# SCIENTIFIC REPORT 2015



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The Maimonides Institute for Biomedical Research of Córdoba (IMIBIC) crystallizes the integrated efforts of individuals and institutions united around the common goal of improving the health of patients and the community, through excellence in science and innovation in biomedical research.

## 1. Director's Foreword

The Maimonides Institute for Biomedical Research of Córdoba (IMIBIC) crystallizes the integrated efforts of individuals and institutions united around the common goal of improving the health of patients and the community, through excellence in science and innovation in biomedical research. The compromise of IMIBIC with quality, talent, and cooperation as keys for translational science continues growing since the inception of the Institute, in 2008, through the integrated agreement and generous contribution of several institutions. In 2011, IMIBIC was endorsed by the Health Institute Carlos III as an accredited Health Research Institute, and the ensuing five years have witnessed a steady progression of IMIBIC in the quest to develop an independent research center of excellence with a translational nature and a vocation to improve the quality of life of patients. The growth and maturation of IMIBIC and its achievements in this intense period are those of the human team that embodies the Institute: over 500 clinicians, nurses, basic and translational researchers, and personnel in technical, management, and administrative areas; an enthusiastic and hardworking crew joined in the quest for this common praiseworthy ambition of improving patient's health through biomedical research.

The year 2015 represented a significant landmark for IMIBIC. The transition to a novel team in the Scientific Direction of the Institute was accompanied by the crucial move to the new facilities, our flagship building for basic and translational research. The new building is located within the University Health Sciences Campus by the Reina Sofía University Hospital. With 10.000 sq, it provides new facilities for researchers, who have at their disposal 5.500 sq for laboratory space plus 900 sq for the new Experimental Animal Service facilities. The building gathers the core of research teams of IMIBIC, in a place where they have at hand everything they need to develop their research.



Along the same lines, we are especially proud of the establishment of the Clinical Research Unit, with two main facilities occupying 2.000 sq. This year 2015 has seen the inauguration of these two new facilities for Clinical Research, located in the Hospital Provincial and the General Hospital's Clinical Research Building, respectively. More than 300 patients have been already treated at these facilities. This enables a significant improvement in the quality of care provided in clinical trials. There has been a 150% increase in independently led new clinical trials, and a 233% increase in the number of new observational studies.

The year 2015 represented a significant landmark for IMIBIC. The transition to a novel team in the Scientific Direction of the Institute was accompanied by the crucial move to the new facilities, our flagship building for basic and translational research, and the Clinical Research Unit.

As per above, the research output of the institute has grown significantly in quantity and quality over the last years. Indeed, despite the complex general situation for research funding nationwide, the intense research activity compiled and summarized in this report illustrates excellent indicators of generation and transfer of knowledge. In 2015, IMIBIC managed to continue increasing its scientific output, with 359 papers, of which 33% were published in collaboration with foreign groups and institutions. The total impact factor was 1303.75 points. The improvement in the quality of our work is commendable, for 26,5% of our publications are found within the first decile journals and 52,1% in first quartile journals.

Moreover, the Institute has made great advances in one of our main objectives: promoting biomedical innovation as a powerful engine for economic and social development. In 2015, 21 property registries were fostered at the heart of the Institute. These facts clearly show that there has been more growth compared to the previous year.

IMIBIC has continued to implement new strategies to increase fundraising through EU and international programmes. A total of 5 projects are active in 2015, including one clinical trial funded by the 7FP, one research project from the Innovative Medicines Initiative, two coordination activities on Pre-commercial Public Procurement of Innovation, and one Marie S. Curie Action. A further three proposals submitted in 2014 and 2015 have been funded, one Pre-commercial Procurement of Innovation Action, one clinical trial on paediatric oncology and one research project on e-health and diabetes. The aim is maintain a level of success that allows a steady increment of funds from international programmes.

The present Scientific Report depicts and summarizes the daily life of IMIBIC in 2015, and will hopefully serve as a portrait and ambassador of our research activity. The human team that comprises the Institute, with the unrestrained support of our institutions, will enthusiastically continue the collaborative research work that should lead us to achieve our mission.

> Justo P. Castaño Scientific Director

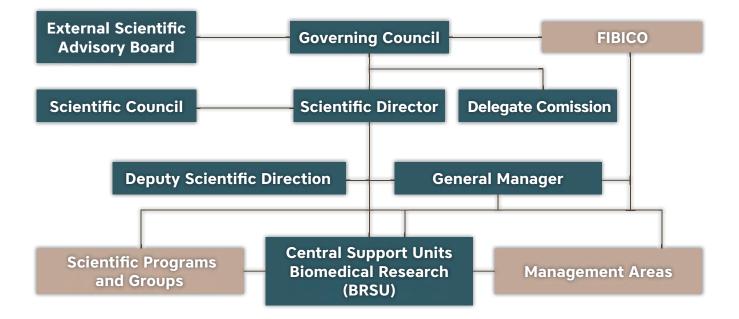




## 2. Human, Technological and Economic Resources. Facilities

#### 2.1. Organization Chart

IMIBIC's governing and representative bodies are detailed below:



#### A. Collegiate Bodies

The collegiate bodies composing IMIBIC are the Governing Board, the Scientific Board and the External Scientific Board. Each body has its competencies and is composed of several specialists.

#### **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

M<sup>a</sup> Isabel Baena Parejo. General Director of Research and Management of Knowledge of the Health Council Marina Álvarez Benito. Managing Director of the Reina Sofia University Hospital and President of FIBICO.

Two representatives from the Regional Ministry of Economy and Knowledge

Manuel García León. General Director for Research and Knowledge Transfer

Manuel Carmona Jiménez . Provincial Delegate of Economy, Innovation, Science and Employment of Córdoba

Two representatives of the University of Córdoba

Antonio Cubero Atienza. Vicerector of Institutional Coordination and Infrastructures Luisa M. Rancaño Martín. Managing Director.

#### IMIBIC's Scientific Director

Justo P. Castaño Fuentes

One representative from the Progress and Health Andalusin Public Foundation **Ana Madera Molano**. Managing Director.

IMIBIC's General Manager José Miguel Guzmán de Damas

#### **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**

Justo P. Castaño Fuentes. Full Professor of Cell Biology of University of Cordoba. He was named scientific director of IMIBIC by the Governing Council at a meeting held on April 08, 2015.

#### **Deputy Scientific Director of Basic Research**

Manuel Tena Sempere. Full Professor of Physiology at the Faculty of Medicine of the University of Córdoba . He was re-named deputy scientific director of IMIBIC by the Governing Council at a meeting held on April 08, 2015.

#### **Deputy Scientific Director of Clinical Research**

José López Miranda. Full professor of the University of Cordoba and Head of the Internal Medicine Unit at Reina Sofia University Hospital. He was named deputy scientific director of IMIBIC by the Governing Council at a meeting held on April 08, 2015.

#### **General Manager**

José Miguel Guzmán de Damas. Hospital Pharmacist. 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 an Executive MBA from the IESE Business School. He obtained his PhD from the Department of Preventive Medicine and Public Health of the University of Malaga. 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:

#### 2.2.1. Active ageing and Frailty

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 patience care assistance. It includes the following lines of research:

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

#### 2.2.2. 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

#### 2.2.3. 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

#### 2.2.4. 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
- Leukemia and Lymphomas
- Digestive Tumors
- Other tumors

#### 2.2.5. 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)	
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 Bárcena 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)	

Code	Title	Researchers
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) Dr. Yolanda Almadén Peña (CO-IR) Dr. Javier Delgado Lista (CO-IR) Dr. Pablo Pérez Martínez (CO-IR)
GC10	Hormonal regulation of energy balance, puberty and reproduc- tion. 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. Bio- technology 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 Artificial Vision PROGRAM 5	Dr. Rafael Medina Carnicer v(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)
GC23	Metabolism in Childhood PROGRAMS 2, 4	Dr. Mercedes Gil Campos (IR)
GE1	Oxidative stress and nutrition. PROGRAMS 1 , 2, 5	Dr. Isaac Túnez Fiñana (IE)
GE2	Knowledge Discovery and Intelligent Systems PROGRAMS 1,2,3	Dr. Sebastián Ventura Soto (IE)
GE3	Skin immune mediate inflammatory diseases (SIMID) PROGRAM 5	Dr. Juan A. Ruano Ruiz (IE)
GE4	Applied Psychology PROGRAM 1	Dr. Carmen Tabernero Urbieta (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)

Code	Title	Researchers
GA3	Pneumology PROGRAMS 2, 4, 5	Dr. Bernabé Jurado Gámez (IA)
GA4	Endocrinology and Nutrition. Insulin resistance, diabetes and metabolism. PROGRAM 2	Dr. Juan Antonio Paniagua González (IA) Dr Mª Ángeles Gálvez Moreno (IA)
GA5	Study of growth. Endocrinology and Child Nutrition. PROGRAM 2	Dr. Ramón Cañete Estrada (IA)
GA6	Clinical Analysis. PROGRAM 2	Dr. Fernando Rodríguez Cantalejo (IA)
GA7	Urology and sexual medicine	Dr. María José Requena Tapia (IA)
UA/	PROGRAM 5	Dr. Rafael Prieto Castro (IA)
GA8	Radiology PROGRAMS 2, 4, 5	Dr. Daniel López Ruiz (IA)
GA9	Cardiology Cardiovascular PROGRAMS 2, 4,	Dr. Ignacio Muñoz Carvajal (IA)
GA10	Nuclear Medicine PROGRAMS 2, 4	Dr. Juan A. Vallejo Casas (IA)
GA11	Learning and Artificial Neural Networks-AYRNA PROGRAMS 2, 3, 4, 5	Dr. César Hervás Martínez (IA)

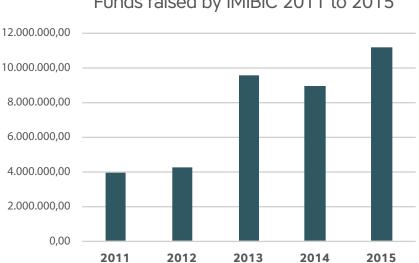
GC- Established Groups. GE - Emerging Groups. GA - Associated Groups

#### 2.4. Economic Resources

The year 2015 is the culmination of the period covered by the First Strategic Plan of IMIBIC, whose start began after achievement of accreditation as an Institute of Health Research granted by the Institute of Health Carlos III in 2011. There have been numerous scientific milestones achieved during this period, which has also enabled a more remarkable increase in economic data to be obtained, all this despite having gone through a difficult economic situation in the sphere of public funding. That is why researchers have turned to new ways to finance their projects, such as Public Procurement of Innovation projects that were achieved in 2013 as well as going to the private sector to raise funds, either through commercial clinic research, or through contracts, agreements and grants to biomedicine. The increase that has occurred in global fundraising figures was as follows:

Among the funds raised include aid received to finance the acquisition of scientific equipment for the new headquarters of both fundamental research and clinical research. However, if we ignore these for a moment, the total amount of economic sources, experienced a significant increase from just 4 million euros in 2011 to 11 million in 2015, reflecting a total volume of funds raised almost reaching 38 million euros in the last 5 years, regardless of infrastructure aid.

One of the goals that had been set in the 2011-2015 Strategic Plan was to strike a balance between funding from public sources and from private sources. In this sense, it has made the impact of private funding increase



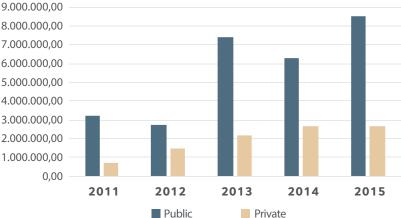
Funds raised by IMIBIC 2011 to 2015

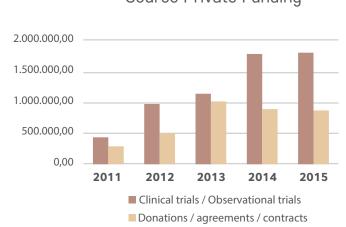
on the annual fundraising figures, as seen in the following graph:

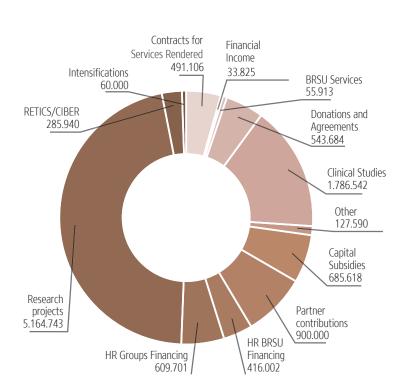
This increase in fundraising from private sources has its origin in the increase of clinical research conducted through clinical trials and observational studies, as well as increased fundraising through agreements, donations, and especially for the provision of scientific research groups to external companies.

As for the volume of revenue from the IMIBIC were managed since 2015, the total executed budget has exceeded 11 million euros, representing an increase of 12% compared to what was initially expected. The previous amount, a total of 2.7 million, forms the structure of the Institute, which includes general costs (maintenances and other supplies) and HR costs of BRSUs, personnel management, cost of supplies and maintenance of buildings and equipment, etc. Meanwhile, the amount allocated to R + D + I, through research projects, clinical studies, RETICs (Networks for Cooperative Research in Health ), CIBERs (Biomedical Research Networking Centers), CIBERs and HR programs aimed at attracting research talent, reached 8.5 million euros. The breakdown of funds executed in 2015 based on their sources are:

Public versus Private Funding







Source Private Funding





## 3. Goals achieved in 2015

Goals achieved in 2015	Comments
1 To evaluate our Strategic Plan for 2011-2015, develop our strategic plan for 2016-2020 and submit it for approval by the Governing Council.	For internal analysis of the new Strategic Plan it has been necessary to assess and review the previous Plan. Final data on the 2015 activity will be available in the first quarter of 2016 for final overall assessment. The new Strategic Plan for 2016 to 2020 has also been developed, which will be pre- sented as a working paper to the various governing bodies of IMIBIC in order to receive suggestions, comments and improvements to it by members of the Governing Council and other organs of IMIBIC and complete its approval at the beginning of 2016.
2 To move our research groups to the new experimental research building.	The 20 groups that had available space in the new building have moved there. The transfer process lasted from January to April 2015 and took place without incident having planned transfer depending on the origin of the group in order to minimize the effective time of the transfer and the economic cost thereof.
3 To develop our Biomedical Research Support Units, espe- cially the isotopes, animal test- ing, microscopy, cytometry and proteomics units.	In January 2015 the favorable authorization was achieved by the Nuclear Safety Council for the implementation of isotope rooms IMIBIC building. With respect to animal testing services, the necessary actions are being implemented for the license to open these services based on the guidelines set by the Director of Animal Ex- perimentation Service of the University. As for the microscopy and cytometry Units, IMIBIC has acquired great technical value teams that will allow the groups to develop quality research projects. Finally, the Proteomics Unit has been reinforced with the addition of two technical support personnel, as well as the acquisition and commis- sioning of equipment of high scientific interest which solidify IMIBIC's role as a leader at the regional level. Additionally, IMIBIC has launched the Genomics Unit, with the addition of two technicians, and with the acquisition of equipment for next-genera- tion sequencing.
4To start up and promote the area of clinical research by in- creasing the development of independent research activities.	In 2015 the activity has been put into practice in the two facilities at the Clinical Re- search Institute, located in the Provincial Hospital and Clinical Research Building Gen- eral Hospital, having served more than 300 patients. Patient quality of care in clinical trialsnhas improved, and a Quality Assurance System and Functional Plan have been developed. The increase in independent clinical research sponsored by IMIBIC has been 150% in new clinical trials (from 2 in 2014 to 5 in 2015) and 233% in new ob- servational trials (3 in 2014 to 10 in 2015). As for the other clinical trials, they have increased by 3% (from 76 in 2014 to 78 in 2015).
5To develop new strategies to promote IMIBIC's image, affili- ations and acknowledgement, and disseminate the scientific results obtained by its research groups.	As of December 2015, the number of publications affiliated correctly has doubled, from 89 in October 2014 to 193 at the end of 2015. IMIBIC is continuing with the strategy reminder of the procedure of affiliation to those Units / Research Groups in which any scientific publication is detected with inadequate affiliation.
6 To promote new strategies to increase fundraising through EU and national calls -including project and HR calls.	The number of requests for international aid programs has reached a total of 16 proposals, including two individuals from human resources. During this year three proposals were resolved favorably for research projects and one for human resources in the H2020 sessions, some of which were presented in 2014. In addition, IMIBIC has begun participation in an ongoing project of 7PM. The total amount of the grant of these 5 projects is $\in$ 1,404,337.
8 To enhance the involvement of Clinical Management Units in IMIBIC activities.	The portfolio of services has been presented with to all CMUs and also has conduct- ed a situation analysis of the objectives of research and innovation for granting each unit. In 2015, the total CMUs (41) of the Hospital Universitario Reina Sofía, 31 units have achieved a new research project or a new patent (78% of the CMUs), and in 2014 30 CMUs. Of the 11 CMUs in 2014 they did not get a project or patent, eight of them have been achieved in 2015.

Goals achieved in 2015	Comments
9 To continue the develop- ment of new strategies for the integration of new clinical and university research groups into the IMIBIC.	The group of the University of applied psychology as an emerging group, led by Dr. Carmen Tabernero Urbieta, has joined us.
10 To develop new strategies for BRSUs to improve the quality of their research projects.	Presentations were raised to all research groups of the portfolio of each BRSU and meetings of technicians with PIs requesting projects in competitive calls, with a view to including services such as BRSU projects and to try to improve the quality of the projects requested by implementing innovative techniques (proteomics, bioinformatics, cytometry, etc.). In all projects that applied and for which funding is requested in competitive public calls (FPS and ISCIII) they have included items of different BRSUs. Today the final resolution of ISCIII research projects has not been published but out of 10 projects granted provisional resolution, 8 have included IMIBIC central services. Projects which were pending resolution also included the BRSUs. (31,000 €).
11 To develop strategies to promote projects aimed at the acquisition of innovative prod- ucts by public entities and foster involvement in new projects.	Of the total number of proposals submitted in 2015 to the FIS call none has been funded. Regarding the call for innovative public international procurement 5 projects have been requested for Horizon 2020. Three of these proposals have been funded, two are Coordination Support Action and one of them is a pre-commercial Public Procurement which has proved to be the first project of ICC International funded in Andalusia in the health sector. A team of managers has been formed at the Institute which coordinates the submis- sion of proposals for national and international ICC. It participates in forums innova- tive public procurement with the aim of making IMIBIC a national benchmark in ICC.
12 To increase IMIBIC's au- tonomous management of re- sources.	The budget structure of IMIBIC has an annual value of around 2.5 million euros. Of this amount only 0.9 million is contributed by the convened entities, so one could say that of every euro invested by such entities, the Institute receives three. With respect to revenue, during the year 2015 IMIBIC has managed to increase the amount of indirect costs, financial income and billing services the BRSUs. Similarly, it has managed to maximize equipment acquired under capital grants in relation to equipment initially requested.



## External Scientific Advisory Board



### 4. External Scientific Advisory Board

The composition of the External Scientific Advisory Board was modified in 2014. The annual ordinary meeting took place in December 16, 2014. Its structure is as follows:

Dr. Lina Badimon. 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)

Mr. Jorge Barrero. General Director of La Fundación Cotec (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 2016.







### 5. 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, IMIBIC is member of the new platforms that support research in health sciences and technologies.

In fact, among the 38 groups integrated in the IMIBIC, 18 participate in partnership programs related to different IS-CIII strategic initiatives. 12 groups are involved in 8 RETICs. Additionally, 6 groups are involved in 3 CIBERs and there are 28 groups involved in the Andalusian Plan for Research, Development & Innovation (PAIDI Program).

#### **CIBER Program**

Our researchers lead the following CIBERs' nodes:

CIBER	Principal Investigator (PI) /Collaborators
CIBER on Obesity and Nutrition (CIBERobn)	José López Miranda (PI)
	Manuel Tena-Sempere (PI)
	Mª Mar Malagón Poyato
	Justo P. Castaño
CIBER on Liver and Digestive Diseases (CIBERehd)	Manuel de la Mata García (PI)
CIBER on Rare Diseases (CIBERER)	Mercedes Gil Campos

#### Plataforms

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 (P)/Collaborators
AIDS Research Network (RIS)	Antonio Rivero Román
	José Peña Martínez
Cooperative Research Thematic Network on Aging and Frailty	Jose Manuel Quesada Gómez (PI)
(RETICEF)	Isaac Túnez Fiñana
	MªDolores Luque de Castro
Spanish Renal Research Network (REDinREN)	Pedro Aljama García (PI)
Spanish Network for Research into Infectious Pathologies (REIPI)	Julián de la Torre Cisneros (PI)
	Rafael Solana Lara
National Biobank Network	Manuel Medina Pérez
Cooperative Research Thematic Network on Cancer (RETICC)	Enrique Aranda Aguilar
Network for Research on Mother-Child Health (RedSAMID)	Mercedes Gil Campos
Research Network on Preventive and Health Promotion in Primary Care (RedIAPP)	Luis A. Pérula de Torres

#### **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	Luis A Pérula de Torres
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
CTS -985	Principal investigator	José Peña Amaro
FQM-227	Principal investigator	María Dolores Luque de Castro
TIC-161	Principal investigator	Rafael Medina Carnicer
TIC-148	Principal investigator	César Hervás Martínez
TIC-122	Principal investigator	Sebastián Ventura Soto
HUM-924	Principal investigator	Juan Antonio Moriana





## 6. Training Activities

#### 6.1. Introduction

The Institute conceives training as a fundamental institutional tool to fulfill and improve its scientific goals. Thus, a multifaceted program is designed on an annual basis to foster and provide high-quality scientific training to our researchers, which is adapted to the different stages of their scientific career. This includes from the organization of an annual program of seminars by known national and international leaders in trending scientific topics, to courses that cover concepts related to our current lines of research as well as practical applications on the latest technologies. Along with these activities, the Institute maintains two key training activities: the annual Young Investigators Meeting, aimed at fostering the interaction and exchange of knowledge among our youngest researchers, and the "Maimonides Commemorative Lecture" which includes lectures by leading experts in Biomedicine, and is intended to recognize and award our top scientists. Finally, the IMIBIC is responsible of a PhD Program in Biomedicine and also participates in two additional PhD programs of the University of Cordoba, that, in all, are aimed to obtain highly qualified researchers, promote teaching and favor professional qualification in the field of biomedical sciences. The Training Coordinator Dr. Rosario López Pedrera, and, from july 2015, Prof. María del Mar Malagón.

#### 6.2. Training

The following sections list the research training activities developed at the IMIBIC during 2015.

#### 6.2.1. PhD in Biomedicine

IMIBIC leads a unique PhD Program in Biomedicine. This program, coordinated by Prof. Francisco Gracia Navarro, PhD, aims to qualify human resources and to stimulate professional qualification in the field of biomedical sciences.

Website. http://www.uco.es/idep/doctorado/programas/biomedicina

#### 6.2.2. Master's Degrees

#### ND PHD

The Master's degree program associated to the IMIBIC encompasses three master's degrees that are led by academic directors who are members of the IMIBIC:

- Translational Biomedical Research

Academic Director: Prof. Socorro García Navarro

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

#### - Research Methods in Health Sciences

Academic Director: Prof. Eduardo Collantes Estévez

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

- Human Nutrition (with Quality Accreditation by ANECA)

#### Academic Director: Prof. Francisco Pérez Jiménez 2014-15 academic course

Prof. Rafael Moreno Rojas 2015-16 academic course

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 areas at IMIBIC have been held during 2015.

#### 6.2.3.1. Courses

IMIBIC organized the following list of activities:

Type of Activity	Title	Duration*(h)
Institutional Event	5th Maimonides Commemorative Lecture	4
Institutional Event	6th IMIBIC Conference of Young Researchers	10
Seminar	Introduction to Systems Biology II	1,5
Seminar	Introduction to Flow Cytometry digital management software and DIVA	3

IMIBIC collaborated in the following list of activities:

Type of Activity	Title	Duration*(h)
COURSE / WORKSHOP	VIII Conference on Presentation of Evidence in Infectious Diseases "em- pirical Management of infectious syndromes"	20
COURSE / WORKSHOP	1st Psoriasis Research Day. A 360 degree approach	6
COURSE / WORKSHOP	6th Seminar Series for Excellence in Research with Cell Trials (Biomedal in collaboration with Celeromics)	2
COURSE / WORKSHOP	Methodological route for the treatment of clinical and epidemiological data through EPIDAT	12
COURSE / WORKSHOP	Preparation and drafting of European proposals in the field of health H2020	11
COURSE / WORKSHOP	3rd Edition transcranial magnetic stimulation and Neuromodulation: present and future neurosciences	35
COURSE / WORKSHOP	New Generation of Cell-based Assays	1
COURSE / WORKSHOP	2020 Health, demographic change and well-being Framework Pro- gramme for Research and Innovation (2014-2020)	4

#### 6.2.3.2. IMIBIC Research Seminars

IMIBIC research seminars promote networking and contribute to strengthen the knowledge of the research community of the Institute.

The seminars organized by the Institute during the course 2014-2015 were:

Date	Speaker	Institution	Title
5/09/2014	Ernst J. Schaefer	Cardiovascular Nutrition Laboratory, Hu- man Nutrition Research Center on Aging at Tufts University (Boston, EEUU)	The Prediction of Diabetes and CVD: Results from Framingham Study
6/11/2014	Pedro Medina Vico	Center for Genomics and Oncology Research	tumoral MicroARNs in tumor development
13/11/2014	Maximilian Bielohuby	Veterinary Specialist for Laboratory An- imal Science. Klinikum der Universität München.Medizinische Klinik und Po- liklinik IV.Endocrine Research Unit	Macronutrient regulation of metabolism and endocrine systems
4/12/2014	Rafael Fernández Chacón	Universidad de Sevilla-IBIS	Translational research in neurosciences -synaptic and extra-synaptic functions of a molecular chaperone
11/12/2014	Mario Fraga	Instituto Universitario de Oncología. Hospital Univ. Central de Asturias	Epigenetic actions during the aging of adult stem cells
18/12/2014	Paloma Alonso Magdalena	Universidad Miguel Hernández (Elche)	New mechanisms of diabesity: Role of en- docrine disruptors in the pathogenesis of diabetes
8/01/2015	José María Tenias Burillo	Escuela Valencia de Estudios para la Salud	Special analytical observational designs. Cross-case studies and hybrid designs
15/01/2015	Javier Aller	Hospital Universitario Puerta de Hierro	Neuroendocrine tumors: the molecular basis to targeted therapies
22/01/2015	Manuel Serrano Ríos	Real Academia Nacional de Medicina	Conference inaugural seminar series. Obesi- ty "metabolically healthy": Fact or Fiction?
29/01/2015	Vincent Prevot	Inserm UMR837, Jean Piere- Aubert Research Centre, Lille (Francia)	Translational research in Metabolic Medi- cine: Tanycytes as Gatekeepers of the Met- abolic Brain
5/02/2015	Fátima Al- Shahrour	Unidad de Bioinformática, Centro Nacio- nal de Investigaciones Oncológicas	Identifying druggable genetic dependencies for personalized cáncer therapy
12/02/2015	Jesús de la Osada García	Universidad de Zaragoza	Animal models in the search for comSpeak- ers responsible for potential anti-atheroscle- rotic of olive oil

Date	Speaker	Institution	Title
26/02/2015	David Epstein	Departamento de Economía Aplicada, Facultad de Ciencias Económicas, Uni- versidad de Granada	Network meta-analysis: comparing multiple interventions in Health Sciences
12/03/2015	Roberto Díez	CSIC	Antibiotics a la carte: a new generation of drugs against bacterial infections
26/03/2015	Loreto Carmona Ortells	Instituto de Salud Musculoesquelética	Research Methodology in Health Sciences
9/04/2015	Mayte Suárez- Fariñas	Laboratory of Investigative Dermatolo- gy/Center for Clinical and Translational Science,The Rockefeller University (New York, USA)	Immunogenetic architecture of psoriasis
16/04/2015	Jesús Rodríguez Baño	Hospital Universitario Virgen Macare- na-Universidad de Sevilla	TitleWhat new scientific evidence can be traslationar to the treatment of infections with ESBL-producing Enterobacteriaceae and / or carbapenemases?
23/04/2015	Albert Lecube	Hospital Universitari Arnau de Vilanova	The lung as a target organ of diabetes-re- lated complications: Sweet Sleep Study
30/04/2015	Mario Durán Prado	Universidad de Castilla-La Mancha (Fac- ultad de Medicina, Ciudad Real) 4	Control of redox balance and bioenergetics in neurological tumors. Role of Coenzyme Q
7/05/2015	Emilio Fernández Espejo	Universidad de Sevilla	Nitrosative origin of Parkinson's disease: role of the thyroid gland
14/05/2015	José Andrés Fernández	Universidad del País Vasco	Image by mass spectrometry: fundamen- tals and application in lipidomic. Xenograft colon cancer.
11/06/2015	Manuel Fernández Rojo	Royal Brisbane Hospital, Brisbane (Aus- tralia)	Caveolin-1 in liver physiology and disease

The Institute has launched a novel cycle of seminars aimed at promoting interactions, sharing idea, and strengthening the bonds among IMIBIC scientists. These seminars are scheduled fortnightly and are presented by young researchers (preferentially postdocs) of our research groups. During 2015, the first seminar was presented by Dr. Víctor Navarro whose title "New insights into the neuroendocrine Control of metabolism and reproduction : a two way road".

#### 6.2.3.3. Institutional Events

#### 6th IMIBIC Conference of Young Researchers

Date: 4<sup>th</sup> and 5<sup>th</sup> May 2015

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

#### Programme

#### Day 1 (4<sup>th</sup> May)

## 9:00-9:30 Opening ceremony. Inscriptions and Posters display

#### 9:30-10:45. Session I. Cancer (Oncology and Oncohematology)

#### I.a 9:30-9:45

Postoperative time course and utility of inflammatory markers in patients with ovarian peritoneal carcinomatosis treated with neoadjuvant chemotherapy, cytoreductive surgery and HIPEC. **Dimas Javier Garcilazo Arismendi** 

#### I.b 9:45-10:00

Identification of new substrates for DYRK2 and its implication in carcinogenesis: Cdc25A regulation in the context of lung cancer. Maribel Lara Chica

#### I.c 10:00-10:15

The role of nitric oxide in generation and maintenance of cancer stem cells: new therapeutic opportunities in cáncer.

#### Jon Peñarando Sáez

#### I.d 10:15-10:30

Visfatin expression is tightly regulated by metformin and could serve as a non-invasive biomarker for prostate cancer.

#### Sebastiano Messineo

#### I.e 10:30-10:45

Metformin exerts antitumoral actions in in vitro and in vivo models of prostate cáncer. André Morais Sarmento

#### 10:45-11:15. Coffee Break. Poster Showcase

### 11:15-13:00. Session II. Nutrition, Endocrine and metabolic diseases.

#### II.a 11:15-11:30

Novel cannabidiol derivatives are dual ppary/cb2 agonists that induce polarization of M2 macrophages and modulate diet-induced obesity. **Inmaculada Velasco Aguayo** 

#### II.b 11:30-11:45

Gonadotropin-inhibitory hormone signaling displays sexually dimorphic roles in the control of energy homeostasis: Studies in the NPFF1 receptor null mouse.

#### Silvia León Téllez

#### II.c 11:45-12:00

Renal damage induced by diets rich in fat and phosphate.

#### **Rafael Ríos Varo**

#### II.d 12:00-12:15

Bone marrow mesenchymal stem cells are morphological, functional and genetically different between patients with type 2 diabetes and healthy donors.

#### Gustavo Díez López

#### II.e 12:15-12:30

Clinical-histological and molecular characteristics of patients with gastrointestinal and pancreatic neuroendocrine tumors.

#### Aura Dulcinea Herrera Marínez

#### II.f 12:30-12:45

Metabolic phenotypes of obesity influence glucose homeostasis in coronary artery disease patients. Juan Francisco Alcalá-Díaz

#### II.g 12:45-13:00

The gut microbial community in metabolic syndrome patients is modified by diet. Carmen María Haro Mariscal

#### 13:00-14:00. Plenary conference

#### Rafael F. Duarte

Hospital Universitario Puerta de Hierro

#### 14:00-16:00. Lunch

16:00-17:45. Session II. Nutrition, Endocrine and metabolic diseases.

#### II.h 16:00-16:15

Central ceramide signaling as novel mediator for the metabolic regulation of puberty: interplay with leptin and kisspeptin.

#### Violeta Heras

#### II.i 16:15-16:30

Contribution of lipid droplet-associated rab proteins to the development of insulin resistance in obesity. **Yoana Rabanal Ruiz** 

#### II.j 16:30-16:45

Phosphate restriction preserves bone volume in early and late stages of CKD in rats. Juan Miguel Díaz Tocados

#### II.k 16:45-17:00

Contributions to the analysis of vitamin D for the study of metabolic diseases. Antonio Mena Bravo

#### 17:00-17:45 Conference. Alejandro Lomniczi "Epigenetics of Puberty: New Answers to Old Ques-

tions"

Division of Neuroscience. Oregon National Primate Research Center (ONPRC)-Oregon Health Science University (OHSU)

#### 17:45-18:15. Poster Showcase.

### 18:15-19:00. Session II. Nutrition, Endocrine and metabolic diseases.

#### II.I 18:15-18:30

Endocrine and metabolic characterization of double somatostatin and cortistatin knockout mice. **Sergio Pedraza Arévalo** 

#### II.m 18:30-18:45

Telomere length and its relation to dietary fat intake in an elderly population with cardiovascular disease: cordioprev study.

#### Andreea Corina Baba

#### II.n 18:45-19:00

The prediabetic status induces a lower metabolic flexibility in patients with established cardiovascular disease.

Ana León Acuña

#### Day 2 (5<sup>th</sup> May)

#### 9:00-10:30. Session III

Chronic and Inflammatory diseases. Infectious and Immunological diseases. Organ transplantation.

#### III.a 9:00-9:15

Acute kidney injury in the meld era of liver transplantation. Are calcineurin inhibitors so problematic for renal function?

#### Irene Gómez Luque

#### III.b 9:15-9:30

Prevalence of urolithiasis in spanish population aged 40 to 65: prelirene study.

#### Luis Angel Perula de Torres

#### III.c 9:30-9:45

FGF23 increases phosphate-induced smooth muscle cells calcification.

Noemi Vergara Segura

#### III.d 9:45-10:00

Prognosis of patients with ulcerative colitis in sustained remission after thiopurines withdrawal. Estefanía Moreno Rincón

#### III.e 10:00-10:15

Circulating miRNAs as potential biomarkers of therapy effectiveness in rheumatoid arthritis patients treated with anti-TNF $\alpha$ .

#### Carlos Pérez Sánchez

#### III.f 10:15-10:30

Aging and chronic kidney disease oxidized albumin promotes cellular senescence and endothelial damage.

#### **Carlos Luna Ruiz**

10:30-11:00. Coffee Break. Poster Showcase

#### 11:00-12:30. Session III

Chronic and Inflammatory diseases. Infectious and Immunological diseases. Organ transplantation

#### III.g 11:00-11:15

Myogenic differentation in skeletal muscle satellite cells and interstitial mononuclear cells in the absence of injury. **Fernando Leiva-Cepas** 

#### III.h 11:15-11:30

Real-time measurements of tissue oxygen microtension as a marker of bile duct viability in liver transplantation.

#### Elena Navarro Rodríguez

#### III.i 11:30-11:45

Knowledge and practices of primary care professionals about the approach of alcohol: results of alco-ap study.

#### Experanza María Romero

#### III.j 11:45-12:00

Caenorhabditis elegans as an animal model in preclinical assays for pharmacogenetic studies of the antipsychotic drugs risperidone and aripiprazole.

#### Jaime Osuna Luque

#### III.k 12:00-12:15

VCE-003.2 is a novel cannabigerol derivative that enhances neuronal stem cell prosurvival and alleviates symtomatology in murine models of Huntington disease.

#### Carmen del Río Mercado

#### III.I 12:15-12:30

Role of monocytes subsets in the atherothrombosis and endothelial dysfunction associated with rheumatoid arthritis: beneficial effects of tocilizumab. **Patricia Ruiz Limón** 

12:30-13:30. Conference. Alvaro Roldán López. Instituto de Salud Carlos III

#### 13:30-14:00. Award-giving and Closing ceremon

#### 5th Maimonides Commemorative Lecture and IMIBIC awards 2015

Date: 15th December Organized by: IMIBIC, UCO and the Regional Government of Andalusia

<b>Carolina Fernández Gándara-GC9</b> . "Analysis of the effect of diet on senescence and associate molecular alterations involved in cell damage i patients with cardiovascular disease"
the effect of diet on senescence and associate molecular alterations involved in cell damage i
the effect of diet on senescence and associate molecular alterations involved in cell damage i patients with cardiovascular disease"
• Prizes for the most relevant research results:
<ul> <li>Category 1. Better initiative involves a new addition to the portfolio of services of the result of the research or participation in a clinical practice wite international quality criteria (AGREE) health work environment.</li> <li>Fatima Guerrero Pavon-GC7. "Development of bioartificial kidney: An approach from the Regent erative Bioengineering"</li> </ul>
<b>Category 2.</b> Award category registration, pater or "spin off" deemed more potential to improv health problems. <b>Raul M. Luque Huertas-GC8</b> . "Using levels GOA enzyme as a marker of prostate cancer"
<ul> <li>Prize for the most relevant scientific publication in collaboration with international groups.</li> </ul>
<b>Carlos Pérez Sánchez-GC5</b> . "Gene profiling reveals specific molecular pathways in the pathor genesis of atherosclerosis and cardiovascula disease in antiphospholipid syndrome, systemi lupus erythematosus and antiphospholipid syndrome with lupus"
<ul> <li>'Enrique Aguilar Benítez de Lugo' Prize for the most relevant publication</li> <li>Patricia Ruiz Limón-GC5. "Atherosclerosis and cardiovascular disease in systemic lupus erythe matosus: effects of in vivo statin treatment"</li> </ul>
12:15h Maimonides Lecture Dr. José María Ordovás (University of Tufts, USA "Nutrigenetics: in search of oneself"

# 6.3. Results of Training Activities

#### **6.3.1. Doctoral Theses**

The training dedication of 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 21 doctoral theses directed by researchers from the Centre during 2015 (only PhD Program in Biomedicine).

Thesis Author	Title	Thesis Director 1	Thesis Director 2
Alejandro Ibáñez Costa*	Identification of novel molecular markers in pituitary tumors: contribution to pathogenesis and therapeu- tic potential	Justo Pastor Castaño Fuentes	Raúl Miguel Luque Huertas
Amanda Cañas Rodríguez	Estrés nitrosativo y alteración de la homeostasis de S-Nitrosotioles en cáncer de mama: implicaciones terapeúticas	Juan Rafael de la Haba Rodriguez	Antonio Rodriguez Ariza
Ángel Custodio Uzcategui Castillo			Oscar Martinez
Aquiles Lozano Rodríguez- Mancheño	Influencia del grado de obesidad sobre la respuesta lipémica postprandial a diferentes tipos de grasa e jóvenes sanos	Francisco Perez Jimenez	José López Miranda
Caridad Dios Guerra	Study of the effect or primary health nurses sched- uled and protocolized hombe visit over and morbidi- ty on multipathological patients of 65 or older.	Maria Aurora Rodríguez Borrego	
Carlos Marquez Vera	Predicción del fracaso y abandono escolar mediante técnica de minería de datos	Cristóbal Romero Morales	Sebastian Ventura Soto
Daniel Falla Fernández	Enseñanza de habilidades de toma de perspectiva viso-espacial en personas con Discapacidad Intelec- tual: una aproximación desde el estudio de las dis- criminaciones condicionales.	Francisco José Alós Cívico	
Esther Cuadrado*	Prosocial Behavior. Commom, motivational determi- nants in contexts of social exclusion and scarcity of environmental resources.	Maria del Carmen Tabernero Urbieta	
José López Aguilera	Fisiopatología de la conducción cardiaca en pacien- tes co estenosis aórtica severa tratados con prote- sis aórtica corevalve. Análisis de predictores de necesidad de marcapasos.	José María Segura Saint-Gerons	Jose Suarez de Lezo Cruz-Conde
Juan Manuel Carmona Torres*	Abuse Study on vulnerable elderly in the family and community in Spain (Andalusia-Cordoba), Portugal (Porto, Azores) and Bolivia (Santa Cruz de la Sierra). Comparative study.	Maria Aurora Rodríguez Borrego	
Julio Manuel Martinez Moreno	Efecto diferencial del calcitriol y del paricalcitol sobre el proceso de calcificación en células de músculo liso vascular. Mecanismos intracelulares implicados.	Yolanda Almaden Peña	Juan Rafael Muñoz Castañeda
Laura Cejudo Diaz del Campo	Terapia celular en la miocardiopatía dilatada.	Miguel Angel Romero Moreno	Jose Suarez de Lezo Cruz-Conde
Luis Santiago Perera Cabrera	Las Microempresas y Cooperativas: una propuesta alternativa para la formación para el trabajo en la Educación Secundaria en Venezuela.	Maria Aurora Rodríguez Borrego	Beatriz Arrieta de Meza
María del Pilar Delgado de la Torre*	Obtainment of high-added value products from residues and winemaking waste.	Maria Dolores Luque de Castro	Feliciano Priego Capote
María Manfredi Lozano*	Analysis of the roles of neuropeptidergic system and micrornas in the control of puberty.	Leonor Pinilla Jurado	Manuel Tena Sempere
María Pérez Ortiz*	Exploiting decomposition methods, kernel algo- rithms and over-sampling techniques for ordinal regression.	Cesar Hervás Martinez	Pedro Antonio Gutiérrez Peña

Thesis Author	Title	Thesis Director 1	Thesis Director 2
María Victoria Noci Sánchez	Daño endotelial en pacientes obesos en respuesta al estrés quirúrgico.	Pedro Jose Carpintero Benitez	Julia Carracedo Añon
Natalia Rocio Moreno Castellanos*			Rafael Manuel Vázquez Martinez
Pablo Jesus López Soto*	The chronobiological pattern as a causative factorMaria Auroraof falls in the population older than 65 years.Rodríguez Borrego		
Paula María Moreno Casado	Marcadores predictivos en el trasplante y la car- Marco Antonio Ángel Salvati cinogénesis pulmonar.Análisis metabolómico y ruta Calzado Canale Velázquez de señalización DYRK2-SIAH2.		Ángel Salvatierra Velázquez
Rafael Soler Torronteras	Estudio de los mecanismos de regulación del factor HIF-1 a por N-acil dopaminas. Implicaciones en neu- roprotección.	Eduardo Muñoz Blanco	Marco Antonio Calzado Canale

\*Theses with International Mention

## 6.4 Research Stays

Throughout the year 2015, 20 researchers IMIBIC completed a research stay in national and international centers. This number reflects clear research dedication and it is dedication and it is orientated towards the creation of networks. In addition, the number of professionals from other national and international centers that stay at IMIBIC is over 16 researchers.

	Type of Internship	Public Scheme	Private Scheme	Internal Scheme
CTAVC	Researchers	6	3	3
STAYS	Duration (months)		66 months	
	Researchers		16	
VISITORS	Duration (months)		50 months	





# 7. Infrastructures

In the 2015 fiscal year many of the running actions have finished that were initiated in 2013 and 2014 related to aid for infrastructure acquisition of a scientific nature for the Institute, which were granted in two years by Ministry of Health (1.5 million) and the Ministry of Economy and Knowledge (2 million).

Specifically, the target in 2015 of the investments made with these performances were as follows:

- For Clinical Research Unit
  - Completion of the work of expansion and reform of the existing space in the old building experimental HURS which was initiated in 2014.
  - Completion of the work or extension of the living freezers for sample storage and conditioning of existing air conditioning. Provision of air conditioning systems and alarm room to freezer.
  - Equipment for day hospital area (7 multiparameter monitors with central monitoring 7 chairs hospital day, two defibrillators, 2 sphygmomanometers (adult and child), an electrocardiograph and two cars stop)
  - Software or 4D ultrasound with 3 probes to be used in existing high performance ultrasound system.
  - 1-phase UPS for maintenance of electrical constant flow freezer room.
  - 1 refrigerator storage registered drug activity related to clinical trials.
- Equipment for Genomics BRSU
  - 1 laminar flow cabinet and prePCR.
  - one centrifugal
  - set of laboratory furniture for the room prePCR.
- Equipment for Animal Experimentation Service:
  - 1 anesthesia equipment for small animal.
  - brightness control system in rooms housing of animals.
  - stainless steel auxiliary furniture.
- For BRSU Microscopy and Cytometry, it has acquired the following equipment:
  - fluorescence microscope 1
- For Isotope BRSU has acquired a set of radiation detectors.
- General and computer equipment for the new headquarters of the Institute (videovigillance, leaded animal testing rooms, fiber optic links, etc.)

As for BRSUs, at year-end 2015, they were set as follows:

During 2015, the BRSU has had a total of 24 technicians, according to the following distribution:

- Methodology and Biostatistics Unit: 1 senior technician
- Microscopy, Cytomics, and Scientific Imaging Unit: 1 senior technician
- Proteomics Unit: 2 senior technicians and 2 technical support
- Service Animal Experimentation: 1 veterinarian and 2 technical support
- Bioinformatics and technological innovation Unit: 4 senior technicians
- Isotope Unit: 1 Technical support
- Genomics Unit: 1 technician and 1 Technical support
- Biobank Unit: 3 Technical support
- Clinical Research Unit: 3 senior technicians, 2 Nurses and 1 Nurse Assistant





# BIOMEDICAL RESEARCH SUPPORT UNITS



# 8. Biomedical Research Support Units

## 8.1. Isotope Unit

#### 8.1.1. Composition

The Isotope Unit personnel is composed of:

#### Supervisor

 Dr. Eduardo Muñoz Blanco fi1muble@uco.es

#### Operator

Antonia Sánchez Arroyo
 antonia.sanchez@imibic.org

#### 8.1.2. Equipment and Facilities

In IMIBIC, we possess two laboratories dedicated to working with radioactive isotopes both  $\gamma$  and  $\beta$ . One is located on the -2 floor and the other on the third floor.

We have had the authorization of the Nuclear Safety Council since December of 2014 to work with the following isotopes:

Isotopes	Maximum Activity (Mbq)
Carbon (C-14)	370
Tritium (H-3)	370
Phosphorous (P-32)	370
Phosphorous (P-33)	370
Sulfur (S-35)	370
Chrome (Cr-51)	370
lodine (I-125)	370

The Radiological Protection Service of the University of Córdoba is responsible for the supervision of this Unit and its operative procedures. This Service is also responsible for checking that the laboratories are free from contamination and is in charge of waste management and removal.

