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## Director's Foreword

### **1.-Director's Foreword**



The Maimonides Institute for Biomedical Research of Córdoba (IMIBIC) continues its development, pursuing the goal of achieving excellence in research and innovation, and bringing its results to the patient and the society. This is made possible by the strong, joint commitment of professionals and institutions, which provides the solid ground that enables a sustained growth in production and quality. After 2015, a year full of changes and challenges for IMIBIC, in 2016

the Institute has consolidated the

development of its regular activities in a new environment, while attaining two most important objectives: the renewal of the accreditation as a Health Research Institute by the National Institute of Health Carlos III, and the elaboration, approval and launching of the new Strategic Plan 2016-2020.

The process of re-accreditation and that of constructing and deploying the Strategic Plan 2016-2020 have shared a key, common basis, which is the involvement of all the IMIBIC community in these endeavours. From researchers focused on basic, clinical or translational science, to nurses and technicians, from personnel in core facilities, or in management and administrative areas, to the governing and scientific boards, all the professionals participated and contributed to the success of these complex and laborious processes.

The challenge will be now to maintain this enthusiastic involvement of all the research community, and to polish and improve our capacities, toward attaining higher levels





of quality, production and efficiency as an independent research center of excellence, with a translational nature and a vocation to improve the quality of life of patients.

This 2016 Scientific Report summarizes the main figures of the research and innovation activities developed by the scientific teams and research support areas of the IMIBIC. A steady growth in the main areas of activity is reflected in the indexes and graphs, but, most importantly, the data depicts the efforts of our research community towards increasing their standards of quality, international collaboration, translation, and innovation. In 2016, IMIBIC continued increasing its scientific output, with 401 publications and a global impact factor of 1528 points.

The Strategic Plan 2016-2020 provides a solid and valuable roadmap for the next years, for it defines our mission, our main and specific goals, and the tools to achieve them, in a precise and specific manner. It is now the time to pursue and achieve these objectives. To this end, our next challenge will also be to foster and enhance the five Scientific Programs, oriented to major health problems, which will pave the way to the future success of truly translational research at IMIBIC. The integrated enthusiastic work of our scientists and institutions will hopefully enable to bring the best results from biomedical research to the patient.

Justo P. Castaño Scientific Director



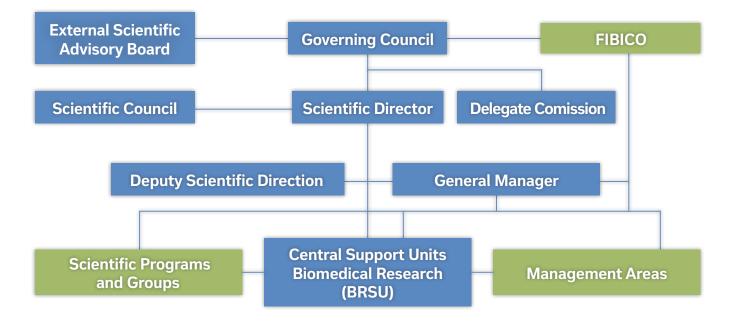


## Human, Technological and Economic Resources

### 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 Equity, Health and Social Policies 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, Innovation, Science and Employment **Manuel García León**. General Director for Research, Technology and Business **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 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 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 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 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

### 2.3. Research Groups

#### GC- Consolidated Groups – GE - Emerging Groups – GA - Associated Groups

Code	Title	Researchers
GC1	Immunology and Allergy PROGRAMS 1, 3, 5	Dr. Rafael Solana Lara (PI)
GC2	Oxidative and nitrosative stress in acute and chronic liver disease. PROGRAMS 3, 4, 5	Dr. Manuel De La Mata García (PI) Dr. José Antonio Bárcena Ruiz (CO-PI)
GC3	Infectious diseases. PROGRAMS 1, 3, 5	Dr. Julián De La Torre Cisneros (PI) Dr. Antonio Rivero Román (CO-PI)
GC4	Inflammation and cancer. PROGRAMS 2, 3, 4, 5	Dr. Eduardo Muñoz Blanco (PI) Dr. Marco A. Calzado (ER)
GC5	Systemic and chronic inflammatory autoimmune diseases of the locomotor system and connective tissue. PROGRAMS 2, 5	Dr. Rosario López Pedrera (PI) Dr. Eduardo Collantes Estévez (CO-PI)
GC6	New therapies in cancer. PROGRAM 4	Dr. Enrique Aranda Aguilar (PI) Dr. Antonio Rodríguez Ariza (CO-PI) Dr. Juan de la Haba Rodríguez (ER)
GC7	Nephrology. Cell damage in chronic inflammation. PROGRAMS 1.5	Dr. Pedro Aljama García (PI) Dr. Julia Carracedo Añón (CO-PI)
GC8	Hormones and cancer. PROGRAMS 2, 4	Dr. Justo P. Castaño Fuentes (PI) Dr. Francisco Gracia Navarro (CO-PI) Dr. Raúl Luque (CO-PI)
GC9	Nutrigenomics. Metabolic syndrome. PROGRAMS 1, 2 , 4, 5	Dr. José López Miranda (PI) Dr. Francisco Pérez Jiménez (CO-PI) Dr. Yolanda Almadén Peña (CO-PI) Dr. Javier Delgado Lista (CO-PI) Dr. Pablo Pérez Martínez (CO-PI)
GC10	Hormonal regulation of energy balance, puberty and re- production. PROGRAMS 2, 4	Dr. Manuel Tena Sempere (PI)
GC11	Metabolism and adipocyte differentiation. Metabolic syn- drome. PROGRAM 2	Dr. María del Mar Malagón Poyato (PI) Dr. Francisco Gracia Navarro (CO-PI)
GC12	Epidemiological Research in Primary Care. PROGRAMS 4, 5	Dr. Luis Ángel Pérula de Torres (PI)
GC13	Calcium metabolism. Vascular calcification PROGRAMS 2, 5	Dr. Mariano Rodríguez Portillo (PI)
GC14	Cell therapy. PROGRAM 5	Dr. I. Concepción Herrera Arroyo (PI)
GC15	Invasive cardiology and cell therapy. PROGRAM 5	Dr. José Suárez De Lezo Cruz-Conde (PI)
GC16	Cell biology in hematology. Hypercoagulability. PROGRAM 4	Dr. Joaquín Sánchez García (PI) Dr. Francisco Velasco Gimena (CO- <b>PI</b> )
GC17	Pathophysiology of the endocrine system of vitamin D. Biotechnology and aging. PROGRAMS 1, 2	Dr. José Manuel Quesada Gómez (PI)
GC18	Translational research in surgery of solid organ trans- plants. PROGRAMS 4, 5	Dr. Javier Briceño Delgado (PI)



GC20	Genetics and behavioural diseases. PROGRAM 5	Dr. Manuel Ruiz Rubio (PI)
GC21	Metabolomics. Identification of bioactive components. PROGRAMS 2 , 4, 5	Dr. María Dolores Luque De Castro (PI) Dr. Feliciano Priego Capote (ER)
GC22	Epigenetics. PROGRAM 4	Dr. Teresa Roldán Arjona (PI)
GC23	Metabolism in Childhood PROGRAMS 2, 4	Dr. Mercedes Gil Campos (PI)
GE1	Oxidative stress and nutrition. PROGRAMS 1 , 2, 5	Dr. Isaac Túnez Fiñana (PI)
GE2	Knowledge Discovery and Intelligent Systems PROGRAMS 1,2,3	Dr. Sebastián Ventura Soto (PI)
GE3	Skin immune mediate inflammatory diseases (SIMID) PROGRAM 5	Dr. Juan A. Ruano Ruiz (PI)
GE4	Applied Psychology PROGRAM 1	Dr. Carmen Tabernero Urbieta (PI)
GE5	Urology and Sexual Medicine PROGRAM 5	Dr. María José Requena Tapia (PI)
GA1	Lung transplantation. Thoracic malignancies. PROGRAM 4	Dr. Ángel Salvatierra Velázquez (PI)
GA2	Comprehensive care nurses - a multidisciplinary perspective. PROGRAMS 1, 5	Dr. María Aurora Rodríguez Borrego (PI)
GA3	Pneumology PROGRAMS 2, 4, 5	Dr. Bernabé Jurado Gámez (PI)
GA4	Endocrinology and Nutrition. Insulin resistance, diabetes and metabolism. PROGRAM <b>2</b>	Dr Mª Ángeles Gálvez Moreno (PI)
GA5	Study of growth. Endocrinology and Child Nutrition. PROGRAM 2	Dr. Ramón Cañete Estrada (PI)
GA6	Clinical Analysis. PROGRAM 2	Dr. Fernando Rodríguez Cantalejo (PI)
GA8	Radiology PROGRAMS 2, 4, 5	Dr. Daniel López Ruiz (PI)
GA9	Cardiology Cardiovascular PROGRAMS 2, 4,	Dr. Ignacio Muñoz Carvajal (PI)
GA10	Nuclear Medicine PROGRAMS 2, 4	Dr. Juan A. Vallejo Casas (PI)
GA11	Learning and Artificial Neural Networks-AYRNA PROGRAMS 2, 3, 4, 5	Dr. César Hervás Martínez (PI)

#### **2.4.- Economic Resources**

The year 2016 marks the start of the period covered by IMIBIC's Second Strategic Plan. It also saw IMIBIC's re-accreditation as a Health Research Institute by the Carlos III Health Institute, as occurred in 2011.

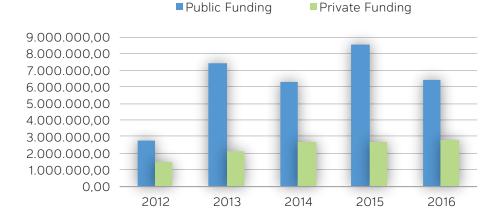
The evolution of the income obtained by IMIBIC in recent years has been marked by the funding of Innovative Public Procurement projects, in the total amount of 9 million euros in the years 2013-2015.

The increase in overall funds raised was as follows:

#### Funds raised by IMIBIC 2012 to 2016



The increase in investments, notably the inauguration of the new IMIBIC headquarters in 2015, as well as the launching of two areas dedicated to clinical research within the Reina Sofía University Hospital in Cordoba. The investment in these facilities and in the purchase of scientific equipment for fundamental research has exceeded 20 million euros. At the same time, it is necessary to maintain a balance between public and private funds obtained. Public funding is obtained from various sources, but it is important to highlight the increase in recent years in international funding, mainly at European level. The breakdown of the funds raised by source is as follows:



#### **Public versus Private Funding**

Public versus Private Funding	2012	2013	2014	2015	2016
Total	4.231.754,11	9.535.436,81	8.915.342,79	11.175.450,20	9.616.514,40
Public Funding	2.764.787,57	7.388.386,12	6.260.590,12	8.518.698,44	6.393.477,67
Private Funding	1.466.966,54	2.147.050,69	2.654.752,67	2.656.751,76	2.868.248,33

As with fundraising in general, this is particularly the case with private funds, which have doubled in just four years. A balance has not yet been achieved public vs. private funding, remaining at 66-33% during the analyzed period 2012-2016. However, as indicated previously, the work that is being done to capture private funding is bearing fruit. Not only has it been doubled in recent years, the sources of such funding have also diversified, and measures have been taken to facilitate private fundraising. In this sense, it is worth highlighting the increase in income obtained from clinical studies, which will surely continue to increase significantly in the coming years thanks to the creation of two units dedicated to clinical research with centralized resources.

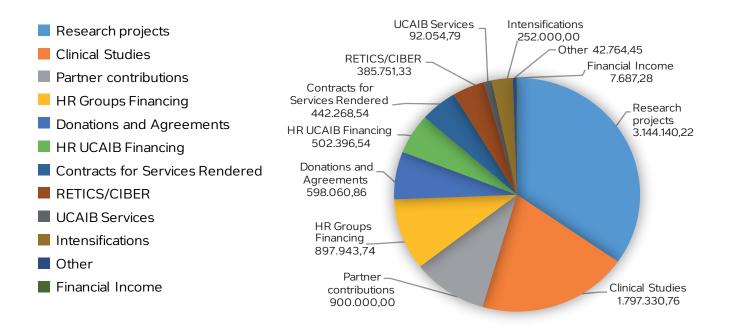


#### **Source of Private Funding**



	2012	2013	2014	2015	2016
Source of Private Funding	1.466.966,54	2.147.050,69	2.654.752,67	2.656.751,76	2.674.432,30
Clinical trials/Observational trials	975.149,79	1.132.818,84	1.772.682,05	1.786.513,67	1.689.229,30
Donations/agreements/contracts	491.816,75	1.014.231,85	882.070,62	870.238,09	985.203,00

The previous sections have all referred to annual fundraising activities, which therefore include funding for several years. As a general rule, research projects receive funding for 3 years on average. All the annuities for research projects, together with the Institute's income and structural expenses (called "centralized resources" - Management and UCAIBs), form the annual budget of the Institute. The total budget for the financial year 2016 amounted to more than 9,6 million euros, which in turn was subdivided into 6 million to finance research activities and 2 million to finance the structure and centralized resources.



The breakdown of the sources of the income making up the budget for the year 2016 is as follows:

	Public	Private	TOTAL
Research projects	3.144.140,22	0	3.144.140,22
Clinical Studies	0	1.797.330,76	1.797.330,76
Partner contributions	900.000,00	0	900.000,00
HR Groups Financing	897.943,74	0	897.943,74
Donations and Agreements	0	598.060,86	598.060,86
HR UCAIB Financing	502.396,54	0	502.396,54
Contracts for Services Rendered	0	442.268,54	442.268,54
RETICS/CIBER	385.751,33	0	385.751,33
UCAIB Services	0	92.054,79	92.054,79
Intensifications	252.000,00	0	252.000,00
Other	5.870,00	36.894,45	42.764,45
Financial Income	0	7.687,28	7.687,28



## Goals achieved in 2016

## 3. Goals achieved in 2016

	Objective for 2016		Current 2016 Status
1	Obtain renewal of accreditation by ISCIII as a Health Research Institute.	Obtain	Over the first semester of 2016, all the documentation required for renewal of IMIBIC's status as a Health Research Institute was prepared. We now receive the final favour- able report.
2	Develop strategies to improve the quality and number of sci- entific publications and the status of IMIBIC researchers as lead authors.	≥ 27% articles in first decile	As at 31 December 2016, 15% of articles were in the first decile; the objective is unlikely to be achieved. A series of improve- ments is planned for 2017.
3	Promote and improve clinical research at IMIBIC, fostering the development, quality and efficiency of independent clini- cal research projects.	≥ 7 trials with IMIBIC as promot- er	As 31 December 2016, IMIBIC is the promoter for 7 trials.
4	Encourage institutional integra- tion.	Opening of IMIBIC animal facility Implementation of direct costs Economic returns via IP	Opening of the animal facility is pending recipient by the Junta de Andalusia inspector authori- sation. It should open at the beginning at the next year. The indirect costs of UCO research projects are being reviewed by the Governing Board. The ques- tion of economic returns on in- tellectual property rights is being examined with the institutions concerned.
5	Strengthen and improve IMIB- IC's self-sustainability, optimis- ing the management of its own resources by obtaining more European funding and com- petitive state funding, and by fostering partnerships with the business sector.	Structural income ≥ 2.2 million euros	Income generated for structural funding at 31 December 2016 was 2.8 million euros
6	Develop a strategy for incorpo- rating new clinical and univer- sity groups, and for promoting existing groups.	≥ 1 group ≥ 1 group	<ul> <li>≥ 1 clinical group: Microbiology</li> <li>≥ 1 group prompted to Emerging: Urology.</li> </ul>



7	Attract more research talent and promote professional de- velopment.	Active competi- tively-funded HR > 5% of 2016 val- ue	As at 31 December 2016, com- petitively-funded HR for any call amounted to 57. This represents an increase of 21% over the pre- vious year
8	Foster, arrange and consolidate international alliances and co- operative ventures.	Apply for > 25 proj- ects	As at 31 December 2016, 33 projects had been presented for international calls.
9	Promote and enhance the pro- tection of the knowledge gen- erated and the transfer of tech- nology to the business sector.	>20% patents in exploitation	19% of patents applied for by 31 December are now in exploita- tion.
10	Assure the quality of the ser- vice provided by UCAIBs and Institute management units and promote transversal inno- vation through them.	User satisfaction ≥ 85%	The user satisfaction survey had been carried at the end of the year.





## 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 Maestro. Director of the Cardiovascular Research Centre (CSIC-ICCC) (Barcelona)

**Dr. Carlos Diéguez González.** 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 Fonticoba. General Director of La Fundación Cotec (Zaragoza).

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.

## Participation in Networks

### **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 ISCIII strategic initiatives.8 groups are involved in 8 RETICs. Additionally, 10 groups are involved in 5 CIBERs and there are 32 groups involved in the Andalusian Plan for Research, Development & Innovation (PAIDI Program).

#### List of CIBER\* projects with IMIBIC participations

\* (Network Biomedical Research Center)

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)
	Mercedes Gil Campos (PI)
	Mª Mar Malagón Poyato
	Justo P. Castaño Fuentes
CIBER on Liver and Digestive Diseases (CIBERehd)	Manuel de la Mata García (PI)
CIBER on Rare Diseases (CIBERER)	Eduardo López Laso
	Rafael Camino León
*CIBER on Fragility and Heathly Aging (CIBERFES)	Jose Manuel Quesada Gómez (PI)
	Feliciano Priego Capote
CIBER on Cancer (CIBERONC)	Enrique Aranda Aguilar (PI)

#### Platforms

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

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

#### **RETICS Program**

List of ISCIII thematic network centers that the IMIBIC is involved in:

Name of the Network	Principal Investigator (P)/Collabo- rators
AIDS Research Network (RIS)	Antonio Rivero Román (PI)
Spanish Renal Research Network (REDinREN)	Pedro Aljama García (PI)
	Mariano Rodríguez Portillo

Spanish Network for Research into Infectious Pathologies (REIPI)	Julián de la Torre Cisneros (PI)
	Luis Martínez Martínez
Research Network on Preventive and Health Promotion in Primary Care (RedIAPP)	Luis A. Pérula de Torres
Spanish Network for asthma, adverse reactions and allergic (ARADYAL)	Carmen Moreno Aguilar (PI)
Spanish Network for Research in inflammation and rheumatic disease (RIER)	Eduardo Collantes Estévez (PI)
Spanish Multiple Sclerosis Network (REEM)	Eduardo Agüera Morales (PI)
	Isaac Túnez Fiñana
Prevention, Early detection, Treatment and Rehabilitation of Ocular Pathologies	José Mª Gallardo Galera (PI)

#### **Others Networks**

Development of novel targeted or immune therapies directed against luminal, HER2-positive and/or triple negative breast cancer.	Juan de la Haba Rodríguez
Spanish Myelodysplastic Syndrome Registry (Resmd)	Joaquín Sánchez García
Observational Immune Tolerance Induction research program (ObsITI)	Francisco Velasco Gimena
Big Data y Análisis de Datos Escalable (BigDADE)	Sebastián Ventura Soto

#### **PAIDI Groups**

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

CTS-208	Principal investigator	José Peña Martínez
BIO 216	Principal investigator	José Antonio Bárcena Ruiz
CTS-647	Principal investigator	Julián Carlos de la Torre Cisneros
BIO-304	Principal investigator	Eduardo Muñoz Blanco
CTS-1004	Principal investigator	Eduardo Collantes Estévez
CTS-234	Principal investigator	Enrique Aranda Aguilar
CTS-260	Principal investigator	Pedro Aljama García
BIO-139	Principal investigator	Justo P. Castaño Fuentes
CTS-212	Principal investigator	Francisco Pérez Jiménez
CTS-525	Principal investigator	José López Miranda
BIO-310	Principal investigator	Manuel Tena Sempere
CTS-179	Principal investigator	Escolástico Aguilera Tejero
BIO-208	Principal investigator	José Suárez de Lezo Cruz Conde
CTS-620	Principal investigator	Francisco Velasco Gimena
CTS-413	Principal investigator	José Manuel Quesada Gómez
TIC-161	Principal investigator	Rafael Medina Carnicer
BIO-272	Principal investigator	Manuel Ruiz Rubio
HUM-924	Principal investigator	Juan Antonio Moriana
FQM-227	Principal investigator	María Dolores Luque de Castro
BIO-301	Principal investigator	Rafael Rodríguez Ariza
CTS-624	Principal investigator	Isaac Túnez Fiñana
CTS -985	Principal investigator	José Peña Amaro



TIC-122	Principal investigator	Sebastián Ventura Soto
HUM-414	Principal investigator	Carmen Tabernero Urbieta
CTS-666	Principal investigator	Aurora Rodríguez Borrego
TIC-148	Principal investigator	César Hervás Martínez
CTS-329	Principal investigator	Ramón Cañete
CTS-992	Principal investigator	Bernabé Jurado Gámez
CTS-651	Principal investigator	Juan Antonio Paniagua González
CTS-639	Principal investigator	María Mercedes Gil Campos
CTS-452	Principal investigator	Luis A. Pérula de Torres
CTS-273	Principal investigator	Manuel de la Mata García





# Training Activities

### **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 Program Director: **Prof. Ma del Mar Malagón, PhD.** 

#### 6.2. Training

The following sections list the research training activities developed at the IMIBIC during 2016.

#### 6.2.1. PhD in Biomedicine

IMIBIC leads a unique PhD Program in Biomedicine. This program, coordinated by Prof. Dr. María M. Malagón, aims to qualify human resources and to promote the development of professional skills in the field of biomedical sciences.

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

#### 6.2.2. Master's Degrees

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, PhD. (2015-16) - Prof. Raúl M Luque Huertas, PhD. (2016-17)** Website: http://www.uco.es/estudios/idep/masteres/investigacion-biomedica-traslacional

#### - Human Nutrition

Academic Director: **Prof. Rafael Moreno Rojas, PhD.** Website: http://www.uco.es/estudios/idep/masteres/nutricion-metabolismo

#### - Biotechnology

Academic Director: **Prof. Nieves Abril Díaz, PhD.** Website: https://www.uco.es/estudios/idep/masteres/biotecnologia

#### 6.2.3. COURSES and other training activities

Specific courses, seminars and other training activities in different research areas have been held during 2016 at the IMIBIC.

#### 6.2.3.1. Training activities

Along the 2016 a number of activities have been organized at the IMIBIC,as:

Type of Activity	Title	Duration *(h)
COURSE	Curso de Bioinformática: Introducción al análisis en biología de sistemas	6h

Type of Activity	Title	Duration *(h)	
COURSE	Curso de Bioinformática: Introducción al análisis en biología de sistemas	6h	
CONGRESS	XVI Jornadas Científicas de Medicina Familiar y Comunitaria de Córdoba		
CONGRESS	Manejo de la Terapia Biologica en procesos dependientes de iGe	3h	
SEMINAR	Determinación de tamaño muestral en estudios biosanitarios	9h	
SEMINAR	El desafío de la medición de desigualdades sociales en salud	9h	
INSTITUTION- AL EVENTS	VII Jornada de Jóvenes Investigadores		
CONGRESS	Alternativas de financiación de empresas innovadoras en el Sector Salud y Agroalimentario	2h	
SEMINAR	Bienvenida Residentes	3h	
CONGRESS	Jornada de Inmunoterapia	4h	
COURSE	New Insights for Multicolor panel design	3h	
CONGRESS	Premios IMIBIC-ROCHE	3h	
COURSE	Data Visualization Course	4,5h	
CONGRESS	"La Nueva Economía del Conocimiento y la Universidad: el Sector eHealth"	6h	
CONGRESS	40 Años de excelencia en alergía a himenópteros	4,5h	
CONGRESS	Diagnóatico del RAS a través de la Biopsia Líquida; beneficios y práctica clínica	3h	
CONGRESS	International workshop on laparoscopic liver surgery	12,5h	
MEETING	Oncología Médica Radioterápica y Urología	11h	
SEMINAR	Microbiota, Dieta y Lácteos	4h	
	Proyecto Diferenciar	8h	
CONGRESS	Meeting Multidisciplinar en Artritis Reumatoide y Enfermedad Pulmonar Intersticial Difusa		
SYMPOSIUM	Symposium Nacional sobre Avances en Especialidades Pediátricas	19h	
CONGRESS	Actualización de nuevas evidencias en CPRCm	2,5h	
CONGRESS	Creación y puesta en marcha de SPIN-OFF (2ª Edición )	25h (online)	
SYMPOSIUM	l Symposio Internacional Transplante Pulmonar	2,5h	
MEETING	Reunión multidisciplinar sobre Cáncer de Próstata Resistente a Castración y con metástasis Óseas.	6h	
COURSE	Curso de Gilead	2h	
CONGRESS	Jornada Enfermedades Raras	10,5h	
CONGRESS	l Jornada Provincial de cronicidad	6,5h	
MEETING	2ª Reunión multidisciplinar sobre el manejo del paciente con Cáncer Colorrectal Metastásico	3,5h	
CONGRESS	New Frontiers in Obesity	26,5h	
COURSE	Taller Consumo de Oxígeno	4,5h	
INSTITUTION- AL EVENT	VI Lección Conmemorativa Maimónides	2h	
WORKSHOP	Recovering life wellbeing through pain self-management techniques involving ICTs	5h	

#### 6.2.3.2. IMIBIC Research Seminars

Regular seminars and research events offer the opportunity to meet recognized national and international speakers covering a diverse range of topics in biomedicine. IMIBIC research seminars promote networking and contribute to strengthen the knowledge of the research community of the Institute. The Institute launches yearly cycle of seminars aimed at promoting interactions, sharing ideas, and strengthening the bonds among IMIBIC scientists. In 2016, a total of 23 seminars were presented.



In addition, young researchers (preferentially postdocs) of our Institute have the opportunity to present their ongoing studies in a fortnight-scheduled cycle of intramural seminars, which was launched for the first time in 2015. In 2016, a total of 14 seminars have been presented.

The seminars organized by the Institute during the course 2016 were:

Month	Week	Seminarios Intramurales	Seminarios Externos
	4-10	-	-
JANUARY	11-17	-	Date: 14/01/2016 Speaker: Natividad Cuende Institution: Iniciativa Andaluza en Terapias Avan- zadas. Junta de Andalucía Title: Soporte a la traslación clínica de la terapia génetica y celular: la Iniciativa Andaluza en Tera- pias Avanzadas.
	18-24	Date: 19/01/2016 Speaker: Sebastián Ventura Group: GE-02 Title: Introducción al análisis de datos y sus aplicaciones a biomedicina	Date: 21/01/2016 Speaker: Matti Poutanen Institution: Department of Physiology. Institute of Biomedicine. University of Turku. (Finlandia) Title: Regulation of tissue-specific sex steroid ac- tion: role of the HSD17B-enzymes in reproductive and metabolic medicine
	25-31	-	Date: 28/01/2016 Speaker: Albert Quintana Institution: Departamento de Biología Celular, Fisiología e Inmunología. Universidad Autónoma de Barcelona Title: Mecanismos moleculares de la susceptibili- dad neuronal a la enfermedad mitocondrial.
	1-7	Date: 02/02/2016 Speaker: Yolanda Jiménez Group: GC-05 Title: Estudio de los mecanismos celulares y moleculares de las vías inflamatoria y osteopro- liferativa en la espondilitis anquilosante. Nuevas dianas terapéuticas	Date: 04/02/2016 Speaker: José López Barneo Institution: Director del IBiS. Title: Factores neurotróficos en el tratamiento de las enfermedades neurodegenerativas
FEBRUARY	8-14	-	Date: 11/02/2016 Speaker: Elena Navarro González Institution: Hospital Universitario Virgen del Ro- cío de Sevilla Title: Epidemiología del cáncer de tiroides
	15-21	Date: 16/02/2016 Speaker: Maribel Lara Chica Group: GC-04 Title: CHK2 stability is regulated by the E3 ubiquitin ligase SIAH2	-
	22-28	-	Date: 25/02/2016 Speaker: Miguel Ángel Martínez Institution: Universidad de Navarra Title: La importancia de la investigación en epi- demiología clínica para mejorar la práctica clínica.

Month	Week	Seminarios Intramurales	Seminarios Externos	
MARCH	29feb-6	Date: 01/03/2016 Speaker: Victoria García Ortiz Group: GC-22 Title: Modificación del epigenoma en células tumorales mediante expresión de desmetilasas vegetales	Date: 03/03/2016 Speaker: Miguel Angel Quintela-Fandiño Institution: Unidad de investigación clínica del cáncer de mama del CNIO Title: Mecanismos de resistencia a tratamientos antiangiogénicos	
	7-13	Date: 08/03/2016 Speaker: Valeria Barresi Group: Department Human Pathology, Univer- sity of Messina Title: Role of pathologist in targeted cancer therapy	Date: 10/03/2016 Speaker: Ana Vivancos Prellezo Institution: Grupo genómica del cáncer del insti- tuto de oncología del Vall D'Hebron Title: Biopsia Líquida: conceptos, tecnología y aplicaciones clínicas".	
	14-20	Date: 15/03/2016 Speaker: Manuel Gahete Ortiz Group: GC-08 Title: Los sistemas somatostatina y ghrelina como ejemplo de convergecia entre hormonas, metabolismo y cáncer	-	
	21-27	Date: 29/03/2016 Speaker: Pablo López Soto Group: GA-02 Title: "Diurnal and twenty-four hour patterning of human diseases: findings in falls in the elder- ly"	-	
	28- 3Apr	-	Date: 30/03/2016 Speaker: Dr. Sollinger Institution: University of Wisconsin School of Medicine and Public Health Title: Terapia génica de la Diabetes	
	4-10	-	Date: 07/04/2016 Speaker: Prof. José Verdú Soriano Institution: Universidad de Alicante Title: "El cuidado de heridas y el paradigma del biofilm bacteriano"	
	11-17	-	-	
APRIL	18-24	Date: 19/04/2016 Speaker: Antonio Rivero-Jurarez Group: GC-03 Title: Virus de la hepatitis E: enfermedad emer- gente en Europa?	-	
	25- 1may	Date: 26/04/2016 Speaker: Antonio Romero Group: GC-10 Title: Estudios fisiopatológicos y mejora diag- nóstica en patologías reproductivas: Embarazo Ectópico, Endometriosis y Síndrome de Ovario Poliquístico	Date: 28/04/2016 Speaker: Susana de la Luna Institution: CRG (Centre for Genomic Regulation) de Barcelona Title: La proteína quinasa DYRK1A como un nue- vo regulador de angiogenesis	



Month	Week	Seminarios Intramurales Seminarios Externos	
MAY	2-8	-	Date: 05/05/2016 Speaker: Luis Carlos Silva Ayçaguer. Institution: Centro Nacional de Información de Ciencias Médicas. INFOMED. Title: El uso ritual de la estadística y sus efectos sobre la construcción de conocimiento.
	9-15	-	Date: 13/05/2016 Speaker: Luke Selth Institution: The University of Adelaide Title: "Novel microRNA regulators of prostate cancer epithelial plasticity and metastasis".
	16-22	-	Date: 19/05/2016 Speaker: Rafael Simó Canonge Institution: Diabetes Research and Metabolism Unit Title: Neurodegeneración y retinopatía diabética: implicaciones terapéuticas
	23-29	Date: 24/05/2016 Speaker: Juanjo Giner Group: Universidad de Córdoba Title: Nanoparticles for Biomedicine	-
JUNE	30may- 5	-	Date: 02/06/2016 Speaker: Marina Pollán Institution: Centro Nacional de Epidemiología (Instituto de Salud Carlos III) Title: Epidemiología del cáncer de mama y densi- dad mamográfica
	6-12	-	Date: 09/06/2016 Speaker: Leocadio Rodríguez Mañas Institution: Jefe de Servicio de Geriatría. Hospital Universitario de Getafe. Coordinador de la Red Temática de Investigación Cooperativa en Enve- jecimiento y Fragilidad (RETICEF) Title: El anciano con diabetes: un abordaje distin- to para un paciente diferente.
	13-19	-	<ul> <li>Date: 16/06/2016</li> <li>Speaker: María D. Mayán Santos</li> <li>Institution: Instituto de Investigación Biomédica de A Coruña (INIBIC).</li> <li>Title: Conexinas y panexinas nuevas dianas en el diagnóstico y la terapéutica.</li> </ul>
	20-26	Date: 22/06/2016 Speaker: Francisco Gómez García Group: GE03 Title: 10 claves prácticas para publicar una re- visión sistemática y un meta-analisis en red en 2016	Date: 23/06/2016 Speaker: Domingo Barber Hernandez. Institution: Director del Instituto de Medicina Molecular Aplicada de la Facultad de Medicina de la Universidad San Pablo-CEU. Title: Inmunoterapia en Alergia
	27-3jul	-	Date: 29/06/2016 Speaker: Graham Pawelec. Institution: University of Tubingen (Alemania). Title: Immunosenescence and Cancer.

Month	Week	Seminarios Intramurales	Seminarios Externos
JULY	4-10	Date: 05/07/2016 Speaker: Francisco Manuel Conde Pérez Group: GC-06 Title: Aproximaciones clásicas y proteómicas para el descubrimiento de biomarcadores pre- dictivos de respuesta a terapias antiángiogéni- cas.	-
	11-17	-	-
	18-24	-	-
	25-31	-	-
AUGUST	-	-	-
	29Aug- 4	-	-
SEPTEMBER	5-11	-	Date: 05/09/2016 Speaker: Francisco Borrego Rabasco Institution: Instituto de Investigación Sanitaria BioCruces Title: Receptores CD300: Papel en la regula- ción de la activación de basófilos mediada por IgE.
0,	12-18	-	-
	19-25	-	-
	26- 20ct	-	-
	3-9	-	Date: 07/10/2016 Speaker: Edgardo Carosella Institution: Jefe del Departamento de Inmuno- logía Aplicada del Hospital Saint Louis Title: La molécula HLA-G: Check Point en la Respuesta Inmune
BER	10-16	-	-
OCTOBER	17-23	-	-
ŏ	24-30	Date: 25/10/2016 Speaker: César Hervás Martínez Group: GA11 Title: Modelos de redes neuronales computa- cionales: Aplicación a problemas de asignación donante receptor en biomedicina de transplan- tes.	-



Month	Week	Seminarios Intramurales	Seminarios Externos
	310ct-6	-	-
3ER	7-13	Date: 08/11/2016 Speaker: Sara Cantisán Bohorquez Group: GC03 Title: Valor de la monitorización inmunológica en el manejo de la infección por citomegalovirus en pacientes trasplantados	-
EM	14-20	-	-
NOVEMBER	21-27	-	Date: 24/11/2016 Speaker: Ángel Nadal Navajas Institution: Universidad Miguel Hernández Title: Regulación de la célula beta por disrupto- res endocrinos y riesgo de diabetes
	28- 4Dec	-	-
	5-11	-	-
~	12-18	-	-
DECEMBER	19-25	_	Date: 20/12/2016 Speaker: Dimitrios P. Mikhailidis Institution: University College London, Depart- ment of Clinical Biochemistry Title: How to write a scientific paper.
	26-1Jan	-	-



# 7<sup>th</sup> IMIBIC YOUNG INVESTIGATORS MEE

## PROGRAMME

9:00-9:30 Opening Ceremony. Registration and Poster display

9:30-10:45 SESSION I. Cancer (Oncology and Oncohema-

La 9:30-9:45 Endothelial nitric oxide synthase in colorectal cancer: a potential new therapeutic target in stem cell-like poor-prognosis subtype. **Jon Peñarando Sáez** 

I.b 9:45-10:00 Potential therapeutic treatment of Biguanides (Met-formin buformin and phenformin) for pituitary adepo-

mas. Mª Carmen Vázquez Borrego

Lc 10:00-10:15 Key proteins regulation of the DNA Damage Response Pathway CHK2 and CDC25A in the context of car cinogenesis. **Maribel Lara Chica** 

I.d 10:15-10:30 HIPECT4. Multicentric randomized controlled trial about the influence of HIPEC in localy advanced color-

I.e 10:30-10:45 Protein expression of FGFR3, PI3K, AKT, p21Waf1/ Cip1 and Cyclin D1 and D3 in patients with T1 bladder

11:15-12:45 SESSION II. Chronic and Inflammatory Diseases Chairs: Dr. Elena Yubero, Dr. Juan Muñoz

comt-4: a crosspoint between dopamine pathways. Ángel Rodríguez Ramos

II.b 11:30-11:45 Potential impact of in vivo Ubiquinol supplementation in the prevention of atherothrombosis in Antiphospho-lipid Syndrome Patients. Preliminary results of a clinical trial. **Iván Arias de la Rosa** 

II.c 11:45-12:00 Assessment of Fatigue in Spondyloarthritis and Its Association with Disease Activity. Clementina López-Me-

II.d 12:00-12:15 Measuring anxiety regulation strategies: development and preliminary validation of an instrument. Rosario Castillo Mayén

II.e 12:15-12:30 TNFalpha-Damaged-HUVECs Microparticles modify Endothelial Progenitor Cell functional activity. **Carlos** 

II.f 12:30-12:45 AP-1 inhibition by SR11302 protects human hepatoma HEPG2 cells form bile acids inducded apoptosis by restoring the NOS-3 expression. Sandra González

13:00-14:00 Plenary Lecture. Dr. Sergi Castellví-Bel (IDIBAPS, Barcelona)

16:00-17:00 SESSION III. Infectious and Immunological Diseases. Organ Transplantation. Chairs: Dr. Juan Francisco Alcalá, Dr. Antonio Romero

III.a 16:00-16:15 Impact of colistin therapy on mortality of multidrug-re-sistant and colistin-sensitive acinetobacter baumannii bacteremia in critically ill patients. **Tania Amat Serna** 

III.b 16:15-16:30 Hepatitis E infection in wild boar as a potential route of transmission to humans: Results of the HepEboar Study. Salvador Barea Chacón

III.c 16:30-16:45 Risk of tuberculosis after lung transplantation: the val-

III.d 16:45-17:00 Effect of hypoxic preconditioning on mesenchymal stem cells functionality of patients with chronic limb

ischemia. Luis Miguel Paco Meza

Emilio Guirao Arrabal

17:00-17:30 Poster Showcas

IMIBIC

ue of pretransplant chest computed tomography and the impact of mTOR inhibitors and azathioprine use.

Luna Ruiz

Rubio

15:30-16:00 Poster Showcase

14:00-15:30 Lunch

Álvaro Sánchez González

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

II.a 11:15-11:30 Neuroligin deficient mutants of C. elegans of

rectal cancer in abscense of carcinomatosis. A protocol study. Rubén García Martín

er: clinical implications and prognostic significance.

e and serotonin

tology) Chairs: Dr. Julián de la Torre, Dr. Juan Roa

## IMIBIC BUILDING • CONFERENCE ROOM • CÓRDOBA, 10-11 MAY, 2016

#### Day 1 (10th May)

- 17:30-19:00 SESSION IV. Nutrition, Endocrine and Metabolic D Chairs: Dr. Nuria Barbarroja, Dr. Manuel D. Gahete
- IV.a 17:30-17:45 Rab34 is a novel regulator of lipid accumulation in adipocytes. Andrés Trávez García
- IV.b 17:45-18:00 Magnesium supplementation improves outcomes but impairs bone mineralization in a rat model of Chronic Kidney Disease-Vascular Calcification. Juan Miguel Díaz Tocados
- IV.c 18:00-18:15 Regulation of endothelial function is modified by two healthy diets in patients with established cardiovascular disease. **José David Torres Peña**
- IV.d 18:15-18:30 Identification of a novel kisspeptin pathway in glial cells: A new contributing circuit for kisspeptin-driven control of puberty?. Encarnación Torres Jiménez
- IVe 18:30-18:45 Does the conten of dietary calcium modifies the urinary excretion of phosphate?. Maria Dolores Salmerón Rodríguez
- IV.f 18:45-19:00 Adipokines directly modulate the function of different pituitary cell types in primates (Papio anubis and Macaca fascic ularis) through common and distinct lar signaling pathways. André Sarmento Cabral

#### Day 2 (11th May)

- 9:00-10:30 SESSION V. Nutrition, Endocrine and Metabolic Di Chairs: Dr. M. Teresa Roldán, Dr. Mercedes Gil
- V.a 9:00-9:15 Chronic consumption of a healthy diet improves post-prandial lipemia response and insulin resistance in dia-betic patients from the CORDIOPREV study. **Beatriz** betic patients fro Gómez Marín
- V.b 9:15-9:30 Changes in the splicing machinery as a tool to predict the development of type-2 diabetes in high-risk pa-tients. Mercedes del Río Moreno
- V.c 9:30-9:45 Relationship between intake and urinary phosphate ex-cretion in patients with chronic kidney disease (CKD). M\* Victoria Pendón
- V.d 9:45-10:00 Factors influencing telomere length and cardiovascular disease. From the CordioPrev Study. **Cristina Hidal-**go Moyano
- V.e 10:00-10:15 Changes in gut microbiota according to the progression of metabolic syndrome. Sonia García-Carpintero Fernández- Pacheco
- V.f 10:15-10:30 Hypothalamic GRK2, via GPR54, modulates puberty onset. Marisol Avendaño Herrador
- 10:30-11:00 Coffee Break

11:00-11:30 Poster Showcase

- 11:30-13:00 SESSION VI. Cancer (Oncology and Oncohe-matology). Active Ageing and Fragility. Chairs: Dr. Rafael Vázquez, Dr. José Antonio Bárcena
- VI.a 11:30-11:45 Differential sensitivity of prostate cancer cells to galiel-lalactone. A proteomic approach. Victor García González
- VI.b 11:45-12:00 Functional role of somatostatin receptor subtype 1 (sst1) in prostate cancer: an in vitro approach. Sergio Pedraza Arévalo
- VI.c 12:00-12:15 Recent advances in human sweat metabolomics for lung cancer screening. Mónica Calderón Santiago
- VI.d 12:15-12:30 Assessment of RIFLE and AKIN criteria to define acute renal dysfunction for HIPEC procedures for and non ovarian peritoneal malignances. Juan Manuel Cabrera Bermón
- VI.e 12:30-12:45 The truncated somatostatin receptor, sst5TMD4, is expressed in prostate cancer, malignant features by altering key signaling pathway suppressors/oncogenes. Juan Manuel tumo liménez Vacas
- VI.f 12:45-13:00 Age related pharamethers can be improved by a medranean diet supplemented in hydroxytyrosol. Andreea Corina Baba

13:00-13:30 Awards and Closing Ceremony

## 6.2.3.3. Institutional Events

## 7<sup>th</sup> IMIBIC Conference of Young **Researchers**

The IMIBIC Young Investigator Meetings is intended to provide the ideal environment to strengthen the skills and knowledge of young scientists, fostering translational research by facilitating the interface between experimental basic science and clinical medicine to improve health and the quality of life. By sharing the results obtained by young researchers at the IMIBIC and related centers, such as other groups of the University of Cordoba, we intend to encourage inter-disciplinarity and, especially, quality training.

