, Madrazo-Atutxa A, Venegas-Moreno E, Benito-Lopez P, Galvez MA, Cano DA, Tinahones FJ, Torres-Vela, E, Soto-Moreno A, Leal-Cerro A. Neurocognitive Function in Acromegaly after Surgical Resection of GH-Secreting Adenoma versus Naive Acromegaly. *PLoS One*. 2013, 8(4):e60041.  
IF: 3,73

Moreno-Fernandez J, Gomez FJ, Gazquez M, Pedroche M, Garcia-Manzanares A, Tenias JM, Benito P, Gomez IR. Real-Time Continuous Glucose Monitoring or Continuous Subcutaneous Insulin Infusion, What Goes First?: Results of a Pilot Study. *Diabetes Technol Ther*. 2013, 15(7):596-600.  
IF: 2,205

Caixas A, Lecube A, Morales MJ, Calanas A, Moreiro J, Cordido F, Diaz MJ, Masmiquel L, Moreno B, Vidal J, Goday A, Arrizabalaga JJ, Garcia-Luna PP, Iglesias P, Burguera B, Rubio MA, Monereo S, Crosby RD, Kolotkin RL. Weight-Related Quality of Life in Spanish Obese Subjects Suitable for Bariatric Surgery is Lower Than in Their North American Counterparts: a Case-Control Study. *Obesity Surgery*. 2013, 23(4):509-514.  
IF: 3,102

Peña-Orihuela P, Camargo A, Rangel-Zuñiga OA, Perez-Martinez P, Cruz-Teno C, Delgado-Lista J, Yubero-Serrano EM, Paniagua JA, Tinahones FJ, Malagón MM, Roche HM, Perez-Jimenez F, Lopez-Miranda J. Antioxidant system response is modified by dietary fat in adipose tissue of metabolic syndrome patients. *J Nutr Biochem*. 2013, 24 (10):1717-1723.  
IF: 4,552

Camargo A, Meneses ME, Rangel-Zuñiga OA, Perez-Martinez P, Marin C, Delgado-Lista J, Paniagua JA, Tinahones FJ, Roche H, Malagón MM, Perez-Jimenez F, Lopez-Miranda J. Endoplasmic reticulum stress in adipose tissue determines

postprandial lipoprotein metabolism in metabolic syndrome patients. *Mol Nutr Food Res*. 2013, 57(12):2166-2176.  
IF: 4,310

### Clinical Trials

0151/11: An open, multicenter, expanded access study of pasireotide s.c. in patients with Cushing disease (Seascape)  
PI: Dr/a Gálvez Moreno, M<sup>a</sup> Ángeles

0235/11: A comparative study of LY2605541 versus insulin glargine as basal treatment in combination with insulin oral agents in insulin-naive patients with type 2 diabetes mellitus: A double-blind, randomized study.  
PI: Dr/a Paniagua González, Juan Antonio

2170: A retrospective, observational study to determine the time elapsed until normal hormone levels are reached by dosis and administration intervals of Somatuline Autogel administered in regular clinical practice to treat acromegaly patients.  
PI: Dr/a Gálvez Moreno, M<sup>a</sup> Ángeles

2138: A retrospective study to assess changes in metabolic control and weight in obese patients with diabetes mellitus type 2 after receiving treatment with GLP-1 receptor antagonists (e-DM-14)  
PI: Dr/a Gálvez Moreno, M<sup>a</sup> Ángeles

# GA 5

## Study of Growth

### Endocrinology and Child Nutrition

#### Team Leader

#### Associated Researcher

Ramón Cañete Estrada  
em1caesr@uco.es

#### Senior Researchers

M<sup>a</sup> Dolores Cañete Vázquez  
Olga Diaz Morales  
Juana M<sup>a</sup> Guzman Cabañas  
Luis Jimenez Reina  
Rosario Martos Estepa  
Cristina Mata Rodriguez  
M<sup>a</sup> José Párraga Quiles  
M<sup>a</sup> Dolores Ruiz Gonzalez  
Inés Tofe Valera  
Javier Torres Borrego  
Miguel Valle Jimenez  
Fernando Vázquez Rueda



## Scientific Activity

Among other lines of research, this group studies obesity in prepubertal children, focusing on children with metabolic syndrome, inflammatory factors, vascular risk biomarkers and adipose tissue gene expression, diet effects on these factors, study of steatohepatitis and physical activity. Another line of research is centered on aspects related to nutrition in children with extrauterine growth retardation, especially in those that might later develop metabolic syndrome. This group also carries out compara-

tive cord blood proteomic analyses of healthy term neonates and neonates with IUGR to identify potential differences that might with associated with IUGR and the likelihood of adverse nutritional effects.

This group also investigates growth-hormone producing cells and morphological, structural and production modifications in animals.

Finally, this group are developing one line of research centered on food allergies, and second line based on the possible health impact on workers in solar thermal plants daily exposed to polycyclic aromatic hydrocarbons.