#### Equipment

-Gamma Counters 3 units:

- Brand: Wizard
- Model: 2470-0100 Beta counter
- -UN Beta Counter (1 unit)
  - Brand: Tricard
  - Model: 2810 TR
- -Microbeta Counter (1 unit)
  - Brand: Microbeta2
  - Model: 2450-0020
- -Harvester Cell
- A sample preparer
  - Brand: Janus
- Two refrigerated ultracentrifuges with capacity for 200 samples.
- -Three exclusive gas cabinets for working with radioactive isotopes, two of which are used with a lead guillotine and the third with a methacrylate guillotine.
- -Two radiation detectors

- Brand: Lamse
- Model: RM 10013-RDM

#### 8.1.3. Portfolio of Services

- Training in the handling of  $\beta$  and  $\gamma$  counters.
- Labeling of proteins with I-125.
- Identification of protein levels in serum, plasma and other biofluidos using the RIA technique.
- In situ hybridization (ISH) with P-33 labelled probes.
- Radioactive techniques for analysis of cell death and proliferation.
- Consultation regarding the different isotopic techniques that are employed in the laboratory.
- Optimization of protocols.

#### 8.1.4. Highlights

In 2015, the Unit has become fully operational, coinciding with the settling of the two brand new laboratories for isotope handing of the new building of IMIBIC. In addition, the Unit has completed the installation of a new cell/body irradiator system, and has incorporated new imaging equipment, including a modern system of ultrasonography for clinical investigation, which is also under the supervision and operational control of the Unit. Altogether, the facilities and materials for isotope detection of the Unit make it one of the best equipped in Biomedical Research Institutes within Spain.

## 8.2. Animal Experimentation Unit

The animal experimentation unit in the IMIBIC is within the Biomedical Research Central Support Units, and is associated to the Animal Experimentation Service (SAEX) of the University of Córdoba.

The unit provides integral support to its users, at consultation and experimental levels, with the objective of carrying out research for the Institute and other associated organizations through the use of animal subjects, mainly rodents (mice and rats) and pigs.

#### 8.2..1 Composition

The personnel of the unit is composed of two qualified technicians and a veterinarian.

- Anabel Pozo Salas sae@imibic.org
- Estefanía Escudero Jabonero
   estefania.escudero@imibic.org
- Rafael Pineda Reyes
   rafael.pineda@imibic.org

### 8.2.2. Equipment and Facilities

IMIBIC's animal experimentation unit comprises:

- 7 rooms for housing rodents.
- 1 healing / metabolism room: This room has a respirometry system and two racks for metabolic cages.
- 5 multi-purpose rooms: These rooms have optogenetics and quantitative analysis equipment as well as a bodily composition MRI, among other equipment.
- Operating Room: Suitable for surgery in both rodents and larger animals, consisting of: 3 3D laparoscopy towers, 7 TV video monitors, 3 anesthesia machines for large animals, 6 surgery tables, 2 rodent anesthesia system with 4 seats, 1 rodent anesthesia system with 2 seats, 6 gas towers, 1 surgical microscope for large animals, 1 high-end ultrasound, 3 magnifiers, 1 microscope and 1 C-arm.
- Quarantine Zone: 4 ventilated racks for rats / mice, 1 replacement cabinet and 1 triple gate SAS.

#### 8.2.3. Highlights

In 2015, many different pieces of equipment were acquired, installed and put into use. Accordingly, the technicians have taken training courses with the aim of opening animal services, as soon as the on-going process of administrative accreditation is completed (expectedly soon).

# 8.3. Microscopy, Cytomics, and Scientific Imaging Unit

The Microscopy, Cytomics and Scientific Imaging Unit is one of the common scientific and technical support platforms used for IMIBIC's research. This Unit is comprised of two technological areas: flow cytometry and advanced optical microscopy (confocal and fluorescence), both of which are considered to be of great importance in the field of biomedical research and health, and are powerful tools used in studies at the cellular, cellular subpopulation, and tissue levels. Its mission is to provide the research community with advanced equipment, and to provide the technical and scientific-methodological support necessary for the optimization of applications of these technologies so as to obtain high-quality results for the development of excellence in translational biomedical research. The Unit services both the research staff of the Institute and other entities of the Andalusian Public Health System, the University, IPOs, as well as private companies that request it.

#### 8.3.1. Composition

The Unit is composed of a superior specialized technician:

 Dr. Esther Peralbo Santaella microscopia.citometria@imibic.org

#### 8.3.2. Equipment and Facilities

#### Area of Flow Cytometry

- This area offers an advanced infrastructure aimed at flow cytometry for the quantification, phenotypical and functional analyses of cellular populations, and cellular sorting.
- The Unit offers the research personnel of IMIBIC the option to use flow cytometers under the "self-service" rule (i.e. without a technical operator present).

#### Equipment

- Flow cytometer LSR Fortessa SORP (Becton Dickinson).
- Flow cytometer FACSCanto (Becton Dickinson).
- Flow cytometer FACSCalibur (Becton Dickinson).
- Flow cytometer Cytomics FC500 MCL (Beckman Coulter)
- Cellular Sorter FACSAria III (Becton Dickinson)

#### Area of Advanced Optic Microscopy

- The area of Advanced Microscoptic Optics is an infrastructure designed for confocal fluorescent microscopy and the imaging associated with these techniques.
- The Unit offers the research personnel of IMIBIC the option to use the microscopic equipment under the "self-service" rule (i.e. without a technical operator present).

#### Equipment

- Spectral LSM 710 confocal microscope (Carl Zeiss), with inverted stand and lighting for brightfiel, DIC and epifluorescence.
- LSM 5 Exciter confocal microscope (Carl Zeiss), with inverted stand and lighting for brightfield and epifluorescence.
- Inverted fluorescence microscope (Nikon Eclipse Ti-S)
- High -Content Bioimager Pathway 855 (Becton Dickinson).

#### 8.3.3. Portfolio of Services

- Education and training in the management of flow cytometers and microscopic equipment, as well as the corresponding result analysis programs.
- Purification and isolation of cell subpopulations via sorting.
- Provision of technical support for the analysis of samples in flow cytometers and confocal microscopy equipment.
- Advice regarding: preparation and marking of samples for flow cytometry, sorting or confocal microscopy, experimental design and interpretation of results.
- Provision of support for data analysis by means of cytometry analysis programs available in the Unit, as well as image analysis.
- Organization of training activities (seminars, courses, etc.) related to the fundamentals and the application of the areas of flow cytometry and advanced optical microscopy.

#### 8.3.4. Highlights

In 2015, the Microscopy Unit, Cytomics and scientific image expanded its equipment with the acquisition and implementation of a new flow cytometer analyzer: BD FACSCanto.

During this year, the Unit provided services to 13 of the 23 consolidated research groups of IMIBIC, as well as 3 external groups belonging to the University of Cordoba.

## 8.4. Proteomics Unit

The Proteomics Unit is located within the IMIBIC research support platforms and provides researchers with state-ofthe-art technologies in the field. Currently, the Proteomics Unit is a specialized platform in quantitative proteomics and MALDI Imaging (or Molecular Imaging).

The Proteomics Unit offers its analytical services for IMIBIC staff and University of Córdoba and to other universities, hospitals and private companies.

The Unit has two main components: (i) a high performance liquid chromatography-mass spectrometry platform that provides researchers with access to high-throughput proteomics analyses, ranging from protein identification and characterization to label-free quantitative proteomics; and (ii) a mass spectrometry-based molecular imaging platform (MALDI-Imaging) that provides spatial information of metabolites, lipids and proteins directly from tissues and biopsies.

As a service for research assistance, the Proteomics Unit provides individualized, fit-for-purpose support including project planning, sample preparation, mass spectrometry analysis and data analysis.

#### 8.4.1. Composition

The Unit is composed of a two superior specialized technicians and two qualified technicians:

- Dr. Ignacio Ortea García
  - ignacio.ortea@imibic.org
- Dr. Eduardo Chicano Gálvez
- eduardo.chicano@imibic.org
- Josune Egea Urra
- Rocío Pérez Espejo

#### 8.4.2. Equipment and Facilities

- Q-TOF Mass spectrometer, Triple TOF 5600+ (Sciex).
- Triple quadrupole mass spectrometer, XevoTQS (Waters).
- MALDI-TOF/TOF Mass spectrometer, 5800 (Sciex).
- nanoHPLC: Eksigent LC400 (Sciex).
- nanoUPLC: nanoAcquity M-Class (Waters).
- Sprayer: Sunchrom Suncollect (Sunchrom, Friedrichdorf, Germany).
- Laser Scanner: Typhoon Trio (GEHealthcare, Uppsala, Sweden).
- Main programs used for data analysis: Protein Pilot, Comet and X!Tandem for protein identification; Peak View, Marker View and Skyline for protein quantification; Tissue View, MSiReader and Cardinal for Maldi Imaging MS.
- Basic laboratory equipment for sample preparation.

#### 8.4.3. Portfolio of Services

The Proteomics Unit offers the following services:

- Identification and characterization of proteins by MALDI-TOF/TOF.
- Identification and characterization of proteins by LC-MS/MS.
- Quantitative Proteomics:
  - SWATH.
  - SRM (Selected Reaction Monitoring)
- pseudoSRM.
- MALDI Imaging mass spectrometry.
- Project supervision and collaboration.
- Training in software used for data analysis.

#### 8.4.4. Highlights

During 2015, the Proteomics Unit started its activities in quantitative proteomics and MALDI-Imaging (MSI) providing services to scientific community. These services include from sample preparation to project supervision, collaborations and training in software for data analysis.

Moreover, this Unit has increased its human resources to include two new technicians that are primarily involved in sample preparation and other pre-analytical procedures.

### 8.5. Bioinformatics Unit

#### 8.5.1. Composition

The Unit is composed of a specialized technician:

David Ovilleiro Fraile
 bioinformatica@imibic.org

### 8.5.2. Equipament and FacilitieS

Bioinformatics Unit covers varying fields and diverse applications such as:

- Analysis of nucleic acids (DNA / RNA )
  - Analysis of peptide sequences, structures, functions, metabolic pathways and interactions with genes
  - Generation of knowledge relative to the study of new drugs
  - Design and development of software
  - Construction of databases for storing biological data
  - Development of algorithms

#### 8.5.3 Portfolio of Services

IMIBIC's Bioinformatics Unit offers services on two levels:

- -Direct analysis of relevant research projects and technical data needed for support
- -Biocomputing tools to support groups conducting relevant research projects

#### 8.5.4. Highlights

- -The mission of the Unit is to attempt to satisfy the Bioinformatic requirements that result from research projects.
- The Unit aims to promote clear and direct communication with the researchers to facilitate a productive collaboration
- -Lastly, the implementation of reporting guidelines pertinent to each particular case (MIAME, MIAPE, etc.) and the use of standardized formats (MAGE-ML, MAGE-TAB, mzML, mzldentM, etc.) is a top priority whose aim is to burnish robust reporting and facilitate the publication of findings.

## 8.6. Genomics Unit

The mission of IMIBIC's Unit of Genomics is to make available to researchers very high level equipment and scientific and technical advice for the development of various analytical techniques to the Institute as well as other public and private institutions. Said equipment and technical knowledge is dedicated to the comprehensive study of DNA and RNA (genotyping / expression / regulation), which in turn will produce high quality results for the development of biomedical research of excellence. To this end, the Unit has cutting-edge, high throughput platforms performance platforms in the field of genomics. It is also important to note the interaction with other BRSU IMIBIC Units, which are located in the same building, such as Bioinformatics, Proteomics or Cytometry.

#### 8.6.1. Composition

The Unit is composed of a superior specialized technician and a qualified technician:

- Álvaro Jiménez Arranz
  - genomica@imibic.org
- Pilar Rubín González de Canales

#### 8.6.2. Equipment and Facilities

Currently, the resources that the Genomic Unit has at its disposal are:

#### a) Illumina MiSeq

MiSeq is an Illumina platform sequencing technology based on SBS (Sequencing by synthesis), which is currently the most widely adopted NGS (Next-Generation Sequencing) technology in the world on account of its speed, accuracy and quality. This sequencer can generate up to 15 Gb / race and is able to perform paired-end reads 2x300, allowing, among others, greater accuracy especially in problem areas such as homopolymeric areas. The MiSeq system allows for DNA-Seq, RNA-Seq and Methyl-Seq, with a wide range of applications.

#### b) NCounter Dx/tecnología Nanostring

The NanoString NCounter system uses a novel technique of molecular rod codes linked to specific probes that allow for the detection and counting of hundreds of targets in a single reaction without amplification, thereby enabling the user to study a large number of mRNAs, miRNAs or DNAs simultaneously with sensitivity and with "gold standard" reproducibility. Among its applications are gene expression analysis, gene fusion, copy-number variation (CNV) and simultaneous analysis of mRNAs and miRNAs and RNAs regulators as IncRNAs.

These applications, along with his Dx / CE-IVD for conducting analysis care quality certificate, also make the NCounter a tool with high potential for clinical use.

#### c) PCR Digital (dPCR): QX200 Droplet Digital PCR System

The digital PCR offers an alternative to conventional qPCR for absolute quantitation and detection of rare alleles without the need for standards or endogenous controls

#### d) Quantitative PCR (qPCR)

The unit currently has 3 platforms aimed at genotyping PCR and gene expression analysis:

- Light Cycler 480 (Plataforma de Placas de 96)
- Light Cycler 96 (Plataforma de Placas de 96)
- 7900 HT Fast (Plataforma de Placas de 384)
- Open Array (Plataforma de Arrays qPCR)

In the case of IMIBIC research staff , the unit offers the possibility of using the qPCR platforms under a "self-service" scheme (without technical operator).

#### e) Others

The Unit has additional appliances designed for quantification, quality analysis and determining the size of nucleic acid fragments:

- Nanodrop ND1000 (Espectrofotómetro)
- DeNovix DS-11 (Espectrofotómetro)
- Quantus (Fluorímetro)
- 2200 TapeStation

Additionally, IMIBIC has a computation cluster (bullx computing node R418-E3), for mandatory use in NGS/Mass Sequencing protocols.

#### 8.6.3. Portfolio of Services

- Technical support and scientific and methodological advice on the choice and optimization of genomic techniques
- Nucleic acids quality control (spectrophotometry, fluorometry and microelectrophoresis)
- Studies of gene expression through nanostring technology
- Gene expression studies using real-time PCR and genotyping studies
- Sequencing NGS (next generation sequencing) illumina miseq
- Training and support in the use of data analysis software related to the unit's technology

#### 8.6.4. Highlights

In 2015, the Unit of Genomics of IMIBIC has acquired high performance equipments for NGS and expression analyses, which have become fully operational and have substantially increased the portfolio of services of the Unit during this year.

## 8.7. Clinical Research Unit

The IMIBIC Clinical Research Unit promotes clinical research at IMIBIC and establishes collaborations with other research centers. Currently, IMIBIC is part of the Spanish Clinical Research Network (SCReN and ECRIN (European Clinical Research Infrastructure Network))."

The IMIBIC Clinical Research Unit focuses on the development of clinical trials including design, feasibility, regulatory affairs, launch, management, monitoring, pharmacovigilance, data management, statistics and delivery of clinical assistance. All operations are GCP compliant as required.

The IMIBIC Clinical Research Unit consists of two facilities: one located at the Provincial Hospital and another by the General Hospital Clinical Research Unit, which have been completed in June 2015. Both have been adapted to perform clinical trials of Phases I-IV in patients.

#### 8.7.1. Composition

#### Head

 Dr. Jose López Miranda jlopezmir@uco.es

#### **Clinical Pharmacologist**

 Dr. María Esther Pacheco Rodriguez esther.pacheco@imibic.org

#### **Project Managers/CRAs**

- Blanca Quijano Ruiz blanca.quijano@imibic.org
- Antonio Luque Pineda
   Antonio.luque@imibic.org

#### **Nurse Coordinator**

 Inés Carmen Rodríguez García inesc.rodriguez.sspa@juntadeandalucia.es

#### Nurse Team

- Pilar Mesa Blanco pilar.mesa@imibic.org
- Manuel Rejano Castañeda manuel.rejano.sspa@juntadeandalucia.es

#### **Nursing Assistants**

- Rubén Sánchez Nieves
- Rafaela Vacas Bueno

#### Administrative Staff

• María Dolores Castro Ortiz

#### 8.7.2. Equipment and Facilities

- Doctor's offices and storehouse
  - 2 hospital wards each containing: crash trolley with semi-automatic defibrillator and emergency medication, intravenous fluids, an insulin pump, healing trolleys, oxygen outlets in all positions and audiovisual system.
  - 14 armchairs and rooms with 3 single beds, all with ongoing monitoring.
  - A pediatric area

12-lead ECGs
Measuring boards and scales
Blood pressure meter in each office.
4 customized Bathrooms.
Individual lockers for patients.
2 Living rooms for patients and family.
1 multi-purpose room
2 Laboratories for sample processing and centrifuges.
Freezers (-80°C and -20°C)
2 storehouse for materials
High Definition Ultrasound Scanner
2 Study coordinators' offices
2 CRAs' offices
2 Archives

#### 8.7.3. Portfolio of Services

- Methodological support
- Launch and Regulatory affairs
- Study development
- Close out
- Pharmacovigilance
- Delivery of clinical assistance

#### 8.7.4. Highlights

During 2015, the Unit provided assistance and support in the start-up, coordination, data-management, and monitoring of 19 independent clinical trials across the following Units , including amongst others, Internal Medicine, Pediatrics, General Surgery, Nephrology, and Rheumatology. Additionally, clinical research activity has increased in 2015 to include a total of 337 patients in the Provincial Hospital Clinical Research Unit and up to 186 patients in the General Hospital Clinical Research Unit. 57 Clinical Trials are currently being conducted. The main areas of activity are Oncology, Nephrology, Dermatology, Internal Medicine and Urology.

As a member of Spanish Clinical Research Network, the Unit has actively participated in 6 clinical trials interacting with different groups within Spain. The Unit also collaborates with several working groups within the network.

## 8.8. Biobank Unit

The Biobank Unit of IMIBIC, is one of the research support platforms whose mission is to act as a liaison between doctors, researchers and patients who donate biological samples for the purpose of biomedical research to uphold the current legal constraints and appropriate ethical safeguards.

The IMIBIC Biobank is part of the Global Framework of Biobank of Andalusian Public Health System (SSPA) Initiative of the Department of Equality, Health and Social Policy. It is part of the National Biobank Network Intiative of the National Institute of Health -Instituto de Salud Carlos III (ISCIII).

#### 8.8.1. Composition

-Unit's Scientific Management

- Dr. Manuel Medina Pérez
  - manuel.medina.sspa@juntadeandalucia.es

-Coordinator

Carmen Pérez Calle

carmen.perez.calle.exts@juntadeandalucia.es

-Technicians:

• Eugenia Carrillo Gil

eugenia.carrillo@imibic.org

 Javier Herruzo javier.herruzo@imibic.org  Desireé Gutiérrez Córdoba desire.gutierrez@imibic.org

#### 8.8.2. Equipment and Facilities

The Unit possesses its own laboratory resources for integral sample handling and processin (Safety booths, PCR Booths, Microtomes, Chryostate, Flotation Bath, Centrifuge, Histobath, Automatized Processor for Paraffin Inclusion, Paraffin Dispenser, etc.) as well as other equipment, including:

-Tissue Safe: fully automated preparation of tissue samples in a vacuum.

-Tissue Arrayer: assembles different tissue samples in a single multiple matrix for subsequent histological analysis.

-Quiacube: Automatic,compact system for analysis of DNA, RNA, plasmids and proteins from varying samples. For sample storage, there are currently several freezer equipments, including: one for temperatures of -20 degrees Celsius, seven for -80 degrees Celsius, as well as paraffin storage rooms for room temperature.

#### 8.8.3. Portfolio of Services

Our service portfolio is divided into four main sections:

- 1. Custody for storing samples at different temperatures.
- 2. Processes for transforming multiple types of biological samples in accordance with the procedures and technical criteria commonly used by researchers in their projects.
- 3. Provision of human samples and data on human health and disease research, selected according to clinical and diagnostic criteria specified by researchers.
- 4. Technical, scientific and ethical consulting regarding the collection, storage, and management of human samples in biomedical research.

#### 8.8.4. Highlights

In 2015, the Biobank Unit experienced an increase in activity in comparison to previous years, having given essential support to 78 research projects. This activity generated a total of 110,000 samples/ bioresources, of which around 18,000 were provided to different researchers. The degree of satisfaction of these users has been assessed via surveys to be 9.3 (out of a possible 10 points).

## 8.9. Methodology and Biostatistics Unit

This Research Support Unit offers methodological consulting and statistical support for IMIBIC's researchers and for healthcare professionals in the Public System in the Province of Córdoba.

The Unit's main objectives are:

- Offering methodological consulting during the course of research projects and activitites (from project and experimental design to completion). This includes methodological support in preparation of project application to competitive funding sources.
- Provide the necessary statistical support to researchers for the creation of databases, the use of statistical techniques and tools of epidemiological clinical research, through advisory or execution of statistical analysis.
- Provide the highest quality possible in design, execution, interpretation and communication of results

#### 8.9.1. Composition

 Dr. Maricarmen Muñoz Villanueva, MD. mc.munoz.exts@juntadeandalucia.es

#### 8.9.2. Equipment and Facilities

The main statistical programs used for data analysis are:

- PASW Statistics 18 (Copyright 2009 by SPSS Inc.)
- IBM SPSS 19 (Copyright 2010 by SPSS Inc.)
- Epidat 4.1 (Consejería de Sanidad, Xunta de Galicia, España; Organización Panamericana da saúde (OPS-OMS); Universidade CES, Colombia. Octube 2014).
- GranMo versión 7 (abril 2012)
- G-stat 2.0 (Copyright 2008 by GSK, SA.)
- Sinergy 3.0 (Copyright 2008 by GSK, SA.)

#### 8.9.3. Portfolio of Services

Through personalized consultations (face to face meetings, telematic or virtual) we cover the different moments of the research process. Specifically, the aid that the Usersdemand include

- -Research design
- Data collection instruments
- Database organization
- Technical statistics options
- Data analysis
- Results interpretation
- Written report of results
- Attention to methodological demands of copy editors.

Specifically, the consulting at the methodological level can include:

- Review of the different sections of the scientific methodology proposed in the research protocol: presentation of hypotheses, formulation of objectives, choice of epidemiological design, operational definition of variables...
- Guidance for literature search techniques
- Advice on the presentation of results for scientific dissemination
- Validation of publication requirements depending on the type of study and quality criteria of scientific publications
- Analysis of the grounds for refusal: review of articles and rejected projects

Consultation and execution of statistical analysis can include:

- Drafting of statistical analysis methodology or strategy.
- Sampling and sample size calculation.
- Design of research databases.
- Exploratory and descriptive analysis of the data.
- Inferential analysis (univariate and multivariate).
- Evaluation of diagnostic tests: sensitivity, specificity, predictive values and ratios of verosimilitudes. ROC curves.
- Validation of questionnaires and other measuring instruments.
- Other statistical techniques (Bayesian analysis, meta-analysis, etc...).

#### 8.9.4. Highlights

In 2015, 123 activities were carried out, most of which (about 60%) were related to consulting and statistical analysis for dissemination of results of research (some publications and conferences). In addition, four teaching activities were implemented; three of which were organized locally by IMIBIC and the other at the nationwide level (collaboration in the Master of Research Methodology of the University of Barcelona). There were also five training activities for updating statistical and epidemiological knowledge.





# HIGHLIGHTS

T and NK immunosenescence. Antiviral immune response



#### **Team Leader**

Principal Investigator (PI): Rafael Solana Lara rsolana@uco.es Red Española de Patología Infecciosa (REIPI) (Collaborator) PAIDI CTS-208 Scientific Group (Collaborator)

#### **Researchers**

Corona Alonso Diaz Rafael González Fernández Aurora Jurado Roger Carmen Moreno Aguilar Berta Ruiz León Pilar Serrano Delgado Vanessa Saiz Sánchez

Post- Doctoral Researchers Carmen Campos Fernández Bárbara Martín Manzanares Alejandra Pera Rojas Pre Doctoral-Researchers (PhD Students y MSc Students)

Estrella Cañones Barceló Laura Castro Orgaz Fakhri Hassouneh Azahara García Gallego Nelson López Sejas Juan Eduardo Molina Alcaide Ana María Navas Romo Oscar Alberio Yarce Bustamante

Other members of the Group (Nursing, Technical, and Administrative Staff) Mercedes Guerra González Mª 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.

#### **Keywords**

Immunosenescence; aging; melanoma; NK cells; NKT cells; NK receptors; CMV; cytotoxic T lymphocytes (CTL).

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Campos C, Lopez N, Pera A, Gordillo JJ, Hassouneh F, Tarazona R, Solana R. Expression of NKp30, NKp46 and DNAM-1 activating receptors on resting and IL-2 activated NK cells from healthy donors according to CMV-serostatus and age. BIOGERONTOLOGY. 16(5):671-683. IF: 3,29

Q: 2

#### **Original Reviews**

Pera A, Campos C, Lopez N, Hassouneh F, Alonso C, Tarazona R, Solana R. Immunosenescence: Implications for response to infection and vaccination in older people. MATURI-TAS. 82(1):50-55. IF: 2,942

Q: 1

#### Papers in Collaboration

Cantisan S, Rodelo-Haad C, Paez-Vega A, Nieto A, Vaquero JM, Poyato A, Montejo M, Farinas MC, Rivero A, Solana R, Martin-Malo A, Torre-Cisneros J. Factors Related to the Development of CMV-Specific CD8+ T cell Response in CMV-Seropositive Solid Organ Transplant Candidates. AMERICAN JOURNAL OF TRANSPLANTATION. 15(3):715-722.

IF: 5,683

Q: 1 D: 1

Ferrando-Martinez S, Ruiz-Mateos E, Casazza JP, de Pablo-Bernal RS, Dominguez-Molina B, Munoz-Fernandez MA, Delgado J, de la Rosa R, Solana R, Koup RA, Leal M. IFN gamma-TNF alpha(-)IL2(-)MIP1 alpha(-)CD107a(+) PRF1(+) CD8 pp65-Specific T-Cell Response Is Independently Associated With Time to Death in Elderly Humans. JOURNALS OF GER-ONTOLOGY SERIES A-BIOLOGICAL SCIENCES AND MEDICAL SCIENCES. 70(10):1210-1218. IF: 5,416

Frias M, Rivero-Juarez A, Gordon A, Camacho A, Cantisan S, Cuenca-Lopez F, Torre-Cisneros J, Pena J, Rivero A. Persistence of Pathological Distribution of NK Cells in HIV-Infected Patients with Prolonged Use of HAART and a Sustained Immune Response. PLOS ONE. 10(3): .

IF: 3,234

Q: 1

Riddell NE, Griffiths SJ, Rivino L, King DCB, Teo GH, Henson SM, Cantisan S, Solana R, Kemeny DM, MacAry PA, Larbi A, Akbar AN. Multifunctional cytomegalovirus (CM-V)-specific CD8(+) T cells are not restricted by telomere-related senescence in young or old adults. IMMUNOLOGY. 144(4):549-560. IF: 3,795 Q: 2

u. 2

El Mouraghi I, Ouarour A, Ghozlani I, Collantes E, Solana R, El Maghraoui A. Polymorphisms of HLA-A, -B, -Cw and DRB1 antigens in Moroccan patients with ankylosing spondylitis and a comparison of clinical features with frequencies of HLA-B\*27. TISSUE ANTIGENS. 85(2):108-116. IF: 2,137

Q: 2

#### **Letters in Collaboration**

Cantisan S, Solana R, Torre-Cisneros J. Response to "Influence of Age and HLA Alleles on the CMV-Specific Cell-Mediated Immunity Among CMV-Seropositive Kidney Transplant Candidates". AMERICAN JOURNAL OF TRANSPLANTATION. 15(9):2527-2528. IF: 5,683 Q: 1 D: 1

#### **Research Funding**

#### National

Jurado Roger, A. HBA1c validation for the diagnosis of gestational diabetes Funding agency: Institute Carlos III Health (ISCIII). Reference: PI11-01064

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

Moreno C - Jurado A. Insect sting anaphylaxis. Search for biomarkers of early response to hymenoptera venom immunotherapy Funding agency: Institute Carlos III Health (ISCIII). Reference: PI1502170

#### International

Moreno C.Towards safe and effective immunotherapy of persistent life-threatening food allergies. Funding Agency: European Commission. Reference: FP7-HEALTH-2007-A-2015

#### **Contracts with Companies**

Solana Lara R. Agreement with Innogenetics Diagnostica Iberia SL.Funging Agency: Innogenetics Diagnostica Iberia SL. Reference:C-CB.0099

#### **Clinical Trials**

0086/15 :A multinational phase IIb study to investigate the efficacy and safety of subcutaneous immunotherapy with a modified fish-parvalbumin given in single rising and maintenance doses to subjects allergic to fish.

PI Dr/a Moreno Aguilar, Carmen

0258/15 : A multicenter international, randomized, double-blind, and placebo-controlled to demonstrate the clinical efficacy and safety of subcutaneous immunotherapy using gpASIT + TM in patients with allergic rhinoconjunctivitis induced grass pollen. PI Dr/a Moreno Aguilar, Carmen

3031 :Insect sting anaphylaxis. Search for biomarkers of early response to hymenoptera venom immunotherapy.

PI Dr/a Moreno Aguilar, Carmen

2739 : Effect of antihypertensive medication in the severity of anaphylaxis and side effects during venom immunotherapy Hymenoptera insects. EADOAS".

PI Dr/a Moreno Aguilar, Carmen

Q: 1 D: 1

# HIGHLIGHTS

# **Oxidative and nitrosative stress** in acute and chronic liver disease



#### **Team Leader**

Principal Investigator (PI) Manuel de la Mata García. hepatoh2hrs.sspa@juntadeandalucia.es CIBER de Enfermedades Hepáticas y Digestivas (CIBERehd) PAIDI CTS-273 Scientific Group

**Co- Principal Investigator (Co-PI)** Jose Antonio Bárcena Ruiz PAIDI BIO-216 Scientific Group



#### **Researchers**

Patricia Aguilar Melero Pilar Barrera Baena José Manuel Benítez Cantero Guadalupe Costán Rodero Mª Valle García Sánchez Federico Gómez Camacho Gustavo Ferrín Sánchez Enrique Fraga Rivas Emilia Martínez Galisteo José Luis Montero Álvarez Alicia Padilla Peña José Peinado Peinado Antonio Poyato Gonzalez Manuel Luis Rodríguez Perálvarez **Post- Doctoral Researchers** Raúl González Ojeda

Pre Doctoral-Researchers (PhD Students y MSc Students) Sandra González Rubio Juan Jurado García Clara Isabel Linares Luna Luis Vida Pérez

Other members of the Group (Nursing, Technical, and Administrative Staff) Rosario Medina Medina Eva María Morcillo Ruiz Mª Luisa García García

#### **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 redoxins 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 invol- ved 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 (satavaptan), acute liver failure (bioartificial liver, MARS) and liver transplantation (immunosuppression strategies).

#### **Keywords**

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

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Gonzalez-Rubio S, Lopez-Sanchez L, Munoz-Castaneda J, Linares CI, Aguilar-Melero P, Rodriguez-Peralvarez M, Sanchez-Sanchez R, Fernandez-Alvarez A, Casado M, Montero-Alvarez JL, Rodriguez-Ariza A, Muntane J, de la Mata M, Ferrin G. GCDCA down-regulates gene expression by increasing Sp1 binding to the NOS-3 promoter in an oxidative stress dependent manner. BIOCHEMICAL PHARMACOLOGY.2015. 96(1):39-51.

- IF: 5,009
- Q: 1 D: 1

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#### **Research Funding**

#### National

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

Montero Álvarez, JL.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. Funding agency: Spanish Ministry of Health, Social Services and Equality.Reference: EC11-185

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

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#### Regional

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

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Padilla Peña. A. Antitumor activity of nitric oxide: regulation of sorafenib by way of mTOR inhibitors of Wnt / β-catenine..Funding Agency: Regional Ministry of Economy, Innovation, Science and Employment (CEICE).. Reference: CTS-6264

Rodríguez Perálvarez, ML.Inhibition of mTOR pathway in patients transplanted for hepatocellular carcinoma and its impact on recurrence Funding agency: Andalusian tumor society of organ and tissue transplants.Reference:SATOT14\_001

Bárcena Ruiz, JA. Molecular systems for defense against oxidative stress and proteomics. Funding Agency Regional Ministry of Economy, Innovation, Science and Employment (CEICE).. Reference: BIO-216 (2015)

#### International

Rodríguez Perálvarez, ML. mTOR pathway inhibition in liver transplant patients with hepatocellular carcinoma and its impact on tumour recurrence. Funding Agency:European Association for the Study for the Liver. Reference: EASL-2014-002

#### Contracts with Companies

De la Mata García, M. Collaboration Agreement between Ciberehd and institution. Funding agency: Centro de Investigación Biomédica en Red en el Área Temática de

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García Sánchez, MV. Sample collection service for the Innpacto project. Funding agency: Fundació Institut de Recerca Hospital Universitari Vall D'hebron. Reference:PSS.0021

De La Mata García, M. Molecular predictors of response to sorafenib as adjuvant Therapy A after resection in Hepatocellular Carcinoma (Bio-Storm). Funding agency:Bayer Pharma AG.Reference:PSS.0036

De La Mata García, M. Agreement with Omniprex (From research to clinical practice). Funding agency: Omniprex SL. Reference: PSS.0055

De La Mata García, M. Contract to manage Database. Funding agency: Bayer Hispania SL. Reference: PSS.0061

García Sánchez, MV.Sponsored research agreement.Funding agency: Merck Sharp & Dohme SA. Reference: PSS.0063

Rodríguez Perálvarez, ML. Inhibition of mTOR pathway in patients transplanted for hepatocellular carcinoma and its impact on recurrence.Reference:PSS.0095

De La Mata García, M. aHCtion Project. Funding agency OMNIPREX SL.Reference PSS.0106

De la Mata García, M. Funding for collaborators at the Digestive Tract Unit . Funding agency: Merck Sharp & Dohme SA. Reference: CCB.0038

De la Mata García, M. Support agreement for collaborators at the Digestive Tract Unit. Funding agency: Merck Sharp & Dohme SA. Reference: CCB.0051

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#### **Clinical Trials**

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

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

PI: Dr/a De La Mata García, Manuel

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

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

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 met diagnostic-high inoperable hepatocellular carcinoma (HCC) treated with one prior systemic therapy PI: Dr/a Montero Alvarez, Jose Luis

0039/13: Radomized, doubled blind, placebo-controlled, multicenter phase III study of regorafenib in patients with hepatocellular carcimona (HCC) after srafenib. PI: Dr/a Barrera Baena, Pilar

0113/13: Multicentric, randomized, open-label, controlled study, of 12 months of follow-up to assess the efect in renal fuction of a immunosupressive treatment based on tarcroimus minimization in combination with everolimus in patients with novo liver transplation. PI: Dr/a De La Mata García, 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

0249/14: An open, multicenter study to assess long-term effects of ABT-450/ritonavir/ ABT-267 (ABT-450/r/ABT-267) and ABT-333 with or without ribavirin (RBV) in adults with chronic infection with genotype 1 (TOPAZ-I) of Hepatitis C virus (HCV).

PI: Dr/a Fraga Rivas, Enrique

\*2952\*; Phase 2, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of ENZALUTAMIDE in patients with advanced hepatocellular carcinoma. PI: Dr/a Montero Alvarez, Jose Luis

0259/15: Open, multicenter, randomized study to evaluate the efficacy and safety of ABT-493 / ABT-530 in adults with chronic infection with hepatitis C genotype 1 (ENDUR-ANCE-1) study.

PI: Dr/a Montero Alvarez, Jose Luis

2061: Predicting short-term response to anti-TNF treatment in patients with Crohn's disease.

PI: Dr/a García Sánchez, Valle

2315: A long-term non-interventionist registration study to assess the safety and efficacy of HUMIRA (adalilumab) in patients with moderately active or very active ulcerative colitis (LEGACY).

PI: Dr/a García Sánchez, Valle

2342: Registry of Telaprevir and Boceprevir in regular clinical practice.

PI: Dr/a De La Mata García, Manuel

2567: Assessing adherence to triple therapy for Hepatitis C. PI: Dr/a Fraga Rivas, Enrique

2572:Defining high risk variceal bleeding: a rational for the use of early tips in acute bleeding and preventing rebleeding. 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

2616: Observational, multicenter, prospective study to assess renal function in patients with liver transplants treated with tacrolimus PI: Dr/a Rodríguez Perálvarez, Manuel Luís

2679: Evolution following discontinuation of anti-TNF treatment in patients with inflammatory bowel disease.

PI: Dr/a García Sánchez, Valle

2845: Evolution following the intensification of anti-TNF treatment in patients with inflammatory bowel disease.

PI: Dr/a García Sánchez, Valle

# GC3

# HIGHLIGHTS

**Infectious diseases** 



#### Researchers

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**Co- Principal Investigator (Co-PI)** Antonio Rivero Roman *AIDS Research Network (RIS) (Collaborator)* 

#### **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.

#### **Scientific Production**

#### **Publications**

#### Original

#### Papers

Torre-Cisneros J, San-Juan R, Rosso-Fernandez CM, Tiago Silva J, Munoz-Sanz A, Munoz P, Miguez E, Martin-Davila P, Lopez-Ruz MA, Vidal E, Cordero E, Montejo M, Blanes M, Farinas MC, Herrero JI, Rodrigo J, Aguado JM. Tuberculosis prophylaxis with levofloxacin in liver transplant patientsis associated with a high incidence of tenosynovitis: safety analysis of a multicenter randomized trial. CLINICAL INFECTIOUS DISEASES.2015. 60(11):1642-1649.

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#### **Original Letters**

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#### **Original Reviews**

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#### **Papers in Collaboration**

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#### **Editorial Material in Collaboration**

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#### **Research Funding**

#### National

De la Torre Cisneros, J. Spanish Network for Research on Infectious Diseases (REIPI). Funding agency: Institute Carlos III Health (IS-CIII). Reference: RD12/0015/0002.

Gracia Ahufinger, I. Study of epigenetic modifications induced by cytomegalovirus as risk and prognostic markers..Funding agency: Institute Carlos III Health (ISCIII).Reference: PI14/01225

#### Regional

Rivero Román, A Predictive value of immediate VHC viral kynetics on the sustained viral response in patients co-infected with the VIH/VHC. Funding Agency: Progress and Health Foundation. Reference: PI-0157-2011

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

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

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

Rivero Juarez, A (node). Study Group for Viral Hepatitis (Grupo de estudio de Hepatitis Viricas "HEPAVIR").Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: RH-0024-2013

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De la Torre Cisneros, J. Study of the kinetics of CD8 + T immunity against CMV in renal transplant patients treated with thymoglobuline. Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0294-2014

#### International

De la Torre Cisneros, J (node). PROYECTO COMBACTE-1 (Combacting Clinical resistance in Europe. Program Innovative Medicines Initiatives (IMI Call IMI-IU-6). Eol Number Eol 115523-1.Funding agency: European Commission. Reference: IMI Call IMI-IU-6-12

De la Torre Cisneros, J (node). PROYEC-TO COMBACTE-2 (Combacting Clinical resistance in Europe. Program Innovative Medicines Initiatives (IMI Call IMI-IU-8). Eol Number 115523.Funding agency: European Commission. Reference: IMI Call IMI-IU-8-12

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

Rivero Juaréz, A (node). Partners of people on Antiretrovirals (ART) New Evaluation of Risk. Estudio de parejas VIH serodiferentes para estimar el porcentaje de transmisión del VIH e investigar los factores asociados con el uso de preservativos. Funding agency: The National Institute for Health Research (NIHR) England.

#### **Contracts with Companies**

De la Torre Cisneros, JC. Contract for the provision of MSD monitoring. Funding agency: Merck Sharp & Dohme de España SA. Reference: PSS.0007

Rivero Román, A. Contract for web design . Funding agency: Janssen-Cilag, S.A. Reference: PSS.0026

Rivero Román, A.Contract to manage BMS-FIBICO. Funding agency: Bristol-Myers Squibb International Corporation (BMSIC). Reference: PSS.0031

Rivero Román, A. Agreement with Gilead Sciences. Funding agency: Gilead Sciences, S.L. Reference: PSS.0038

De la Torre Cisneros, JC. Agreement with Brahms Iberia (Conference Infectious Pathology).Funding agency: Brahms Iberia, S.L.Reference: PSS.0045 De la Torre Cisneros, JC. Agreement with Pizfer. Funding agency: PFIZER, S.L.U.Reference: PSS.0058

De la Torre Cisneros, JC. Agreement with SET. Funding agency: SOCIEDAD ESPAÑOLA DE TRASPLANTES.Reference: PSS.0074

Rivero Román, A. Cooperation Agreement for a scientific research grants programme.. Funding agency: JANSSEN-CILAG, S.A. Reference: CCB.0113\_01

De la Torre Cisneros, JC. Agreement with Roche Pharma.Funding Agency:Roche Pharma, S.A.Reference: CCB.0004

Rivero Román, A. Programme combined HIV/ AIDS. Funding agency: Bristol-Myers Squibb, S.A.U.Reference: CCB.0049

Rivero Román, A.Agreement with Merck Sharp & Dohme. Funding agency: Merck Sharp & Dohme de España A Reference: CCB.0058

Rivero Román, A.Agreement with Merck Sharp & Dohme. Funding agency: Merck Sharp & Dohme de España SA. Reference: CCB.0073

Rivero Román, A.Agreement with Roche Pharma. Funding Agency: Roche Pharma, S.A Reference:CCB.0075

De la Torre Cisneros, JC. Agreement with Roche Pharma (Publications).Funding Agency:Roche Pharma, S.A.Reference: CCB.0076

De la Torre Cisneros, JC. Agreement with Astellas Pharma.Funding Agency: Astellas Pharma, S.A..Reference: CCB.0092

Rivero Román, A.Agreement with Abbvie. Funding Agency: Abbvie Spain S.L.U.Reference:CCB.0093

Rivero Román, A.Agreement with MSD. Funding Agency: Merck Sharp & Dohme de España Sa.Reference:CCB.0102

#### **Clinical Trials**

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

0121/11:A randomized, controlled, partially-blind Phase IIb trial to assess the safety, effectiveness and dose-reponse 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

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 AT-V7RTV plus 3TC.

PI: Dr/a Rivero Román, Antonio

0101/11: Early access program, multicenter, open-label, telaprevir in combination with pegylated interferon alfa and ribavirin for the

treatment of chronic infection with genotype 1 hepatitis C virus in patients with advanced fibrosis or compensated cirrhosis PI: Dr/a Rivero Román, Antonio

0007/12: Clinical Trial Phase IIb, randomized, controlled, partially blinded, to investigate the safety, efficacy and dose-response of BMS-986001 in patients with HIV-1 who have not received prior treatment followed by a period when open to the recommended dosagePI: Dr/a Rivero Román, Antonio

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

PI: Dr/a Rivero Román, Antonio

0072/12: An open study to assess the safety, antiviral activity and pharmacokynetics 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 (SAP-PHIRE-III).

PI: Dr/a Rivero Román, Antonio

28/13: A randomized, open, controlled, single-pattern, phase III study with active product of bi 207127 in combination with faldaprevir and ribavirian 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: Steral 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

0039/14: A randomized, multicenter, open-label, controlled, phase III trial to assess the efficacy of fosfomycin vs. meropenem in targeted therapies for bacteremic urinary tract infection with extended-spectrum beta-lactamase (ESBL). PI: Dr/a Natera Kindelan, Clara

0062/14:Optimal duration of the antimicribial treatment for bloodstream infections produced by Enterobacteriaceae. Clinical trial SHORTEN. PI: Dr/a Natera Kindelan, Clara

0081/14. A randomized, open-label study to assess the efficacy of darunavir/ritonavir plus lamivudine once a day vs. continuing treatment with darunavr/ritonavir once a day plus tenofovir/emtricitabine or abacavir/lamivudine in HIV patients with suppressed viremia. DUAL study. Pl: Dr/a Rivero Román, Antonio 0272/14: Phase 3, randomized, active-controlled, open-label treatment to evaluate the change in treatment regimen in a single tablet taken once daily darunavir / cobicistat / emtricitabine / alafenamida tenofovir (D / C / F / TAF) front the continuation of the current regime consists of an inhibitor boosted protease (PPI) in combination with emtricitabine / tenofovir disoproxil fumarate (FTC / TDF) in patients infected with HIV type 1 (HIV-1) with virologic suppression subjects PI: Dr/a Rivero Román, Antonio

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0009/10/2: Long-term follow-up of participants in a phase II or III SCH 503034 trial for the treatment of chronic Hepatits C. PI: Dr/a Rivero Román, Antonio

0124/15: Switch to MK-1439A in HIV-1-Infected Subjects Virologically Suppressed on a Regimen of a Ritonavir-boosted Protease Inhibitor and Two Nucleoside Reverse Transcriptase Inhibitors (NRTIs).

PI: Dr/a Rivero Román, Antonio

0114/15: Phase 3 trial, randomized, active-controlled, double-blind treatment to evaluate the safety and efficacy of the combined regimen of darunavir / cobicistat / emtricitabine / alafenamida tenofovir (D / C / F / TAF) administered once daily against the consistent treatment in the combination of darunavir / cobicistat co-administered with combination emtricitabine / tenofovir disoproxil fumarate in antiretroviral treatment naive subjects infected with human immunodeficiency virus type 1. PI: Dr/a Rivero Román, Antonio

0298/15: Clinical trial of suspension of prophylaxis with valganciclovir in CMV-seropositive kidney transplant recipients that maintain cellular immunity CMV-specific CD8 + after receiving thymoglobuline.

PI: Dr/a De la Torre Cisneros, Julián Carlos

0062/15: Immune Response, and Safety Study of Clostridium difficile Toxoid Vaccine in Subjects at Risk for C. difficile Infection. PI: Dr/a De la Torre Cisneros, Julián Carlos

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

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

2548: Hepatic safety of Evilplera in HIV/hepatitis C (HCV)-coinfected patients without HCV treatment in the The HEPAVIR HEPATIC SAFE-TY Cohort. hEPAtic study PI: Dr/a Rivero Román, Antonio

2649: Effectiveness and safety of treatment against hepatitis C virus based on direct acting antivirals in actual use conditions: Cohort GEHEP PI: Dr/a Rivero Román, Antonio

2854:B-Lactam / B-Lactam inhibitor combinations versus carbapemens for the treatment of bacteremia due to extended-spectrum B-Lactamase-producing Gram-negative bacilli in neutropenic hematologic patients. PI: Dr/a De la Torre Cisneros, Julián Carlos 2851:Efficacy and Safety of Entecavir for chronic hepatitis B in patients coinfected with HIV / HBV

PI: Dr/a Rivero Román, Antonio

2595: Intestinal colonization by multiresistant enterobacteria in patients with renal and liver transplant: multicenter cohort study PI: Dr/a Gracia Ahufinger, Irene

2848: Evaluation of mortality associated with different clinical management strategies of Klebsiella pneumoniae bacteremia resistant to carbapenems and colistin. KAPECOR study. PI: Dr/a Machuca Sanchez, Isabel Maria

2849 Effectiveness of intestinal decontamination in patients colonized by Klebsiella resistant to carbapenems and colistin pneumoniae.