The objectives of the Meetings are:

- To provide a platform to discuss the latest knowledge and methods in translational medical research.
- To promote interactions and the exchange of ideas between pre- and post-doctoral scientists and strengthen the bonds among research groups.
- To facilitate interdisciplinary actions and communication to bring together basic and clinical research.
- To foster and provide high-quality scientific training to young researchers.
- To consolidate the annual IMIBIC Meetings as a youthful and fresh reference forum for the research community and, in particular, for our young researchers.

The 7th Meeting took place at the IMIB-IC Building, 10-11 May, 2016. The Meeting program included different sessions encompassing the IMIBIC Scientific Programs, as follows:



## 6<sup>th</sup> Maimonides Commemorative Lecture and IMIBIC awards 2016

The aim of this initiative is to recognize the biomedical research carried out by IMIBIC staff and to emphasize the importance of the work carried out at the Institute. Additionally, in each edition, a professional of recognized international prestige in the field of biomedicine is invited to give the so-called "Maimónides Lecture", a conference focusing on the latest knowledge on biomedical subjects of special interest in which the lecturer is an expert.

This year, the guest was Dr. Antonio Vidal Puig, PhD in Medicine and Professor of Molecular Nutrition and Metabolism at the University of Cambridge and Honorary Consultant in Metabolic Medicine at Addenbrooke Hospital, Cambridge. Dr. Vidal is a Senior Research Fellow at the BHF Cambridge Cardiovascular Centre for Research Excellence at the University of Cambridge. Dr. Vidal has developed his career at Harvard University and, since 2000, at the University of Cambridge. His works have contributed fundamentally to our current knowledge on obesity and the development of associated metabolic diseases, which has been recognized through different distinctions, such as the Distinguished Career Award in the field of Endocrinology, Nutrition and Obesity, granted by The Lilly Foundation at its 2015 Biomedical Research Awards. Dr. Vidal has also contributed to the training of numerous young researchers, including some members of IMIBIC, receiving them at his laboratory in Cambridge during their research placements.

In addition to the IMIBIC awards conference, the winning studies participating this



year for each of the IMIBIC awards, including the "Enrique Aguilar Benítez de Lugo" Prize for the most relevant scientific publication in collaboration with international groups, the Award for the best master's degree thesis, and the Awards for the most relevant translational research results, were given. Another prize was awarded for the journalistic news report most valu-able to IMIBIC.

In addition to the aforementioned prizes, a special prize was awarded to the Reina Sofía University Hospital in Córdoba, for its contribution to the advancement of biomedical and health research, commemorating the 40th anniversary of its creation.

# 6.3. Results of Training Activities

# 6.3.1. Doctoral Theses

The Institute offers the PhD Program in Biomedicine, which helps prepare young scientists in biomedical and clinical research. Experienced mentors in the IMIBIC supervise the research training in health and health-related areas of a considerable number of predoctoral students. In total 27 researchers of IMIBIC completed their Doctoral Thesis during 2016. Of those 16 were PhD in Biomedicine supervised by senior researchers from the Institute, and 11 in other PhD programs of the University of Cordoba.

## **PhD Program in Biomedicine**

Author	Title	Supervisor(s)	
Alonso García, Pedro Enrique	Implicación de los alcaloides de las solanáceas co- mestibles en la etiopatogenia del prurito cicatricial	Rodriguez Portillo, Juan Mariano	
Baeza Garzón, Mª Flor	Seguimiento a largo plazo de pacientes con miocar- diopatía dilatada idiopática tras infusión intracoronaria de células de médula ósea	Romero Moreno, Miguel Angel	Suarez de Lezo Cruz-Conde, Jose
Calvo Rodríguez, Rafael	Estado de los marcadores tumorales en el cáncer de colon obstructivo: papel de las prótesis autoexpansibles.	Gallardo Valverde, José María	
Castro Villegas, María del Carmen	Cambios en la expresión de los niveles de micrornas en suero de pacientes con artritis reumatoide en res- puesta al tratamiento con la terapia bloqueadora del factor de necrosis tumoral alfa	Collantes Estevez, Eduardo	López Pedrera, Rosario
Delgado Domínguez, Carlos Jesús	Bases temperamentales del sentido del humor y acti- vidad de la enfermedad en pacientes con espondilitis anquilosante y artritis reumatoide	Collantes Estevez, Eduardo	Carretero Dios, Hugo
Haro Mariscal, Carmen María*	The dysbiosis of the bacterial population of the di- gestive system (intestinal microbiota) in patients with metabolic syndrome improves after two models of healthy diets: a diet rich in complex carbohydrates and a mediterranean diet. CORDIOPREV study	Perez Jimenez, Francisco	Camargo García, Antonio
Khraiwesh , Husam Mohammad*	Adaptación metabólica y estructural de tejidos mitóti- cos y postmitóticos a condiciones de restricción caló- rica en el ratón. Efecto del tipo de grasa en la dieta	Gonzalez Reyes, Jose Antonio	Villalba Montoro, Jose Manuel
Martínez-Dueñas López-Marín, Loreto	Prevalencia del virus de la hepattis e en pacientes infectados por vih	Rivero Román, Antonio	Antonio Rivero Juárez
Moreno Fernández, Jesús	Utilidad clínica de la introducción precoz de la monito- rización continua de glucosa en tiempo real combina- da con infusión subcutánea continua de insulina en el tratamiento de pacientes con diabetes mellitus tipo 1	Galvez Moreno, Maria Angeles	Castaño Fuentes, Justo Pastor
Rincón Fernández Pa- checo, David*	Papel y regulación de las nuevas variantes de splicing hsst5tmd4 y In1-ghrelina en cáncer de mama.	Castaño Fuentes, Justo Pastor	Gahete Ortiz, Manuel David
Romero Saldaña, Ma- nuel	Nuevas variables predictoras en la incidencia de sín- drome metabólico y diabetes mellitus tipo 2. Estudio longitudinal en población trabajadora	Vaquero Abellan, Manuel	Fuentes Jiménez, Francisco José
Ruiz González, María Dolores	Alteraciones proteómicas en suero de recién nacidos con retraso del crecimiento intrauterino.	Cañete Estrada, Ramon	
Ruíz Limón, Patricia*	Análisis de los mecanismos celulares y moleculares reguladores del efecto de la Fluvastatina y nuevos fármacos antioxidantes en la prevención de la trom- bosis y la aterotrombosis asociadas al Síndrome Anti- fosfolípido y al Lupus Eritematoso Sistémico. Estudio Genómico y Proteómico.	López Pedrera, Rosario	Barbarroja, Nuria
Salido Vallejo, Rafael	Sirolimus tópico en el tratamiento de angiofibromas faciales asociadas a esclerosis tuberosa	Velez Garcia-Nie- to, Antonio Jose	
Valverde Estepa, Araceli María	Inhibición combinada del receptor del factor de creci- miento epidérmico y de la ciclooxigenasa-2 en cáncer colorrectal: mecanismos celulares y moleculares e implicaciones terapéuticas	Rodriguez Ariza, Antonio	



Author	Title	Supervisor(s)	
Villa Osaba, Alicia	Papel fisiológico e implicaciones fisiopatológicas y te- rapéuticas de los sistemas somatostatina, cortistatina y sus receptores en el cáncer de mama y obesidad	Castaño Fuentes, Justo Pastor	Luque Huertas, Raúl Miguel

\*Theses with International Mention

## **Other PhD Programs**

Author	Title	Supervisor(s)	
Aguilera Aguilera, Eu- sebio Jesus     Contribuciones sobre métodos óptimos y subóptimos de aproximaciones poligonales de curvas 2-d.		Angel Carmona Poyato	Francisco Madrid Cuevas
Garrido Jurado, Sergio	Contribuciones a la estimación de la pose de cámara y reconstrucción tridimensional	Rafael Muñoz Salinas	
Guerrero Alonso, Maria Soledad	Control múltiple en discriminaciones simples y condi- cionales: aplicaciones para la enseñanza y estudio procedimental	Francisco Alós Cívico	Juan Antonio Mo- riana Elvira
López Fernández, Da- vid	Contribución a la estimación de posturas usando múl- tiples vistas	Francisco Madrid Cuevas	Angel Carmona Poyato
López Quintero, Manu- el Ignacio	Estimación de la pose humana 2D en imágenes es- téreo	Manuel Jesus Marin Jimenez	Rafael Muñoz Salinas
Mondejar Guerra, Vic- tor Manuel	Contribuciones a la estimación de pose de Cámara	Rafael Muñoz Salinas	Rafael Medina Carnicer
Moreno Osella, Eliana María	El abordaje de problemas psicológicos y de salud mental en sistemas públicos de salud: hacia la imple- mentación de estrategias y tratamientos basados en la evidencia	Juan Antonio Mo- riana Elvira	
Parrilla Doblas, Jara Teresa	DNA demethylation through 5-methylcytosine exci- sion. Molecular basis and potential applications	Mª Teresa Roldan Arjona	Rafael Rodriguez Ariza
Peralbo Molina, Ángela	Avances en metabolómica basados en la preparación de muestra y en plataformas analiticas de cromato- grafía y espectrometría de masas	Feliciano Priego Capote	Mª Dolores Luque de Castro
Ramiro Merina, Ángel	Análisis molecular y funcional de la proteína MBD4 de Arabidopsis thaliana	Mª Teresa Roldan Arjona	Rafael Rodriguez Ariza
Villanueba Fernández, Elena	Técnica de la guía encarcelada en el tratamiento percutáneo de las bifurcaciones coronarias tratadas con stents: estudio aleatorizado con microcopía es- tereoscópica	Manuel Pan Álva- rez-Ossorio	Manuel Suárez de Lezo Cruz-Conde

# 6.4 Research Stays

IMIBIC is committed to foster training of our PhD students in national and international centers of reference in biomedical research in order to allow the opportunity to experience research in a foreign environment, facilitate the integration of graduates into the scientific community and create networks. Seventeen researchers from the IMIBIC completed a research stay in national or international centers in 2016. Likewise, external visitors are invited to carry out their research in our Institute. Specifically, the number of professional from other national and international centers that stay at IMIBIC is 18.

	Type of Internship	Public Scheme	Private Scheme	Internal Scheme
STAYS	Researchers	5	2	10
	Duration (months)	53 months		
VISITORS	Researchers	18		
	Duration (months)	41 months		

# Biomedical Research Support Units

# 7. Biomedical Research Support Units

In 2016 the new Strategic Plan of The Maimonides Institute of Biomedical Research of Córdoba (IMIBIC) 2016-2020 was approved, coinciding in turn with IMIBIC's re-accreditation as a Health Research Institute by the Carlos III Health Institute. This has logically led to the renewal of the Infrastructure Plan which forms part of the Strategic Plan. In con-trast to the objectives set in the previous Plan covering the period 2011-2015, which envisaged the creation of different Central Biomedical Research Support Units ("Unidades Centrales de Apoyo a la Investigación Biomédica" - UCAIBs - in Spanish), the new Plan foresees the development and consolidation of the existing units.

At the date of presentation of IMIBIC's scientific report, the UCAIBs (Central Biomedical Research Support Units) were configured as follows:

- 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

The UCAIBs have been assigned different goals in the New Infrastructure Plan, relating to both scientific research and for budgetary balance purposes, for example. These UCAIBs receive institutional support to enable them to carry out their activities in support of the Institute's research groups, as well as for the development of new techniques related to the area of experience of each unit and even for the performance of different training activities aimed at IMIBIC researchers and for the development of technical staff.

# 1. Isotope Unit

## **1.1. Composition**

The Isotope Unit personnel is composed of:

Supervisor: Eduardo Muñoz Blanco PhD fi1muble@uco.es

Operator: Antonia Sánchez Arroyo

antonia.sanchez@imibic.org

# **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

# 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.

# 1.4. Highlights

During 2016, the main milestone achieved by this unit was the implementation of state-of-the-art ultrasound equip-ment for use **of** the development of clinical research projects through the combination of resonance and ultrasound images, which undoubtedly represents a breakthrough in diagnostic imaging-related research.

# 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.



# 2.1. Composition

The Animal Experimentation Unit personnel is composed of:

Director of SAEX Ana M<sup>a</sup> Molina López

and two technicians and a veterinarian:

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

# 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.

# 2.3. Highlights

In 2016, many different pieces of equipment were acquired, installed and put into use. Accordingly, the technicians have taken training courses with the aim of opening the animal services. In addition, the multi-purpose rooms have been renovated in order to optimize these spaces.

# 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 mi-croscopy (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 **gives** services **to** both the research staff of the Institute and other entities of the SSPA, the University, IPOs, as well as private companies that request it.

# 3.1. Composition

The Unit is composed of a superior specialized technician:

## Esther Peralbo Santaella, PhD

microscopia.citometria@imibic.org

# 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 **being** 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 Microscoptic Optics

- 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).

# **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 .

# 3.4. Highlights

In 2016, the Unit provided services to 15 research groups of IMIBIC such as, "Nephrology", "Cell biology in hematology. Hypercoagulability", "Systemic and chronic inflammatory autoimmune diseases of the locomotor system and connective", "Nutrigenomics", etc.

Articles published in 2016 with IMIBIC's groups:

- Ruiz-Limón P, Ortega R, Arias de la Rosa I, Abalos-Aguilera MD, Perez-Sanchez C, Jimenez-Gomez Y, Peralbo-Santaella E, Font P, Ruiz-Vilches D, Ferrin G, Collantes-Estevez E, Escudero-Contreras A, López-Pedrera C, Barbarroja N. Tocilizumab improves the proatherothrombotic profile of rheumatoid arthritis patients modulating endothelial dysfunction, NETosis, and inflammation. Transl Res. 2016 Dec 9. pii: S1931-5244(16)30423-6.
- Martinez-Moreno JM, Herencia C, Montes de Oca A, Muñoz-Castañeda JR, Rodríguez-Ortiz ME, Díaz-Tocados JM, Peralbo-Santaella E, Camargo A, Canalejo A, Rodriguez M, Velasco-Gimena F, Almaden Y. Vitamin D modulates tissue factor and protease-activated receptor 2 expression in vascular smooth muscle cells. FASEB J. 2016 Mar; 30(3):1367-76.

# 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.

# 4.1. Composition

The Unit is composed of two specialized technicians:

- Ignacio Ortea García, PhD ignacio.ortea@imibic.org
- Eduardo Chicano Gálvez, PhD eduardo.chicano@imibic.org

and two assistant technicians:

- Rocío Pérez
- Josune Egea (till October 2016) / Natalia Fernández (from October 2016)

# 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 XITandem 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.

# 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.

# 4.4.Highlights

During 2016, the Proteomics Unit increased its activities in quantitative proteomics and MALDI-Imaging (MSI) providing services to scientific community. These services **range** from sample preparation to project supervision, collaborations and training in software for data analysis.

Moreover, the Proteomics Unit has published two scientific articles, presented six studies at international/national congresses, and has participated in two international interlaboratory proficiency studies.

Articles published in 2016 with IMIBIC's groups:

- Ortea, I., Rodríguez-Ariza, A., Chicano-Gálvez, E., Arenas Vacas, M.S., Jurado Gámez, B. Discovery of potential protein biomarkers of lung adenocarcinoma in bronchoalveolar lavage fluid by SWATH MS data-independent acquisition and targeted data extraction. Journal of Proteomics 2016, 138, 106-114.
- Ortea I, Rodríguez-Ariza A, Chicano-Gálvez E, Arenas Vacas MS, Jurado Gámez B. Discovery of potential protein biomarkers of lung adenocarcinoma in bronchoalveolar lavage fluid by SWATH MS data-independent acquisition and targeted data extraction. Rev. Esp. Patol. Torac. 2016, 2(3), 164-170.

Articles published in 2016 with external groups:

- Ortea, I; O'Connor, G; Maquet, A. Review on proteomics for food authentication. Journal Of Proteomics.2016. 138:106-14
- Ortea I, Roschitzki B, López-Rodríguez R, Tomero EG, Ovalles JG, López-Longo J, et al. Independent Candidate Serum Protein Biomarkers of Response to Adalimumab and to Infliximab in Rheumatoid Arthritis: An Exploratory Study.2016. PLoS ONE 11(4): e0153140.
- Prado, M, Ortea, I, Vial, S, Rivas, J, Calo-Mata, P, Barros-Velazquez, J. Advanced DNA- and Protein-based Methods for the Detection and Investigation of Food Allergens. Critical Reviews In Food Science And Nutrition.2016. 147:212-225

# **5. Bioinformatics Unit**

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

Bioinformatics 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

## **Objectives of the Bioinformatics Unit**

-The mission of the Unit is to satisfy the Bioinformatic requirements that result from research projects.

-Clear and direct communication with the researchers facilitates this 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.

# 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 the public and private spheres. 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 peak performance platforms in the field of genomics. It is also important to note the use of interaction with other UCAIB IMIBIC Units, which are located in the same building, such as bioinformatics, proteomics or Cytometry.

# 6.1. Composition

The Unit is composed of a superior specialized technician, coordinator of this Core Facility, and a laboratory technician.

Álvaro Jiménez Arranz (superior specialized technician) genomica@imibic.org / alvaro.jimenez@imibic.org Pilar Rubín González de Canales (laboratory technician) Email: pilar.rubin@imibic.org

# **6.2. Equipment and Facilities**

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

## 6.2.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/run 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, Methyl-Seq and ChIP-Seq, with a wide range of applications.

# 6.2.b. NCounter Dx/tecnología Nanostring

The NanoString NCounter system uses a novel technique of molecular barcodes 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 RNAs regulators as miRNAs or lncRNAs.

These applications, along with Dx / CE-IVD for conducting analysis care quality certificate, also make the NCounter a tool with high potential for clinical use. Currently there is already on the market a CE marked test for in vitro diagnostics (CE-IVD) which has approved by the FDA for breast cancer (Prosigna-PAM50), based on the molecular analysis of gene expression of 50 genes. This allows it to classify the tumor into one of 4 intrinsic subtypes, related to disease prognosis and choice of treatment. In addition, it is currently in the process of launching another validated kit for in vitro diagnostics (CE-IVD / FDA), based on the pattern of differential expression of 20 genes, aimed at determining subtypes LDBG (diffuse lymphoma of large B cells), related disease treatment.

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

The digital PCR offers a more precise and sensitive alternative to conventional qPCR for absolute quantitation and detection of rare alleles without the need for standards or endogenous controls thanks to droplet partitioning.

## 6.2.d. Quantitative PCR (qPCR)

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

- Light Cycler 480 (96-well platform)
- Light Cycler 96 (96-well platform)
- 7900 HT Fast (384-well platform)

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).

## 6.2.e. Others:

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

- Nanodrop ND1000 (Spectrophotometer)
- DeNovix DS-11 (Spectrophotometer)
- Quantus (Fluorometer)
- 2200 TapeStation (Microelectrophoresis)

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

# 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 by Nanostring technology
- PAM50-signature Analysis (Prosigna<sup>™</sup>) for Breast Cancer Prognosis
- miRNAs analysis in tissue, peripheral blood cells and serum/plasma by Nanostring Technology
- Gene expression and genotyping studies using real-time PCR
- Technical and scientific support in the use of qPCR platforms and probes design
- Absolute quantification by Droplet Digital PCR System (viral load analysis...)
- NGS library preparation

- Sequencing NGS (Next Generation Sequencing) by Illumina Miseq
- Training and support in the use of data analysis software related to the Unit's technology

## 6.4. Highlights

In 2016, a new pre-PCR room was designed and built. The Unit has improved the protocols and services started last year, has initiated new services indicated in this report and was validated for analysis of PAM50-signature (Prosigna™) for Breast Cancer Prognosis.

# 7. Clinical Research Unit

The IMIBIC Clinical Research Unit is located within the IMIBIC research support platforms. Its purpose is to promote clinical research at IMIBIC (Instituto Maimónides de Investigación Biomédica de Córdoba) and at Hospital Universitario Reina Sofía as well as to establish collaborations with other research centers. Currently, IMIBIC is part of the Spanish Clinical Research Network (SCReN).

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: the Provincial Hospital Clinical Research Unit and the General Hospital Clinical Research Unit. Both are adapted to perform clinical trials of phases I-IV in patients.

# 7.1. Composition

Unit Head Dr. Jose López Miranda jlopezmir@uco.es

## **Clinical Pharmacologist**

María Esther Pacheco Rodriguez, MD 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

Manuel Rejano Castañeda manuel.rejano.sspa@juntadeandalucia.es Pilar Mesa Blanco pilar.mesa@imibic.org Araceli Chicano Gálvez araceli.chicano@imibic.org

## **Nursing Assistants**

Rubén Sánchez Nieves Rafaela Vacas Bueno

## **Administrative Staff**

María Dolores Castro Ortiz



# 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
- 2 Waiting 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

# 7.3. Portfolio of Services

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

# 7.4. Highlights

During 2016, the Unit provided assistance and support in the start-up, coordination, data management or monitoring of 24 independent clinical research projects in the following Units, among others, Internal Medicine, Pediatrics, General Surgery, Nephrology and Rheumatology, Infectious diseases. Additionally, research activity has been increasing to 898 patients treated at the facilities of the Clinical Research Unit. 78 clinical research projects have been carried out. The main areas that have developed their activity in the unit are Oncology, Internal Medicine, Nephrology, Infectious Diseases, Dermatology and Urology.

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

To promote clinical research, the Unit has organized working meetings with health professionals in different areas: Neurosurgery, Intensive Care, Allergology, Otorhinolaryngology, Endocrinology, Pediatrics, Hematology, Neurology, Pulmonology. The research lines of the main pharmaceutical companies and the capacity of participation of these units have been evaluated. Meetings have been organized with the medical departments of the pharmaceutical companies.

# 8. Biobank Unit

The Biobank Unit of Maimonides Institute for Biomedical Research of Cordoba (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 Andalusia Public Health System (SSPA) Initiative of the Department of Equality, Health and Social Policy. It is part of the Biobank Network Theme Hospital (National Biobank Network) Initiative Carlos III Health Institute (ISCIII), which is itself within the subprogram Thematic Networks for Cooperative Research in Health (RETICS).

# 8.1. Composition of Biobank Unit

## -Unit's Scientific Management

Manuel Medina Pérez, PhD

manuel.medina.sspa@juntadeandalucia.es

## -Individual in charge of coordination

Carmen Pérez Calle

carmen.perez.calle.exts@juntadeandalucia.es

-Technician: Javier Herruzo

javier.herruzo@imibic.org

# 8.2. Biobank Unit Equipment

The Unit possesses its own laboratory resources for use of sample transformations (Safety booths, PCR Booths, Microtomes, Chryostate, Flotation Bath, Centrifuge, Histobath, Automatized Processor for Paraffin Inclusion, Paraffin Dispenser, etc.) as well as other machinery such as:

-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 two freezers: one for temperatures of -20 degrees Celsius, seven for -80 degrees Celsius, as well as paraffin storage rooms for room temperature.

# 8.3. Biobank Unit Service Portfolio

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, selecte daccording 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.

# 8.4. Highlights

In 2016, the Biobank Unit experienced an increase in its activity in comparison to previous years, having given essential support to 63 research projects. This activity generated a total of 20 390 samples/ bioresources, of which around 6515 were awarded to different researchers. The degree of satisfaction of these users has been assessed via surveys to be 9.2 points (out of a possible 10).

# 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 to:

- Offering methodological consulting in the beginning or development of the studies of research in the phases prior to the presentation of proposals/reports to the relevant financial entities and in general throughout the projects' life cycles.
- 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

# 9.1. Composition

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

# 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.)

# 9.3. Portfolio of Services

Through personalized consultations (face to face meetings, telematic or virtual) we cover the different **stages** of the research process. Specifically, the aid that they request may be:

- 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...).

# 9.4. Highlights

In 2016, 107 activities were carried out, most of which (about 60%) were related to consultancy and statistical analysis for the dissemination of research results (publications and conferences, doctoral theses, master's dissertations). Three training activities were also carried out to update the statistical and epidemiological knowledge

Articles published in 2016 with IMIBIC's groups:

- Beltran-Aroca CM, Girela-Lopez E, Collazo-Chao E, Montero-Perez-Barquero M, Munoz-Villanueva MC. Confidentiality breaches in clinical practice: what happens in hospitals?. BMC medical ethics.2016. 17(1):52-52.





# Scientific Production

# **GC1 • Immunology and Allergy**

# HIGHLIGHTS



## **Team Leader**

## Principal Investigator (PI) Rafael Solana Lara

rsolana@uco.es

Spanish Network for Research into Infectious Pathologies (REIPI) (Collaborator) Spanish Network for asthma, adverse reactions and allergic (ARADYAL) (PI: Carmen Moreno Aguilar) PAIDI CTS 208 Scientific Group (Collaborator)

## Researchers

Alonso Diaz; Corona Barasona Villarejo; Mª José González Fernández; Rafael Jurado Roger; Aurora Moreno Aguilar; Carmen Saiz Sánchez; Vanessa Serrano Delgado; María del Pilar

## **Post-Doctoral Researchers**

Campos Fernández; Carmen Castro Orgaz; Laura Manzanares Martin; Barbara Pera Rojas; Alejandra (Collaborator) Ruiz León; Berta

# Pre-Doctoral Researchers (PhD Students y MSc Students)

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

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

Velarde Martínez; Mª Luisa Fisichella; Marco Guerra González; Mercedes

## **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

Cantisan S, Paez-Vega A, Perez-Romero P, Montejo M, Cordero E, Gracia-Ahufinger I, Martin-Gandul C, Maruri N, Aguado R, Solana R\*, Torre-Cisneros J\*. Spanish Network for Research in Infectious Diseases (REIPI). Prevention strategies differentially modulate the impact of cytomegalovirus replication on CD8(+) T-cell differentiation in high-risk solid organ transplant patients..Antiviral Research.2016.132:244-51. IF:4,909

Q:1 D1

Pita-Lopez ML, Pera A, Solana R.Adaptive Memory of Human NK-like CD8(+) T-Cells to Aging, and Viral and Tumor Antigens.Frontiers In Immunology.2016.(7):-616. IF:5,695 Q:1

Lopez-Sejas N, Campos C, Hassouneh F, Sanchez-Correa B, Tarazona R, Pera A, Solana R.Effect of CMV and Aging on the Differential Expression of CD300a, Cd161, T-bet, and Eomes on NK Cell Subsets.Frontiers In Immunology.2016.7:476. IF:5,695

Q:1

Morales-Estevez C, De la Haba-Rodriguez J, Manzanares-Martin B, Porras-Quintela I, Rodriguez-Ariza A, Moreno-Vega A, Ortiz-Morales MJ, Gomez-Espana MA, Cano-Osuna MT, Lopez-Gonzalez J, Chia-Delgado B, Gonzalez-Fernandez R, Aranda-Aguilar E.KIR Genes and Their Ligands Predict the Response to Anti-EGFR Monoclonal Antibodies in Solid Tumors.Frontiers in Immunology.2016.7:561. IF:5,695 Q:1

Tarazona R, Duran E, Solana R.Natural Killer Cell Recognition of Melanoma: New Clues for a More effective immunotherapy.Frontiers In Immunology.2016.6:649. IF:5,695

Q:1

Solana R, Tarazona R.Challenges of vaccination in older people. Can we circumvent immunosenescence?.Maturitas.2016.90:1-2. IF:3,12

Q:2

Hassouneh F, Campos C, Lopez-Sejas N, Alonso C, Tarazona R, Solana R, Pera A.Effect of age and latent CMV infection on CD8+CD56+ T cells (NKT-like) frequency and functionality..Mechanisms Of Ageing And Development.2016.158:38-45. IF:2,892 Q:3

Penuelas E, Serrano P, Barasona MJ, Saiz V, Fernandez L, Moreno C.Sensitization to Minor Allergens Has a Direct Influence on the Outcome of Subcutaneous Immunotherapy in Olive-Allergic Patients.Journal Of Investigational Allergology And Clinical Immunology.2016.26(3):202-204. IF:2,131

Q:3

Ruiz B, Serrano P, Moreno C.IgE-Api m 4 Is Useful for Identifying a Particular Phenotype of Bee Venom Allergy.J Investig Allergol Clin Immunol.2016.26(6):355-361. IF 2,131 Q:3

## **In Collaboration**

Borrego F, Larrucea S, Solana R, Tarazona R.Editorial: NK Cell-Based Cancer immunotherapy.Frontiers In Immunology.2016.7:249. IF:5,695 Q:1

Sanchez-Correa B, Campos C, Pera A, Bergua JM, Arcos MJ, Banas H, Casado JG, Morgado S, Duran E, Solana R, Tarazona R.Natural killer cell immunosenescence in acute myeloid leukaemia patients: new targets for immuno-therapeutic strategies?.Cancer Immunology Immunotherapy.2016.65(4):453-463. IF:4,846 Q:1

Nunez IG, Marmol MAA, Villarejo MJB, Vergara MS, Gonzalez FE, Ariza ER.Kounis Syndrome After Levofloxacin Intake: A Clinical Report and Cross-reactivity Study.Journal Of Investigational Allergology And Clinical Immunology.2016.26(5):335-336. IF:2,131

Q:3

Planelles D, Vilches C, Gonzalez-Escribano F, Muro M, Gonzalez-Fernandez R, Sanchez F, Ocejo JG, Eiras A, Caro JL, Palou E, Campillo JA, de Juan MD, Montes O, Balas A, Marin L, Torio A, Fernandez-Arquero M, Gonzalez-Roiz C, Lopez-Vazquezr A, Cisneros E, Abad-Molina C, Lopez R, Abad-Alastruey ML, Serra C, Garcia-Alonso AM, Vicario JL.Report From the First and Second Spanish Killer Immunoglobulin-Like Receptor Genotyping Workshops: External Quality Control for Natural Killer Alloreactive Donor Selection in Haploidentical Stem Cell Transplantation.Transplantation Proceedings.2016.48:3043-3045. IF:0,867 Q:4

## **Research Funding**

## National

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: PI15/02170

Moreno C. Anaphylaxis by insect bites. Search for biomarkers of early response to immunotherapy with Hymenoptera venom. Funding agency: Society Andalusian of Allergology and Clinical Immunology. Reference: Alergosur16

Moreno C. Anaphylaxis by insect bites. Search for biomarkers of early response to immunotherapy with Hymenoptera venom. Funding agency: Society Andalusian of Allergology and Clinical Immunology. Reference: SEAIC\_15

Solana R. Relevance of immunosenescence in the design of new NK cell-based immunotherapy protocols in melanoma and acute myeloid leukaemia models. Funding agency: Institute of Health Carlos III (ISCIII). Reference: PI16/01615

Expected starting date:during 2017

Moreno C. Spanish Network for asthma, adverse reactions and allergic (ARADYAL). Funding agency: Institute of Health Carlos III (ISCIII). Reference:RD16/0006/0018 Expected starting date:during 2017

### Regional

Ruiz León, M. Role of Microbioma by lipid transfer proteins in allergic disease. Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference:-PI-0119-2016

Expected starting date:during 2017

### 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

Solana Lara R. Agreement with Spanish Cancer Association.Funging Agency: Spanish Cancer Association. Reference:CCB.0104

Moreno C. Agreement with Novartis.Funging Agency: Novartis Farmaceutica, S.A. PSS.0117

Moreno C. Agreement with Alk-Abello. Funging Agency: Alk-Abello S.A .Reference.PSS.0138

## **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 gp-ASIT + 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

2769. Control observational study with allergic rhinitis moderate/grave in Spain. PI Dr/a Barasona Villarejo, Mª José

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





# **GC2** • Oxidative and nitrosative stress in acute and chronic liver disease

# HIGHLIGHTS



## **Team Leader**

## Principal Investigator (PI) Manuel de la Mata García

hepatoh2hrs.sspa@juntadeandalucia.es CIBER on Liver and Digestive Diseases (CIBERehd) PAIDI CTS-273 Scientific Group Co- Principal Investigator (Co-PI): Jose Antonio Bárcena Ruiz PAIDI BIO-216 Scientific Group

## Researchers

Aguilar Melero; Patricia Barrera Baena; Pilar Benítez Cantero; José Manuel Costán Rodero; Guadalupe Ferrín Sánchez; Gustavo Fraga Rivas; Enrique García Sánchez; Mª Valle Gómez Camacho; Federico Martínez Galisteo; Emilia Montero Álvarez; José Luis Padilla Peña; Alicia Peinado Peinado; José Poyato González; Antonio

## Post-Doctoral Researchers Requejo Aguilar; Raquel Rodríguez Perálvarez; Manuel Luis

## Pre-Doctoral Researchers (PhD Students y MSc Students)

González Rubio; Sandra Jurado García; Juan Linares Luna; Clara Isabel Vida Pérez; Luis

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

García García; Mª Luisa Medina Medina; Rosario Morcillo Ruiz; Eva María

# **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 involved in the development of a large number of phase II, III and IV clinical trials in the areas of viral hepatitis (boceprevir), hepatocellular carcinoma (sorafenib), liver cirrhosis (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

Pedrajas JR, McDonagh B, Hernandez-Torres F, Miranda-Vizuete A, Gonzalez-Ojeda R, Martinez-Galisteo E, Padilla CA, Barcena JA.Glutathione Is the Resolving Thiol for Thioredoxin Peroxidase Activity of 1-Cys Peroxiredoxin Without Being Consumed During the Catalytic Cycle.Antioxidants & Redox Signaling.2016.24(3):115-128. IF:7,093 Q:1 D1

Requejo-Aguilar, Raquel, Ana Alastrue-Agudo, Marta Cases-Villar, Eric Lopez-Mocholi, Richard England, María J Vicent, and Victoria Moreno-ManzanoCombined Polymer-Curcumin Conjugate and Ependymal Progenitor/ Stem Cell Treatment Enhances Spinal Cord Injury Functional Recovery. Biomaterials. 2017. Epub 2016;113:18-30. IF: 8,387

Q:1 D1

Requejo-Aguilar R, Bolanos JP.Mitochondrial control of cell bioenergetics in Parkinson's disease.Free Radical Biology And Medicine.2016.100:123-137. IF:5,784

Q:1

Gonzalez-Rubio S, Linares CI, Aguilar-Melero P, Rodriguez-Peralvarez M, Montero-Alvarez JL, de la Mata M, Ferrin G.AP-1 Inhibition by SR 11302 Protects Human Hepatoma HepG2 Cells from Bile Acid-Induced Cytotoxicity by Restoring the NOS-3 Expression.PloS One.2016.11(8):e0160525. IF:3,057 Q:1

Jurado-Garcia J, Munoz Garcia-Borruel M, Rodriguez-Peralvarez ML, Ruiz-Cuesta P, Poyato-Gonzalez A, Barrera-Baena P, Fraga-Rivas E, Costan-Rodero G, Briceno-Delgado J, Montero-Alvarez JL, de la Mata-Garcia M.Impact of MELD Allocation System on Waiting List and Early Post-Liver Transplant Mortality..Plos One.2016.11(6):e0155822. IF:3,057 Q:1

Rodriguez-Peralvarez M, Rico-Juri JM, Tsochatzis E, Burra P, De la Mata M, Lerut J.Biopsy-proven acute cellular rejection as an efficacy endpoint of randomized trials in liver transplantation: a systematic review and critical appraisal.Transplant International.2016.29(9):961-973. IF:2,835

Q:1

Coppo, Lucia, Sergio J Montano, Alicia C Padilla, and Arne Holmgren.Determination of Glutaredoxin Enzyme Activity and Protein S-Glutathionylation Using Fluorescent Eosin-Glutathione.Analytical Biochemistry.2016.499:24-33. IF:2,243 Q:2 Caston JJ, Castells L, Varo E, Gomez MA, de la Mata M, Campos-Varela I, Lumbreras C, Gonzalez-Dieguez L, Fabregat J, Herrero I, Salcedo M, Sanchez-Antolin G, Torre-Cisneros J.Impact of Cytomegalovirus Infection on Severe Hepatitis C Recurrence in Patients Undergoing Liver Transplantation.Transplantation.2016.100(3):593-599. IF:3,69

Q:2

Ruiz-Cuesta P, Gonzalez-Alayon C, Jurado-Garcia J, Iglesias-Flores EM, Barranco-Quintana JL, Garcia-Garcia L, Salgueiro-Rodriguez IM, Benitez-Cantero JM, Garcia-Sanchez V.Adherence to a predefined vaccination program in patients with inflammatory bowel disease.Gastroenterologia y Hepatologia.2016.39(6):385-92. IF:0.8

Q:4

Guerrero Puente L, Munoz Garcia-Borruel M, Barrera Baena P, de la Mata Garcia M.Inflammatory pseudotumor of the liver: A propos of a case.Gastroenterologia yHepatologia.2016.39(5):329-331.