## Keywords

Child obesity, metabolic syndrome in children, diet, endothelium, inflammation, cardiovascular biomarkers, gene expression, proteomics, neonates with intrauterine growth retardation (IUGR), metabolic syndrome in IUGR, basic research on growth producing cells with different external stimuli. Food allergy

## Publications

### Originals Publications

Gonzalez-Gonzalez A, Muñoz-Serrano A, Tenias-Burillo JM, Falero-Gallego P, Garcia-Fuentes E, Gutierrez-Repiso C, Canete R. Interobserver agreement in detecting goitre by palpation in a school population. *An Pediatr (Barc)*. 2013, 79(3):182-186.  
IF: 0,867

Valle Jiménez M, Martos R, Morales RM, Valle R, Cañete MD, Urbano MM, Bermudo F, Cañete R. Relationship between Changes in Plasma Leptin Concentrations and Plasminogen Activator Inhibitor-1 in Obese Prepubertal Children after Nine Months of Treatment. *Ann Nutr Metab*. 2013, 63(3):216-222.  
IF:1,661

Alcoba-Conde AA, Rueda FV, Estrada RC. Cervical ectopic thymus: a rare condition. *An Pediatr*. 2013, 79(3):202-203.  
IF:0,867

### Joint Publications

Moral L, Torres-Borrego J, Murua JK, Valverde-Molina J, Belinchon JP, Praena-Crespo M, Casanueva CO, Callen-Bleuca MT, Fernandez-Llamazares CM, Rey CC. Association between paracetamol exposure and asthma: update and practice guidelines. *An Pediatr (Barc)*. 2013, 79(3):188-188.  
IF:0,867

Rupérez AI, López-Guarnido O, Gil F, Olza J, Gil-Campos M, Leis R, Tojo R, Cañete R, Gil A, Aguilera CM. Paraoxonase 1 activities and genetic variation in childhood obesity. *Br J Nutr*. 2013, 110(9):1639-1647.  
IF:3,302

Rupérez AI, Olza J, Gil-Campos M, Leis R, Mesa MD, Tojo R, Cañete R, Gil A, Aguilera CM. Are Cata-

lase -844A/G Polymorphism and Activity Associated with Childhood Obesity?. *Antioxid Redox Signal*. 2013, 19(16):1970-1975.  
IF:7,189

Olza J, Gil-Campos M, Leis R, Rupérez AI, Tojo R, Canete R, Gil A, Aguilera CM. Influence of variants in the NPY gene on obesity and metabolic syndrome features in Spanish children. *Peptides*. 2013, 45:22-27.  
IF:2,521

Olza J, Rupérez AI, Gil-Campos M, Leis R, Fernandez-Orth D, Tojo R, Cañete R, Gil A, Aguilera CM. Influence of FTO variants on obesity, inflammation and cardiovascular disease risk biomarkers in Spanish children: a case-control multicentre study. *BMC Med Genet*. 2013, 14(123):  
IF:2,536

Mateos ME, Beyer K, Lopez-Laso E, Siles JL, Perez-Navero JL, Pena MJ, Guzman J, Matas J. Simpson-golabi-behmel syndrome type 1 and hepatoblastoma in a patient with a novel exon 2-4 duplication of the GPC3 gene. *Am J Med Gen*. 2013, 161(5):1091-1095.  
IF:2,304

García P, San Feliciano L, Benito F, García R, Guzman J, Salas S, Fernandez C, del Prado N, Ciprian D, Figueras J. Outcome at two years corrected age of a cohort of very low birth weight infants from hospitals within the neonatal SEN1500 network. *An Pediatr*. 2013, 79(5):279-287.  
IF: 0,867

Luque RM, Ibáñez-Costa A, López-Sánchez LM, Jiménez-Reina L, Venegas-Moreno E, Gálvez MA, Villa-Osaba A, Madrazo-Atutxa AM, Japón MA, de la Riva A, Cano DA, Benito-López P, Soto-Moreno A, Gahete MD, Leal-Cerro A, Castaño JP. A cellular and molecular basis for the selective desmopressin-induced ACTH release in Cushing disease patients: key role of AVPR1b receptor and potential therapeutic implications. *J Clin Endocrinol Metab*. 2013, 98:4160-4169  
IF:6,429

Ruiz Hierro C, Vázquez Rueda F, Vargas Cruz V, Lasso Betancor CE, Ayala Montoro J. Focal nodular hyperplasia on accessory lobe of the liver: preoperative diagnosis and management. *J Pediatr Surg*. 2013, 48:251-254  
IF:1,383

Baena-Gomez MA, Torres-Borrego J, Teran ABM, Gil DA, Herrera AMC. Sleep apnea-hypopnea syndrome in type I Chiari malformation. *An Pediatr*. 2013, 79(4):23-274.  
IF:0,867

## Research Projects

Cañete Estrada, R. Clinical trial on the effect of metformin on pediatric obesity: effects on body mass, profile of inflammatory biomarkers and cardiovascular risk, and impact on factors related to the metabolic syndrome. Metabolic. Sponsored by: Ministry of Health, Social Services and Equality. Reference: EF10-243

## Collaboration Agreements

Cañete Estrada, R. HEALTHCARE - Occupational exposure and polycyclic aromatic hydrocarbons in thermal plants: early analysis of their potential impact on health. Sponsored by: Pfizer, S.A. Reference: CCB.UCO0050

Cañete Estrada, R. Protein expression of prepubertal children with GH deficit. Sponsored by: Pfizer, S.A. Reference: CCB.UCO0051

## Clinical Trials

0275/10: Clinical trial on the effect of metformin on pediatric obesity: effects on body weight, profile of inflammatory biomarkers and cardiovascular risk, and impact on factors related to the metabolic syndrome.  
PI: Dr /a Cañete Estrada, Ramón

0090/11: A randomized, phase III, double-blind, prospective, comparative study of rhBSSL vs. placebo added to the infant formula or to breast milk for four weeks of treatment administered to preterm infants born before a gestational age of 32 weeks.

PI: Dr/a Guzman Cabañas, Juana Maria

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0291/11: A randomized, multicenter, blind trial with topiramato vs. placebo for the treatment of newborns with perinatal asphyxia treated with moderate whole-body hypothermia.

PI: Dr/a Guzman Cabañas, Juana Maria

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0180/12: A multicenter, randomized, observer-blind, active-controlled study to evaluate the safety, tolerability, pharmacokinetics and efficacy of ceftaroline versus ceftriaxone in pediatric patients with bacterial pneumonia requiring hospitalization

PI: Dr/a Torres Borrego, Javier

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1693: An epidemiological study of early diagnosis of invasive candidiasis in very-low-weight preterm neonates

PI: Dr/a Guzman Cabañas, Juana Maria

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2270: A randomized, double-blind, parallel-group nutritional intervention study to assess the effect of taking *Lactobacillus fermentum* CECT5716 on the incidence of mastitis.