PI: Dr/a Machuca Sanchez, Isabel Maria

2907: Impact of specific antimicrobials and MIC valueson the outcome of bloodstream infections due to ESBL-or carbapenemase-producing Enterobacteriaceae in Solid Organ Transplantation: an observational multinationalstudy.

PI: Dr/a De la Torre Cisneros, Julián Carlos

2933:Study of the kinetics of T Cd8 positive immunity against CMV in renal transplant patients treated with thymoglobuline.

PI: Dr/a De la Torre Cisneros, Julián Carlos

# GC4

# HIGHLIGHTS

Team Leaders

Principal Investigator (PI) Eduardo Muñoz Blanco fi1muble@uco.es PAIDI BIO-304 Scientific Group

**Emerging Researcher (ER)** Marco Antonio Calzado Canale

# Inflammation and cancer



#### Researchers Irene Cantarero Carmona Carmen Navarrete Rueda Paula Moreno Casado Noel García Medel

Pre Doctoral-Researchers (PhD Students y MSc Students)

Belén Palomares Cañero Carla Jiménez Jiménez Carmen del Río Mercado Estrella Millán Ortega Mª Isabel Lara Chica Martín Garrido Rodríguez-Córdoba Rosario Morrugares Carmona Víctor García Gonzalez Other members of the Group (Nursing, Technical, and Administrative Staff) Juan Antonio Collado Rojas Rosario Molina Moran

#### **Scientific Activity**

The group "Inflammation and Cancer" is a consolidated group (GC-04) of the IMIBIC and participates in the research program Chronic Inflammatory Diseases that is described in the Institute strategic plan. Overall the research undertaken by the group is very collaborative with other national and international research groups and with SMEs. The main research lines are:

- 1. Study of the mechanism of action of cannabinoids (endocannabinoids, phytocannabinoids and synthetic cannabinoids) (IP. Eduardo Muñoz). In this line of research we are very focused on studying the mechanism of action of some phytocannabinoids and endocannabinoids in order to explore its therapeutic potential in inflammatory and neurogenerative diseases. On the one hand we are identifying the hyoximimetic mechanism of action of endocannabinoids type N-acyl dopamines and exploring pharmacological strategies to increase the levels of these endocannabinoids in the CNS. Also we are investigating the pharmacological potential of new semi-synthetic compounds derived from phytocannabinoids Cannabidiol and Cannabigerol by studying novel mechanisms of actions and its efficacy in different in vivo models of neuroinflammation and fibrosis.
- 2. Molecular identification of signaling pathways that regulate certain processes involved in inflammation and cancer (IP. Marco A. Calzado). This line is aimed to identify the role of the ubiquitin ligase SIAH2 in response to hypoxia and other endogenous mediators. One of the main objectives is to identify new molecular targets for the development of novel potential therapies. Moreover, we are studying the metabolomic profile in human lung cancer and in murine models of prostate cancer. In this research line we also have a particular interest in the study of new chemical entities able to inhibit molecular targets of pharmacological interest in cancer.

#### **Keywords**

Inflammation; cancer; tissue regeneration; cannabinoids; SIAH2; pharmacology and Nutraceuticals.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Valdeolivas S, Navarrete C, Cantarero I, Bellido ML, Munoz E\*, Sagredo O\*. Neuroprotective Properties of Cannabigerol in Huntington's Disease: Studies in R6/2 Mice and 3-Nitropropionate-lesioned Mice. NEU-ROTHERAPEUTICS.2015. 12(1):185-199. (\* Equal senior authors)

- IF: 5,054 Q: 1 D: 1
- Q. 1 D.

Moreno P, Lara-Chica M, Soler-Torronteras R, Caro T, Medina M, Alvarez A, Salvatierra A, Munoz E, Calzado MA. The Expression of the Ubiquitin Ligase SIAH2 (Seven In Absentia Homolog 2) Is Increased in Human Lung Cancer. PLOS ONE.2015.;10(11):e0143376. IF: 3,234

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Appendino G, Minassi A, Collado JA, Pollastro F, Chianese G, Taglialatela-Scafati O, Ayyari M, Garcia V, Munoz E. The Thia-Michael Reactivity of Zerumbone and Related Cross-Conjugated Dienones: Disentangling Stoichiometry, Regiochemistry, and Addition Mode with an NMR-Spectroscopy-Based Cysteamine Assay. EUROPEAN JOURNAL OF ORGANIC CHEMIS-TRY.2015. 17:3721-3726. IF: 3,065

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#### **Papers in Collaboration**

Díaz L, Martínez-Bonet M, Sánchez J, Fernández-Pineda A, Jiménez JL, Muñoz E, Moreno S, Álvarez S, Muñoz-Fernández MÁ. Bryostatin activates HIV-1 latent expression in human astrocytes through a PKC and NF-κB-dependent mechanism. SCIENTIFIC REPORTS. 2015 .1 22;5:12442 IF: 5,578

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Martínez-Bonet M, Clemente MI, Álvarez S, Díaz L, García-Alonso D, Muñoz E, Moreno S, Muñoz-Fernández MÁ. Antiretroviral drugs do not interfere with bryostatin-mediated HIV-1 latency reversal. ANTIVIRAL RESEARCH. 2015.;123:163-71.

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IF: 3,30 Q:1

Q. 1

#### **Research Funding**

#### National

Muñoz Blanco, E. Pre-clinical development of new cannabinoid derivatives for the treatment of sclerodermia and ALS. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: RTC-2014-1877-1 Muñoz Blanco, E Hypoximimetic activity of new derivatives of cannabidiol. therapeutic implications. Funding agency: Spanish Ministry of Economy and Competitiveness (MINE-CO). Reference: SAF2014-53763-P

Lopez Miranda JM (Calzado Canale, M: Co-PI). Early predictor and causes of loss of phenotypic flexibility as individual risk factor of metabolic disease: towards a personalized medicine. Agency: Institute of Health Carlos III (ISCIII) Reference: PIE14/00005

Muñoz Blanco, E . Preclinical development of VCE-003.2 for the treatment of Huntington's Disease (CANNADERIV) Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: RTC-2015-3364-1

#### Regional

Calzado Canale, MA. Analysis of the metabolic footprint of lung cancer. Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0246-2013

Casado Moreno, P Impact of oxigenator of extracorporeal membrane on dysfunctional lung graft in a standardized porcine model of a unipulmonary transplant .Funding agency: Andalusian Progress and Health and Social Policies (FPS).Reference: PI-0296-2014

#### **Contracts with Companies**

Muñoz Blanco, E. Natural Ingredientes. Funding agency: SimCosmetic Biotech S.L.. Reference:12015022

Muñoz Blanco, E. Outsourcing within the INNTERCONECTA project: ATENA-"Olive oil and other healthy fats. Technological applications for the transformation of olive oil fats into high value added products. Funding agency: Phytoplant Research S.L. Reference: 12013097

Muñoz Blanco, E. Prolonged.Outsourcing within the INNTERCONECTA project SNC-IN-TEGRA. "Integration of technological platforms for the development of drugs for the treatment of central neural system diseases". Funding agency: Vivacell Biotechnology Spain SL. Reference: 12012115

## HIGHLIGHTS

Systemic and chronic inflammatory autoimmune diseases of the locomotor system and connective tissue



#### Team Leader

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



#### Researchers

M<sup>a</sup> Ángeles Aguirre Zamorano Miguel Ángel Caracuel Ruiz Alejandro Escudero Contreras Pilar Font Ugalde Inmaculada Gómez Gracia Verónica Pérez Guijo

Post- Doctoral Researchers Nuria Barbarroja Puerto Yolanda Jiménez Gómez Pre Doctoral-Researchers (PhD Students y MSc Students) Jerusalem Calvo Gutiérrez María Del Carmen Castro Villegas Rocío Jiménez Gasco Clementina López Medina Maria Dolores López Montilla Rafaela Ortega Castro Carlos Pérez Sánchez Patricia Ruiz Limón

Other members of the Group (Nursing, Technical, and Administrative Staff) M<sup>a</sup> Carmen Abalos Aguilera Cristina Carmona Moriel Desiré Ruiz Vílchez

Our research team works in two main investigation areas, which involve systemic autoimmune diseases (mainly Systemic Lupus Erythematosus, Primary Antiphospholipid Syndrome and Rheumatoid Arthritis) and chronic arthropaties (with special emphasis on Spondyloarthritis including Psoriatic Arthritis). We use synergistically clinical-therapeutic, molecular and cellular approaches.

#### 1. Research Area: Systemic autoinmune diseases

1.1 Atherothrombosis in Systemic autoinmune diseases. IR: Rosario López Pedrera.

Description: Our team studies the cellular and molecular mechanisms of atherothrombosis development in three systemic autoimmune diseases: Systemic Lupus Erythematosus (SLE), Antiphospholipid syndrome (APS) and Rheumatoid Arthritis (RA). We further analyze the regulatory mechanisms promoted by new therapeutic approaches such as Statins, biological therapies (i.e. anti-TNF, anti-IL6, anti-Blyss), biosimilars, and new drugs with antioxidant and anti-inflammatory effects (i.e. Coenzyme Q10)

#### Main Objectives

Study of cellular and molecular mechanisms of atherothrombosis in Systemic Autoimmune Diseases (EAS): Implementation of genomic, epigenetic and proteomics approaches to identify new biomarkers to delineate unique pathogenic mechanisms in each autoimmune condition.

Analysis of the mitochondrial dysfunction and oxidative stress in EAS as key mechanisms in the evolution of cardiovascular disease and in the response to new therapeutic approaches.

Study of the cellular and molecular mechanisms that regulate the effects of statins, CoQ10 and other biologic therapies in the prevention of atherothrombosis in EAS.

Molecular and cellular mechanisms involved in the metabolic complications associated with autoimmune diseases: Systemic lupus erythematosus, Rheumatoid arthritis and antiphospholipid syndrome. Effects of mainstream and biological therapies in the prevention of these disorders.

1.2. Biomarkers for Systemic Autoimmune Diseases. IR: Eduardo Collantes Estévez and Rosario López Pedrera. Description and objectives: Our research group also investigates new molecular biomarkers involved in the development of systemic autoimmune diseases. Specifically, the group conducts various research projects among which we can detach the so-called PRECISESADS (Molecular Reclassification to Find clinically Useful Biomarkers for Systemic Autoimmune Diseases), an European project funded by the "Innovative Medicines Initiative (IMI)". The aim of PRECISESADS is the use of -omics and bioinformatics tools for the reclassification of EAS that share common pathophysiological mechanisms. The project aims to push for personalized medicine based on clinical and molecular profiles of the individual by promoting a substantial improvement in the processes of prediction, diagnosis, and clinical developments as well as in monitoring therapeutic response.

2. Research Area: Inflammation and Chronic Arthropathies. IR: Eduardo Collantes Estévez.

Description: Our group has 3 lines of research in this field:

Clinical and epidemiological aspects of ankylosing spondylitis (AS) (activity and disease severity) at local, national (Spanish Registry EA: REGISPONSER) and international levels (European and Latin American Registry of EA (E: RE-SPONDIA). In the two former we are coordinators. 2) Development of a new system for evaluating the mobility of patients with AS (as an expression of structural damage and disease severity) by informatics technologies developed by our group (UCOTRACK. computerized motion capture using artificial vision; patented). 3) Study of the cellular and molecular mechanisms of the inflammatory and osteoproliferative pathways, in order to find new therapeutic targets. Main Objectives.-

To describe and analyze the clinical, epidemiological, demographic, genetic, radiographic, of therapeutic and pathophysiological response of patients with AS in Spain and compare that data with the ones obtained in Latin American patients. The most interesting point will be to known if the differences in the clinical manifestations are due to the genetic load that derive from the same genotype (in relation to HLA-B27) and its relationship to the interaction with the environment.

To apply the new patented system (UCOTRACK) to evaluate the mobility of patients with AS.

To assess the relevance of the overall oxidative status, mitochondrial dysfunction and endoplasmic reticulum stress as agents involved in the development of inflammation and / or structural damage present in this disease.

#### **Keywords**

Systemic autoimmune diseases (Primary Antiphospholipid Syndrome, Systemic Lupus Erythematosus, Rheumatoid Arthritis); oxidative stress; microRNAs; proteomics; inflammation; cardiovascular disease; new therapies; spondy-loarthropathies; epidemiology; diagnostic criteria, structural damage.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Ruiz-Limon P, Barbarroja N, Perez-Sanchez C, Aguirre MA, Bertolaccini ML, Khamashta MA, Rodriguez-Ariza A, Almaden Y, Segui P, Khraiwesh H, Gonzalez-Reyes JA, Villalba JM Collantes-Estevez E, Cuadrado MJ, Lopez-Pedrera C. Atherosclerosis and cardiovascular disease in systemic lupus erythematosus: effects of in vivo statin treatment. ANNALS OF THE RHEUMATIC DISEASES. 2015. 74(7):1450-1458. IF: 10.377 Q: 1 D: 1

Perez-Sanchez C, Barbarroja N, Messineo S, Ruiz-Limon P, Rodriguez-Ariza A, Jimenez-Gomez Y, Khamashta MA, Collantes-Estevez E, Cuadrado MJ, Aguirre MA, Lopez-Pedrera C. Gene profiling reveals specific molecular pathways in the pathogenesis of atherosclerosis and cardiovascular disease in antiphospholipid syndrome, systemic lupus erythematosus and antiphospholipid syndrome with lupus. ANNALS OF THE RHEUMATIC DISEAS-ES. 2015. 74(7):1441-1449. IF: 10.377

Q: 1 D: 1

Barbarroja N, Rodriguez-Cuenca S, Nygren H, Camargo A, Pirraco A, Relat J, Cuadrado I, Pellegrinelli V, Medina-Gomez G, Lopez-Pedrera C, Tinahones FJ, Symons JD, Summers Scott A, Oresic M, Vidal-Puig A. Increased Dihydroceramide/Ceramide Ratio Mediated by Defective Expression of degs1 Impairs Adipocyte Differentiation and Function. DIABETES. 2015. 64(4):1180-1192.

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Calvo-Gutierrez J, Garrido-Castro JL. Gil-Cabezas J, Gonzalez-Navas C, Font Ugalde P, Carmona L, Collantes-Estevez E. Is Spinal Mobility in Patients With Spondylitis Determined By Age, Structural Damage, and Inflammation? ARTHRITIS CARE & RESEARCH 2015; 67(1):74-79.

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Q: 1

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Lopez-Pedrera C, Aguirre MA, Ruiz-Limon P, Perez-Sanchez C, Jimenez-Gomez Y, Barbarroja N, Cuadrado MJ. Immunotherapy in antiphospholipid síndrome. INTERNATIONAL IMMUNOPHARMACOLOGY. 2015. 27(2):200-208.

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#### **Original Editorial Material / Correc**tion

Collantes-Estevez E, Espinoza LR. Nonradiographic axial spondyloarthritis. What brings the new concept? CLINICAL RHEUMATOLOGY 2015: 34(2):195-197. IF: 1,696 Q: 3

#### **Papers in Collaboration**

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54(7):1236-1243.

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Canet LM, Filipescu I, Caliz R, Lupianez CB, Canhao H, Escudero A, Segura-Catena J, Soto-Pino MJ, Ferrer MA, Garcia A, Romani L, Perez-Pampin E, Gonzalez-Utrilla A, Nevot MAL, Collantes E, Fonseca JE, Sainz J. Genetic variants within the TNFRSF1B gene and susceptibility to rheumatoid arthritis and response to anti-TNF drugs: a multicenter study. PHARMACOGENETICS AND GENOM-ICS. 2015.25(7):323-333.

IF: 3,481

Q: 1

Valverde A, Penarando J, Canas A, Lopez-Sanchez LM, Conde F, Hernandez V, Peralbo E, Lopez-Pedrera C, de la Haba-Rodriguez J, Aranda E, Rodriguez-Ariza A. Simultaneous Inhibition of EGFR/VEGFR and Cyclooxygenase-2 Targets Stemness-Related Pathways in Colorectal Cancer Cells. PLOS ONE 2015; 10(6):e0131363 IF: 3,234

Q: 1

El Mouraghi I, Ouarour A, Ghozlani I, Collantes E, Solana R, El Maghraoui A. Polymorphisms of HLA-A, -B, -Cw and DRB1 antigens in Moroccan patients with ankylosing spondylitis and a comparison of clinical features with frequencies of HLA-B\*27. TISSUE ANTI-GENS.2015. 85(2):108-116. IF: 2,137

Q: 2

Herencia C, Almadén Y, Martínez-Moreno JM, Espejo I, Herrera C, Pérez-Sánchez C, Guerrero F. Ciria R. Briceño FJ. Ferrín G. de la Mata M, Muñoz-Castañeda JR. Human mesenchymal stromal cell lysates as a novel strategy to recover liver function. Regen Med. 2015;10(1):25-38. doi: 10.2217/rme.14.59. PubMed PMID: 25562350. IF: 2,786

Q: 2

Gomez-Gomez E, Carrasco-Valiente J, Valero-Rosa J, Campos-Hernandez JP, Anglada-Curado FJ, Carazo-Carazo JL, Font-Ugalde P, Requena-Tapia MJ. Impact of 3D vision on mental workload and laparoscopic performance in inexperienced subjects. ACTAS UROLOGICAS ESPANOLAS. 39(4):229-235. IF: 1,022

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#### **Reviews in Collaboration**

Rodriguez-Cuenca S, Barbarroja N, Vidal-Puig A. Dihydroceramide desaturase 1, the gatekeeper of ceramide induced lipotoxicity. BIO-CHIMICA ET BIOPHYSICA ACTA-MOLECULAR AND CELL BIOLOGY OF LIPIDS. 1851(1):40-50. IF: 5,162 Q: 1 D: 2

#### **Research Funding**

#### National

Lopez Pedrera, R. Mechanisms of atherosclerosis and cardiovascular disease in systemic autoinmmune diseases'. New therapeutic approaches. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI12/01511

Font Ugalde, P. Characterization of new molecular targets involved in the inflammation and bone neoformation in the Ankylosing Spondylitis. Therapeutic alternatives. Fundaning agency: Fundacion Española de Reumatologia (Spanish Rheumatology Foundation). Reference: FER14.001

Barbarroja Puerto, N. Role of inflamed joints in the development of global insulin resistance and atherosclerosis associated with Rheumatoid Arthritis. Funding agency: Institute Carlos III Health (ISCIII). Reference: CP15/00158

#### Regional

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. Funding agency: Andalusian Progress and Health Foundation (FPS).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. Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0314-2012.

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

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

#### International

Collantes Estevez, E. PRECISESADS > 'Molecular reclassification to find clinically useful biomarker for systemic autoimmune diseases'. Funding agency: European Commission Reference: IMI/0002

#### Contracts with Companies

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

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

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

Collantes Estevez, E. Agreement Rheumatoid arthritis.Funding agency: Fundacion Española de Reumatologia (Spanish Rheumatology Foundation). Reference:CCB.0013

Pérez Sanchez, C. Agreement between the Clinical Management Unit of Reumatology and UCB Pharma. Funding agency: 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.Funding agency: 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.Funding agency: Fundacion Española de Reumatologia (Spanish Rheumatology Foundation). Reference: CCB.0045 Collantes Estevez, E. Agreement between MSD and the UGC of Reumatology. Funding agency: Merck Sharp & Dohme de España SA.Reference:CCB.0042

Collantes Estevez, E. Sponsored Research Agreement (Publications) Funding agency: PFIZER S.L.U. Reference: CCB.0050

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

Collantes Estevez, E. Sponsored Research Agreement ROCHE.Funding agency: Roche Farma SA. Reference: CCB.0067

Font Ugalde, P. Sponsored Research Agreement FER.Funding agency: FUNDACION ESPAÑOLA DE REUMATOLOGIA.Reference: CCB.0080

Collantes Estevez, E. Sponsored Research Agreement ROCHE..Funding agency: ROCHE FARMA, S.A.Reference: CCB.0100

#### **Clinical Trials**

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

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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 rheutmatoid 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. Pl: Dr/a Aguirre Zamorano, Mª Ángeles

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

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 rheutmatoid arthritis with unadequate

response to methotrexate alone. PI: Dr/a Escudero Contreras, Alejandro

0106/13: A multicenter, randomized, double-blind study to compare the effectiveness and safety of continuous treatment with adalimumab vs. discontinuation of treatment with adalimumab as maintenance therapy in patients with axial spondyloarthritis.

PI: Dr/a Collantes Estevez, Eduardo

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 rheutmatoid arthritis.

PI: Dr/a Escudero Contreras, Alejandro

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

PI: Dr/a Collantes Estevez, Eduardo

0054/14:A non-controlled study to assess the effectiveness of tocilizumab in patients with moderate or severe rheumatoid arthritis who are candidate for monotherapy with a biological agent

PI: Dr/a Escudero Contreras, Alejandro

0205/14: A phase 3 randomized, double-blind study assessing the efficacy and safety of PF-06410293 and adalimumab in combination with methotrexate in subjects with moderately to severely active rheumatoid arthritis who have had an inadequate response to methotrexate

PI: Dr/a Escudero Contreras, Alejandro

0253/15: "Phase III study randomized, double-blind, parallel group to demonstrate equivalent efficacy and compare the safety and immunogenicity of GP2015 and Enbrel (authorized in the EU) in patients with active rheumatoid arthritis.

PI: Dr/a Escudero Contreras, Alejandro

\*2953\*: Randomized controlled trial, multicenter, double-blind, etanercept and methotrexate in combination or as monotherapy in patients with psoriatic arthritis.

PI: Dr/a Calvo Gutiérrez, Jerusalem

0220/10: Randomized, double-blind, parallel group placebo-controlled study to evaluate the safety and reduction of signs and symptoms during treatment with tocilizumab (TCZ) compared to placebo in patients with ankylosing spondylitis who have had an inadequate response to treatment study prior to TNF antagonist

PI: Dr/a Collantes Estevez, Eduardo

0219/10: Randomized, double-blind, parallel group placebo-controlled study to evaluate the safety and reduction of signs and symptoms during treatment with tocilizumab (TCZ) compared to placebo in patients with ankylosing spondylitis who have had an inadequate response to treatment study prior to TNF antagonist

PI: Dr/a Collantes Estevez, Eduardo

0363/14: Phase IIb study, multicenrico, randomized, double-blind, ALX-0061 as monotherapy administered subcutaneously in subjects with rheumatoid arthritis with moderate to severe intolerance to methotrexate or for whom continued treatment with medication. PI: Dr/a Escudero Contreras, Alejandro

0029/15: A randomized, double-blind, placebo-controlled study with an open label extension to evaluate the safety and efficacy of brodalumab in subjects with axial spondyloarthritis.

PI: Dr/a Collantes Estevez, Eduardo

0040/15: Phase III, multicenter, randomized, double-blind, placebo-controlled secukinumab (150mg) po subcutaneously with or without a loading dose subcutaneously with or without a loading dose subcutaneously to evaluate the efficacy, safety and tolerability for up to 2 years in patients with active ankylosing spondylitis. PI: Dr/a Collantes Estevez, Eduardo

0146/15 A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of Ustekinumab in the Treatment of Anti-TNF (alpha) Refractory Subjects With Active Radiographic Axial Spondyloarthrit.

PI: Dr/a Collantes Estevez, Eduardo

0064/15: A Phase II Multicenter, Open-Label Extension Study Assessing the Long Term Efficacy and Safety of Subcutaneous ALX-0061 in Subjects with Moderate to Severe Rheumatoid Arthritis who Have Completed One of the Preceding Phase iib Studies with ALX-0061 PI: Dr/a Escudero Contreras, Alejandro

0071/15: Randomized, 16-week, multiphase, double-blind, placebo-controlled study to evaluate the safety, tolerability, and efficacy of fulranumab as adjunctive therapy in subjects with signs and symptoms of osteoarthritis of the hip or knee PI: Dr/a Caracuel Ruiz, Miguel Ángel

1789: Assessing cardiovascular risk and its determinants in patients with rheutmatoid arthritis, ankylosing spondylitis and psoriatic arthritis. PI: Dr/a Collantes Estevez, Eduardo

2031: Immunogenicity in anti-TNF therapies in patients with rheumatic diseases. PI: Dr/a Castro Villegas, Mª Carmen

2219: Beneficial effects of coenzyme Q10 treatment on the mitocondrial dysfunction and oxidative sress associated to athero-thrombosis 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

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

2541: A study of treatment adherence in patients with rheumatoid arthritis receiving subcutaneous administration of biological agents. Arco study

PI: Dr/a Escudero Contreras, Alejandro

2611:GEMA 2 project. Evaluation and management.

PI: Dr/a Escudero Contreras, Alejandro

2687: Assessing and certifying healthcare quality in the clinical management of rheumatoid arthritis according to the Tream to Target (T2T) strategy.

PI: Dr/a Escudero Contreras, Alejandro

2686:ASCORE study about long-term experience with abatacept s.c. in habitual clinical practice.

PI: Dr/a Escudero Contreras, Alejandro

2736 A non-interventional study to assess the effectiveness of Certolizumab Pegol In patients with axial Spondyloa PI: Dr/a Collantes Estevez, Eduardo

2880:Spanish Registry of adverse events in biological and biosimilar therapies in rheumatic illnesses. Phase III

PI: Dr/a Collantes Estevez, Eduardo

## HIGHLIGHTS

**New Therapies in Cancer** 



#### **Team Leaders**

Principal Investigator (PI) Enrique Aranda Aguilar earandaa@seom.org Red Temática de Investigación Cooperativa en Cáncer (RETICC)

**Co-Principal Investigator (Co-PI)** Antonio Rodríguez Ariza *Nicolás Monardes Contract PAIDI CTS-234 Scientific Group (collaborator)* 

**Emerging Researcher (ER)** Juan Rafael de la Haba Rodríguez PAIDI CTS-234 Scientific Group (collaborator)



#### Researchers

Isidoro Barneto Aranda Francisco Manuel Conde Perez Maria Auxiliadora Gomez España Elena Fuentes Vaamonde Estefanía Gómez Rodríguez Antonio Martinez Peinado Maria Jose Méndez Vidal María Jesús Rubio Pérez Carlos Villar Pastor Laura María López Sánchez Gema Mª Varo Sánchez

Pre Doctoral-Researchers (PhD Students y MSc Students) Amanda Cañas Rodríguez Jon Peñarando Saez Marta Toledano Fonseca Araceli Valverde Estepa Other members of the Group (Nursing, Technical, and Administrative Staff) M<sup>a</sup> Ángeles Diaz Diaz Vanesa Hernández Nieto Isabel Jaraba Mezquida Amalia Leña Barranco Maria López Garcia Jacinta Marin Serrano Maria Jose Marin Serrano Rosario Miranda Garcia Sonia Rodriguez De Julian Asunción Aranda Aguila M<sup>a</sup> Pilar Mesa Blanco

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 currently 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 different 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.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Martin M, Loibl S, von Minckwitz G, Morales S, Martinez N, Guerrero A, Anton A, Aktas B, Schoenegg W, Munoz M, Garcia-Saenz JA, Gil M, Ramos M, Margeli M, Carrasco E, Liedtke C, Wachsmann G, Mehta K, De la Haba-Rodriguez JR. Phase III Trial Evaluating the Addition of Bevacizumab to Endocrine Therapy As First-Line Treatment for Advanced Breast Cancer: TheLetrozole/Fulvestrant and Avastin (LEA) Study. JOURNAL OF CLINICAL ON-COLOGY. 2015. 33(9):1045-

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Q: 1 D: 1

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Q: 1

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Q:3

#### Papers in Collaboration

Martín M, Ruiz Simón A, Ruiz Borrego M, Ribelles N, Rodríguez-Lescure Á, Muñoz-Mateu M, González S, Margelí Vila M, Barnadas A, Ramos M, Del Barco Berron S, Jara C, Calvo L, Martínez-Jáñez N, Mendiola Fernández C, Rodríguez CA, Martínez de Dueñas E, Andrés R, Plazaola A, de la Haba-Rodríguez J, López-Vega JM, Adrover E, Ballesteros AI, Santaballa A, Sánchez-Rovira P, Baena-Cañada JM, Casas M, Del Carmen Cámara M, Carrasco EM, Lluch A. Epirubicin plus cyclophosphamide followed by docetaxel versus epirubicin plus docetaxel followed by capecitabine as adjuvant therapy for node-positive early breast cancer: results from the GEICAM/2003-10 Study. J CLIN ON-COL. 2015.10;33(32):3788-95. IF:18,428

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Q: 3

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#### **Reviews in Collaboration**

Suarez C, Puente J, Gallardo E, Mendez-Vidal MJ, Climent MA, Leon L, Olmos D, Garcia del Muro X, Gonzalez-Billalabeitia E, Grande E, Bellmunt J, Mellado B, Maroto P, Gonzalez del Alba A. New advances in genitourinary cancer: evidence gathered in 2014. CANCER AND METASTASIS REVIEWS. 2015.34(3):443-464. IF: 7,234

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#### **Research Funding**

#### National

Aranda Aguilar, E. Red Temática de Investigación Cooperativa Cancer. Funding agency: Institute Carlos III Health (ISCIII). Reference:RD12/0036/0038

De la Haba Rodríguez, J R.Analysis of polymorphisms related to hypertension as a predictor of response to antiogenic treatment in cancer. Funding agency: 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.Funding agency: 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.Funding agency: Institute Carlos III Health (ISCIII). Reference:PI13/00553

Rodríguez Ariza, A.ONCOVER: Detection system of volatile compounds for early diagnosis of lung and colon cancer. Funding agency: Collaboration Agreements between entre el MINECO (FEDER) and the Univeristy of Cordoba for the implementation of a biomedical research project.Reference:CCB.030PM

Aranda Aguilar, E. Design and production of biomimetic microfluidic devices for the devel-

opment of predictors in anti-angiogenic therapy for cancer. Funding agency: FUNDACION SALUD 2000. Reference: FS2000-SEOM-14-01

Aranda Aguilar, E. Using polymorphisms of the angiotensin-converting enzyme to predict response to anti-angiogenic therapy for cancer.Funding agency: Fundación para la innovación y la prospectiva para la salud en españa. Reference: FIPSE2014 001

#### Regional

López Sáncher, M. Protein Study for the identification of new biomarkers in breast cancer stem cells Cancer.Funding Agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Andlusian Reference: PI-0268-2014

Aranda Aguilar, E. Genetic variations associated with hypertension and thrombosis as predictors of response to antiangiogenic therapy in patients with colon cancer.Funding agency: Asociación española contra el cancer.Reference: AECC14/002

#### **Contracts with Companies**

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

Aranda Aguilar, E. Contract for determination of gene activity NRAS .Funding agency: MER-CK, S.L.Reference:PSS.0050

Aranda Aguilar, E. Contract for determination of biomarkers KRAS / NRAS. Funding agency: AMGEN SA.Reference: PSS.0053

Aranda Aguilar, E. Contract for determination of biomarkerr rAS .Funding agency:Treatment of digestive tumours (TTD Group). Reference: PSS.0054

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

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.Funding agency: Roche Farma, S.A.Reference:C-CB.0028

#### **Clinical Trials**

0198/05: An open, multicenter, randomized phase IV-III study to assess the effectiveness of maintenance threatment with capcitabin (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

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 + Exemastane.

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

0234/06: Multicenter, randomized, double-blind placebo-controlled maintenance

treatment study of Abagomovab in patients with epithelial ovarian cancer after complete response to first-line chemotherapy. PI: Dr/a Rubio Pérez, María Jesús

0090/07: An open, multicenter, randomized, phase III study of lapatinib, trastuzumab sequentially administered or administered in combination 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 ofadjuvant chemotherapy indvidualized according to BRCA1 ARNm levels in patients with nonsmall cell lung cancer.

PI: Dr/a Barneto Aranda, Isidoro

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 posmenopausal women with early hormone-receptor positive breast cancer.

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

0144/08: A randomized, phase II clinical study of radiotheraphy, 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

0265/08: Topotecan plus carboplatin vs standard treatment (pacitaxel 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

0048/09: A randomized, phase II study of citabin + Bevacizumab + external radiotherapy versus Capecitabin+external radiotherapy as preoperative treatment in patients with resectable locally advanced rectal cancer. PI: Dr/a Aranda Aguilar, Enrique

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 HER-2/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 contomitantly to a non-anthracycline chemotherapy as neoadjuvant treatment in patients with breast cancer.

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

0002/10: A phase II study of capacitabin-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-lline 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 regimes 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

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, María Jesús

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

PI: Dr/a Aranda Aguilar, Enrique

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

PI: Dr/a Aranda Aguilar, Enrique

0259/10: Open and randomized phase II study of lapatinib plus trastuzumab plus chemotherapy compared to chemotherapy as first-line treatment of women with HER2-positive metastatic breast cancer and p95HER2-positive

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

0152/10: Phase II Clinical Trial uncontrolled. prospective multicenter to determine the clinical benefit and toxicity of Pazopanib, multitarget inhibitor of receptor tyrosine kinase activity (VEGFR-1, -2, -3, PDGFR-beta and Allfa and C-Kit) in patients with advanced ovarian cancer resistant to platinum

PI: Dr/a Rubio Pérez, María Jesús

0268/10: Randomized Phase II clinical trial of docetaxel-carboplatin in combination with niparib (BSI-201) and docetaxel-carboplatin as neoadjuvant treatment of patients with early stage breast cancer and triple-negative phenotype

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

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

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, Maria 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, Maria Jose

0285/11: A randomized phase II trial to assess the efficacy and safety of an individualized neoadjuvant chemotherapy scheme based on the level of brca1 for primary her-2 negative breast cancer (BERNAQ).

PI Dr/a De la Haba Rodríguez, Juan Rafael

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

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

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-233 chloride (Alphardin) in patients with castration-resistant (hormone-resistant) prostate cancer with bone metastasis.

PI: Dr/a Méndez Vidal, María Jose

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

0229/12: A multicenter, single-arm study of trastuzumab emtansine (TDM1) in patients with metastastic 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

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, Maria 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

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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

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 Jesús

0136/13: A multicenter, randomized, double-blind, placebo-controlled, phase III study

of maintenance therapy with Olaparib alone in patients with FIGO stage IIIb-IV ovarian cancer with complete or partial response after platinum-based first-line chemotherapy. PI: Dr/a Rubio Pérez, María Jesús

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

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

0181/13: Ensayo en fase III, aleatorizado, de ganetespib en combinación con docetaxel frente a docetaxel solo en pacientes con adenocarcinoma de pulmón no microcítico avanzado

PI Dr/a Barneto Aranda, Isidoro

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, sinlge-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: Abirateriona 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, Maria 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, Maria Jose

0323/13: El estudio MILO (Inhibidor de la MEK para el Tratamiento del Cáncer Seroso de Ovario de Bajo Grado): Estudio fase 3, multinacional, aleatorizado y abierto de MEK162 frente a la quimioterapia elegida por el médico en pacientes con carcinomas serosos en bajo grado, recurrentes o persistentes de ovario, trompas de Falopio o peritoneales primarios.

PI: Dr/a Rubio Pérez, María Jesús

65/13:Quimioterapia neoadyuvante con nab-paclitaxel en pacientes con cáncer de mama her2 negativo de alto riesgo (ETNA) PI: Dr/a De la Haba Rodríguez, Juan Rafael

82/13: Estudio abierto de afatinib en pacientes no tratados (primera linea) o tratados previamente con qumioterapia con cáncer de pulmón no microcítico (cpnm) localmente avanzado o matastásico portadores de mutación de EGFR.

PI: Dr/a Barneto Aranda, Isidoro

97/13: Estudio de fase 3, aleatorizado y doble ciego para comparar Vintafolida (EC 145) y doxorubicina liposómica pegilada (DLP/Doxil®/Caelvx®) en combinación frente a DLP en pacientes con cáncer de ovario resistente al platino.

PI: Dr/a Rubio Pérez, María Jesús

0215/13: Phase III Palbociclib (PD-0332991) study in combination with Exemestane versus chemotherapy (capecitabine) in patients with Advanced Breast Cancer (ABC) with positive hormone receptors (HR) and negative HER2 inhibitor resistance to Aroma inhibitors PI: Dr/a De la Haba Rodríguez, Juan Rafael

0281/13: Safety study retreatment radium-223 dichloride in castration-resistant prostate cancer patients with bone metastases who received an initial regimen of six doses of radium-223 dichloride 50 kBq / kg every four weeks .

PI: Dr/a Méndez Vidal, Maria Jose

0323/13: The MILO study (inhibitor of MEK for Low Grade Serous Ovarian Cancer Treatment): Phase III, multinational, randomized, open MEK162 versus chemotherapy chosen by the physician in patients with serous carcinomas in low-grade recurrent or persistent ovarian, fallopian tube, or primary peritoneal. PI: Dr/a Rubio Pérez, María Jesús

0026/14: Estudio de fase II abierto, aleatorizado, de tres grupos, de dicloruro de radio-223 de 50kBq/kg en comparación con 80 kBq/kg y 50 kBq/kg en un programa de dosis ampliado en pacientes con cáncer de próstata resistente a la castración con metástasis ósea PI: Dr/a Méndez Vidal, Maria Jose

0036/14: A PHASE II randomized, double-blind study of neoadiuvant letrozole plus GDC-0032 versus letrozole plus placebo in postmenopausal women with er positive/ her2-negative, early stage breast cancer. PI: Dr/a De la Haba Rodríguez, Juan Rafael

0037/14: Phase III, international, randomized trial of more pegylated doxorubicin liposomal trabedectine (DLP) compared to carboplatin plus DLP in patients with ovarian cancer who have experienced progression in the last 6-12 months following treatment.

PI: Dr/a Rubio Pérez, María Jesús

0050/14: An open-label, phase II trial of Orteronel (TAK-700) for metastatic or advanced non-resectable granulosa cell ovarian tumors. GreKo study II.

PI Dr/a Rubio Pérez, María Jesús

0052/14 : A multicenter, randomized, open, controlled, phase III study to assess the efficacy and safety of olaparib alone vs. chemotherapy of choice in patients with metastatic breast cancer with mutations.

PI Dr/a De la Haba Rodríguez, Juan Rafael

0059/14: A phase III study to assess the efficacy of palbociclib (PD-0332991), a cyclin-dependent kinase 4/6 inhibitor in patients with primary HR positive breast cancer and normal HER2 at high risk of relapse following chemotherapy.

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

0065/14: A phase II study of Regorafenib alone in patients with metastatic colorectal cancer with mutations in RAS or BRAF previously treated with FOLFOXIRI PLUS bevacizumab.

PI Dr/a Aranda Aguilar, Enrique

0094/14: A randomised, double-blind, placebo-controlled, multicentre phase ii study to compare the efficacy, safety and tolerability of olaparib versus placebo when given in addition to abiraterone treatment in patients with metastatic castrate-resistant prostate cancer who have received prior chemotherapy containing docetaxel

PI Dr/a Méndez Vidal, María José

0105/14: A multinational, multicenter, phase Il study to assess the efficacy of pertuzumab plus trastuzumab and neoadjuvant chemotherapy based on anthracyclines in patients with locally advanced, inflammatory or early positive her2 breast cancer.

PI Dr/a De la Haba Rodríguez, Juan Rafael

0107/14: A multicenter, randomized, double-blind phase II study to assess the efficacy and safety of RO5520985 plus FOLFOX vs. bevacizumab plus FOLFOX in patients with naive metastatic colorectal cancer. PI Dr/a Aranda Aguilar, Enrique

0124/14: A multicenter, randomized, placebo-controlled, parallel-group phase III study to assess the efficacy and safety of olaparib as neoadjuvant treatment in patients with high-risk HER2 negative breast cancer. PI Dr/a De la Haba Rodríguez, Juan Rafael

0151/14: Assessing an immunomodulatory maintenance therapy in patients with metastatic colorectal cancer with tumor shrinkage during induction therapy. A phase III trial. PI Dr/a Aranda Aguilar, Enrique

0177/14: A multicenter, open-label, single-arm, extension study in patients with solid tumors receiving treatment with bevacizumab in any of the studies sponsorized by F. Hoffmann- La Roche and/or Genentech. PI Dr/a Rubio Pérez, María Jesús

0191/14: A randomized, open-label, phase III study to assess the effectiveness of including denosumab in standard first-line chemotherapy for advanced small cell lung cancer. PI Dr/a Barneto Aranda, Isidoro

0265/14: Phase II of pazopanib and weekly paclitaxel administration in patients with locally advanced metastatic squamous cell carcinoma of the penis or have been previously treated with chemotherapy regimens that include platinum study. PI: Dr/a Méndez Vidal, Maria Jose

0267/14: Phase II multicenter study that analyzes the predictive value of response to ENZALUTAMIDE fusion gene TMPRSS2 -ETS in patients with metastatic CRPC previously treated with chemotherapy.

PI: Dr/a Méndez Vidal, Maria Jose

0270/14: Phase II randomized double-blind study comparing treatment every 3 weeks with carboplatin (AUC 5) + 175 mg / m2 of paclitaxel, with or without concomitant nintedanib and maintenance in advanced or recurrent cervical carcinoma .

PI Dr/a Rubio Pérez, María Jesús

0311/14:Phase III study, open, multicenter, randomized trial to investigate the efficacy and safety of mpdl3280a (anti-pd-l1) compared to chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after fault based regime platinum chemotherapy. PI: Dr/a Méndez Vidal, Maria Jose

0341/14: Phase III trial to compare the safety and efficacy of lapatinib plus trastuzumab plus an aromatase inhibitor (AI) versus trastuzumab plus an AI and against lapatinib plus an AI as first or second line therapy in postmenopausal patients with cancer metastatic breast cancer (MBC) HER2 positive and hormone receptor-positive who have received prior treatment with trastuzumab and endocrine therapy

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

0362/14: Phase II Clinical Trial of Pembrolizumab (MK-3475) in Subjects with Advanced/ Unresectable or Metastatic Urothelial Cancer. PI: Dr/a Méndez Vidal, Maria Jose

0358/14: A multicenter phase ii clinical trial of lurbinectedin (pm01183) in selected advanced solid tumors.

PI Dr/a Rubio Pérez, María Jesús

0309/14:A Randomized, multicenter, open label study os MM-302 plus Trastuzumab vs. chemotherapy pf physician's choice plus trastuzumab in anthracycline naive patients with locally advenced/metastatic HER2-Positive breast cancer

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

0194/14: A multinational randomised, double-blind, placebo-controlled, phase III efficacy and safety study of ODM-201 in men with high-risk non-metastatic castration-resistant prostate cancer.

PI: Dr/a Méndez Vidal, Maria Jose

0005/15: Multicenter, open single-arm safety study of herceptin s.c. in combination with docetaxel PERJETA and in the treatment of patients with advanced HER2 positive (metastatic or locally recurrent) breast cancer. PI: Dr/a De La Haba Rodríguez, Juan Rafael

0055/15:A phase iii, open-label, randomized study of mpdl3280a (anti-pdl1 antibody) in combination with carboplatin - paclitaxel with or without bevacizumab compared with carboplatin -paclitaxel -bevacizumab in chemotherapy naïve patients with stage iv nonsquamous non-small cell lung cancer. PI Dr/a Barneto Aranda, Isidoro

0060/15: A phase iii, open-label, multicenter, randomized study evaluating the efficacy and safety of mpdl3280a (anti-pd-l1 antibody) in combination with carboplatin - paclitaxel or mpdl3280a in combination with carboplatinnab paclitaxel versus carboplatin - nab-paclitaxel in chemotherapy naïve patients with stage iv squamous non-small cell lung cancer PI Dr/a Barneto Aranda, Isidoro

0066/15: Multicenter open-label study, randomized controlled phase III to assess the efficacy and safety of olaparib monotherapy versus chemotherapy with single agent lesson by her doctor in the treatment of ovarian cancer relapsed platinum-sensitive in patients carrying germline mutations BRCA1 /2 PI Dr/a Rubio Pérez, María Jesús

0144/15: A Randomized, Active-Controlled, Partially Blinded, Biomarker Select, Phase III Clinical Trial of Pembrolizumab as Monotherapy and in Combination with Cisplatin+5-Fluorouracil versus Placebo+Cisplatin+5- Fluorouracil as First-Line Treatment in Subjects with Advanced Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma PI: Dr/a Aranda Aguilar, Enrique

0176/15: Phase II. multicenter, randomized. double-blind, parallel group study to compare the efficacy and tolerability of fulvestrant (FaslodexTM) 500 mg with placebo and Fulvestrant (FaslodexTM) 500 mg in combination with PD-0332991 (Palbociclib) as first-line treatment for postmenopausal patients with metastatic breast cancer and hormone receptor positive. FLIPPER study

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

0226/15:Phase 0 study, pharmacokinetic / pharmacodynamic, multicenter, to evaluate the effect inhibitor AZD2281 (olaparib) before surgery in patients concarcinoma with the endometrium located.

PI Dr/a Rubio Pérez, María Jesús

0140/15:Evaluation of the effect of lurbinectedina (PM1183) in cardiac repolarization (QTc duration) in selected patients with solid tumors.

PI Dr/a Rubio Pérez, María Jesús

0045/15:A Randomized, Double-blind, Placebo-Controlled, Phase 2 Study to Assess the Efficacy and Safety of Farletuzumab (MORAb 003) in Combination with Carboplatin plus Paclitaxel or Carboplatin plus Pegylated Liposomal Doxorubicin (PLD) in Subjects with Low CA125 Platinum-Sensitive Ovarian Cancer. PI Dr/a Rubio Pérez, María Jesús

0295/15: Multicenter randomized clinical trial on maintenance of treatment based on biomarkers for first line metastatic colorectal cancer (modul).

PI: Dr/a Aranda Aguilar, Enrique

0026/15:Phase II study randomized, multicenter, open to evaluate the efficacy and safety of palbociclib in combination with fulvestrant or letrozole in patients with HER2 negative metastatic breast cancer, ER + (PAR-SIFAL 1)

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

0019/15 :Phase III, randomized, open MP-DL3280A (anti PD-L1) in combination with BEVAZUMAB compared to sunitinib in patients with advanced untreated renal cell carcinoma. PI: Dr/a Méndez Vidal, Maria Jose

0195/15:Phase III randomized trial with the monoclonal anti-PD-1 pembrolizumab (MK-3475) antibody compared to placebo in patients with NSCLC in early stages after resection and completion of adjuvant treatment reference (PEARLS).