Q:4

Vida Perez L, Montero Alvarez JL, Poyato Gonzalez A, Briceno Delgado J, Costan Rodero G, Fraga Rivas E, Barrera Baena P, De la Mata Garcia M.Prevalence and Predictors of Metabolic Syndrome After Liver Transplantation.Transplantation Proceedings.2016.48(7):2519-2524. IF:0,867 O:4



## In Collaboration

Castells L, Rimola A, Manzardo C, Valdivieso A, Montero JL, Barcena R, Abradelo M, Xiol X, Aguilera V, Salcedo M, Rodriguez M, Bernal C, Suarez F, Antela A, Olivares S, del Campo S, Laguno M, Fernandez JR, de la Rosa G, Agueero F, Perez I, Gonzalez-Garcia J, Esteban-Mur JI, Miro JM.Pegylated interferon plus ribavirin in HIV-infected patients with recurrent hepatitis C after liver transplantation: A prospective cohort study (vol 62, pg 92, 2015). Journal Of Hepatology.2016.64(3):757-757. IF:10,59

Q:1 D1

Hernandez-Breijo B, Chaparro M, Cano-Martinez D, Guerra I, Iborra M, Cabriada JL, Bujanda L, Taxonera C, Garcia-Sanchez V, Marin-Jimenez I, Barreiro-de Acosta M, Vera I, Martin-Arranz MD, Mesonero F, Sempere L, Gomollon F, Hinojosa J, Gisbert JP, Guijarro LG.Standardization of the homogeneous mobility shift assay protocol for evaluation of anti-infliximab antibodies. Application of the method to Crohn's disease patients treated with infliximab.Biochemical Pharmacology.2016.122:33-41. IE-5.091

Q:1 D1

Taxonera C, Barreiro-de-Acosta M, Bastida G, Martinez-Gonzalez J, Merino O, Garcia-Sanchez V, Gisbert JP, Marin-Jimenez I, Lopez-Serrano P, Gomez-Garcia M, Iglesias E, Lopez-Sanroman A, Chaparro M, Saro C, Bermejo F, Perez-Carazo L, Plaza R, Olivares D, Alba C, Mendoza JL, Fernandez-Blanco I.Outcomes of Medical and Surgical Therapy for Entero-urinary Fistulas in Crohn's Disease.Journal Of Crohns & Colitis.2016.10(6):657-662. IF:6,585 Q:1

Martinez-Cecilia D, Reyes-Diaz M, Ruiz-Rabelo J, Gomez-Alvarez M, Munoz Villanueva C, Alamo J, Muntane J, Padillo FJ.Oxidative stress influence on renal dysfunction in patients with obstructive jaundice: A case and control prospective study.Redox Biology.2016.8:160-164. IF:6,235 Q:1

Gisbert JP, Barreiro-de Acosta M, Esteve M, Garcia-Sanchez V, Gomollon F, Guardiola J, Hinojosa J, Martin Arranz MD, Minguez M, Taxonera C, Vera I.Physician Perspectives on Unresolved Issues in the Management of Ulcerative Colitis: The UC Horizons Project.Inflammatory Bowel Diseases.2016.22(3):583-98. IF:4,358 Q:1

Khorrami S, Ginard D, Marin-Jimenez I, Chaparro M, Sierra M, Aguas M, Sicilia B, Garcia-Sanchez V, Suarez C, Villoria A, Taxonera C, Velasco-Guardado A, Martinez-Gonzalez J, Gisbert JP.Ustekinumab for the Treatment of Refractory Crohn's Disease: The Spanish Experience in a Large Multicentre Open-label Cohort..Inflammatory Bowel Diseases.2016.22(7):1662-1669. IF:4,358

Q:1

Guerra I, Perez-Jeldres T, Iborra M, Algaba A, Monfort D, Calvet X, Chaparro M, Manosa M, Hinojosa E, Minguez M, Ortiz de Zarate J, Marquez L, Prieto V, Garcia-Sanchez V, Guardiola, J, Rodriguez GE, Martin-Arranz MD, Garcia-Tercero I, Sicilia B, Masedo A, Lorente R, Rivero M, Fernandez-Salazar L, Gutierrez A, Van Domselaar M, Lopez-SanRoman A, Ber Y, Garcia-Sepulcre M, Ramos L, Bermejo F, Gisbert JP.Incidence, Clinical Characteristics, and Management of Psoriasis Induced by Anti-TNF Therapy in Patients with Inflammatory Bowel Disease: A Nationwide Cohort Study.Inflammatory Bowel Diseases.2016.22(4):894-901. IF:4,358 O:1

Rodriguez-Novoa S, Garcia-Samaniego J, Prieto M, Calleja JL, Pascasio JM, Blanco MD, Crespo J, Buti M, Vidal MLB, Tapiador JAR, Fernandez-Rodriguez C, Sola R, Fraga E, Dieguez LG, Nunez O, Praga M, del Pino-Montes J, Romero-Gomez M, Morillas R, Diago M, Castro A.Altered Underlying Renal Tubular Function in Patients With Chronic Hepatitis B Receiving Nucleos(t)ide Analogs in a Real-World Setting The MENTE Study.Journal Of Clinical Gastroenterology.2016.50(9):779-789. IF:3,163 Q:2

Alvarez-Sotomayor D, Satorres C, Rodriguez-Medina B, Herrero I, de la Mata M, Serrano T, Rodriguez-Peralvarez M, D'Avola D, Lorente S, Rubin A, Berenguer M.Controlling Diabetes After Liver Transplantation: Room for Improvement.Transplantation.2016.100:E66-E73. IF:3,69 Q:2

Pique N, Ponce M, Garrigues V, Rodrigo L, Calvo F, Martin de Argila C, Borda F, Naranjo A, Alcedo J, Soria MJ, Rey E, Bujanda L, Gisbert JP, Suarez D, Calvet X, Ponce J.Prevalence of severe esophagitis in Spain. Results of the PRESS study (Prevalence and Risk factors for Esophagitis in Spain: A cross-sectional study). United European Gastroenterology Journal.2016.4(2):229-235. IF:2,933

Q:2

R-Grau MD, Chaparro M, Mesonero F, Barreiro-de Acosta M, Castro L, Castro M, Domenech E, Mancenido N, Lazaro Perez-Calle J, Taxonera C, Barrio J, De Francisco R, Fernandez-Salgado E, Luzon L, Merino O, Oltra L, Saro C, Bermejo F, Garcia-Sanchez V, Ginard .Effectiveness of anti-TNF alpha drugs in patients with Crohn's disease who do not achieve remission with their first anti-TNF alpha agent.Digestive And Liver Disease.2016.48(6):613-619. IF:2,719 Q:3

Cervoni JP, Amoros A, Banares R, Montero JL, Soriano G, Weil D, Moreau R, Pavesi M, Thevenot T, Di Martino V.Prognostic value of C-reactive protein in cirrhosis: external validation from the CANONIC cohort.European Journal Of Gastroenterology & Hepatology.2016.28(9):1028-1034. IF:2,093

Castro-Laria L, Argueelles-Arias F, Garcia-Sanchez V, Benitez JM, Fernandez-Perez R, Trapero-Fernandez AM, Gallardo-Sanchez F, Pallares-Manrique H, Gomez-Garcia M, Cabello-Tapia MJ, Talavera-Fabuel A, Bejarano-Garcia A, Leo-Carnerero E, Hernandez-Martinez.Initial experience with golimumab in clinical practice for ulcerative colitis. Revista Espanola De Enfermedades Digestivas.2016.108(3):129-132. IE:1.455

Q:4

Q:3

## **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

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

De la Mata García, M. The role of the immune system activation to eliminate circulating tumour cells and to prevent hepatocellular carcinoma recurrence after liver transplantation. Funding agency: Institute of Health Carlos III (ISCIII). Reference: PI14/01469

Garcia Sánchez V.Proteomic markers of response to infliximab biosimilars in patients with ulcerative colitis. Funding agency: Institute of Health Carlos III (ISCIII). Reference: PI15/01352

Bárcena Ruiz, JA. Role of peroxiredoxins in the homeostasis celular as Antioxidants and Gignalling. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO) Reference: BFU2016-80006-P

## Regional

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

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

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

Benítez Cantero, JM. Evolution after the "desintensificación" of anti-TNF in patients with inflammatory bowel disease.Funding agency: Andalusian society of digestive pathology.Reference: SAPD2015\_001

## **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 Enfermedades Hepáticas y Digestivas (CIBER on Liver and Digestive Diseases (CIBERehd)). Reference: MCI.CIBEREHD

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. 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

García Sánchez, MV.Prognosis of patients with ulcerative colitis in sustained remission after thiopurines withdrawal. Merck Sharp & Dohme SA. Reference: PSS.0091

Rodríguez Perálvarez, ML. Support agreement for collaborators at the Digestive Tract Unit.Funding agency: Tumor Andalusian society of transplants of organs and tissues.Reference:PSS.0095

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

De la Mata García, M. aHCtion Project .Funding agency: Abbvie Spain S.L.U.Reference:PSS.0144

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.072

De la Mata García, M. Support agreement for collaborators at the Digestive Tract Unit. Funding agency: Adalia Farma S.L.Reference: CCB.0084

De la Mata García, M. Support agreement for collaborators at the Digestive Tract Unit. Funding agency: Astellas Pharma, S.A.Reference: CCB.0124

De la Mata García, M. Support agreement for collaborators at the Digestive Tract Unit. Funding agency: Merck Sharp & Dohme de España SA.Reference: CCB.0130

De la Mata García, M. Support agreement for collaborators at the Digestive Tract Unit. Funding agency: Mutual Médica de Cataluña y Baleares.Reference: CCB.0132

## **Clinical Trials**

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

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). Pl: Dr/a Fraga Rivas, Enrique

0349/14.A Phase 1b Study to Assess the Safety and Anti-tumour Activity of Dexanabinol Monotherapy and Dexanabinol in Combination with Chemotherapy in Patients with Advanced Tumours

PI: Dr/a Montero Alvarez, Jose Luis

0257/15.A Study of Safety, Tolerability, and Clinical Activity of MEDI4736 and Tremelimumab Administered as Monotherapy and in Combination to Subjets with Unresectable Hepatocellular Carcinoma. Pl: Dr/a Fraga Rivas, Enrique

0219/15. A Phase II/III, randomiezed, double-blind and placebo-controlled study, to evaluate the efficacy and safety the treatment of induction and maintenance GS-5745 in which patients with active mild to moderate ulcerative colitis. PI: Dr/a García Sánchez, Valle

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 (ENDURANCE-1) study. PI: Dr/a Montero Alvarez, Jose Luis

0311/15.A phase 3b, randomized, contrtrolled, multicenter study with oral ferric maltol (Feraccru) or intravenous iron (FCM), for the treatment of iron deficiency anemia in subjects with inflamatory bowel disease. PI: Dr/a García Sánchez, Valle

\*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

\*3002.A Phase 3, randomized, double-blind, placebo-controlled, multicenter study to investigate the efficacy and safety of mongersen (GED-0301) for the treatment of subjects with active Crohn's disease. Pl: Dr/a García Sánchez, Valle

\*3024.A Phase 3, long-term active treatment

extension study of mongersen (GED-0301) in subjects with Crohn's disease Pl: Dr/a García Sánchez, Valle

\*3182.Suspension of treatment ANTI-TNF in patients inflammatory bowel disease: Multicenter trial, prospective and randomized. PI: Dr/a Benítez Cantero, José Manuel

\*3184. A phase II, multicentre and open study to evaluate the efficacy and safety of combination with fixed-dosis of sofosbuvir/velpatasvir in patients with chronic HCV infection who received a liver transplant. PI: Dr/a Montero Alvarez, Jose Luis

\*3127. Open and a single group study to evaluate the safety and efficacy ABT-493/ABT-530 in adults who have been recipients of a liver or kidney transplant, with chronic infection Hepatitis C (VHC) genotipo 1-6 (MAGELLAN-2). PI: Dr/a Montero Alvarez, Jose Luis

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). Pl: 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

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. Pl: Dr/a De La Mata García, Manuel

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

2845.Evolution following the intensification of anti-TNF treatment in patients with inflammatory bowel disease. PI: Dr/a García Sánchez, Valle

2986. Evolution following an exchange to inflisimab bisiolar in in patients with inflammatory bowel disease in remission PI: Dr/a García Sánchez, Valle

3006.Cancer and seriously infecctions across Europe: I-CARE. Pl: Dr/a Benítez Cantero, José Manuel

3044. Effectiveness and safey/tolerability of

Viekirax y Exviera in diagnosed patients HCV, co-infected or not with VIH-1, GT1 o 4, and chronic kidney disease in stage IIIb to V, inluding those in dialysis, usual clinical practice in Spain. Vie-kinD Stuyd. PI: Dr/a Montero Alvarez, Jose Luis

3132. Epidimiologic study in incidence in inflammatory bowel disease in adult spanish population.

PI: Dr/a García Sánchez, Valle

3194. Exploratory observational study, describing the profiles of patients with Hepatitis C with 18 age old or treated without interferon in accordance with the ribavirin addiction in Spain. ConRiba-15 Study. PI: Dr/a Montero Alvarez, Jose Luis

3278. Evidence on the effectiveness of Paritaprevir/r/Ombitasvir ± Dasabuvir (RÉGIMEN ABBVIE) ± Ribavirina in pacientes with chronic hepatitis C. Retrospective observational study PI: Dr/a Poyato González, Antonio

3279. Evolution of patients with inflammatory bowel disease in remission after the exchange to infliximab biosimilar. PI: Dr/a García Sánchez, Valle



# **GC3** • Infectious diseases

# HIGHLIGHTS









## **Team Leader**

## Principal Investigator (PI) Julián de la Torre Cisneros

julian.torre.sspa@juntadeandalucia.es Spanish Network for Research into Infectious Pathologies (REIPI) PAIDI CTS-647 Scientific Group

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

## Researchers

Camacho Espejo; Angela Castón Osorio; Juan José García Lázaro; Milagros Gracia Ahufinger; Irene Jurado Jimenez; Rafael Kindelan Jaquotot; José Mª Machuca Sánchez; Isabel Natera Kindelan; Clara Rodríguez López; Fernando Carlos Rumbao Aguirre; José Vidal Verdu; Elisa

## **Post-Doctoral Researchers**

Aguado Álvarez; Rocio Cantisan Bohorquez; Sara Frias Casas; Mario Perez Nadales; Elena Rivero Juarez; Antonio

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Paez Vega; Aurora Cano Yuste; Angela Cuenca López; Francisca Rodríguez Cano; Diego López López; Pedro

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

Añon Gámez; Mª Teresa Palomo Buitrago; María de la Encarnación Brieva Herrero; Teresa De la Torre Giménez; Julián Ruiz Torres; Laura Zafra Soto; Ismael Cantueso Méndez; Inmaculada

# **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

Rivero-Juarez A, Rivero A.Sustained virological response with sofosbuvir and ledipasvir for hepatitis C virus genotype 5.Lancet Infectious Diseases.2016.120(4):392-393. IF:21,372 Q:1 D1

Caston JJ, Cantisan S, Gonzalez-Gasca F, Paez-Vega A, Abdel-Hadi H, Illescas S, Alonso G, Torre-Cisneros J.Interferon-gamma production by CMV-specific CD8+T lymphocytes provides protection against cytomegalovirus reactivation in critically ill patients.Intensive Care Medicine.2016.42(1):420-53. IF:10,125 O:1 D1

Rivero-Juarez A, Frias M, Rodriguez-Cano D, Cuenca-Lopez F, Rivero A.Isolation of Hepatitis E Virus From Breast Milk During Acute Infection. Clinical Infectious Diseases.2016.62(11). 1464. IF:8,732 Q:1 D1

Cantisan S, Paez-Vega A, Perez-Romero P, Montejo M, Cordero E, Gracia-Ahufinger I, Martin-Gandul C, Maruri N, Aguado R, Solana R, Torre-Cisneros J. Spanish Network for Research in Infectious Diseases (REIPI). Prevention strategies differentially modulate the impact of cytomegalovirus replication on CD8(+) T-cell differentiation in high-risk solid organ transplant patients..Antiviral Research.2016.132:244-51. IF:4,909

Q:1 D1

Garcia-Martinez L, Gracia-Ahulfinger I, Machuca I, Cantisan S, De La Fuente S, Natera C, Perez-Nadales E, Vidal E, Rivero A, Rodriguez-Lopez F, Del Prado JR, Torre-Cisneros J.Impact of the PROVAUR stewardship programme on linezolid resistance in a tertiary university hospital: a before-and-after interventional study.Journal of Antimicrobial Chemotherapy.2016.71(9): 2606-2611. IF:4,919 Q:1 D1

Machuca I, Gutierrez-Gutierrez B, Cortes SP, Gracia-Ahufinger I, Serrano J, Madrigal MD, Barcala J, Rodriguez-Lopez F, Rodriguez-Bano J, Torre-Cisneros J.Oral decontamination with aminoglycosides is associated with lower risk of mortality and infections in high-risk patients colonized with colistin-resistant, KPC-producing Klebsiella pneumoniae. Journal of Antimicrobial Chemotherapy.2016.71(11):3242-3249. IF:4,919 O:1 D1

Blanco JR, Rivero-Juarez A.HCV genotype 3: a wolf in sheep's clothing.Expert Review of Anti-Infective Therapy.2016.14(2):149-152. IF:3,542 Q:1

Rivero-Juarez A, Frias M, Rivero A.Current views on interferon therapy for HIV.Expert Opinion on Biological Therapy.2016.120(9):1135-1142. IF:3,438 Q:1

Blanco JR, Rivero-Juarez A.The risk of hepatocellular carcinoma after sustained virological response in patients treated with the new direct-acting antiviral drugs: should we be worry about it?.Expert Rev Anti-Infe.2016.14(11):993-9920. IF:3,542

Q:1

Caston JJ, Torre-Cisneros J.Cytomegalovirus infection in adults. Must it be treated?.Medicina Clinica.2016.147(8):345-347. IF:1,2207 Q:2 Caston JJ, Castells L, Varo E, Gomez MA, de la Mata M, Campos-Varela I, Lumbreras C, Gonzalez-Dieguez L, Fabregat J, Herrero I, Salcedo M, Sanchez-Antolin G, Torre-Cisneros J.Impact of Cytomegalovirus Infection on Severe Hepatitis C Recurrence in Patients Undergoing Liver Transplantation.Transplantation.2016.100(3):593-599. IF:3,69

Q:2

Torre-Cisneros J, Aguado JM, Caston JJ, Almenar L, Alonso A, Cantisan S, Carratala J, Cervera C, Cordero E, Farinas MC, Fernandez-Ruiz M, Fortun J, Frauca E, Gavalda J, Hernandez D, Herrero I, Len O, Lopez-Medrano F, Manito N, Marcos MA, Martin-Davila P, Monforte V, Montejo M, Moreno A, Munoz P, Navarro D, Perez-Romero P, Rodriguez-Bernot A, Rumbao J, San Juan R, Vaquero JM, Vidal E Spanish Society of Transplantation (SET); Group for Study of Infection in Transplantation of the Spanish Society of Infectious Diseases and Clinical Microbiology (GESI-TRA-SEIMC); Spanish Network for Research in Infectious Diseases (REIPI). Management of cytomegalovirus infection in solid organ transplant recipients: SET/GESITRA-SEIMC/ REIPI Recommendations.Transplantation Reviews.2016.30(3):119-43. IF:3,915 Q:2

Rodriguez-Gomez J, Leon R, Robles JC, de la Torre-Cisneros J.Adult pneumoccocical sepsis: Should we rule out congenital anesplenia?.Enfermedades Infecciosas y Microbiologia Clinica.2016.34(9):2007-2008. IF:1,53

Q:3

Rivero A, Polo R, Lopez Aldeguer J, Lozano F, Antela A, Aguirrebengoa K, Ramon Arribas J, Asensi V, Berenguer J, Ramon Blanco J, Boix V, Casado JL, Clotet B, Crespo M, Domingo P, Duenas C, Estrada V, Garcia F, Gatell JM, Go-



mez-Sirvent JL, Gonzalez-Garcia J, Gutierrez F, Iribarren JA, Knobel H, Llibre JM, Losa JE, Mallolas J, Marino A, Miro JM, Moreno S, Palacios R, Pineda JA, Pulido F, Ribera E, Rubio R, Sanz Moreno J, Sanz Sanz J, Tellez MJ, de la Torre J, Tuset M, Perez Molina JA Spanish Soc Infectious.Executive summary of the GESIDA/ National AIDS Plan Consensus Document on Antiretroviral Therapy in Adults Infected by the Human Immunodeficiency Virus (Updated January 2016). Enfermedades infecciosas y microbiologia clinica.2016.34(7):439-451. IF:1,53 Q:3

Guirao-Arrabal E, Santos F, Redel-Montero J, Vaquero JM, Cantisan S, Vidal E, Torre-Gimenez A, Rivero A, Torre-Cisneros J.Risk of tuberculosis after lung transplantation: the value of pretransplant chest computed tomography and the impact of mTOR inhibitors and azathioprine use.Transplant Infectious Disease.2016.18(4):512-519. IF:1,459

Q:4

#### In Collaboration

Aguero F, Forner A, Manzardo C, Valdivieso A, Blanes M, Barcena R, Rafecas A, Castells L, Abradelo M, Torre-Cisneros J, Gonzalez-Dieguez L, Salcedo M, Serrano T, Jimenez-Perez M, Herrero JI, Gastaca M, Aguilera V, Fabregat J, del Campo S, Bilbao I, Jimene. FIPSE Investigators. Human Immunodeficiency Virus Infection Does Not Worsen Prognosis of Liver Transplantation for Hepatocellular Carcinoma. Hepatology.2016.203(2):488-498.

IF:11,711 Q:1 D1

Gutierrez-Gutierrez B, Salamanca E, de Cueto M, Hsueh PR, Viale P, Pano-Pardo JR, Mario Venditti Tumbarello M, Daikos G, Pintado V, Doi YH, Tuon FF, Karaiskos I, Machuca I, Schwaber MJ, Azap OK, Souli M, Roilides E, Pournaras S, Akova M, Perez F, Bermejo J, Oliver A, Almela M, Lowman W, Almirante B, Bonomo RA, Carmeli Y, Paterson DL, Pascual A, Rodriguez-Bano J.A.REIPI ESGBIS INCREMENT Grp.Predictive Model of Mortality in Patients With Bloodstream Infections due to Carbapenemase-Producing Enterobacteriaceae. Mayo Clinic Proceedings.2016.91(10):13202-1371. IF:5,92 Q:1 D1

Machuca J, Lopez-Cerero L, Fernandez-Cuenca F, Gracia-Ahufinger I, Ruiz-Carrascoso G, Rodriguez-Lopez F, Pascual A .Characterization of an outbreak due to CTX-M-15-producing Klebsiella pneumoniae lacking the bla(OXA-48) gene belonging to clone ST405 in a neonatal unit in southern Spain. Journal of Antimicrobial Chemotherapy.2016.71(8):2353-2355. IF:4,919 Q:1 D1

Montes ML, Nelson M, Girard PM, Sasadeusz J, Horban A, Grinsztejn B, Zakharova N, Rivero A, Durant J, Ortega-Gonzalez E, Lathouwers E. Janssen K. Ouwerkerk-Mahadevan S. Witek J, Gonzalez-Garcia J.Telaprevir-based therapy in patients coinfected with chronic hepatitis C virus infection and HIV: INSIGHT study.Journal of Antimicrobial Chemotherapy.2016.71(1):244-250. IF-4 919

Q:1 D1

Hamprecht A, Prim N, Tumbarello M, Bou G, Viale P, Tacconelli E, Almela M, Perez F, Giamarellou H, Cisneros JM, Schwaber MJ, Venditti M, Lowman W, Bermejo J, Hsueh PR, Mora-Rillo M, Gracia-Ahulfinger I, Pascual A, Rodriguez-Bano J. REIPI ESGBIS INCREMENT Grp Ertapenem for the treatment of bloodstream infections due to ESBL-producing Enterobacteriaceae: a multinational pre-registered cohort study.Journal of Antimicrobial Chemotherapy.2016.71(20):12072-12080. IF:4,919

Q:1 D1

Fortun J, Muriel A, Martin-Davila P, Montejo M, Len O, Torre-Cisneros J, Carratala J, Munoz P, Farinas C, Moreno A, Fresco G, Goikoetxea J, Gavalda J, Pozo JC, Bodro M, Vena A, Casafont F, Cervera C, Tiago Silva J, Aguado JM. Grp Estudio Infeccion Pacientes.Caspofungin versus fluconazole as prophylaxis of invasive fungal infection in high-risk liver transplantation recipients: A propensity score analysis.Liver Transplantation.2016.22(4):427-435. IF:3.951

Q:1 D1

Gutierrez-Gutierrez B, Perez-Galera S, Salamanca E, de Cueto M, Calbo E, Almirante B, Viale P, Oliver A, Pintado V, Gasch O, Martinez-Martinez L, Pitout J, Akova M, Pena C, Molina J, Hernandez A, Venditti M, Prim N, Origuen J, Bou G, Tacconelli E, Tumbarello M, Hamprecht A, Giamarellou H, Almela M, Perez F, Schwaber MJ, Bermejo J, Lowman W, Hsueh PR, Mora-Rillo M, Natera C, Souli M, Bonomo RA, Carmeli Y, Paterson DL, Pascual A, Rodriguez-Bano J. REIPI ESGBIS INCREMENT Grp. A Multinational, Preregistered Cohort Study of beta-Lactam/beta-Lactamase Inhibitor Combinations for Treatment of Bloodstream Infections Due to Extended-Spectrum-beta-Lactamase-Producing Enterobacteriaceae.Antimicrobial Agents and Chemotherapy.2016.200(7):4159-41209. IF:4,415

Cuervo G, Gasch O, Shaw E, Camoez M, Dominguez MA, Padilla B, Pintado V, Almirante B, Lepe JA, Lopez-Medrano F, Ruiz de Gopequi E, Martinez JA, Montejo JM, Perez-Nadales E, Arnaiz A, Goenaga MA, Benito N, Horcajada JP, Rodriguez-Bano J, Pujol M. REIPI GEIH Study Grp.Clinical characteristics, treatment and outcomes of MRSA bacteraemia in the elderly. Journal of Infection.2016.72(3):309-3120. IF:4,382

Q:1

Q:1

Gutierrez-Gutierrez B, Bonomo RA, Carmeli Y, Paterson DL, Almirante B, Martinez-Martinez L, Oliver A, Calbo E, Pena C, Akova M, Pitout J, Origuen J, Pintado V, Garcia-Vazquez E, Gasch O. Garcia-Alegria E. Lafita-Navarro MC. Aguado R, Garcia-Gutierrez L, Sarnataro K, Ruiz-Herguido C, Martin F, Bigas A, Canelles M, Leon J.NUMB inactivation confers resistance to imatinib in chronic myeloid leukemia cells.Cancer Letters.2016.375(1):92-99. IF:5.992

Q·1

Nunez-Torres R Macias J Mancebo M Frias M Dolci G. Tellez F. Merino D. Merchante N. Gomez-Mateos J, Guaraldi G, Rivero-Juarez A, Pineda JA, Real LM.The PNPLA3 Genetic Variant rs738409 Influences the Progression to Cirrhosis inHIV/Hepatitis C Virus Coinfected Patients .PloS One.2016.11(12):-e012082205. IF:3,057 Q:1

Neukam K, Espinosa N, Collado A, Delgado-Fernandez M, Jimenez-Aguilar P, Rivero-Juarez A, Hontanon-Antonana V, Gomez-Berrocal A, Ruiz-Morales J, Merino D, Carrero A, Tellez F, Rios MJ, Hernandez-Quero J, de Lagarde-Sebastian M, Perez-Camacho Vera-Mendez F, Macias J, Pineda JA. hE-PAtic Study Grp Hepatic Safety of Rilpivirine/ Emtricitabine/Tenofovir Disoproxil Fumarate Fixed-Dose Single-Tablet Regimen in HIV-Infected Patients with Active Hepatitis C Virus Infection: The hEPAtic Study.Plos One.2016.11(5):-e0155842. IF:3,057

Q:1

Q:2

Q:2

Neukam K, Mira JA, Collado A, Rivero-Juarez A, Monje-Agudo P, Ruiz-Morales J, Rios MJ, Merino D, Tellez F, Perez-Camacho I, Galvez-Contreras MC, Rivero A, Pineda JA. HEPAVIR SEG-HEP-2007 Study Grp Soc.Liver Toxicity of Current Antiretroviral Regimens in HIV-Infected Patients with Chronic Viral Hepatitis in a Real-Life Setting: The HEPAVIR SEG-HEP Cohort.Plos One.2016.11(2):-e0148104. IF:3,057 Q:1

Herrero R, Pineda JA, Rivero-Juarez A, Echbarthi M, Real LM, Camacho A, Macias J, Fibla J, Rivero A, Caruz A.Common haplotypes in CD209 promoter and susceptibility to HIV-1 infection in intravenous drug users.Infection Genetics and Evolution.2016.(45):20-25. IF:2,591

Macias J, Real LM, Rivero-Juarez A, Merchante N, Camacho A, Neukam K, Rivero A, Mancebo M, Pineda JA.Changes in liver steatosis evaluated by transient elastography with the controlled attenuation parameter in HIV-infected patients.HIV MEDI-CINE.2016.17(10):72020-773. IF:3,341

Pascual, Julio; Royuela, Ana; Fernandez, Ana M; Herrero, Ignacio; Delgado, Juan F; Sole, Amparo; Guirado, Lluis; Serrano, Trinidad; de la Torre-Cisneros, Julian; Moreno, Asuncion; Cordero, Elisa; Gallego, Roberto; Lumbreras, Carlos; Aguado, Jose M. Spanish Society of Transplantation Virological and Immune Response Investigation Study Group.Role of mTOR inhibitors for the control of viral infection in solid organ transplant recipients..Transplant infectious disease : an official journal of the Transplantation Society.2016.():-. IF:1,59

0.3

Berenquer J, Rivero A, Javier Blasco A, Arribas JR. Boix V. Clotet B. Domingo P. Gonzalez-Garcia J, Knobel H, Lazaro P, Lopez JC, Llibre JM, Lozano F, Miro JM, Podzamczer D, Tuset M, Gatell JM. GeSIDA Antiretroviral Therapy.Costs and cost-effectiveness analysis of 2015 GESI-DA/Spanish AIDS National Plan recommended guidelines for initial antiretroviral therapy in HIV-infected adults.Enfermedades Infecciosas y Microbiologia Clinica.2016.34(20):3201-371. IF153 Q:3

Iribarren JA, Rubio R, Aguirrebengoa K, Arribas JR, Baraia-Etxaburu J, Gutierrez F, de Quiros JCLB. Losa JE. Miro JM. Moreno S. Molina JP. Podzamczer D, Pulido F, Riera M, Rivero A, Moreno JS, Amador C, Antela A, Arazo P, Arrizabalaga J, Bachiller P, Barros C, Berenguer J, Cayla J, Domingo P, Estrada V, Knobel H, Locutura J, Aldeguer JL, Llibre JM, Lozano F, Mallolas J, Malmierca E, Miralles C, Miralles P, Munoz A, Ocampo A, Olalla J, Perez I, Elias MJP, Arellano JLP, Portilla J, Ribera E, Rodriguez F, Santin M, Sanz JS, Tellez MJ, Torralba M, Valencia E, Von Wichmann MA. GESIDA SEIMC Writing Comm.Executive summary: Prevention and treatment of opportunistic infections and other coinfections in HIV-infected patients: May 2015. Enfermedades Infecciosas y Microbiologia Clinica.2016.34(8):517-523. IF:1,53

Q:3

Por:Pascual, J, Royuela, A, Fernandez, AM, Herrero, I, Delgado, JF, Sole, A, Guirado, L, Serrano, T, de la Torre-Cisneros, J, Moreno, A, Cordero, E, Gallego, R, Lumbreras, C, Aguado, JM.GESIDA/ SEIMC Writing Committee. Prevention and treatment of opportunist icinfections and other coinfections in HIV-infected patients: May2015. Enfermedades infecciosas y microbiologia clinica.2016.34(8):5120.e1-5120.e18. IF:1,53 O:3

Serrano-Villar S, Gutierrez F, Miralles C, Berenguer J, Rivero A, Martinez E, Moreno S.Human Immunodeficiency Virus as a Chronic Disease: Evaluation and Management of Nonacquired Immune Deficiency Syndrome-Defining Conditions.Open Forum Infectious Diseases.2016.3(2):ofw097.

Berenguer J, Rivero A, Jarrin I, Nunez MJ, Vivancos MJ, Crespo M, Tellez MJ, Domingo P, Iribarren JA, Artero A, Marquez M, Santos I, Moreno J, Montero M, Gonzalez-Garcia J. Human Immunodeficiency Virus/Hepatitis C Virus Coinfection in Spain: Prevalence and Patient Characteristics. Open Forum Infectious Diseases.2016.3(2):ofw059.

Perez-Latorre L, Rivero-Juarez A, Hontanon V, Diez C, Cuenca F, Martin-Carbonero ML, Montes ML, Bellon JM, Aldamiz-Echevarria T, Carrero A, Rivero A, Gonzalez-Garcia J, Berenguer J.Prognostic Value of Transient Elastography in Human Immunodeficiency Virus-Infected Patients With Chronic Hepatitis C. Open Forum Infectious Diseases 2016.3(4):

# **Research Funding**

#### National

De la Torre Cisneros, J. Spanish Network for Research on Infectious Diseases (REIPI).Funding agency: Institute Carlos III Health (ISCIII). 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

De la Torre Cisneros, J. Clinical trial to stop valganciclovir prophylaxis in CMV-seropositive renal transplant patients who maintain CD8+ CMV-specific cellular immunity after receiving thymoglobulin. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI15/00402

Rivero Román, A. Andalusia prospective follow-up cohort of chronically HCV infected patients co-infected with HIV. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI15/01017 Cantisan Bohrquez, S. Impact of the lack of CMV-specific CD8+ T cell response in CMV-seropositive donors on CMV reactivation after hematopoietic stem cells transplant in CMV-seropositive recipients Funding agency: Institute Carlos III Health (ISCIII). Reference: PI15/01419

De la Torre Cisneros, J. Spanish Network for Research on Infectious Diseases (REIPI).Funding agency: Institute Carlos III Health (ISCIII). Reference: RD16/0016/0008 . Expected starting date:2017

Rivero Román, A.AIDS Research Network (RIS).Funding agency: Institute Carlos III Health (ISCIII). Reference: RD16/0025/0034 Expected starting date:2017

Rivero Juarez A. Impact of the acute Hepatitis e Virus Infection in HIV Infected Patients Funding agency: Institute Carlos III Health (ISCIII). Reference: PI16/01297 Expected starting date:2017

Perez Nadales, E. Risk factors for bacterial load of colonization, dissemination to the community, and mortality by arbapenemase-producing Klebsiella pneumoniae (Klebcom Study). Funding agency: Institute Carlos III Health (IS-CIII). Reference: P116/01631 Expected starting date: 2017

#### Regional

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. Study Group for Viral Hepatitis.Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: RH-0024-2013

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 Number 115523-1.Funding agency: European Commission. Reference: IMI Call IMI-IU-6-12

De la Torre Cisneros, J (node). PROYECTO 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. Agreement with JANSSEN. Funding agency: JANSSEN-CILAG, S.A. Reference: PSS.0090\_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.F Agreement with Merck Sharp & Dohme. Funding agency: Merck Sharp & Dohme de España SA. Reference:C-CB.0110



Rivero Román, A. Agreement with JANSSEN. Funding agency: JANSSEN-CILAG, S.A.Reference:CCB.0113\_01

De la Torre Cisneros, JC. Agreement.Funding Agency: FPS.Reference:CCB.0114

Rivero Román, A. Agreement with JANSSEN. Funding agency: Janssen-Cilag, S.A. Reference: CCB.0115

Rivero Román, A. Agreement with JANSSEN. Funding agency: Janssen-Cilag, S.A. Reference: CCB.0123

Rivero Román, A. Agreement with GILEAD. Funding agency: Gilead Sciences, S.L Reference CCB.0120

Rivero Román, A. Agreement with GILEAD. Funding agency: Gilead Sciences, S.L .Reference: CCB.0121

#### **Clinical Trials**

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.

PI: 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

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. Pl: 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

0369/15. A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Switching From a Regimen of Dolutegravir and ABC/3TC, or a Fixed Dose Combination (FDC) of ABC/DTG/3TC to a FDC of GS-9883/F/TAF in HIV-1 Infected Subjects Who Are Virologically Suppressed. Pl: Dr/a Rivero Román, Antonio

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

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

\*3192.A Phase III, randomised, double-find, multicentre, parallelgroup, non-inferiority study evaluating the efficacy, safety, and tolerability of dolutegravir plus lamivudine compared to dolutegravir plus tenofovir/emtricitabine in HIV-1-infected treatment-naive adults PI: Dr/a Rivero Román, Antonio

\*3186.A Phase 2, Multicenter, Randomized, Open-Label Study to Evaluate the Efficacy and Safety of Sofosbuvir/Velpatasvir Fixed Dose Combination (FDC) and Sofosbuvir/Velpatasvir FDC and Ribavirin in Subjects With Chronic Genotype 3 HCV Infection and CirrhosisPI: Dr/a Rivero Román, Antonio

\*3124 A Phase 3 Randomized Double-Blind Study to Evaluate the Safety and Efficacy of GS-9883/Emtricitabine/Tenofovir Alafenamide Versus Abacavir/Dolutegravir/Lamivudine in HIV-1 Infected, Antiretroviral Treatment-Naïve Adults

PI: Dr/a Rivero Román, Antonio

\*3125.A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of GS-9883/Emtricitabine/Tenofovir Alafenamide Versus Dolutegravir + Emtricitabine/Tenofovir Alafenamide in HIV-1 Infected, Antiretroviral Treatment-Naïve Adults. Pl: Dr/a Rivero Román. Antonio

\*3248.A Phase III, Randomized, Multicenter, Parallel-group, Non-inferiority, Open-label Study Evaluating the Efficacy, Safety, and Tolerability of Switching to Long-acting Cabotegravir Plus Long-acting Rilpivirine From Current INI- NNRTI-, or PI-based Antiretroviral Regimen in HIV-1-infected Adults Who Are

Virologically Suppressed Pl: Dr/a Rivero Román, Antonio

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

PI: Dr/a Rivero Román, Antonio

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 Bohorguez, Sara

2548.Hepatic safety of Evilplera in HIV/hepatitis C (HCV)-coinfected patients without HCV treatment in the The HEPAVIR HEPATIC SAFETY Cohort. hEPAtic study 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

2649. Effectiveness and safety of treatment against hepatitis C virus based on direct acting antivirals in actual use conditions: Cohort GE-HFP

PI: Dr/a Rivero Román, Antonio

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 Sánchez, Isabel María

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

2849.Effectiveness of intestinal decontamination in patients colonized by Klebsiella resistant to carbapenems and colistin pneumoniae. PI: Dr/a Machuca Sanchez, Isabel Maria

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

3044/2. Efficacy and safety/tolerability of Viekirax and Exviera in patients with diagnosed HCV, whether or not displaying coinfection with HIV-1, GT1 or GT4, and Stage IIIB-V chronic kidney disease, including patients undergoing dialysis, in routine clinical practice in Spain. ViekinD Study.

PI: Dr/a Rivero Román, Antonio

3131. Rescue therapy using ceftolozane-tazobactam in infection caused by multidrug-resistant Pseudomonas aeruginosa. PI: Dr/a De la Torre Cisneros. Julián Carlos.

3162. Spanish bacteremia cohort 2016: epidemiology, clinical management and prognostic factors at diagnosis. PRO-BAC 2016 Study. PI: Dr/a Natera Kindelan, Clara

3009.Prospective observational study to assess the risk factors, clinical management outcomes of hospitalized patients with serious infections caused by carbapenen-resistant Enterobacteriaceae and acinetobacter baumannii. PI: Dr/a De la Torre Cisneros, Julián Carlos

3081. Impact of ceftazidime/Avibactam treatment on mortality associated with bacteremia caused by carbapenemase-producing Enterobacteriaceae in haematological patients. PI: Dr/a De la Torre Cisneros, Julián Carlos

3055.Experience of patients treated with ceftazidime-avibactam for infections caused by carbapenem-resistant organisms: a case series from the compassionate-use program. PI: Dr/a De la Torre Cisneros, Julián Carlos

# **GC4** • Inflammation and cancer

# HIGHLIGHTS



# **Team Leaders**

Principal Investigator (PI) Eduardo Muñoz Blanco

fi1muble@uco.es PAIDI BIO-304 Scientific Group

**Emerging Researcher (ER)** Marco Antonio Calzado Canale Post-Doctoral Researchers Cantarero Carmona; Irene García Medel; Noel Navarrate Rueda; Carmen

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Del Río Mercado; Carmen García González; Víctor Lara Chica; Mª Isabel Palomares Cañero; Belén

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

Garrido Rodríguez-Córdoba; Martín Jiménez Jiménez;Carla Millán Ortega; Estrella Carranza Valencia; Juan Collado Rojas; Juan Antonio Molina Moran; Rosario Ramírez Balsera; Carmen



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

Garcia-Limones C, Lara-Chica M, Jimenez-Jimenez C, Perez M, Moreno P, Munoz E, Calzado MA.CHK2 stability is regulated by the E3 ubiquitin ligase SIAH2.Oncogene.2016.35 (33):4289-301. IF:7.932

Q:1 D1

del Rio C, Navarrete C, Collado JA, Bellido ML, Gomez-Canas M, Ruth Pazos M, Fernandez-Ruiz J, Pollastro F, Appendino G, Calzado MA, Cantarero I, Munoz E.The cannabinoid quinol VCE-004.8 alleviates bleomycin-induced scleroderma and exerts potent antifibrotic effects through peroxisome proliferator-activated receptor-gamma and CB2 pathways.Scientific Reports.2016.6():-21703. IF:5,228 O:1

Diaz-Alonso J, Paraiso-Luna J, Navarrete C, del Rio C, Cantarero I, Palomares B, Aguareles J, Fernandez-Ruiz J, Bellido ML, Pollastro F, Appendino G, Calzado MA, Galve-Roperh I, Munoz E.VCE-003.2, a novel cannabigerol derivative, enhances neuronal progenitor cell survival and alleviates symptomatology in murine models of Huntington's disease.Scientific Reports.2016.6:29789.

IF:5,228 Q:1

Garcia V, Lara-Chica M, Cantarero I, Sterner O, Calzado MA, Munoz E.Galiellalactone induces cell cycle arrest and apoptosis through the ATM/ATR pathway in prostate cancer cells. Oncotarget.2016.7(4):4490-4506. IF:5,008 Q:1

#### In Collaboration

Hanus LO, Meyer SM, Munoz E, Taglialatela-Scafati O, Appendino G.Phytocannabinoids: a unified critical inventory.Natural Product Reports.2016.33:1357-1392. IF:10,986 Q:1 D1

Gomez-Canas M, Morales P, Garcia-Toscano L, Navarrete C, Munoz E, Jagerovic N, Fernandez-Ruiz J, Garcia-Arencibia M, Pazos MR.Biological characterization of PM226, a chromenoisoxazole, as a selective CB2 receptor agonist with neuroprotective profile.Pharmacological Research.2016.110 ():205-215. IF:4,816 Q:1

Gutierrez C, Serrano-Villar S, Madrid-Elena N, Perez-Elias MJ, Martin ME, Barbas C, Ruiperez J, Munoz E, Munoz-Fernandez MA, Castor T, Moreno S.Bryostatin-1 for latent virus reactivation in HIV-infected patients on antiretroviral therapy.AIDS (London, England).2016.30 (9):1385-92. IF: 4,407

Q:1

Pollastro F, Golin S, Chianese G, Putra MY, Moriello AS, De Petrocellis L, Garcia V, Munoz E, Taglialatela-Scafati O, Appendino G.Neuroactive and Anti-inflammatory Frankincense Cembranes: A Structure-Activity Study.Journal of Natural Products.2016.79 (7):1762-1768. IF:3,662 Q:1 Del Prete D, Millan E, Pollastro F, Chianese G, Luciano P, Collado JA, Munoz E, Appendino G, Taglialatela-Scafati O.Turmeric Sesquiterpenoids: Expeditious Resolution, Comparative Bioactivity, and a New Bicyclic Turmeronoid. Journal of Natural Products.2016.79 (2):267-273. IF:3,662

Q:1

Deiana V, Gomez-Canas M, Pazos MR, Fernandez-Ruiz J, Asproni B, Cichero E, Fossa P, Munoz E, Deligia F, Murineddu G, Garcia-Arencibia M, Pinna GA.Tricyclic pyrazoles. Part 8. Synthesis, biological evaluation and modelling of tricyclic pyrazole carboxamides as potential CB2 receptor ligands with antagonist/inverse agonist properties.European Journal of Medicinal Chemistry.2016.112 ():66-80. IE:3.902

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. Hypoxia Mimetic 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 phe-



notypic 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

Calzado Canale, MA. Identification of new functions and substrates of protein kinase Dyrk2 and their implications for carcinogenesis. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO).Reference: SAF2016-75228-R.