PI: Dr/a Guzman Cabañas, Juana Maria

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2343: Tolerance to two highly hydrolysed formulas based on rice protein and casein in infants allergic to cow's milk proteins.

PI: Dr/a Torres Borrego, Javier

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# GA6

## Clinical Analysis

### Team Leader

#### Associated Researcher

Cristóbal Aguilera Gamiz

[Cristobal.aguilera.sspa@juntadeandalucia.es](mailto:Cristobal.aguilera.sspa@juntadeandalucia.es)

#### Other researchers

Fernando Rodríguez Cantalejo

Javier Caballero Villarraso

#### Senior Researchers

Enrique Bellido Muñoz

Francisco Gavilán León

María López García

Antonio Martínez Peinado

Rosario Miranda García

Rafael Molero Payán



## Scientific Activity

Our group is currently developing two lines of research related to the assessment of the diagnostic accuracy of new technologies. On the one hand, we are assessing the diagnostic efficacy of the methodologies used for prenatal diagnosis of aneuploidy such as cho-

ronic villus sampling in screening for aneuploidy in the first trimester and the karyotype study in the first and second trimester of pregnancy. On the other hand, we are assessing new point-of-care testing (POCT) methodologies as gas, blood metabolite and ion determination; diagnosis and evolution of celiac disease, and use of POCT methods in

coagulometry for to the follow-up of anticoagulated patients.

## Keywords

New methodologies, chorionic villus sampling, prenatal screening, karyotype, POCT.

## Publications

### Joint Publications

Yubero-Serrano EM, Gonzalez-Guardia L, Rangel-Zuñiga O, Delgado-Casado N, Delgado-Lista J, Perez-Martinez P, Garcia-Rios A, Caballero J, Marin C, Gutierrez-Mariscal FM, Tinahones FJ, Villalba JM, Tunes I, Perez-Jimenez F, Lopez-Miranda J. Postprandial antioxidant gene expression is modified by Mediterranean diet supplemented with coenzyme Q(10) in elderly men and women. *Age*. 2013, 35(1):159-170.  
IF: 4,084

De Hoyo M, Carrasco L, Da Silva-Grigoletto ME, Sanudo B, Caballero-Villarraso J, Arriaza E, Escobar MD. Impact of an acute bout of vibration on muscle contractile properties, creatine kinase and lactate dehydrogenase response. *Eur J Sport Sci*. 2013, 13(6):666-673.  
IF: 1,146

Pendón-Ruiz de Mier MV, Alvarez-Lara MA, Ojeda-López R, Martín-Malo A, Carracedo J, Caballero-Villarraso J, Alonso C, Aljama P. Effectiveness of haemodiafiltration with ultrafiltrate regeneration in the reduction of light chains in multiple myeloma with renal failure. *Nefrologia*. 2013, 33:788-796.  
IF: 1,274

Perez-Caballero AI, Alcalá-Díaz JF, Perez-Martinez P, Garcia-Rios A, Delgado-Casado N, Marin C, Yubero-Serrano E, Camargo A, Caballero J, Malagón MM, Tinahones FJ, Perez-Jimenez F, Lopez-Miranda J, Delgado-Lista J. Lipid metabolism after an oral fat test meal is affected by age-associated features of metabolic syndrome. *Atherosclerosis*. 2013, 226(1):258-262.  
IF: 3,706

Lozano A, Perez-Martinez P, Marin C, Tinahones FJ, Delgado-Lista J, Cruz-Teno C, Gomez-Luna P, Rodriguez-Cantalejo F, Perez-Jimenez F, Lopez-Miranda J. An acute intake of a walnut-enriched meal improves postprandial adiponectin re-

sponse in healthy young adults. *Nutr Res*. 2013, 33(12):1012-8.  
IF: 2,142

Casado-Díaz, A, Cuenca-Acevedo, R, Navarro-Valverde, C, Díaz-Molina, C, Caballero-Villarraso, J, Santiago-Mora, R, Dorado, G, Quesada-Gomez, JM. Vitamin D status and the Cdx-2 polymorphism of the vitamin D receptor gene are determining factors of bone mineral density in young healthy postmenopausal women. *J SteroidBiochem Mol. Biol*. 2013, 136:187-189.  
IF: 3,984

# GA7

## Urology and Sexual Medicine

### Team Leaders

#### Associated Researcher

M<sup>º</sup> Jose Requena Tapia

[josefa.requena.sspa@juntadeandalucia.es](mailto:josefa.requena.sspa@juntadeandalucia.es)

#### Other Researcher

Rafael Prieto Castro

#### Senior Researcher

Julia Carrasco Valiente

#### Post-doctoral Researcher

Ana M<sup>º</sup> Blanca Pedregosa

#### Pre-doctoral Researchers

Francisco Anglada Jurado

Daniel Gil Contreras

Juan P Campos Hernández

Jesús Ruiz García

Javier Márquez López

Enrique Gómez Gómez





## Scientific Activity

This Group is centered on the study of urologic tumors from a new epidemiological approach and the search for diagnostic / prognostic markers. Additionally, this Group is involved in

research on renal transplantation and developing new strategies to improve prognosis after organ transplantation. In the field of sexual medicine, our group has focused its efforts on the study of erectile dysfunction (ED), especially on secondary ED, which is associated with

radical prostatectomy. At present, we are looking for new invasive pharmacological therapeutic lines.