PI Dr/a Barneto Aranda, Isidoro

0020/15: Phase III open randomized clinical trial pembrolizumab (MK-3475) versus paclitaxel in patients with gastric adenocarcinoma or advanced gostroesophagic which have submitted progression after first-line treatment with platinum and fluoropyrimidine PI: Dr/a Aranda Aguilar, Enrique

0192/15: Phase III study, open, randomized trial to investigate the efficacy and safety of Atelizumab (anti-PD-L1 antibody) compared to tratamientode optimal support after adjuvant cisplatin-based chemotherapy in selected PD-L1 with completely resected lung cancer patients in small cell stage IB-IIIA . PI Dr/a Barneto Aranda, Isidoro

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

PI: Dr/a Aranda Aguilar, Enrique

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

2149:Prospective obervational study for the purpose of assessing the impact of the determination of the intrinsic subtypes of breast cancer by PAM50 technology manostring adyuvamant in the use of chemotherapy in women with breast cancer with positive and negative lymph hromonales receptors. NanoString study

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

2178: A post-authorization, 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 carcinome on first-line treatment.

PI: Dr/a Méndez Vidal, Maria Jose

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

PI: Dr/a Méndez Vidal, Maria 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

2456: An epidemiologic study of the natural course and management of locally advanced or metastatic breast cancer: CASCADE study. PI Dr/a De la Haba Rodríguez, Juan Rafael

2571: ROSE project: Management of advanced ovarian cancer in Spain between 2008 and 2010.

PI Dr/a Rubio Pérez, María Jesús

2573: Molecular profiling of gestational breast cancer.

PI Dr/a De la Haba Rodríguez, Juan Rafael

2613/2: Epidemiological prospective observational study for the purpose of evaluating the relationship between burnout syndrome in doctors and chronic pain relief in patients. PI: Dr/a Barneto Aranda, Isidoro

2632: Improving the selection of patients with metastatic colorectal cancer who are candidate for biological therapies: Expanded genotyping using next-generation platforms with different sensitivities.

PI Dr/a Aranda Aguilar, Enrique

2636: A retrospective study to assess the efficacy and safety of targeted therapies following first-line therapy with pazopanib in patients with metastatic renal cell cancer in regular clinical practice.

PI Dr/a Méndez Vidal, María José

2683: Multicenter prospective study of prognostic factors in prostate cancer resistant to castration treated with abiraterone PI Dr/a Méndez Vidal, María José

2684: Multicenter prospective study of prognostic factors in castration resistant treated with docetaxel or cabazitaxel prostate cancer. PI Dr/a Méndez Vidal, María José

2735: Postlicensing retrospective multicenter study to analyze the efficacy and safety of the combination of trabectedin and pequlated liposomal doxorubicin (PLD) for the treatment of patients with recurrent ovarian cancer (ROC) sensitive to platinum, according to data sheet.

PI Dr/a Rubio Pérez, María Jesús

2902: Prospective Development of predictive and prognostic tools for optimization Frontline therapy with Bevacizumab in Patients with Metastatic Breast Cancer HER-2 negative and aggressive illness criteria observational study. PI Dr/a De la Haba Rodríguez, Juan Rafael

2906: Perfil clínico y manejo terapéutico de los pacientes con cáncer de páncreas: Registro en los Servicios Hospitalarios de Oncologia Médica de España

PI Dr/a Aranda Aguilar, Enrique

2928 : European non-interventional, multicenter, prospective study to describe the efficacy of trabectedin + pegylated liposomal doxorubicin (PLD) in the treatment of patients with recurrent ovarian cancer (ROC) according to data sheet despite prior use of an anti-angiogenic drug .

PI Dr/a Rubio Pérez, María Jesús

2930: The T790M mutation detection technology by BEAMing in patients with NSCLC and EGFR mutated in stage IV. LUNGBEAM study.

PI: Dr/a Barneto Aranda, Isidoro

2984: Monitoring by liquid biopsy of patients with metastatic colorectal cancer: comparison of next generation platforms for genotyping of circulating tumor DNA. PI Dr/a Aranda Aguilar, Enrique

## HIGHLIGHTS

## Nephrology. Cell damage in chronic inflammation



#### Researchers

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#### Pre Doctoral-Researchers (PhD Students v MSe Students)

Students y MSc Students) Oscar Andrés Calle Mafla Ney Arencibia Pérez Rodolfo Crespo Montero Elvira Esquivias de Motta Aldo René Hurtarte Sandoval Carlos Luna Ruiz María López Andreu Isabel López López María Victoria Pendón Ruiz de Mier Ana Isabel Robles López Cristian Roberto Rodelo Haad Cristina Rabasco Ruiz María Dolores Salmerón Rodríguez Marina Sánchez-Agesta Martínez Luis González Burdiel

Other members of the Group (Nursing, Technical, and Administrative Staff) Maria José Jimenez Moral M<sup>a</sup> Rosa Moyano García

#### TeamLeaders

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**Co-Principal Investigator (Co-PI)** Julia Carracedo Añón Nicolás Monardes Contract

- 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 produce pathological complications when combined with other low-intensi- ty 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.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Buendia P, Carracedo J, Soriano S, Madueno JA, Ortiz A, Martin-Malo A, Aljama P, Ramirez R.

Klotho Prevents NF B Translocation and Protects Endothelial Cell From Senescence Induced by Uremia.. JOURNALS OF GERON-TOLOGY SERIES A-BIOLOGICAL SCIENCES AND MEDICAL SCIENCES. 2015.70(10):1198-1209.

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- IF: 3,309 Q: 1 D: 1
- Q. I D. I

Buendia P, Montes de Oca A, Madueno JA, Merino A, Martin-Malo A, Aljama P, Ramirez R, Rodriguez M, Carracedo J. Endothelial microparticles mediate inflammation-induced vascular calcification.. FASEB JOURNAL. 2015.29(1):173-181.

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Aguera ML, Martin-Malo A, Alvarez-Lara MA, Garcia-Montemayor VE, Canton P, Soriano S, Aljama P. Efficiency of original versus generic intravenous iron formulations in patients on haemodialysis. PLOS ONE.2015. 10(8):e0135967

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Luna C, Carmona A, Alique M, Carracedo J, Ramirez R. TNF alpha-Damaged-HUVECs Microparticles Modify Endothelial Progenitor

Cell Functional Activity. FRONTIERS IN PHYSI-OLOGY.2015 6:395 IF: 3,534 Q: 1 Espinosa M, Hernandez J, Arenas MD, Carnicer F, Caramelo C, Fabrizi F. Pegylated Interferon (Alone or With Ribavirin) for Chronic Hepatitis C in Haemodialysis Population. KID-NEY & BLOOD PRESSURE RESEARCH.2015. 40(3):258-365. IF: 2,123 Q: 2 Rosati A, Tetta C, Merello JI, Palomares I, Perez-Garcia R, Maduell F, Canaud B, Aljama Garcia P. Cumulativeirondose and resistance to erythropoietin. JOURNAL OF NEPHROLO-GY. 2015.28(5):603-613. IF: 1,454 Q: 3 Pendon-Ruiz de Mier V, Navarro Cabello MD, Martinez Vaquera S, Lopez-Andreu M, Aguera Morales ML, Rodriguez-Benot A, Ruiz Rabelo J, Campos Hernandez P, Requena Tapia MJ, Aljama Garcia P. Index High Insulin Resistance in Pancreas-Kidney Transplantation Contributes to Poor Long-term Survival of the Pancreas Graft.. TRANSPLANTATION PROCEED-INGS.2015. 47(1):117-119. IF: 0,982

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Rodelo-Haad C, Aguera ML, Martinez-Vaquera S, Pendon-Ruiz de Mier MV, Salmeron-Rodriguez MD, Esquivias E, Navarro MD, Rodriguez-Benot A, Aljama P. Tyrosine-phosphatase and glutamate-decarboxylase antibodies after simultaneous pancreas kidney transplantation: do they have an impact on pancreas graft survival?.TRANSPLANTATION PROCEEDINGS. 2015.47(1):107-111. IF: 0,982

Pendon-Ruiz de Mier V, Navarro Cabello MD, Martinez Vaquera S, Lopez-Andreu M, Aguera Morales ML, Rodriguez-Benot A, Aljama Garcia P. Incidence and Long-Term Prognosis of Cancer After Kidney Transplantation. TRANSPLANTATION PROCEEDINGS. 2015.47(9):2618-2621. IF: 0,982

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Garcia Montemayor V, Agueera ML, Rabasco C, Navarro MD, Rodriguez Benot A, Aljama P. Development of Donor-Specific Anti-HLA Antibodies After Restarting Hemodialysis Due to Graft Failure. TRANSPLANTATION PROCEED-INGS. 2015.47(9):2626-2630. IF: 0,982

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#### **Papers In Collaboration**

Cantisan S, Rodelo-Haad C, Paez-Vega A, Nieto A, Vaquero JM, Poyato A, Montejo M, Farinas MC, Rivero A, Solana R, Martin-Malo A, Torre-Cisneros J. FactorsRelated to theDevelopment of CMV-Specific CD8+ T cell Response in CMV-Seropositive Solid Organ-TransplantCandidates. AMERICAN JOURNAL OF TRANSPLANTATION.2015. 15(3):715-722. IF: 5,683

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Rabasco C, Cavero T, Roman E, Rojas-Rivera J, Olea T, Espinosa M, Cabello V, Fernandez-Juarez G, Gonzalez F, Avila A, Baltar JM, Diaz M, Alegre R, Elias S, Anton M, Frutos MA, Pobes A, Blasco M, Martin F, Bernis C, Macias M, Barroso S, de Lorenzo A, Ariceta G, Lopez-Mendoza M, Rivas B, Lopez-Revuelta

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Q: 3

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K, Campistol JM, Mendizabal S, Rodriguez de Cordoba S, Praga M. SpanishGrpStudy Glomerular Dis. Effectiveness of mycophenolatemofetil in C3 glomerulonephritis. KIDNEY INTERNATIONAL. 2015.88(5):1153-1160. IF: 5,683

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Fernandez-Ruiz M, Corrales I, Arias M, Campistol JM, Gimenez E, Crespo J, Lopez-Oliva MO, Beneyto I, Martin-Moreno PL, Llamas-Fuente F, Gutierrez A, Garcia-Alvarez T, Guerra-Rodriguez R, Calvo N, Fernandez-Rodriguez A, Tabernero-Romo JM, Navarro MD, Ramos-Verde A, Aguado JM, Navarro D. OP-ERA Study Grp.Association Between Individual and Combined SNPs in Genes Related to Innate Immunity and Incidence of CMV Infection in Seropositive Kidney Transplant Recipients AMERICAN JOURNAL OF TRANSPLAN-TATION.2015.15 (5);1323-1335 IF: 5,683

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Q3

#### **Reviews In Collaboration**

Alique M, Luna C, Carracedo J, Ramirez R. LDL biochemical modifications: a link between atherosclerosis and aging. FOOD & NUTRITION RESEARCH. 2015.201559: . IF: 2,162 Q: 1

Campistol JM, Arias M, Ariceta G, Blasco M, Espinosa L, Espinosa M, Grinyo JM, Macia M, Mendizabal S, Praga M, Roman E, Torra R, Valdes F, Vilalta R, Rodriguez de Cordoba S. An update for atypical haemolytic uraemic syndrome: Diagnosis and treatment. A consensus document.NEFROLOGIA. 2015.35(5):421-447. IF: 0,982

Q: 3

Q. J

#### **Editorial Material in Collaboration**

Martinez-Castelao A, Gorostidi M, Gorriz JL, Olmo RS, Bover J, Segura J. Reflections on two consensus documents about chronic kidney disease. NEFROLOGIA.2015. 35(2):127-130.

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Q: 3

#### **Research Funding**

#### National

Carracedo Añón, J. Inflammation and calcifying vascular disease in uremia.Funding agency: 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. Funding agency: Institute Carlos III Health (ISCIII). Reference:PI12/01866

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

Martín Malo, A.Artificial Intelligence: a new alternative to analyze the associations among the concentrations of calcium, phosphorous and pth in hemodialisis patients as well as predicting cardiovascular risk Funding agency: Andalusian Progress and Health Foundation (FPS) Reference: PI-0311-2014

#### Regional

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

#### **Clinical Trials**

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 Santamaría 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 Santamaría Olmo, Rafael

0102/13: Efficacy and safety of paricalcitol in reducing secondary hyperparathyroidism after kidney transplantation.

PI: Dr/a Rodríguez Benot, Alberto

0184/13: A phase 2 multicenter, randomized, open label, multiple dose study of intravenous and subcutaneous administration of sotatercept (ACE-011) in replacement of hematopoiesis -stimulating agents in patients with end stage renal nephropathy.

PI: Dr/a Álvarez de Lara Sánchez, Mª Antonia

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 Santamaría 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 kideney disease requiring hemodialysis receiving recombinant human erythropoietin. PI: Dr/a Álvarez de Lara Sánchez, Mª Antonia

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

0239/13: Randomized open and controlled phase III study with active treatment to assess the efficacy and safety of FG-4592 in the treatment of anemia in patients with chronic renal insufficience untreated by dialisis PI: Dr/a Sagrario Soriano, Sagrario

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

0264/13: A randomized, multicenter, open-label, parallel-group study to assess the efficacy and safety of oral administration of BAY 85-3934 and an active comparator (darbepoetinalfa) as maintenance treatment for anemia prior to dialvsis.

PI Dr/a Soriano Cabrera, Sagrario

0265/13: A multicenter, open-label, parallel-group, extension study to assess the efficacy and safety of oral administration of BAY 853934 and an active comparator (darbepoetinalfa) in long-term treatment for anemia prior to stable dialysis.

PI Dr/a Soriano Cabrera, Sagrario

0048/14: A randomized, multicenter, controlled, open-label study to assess the efficacy of sequential treatment with Tacrolimus-Rituximab vs. steroids plus Cyclophosphamide in patients with primary membranous nephropathy.

PI :Dr. Espinosa Hernández; Mario

0145/14: A randomized, double-blind, placebo-controlled, phase II study to assess the efficacy and safety of the ASP0113 vaccine in CMV-seronegative donors.

PI Dr. Navarro Cabello; Maria Dolores

0229/14: A randomized, open, phase III study controlled with an active treatment to assess the efficacy and safety of roxadustat as maintenance therapy for anemia in end-stage renal failure patients receiving stable dialysis. PI Dr/a Alvarez De Lara Sánchez; Maria Antonia

0024/15Multicentered open randomized study of two parallel groups to assess the efficacy and safety of Envarsus compared to tacrolimus used in accordance with current clinical practice as initial maintenance in-patient treatment.

PI Dr/a Rodríguez Benot, Alberto Manuel

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, Mª 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 Santamaría Olmo, Rafael

2079: A multinational, multicenter, observational, non-interventional study of patients with atypical hemolytic uremic syndrome (SHUA register).

PI Dr/a Espinosa Hernández; Mario

2391: A multicenter, retrospective study to determine the factors affecting survival in patients who have received pancreas transplants. EFISPAN study

PI Dr/a Navarro Cabello; Maria Dolores

2591: ADAPTATION: Observational Study of Correction of Anaemia with Darbepoetin Alfa at Monthly Dose Frequency in EU and Australian patients with Chronic Kidney Disease not on Dialisis).

PI:Dr/a Soriano Cabrera; Sagrario

2612: A Long-term follow-up study involving adults who received kidney and liver allografts and had previously taken part in a trial with Tacrolimus (Advagraft). A multicenter, non-interventional, post-authorization study. PI Dr/a Rodríguez Benot; Alberto Manuel

## HIGHLIGHTS

**Hormones and Cancer** 



Researchers Antonio Jesús Martínez Fuentes

Post-Doctoral Researchers Manuel D. Gahete Ortiz Alejandro Ibáñez Costa

#### PhD Researchers

Cristóbal José Blanco Acevedo André Cabral Morais Sarmento Borges Mercedes del Río Moreno Daniel Hormaechea Agulla Jesús Moreno Fernández David Rincón Fernández-Pacheco Sergio Pedraza Arévalo Ramón Santamaría Peiteado Álvaro Toledano Delgado Mª Carmen Vázquez Borrego Alicia Villa Osaba Pre Doctoral-Researchers (PhD Students y MSc Students) Emilia Mª Alors Pérez Patricia Borges de Souza Antonio Carlos Fuentes Fayos María del Señor Gómez Marín Vicente Herrero Aguayo Juan Manuel Jiménez Vacas Bethan Mansfield Mª Eugenia Prados González Virginia Ruiz Murillo

Other members of the Group (Nursing, Technical, and Administrative Staff) Esther Rivero Cortés Fernando López López

#### **Team Leaders**

Principal Investigator (PI) Justo P. Castaño Fuentes justo@uco.es IMIBIC's Scientific Director CIBER on Obesity and Nutrition (CI-BERobn) (Collaborator)

**Co-Principal Investigator (Co-PI)** Francisco Gracia Navarro *PAIDI BIO-139 Scientific Group* 

**Co-Principal Investigator (Co-PI)** Raúl M. Luque Huertas *CIBER on Obesity and Nutrition (CI-BERobn) (Collaborator)* 

Our group investigates the cellular and molecular mechanisms underlying the physiological regulation neuroendocrine-metabolic processes and their dysfunctions in tumours and cancer. Special emphasis is dedicated to the role played by key neuropeptide-receptor systems and their receptors, and to emerging molecular regulatory mechanisms in cancer such as alternative splicing. From original studies of pituitary somatotropes producing 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 neuro-endocrine cell types (e.g. corticotropes, gonadotropes, pancreatic beta cells, prostate and breast cells, etc.) and the global role of these molecules in metabolic homeostasis and the development of tumour pathologies, including pituitary and neuroendocrine tumors, and prostate and breast cancer, etc.

To achieve these aims, we use a wide range of techniques, including primary cultures of normal and tumour cells, cell lines, genetically modified animals, hormone secretion measurements, quantification of second messengers, measurements of protein and gene expression levels, dynamics of association/ dissociation studies and membrane protein trafficking using FRET, confocal microscopy in living cells, etc. Our studies have led to the discovery and characterization of new ligands, receptors, functions and mechanisms of action for different neuroendocrine-metabolic signals and drugs involved in the control of hormone secretion, tumorigenesis, or cell survival and death in various normal and pathological cell types (e.g. pituitary tumours, breast and prostate cancer, diabetes, obesity), with the ultimate aim of contributing to the future design of innovative therapeutic strategies.

#### **Keywords**

Cellular and Molecular Endocrinology and Endocrine Oncology; Hypothalamus; Pituitary; Somatostatin, cortistatin, ghrelin, GHRH, kisspeptins and their receptors; Expression and secretion of hormones (GH, PRL, IGF-I, insulin) and intracellular signalling pathways; Regulation of the somatotropic axes; Obesity and Diabetes; Pituitary tumours; Neuroendocrine tumors; Prostate cancer; Breast cancer.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Lugue RM, Sampedro-Nunez M, Gahete MD, Ramos-Levi A, Ibanez-Costa A, Rivero-Cortes E, Serrano-Somavilla A, Adrados M, Culler MD, Castaño JP, Marazuela M. In1-ghrelin, a splice variant of ghrelin gene, is associated with the evolution and aggressiveness of human neuroendocrine tumors: Evidence from clinical, cellular and molecular parameters. ONCOTARGET.2015. 6(23):19619-19633. IF: 6.359

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Ibáñez-Costa A, Gahete MD, Rivero-Cortes E, Rincón-Fernández D, Nelson R, Beltrán M, de la Riva A, Japón M A, Venegas-Moreno E, Gálvez MA, García-Arnés JA, Soto-Moreno A, Morgan J, Tsomaia N, Culler MD, Diéguez C, Castaño JP, Luque RM. In1-ghrelin splicing variant is overexpressed in pituitary adenomas and increases their aggressive features. SCIENTIFIC REPORTS.2015. 5:8714.

IF: 5,578 Q: 1 D: 1

Luque RM, Ibáñez-Costa A, Neto LV, Taboada GF, Hormaechea-Agulla D, Kasuki L, Venegas-Moreno E, Moreno-Carazo A, Gálvez MÁ, Soto-Moreno A, Kineman RD, Culler MD, Gahete MD, Gadelha MR, Castaño JP. Truncated somatostatin receptor variant sst5TMD4 confers aggressive features (proliferation, invasion and reduced octreotide response) to somatotropinomas. CANCER LETTERS. 2015.359(2):229-306. IF: 5.621

Villa-Osaba A, Gahete MD, Córdoba-Chacón J, de Lecea L, Pozo-Salas AI, Delgado-Lista FJ, Álvarez-Benito M, López-Miranda J, Luque RM, Castaño JP. Obesity alters gene expression for GH/IGF-I axis in mouse mammary fat pads: Differential role of cortistatin and somatostatin. PLOS ONE. 2015.10(3):e0120955. IF: 3,234

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Ibáñez-Costa A. Córdoba-Chacon J. Gahete MD, Kineman RD, Castaño JP, Luque RM. Melatonin regulates somatotrope and lactotrope function through common and distinct signaling pathways in culture primary pituitary cells from female primates. ENDOCRINOLO-GY.2015. 156(3):1100-1110. IF: 4,503

Q: 1

Pedraza-Arévalo S, Córdoba-Chacón J, Pozo-Salas AI, Lopez FL, de Lecea L, Gahete MD, Castaño JP, Luque RM. Not so giants: Mice lacking both somatostatin and cortistatin have high GH levels but show no changes in growth rate or IGF-1 levels. ENDOCRINOL-OGY. 2015.156(6):1958-1964. IF: 4,503 Q: 1

#### **Papers In Collaboration**

Yubero-Serrano EM, Delgado-Lista J, Tierney AC, Perez-Martinez P, Garcia-Rios A, Alcala-Diaz JF, Castaño JP, Tinahones FJ, Drevon CA, Defoort C, Blaak EE, Dembinska-Kiec A, Riserus U, Lovegrove JA, Perez-Jimenez F, Roche HM, Lopez-Miranda J. Insulin resistance determines a differential response to changes in dietary fat modification on metabolic syndrome risk factors: the LIPGENE study. AMERICAN JOURNAL OF CLINICAL

NUTRITION. 2015. 102(6):1509-1517. IF: 6.77 Q: 1 D: 1

Martin-Rodríguez JF, Muñoz-Bravo JL. Ibáñez-Costa A, Fernández-Maza L, Balcerzyk M, Leal-Campanario R, Luque RM, Castaño JP, Venegas-Moreno E, Soto-Moreno A, Leal-Cerro A, Cano DA. Molecular characterization of growth hormone-producing tumors in the GC rat model of acromegaly. SCIENTIFIC REPORTS. 2015. 5:16298.

IF: 5,578 Q: 1 D: 1

Sánchez-Garrido MA, Ruiz-Pino F, Manfredi-Lozano M, Leon S, Heras V, Castellano JM, Castaño JP, Luque RM, Vazquez MJ, Roa J, Romero-Ruiz A, Diéguez C, Pinilla L, Tena-Sempere M. Metabolic and gonadotropic impact of sequential obesogenic insults in the female: Influence of the loss of ovarian secretion. ENDO-CRINOLOGY. 2015.156(8):2984-2998. IF: 4,503

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Garcés MF, Vallejo SA, Sánchez E, Palomino-Palomino MA, Leal LG, Angel-Muller E, Díaz-Cruz LA, Ruiz-Parra AI, González-Clavijo AM, Castaño JP, Abba M, Lacunza E, Diéguez C, Nogueiras R, Caminos JE. Longitudinal analysis of maternal serum Follistatin concentration in normal pregnancy and preeclampsia. CLINICAL ENDOCRINOLOGY. 2015.83(2):229-235.

IF: 3,457 Q: 2

Molè D, Gentilin E, Ibañez-Costa A, Gagliano T, Gahete MD, Tagliati F, Rossi R, Pelizzo MR, Pansini G, Luque RM, Castaño JP, degliUberti E, Zatelli MC. The expression of the truncated isoform of somatostatin receptor subtype 5

Q: 1

associates with aggressiveness in medullary thyroid carcinoma cells. ENDOCRINE.2015. 50(2):442-452. IF: 3.878

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Q: 4

Cordoba-Chacon J, Majumdar N, Pokala NK, Gahete MD, Kineman RD. Is let insulin content and release are increased in male mice with elevated endogenous GH and IGF-I, without evidence of systemic insulin resistance or alterations in beta-cell mass. GROWTH HOR-MONE & IGF RESEARCH. 25(4):189-195. IF: 1,407

Q: 4

#### **Research Funding**

#### Regional

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 (sst5T-MD4/5) in pituitary tumors and in breast and prostate cancer. Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0639-2012

Gahete Ortiz, M D. Determining the molecular footprint of predictive splicing in the development of prostate cancer and application in the diagnosis and treatment of the disease. Funding agency:Regional Ministry of Health and Social Policy (CISPS). Reference: PI-0541-2013

Luque Huertas, RM. Therapeutic opportunities of somatostatin, ghrelin and their receptors in pituitary pathologies: identification of novel molecular targets and contribution of the mechanism of alternative splicing. Funding agency: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: CTS1406

#### National

Castaño Fuentes, JP. Role of alternative splicing and its (dys)regulation in tumoral pathologies and cancer: diagnostic and therapeutic potential. Funding agency: Ministry of Economy and Competitiveness (MINECO).Reference: BFU2013-43282-R

Luque Huertas, RM. Molecular, cellular, Endocrine-Metabolic and inflammatory factors involved in the pathological interaction between obesity and prostate cancer. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI13/00651

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. Funding agency: Merck Serono Research Grants. Reference: MERCK Castaño Fuentes, JP; Martínez Fuentes, AJ. Characterization of gene expression in gastro-entero-pancreatic neuroendocrine tumors and its correlation with clinical aspects and behavior of the tumor. Funding agency: Grupo Español de Tumores Neuroendocrinos (GETNE). Reference: GETNE

Castaño Fuentes, JP (This project was funded as a collaborative initiative among different research groups). Detection system for volatile compounds for the precocious diagnostic of cancer (Project ONCOVER). Funding agency: MINECO/FEDER/UCO

López Miranda, J (This project was funded as a collaborative initiative among different research groups). Early predictors and causes of loss of phenotypic flexibility as individual risk factor of metabolic disease: towards a personalized medicine (FLEXI-MET). Funding agency: Institute Carlos III Health (ISCIII). REF: PIE/1400005

#### **Contracts with Companies**

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

## HIGHLIGHTS

### Nutrigenomics. Metabolic syndrome



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**Co- Principals Investigators (CO-PI)** Yolanda Almadén Peña Javier Delgado Lista Pablo Pérez Martínez

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#### Other members of the Group (Nursing, Dietists, Technical, and Administrative Staff)

Rosario Carreras Calero Pilar Gómez Arcas Beatriz Lucena Porras Vanesa Navarro Martos José Andrés Morales Martínez Gracia Mª Quintana Navarro Isabel Pérez Corral

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 and gut microbiota on atherogenic mechanisms such as oxidative stress, inflammation, endothelial function, hemostasis, cellular signalling mechanisms and the activation of genes involved in atherogenesis. Finally we have ongoing a clinical trial to rest the comparative effects of two healthy directs on clinical events in a coronary heart disease population.

#### **Keywords**

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

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Yubero-Serrano EM, Delgado-Lista J, Tierney AC, Perez-Martinez P, Garcia-Rios A, Alcala-Diaz JF, Castano JP, Tinahones FJ, Drevon CA, Defoort C, Blaak EE, Dembinska-Kiec A, Riserus U, Lovegrove JA, Perez-Jimenez F, Roche HM, Lopez-Miranda J. Insulin resistance determines a differential response to changes in dietary fat modification on metabolic syndrome risk factors: the LIPGENE study. AMERICAN JOURNAL OF CLINICAL NUTRITION.2015. 102(6):1509-1517.

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Gonzalez-Guardia L, Yubero-Serrano EM, Delgado-Lista J, Perez-Martinez P, Garcia-Rios A, Marin C, Camargo A, Delgado-Casado N, Roche HM, Perez-Jimenez F, Brennan L, Lopez-Miranda J. Effects of the Mediterranean diet supplemented with coenzyme q10 on metabolomic profiles in elderly men and women. JOURNALS OF GERONTOLOGY SE-RIES A-BIOLOGICAL SCIENCES AND MEDICAL SCIENCES.2015. 70(1):78-84.

IF: 5,416

Q: 1 D: 1

Gomez-Delgado F, Garcia-Rios A, Alcala-Diaz JF, Rangel-Zuñiga O, Delgado-Lista J, Yubero-Serrano EM, Lopez-Moreno J, Tinahones FJ, Ordovas JM, Garaulet M,Lopez-Miranda J, Perez-Martinez P. Chronic consumption of a low-fat diet improves cardiometabolic risk factors according to the CLOCK gene in patients with coronary heart disease. MOLECULAR NUTRITION & FOOD RE-SEARCH.2015;59(12):2556-64. IF :4,603 Q: 1 D: 1

Fuentes F, Alcala-Diaz JF, Watts GF, Alonso R, Muniz O, Diaz-Diaz JL, Mata N, Munoz-Torrero JF, Sanchez Brea A, Galiana J, Figueras R, Aguado R, Piedecausa M, Cepeda JM, Vidal JI, Rodriguez-Cantalejo F, Lopez-Miranda J, Mata P. Statins do not increase the risk of developing type 2 diabetes in familial hypercholesterolemia: The SAFEHEART study. INTER-NATIONAL JOURNAL OF CARDIOLOGY.2015. 79-84

- IF: 4,036
- Q: 1

Montero-Perez-Barquero M, Manzano L, Formiga F, Roughton M, Coats A, Rodriguez-Artalejo F, Diez-Manglano J, Bettencourt P, Llacer P, Flather M. RICA investigators. Utility of the SENIORS elderly heart failure risk model applied to the RICA registry of acute heart failure. INTERNATIONAL JOURNAL OF CARDIOLOGY.2015. 182:449-453.

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Yubero-Serrano EM, Woodward M, Poretsky L, Vlassara H, Striker Gary E. AGE-less Study Grp. Effects of Sevelamer Carbonate on Advanced Glycation End Products and Antioxidant/Pro-Oxidant Status in Patients with Diabetic Kidney Disease. CLINICAL JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLO-GY.2015. 10(5):759-766. IF: 4.613

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Rangel-Zuniga OA, Camargo A, Marin C, Pena-Orihuela P, Perez-Martinez P, Delgado-Lista J, Gonzalez-Guardia L, Yubero-Serrano EM, Tinahones FJ, Malagon MM, Perez-Jimenez F, Roche HM, Lopez-Miranda J . Proteome from patients with metabolic syndrome is regulated by quantity and quality of dietary lipids. BMC GENOMICS.2015. 16: 509

IF: 3,986

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Cerrada JC, Sanchez FJC, Perez-Calvo JI, Manzano L, Formiga F, Bodas OA, Conde A, Quiros R, Bocanegra CP, Montero-Perez-Barquero M. RICA Investigators. Prognostic value of glomerular filtration rate estimation equations in acute heart failure with preserved versus reduced ejection fraction. INTERNATIONAL JOURNAL OF CLINICAL PRACTICE.2015. 69(8):829-839. IF: 2,566

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Herencia C, Rodriguez-Ortiz ME, Munoz-Castaneda JR, Martinez-Moreno JM, Canalejo R, Montes de Oca A, Diaz-Tocados JM, Peralbo-Santaella E, Marin C, Canalejo A, Rodriguez M, Almaden Y. Angiotensin II prevents calcification in vascular smooth muscle cells by enhancing magnesium influx. EUROPE-AN JOURNAL OF CLINICAL INVESTIGATION. 2015.45(11):1129-1144.

IF: 2,734

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IF: 1,04

Q: 4

#### **Research Funding**

#### National

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

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. Funding agency: 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. Funding agency: Institute Carlos III Health (ISCIII.)Reference:-PI13/00185

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

García Rios, A. PREDIMED+DM: Effect of a hypocaloric Mediterranean diet and physical activity promotion on the prevention of type 2 diabetes mellitus in subjects with the Metabolic Syndrome. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI14/00618

Almaden Peña, Y. Association between mineral metabolism parameters and cardiovascular Disease. Influence of the Mediterranean diet .Funding agency: Institute Carlos III Health (ISCIII).Reference: PI14/00872

López Miranda J. Early predictors and causes of loss of phenotypic flexibility as individual risk factor of metabolic disease: towards a personalized medicine (FLEXI-MET) .Funding agency: Institute Carlos III Health (ISCIII).Reference: PIE14/00005

López Miranda, J.(CO-IP) Understanding obesity (Ob), metabolic syndrome (MetS), type 2 diabetes (T2DM) and fatty liver disease (FL): a multidisciplinary approach. Funding agency: Institute Carlos III Health (ISCIII).Reference: PIE 14/00031

Pérez Jiménez, F. Formalization of Economic Compensation Agreement. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO) Reference MCI.CIBEROBN

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. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO) .Reference:AGL2012-39615

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. Funding agency: Fundacion Salud 2000. Reference: MS01-2011

Hinojosa Marin, C. Interaction between diet and molecular mechanisms involved on endothelial dysfunction in patients with cardiovascular disease. Funding agency: Institute Carlos III Health (ISCIII).Reference: CP11/00185

Camargo A .Microbiota, sex hormones, and cardiovascular disease. Funding agency: Institute Carlos III Health (ISCIII).Reference:CP14/00114

#### Regional

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. Funding agency: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference CVI-7450

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

#### International

Lopez Miranda, J.(NUTRITECH). Application on new technologies and methods in nutrition research-the example of phenotypic flexibility. Funding agency: European Comission / 7pm- Programa Cooperación -Tema Salud-Single Stage- 2011.Reference: FP7-289511

#### **Contracts with Companies**

López Miranda, J. Astrazeneca agreement. Funding agency: Astrazeneca Farmaceutica Spain S.A. Reference:CCB.0046

Montero Pérez-Barquero, M. Pzifer agreement. Funding agency: Pfizer, S.L.U. Reference: CCB.0070

Pérez Jiménez, F. Gendiag agreement. Funding agency: Gendiag Exe, S.L. Reference: 12011136

Pérez Jiménez, F. Nutritional Intervention Study to assess the evolution of health benefits derived from the consumption of hake in populations at high cardiovascular risk. PESCANOVA project. Funding agency: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. Funding agency: Tno Earth, Enviromental and LS. Reference: PSS.0014

Montero Pérez-Barquero, M. Laboratorios Servier Agreement. Funding agency: Laboratorios Servier, S.L. Reference: PSS.0051

Pérez Jiménez, F .Sponsored Agreement with Biomaslinic. Funding agency: Biomaslinic S.L. Reference: PSS.0070

#### **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

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, José

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, José

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. Pl: Dr/a López Miranda, José

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

0314/12: EA randomized, double-blind, placebo-controlled, parallel-group trial to assess the effect of SAR236553/REGN727 on the occurrence of cardiovascular events in patients who recently had acute coronary syndrome.

PI: Dr/a Fuentes 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/fluricasone. 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 hypercholestorolemia.

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, José

0205/13: An open, extension study of the trials EFC12492, R727-CL-1112, EFC12732 and LTS11717 to assess the safety and long-term efficacy of Alirocumab in patients with heterozygous familial hypercholesterolemia. PI: Dr/a Fuentes Jiménez, Francisco

0216/13: A randomized, double-blind, parallel-group, active-control trial to assess the efficacy and safety of LCZ696 versus Valsartan on morbidity and mortality in patients with heart failure NYHA Class II-IV)

PI: Dr/a Montero Pérez-Barquero, Manuel

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 hypercholestorolemia.

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 hypercholestorolemia.

PI: Dr/a Pérez Martínez, Pablo

#### 0005

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 Canaglifozin in renal

events in adult subjects with Diabetes Mellitus Type 2.

PI: Dr/a Fuentes Jiménez, Francisco

0197/15: Multinational, Multicenter, Single Group and Open Study to document the safety, tolerability and effect on atherogenic lipoproteins Alirocumab in High-Risk Cardiovascular Patients with Severe Hypercholesterolemia not adequately controlled with Conventional Treatments Lipid PI: Dr/a López Miranda, José

0090/15: Randomized, double-blind, multicenter, placebo-controlled, parallel group to describe the efficacy, safety and tolerability of evolocumab administered for 24 weeks, as adjunctive therapy of diet and lipid-lowering therapy in reducing the colesterolligado to LDL density (LDL-C) in pediatric subjects 10-17 years of age with heterozygous familial hypercholesterolemia (HeFH).

PI: Dr/a Fuentes Jiménez, Francisco

0049/15:Long-term study, randomized, double-blind, placebo-controlled trial to determine the effect of albiglutide, when added to standard glucose-lowering therapy on cardiovascular events in patients with Type 2 Diabetes Mellitus

PI: Dr/a Delgado Lista, Francisco Javier

2053: Xalia-Xarelto ® for initial long-term anticoagulation in venous thromboembolism (VTE).

PI: Dr/a Blanco Molina, Mª Ángeles

2488: Protocol Gaucher Registry PI: Dr/a Fernández De La Puebla Giménez, Rafael Ángel

2566: Validating the ACTS questionnaire for patients with atrial fibrillation treated with oral anticoagulants in Internal Medicine and Neurology units in Spain. ALADI study. PI: Dr/a Montero Pérez-Barquero, Manuel

2615/2: General, long-term registry of atrial fibrilation. EORP registry.

PI: Dr/a Montero Pérez-Barquero, Manuel

2717: Hydroxytyrosol influence on lipid profile, the metabolism of carbohydrates and endothelial function in individuals over 65 years of age.

PI: Dr/ Pérez Jiménez, Francisco

2766: Study tracked the clinical practice of the recommendation on the treatment with oral anticoagulants (OACs) in elderly patients with atrial fibrillation. ESPARTA study PI: Dr/a López Jimenez, Luciano

2773: Hyperglycemia from stress as a prognostic marker in patients hospitalized for cardio-respiratory processes in internal medicine.

PI: Dr/a Montero Pérez-Barquero, Manuel

2847:Global anticoagulant registry in the field observing treatment and putcomes in patients with treated acute venous thromboembolic events in the real world.

PI: Dr/a López Jimenez, Luciano

### HIGHLIGHTS

### Hormonal Regulation of Energy Balance, Puberty and Reproduction



#### **Team Leader**

Principal Investigator (PI) Manuel Tena-Sempere filtesem@uco.es IMIBIC Deputy Scientific Director Group leader: CIBER Obesity and Nutrition (CIBERobn) Responsible researcher: PAIDI BIO-310 Scientific Group

#### Researchers Francisco Gaytan Luna Leonor Pinilla Jurado Antonio Romero Ruiz

#### **Post- Doctoral Researchers**

Marisol Avendaño Herrador Juan Manuel Castellanos Rodríguez Silvia León Téllez María Manfredi Lozano Juan Roa Rivas Miguel Sánchez-Garrido Nogueras María Jesús Vázquez Villar Students y MSc Students) Violeta Heras Domínguez Alexia Barroso Romero Daniela Fernandois Vicencio (Visiting fellow) Leman Gizem Erkan (Visiting fellow) Bárbara Lobato Delgado Carmen Mª López Rodríguez Cecilia Mª Perdices López Francisco Ruiz Pino José Manuel Ruíz Rodríguez Encarnación Torres Jiménez Inmaculada Velasco Aguayo

Pre Doctoral-Researchers (PhD

Other members of the Group (Nursing, Technical, and Administrative Staff) Roció Onieva Jimenez Ana Belén Pedraza Casado Mª Jesús Sánchez Tapia Ana Rodríguez Sánchez

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. In this context, we have made substantial contributions to the characterization of the physiological role, mechanisms of action, and pathophysiological and therapeutic implications of kisspeptins in the control of puberty, ovulation, the secretion of gonadotropins and the metabolic regulation of fertility. In addition, we have characterized the actions of different gastrointestinal hormones (ghrelin, PYY) and adipose tissue factors (leptin, resistin, adiponectin) in the regulation of puberty and reproductive function. Additionally, we have defined the role in the reproductive axis of different neuropeptides (GALP, neuromedins, 26/43RFa, VGF) primarily involved in the control of food intake. More recently, we have undertaken research activities on the regulatory roles of microRNAs and cellular energy sensors in the control of puberty, fertility and metabolism. Even if our research activity is basic in nature, our projects have allowed us to identify novel mechanisms of action and pharmacological effects of practical interest for a broad group of neuroendocrine factors, with high potential for translation in the context of increasingly prevalent diseases such as obesity and other body weight disorders, changes of puberty and various forms of infertility. In addition, translational studies in the fields of gynaecology, urology and paediatrics have been recently initiated in close collaboration with clinical groups within IMIBIC.

#### **Keywords**

Body weight; obesity; puberty; fertility; kisspeptins; GPR54; gonadotropins; GnRH; leptin; ghrelin; adipokines; neuro-peptides; microRNAs; Polycystic ovary syndrome (PCOS).

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Lopez M, Tena-Sempere M. Estrogens and the control of energy homeostasis: a brain perspective. TRENDS IN ENDOCRINOLOGY AND METABOLISM. 2015.26(8):411-421. IF: 9,392

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Sangiao-Alvarellos S, Manfredi-Lozano M, Ruiz-Pino F, Leon S, Morales C, Cordido F, Gaytan F, Pinilla L, Tena-Sempere M. Testicular expression of the Lin28/let-7 system: Hormonal regulation and changes during postnatal maturation and after manipulations of puberty. SCIENTIFIC REPORTS. 2015.5: 15683.

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Sanchez-Garrido MA, Ruiz-Pino F, Manfredi-Lozano M, Leon S, Heras V, Castellano JM, Castano JP, Luque RM, Vazquez MJ, Roa J, Romero-Ruiz A, Dieguez C, Pinilla L, Tena-Sempere M. Metabolic and Gonadotropic Impact of Sequential Obesogenic Insults in the Female: Influence of the Loss of Ovarian Secretion. ENDOCRINOLOGY. 2015.156(8):2984-2998.

IF: 4,503

Ruiz-Pino F, Garcia-Galiano D, Manfredi-Lozano M, Leon S, Sanchez-Garrido MA, Roa J, Pinilla L, Navarro VM, Tena-Sempere M. Effects and Interactions of Tachykinins and Dynorphin on FSH and LH Secretion in Developing and Adult Rats. ENDOCRINOLOGY. 2015.156(2):576-588.

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Gaytan F, Morales C, Leon S, Garcia-Galiano D, Roa J, Tena-Sempere M. Crowding and Follicular Fate: Spatial Determinants of Follicular Reserve and Activation of Follicular Growth in the Mammalian Ovary. PLOS ONE.2015. 10(12): :e0144099 IF: 3,234 Q: 1 Vazquez MJ, Romero-Ruiz A, Tena-Sempere M. Roles of Leptin in Reproduction, Pregnancy and Polycystic Ovary Syndrome: Consensus Knowledge and Recent Developments. METABOLISM-CLINICAL AND EXPERIMEN-TAL.2015. 64(1):79-91. IF: 3,894 Q: 2

#### Papers in Collaboration

Boehm U, Bouloux PM, Dattani MT, de Roux N, Dode C, Dunkel L, Dwyer AA, Giacobini P, Hardelin JP, Juul A, Maghnie M, Pitteloud N, Prevot V, Raivio T, Tena-Sempere M, Quinton R, Young J. EXPERT CONSENSUS DOCUMENT European Consensus Statement on congenital hypogonadotropic hypogonadism-pathogenesis, diagnosis and treatment. NATURE REVIEWS ENDO-CRINOLOGY.2015. 11(9):547-564. IF: 13,281

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Epigenetic regulation of puberty via Zinc finger protein-mediated transcriptional repression. NATURE COMMUNICATIONS.2015. 6(10195). IF: 11,470

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Ferno J, Senaris R, Dieguez, C, Tena-Sempere, M, Lopez M. Orexins (hypocretins) and energy balance: More than feeding. MOLECU-LAR AND CELLULAR ENDOCRINOLOGY.2015. 418;17-26. IF: 4,505

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Mela V, Diaz F, Lopez-Rodriguez AB, Vazquez MJ, Gertler A, Argente J, Tena-Sempere M, Viveros MP, Chowen JA. Blockage of the Neonatal Leptin Surge Affects the Gene Expression of Growth Factors, Glial Proteins, and Neuropeptides Involved in the Control of Metabolism and Reproduction in Peripubertal Male and Female Rats. ENDOCRINOLOGY. 2015.156(7):2571-2581. IF: 4,503

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Castro-Gonzalez D, Fuente-Martin E, Sanchez-Garrido MA, Argente-Arizon P, Tena-Sempere M, Barrios V, Chowen JA, Argente J. Increased prepubertal body weight enhances leptin sensitivity in proopiomelanocortin and neuropeptide y neurons before puberty onset in female rats. ENDOCRINOLOGY. 2015. 156(4):1272-1282. IF: 4,503

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Martinez de Morentin PB, Lage R, Gonzalez-Garcia I, Ruiz-Pino F, Martins L, Fernandez-Mallo D, Gallego R, Ferno J, Senaris R, Saha AK, Tovar S, Dieguez C, Nogueiras R, Tena-Sempere M, Lopez M. Pregnancy Induces Resistance to the Anorectic Effect of Hypothalamic Malonyl - CoA and the Thermogenic Effect of Hypothalamic AMPK Inhibition in Female Rats. ENDOCRINOLOGY. 2015. 156(3):947-960.

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IF: 5,578 Q: 1 D: 1

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Pinto FM, Bello AR, Gallardo-Castro M, Valladares F, Almeida TA, Tena-Sempere M, Candenas L. Analysis of the Expression of Tachykinins and Tachykinin Receptors in the Rat Uterus During Early Pregnancy. BIOLOGY OF REPRODUCTION.2015. 93(2): 51 IF: 3,318

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#### **Research Funding**

#### Regional

Tena-Sempere, M. MicroRNAs and reproductive health: Mechanistic and Translational studies. Funding agency: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: FQM1943

Vázquez Villar, MJ. Etiopatogenic roles and diagnostic implications of microRNAs in the Polycystic Ovary Syndrome. Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0186-2013

#### National

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

Tena Sempere, M. MicroRNAs and Polycystic Ovary Syndrome: Search of novel biomarkers for improvement of diagnosis. Funding agency: FUNDANCION SALUD 2000. Reference: 13-MS-005

Tena-Sempere, M. Dissecting the roles of kisspeptin pathways as major determinants of puberty: Novel interactions, regulatory mechanisms and metabolic implications. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: BFU2014-57581-P

López Miranda, J (This project was funded as a collaborative initiative among different research groups). Early predictors and causes of loss of phenotypic flexibility as individual risk factor of metabolic disease: towards a personalized medicine (FLEXI-MET). Funding agency: Institute Carlos III Health (ISCIII). REF: PIE/1400005

Castellano Rodríguez, JM (Tutor: M. Tena-Sempere). Overweight-induced hypogonadism as an inductive factor of metabolic comorbidities associated with overweight: Contribution of epigenetic mechanisms. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: SAF 2014-56995 JIN

#### International

Tena-Sempere, M. Epi-puberty-metabolic control of puberty: role of epigenetic regulatory mechanisms. Funding agency: European Commission. Reference: PI-OF-GA-2010-273034

Tena-Sempere, M. New Frontiers in Reproductive medicine: Exploring novel mechanisms for the control of puberty and fertility, and their interplay with metabolic homeostasis and disease. Funding agency: FiDiPro Program (Finnish Distinguished Professorship Program) 2015-2020, Academy of Finland

Tena-Sempere, M. Reprobesity: Overweight-induced Hypogonadism as major factor for the generation and/or perpetuation of Metabolic Co-morbidities of Obesity: Contribution of Epigenetic Regulatory Mechanisms. Funding agency: European Commission. Reference: MSCA-EF-2014-002

#### **Contracts with Companies**

Tena-Sempere, M. Proof-of-principle studies for the validation of Gpr54 agonists as therapeutic tool in preclinical (rodent) models of functional hypogonadotropic hypogonadism and ovulatory dysfunction. Extension. Funding agency: Ferring. Reference: 12013091.