Malagón MM (Calzado Canale, M: Co-PI). Integration of platforms for the identification of therapeutic targets and the development of new products for the prevention and/or treatment of radiodermatitis. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO).Reference: RTC-2016-4589-1

#### 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

# **Contracts with Companies**

Muñoz Blanco, E. Biological screening in different biochemical and cellular tests on collection natural ingredients.Funding agency: Innovativehealth Group S.L.Reference: PSS.0145

Muñoz Blanco, E. Biomolecules design through multivariate analysis process for obtaining active compounds (INTERCONNEC-TA). Funding agency: Vivacell Biotechnology Spain SL.

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

Muñoz Blanco, E. Outsourcing within the IN-NTERCONECTA 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. Bioligical activity of natural biomedical products.Funding agency: Beros Consulting S.L. Reference: ccb.uco0040

Muñoz Blanco, E. Project for the prodyuction and resarch on hemp and derivatives. Funding agency: Phytoplant Research S.L. Reference: 12012129



# **GC5** • Systemic and chronic inflammatory autoimmune diseases of the locomotor system and connective tissue

# PUBLICATIONS







# Team Leader

# Principal Investigator (PI) Rosario López Pedrera rosario.lopez.exts@juntadeandalucia. es Nicolás Monardes Contract

# Co-Principal Investigator (Co-PI)

Eduardo Collantes Estévez Professor at University of Cordoba. Head of the Clinical Management Unit of Rheumatology Spanish Network for Research in inflammation and rheumatic disease (RIER) PAIDI CTS-1004 Scientific Group

# Researchers

Aguirre Zamorano; M<sup>a</sup>Angeles Caracuel Ruiz; Miguel Ángel Escudero Contreras; Alejandro Font Ugalde; Pilar Gómez Gracia; Inmaculada Pérez Guijo; Verónica López Medina; Clementina López Montilla; María Dolores

# **Post-Doctoral Researchers**

Barbarroja Puerto; Nuria Calvo Gutierrez; Jerusalem Castro Villegas; Mª Del Carmen Jiménez Gómez; Yolanda Ortega Castro; Rafaela Ruiz Limon; Patricia

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Arias de la Rosa; Iván Jiménez Gasco; Rocío Guerrero Sánchez; Víctor Manuel Peñafiel Benavides; Manuel Perez Sanchez; Carlos

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

Abalos Aguilera; Mª Carmen Carmona Moriel; Cristina Elena Ruiz Vílchez; Desiree

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. PI: 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. PI: 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: RESPONDIA). 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; spondyloar-thropathies; epidemiology; diagnostic criteria, structural damage.



# **Scientific Production**

## Publications

#### Original

Ruiz-Limón P, Ortega R, Arias de la Rosa I, Abalos-Aguilera MD, Perez-Sanchez C, Jimenez-Gomez Y, Peralbo-Santaella E, Font P, Ruiz-Vilches D, Ferrin G, Collantes-Estevez E, Escudero-Contreras A, López-Pedrera C, Barbarroja N. Tocilizumab improves the proatherothrombotic profile of rheumatoid arthritis patients modulating endothelial dysfunction, NETosis, and inflammation. Transl Res. 2016 (epub). pii: S1931-5244(16)30423-6. IE: 4,557 Q:1D1

Canas A, Lopez-Sanchez LM, Penarando J, Valverde A, Conde F, Hernandez V, Fuentes E, Lopez-Pedrera C, de la Haba-Rodriguez JR, Aranda E, Rodriguez-Ariza A.Altered S-nitrosothiol homeostasis provides a survival advantage to breast cancer cells in HER2 tumors and reduces their sensitivity to trastuzumab. Biochimica Et Biophysica Acta-Molecular Basis Of DiseasE.2016.1862(4):601-10. IF:5,158

Q:1

Perez-Sanchez C, Aguirre MA, Ruiz-Limon P, Barbarroja N, Jimenez-Gomez Y, de la Rosa IA, Rodriguez-Ariza A, Collantes-Estevez E, Segui P, Velasco F, Cuadrado MJ, Teruel R, Gonzalez-Conejero R, Martinez C, Lopez-Pedrera Ch:Atherothrombosis-associated microRNAs in Antiphospholipid syndrome and Systemic Lupus Erythematosus patients'.Scientific Reports.2016.6:31375.

IF:5,228 Q:1

Lopez-Medina C, Schiotis RE, Font-Ugalde P, Castro-Villegas MC, Calvo-Gutierrez J, Ortega-Castro R, Jimenez-Gasco R, Escudero-Contreras A, Collantes-Estevez E.Assessment of Fatigue in Spondyloarthritis and Its Association with Disease Activity.Journal Of Rheumatology.2016.43(4):751-757. IF:3,236

Gratacos J, Moreno Martinez-Losa M, Font P, Montilia C, Fernandez-Espartero C, Linares LF, Brito E, Oliva JC, Collantes-Estevez E.Etoricoxib in ankylosing spondylitis: is there a role for active patients refractory to traditional NSAIDs?.Clinical And Experimental Rheumatology.2016.34(1):94-99.

IF:2,495 Q:2

Q:2

Q:2

Calvo-Gutierrez, J; Garrido-Castro, J L; Gonzalez-Navas, C; Castro-Villegas, M C; Ortega-Castro, R; Lopez-Medina, C; Font-Ugalde, P; Escudero-Contreras, A; Collantes-Estevez, E.Inter-rater reliability of clinical mobility measures in ankylosing spondylitis.BMC Musculoskeletal Disorders.2016.17(1):-382382. IF:1,684

strategy in established rheumatoid arthritis:

results of the CREATE registry. Rheumatology

Cardenas M, de la Fuente S, Castro-Villegas MC, Romero-Gomez M, Ruiz-Vilchez D, Calvo-Gutierrez J, Escudero-Contreras A, Del Prado JR, Collantes-Estevez E, Font P.Cost-effectiveness of clinical remission by treat to target International.2016.36(12):1627-1632. IF:1,702 Q:3

Cardenas M, de la Fuente S, Font P, Castro-Villegas MC, Romero-Gomez M, Ruiz-Vilchez D, Calvo-Gutierez J, Escudero-Contreras A, Casado MA, Del Prado JR, Collantes-Estevez E.Real-world cost-effectiveness of infliximab, etanercept and adalimumab in rheumatoid arthritis patients: results of the CREATE registry.Rheumatology International.2016.36(2):231-241. IF:1,702

IF:1,70∠ Q:3

#### **In Collaboration**

Zhao M, Zhou Y, Zhu BC, Wan MJ, Jiang TT, Tan QQ, Liu Y, Jiang JQ, Luo SHT, Tan YX, Wu HJ, Renauer P, Gutierrez MDA, Palma MJC, Castro RO, Fernandez-Roldan C, Raya E, Faria R, Carvalho C, Alarcon-Riquelme ME, Xiang ZY, Chen JW, Li F, Ling GH, Zhao HJ, Liao XP, Lin YK, Sawalha AH, Lu QJ.IFI44L promoter methylation as a blood biomarker for systemic lupus erythematosus.Annals Of The Rheumatic Diseases.2016.75(11):1998-2006. IF:12,384

Q:1 D1

Sepriano A, Landewe R, van der Heijde D, Sieper J, Akkoc N, Brandt J, Braun J, Collantes-Estevez E, Dougados M, Fitzgerald O, Huang F, Gu J, Kirazli Y, Maksymowych WP, Marzo-Ortega H, Olivieri I, Ozgocmen S, Roussou E, Scarpato S, Sorensen IJ, Valle-Onate R, Van den Bosch F, van der Horst-Bruinsma I, Weber U, Wei J, Rudwaleit M.Predictive validity of the ASAS classification criteria for axial and peripheral spondyloarthritis after follow-up in the ASAS cohort: a final analysis.Annals Of The Rheumatic Diseases.2016.75(6):1034-1042. IF:12,384

Q:1 D1

Molto A, Etcheto A, van der Heijde D, Landewe R, van den Bosch F, Bautista Molano W, Burgos-Vargas R, Cheung PP, Collantes-Estevez E, Deodhar A, El-Zorkany B, Erdes S, Gu J, Hajjaj-Hassouni N, Kiltz U, Kim TH, Kishimoto M, Luo SF, Machado PM, Maksymowych WP, Maldonado-Cocco J, Marzo-Ortega H, Montecucco CM, Ozgocmen S, van Gaalen F, Dougados M. Prevalence of comorbidities and evaluation of their screening in spondyloarthritis: results of the international cross-sectional ASAS-COMOSPA study.Annals Of The Rheumatic Diseases.2016.75(6):1016-1023. IF:12,384

Q:1 D1

Jamin C, Le Lann L, Alvarez-Errico D, Barbarroja N, Cantaert T, Ducreux J, Dufour AM, Gerl V, Kniesch K, Neves E, Trombetta E, Alarcon-Riquelme M, Maranon C, Pers JO.Multi-center harmonization of flow cytometers in the context of the European PRECISESADS project.Autoimmunity Reviews.2016.15(11):1038-1045. IF:6,972

Q:1 D1

Sciascia S, Lopez-Pedrera Ch, Cecchi I, Pecoraro C, Roccatello D, Cuadrado MJ.Non-vitamin K antagonist oral anticoagulants and antiphospholipid syndrome.Rheumatology (Oxford, England).2016.55(10):1726-1735. IF:4,524 Q:1 Delgado-Domínguez CJ, Escudero-Contreras A, Font-Ugalde P, Ruiz-Vilchez D, Collantes-Estévez E, Carretero-Dios H.Upswings in Cheerful Mood and Disease Activity in Patients with Rheumatoid Arthritis.International Journal Of Behavioral Medicine.2016.23(5):606-610. IF:1,872 Q:2

Galindo-Izquierdo M, Rodriguez-Almaraz E, Pego-Reigosa JM, Lopez-Longo FJ, Calvo-Alen J, Olive A, Fernandez-Nebro A, Martinez-Taboada V, Vela-Casasempere P, Freire M, Narvaez FJ, Rosas J, Ibanez-Barcelo M, Uriarte E, Tomero E, Zea A, Horcada L, Tor-rente V, Castellvi I, Calvet J, Menor-Almagro R, Zamorano MAA, Raya E, Diez-Alvarez E, Vazquez-Rodriguez T, de la Pena PG, Movasat A, Andreu JL, Richi P, Marras C, Montilla-Morales C, Hernandez-Cruz B, de la Fuente JLM, Gantes M, Ucar E, Alegre-Sancho JJ, Manero J, Ibanez-Ruan J, Rodriguez-Gomez M, Quevedo V, Hernandez-Beriain J, Silva-Fernandez L, Alonso F, Perez S, Rua-Figueroa I.Characterization of Patients With Lupus Nephritis Included in a Large Cohort From the Spanish Society of Rheumatology Registry of Patients With Systemic Lupus Erythematosus (RELESSER). Medicine.2016.95(9): e2891. IF:1,206

Q:3

Torrente-Segarra V, Urruticoechea Arana A, Sanchez-Andrade Fernandez A, Tovar Beltran JV, Munoz Jimenez A, Martinez-Cristobal A, Gonzalez Ferrandez JA, Fernandez Prada M, Vazquez Fuentes N, Corominas H, Garcia-Diaz S, Acosta Pereira A, Ruiz Martin JM, Riazuelo JRL Moliner RE Vilchez DR, Cabello RV, Fernandez JC, Pons JRN, Punal NPG, Celimendiz PG, Verdu RC, Diez AA, Roura CT, Turudi CM, Torrent DT, Santirso FJR, Garrido JJL, Portales RG, Palau SO, Gonzalez-Albo SP, Perez AG, Mateos AC, Alen JC, Gil JG, Alonso MPN, Blasco MJM. RENACER study: Assessment of 12-month efficacy and safety of 168 certolizumab PEGol rheumatoid arthritis-treated patients from a Spanish multicenter national database.Modern Rheumatology.2016.26(3):336-341. IF:1.843

Q:3

# **Research Funding**

#### National

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

López Pedrara, R. Study of the mechanisms of atherothrombosis in systemic autoimmune diseases by integration of immunological, molecular and epigeticos analysis. New therapies. Funding agency: Institute Carlos III Health (IS-CIII). Reference: PI15/01333

Collantes Estevez, E. Spanish Network for Research in inflammation and rheumatic disease (RIER). Funding agency: Institute Carlos III Health (ISCIII). Reference: RD16/0012/0015 Expected starting date: 2017

#### Regional

López Pedrara, R. Cellular and Molecular Mechanisms. Funding Agency: Regional Ministry of Economy, Innovation, Science and Empoyment (CEICE). Reference: CTS-7940

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

Collantes Estevez, E. Can Inertial Movement Sensors (IMUs) provide a valid and reliable way of measuring Spinal Mobility in Axial Spondyloarthritis (axSpa): a Clinimetric Evaluation. Funding Agency: Foundation for Research in Rheumatology.Reference: FOREUM-2015-001 Expected starting date:2017

#### **Contracts with Companies**

Collantes Estevez, E. Agreement between MSD and the UGC of Reumatology. Funding agency: Merck Sharp & Dohme de España SA.Reference:CCB.0042

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. 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

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

Collantes Estevez, E. Sponsored Research Agreement UCOTRACK.Funding agency: MERCK SHARP & DOHME DE ESPAÑA SA.Reference: CCB.0107 Collantes Estevez, E. Sponsored Research Agreement ROCHE..Funding agency: ROCHE FARMA, S.A. Reference: CCB.0122

### **Clinical Trials**

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

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, M<sup>a</sup> Ángeles

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.

Pl: Dr/a Collantes Estevez, Eduardo

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

0318/14. GO-VIBRANT A Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Golimumab, an Anti-TNF alpha Monoclonal Antibody, Administered Intravenously, in Subjects with Active Psoriatic Arthritis PI: Dr/a Lopez Montilla, M<sup>a</sup> Dolores

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

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, multi-phase, 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

0107/15.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 Lopez Montilla, M<sup>a</sup> Dolores

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.

Pl: Dr/a Collantes Estevez, Eduardo

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

0293/15. A Multicenter Double-Blind, Randomized Controlled Study of Etanercept and Methotrexate in Combination or as Monotherapy in Subjects With Psoriatic Arthritis PI: Dr/a Lopez Montilla, M<sup>a</sup> Dolores

0271/15.A Comparative Study to Assess the Efficacy, Safety and Immunogenicity of YLB113 and Enbrel for the Treatment of Rheumatoid Arthritis.

PI: Dr/a Escudero Contreras, Alejandro

0306/15. A Randomized, Double-blind, Placebo-controlled, Proof-of-concept Study to Evaluate the Efficacy of UCB5857 Over 12 Weeks in Subjects With Primary Sjorgen's Syndrome. Pl: 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

\*2950. A Phase 3 Randomized, Double-blind, Placebo-controlled, Multicenter Study Of The Analgesic Efficacy And Safety Of The Subcutaneous Administration Of Tanezumab In Subjects With Osteoarthritis Of The Hip Or Knee. Pl: Dr/a Caracuel Ruiz, Miguel Ángel

2959. A Phase 3, Multicenter, Long-term Observational Study Of Subjects From Tanezumab Studies Who Undergo A Total Knee, Hip Or Shoulder Replacement PI: Dr/a Caracuel Ruiz, Miguel Ángel

\*2894. A Multicenter, Open-label (Part A) Followed by a Randomized, Double-blind, Parallel-group, Placebo Controlled Study (Part B) to Evaluate Maintenance of Remission in Subjects With Active Axial Spondyloarthritis (axSpA) Receiving Either Certolizumab Pegol 200 mg Q2W or 200 mg Q4W as Compared

PI: Dr/a Collantes Estevez, Eduardo

to Placebo

\*3235. MAXIMISE (Managing AXIal Manifestations in Psorlatic Arthritis With SEcukinumab), a Randomized, Double-blind, Placebo-con-



trolled, Multicenter, 52 Week Study to Assess the Efficacy and Safety of Secukinumab 150 mg or 300 mg s.c. in Participants With Active Psoriatic Arthritis and Axial Skeleton Involvement Who Have Inadequate Response to Non Steroidal Anti-inflammatory Drugs (NSAIDs). Pl: Dr/a López Montilla, M<sup>a</sup> Dolores

\*3026. A Multicenter, Randomized, Double-Blind, Placebo- Controlled 16-Week Study Followed by Long-Term Evaluation of Efficacy and Safety of Ixekizumab (LY2439821) in TN-Fi-Experienced Patients With Radiographic Axial Spondyloarthritis.

PI: Dr/a Collantes Estevez, Eduardo

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

PI: Dr/a Collantes Estevez, Eduardo

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

PI: Dr/a López Pedrera, Rosario

2273. Spanish registry of patients with axial ankylosing spondylitis treated with anti-TNF. PI: Dr/a Collantes Estevez, Eduardo

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

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

PI: Dr/a Escudero Contreras, Alejandro

2703.Spanish Registry of psoriatic arthritis. PI: Dr/a López Montilla, Mª Dolores

2702. Validation of the EARP questionnaire for the detection of psoriatic arthritis in the Spanish population. VALS Study. PI: Dr/a López Montilla, M<sup>a</sup> Dolores

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

2817. Clinical applicability of a standardised dose-reduction protocol in patients with diagnosed rheumatoid arthritis (RA) displaying persistent clinical remission with anti-TNF therapy.

PI: Dr/a Font Ugalde, Pilar

2880.Spanish Registry of adverse events in biological and biosimilar therapies in rheumatic illnesses. Phase III PI: Dr/a Collantes Estevez, Eduardo

3160.0bservational study of the reproducibility of UCOTRACK, an automated system for measuring mobility in patients with axial spondyloarthritis.

PI: Dr/a Collantes Estevez, Eduardo

3161.An Observational, Prospective Cohort Stury to Evaluate Safety and Efficacy of RemsimaTM in Patients with Rheumatoid Arthritis. PI: Dr/a Escudero Contreras, Alejandro



# **GC6** • New therapies in cancer

# HIGHLIGHTS



# **Team Leaders**

# **Principal Investigator (PI)** Enrique Aranda Aguilar

earandaa@seom.org CIBER on Cancer (CIBER-ONC) PAIDI CTS-234 Scientific Group

**Co-Principal Investigator (Co-PI)** Antonio Rodríguez Ariza *Nicolás Monardes Contract* 

**Emerging Researcher (ER)** Juan Rafael de la Haba Rodríguez

# Researchers

Barneto Aranda; Isidoro C. Cano Osuna; María Teresa Fuentes Vaamonde; Elena Gomez España; María Auxiliadora Méndez Vidal; María José Moreno Vega; Alberto Luis Porras Quintela; Ignacio Rubio Pérez; María Jesús Sánchez Mauriño; Pedro Varo Sánchez; Gema Mª Villar Pastor; Carlos Martinez Peinado; Antonio Conde Perez; Francisco Manuel López Sanchez; Laura María

# **Post-Doctoral Researchers**

Cañas Rodriguez; Amanda Guil Luna; Silvia Valverde Estepa; Araceli

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Gómez Rodríguez, Estefanía Gómez Solís; Ángel Mellado Fuentes; Ana María Mena Osuna; Rafael Morales Estévez; Cristina Navas Navas; Patricia Ortíz Morales; María José Peñarando Saez; Jon Toledano Fonseca; Marta

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

Díaz Díaz; Mª Ángeles Hernández Nieto; Vanesa Jaraba Mezquida; Isabel Leña Barranco; Amalia López García; María Marín Serrano; Jacinta Marín Serrano; María José Mesa Blanco ; Mª Pilar Miranda García; Rosario Rodríguez De Julián; Sonia

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 reported the development of predictive biomarkers of response to antiangiogenic therapy. We participate very actively in the development of new therapeutic strategies using drugs aimed at specific targets. To achieve this, we are currently studying the association between antitumoral immune response and response to antiangiogenic therapy in cancer, to define predictive markers of response to antiangiogenic drugs. 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 cancer. 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. Results in our laboratory data support the hypothesis that the metabolism of nitric oxide (NO) plays an important role in the onset and progression of cancer, confirming a close relationship between NO and stem/mesenchymal characteristics in tumors. Therefore the main objective in this area is to characterize the mechanisms by which NO is involved in the onset and progression of cancer, and identify new therapeutic strategies for the treatment of this disease. Finally, our group is actively performing clinical validation studies to assess whether the determination of RAS mutational status using liquid biopsy tools may optimize the rational use of anti-EGFR therapies in colorectal cancer. Likewise, our group is applying liquid biopsy tools in other gastrointestinal tumors such as pancreatic cancers. Also, more translational studies are being undertaken in our laboratory to explore other plasma components, such as miRNAs and exosomes.

#### **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

Canas A, Lopez-Sanchez LM, Penarando J, Valverde A, Conde F, Hernandez V, Fuentes E, Lopez-Pedrera C, de la Haba-Rodriguez JR, Aranda E, Rodriguez-Ariza A.Altered S-nitrosothiol homeostasis provides a survival advantage to breast cancer cells in HER2 tumors and reduces their sensitivity to trastuzumab.. BIOCHIMICA ET BIOPHYSICA ACTA-MOLEC-ULAR BASIS OF DISEASE.2016.1862(4):601-10. IF:5,158 Q:1

Perez-Sanchez C, Aguirre MA, Ruiz-Limon P, Barbarroja N, Jimenez-Gomez Y, de la Rosa IA, Rodriguez-Ariza A, Collantes-Estevez E, Segui P, Velasco F, Cuadrado MJ, Teruel R, Gonzalez-Conejero R, Martinez C, Lopez-Pedrera Ch.'Atherothrombosis-associated microRNAs in Antiphospholipid syndrome and Systemic Lupus Erythematosus patients.'Scientific Reports.2016.6:31375. IF:5,228

Morales-Estevez C, De la Haba-Rodriguez J, Manzanares-Martin B, Porras-Quintela I, Rodriguez-Ariza A, Moreno-Vega A, Ortiz-Morales MJ, Gomez-Espana MA, Cano-Osuna MT, Lopez-Gonzalez J, Chia-Delgado B, Gonzalez-Fernandez R, Aranda-Aguilar E.KIR Genes and Their Ligands Predict the Response to Anti-EGFR Monoclonal Antibodies in Solid Tumors. Frontiers in Immunology.2016.(7):561. IF:5,695 O:1 Barrios P, Losa F, Gonzalez-Moreno S, Rojo A, Gomez-Portilla A, Bretcha-Boix P, Ramos I, Torres-Melero J, Salazar R, Benavides M, Massuti T, Aranda E.Recommendations in the management of epithelial appendiceal neoplasms and peritoneal dissemination from mucinous tumours (pseudomyxoma peritonei).Clinical & Translational Oncology.2016.18(5):437-448. IF:2,075 Q:3

#### **In Collaboration**

Gianni L, Pienkowski T, Im YH, Tseng LM, Liu MC, Lluch A, Staroslawska E, de la Haba-Rodriguez J, Im SA, Pedrini JL, Poirier B, Morandi P, Semiglazov V, Srimuninnimit V, Bianchi GV, Magazzu D, McNally V, Douthwaite H, Ross G, Valagussa P.5-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 2 randomised trial.Lancet Oncology.2016.17(6):791-800. IF:26,509 Q:1 D1

Van Cutsem E, Cervantes A, Adam R, Sobrero A, Van Krieken JH, Aderka D, Aranda Aguilar E, Bardelli A, Benson A, Bodoky G, Ciardiello F, D'Hoore A, Diaz-Rubio E, Douillard JY, Ducreux M, Falcone A, Grothey A, Gruenberger T, Haustermans K, Heinemann V, Hoff P, Kohne CH, Labianca R, Laurent-Puig P, Ma B, Maughan T, Muro K, Normanno N, Osterlund P, Oyen WJG, Papamichael D, Pentheroudakis G, Pfeiffer P, Price TJ, Punt C, Ricke J, Roth A, Salazar R, Scheithauer W, Schmoll HJ, Tabernero J, Taieb J, Tejpar S, Wasan H, Yoshino T, Zaanan A, Arnold D.ESMO consensus guidelines for the management of patients with metastatic colorectal cancer.Annals Of Oncology.2016.27(8):1386-1422. IF:9,269 Q:1 D1

Lindemann K, Kristensen G, Mirza MR, Davies L, Hilpert F, Romero I, Ayhan A, Burges A, Rubio MJ, Raspagliesi F, Huizing M, Creemers GJ, Lykka M, Lee CK, Gebski V, Pujade-Lauraine E.Poor concordance between CA-125 and RE-CIST at the time of disease progression in patients with platinum-resistant ovarian cancer: analysis of the AURELIA trial.Annals of Oncology.2016.27(8):1505-10. IF:9,269 O:1 D1

Perez-Valderrama B, Arranz Arija JA, Rodriquez Sanchez A, Pinto Marin A, Borrega Garcia P, Castellano Gaunas DE, Rubio Romero G, Maximiano Alonso C, Villa Guzman JC, Puertas Alvarez JL, Chirivella Gonzalez I, Mendez Vidal MJ, Juan Fita MJ, Leon-Mateos L, Quintela ML, Dominguez RG, Garcia JMJ, de Mendizabal EV, Sorrosal JJL, Carbonero IG, del Alba AG, Rodriguez CS, Gallego PJ, Garcia JAM, Marrero RDG, Borau PG, Lobera CS, Palau CM, Brea ML, Parra EMF, Torras OR, Badiola LB, Estevez SV, Larriba JLG.Validation of the International Metastatic Renal-Cell Carcinoma Database Consortium (IMDC) prognostic model for firstline pazopanib in metastatic renal carcinoma: the Spanish Oncologic Genitourinary Group (SOGUG) SPAZO study.Annals of Oncology.2016.27(4):706-711. IF:9,269

Q:1 D1

Alba E, Lluch A, Ribelles N, Anton-Torres A, Sanchez-Rovira P, Albanell J, Calvo L, Lopez Garcia-Asenjo JA, Palacios J, Ignacio Chacon J, Ruiz A, De la Haba-Rodriguez J, Segui-Palm-



<sup>∩.0</sup> 

er MA, Cirauqui B, Margeli M, Plazaola A, Barnadas A, Casas M, Caballero R, Carrasco E, Rojo F.High Proliferation Predicts Pathological Complete Response to Neoadjuvant Chemotherapy in Early Breast Cancer.Oncologist.2016.21(2):150-155. IF:4,789 Q:1

Caba O, Irigoyen A, Jimenez-Luna C, Benavides M, Ortuno FM, Gallego J, Rojas I, Guillen-Ponce C, Torres C, Aranda E, Prados J.Identification of gene expression profiling associated with erlotinib-related skin toxicity in pancreatic adenocarcinoma patients.Toxicology and Applied Pharmacology.2016.311:113-116. IF:3,847 Q:1

Camps C, Albanell J, Anton A, Aranda E, Carrato A, Cassinello J, Castellano D, Cruz JJ, Garrido P, Guillem V, Gravalos C, Lopez G, Llorente C, Lorenzo A, Lluch A, Ignacio E, Diaz-Rubio E.Quality Indicators to Assure and Improve Cancer Care in Spain Using the Delphi Technique.Journal of The National Comprehensive Cancer Network.2016.14(5):553-558. IF:4,262 Q:1

Ortea I, Rodriguez-Ariza A, Chicano-Galvez E, Arenas Vacas MS, Jurado Gamez B.Discovery of potential protein biomarkers of lung adenocarcinoma in bronchoalveolar lavage fluid by SWATH MS data-independent acquisition and targeted data extraction.Journal Of Proteomics. 2016.138:106-14. IF:3,867

Q:1

Gonzalez-Martin A, Alba E, Ciruelos E, Cortes J, Llombart A, Lluch A, Andres R, Alvarez I, Aramenda JM, Ayala de la Pena F, Barnadas A, Batista N, Calvo L, Galve E, Garcia-Palomo A, Garcia-Saenz JA, de la Haba J, Lopez R, Lopez-Vivanco G, Martinez-Janez N, de Duenas EM, Plazaola A, Rodriguez-Lescure A, Ruiz M, Sanchez-Rovira P, Santaballa A, Segui MA, Tusquets I, Zamora P, Martin M.Nab-Paclitaxel in Metastatic Breast Cancer: Defining the Best Patient Profile.Current Cancer Drug Targets.2016.16(5):415-428. IF:3,707

Q:2

Lainez N, Garcia-Donas J, Esteban E, Puente J, Isabel Saez M, Gallardo E, Pinto-Marin A, Vazquez-Estevez S, Leon L, Garcia-Carbonero I, Suarez-Rodriguez C, Molins C, Climent-Duran MA, Lazaro-Quintela M, Gonzalez del Alba A, Mendez-Vidal MJ, Chirivella I, Afonso FJ, Lopez-Brea M, Sala-Gonzalez N, Domenech M, Basterretxea L, Santander-Lobera C. Gil-Arnaiz I. Fernandez O. Caballero-Diaz C, Mellado B, Marrupe D, Garcia-Sanchez J, Sanchez-Escribano R, Fernandez Parra E, Villa Guzman JC, Martinez-Ortega E, Gonzalez MB, Moran M, Suarez-Paniagua B, Lecumberri MJ, Castellano D.Impact on clinical practice of the implementation of guidelines for the toxicity management of targeted therapies in kidney cancer. The protect-2 study.BMC Cancer 2016 16:135

IF:3,265

Q:2

Puente J, Garcia del Muro X, Pinto A, Lainez N, Esteban E, Arranz JA, Gallardo E, Mendez MJ, Maroto P, Grande E, Suarez C.Expert Recommendations for First-Line Management of Metastatic Renal Cell Carcinoma in Special Subpopulations.Targeted Oncology. 2016.11 (2): 129-141. IF:3,197

Q:2

Aldecoa I, Atares B, Tarragona J, Bernet L, Sardon JD, Pereda T, Villar C, Mendez MC, Gonzalez-Obeso E, Elorriaga K, Alonso GL, Zamora J, Planell N, Palacios J, Castells A, Matias-Guiu X, Cuatrecasas M.Molecularly determined total tumour load in lymph nodes of stage I-II colon cancer patients correlates with high-risk factors. A multicentre prospective study.Virchows Archiv.2016.469(4):385-3940. IF:2,627

Q:2

Munoz-Casares FC, Medina-Fernandez FJ, Arjona-Sanchez A, Casado-Adam A, Sanchez-Hidalgo JM, Rubio MJ, Ortega-Salas R, Munoz-Villanueva MC, Rufian-Pena S, Briceno FJ.Peritonectomy procedures and HIPEC in the treatment of peritoneal carcinomatosis from ovarian cancer: Long-term outcomes and perspectives from a high-volume center.European Journal Of Surgical Oncology.2016.42(2):224-33. IF:2,94

Q:2

Gonzalez-Flores E, Losa F, Pericay C, Polo E, Rosello S, Safont MJ, Vera R, Aparicio J, Cano MT, Fernandez-Martos C.SEOM Clinical Guideline of localized rectal cancer (2016).Clinical & Translational Oncology.2016.18(12):1163-1171. IF:1,74 Q:3

# **Research Funding**

#### National

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

Aranda Aguilar, E. Design and production of biomimetic microfluidic devices for the development of predictors in anti-angiogenic therapy for cancer. Funding agency: FUN-DACION 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

Rodríguez Ariza, A. Proteomic identification of biomarkers defining molecular subtypes of colorectal cancer and their possible use as prognostic or therapy-response factors. Funding agency: FUNDACIÓN SALUD 2000. Reference: 15-MS-002

Rodríguez Ariza, A. Development of anti-cancer stem cell (CSC) drugs by screening synthetic libraries using inhibitors of GPCR kinase and the NFAT-calcineurin interaction.Funding agency: Ministry of Economy, Innovation, Science and Employment (MINECO). Reference: RTC-2015-3386-1\_2

De la Haba JR. Epigenetic profile in cancer patients with increased blood pressure secondary to anti-VEGF treatment.Funding agency: Institute Carlos III Health (ISCIII). Reference: PI15/00516

Aranda Aguilar, E. The association among anti-tumor immunity, the renin-angiotensin system and response to antiangiogenic therapy in colorectal cancer. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI16/01271 Expected starting date:2017

Aranda Aguilar, E. CIBER-OBN.Funding agency: Institute Carlos III Health (ISCIII). Reference: CB16/12/00349 Expected starting date:2017

Rodríguez Ariza, A. Relationships between nitric oxide and molecular subtypes in colorectal cancer: identification of new therapeutic strategies. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI16/01508 Expected starting date:2017

#### 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

Aranda Aguilar, E. Microangiothecan. Funding Agency: CIBER-BBN. Reference: Ciberbbn-Imibic14-1

#### **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 AGTR-1. Funding agency: Treatment of digestive tumours (TTD Group). Reference: PSS.0052

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

Barneto Aranda, I. BRAF project. Funding agency: Glaxosmithkline, S.A. Reference: PSS.0057

Aranda Aguilar, E. Oncobeam Contract Centre of excellence. Funding agency: Sysmex España S.L. Reference: PSS.0108

Díaz López, C. Convidien Agreement.Funding agency: Covidien Spain S.L.Reference: PSS.0122 Aranda Aguilar, E. Tactics Agreement. Funding agency:Tactics Medicina Y Desarrollo, S.L.Reference: PSS.0140

Aranda Aguilar, E. TTD Agreement.Funding agency: Treatment of digestive tumours (TTD Group). Reference: PSS.0147

Aranda Aguilar, E. Boehringer Agreement. Funding agency: Boehringer Ingelheim International Gmbh. Reference: PSS.0153

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:CCB.0028

Villa Pastor, C. Roche Agreeement. Funding agency: Roche Farma, S.A.Reference:C-CB.0041

Sánchez Mauriño, P.Roche Agreeement. Funding agency: Roche Farma, S.A.Reference:CCB.0069

Aranda Aguilar, E. Rovi Agreement. Funding agency: Laboratorios Farmaceuticos Rovi, SA. Reference:CCB.0094

Aranda Aguilar, E. FS2000 Agreement.Funding agency: Fundación Salud 2000. eference:CCB.0119

#### **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.

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

0090/07.An open, multicenter, randomized, phase III study of lapatinib, trastuzumab sequentially administered or administered in combination as adjuvant treatment in a patient with HER2/ERbB2-positive breast cancer. PI: Dr/a De la Haba Rodríguez, Juan Rafael

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. Pl: Dr/a Rubio Pérez, María Jesús

0255/08. A Randomized, Open Label, Multi-center Phase III Study to Evaluate the Efficacy and Safety of Nilotinib Versus Imatinib in Adult Patients With Unresectable or Metastatic Gastrointestinal Stromal Tumors (GIST). PI: Dr/a Aranda Aguilar, Enrique 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.

Pl: 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

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

0172/11. A Randomized, Multi-Center Cross-Over Study to Evaluate Patient Preference and Health Care Professional (HCP) Satisfaction With Subcutaneous (SC) Administration of Trastuzumab in HER2-Positive Early Breast Cancer (EBC).

PI: Dr/a Porras Quintela, Ignacio

0190/11.Phase II Clinical Trial of Dovitinib (TKI-258) in First-line Metastatic or Locally Advanced Non-resectable Adrenocortical Carcinoma. PI: Dr/a Méndez Vidal, María José

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

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.

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

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).

Pl: 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.

Pl: 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

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.

Pl: 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.

Pl: 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. Pl: 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

trial of PROSTVAC-V/F ± FEC-GM in patients with asymptomatic or minimally symptomatic castration-resistant prostate cancer. PI: Dr/a Méndez Vidal, María José

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 Da-



comitinib (PF-00299804) vs. Gefitinib in firstline treatment of locally advanced or metastatic non-small cell lung cancer in patients with activating mutation(s) of the epidermal growth factor (EGF) receptor.

PI: Dr/a Barneto Aranda, Isidoro

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

PI: Dr/a Aranda Aguilar, Enrique

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

65/13. Neoadjuvant Chemotherapy With Nab-paclitaxel in Women With HER2-negative High-risk Breast Cancer " ETNA (Evaluating Treatment With Neoadjuvant Abraxane) PI: Dr/a De la Haba Rodríguez, Juan Rafael

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 plati-

num-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).

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

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

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, María José

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, María José

0312/13. A Phase II Randomized Clinical Trial Evaluating Neoadjuvant Therapy Regimens With Weekly Paclitaxel Plus Neratinib or Trastuzumab or Neratinib and Trastuzumab Followed by Doxorubicin and Cyclophosphamide With Postoperative Trastuzumab in Women With Locally Advanced HER2-Positive Breast Cancer

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

0323/13. A Study of MEK162 vs. Physician's Choice Chemotherapy in Patients With Lowgrade Serous Ovarian, Fallopian Tube or Peritoneal Cancer.

PI: Dr/a Rubio Pérez, María Jesús

0333/13. A Randomized Phase III, Factorial Design, of Cabazitaxel and Pelvic Radiotherapy in Patients With Localized Prostate Cancer and High-risk Features of Relapse PI: Dr/a Méndez Vidal, María José

0036/14. A Phase II randomized, double-blind study of neoadjuvant 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 highrisk 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

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, María José

0267/14. Phase II multicenter study that analyzes the predictive value of response to EN-ZALUTAMIDE fusion gene TMPRSS2 -ETS in patients with metastatic CRPC previously treated with chemotherapy. PI: Dr/a Méndez Vidal, María José

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

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

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, María José

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 Pl: 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, María José

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

PI: Dr/a Rubio Pérez, María Jesús

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

0019/15 .Phase III, randomized, open MPD-L3280A (anti PD-L1) in combination with BEV-AZUMAB compared to sunitinib in patients with advanced untreated renal cell carcinoma . PI: Dr/a Méndez Vidal, María José

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

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 + (PARSIFAL 1) PI: Dr/a De La Haba Rodríguez, Juan Rafael

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. Pl: Dr/a Rubio Pérez, María Jesús

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. Pl: 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

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

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 Pl: 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

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

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

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

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

0233/15. Randomised phase II study comparing, as first-line chemotherapy, single-agent oral vinorelbine administered with two different schedules in patients with advanced breast cancer. TempoBreast 1.

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

0256/15. Randomized, double-blind, phase iii trial olaparib vs. Placebo patients with advanced figo stage iiib-iv high grade serious or endometrioid ovarian, fallopian tube, or peritoneal cancer treated standard first-line treatment.

PI: Dr/a Rubio Pérez, María Jesús

0261/15.A phase III Trial of postoperative chemotherapy or no further treatment for patients with node-negative stage I-II intermediate or high risk endometrial cancer. PI Dr/a Rubio Pérez, María Jesús

0264/15. A Phase 2a Randomized, Open-label Study to Assess the Safety, Tolerability, and Efficacy of BAX69 in Combination With 5-FU/ Leucovorin or Panitumumab Versus Standard of Care in Subjects With Metastatic Colorectal Cancer.

Pl: Dr/a Aranda Aguilar, Enrique

0265/15. Safety and efficacy of LONQUEX®a (lipegfilgrastim) versus pegfilgrastim (Neulasta®, Amgen Inc.) and placebo in patients with non-microcytic lung cancer receiving first-line chemotherapy.

PI: Dr/a Barneto Aranda, Isidoro

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

0371/15.Estudio en Fase II con MPDL3280A preoperatorio en carcinoma operable de células transicionales de vejiga (ABACUS). Pl: Dr/a Méndez Vidal, María José

0015/16. An Open-label, Randomised, Non-comparative Phase 2 Study Evaluating S 95005 (TAS-102) Plus Bevacizumab and Capecitabine Plus Bevacizumab in Patients With Previously Untreated Metastatic COlorectal Cancer Who Are Non-eligible for Intensive Therapy

PI: Dr/a Aranda Aguilar, Enrique

0018/16. A Phase III, Multicenter, Randomized, Placebo-Controlled Study of Atezolizumab (Anti-PD-L1 Antibody) in Combination With Nab-Paclitaxel Compared With Placebo With Nab-Paclitaxel for Patients With Previously Untreated Metastatic Triple-Negative Breast Cancer

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

\*2898 A Phase III Double-Blinded, Placebo Controlled Study of Xilonix for Improving Survival in Metastatic Colorectal Cancel (Trial). Pl: Dr/a Aranda Aguilar, Enrique

\*3246 Estudio fase 2 de eficacia y seguridad de Niraparib en hombres con cáncer de próstata metastásico resistente a castración y anomalías en la reparación de AND. Pl: Dr/a Méndez Vidal, María José

\*2893 EUTROC-PiSARRO. p53 Suppressor Activation in Recurrent High Grade Serous Ovarian Cancer, a Phase Ib/II Study of Systemic Carboplatin/Pegylated Liposomal Doxorubicin Combination Chemotherapy With or Without APR-246.