## Keywords

Bladder cancer, renal cancer, renal transplant, erectile dysfunction

## Publications

### Originals Publications

Gutierrez-Hernandez PR, Puigvert-Martinez A, Prieto-Castro R. The partner of the male with erectile dysfunction: The Primary Care physicians opinion of the role of the partner in erectile dysfunction diagnosis and treatment in Spain. *Rev Int Androl.* 2013, 11(4):128-137. IF: 0,256

Regueiro JC, Carrasco JC, Alvarez J, Prieto R, Leva ME, Requena MJ. Surgical Treatment Options in Bulbar Urethral Stenosis. *Actas Urol Esp.* 2013, 37(3):167-173. IF: 1,144

Santiago-Agredano B, Alvarez-Kindelán J, Font-Ugalde P, Blanca-Pedregosa A, López-Beltrán A, Requena-Tapia MJ. Prognostic value of microvascular invasion in predicting survival in renal cell carcinoma. *Actas Urol Esp.* 2013, 37:504-512. IF: 1,144

Anglada-Curado FJ, Campos-Hernandez P, Carrasco-Valiente J, Anaya-Henares F, Carazo-Carazo JL, Alvarez-Kindelán J, Regueiro-Lopez JC, Requena-Tapia MJ. Extracorporeal shock wave lithotripsy for distal ureteral calculi: Improved efficacy using low frequency. *Int J Urol.* 2013, 20(2):214-219. IF: 1,734

Rosa JV, Lopez JM, Hernández PC, Martínez AP, Castro RP. Current recommendations about the diagnosis and treatment of testosterone deficit syndrome: Clinical guidelines. *Arch Esp Urol.* 2013, 66(7):737-744. IF: 0

López-Beltrán A, Vidal A, Blanca A. Biobanking: the basis for molecular research in uro-oncology. *Arch Esp Urol.* 2013, 66(5):416-22. IF: 0

García-Rubio JH, García JR, Hernández PC, López JM, Curado FA, Vallejo ML, López JC, Gómez EG, Aljama P, Tapia MJR. Correlation between dual kidney biopsy in expanded-criteria donors and transplant survival. *Transplant Proc.* 2013, 45(10):3606-3608. IF: 0,952

Gómez EG, Hernández JP, López FJ, García JR, Montemayor VG, Curado FA, Vallejo ML, López

JC, Cabello MD, Aljama P, Tapia MJR. Long-term Allograft Survival After Kidney Transplantation. *Transplant Proc.* 2013, 45(10):3599-3602. IF: 0,951

Alfaro AG, Hernández PC, Gómez EG, García JR, Carazo JL, López FM, Curado FJ, Vallejo ML, López JC, Aljama P, Tapia MJR. Variations in initial renal transplant function by type of organ retrieval. *Transplant Proc.* 2013, 45(10):3603-3605. IF: 0,951

### Joint Publications

Puigvert-Martinez A, Cortada-Robert J, Astobizeta-Odrizola A, Becerra-Fernandez A, Prieto-Castro R. Grp Estudio HIT, Asociac Española Andrología Med Se. Testosterone deficit syndrome in patients with sexual dysfunction: Prevalence and relationship between testosterone fractions, patients characteristics and symptoms. *Rev Int Androl.* 2013, 11(1):2-8. IF: 0,256

Lopez-Beltran A, Cheng L, Vidal A, Scarpelli M, Kirkali Z, Blanca A, Montironi R. Pathology of Renal Cell Carcinoma An Update. *Anal Quant Cytol Histol.* 2013, 35:61-76. IF: 0,560

Beltran AL, Ordóñez JL, Otero AP, Blanca A, Sevillano V, Sanchez-Carbayo M, Kirkali Z, Cheng L, Montironi R, Prieto R, De Alava E. Fluorescence in situ hybridization analysis of CCND3 gene as marker of progression in bladder carcinoma. *J Biol Regul Homeost Agents.* 2013, 27(2):559-567. IF: 0

### Research Projects

Requena Tapia, M<sup>a</sup> J. BROCA Project. Sponsored by: University of Cordoba. Reference: CCB.029PM

### Collaboration Agreements

Requena Tapia, M<sup>a</sup> J. Collaboration with Gsk. Introduction to the Bayesian inference. Sponsored by: GlaxoSmithKline, S.A. Reference: CCB.0040

Requena Tapia, M<sup>a</sup> J. Collaboration with GSK. Bayesian Inference Sponsored by: GlaxoSmithKline, S.A. Reference: CCB.0062

## Clinical Trials

0216/10: Comparative efficacy of DUODART (r) and lifestyle patterns versus watchful waiting and lifestyle patterns with or without escalation to tamsulosin in the management of treatment of naive patients with moderate symptoms of prostatic hyperplasia and prostate growth. PI: Dr/a Requena Tapia, María José

0280/12: A randomized, double-blind, comparative study of ZYTIGA (abiraterone acetate) plus prednisone at low dose plus androgen deprivation therapy (ADT) against TPA alone in subjects with a new diagnosis of high-risk metastatic hormone-naive prostate cancer (mHNPC). PI: Dr/a Requena Tapia, María José

1658: Epidemiological study estimating the incidence of prostate cancer in Spain 2010. PI: Dr/a Requena Tapia, María José

1735: A study to assess the impact of androgen deprivation therapy in the incidence of metabolic abnormalities in patients with prostate cancer. PI: Dr/a Anglada Curado, Francisco José

1809: A study to assess overactive bladder and detrusor overactivity in men with lower urinary tract filling symptoms (LUTS) attending functional urology and urodynamics units. PI: Dr/a Ruiz García, Jesús Manuel

1856: An epidemiological, observational study of disease progression and therapeutic approach in patients with prostate cancer. PI: Dr/a Requena Tapia, María José

2363: A study on regular practice in patients with Bladder Pain Syndrome (BPS) in Funcional Urology and Urodynamics units. PI: Dr/a Ruiz García, Jesús Manuel