Tena-Sempere, M. Physical, chemical and biological characterization of active compounds (BIONATURIS). Funding agency: Bioorganic Research and Services, S.A. Reference: PSS.0044

## HIGHLIGHTS

### Metabolism and Adipocyte Differentiation. Metabolic Syndrome



#### **Team Leaders**

Principal Investigator (PI) M<sup>a</sup> del Mar Malagón Poyato bc1mapom@uco.es CIBER Physiopathology of obesity and nutrition (CICIBERobn) (Collaborate)

**Co- Principal Investigator (PI)** Francisco Gracia Navarro *PAIDI BIO-139 scientific group* 



#### Researchers Socorro García Navarro Rafael Vázquez Martínez Andrés Trávez García Mª del Carmen Navarro Ruiz Alejandro Fernández Vega Julia Sánchez Ceinos

**Post- Doctoral Researchers** Rocio Guzmán Ruiz Pre Doctoral-Researchers (PhD Students y MSc Students) Jaime López Alcalá José Manuel Jiménez Pastor M<sup>a</sup> del Carmen Soler Vázquez Sandra Díaz del Moral Carmen Tercero Alcázar

Other members of the Group (Nursing, Technical, and Administrative Staff) Laura Molero Murillo

This research group investigates the cellular and molecular mechanisms that control adipose tissue function. Thus, this group is focused on the central role of adipose tissue in the regulation of lipid metabolism and in the response to insulin and other hormonal regulators of metabolic homeostasis, as well as on its role as an endocrine organ. Specifically, this group analyzes the different components of adipose tissue, mature adipocytes and the stromal vascular fraction, including the study of preadipocytes and adipogenesis. In particular, this group is interested in the identification and characterization of novel biomarkers related to fundamental processes in adipocytes, including the control of lipid transport, accumulation and mobilization, as well as the signaling/metabolic pathways underlying these processes. In addition, the relationship between cell stress processes (oxidative stress, endoplasmic reticulum stress, inflammation, mechanical stress, fibrosis, etc) is analyzed using in vitro models of insulin resistance. These studies are performed in the context of disorders associated with adipose tissue dysfunction, obesity and lipodystrophy, which result in the development of metabolic disease. Finally, this group also investigates the effects of interventions that improve the metabolic profile of morbidly obese subjects (bariatric surgery, lifestyle or pharmacological interventions,). To address these goals, this group employs multiple experimental approaches, including the application of comparative proteomics and lipidomics (including MALDI imaging) to the adipose tissue under different experimental conditions and model organisms. In addition, gene expression studies, protein interaction analyses, confocal microscopy and real-time videomicroscopy, and functional studies (gene overexpression or silencing) using primary cells or cell lines are also carried out.

#### **Keywords**

Adipose tissue, adipocyte, lipid metabolism, adipogenesis, proteomics, lipidomics, intracellular trafficking, intracellular signaling, adipokines, receptors, obesity, lipodystrophy, insulin resistance, metabolic syndrome.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Diaz-Ruiz A, Guzman-Ruiz R, Moreno NR, Garcia-Rios A, Delgado-Casado N, Membrives A, Tunez I, El Bekay R, Fernandez-Real JM, Tovar S, Dieguez C, Tinahones FJ, Vazquez-Martinez R, Lopez-Miranda J, Malagon MM. Proteasome Dysfunction Associated to Oxidative Stress and Proteotoxicity in Adipocytes Compromises Insulin Sensitivity in Human Obesity. ANTIOXIDANTS & REDOX SIGNALING. 2015, 23(7):597-612. IE: 7.407

Q: 1 D: 1

#### **Papers in Collaboration**

Prevost G, Jeandel L, Arabo A, Coeffier M, El Ouahli M, Picot M, Alexandre D, Gobet F, Leprince J, Berrahmoune H, Dechelotte P, Malagon M, Bonner C, Kerr-Conte J, Chigr F, Lefebvre H, Anouar Y, Chartrel N. Hypothalamic Neuropeptide 26RFa Acts as an Incretin to Regulate Glucose Homeostasis. 2015, DIA-BETES. 64(8):2805-2816.

IF: 8,095

Q: 1 D: 1

Rodriguez A, Moreno NR, Balaguer I, Mendez-Gimenez L, Becerril S, Catalan V, Gomez-Ambrosi J, Portincasa P, Calamita G, Soveral G, Malagon MM, Fruehbeck G. Leptin administration restores the altered adipose and hepatic expression of aquaglyceroporins improving the non-alcoholic fatty liver of ob/ ob mice. 2015, SCIENTIFIC REPORTS. 5: . IF: 5.578

Q: 1 D: 1

Q. 1 D.

Ortega FJ, Mercader JM, Moreno-Navarrete JM, Nonell L, Puigdecanet E, Rodriquez-Hermosa JI, Rovira O, Xifra G, Guerra E, Moreno M, Mayas D, Moreno-Castellanos N, Fernandez-Formoso JA, Ricart W, Tinahones FJ, Torrents D, Malagon MM, Fernandez-Real JM. Surgery-Induced Weight Loss Is Associated With the Downregulation of Genes Targeted by MicroRNAs in Adipose Tissue. 2015, JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM. 100(11):1467-1476. IF: 6,209 G: 1 D: 2

Rangel-Zuniga OA, Camargo A, Marin C, Pena-Orihuela P, Perez-Martinez P, Delgado-Lista J, Gonzalez-Guardia L, Yubero-Serrano EM, Tinahones FJ, Malagon MM, Perez-Jimenez F, Roche HM, Lopez-Miranda J. Proteome from patients with metabolic syndrome is regulated by quantity and quality of dietary lipids. 2015, BMC GENOMICS. 16:509. IF: 3,986 Q: 1 D: 2

#### **Research Funding**

#### Regional

Malagón, MM. Identifying markers for Adipose Tissue Dysfunction in Insulin Resistance Conditions. Funding Agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0200-2013

Malagón, MM. High-performance proteomic approaches to identify markers of adipose tissue obesity. Alterations in the adipocyte phosphoproteome associated with insulin resistance. Funding Agency: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: P10-CTS-6606

#### National

Malagón, MM. Characterization of novel pathways in the regulation of lipid metabolism in adipocytes. Alterations in obesity. Funding Agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: BFU-2013-44229-R

López Miranda, J (This project was funded as a collaborative initiative among different research groups). Early predictors and causes of loss of phenotypic flexibility as individual risk factor of metabolic disease: towards a personalized medicine (FLEXI-MET). Funding agency: Institute Carlos III Health (ISCIII). REF: PIE/1400005

Malagón MM (node Córdoba), Villarroya, F(PI). Research network on adipose plasticity pathophysiologic impact.Funding Agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: BFU2015-70454-REDT

## HIGHLIGHTS

### Epidemiological Research in Primary Care



#### **Team Leaders**

Principal Investigator (PI) Luis Ángel Pérula de Torres langel.perula.sspa@juntadeandalucia.es Research Network on preventive actions and health promotion in primary care (RedIAPP) Responsible Researcher: GIEAP Group PAIDI CTS-452 Scientific Group

#### Researchers

María José Acosta García Cristina Aguado Taberné María Antonia Alba Dios Joaquín Ruiz de Castroviejo Del Campo Antonio Blanco Hungría Javier Fonseca del Pozo José Ángel Fernández García Miguel Ángel Fernández Fernández Juan Ignacio González Carretero Jesús Gonzalez Lama Celia Jimenez García Antonio Manuel Jodral Segado Enrique Martin Rioboo Inmaculada Olaya Caro José Antonio Prados Castillejo Juan Manuel Parras Rejano Carlos Perula De Torres Antonio Ranchal Sánchez Juana Redondo Sánchez Roger Ruiz Moral Francisco Javier Ruiz Moruno Javier Serrano Merino Luis Carlos Silva Aycaguer Antonio Valero Martin Manuel Vaguero Abellán Francisco José Varas Fabra

Post- Doctoral Researchers Manuel Rich Ruiz

#### Pre Doctoral-Researchers (PhD Students y MSc Students) Margarita Criado Larumbe

Fernando Leiva Cepas Esperanza María Romero Rodríguez Carlos Ortega Millán

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 healthcare, clinical interviews. Medical education.

#### **Keywords**

Epidemiology; Preventive Medicine and Public Health; Primary Health Care.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Moral RR, Pérula de Torres LA, Pulido Ortega L, Criado Larumbe M, Roldán Villalobos A, Fernández García JA; Parras Rejano JM. Effectiveness of motivational interviewing to improve therapeutic adherence in patients over 65 years old with chronic diseases: A cluster randomized clinical trial in primary care. PATIENT EDUCATION AND COUNSEL-ING.2015;98:977-83. IF: 2,199

Q: 1 D:1

Q. I D.I

Bóveda-Fontán Julia, Barragán-Brun Nieves, Campiñez-Navarro Manuel, Pérula-de Torres Luís, Bosch-Fontcuberta Josep, Martín-Álvarez Remedios, Arbonies-Ortiz Juan, Novo-Rodríguez Jesús, Criado-Larumbe Margarita, Fernández-García Jose, Martín-Rioboó Enrique, Collaborative Group Estudio Dislip-EM. Effectiveness of motivational interviewing in patients with dyslipidemia: a randomized cluster trial. BMC FAM PRACT. 2015;16:151. FI: 1.669

Q: 2

С.

Perula-de-Torres LA, Marzo-Castillejo M, Ranchal-Sanchez A, Bartolome-Moreno C, Parras-Rejano JM, Bellas-Beceiro B, Vela-Vallespin C, Nuin-Villanueva MA, Melus-Palazon E, Vilarrubi-Estrella M, Martin-Rabadan Muro M, Martin-Carrillo Domingez P, Magallon-Botaya R. Group CECC-AP study. European Code Against Cancer: what does the Spanish population know and think about its recommendations?. EUROPEAN JOURNAL OF CANCER. PREVENTION. 2015:24(2):69-75.

IF: 3,031 Q: 2

Q. 2

Ruiz-Moral R, Palenzuela-Paniagua S, Magallon-Botaya R, Jimenez-Garcia C, Fernandez Garcia JA, Perula de Torres LA. Opinions and beliefs held by Spanish teenagers regarding tobacco and alcohol consumption: a descriptive study. BMC PUBLIC HEALTH. 2015:15: 61.

- IF: 2,264
- Q: 2

Alba Dios MA, Pérula de Torres CJ, Pérula de Torres LA, Pulido Ortega L, Ortega Ruiz R, Jiménez García C y Grupo colaborativo Estudio ATEM-AP. Adherencia terapéutica y calidad de vida relacionada con la salud en pacientes crónicos polimedicados de más de 65 años. Med Fam (And) 2015; 2: 111-24. IF:0

Ranchal-Sánchez A, Font P, López-Cabello P, Pérula de Torres LA. Winmedtrad utility to know the smoking addiction prevalence in a reference hospital. Med Segur Trab (Internet) 2015; 61:172-83. IF:0

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#### Papers in Collaboration

Carratala-Munuera C, Gil-Guillen VF, Orozco-Beltran D, Maiques-Galan A, Lago-Deibe F, Lobos-Bejarano JM, Brotons-Cuixart C, Martin-Rioboo E, Alvarez-Guisasol F, Lopez-Pineda A.Barriers to improved dyslipidemia control: Delphi survey of a multidisciplinary panel. FAMILY PRACTICE.2015. 32(6);672-680 IF:1,861

Q: 2

Cano-Castiñeira R, Carrasco-Valiente J, Perula-de-Torres LA, Jimenez-Garcia C, Olaya-Caro I, Criado-Larumbe M, Requena-Tapia MJ Prevalence of Renal Stones in Andalusian Population: Results of PreLiRenA Study. ACTAS UROLOGI-CAS ESPANOLAS. 2015;39(1); 26-31

IF:1,022 Q:4

Q.4

Alonso JV, Fonseca del Pozo FJ, Carmona Simon J, Valenzuela S, Perez Gomez F, Lopera E.Limb-Shaking TIA Presenting as Hemichorea-Hemiballismus: TIA Chameleons Diagnostic Challenge in the Emergency Department. JOURNAL OF STROKE & CEREBROVASCULAR DISEASES.2015. 24(11);E327-E331

IF: 1,699

Q:4

Bóveda-Fontán Julia, Barragán-Brun Nieves, Campiñez-Navarro Manuel, Pérula-de Torres Luís, Bosch-Fontcuberta Josep, Martín-Álvarez Remedios, Arbonies-Ortiz Juan, Novo-Rodríguez Jesús, Criado-Larumbe Margarita, Fernández-García Jose, Martín-Rioboó Enrique, Collaborative Group Estudio Dislip-EM. Effectiveness of motivational interviewing in patients with dyslipidemia: a randomized cluster trial. BMC FAMILY PRAC-TICE.2015 IE: 1.699

Q:2

Q.2

Mengibar Ariza E, López Sánchez C, Bóveda Fontán J, Campiñez Navarro M, Pérula de Torres LA, Lora Coronado MP y grupo colaborativo estudio Dislip-EM. Evaluación del manejo de la dislipemia en consultas de atención primaria: resultados de una auditoria clínica. Med fam And 2015;16:213-21 IE:0

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#### **Research Funding**

#### National

Pérula de Torres, LA. (Colloborate Investigator); IP: Sonia Soto Díaz . A randomized clinical trial to evaluate the effectiveness to evaluate the effectiveness of a multimodal intervention based on person-centered communication with health outcomes and safety in diabetic patients. COMUNICARE Study". Funding Agency: Institute Carlos III Health (ISCIII).Reference: PI10/00667(Prorogued to 2016). Pérula de Torres, LA. Preferences of physicians and patients concerning their participation in the decision-making process and coherence of their actions in real clinical scenarios. Funding Agency: Institute Carlos III Health (ISCIII).Reference:PI11-00771.

Parras Rejano, JM (Collaborator Investigator). IP: Gayoso,P. Renal function (RF) and markers of inflammation in Relation to Mortality, Cardiovascular Events and Impaired RF. Study of cohorts in general adult population: EPIRCE II". Funding Agency: Institute Carlos III Health (ISCIII).Reference:PI13/02031.

#### Regional

Pérula de Torres, LA. Effectiveness of opportunistic detection of atrial fibrillation in people aged 65 years or more in primary care. Dofa-Ap. Project.Funding Agency: Andalusian Progress and Health Foundation (FPS). Reference:PI-0117-2011

Pérula de Torres, LA. Effect on the quality of life from treatment with positive pressure devices (PPDs) in patients older than 65 with apnea-hypopnea (SAHS).Funding Agency: Andalusian Progress and Health Foundation (FPS). Reference: PI-0281-2014

Pérula de Torres, LA. Effect on the quality of life from treatment with positive pressure devices (PPDs) in patients older than 65 with apnea-hypopnea (SAHS).Funding Agency: Andalusian Progress and Health Foundation (FPS). Reference:PI-0025-2015

Romero Rodríguez, E. Knowledge, attitudes and practices of primary care professionals in preventive interventions in high-risk drinkers or patients with problems related to alcohol consumption: STUDY ALCO-AP.Funding Agency: Sociedad andaluza medicina familiar y comunitaria. Reference: 130/15:

#### **Clinical Trials**

2883/2: Multicenter observational study to establish the prevalence, clinical profile and therapeutic management of patients with suppurative hydradenitis from dermatology hospital services and health centers in Spain. PI Dr/a Ruiz Moruno, Francisco Javier

2883/3: Multicenter observational study to establish the prevalence, clinical profile and therapeutic management of patients with suppurative hydradenitis from dermatology hospital services and health centers in Spain. PI Dr/a Redondo Sánchez, Juana

2742: Observational cross-sectional study to evaluate the sociodemographic and clinical characteristics of patients diagnosed with irrigation NVAF stroke or systemic embolism, receiving treatment for adequate control of their clotting who are also treated in primary care. Study SILVER-AP PI Dr/a Martín Rioboo, Enrique

2742/2: Retrospective and prospective study on the degree of GEMA compliance with 2009 guidelines vs the 2015 guidelines, and its impact on the degree of control of asthma patients in primary care

PI Dr/a Aguado Taberné, Cristina

2929: Retrospective and prospective study on the degree of GEMA compliance with 2009 guidelines vs the 2015 guidelines, and its impact on the degree of control of asthma patients in primary care. PI Dr/a Ruiz Moruno, Francisco Javier

## HIGHLIGHTS

### Calcium metabolism. Vascular calcification



#### **Team Leader**

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#### Researchers

Escolástico Aguilera Tejero Antonio Canalejo Raya (Collaborator) Ignacio López Villalba Ana Raya Bermúdez

**Post- Doctoral Researchers** 

Addy Montes de Oca Gonzalez Carmen Herencia Bellido Julio Manuel Martínez Moreno Juan Rafael Muñoz Castañeda Carmen Pineda Martos Mª Encarnación Rodríguez Ortiz **Pre Doctoral-Researchers (PhD Students y MSc Students)** Rafael Ríos Varo Juan Miguel Tocados Díaz Noemí Vergara Segura

Other members of the Group (Nursing, Technical, and Administrative Staff) Sandra García Valdivia Erena Ruiz Mora

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 calcification 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 analyses 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; HPTH2°; vascular calcification; renal failure VDR; CaR. Mesenchymal stem cells; Wnt / beta-catenin.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Buendia P, Montes de Oca A, Madueno JA, Merino A, Martin-Malo A, Aljama P, Ramirez R, Rodriguez M, Carracedo J. Endothelial microparticles mediate inflammation-induced vascular calcification. FASEB JOURNAL.2015. 29(1):173-181. IF: 5,043

Q: 1 D: 1

Gonzalez-Rubio S, Lopez-Sanchez L, Munoz-Castaneda J, Linares CI, Aguilar-Melero P, Rodriguez-Peralvarez M, Sanchez-Sanchez R, Fernandez-Alvarez A, Casado M, Montero-Alvarez JL, Rodriguez-Ariza A, Muntane J, de la Mata M, Ferrin G. GCDCA down-regulates gene expression by increasing Sp1 binding to the NOS-3 promoter in an oxidative stress dependent manner. BIOCHEMICAL PHARMACOLOGY. 2015.96(1):39-51.

IF: 5,009 Q: 1 D: 1

G. I D.

Noci MV, Ramirez R, Lluch M, Rodriguez M, Carracedo J. Changes in endothelial microparticles and endothelial progenitor cells in obese patients in response to surgical stress. JOURNAL OF BONE AND JOINT SURGERY-BRITISH VOL-UME. 2015.97(5):353-358.

IF: 3,309

Q: 1 D: 1

Herencia C, Rodriguez-Ortiz ME, Munoz-Castaneda JR, Martinez-Moreno JM, Canalejo R, Montes de Oca A, Diaz-Tocados JM, Peralbo-Santaella E, Marin C, Canalejo A, Rodriguez M, Almaden Y. Angiotensin II prevents calcification in vascular smooth muscle cells by enhancing magnesium influx. EUROPEAN JOURNAL OF

CLINICAL INVESTIGATION. 2015.45(11):1129-1144. IF: 2,734 Q: 1 Herencia C, Almaden Y, Martinez-Moreno JM, Espejo I, Herrera C, Perez-Sanchez C, Guerrero F, Ciria R, Briceno FJ, Ferrin G, de la Mata M, Munoz-Castaneda JR. Human mesenchymal stromal cell lysates as a novel strategy to recover liver function. REGENERATIVE MEDICINE. 2015.10(1):25-38. IF: 2,786 Q: 2Herencia C, Almaden Y, Ferrin G, Martinez-Romero R, de la Mata M, Ciria R, Briceno FJ, Munoz-Castaneda JR. Cardiotrophin-1 decreases liver apoptosis through calpastatin induction. JOURNAL OF SURGICAL RESEARCH. 2015.193(1):119-125. IF: 1,936 Q:2Pineda C, Aguilera-Tejero E, Raya Al, Montes de Oca A, Rodriguez M, Lopez I. Effects of two calculolytic diets on parameters of feline mineral metabolism. JOURNAL OF SMALL ANIMAL PRACTICE. 2015 .56(8):499-504. IF: 1,089 Q: 2 Felsenfeld AJ, Levine BS, Rodriguez M. Pathophysiology of Calcium, Phosphorus, and Magne-

physiology of Calcium, Phosphorus, and Magnesium Dysregulation in Chronic Kidney Disease. SEMINARS IN DIALYSIS. 201528(6):564-577. IF: 1,745

Q: 3

#### **Original Review**

Rodriguez M, Rodriguez-Ortiz ME. Advances in pharmacotherapy for secondary hyperpara-

thyroidism. EXPERT OPINION ON PHARMACO-THERAPY. 2015.16(11):1703-1716. IF: 3,534

Rodriguez M, Goodman WG, Liakopoulos V, Messa P, Wiecek A, Cunningham J. The Use of Calcimimetics for the Treatment of Secondary Hyperparathyroidism: A 10 Year Evidence Review. SEMINARS IN DIALYSIS. 2015.28(5): 497-507

Q. 5

#### **Papers in Collaboration**

Block GA, Fishbane S, Rodriguez M, Smits G, Shemesh S, Pergola PE, Wolf M, Chertow GM. A 12-Week, Double-Blind, Placebo-Controlled Trial of Ferric Citrate for the Treatment of Iron Deficiency Anemia and Reduction of Serum Phosphate in Patients With CKD Stages 3-5. AMERICAN JOURNAL OF KIDNEY DISEASES. 2015.65(5):728-736.

IF: 5,9 Q: 1 D: 1

Q. ID

Salem S, Jankowski V, Asare Y, Liehn E, Welker P, Raya-Bermudez A, Pineda-Martos C, Rodriguez M, Muñoz-Castañeda JR, Bruck H, Marx N,Machado FB, Staudt M, Heinze G, Zidek W, Jankowski J. Identification of the Vasoconstriction-Inhibiting Factor (VIF), a Potent Endogenous Cofactor of Angiotensin II Acting on the Angiotensin II Type 2 Receptor. CIRCU-LATION. 2015.131(16):1426-1434. IF: 14.43

Q: 1 D: 1

Acevedo LM, Peralta-Ramirez A, Lopez I, Chamizo VE, Pineda C, Rodriguez-Ortiz ME, Rodriguez M, Aguilera-Tejero E, Rivero JL. Slow- and fast-twitch hindlimb skeletal mus-

Q: 1

IF: 1,745 Q: 3

cle phenotypes 12 wk after 5/6 nephrectomy in Wistar rats of both sexes. AMERICAN JOURNAL OF PHYSIOLOGY-RENAL PHYSIOLO-GY.2015. 309(7);638-647. IF: 3,248

Q: 1

#### **Research Funding**

#### National

Rodríguez Portillo, JM. Vascular calcification. Regulation of osteogenic gene expression in vascular smooth muscle cells and smooth muscle mesenchymal progenitor cells via Wht / Beta-Catenin and SMAD. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI11-02055

Muñoz Castañeda JR; Rodriguez Portillo J. Influence of urinary phosphorous excretion on the renal injury progression. Mechanisms and clinical studies. Funding agency: Institute Carlos III Health (ISCIII).Reference: PI14/00638

#### International

Rodríguez Portillo, JM. (SYSKID). Systems biology towards novel chronic kidney disease diagnosis and treatment. Funding agency: European Commission Reference: FP7-241544

#### Regional

Rodríguez Portillo, JM. Role of adult stem cells and vascular smooth muscle in damage induced by vascular calcification. Relationship between phosphorus wat / beta-catenin and osteogenesis. Funding agency:Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: P09-CTS-5205

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. Funding agency:Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: CVI-7925

López Villalba,I . Conexiones entre el metabolismo mineral y el metabolismo energético: efecto de la dieta hirpercalorica en el balance del fosforo y la función renal.Funding Agency: Andalusian Progress and Health Foundation (FPS). Reference: PI-0272-2014

#### **Contracts with Companies**

Rodriguez Portillo, JM. Effect of paricalcitol on vascular smooth muscle cells.Fundingagency:AbbVie Farmaceutica S.L.U. Reference: PSS.0015

Rodriguez Portillo, JM. Research Program Agreement for measuring AMG 416 activity against isolated rat PTG. Funding agency: Amgen Inc. S.A. Reference: PSS.0020

#### **Clinical Trials**

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. Pl: Dr/a Rodríguez Portillo, J. Mariano

0010/14: A multicenter, single-arm, extension study to assess long-term safety of AMG 416 (Velcalcetide) for secondary hyperparathyroidism in patients with chronic renal failure undergoing hemodialysis.

PI: Dr/a Rodríguez Portillo, J. Mariano

0039/15: Open phase II clinical trial for assessment of the effectiveness of the decrease of intestinal absorption of phosphorous in the progression of kidney disease in patients with metabolic syndrome

PI: Dr/a Rodríguez Portillo, J. Mariano

## HIGHLIGHTS

**Cell Therapy** 



#### **Team Leader**

Principal Investigator (PI) Inmaculada C. Herrera Arroyo inmaculada.herrera.sspa@juntadeandalucia.es



#### Researchers Miguel Canis López Macarena Centeno Haro (collaborator) M<sup>a</sup> Sagrario Cañadillas Lopez José García-Revillo García Vanesa Martin Palanco Sonia Nogueras Martin Rosa Ortega Salas (collaborator)

Post- Doctoral Researchers Rosario Jimenez Moreno Pre Doctoral-Researchers (PhD Students y MSc Students) Maria Dolores Carmona Luque María Muñoz Calero Laura López Galvez Luis Miguel Paco Meza

Other members of the Group (Nursing, Technical, and Administrative Staff) María Luisa Castilla Rodríguez Antonia de la Torre Murillo Rosario Gutiérrez Fernández María Luque Zafra Teresa Muñoz Liñan

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.

#### **Scientific Production**

#### **Publications**

#### **Papers in Collaboration**

Baragano Raneros A, Martin-Palanco V, Fernandez AF, Rodriguez RM, Fraga MF, Lopez-Larrea C, Suarez-Alvarez B. Methylation of NKG2D ligands contributes to immune system evasion in acute myeloid leukemia. GENES AND IMMUNITY. 2015; 16(1):71-82. IF: 2,913 Q:2

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Herencia C, Almaden Y, Martinez-Moreno JM, Espejo I, Herrera C, Perez-Sanchez C, Guerrero F, Ciria R, Briceno FJ, Ferrin G, de la Mata M, Munoz-Castaneda JR. Human mesenchymal stromal cell lysates as a novel strategy to recover liver function. REGENERATIVE MEDI-CINE.2015. 10(1):25-38. IF: 2,786

Q: 2

#### Letters In Collaboration

Baeza Garzon F, Romero M, Suarez de Lezo J, Ojeda Pineda S, Herrera C, Suarez de Lezo J. Idiopathic Dilated Cardiomyopathy Treated With Intracoronary Infusion of Autologous Bone Marrow Cells: Long-term Follow-up. REVISTA ESPANOLA DE CARDIOLOGIA.2015. 68(8):726-728. IF: 3.792

Q: 2

#### **Research Funding**

#### National

Herrera Arroyo, Inmaculada C. Cell preservation system project. Funding agency: University of Córdoba. Reference: CCB.031PM

Cañadillas López, M<sup>a</sup> Sagrario. Effect of hypoxia on the regenerative potential of Adipose Derived Mesenchymal Cells (ASCs). Study in adiabetic nephropathy rat model.. Funding Agency: Institute Carlos III Health (ISCIII). Reference: PI14/00087

#### Regional

Cañadillas López, MS. Combination therapy with mesenchymal stem cells and erythropoietin in the treatment of chronic renal failure in an experimental study in rats. Funding agency: Andalusian Progress and Health Foundation (SAS). 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.Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference:-PI-0551-2012

#### **Contracts with Companies**

Herrera Arroyo, Inmaculada C. Agreement with Janssen. Funding agency: Janssen-Cilag, S.A. Reference: PSS.0040

Herrera Arroyo, Inmaculada C. Agreement with Roche (SESIÓN CLÍNIC). Funding agency: Roche Reference: PSS.0066

Herrera Arroyo, Inmaculada C. Agreement with Eusa Pharma (Professional Training) Funding agency: Eusa Pharma Iberia S.L. Reference: PSS.0068

Herrera Arroyo, Inmaculada C. Agreement with Bristol Mayers (Professional Training) Funding agency: Bristol Mayers.Reference: PSS.0069

Herrera Arroyo, Inmaculada C. Agreement with JANSSEN. Funding agency: JANS-SEN-CILAG, S.A.. Reference: PSS.0075

Herrera Arroyo, Inmaculada C. Cooperation Agreement for a scientific research grants programme. Funding agency: JANSSEN- CI-LAG, S.A.Reference: CCB.0113\_02

Herrera Arroyo, Inmaculada C. Agreement with JANSSEN. Funding agency: JANS-SEN-CILAG, S.A.Reference: : PSS.0103

Herrera Arroyo, Inmaculada C. Conference sponsored by Pzifer Funding agency: Pzifer. Reference: CCB.0078

Herrera Arroyo, Inmaculada C. Conference sponsored by Celgene.Funding agency: Celgene Reference: CCB.0108

#### **Clinical Trials**

0274/13: Phase II clinical trial to evaluate the efficacy of obinutuzumab (R05072759)+ bendamustine in patients with relapsed or refractory leukemia linfaticacronica. PI: Dr/a Herrera Arroyo, Inmaculada C.

## HIGHLIGHTS

Invasive cardiology and cell therapy



#### **Team Leader**

Principal Investigator (PI) José Suárez de Lezo Cruz-Conde jose.suarezlezo.sspa@juntadeandalucia

> Researchers Francisco Mazuelos Bellido Soledad Ojeda Pineda Manuel Pan Alvarez-Ossorio Djordje Pavlovic Djurovic Miguel Ángel Romero Moreno Jose Mª Segura Saint-Gerons Javier Suarez de Lezo Herreros De Tejada

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.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Suarez de Lezo J, Romero M, Pan M, Suarez de Lezo J, Segura J, Ojeda S, Pavlovic D, Mazuelos F, Lopez Aguilera J, Espejo Perez S. Stent Repair for Complex Coarctation of Aorta. JACC-CARDIOVASCULAR INTERVEN-TIONS.2015. 8(10):1368-1379.

- IF: 7,345 Q: 1 D: 1

Pan M, Romero M, Ojeda S, Suarez de Lezo J, Segura J, Mazuelos F, Martin P, Medina A, Suarez de Lezo J. Fracture of Bioresorbable Vascular Scaffold After Side-Branch Balloon Dilation in Bifurcation Coronary Narrowings. AMERICAN JOURNAL OF CARDIOLOGY. 2015.116(7):1045-1049. IF: 3,276

#### Q: 2

Ojeda S, Pan M, Romero M, Suarez de Lezo J, Mazuelos F, Segura J, Espejo S, Morenate C, Blanco M, Martin P, Medina A, Suarez de Lezo J. Outcomes and computed tomography scan follow-up of bioresorbable vascular scaffold for the percutaneous treatment of chronic total coronary artery occlusion. AMERICAN JOURNAL OF CARDIOLOGY.

2015.115(11):1487-1493.

IF: 3,276

Q: 2

Villanueva E, Pan M, Ojeda S, Suarez de Lezo J, Romero M, Martin P, Mazuelos F, Segura J, Medina A, Suarez de Lezo J. Structural Damage to Jailed Guidewire During the Treatment of Coronary Bifurcations: Microscopic Evaluation. REVISTA ESPANOLA DE CARDIOLOGIA. 2015.68(12):1111-1117.

IF: 3,792

Q: 2

Ruiz Ortiz M, Pena ML, Mesa D, Delgado M, Romo E, Santisteban M, Puentes M, Lopez Granados A, Castillo JC, Arizon JM Suarez de Lezo J. Impact of Asymptomatic Acute Cellular Rejection on Left Ventricle Myocardial Function Evaluated by Means of Two-Dimensional Speckle Tracking Echocardiography in Heart Transplant Recipients. ECHOCARDIOG-RAPHY-A JOURNAL OF CARDIOVASCULAR ULTRASOUND AND ALLIED TECHNIQUES. 2015.32(2):229-237.

- IF: 1,254
- Q: 3

#### **Original Letters**

Amat-Santos IJ, Messika-Zeitoun D, Eltchaninoff H, Kapadia S, Lerakis S, Cheema AN, Gutierrez-Ibanes E, Munoz A, Pan M, Webb JG, Herrmann H, Kodali S, Nombela-Franco L, Tamburino C, Jilaihawi H, Masson JB, de Brito FS, Ferreira MC, Lima VC, Mangione JA, Lung B, Vahanian A, Durand E, Tuzcu M, Hayek SS, Angulo-Llanos R, Gomez-Doblas JJ, Castillo JC, Dvir D, Leon MB, Garcia E, Cobiella J, Barbanti M, Makkar R, Ribeiro HB, Urena M, Dumont E, Pibarot P, Lopez J, San Roman A, Rodes-Cabau J. Response to Letters Regarding Article, "Infective Endocarditis After Transcatheter Aortic Valve Implantation: Results From a Large Multicenter Registry". CIR-CULATION.2015. 132(23):372-374. IF: 15,073

Q: 1 D: 1

Castillo FJ, Anguita M, Castillo JC, Ruiz M, Mesa D, Suarez de Lezo J. Changes in Clinical Profile, Epidemiology and Prognosis of Left-sided Native-valve Infective Endocarditis Without Predisposing Heart Conditions. RE-VISTA ESPANOLA DE CARDIOLOGIA (ENGLISH ED.). 2015.68(5):445-448.

IF: 3,792 Q: 2

Q. Z

Castillo FJ, Anguita M, Castillo JC, Ruiz M, Mesa D, Suarez de Lezo J. Use of the New Antiplatelet Agents in Acute Coronary Syndromes: Limitations Related to Patient Characteristics. REVISTA ESPANOLA DE CARDIO-LOGIA.2015. 68(5):448-450. IF: 3,792

Q: 2

Q. 2

Baeza Garzon F, Romero M, Suarez de Lezo J, Ojeda Pineda S, Herrera C, Suarez de Lezo J. Idiopathic Dilated Cardiomyopathy Treated With Intracoronary Infusion of Autologous Bone Marrow Cells: Long-term Follow-up. REVISTA ESPANOLA DE CARDIOLOGIA.2015. 68(8):726-728. IF: 3,792 Q:2

Q.1\_

#### **Papers in Collaboration**

Amat-Santos IJ, Messika-Zeitoun D, Eltchaninoff H, Kapadia S, Lerakis S, Cheema AN, Gutierrez-Ibanes E, Munoz-Garcia AJ, Pan M, Webb JG, Herrmann HC, Kodali S, Nombela-Franco L. Infective endocarditis after transcatheter aortic valve implantation: results from a large multicenter registry. CIRCULA-TION. 2015.131(18):1566-1574. IF: 14,43 Q: 1 D: 1 Latib A, Naganuma T, Abdel-Wahab M, Danenberg H, Cota L, Barbanti M, Baumgartner H, Finkelstein A, Legrand V, de Lezo JS, Kefer J, Messika-Zeitoun D, Richardt G, Stabile E, Kaleschke G, Vahanian A, Laborde JC, Leon MB, Webb JG, Panoulas VF, Maisano F, Alfieri O, Colombo A. Treatment and clinical outcomes of transcatheter heart valve thrombosis. CIRCULATION-CARDIOVASCULAR IN-TERVENTIONS. 2015.8(4): .

IF: 6,218 Q: 1 D: 1

Q. 1

Jimenez-Jaimez J, Peinado R, Zorio Grima E, Segura F, Morina P, Sanchez Munoz JJ, Mazuelos F, Cozar R, Gimeno JR, Heras RP, Monserrat L, Domingo D, Ortiz-Genga M, Fernandez Pastor J, Alvarez M, Tercedor L. Diagnostic Approach to Unexplained Cardiac Arrest (from the FIVI-Gen Study). AMERICAN JOURNAL OF CARDIOLOGY. 2015.115(6):894-899. IF: 3,276

Q: 2

#### **Reviews in Collaboration**

Tamburino C, Latib A, van Geuns RJ, Sabate M, Mehilli J, Gori T, Achenbach S, Alvarez MP, Nef H, Lesiak M, Di Mario C, Colombo A, Naber CK, Caramanno G, Capranzano P, Brugaletta S, Geraci S, Araszkiewicz A, Mattesini A, Pyxaras SA, Rzeszutko L, Depukat R, Diletti R, Boone E, Capodanno D, Dudek D. Contemporary practice and technical aspects in coronary intervention with bioresorbable scaffolds: a European perspective. EUROINT-ERVENTION.2015.11(1):45-52.

IF: 3,769 Q: 2

Q. 1

#### **Research Funding**

#### National

Pan Álvarez-Ossorio, M. Use of the "jailed guidewire" technique in the percutaneous treatment of coronary bifurcation stenting: A randomized study of stereoscopic microcospy.Funding agency:Institute Carlos III Health (ISCIII).Reference: PI12/00440

#### Regional

Rodríguez Pan Álvarez-Ossorio, M. Revascularization and Myocardial regeneration in Patients with Chronic Coronary Occlusion and Ventricular Dysfunction. Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0315-2012

#### **Clinical Trials**

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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 Mª

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 Mª

\*2961\*: EBC MAIN: Study conducted by the European Bifurcation Club: randomized comparison of the implementation of one or two stents to treat bifurcation lesions of the common trunk of the left coronary artery. PI: Dr/a Pan Álvarez-Ossorio, Manuel

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. Pl: Dr/a Pan Álvarez-Ossorio, Manuel

## HIGHLIGHTS

### Cell biology in hematology. Hypercoagulability



#### Team Leader

#### Principal Investigator (PI) Joaquín Sánchez García Joaquin.sanchez.garcia.sspa@juntadeandalucia.es Spanish Myelodysplastic Syndrome Registry (Resmd) (Collaborator)

**Co-Principal Investigator (CO-PI)** Francisco Velasco Gimena Observational Immune Tolerance Induction research program (ObsITI) (Collaborator) PAIDI CTS-620 Scientific Group



#### Researchers

Miguel A. Álvarez Rivas Víctor Arqueros Martínez Javier Casaño Sánchez Pedro Gómez García Carmen Martín Calvo José Ramón Molina Hurtado Antonia Rodríguez Villa Rafael Rojas Contreras Josefina Serrano López **Post- Doctoral Researchers** Francisco Miguel Gutiérrez Mariscal Juana Serrano López

Pre Doctoral-Researchers (PhD Students y MSc Students) David Flores Mesa Estefanía García Torres Carmen Martínez Losada

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 processes. 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**

Inmunology of hematopoietic transplantation; Cell biology of acute leukemias.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Garcia E, Buenasmañanas D, Martin C, Rojas R. Sirolimus associated pneumonitis in a hematopoietic stem cell transplant patient. ME-DICINA CLINICA.2015. 145(1):21-23. IF: 1,417

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Q: 2
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Buenasmañanas-Cervantes D\*, Garcia-Torres E, Serrano-Lopez J, Extramedullary Hematopoiesis in a Non-Transfused Elderly Patient Diagnosed with Beta Thalassemia Minor Arqueros-Martinez V, Rojas-Contreras R and Sanchez-Garcia J.Journal of Hematology and Blood Disorders. 2015; 1:1 IF:0

#### **Papers in Collaboration**

Privette Vinnedge LM, Benight NM, Wagh PK, Pease NA, Nashu MA, Serrano-Lopez J, Adams AK, Cancelas JA, Waltz SE, Wells SI. The DEK oncogene promotes cellular proliferation through paracrine Wnt signaling in Ron receptor-positive breast cancers. ONCOGENE. 2015.34(18):2325-2336.

IF: 8,459 Q: 1 D: 1

Rubio MT, Labopin M, Blaise D, Socié G, Contreras RR, Chevallier P, Sanz MA, Vigouroux S, Huynh A, Shimoni A, Bulabois CE, Caminos N, López-Corral L, Nagler A, Mohty M. The impact of graft-versus-host disease prophylaxis in reduced-intensity conditioning allogeneic stem cell transplant in acute myeloid leukemia: a study from the Acute Leukemia Working Party of the European Group for Blood and Marrow Transplantation. HAEMATOLOG-ICA.2015. 100(5):683-689.

- IF: 5,814 Q: 1 D: 1

Sanz MA, Montesinos P, Casale MF, Diaz-Mediavilla J, Jimenez S, Fernandez I, Fernandez P, Gonzalez-Campos J, Gonzalez JD, Herrera P, de Lisa E, Olave T, Rojas R, Salamero O, Sayas MJ, Pellicer A, Perales A. Maternal and fetal outcomes in pregnant women with acute

promyelocytic leukemia. ANNALS OF HEMA-TOLOGY. 2015.94(8):1357-1361. IF: 2,634 Q: 2

Herrera-Martinez AD, Alhambra Exposito MR, Manzano Garcia G, Molina Puerta MJ, Calanas Continente A, Bahamondes Opazo R, Munoz Jimenez C, Rojas Contreras R, Galvez Moreno MA.Use of glutamine in total parenteral nutrition of bone marrow transplantpatients.NU-TRICION HOSPITALARIA. 2015; 31(4):1620-1624.

IF: 1,04

Q: 4

Acevedo CC, Velasco F, Herrera C.Reversal of rivaroxaban anticoagulation by nonactivated prothrombin complex concentrate in urgent surgery.Future Cardiol. 2015 .19:1-5. IF:0

#### **Research Funding**

#### **National**

Sánchez García, J. Analysis of Phenotype, genotype, and sensitivity to new leukemia stem cell pharmaceutical products in LAM and LAL " Funding Agency: Sociedad Española De Hematología-Hemoterapia.

García Torres, E. Effect of immunomodulators (lenadomide and pomalidomide) in lymphoid populations and their impact on the development of the disease Funding Agency: Sociedad Española De Hematología-Hemoterapia. Reference: AAHH2015\_001

#### **Contracts with Companies**

Sánchez García, J. Collaboration agreement with Janssen. Identifying markers and newcellular therapeutic targets of Graft-Versus-Host-Disease (GVHD) using T lymphocytes gene expression arrays for T-cell activation. Funding agency: Janssen-Cilag, S.A. Reference:PSS.0039.

Molina Hurtado, J. Collaboration agreement with Pzifer. Funding agency:PFIZER, S.L.U. Reference: PSS.0043

Álvarez Rivas, MA. Collaboration agreement

with Celgene. Funding agency: CELGENE, S.L.U.Reference: PSS.0104

Serrano López J. Collaboration agreement with Pzifer. Funding agency:PFIZER, S.L.U. Reference: CCB.0068

#### **Clinical Trials**

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, Joaquin

0299/10: Maintenance treatment 5-Azacitidine in patients with acute myelog-

enous leukemia ineligible for intensive treatment with partial or complete response to induction chemotherapy.

with

PI: Dr/a Serrano López, Josefina

0070/11: multicenter, А 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

0279/11: Intergroup trial for children or teens with LNH-B o LLA-B (LLA-L3): Evaluation of the efficacy and safety of Rituximab for highrisk patients.

PI: Dr/a Gómez García Pedro

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 Martin Calvo, Mª Carmen

0293/12: A randomized, double-blind, placebo-controlled, phase 3 study of the efficacy and safety of oral azacytidine plus the best supportive treatment vs. the best supportive treatment as maintenance therapy in patients with acute myelogenous leukemia i complete remission.

PI: Dr/a Serrano López, Josefina

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 treatements of different durations. PI: Dr/a Molina Hurtado, José Ramón

0123/13: Phase 3 randomized, double-blind, placebo-controlled study to evaluate the protective efficacy and safety of a therapeutic vaccine, ASP0113, recipients seropositive for cytomegalovirus (CMV) underwent allogeneic cells.

PI: Dr/a Rojas Contreras, Rafael

0148/13: Multicenter phase IIIB study, international, open-label, single treatment group to assess the safety of obinutuzumab as a single agent or in combination with chemotherapy in patients with lymphatic leukemia relapsed / refractory chronic PI: Dr/a Molina Hurtado José Ramón

PI: Dr/a Molina Hurtado Jose Ramon

0165/13: An open, phase IIIb trial to assess the safety of changin intravenous rituximab to subcutaneous rituximab in the course of firstline treatment of CD20+ Follicular and Diffuse Non-Hodgkin's Large B-Cell Lymphoma. PI: Dr/a Sánchez García, Joaquin

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, Joaquin

0041/14: Clinical trial, phase III, case series on the reversal of the anticoagulant effect of dabigatran, by intravenous administration of 5.0 g of idarucizumab (BI 655 075) in patients treated with dabigatran etexilate. PI Dr/a Velasco Gimena, Francisco

0112/14 : A Phase III, randomized, placebo-controlled, double-blind maintenance treatment with oral citrate ixazomib (MLN9708) in patients with multiple myeloma after autologous stem cell transplantation. PI Dr/a Alvarez Rivas, Miguel Angel

0148/14: Phase III, multicenter, randomized, open-azacytidine (Vidaza®) versus fludarabine and cytarabine (fluga scheme) in elderly patients with acute myeloid leukemia new diagnostic.

PI Dr/a Serrano López, Josefina

0171/14: A Phase II, randomized, double-blind, placebo-controlled study of azacitidine with or without birinapant with an open run-in phase one group in patients with myelodysplastic syndrome or highest risk chronic myelomonocytic leukemia.

PI Dr/a Sánchez García, Joaquin

0181/14: A Phase Ib / II trial to evaluate the safety and efficacy of PF 04449913, oral inhibitor of the Hedgehog pathway, in combination with intensive chemotherapy, low dose ara-C or decitabine, given to patients with acute myeloid leukemia or syndrome PI Dr/a Serrano López, Josefina

0310/14: A Phase 3, Randomized, controlled, open-label study of VELCADE (Bortezomib) Melphalan-Prednisone (VMP) Compared to Daratumumab in Conbination with VMP (D VMP) in subjects with previously untreated multiple myeloma who are ineligibl for high-dose-therapy- ALCYONE PI Dr/a Alvarez Rivas, Miguel Angel

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 Martin Calvo, M<sup>a</sup> Carmen

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, Joaquin

2224: A multicenter, retrospective study to describe the effectiveness and safety of clofarabine as compassionate use treatment in adult patients with relapsed/refractary acute leukemia prior to hematopoietic stem cell transplantation.