PI: Dr/a Rubio Pérez, María Jesús

\*3001. A Phase 3, Randomized, Controlled, Multi-Center, Open-Label Study to Compare Tivozanib Hydrochloride to Sorafenib in Subjects With Refractory Advanced Renal Cell Carcinoma.

PI: Dr/a Méndez Vidal, María José

\*3183. A Phase 3, Multicenter, Randomized, Open-label Study Of Avelumab (msbO010718c) Alone Or In Combination With Pegylated Lipossomal Doxorubicin Versus Pegylated Liposomal Doxorubicin Alone In Patients With Platinum-resistant/Refractory Ovarian Cancer. Pl: Dr/a Rubio Pérez, María Jesús

\*3123. A Randomized, Multicenter, Double Blind, Phase III Study of Adjuvant Nivolumab or Placebo in Subjects With Resected Esophageal, or Gastroesophageal Junction Cancer. Pl: Dr/a Aranda Aguilar, Enrique

\*3240 A randomised, Parallel, Double Blinded Study to Compare the Efficacy and Safety of FKB238 to Avastin in 1st line treatment for patients with Advanced/Recurrent Non-Squamous non-small cell lung cancer in combination of paclitaxel and carboplatin. Pl: Dr/a Barneto Aranda, Isidoro

\*3267. A Study to Investigate Efficacy and Safety of Cobimetinib Plus Atezolizumab and Atezolizumab Monotherapy Versus Regorafenib in Participants With Metastatic Colorectal Adenocarcinoma

Pl: Dr/a Aranda Aguilar, Enrique

\*3325. A Study of Atezolizumab in Locally Advanced or Metastatic Urothelial or Non-Urothelial Carcinoma of the Urinary Tract. PI: Dr/a Méndez Vidal, María José

\*3238 Multicenter, Double-Blind, Randomized, Parallel-Group Study to Assess the Efficacy and Safety of MYL-14020 Compared with Avastin, in the First-line Treatment of Patients with Stage IV Non-Squamous Non-Small Cell Lung Cancer PI: Dr/a Barneto Aranda, Isidoro

\*3247. Phase III Randomized Clinical Trial of Lurbinectedin (PM01183)/Doxorubicin (DOX) Versus Cyclophosphamide (CTX), Doxorubicin (DOX) and Vincristine (VCR) (CAV) or Topotecan as Treatment in Patients With Small-Cell Lung Cancer (SCLC) Who Failed One Prior Platinum-containing Line (ATLANTIS Trial). PI: Dr/a Barneto Aranda, Isidoro

\*3189. A Study to Evaluate the Efficacy and Safety of Trastuzumab Emtansine in Combination With Atezolizumab or Atezolizumab-Placebo in Participants With Human Epidermal Growth Factor-2 (HER2) Positive Locally Advanced or Metastatic Breast Cancer Who Have Received Prior Trastuzumab and Taxane Based Therapy (KATE2).

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

\*3333. A Phase III, Multicenter, Randomized, Placebo-Controlled, Double-Blind Study of Atezolizumab (Anti-PD-L1 Antibody) as Adjuvant Therapy in Patients With Renal Cell Carcinoma at High Risk of Developing Metastasis Following Nephrectomy. PI: Dr/a Méndez Vidal, María José

\*3122. A Randomized Phase 2 Study Comparing Different Dose Approaches of Induction Treatment (First Cycle) of Regorafenib in Metastatic Colorectal Cancer (mCRC) Patients PI: Dr/a Aranda Aquilar, Enrique

\*3220. A Phase II Trial to Assess FOLF-IRI+Aflibercept Efficacy in Patients With Oxaliplatin-pretreated Metastatic Colorectal Cancer With or Without ACE Polymorphisms PI: Dr/a Gómez España, Maria Auxiliadora

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

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 firstline treatment.

PI: Dr/a Méndez Vidal, María José

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, María José

2524. Translational, observational and prospective study to determine factors predicting the anti-angiogenic efficacy of bemiparin in patients with advanced cancer. PI: Dr/a Sánchez Mauriño, Pedro

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

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. Clinical profile and therapeutic management of patients with pancreas cancer; Registry of Hospital Medical Oncology services in Spain.

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. Pl: 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

3074. Clinical evaluation of OncoBEAM using an extended panel of 34 RAS mutations. comparison of RAS mutation detection in circulating tumor DNA and sample tissue in patients with metastatic colorectal cancer. PI: Dr/a Aranda Aguilar, Enrique

3221. Multi-centre observational prospective study on fatigue- and hand-foot syndrome-related quality of life in patients with metastatic renal cell carcinoma receiving a tyrosine kinase inhibitor as first-line treatment. PI: Dr/a Méndez Vidal, María José

3223. Prospective registry study in patients with unresectable locally advanced or metastatic breast cancer (MBC). RegistEM Study PI: Dr/a De la Haba Rodríguez, Juan Rafael

3295. Validation of the International Metastatic Renal-Cell Carcinoma Database Consortium (IMDC) prognostic model for second-line directed therapy (ITC/mTOR inhibitors) following first-line treatment with pazopanib (SPAZO-2) PI: Dr/a Méndez Vidal, María José

3252. Retrospective observational study on the treatment of metastatic colorectal cancer (mCRC) in Spain. PI: Dr/a Aranda Aquilar. Enrique

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# **GC7** • Nephrology. Cell damage in chronic inflammation

# HIGHLIGHTS



# **TeamLeaders**

# Principal Investigator (PI) Pedro Aljama García pedro.aljama.sspa@juntadeandalucia.es Spanish Renal Research Network (REDinREN) PAIDI CTS-260 Scientific Group

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

# Researchers

Álvarez De Lara Sánchez; Mª Antonia Espinosa Hernández; Mario Navarro Cabello; María Dolores Martin Malo; Alejandro Rodríguez Benot; Alberto Santamaría Olmo; Rafael Soriano Cabrera; Sagrario

# **Post-Doctoral Researchers**

Agüera Morales; María Luisa Ariza Fuentes; Francisco Javier Buendia Bello; Paula

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Arencibia Pérez; Ney Calle Mafla; Oscar Andrés Carmona Muñoz; Andrés Crespo Montero; Rodolfo Esquivias de Motta; Elvira García Montemayor; Victoria Eugenia González Burdiel; Luis Hurtarte Sandoval; Aldo René López Andreu; María Luna Ruiz; Carlos Rabasco Ruiz; Cristina Rodelo Haad;Cristian Roberto

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

Guerrero Pavón; Fátima Jiménez Moral; María José López López; Isabel Moyano García; Mª Rosa Robles López; Ana Isabel Sánchez-Agesta Martínez; Marina



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

Rodriguez M, Salmeron MD, Martin-Malo A, Barbieri C, Mari F, Molina RI, Costa P, Aljama P.A New Data Analysis System to Quantify Associations between Biochemical Parameters of Chronic Kidney Disease-Mineral Bone Disease.Plos One.2016.11(1):-e0146801. IF:3,057 Q:1

Buendia P, Ramirez R, Aljama P, Carracedo J.Klotho Prevents Translocation of NF kappa B.KLOTHO colecction: Vitamins and Hormones.2016.101:119-50. IF:2,161

Q:3

Luna C, Alique M, Navalmoral E, Noci MV, Bohorquez-Magro L, Carracedo J, Ramirez R.Aging-associated oxidized albumin promotes cellular senescence and endothelial damage. Clinical Interventions In Aging.2016.11():225-236. IF:2,133 Q:3

Cabezas-Reina CJ, Esquivias-de-Motta E, Estevez-Maria JC, Sanchez-Agesta-Martinez M.Amyloid angiopathy in the context of hemodialysis: An unknown field.Nefrologia.2016.36(5):571-572. IF:1,207 Q:4

Aguere ML, Hurtarte AR, de Lara MAA, Aumente MD, Carmona A, Carracedo J, Aljama P, Benot AR.Donor-Specific Antibodies After Starting Hemodialysis in Nonrenal Solid Organ Transplant Recipients: Role of TH17.Transplantation Proceedings.2016.48():2920-2923. IF:0,867 Q:4

Arencibia N, Aguera ML, Rodelo C, Lopez I, Sanchez-Ageste M, Hurtarte A, Navarro MD, Rodriguez-Benot A.Short-Term Outcome of Untreated Versus Treated Asymptomatic Bacteriuria in Renal Transplant Patients.Transplantation Proceedings.2016.48():2941-2943. IF:0,867

Q:4

# **In Collaboration**

Maduell F, Ramos R, Varas J, Martin-Malo A, Molina M, Perez-Garcia R, Marcelli D, Moreso F, Aljama P, Merello JI.Hemodialysis patients receiving a greater Kt dose than recommended have reduced mortality and hospitalization risk.Kidney International.2016.90():1332-1341. IF:7,683 O:1 D1

Fakhouri F, Hourmant M, Campistol JM, Cataland SR, Espinosa M, Gaber AO, Menne J, Minetti EE, Provot F, Rondeau E, Ruggenenti P, Weekers LE, Ogawa M, Bedrosian CL, Legendre CM.Terminal Complement Inhibitor Eculizumab in Adult Patients With Atypical Hemolytic Uremic Syndrome: A Single-Arm, Open-Label Trial.American Journal Of Kidney Diseases.2016.68(1):84-93. IF:6,269 Q:1 D1

Torre-Cisneros J, Aguado JM, Caston JJ, Almenar L, Alonso A, Cantisan S, Carratala J, Cervera C, Cordero E, Farinas MC, Fernandez-Ruiz M, Fortun J, Frauca E, Gavalda J, Hernandez D, Herrero I, Len O, Lopez-Medrano F, Manito N, Marcos MA, Martin-Davila P, Monforte V, Montejo M, Moreno A, Munoz P, Navarro D, Perez-Romero P, Rodriguez-Bernot A, Rumbao J, San Juan R, Vaquero JM, Vidal E .Management of cytomegalovirus infection in solid organ transplant recipients: SET/GES-ITRA-SEIMC/REIPI recommendations. Transplantation Reviews.2016.30(3):119-43. IF:3,915 0;2

Arjona-Sanchez A, Cadenas-Febres A, Cabrera-Bermon J, Munoz-Casares FC, Casado-Adam A, Sanchez-Hidalgo JM, Lopez-Andreu M, Briceno-Delgado J, Rufian-Pena S.Assessment of RIFLE and AKIN criteria to define acute renal dysfunction for HIPEC procedures for ovarian and non ovarian peritoneal malignances.European Journal Of Surgical Oncology.2016.42(6):869-876. IF:2,94

Q:2

Perez-Garcia R, Palomares I, Merello JI, Ramos R, Maduell F, Molina M, Aljama P, Marcelli D.Hyponatraemia, mortality and haemodialysis: An unexplained association. Nefrologia.2016.36(1):42-50. IF:1,207 Q:4

Torres A, Torregrosa V, Marcen R, Campistol JM, Arias M, Hernandez D, Fernandez C, Esforzado N, Paschoalin R, Perez N, Garcia AI, Del Amo M, Pomes J, Gonzalez Rinne A, Marrero D, Pereza E, Henriquez F, Diaz JM, Silva I, Lopez V, Perello M, Ramos D, Beneyto I, Cruzado JM, Martinez Castelaok A, Bravo J, Rodriguez M, Diaz C, Crespo J, Anaya F, Rodriguezo ML, Cubero JJ, Pascual P, Romero R, Belmonte AA, Checa MD, Jimenez C, Escuin F, Crespo M, Mir M, Gomez G, Bayes B, Gonzalez MJ, Gutierrez A, Cuberes M, Rodriguez Benoit A, Garcia T, Llamas F, Ortega A, Conde JL, Gomez Alamillo C.Mineral metabolism disorders, vertebral fractures and aortic calcifications in stable kidney transplant recipients: The role of gender (EMITRAL study). Nefrologia.2016.36(3):255-267. IF:1,207 Q:4

Arenas-Bonille AJ, Campos-Hernandez JP, Carrasco-Valiente J, Marquez-Lopez FJ, Ruiz-Garcia JM, Sanchez-Gonzaleza A, Salamanca-Bustos JJ, Regueiro-Lopez JC, Navarro-Cabello MD, Requena-Tapia MJ.Influence of Donor and Recipient Ages in Survival of Simultaneous Pancreas-Kidney Transplantation.Transplantation Proceedings.2016.48:3033-3036. IF:0,867

Q:4

Mazuecos A, Alvarez A, Nieto A, Gentil MA, Cabello M, Rodriguez-Benot A, Gracia C, Gonzalez F, Castro P, Alonso M.Kidney Transplantation Results in Very Highly Sensitized Patients Included in a Virtual Crossmatch Program: Analysis of Kidney Pairs.Transplantation Proceedings.2016.48:2899-2902. IF:0,867

Q:4

Gentil MA, de la Nuez PC, Gonzalez-Corvillo C, de Gracia MG, Cabello M, Mazuecos MA, Rodriguez-Benot A, Ballesteros L, Osuna A, Alonso M.Non-Heart-Beating Donor Kidney Transplantation Survival Is Similar to Donation After Brain Death: Comparative Study With Controls in a Regional Program.Transplantation Proceedings.2016.48:2867-2870. IF:0,867

Q:4



Ramponi F, Ronco C, Mason G, Rettore E, Marcelli D, Martino F, Neri M, Martin-Malo A, Canaud B, Locatelli F.Cost-effectiveness analysis of online hemodiafiltration versus highflux hemodialysis.Clinicoeconomics And Outcomes Research.2016.8:531-540.

#### **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:Pl12/01866

Aljama García, P. Kidney Research Network **REDINRENFunding agency: Institute Carlos III** Health (ISCIII). Reference: RD12/0021/0011

Carracedo Añón, J. CD14+CD16+ and endothelial cell interaction mediated induction of vascular calcification in patients with chronic kidney disease Funding agency: Institute Carlos III Health (ISCIII). Reference: PI15/01785

Aljama García, P.Kidney Research Network REDINREN. Funding agency: Institute Carlos III Health (ISCIII). Reference: RD16/0009/0034. Expected starting date:2017

#### Regional

Carracedo Añón, 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

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

Soriano Cabrera,S. Role of Fgf3 in the progression of vascular damage associated to uremia:Basics and Clinics Studies.Funding agency: Regional Ministry of Health and Social Policy (CISPS)Reference: PI-0136-2016 Expected starting date:2017

#### **Contracts with Companies**

Aljama García, P.Agreement FMC. Funding agency: F.M.C. SERVICES ANDALUCIA, S.A. Reference: CCB.0114 2

Aljama García, P. Agreement FRESENIUS. Funding agency:FRESENIUS MEDICAL CARE ESPAÑA, S.A.Reference: CCB.0125

#### **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. Pl: Dr/a Santamaría Olmo, Rafael

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.

Pl: Dr/a Santamaría Olmo, Rafael

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, Mª Luisa

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/a 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/a Navarro Cabello; María 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 Álvarez De Lara Sánchez; María Antonia

0024/15.Multicentered 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

\*3274. A multicenter, single-arm study of the effects of atrasentan on apermatogenesis and testicular function. Pl: Dr/a Santamaría Olmo, Rafael

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

2079/2. A multinational, multicenter, observational, non-interventional study of patients with atypical hemolytic uremic syndrome (SHUA register).

PI: Dr/a Espinosa Hernández; Mario

2932. Scrutiny of FABRY disease in patients Segmental Focal Glomerulosclerosis. PI: Dr/a Espinosa Hernández; Mario

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.

Pl: Dr/a Soriano, 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



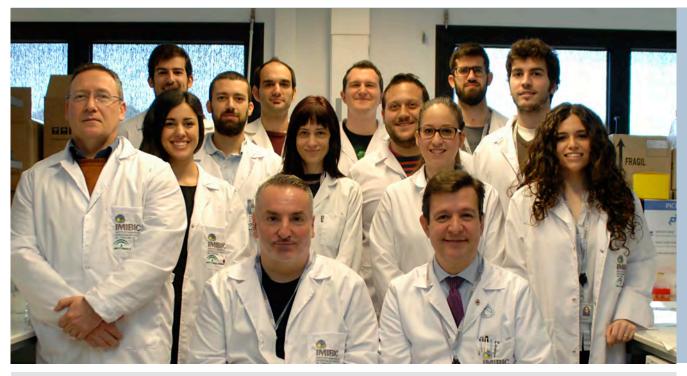
# **GC8** • Hormones and cancer

# HIGHLIGHTS









# **Team Leaders**

# Principal Investigator (PI)

Justo P. Castaño Fuentes justo@uco.es

IMIBIC's Scientific Director CIBER on Obesity and Nutrition (CI-BERobn) (Collaborator) PAIDI BIO-139 Scientific Group

**Co-Principal Investigator (Co-PI)** Francisco Gracia Navarro

**Co-Principal Investigator (Co-PI)** Raúl M. Luque Huertas Researchers Martínez Fuentes: Antonio Jesús

# **Post-Doctoral Researchers**

Gahete Ortiz; Manuel David Ibáñez Costa; Alejandro Moreno Fernández; Jesús Rincón Fernández-Pacheco; David Villa Osaba; Alicia

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Alhambra Expósito;María Rosa Alors Pérez; Emilia Mª Bathan; Mansfield Blanco Acevedo; Cristobal José Borges de Souza; Patricia Cabral Morais Sarmento Borges; André Del Río Moreno; Mercedes Fuentes Fayos; Antonio Carlos Gómez Gómez;Enrique Gómez Marin; María del Señor Herrera Martínez;Aura Dulcinea Herrero Aguayo; Vicente Hormaechea Agulla; Daniel Jiménez Vacas; Juan Manuel Martínez López; Ana Moreno Moreno; Paloma Pedraza Arevalo; Sergio Sáez Martínez; Prudencio Sánchez Medianero; Mª Teresa Spina; Andrea Toledano Delgado; Álvaro Vázquez Borrego; Mª Carmen

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

López López; Fernando



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

Hormaechea-Agulla D, Gomez-Gomez E, Ibanez-Costa A, Carrasco-Valiente J, Rivero-Cortes E, L-Lopez F, Pedraza-Arevalo S, Valero-Rosa J, Sanchez-Sanchez R, Ortega-Salas R, Moreno MM, Gahete MD, Lopez-Miranda J, Requena MJ, Castano JP, Luque RM.Ghrelin O-acyltransferase (GOAT) enzyme is overexpressed in prostate cancer, and its levels are associated with patient's metabolic status: Potential value as a non-invasive biomarker.Cancer Letters.2016.383(1):125-134. IF:5,992 Q:1 2

Luque RM, Cordoba-Chacon J, Pozo-Salas AI, Porteiro B, de Lecea L, Nogueiras R, Gahete MD, Castano JP.Obesity- and gender-dependent role of endogenous somatostatin and cortistatin in the regulation of endocrine and metabolic homeostasis in mice.Scientific Reports.2016.6():-37992. IF:5,228

Fernandez-Peralbo MA, Gomez-Gomez E, Calderon-Santiago M, Carrasco-Valiente J, Ruiz-Garcia J, Requena-Tapia MJ, de Castro MDL, Priego-Capote F.Prostate Cancer Patients-Negative Biopsy Controls Discrimination by Untargeted Metabolomics Analysis of Urine by LC-QTOF: Upstream Information on Other Omics. Scientific Reports.2016.(6):-38243. IF:5.228

Q:1

Q:1

Luque RM, Villa-Osaba A, L-Lopez F, Pozo-Salas AI, Sanchez-Sanchez R, Ortega-Salas R, de Lecea L, Alvarez-Benito M, Lopez-Miranda J, Gahete MD, Castano JP.Lack of cortistatin or somatostatin differentially influences DM-BA-induced mammary gland tumorigenesis in mice in an obesity-dependent mode.Breast Cancer Research.2016.18(1):29-29. IF:5,211 Q:1

Gahete, MD; Luque, RM; Castano, JP.Models of GH deficiency in animal studies.Best Practice & Research Clinical Endocrinology & Metabolism.2016.30(6):693-704. IF:5,07 Q:1

Sampedro-Nunez M, Luque RM, Ramos-Levi AM, Gahete MD, Serrano-Somavilla A, Villa-Osaba A, Adrados M, Ibanez-Costa A, Martin-Perez E, Culler MD, Marazuela M, Castano JP.Presence of sst5TMD4, a truncated splice variant of the somatostatin receptor subtype 5, is associated to features of increased aggressiveness in pancreatic neuroendocrine tumors. Oncotarget.2016.7(6):6593-608. IF:5,008 Q:1

Gahete MD, Rincon-Fernandez D, Duran-Prado M, Hergueta-Redondo M, Ibanez-Costa A, Rojo-Sebastian A, Gracia-Navarro F, Culler MD, Casanovas O, Moreno-Bueno G, Luque RM, Castano JP.The truncated somatostatin receptor sst5TMD4 stimulates the angiogenic process and is associated to lymphatic metastasis and disease-free survival in breast cancer patients.Oncotarget.2016.7(37):60110-60122. IF:5,008 Q:1 Ibanez-Costa A, Rivero-Cortes E, Vazquez-Borrego MC, Gahete MD, Jimenez-Reina L, Venegas-Moreno E, de la Riva A, Arraez MA, Gonzalez-Molero I, Schmid HA, Maraver-Selfa S, Gavilan-Villarejo I, Garcia-Arnes JA, Japon MA, Soto-Moreno A, Galvez MA, Luque RM, Castano JP.Octreotide and pasireotide (dis)similarly inhibit pituitary tumor cells in vitro.Journal Of Endocrinology.2016.231(2):135-145. IF:4,498

Q:1

Cordoba-Chacon J, Gahete MD, Pozo-Salas AI, de Lecea L, Castano JP, Luque RM.Cortistatin Is a Key Factor Regulating the Sex-Dependent Response of the GH and Stress Axes to Fasting in Mice.Endocrinology.2016.157(7):2810-23. IF:4,159 O:1

Villa-Osaba A, Gahete MD, Cordoba-Chacon J, de Lecea L, Castaño JP, Luque RM.Fasting modulates GH/IGF-I axis and its regulatory systems in the mammary gland of female mice: Influence of endogenous cortistatin.Mo-lecular and Cellular Endocrinoly.2016.(437):14-

24. IF:3,859 Q:2

Villa-Osaba A, Gahete MD, Cordoba-Chacon J, de Lecea L, Castano JP, Luque RM.Fasting modulates GH/IGF-I axis and its regulatory systems in the mammary gland of female mice: Influence of endogenous cortistatin.Molecular and Cellular Endocrinology.2016.434(C):14-24. IF:3,859 Q:2

Gahete MD, Vaquez-Borrego MC, Martinez-Fuentes AJ, Tena-Sempere E, Castano



JP, Luque RM.Role of the Kiss1/Kiss1r system in the regulation of pituitary cell function. Molecular and Cellular Endocrinology.2016. (438):100-106. IF:3,859 O;2

Moreno-Fernandez J, Gomez FJ, Moreno MAG, Castano JP.Clinical Efficacy of Two Different Methods to Initiate Sensor-Augmented Insulin Pumps: A Randomized Controlled Trial.Journal of Diabetes Research.2016.(2016):-4171789. IF:2,431 Q:3

Gomez EG, Hernandez JPC, Cazalilla M, Trivino F, Barbudo J, Prieto R, Tapia MJR.Partial thrombosis of the corpus cavernosum: should we dig deeper into coagulopathy disorders?. Andrologia.2016.48():1313-1316. IF:1,441 Q:3

Gomez-Gomez E, Malde S, Spilotros M, Shah PJ, Greenwell TJ, Ockrim JL.A tertiary experience of ileal-ureter substitution: Contemporary indications and outcomes.Scandinavian Journal Of Urology.2016.50(3):192-199. IF:1,346 Q:3

Valero-Rosa J, Campos-Hernandez JP, Carrasco-Valiente J, Gomez-Gomez E, Marquez-Lopez FJ, Ruiz-Garcia J, Garcia-Rubio JH, Requena-Tapia MJ, Prieto-Castro R.Prognostic value of penile colour doppler ultrasonography for recovering erectile function after radical prostatectomy.Actas Urologicas Espano-IaS.2016.40(8):507-512. IF:0,964

Q:4

Luque RM, Ibanez-Costa A, Sanchez-Tejada L, Rivero-Cortes E, Robledo M, Madrazo-Atutxa A, Mora M, Alvarez CV, Lucas-Morante T, Alvarez-Escola C, Fajardo C, Castano L, Gaztambide S, Venegas-Moreno E, Soto-Moreno A, Galvez MA, Salvador J, Valassi E, Webb SM, Pico A, Puig-Domingo M, Gilabert M, Bernabeu I, Marazuela M, Leal-Cerro A, Castano JP.The Molecular Registry of Pituitary Adenomas (REMAH): A bet of Spanish Endocrinology for the future of individualized medicine and translational research.Endocrinologia y Nutricion.2016.63(6):274-284. IE:0

#### **In Collaboration**

Gomez-Delgado F, Delgado-Lista J, Lopez-Moreno J, Rangel-Zuñiga OA, Alcala-Diaz JF, Leon-Acuña A, Corina A, Yubero-Serrano E, Torres-Peña JD, Camargo A, Garcia-Rios A, Caballero J, Castaño J, Ordovas JM, Lopez-Miranda J, Perez-Martinez P.Telomerase RNA Component Genetic Variants Interact With the Mediterranean Diet Modifying the Inflammatory Status and its Relationship With Aging: CORDIOPREV Study.Journals of Gerontoly. Series A, Biologycal Sciences and Medical Sciences.2016: pii: glw194

IF:5,476 Q:1 D1

Sandoval-Alzate HF, Agudelo-Zapata Y, Gonzalez-Clavijo AM, Poveda NE, Espinel-Pachon CF, Escamilla-Castro JA, Marquez-Julio HL, Alvarado-Quintero H, Rojas-Rodriguez FG, Arteaga-Diaz JM, Eslava-Schmalbach JH, Garces-Gutierrez MF, Vrontakis M, Castano JP, Luque RM, Dieguez C, Nogueiras R, Caminos JE.Serum Galanin Levels in Young Healthy Lean and Obese Non-Diabetic Men during an Oral Glucose Tolerance Test.Scientific Reports.2016.6():-31661. IF:5,228

Q:1

Rubio-Briones J, Borque A, Esteban LM, Iborra I, Lopez PA, Gil JM, Pallas Y, Fumado L, Martinez-Breijo S, Chantada V, Gomez E, Quicios C, Congregado CB, Medina R, Ortiz M, Montesino M, Clar F, Soto J, Campa JM.Preliminary results of the Spanish Association of Urology National Registry in Active Surveillance for prostate cancer.Actas Urologicas Espanolas.2016.40(1):3-10. IF:0,964

Q:4

Sanchez-Gonzalez A, Carrasco-Valiente J, Arenas-Bonilla AJ, Campos-Hernandez JP, Blanca-Pedregosa A, Ruiz-Garcia JM, Valero-Rosa J, Gomez-Gomez E, Salamanca-Bustos JJ, Navarro-Cabello D, Requena-Tapia MJ.Graft Survival in Patients Who Received Second Allograft, Comparing Those With or Without Previous Failed Allograft Nephrectomy.Transplantation Proceedings.2016. 48(9) :2895-2898 IF 0,867 Q:4

Messineo S, Laria AE, Arcidiacono B, Chiefari E, Huertas RML, Foti DP, Brunetti A.Cooperation between HMGA1 and HIF-1 Contributes to Hypoxia-Induced VEGF and Visfatin Gene Expression in 3T3-L1 Adipocytes.Frontiers In Endocrinology.2016.7:73. IE:0

# **Research Funding**

#### 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: 13-MS-007-CCB.0052

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

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

Gahete Ortiz, MD.Pathological Implication of aberrant alternative splicing in hepatocellular carcimona: Identification to predictive, prognostic and therapeutic markers. Funding agency: Institute Carlos III Health (ISCIII). Reference: CP15/00156

Castaño Fuentes, JP. Alterations in equipment of alternative splicing in pancreas cancer: Identifications of new diagnostics, prognostics and therapeutics biomarkers.Funding agency: Ministry of Economy and Competitiveness (MINECO).Reference: BFU2016-80360-R.

Luque Huertas, RM.New molecular mechanisms in the pathological interaction between obesity and prostate cancer: alternative splicing and miRNAs as potential biomarkers and therapeutic targets. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI16/00264

Expected starting date:2017

#### Regional

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

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

Castaño Fuentes, JP. Splicing alternative process in pituitary tumor pathology: A possible usefulness diagnostic and therapeutic effect. Funding agency: Sociedad Andaluza de Endocrinología, Diabetes y Nutrición. Reference:-SAEDYN15\_001

Luque Huertas, RM. Grant Mobility II: Protection of research results of Galileo innovation and technology transfer II Plan from Universidad de Córdoba. Funding agency: Universidad de Cordoba. Reference:II Plan Propio GALILEO

Martínez Fuentes, A. Presence and anti-tumoral activity of the KISS-1/KISS1-R system in pancreatic neuroendocrine tumors: potential as biomarker and therapeutic target. Funding agency: Regional Ministry of Health and Social Policy (CISPS). Reference: PI-0077-2016. Expected starting date:2017



# **GC9** • Nutrigenomics. Metabolic syndrome

# HIGHLIGHTS



# **Team Leader**

# Principal Investigator (PI)

José López Miranda jlopezmir@uco.es IMIBIC Deputy Scientific Director CIBER on Obesity and Nutrition (CI-BERobn) PAIDI CTS-525 Scientific Group

**Co- Principal Investigator (CO-PI)** Francisco Pérez Jiménez PAIDI CTS-212 Scientific Group

# Co- Principals Investigators (CO-PI)

Yolanda Almadén Peña Nicolás Monardes Contract Javier Delgado Lista Pablo Pérez Martínez

Emerging Researchers (ER): Antonio Camargo García Carmen Marín Hinojosa

# Researchers

Arenas De Larriva; Antonio Blanco Molina; Mª Ángeles Fernández De La Puebla; Rafael Ángel Fuentes Jiménez; Francisco Herruzo Gómez; Ezequiel López Jiménez; Luciano Navarro Martos; Vanesa Montero Pérez-Barquero; Manuel Pérez Caballero; Anabel Sánchez García; Esther Torres Peña; José David Torres Roldan; Amalia

# **Post-Doctoral Researchers**

Blanco Rojo; Ruth Criado García; Juan Cruz Teno; Cristina Delgado Casado; Nieves García Ríos; Antonio Gómez Delgado; Francisco Gómez Luna; Purificación Haro Mariscal; Carmen Mª Jiménez Morales; Anabel Peña Orihuela; Patricia Judith Rangel Zuñiga; Oriol Alberto Yubero Serrano; Elena Roncero Ramos; Irene

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Alcalá Díaz; Juan Francisco Corina Baba; Andreaa Jiménez Lucena; Rosa Santos Marcos, José Antonio Blancas Sánchez; Isabel María López Moreno, Javier Vaquero Álvarez; Manuel León Acuña; Ana Gcia-Carpintero Fdez-Pacheco; Sonia Jiménez Izquierdo; Rafael Manuel

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

De Lara Santos; Gloria Gavilán Sánchez; José Gutiérrez González; Antonio Manuel Morales Martínez; José Andrés Pérez Corral; Isabel Quintana Navarro; Gracia M<sup>a</sup> Redondo Garrido, Ana



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**

#### **Originals**

Blanco-Rojo R, Delgado-Lista J, Lee YC, Lai CQ, Perez-Martinez P, Rangel-Zuniga O, Smith CE, Hidalgo B, Alcala-Diaz JF, Gomez-Delgado F, Parnell LD, Arnett DK, Tucker KL, Lopez-Miranda J, Ordovas JM.Interaction of an S100A9 gene variant with saturated fat and carbohydrates to modulate insulin resistance in 3 populations of different ancestries.American Journal of Clinical Nutrition.2016.104(2):508-17. IF:6,703 O:1 D1

Blanco-Rojo R, Alcala-Diaz JF, Wopereis S, Perez-Martinez P, Quintana-Navarro GM, Marin C, Ordovas JM, van Ommen B, Perez-Jimenez F, Delgado-Lista J, Lopez-Miranda J.The insulin resistance phenotype (muscle or liver) interacts with the type of diet to determine changes in disposition index after 2 years of intervention: the CORDIOPREV-DIAB randomised clinical trial.Dlabetologia.2016.59(1):67-76. IF:6,206 Q:1 D1

Delgado-Lista J, Perez-Martinez P, Garcia-Rios A, Perez-Caballero AI, Perez-Jimenez F, Lopez-Miranda J.Mediterranean Diet and Cardiovascular Risk: Beyond Traditional Risk Factors.Critical Reviews in Food Science and Nutrition.2016.56(5):788-801. IF:5,492 Q:1 D1

Gomez-Delgado F, Delgado-Lista J, Lopez-Moreno J, Rangel-Zuñiga OA, Alcala-Diaz JF, Leon-Acuña A, Corina A, Yubero-Serrano E, Torres-Peña JD, Camargo A, Garcia-Rios A, Caballero J, Castaño J, Ordovas JM, Lopez-Miranda J, Perez-Martinez P.Telomerase RNA Component Genetic Variants Interact With the Mediterranean Diet Modifying the Inflammatory Status and its Relationship With Aging: CORDIOPREV Study.Journals of Gerontoly. Series A, Biologycal Sciences and Medical Sciences.2016.pii: glw194 IF:5.476

Q:1 D1

Martinez-Moreno JM, Herencia C, Montes de Oca A, Munoz-Castaneda JR, Rodriguez-Ortiz ME, Diaz-Tocados JM, Peralbo-Santaella E, Camargo A, Canalejo A, Rodriguez M, Velasco-Gimena F, Almaden Y.Vitamin D modulates tissue factor and protease-activated receptor 2 expression in vascular smooth muscle cells. Faseb Journal.2016.30(3):1367-1376. IF:5,299 Q:1 D1

Perez-Martinez P, Alcala-Diaz JF, Kabagambe EK, Garcia-Rios A, Tsai MY, Delgado-Lista J, Kolovou G, Straka RJ, Gomez-Delgado F, Hopkins PN, Marin C, Borecki I, Yubero-Serrano EM, Hixson JE, Camargo A, Province MA, Lopez-Moreno J, Rodriguez-Cantalejo F, Tinahones FJ, Mikhailidis DP, Perez-Jimenez F, Arnett DK, Ordovas JM, Lopez-Miranda J.Assessment of postprandial triglycerides in clinical practice: Validation in a general population and coronary heart disease patients.Journal of Clinical Lipidology.2016.10(5):1163-1171. IF:4,906 0-1 D1

Beltran-Aroca CM, Girela-Lopez E, Collazo-Chao E, Montero-Perez-Barquero M, Munoz-Villanueva MC.Confidentiality breaches in clinical practice: what happens in hospitals?. BMC medical ethics.2016.17(1):52-52. IF:1,84 Q:1 D1

Hormaechea-Agulla D, Gomez-Gomez E, Ibanez-Costa A, Carrasco-Valiente J, Rivero-Cortes E, L-Lopez F, Pedraza-Arevalo S, Valero-Rosa J, Sanchez-Sanchez R, Ortega-Salas R, Moreno MM, Gahete MD, Lo pez-Miranda J, Requena MJ, Castano JP, Luque RM.Ghrelin O-acyltransferase (GOAT) enzyme is overexpressed in prostate cancer, and its levels are associated with patient's metabolic status: Potential value as a non-invasive biomarker.Cancer Letters.2016.383(1):125-134. IF:5,992 O:1

Haro C, Montes-Borrego M, Rangel-Zuniga OA, Alcala-Diaz JF, Gomez-Delgado F, Perez-Martinez P, Delgado-Lista J, Quintana-Navarro GM, Tinahones FJ, Landa BB, Lopez-Miranda J, Camargo A, Perez-Jimenez F.Two Healthy Diets Modulate Gut Microbial Community Improving Insulin Sensitivity in a Human Obese Population.Journal Of Clinical Endocrinology & Metabolism . 2016.101(1):232-241. IF:5,531

Q:1

Raya Al, Rios R, Pineda C, Rodriguez-Ortiz ME, Diez E, Almaden Y, Munoz-Castaneda JR,

Rodriguez M, Aguilera-Tejero E, Lopez I.Energy-dense diets increase FGF23, lead to phosphorus retention and promote vascular calcifications in rats.Scientific Reports.2016.6:36881. IF:5,228 Q:1

Haro C, Garcia-Carpintero S, Alcala-Diaz JF, Gomez-Delgado F, Delgado-Lista J, Perez-Martinez P, Rangel Zuniga OA, Quintana-Navarro GM, Landa BB, Clemente JC, Lopez-Miranda J, Camargo A, Perez-Jimenez F.The gut microbial community in metabolic syndrome patients is modified by diet.Journal of Nutritional Biochemistry.2016.27:27-31. IF:4,668 Q:1

Fuentes F, Alcala-Diaz JF, Watts GF, Mata P.Diabetes, statins and FH.International Journal of Cardiology.2016.203:575-575. IF:4.638

Q:1

Arevalo-Lorido JC, Gomez JC, Formiga F, Conde-Martel A, Carrera-Izquierdo M, Muela-Molinero A, Davila-Ramos MF, Serrado-Iglesias A, Manzano-Espinosa L, Montero-Perez-Barquero M.High serum osmolarity at admission determines a worse outcome in patients with heart failure: Is a new target emerging?.International Journal of Cardiology.2016.221:238-242. IF:4,638

Q:1

Salamanca-Bautista P, Conde-Martel A, Aramburu-Bodas O, Formiga F, Carles Trullas J, Quesada-Simon MA, Casado-Cerrada J, Ruiz-Laiglesia F, Manzano L, Montero-Perez-Barquero M.Precipitating factors of heart failure admission: Differences related to age and left ventricular ejection fraction.International Journal of Cardiology.2016.219:150-155. IF:4,638 Q:1

Leon-Acuna A, Alcala-Diaz JF, Delgado-Lista J, Torres-Pena JD, Lopez-Moreno J, Camargo A, Garcia-Rios A, Marin C, Gomez-Delgado F, Caballero J, Van-Ommen B, Malagon MM, Perez-Martinez P, Lopez-Miranda J.Hepatic insulin resistance both in prediabetic and diabetic patients determines postprandial lipoprotein metabolism: from the CORDIOPREV study. Cardiovascular Diabetology.2016.15:68. IF:4,534

Q:1



Delgado-Lista J, Perez-Martinez P, Garcia-Rios A, Alcala-Diaz JF, Perez-Caballero AI, Gomez-Delgado F, Fuentes F, Quintana-Navarro G, Lopez-Segura F, Ortiz-Morales AM, Delgado-Casado N, Yubero-Serrano EM, Camargo A, Marin C, Rodriguez-Cantalejo F, Gomez-Luna P, Ordovas JM, Lopez-Miranda J, Perez-Jimenez F.CORonary Diet Intervention with Olive oil and cardiovascular PREVention study (the CORDIOPREV study): Rationale, methods, and baseline characteristics: A clinical trial comparing the efficacy of a Mediterranean diet rich in olive oil versus a low-fat diet. American Heart JournaL.2016.177:42-50. IF:4,332

Q:1

Yubero-Serrano EM, Delgado-Lista J, Alcala-Diaz JF, Garcia-Rios A, Perez-Caballero AI, Blanco-Rojo R, Gomez-Delgado F, Marin C, Tinahones FJ, Caballero J, Ordovas JM, van Ommen B, Perez-Jimenez F, Perez-Martinez P, Lopez-Miranda J.A dysregulation of glucose metabolism control is associated with carotid atherosclerosis in patients with coronary heart disease (CORDIOPREV-DIAB study).Atherosclerosis.2016.(253):178-185. IF:3,942

Q:1

Lopez-Moreno J, Quintana-Navarro GM, Delgado-Lista J, Garcia-Rios A, Delgado-Casado N, Camargo A, Perez-Martinez P, Striker GE, Tinahones FJ, Perez-Jimenez F, Lopez-Miranda J, Yubero-Serrano EM.Mediterranean Diet Reduces Serum Advanced Glycation End Products and Increases Antioxidant Defenses in Elderly Adults: A Randomized Controlled Trial.Journal of The American Geriatrics Society.2016.64(4):901-904.