# GA8

## Radiology

### Team Leader

#### Associated Researcher

Marina Alvarez Benito

[marinaalvarezbenito@telefonica.net](mailto:marinaalvarezbenito@telefonica.net)

#### Senior Researchers

Alberto Benito Ysamat

Antonio Cano Sánchez

María Cara García

Fernando Delgado Acosta

María José García Ortega

José García-Revilla García

Lucía Nuria Izquierdo Palomares

Rafaela Muñoz Carrasco

Elisa Roldán Romero

Ana Luz Santos Romero

Roser Ysamat Marfa



## Scientific Activity

Continuous advances in diagnostic imaging techniques have allowed physician to make highly accurate diagnoses, perform a close follow-up of the evolution of the disease, and assess TJE response of a large number of nosologic entities to a range of drugs and therapies. The collaboration of the Diagnostic Radiology Unit has allowed to assess the effect of new drugs on the evolution of a large number of neoplasms, rheumatologic diseases,

demyelinating diseases of the central nervous system or inflammatory diseases of the digestive tract. In other cases, this Unit has helped our researchers to quantify the prevalence of certain complications associated to different therapies such as corticosteroids-based therapies.

Appart from strictly diagnostic scans, the Diagnostic Radiology Unit also performs innovative interventional procedures. Among them, it is worth mentioning the intraarterial infusion of autologous bone marrow mononu-

clear cells in diabetic and non-diabetic patients with chronic critical ischemia of the lower limbs.

## Keywords

Stem cells, arterial ischemia of the lower limbs, therapeutic angiogenesis, neoplasms, demyelinating diseases, rheumatic diseases, pathochrony, radiological assessment of response to drugs, diagnostic radiological scans, therapeutic radiological scans.

## Publications

### Originals Publications

Fernandez-Valverde F, Jimenez-Gomez E, Roldan-Romero E, Bravo-Rodriguez F. Presurgical endovascular treatment of symptomatic carotid stenosis caused by a meningioma of the planum sphenoidale. *Rev Neurol*. 2013; 56(3):157-160. IF:1,179

Carrasco RM, Benito MA, del Campo ER. Value of mammography and breast ultrasound in male patients with nipple discharge. *Eur J Radiol*. 2013; 82(3):478-484. IF:2,512

Munoz-Guillen NM, Leon-Lopez R, Tunez-Finana I, Cano-Sanchez A. From vasospasm to early brain injury: new frontiers in subarachnoid haemorrhage research. *Neurologia*. 2013; 28(5):309-316. IF:1,322

Galera SL, Romero ER, Rodriguez FB. Whipple's disease: presentation of an unusual case with isolated cerebral involvement. *Neurologia*. 2013; 28(5):317-319. IF:1,322

### Joint Publications

Kovacs FM, Arana E, Royuela A, Cabrera A, Casillas C, Pinero P, Vega M, Asenjo B, Estremera A, Amengual G, Sarasibar H, Ferrer P, Manjarres A, Zamarro J, Bravo-Rodriguez F, Paniagua JC, Mota J, Sanchez-Sagrado T, Abreira V, Martinez C. Appropriateness of lumbar spine magnetic resonance imaging in Spain. *Eur J Radiol*. 2013; 82(6):1008-1014. IF:2,512

Escribano JA, Solivera J, Vidal E, Rivin E, Lozano J. Orogenic Cerebellar Abscess by *Enterococcus avium*, a Very Rare Infectious Agent. *J Neurol Surg A Cent Eur Neurosurg*. 2013; 74(Supl 1):155-158. IF:0

Fernandez FJM, Teran MDA, Galera MSL, Torres PR, Estudillo GB, Pena SR. Resection margins in conservative breast cancer surgery. *Cir Esp*. 2013; 91(7):404-412. IF:0,871

## Resercher Projets

### In collaborations with others IMBIC Groups:

Castaño Fuentes JP. Role of Somatostatin, cortistanina and ghrelin in the pathological interaction between obesity and breast cancer. Sponsored by: Ministry of Economy and Competitiveness (MINECO). Reference: BFU2010-19300

Pan Álvarez-Ossorio, M. Revascularization and Myocardial regeneration in patients with Chronic Coronary Occlusion and Ventricular Dysfunction. Sponsored by: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0315-2012

Rodríguez Ariza, A. Role of nitric oxide and nitrosothiols homeostasis in the generation and maintenance of tumor stem cells: new approaches to colon and breast cancer. Sponsored by: Institute Carlos III Health (ISCIII). Reference: PI13/00553

## Third Party Services

Alvarez Benito, M. Preoperative breast mri in clinical practice: multiple international prospective meta-analysis of individual woman data (the MIPA study). Sponsored by: EIBIR Gemeinnützige GmbH. Reference: PSS.0030

## Clinical Trials

0019/10: An open label, multi-center, phase 3 study with corresponding blinded image reading to determine the efficacy and safety of a

single intravenous injection of 0.1 mmol/kg body weight of gadobutrol 1.0 molar (Gadovist®) in patients with newly diagnosed breast cancer referred for contrast-enhanced breast MR. PI: Dr/a Alvarez Benito, Marina

1892: Study to evaluate the safety and tolerability of de Gadovist® for patients who need una magnetic resonance realized for contrast. PI: Dr/a Alvarez Benito, Marina

### In collaborations with others IMBIC Groups:

0139/09: A multicenter, open, randomized, two-arm, phase III study of bevacizumab plus chemotherapy vs chemotherapy alone for the treatment of patients with platinum-resistant primary peritoneal carcinoma, fallopian tube carcinoma or epithelial ovarian carcinoma. PI: Dr/a Rubio Pérez, Maria José