PI: Dr/a Serrano López, Josefina

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2257: A study to validate an ex vivo individualized test for acute lymphoblastic leukemia. PI: Dr/a Serrano López, Josefina

2512: PUCHS' Study. A multicenter non-interventional , retrospective prevalence of hemophilia in Spain .

PI: Dr/a Velasco Gimena, Francisco

2570: Prospective observational study to identify clinical aspects leading to therapeutic decision making in patients with myelofibrosis PI: Dr/a Molina Hurtado, José Ramón

2634: Ex vivo pharmacology study treatments in hematological malignancies characterization by using automated flow cytometry platform ExviTch

PI: Dr/a Sánchez García, Joaquin

2641: Non-interventional post-authorization Registration patients with relapsed and refractory multiple myeloma treated with pomalidomide, who have received at least two prior treatments including lenalidomide and bortezomib, and who have experienced a proautologous hematopoietic stem cell transplant (VERSA STUDY).

PI: Dr/a Álvarez Rivas, Miguel Ángel

2638: PASS Post-Authorization Safety Study (PASS) prospective, non-interventionist, designed as Disease Registry of patients with myelodysplastic syndromes (MDS) low risk (IPSS low and intermediate-1) cin isolated 5q deletion and transfusion dependence. PI: Dr/a Sánchez García, Joaquin

2678: Post-authorization safety study (PASS) ma25101: observational cohort study of the safety of brentuximab vedotin in the treatment of relapsed or refractory cd3o Hodgkins lymphoma lymphoma and systemic anaplastic large relapsed or refractory cells PI: Dr/a Molina Hurtado, José Ramón

2699: A Study to the validation of a test ex vivo personalized medicine in Multiple Myeloma

PI: Dr/a Álvarez Rivas, Miguel Ángel

## HIGHLIGHTS

### Pathophysiology of the endocrine system of vitamin D. Biotechnology and aging



PhD Researchers Antonio Casado Diaz Rafael Cuenca Acevedo Jose Maria Mata Granados Raquel Santiago Mora Ignacio Serrano Alferez

#### **Team Leader**

Principal Investigator (PI) José Manuel Quesada Gómez md1qugoj@uco.es Thematic Network of Research Partnerships on Aging-Frailty (RETICEF).

nerships on Aging-Frailty (RETICEF). PAIDI CTS-413 Scientific Group

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 sociated 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 (MSCh) of adult adipocytes; osteoblasts; polyphenols; gene expression; proteomics; nutrigenetics; and nutrigenomics.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Quesada-Gomez JM, Santiago-Mora R, Navarro-Valverde C, Dorado G, Casado-Diaz A. Stimulation of in-vitro angiogenesis by low concentrations of risedronate is mitigated by 1,25-dihydroxyvitamin D-3 or 24,25-dihydroxyvitamin D-3. JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY. 148:214-218.

IF: 3,628 Q: 2

Navarro Valverde C, Quesada Gómez JM. Vitamin D, determinant of bone and extrabone health. Importance of vitamin D supplementation in milk and dairy products. NUTRICION HOSPITALARIA2015.-7;31 Suppl 2:18-25. IF: 1.040

Q: 4

#### **Papers in Collaboration**

Mena-Bravo A, Ferreiro-Vera C, Priego-Capote F, Maestro MA, Mourino A, Quesada-Gomez JM, Luque de Castro MD. Quantitative analytical method to evaluate the metabolism of vitamin D. CLINICA CHIMICA ACTA; INTERNATIONAL JOURNAL OF CLINI-CAL CHEMISTRY. 442:6-12. IF: 2,824 Q: 1

Q. 1

#### **Research Funding**

#### National

Quesada Gómez, JM. Evaluation of the healing effect in an in vivo model. Funding agency: Carlos III Health Institute (ISCIII). Reference:PI12/02315 Quesada Gómez, JM. RETICEF. Funding agency: Carlos III Health Institute (ISCIII). Reference: RD12/0043/0028

#### Regional

Quesada Gómez, JM. Study of the effect of Oleuropein on fibroblasts. Implications in the treatment of diabetic foot .Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0335-2012

#### **Contracts with Companies**

Quesada Gómez JM. Collaboration agreements with Lilly SA (Formation) .Funding Agency: LILLY, S.A.Reference:CCB.0079 GC17

## HIGHLIGHTS

Translational research in surgery of solid organ transplants





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Pre Doctoral-Researchers (PhD Students y MSc Students) Elena Navarro Rodríguez

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 develop 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.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Medina Fernandez FJ, Munoz-Casares FC, Arjona-Sanchez A, Casado-Adam A, Gomez-Luque I, Garcilazo Arismendi DJ, Thoelecke H, Rufian Pena S, Briceno Delgado J. Postoperative Time Course and Utility of Inflammatory Markers in Patients with Ovarian Peritoneal Carcinomatosis Treated with Neoadjuvant Chemotherapy, Cytoreductive Surgery, and HIPEC. ANNALS OF SURGICAL ONCOLOGY. 2015. 22(4):1332-1340. IF: 3.93

Q: 1 D: 1

Q. 1 D.

Ruiz-Rabelo JF, Navarro-Rodriguez E, Luigi Di-Stasi L, Diaz-Jimenez N, Cabrera-Bermon J, Diaz-Iglesias C, Gomez-Alvarez M, Briceno-Delgado J. Validation of the NASA-TLX Score in Ongoing Assessment of Mental Workload During a Laparoscopic Learning Curve in Bariatric Surgery. OBESITY SURGERY. 2015. 25(12):2451-2456.

IF: 3,747

Q: 1 D: 1

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Ciria R, Lopez-Cillero P, Gallardo AB, Cabrera J, Pleguezuelo M, Ayllon MD, Luque A, Zurera L, Espejo JJ, Rodriguez-Peralvarez M, Montero JL, de la Mata M, Briceno J. Optimizing the management of patients with BCLC stage-B hepatocellular carcinoma: Modern surgical resection as a feasible alternative to transarterial chemoemolization. EUROPE-AN JOURNAL SURGERY ONCOLOGY. 2015. 41(9):1153-1161.

IF: 3,009

Q: 1

Pozo-Laderas JC, Pontes-Moreno A, Robles-Arista JC, Bautista-Rodriguez MD, Candau-Alvarez A, Caro-Cuenca MT, Linares-Sicilia MJ. Mixed invasive fungal infection due to Rhizomucor pusillus and Aspergillus niger in an immunocompetent patient. REVISTA IBEROAMERICANA DE MICOLOGIA. 2015. 32(1):46-50. IF: 1,056

Q: 4

Q. -

Pardo F, Pons JA, Briceno J. Soc Espanola Trasplante Hepatico. V Consensus Meeting of the Spanish Society for Liver Transplant on high-risk recipients, immunosupression scenarios and management of hepatocarcinoma on the transplant waiting. GASTROENTERO-LOGIA Y HEPATOLOGIA. 2015. 38(10):600-618.

- IF: 0,838
- Q: 4

Pardo F, Pons JA, Briceno J. Soc Espanola Trasplante Hepatico. V Consensus Meeting of the Spanish Society for Liver Transplant on high-risk recipients, immunosupression scenarios and management of hepatocarcinoma on the transplant waiting list. CIRUGIA ESPANOLA. 2015. 93(10):619-637. IF: 0,743 Q: 4

#### **Original Review**

Pozo Laderas JC, Pontes Moreno A, Pozo Salido C, Robles Arista JC, Linares Sicilia MJ. Disseminated mucormycosis in immunocompetent patients: A disease that also exists. REVISTA IBEROAMERICANA DE MICOLOGIA. 2015. 32(2):63-70. IF: 1,056

Q: 4

#### **Papers in Collaboration**

Ferrin G, Rodriguez-Peralvarez M, Aguilar-Melero P, Ranchal I, Llamoza C, Linares CI, Gonzalez-Rubio S, Muntane J, Briceno J, Lopez-Cillero P, Montero-Alvarez JL, de la Mata M. Plasma Protein Biomarkers of Hepatocellular Carcinoma in HCV-Infected Alcoholic Patients with Cirrhosis. PLOS ONE. 2015. 10(3): e0118527 IF: 3,234

Q: 1

Morise Z, Ciria R, Cherqui D, Chen KH, Belli G, Wakabayashi G. Can we expand the indications for laparoscopic liver resection? A systematic review and meta-analysis of laparoscopic liver resection for patients with hepatocellular carcinoma and chronic liver disease. JOURNAL OF HEPATO-BILIARY-PAN-CREATIC SCIENCES. 2015. 22(5):342-352. IF: 2,994

Q: 1

Herencia C, Almaden Y, Martinez-Moreno JM, Espejo I, Herrera C, Perez-Sanchez C, Guerrero F, Ciria R, Briceno FJ, Ferrin G, de la Mata M, Munoz-Castaneda JR. Human mesenchymal stromal cell lysates as a novel strategy to recover liver function. REGENERATIVE MEDI-CINE. 2015. 10(1): 25-38. IF: 2,786

Q: 2

Herencia C, Almaden Y, Ferrin G, Martinez-Romero R, de la Mata M, Ciria R, Briceno FJ, Munoz-Castaneda JR. Cardiotrophin-1 decreases liver apoptosis through calpastatin induction. JOURNAL OF SURGICAL RE-SEARCH.2015. 193(1):119-125. IF: 1,936

Q: 2

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Rodriguez-Peralvarez M, Perez-Medrano I, Guerrero-Misas M, Gonzalez V, Poyato A, Barrera P, Ferrin G, Pozo JC, Sanchez-Frias M, Ciria R, Briceno J, Montero JL, De la Mata M. Everolimus is safe within the first month after liver transplantation. TRANSPLANT IMMU-NOLOGY.2015. 33(2):146-151.

IF: 1,457 Q: 3

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Pendon-Ruiz de Mier V, Navarro Cabello MD, Martinez Vaquera S, Lopez-Andreu M, Aguera Morales ML, Rodriguez-Benot A, Ruiz Rabelo J, Campos Hernandez P, Requena Tapia MJ, Aljama Garcia P. Index High Insulin Resistance in Pancreas-Kidney Transplantation Contributes to Poor Long-term Survival of the Pancreas Graft. TRANSPLANTATION PROCEED-INGS.2015. 47(1):117-119.

IF: 0,982 Q: 3

Hernandez JPC, Gomez EG, Valiente JC, Lopez FJM, Garcia JR, Curado FJA, Castro RP, Rabelo JR, Cabello MLN, Tapia MJR. Influence of Surgical Complications on Kidney Graft Survival in Recipients of Simultaneous Pancreas Kidney Transplantation. TRANSPLAN-TATION PROCEEDINGS.2015. 47(1):112-116. IF: 0,982 Q: 3

Q.

Moya-Herraiz A, Munoz-Bellvis L, Ferrer-Fabrega J, Municio AM, Perez-Daga JA, Munoz-Casares C, Alarco-Hernandez A, Gomez-Gutierrez M, Casanova-Rituerto D, Sanchez-Bueno F, Jimenez-Romero C, Perez LFC. Cooperative study of the Spanish Pancreas Transplant Group (GETP): Surgical complications. CIRUGIA ESPANOLA.2015. 93(5):300-306. IF: 0,743

Q: 4

#### **Research Funding**

#### National

Ciria Bru, R.Condition mechanisms discarded teatotic liver grafts after cold storage by normo or subnormo thermic machine perfusion . Funding Agency: Institute Carlos III Health (ISCIII).Reference: PI14/01559

Ciria Bru, R. Rescue paragraph liver transplant grafts discarded normothermic extracorporeal perfusion. Funding Agency: Fundación Mutua Madrileña Reference: FMM-14-002

#### Regional

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.Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Referenc: PI-0543-2012

J, Car Aljam Sa- in Par 1J. utes 1 Muñoz Casares, FC. Efficacy and safety of early postoperative intraperitoneal chemotherapy with paclitaxel in radical surgical treatment of ovarian peritoneal carcinomatosis. Funding agency: 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.Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0340-2013

Briceño Delgado, FJ. External validation of donor-recipient pairing model in liver transplants based on artificial neural networks Funding Agency: Andalusian Progress and Health Foundation (FPS). Reference: PI-0312-2014

#### **Contracts with Companies**

Briceño Delgado, FJ.Stand in course on advanced liver surgery.Funding agency: Covidien Spain, S.L. Reference:PSS.0041

Briceño Delgado, FJ.Agreement with SANOFI Funding agency: SANOFI-AVENTIS, S.A... Reference: PSS.0080

Briceño Delgado, FJ.Agreement with TAKEDA. Funding agency: TAKEDA FARMACEUTICA ESPAÑA S.A... Reference: PSS.0081

Membrives Obreroa, A. Agreement with J&J. Funding agency: JOHNSON & JOHNSON S.AReference: PSS.0082

Briceño Delgado, FJ.Agreement with ADALIA. Funding agency: ADALIA FARMA S.L.. Reference: CCB.0085

#### **Clinical Trials**

0290/10: Phase IV randomized clinical trial, open, multicenter, non-inferiority for the purpose of comparing the safety and efficacy of colistin iv. with meropenem iv. in the treatment of ventilator-associated pneumonia PI: Dr/a Pozo Laderas, Juan Carlos

0239/11: Role of intraoperative introperitoneal paclitaxel chemotherapy in radical surgical treatment of ovarian-origin petoneal cacinomatosis: hyperthermia versus normotemia. Pl: Dr/a Rufián Peña, Sebastián

0218/14: Efficacy and safety of early postoperative intraperitoneal chemotherapy (EPIC) with paclitaxel in the radical surgical treatment of ovarian peritoneal carcinomatosis. PI: Dr/a Muñoz Casares, Francisco C.

0131/15: Multicenter randomized clinical trial to evaluate the efficacy and safety of hyperthermic intraperitoneal chemotherapy (HIPEC) with mitomycin C associated with surgery in the treatment of locally advanced colorectal carcinoma.

PI: Dr/a Arjona Sánchez, Álvaro

2168: Observational, prospective, multicenter study in intensive Care to evaluate the diagnostic reliability of PCR study (reacted in a polymerase chain) in patients receiving empirical antifungal treatment for suspected invasive candidiasis

PI: Dr/a Robles Ariza, Juan Carlos

## HIGHLIGHTS

**Applications of Artificial Vision** 





Principal Investigator (PI) Rafael Medina Carnicer rmedina@uco.es PAIDI TIC-161 Scientific Group



Researchers Angel Carmona Poyato Nicolás Luis Fernández García Juan Luis Garrido Castro Francisco José Madrid Cuevas Manuel Jesus Marín Jiménez Rafael Muñoz Salinas Enrique Yeguas Bolívar Pre Doctoral-Researchers (PhD Students y MSc Students) Eusebio Jesús Aguilera Aguilera Sergio Garrido Jurado David López Fernández Manuel Ignacio López Quintero Víctor Manuel Mondejar Guerra

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, Augmented Reality, Virtual Reality.

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; Tracking; Object Recognition 3D-Vision; Augmented Reality; Gesture Recognition.

#### Scientific Production

#### **Publications**

#### **Original Papers**

Mondejar-Guerra VM, Munoz-Salinas R, Marin-Jimenez MJ, Carmona-Poyato A, Medina-Carnicer R. Keypoint descriptor fusion with Dempster-Shafer theory. INTERNATION-AL JOURNAL OF APPROXIMATE REASON-ING.2015. 60:57-70.

IF: 2,451

Q: 1

Aguilera-Aguilera Ej., Carmona-Poyato A, Madrid-Cuevas fj, Muñoz-Salinas R. Novel method to obtain the optimal polygonal approximation of digital planar curves based on Mixed Integer Programming. JOURNAL OF VISUAL COMMUNICATION AND IMAGE REP-RESENTATION. 2015.30 106–116. IF: 1,218

Q: 2

López-Fernández D, Madrid-Cuevas FJ, Carmona-Poyato A, Muñoz-Salinas R, R. Medina-Carnicer. Entropy volumes for viewpoint-independent gait recognition. MACHINE VISION AND APPLICATIONS (2015) 26:1079– 1094.

IF: 1,351 . Q: 2

Reta C, Altamirano L, Gonzalez JA, Medina-Carnicer R. Three hypothesis algorithm with occlusion reasoning for multiple people tracking. JOURNAL OF ELECTRONIC IMAG-ING.2015. 24(1): . IF: 0,672

Q: 3

#### **Papers in Collaboration**

Cozar, JR; Marin-Jimenez, MJ; Gonzalez-Linares, JM; Guil, N; Gomez-Luna, J.Calculation of dense trajectory descriptors on a heterogeneous embedded architecture. JOURNAL OF SYSTEMS ARCHITECTURE.2015.61(10); 659-667 IF: 0,44 Q: 4

#### Research Funding

#### National

Medina Carnicer, R. Svsmem: 3D Vision system without markers for unsupervised assessment of mobility . Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: TIN2012-32952

Medina Carnicer, R (Co-IP). Collaboration in the development of the "BROCA" project (development of a surgical robot with 3D vision). Requena Tapia, MJ (IP) . BROCA Project. Funding agency: Collaboration Agreements between MINECO (FEDER) and the University of Cordoba for the implementation of a biomedical research project. Reference: CCB.029PM

#### **Contracts with Companies**

Medina Carnicer, R. Implementing a 3D vision system (SVCS) for determining irregular object geometries in CN. Jose Cabrera. Funding agency:Enresa



### HIGHLIGHTS

9

Publications

diseases

Impact Factor **7,072** 

**Genetics and behavioural** 

Average Impact Factor **0,786** 



#### Researchers

Encarna Alejandre Duran Francisco José Alós Cívico Rafael Burgos Marín Teresa Guijarro Granados M<sup>a</sup> Salud Jiménez Romero Pilar Martin Borreguero Juan Antonio Moriana (PAIDI HUM-924 Scientific Group) María Auxiliadora Romero Balsera M<sup>a</sup> Araceli Sánchez Raya Vicente Sánchez Vázquez Post- Doctoral Researchers M Del Mar Gámez Del Estal Francisco Mariano García Torres

Pre Doctoral-Researchers (PhD Students y MSc Students) Ángel Rodríguez Ramos Jaime Osuna Luque

#### **Team Leader**

Principal Investigator (PI) Manuel Ruiz Rubio ge1rurum@uco.es PAIDI BIO-272 Scientific Group

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.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Gálvez-Lara, M., Moriana, J.A., Vilar, R., Fasfous, A., Hidalgo, N. y Pérez, M. Validation of the Cross-Linguistic Naming Test: A naming test for different cultures. A preliminary study in Spanish population. JOURNAL OF CLINI-CAL AND EXPERIMENTAL NEUROPSYCHOLO-GY.2015. 37, 102-112. IF: 2,083 Q:2 Langer, A., Cangas, A., Lysaker, P. y Moriana, J.A. Hallucination-like Experiences: Interpretation, Emotional Reactions and Daily Life Implications' in Clinical and Nonclinical Populations. PSICOTHEMA.2015. 27,19-25 IF: 1,120

Q:2

Guerrero, M.; Alós, F.; Moriana., JA (2015). Emergent Relations with Compound Stimuli in Conditional and Simple Discriminations: an Experimental Application in Children. PSYCHO-LOGICAL RECORD.2015. 65 - 3, pp.475 - 486. IF: 0,879 Q:3

Q:3

Valencia, M., Moriana, J.A., Kopelowicz, A., López, S., Liberman, R.P. (2015). Social-Skills Training for Spanish-Speaking Persons with Schizophrenia: Experiences From Latin America, Spain, and the United States. AMERICAN JOURNAL OF PSYCHIATRIC REHABILITA-TION.2015. 18 - 3, pp. 209 - 246. IF: 0,576

Garcia-Torres F, Alós FJ, Pérez-Dueñas C. Posttraumatic stress disorder in cancer survivors: A review of the psychological treatments available.PSICOONCOLOGIA 2015; 12(2-3): 293-301.

- IF: 0,145
- Q:4

Garcia-Torres F, Alós FJ. Efficacious psychological treatments for reducing fatigue in cancer survivors: The state of the question and future prospects. PAPELES DEL PSICÓLOGO 2015; 36(2): 3-13. IF: 0,186 Q:4

Sánchez, A., Martínez, E., Moriana, J.A., Alós, F. y Luque, B. L Early intervention in autism spectrum disorders (ASD). Psicología de la Educación. 2015.21 - 1 IF: 0.00

Moriana, J.A., Liberman, R:P., Kopelowicz, Luque, B., Cangas, A. y Alós, F. Habilidades sociales en la esquizofrenia. Psicología Conductual/Behavioural Psychology.2015. 23, 5-24. IF: 0,00

#### **Research Funding**

Moriana, J.A. Evidence-based short psychological treatments for common disorders. A randomized trial in the specialized primary care setting. Funding agency: Spanish Ministry of Economy and Competitiveness (MINE-CO). Reference: PSI2014-56368-R

Moriana, J.A. New smartphone app for early detection of autism and the development of therapeutic activities on the part of parents and keepers. Funding agency: Fundación Privada Cajasur

#### **Contracts with Companies**

Ruiz Rubio, M. Caenorhabditis elegans as models of neurological diseases.Funding agency: Canvax Biotech S.L. Reference:INTER.0002

Sánchez-Raya, A., Luque, B. y Moriana, J.A. Agreement with the CISPS for the creation of the Early Child Care Center (Centro de Atención Infantil Temprana) of the University of Cordoba.

#### **Clinical Trials**

2013-001955-11. PSICAP Project. Pilot Project to treat emotional disorders in primary care with psychological techniques evidence-based project. A randomized controlled trial.

PSI2014-56368-R PSIBRIEF Project. Evidence-based short psychological treatments for common disorders. A randomized trial in the specialized primary care setting.

Q:4

## HIGHLIGHTS

## Metabolomics. Identification of bioactive components



#### Team Leader

Principal Investigator (PI) Mª Dolores Luque de Castro qa1lucam@uco.es PAIDI FQM-227 Scientific Group Emerging Researcher (ER): Feliciano Priego Capote



Researchers Mª del Mar Delgado Povedano María Auxiliadora Fernández Peralbo Antonio Mena Bravo María Molina Calle Asunción López Bascón Carlos Augusto Ledesma Escobar Angela Peralbo Molina Post- Doctoral Researchers Carlos Ferreiro Vera, Mónica Calderón Santiago Verónica Sánchez de Medina Baena María Pilar Delgado De La Torre

Pre Doctoral-Researchers (PhD Students y MSc Students) Laura Castillo Peinado Diego Luque Córdoba

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, nutrimetabolomics 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.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Mena-Bravo A, Priego-Capote F, Luque de Castro MD. Study of blood collection and sample preparation for analysis of vitamin D and its metabolites by liquid chromatography-tandem mass spectrometry. ANALYTICA CHIMICA ACTA. 879:69-76.

Q: 1 D: 1 Peralbo-Molina A, Calderon-Santiago M, Priego-Capote F, Jurado-Gamez B, Luque de Castro MD. Development of a method for metabolomic analysis of human exhaled breath condensate by gas chromatography-mass spectrometry in high resolution mode. ANA-LYTICA CHIMICA ACTA. 887:118-126. IF: 4,513

Q: 1 D: 1

IF: 4,513

Lopez-Bascon MA, Priego-Capote F, Calderon-Santiago M, de Medina VS, Moreno-Rojas JM, Garcia-Casco JM, Luque de Castro MD. Determination of Fatty Acids and Stable Carbon Isotopic Ratio in Subcutaneous Fat to Identify the Feeding Regime of Iberian Pigs. JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY. 63(2):692-699.

IF: 2,912

Q: 1 D: 1

Delgado de la Torre MP, Priego-Capote F, Luque de Castro MD. Characterization and Comparison of Wine Lees by Liquid Chromatography-Mass Spectrometry in High-Resolution Mode. JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY. 63(4):1116-1125. IF: 2,912

Q: 1 D: 1

Mena-Bravo A, Ferreiro-Vera C, Priego-Capote F, Maestro MA, Mourino A, Quesada-Gomez JM, Luque de Castro MD. Quantitative analytical method to evaluate the metabolism of vitamin D. CLINICA CHIMICA ACTA; INTERNATIONAL JOURNAL OF CLINI-CAL CHEMISTRY. 442:6-12. IF: 2,824

- Q: 1

Calderon-Santiago M, Priego-Capote F, Luque de Castro MD. Enhancing detection coverage in untargeted metabolomics analysis by sol-

id-phase extraction on-line coupled to LC-MS/MS. ELECTROPHORESIS. 36(18):2179-2187 IF: 3.028 Q: 1 Calderon-Santiago M, Priego-Capote F, Turck N, Robin X, Jurado-Gamez B, Sanchez JC, Luque de Castro MD. Human sweat metabolomics for lung cancer screening. ANA-LYTICAL AND BIOANALYTICAL CHEMISTRY. 407(18):5381-5382. IF: 3,436 Q: 1 Fernandez-Peralbo MA, Calderon Santiago M, Priego-Capote F, Luque de Castro MD. Study of exhaled breath condensate sample preparation for metabolomics analysis by LC-MS/MS in high resolution mode. TALANTA. 144:1360-1369. IF: 3,545 Q: 1 Molina-Calle M, Priego-Capote F, Luque de Castro MD. Ultrasound-assisted emulsification-extraction of orange peel metabolites prior to tentative identification by LC-QTOF MS/MS. TALANTA. 141:150-157. IF: 3,545 Q: 1 Molina-Calle M, Priego-Capote F, Lugue de Castro MD. Development and application of a quantitative method for determination of flavonoids in orange peel: Influence of sample pretreatment on composition. TALANTA. 144:349-355. IF: 3,545 Q: 1 Sanchez de Medina V, Priego-Capote F, Luque de Castro MD. Characterization of monovarietal virgin olive oils by phenols profiling. TA-LANTA. 132:424-432. IF: 3,545 Q: 1 Ledesma-Escobar CA, Priego-Capote F, Luque de Castro MD. Comparative study of the effect of auxiliary energies on the extraction of Citrus fruit components. TALANTA. 144:522-528. IF: 3,545 Q: 1

Sanchez de Medina V, El Riachy M, Priego-Capote F, Luque de Castro MD. Composition of fatty acids in virgin olive oils from cross breeding segregating populations by gas chromatography separation with flame ionization detection. JOURNAL OF THE SCIENCE OF FOOD AND AGRICULTURE. 95(14):2892-2900.

- IF: 1,714
- Q: 1

Ledesma-Escobar CA, Priego-Capote F, Luque de Castro MD. Characterization of lemon (Citrus limon) polar extract by liquid chromatography-tandem mass spectrometry in high resolution mode. JOURNAL OF MASS SPECTROMETRY. 50(11):1196-1205. IF: 2,379

- Q: 2

de la Torre MPD, Priego-Capote F, Luque de Castro MD. Comparison of the volatile profile of vine-shoots and oak chips by headspace-gas chromatography-mass spectrometry (HS-GC-MS). ANALYTICAL METHODS. 7(5):1758-1769.

IF: 1,821

Q: 2

de la Torre MPD, Priego-Capote F, Luque de Castro MD . Tentative identification of polar and mid-polar compounds in extracts from wine lees by liquid chromatography-tandem mass spectrometry in high-resolution mode. JOURNAL OF MASS SPECTROMETRY. 50(6):826-837.

- IF: 2,379
- Q: 2

Sanchez de Medina V, Priego-Capote F, Luque de Castro MD. The effect of genotype and ripening index on the phenolic profile and fatty acids composition of virgin olive oils from olive breeding programs. EUROPEAN JOURNAL OF LIPID SCIENCE AND TECHNOL-OGY. 117(7):954-966.

- IF: 1,812
- Q: 2

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Sanchez de Medina V, Calderon-Santiago M, El Riachy M, Priego-Capote F, Luque de Castro MD. Influence of genotype on the fatty acids composition of virgin olive oils from advanced selections obtained by crosses between Arbequina, Picual, and Frantoio cultivars along the ripening process. EUROPEAN JOURNAL OF LIPID SCIENCE AND TECHNOL-OGY. 117(8):1261-1270.

- IF: 1,812
- Q: 2

#### **Original Reviews**

Delgado-Povedano MM, Luque de Castro MD. A review on enzyme and ultrasound: A controversial but fruitful relationship. ANALYTICA CHIMICA ACTA. 889:1-21. IF: 4,513

Q: 1 D: 1

#### Papers in Collaboration

Rojano-Delgado MA, Priego-Capote F, Luque de Castro MD, De Prado R. Mechanism of imazamox resistance of the ClearfieldA (R) wheat cultivar for better weed control. AGRONOMY FOR SUSTAINABLE DEVELOP-MENT. 35(2):639-648. IF: 3,992 Q: 1 D: 1

Saez-Bastante J, Pinzi S, Jimenez-Romero FJ, Luque de Castro MD, Priego-Capote F, Dorado MP. Synthesis of biodiesel from castor oil: Silent versus sonicated methylation and

oil: Silent versus sonicated methylation and energy studies. ENERGY CONVERSION AND MANAGEMENT. 96:561-567. IF: 4,38

Q: 1 D: 1

Finamore F, Priego-Capote F, Nolli S, Zufferey A, Fontana P, Sanchez JC. Characterisation of the influences of aspirin-acetylation and glycation on human plasma proteins. JOURNAL OF PROTEOMICS. 114:125-135. IF: 3,888

Q: 1

#### **Research Funding**

#### National

Luque de Castro MD.Study of the relevance of ultrasound frequency in improving sample preparation stages in proteomics, metabolomics and degradation processes. Funging agency:Spanish Ministry of Economy and Competitiveness (MINECO). Reference: CTQ2012-37428 (finished in Dec 2015)

López Miranda, J (This project was funded as a collaborative initiative among different research groups). Early predictors and causes of loss of phenotypic flexibility as individual risk factor of metabolic disease: towards a personalized medicine (FLEXI-MET). Funding agency: Institute Carlos III Health (ISCIII). REF: PIE/1400005

Priego Capote, F. Development strategies for improving spectrometric detection metabolomic mass oriented analysis and global applied to clinical and nutrition. Funding Agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: CTQ2015-68813-R

#### Regional

Luque de Castro, MD. Optimizing and applying metabolomic platforms for non-invasive analysis of biofluids to determine markers for early diagnosis of lung cancer.Funging agency:Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: FQM1602-2012

#### **Contracts with Companies**

Luque de Castro, MD.Completing the development of active plant compound extraction methods for their identification and quantification. Funging agency: Phytoplant Research, S. L.

Luque de Castro, MD. Identification by LC-QTIF, measurement by triple quadrupole LC-MS/MS and ionization by APCI of compounds in vegetable extracts.Funding Agency: Phytoplant Research, S. L.

Luque de Castro, MD/Priego Capote, F. Identification and quantification of components of black garlic and compared with fresh garlic. Funding Agency: La abuela Carmen

Luque de Castro, MD/Priego Capote, F. Identification -quantification of the components of the Stevia' plant. Funding Agency: Vitrosur

Luque de Castro, MD/Priego Capote, F. Analysis of vitamin D and its metabolites in human serum samples . Funding Agency: Institute of Health Carlos III (ISCIII).

Luque de Castro, MD. Determination of vitamin D and its 25(OH)D 1,25(OH)2D and 24,25(OH)D metabolites (potentially also the C3 epimer) in serum samples provided by the organisation. Funding agency: Ospedale San Raffaele S.R.L.Reference: PSS.0112

Luque de Castro, MD. Postprandial study after eating sausages with modified fat in obese patients and healthy adults and children. Funding Agency: ACEITES DEL SUR-COOSUR S.A.Reference: ITC-20151323



### HIGHLIGHTS

**Team Leader** 

Principal Investigator (PI) Teresa Roldán Arjona ge2roarm@uco.es

Researchers Rafael Rodríguez Ariza

## **Epigenetics**





Post- Doctoral Researchers M<sup>a</sup> Dolores Córdoba Cañero M<sup>a</sup> Victoria García Ortiz M<sup>a</sup> Teresa Morales Ruiz Pre Doctoral-Researchers (PhD Students y MSc Students) Casimiro Barbado García-Gil Iván Devesa Guerra Macarena Dorado León Jara Teresa Parrilla Doblas

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 mecitosina 5-DNA glycosylase activity, and initiate the deletion of 5-mec by a mechanism 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 demethylation 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.

#### **Scientific Production**

#### **Publications**

#### Papers In Collaboration

Li Y, Cordoba-Canero D, Qian W, Zhu X, Tang K, Zhang H, Ariza RR, Roldan-Arjona T, Zhu JK. An AP Endonuclease Functions in Active DNA Demethylation and Gene Imprinting in Arabidopsis. PLOS GENETICS.2015. 11(1): e1004905. IF: 7,528 Q: 1 D: 1

#### **Research Funding**

#### National

Roldán Arjona, Mª T. DNA demethylation: basic molecular mechanisms and their relevance to the reversal of epigenetic silencing. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO).Reference: BFU2013-43269-P

#### International

Roldán Arjona, M<sup>a</sup> T. Epigenetic Chemical Biology (EPICHEM). Funding agency: European Commision. Reference: CMST COST Action CM1406 http://www.cost.eu/COST\_Actions/cmst/Ac-

http://www.cost.eu/COST\_Actions/cmst/Actions/CM1406?management

#### Regional

Roldán Arjona, M<sup>a</sup> T. Molecular mechanisms of DNA demethylation and implications in epigenome reprogramming. Funding agency: Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Reference: CVI-7576

#### **Contracts with Companies**

Roldán Arjona, M<sup>a</sup> T. Services provided for Canvax. Funding agency: Canvax Biotech S.L. Reference:PSS.0032



### HIGHLIGHTS

Principal Investigator (PI) Mercedes Gil Campos h02gicam@uco.es;

Research Network on Maternal and Child Health (RedSAMID) and associated Centro de Investigación Biomédica en Red de Enfermedades

PAIDI CTS-639 Scientific Group

**Team Leader** 

Raras (CIBERER)

**Metabolism in Childhood** 



Researchers Montserrat Antón Gamero M<sup>a</sup> José de la Torre Aguilar José Fernando Fernández Gutiérrez Ignacio Ibarra De La Rosa Eduardo López Laso María Elena Mateos Gonzalez Juan Luis Perez Navero Maria Esther Ulloa Santamaria Maria Jose Velasco Jabalquinto Katherine Flores Rojas Post- Doctoral Researchers Francisco Jesus Llorente Cantarero

Our group studies infectious diseases from two approaches:

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 address neuropediatrics, and particular, the inborn errors of metabolism.

#### **Keywords**

Obesity; metabolic syndrome; arteriosclerosis; inflammation; oxidative stress; gene expression; proteomics; nutrigenetics; nutrigenomics.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

de la Oliva P, Menendez-Suso JJ, Iglesias-Bouzas M, Alvarez-Rojas E, Gonzalez-Gomez JM, Rosello P, Sanchez-Diaz JI, Jaraba S. Spanish Grp Preload Responsiveness. Cardiac preload responsiveness in children with cardiovascular dysfunction or dilated cardiomyopathy: A Multicenter Observational Study PEDIATRIC CRITICAL CARE MEDICINE.2015 16(1):45-53. IF: 2,338

Q:1

Baena-Gomez MA, De La Torre Aguilar MJ, Mesa MD, Perez Navero JL, Gil-Campos M. Changes in antioxidant defense system using different lipid emulsions in parenteral nutrition in children after hematopoietic stem cell transplantation. NUTRIENTS. 7(9):7242-7255. IF: 3,27

Q:2

Moreno-Solis G, Fernandez-Gutierrez F, Torres-Borrego J, Torcello-Gaspar R, Gomez-Chaparro Moreno JL, Perez-Navero JL. Lowserum 25-hydroxyvitamin D levels and bronchiolitis severity in Spanish infants. EU-ROPEAN JOURNAL OF PEDIATRICS.2015. 174(3):365-372.

IF: 1,89

Q: 2

Candau-Alvarez A, Gil-Campos M, De la Torre-Aguilar MJ, Llorente-Cantarero F, Lopez-Miranda J, Luis Perez-Navero J. Early modification in drainage of interleukin-1 beta and tumor necrosis factor-alpha best predicts surgical-site infection after cervical

neck dissection for oral cancer JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY.2015. 73(6):1189-1198.

- IF: 1,425 Q: 2
- Q

Candau-Alvarez A, Linares-Sicilia MJ, Dean-Ferrer A, Perez-Navero JL. Role of culture of postoperative drainage fluid in the prediction of infection of the surgical site after majoronco logical operations of the head and neck. BRITISH JOURNAL OF ORAL & MAXILLOFACIAL SURGERY. 2015.53(2): IF: 1,076

Q:3

Moreno-Solis G, Torres-Borrego J, de la Torre-Aguilar MJ, Fernandez-Gutierrez F, Llorente-Cantarero FJ, Perez-Navero JL. Analysis of the local and systemic inflammatory response in hospitalized infants with respiratory syncitial virus bronchiolitis. AL-LERGOLOGIA ET IMMUNOPATHOLOGIA.2015. 43(3):264-271. IF: 1.748

Q:4

#### **Papers in Collaboration**

Maldonado-Lobon JA, Gil-Campos M, Maldonado J, Lopez-Huertas E, Flores-Rojas K, Valero AD, Rodriguez-Benitez MV, Banuelos O, Lara-Villoslada F, Fonolla J, Olivares M. Long-term safety of early consumption of Lactobacillus fermentum CECT5716: A 3-year follow-up of a randomized controlled trial. PHARMACOLOGICAL RESEARCH.2015. 95(96):12-19. IF: 4.408

Q: 1

Aguilera CM, Gomez-Llorente C, Tofe I, Gil-Campos M, Canete R, Gil A. Genome-Wide Expression in Visceral Adipose Tissue from Obese Prepubertal Children INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES.2015. 16(4):7723-7737. IF: 2.862

Q: 2

Zimoń M, Battaloğlu E, Parman Y, Erdem S, Baets J, De Vriendt E, Atkinson D, Almeida-Souza L, Deconinck T, Ozes B, Goossens D, Cirak S, Van DammeP,Shboul M, Voit T, Van Maldergem L, Dan B, El-Khateeb MS, Guergueltcheva V, Lopez-Laso E, Goemans N, Masri A, Züchner S, Timmerman V, Topaloğlu H, De Jonghe P, Jordanova A. Unraveling the genetic landscape of autosomal recessive Charcot-Marie-Tooth neuropathies using a homozygosity mapping approach.NEUROGE-NETICS. 2015.16(1): 33-42. IF: 2.884

Q:2

Q.2

Olza J, Aguilera CM, Gil-Campos M, Leis R, Bueno G, Valle M, Canete R, Tojo R, Moreno LA, Gil A. A Continuous Metabolic Syndrome Score Is Associated with Specific Biomarkers of Inflammation and CVD Risk in Prepubertal Children. ANNALS OF NUTRITION AND ME-TABOLISM.2015. 66(2-3):72-79. IF: 2.618

⊪: 2,t

Q:2

GarciaCastano A, Perez de Nanclares G, Madariaga L, Aguirre M, Chocron S, Madrid A, Lafita Tejedor FJ, Gil Campos M, Sanchez del Pozo J, Ruiz Cano R, Espino M, Gomez Vida JM, Santos F, Garcia Nieto VM, Loza R, Miguel Rodriguez L, Hidalgo Barquero E, Printza N, Camacho JA, Castano L, Ariceta G. RenalTubeGrp. Novel mutationsassociatedwithnephrogenic diabetes insipidus. A clinical-geneticstudy. EUROPEAN JOURNAL OF PEDIATRICS. 174(10):1373-1385. IF: 1,89

Q: 2

Fernandez-Ramos JA, Lopez-Laso E, Camino-Leon R, Gascon-Jimenez FJ, Jimenez-Gonzalez MD.Experience in molecular diagnostic in hereditary neuropathies in a pediatric tertiary hospital. REVISTA DE NEU-ROLOGIA.2015. 61(11);490-498

IF: 0,83 Q: 4

Mercedes Gil-Campos, Miguel Ángel San José González, Juan José Díaz Martín y Comité de Nutrición de la Asociación Española de Pediatría. Uso de azúcares y edulcorantes en la alimentación del niño. Recomendaciones del comité de nutrición de la asociación española de pediatría. An Pediatr (Barc) 2015; 83(5):353.e1-353.e7.

IF: 0,722 Q: 4

#### **Research Funding**

#### National

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

#### Regional

Gil Campos, M.Search for cardiovascular risk biomarkers and antioxidant defense system in prepubertal children with a history of extrauterine growth retardation (biorica). Funding Agency:Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0480-2012

Perez Navero JL. Possibles biomonitoring of inflammatory markers, oxidative stress, intestine microbiota and exposure to heavy metals in autism spectrum disorder in childhood.

Q.

#### **Contracts with Companies**

Gil Campos, M. Design and development of nutritionally balanced foods, appealing and comfortable/easy to handle specified for ages 3 and 4. Reference ITC-20151270

Gil Campos, M. Development of advanced fats. Reference ITC-20151323

#### **Clinical Trials**

0061/11: European Neuroblastoma Treatment Protocol for low or intermediate risk / European Low and Intermediate Risk Neuroblastoma

PI: Dr/a Mateos Gonzalez, Maria Elena

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

1783: Register of patients with type C Nlemann-Pick.

PI: Dr/a López Laso, Eduardo

2060: An international registry which collects data on disease manifestations, interventions and outcomes in patients with tuberous sclerosis complex PI: Dr/a López Laso, Eduardo

2622: Randomized clinical trial of parallel group, double-blind, placebo control to evaluate the efficacy and safety of docoxahenoicic acid in the coajuvant treatment of children on the spectrum of the autism disorder. Pl: Dr/a Gil Campos, Maria Mercedes

2414: Nutritional intervention study , multicenter , randomized, blinded , parallel group to evaluate the effect to evaluate the effect of the consumption of Lactobacillus fermentum CECT5716 on the duration of acute diarrhea in children .

PI: Dr/a Gil Campos, Maria Mercedes

Gil Campos, M. P035 Diarrhea treatment Study of nutritional intervention. Multicenter, randomized, blind, parallel group study to evaluate the effect of consumption of Lactobacillus fermentum CECT5716 on the duration of acute diarrhea in children

## HIGHLIGHTS

Team Leader

Principal Investigator (PI) Isaac Túnez Fiñana fm2tufii@uco.es PAIDI CTS-624 scientific group

## **Oxidative Stress and Nutrition**





Researchers Antonio Cruz Guerrero Félix Gascón Luna Ignacio Jimena Medina Rafael Lillo Roldán Evelio Luque Carabot José Peña Amaro Mª Concepción Ruiz Villen

Post- Doctoral Researchers Fernando Sánchez López Pre Doctoral-Researchers (PhD Students y MSc Students) Eduardo Agüera Morale Mª Carmen Bahamonde Román Cristina Conde Gavilán Antonio Cruz Guerrero Alberto Galván Jurad

Other members of the Group (Nursing, Technical, and Administrative Staff) Ana Isabel Giraldo Polo Manuel La Torre Luque

Our group studies the effect of different antioxidant agents, as well as transcraneal 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.

### **Scientific Production**

#### **Publications**

#### **Original Papers**

Colin-Gonzalez AL, Aguilera G, Serratos IN, Escribano BM, Santamaria A, Tunez I. On the Relationship Between the Light/Dark Cycle, Melatonin and Oxidative Stress. CURRENT PHARMACEUTICAL DESIGN. 21(24): 3477-3488.

IF: 3,452 Q: 1

Luque E, Ruz-Caracuel I, Medina FJ, Leiva-Cepas F, Aguera E, Sanchez-Lopez F, Lillo R, Aguilar-Luque M, Jimena I, Tunez I, Pena J. Skeletal muscle findings in experimental autoimmune encephalomyelitis. PATHOLOGY RESEARCH AND PRACTICE. 211(17): 493-504.

IF: 1,397

Q: 4

#### Papers in Collaboration

Bocchetta M, Galluzzi S, Kehoe PG, Aguera E, Bernabei R, Bullock R, Ceccaldi M, Dartigues JF, de Mendonca A, Didic M, Eriksdotter M, Felician O, Frolich L, Gertz HJ, Hallikainen M, Hasselbalch SG, Hausner L, Heuser I, Jessen F, Jones RW, Kurz A, Lawlor B, Lleo A, Martinez-Lage P, Mecocci P, Mehrabian S, Monsch A, Nobili F, Nordberg A, Rikkert MO, Orgogozo JM, Pasquier F, Peters O, Salmon E, Sanchez-Castellano C, Santana I, Sarazin M, Traykov L, Tsolaki M, Visser PJ, Wallin AK, Wilcock G, Wilkinson D, Wolf H, Yener G, Zekry D, Frisoni GB. The use of biomarkers for the etiologic diagnosis of MCI in Europe: An EADC survey. ALZHEIMERS & DEMENTIA. 11(2): 195-206. IF: 13,324

Q: 1 D: 1

Villar LM, Costa-Frossard L, Masterman T, Fernandez O, Montalban X, Casanova B, Izquierdo G, Coret F, Tumani H, Saiz A, Arroyo R, Fink K, Leyva L, Espejo C, Simo-Castello M, Garcia-Sanchez MI, Lauda F, Llufriu S, Alvarez-Lafuente R, Olascoaga J, Prada A, Oterino A, de Andres C, Tintore M, Ramio-Torrenta L, Rodriguez-Martin E, Picon C, Comabella M, Quintana E, Aguera E, Diaz S, Fernandez-Bolanos R, Garcia-Merino JA, Landete L, Menendez-Gonzalez M, Navarro L, Perez D, Sanchez-Lopez F, Serrano-Castro PJ, Tunon A, Espino M, Muriel A, Bar-Or A, Alvarez-Cermeno JC. Lipid-Specific Immunoglobulin M Bands in Cerebrospinal Fluid Are Associated with a Reduced Risk of Developing Progressive Multifocal Leukoencephalopathy during Treatment with Natalizumab. ANNALS OF NEUROLOGY. 77(3): 447-457. IF: 9.977

Q: 1 D: 1

Estrada, C; Fernandez-Gomez, FJ; Lopez, D; Gonzalez-Cuello, A; Tunez, I; Toledo, F; Blin, O; Bordet, R; Richardson, JC; Fernandez-Villalba, E; Herrero, MT Transcranial magnetic stimulation and aging: Effects on spatial learning and memory after sleep deprivation in Octodon degus NEUROBIOLOGY OF LEARNING AND MEMORY.2015.125;274 IF: 3,652

Q: 1 D: 1

Estrada C, Lopez D, Conesa A, Fernandez-Gomez F, Gonzalez-Cuello A, Toledo F, Tunez I, Blin O, Bordet R, Richardson JC, Fernandez-Villalba E, Herrero MT. Cognitive Impairment After Sleep Deprivation Rescued by Transcranial Magnetic Stimulation Application in Octodon degus. NEUROTOXICITY RE-SEARCH. 28(4): 361-371.