IF:3,842

Q:1

Rangel-Zuniga OA, Corina A, Lucena-Porras B, Cruz-Teno C, Gomez-Delgado F, Jimenez-Lucena R, Alcala-Diaz JF, Haro-Mariscal C, Yubero-Serrano EM, Delgado-Lista J, Lopez-Moreno J, Rodriguez-Cantalejo F, Camargo A, Tinahones FJ, Ordovas JM, Lopez-Miranda J, Perez-Martinez P.TNFA gene variants related to the inflammatory status and its association with cellular aging: From the CORDIOPREV study. Experimental Gerontology.2016.83:56-62. IF:3,35 Q:1

Talavera-Garcia E, Delgado-Lista J, Garcia-Rios A, Delgado-Casado N, Gomez-Luna P, Gomez-Garduno A, Gomez-Delgado F, Alcala-Diaz JF, Yubero-Serrano E, Marin C, Perez-Caballero AI, Fuentes-Jimenez FJ, Camargo A, Rodriguez-Cantalejo F, Tinahones FJ, Ordovas JM, Perez-Jimenez F, Perez-Martinez P, Lopez-Miranda J.Influence of Obesity and Metabolic Disease on Carotid Atherosclerosis in Patients with Coronary Artery Disease (CordioPrev Study).Plos One.2016.11(4):e0153096. IF:3,057

Q:1

Haro C, Rangel-Zuniga OA, Alcala-Diaz JF, Gomez-Delgado F, Perez-Martinez P, Delgado-Lista J, Quintana-Navarro GM, Landa BB, Navas-Cortes JA, Tena-Sempere M, Clemente JC, Lopez-Miranda J, Perez-Jimenez F, Camargo A.Intestinal Microbiota Is Influenced by Gender and Body Mass Index..Plos One.2016.11(5):e0154090. IF:3.057

Q:1

Herencia C, Diaz-Tocados JM, Jurado L, de Oca AM, Rodriguez-Ortiz ME, Martin-Alonso C, Martinez-Moreno JM, Vergara N, Rodriguez M, Almaden Y, Munoz-Castaneda JR.Procaine Inhibits Osteo/Odontogenesis through Wnt/beta-Catenin Inactivation.Plos One.2016.11(6):e0156788. IF:3,057

Q:1

Meza-Miranda ER, Rangel-Zuniga OA, Marin C, Perez-Martinez P, Delgado-Lista J, Haro C, Pena-Orihuela P, Jimenez-Morales AI, Malagon MM, Tinahones FJ, Lopez-Miranda J, Perez-Jimenez F, Camargo A.Virgin olive oil rich in phenolic compounds modulates the expression of atherosclerosis-related genes in vascular endothelium.European Journal Of Nutrition. 2016.55(2):519-527. IF:3,239

Q:2

Romero-Saldana M, Fuentes-Jimenez FJ, Vaquero-Abellan M, Alvarez-Fernandez C, Molina-Recio G, Lopez-Miranda J.New non-invasive method for early detection of metabolic syndrome in the working population.European Journal Of Cardiovascular Nursing.2016.15:549-558. IF:2,491

Q:2

Trullas JC, Manzano L, Formiga F, Aramburu-Bodas O, Quesada-Simon MA, Arias-Jimenez JL, Garcia-Escriva D, Romero-Requena JM, Jordana-Comajuncosa R, Montero-Perez-Barquero M.Heart Failure with Recovered Ejection Fraction in a Cohort of Elderly Patients with Chronic Heart Failure. Cardiology.2016.135(3):196-201. IF:1,994 Q:3

Montero-Perez-Barquero M, Morales-Rull JL.Organ protection possibilities in acute heart failure.Revista Clinica Espanola.2016.216(3):157-164. IF:0,76 Q:3

Sanchez-Sanchez C, Martin-Casado M, Formiga F, Montero-Perez-Barquero M.Reply to Spironolactone in patients with heart failure and preserved ejection fraction.Revista Clinica Espanola.2016.216(2):112-112. IF:0,76 Q:3

# In Collaboration

Perez de Isla L, Alonso R, Mata N, Saltijeral A, Muniz O, Rubio-Marin P, Diaz-Diaz JL, Fuentes F, de Andres R, Zambon D, Galiana J, Piedecausa M, Aguado R, Mosquera D, Vidal JI, Ruiz E, Manjon L, Mauri M, Padro T, Miramontes JP, Mata P.Coronary Heart Disease, Peripheral Arterial Disease, and Stroke in Familial Hypercholesterolaemia: Insights From the SAFEHEART Registry (Spanish Familial Hypercholesterolaemia Cohort Study).Arteriosclerosis Thrombosis And Vascular Biology.2016.36(9):2004-2010. IF:5,969 Q:1 D1

El Bekay R, Coin-Araguez L, Fernandez-Garcia D, Oliva-Olivera W, Bernal-Lopez R, Clemente-Postigo M, Delgado-Lista J, Diaz-Ruiz A, Guzman-Ruiz R, Vazquez-Martinez R, Lhamyani, S, Roca-Rodriguez MM, Fernandez Veledo S, Vendrell J, Malagon MM, Tinahones FJ.Effects of glucagon-like peptide-1 on the differentiation and metabolism of human adipocytes.British Journal Of Pharmacology.2016.173(11):1820-1834. IF:5,259

Q:1 D1

Alonso R, Diaz-Diaz JL, Arrieta F, Fuentes-Jimenez F, de Andres R, Saenz P, Ariceta G, Vidal-Pardo JI, Almagro F, Argueso R, Prieto-Matos P, Miramontes JP, Pinto X, Rodriguez-Urrego J, de Isla LP, Mata P.Clinical and molecular characteristics of homozygous familial hypercholesterolemia patients: Insights from SAFEHEART registry.Journal Of Clinical Lipidology.2016.10(4):953-961. IF:4,906

Q:1 D1

Moreno-Indias I, Oliva-Olivera W, Omiste A, Castellano-Castillo D, Lhamyani S, Camargo A, Tinahones FJ.Adipose tissue infiltration in normal-weight subjects and its impact on metabolic function.Translational Research.2016.172:6-17. IF:4.557

Q:1 D1

Q:1

Luque RM, Villa-Osaba A, L-Lopez F, Pozo-Salas AI, Sanchez-Sanchez R, Ortega-Salas R, de Lecea L, Alvarez-Benito M, Lopez-Miranda J, Gahete MD, Castano JP.Lack of cortistatin or somatostatin differentially influences DM-BA-induced mammary gland tumorigenesis in mice in an obesity-dependent mode.Breast Cancer Research.2016.18(1):29-29. IF:5,211

Moreno-Indias I, Sánchez-Alcoholado L, Sánchez-Garrido MÁ, Martín-Núñez GM, Pérez-Jiménez F, Tena-Sempere M, Tinahones FJ, Queipo-Ortuño MI.Neonatal Androgen Exposure Causes Persistent Gut Microbiota Dysbiosis Related to Metabolic Disease in Adult Female Rats.ENDOCRINOL-OGY.2016.157:4888-4898. IF:4,159

Q:1

Alonso R, Mata P, Muniz O, Fuentes-Jimenez F, Diaz JL, Zambon D, Tomas M, Martin C, Moyon T, Croyal M, Thedrez A, Lambert G.PCSK9 and lipoprotein (a) levels are two predictors of coronary artery calcification in asymptomatic patients with familial hypercholesterolemia. Atherosclerosis.2016.(254):249-253. IF:3,942

Q:1

Monfort-Pires M, Delgado-Lista J, Gomez-Delgado F, Lopez-Miranda J, Perez-Martinez P, Ferreira SRG.Impact of the Content of Fatty Acids of Oral Fat Tolerance Tests on Postprandial Triglyceridemia: Systematic Review and Meta-Analysis.Nutrients.2016.8(9):580. IF:3,759

Q:1

Q·1

Hernandez-Aguilera A, Fernandez-Arroyo S, Cuyas E, Luciano-Mateo F, Cabre N, Camps J, Lopez-Miranda J, Menendez JA, Joven J.Epigenetics and nutrition-related epidemics of metabolic diseases: Current perspectives and challenges.Food And Chemical Toxicology.2016.96:191-204. IF:3,584

Lacruz B, Tiberio G, Nunez MJ, Lopez-Jimenez L, Riera-Mestre A, Tiraferri E, Verhamme P,

Mazzolai L, Gonzalez J, Monreal M.Venous thromboembolism in centenarians: Findings from the RIETE registry.European Journal Of Internal Medicine.2016.36:62-66. IF:2,591

Q:1

DeFilipp Z, Duarte RF, Snowden JA, Majhail NS, Greenfield DM, Miranda JL, Arat M, Baker KS, Burns LJ, Duncan CN, Gilleece M, Hale GA, Hamadani M, Hamilton BK, Hogan WJ, Hsu JW, Inamoto Y, Kamble RT, Lupo-Stanghellini MT, Malone AK, McCarthy P, Mohty M, Norkin M, Paplham P, Ramanathan M, Richart JM, Salooja N, Schouten HC, Schoemans H, Seber A, Steinberg A, Wirk BM, Wood WA, Battiwalla M, Flowers MED, Savani BN, Shaw BE .Metabolic Syndrome and Cardiovascular Disease after Hematopoietic Cell Transplantation: Screening and Preventive Practice Recommendations from the CIBMTR and EBMT. Biology Of Blood And Marrow Transplantation.2016.22(8):1493-503. IF:3,98

Q:2

Giraldo P, Perez-Lopez J, Nunez R, Fernandez de la Puebla R, Luno E, Saura-Grau S, Carlos Bureo J, Plaza S, de la Serna J.Patients with type 1 Gaucher disease in Spain: A cross-sectional evaluation of health status.Blood Cells

Molecules And Diseases.2016.56(1):23-30. IF:2,731 Q:2

Moreno-Indias I, Sanchez-Alcoholado L, Perez-Martinez P, Andres-Lacueva C, Cardona F, Tinahones F, Queipo-Ortuno MI.Red wine polyphenols modulate fecal microbiota and reduce markers of the metabolic syndrome in obese patients.Food & Function.2016.7(4):1775-1787. IF:2,686 Q:2

Ruiz-Irastorza G, Garcia M, Espinosa G, Cabezas-Rodriguez I, Mitjavila F, Gonzalez-Leon R, Sopena B, Perales I, Pinilla B, Rodriguez-Carballeira M, Lopez-Dupla JM, Callejas JL, Castro A, Tolosa C, Sanchez-Garcia ME, Perez-Conesa M, Navarrete-Navarrete N, Rodriguez AP, Herranz MT, Pallares L.Patterns of drug therapy in newly diagnosed Spanish patients with systemic lupus erythematosus.Clinical And Experimental Rheumatology.2016.34(3):466-472. IF:2,495 O:2

Trullas JC, Miro O, Formiga F, Martin-Sanchez FJ, Montero-Perez-Barquero M, Jacob J, Quiros-Lopez R, Herrero Puente P, Manzano L, Llorens P.The utility of heart failure registries: a descriptive and comparative study of two heart failure registries.Postgraduate Medical Journal.2016.92(1087):260-266. IF:1,633 O:2

Suarez C, Pose A, Montero-Perez-Barquero M, Roquer J, Gallego J, Rafols C, Cazorla D, Vivancos J.Validation of satisfaction questionnaire ACTS in outpatients with atrial fibrillation treated with oral anticoagulants in Spain. ALA-DIN Study.Medicina Clinica.2016.147(5):192-8. IF:1,267 Q:2

Manito Lorite N, Manzano Espinosa L, Llorens Soriano P, Masip Utset J, Comin Colet J, Formiga Perez F, Herrero Puente P, Delgado Jimenez J, Montero-Perez-Barquero M, Rodriguez JJ, Areses ELD, Perez Calvo JI, Martin-Sanchez FJ, Miro Andreu O.Consensus for improving the comprehensive care of patients with acute heart failure: summarised version. Revista Clinica Espanola.2016.216(5):260-270. IF:0,76 O:3

Cerqueiro JM, Gonzalez-Franco A, Montero-Perez-Barquero M, Llacer P, Conde A, Davila MF, Carrera M, Serrado A, Suarez I, Perez-Silvestre J, Satue JA, Arevalo-Lorido JC, Rodriguez A, Herrero A, Jordana R, Manzano L.Reduction in hospitalisations and emergency department visits for frail patients with heart failure: Results of the UMIPIC healthcare programme.Revista Clinica Espanola.2016.216(1):8-14. IF:0,76

Q:3

Cerqueiro JM, Gonzalez-Franco A, Montero-Perez-Barquero M, Manzano L.Reply to Heart failure in elderly patients, a global perspective.Revista Clinica Espanola.2016.216(7):406-406. IF:0,76

Q:3

Souki A, Arraiz N, Prieto C, Perez Jimenez F, Valero P, Amell A, Cano-Ponce C.Association between resistin serum levels and dimension and body composition variables in children and adolescents.Revista Medica De Chile.2016.144(3):307-316. IF:0.44

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# **Research Funding**

#### National

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

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 (IS-CIII).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 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

Lopez 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.Reference: AGL2015-67896-P

Marin Hinojosa, C.Identification of novel therapeutic biomarkers in the progression of intima-media thickness of carotid arteries through on nutritional epigenetics. Funding agency: Institute Carlos III Health (ISCIII).Reference: PI15/00733

Pérez Jiménez, F. Mediterranean diet associated with probiotics improves the cognitive function in patients with mild cognitive impairment modulating the axis microbiota-gut-brain. Funding agency: Institute Carlos III Health (ISCIII).Reference: PI16/01777 Expected starting date:2017

#### 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

Haro Mariscal C. Early diagnostic colorectal cancer tool based in intestine microbiota.Funding agency: Regional Ministry of Health and Social Policy (CISPS). Reference:PIN-0156-2016



#### International

Delgado Lista, J. POWER2DM - Predictive model-based decision support for diabetes patient empowerment.Funding Agency: PER-SONALISING HEALTH AND CARE 2015 - SIN-GLE STAGE EUROPEA COMISION. Reference: PHC28-2015-001

#### **Contracts with Companies**

Montero Pérez-Barguero, M. Pzifer agreement. Funding agency: Pfizer, S.L.U. Reference<sup>-</sup> CCB 007

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

Montero Pérez-Barguero, 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

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. PI: 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

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.

Pl: 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. Pl: 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. Pl: Dr/a Pérez Martínez, Pablo

0295/13. A randomized, multicenter, double-blind, double-blind, placebo-controlled, parallel-group study to assess the efficacy, safety and tolerability of PF-04950615 in reducing the number of severe cardiovascular evetns in high-risk patients. Pl: 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 evetns in high-risk patients. Pl: 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.

Pl: Dr/a Fuentes Jiménez, Francisco

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).

Pl: 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

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

\*3121 . Open-label, Single-Arm, Multicenter Study to Evaluate the Safety, Tolerability and Efficacy of Evolocumab for LDL-C Reduction, as Add-on to Diet and Lipid-lowering Therapy, in Pediatric Subjects From 10 to 17 Years of Age With Heterozygous Familial Hypercholesterolemia (HeFH) or Homozygous Familial Hypercholesterolemia (HoFH). PI: Dr/a Fuentes Jiménez, Francisco

\*3237 . An 8-Week Open-Label, Sequential, Repeated Dose-Finding Study to Evaluate the Efficacy and Safety of Alirocumab in Children and Adolescents With Heterozygous Familial Hypercholesterolemia Followed by an Extension Phase.

PI: Dr/a Fuentes Jiménez, Francisco

\*3245. Safety and Efficacy of the Combination of Loop Diuretics With Thiazide-type Diuretics in Patients With Decompensated Heart Failure. a Double-blind, Randomized, Placebo-controlled Trial (CLOROTIC Trial). PI: Dr/a Montero Pérez-Barquero, Manuel

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

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 Jiménez, Luciano

# **GC10** • Hormonal regulation of energy balance, puberty and reproduction

HIGHLIGHTS

**PUBLICATIONS** 

16







# **Team Leader**

# Principal Investigator (PI) Manuel Tena-Sempere

fi1tesem@uco.es

IMIBIC Deputy Scientific Director CIBER on Obesity and Nutrition (CIBERobn) PAIDI BIO-310 Scientific Group

# Researchers

Gaytan Luna; Francisco Pinilla Jurado, Leonor

# **Post-Doctoral Researchers**

Avedaño Averrado; M <sup>a</sup>Soledad Castellano Rodríguez, Juan Manuel Franssen; Delphine García Galiano; David Manfredi Lozano; María Roa Rivas; Juan Romero; Antonio Ruchorian; Suvi (visiting fellow) Sánchez-Garrido Nogueras; Miguel Vázquez Villar; María Jesús

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Barroso Romero; Alexia Gizem Erkan; Leman (visiting fellow) Fernandois Vicencio, Daniela (visiting fellow)

Heras Domínguez; Violeta Lobato Delgado; Bárbara López Rodríguez; Carmen María Perdices López; Mª Cecilia Pineda Reyes; Beatriz Ruíz Pino; Francisco Ruíz Rodríguez; José Manuel Torres Jiménez; Encarnación Velasco Aguayo; Inmaculada

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

Onieva Jiménez; Rocío Rodríguez Sánchez; Ana Sánchez Tapia; Mª Jesús



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

Manfredi-Lozano M, Roa J, Ruiz-Pino F, Piet R, Garcia-Galiano D, Pineda R, Zamora A, Leon S, Sanchez-Garrido MA, Romero-Ruiz A, Dieguez C, Vazquez MJ, Herbison AE, Pinilla L, Tena-Sempere M.Defining a novel leptin-melanocortin-kisspeptin pathway involved in the metabolic control of puberty.Molecular Metabolism.2016.5(10):844-857. IF:5,363 O:1

Leon S, Fernadois D, Sull A, Sull J, Calder M, Hayashi K, Bhattacharya M, Power S, Vilos GA; Vilos AG, Tena-Sempere M, Babwah AV.Beyond the brain-Peripheral kisspeptin signaling is essential for promoting endometrial gland development and function.Scientific Reports. 2016. 6:29073-29073. IF:5,228 Q:1

Leon S, Barroso A, Vazquez MJ, Garcia-Galiano D, Manfredi-Lozano M, Ruiz-Pino F, Heras V, Romero-Ruiz A, Roa J, Schutz G, Kirilov M, Gaytan F, Pinilla L, Tena-Sempere M.Direct Actions of Kisspeptins on GnRH Neurons Permit Attainment of Fertility but are Insufficient to Fully Preserve Gonadotropic Axis Activity.Scientific Reports.2016.6:19206. IF:5,228 O:1

Lopez M, Tena-Sempere M.Estradiol and brown fat.Best Practice & Research Clinical Endocrinology & Metabolism.2016.30(4):527-536. IF:5,07

Q:1

Castellano JM, Tena-Sempere M.Metabolic control of female puberty: potential therapeutic targets. Expert Opinion On Therapeutic Targets.2016.20(10):1181-1193. IF:4,798 Q:1

Tena-Sempere M.The Endocrine Society Centennial: Genes and Hormones in Obesity or How Obesity Met Endocrinology.Endocrinology.2016.157(3):979-82. IF:4,159 O:1

Haro C, Rangel-Zuniga OA, Alcala-Diaz JF, Gomez-Delgado F, Perez-Martinez P, Delgado-Lista J, Quintana-Navarro GM, Landa BB, Navas-Cortes JA, Tena-Sempere M, Clemente JC, Lopez-Miranda J, Perez-Jimenez F, Camargo A.Intestinal Microbiota Is Influenced by Gender and Body Mass Index.Plos One.2016.11(5):e0154090. IF:3,057

Q:1

Gahete MD, Vaquez-Borrego MC, Martinez-Fuentes AJ, Tena-Sempere E, Castano JP, Luque RM.Role of the Kiss1/Kiss1r system in the regulation of pituitary cell function.Molecular and Cellular Endocrinology.2016.(438):100-106. IF:3,859 Q:2

Castellano JM, Tena-Sempere M.Animal Modeling of Early Programming and Disruption of Pubertal Maturation.Endocrine Development.2016.29:87-121 IF-0

Leon S, Tena-Sempere M .Dissecting the Roles of Gonadotropin-Inhibitory Hormone in Mammals: Studies Using Pharmacological Tools and Genetically Modified Mouse Models.Frontiers In Endocrinology. 2016.6:189. IF:0

#### In Collaboration

Messina A, Langlet F, Chachlaki K, Roa J, Rasika S, Jouy N, Gallet S, Gaytan F, Parkash J, Tena-Sempere M, Giacobini P, Prevot V.A microRNA switch regulates the rise in hypothalamic GnRH production before puberty.Nature Neuroscience.2016.19(6):835-834. IF:16,724

Q:1 D1

Lopez M, Nogueiras R, Tena-Sempere M, Dieguez C.Hypothalamic AMPK: a canonical regulator of whole-body energy balance.Nature Reviews Endocrinology.2016.12(7):421-432. IF:15,432 Q:1 D1

Martins L, Seoane-Collazo P, Contreras C, Gonzalez-Garcia I, Martinez-Sanchez N, Gonzalez F, Zalvide J, Gallego R, Dieguez C, Nogueiras R, Tena-Sempere M, Lopez M.A Functional Link between AMPK and Orexin Mediates the Effect of BMP8B on Energy Balance.Cell Reports.2016.16(8):2231-2242. IF:7,87 O:1

Moreno-Indias I, Sánchez-Alcoholado L, Sánchez-Garrido MÁ, Martín-Núñez GM, Pérez-Jiménez F, Tena-Sempere M, Tinahones FJ, Queipo-Ortuño MI.Neonatal Androgen Exposure Causes Persistent Gut Microbiota Dysbiosis Related to Metabolic Disease in Adult Female Rats.ENDOCRINOL-OGY.2016.157:4888-4898. IF:4,159

Q:1

Argente-Arizon P, Ros P, Diaz F, Fuente-Martin E, Castro-Gonzalez D, Sanchez-Garrido MA, Barrios V, Tena-Sempere M, Argente J, Chowen JA.Age and sex dependent effects of early overnutrition on metabolic parameters and the role of neonatal androgens.Biology Of Sex



Differences.2016.7:26. IF:3,237 Q:2

Mela V, Diaz F, Vazquez MJ, Argente J, Tena-Sempere M, Viveros MP, Chowen JA.Interaction between neonatal maternal deprivation and serum leptin levels on metabolism, pubertal development, and sexual behavior in male and female rats.Biology Of Sex Differences.2016.7:2. IF:3,237 Q:2

**Research Funding** 

#### National

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

Castellano Rodríguez, JM (CO-PI: 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

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

Roa Rivas J. Etiophatogenic role and diagnostic/therapeutic implications of MicroRNAs on early puberty in obesity. Funding agency: Institute Carlos III Health (ISCIII). Reference: CP15/00047

Roa Rivas J. Puberty and metabolic risk in obese children: Epigenetic alterations and pathophysiological and diagnostic implications. PUBMEP Study.Funding agency: Institute Carlos III Health (ISCIII). Reference; PI16/01243 Expected starting date:2017

#### 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 Avendaño Herrador, MS. Pathophysiological, prognosis and diagnosis role of circulating MicroRNAs in hypogonadism associated with obesity. Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0370-2016

#### International

Tena-Sempere, M. GnRH deficiency: Elucidation of the neuroendocrine control of human reproduction. Funding Agency: Comission European.Reference: oc-2011-1-9031

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

# **GC11 • Metabolism and Adipocyte Differentiation. Metabolic Syndrome**

# HIGHLIGHTS



# **Team Leaders**

# Principal Investigator (PI) Mª del Mar Malagón Poyato

bc1mapom@uco.es CIBER on Obesity and Nutrition (CIBERobn) (Collaborator) PAIDI BIO-139 scientific group (Collaborator)

**Co- Principal Investigator (PI):** Francisco Gracia Navarro Researchers García Navarro, Socorro Vázquez Martínez, Rafael

# Post-Doctoral Researchers

Cayuela Marín, Angelina Guzmán Ruíz, Rocío

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Baker, Matthew Díaz Del Moral, Sandra Fernández Vega, Alejandro Navarro Ruiz, Mª Del Carmen López Alcalá, Jaime Tercero Alcázar, Carmen Travéz García, Andrés Sá Gomes, Andreia Cristina Sánchez Ceinos, Julia Soler Vázquez, Mª Del Carmen

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



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.

Meza-Miranda ER, Rangel-Zuniga OA, Marin

C, Perez-Martinez P, Delgado-Lista J, Haro C, Pena-Orihuela P, Jimenez-Morales AI,

Malagon MM, Tinahones FJ, Lopez-Miranda J, Perez-Jimenez F, Camargo A.Virgin olive oil

rich in phenolic compounds modulates the

expression of atherosclerosis-related genes

in vascular endothelium.European Journal Of

# Scientific Production

#### **Publications**

#### Original

El Bekay R, Coin-Araguez L, Fernandez-Garcia D, Oliva-Olivera W, Bernal-Lopez R, Clemente-Postigo M, Delgado-Lista J, Diaz-Ruiz A, Guzman-Ruiz R, Vazquez-Martinez R, Lhamyani, S, Roca-Rodriguez MM, Fernandez Veledo S, Vendrell J, Malagon MM\*, Tinahones FJ\*.Effects of glucagon-like peptide-1 on the differentiation and metabolism of human adipocytes.British Journal Of Pharmacology.2016.173(11):1820-1834. IF:5,259 O:1 D1

Moreno-Castellanos N, Guzman-Ruiz R, Cano DA, Madrazo-Atutxa A, Peinado JR, Pereira-Cunill JL, Garcia-Luna PP, Morales-Conde S, Socas-Macias M, Vazquez-Martinez R, Leal-Cerro A, Malagon MM.The Effects of Bariatric Surgery-Induced Weight Loss on Adipose Tissue in Morbidly Obese Women Depends on the Initial Metabolic Status.Obesity Surgery.2016.26(8):1757-1767. IF:3.346

Q:1

# In Collaboration

Leon-Acuna A, Alcala-Diaz JF, Delgado-Lista J, Torres-Pena JD, Lopez-Moreno J, Camargo A, Garcia-Rios A, Marin C, Gomez-Delgado F, Caballero J, Van-Ommen B, Malagon MM, Perez-Martinez P, Lopez-Miranda J.Hepatic insulin resistance both in prediabetic and diabetic patients determines postprandial lipoprotein metabolism: from the CORDIOPREV study. Cardiovascular Diabetology.2016.15:68. IF:4,534 Q:1

Tina-Ti

IF:3.239

Q:2

Nutrition. 2016.55(2):519-527.

disue dysfunction in insulin resistance conditions. Funding Agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0200-2013

Guzmán Ruíz, R. Identification of biomarkers predictive of response to bariatric surgery in morbidly obese patients. Advanced proteomics techniques and applications. Funding agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0159-2016

#### 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

Malagón, MM. Characterization of extracellular and intracellular constituents that define expensed adipose tissue.Funding Agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: BFU2016-76711-R

Malagón MM (Calzado Canale, M: Co-PI). Integration of platforms for the identification of therapeutic targets and the development of new products for the prevention and/or treatment of radiodermatitis. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO).Reference: RTC-2016-4589-1



BIC

# **GC12 • Epidemiological Research in Primary** Care

HIGHLIGHTS



# **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) PAIDI CTS-452 Scientific Group

# Researchers

Acosta García; María José Aguado Taberne; Cristina Alba Dios; María Antonia Aycaguer Silva; Luis Carlos Blanco Hungría; Antonio Fernández Fernández; Miguel Ángel Fernández García; José Ángel Fonseca del Pozo; Francisco Javier González Carretero; Juan Ignacio González Lama; Jesús Hidalgo Requena; Antonio Jiménez García; Celia Jiménez Rodríguez; J. M. (Collaborator) Jodral Segado; Antonio Manuel Olaya Caro; Inmaculada Parras Rejano; Juan Manuel Perula De Torres; Carlos Prados Castillejo; José Antonio Ranchal Sánchez; Antonio Redondo Sánchez; Juana Martin Rioboo; Enrique Roldán Villalobos;Ana R. De Castroviejo Del Campo; Joaquín Ruiz Moruno; Fco. Javier

Valero Martin; Antonio Vaquero Abellán; Manuel Varas Fabra; Francisco José

# **Post-Doctoral Researchers**

Blanco Aguilera; Antonio Rich Ruiz; Manuel Romero Rodríguez; Esperanza María

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Leiva Cepas;Fernando Ortega Millán; Carlos Serrano Merino; Jesús Criado Larumbe; Margarita Marín González; Beatriz

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

Campinez Navarro M, Perula de Torres LA, Bosch Fontcuberta JM, Barragan Brun N, Arbonies Ortiz JC, Novo Rodriguez JM, Boveda Fontan J, Martin Alvarez R, Prados Castillejo JA, Rivas Doutreleau GR, Domingo Pena Castro Moreno JJ, Romero Rodriguez EM.Measuring the quality of motivational interviewing in primary health care encounters: The development and validation of the motivational interviewing assessment scale (MIAS).European Journal Of General Practice.2016.22(3):182-188. IF:1,364

0.3

Arias Vega MR, Perula de Torres LA, Carrasco Valiente J, Requena Tapia MJ, Jimenez Garcia C, Silva Aycaguer LC.Prevalence of urolithiasis in the 40 to 65 year old Spanish population: The PreLiRenE study.Medicina Clinica.2016.146(12):525-531. IF:1,267

Q:2

Blanco-Hungria A, Blanco-Aguilera A, Blanco-Aguilera E, Serrano-del-Rosal R, Biedma-Velazquez L, Rodriguez-Torronteras A, Segura-Saint-Gerons R. Prevalence of the different Axis I clinical subtypes in a sample of patients with orofacialpain and temporomandibular disorders in the Andalusian Healthcare Service.Medicina Oral Patologia Oral Y Cirugia Bucal. 2016. 21(2): E169-E-177. IF:1,087

Q:3

Girela-Lopez E, Ruz-Caracuel I, Beltran C, Jimena I, Leiva-Cepas F, Jimenez-Reina L, Pena J.Histological Changes in Skeletal Muscle During Death by Drowning: An Experimental Study.American Journal Of Forensic Medicine And Pathology.2016.37(2):118-26. IE 0 795

Q·4

Fonseca del Pozo FJ, Valle Alonso J, Canales Velis NB, Andrade Barahona MM, Siggers A, Lopera Lopera E.Basic life support knowledge of secondary school students in cardiopulmonary resuscitation training using a song.International Journal Medical Education.2016.7:237-241. IF.0

#### In Collaboration

Romero-Saldana M. Fuentes-Jimenez FJ. Vaquero-Abellan M, Alvarez-Fernandez C, Molina-Recio G, Lopez-Miranda J.New non-invasive method for early detection of

metabolic syndrome in the working population.European Journal Of Cardiovascular Nursing.2016.15:549-558. IF:2,491 Q:2

Alonso JV, del Pozo FJF, Alvarez MV, Lopera EL, Segura MF, Arevalo RG.Comparison of the Canadian CT head rule and the New Orleans criteria in patients with minor head injury in a Spanish hospital.Medicina Clinica.2016.147(12):523-530. IF:1.267

0.5

Puentes Torres RC, Aguado Taberne C, Perula de Torres LA, Espejo Espejo J, Castro Fernandez C, Fransi Galiana L.Acceptability of the opportunistic search for human immunodeficiency virus infection by serology in patients recruited in Primary Care Centres in Spain. Atencion Primaria.2016.48(6):383-393. IF:1.098 Q:3

Aguera E, Castilla S, Luque E, Jimena I, Leiva-Cepas F, Ruz-Caracuel I, Pena J .Muscular hypertrophy and atrophy in normal rats provoked by the administration of normal and denervated muscle extracts.Histology And Histopathology.2016.31(12):1367-79. IF:1.875

Q:4

#### **Research Funding**

#### National

Rich Ruíz, M. Efficacy of the Otago Exercise Program (OEP) delivered as group training versus individually tailored training in community-dwelling adults between 65 and 80 years old Funding Agency: Institute Carlos III Health (ISCIII).Reference:PI16/01520

Martín Rioboo, E.Knowledge, availability and use of current resources for monitoring and diagnostic arterial hypertension in health care professionals. Funding Agency: Laboratorios Esteve.

## Regional

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

Pérula de Torres, LA. Knowledge, availability and use of current resources for monitoring and diagnostic arterial hypertension in health care professionals. Funding Agency: SAMFYC. Reference: SAMFYC14/001

#### **Contracts with Companies**

Rich Ruíz, M. Efficacy of the Otago Exercise Program (OEP) delivered as group training versus individually tailored training in community-dwelling adults between 65 and 80 years old. Funding Agency: Universidad De Cordoba. Reference: PSS.0164

#### **Clinical Trials**

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

3249.Glycemic control in patients with high cardiovascular risk and type 2 diabetes mellitus in primary care and cardiology consultation

PI Dr/a Martín Rioboo, Enrique

3010.Prospective, multi Centre, international registry of male and female patients newly diiagnosed with atrial fibrillation and treated with Rivaroxaban.

PI Dr/a González Lama, Jesús



# **GC13 • Calcium metabolism. Vascular** calcification

# HIGHLIGHTS



# **Team Leader**

# Principal Investigator (PI) Mariano Rodríguez Portillo

juanm.rodriguez.sspa@juntadeandalucia.es Spanish Renal Research Network (REDinREN) (Collaborator) PAIDI CTS-179 Scientific group (Collaborator)

# Researchers

Aguilera Tejero; Escolástico Canalejo Raya; Antonio (Collaborator) Raya Bermúdez;Ana Isabel López Villalba; Ignacio Muñoz Castañeda; Juan Rafael (Nicolas Monardes Contract)

# **Post-Doctoral Researchers**

Pineda Martos; Carmen María Herencia Bellido; Carmen Martínez Moreno; Julio Manuel Pendón Ruiz de Mier; Mª Victoria Rodríguez Ortiz; Mª Encarnación

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Pendón Ruiz de Mier; Mª Victoria Ríos Varo; Rafael Salmerón Rodríguez; María Dolores Tocados Díaz; Juan Miguel Vergara Segura; Noemí

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

García Valdivia; Sandra Ruiz Mora; Erena López Baltanás; Rodrigo

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 kid-ney 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

Martinez-Moreno JM, Herencia C, Montes de Oca A, Munoz-Castaneda JR, Rodriguez-Ortiz ME, Diaz-Tocados JM, Peralbo-Santaella E, Camargo A, Canalejo A, Rodriguez M, Velasco-Gimena F, Almaden Y.Vitamin D modulates tissue factor and protease-activated receptor 2 expression in vascular smooth muscle cells. Faseb Journal.2016.30(3):1367-1376. IF:5,299 Q:1 D1

Raya AI, Rios R, Pineda C, Rodriguez-Ortiz ME, Diez E, Almaden Y, Munoz-Castaneda JR, Rodriguez M, Aguilera-Tejero E, Lopez I.Energy-dense diets increase FGF23, lead to phosphorus retention and promote vascular calcifications in rats.Scientific Reports.2016.6: 36881.

Q.1

Rodriguez M, Salmeron MD, Martin-Malo A, Barbieri C, Mari F, Molina RI, Costa P, Aljama P.A New Data Analysis System to Quantify Associations between Biochemical Parameters of Chronic Kidney Disease-Mineral Bone Disease.PLOS ONE.2016.11(1):-e0146801. IF:3,057 Q:1

Herencia C, Diaz-Tocados JM, Jurado L, de Oca AM, Rodriguez-Ortiz ME, Martin-Alonso C, Martinez-Moreno JM, Vergara N, Rodriguez M, Almaden Y, Munoz-Castaneda JR.Procaine Inhibits Osteo/Odontogenesis through Wnt/beta-Catenin Inactivation.PLOS ONE.2016.11(6):-e0156788. IF:3,057 Q:1

Bover J, Ureňa-Torres P, Górriz JL, Lloret MJ, da Silva I, Ruiz-García C,Chang P, Rodríguez M, Ballarín J..Cardiovascular calcifications in chronic kidney disease: Potential therapeutic implications .Nefrologia.2016.36(6);597:608 IF:1,21 Q:4

Bover J, Górriz JL, Ureña-Torres P, Lloret MJ, Ruiz-García C, daSilva I, Chang.Detection of cardiovascular calcifications: Is it a useful tool for nephrologists?.Nefrologia.2016. 36(6):587-596

IF:1,21 Q:4

#### **In Collaboration**

Acevedo LM, Lopez I, Peralta-Ramirez A, Pineda C, Chamizo VE, Rodriguez M, Aguilera-Tejero E, Rivero JLL.High-phosphorus diet maximizes and low-dose calcitriol attenuates skeletal muscle changes in long-term uremic rats.Journal Of Applied Physiology.2016.120(9):1059-1069. IF:3,004 Q:2

# **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 Wnt / Beta-Catenin and SMAD. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI11-02055

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

Aguilar Tejero, E. Influence of dietary calorie content on the phosphorus balance: implications in kidney disease. Funding agency: Institute Carlos III Health (ISCIII).Reference: PI14/00467

Muñoz Castañeda , JR. New therapy for the treatment of degenerative osteoarthrosis based on a modification of adipose-tissue-derived mesenchymal stem cells.Funding agency: Institute Carlos III Health (ISCIII).Reference: DTS.16/00061

Expected starting date:2017

#### Regional

Muñoz Castañeda, JR. Hepatocyte differentiation from two pluripotent cell types in bone marrow. Application for cell regeneration in two experimental models of hepatic lesion. Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: ICE02137.