0196/09: A multicenter, randomized, double-blind, parallel-group study to assess the safety, disease remission and prevention of articular structural damage in patients with early, moderate to severe rheumatoid arthritis on tocilizumab monotherapy. PI: Dr/a Escudero Contreras, Alejandro

0028/10: A multicenter, double-blind, parallel-group, placebo-controlled phase III to assess the effectiveness and safety of certolizumab pegol in adult patients with active, progressive psoriatic arthritis. PI: Dr/a Collantes Estevez, Eduardo

0261/10: A multicenter, randomized, double-blinded, placebo-controlled, 12-week duration study of etanercept with a base NSAIDs in the treatment of adult subjects with axial ankylosing spondylitis without radiographic signs, with an open extension of 92 weeks PI: Dr/a Collantes Estevez, Eduardo

0291/10: A multicenter, randomized, semi-crossover, double-blind, phase I/II clinical trial to assess the safety and feasibility of systemic

therapy with mesenchymal cells derived from autologous bone marrow in patients with multiple sclerosis.

PI: Dr/a Sánchez López, Fernando

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0133/11: A Randomized Phase III Study of Weekly ABI-007 plus Gemcitabine versus Gemcitabine alone in patients with metastatic Adenocarcinoma of the Pancreas.

PI: Dr/a Pulido Cortijo, Gema

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0145/11: A multicenter, extension, dose-blind frequency study to determine the safety and efficacy of long-term pegylated interferon beta-1a (BIB017) therapy in patients with relapsing multiple sclerosis

PI: Dr/a Sánchez López, Fernando

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0232/11: A multicenter, randomized, double-blind parallel-group trial to assess the effectiveness of Adalimumab versus Azathioprina in the prevention of postsurgical recurrence of Crohn disease after 52 weeks.

PI: Dr/a García Sánchez, Valle

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0067/12 : A phase III, randomised, double-blind, parallel group, placebo controlled, multicentre study to assess efficacy and safety of expanded allogeneic adipose-derived stem cells (eASCs) for the treatment of perianal fistulising Crohn's disease over a period of 24 weeks. ADMIRE –CD study.

PI: Dr/a Gallardo Valverde, M<sup>o</sup> José

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0081/12: An open, multicenter, single-arm, non-randomized, phase II study to assess the effectiveness of oral TKI258 as second-line therapy in patients with advanced and/or metastatic endometrial cancer with mutated or wild-type FGFR2.

PI: Dr/a Rubio Pérez, María Jesús

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0235/12: A Randomized, Double-blind, Phase 3 Efficacy Trial of PROSTVAC-V/F ± GM-CSF in Men With Asymptomatic or Minimally Symptomatic Metastatic, Castrate-Resistant Prostate Cancer

PI: Dr/a Rubio Pérez, María José

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0280/12: A randomized, double-blind, comparative study of ZYTIGA (abiraterone acetate) plus prednisone at low dose plus androgen deprivation therapy (ADT) against TPA alone in subjects with a new diagnosis of high-risk metastatic hormone-naïve prostate cancer (mHNPc).

PI: Dr/a Requena Tapia, María José

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0230/13: A randomized, double-blind, placebo-controlled, phase III study of adjuvant regorafenib vs. placebo in patients with IV stage colorectal cancer after curative treatment of liver metastasis.

PI: Dr/a Aranda Aguilar, Enrique

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09

**Scientific Production  
at a glance**



# 09

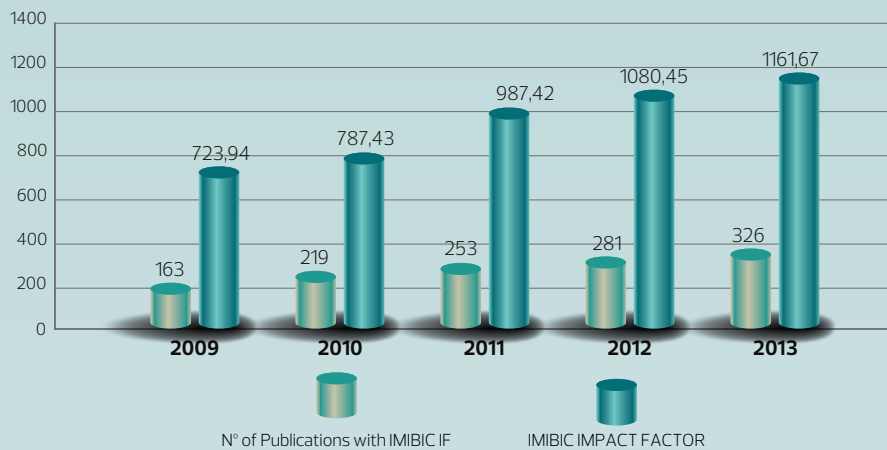
## Scientific Production at a glance

### 9.1 SUMMARY OF PUBLICATIONS

The scientific activities carried out by researchers in their respective groups have led to the following global production:

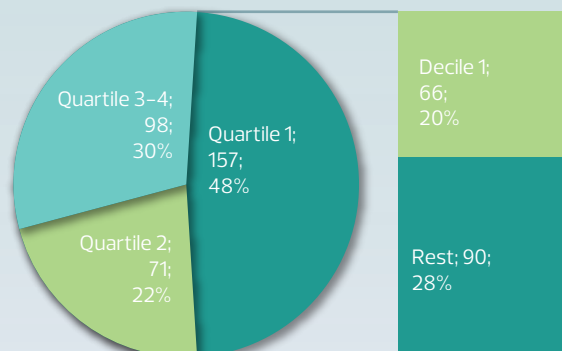
- 330 published articles, 326 indexed and 5 unindexed, with a notable improvement in the quality of our work, with 20% in the first decile and 48% in the first quartile.
- A total impact factor of 1161.167 points, with an Average Impact Factor of 3.56 (including indexed articles only)

The following graph shows the evolution of IF over the past five years:

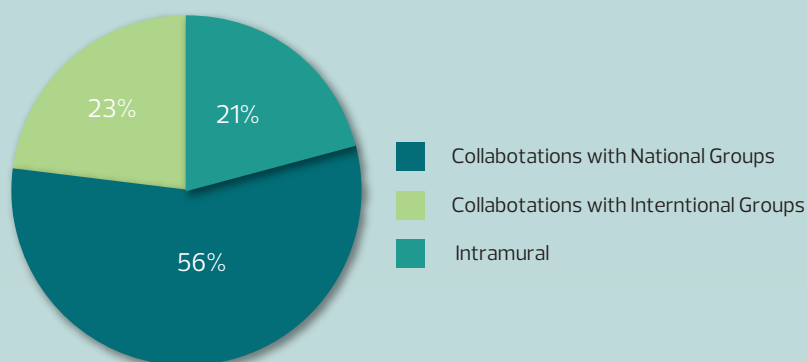


As regards authorship of the works, 53% of the published articles have an IMBIC researcher as first/last author, compared the remaining 47% which were published as co-authors.

In turn, these publications mainly appear in journals in the first two quartiles, which speaks volumes for the scientific quality of the published papers.



As for the affiliation of the authors, the papers published in collaboration with groups from other research centers are shown in the pie chart below:



## 9.2 List of journals where our work has been published

Scientific Journals	International/National	Quartile	Decile
AIDS	International	1	1
Am J Clin Nutr	International	1	1
Am J Gastroenterol	International	1	1
Am J Transplant	International	1	1
Anal Chim Acta	International	1	1
Ann Rheum Dis	International	1	1
Antioxid Redox Signal	International	1	1
Arthritis Rheum	International	1	1
Cell Metab	International	1	1
Circulation Res	International	1	1
Clin Cancer Res	International	1	1
Clin Infect Dis	International	1	1
Cochrane DB Syst Rev	International	1	1
Curr Top Dev Biol	International	1	1
Diabetes	International	1	1
Diabetes Care	International	1	1
Equine Vet J	International	1	1
Fertil Steril	International	1	1
Food Chem	International	1	1
Gastroenterology	International	1	1
Gut	International	1	1
Hepatology	International	1	1
Horm Behav	International	1	1
J Agric Food Chem	International	1	1
J Antimicrob Chemother	International	1	1
J Chromatogr A	International	1	1
J Clin Endocrinol Metab	International	1	1
J Hepatol	International	1	1
J Nutr Biochem	International	1	1
J Sci Food Agric	International	1	1
J Thorac Cardiovasc Surg	International	1	1
Lancet Infect Dis	International	1	1
Liver Transplantation	International	1	1



Mol Nutr Food Res	International	1	1
Nat Commun	International	1	1
Nat Neurosci	International	1	1
Neuropsychopharmacology	International	1	1
Nucleic Acids Res	International	1	1
Radiother Oncol	International	1	1
Trac-Trends Analytical Chemistry	International	1	1
Transplantation	International	1	1
Trends Food Sci Technol	International	1	1
Vet J	International	1	1
Age	International	1	
Am J Hematol	International	1	
Am J Physiol Endocrinol Metab	International	1	
Anal Bioanal Chem	International	1	
Analyst	International	1	
Andrology	International	1	
Atherosclerosis	International	1	
Biol Blood Marrow Transplant	International	1	
Br J Hematol	International	1	
Br J Nutr	International	1	
Brain Stimulation	International	1	
Cell Death Dis	International	1	
Clin Microbiol Infect	International	1	
Clin Nutr	International	1	
Comp Biochem Physiol A-Mol Integr Physiol	International	1	
Curr Opin Nephrol Hypertens	International	1	
Curr Opin Rheumatol	International	1	
Curr Pharm Des	International	1	
DNA Repair	International	1	
Electrophoresis	International	1	
Endocrinology	International	1	
Eur J Cardiothorac Surg	International	1	
Eur J Clin Invest	International	1	
Exp Gerontol	International	1	
Genes Brain Behav	International	1	
Haematologica	International	1	
Heart	International	1	
Histopathology	International	1	
Inflamm Bowel Dis	International	1	
Int J Clin Pract	International	1	
Int Rev Immunol	International	1	
J Biol Chem	International	1	
J Bone Min Res	International	1	
J Chemometr	International	1	
J Eur Acad Dermatol Venereol	International	1	
J Funct Foods	International	1	
J Gerontol Ser A-Biol Sci Med Sci	International	1	
J Immunol	International	1	
J Infect	International	1	
J Nat Prod	International	1	

J Nutri Biochem	International	1
J Proteomics	International	1
J Virol	International	1
Langmuir	International	1
Liver Int	International	1
Nephrol Dial Transplant	International	1
Neurogenetics	International	1
Nutr Metab Cardiovasc Dis	International	1
Obesity	International	1
Obesity Surgery	International	1
Pediatr Blood Cancer	International	1
Phytochemistry	International	1
PLoS One	International	1
Reprod Domest Anim	International	1
Rheumatology (Oxford)	International	1
Talanta	International	1
Thromb Res	International	1
Emergencias	National	1
Hematologica	National	1

10

**Knowledge Transfer**



# 10

## Knowledge Transfer

One of the main issues science and technology still have to address in our country is innovation. For instance, the data presented in the 2013 COTEC Report show that while Spain ranks tenth in the generation of knowledge, it lags behind in 30th position in terms of innovation.

IMIBIC has been aware of this situation for some time and has worked hard through its Innovation Management Department, setting targets for 2013 where we have obtained results far beyond those initially set. Thus, it has brought greater stability and will permit the future development of this department.

Developing an innovation department in a health-related organization is definitely an essential tool to face future challenges successfully. The health sector is one of the most profitable ones, in business terms, so the opportunity is clear: in a growing market, we own valuable raw material.