IF: 3,538

Q: 2

Colin-Gonzalez AL, Becerril H, Flores-Reyes BR, Torres I, Pinzon E, Santamaria-Del Angel D, Tunez I, Serratos I, Pedraza-Chaverri J, Santamaria A, Maldonado PD. Acute restraint stress reduces hippocampal oxidative damage and behavior in rats: Effect of S-allyl cysteine. LIFE SCIENCES. 135: 165-172. IF: 2,702

Q: 2

#### **Reviews in Collaboration**

Colin-Gonzalez AL, Ali SF, Tunez I, Santamaria A. On the antioxidant, neuroprotective and anti-inflammatory properties of S-allyl cysteine: An update. NEUROCHEMISTRY INTERNA-TIONAL. 89: 83-91.

IF: 3,092

Q: 2

#### **Research Funding**

#### National

Túnez Fiñana, I. Drug development against tumor cells mothers (CSC) by screening libraries using synthetic kinase inhibitors of GPCRs and NFAT - calcineurin interaction.Funding Agency: Ministry of Economy and Competitiveness (MINECO). Referenece: RTC-2015-3386-1\_1

#### **Contracts with Companies**

Túnez Fiñana, I. Development of in vitro CNS disease models and trial of the activity of active compounds identified using FRIDA. Funding agency Canvax Biotech S.L. Reference: INTER.0001

Agüera A. Phase study and verification method SharpMind ("Mentágil") cognitive stimulation.) Reference:AC-2015-FIBICO-001

#### **Clinical Trials**

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

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, doseblind 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

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 methylthioninium 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

0227/13: A prospective, single-arm study in a clinical setting to assess the efficacy, tolerability and convenience of teriflunomide according to patient reported outcomes (PRO) in patients with multiple sclerosis. PI: Dr/a Sánchez López, Fernando

0255/13: An opne multicenter, randomized, placebo-controlled, triple-blind phase II clinical trial to assess the effectiveness of blood mononuclear cells intra infusion of autologous bone marrow in patients with ischemic stroke

PI: Dr/a Sánchez López, Fernando

0301/13: A prospective, multicenter, randomized, double-blind, parallel-group, placebo-controlled, phase III 96-week duration study to assess the efficacy and safety of masitinib 4.5mg/kg/day vs placebo. PI: Dr/a Agüera Morales, Eduardo

0011/14 : A multicenter, randomized, double-blind, placebo-controlled study to assess the safety and efficacy of eculizumab in patients with recurrent optic neuromyelitis (NMO). PI: Dr/a Sánchez López, Fernando

0012/14: An open, phase III extension study of ECU-NMO-301 to assess the efficacy and safety of eculizumab in patients with recurrent optic neuromyelitis (NMO). PI: Dr/a Sánchez López, Fernando

0082/14: An open, multicenter study to assess the efficacy of oral Tecfidera™ (dimethyl fumarate) in EM activity and in patient reported outcomes in patients with remitting-relapsing multiple sclerosis in real practice (PROTEC).

PI: Dr/a Sánchez López, Fernando

0235/14: An open, multicenter, aletorizared study to assess the impact of natalizumab against tissue damage fingolimod in central nervous system and in recovery of subjects with multiple sclerosis

PI: Dr/a Sánchez López, Fernando

0150/15: A phase 3 multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of aducanumab (biib037) in subjets with early alzheimer's disease.

PI: Dr/a Agüera Morales, Eduardo

0050/15:A phase 3 , prospective, multicenter, randomized, double-blind, placebo-controlled, parallel-group to compare the efficacy and safety of masitinib versus placebo in patients with cognitive impairment associated with Parkinson's disease. 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

2487: An observational, multicenter , multinational paragraph gather information on security and document the pharmaceutical use of Fampyra When are US in Medical Practice . PI: Dr/a Agüera Morales, Eduardo

2878: Evaluation of patient preferences towards different options disease modifying treatments in multiple sclerosis relapsing-remitting .

PI: Dr/a Sánchez López, Fernando

2660: A retrospective, observational, multicenter, national study to assess the use of fingolimod Gilenya in patients with remitting-relapsing multiple sclerosis in clinical practice. Estudio NEXT

PI: Dr/a Agüera Morales, Eduardo

2681: A retrospective, observational to describe the tolerability of Gilenya (Fingolimod) at the start of treatment in clinical practice habituate. MS Right Study

PI: Dr/a Agüera Morales, Eduardo

2660/2: A retrospective, observational , multicenter antional, to evaluate the experience in clinical practice Gilenya fingolimod treatment in patients with relapsing remitting multiple sclerosis. NEXT Study

PI: Dr/a Sánchez López, Fernando

# GE2

## HIGHLIGHTS

Knowledge Discovery and Intelligent Systems





Researchers Carlos García Martínez Gibaja Galindo; Eva Lucrecia Zafra Gómez; Amelia Romero Morales; Cristóbal Romero Salguero; José Raúl

**Post-PhD Researchers** Luna Ariza; José María Cano Rojas; Alberto Pre Doctoral-Researchers (PhD Students y MSc Students) Robles Berumen; Hermes Ramírez Quesada; Aurora Reyes Pupo; Oscar Gabriel Guerrero Enamorado; Alain

#### Team Leader

Principal Investigator (PI) Sebastián Ventura Soto sventura@uco.es

In the KDIS research group, our interests mainly focus on the development of knowledge discovery methods, and its application to different real problems.

We are devoted to the development of algorithms for solving classification problems in different types of problems:

- Conventional data problems.
- Multi-label data problems.
- Multi-instance problems.
- Multi-view problems.

From the applications perspective, we are interested in applying our algorithms to several real problems, focusing on aspects such as scalability or interpretability of the obtained results. Our wider expertise has been in the field of educational data, although in the last years we have also work in several health problems, like predicting diabetes from clinical data and the analysis of clinical histories to develop automatic diagnosis methods.

#### Keywords

Data Mining; Big Data Mining; Machine Learning; Classification; Clustering; Association; Educational Data Mining; Clinical Data Mining; Health Informatics.

#### **Scientific Production**

#### Original

#### Article

Ramirez A, Romero JR, Ventura S. An approach for the evolutionary discovery of software architectures. INFORMATION SCIENCES. 305:234-255. IF: 4,038 Q: 1 D: 1 Gibaja E, Ventura S. A Tutorial on Multila-

bel Learning. ACM COMPUTING SURVEYS. 47(3): e52. IF: 3,373 Q: 1 D: 1

Cano A, Luna JM, Zafra A,Ventura S.A classification module for Genetic Programming Algorithms in JCLEC. JOURNAL OF MACHINE LEARNING RESEARCH.2015.16;491-494 IF:2,473 Q: 1 D: 1

Cano A, Zafra A, Ventura S. Speeding up multiple instance learning classification rules on GPUs. KNOWLEDGE AND INFORMATION SYS-TEMS. 44(1):127-145. IF: 1,782

Q: 1

Reyes O, Morell C, Ventura S. Scalable extensions of the ReliefF algorithm for weighting and selecting features on the multi-label learning context. NEUROCOMPUTING. 161:168-182. IF: 2,083 Q: 2

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Q. Z
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#### **Research Funding**

#### National

Ventura-Soto, S. Data Mining with More Flexible Representations. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: TIN2014-55252-P

#### **Contracts with Companies**

Ventura S. Incorporating educational processes data mining to various e-learning applications Santillana Group : Analysis and preparation of the information .. Funding Agency: Santillana Group.Reference: Contrato Art. 83 .

# GE3

## HIGHLIGHTS

**Team Leader** 

Principal Investigator (PI): Juan A. Ruano Ruiz juanruanoruiz@mac.com

## Inflammatory immune-mediated cutaneous diseases



Researchers Beatriz Isla Tejera Antonio Vélez García-Nieto

Post- Doctoral Researchers Marcelino González Padilla Pre Doctoral-Researchers (PhD Students y MSc Students) Pedró Jesús Carmona Fernández F Jesús Gay Mimbreva Francisco Gómez García Ana Lorente Lavirgen Juan Luis Sanz Cabanillas

Other members of the Group (Nursing, Technical, and Administrative Staff) Carmen Clemente Millán María López García Carmen López González

Our research group is focused on prevalent or severe inflammatory skin diseases such as psoriasis. Psoriasis is a chronic inflammatory disease that is genetically complex and primarily affects skin and other organs such as joints. It is estimated that psoriasis affects 2-3% of the population and it is one of the most prevalent types of immunological diseases worldwide.

Our research group has developed a strategic plan including several lines of action.

- 1: Several research projects have been developed to identify the clinical, sociodemographic and molecular factors that influence variability in response to biological drugs in patients with psoriasis. To such purpose, we have created the largest collection of biological samples donated by patients with moderate to severe psoriasis that are currently stored at the reina Sofía University Hospital of Cordoba, Spain, which belongs to the Spanish National Biobank Network (Red Nacional de Biobancos). In the coming years, we are determining the role of some genetic polymorphisms, as well as of some patterns of CpG methylation of CpG sites in different genes, plasma concentrations of certain interleukins, or the profile of circulating miRNA.
- 2: We are interested in the development of new drugs for psoriasis. In 2015, we established a collaboration agreement with Canvax Biotech S.L within the framework of a project funded by public entities to carry out pre-clinical and clinical phase I trials to assess the efficacy and safety of the new compound CVX-785 for the treatment of psoriasis.
- 3: Being aware that translational medicine involves a multidimensional, multidisciplinary approach, we have integrated experts from different areas such as Immunology, Physics, Pharmacy, Genetics or Health Economics in diverse research groups through collaboration with the Department of Physics of the University of Cordoba, Department of Applied Economics of the University of Granada, the Laboratory of Investigative Dermatology, The Rockefeller University, New York (EEUU) or the Pharmacogenomics Laboratory, College of Pharmacy, Pharmacotherapy Education and Research Center (PERC), University of Texas Health Science Center at San Antonio (UTHSCSA), (TX, EEUU).
- 4: Finally, it is worth mentioning our commitment to innovation materialized in the form of collaboration agreements with the IT industry, namely, Canvax Biotech S.L., The Zebra Fish Lab S.L., and Lynhce Diagnostics S.L. A spin-off company called info4CURE S.L has been set up to exploit patent licenses or the potential utility models resulting from such patents.

#### Keywords

Psoriasis, Biobank, genetic polymorphisms, predictors of therapeutic response, cost-efficiency, monoclonal antibodies, immune response, cold atmospheric plasma.

#### **Scientific Production**

#### **Publications**

#### **Papers In Collaboration**

Carretero G, Ferrandiz C, Dauden E, Vanaclocha Sebastian F, Gomez-Garcia FJ, Herrera-Ceballos E, De la Cueva-Dobao P, Belinchon I, Sanchez-Carazo JL, Alsina-Gibert M, Lopez-Estebaranz JL, Ferran M, Torrado R, Carrascosa JM, Carazo C, Rivera R, Jimenez-Puya R, Garcia-Doval I. Risk of adverse events in psoriasis patients receiving classic systemic drugs and biologics in a 5-year observational study of clinical practice: 2008-2013 results of the Biobadaderm registry. JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLO-GY AND VENEREOLOGY. 29(1):156-163. IF: 2,826 Q: 1 D: 1

Medina C, Carretero G, Ferrandiz C, Dauden E, Vanaclocha F, Gomez-Garcia FJ, Herrera-Ceballos E, De la Cueva-Dobao P, Belinchon I, Sanchez-Carazo JL, Alsina M, Lopez-Estebaranz JL, Ferran M, Carrascosa JM, Torrado R, Argila D, Rivera R, Jimenez-Puya R, Garcia-Doval I. Safety of classic and biologic systemic therapies for the treatment of psoriasis in elderly: an observational study from national BIOBADADERM registry. JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY. 29(5):858-864. IF: 2,826 Q: 1 D: 1

#### Research Funding

#### National

Ruano Ruiz, J. Multicenter randomized clinical trial to evaluate in terms of cost-efficiency a predictive model of responseto anti-TNF drugs in patients with moderate-severe psoriasis. Funding agency: Institute Carlos III Health (ISCIII). Reference: ICI1400136

#### International

Ruano Ruiz, J .Skin biopsy for analysis of cell growth, cell differentiation, and inflammation in the skin.Funding Agency: Mount Sinai Hospital (NY, USA). Reference: JRR-SKIN-2015

#### **Contracts with Companies**

Ruano Ruiz, J. Collaboration Agreement with Canvax. Funding Agency: Canvax Biotech SL. Reference: PSS.0065 Jimenez Puya, R. Collaboration Agreement with PFIZER. Funding Agency: Pfizer, SLU. Reference: PSS.0060

Ruano Ruiz, J. Sponsored Conference of Research PSORIASIS. Funding Agency: Janssen-Cilag, SA. Reference: PSS.0072

Ruano Ruiz, J. Agreement with Pfizer. Funding Agency: Pfizer, SLU. Reference: CCB.0048

Ruano Ruiz, J. Development of systemic diagnosis tools. Funding Agency: LYNHCE. Reference: AC-2015-FIBICO-006

Ruano Ruiz, J. Development of new models in Biomedince in Zebrafish.Funding Agency: IKAN BIOTECH. References: 2015-FIBICO-007

Ruano Ruiz, J. The expression recombinant phage proteins and labeling for use in diagnosis Funding Agency: CANVAX BIOTECH

#### **Clinical Trials**

0140/12:. Study of Efficacy and Safety of Brodalumab Compared With Placebo and Ustekinumab in Moderate to Severe Plaque Psoriasis Subjects (AMAGINE-3). ClinicalTrials.gov Identifier: NCT01708629.

PI: Dr/a Ruano Ruiz, Juan Alberto

0251/14: A Phase 3, Multicenter, Randomized, Double-blind, Placebo and Active Comparator-controlled Study Evaluating the Efficacy and Safety of Guselkumab for the Treatment of Subjects with Moderate to Severe Plaquetype Psoriasis (CNT01959PS03001)-VOYAGE 1. EudraCT Number: 2014-000719-15. Pl: Dr/a Ruano Ruiz, Juan Alberto

0032/15: Long term clear skin maintenance treatment optimization in patients with moderate to severe chronic plaque psoriasis: A randomized, multicenter, open-label with blinded-assessment, comparative, 52 week study to evaluate the efficacy, safety and tolerability of secukinumab 300 mg s.c.(CAIN-457A3302)-OPTIMISE. EudraCT Number: 2014-005339-15.

PI: Dr/a Ruano Ruiz, Juan Alberto

0104/15: A multicenter, randomized, double-blind, placebo and active-controlled phase IIB dose-finding study of QGE031 as add-on therapy to investigate the efficacy and safety in patients with Chronic Spontaneous Urticaria (CSU)- (CQGE031C2201). Pl: Dr/a Ruano Ruiz, Juan Alberto

0125/15: A randomized, double-blind,parallel groups and active to compare the efficacy and safety of Humira versus CHS -1420 in patients with chronic plaque psoriasis (CHS-1420-02) (PsOsim) control. PI: Dr/a Ruano Ruiz, Juan Alberto

2016: An epidemiological, observational study to assess retention in treatment of patients with moderate to severe psoriasis in clinical practice. PI: Dr/a Jimenez Puya, Rafael

2032: Effect of the immunogenicity of anti-TNF therapies on the therapeutic response in patients with moderate to severe plaque psoriasis. PI: Dr/a Jimenez Puya, Rafael

2095: Cardiovascular risk factors in a population of Spanish patients with moderate to severe plaque psoriasis vulgaris with or without associated arthritis treated with anti-TNF alfa in real clinical practice conditions. Analysing the influence of the syndrome. PI: Dr/a Ruano Ruiz, Juan Alberto

2401: Influence of genetic polymorphisms associated with cardiovascular immunity and disease in relation to the effectiveness of anti-TNF-a drugs in moderate to severe psoriasis and the presence of cardiovascular risk factors.

PI: Dr/a Ruano Ruiz, Juan Alberto

2550: An observational study to assess relapse in patients with moderate to severe psoriasis treated with biological drugs according to clinical practice in Spain. PI: Dr/a Vélez Garcia-Nieto, Antonio

2635: Survival of etanercept among the elderly. PI: Dr/a Jimenez Puya, Rafael

2700: Development of a predictive model of response to anti - TNF used for the treatment of moderate to severe psoriasis in routine clinical practice drugs.

PI: Dr/a Ruano Ruiz, Juan Alberto

2702: Validation of the EARP for detection of psoriatic arthritis in Spanish population. VALS study.

PI: Dr/a Vélez Garcia-Nieto, Antonio

2719: Evaluation of patients with chronic urticaria refractory to treatment with antihistamines worldwide. Chronic urticaria observational study to collect clinical data in clinical practice on the impact of treatment, diagnosis and management of chronic urticaria in patients refrectarios at least one course of treatment with antihistamines H1. AWARE Study.

PI: Dr/a Ruano Ruiz, Juan Alberto

2740: Application of genomic techniques and image processing using artificial intelligence for obtaining a predictor melamona risk model .PI: Dr/a Ruano Ruiz, Juan Alberto

2883: An observational multicentre study to establish the prevalence , clinical profile and therapeutic management of patients with hidradenitis suppurativa in Dermatology Hospital Services and Health of Spain .

PI: Dr/a Lorente Lavirgen, Ana Isabel

# GE4

## HIGHLIGHTS

Principal Investigator (PI) Carmen Tabernero Urbieta carmen.tabernero@uco.es

## **Applied Psychology**



Researchers Antolí Cabrera, Adoración Arenas Moreno, Alicia Luque Salas, Bárbara Moyano Pacheco, Manuel Pérez Dueñas, Carolina Rubio García, Sebastián Post- Doctoral Researchers Cuadrado, Esther Castillo Mayén, Rosario

Pre Doctoral-Researchers (PhD Students y MSc Students) Gutiérrez Domingo, Tamara

Our research group investigates the influence of psychosocial variables (age, sex, socioeconomic status, educational level, perceived social support) and motivational processes (cognitive, affective and personality variables) on dietary adherence, life satisfaction and quality of life of patients with cardiovascular disease. We analyse the behaviour of patients with cardiovascular disease from a cognitive approach to develop social intervention programs based on health promotion.

More specifically, we intend to validate a structural equation model that allows us to determine the weight and interaction of psychosocial and motivational variables in adherence to diet, quality of life and well-being of patients with cardiovascular disease. Subsequently, we intend to test the effectiveness of an intervention program based on self-monitoring assessment processes of patients with cardiovascular disease. We present a management training program for the regulation of emotions to cope with stressful events. The intervention program will provide to patients the keys to self-regulation of emotions through e-HEALTH platforms. Finally, we propose to evaluate the relationship and impact of psychosocial and motivational variables with other biomedical variables analysed from other IMIBIC research teams.

This is a first collaboration project; however our research team seeks greater openness and collaboration with different IMIBIC teams and research areas.

#### **Keywords**

Motivation, self-efficacy, positivity, emotions, diet, cardiovascular disease, cope with stress, emotional self-regulation, management training programs, e-health

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Cuadrado E, Tabernero C. Affective Balance, Team Prosocial Efficacy and Team Trust: A Multilevel Analysis of Prosocial Behavior in Small Groups. PLOS ONE.2015. 10(8): e0136874. IF: 3,234 Q: 1 Tabernero C, Hernandez B, Cuadrado E,

Luque B, Pereira Cicero R. A multilevel perspective to explain recycling behaviour in communities. JOURNAL OF ENVIRONMENTAL MANAGEMENT.2015. 159: 192-201. IF: 3,12

Q: 1

Cuadrado E, Tabernero C, Steinel W. Determinants of prosocial behavior in included versus excluded contexts. FRONTIERS IN PSYCHOL-OGY.2015.6: 1 - 16.

IF: 2,560 Q: 1

Arenas, A.; Giorgi, G.; Mancuso, S.; Montani, F.; Fiz-Perez, J.; Mucci, N.; Arcangeli, G. Workplace bullying in a sample of Italian and Spanish employees and its relationship with job satisfaction, and psychological well-being. FRONTIERS IN PSYCHOLOGY.2015.6.e1912 IF: 2,56

Q: 1

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Giorgi G, León-Pérez JM, Arenas A. Are bullying behaviors tolerated in some cultures? evidence for a curvilinear relationship between workplace bullying and job satisfaction among Italian workers. JOURNAL OF BUSI-NESS ETHICS.2015. 131(1); 227 - 237. IF: 1,33

Q: 1

Cuadrado E, Tabernero C, Steinel W. Motivational determinants of prosocial behavior:

What do included, hopeful excluded, and hopeless excluded individuals need to behave prosocially? MOTIVATION AND EMO-TION.2015. 39(3): 344-358. IF: 1,844 Q: 2 Leon-Perez JM, Medina FJ, Arenas A, Munduate L. The Relationship between Interpersonal Conflict and Workplace Bullying. JOURNAL OF MANAGERIAL PSYCHOLOGY.2015.30 (3): 250-263. IF: 1,20 Q: 3 Freixas, A., Luque, B., Reina, A. Sexuality in older Spanish women: Voices and reflections. JOURNAL OF WOMEN & AG-ING.2015. 27(1): 35-58. IF: 0,60 Q: 3 Moyano M, Tabernero C, Melero R, Trujillo HM. Spanish version of the Cultural Intelligence Scale (CQS). REVISTA DE PSICOLOGIA SOCIAL.2015. 30(1): 182-216. IF: 0,475 Q: 4 Aranda, M., Montes-Berges, B., Castillo-Mayén, M. R. The social dominance orientation in adolescence: the role of gender identity and stereotypical male and female traits. REVISTA DE PSICOLOGÍA SOCIAL: IN-TERNATIONAL JOURNAL OF SOCIAL PSY-CHOLOGY.2015. 30(2): 241-263. IF: 0.475 Q: 4 Arenas A, Leon-Perez JM, Munduate L, Medina FJ. Workplace Bullying as a Conflict Escalation Process: The Role of Supervisor's Power. REVISTA DE PSICOLOGÍA SOCIAL.2015. 30(2): 295-322. IF: 0.286

Q: 4

Merida R, Serrano A, Tabernero C. Design and validation of a questionnaire for children's self-esteem assessment.RIE-REVISTA DE INVESTIGACION EDUCATIVA.2015. 33(1): 149-162 IF: 0,00

#### **Papers In Collaboration**

Moriana J A, Liberman RP, Kopelowicz A, Luque B, Cangas AJ, Alós F. Social skills training for schizophrenia. BEHAVIORAL PSY-CHOLOGY.2015. 23 (1): 5-24. IF: 0,83 Q: 4

Aranda M, Castillo-Mayén MR, Montes-Berges B. Has the traditional social perception of nurses changed? Current attribution of stereotypes and gender roles. ACCIÓN PSI-COLÓGICA.2015. 12(1): 103-112. IF : 0,362

Q: 4

Sánchez A, Martínez E, Moriana JA, Alós F, Luque B. Early intervention in autism spectrum disorders (ASD). Psicología de la Educación. 2015. 21: 155-163. IF: 0,00

#### **Research Funding**

#### National

Tabernero Urbieta, C. La influencia de la autoeficacia y otras variables motivacionales en la adherencia a la dieta, la calidad de vida y el bienestar de pacientes con enfermedad cardiovascular. Funding agency: MINISTRY OF ECONOMY AND COMPETITIVENESS (MINE-CO).Reference: PSI2014-58609-R

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# GA1

## HIGHLIGHTS

### Lung transplantation. Thoracic malignancies



#### **Team Leader**

Associated Researcher Ángel Salvatierra Velázquez angel.salvatierra.sspa@juntadeandalucia.es

> Researchers Francisco Javier Algar Algar José Ayala Montoro Antonio Álvarez Kindelan Carlos Baamonde Laborda Francisco Cerezo Madueño Dionisio Espinosa Jiménez

**Pre-PhD Researchers** Guadalupe Carrasco Fuentes Hugo Dario Guamán Arcos Francisco Javier Gonzalez García Diego Alejandro Murillo Brito

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. 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 signalling mechanisms.

#### **Keywords**

Lung preservation; chronic rejection; bronchiolitis obliterans; endothelium; inflammation; oxidative stress; proteomics; genomics.

#### **Scientific Production**

#### **Publications**

#### **Papers Original**

Betancourth-Alvarenga JE, Vazquez-Rueda F, Vargas-Cruz V, Paredes-Esteban RM, Ayala-Montoro J. Surgical management of aplasia cutis congénita. ANALES DE PEDIATRIA.2015. 83(5):341-345. IF: 0.833

Q: 4

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Arango Tomas E, Cerezo Madueno F, Salvatierra Velazquez A. Technique Resource for Difficult Auricular Anastomosis in Lung Transplantation. TRANSPLANTATION PROCEED-INGS.2015. 47(9):2653-2655. IF: 0,982

Q: 3

Arango Tomas EA, Algar Algar FJ, Cerezo Madueno F, Salvatierra Velazquez A. Evolution and Risk Factors for Early Mortality After Lung Transplantation for Idiopathic Pulmonary Fibrosis: An Experience of 20 Years. TRANSPLANTATION PROCEEDINGS. 2015. 47(9):2656-2658. IF: 0,982

Q: 3

#### **Original Editorial Material**

Arango Tomas E, Baamonde Laborda C, Algar Algar FJ, Salvatierra Velazquez A. Single-port thoracoscopic access for a mediastinal ectopic goiter. CIRUGIA ESPANOLA.2015. 93(4):264-266. IF: 0,743 Q:4

#### **Papers in Collaboration**

Moreno P, Lara-Chica M, Soler-Torronteras R, Caro T, Medina M, Alvarez A, Salvatierra A, Munoz E, Calzado MA. The Expression of the Ubiquitin Ligase SIAH2 (Seven In Absentia Homolog 2) Is Increased in Human Lung Cancer. PLOS ONE. 2015. 10(11): . IF: 3,234

Q: 1

#### **Research Funding**

#### Regional

Álvarez Kindelán, A.Beca Neumosur Nº 3/2010. Funding agency: Asociación de neumología y cirugía torácica del sur. Reference:Proyecto Neumosur

Álvarez Kindelán, A.Beca Neumosur 20/2011. Funding agency: Asociación de neumología y cirugía torácica del sur.Reference: Proyecto Neumosur 4

#### **Contracts with Companies**

Salvatierra Velazquez, A. 20 years of Andalusian lung transplant program functionality. Funding agency: Novartis farmaceutica, S.A.Reference:PSS.003

#### **Clinical trials**

2812: Study on the incidence of pulmonary thromboembolsism in patients surgically intervened on by bronchogenic carcinoma PI: Dr/a Álvarez Kindelán, Antonio

# GA2

## HIGHLIGHTS

Comprehensive nursing care. Multidisciplinary perspective



Researchers África Ruiz Gándara (Collaborator) Rosane Gonçalves Nitschke

Post- Doctoral Researchers Juan Manuel Carmona Torres Caridad Dios Guerra Clara Inés Florez Almonacid Dolores Guerra Martin Pablo Jesús López Soto Pre Doctoral-Researchers (PhD Students y MSc Students)

Jesús Fernández Luna Patricia Luque Carrillo Rosa Miñarro Del Moral Ignacio Morales Cané Ángeles Peinado Valeriano Pedro Manuel Rodríguez Muñoz Macarena Ruiz Cañete

### Team Leader

Associated Researcher M<sup>a</sup> Aurora Rodríguez Borrego. en1robom@uco.es PAIDI CTS-666 scientific group

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.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

López-Soto PJ, Manfredini R, Smolensky MH, Rodríguez-Borrego MA. 24-hour pattern of falls in hospitalized and long-term care institutionalized elderly persons: A systematic review of the published literature. Chronobiol Int. 2015 May;32(4):548-56. IF: 3,343 Q:1 D1

Lopez-Soto PJ, De Giorgi A, Senno E, Tiseo R, Ferraresi A, Canella C, Rodriguez-Borrego MA, Manfredini R, Fabbian F. Renal disease and accidental falls: a review of published evidence. BMC NEPHROLOGY. 16: .

IF: 1,69 Q: 3

Dios-Guerra C, Carmona-Torres JM, Ruíz-Gándara Á, Muñoz-Alonso A, Rodríguez-Borrego MA.Programmed home visits by nursing professionals to older adults: prevention or treatment? Rev Lat Am Enfermagem. 2015 May-Jun;23(3):535-42.

IF: 0,534

Q: 4

#### **Research Funding**

#### National

Rodríguez Borrego, M<sup>a</sup> A. Violence in couples formed by health professionals working at the Spanish National Health System. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI13/01253

#### Local

Rodríguez Borrego, M<sup>a</sup> A. Gambling, therapeutic strategy in administering palliative care Funding agency: University of Cordoba. Reference: 2015-2-3004

#### International

Rodríguez Borrego, Mª A. The chronobiological pattern as a causative factor of falls in the population older than 65 years.Funding Agency: MAPFRE FOUNDATION – 2014 Ignacio Hernando de Larramendi research funds.



## HIGHLIGHTS

**Team Leader** 

Bjgamez@uco.es

Associated Researcher Bernabé Jurado Gámez Pneumology



### Researchers

Nuria Feu Collado Francisco Luis García Gil Luis M. Entrenas Costa Rafael Lama Martínez Natalia Pascual Martínez Javier Redel Montero Francisco Santos Luna Post- Doctoral Researchers Marisol Arenas De Larriva Antonio Pablo Arenas Vacas Luis M. Entrenas Costa Luis Muñoz Cabrera

Pre Doctoral-Researchers (PhD Students y MSc Students) Montserrat Castillo Jurado Inmaculada García Porcuna

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 (COPD, 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.

#### Scientific Production

#### Publications

Original

#### Papers

Jurado-Gamez B, Guglielmi O, Gude-Sampedro F, Buela-Casal G. Effect of CPAP therapy on job productivity and psychosocial occupational health in patients with moderate to severe sleep apnea. SLEEP AND BREATH-ING.2015. 19(4):1293-1299.

IF: 2,482 Q: 2

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Jurado-Gamez B, Bardwell WA, Cordova-Pacheco LJ, Garcia-Amores M, Feu-Collado N, Buela-Casal G. A basic intervention improves CPAP adherence in sleep apnoea patients: a controlled trial. SLEEP AND BREATHING.2015. 19(2):509-514.

- IF: 2,482
- Q: 2

Sole A, Zurbano F, Borro JM, Monforte V, Ussetti P, Santos F. Prevalence and Diagnosis of Chronic Kidney Disease in Maintenance Lung Transplant Patients: ICEBERG Study. TRANS-

PLANTATION PROCEEDINGS. 2015.

47(6):1966-1971.

IF: 0,982 Q: 3

Q. .

Jurado-Gámez B, Guglielmi O, Gude F, Buela-Casal G. Workplace Accidents, Absenteeism and Productivity in Patients with Sleep Apnea. ARCHIVOS DE BRONCONEUMOLO-GIA.2015. 51(5):213-218.

- IF: 1,823
- Q: 3

Ordonez Dios IM, Montoro Ballesteros F, Vaquero Barrios JM, Cobos Ceballos MJ, Redel Montero J, Santos Luna F. Analysis of the Incidence of Noncutaneous Neoplasia After Lung Transplantation and Its Impact on Prognosis. TRANSPLANTATION PROCEEDINGS.2015. 47(9):2659-2660. IF: 0,982 Q: 3

#### **Papers in Collaboration**

Isetta V, Negrin MA, Monasterio C, Masa JF, Feu N, Alvarez A, Campos-Rodriguez F, Ruiz C, Abad J, Vazquez-Polo FJ, Farre R, Galdeano M, Lloberes P, Embid C, de la Pena M, Puertas J, Dalmases M, Salord N, Corral J, Jurado B, Leon C, Egea C, Munoz A, Parra O, Cambrodi R, Martel-Escobar M, Arque M, Montserrat JM. A Bayesian cost-effectiveness analysis of a telemedicine-based strategy for the management of sleep apnoea: a multicentre randomised controlled trial. THO-RAX.2015. 70(11):1054-1061. IF: 8,562

Q: 1 D: 1

Casanova C, Marin JM, Martinez-Gonzalez C, de Lucas-Ramos P, Mir-Viladrich I, Cosio B, Peces-Barba G, Solanes-García I, Agüero R, Feu-Collado N, Calle-Rubio M, Alfageme I, de Diego-Damia A, Irigaray R, Marín M, Balcells E, Llunell A, Galdiz JB, Golpe R, Lacarcel C, Cabrera C, Marin A, Soriano JB, Lopez-Campos JL, Soler-Cataluña JJ, de-Torres JP; COPD History Assessment in Spain (CHAIN) Cohort, Differential Effect of Modified Medical Research Council Dyspnea, COPD Assessment Test, and Clinical COPD Questionnaire for Symptoms Evaluation Within the New GOLD Staging and Mortality in COPD. Chest. 2015 Jul;148(1):159-68. doi: 10.1378/ chest.14-2449. IF: 7.483

Q: 1 D: 1

Q. TD.

Cosio BG, Soriano JB, López-Campos JL, Calle-Rubio M, Soler-Cataluna JJ, de-Torres JP, Marín JM, Martínez-Gonzalez C, de Lucas P, Mir I, Peces-Barba G, Feu-Collado N, Solanes I, Alfageme I, Casanova C. Defining the Asthma-COPD overlap syndrome in a COPD cohort. Chest. 2015 Aug 20. doi: 10.1378/ chest.15-1055 JE: 7.483

Peralbo-Molina A, Calderon-Santiago M, Priego-Capote F, Jurado-Gamez B, Luque de Castro MD. Development of a method for metabolomic analysis of human exhaled breath condensate by gas chromatography-mass spectrometry in high resolution mode. ANA-LYTICA CHIMICA ACTA.2015. 887:118-126. IF: 4,513

Cantisan S, Rodelo-Haad C, Paez-Vega A, Nieto A, Vaquero JM, Poyato A, Montejo M, Farinas MC, Rivero A, Solana R, Martin-Malo A, Torre-Cisneros J. Factors Related to the Development of CMV-Specific CD8+ T cell Response in CMV-Seropositive Solid Organ Transplant Candidates. AMERICAN JOURNAL OF TRANS-PLANTATION.2015. 15(3): 715-722. IF: 5,683

Calderon-Santiago M, Priego-Capote F, Turck N, Robin X, Jurado-Gamez B, Sanchez JC, de Castro MDL. Human sweat metabolomics for lung cancer screening. ANALYTICAL AND BIOANALYTICAL CHEMISTRY.2015. 407(18):5381-5382.

Q: 1

Miravitlles M, Alcázar B, Alvarez FJ, Bazús T, Calle M, Casanova C, Cisneros C, de-Torres JP, Entrenas LM, Esteban C, García-Sidro P, Cosio BG, Huerta A, Iriberri M, Iz-

Q: 1 D: 1

Q: 1 D: 1

Q: 1 D: 1

IF: 3,436

quierdo JL, López-Viña A, López-Campos JL, Martínez-Moragón E, Pérez de Llano L, Perpiñá M, Ros JA, Serrano J, Soler-Cataluña JJ, Torrego A, Urrutia I, Plaza V. What pulmonologists think about the asthma-COPD overlap syndrome. INTERNATIONAL JOUR-NAL OF CHRONIC OBSTRUCTIVE PULMO-NARY DISEASE.2015. 51(5):213-218. IF: 1.823

Q:3

#### **Reviews in Collaboration**

Guglielmi O, Jurado-Gamez B, Gude F, Buela-Casal G. Occupational health of patients with obstructive sleep apnea syndrome: a systematic review. SLEEP AND BREATH-ING.2015. 19(1):35-44. IF: 2,482

Q:2

#### Research Funding

#### Regional

Arenas de Larriva, MS. 03/2011 Neumosur Grant.Funding agency: Asociación de Neumología y cirugía torácica del sur(Spanish Pneumology Association).Reference: Project Neumosur 5

#### National

Muñoz Cabrera, L. Metabolomics contribution to the study of exhaled breath condensate for differentiation and the establishment of pathophysiological bases in the phenotypes of chronic obstructive pulmonary disease. Funding agency: Respira. Fundación Española sel Pulmón.Separ.Reference: SEPAR-02-2013

Jurado Gámez B. Metabolomics contribution in the sweat analysis for the identification of biomarkers in the diagnosis of lung cancer .Funding agency: Respira. Fundación Española del Pulmón.SEPAR.Reference: 78/2013.

#### **Clinical Trials**

0290/13 :Macitentan phase IIIb, multicenter, open, one single branch in patients with pulmonary arterial hypertension to validate psychometrically French, Italian and Spanish versions of PAH-SYMPACT tm study. PI: Dr/a Santos Luna, Francisco

0292/13: Extension of the AC-055-310 study, phase IIIb study with Macitentan, multicenter, open, one single branch in patients with pulmonary arterial hypertension to psychometrically validate the French, Italian and Spanish PAH-SYMPACT tm.

PI: Dr/a Santos Luna, Francisco

0044/14: Study rospective, multicenter, randomized, open, and 12 weeks to evaluate the efficacy and safety of glycopyrronium (50 micrograms 1 v / d) or fixed dose combination of indacaterol maleate and glycopyrronium bromide (110/50 microg) PI: Dr/a Jurado Gámez, Bernabé

0108/15: Randomized, double-blind, placebo-controlled, parallel group to evaluate the efficacy and safety of dupilumab in patients with persistent asthma

PI: Dr/a Entrenas Costa, Luis Manuel

2392: Multicenter prospective observational study to evaluate the specific immune response against Cytomegalovirus (CMV) measured by QuantiFERON and overall immune response measured by ImmuKnow in lung transplant patients with serolog PI: Dr/a Santos Luna, Francisco

2733: Multicenter retrospective observational study to describe the most frequent clinical phenotypes of patients with severe persistent asthma treated with omalizumab in routine clinical practice phenome.

PI: Dr/a Arenas Vacas, Antonio Pablo

2850: Prospective study of a single branch and longitudinal cohort to evaluate biomarkers in patients with severe asthma in usual clinical practice conditions. PI: Dr/A Entrenas Costa, Luis Manuel

2711: Randomized clinical trial on the effect of a program of aerobic exercise in patients with moderate to severe sleep apnea. PI: Dr/a Feu Collado, María Nuria

2741:Pprevalence of breathing disorders during sleep in patients with cop. PI: Dr/a Feu Collado, María Nuria

2856: Phase IV observational, multinational study on disease control. Findings reported by patients treated with inhalers of a dosage combination set for persistent asthma and COPD in clinical practice (SPRINT) PI: Dr/a Entrenas Costa, Luis Manuel

2639: Evaluation of early conversion to prolonge-release tacrolimus (advagraf) in lung transplantation. PI: Dr/a Santos Luna, Francisco

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## HIGHLIGHTS

### Endocrinology and Nutrition. Insulin resistance, diabetes and metabolism



#### **Team Leader**

Associated Researcher Juan Antonio Paniagua González japaniaguag@yahoo.es PAIDI CTS-651 Scientific Group

Other Associated Researcher Mª Ángeles Gálvez Moreno



#### Researchers

Enrique Bellido Muñoz Francisco José Berral De La Rosa Alfonso Calañas Continente Mª Sierra Corpas Jiménez Carmen Gutiérrez Alcántara Mª José Molina Puertas Rafael Palomares Ortega Remedios Vigara Madueño Pre Doctoral-Researchers (PhD Students y MSc Students) Juan Manuel Escandell Morales Zahira Noemi Fernández Bedmar

Post- Doctoral Researchers Magdalena Romero Jimenez

Other members of the Group (Nursing, Technical, and Administrative Staff) María del Rosario Torres Roldan

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.Soriguer in the performance of epidemiological studies of diabetes mellitus type 2 and in the prevention of diabetes through a behaviour modification programme 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 redistribution, 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; β-pancreatic dysfunction; prediabetes; metabolic syndrome; and adipotoxicidad adipose tissue; inflammation, oxidative stress; gene expression; metabolomics; Pituitary Adenoma; Somatostatin receptors; Vitamin D; Metabolic Sindome Prevalence of Diabetes Mellitus Type 2; Diabetes Mellitus and Pregnancy.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Herrera-Martinez AD, Padillo-Cuenca JC, Calanas Continente A, Bahamondes-Opazo R, Munoz-Jimenez C, Galvez Moreno MA.Invasive techniques and intraoperative echography in the localization of insulinomas; a case report. NUTRICION HOSPITALARIA.2015. 32(1):426-429. IF: 1,04

IF: 1,0 Q: 4

Q. -

Herrera Martinez A, Vinals Torras M, MunozJimenez MC, Arenas de Larriva AP, Molina Puerta MJ, Manzano Garcia G, Galvez Moreno MA, Calanas-Continente A.Metabolic encephalopathy secondary to vitamin d intoxication. NUTRICION HOSPITALARIA.2015. 31(3):1449-1451.

IF: 1,04

Q: 4

Herrera-Martinez AD, Alhambra Exposito MR, Manzano Garcia G, Molina Puerta MJ, Calanas Continente A, BahamondesOpazo R, Munoz-Jimenez C, Rojas Contreras R, Galvez Moreno MA.Use of glutamine in total parenteral nutrition of bone marrow transplantpatients.NU-TRICION HOSPITALARIA. 2015. 31(4):1620-1624.

- IF: 1,04
- Q: 4

Martinez-Brocca MA, Morales C, Rodriguez-Ortega P, Gonzalez-Aguilera B, Montes C, Colomo N, Piedrola G, Mendez-Muros M, Serrano I, Soledad Ruiz de Adana M, Moreno A, Fernandez I, Aguilar M, Acosta D, Palomares R. Implementation of subcutaneous insulin protocol for non-critically ill hospitalized patients in Andalusian tertiary care hospitals. ENDOCRINOLOGIA Y NUTRICION. 2015.62(2):64-71. IF: 0

#### **Papers in Collaboration**

Ibanez-Costa A, Gahete MD, Rivero-Cortes E, Rincon-Fernandez D, Nelson R, Beltran M, de la Riva A, Japon M A, Venegas-Moreno E, Galvez MA, Garcia-Arnes JA, Soto-Moreno A, Morgan J, Tsomaia N, Culler MD, Dieguez C, Castano JP, Luque RM. In 1-ghrelin splicing variantis over expressed in pituitary adenomas and increases their aggressive features. SCIENTIFIC REPORTS.2015. 4;5:8714. IF: 5,578 Q: 1 D: 1

Luque RM, Ibáñez-Costa A, Neto LV, Taboada GF, Hormaechea-Agulla D, Kasuki L, Venegas-Moreno E, Moreno-Carazo A, Gálvez MÁ, Soto-Moreno A, Kineman RD, Culler MD, Gahete MD, Gadelha MR, Castaño JP. Truncated somatostatin receptor variant sst5TMD4 confers aggressive features (proliferation, invasion and reduced octreotide response) to somatotropinomas.CANCER LET-TERS.2015. 359(2):299-306. IE- 5.621





Jodar-Gimeno E, Alvarez-Guisasola F, Avila-Lachica L, Palomares-Ortega R, Roldan-Suarez C, Lizan-Tudela L. Quality of life and fearforhypoglycaemia in patients with type 2 diabetes mellitus. REVISTA CLINICA ESPANO-LA. 2015.(2):91-97.

IF: 1,063 Q: 3

#### **Contracts with Companies**

Gálvez Moreno, MA. Development of advanced fats Innovation. Funding agency: ACEITES DEL SUR-COOSUR S.A.Reference: ITC-20151323

Gálvez Moreno, MA. Risk of lactic acidosis associated with the use of metformin in type 2 diabetic patients with moderate to severe chronic kidney disease. Case-control study.

#### **Clinical Trials**

0082/15: Phase III trial, multicenter, randomized, open and controlled comparator to evaluate the safety and tolerability of weekly TV-1106 dose compared with rhGH (Genotropin) at daily doses in adults with growth hormone deficiency.

PI: Dr/a Gálvez Moreno, Mª Ángeles

\*2980\* : A Phase III, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety and tolerability of TV-1106 in adults with deficiency of growth hormone are not currently treated with recombinant human growth hormone (rhGH) . PI: Dr/a Gálvez Moreno, Mª Ángeles

0303/15: Intravenous versus subcutaneous basal insulin in diabetic non-critical hospitalized patients receiving total parenteral nutrition.

PI: Dr/a Molina Puerta, Mª José

0230/15: Pragmatic real-world test, 26 weeks with 6-month extension, randomized, open, 2 parallel arms, to evaluate the results of clinical and health benefits of the transition to ToujeoR compared to insulins and Standard Treatment in Patients with Type 2 Diabetes Mellitus Inadequately Controlled with basal insulin Treaties

PI: Dr/a Gálvez Moreno, Mª Ángeles

2520: Assessing the effectiveness of telemedicine in achieving metabolic control in patients with type 1 mellitus diabetes taking multiple insulin doses in Andalusia. PI: Dr/a Palomares Ortega, Rafael

## GA5

## HIGHLIGHTS

Team Leader

Associated Researcher Ramón Cañete Estrada em1caesr@uco.es

## Study of growth. Endocrinology and Child Nutrition



Researchers M<sup>a</sup> Dolores Cañete Vázquez Juana M<sup>a</sup> Guzmán Cabañas Luis Jiménez Reina Rosario Martos Estepa Cristina Mata Rodríguez M<sup>a</sup> José Parraga Quiles M<sup>a</sup> Dolores Ruiz Gonzalez Inés Tofe Valera Javier Torres Borrego Miguel Valle Jiménez Fernando Vázquez Rueda

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 comparative 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.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Ruis-Gonzalez MD, Cañete MD, Gomez-Chaparro JL, Abril N, Cañete R, Lopez-Barea J. Alterations of protein expression in serum of infants with intrauterine growth restriction and different gestational ages. JOURNAL OF PROTEOMICS. 2015.119:169-182.

IF: 3,888 Q: 1

Q.