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



IF:5,228 Q·1

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

#### International

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

# **Contracts with Companies**

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

Muñoz Castañeda, JR. Preclinical Research Program Agreement for anti-PCSK9 mAb1. Funding agency: JYC Ediciones Medicas. Reference: PSS.0162

# **Clinical Trials**

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



# **GC14 • Cell therapy**

# HIGHLIGHTS









# **Team Leader**

Principal Investigator (PI) Inmaculada C. Herrera Arroyo inmaculada.herrera.sspa@juntadeandalucia.es

# Researchers

Canis López ;Miguel Cañadillas López; Mª Sagrario Martin Palanco;Vanesa Nogueras Martin; Sonia Ortega Salas; Rosa Centeno Haro; Macarena García-Revillo García; José

Post-Doctoral Researchers Jiménez Moreno; Rosario

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Carmona Luque; María Dolores Trujillo Aguilar ; Cristina López Gálvez; Laura Muñoz Calero;María Paco Meza; Luis Miguel

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

Castilla Rodríguez; María Luisa De la Torre Murrilo; Antonia Gutiérrez Fernández; Rosario Luque Zafra; María Muñoz Liñán; Teresa

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 Productions**

# **Publications**

#### **In Collaboration**

Hormaechea-Agulla D, Gomez-Gomez E, Ibanez-Costa A, Carrasco-Valiente J, Rivero-Cortes E, L-Lopez F, Pedraza-Arevalo S, Valero-Rosa J, Sanchez-Sanchez R, Ortega-Salas R, Moreno MM, Gahete MD, Lo pez-Miranda J, Requena MJ, Castano JP, Luque RM.Ghrelin O-acyltransferase (GOAT) enzyme is overexpressed in prostate cancer, and its levels are associated with patient's metabolic status: Potential value as a non-invasive biomarker.Cancer Letters.2016.383(1):125-134. IF:5,992 O:1

Luque RM, Villa-Osaba A, L-Lopez F, Pozo-Salas AI, Sanchez-Sanchez R, Ortega-Salas R, de Lecea L, Alvarez-Benito M, Lopez-Miranda J, Gahete MD, Castano JP.Lack of cortistatin or somatostatin differentially influences DM-BA-induced mammary gland tumorigenesis in mice in an obesity-dependent mode.Breast Cancer Research.2016.18(1):29-29. IF:5,211 O:1

Koenecke C, Heim D, van Biezen A, Heuser M, Aljurf M, Kyrcz-Krzemien S, Volin L, de Souza CA, Gedde-Dahl T, Sengeloev H, Schanz U, Komarnicki M, Arroyo CH, Tholouli E, Gluckman E, Esquirol A, Yakoub-Agha I, Gürman G, Olavarria E, Kröger N. Outcome of patients with chronic myeloid leukemia and a low-risk score: allogeneic hematopoietic stem cell transplantation in the era of targeted therapy. A report from the EBMT Chronic Malignancies Working Party.Bone Marrow Transplantation.2016.51:1259-1261. IF:3,636 Q:2

Izeta A, Herrera C, Mata R, Astori G, Giordano R, Hernandez C, Leyva L, Arias S, Oyonarte S, Carmona G, Cuende N.Cell-based product classification procedure: What can be done differently to improve decisions on borderline products?.Cytotherapy.2016.18(7):809-815. IF:3,625

#### Q:3

#### **Research Funding**

#### National

Cañadillas López, S. 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

Herrera Arroyo, Inmaculada C. Preclinical development of gene cell therapy based on a new drug comprising allogenic T cells with inducible expression of anti-cd19 chimeric antigen receptor (CAR) for the treatment of refractory B-cell tumors. Funding Agency: Regional Ministry of Equality, Health and Social Policies (CISPS).Reference: SALUD-201600073092-TRA

# **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 Janssen. Funding agency: Janssen-Cilag, S.A.Reference:PSS.0103

Herrera Arroyo, Inmaculada C. Agreement with Bristol-Meyers. Funding agency: Bristol-Myers Squibb, S.A.U.Reference:PSS.0129

Herrera Arroyo, Inmaculada C. Agreement with Janssen. Funding agency: Janssen-Cilag, S.A.Reference:PSS.0130

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

Herrera Arroyo, Inmaculada C. Agreement with JANSSEN. Funding agency: Janssen-Cilag, S.A.Reference: CCB.0113\_02

# **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.



# **GC15** • Invasive cardiology and cell therapy

# HIGHLIGHTS

**PUBLICATIONS** 

20







# **Team Leader**

# Principal Investigator (PI)

José Suárez de Lezo Cruz-Conde jose.suarezlezo.sspa@juntadeandalucia PAIDI BIO 208 Scientific Group Other Researcher Manuel Pan Álvarez-Ossorio

# Researchers

Mazuelos Bellido; Francisco Ojeda Pineda; Soledad Pavlovic Djurovic; Djordje Romero Moreno; Miguel Ángel Segura Saint-Gerons; José Mª Suarez De Lezo Herreros De Tejada; Javier



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

Pan M, Ojeda S, Villanueva E, Chavarria J, Romero M, de Lezo JS, Mazuelos F, Segura J, Carrasco F, Hidalgo F, Aguilera JL, Rodriguez S, Puente M, de Lezo JS.Structural Damage of Jailed Guidewire During the Treatment of Coronary Bifurcation Lesions A Microscopic Randomized Trial.JACC-Cardiovascular Interventions.2016.9(18):1917-1924. IF:7.63

Q·1

Hidalgo F, Anguita M, Castillo JC, Rodriguez S, Pardo L, Duran E, Sanchez JJ, Ferreiro C, Pan M, Mesa D, Delgado M, Ruiz M.Effect of early treatment with ivabradine combined with beta-blockers versus beta-blockers alone in patients hospitalised with heart failure and reduced left ventricular ejection fraction (ETH-IC-AHF): A randomised study.International Journal Of Cardiology.2016.217():7-11. IF:4,638 Q:1

Lopez-Aguilera J, Segura Saint-Gerons JM, Mazuelos Bellido F, Suarez de Lezo J, Ojeda Pineda S, Pan Alvarez-Ossorio M, Romero Moreno MA, Pavlovic D, Espejo Perez S, Suarez de Lezo J.Atrioventricular Conduction Changes After CoreValve Transcatheter Aortic Valve Implantation.Revista Espanola De Cardiologia.2016.69(1):28-36. IF:4,596 Q:1

Suarez de Lezo J, Martin P, Pan M, Ojeda S, Novoa J, Segura J, Mazuelos F, Romero M, Medina A, Suarez de Lezo J.Bioresorbable Vascular Scaffold for the Treatment of Coronary Bifurcation Lesions: Immediate Results and 1-year Follow-up.Revista Espanola De Cardiologia.2016 .69(6):554-62. IF:4,596 O:1

Lopez-Aguilera J, Segura JM, Suarez de Lezo J. Time of Pacemaker Implantation After Percutaneous Aortic Valve Replacement. Response.Revista Espanola De Cardiologia.2016.69 (6):631-632. IF:4,596 Q:1

Estevez-Loureiro R, Arzamendi D, Carrasco-Chinchilla F, Amat-Santos IJ, Freixa X, Suarez de Lezo J.Usefulness of MitraClip for the Treatment of Mitral Regurgitation Secondary to Failed Surgical Annuloplasty.Revista Espanola De Cardiologia.2016.69(4):446-448. IF:4,596 Q:1

Hidalgo, F, Mesa, D, Ruiz, M, Delgado, M, Rodríguez, S, Pardo, L, Pan, M, López, A, Romero, MA, Suárez de Lezo, J.Effects of Mitral Annulus Remodeling Following MitraClip Procedure on Reduction of Functional Mitral Regurgitation .Revista Espanola De Cardiologia.2016. 69(11) :1020-1045. IF:4,596 Q:1

Jiménez-Quevedo P, Serrano A, Pérez de Prado A, Pan M. Spanish Cardiac Catheterization and Coronary Intervention Registry. 25th Official Report of the Spanish Society of Cardiology Working. Group on Cardiac Catheterization and Interventional Cardiology (1990-2015).Revista Espanola De Cardiologia.2016.69(12):1180-1189. IF:4,596

Carrasco F, Anguita M, Ruiz M, Castillo JC, Delgado M, Mesa D, Romo E, Pan M, Suarez de Lezo J.Clinical features and changes in epidemiology of infective endocarditis on pacemaker devices over a 27-year period (1987-2013). Europace.2016.18(6):836-41. IF:4,021 Q:2

Ojeda S, Pan M, Suarez de Lezo J, Martin P, Mazuelos F, Romero M, Novoa J, Espejo S, Segura J, Morenate C, Medina A, Suarez de Lezo J.Patency of coronary side branches covered by an everolimus-eluting bioresorbable vascular scaffold: clinical outcomes and computed tomography scan follow-up.Eurointervention.2016.11(11): e1283-90 IF:3,712 Q:2

Lopez-Aguilera J, Saint-Gerons JMS, Bellido FM, de Tejada JSDH, Pineda SO, Alvarez-Ossorio MP, Moreno MAR, Pavlovic D, Conde JSDL.Effect of New-Onset Left Bundle Branch Block After Transcatheter Aortic Valve Implantation (CoreValve) on Mortality, Frequency of Re-Hospitalization, and Need for Pacemaker.American Journal Of Cardiology.2016.118(9):1380-1385. IF:3,154

Q:2

Q:1

Jorge E, Pan M, Baptista R, Romero M, Ojeda S, Suarez de Lezo J, Faria H, Calisto J, Monteiro P, Pego M, Suarez de Lezo J.Predictors of Very Late Events After Percutaneous Mitral Valvuloplasty in Patients With Mitral Stenosis.American Journal Of Cardiology.2016. 117(12):1978-1984. IF:3,154

0·2

Bernal FJC, Sanchez MPA, Dominguez JCC, Avalos FC, Ortiz MR, Ortega MD, Penas ER, Rubio DM, Cruzconde JSD.Left-sided native valve infective endocarditis: Influence of age and the presence of underlying heart disease. Medicina Clinica.2016.147:475-480. IF:1,267 Q:2

Suarez de Lezo J, Martin P, Mazuelos F, Novoa J, Ojeda S, Pan M, Segura J, Hernandez E, Romero M, Melian F, Medina A, de Lezo JS.Direct bioresorbable vascular scaffold implantation: Feasibility and midterm results. Catheterization And Cardiovascular Interventions.2016.87(5):E173-82. IF:2,181

Q:3

# In Collaboration

Azzalini L, Giustino G, Ojeda S, Serra A, La Manna A, Ly HQ, Bellini B, Benincasa S, Chavarria J, Gheorghe LL, Longo G, Micciche E, D'Agosta G, Picard F, Pan M, Tamburino C, Latib A, Carlino M, Chieffo A, Colombo A.Procedural and Long-Term Outcomes of Bioresorbable Scaffolds Versus Drug-Eluting Stents in Chronic Total Occlusions The BONITO Registry (Bioresorbable Scaffolds Versus Drug-Eluting Stents in Chronic Total Occlusions).Circulation-Cardiovascular Interventions.2016.9(10):e004284. IF:5,706

Q:1

Hildick-Smith D, Behan MW, Lassen JF, Chieffo A, Lefevre T, Stankovic G, Burzotta F, Pan M, Ferenc M, Bennett L, Hovasse T, Spence MS, Oldroyd K, Brunel P, Carrie D, Baumbach A, Maeng M, Skipper N, Louvard Y.The EBC TWO Study (European Bifurcation Coronary TWO): A Randomized Comparison of Provisional T-Stenting Versus a Systematic 2 Stent Culotte Strategy in Large Caliber True Bifurcations.Circulation-Cardiovascular Interventions.2016.9 (9):e003643. IF:5,706

Q:1



Jorge E, Baptista R, Calisto J, Faria H, Silva C, Monteiro P, Pan M, Pego M.Pulmonary vascular remodeling in mitral valve disease: An optical coherence tomography study.International Journal Of Cardiology.2016.203:576-578. IF:4,638 Q:1

Jorge E, Baptista R, Calisto J, Faria H, Monteiro P, Pan M, Pego M.Optical coherence tomography of the pulmonary arteries: A systematic review.Journal Of Cardiology.2016.67(42401):6-14. IF:2,405 Q:2

Azzalini L, Dautov R, Ojeda S, Serra A, Benincasa S, Bellini B, Giannini F, Chavarría J, Gheorghe LL, Pan M, Carlino M, Colombo A, Rinfret S.Long-term outcomes of rotational atherectomy for the percutaneous treatment of chronic total occlusions.Catheter Cardiovasc Interv.2016.epub IF:2,181 Q:3

Vaquerizo B, Fernandez-Nofreiras E, Oategui I, De Lezo JS, Rumoroso JR, Martin P, Routledge H, Tizon-Marcos H.Second-Generation Drug-Eluting Balloon for Ostial Side Branch Lesions (001-Bifurcations): Mid-Term Clinical and Angiographic Results. Journal Of Interventional Cardiology.2016.29(3):285-292. IF:1,327 Q:3

#### **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 (IS-CIII).Reference: PI12/00440

#### **Clinical Trials**

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 Romero Moreno; Miguel Ángel

\*3341.An Open-label, 2 x 2 Factorial, randomized controlled, clinical trial to evaluate the safety of apixaban vs Vitamin K antagonist and aspirin placebo in patients with atrial fibrillation and acute coronary syndrome or percutaneous coronary intervention. PI: Dr/a Pavlovic Djurovic; Djordje

\*3126. A Phase III, Double-blind, Randomized Placebo-controlled Study to Evaluate the Effects of Dalcetrapib on Cardiovascular (CV) Risk in a Genetically Defined Population With a Recent Acute Coronary Syndrome (ACS): The Dal-GenF Trial

PI: Dr/a Pavlovic Djurovic; Djordje

1681.European study of coronary bifurcations: a randomized study to compare the provisional stenting strategy vs the systematic implantation of two stents in true bifurcation lesions located in large vessels. PI: Dr/a Pan Álvarez-Ossorio, Manuel

2648.Ambulatory electrocardiographic monitoring fot the detection of high-degree atrio-ventricular block in patients with new-onset persistent left bundle branco block alter transcatheter aortic valve implantation. PI: Dr/a Romero Moreno; Miguel Ángel

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

# **GC16 • Cell biology in hematology.** Hypercoagulability

# HIGHLIGHTS



# **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

Arqueros Martínez; Víctor García Torres; Estefanía Martin Calvo; Carmen Molina Hurtado; José Ramón Rodríguez Villa; Antonia Rojas Contreras; Rafael Serrano López; Josefina

# **Post-Doctoral Researchers**

Gutiérrez Mariscal; Francisco Miguel Serrano López; Juana

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Álvarez Rivas; Miguel A. Flores Mesa; David Martínez Losada; Carmen Casaño Sánchez; Javier



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

Serrano-Lopez J, Cancelas JA.Mom Knows better: Imprinted control of Hematopoelic stem cell quiescence.Cell Stem Cell.2016.18(2):158-160. IF:22,387 O:1 D1

Martinez-Moreno JM, Herencia C, Montes de Oca A, Munoz-Castaneda JR, Rodriguez-Ortiz ME, Diaz-Tocados JM, Peralbo-Santaella E, Camargo A, Canalejo A, Rodriguez M, Velasco-Gimena F, Almaden Y.Vitamin D modulates tissue factor and protease-activated receptor 2 expression in vascular smooth muscle cells. Faseb Journal.2016.30(3):1367-1376. IF:5,299 O:1 D1

Perez-Sanchez C, Aguirre MA, Ruiz-Limon P, Barbarroja N, Jimenez-Gomez Y, de la Rosa IA, Rodriguez-Ariza A, Collantes-Estevez E, Segui P, Velasco F, Cuadrado MJ, Teruel R, Gonzalez-Conejero R, Martinez C, Lopez-Pedrera Ch.Atherothrombosis-associated microRNAs in Antiphospholipid syndrome and Systemic Lupus Erythematosus patients.Scientific Reports. 2016.6:31375. IF:5,228

Q:1

Mari-Jimenez P, Martinez-Losada C, Centeno-Haro M, Rodriguez-Garcia G, Perez-Seoane C, Sanchez-Garcia J.A rare composite lymphoma: follicular and in situ mantle cell.Annals Of Hematology.2016.95(8):1351-2. IF:3,022

Q:2

Yebenes-Ramirez M, Serrano J, Martinez-Losada C, Sanchez-Garcia J.Clinical and biological prognostic factors in relapsed acute myeloid leukemia patients.Medicina CLINI-CA.2016.147(5):185-91. IF:1,267

0.5

Chic-Acevedo, Garcia-Torres E, Alvarez-Rivas MA.Cold agglutinin disease of IgA class as ear-

ly manifestation of multiple myeloma and resolution after treatment with new anti-myeloma drugs].Medicina Clinica.2016.147(11):e63-e64. IF:1,267 Q:2

#### In Collaboration

Bernal T, Martinez-Camblor P, Sanchez-Garcia J, Sanz G.Effectiveness of azacitidine for the treatment of higher-risk myelodysplastic syndromes in daily practice: the authors' reply. Leukemia.2016.30(3):740-741. IF:12,104

Q:1 D1

Roy NBA, Wilson EA, Henderson S, Wray K, Babbs C, Okoli S, Atoyebi W, Mixon A, Cahill MR, Carey P, Cullis J, Curtin J, Dreau H, Ferguson DJP, Gibson B, Hall G, Mason J, Morgan M, Proven M, Qureshi A, Garcia JS, Sirachainan N, Teo J, Tedgard U, Higgs D, Roberts D, Roberts I, Schuh A.A novel 33-Gene targeted resequencing panel provides accurate, clinical-grade diagnosis and improves patient management for rare inherited anaemias.British Journal Of Haematology.2016.175:318-330. IF:5,812

Q:1

Bergua JM, Montesinos P, Martinez-Cuadron D, Fernandez-Abellan P, Serrano J, Sayas MJ, Prieto-Fernandez J, Garcia R, Garcia-Huerta AJ, Barrios M, Benavente C, Perez-Encinas M, Simiele A, Rodriguez-Macias G, Herrera-Puente P, Rodriguez-Veiga R, Martinez-Sanchez MP, Amador-Barciela ML, Riaza-Grau R, Sanz MA.A prognostic model for survival after salvage treatment with FLAG-Ida +/- gemtuzumab-ozogamicine in adult patients with refractory/relapsed acute myeloid leukaemia.British Journal of Haematology.2016.174(5):700-710. IF:5,812 Q:1

"Machuca I, Gutierrez-Gutierrez B, Cortes SP, Gracia-Ahufinger I, Serrano J, Madrigal MD, Barcala J, Rodriguez-Lopez F, Rodriguez-Bano J, Torre-Cisneros J.Oral decontamination with aminoglycosides is associated with lower risk of mortality and infections in high-risk patients colonized with colistin-resistant, KPC-producing Klebsiella pneumoniae.Journal Of Antimicrobial Chemotherapy.2016.71(11):3242-3249. IF:4,919 Q:1

Nomdedeu M, Calvo X, Pereira A, Carrio A, Sole F, Luno E, Cervera J, Vallespi T, Munoz C, Gomez C, Arias A, Such E, Sanz G, Grau J, Insunza A, Calasanz MJ, Ardanaz MT, Hernandez-Rivas JM, Azaceta G, Alvarez S, Sanchez J, Martin ML, Bargay J, Gomez V, Cervero CJ, Allegue MJ, Collado R, Campo E, Esteve J, Nomdedeu B, Costa D.Prognostic impact of chromosomal translocations in myelodysplastic syndromes and chronic myelomonocytic leukemia patients. A study by the spanish group of myelodysplastic syndromes.Genes Chromosomes & Cancer.2016.55(4):322-327.

IF:3,96 Q:2

> Kreuz W, Ettingshausen CE, Vdovin V, Zozulya N, Plyushch O, Svirin P, Andreeva T, Bubanska E, Campos M, Benedik-Dolnicar M, Jimenez-Yuste V, Kitanovski L, Klukowska A, Momot A, Osmulskaya N, Prieto M, Salek SZ, Velasco F, Pavlova A, Oldenburg J, Knaub S, Jansen M, Belyanskaya L, Walter O.First prospective report on immune tolerance in poor risk haemophilia A inhibitor patients with a single factor VIII/von Willebrand factor concentrate in an observational immune tolerance induction study.Haemophilia.2016.22(1):87-95. IF:2,673

Q:2

Garza E, Del Poeta G, Martinez-Losada C, Catalano G, Borgia L, Piredda ML, Fabiani E, Gattei V, Lo-Coco F, Noguera NI.A cese of SRSF2 mutation in chronic lymphocytic leukemia. Leukemia Research Reports.2016. 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. Reference: FEHH15\_001



García Torres, E. Effect of immunomodulators (lenadomide and pomalidomide) in lymphoid populations and their impact on the development of the disease. Funding Agency: Asociacion Andaluza de Hematologia y Hemoterapia. Reference: AAHH2015\_001

Losada Martínez, C. Effect of immunomodulators (lenadomide and pomalidomide) in lymphoid populations and their impact on the development of the disease.Funding Agency: AAHH2016\_001

#### Regional

Serrano Lopez, J. Analysis of gene expression using a nanostring platform and of myd88l265p mutation in paraffin-embedded samples for the personalised treatment of diffuse large B-cell lymphoma. Funding agency: Regional Ministry of Health and Social Policy (CISPS).Reference: PIN-0364-2016

## **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

Sánchez García, J. Identification of biomarkers and new therapeutic cell targets of graft-versus-host disease by gene-expression arrays of t-lymphocytes Funding agency: Pfizer Gep SLU.Reference:PSS.0116

Álvarez Rivas, MA. Collaboration agreement with Celgene. Funding agency: Celgene International SARL. Reference: PSS.0120

Sánchez García, J. Gene expression analysis and MYD88 L265 mutation in paraffin embedded samples of diffuse large B cell lymphomas Celgene S.L.U.PSS.0152

Serrano López J. Collaboration agreement with Pzifer. Funding agency:Pfizer, S.L.U. Reference: CCB.0068

#### **Clinical Trials**

0070/11. A multicenter, prospective, open-label, single-arm, phase I-II clinical trial to analyze the induction treatment with a combination of fludarabine, idarubicin, cytarabine, G-CSF and plerixafor for the treatment of young patients with recurrent or resistant LM. PI: Dr/a Serrano López, Josefina

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

PI: Dr/a Gomez Garcia 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.

Pl: 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

0313/12. CLLM1-Protocol of the German CLL-Study Group (GCLLSG) A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study of the Efficacy and Safety of Lenalidomide (Revlimid®) as Maintenance Therapy for High-risk Patients With Chronic Lymphocytic Leukemia Following First-line Therapy.

PI: Dr/a Arqueros Martínez; Víctor

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. Pl: 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

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. Pl: 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. Pl: 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.

Pl: 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.

Pl: 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

0298/14. A phase II multicenter study of carfilzomib, lenalidomide and dexamethasone (KRd) plus high-dose therapy with melphalan-200 and autologous stem cell transplantation, followed by consolidation with KRd, and maintenance with lenalidomide and dexamethasone in patients with high risk smoldering multiple myeloma (SMM) under 65 years. PI: Dr/a Alvarez Rivas, Miguel Angel

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

0024/16.Estudio piloto (Fase II) de combinación de pomalidomida/dexametasona asociado a baja dosis de ciclofosfamida en pacientes con mieloma múltiple refractario que han recibido lenalidomida y bortezumib. Pl: Dr/a Alvarez Rivas, Miguel Angel

\*3269. A Phase 2/3 Multi-center Study to Evaluate the Safety and Efficacy of Blinatumomab in Subjects With Relapsed/Refractory Aggressive B-Cell Non Hodgkin Lymphoma. Pl: Dr/a Sánchez García, Joaquin

\*3218. A Phase 3, Double-Blind, Placebo-controlled Study of Quizartinib (AC220) Administered in Combination With Induction and Consolidation Chemotherapy, and Administered as Maintenance Therapy in Subjects 18 to 75 Years Old With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia.

Pl: Dr/a Serrano López, Josefina

\*3190. A Randomized, Double-Blind Study Evaluating the Efficacy, Safety and Immunogenicity of ABP 798 Compared With Rituximab in Subjects With CD20 Positive B-Cell Non-Hodgkin Lymphoma (NHL).

PI: Dr/a Sánchez García, Joaquin

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

2257. A study to validate an ex vivo individualized test for acute lymphoblastic leukemia. PI: Dr/a Serrano López, Josefina

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

2638. PASS Post-Authorization Safety Study (PASS) prospective, non-interventionist, de-

signed 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

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

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 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

2852.A retrospective study of clinical, phenotypic and genetic factors of peripheral T-cell lymphomas in the Spanish population. Pl: Dr/a Sánchez García, Joaquin

# **GC17** • Pathophysiology of the endocrine system of vitamin D. Biotechnology and aging

HIGHLIGHTS



# **Team Leader**

Principal Investigator (PI) José Manuel Quesada Gómez md1qugoj@uco.es CCIBER on Fragility and Heathly Aging (CIBERFES) (Collaborator)

# Researchers

Casado Díaz; Antonio Mata Granados; José María Santiago Mora; Raquel Serrano Alférez; Ignacio

Pre-Doctoral Researchers (PhD Students y MSc Students) Cuenca Acevedo; Rafael



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

Casado-Diaz A, Anter J, Dorado G, Quesada-Gomez JM.Effects of quercetin, a natural phenolic compound, in the differentiation of human mesenchymal stem cells (MSC) into adipocytes and osteoblasts.Journal Of Nutritional Biochemistry.2016.32:151-162. IF:4,668 Q:1

Navarro-Valverde C, Sosa-Henriquez M, Alhambra-Exposito MR, Quesada-Gomez JM.Vitamin D-3 and calcidiol are not equipotent. Journal Of Steroid Biochemistry And Molecular Biology.2016.164:205-208. IF:3,985 Q:2

Anter J, Quesada-Gomez JM, Dorado G, Casado-Diaz A.Effect of hydroxytyrosol on human mesenchymal stromal/Stem Cell Differentiation into Adipocytes and osteoblasts.Archives Of Medical Research.2016.47(3):162-71. IF:2,219 Q:3

## **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

Quesada Gómez, JM. Effect of the PTH (1-34) and vitamin D3 on mobilization of endothelial precursor cells and their role in regenerative medicine applied to the skin ulcers healing in diabetics. Funding agency: Carlos III Health Institute (ISCIII). Reference: PI15/01857

Casado Días, A. Effect of the PTH (1-34) and vitamin D3 on mobilization of endothelial precursor cells and their role in regenerative medicine applied to the skin ulcers healing in diabetics. Funding agency: Fundación Española de investigación ósea y del metabolismo nineral. Reference: FEIOMM2016\_001

Quesada Gómez, JM. Fragility and Healthy Aging (Ciberfes). Funding agency: Carlos III Health Institute (ISCIII). Reference: CB16/10/00501 Expected starting date:2017

#### 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

# **Clinical Trials**

3071. Non-interventional study with Binosto 70 mg effervescent tablets once weekly investigating gastro-intestinal events and medication errors.

PI: Dr/a Quesada Gómez, José Manuel

# **GC18** • Translational research in surgery of solid organ transplants

# HIGHLIGHTS

PUBLICATIONS

Імраст Fасток **37,932** 





# Team Leader

Principal Investigator (PI): Francisco Javier Briceño Delgado javibriceno@hotmail.com

# Researchers

Ciria Bru; Rubén Rufián Peña; Sebastián Leva Vallejo; Manuel López Cillero; Pedro Muñoz Casares;Francisco Cristobal Padial Aguado;Ana Cristina Pozo Laderas; Juan Carlos Regueiro López;Juan Carlos Robles Ariza;Juan Carlos Ruiz Rabelo; Juan Post-Doctoral Researchers Arjona Sánchez; Álvaro Pleguezuelo Navarro; María

Pre-Doctoral Researchers (PhD Students y MSc Students) Gómez Gómez; Irene Jiménez Gómez; Jesús Navarro Rodríguez; Elena

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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

Ciria R, Cherqui D, Geller DA, Briceno J, Wakabayashi G.Comparative Short-term Benefits of Laparoscopic Liver Resection: 9000 Cases and Climbing.Annals Of Surgery.2016.263(4):761-77. IF:8,569 Q:1 D1

Arjona-Sanchez A, Cadenas-Febres A, Cabrera-Bermon J, Munoz-Casares FC, Casado-Adam A, Sanchez-Hidalgo JM, Lopez-Andreu M, Briceno-Delgado J, Rufian-Pena S.Assessment of RIFLE and AKIN criteria to define acute renal dysfunction for HIPEC procedures for ovarian and non ovarian peritoneal malignances". European Journal Of Surgical Oncology. 2016. 42(6):869-876.

IF:2,94

Q:2

Munoz-Casares FC, Medina-Fernandez FJ, Arjona-Sanchez A, Casado-Adam A, Sanchez-Hidalgo JM, Rubio MJ, Ortega-Salas R, Munoz-Villanueva MC, Rufian-Pena S, Briceno FJ.Peritonectomy procedures and HIPEC in the treatment of peritoneal carcinomatosis from ovarian cancer: Long-term outcomes and perspectives from a high-volume center.European Journal Of Surgical Oncology.2016.42(2):224-33. IF:2,94

0.5

Medina-Fernandez FJ, Garcilazo-Arismendi DJ, Garcia-Martin R, Rodriguez-Ortiz L, Gomez-Barbadillo J, Gallardo-Valverde JM, Martinez-Duenas JL, Navarro-Rodriguez E, Torres-Tordera E, Diaz-Lopez CA, Briceno J.Validation in colorectal procedures of a useful novel approach for the use of C-reactive protein in postoperative infectious complications. Colorectal Disease.2016.18(3):O111-O118. IF:2,452 O:3

#### **In Collaboration**

Rodriguez AH, Aviles-Jurado FX, Diaz E, Schuetz P, Trefler SI, Sole-Violan J, Cordero L, Vidaur L, Estella A, Pozo Laderas JC, Socias L, Vergara JC, Zaragoza R, Bonastre J, Guerrero JE, Suberviola B, Cilloniz C, Restrepo MI, Martin-Loeches I.Procalcitonin (PCT) levels for ruling-out bacterial coinfection in ICU patients with influenza: A CHAID decision-tree analysis. Journal Of Infection.2016.72(2):143-151. IF:4,382

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Q:1

Jurado-Garcia J, Munoz Garcia-Borruel M, Rodriguez-Peralvarez ML, Ruiz-Cuesta P, Poyato-Gonzalez A, Barrera-Baena P, Fraga-Rivas E, Costan-Rodero G, Briceno-Delgado J, Montero-Alvarez JL, de la Mata-Garcia M.Impact of MELD Allocation System on Waiting List and Early Post-Liver Transplant Mortality.Plos One.2016.11(6):-e0155822. IF:3,057

Krawczyk M, Grat M, Adam R, Polak WG, Klempnauer J, Pinna A, Di Benedetto F, Filipponi F, Senninger N, Foss A, Rufian-Pena S, Bennet W, Pratschke J, Paul A, Settmacher U, Rossi G, Salizzoni M, Fernandez-Selles C, de Rituerto STM, Gomez-Bravo MA, Pirenne J, Detry O, Majno PE, Nemec P, Bechstein WO, Bartels M, Nadalin S, Pruvot FR, Mirza DF, Lupo L, Colledan M, Tisone G, Ringers J, Daniel J, Torra RC, Gonzalez EM, Canizares RB, Martinez VCM, Rodriguez FSJ, Yilmaz S, Remiszewski P.Liver Transplantation for Hepatic Trauma: A Study From the European Liver Transplant Registry. Transplantation.2016.100(11):2372-2381. IF:3,69 Q:2

Cascales-Campos PA, Lopez-Lopez V, Munoz-Casares FC, Feliciangeli E, Torres Melero J, Barrios P, Morales R, Ramos I, Ortega G, Camps B, Gonzalez-Bayon L, Bretcha-Boix P, Farre-Alegre J, Gonzalez-Moreno S, Gil J.Morbidity and mortality outcomes after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in patients aged 75 years and over: Spanish group of peritoneal cancer surgery (GECOP) multicenter study.Surgical Oncology-Oxford.2016.25(2):111-116. IF:3,514

Q:2

Q:1

Sleightholm R, Foster JM, Smith L, Ceelen W, Deraco M, Yildirim Y, Levine E, Munoz-Casares C, Glehen O, Patel A, Esquivel J.The American Society of Peritoneal Surface Malignancies Multi-Institution evaluation of 1,051 advanced ovarian cancer patients undergoing cytoreductive surgery and HIPEC: An introduction of the peritoneal surface disease severity score.Journal Of Surgical Oncology.2016.114(7):779-784. IF:3,151

Q:2

Arenas-Bonille AJ, Campos-Hernandez JP, Carrasco-Valiente J, Marquez-Lopez FJ, Ruiz-Garcia JM, Sanchez-Gonzaleza A, Salamanca-Bustos JJ, Regueiro-Lopez JC, Navarro-Cabello MD, Requena-Tapia MJ.Influence of Donor and Recipient Ages in Survival of Simultaneous Pancreas-Kidney Transplantation.Transplantation Proceedings.2016.48:3033-3036. IF:0,867 O:4 Salamanca-Bustos JJ, Campos-Hernandez JP, Sanchez-Hidalgo JM, Arjona-Sanchez A, Sanchez-Gonzalez A, Arenas-Bonilla AJ, Ruiz-Rabelo J, Carrasco-Valiente J, Ruiz-Garcia J, Regueiro-Lopez JC, Briceno-Delgado J, Requena-Tapia MJ.Validation of the Pancreatic Donor Risk Index in Simultaneous Pancreas-Kidney Transplantation Performed in Cordoba Hospital From 2000 to 2015.Transplantation Proceedings.2016.48:3037-3039. IF:0,867 Q:4

Rodriguez-Gomez J, Leon R, Robles JC, de la Torre-Cisneros J.Adult pneumoccocical sepsis: Should we rule out congenital anesplenia?.Enfermedades Infecciosas Y Microbiologia Clinica.2016.34(9):2007-2008. IF:1,53

# **Research Funding**

#### National

Q:3

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 (IS-CIII).Reference: PI14/01559

Ciria Bru, R. Rescue paragraph liver transplant grafts discarded normothermic extracorporeal perfusion. Funding Agency: Fundación Mutua Madrileña Reference: FMM-14-002

Briceño Delgado, FJ. External validation of a donor-recipient matching model in liver transplantation based on artificial neural networks. Funding Agency: Institute Carlos III Health (IS-CIII).Reference: PI15/01570

#### Regional

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 Microgenics. Funding agency: Microgenics GMBH. Reference: PSS.0105

Briceño Delgado, FJ.Agreement with ADALIA. Funding agency: ADALIA FARMA S.L. Reference: CCB.0085

# **Clinical Trials**

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

# **GC19** • Applications of machine vision

# HIGHLIGHTS









# **Team Leader**

Principal Investigator (PI): Rafael Medina Carnicer rmedina@uco.es PAIDI TIC-161 Scientific Group

# Researchers

Carmona Poyato; Ángel Fernández García; Nicolás Luis Garrido Castro; Juan Luis Madrid Cuevas; Francisco José Marín Jiménez; Manuel Jesús Muñoz Salinas;Rafael Yeguas Bolivar;Enrique Post-Doctoral Researchers Romero Ramírez; Francisco José

Pre-Doctoral Researchers (PhD Students y MSc Students) Cazzato; Dario



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

Garrido-Jurado S, Munoz-Salinas R, Madrid-Cuevas FJ, Medina-Carnicer R.Generation of fiducial marker dictionaries using Mixed Integer Linear Programming.Pattern Recognition.2016.51:481-491. IF:3,399 Q:1

Lopez-Fernandez D, Madrid-Cuevas FJ, Carmona-Poyato A, Munoz-Salinas R, Medina-Carnicer R.A new approach for multi-view gait recognition on unconstrained paths. Journal Of Visual Communication And Image Representation.2016.38:396-406. IF:1,53 Q:2

Fernandez-Garcia NL, Del-Moral Martinez L, Carmona-Poyato A, Madrid-Cuevas FJ, Medina-Carnicer R.A new thresholding approach for automatic generation of polygonal approximations. Journal Of Visual Communication And Image Representation.2016.35:155-168. IF:1,53 Q:2

Madrid-Cuevas FJ, Aguilera-Aguilera EJ, Carmona-Poyato A, Munoz-Salinas R, Medina-Carnicer R, Fernandez-Garcia NL.An efficient unsupervised method for obtaining polygonal approximations of closed digital planar curves.Journal Of Visual Communication And Image Representation.2016.39:152-163. IF:1,53

Q:2

Garrido-Jurado S, Munoz-Salinas R, Madrid-Cuevas FJ, Marin-Jimenez MJ.Simultaneous reconstruction and calibration for multi-view structured light scanning.Journal Of Visual Communication And Image RepresentatioN.2016.39:120-131. IF:1,53

Q:2

Lopez-Fernandez D, Madrid-Cuevas FJ, Carmona-Poyato A,

MJ. Marin-Jimenez Munoz-Salinas R, Medina-Carnicer R.Viewpoint-independent gait recognition through morphological descriptions of 3D human reconstructions.Image And Vision Computing.2016.48(49):1-13. IF:1,766 Q:2

Aguilera-Aguilera,Carmona-Poyato,A., Madrid-Cuevas, F., Marín Jiménez, M.. Fast computation of optimal polygonal approximations of digital planar closed curves.Graphics Models.2016.84:15-27. IF:0,821 Q:3

Lopez-Quintero MI, Marin-Jimenez MJ, Munoz-Salinas R, Madrid-Cuevas FJ, Medina-Carnicer R.Stereo Pictorial Structure for 2D articulated human pose estimation.Machine Vision And Applications.2016.27(2):157-174. IF:1,272 Q:3

### In Collaboration

Castro FM, Marin-Jimenez MJ, Guil N.Multimodal features fusion for gait, gender and shoes recognition.Machine Vision And Applications.2016.27(8):1213-1228. IF:1,272 Q:3

# **Research Funding**

#### National

Medina Carnicer, R. Vision system for tracking and mapping, fusing markers, characteristic points, 3D information and color, and its application to 3-dimensional reconstruction and augmented reality. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: TIN2016-75279-P

Salinas Muñoz, R.Volumetric Measuring System. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference: RTC-2016-5661-1\_01

#### Regional

Garrido Castro, JL. Development and validation of inertial sensors applied to metrology in patients with axial spondyloarthritis. Funding Agency: Regional Ministry of Health and Social Policy (CISPS). Reference: PIN-0079-2016



# **GC20** • Genetics and behavioural diseases

# HIGHLIGHTS



# **Team Leader**

Principal Investigator (PI) Manuel Ruiz Rubio ge1rurum@uco.es PAIDI BIO-272 Scientific Group PAIDI HUM-924 Scientific Group (PI: Juan Antonio Moriana)

#### **Researchers**

Moriana; Juan Antonio Alejandre Duran; Encarna Alós Cívico, Francisco José Burgos Marín; Rafael Guijarro Granados; Teresa Jiménez Romero; Mª Salud Martin Borreguero; Pilar Romero Balsera; María Auxiliadora Sánchez Raya; Mª Araceli Sánchez Vázquez; Vicente Post-Doctoral Researchers García Torres; Francisco Mariano Gámez Del Estal; M Del Mar

Pre-Doctoral Researchers (PhD Students y MSc Students) Osuna Luque; Jaime Rodríguez Ramos, Ángel



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

Moreno EM, Moriana JA.User involvement in the implementation of clinical guidelines for common mental health disorders: a review and compilation of strategies and resources.Health Research Policy And Systems.2016.14:61. IF:2,107

Q:2

Moreno EM, Moriana JA.Clinical guideline implementation strategies for common mental health disorders.Revista De Psiquiatria Y Salud Mental.2016.9(1):51-62. IF:1,65 Q:4

#### In Collaboration

Muñoz-Navarro R, Cano-Vindel A, Wood CM, Ruíz-Rodríguez P, Medrano LA, Limonero JT, Tomás-Tomás P, Gracia-Gracia I, Dongil-Collado E, Iruarrizaga MI; PsicAP Research Group.. The PHQ-PD as a screening tool for panic disorder in the primary care setting in Spain.Plos One.2016.11(8):e0161145. IF:3,057 O:1

Spangenberg L, Zenger M, Garcia-Torres F, Mueller V, Reck M, Mehnert A, Vehling S.Dimensionality, Stability, and Validity of the Beck Hopelessness Scale in Cancer Patients Receiving Curative and Palliative Treatment. Journal Of Pain And Symptom Management. 2016.51:615-622. IF:2,649 Q:1

Cuadrado, F., Rosar, M., Moriana, J.A., & Antolí, A.Alzheimer's disease representation in the picture books.Ocnos.2016.15:7-20. IF:0

# **Research Fundings**

#### National

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

#### Regional

Sánchez Raya, A.Mobile computing applicationfor early detection, diagnosis and intervention in health care and its integration of clinical management system.Funding Agency: Regional Ministry of Health and Social Policy (CISPS). Reference: PIN-0072-2016

#### **Contracts with Companies**

Ruiz Rubio, M. Caenorhabditis elegans as models of neurological diseases.Funding agency: Canvax Biotech S.L. Reference:INTER.0002

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

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.



# **GC21 • Metabolomics. Identification of bioactive components**

HIGHLIGHTS



# Team Leader

# Principal Investigator (PI):

M<sup>a</sup> Dolores Luque de Castro

qa1lucam@uco.es PAIDI FQM-227 Scientific Group Emerging Researcher (ER) CIBER on Fragility and Heathly Aging (CIBERFES) (Collaborator)

# Emerging Researcher (ER) Feliciano Priego Capote

# Researchers

Delgado Povedano; Mª del Mar Fernández Peralbo; María Auxiliadora Ledesma Escobar, Carlos Augusto Mena Bravo; Antonio Molina Calle; María Peralbo Molina; Angela Post-Doctoral Researchers Calderón Santiago; Mónica Delgado De La Torre; María Pilar Sánchez De Medina Baena; Verónica

Pre-Doctoral Researchers (PhD Students y MSc Students) Castillo Peinado; Laura Luque Córdoba; Diego



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. sampleOne 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

Delgado-Povedano Md, Sanchez de Medina V, Bautista J, Priego-Capote F, Luque de Castro MD.Tentative identification of the composition of Agaricus bisporus aqueous enzymatic extracts with antiviral activity against HCV: A study by liquid chromatography-tandem mass spectrometry in high resolution mode.Journal Of Functional Foods.2016.24:403-419. IF:3,973 Q:1 D1

Fernandez-Peralbo MA, Gomez-Gomez E, Calderon-Santiago M, Carrasco-Valiente J, Ruiz-Garcia J, Requena-Tapia MJ, de Castro MDL, Priego-Capote F.Prostate Cancer Patients-Negative Biopsy Controls Discrimination by Untargeted Metabolomics Analysis of Urine by LC-QTOF: Upstream Information on Other Omics.Scientific Reports.2016. (6):38243. IF:5,228

Q:1

Peralbo-Molina A, Calderon-Santiago M, Priego-Capote F, Jurado-Gamez B, Luque de Castro MD.Identification of metabolomics panels for potential lung cancer screening by analysis of exhaled breath condensate.Journal Of Breath Research.2016.10(2):2600. IF:4,177 Q:1

Peralbo-Molina A, Calderon-Santiago M, Priego-Capote F, Jurado-Gamez B, Luque de Castro MD.Metabolomics analysis of exhaled breath condensate for discrimination between lung cancer patients and risk factor individuals.Journal Of Breath Research.2016.10(1):16011-16011. IF:4,177 O:1

Lopez-Bascon MA, Calderon-Santiago M, Priego-Capote F.Confirmatory and quantitative analysis of fatty acid esters of hydroxy fatty acids in serum by solid phase extraction coupled to liquid chromatography tandem mass spectrometry.Analytica Chimica Acta.2016.943:82-88. IE:4.712

Q:1

Delgado-Povedano MM, Calderon-Santiago M, Priego-Capote F, Luque de Castro MD.Development of a method for enhancing metabolomics coverage of human sweat by gas chromatography-mass spectrometry in high resolution mode.Analytica Chimica Acta.2016.905:115-125. IF:4,712 Q:1

Castillo-Peinado LS, Luque de Castro MD.Present and foreseeable future of metabolomics in forensic analysis. Analytica Chimica Acta.2016.925:1-15. IF:4.712

Q:1

Molina-Calle M, Sanchez de Medina V, Delgado de la Torre MP, Priego-Capote F, Luque de Castro MD.Development and application of a quantitative method based on LC-QqQ MS/ MS for determination of steviol glycosides in Stevia leaves.Talanta.2016.154:263-9. IF:4,035 Q:1

Ledesma-Escobar CA, Priego-Capote F, Luque de Castro MD.Effect of sample pretreatment on the extraction of lemon (Citrus limon) components.Talanta.2016.153:386-391. IF:4,035 Q:1

Lopez-Bascon MA, Priego-Capote F, Peralbo-Molina A, Calderon-Santiago M, Luque de Castro MD.Influence of the collection tube on metabolomic changes in serum and plasma. Talanta. 2016. 150:681-689. IF:4,035

Q:1

Delgado-Povedano MM, Calderon-Santiago M, Priego-Capote F, Luque de Castro MD. Study of sample preparation for quantitative analysis of amino acids in human sweat by liquid chromatography-tandem mass spectrometry.Talanta.2016.146:310-317. IF:4,035 Q:1

Mena-Bravo A, Priego-Capote F, Luque de Castro MD.Two-dimensional liquid chromatography coupled to tandem mass spectrometry for vitamin D metabolite profiling including the C3-epimer-25-monohydroxyvitamin D3. Journal Of Chromatography.2016.1451:50-7. IF:3,926 Q:1 Calderon-Santiago M, Fernandez-Peralbo MA, Priego-Capote F, Luque de Castro MD.MSCombine: a tool for merging untargeted metabolomic data from high-resolution mass spectrometry in the positive and negative ionization modes. Metabolomics.2016.12(3):-UNSP 43. IF:3,661 Q:2

Delgado-Povedano MD, Calderon-Santiago M, Priego-Capote F, Jurado-Gamez B, de Castro MDL.Recent advances in human sweat metabolomics for lung cancer screening.Metabolomics.2016.12(11):-166. IF:3,661 Q:2

Molina-Calle M, Priego-Capote F, Luque de Castro MD.HS-GC/MS volatile profile of different varieties of garlic and their behavior under heating.Analytical And Bioanalytical Chemistry.2016.408(14):3843-3852. IF:3,125 Q:2

Ledesma-Escobar CA, Priego-Capote F, Luque de Castro MD.Comparative Study of the Effect of Sample Pretreatment and Extraction on the Determination of Flavonoids from Lemon (Citrus limon)..Plos One.2016.11(1):-e0148056. IF:3,057 Q:1

Luque de Castro MD.Sweat as a clinical sample: what is done and what should be done. Bloanalysis.2016.8(2):85-88. IF:2,813

Q:2

Castillo-Peinado LD, de Castro MDL.The role of ultrasound in pharmaceutical production: sonocrystallization.Journal Of Pharmacy And Pharmacology.2016.68(10):1249-1267. IF:2,363 Q:2

Luque de Castro MD.Could metabolomics clarify the multiple sclerosis-vitamin D metabolites relationship?.Journal of Multiple Sclerosis.2016.3:1710. IF:0

# In Collaboration

Serrano-Rodriguez JM, Gomez-Diez M, Esgueva M, Castejon-Riber C, Mena-Bravo A,



Priego-Capote F, Serrano Caballero JM, Munoz A.Pharmacokinetics and pharmacodynamics of ramipril and ramiprilat after intravenous and oral doses of ramipril in healthy horses.Veterinary Journal.2016.208:38-43. IF:1,68 Q:1

# **Research Funding**

#### National

López Miranda, J (Priego Capote F (CO-PI) 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. Strategy development for improving the mass-spectrometric detection in guided metabiological 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

#### International

Priego Capote, F.Interreg-Med Aristoil Project. Funging agency:European Comission. Reference: MED-1033

#### **Contracts with Companies**

Luque de Castro, MD.Determination of vitamin D and serum samples metabolites from women with osteoporosis. Funding Agency: Institute of Health Carlos III (ISCIII). Reference: 12014156

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.Reference: 12014165

Priego Capote, F. Extraction of stevia plants: identifying the components of the extract and optimizing the extraction and purification of the compounds of interest. Funging agency: Consortium with "Campus de Excelencia Internacional en Agroalimentación (ceiA3)"( Agrifood Campus of International Excellence)

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). Reference:12015111

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 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.Determination of vitamin D and its 25(OH)D 1,25(OH)2D and 24,15(OH)2D metabolites in serum samples provided by the Organisation.Funding Agency: Ospedale San Raffaele S.R.L. Reference: PSS.0146

Luque de Castro, MD.Metabolomics profile of sweat samples by GC-QTOF (in the latter case in positive and negative ionization modes). Identificaction by public databases and the private database of the Research Group. Funding Agency: Beiersdorf AG. Reference:PSS.0137

# **GC22** • Epigenetics

# HIGHLIGHTS

**ACTIVE PROJETS** 





#### **Team Leader**

#### Principal Investigator (PI): Teresa Roldán Arjona

ge2roarm@uco.es PAIDI BIO-301 Scientific Group Researchers Rodríguez Ariza; Rafael

#### Post-Doctoral Researchers Cordoba Cañero; Mª Dolores García Ortiz; Mª Victoria Morales Ruiz; Mª Teresa Parrilla Doblas; Jara Teresa Oliveira Ricon; Raphael

Pre-Doctoral Researchers (PhD Students y MSc Students) Arroyo de Alba; Noelia Barbado García-Gil; Casimiro Devesa Guerra; Iván Dorado León; Macarena



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.