The key, as we perceive it in IMIBIC, is to develop the right processes so that our know-how is converted efficiently into new resources. For this reason, the Innovation Management Department is a sound future investment. In this context, the Innovation Management Department has built on the previous years' work and has carried out the following activities during 2013

1. Accreditation of its Head as Assistant Technician for Technology Transfer by the Ministry of Economy and Competition. This distinction was awarded to the top 20 CVs presented in the competition set up for that purpose. The award provides funding of up to €16,000 a year for 3 years to cover the award winner's salary.
2. Including the IMIBIC Innovation Management Department as a partner in the ITEMAS platform. This has given the innovation department access to new resources, both in financial and personal terms. In this case, including IMIBIC in this platform has permitted us to contract two people, thus ensuring the stability and development of the department for the next 4 years.  
The Medical Technology Innovation Platform (ITEMAS) is one of the Thematic Platforms promoted by the Health Institute Carlos III (ISCIII) as part of their integrated vision of innovation in their environment. The ITEMAS Platform seeks to promote innovation in health technology as a fundamental tool to make the National Health Service more sustainable, supporting the development of the innovative culture necessary to allow the integration of the scientific-industrial network into the field of medical technology. The core of the ITEMAS Platform is currently made up of innovation units in the largest hospitals in the National Health Service.
3. Over 90 meetings with researchers were held. At these meetings, the transfer process was explained to researchers and those ideas, innovations and research results with potential for some kind of industrial or intellectual property were identified.
4. Several trade fairs, meetings and conferences were attended, not only to give lectures and seminars, but also to meet representatives from many companies to offer IMIBIC services and forge links.

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PRE-COMMERCIAL PROCUREMENT AND PUBLIC PROCUREMENT OF INNOVATIVE SOLUTIONS: New Instruments for more efficient public services and advantages for industry and SMEs

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2nd Andalusian Congress of Industrial Law

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TT Symposium at the VII Congress of the Spanish Federation of Biotechnologists, BAC2013

FENIN-REGIC-SEMYUC Forum

Practical Technology Commercialization Workshop: Converting Technology to Wealth. CEIC Granada

Innovation Procurement Conference in Poland on 14-15 November 2013

9th Andalusian Conference Days for Tutors of Family and Community Medicine

REGIC Meeting - presentation of services portfolio

Public Workshop. 10th Conference Days "Health Investigates"

As a result of this intense work, these are the results obtained:

EVOLUTION OF RESULTS						
	2008	2009	2010	2011	2012	2013
Industrial/intellectual property	1	1	4	5	6	12
National Phase	-	-	-	1	1	1
PCTs	-	1	1	2	3	3
Licensed Patents	-	-	-	-	4	4
SPIN-OFFs	-	-	-	1	2	-

## Industrial /intellectual property

During 2013, a total of 16 industrial/intellectual property were applied for.

Reference	Title	Patent Type	Owner
IMIBIC-53	UCInnova Management Software	Intellectual Property Registry	SAS
IMIBIC-54	Icontraception for iOS	Intellectual Property Registry	SAS
IMIBIC-55	Removable dressing for nasal packing	National Patent	SAS & UCO
IMIBIC-56	Polymorphisms of the enzyme converting angiotensin to predict or forecast the response to anti-angiogenic therapy cancer	National Patent	SAS & UCO
IMIBIC-57	Icontraception for Android	Intellectual Property Registry	SAS
IMIBIC-58	Compositions for the treatment of liver damage	National Patent	SAS & UCO
IMIBIC-59	Method to predict the risk of CMV replication after a transplant	National Patent	SAS & UCO
IMIBIC-60	Method of classification, diagnosis and follow-up of individuals at risk for lung cancer using analysis of sweat	National Patent	SAS & UCO
IMIBIC-61	Device used to induce ischemia in members	National Patent	SAS
FIBICO 72	Method to obtain data to predict response to Hepatitis C treatment	Patent Cooperation Treaty	SAS & UCO
IMIBIC-63	Posture chair	National Patent	SAS
IMIBIC-64	Device for rectum amputations	National Patent	SAS
IMIBIC-65	UCOTRACK	Intellectual Property Registry	SAS & UCO

IMBIC-66	Using growth factor derived from platelets or from a selective agonist of the at2 receptor for the treatment of vascular calcification	National Patent	SAS & UCO
IMBIC-67	Bone fixing device as reference star for surgical navigation	Patent Cooperation Treaty	SAS
IMBIC-68	Using growth factor derived from platelets or from a selective agonist of the at2 receptor for the treatment of vascular calcification	Patent Cooperation Treaty	SAS & UCO





11

**Goals for 2014**



# 11

## Goals for 2014

1. To transfer the research groups to the IMIBIC premises (new building).
2. To increase the number of publications whose affiliation includes IMIBIC, Reina Sofia University Hospital and University of Córdoba.
3. To implement the Clinical Research and Clinical Trial Unit Platform, including the Phase I Clinical Trial Unit.
4. To introduce the infrastructure and equipment obtained via the competitive grants of 2007, 2008 and 2010, and setting up of this equipment in the UCAIB area of the Institute.
5. To promote strategies to develop the Medical Technology Innovation Platform (ITEMAS).
6. To implement centralized special units, such as the Isotope Lab and the Experimental Animal Service
7. To continue the strategy for raising funds through public procurement strategy.
8. To raise more competitive funds from public sources, as well as from donations and companies.
9. To launch the IMIBIC node in the ProteoRed-ISCIII network.
10. To increase funding for the Biobank and the volume of sample transfer.
11. To increase the number of research groups becoming part of IMIBIC in the health care sector.
12. To continue with the Integration Plan strategy and starting a new agreement between the institutions involved in IMIBIC.



**IMIBIC**

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