Valle M, Martos R, Cañete MD, Valle R, van Donkelaar EL, Bermudo F, Cañete R. Association of serum uric acid levels to inflammation biomarkers and endothelial dysfunction in obese prepubertal children. PEDIATRIC DIA-BETES. 16(6):441-447. IF: 2,569

Q: 1

#### **Papers in Collaboration**

Perez-Yarza, EG; Moreno-Galdo, A; Ramilo, O; Rubi, T; Escribano, A; Torres, A; Sardon, O; Oliva, C; Perez, G; Cortell, I; Rovira-Amigo, S; Pastor-Vivero, MD; Perez-Frias, J; Velasco, V; Torres-Borrego, J; Figuerola, J; Barrio, MI; Garcia-Hernandez, G; Mejias, A Risk factors for bronchiolitis, recurrent wheezing, and related hospitalization in preterm infants during the first year of life. PEDIATRIC ALLERGY AND IMMUNOLOGY .2015. 26(8); 797-804

IF: 3,397

Q:1 D:1

Carbonell-Estrany X, Perez-Yarza EG, Garcia LS, Cabanas JMG, Boria EV, Atienza BB. IRIS Infeccion Respiratoria Infan. Long-Term Burden and Respiratory Effects of Respiratory Syncytial Virus Hospitalization in Preterm Infants-The SPRING Study. 2015.PLOS ONE. 10(5) IF: 3,234

Q: 1

Q. 1

Olza J, Aguilera CM, Gil-Campos M, Leis R, Bueno G, Valle M, Canete R, Tojo R, Moreno LA, Gil A. A Continuous Metabolic Syndrome Score Is Associated with Specific Biomarkers of Inflammation and CVD Risk in Prepubertal Children. ANNALS OF NUTRITION AND ME-TABOLISM. 2015.66(2-3):72-79. IF: 2,618 Q: 2 Aguilera CM, Gomez-Llorente C, Tofe I, Gil-Campos M, Canete R, Gil A. Genome-Wide Expression in Visceral Adipose Tissue from Obese Prepubertal Children. IN-TERNATIONAL JOURNAL OF MOLECULAR SCIENCES. 2015.16(4):7723-7737. IF: 2,862 Q: 2

Moreno-Solis G, Torres-Borrego J, de la Torre-Aguilar MJ, Fernandez-Gutierrez F, Llorente-Cantarero FJ, Perez-Navero JL. Analysis of the local and systemic inflammatory response in hospitalized infants with respiratory syncitial virus bronchiolitis. ALLERGOLOGIA ET IMMUNOPATHOLOGIA. 2015.43(3);264-271 IF: 1,748

Q: 4

Betancourth-Alvarenga JE, Vazquez-Rueda F, Vargas-Cruz V, Paredes-Esteban RM, Ayala-Montoro J. Surgical management of aplasia cutis congénita. ANALES DE PEDIATRIA.2015. 83(5):341-345. IF: 0,833

#### Q: 4

#### **Contracts with Companies**

Cañete Estrada, R. HEALTHCARE - Occupational exposure and polycyclic aromatic hydrocarbons in thermal plants: early analysis of their potential impact on health. Funding agency:Pfizer, S.A. Reference: CCB.UCO0050

Cañete Estrada, R. Protein expression of pre-pubertal children with GH déficit. Funding agency: Pfizer, S.A. Reference: CCB.UCO0051

### **Clinical Trials**

0291/11: A randomized, multicenter, blind trial with topiramato vs. placebo for the treat-

ment of newborns with perinatal asphyxia treated with moderate whole-body hypothermia.

PI: Dr/a Guzman Cabañas, Juana Maria

2738: STUDY OF SEQUENCING postlicensing PROSPECTIVE (EPA-SP), center study evaluating the noninferiority of a pattern PRO-co-seasonal FACE A PATTERN OF Depigoid DUO PERENNIAL GRASSES / OLIVO A 2000 DPP / ML in pediatric patients with O Rhinitis

PI: Dr/a Torres Borrego, Javier

2876: Observational cross-sectional study to assess the quality of life of patients with a diagnosis of seasonal allergic rhinitis or rhinoconjunctivitis with or without asthma caused by pollen olive or olive more grasses treated with immunotherapy

PI: Dr/a Torres Borrego, Javier



## HIGHLIGHTS

**Team Leader** 

**Associated Researcher** Fernando Rodríguez Cantalejo **Clinical Analysis** 



Researchers Javier Caballero Villarraso Antonio Martínez Peinado Rafael Molero Payan

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 chorionic 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**

**Publications** 

New methodologies; chorionic villus sampling; prenatal screening; karyotype; POCT.

#### Scientific Production

#### Papers In Collaboration

Fuentes F, Alcala-Diaz JF, Watts GF, Alonso R, Muniz O, Diaz-Diaz JL, Mata N, Munoz-Torrero JF, Sánchez Brea A, Galiana J, Figueras R, Aguado R, Piedecausa M, Cepeda JM, Vidal JI, Rodriguez-Cantalejo F, Lopez-Miranda J, Mata P. Statins do not increase the risk of developing type 2 diabetes in familial hypercholesterolemia: The SAFEHEART study. INTER-NATIONAL JOURNAL OF CARDIOLOGY.2015. 201:79-84.

IF: 4,036 Q: 1

Vega Almazan M, Ortega E, Moreno Torres R, Tovar M, Romero J, Lopez-Casado MA, Jaimez L, Jimenez-Jaimez J, Ballesteros A, Caballero-Villarraso J, Maldonado J. Diagnostic screening for subclinical celiac disease using a rapid test in children aged 2-4. PEDIATRIC RESEARCH.2015. 78(3):280-285. IF: 2,314

Q: 1

Moreno-Muñoz D, de la Haba-Rodríguez JR, Conde F, López-Sánchez LM, Valverde A, Hernández V, Martínez A, Villar C, Gómez-España A, Porras I, Rodríguez-Ariza A, Aranda E. Genetic variants in the renin-angiotensin system predict response to bevacizumab in cancer patients. Eur J Clin Invest. 2015 Dec;45(12):1325-32. IF: 2,734

Q: 1

#### **Letters in Collaboration**

Rivero-Juarez A, Martinez-Duenas L, Martinez-Peinado A, Camacho A, Cifuentes C, Gordon A, Frias M, Torre-Cisneros J, Pineda JA, Rivero A.Absence of occult Hepatitis E virus infection among HIV immune suppressed patients.JOURNAL OF INFECTION.2015. 70(6):680-683.

#### **Research Funding**

#### National

Caballero Villarraso, J. HEALTHCARE - Occupational exposure and polycyclic aromatic hydrocarbons in thermal plants: early analysis of their potential impact on health.Funding agency: Corporación Tecnológica de Andalucía (CTA), an initiative promoted by the Regional Ministry of Economy, Innovation, Science and Employment (CEICE). Acting in a consortium with MAGTEL INGENIERÍA S.L.U.

IF: 5,416 Q: 1 D: 1

# GA7

## HIGHLIGHTS

Urology and sexual medicine



Researcher Francisco Anglada Curado Juan Pablo Campos Hernández Rafael Prieto Castro

Post- Doctoral Researchers Ana María Blanca Pedregosa Julia Carrasco Valiente **Pre Doctoral-Researchers (PhD Students y MSc Students)** Enrique Gómez Gómez Javier Márquez López Jesús Ruiz García José Valero Rosa

Other members of the Group (Nursing, Technical, and Administrative Staff) Daniel Gil Contreras

#### Team Leader

Associated Researcher M<sup>a</sup> Jose Requena Tapia josefa.requena.sspa@juntadeandalucia.es

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; prostate cancer; lower urinary tract symptomatology; renal cancer; renal transplant; erectile dysfunction; kidney stone.

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

Hernandez JPC, Gomez EG, Valiente JC, Lopez FJM, Garcia JR, Curado FJA, Castro RP, Rabelo JR, Cabello MLN, Tapia MJR. Influence of Surgical Complications on Kidney Graft Survival in Recipients of Simultaneous Pancreas Kidney Transplantation. TRANS-PLANTATION PROCEEDINGS. 47(1):112-116. IF: 0,982

Q: 3

Bonilla AJA, Alfaro AG, Henandez JPC, Rubio JHG, Gomez EG, Valiente JC, Garcia JMR, Lopez JM, Tapia MJR. Review of a transplantectomy series. TRANSPLANTATION PROCEED-INGS. 47(1):81-83.

IF: 0,982

Q: 3

Salmeron-Rodriguez MD, Navarro-Cabello MD, Aguera-Morales ML, Lopez-Andreu M, Rodriguez-Benot A, Robles-Arista JC, Duenas-Jurado JM, Campos-Hernandez JP, Requena-Tapia M J Aljama-Garcia P. Short-Term Evolution of Renal Transplant With Grafts From Donation After Cardiac Death: Type III Maastricht Category. TRANSPLANTATION PROCEEDINGS. 47(1): 23-26.

IF: 0,982

Q: 3

Garcia-Rubio, J. H.; Carrasco Valiente, J.; Campos Hernandez, J. P.; Ruiz Garcia, J.; Márquez Lopez, J.; Regueiro Lopez, J. C.; Cano Castiñeira, R.; Ruiz de Mier, M. V. Pendon; Requena Tapia, M. J. Graft Survival in Patients With Polycystic Kidney Disease With Nephrectomy of Native Kidney Pretransplant. TRANSPLANTATION PROCEEDINGS. 47(9):2615-2617.

- IF: 0.982
- Q:3

Gomez-Gomez E, Ramirez M, Gomez-Ferrer A, Rubio-Briones J, Iborra I, Carrasco-Valiente J, Campos JP, Ruiz-Garcia J, Requena-Tapia MJ, Solsona E. Assessment and clinical factors associated with pain in patients undergoing transrectal prostate biopsy. ACTAS UROLOG-ICAS ESPANOLAS. 39(7):414-419. IF: 1,022

Q: 4

Puigvert-Martinez A, Prieto-Castro R. Grp Estudio Atlas Disfuncion Erect. Diagnosis and treatment of erectile dysfunction in Spain: The opinion of primary care physicians "Atlas of the erectile dysfunction in Spain" Project. REVISTA INTERNACIONAL DE ANDROLOGIA. 13(3):92-98. IF: 1,022 Q: 4 Cano-Castineira R, Carrasco-Valiente J, Peru-

la-de-Torres LA, Jimenez-Garcia C, Olaya-Caro I, Criado-Larumbe M, Requena-Tapia MJ. Prevalence of Renal Stones in Andalusian Population: Results of PreLiRenA Study. AC-TAS UROLOGICAS ESPANOLAS. 39(1):26-31. IF: 1,022

Q: 4

Regueiro Lopez JC, Gomez-Gomez E, Alonso Carrillo A, Cano Castineira R, Requena Tapia MJ. Perineostomy: the last oportunity. INTER-NATIONAL BRAZ J UROL. 41(1):91-98. IF: 0,875 Q: 4

Marquez-Lopez J, Gomez-Gomez E, Anaya-Henares F, Robles-Casilda R, Requena-Tapia MJ. When should we perform a bone scintigraphy in patients with new diagnosis of asymptomatic prostate cancer in order to detect bone metastasis? ARCHIVOS ESPANOLES DE UROLOGIA. 68(2):135-141. IF: 0,309 Q: 4

Gomez-Gomez E, Carrasco-Valiente J, Valero-Rosa J, Campos-Hernandez JP, Anglada-Curado FJ, Carazo-Carazo JL, Font-Ugalde P, Requena-Tapia MJ. Impact of 3D vision on mental work load and laparoscopic performance in inexperienced subjects. ACTAS UROLOGICAS ESPANOLAS. 39(4):229-235. IF: 0.227

Q: 4

#### **Papers in Collaboration**

Jimenez-Cidre MA, Lopez-Fando L, Esteban-Fuertes М, Prieto-Chaparro L, Llorens-Martinez FJ, Salinas-Casado J, Castro-Diaz D, Mueller-Arteaga C, Adot-Zurbano JM, Rodriguez-Escobar F, Gutierrez C, Arlandis-Guzman S, Bonillo-Garcia MA, Madurga-Patuel B, Leva-Vallejo M, Franco de Castro A, Peri-Cusi L, Conejero-Sugranes J, Jimenez-Calvo J, Rebollo P, Mora A.The 3-Day Bladder Diaryls a Feasible, Reliable and Valid Tool to Evaluate the Lower Urinary Tract Symptoms in Women. NEUROUROLOGY AND URODYNAMICS. 34(2):128-132. IF: 2,873

Q: 1

Pendon-Ruiz de Mier V, Navarro Cabello MD, Martinez Vaquera S, Lopez-Andreu M, Aguera Morales ML, Rodriguez-Benot A, Ruiz Rabelo J, Campos Hernandez P, Requena Tapia MJ, Aljama Garcia P. Index High Insulin Resistance in Pancreas-Kidney Transplantation Contributes to Poor Long-term Survival of the Pancreas Graft. TRANSPLANTATION PROCEED-INGS. 47(1):117-119.

IF: 0,982 Q: 3

Cozar JM, Minana B, Palou-Redorta J, Medina

RA, de la Rosa-Kehrmann F, Lozano-Palacio F, Ribal-Caparros MJ, Hernandez-Fernandez C, Castineiras-Fernandez JJ, Requena MJ, Moreno-Sierra J, Carballido-Rodriguez J, Baena-Gonzalez V. Comparative analysis of the incidence of bladder cancer in the communities of Andalusia, Catalonia and Madrid in 2011. ACTAS UROLOGICAS ESPANOLAS. 39(7):420-428.

IF: 1,022 Q: 4

#### **Research Funding**

#### National

Requena Tapia, MJ. BROCA Project.Funding agency: Collaboration Agreements between MINECO (FEDER) and the University of Cordoba for the implementation of a biomedical research project. Reference: CCB.029PM

Requena Tapia, MJ.Estudio de los niveles de expresión de las proteínas de la ruta de señalización PI3CA/AKT y su papel diagnóstico y pronóstico/predictivo en cáncer de vejiga urinaria.Funding agency: Asociacion Española De Urologia. Reference: FIU14/002

#### Participation in other researchs projects from IMIBIC Groups

\*Rodríguez Ariza, A.ONCOVER: Detection system of volatile compounds forearly diagnosis of lung and colon cancer. Funding agency: Collaboration Agreements between entre el MINECO (FEDER ) and the University of Cordoba for the implementation of a biomedical research project.Reference:CCB.030PM

#### Regional

Requena Tapia, MJ. Impartation transrectal prostate and bladder catheterization workshop on exploration simulation dolls.Funding agency:; University of Córdoba.

#### **Contracts with Companies**

Requena Tapia, M<sup>a</sup> J. Collaboration with GSK.Bayesian Inference. Funding agency: GlaxosMithKline, S.A. Reference:CCB.0062

Requena Tapia, M<sup>a</sup> J. Collaboration with JANSSEN-CILAG, S.A.Bayesian Inference. Funding agency: JANSSEN-CILAG, S.A.Reference: PSS.0078

Requena Tapia, M<sup>a</sup> J. Collaboration with MECWINS.Bayesian Inference. Funding agency: MECWINS S.A..Reference: PSS.0114

#### **Clinical Trials**

0280/12: A randomized, double-bind, 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

0344/14: Phase III, randomized, placebo-controlled, double-blind JNJ-56021927 in combination with abiraterone acetate and prednisone compared with abiraterone acetate and prednisone in patients with metastatic-resistant prostate cancer

PI: Dr/a Requena Tapia, María José

0215/15: Phase 3 randomized, double-blind, placebo-controlled JNJ-56021927 more androgen deprivation therapy (TPA) versus TPA in patients with prostate cancer metastasic-hormono-sensitive (PCmHS) low tumor burden

PI: Dr/a Requena Tapia, María José

1856: An epimediological, 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

2446: Elaboration of a predictive model of Cystoscopy, based on BTA-stat test for monitoring patients with low grade non-muscle invasive bladder carcinoma. (Estudio PreCis BTA)

PI: Dr/a Requena Tapia, María José

2458: Observational, prospective, longitudinal, multinational study to describe patterns of care and outcomes in men with high risk of adverse clinical outcomes after experiencing a biochemical failure following treatment of definitive prostate cancer in men with castration-resistant prostate cancer and in men with metastatic prostate cancer at the time of initial diagnosis

PI: Dr/a Carrasco Valiente, Julia



## HIGHLIGHTS

Team Leader

Associated Researcher Daniel López Ruiz danieljIruiz@gmail.com

## Radiology



Researchers Alberto Benito Ysamat Antonio Cano Sánchez María Cara García Fernando Delgado Acosta José García-Revillo García María José García Ortega Lucia Nuria Izquierdo Palomares Rafaela Muñoz Carrasco Ana Luz Santos Romero Elisa Roldán Romero

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, reumatologic 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 mononuclear 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.

#### **Scientific Production**

#### **Publications**

#### **Papers in Collaboration**

Ruiz-Limon P, Barbarroja N, Perez-Sanchez C, Aguirre MA, Bertolaccini ML, Khamashta MA, Rodriguez-Ariza A, Almaden Y, Segui P, Khraiwesh H, Gonzalez-Reyes JA, Villalba JM Collantes-Estevez E, Cuadrado MJ, Lopez-Pedrera C. Atherosclerosis and cardiovascular disease in systemic lupus erythematosus: effects of in vivo statin treatment ANNALS OF THE RHEUMATIC DIS-EASES.2015;74(7);1450-1458 IF:10,377 Q:1 D:1

Q:TD:

Villa-Osaba A, Gahete MD, Cordoba-Chacon J, de Lecea L, Pozo-Salas AI, Delgado-Lista FJ, Alvarez-Benito M, Lopez-Miranda J, Luque RM, Castaño JP. Obesity Alters Gene Expression for GH/IGF-I Axis in Mouse Mammary Fat Pads: Differential Role of Cortistatin and Somatostatin. PLOS ONE.2015. 10(3): . IF: 3,234

Q: 1

Jimenez-Gomez E, Sánchez AC, Fernández RO, Alvarado SV, Bravo-Rodriguez F, Acosta FD. Unprotected carotid artery stenting in symptomatic elderly patients: a single-center experience. JOURNAL OF NEUROINTERVEN-TIONAL SURGERY.2015. 7:341-345.

- IF: 2,774
- Q: 1

Ciria R, Lopez-Cillero P, Gallardo AB, Cabrera J, Pleguezuelo M, Ayllon MD, Luque A, Zurera L, Espejo JJ, Rodriguez-Peralvarez M, Montero JL, de la Mata M, Briceno J.Optimizing the management of patients with BCLC stage-B hepatocellular carcinoma: Modern surgical resection as a feasible alternative to transarterial chemoemolization European Journal Surgery Oncology.2015.41(9).1153-1161.

IF: 3,009 Q:1

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Zurera LJ, Espejo JJ, Lombardo S, Gilbert JJ, Canis M, Ruiz C. Safety and efficacy of expanded polytetrafluoroethylene-covered transjugular intrahepatic portosystemic shunts in children with acute or recurring upper gastrointestinal bleeding. PEDIATRIC RA-DIOLOGY.2015 45(3):422-429. IF: 1,57 Q: 2

#### **Resercher Fundings**

#### National

Álvarez Benito, M (IP), Cara García, A Luz Santos, A. Pilot endovascular recanalization study of stroke beyond 8 hours from the selected start via imaging techniques.Funding Agency: Sociedad Española de Radiología Medica. Reference:Seram14.001

### Participation in other researchs projects from IMIBIC Groups

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. Funding agency: Carlos III Health Institute (ISCIII). Reference:PI13/00553

#### **Clinical Trials**

2802:Pilot endovascular recanalization study of stroke beyond 8 hours from the selected start via imaging techniques PI: Dr/a Delgado Acosta, Fernando

2763: Primary post-angioplasty permeability of native dysfunctional arteriovenous fistulas in hemodialysis: treatment by means of balloon versus conventional pre-loaded balloon. PI: Dr/a García-Revillo García, José

#### \*Participation in other researchers' clinical trials from IMIBIC Groups.

0145/11: A multicenter, extension, doseblind 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

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

0106/13: Multicenter, randomized, double-blind study comparing the efficacy and safety of continuing versus withdrawing adalimumab theraphy in mantaining remission in patients with non-radiographic axial spondyloarthritis.

PI: Dr/a Collantes Estévez, Eduardo

0300/13: Randomized, double-blind, placebo-controlled phase III study to evaluate the efficacy, safety and effect on radiographic progression of brodalumab in patients with psoriatic arthritis.

PI: Dr / Montilla López, María Dolores

0267/14: multicenter phase II study to analyze the predictive value of response to Enzalutamide of fusion TMPRSS2-ETS gene in patients with metastatic CRPC previously untreated with chemotherapy.

PI: Dr / Mendez Vidal, Mª José

0040/15: A Phase III, randomized, double-blind, placebo controlled multi-center study of subcutaneous secukinumab (150 mg and 300 mg) in prefilled syringe to demonstrate efficacy (including inhibition of structural damage), safety, and tolerability up to 2 years in subjects with active psoriatic arthritis (FUTURE 5)

PI: Dr/a Collantes Estévez, Eduardo

NCT01556490:A Phase III Clinical Trial of Intra-arterial TheraSphere™ in the Treatment of Patients with Unresectable Hepatocellular Carcinoma (HCC)

PI: Dr/a Zurera Tendero, Luis J

## GA9

## HIGHLIGHTS

**Cardiovascular Pathology** 





Associated Reseacher Ignacio Muñoz Carvajal ignacio.munoz.carvajal.sspa@juntadeandalucia.es PAIDI TEP-226 PRINIA Scientific Group (Project Engineering and Automation) (Collaborator)



#### Researchers

Pedro Jose Alados Arboledas Francisco Javier Arias Dachary Maria del Valle Blazquez Ruiz Miguel Canis López Jose Garcia-Revillo Garcia Jaime Guillermo Casares Mediavilla Antonio Chacón Quevedo Azahara Fernández Carbonell Daniela Hervas Sotomayor Agustina Jiménez Castilla Aurea Jurado Morata Carlos Manuel Merino Cejas Javier Moya González Bibián Ortega Lopera Isabel Pernía Orena Jose Maria Turegano Cisneros Federico Zurita Martinez

Pre Doctoral-Researchers (PhD Students y MSc Students) Mª Teresa Conejero Jurado Diana Valencia Núñez

Other members of the Group (Nursing, Technical, and Administrative Staff) Rafael Canales Ruiz M<sup>a</sup> del Carmen Romero Morales Manuel Recio Rufián Raquel Riballo Cortes Noelia M<sup>a</sup> Romero Mata

#### **Research Funding**

#### National

### Participation in other researchs projects as CO-IP

Requena Tapia, M<sup>a</sup> J. BROCA Project. Funding agency:Collaboration Agreements between entre el MINECO (FEDER) and the Univeristy of Cordoba for the implementation of a biomedical research project. Reference: CCB.029PM

#### **Contracts with Companies**

Casares Mediavilla, J. Agreement with Genzyme Polycolnals. Funding agency:GENZYME POLYCLONALS S.A.S. Reference: CCB.0006

Muñoz Carvajal, I. Agreement with C.S.A TECNICAS MEDICAS.Funding Agency: C.S.A. TECNICAS MÉDICAS, S.L.Reference: CCB.0044

Muñoz Carvajal, I. PROYECTO CARELINK. Funding agency: C.S.A. Tecnicas Médicas, S.L.Reference: CCB.0065

#### **Clinical Trials**

2610: Pre-operation factors that exert influence in the presence of complications and post-surgery cardiac morbidity in patients with sever ventricular dysfunction. Prosepctive observational study.

PI: Dr/a Muñoz Carvajal, Ignacio

Study of remote monitoring implantable devices.(Carelink Express Study) PI: Dr/a Muñoz Carvajal, Ignacio

Using circulatory assistance devices as shortterm bridge urgent heart transplant in Spain: efficacy, safety and cost analysis ( ASIS -TC ) . PI (node Córdoba): Dr/a Daniela Hervas Sotomayor

#### \*Participation in other researchers' clinical trials from IMIBIC Groups

\*0062/15: Immune response, and safety study of clostridium difficile toxoid vaccine in subjects at risk for C. difficile Infection. PI: Dr/a De la Torre Cisneros, Julián Carlos

# GA10

## HIGHLIGHTS

**Nuclear Medicine** 





Researcher Elviria Carmona Asenjo F° Roberto Maza Muret, Luisa Mena Bares

Pre Doctoral-Researchers (PhD Students y MSc Students) Maria Victoria Guiote Moreno Other members of the Group (Nursing, Technical, and Administrative Staff) Estefanía Moreno Ortega Antonio Martin Ruiz Anahi Rojas Arroyo

#### Team Leader

Associated Researcher Juan Antonio Vallejo Casas jantonio.vallejo.sspa@juntadeandalucia.es

#### **Scientific Activity**

The Group work now in the development of new treatment lines for Differentiated Thyroid carcinoma, as active part of SEMNIM Group, and also, participating in International meetings.

Also, we continue with the clinical trials activity, and specifically in the use of new radioisotopic treatment for Prostate Cancer and Limphoma.

We was initiated this year the collaboration with others groups for the implementation of PET/CT in clinicals situation, especially in the evaluation of therapeutic response.

#### **Scientific Production**

#### **Publications**

#### **Original Editorial Material**

Mena LM, Carmona E, Maza FR, Guiote MV, Moreno E, Vallejo JA. Malignant ovarian Brenner tumor. A case report evaluated with F-18-FDG PET/CT. REVISTA ESPANOLA DE MEDICINA NUCLEAR E IMAGEN MOLECULAR. 34(5):337-338. IF: 1,054 Q: 4

## GA11

## HIGHLIGHTS

## Learning and Artificial Neural Networks-AYRNA



#### **Team Researchers**

Researchers Pedro Antonio Gutiérrez Juan Carlos Fernández Caballero Carlos García Alonso Mercedes Torres Jiménez Mariano Carbonero Ruz Francisco José Martínez Estudillo Alfonso Carlos Martínez Estudillo David Becerra Alonso Francisco Fernández Navarro Javier Sánchez Monedero María Pérez Ortiz Mónica de la Paz Marín Pre Doctoral-Researchers (PhD Students y MSc Students) Manuel Dorado Moreno Antonio Manuel Durán Rosal David Guijo Rubio

#### Team Leader

Associated Researcher César Hervás Martínez chervas@uco.es PAIDI TIC-148 Scientific Group

#### **Scientific Activity**

The Learning and Artificial Neural Networks AYRNA research group (code TIC-148 - Junta de Andalucía) was founded mainly focused in the field of Artificial Neural Networks (ANNs). In the last years, the group has diversified its interest areas working on the resolution of different problems through soft computing techniques (artificial neural networks, evolutionary algorithms and other pattern recognition algorithms). Regarding the biomedical field, we work on artificial neural networks in donor-recipient matching in liver and lung transplants.

#### **Keywords**

Data science; multiobjective evolutionary algorithms; machine learning; ordinal classification; teaching innovation; time series segmentation; time series prediction; new basis functions for artificial neural networks; evolutionary artificial neural networks; distributed systems;

#### **Scientific Production**

#### **Publications**

#### **Original Papers**

A. Sáez, J. Sánchez-Monedero, P. A. Gutiérrez y C. Hervás-Martínez. "Machine learning methods for binary and multiclass classification of melanoma thickness from dermoscopic images", IEEE Transactions on Medical Imaging, Vol. 35. 2015, pp. 1036-1045. IF: 3,39

Q:1 D:1

Pérez-Ortiz M., Gutiérrez P.A., Tino P. and Hervás-Martínez C. Over-sampling the minority class in the feature space.IEEE Transactions on Neural Networks and Learning Systems, 2015.

IF: 4.291.

Q:1 D:1

Pérez-Ortiz M, Peña JM, Gutiérrez PA, Torres-Sánchez, J, Hervás-Martínez C, López-Granados F.A semi-supervised system for weed mapping in sunflower crops using unmanned aerial vehicles and a crop row detection method. Applied Soft Computing. 2015.37. 533-544.

IF:2.81

Q:1 D:1

Fernandez JC, Salcedo-Sanz S, Gutiérrez, PA, Alexandre E, Hervás-Martínez, C. Significant wave height and energy flux range forecast with machine learning classifiers. Engineering Applications of Artificial Intelligence.2015.43. 44-53.

IF:2.207 Q:1 D:1

Pérez-Ortiz M, Gutiérrez PA, Hervás-Martínez C, Yao X. Graph-Based Approaches for Over-sampling in the context of Ordinal Regression. IEEE Transactions on Knowledge and Data Engineering.2015.27.1233-1245. IF: 2.067

Q:1 D:1

Marin MP, Gutiérrez, PA, Hervás-Martínez, C. Classification of countries' progress toward a knowledge economy based on machine learning classification techniques. Expert Systems with Applications. 2015.42.562–572. IF:2,24

Q:1 D:1

Torres-Jiménez M, García C, Salvador AL., Fernández V. Evaluation of system efficiency using the Monte-Carlo DEA: The case of small

health areas. European Journal of Operational Research.2015.242. 525-535. IF2,358 Q:1 D:1 Fernandez-Navarro F, Riccardi A, Carloni S. Ordinal Regression by a Generalized Force-Based Model, IEEE Transaction on Cybernetics.2015.45.844-857. IF:3.469 Q:1 D:1 P. Gómez-Rey, F. Fernández-Navarro y E. Barbera-Gregori. "Ordinal Regression by a Gravitational Model in the field of Educational Data Mining", Expert Systems. 2015, pp. 1-12. IF:2,24

Q:1 D:1 Nikolaou, Gutiérrez PA, Durán-Rosal AM., Dicaire I, Fernandez-Navarro F, Hervás-Martínez C. Detection of early warning signals in paleoclimate data using a genetic time series segmentation algorithm. Climate Dynamic. 2015. 44.1919-1933.

IF:4,673 Q:1

A. Castaño-Méndez, F. Fernández-Navarro, A. Riccardi y C. Hervás-Martínez. "Enforcement of the principal component analysis-extreme learning machine algorithm by linear discriminant analysis", Neural Computing and Applications, Vol. -. 2015, pp. 1-12. IF: 1.569

Q:2

Rodero E, González A, Dorado-Moreno M, Luque M ,Hervás-Martínez C. Classification of goat genetic resources using morphological traits. Comparison of machine learning techniques with linear discriminant analysis. Livestock Science. 2015. 180;14-21.

IF: 1,171

Q:2

M. Dorado-Moreno, A. Sianes y C. Hervás-Martínez. "From outside to hyper-globalisation: an Artificial Neural Network ordinal classifier to measure the extent of globalisation", Quality & Quantity. 50; 549-576. 2015. IF: 0.720

Q:2

Pérez-Ortiz, M, Gutiérrez, PA, Cruz-Ramirez M, Sánchez-Monedero J, Hervás-Martínez C. Kernelising the Proportional Odds Model through Kernel Learning techniques. Neurocomputing. 2015. 164.23-33 IF: 2,083

Q:1

#### Papers in Collaboration

Tang F. Tino P. Gutiérrez, PA, Chen H. The Benefits of Modelling Slack Variables in SVMs. Neural Computation.2015.25.954-981. IF:2,207 Q:1 D:1

#### **Research Funding**

#### National

Hervás-Martínez C. Ordinal classification and prediction algorithms in renawable energy, Orca-Re. Funding Agency: Ministry of Economy and Competitiveness (MINECO). Reference: TIN2014-54583-C2-1-R

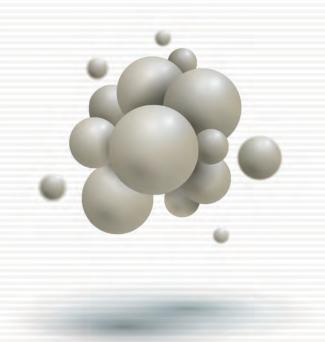
Figueiras Vidal AR; Gutiérrez Peña PA. Advanced Diversification for Learning Machines. Funding Agency: Ministry of Economy and Competitiveness (MINECO). Reference: TIN2015-70308-REDT.

#### **Contrats with Companies**

Hervás-Martínez C. Agreement with Abengoa S.A.. Funging Agency: Abengoa S.A.Reference:CCB.001UCO

Hervás-Martínez C. Agreement with Astellas Pharma S.A. Funging Agency: Astellas Pharma S.A.Reference:CCB.00UCO





## **10. Scientific Production at a glance**

#### **10.1 Summary of Publications**

The scientific activities carried out by researchers in their respective groups have led to the following global production:

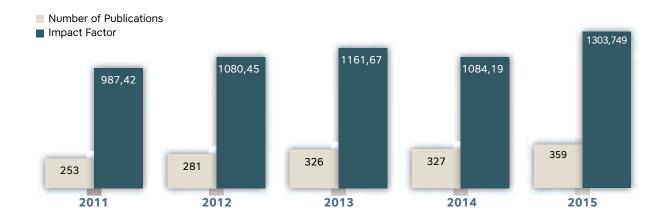
### Publications



The following graph shows the evolution of IF over the past five years:

Evolution in the last five years

Year	Publications	IMIBIC Impact Factor
2011	253	987,42
2012	281	1080,45
2013	326	1161,17
2014	327	1084,19
2015	359	1303,749

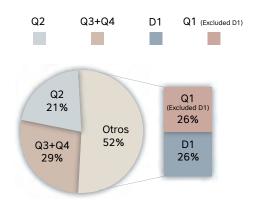


Of note, more than half of these publications appeared in journals within the first quartile, and of those, 26,5% in the first decile, which underscores the growing rates of scientific quality of the published papers.

Regarding the authorship of the works, 57,94%, of the published articles have an IMIBIC researcher at the first/last author and corresponding author, whereas the remaining 42,06 % corresponds to co-authorships in the frame of collaborative research projects.

Distribution of Publications per Quartiles and first Deciles

Total IF	No. of publications
365,418	92
625,578	95
192,741	74
86,226	57
33,786	41
1303,749	359
	IF 365,418 625,578 192,741 86,226 33,786



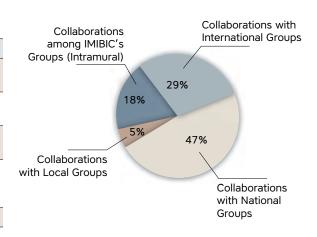
Distribution of International and National Journals

N° of Publications with IF	Total IF	No. of publications	%
International journals	1244,205	316	88%
National journals	59,544	43	12%
Total	1303,749	359	100%

Regarding the affiliation of the authors, the papers published in collaboration with groups from other research centers are shown in the pie chart below:

Distribution of the afiliation of the authors

	Total IF	No. of publications	%
Collaborations with International Groups	494,632	105	29%
Collaborations with National Groups	58,009	19	47%
Collaborations with Local Groups	522,541	169	5%
Collaborations among IMIBIC's Groups (Intramural)	228,567	66	18%
	1303,749	359	100%



#### 10.2- List of Journals

Scientific Journals	Quartile	Decil 1	International/National
ACM Computing Surveys	1	D1	International
Agronomy for Sustainable Development	1	D1	International
AIDS	1	D1	International
Alimentary Pharmacology & Therapeutics	1	D1	International
Alzheimers & Dementia	1	D1	International
American Journal of Clinical Nutrition	1	D1	International
American Journal of Kidney Diseases	1	D1	International
American Journal of Transplantation	1	D1	International
Analytica Chimica Acta	1	D1	International

Scientific Journals	Quartile	Decil 1	International/National
Annals of Neurology	1	D1	International
Annals of Oncology	1	D1	International
Annals of Surgical Oncology	1	D1	International
Annals of the Rheumatic Diseases	1	D1	International
Antimicrobial Agents and Chemotherapy	1	D1	International
Antioxidants & Redox Signaling	1	D1	International
Applied Soft Computing	1	D1	International
Biochemical Pharmacology	1	D1	International
Cancer and Metastasis Reviews	1	D1	International
Chest	1	D1	International
Chronobiology International	1	D1	International
Circulation	1	D1	International
Circulation-Cardiovascular Interventions	1	D1	International
Clinical Infectious Diseases	1	D1	International
Clinical Microbiology and Infection	1	D1	International
Diabetes	1	D1	International
Energy Conversion and Management	1	D1	International
Engineering Applications of Artificial Intelligence	1	D1	International
European Journal of Heart Failure	1	D1	International
European Journal of Operational Research	1	D1	International
Expert Systems with Applications	1	D1	International
Food Chemistry	1	D1	International
Gastroenterology	1	D1	International
Haematologica	1	D1	International
Hepatology	1	D1	International
IEEE Transaction on Cybernetics	1	D1	International
IEEE Transactions on Knowledge and Data Engineering	1	D1	International
Information Sciences	1	D1	International
JACC-Cardiovascular Interventions	1	D1	International
Journal of Agricultural and Food Chemistry	1	D1	International
Journal of Allergy and Clinical Immunology	1	D1	International
Journal of Antimicrobial Chemotherapy	1	D1	International
Journal of Bone and joint Surgery-British Volume	1	D1	International
Journal of Business Ethics	1	D1	International
Journal of Clinical Oncology	1	D1	International
Journal of Heart and Lung Transplantation	1	D1	International
Journal of Hepatology	1	D1	International
Journal of Infection	1	D1	International
Journal of Machine Learning Research	1	D1	International
Journal of Physiology-London	1	D1	International
Journal of the European Academy of Dermatology and Venereology	1	D1	International
Journals of Gerontology Series A-Biological Sciences and Medical Sciences	1	D1	International
Kidney International	1	D1	International
Lancet Infectious Diseases	1	D1	International
Leukemia	1	D1	International
Medicine	1	D1	International
		D1	International

Scientific Journals	Quartile	Decil 1	International/National
Movement Disorders	1	D1	International
Nature Reviews Endocrinology	1	D1	International
Neural Computation	1	D1	International
Neurobiology of Learning and Memory	1	D1	International
Neurotherapeutics	1	D1	International
Obesity Surgery	1	D1	International
Oncogene	1	D1	International
Oncotarget	1	D1	International
Pediatric Allergy and Immunology	1	D1	International
Pediatrics	1	D1	International
PLOS Genetics	1	D1	International
Scientific Reports	1	D1	International
Surgery for Obesity and Related Diseases	1	D1	International
Thorax	1	D1	International
Trends in Endocrinology and Metabolism	1	D1	International
American Journal of Physiology-Renal Physiology	1		International
Analytical and Bioanalytical Chemistry	1		International
Antiviral Research	1		International
Antiviral Research	1		International
Arthritis Care & Research	1		International
Biochimica et Biophysica Acta-Molecular and Cell Biology of Lipids	1		International
Biology of Reproduction	1		International
BMC Genomics	1		International
Cancer Letters	1		International
Climate Dynamics	1		International
Clinica Chimica Acta; International Journal of Clinical Chemistry	1		International
Clinical Journal of the American Society of Nephrology	1		International
Critical Reviews in Oncology Hematology	1		International
Current Medical Research and Opinion	1		International
Current Pharmaceutical Design	1		International
Electrophoresis	1		International
Endocrinology	1		International
EUR J Clin Invest.	1		International
European Journal of Cancer	1		International
European Journal of Cardio-Thoracic Surgery	1		International
European Journal of Clinical Investigation	1		International
European Journal of Internal Medicine	1		International
European Journal of Organic Chemistry	1		International
Expert Opinion on Pharmacotherapy	1		International
Faseb Journal	1		International
Food & Nutrition Research	1		International
Frontiers in Physiology	1		International
Inflammatory Bowel Diseases	1		International
International Journal of Approximate Reasoning	1		International
International Journal of Cardiology	1		International
International Journal of Clinical Practice	1		International

Scientific Journals	Quartile	Decil 1	International/National
Journal of Clinical Endocrinology & Metabolism	1		International
Journal of Environmental Management	1		International
Journal of Hepato-Biliary-Pancreatic Sciences	1		International
Journal of Natural Products	1		International
Journal of Neurointerventional Surgery	1		International
Journal of Proteomics	1		International
Journal of Shoulder and Elbow Surgery	1		International
Journal of the Science of Food and Agriculture	1		International
Knowledge and Information Systems	1		International
Liver Transplantation	1		International
Maturitas	1		International
Molecular and Cellular Endocrinology	1		International
Nephrology Dialysis Transplantation	1		International
Neurourology and Urodynamics	1		International
Oncologist	1		International
Pediatric Critical Care Medicine	1		International
Pediatric Diabetes	1		International
Pediatric Research	1		International
Pharmacogenetics and Genomics	1		International
Pharmacological Research	1		International
Plos One	1		International
Reproduction	1		International
Rheumatology	1		International
Talanta	1		International
Thrombosis and Haemostasis	1		International
Veterinary Journal	1		International
World Journal of Surgery	1		International

# 11 Knowledge Transfer



## **11. Knowledge Transfer**

IMIBIC is aware that one of the main issues which science and technology still has to address in our country is innovation. Thus, IMIBIC has the commitment of encouraging its researchers to innovate and wants therefore to create and transmit a culture of innovation among their researchers, aiming to produce an excellent translational research. Hence, to provide support to this objective, the Innovation Department has grown and it is now able to reach to a greater number of healthcare professionals.

During 2015, one of the priority areas from the Innovation Management area has been to strengthen the links with the business fabric. Therefore, main emphasis was set in public-private collaborations and generating more contacts with companies. IMIBIC's perspective is that the key for successful innovation in healthcare is to efficiently translate the know-how generated by our researchers into new products, services, procedures... In this context, the Innovation Department has carried out the following activities during 2015:

- IMIBIC is part of ITEMAS platform (Innovation Platform in Medical and Health Technologies) funded by ISCIII (Instituto de Salud Carlos III) that seeks to promote innovation in health technology as a key tool to provide sustainability to the National Health System since 2013. As part of ITEMAS platform, the Innovation Management Area has actively participated in two of the Work Groups stablished on this platform: Entrepreneurship and Innovative Public Procurement. Furthermore, Innovation Management area and it is collaborating actively on their activities.
- 2. In the scope of the Innovation Department activities, more than 100 meetings with healthcare professionals and researchers took place. During these meetings, basics of innovation and technology transfer process were explained to them. Innovation culture was disseminated through those meetings, and insights were shared regarding the process of detecting ideas, innovations and research results that could potentially be protected by means of intellectual property.
- 3. With the purpose of creation an innovation culture, several presentations took place in different Medical Services within the hospital and other healthcare centers, to different healthcare professionals (medical doctors, nurses...) in the scope of the hospital, allowing us to reach a huge number of professionals:
  - a. Retos-Colaboración 2015 Call Workshop, 15th January, Madrid (Spain).
  - b. REGIC (Management Foundations Network) Workshop, 18-19th May, Córdoba (Spain).
  - c. 1st Major EAFIP (European Assistance for Innovation Procurement) Event, 27th–28th October, Paris (France).
  - d. Workshop "Bioinformatics as a driver of innovation", 12th November, Madrid (Spain).

- e. "Salud Conectada", organized by Healthcare Informatics Society (SEIS), 23-25th November, Sevilla (Spain).
- f. IV Meeting of Technological Platform for Healthcare Innovation, 25-26th November, Sevilla (Spain).
- g. Asamblea ITEMAS 2015, 26th November, Valencia (Spain).
- h. WeHealth meetings. WeHealth is an interdisciplinary community where developers, healthcare professionals, researchers...come together with the aim of promoting initiatives to improve healthcare and quality of life through ICT's.
- 4. The Innovation Management area participated in two European projects, that started in 2015 in the modality of Coordination Support Actions (CSA), for the preparation of Pre Commercial Procurement tenders on the fields of e-health solutions and emergency services. Furthermore, they collaborated in the consortium creation of another PCP (Pre Commercial Procurement) project on the field of chronic pain management that was requested and got funded during 2015. This PCP project will start in 2016.
- 5. A Technology Innovation area within the Innovation Management area was created during 2014, after the Innovation Management area detected the need of a more technological area, as several of our innovations are related to ICTs. Since its creation, the Technology Innovation area has taken part in several research projects where application of technologies was needed. Their participation in research and innovation projects has increased during 2015, as more researchers became aware of the importance of ICTs and data analysis applied to their research projects.
- 6. Participation in FIPSE call "Feasibility studies for Healthcare Innovations". Four projects were presented to this call but unfortunately none got funded. This call helped the Innovation Management area to select projects that needed validation and/or feasibility studies, and to make the involved researchers aware of the importance of validation and other steps needed to successfully transfer their knowledge to the society.
- 7. The Innovation Management area has promoted the participation of different research groups from IMIBIC in private-public collaboration calls. Specifically, they have requested funding for 8 INNTERCONECTA projects and 1 RETOS project. Finally, 4 INNTERCONECTA and 1 RETOS projects obtained funding during 2015.
- 8. Aiming to strengthen IMIBIC links with the industrial network, the Innovation Management area has started a program where companies come to IMIBIC and present their main R+D activities to the researchers in order to encourage synergies between the companies and IMIBIC.

As a result of all the activities described, the results shown in the table below were obtained:

Evolution of Results	2011	2012	2013	2014	2015
Patents	6	8	13	11	14
PCTs	2	3	3	4	7
Licenses	0	4	4	2	2
Companies	1	2	0	1	0

#### Industrial and intellectual property patents

During 2015, a total of 21 industrial/intellectual property patents were applied for:

Title	Registry type	Owner Entity
Method for obtaining useful data for diagnosis of hepatocellular carcinoma on alcoholic patients suffering from hepatitis C	National Patent	SAS, CIBER
Method for obtaining useful data for predicting and forecasting of the de- velopment of interferon-induced thrombocytopenia	National Patent	SAS, UCO
Prediction method for atypical fractures	European Patent	SAS, IMIN
Use of derivatives of aureolic acid on the production of a medicine for cholestasis treatment	National Patent	SAS, CIBER, UCO
Use of derivatives of anthranilic acid on the production of a medicine for cholestasis treatment	National Patent	SAS, CIBER, UCO
Laparoscopic Extractor	National Patent	SAS
Diagnosis kit for the identification of bacterial agents causing systemic in- fections	National Patent	SAS, IKAN BIOTECH CANVAX BIOTECH
Biomarkers in exhaled breath condensate for the diagnosis, classification and monitoring of lung cancer	National Patent	SAS, UCO
Intraocular device for retina protection	National Patent	SAS
Software for the management and registration of hospital infections	Intellectual Property Registry	SAS
Electronic Data Record Software	Intellectual Property Registry	SAS, UCO, CIBER
Use of a composition comprising an agent AP-1 inhibitor for the manufac- ture of a medicament for the treatment of cholestasis	National Patent	SAS, CIBER, UCO
Using the GOAT enzyme levels as a marker of prostate cancer. "Ghrelin -O - acyltransferase (GOAT) and its uses."	National Patent	SAS, UCO
Predicting response method for patients with rheumatoid arthritis in the anti-TNF therapy	PCT	SAS, UCO, FIBICO
Method for obtaining useful data for diagnosis of hepatocellular in alcoholic patients with hepatitis C	PCT	SAS, UCO, CIBER
Mesenchymal stem cells lysates for the treatment of musculoskeletal injuries	PCT	SAS, UCO
Quality Control device for ionizing radiations emitting equipment	РСТ	SAS
Method for obtaining useful data for the detection of patients with lung cancer	РСТ	SAS, UCO
Procedure to obtain useful data to detect angiogenesis on lower limbs	PCT	SAS
Laryngoscope with consumable blade	PCT	SAS
Method and kit for predicting or forecasting response to antiangiogenic	National Phases	SAS, UCO

SAS: Andalusian Health Service ; UCO: University of Cordoba ; CIBER: Biomedical Research Networking Centres





## 12. Goals for 2016

1	Obtain the reaccreditation of ISCIII as a Health Research Institute.
2	Develop strategies to increase the quality and number of scientific publications and leadership within IMIBIC's researchers.
3	Promote and improve clinical research in the IMIBIC, increasing development, quality and efficiency of independent clinical research projects.
4	Encourage institutional integration.
5	Strengthen and improve the self-sustainability of IMIBIC, optimizing the management of their own resources, by increasing uptake of European funds and competitive public funds as well as through the promotion of collaboration with the business community.
6	Develop a strategy for incorporating new clinical groups and academics, as well as for the promotion of existing groups.
7	Attract research talent and promote their professional development.
8	Promote, attain and strengthen partnerships and international collaborations.
9	Promote and increase the protection of knowledge generated and the transfer of technology to the business fabric
10	Ensure the quality of service provided by the BRSUs and management units of the Institute and promote innovation through across them.



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