#### **Research Funding**

#### National

Roldán Arjona, M<sup>a</sup> 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

Roldán Arjona, M<sup>a</sup> T. Dynamization Actions Europe Researchs.Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference 201460000027968

Roldán Arjona, M<sup>a</sup> T. DNA repairs by base escision: from genome maintenance to epigenome issue. Funding agency: Spanish Ministry of Economy and Competitiveness (MINE-CO). Reference: BFU2016-80728-P. Expected starting date:2017

#### 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

#### International

Roldán Arjona, M<sup>a</sup> T. Epigenetic Chemical Biology (EPICHEM). Funding agency: European Commision. Reference: CMST COST Action CM1406 http://www.cost.ou/COST Actions/cmst/Ac-

http://www.cost.eu/COST\_Actions/cmst/Actions/CM1406?management

#### **Contracts with Companies**

Roldán Arjona, M<sup>a</sup> T. Services provided for Canvax. Funding agency: Canvax Biotech S.L. Reference:PSS.0032



# **GC23** • Metabolism in Childhood

# HIGHLIGHTS



# **Team Leader**

# **Principal Investigator (PI)** Mercedes Gil Campos h02gicam@uco.es CIBER on Obesity and Nutrition (CIBERobn) CIBER on Rare Diseases (CIBERER) (Collaborator :Eduardo López Laso) PAIDI CTS-639 Scientific Group

# **Researchers**

Pérez Navero; Juan Luis Antón Gamero; Montserrat De La Torre Aguilar; Mª José Fernández Gutiérrez; José Fernando Flores Rojas; Katherine Ibarra De La Rosa; Ignacio López Laso; Eduardo Mateos González; María Elena Ulloa Santamaría; María Esther Velasco Jabalquinto; María José

**Post-Doctoral Researchers** Llorente Cantarero; Francisco Jesús

Pre-Doctoral Researchers (PhD Students y MSc Students) Ordoñez; María Dolores



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

Pérez-Navero JL, de la Torre-Aguilar MJ, Ibarra de la Rosa I, Gil-Campos M, Gómez-Guzmán E, Merino-Cejas C, Muñoz-Villanueva MC, Llorente-Cantarero FJ.Cardiac Biomarkers of Low Cardiac Output Syndrome in the Postoperative Period.Rev Esp Cardiol.2016. 70(4):267-274

IF:4,596 Q·1

Baena-Gomez MA, de la Torre-Aguilar MJ, Aguilera-Garcia CM, Olza J, Perez-Navero JL, Gil-Campos M.Inflammatory Response Using Different Lipid Parenteral Nutrition Formulas in Children After Hematopoietic Stem Cell Transplantation.Nutrition And Cancer-An International Journal.2016.68(5):804-810. IF:2,241 O:3

Priego Ruiz MP, Lopez Laso E, Munoz Sanchez R, Perez Navero JL.Acute myelopathy: importance of early diagnosis.Anales De Pediatria.2016.84(6):348-349. IF:0,773 0:4

#### In Collaboration

McEntagart M, Williamson KA, Rainger JK, Wheeler A, Seawright A, De Baere E, Verdin H, Bergendahl LT, Quigley A, Rainger J, Dixit A, Sarkar A. Lopez Laso E. Sanchez-Carpintero R. Barrio J. Bitoun P. Prescott T. Riise R. McKee S. Cook J, McKie L, Ceulemans B, Meire F, Temple IK, Prieur F, Williams J, Clouston P, Nemeth AH, Banka S, Bengani H, Handley M, Freyer E, Ross A, van Heyningen V, Marsh JA, Elmslie F, FitzPatrick DR.A Restricted Repertoire of De Novo Mutations in ITPR1 Cause Gillespie Syndrome with Evidence for Dominant-Negative Effect.American Journal Of Human Genetics.2016.98(5):981-992. IF:10,794 Q:1 D1

M. Simon, M. Azkargorta, L. Guerra, L. Nonell, M. López-Santamaria, M. Garrido, M.E. Mateos, C. Belendez, D. Plaza, F. Hernandez, M. Mendiola, I. Ojanguren, M. Childs, P. Czauderna, R. Maibach, B. Morland, M.A. Buendia, F. Elortza, R. Planas, M.-R. Sarrias, M. Sala, C. Armengol.Comprehensive Proteomic study of hepatoblatoma: identification of a prognosti signature and deregulated pathways.Journal of Hepatology .2016.64 (2): S302 IF:10,57 Q:1 D1

Ng YS, Alston CL, Diodato D, Morris AA, Ulrick N, Kmoch S, Houstek J, Martinelli D, Haghighi A, Atiq M, Gamero MA, Garcia-Martinez E, Kratochvilova H, Santra S, Brown RM, Brown GK, Ragge N, Monavari A, Pysden K, Ravn K, Casey JP, Khan A, Chakrapani A, Vassallo G, Simons C, McKeever K, O'Sullivan S, Childs AM, Ostergaard E, Vanderver A, Goldstein A, Vogt J, Taylor RW, McFarland R.The clinical, biochemical and genetic features associated with RM-ND1-related mitochondrial disease.Journal Of Medical Genetics.2016.53(11):768-775. IF:5,65

Palomo Atance E, Bahillo Curieses P, Bueno Lozano G, Feliu Rovira A, Gil-Campos M, Lechuga-Sancho AM, Ruiz Cano R, Vela Desojo A.Recommendations of the Spanish Paediatric Endocrinology Society Working Group on Obesity on eating habits for the prevention of obesity and cardiovascular risk factors in childhood.Anales de Pediatria.2016.84(3):178-178. IF:0,773 Q:4

Opladen T, Cortes-Saladelafont E, Mastrangelo M, Horvath G, Pons R, Lopez-Laso E, Fernandez-Ramos JA, Honzik T, Pearson T, Friedman J, Scholl-Burgi S, Wassenberg T, Jung-Klawitter S, Kuseyri O, Jeltsch K, Kurian MA, Garcia-Cazorla A.The International Working Group on Neurotransmitter related Disorders (iNTD): A worldwide research project focused on primary and secondary neurotransmitter disorders.Molecular Genetics And Metabolism Reports.2016.(9):61-66. IE:0

#### **Research Funding**

#### National

Q:1

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:Institute Carlos III Health (ISCIII).Reference: PI13/01245 Ordeñez MD. Research Grant: Clinical trial to effectiveness lactoferrin assessment.Funding agency: Fundacion Agrupacion Mutua. Reference: F.AGRUPACIO\_002

Gil Campos, M.CIBERObn. Funding agency:Institute Carlos III Health (ISCIII).Reference: CB15/00131

Gil Campos, M.Volumetric Measuring System. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO).Reference: RTC-2016-5661-1\_02 Expected starting date:2017

#### Regional

Anton Gamero,M. Developing of clinical decision supports system for management chronic kidney disease no terminal in children based on data mining about REPIR I. Funding Agency: Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PIN-0385-2016 Expected starting date:2017

Ordeñez MD. Lactoprem: Clinical trial to effectiveness lactoferrin assessment in the prevention of sepsis in preterm neonates. Biomonitoring antiinflamtories mechanisms, antioxidants, and the intestine microbiota. Regional Ministry of Equality, Health and Social Policies (CISPS). Reference: PI-0323-2016 Expected starting date:2017

#### International

Perez Navero JL.Search EUCLIDS -The genetic basis of meningococcal and other life threatening bacterial infections of childhood. Funding Agency: European Comission.Reference: OPI2010/200

Mateos Gonzalez, ME.Search ChiLTERN - Children's Liver Tumour European Research Network Fundign Agency: European Comission. Reference:PHC-18-2015-001

#### **Contratcs with Companies**

Gil Campos, M. Design and development of nutritionally balanced foods, appealing and comfortable/easy to handle specified for ages 3 and 4. Funding agency: Grupo Sada P.A.S.L.Reference ITC-20151270



Gil Campos, M. Development of advanced fats. Funding agency: Aceites Del Sur-Coosur S.A.Reference: ITC-20151323

#### **Clinical Trials**

0061/11. European Neuroblastoma Treatment Protocol for low or intermediate risk / European Low and Intermediate Risk Neuroblastoma. Pl: Dr/a Mateos González, María Elena

0316/15. An International Prospective Study on Clinically Standard-risk Medulloblastoma in Children Older Than 3 to 5 Years With Lowrisk Biological Profile (PNET 5 MB-LR) or Average-risk Biological Profile (PNET 5 MB-SR). Pl: Dr/a Mateos González, María Elena

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

\*International patientes registration with Niemann-Pick tipo C. PI: Dr/a López Laso, Eduardo

\*\*Patient Registry of International working group on inborn errors of neurotransmitter metabolism. PI: Dr/a López Laso, Eduardo



# **GE1** • Oxidative stress and nutrition

# HIGHLIGHTS



# **Team Leader**

# Principal Investigator (PI) Isaac Túnez Fiñana fm2tufii@uco.es

Cooperative Research Thematic Network on Aging and Frailty (RETICEF) (Collaborator) PAIDI CTS-624 scientific group Spanish Multiple Sclerosis Network (REEM) (PI: Eduardo Agüera Morales)

#### Researchers

Agüera Morales; Eduardo Cruz Guerrero; Antonio Gascón Luna; Félix Jimena Medina; Ignacio Lillo Roldán; Rafael Luque Carabot; Evelio Peña Amaro; José Ruiz Villen; María Concepción Post-Doctoral Researchers Sánchez López; Fernando

Pre-Doctoral Researchers (PhD Students y MSc Students) Aguilar Luque; Macarena Bahamonde Román; María del Carmen Conde Gavilán; Cristina Galván Jurado; Alberto

# Other members of the Group (Nursing; Technical; and Administrative Staff) Giraldo Polo; Ana Isabel

Gómez Chaparro; José María La Torre Luque; Manuel

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

Escribano BM, Aguilar-Luque M, Bahamonde C, Conde C, Lillo R, Sanchez-Lopez F, Giraldo AI, Cruz AH, Luque E, Gascon F, Aguera E, Tunez I. Natalizumab Modifies Catecholamines Levels Present in Patients with Relapsing-Remitting Multiple Sclerosis. Current Pharmaceutical Design. 2016. 22(31):4876-4880. IF:3,052

Escribano BM, Santamaria A, de Lima ME, Medina-Fernandez FJ, Bashir S, Tunez I.Brain Magnetic Stimulation in Animal Models: A Valuable Lesson for Clinical Applications. CNS & Neurological Disorders-Drug Targets. 2016. 15(7):845-856. IF:2,188

Q:3

Q:2

Aguera E, Castilla S, Luque E, Jimena I, Leiva-Cepas F, Ruz-Caracuel I, Pena J .Muscular hypertrophy and atrophy in normal rats provoked by the administration of normal and denervated muscle extracts. Histology and Histopathology. 2016. 31(12):1367-79. IF:1,875 0:4

Girela-Lopez E, Ruz-Caracuel I, Beltran C, Jimena I, Leiva-Cepas F, Jimenez-Reina L, Pena J.Histological Changes in Skeletal Muscle During Death by Drowning: An Experimental Study. American Journal of Forensic Medicine and Pathology. 2016. 37(2):118-26. IF:0,795 Q:4

#### **Research Funding**

#### National

Túnez Fiñana, I. Drug development against tumor cells mothers (CSC) by screening libraries using synthetic kinase inhibitors of GPCRs and NFAT - calcineurininteraction. Funding Agency: Ministry of Economy and Competitiveness (MINECO). Reference: RTC-2015-3386-1\_1 Agüera Morales, E. Spanish Multiple Sclerosis Network. Funding agency: Institute of Health Carlos III (ISCIII). Reference: RD16/0015/0026 To Begin in 2017

#### **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

Tunez Fiñana, I. Agreement with MBT. Funding agency: MBT SL. Reference: PSS.0115

Agüera Morales, E. Agreement with Biogen. Funding agency: Biogen Spain S.L.U. Reference: PSS.0056

Tunez Fiñana, I. Agreement with Canvax.. Funding agency: Canvax Biotech S.L. Reference: PSS.0135

# **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

0106/11.A long-term, prospective, observational safety study of patients with multiple sclerosis who participated in clinical trials with cladribine

PI: Dr/a Sánchez López, Fernando

0145/11. A multicenter, extension, dose-blind frequency study to determine the safety and efficacy of long-term pegylated interferon beta-1a (BIB017) therapy in patients with relapsing multiple sclerosis PI: Dr/a Sánchez López, Fernando

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 highyield 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. Pl: 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. Pl: 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

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. Pl: Dr/a Aqüera 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

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). Pl: 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 Pl: 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. Pl: Dr/a Agüera Morales, Eduardo

0321/15.Multicenter Follow-Up Study to Assess Log-Term Electrophysiologyc and Clinical Outcomes in Subjects Previously Enrrolled in Study 215ON201.

PI: Dr/a Agüera Morales, Eduardo

\*3268.Open-Label, Randomised, Multicenter, Multiple-Dose, Active Controlled, Parallel-Group, Efficacy and Safety Study of BG00012 in Children from 10 to less than 18 years of age with relapsing-remitting multple sclerosis, with optional open-label extension. Pl: Dr/a Agüera Morales, Eduardo

\*3069.A 24-Month, multicenter, randomized, double-blind, placebo-controlled, parallel-group, efficacy, safety, tolerability, biomarker, and pharmacokinetic study of AZD3293 in early alzheimer disease (the amaranth study). Pl: Dr/a Agüera Morales, Eduardo

\*3066.An International, Double-blind, Randomised, Placebo-controlled Phase IIb Trial to Assess the Efficacy, Safety, and Pharmacokinetics of GNbAC1 in Patients With Relapsing Remitting Multiple Sclerosis. Pl: Dr/a Agüera Morales, Eduardo

\*3120.An Open-Label Study To Evaluate the Efficacy and Safety of Ocrelizumab in Patients With Relapsing Multiple Sclerosis Who Have A Suboptimal Response to an Adequate Course of Disease-Modifying Treatment. PI: Dr/a Agüera Morales, Eduardo

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

2813. Multi-centre, observational, non-interventional, prospective study to evaluate patient satsifaction with the Extavia treatmented administered using a new autoinjector, ExtraviProTM, in patients with multiple sclerosis. (EXCHANGE)

PI: Dr/a Sánchez López, Fernando

2878. Evaluation of patient preferences towards different options disease modifying treatments in multiple sclerosis relapsing-remitting.

PI: Dr/a Sánchez López, Fernando

2879. Prospective, multicenter, observational post-authorization safety study to evaluate the long term safety profile of lemtrada® (alemtuzumab) treatment in patients with relapsing forms of multiple sclerosis. Pl: Dr/a Agüera Morales, Eduardo 2882. Observational study to collect information on safety and to document the drug utilization of Fampyra when used in routine medical practice (LIBERATE). PI: Dr/a Agüera Morales, Eduardo

3007.Spanish patient registration treated with glatiramer acetate (Copaxone®) 40mg/ml. Pl: Dr/a Agüera Morales, Eduardo

3012. Retrospective epidemiological study to analyse clinical and radiological disease activity in patients with relapsing-remitting multiple sclerosis following withdrawal of Natalizumab in routine medical practice. PI: Dr/a Agüera Morales, Eduardo

3163.Plegridy (peginterferon) Real World Effectiveness and Safety Observational Program.

PI: Dr/a Agüera Morales, Eduardo

3196. Retrospective study of adharence to the spanish consensus to treatments for spasticity in multiple sclerosis in Spain. PI: Dr/a Agüera Morales, Eduardo

3222.A multicenter, global, retrospective, observational study to characterize real-world clinical outcomes in patients with relapsing-remitting multiple sclerosis treated with disease-modifying therapies (Tecfidera, Copaxone, Aubagio, or Gilenya) (EFFECT) PI: Dr/a Agüera Morales, Eduardo



# **GE2** • Knowledge Discovery and Intelligent Systems

# HIGHLIGHTS

**PUBLICATIONS** 

7







# **Team Leader**

Principal Investigator (PI) Sebastián Ventura Soto sventura@uco.es PAIDI TIC-122 Scientific Group

#### Researchers

García Martínez; Carlos Gibaja Galindo; Eva Lucrecia Romero Morales; Cristóbal Romero Salguero; José Raúl Zafra Gómez; Amelia Post-Doctoral Researchers Cano Rojas; Alberto Luna Ariza; José María Olmo Ortiz; Juan Luis

Pre-Doctoral Researchers (PhD Students y MSc Students)

Delgado Osuna; José Antonio Guerrero Enamorado; Alain Ramírez Quesada; Aurora Reyes Pupo; Oscar Gabriel Robles Berumen; Hermes



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

Luna JM, Cano A, Sakalauskas V, Ventura S. Discovering useful useful patterns from multiple instance data. Information Sciences. 2016. 357:23-38. IF:3,364 O:1 D:1

Reyes O, Morell C, Ventura S. Effective lazy learning algorithm based on a data gravitation model for multi-label learning. Information Sciences. 2016. 340:159-174. IF:3,364 Q:1 D:1

Cano A, Luna JM, Gibaja EL, Ventura S. LAIM discretization for multi-label data. Information Sciences. 2016. 330: 370-384 IF:3,364 Q:1 D:1

Luna JM, Pechenizkiy M, Ventura S. Mining exceptional relationships with grammar-guided genetic programming. Knowledge and Information Systems. 2016. 47(3):571-594. IF:1,702 Q:2

Cano A, Nguyen DT, Ventura S, Cios KJ.ur-CAIM: improved CAIM discretization for unbalanced and balanced data. Soft Computing. 2016. 20(1):173-188. IF:1,63

Q:2

Q:3

Marquez-Vera C, Cano A, Romero C, Noaman AYM, Fardoun HM, Ventura S. Early dropout prediction using data mining: a case study with high school students. Expert Systems. 2016.33(1):107-124. IF:0,947

Guerrero-Enamorado A, Morell C, Noaman AY, Ventura S. An algorithm evaluation for discovering classification rules with gene expression programming. INTERNATIONAL Journal of Computational Intelligence Systems. 2016. 9(2):263-280. IF:0.391

Q:4

# **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



# **GE3 • Skin immune mediated inflammatory diseases (SIMID)**

HIGHLIGHTS



# **Team Leader**

Principal Investigator (PI) Juan A Ruano Ruíz juanruanoruiz@mac.com

#### Researchers

Gay Mimbreva; Jesús Hernández Romero; José Luis Isla Tejera; Beatriz Vélez García-Nieto; Antonio

Post-Doctoral Researchers González Padilla; Marcelino Pre-Doctoral Researchers (PhD Students y MSc Students) Aguilar Luque; Macarena

Carmona Fernández; Pedro Jesús Gómez García; Francisco Lorente Lavirgen; Ana Sanz Cabanillas; Juan Luis

Other members of the Group (Nursing; Technical; and Administrative Staff) Alcalde Mellado; Patricia (Collaborator) López García; María Maestre López; Beatriz (Collaborator)



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 reinaSofía 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, Pharmacy, Genetics or Health Economics in diverse research groups through collaboration with the Department of Applied Economics of the University of Granada, the Laboratory of Investigative Dermatology, The Rockefeller University, New York (EEUU) o el Pharmacogenomics Laboratory, College of Pharmacy, Pharmacotherapy Education and Research Center (PERC), and the 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. 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, biobanking, genetic polymorphisms, predictors of therapeutic response, cost-efficiency, monoclonal antibodies, immune response.

# **Scientific Production**

#### **Publications**

#### Original

Alcantara-Reifs CM, Velez Garcia-Nieto A. Mycoplasma pneumoniae-associated mucositis. Canadian Medical Association Journal. 2016. 188(10):753-753. IF:6,724

Q:1 D:1

Alcantara-Reifs CM, Salido-Vallejo R, Garnacho-Saucedo G, de la Corte-Sanchez S, Garcia-Nieto AV. Eslicarbazepine-induced toxic epidermal necrolysis. Epilepsia. 2016. 57(5):853-854. IF:4,706

Q:1

Ruano J, Suarez-Farinas M, Shemer A, Oliva M, Guttman-Yassky E, Krueger JG. Molecular and Cellular Profiling of Scalp Psoriasis Reveals Differences and Similarities Compared to Skin Psoriasis. Plos One. 2016. 11(2):Núm art e0148450. IF:3,057

Q:1

Salido-Vallejo R, Cuevas-Asencio I, Garnacho-Sucedo G, Gonzalez-Menchen A, Alcantara-Reifs C, De la Corte-Sanchez S, Velez A, Moreno-Gimenez JC.Neoadjuvant intralesional methotrexate in cutaneous squamous cell carcinoma: a comparative cohort study. Journal of the European Academy of Dermatology and Venereology. 2016. 30(7):1120-1124. IF:3,029 Q:1

Gay-Mimbrera J, Garcia MC, Isla-Tejera B, Rodero-Serrano A, Velez Garcia-Nieto A, Ruano J.Clinical and Biological Principles of Cold Atmospheric Plasma Application in Skin Cancer. Advances in Therapy. 2016. 33(6): 894-909. IF:2,503 Q:2

Alcantara-Reifs CM, Salido-Vallejo R, Garnacho-Saucedo G, Rizo-Barrios A, Garcla-Nieto AV.Asymptomatic angiomatous lesions on the face and limbs of an adult woman. Indian Journal of Dermatology Venereology & Leprology. 2016. 82(3):356-7. IF:1,488

Q:3

Alcantara-Reifs CM, Salido-Vallejo R, Gonzalez-Menchen A, Garcia-Nieto AV.Linear basal cell carcinoma: Report of three cases with dermoscopic findings. Indian Journal Of Dermatology Venereology & Leprology. 2016. 82(6):708-711. IF:1,488

Q:3

Rodriguez-Martin AM, Ruano-Ruiz J, Velez-Garcia-Nieto A. Cutaneous metastases: clinical and dermatoscopically simulating multiple dermatofibromas. International Journal of Dermatology. 2016. 55(5):574-576. IF:1,415 O:3

Alcantara-Reifs CM, Salido-Vallejo R, Garnacho-Saucedo GM, Velez Garcia-Nieto A. Classic Kaposi's sarcoma treated with topical 0.5% timolol gel. Dermatologic Therapy. 2016. 29(5):309-311. IF:1,268

Alcantara-Reifs CM, Salido-Vallejo R, Garnacho-Saucedo G, Velez Garcia-Nieto A. Otophyma: a rare variant of phymatous rosacea. American Journal Otolaryngology. 2016. 37(3):251-4. IF:0.933

Reifs CMA, Salido-Vallejo R, Garnacho-Saucedo GM, De la Corte-Sanchez S, Gonzalez-Menchen A, Garcia-Nieto AV.Alemtuzumab in refractory Sezary syndrome. Anais Brasileiros de Dermatologia. 2016. 91:642-644. IF:0,88 Q:4

Salido-Vallejo R, Garnacho-Saucedo G, Velez A. Elucidation of the mTOR Pathway and Ther-



Q:3

Q:4

apeutic Applications in Dermatology. Actas Dermo-Sifiliograficas. 2016. 107(5):379-390. IF:0

#### In Collaboration

Garcia AA, Rodriguez Martin AM, Serra Baldrich E, Manubens Mercade E, Puig Sanz L. Allergic contact dermatitis to silver in a patient treated with silver sulphadiazine after a burn. Journal of the European Academy of Dermatology and Venereology. 2016. 30(2):365-366. IF:3,029 Q:1

Davila-Seijo P, Dauden E, Carretero G, Ferrandiz C, 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, Torrado R, Carrascosa JM, Llamas M, Rivera R, Jimenez-Puya R, Garcia-Doval I. Survival of classic and biological systemic drugs in psoriasis: results of the BIOBADADERM registry and critical analysis. Journal of the European Academy of Dermatology and Venereology. 2016. 30(11):1942-1950.

IF:3,029 Q:1

Garcia-Doval I, Perez-Zafrilla B, Ferrandiz C, Carretero G, Dauden E, de la Cueva P, Gomez-Garcia FJ, Herrera-Ceballos E, Belinchon-Romero I, Sanchez-Carazo JL, Lopez-Estebaranz JL, Alsina M, Ferran M, Torrado R, Carrascosa JM, Rivera R, Vanaclocha F. Development of clinical prediction models for good or bad response to classic systemic drugs, anti-TNFs, and ustekinumab in psoriasis, based on the BIOBADADERM cohort. Journal of Dermatological Treatment. 2016. 27(3):203-209. IF:1,857

Q:2

Moreno-Ramirez D, Ruiz-Villaverde R, de Troya M, Reyes-Alcazar V, Alcalde M, Galan M, Garcia-Lora E, Garcia El, Linares M, Martinez L, Pulpillo A, Suarez C, Velez A, Torres A. Process of Care for Patients With Benign Cysts and Tumors: Consensus Document of the Andalusian Regional Section of the Spanish Academy of Dermatology and Venereology (AEDV). Actas Dermo-Sifiliograficas. 2016. 107(5):391-399. IE-0

Ruiz-Villaverde R, Moreno-Ramirez D, Galan-Gutierrez M, de Troya M, Reyes-Alcazar V, Alcalde M, Garcia EI, Linares M, Martinez L, Pulpillo A, Suarez C, Velez A, Garcia-Lora E, Torres A. Clinical Pathway for Patients with Acute or Chronic Urticaria: A Consensus Statement of the Andalusian Section of the Spanish Academy of Dermatology and Venereology (AEDV). Actas Dermo-Sifiliograficas. 2016. 107(6):482-488. IE.O

#### **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. Inflammatory Skin Disease Summit. Funding agency: Icahn School Of Medicine Mount Sinai. Reference: ISDS 2016-001

#### **Clinical Trials**

0140/12.A phase III study to assess the efficacy and safety of induction and maintenance treatment with brodalumab versus placebo and ustekinumab in patients with moderate to severe plaque psoriasis. AMAGINE-2 PI: Dr/a Ruano Ruiz, Juan A.

0251/14. Phase 3, Multicenter, Randomized, Double-blind, Placebo and Active Comparator-controlled Study Evaluating the Efficacy and Safety of Guselkumab in the Treatment of Subjects With Moderate to Severe Plaquetype Psoriasis.

Pl: Dr/a Ruano Ruiz, Juan A.

0032/15. Long Term Clear Skin Maintenance Treatment Optimization in Patients With Moderate to Severe Chronic Plague 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.Pl: Dr/a Ruano Ruiz, Juan A.

0104/15. A multicenter, randomized, double-blind, placebo and active-controlled phase 2b dose-finding study of QGE031 as add-on therapy to investigate the efficacy and safety in patients with Chronic Spontaneous Urticaria (CSU)

PI: Dr/a Ruano Ruiz, Juan A.

0020/16. An Open Label, Multicenter, Extension Study to Evaluate the Long-term Safety of QGE031 240 mg s.c. Given Every 4 Weeks for 52 Weeks in Chronic Spontaneous Urticaria Patients Who Completed Study CQGE031C2201.

Pl: Dr/a Ruano Ruiz, Juan A.

\*3247. A Multicentre, Randomized, Double-blind, Parallel-group, Controlled Study, to Assess the Efficacy and Safety of P-3074 Cutaneous Spray, Solution, in the Treatment of Male Pattern Baldness PI: Dr/a Ruano Ruiz, Juan A.

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. Pl: Dr/a Ruano Ruiz, Juan A.

2550.An observational study to assess relapse in patietns with moderate to severe psoriasis treated with biological drugs according to clinical practice in Spain. PI: Dr/a Vélez Garcia-Nieto, A.

2700. Construction of a model to predict the response to anti-TNF drugs used for the treatment of moderate-to-severe psoriasis in routine medical practice.

PI: Dr/a Ruano Ruiz, Juan Alberto

2702. Validation of the EARP questionnaire for the detection of psoriatic arthritis in the Spanish population. VALS Study. PI: Dr/a Vélez Garcia-Nieto, A.

2719: World-wide antihistamine-refractory chronic urticaria patient evaluation. AWARE Study

PI: Dr/a Ruano Ruiz, Juan A.

2740. Application of genomic techniques and image processing using artificial intelligence to obtain a predictor model for risk of melanoma.

PI: Dr/a Ruano Ruiz, Juan A.

2883. Multi-centre observational study to establish the prevalence, clinical profile and therapeutic management of patients with suppurative hydradenitis in hospital dermatology units and health centres in Spain Pl: Dr/a Lorente Lavirgen, A.I.

# **GE4** • Applied Psychology

HIGHLIGHTS



# **Team Leader**

Principal Investigator (PI) Carmen Tabernero Urbieta carmen.tabernero@uco.es PAIDI HUM-414 Scientific Group

#### **Researchers**

Antolí Cabrera; Adoración Arenas Moreno; Alicia Luque Salas; Bárbara Pérez Dueñas; Carolina Rubio García; Sebastián

#### Post-Doctoral Researchers Cuadrado; Esther Castillo Mayén; Rosario Moyano Pacheco; Manuel

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 analyze the behavior 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 analyzed 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 Productions**

#### **Publications**

#### Original

Cuadrado E, Tabernero C, Steinel W. Determinants of Prosocial Behavior in Included Versus Excluded Contexts. Frontiers in Psychology. 2016. 6: Núm art 2001. IF:2,463 Q:1

Cuadrado E, Tabernero C, Steinel W. Prosocial behaviour, inclusion and exclusion: why and when do we behave prosocially?. Revista de Psicologia Social. 2016. 31(3):463-499. IF:0,458 Q:4

Tabernero C, Cuadrado E, Luque B, Signoria E, Prota R. The importance of achieving a high customer satisfaction with recycling services in communities. Environment Development and Sustainability. 2016. 18(3):763-776. IF:0

#### **In Collaboration**

Abad-Merino S, Dovidio JF, Tabernero C, Gonzalez I. Gender and Intergroup Helping: Forms of Prosocial Behavior as Differential Social Control Mechanisms for Women and Men. Spanish Journal of Psychology.2016.19: Núm art e70. IF:0,493 Q:4

#### **Research Funding**

#### National

Tabernero Urbieta, CM. Influence of self-efficacy and other motivational variables on diet compliance, quality of life and well-being of patients with cardiovascular disease. Funding agency: Ministry of Economy and Competitiveness (MINECO).Reference: PSI2014-58609-R



# **GE5** • Urology and Sexual Medicine

# HIGHLIGHTS









#### **Team Leader**

Principal Investigator María José Requena Tapia josefa.requena.sspa@juntadeandalucia.es

#### Researchers

Anglada Jurado; Francisco Campos Hernández; Juan Pablo Prieto Castro; Rafael

Post-Doctoral Researcher Blanca Pedregosa; Ana María Carrasco Valiente; Julia

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Gil Contreras; Daniel Márquez López; Javier Ruiz García; Jesús Sanchez-Bayton Griffith; Christian Valero Rosa; José



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

Hormaechea-Agulla D, Gomez-Gomez E, Ibanez-Costa A, Carrasco-Valiente J, Rivero-Cortes E, L-Lopez F, Pedraza-Arevalo S, Valero-Rosa J, Sanchez-Sanchez R, Ortega-Salas R, Moreno MM, Gahete MD, Lopez-Miranda J, Requena MJ, Castano JP, Luque RM.Ghrelin O-acyltransferase (GOAT) enzyme is overexpressed in prostate cancer, and its levels are associated with patient's metabolic status: Potential value as a non-invasive biomarker. Cancer Letters. 2016. 383(1):125-134. IF:5,992 Q:1

Fernandez-Peralbo MA, Gomez-Gomez E, Calderon-Santiago M, Carrasco-Valiente J, Ruiz-Garcia J, Requena-Tapia MJ, de Castro MDL, Priego-Capote F.Prostate Cancer Patients-Negative Biopsy Controls Discrimination by Untargeted Metabolomics Analysis of Urine by LC-QTOF: Upstream Information on Other Omics. Scientific Reports. 2016. 6:Núm art 38243. IF:5,228

Q:1

Blanca A, Requena MJ, Alvarez J, Cheng L, Montironi R, Raspollini MR, Reymundo C, Lopez-Beltran A. FGFR3 and Cyclin D3 as urine biomarkers of bladder cancer recurrence. Biomarkers in Medicine. 2016. 10(3):243-253. IF:2,179 Q:3

Arias Vega MR, Perula de Torres LA, Carrasco Valiente J, Requena Tapia MJ, Jimenez Garcia C, Silva Aycaguer LC.Prevalence of urolithiasis in the 40 to 65 year old Spanish population: The PreLiRenE study. Medicina Clinica. 2016. 146(12):525-531. IF:1,267

Valero-Rosa J, Campos-Hernandez JP, Carrasco-Valiente J, Gomez-Gomez E, Marquez-Lopez FJ, Ruiz-Garcia J, Garcia-Rubio JH, Requena-Tapia MJ, Prieto-Castro R. Prognostic value of penile colour doppler ultrasonography for recovering erectile function after radical prostatectomy. Actas Urológicas Españolas. 2016. 40(8):507-512. IF:0,964

Q:4

Q:2

Arenas-Bonille AJ, Campos-Hernandez JP, Carrasco-Valiente J, Marquez-Lopez FJ, Ruiz-Garcia JM, Sanchez-Gonzaleza A, Salamanca-Bustos JJ, Regueiro-Lopez JC, Navarro-Cabello MD, Requena-Tapia MJ. Influence of Donor and Recipient Ages in Survival of Simultaneous Pancreas-Kidney Transplantation.Transplantation Proceedings. 2016. 48:3033-3036. IF:0,867

Q:4

Sanchez-Gonzalez A, Carrasco-Valiente J, Arenas-Bonilla AJ, Campos-Hernandez JP, Blanca-Pedregosa A, Ruiz-Garcia JM, Valero-Rosa J, Gomez-Gomez E, Salamanca-Bustos JJ, Navarro-Cabello D, Requena-Tapia MJ. Graft Survival in Patients Who Received Second Allograft, Comparing Those With or Without Previous Failed Allograft Nephrectomy. Transplantation Proceedings. 2016. 48:2895-2898. IF:0,867 Q:4

Salamanca-Bustos JJ, Campos-Hernandez JP, Sanchez-Hidalgo JM, Arjona-Sanchez A, Sanchez-Gonzalez A, Arenas-Bonilla AJ, Ruiz-Rabelo J, Carrasco-Valiente J, Ruiz-Garcia J, Regueiro-Lopez JC, Briceno-Delgado J, Requena-Tapia MJ. Validation of the Pancreatic Donor Risk Index in Simultaneous Pancreas-Kidney Transplantation Performed in Cordoba Hospital From 2000 to 2015. Transplantation Proceedings. 2016.48:3037-3039. IF:0,867

Q:4

#### In Collaboration

Raspollini MR, Luque RJ, Menendez CL, Bottito E, Brunetti M, Martignoni G, Montironi R, Cheng L, Blanca A, Baroni G, Minervini A, Lopez-Beltran A.T1 high-grade bladder carcinoma outcome: the role of p16, topoisomerase-II alpha, survivin, and E-cadherin. Human Pathology. 2016. 57:78-84. IF:2,791

Q:2

#### **Research Funding**

#### Regional

Carrasco Valiente, J. Prostate cancer management patterns in Andalusia and evaluation of health outcomes in prostate cancer. Funding agency: Regional Ministry of Equality, Health and Social Policy (CISPS). Reference:-PI-0126-2016

#### National

Requena Tapia, M.J. Improved patient wellbeing and safety in management procedures using collaborative systems. m-LISTABLE. Funding agency: Spanish Ministry of Economy and Competitiveness (MINECO). Reference:RTC-2016-5149\_003

Requena Tapia, MJ. Study of PI3CA/AKT signalling pathway protein expression and its diagnostic and prognostic /predictive role in bladder cancer.Funding agency: Asociacion Española De Urologia. Reference: FIU14/002

#### **Contracts with Companies**

Requena Tapia, M.J. Agreement with Janssen. Bayesian Inference. Funding agency: Janssen-Cilag, S.A. Reference: PSS.0078

Requena Tapia, M.J. Agreement with Janssen. Funding agency: Janssen-Cilag, S.A. Reference: PSS.0079

Requena Tapia, M.J. Agreement with Mecwins. Bayesian Inference. Funding agency: Mecwins S.A. Reference: PSS.0114

Requena Tapia, M.J. Agreement with Janssen. Funding agency: Janssen-Cilag, S.A. Reference: PSS.0124

Requena Tapia, M.J. Agreement with Janssen. Funding agency: Janssen-Cilag, S.A. Reference: PSS.0125

Requena Tapia, M.J. Agreement with Fundación para la investigación en Urología. Funding agency: Fundación para la investigación en Urología. Reference: PSS.0126

Requena Tapia, M.J. Agreement with Bayer . Funding agency: Bayer Hispania S.L.. Reference:  $\mathsf{PSS.0157}$ 

#### **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).

IP: Dr/a Requena Tapia, María José

0344/14.Phase III, randomized, placebo-controlled, double-blind JNJ-56021927 in combi-



nation with abiraterone acetate and prednisone compared with abiraterone acetate and prednisone in patients with metastatic-resistant prostate cancer IP: 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.

IP: Dr/a Requena Tapia, María José



# **GA1 • Lung transplantation. Thoracic** malignancies

# HIGHLIGHTS



# **Team Leader**

Principal Investigator Ángel Salvatierra Velázquez angel.salvatierra.sspa@juntadeandalucia.es

# Researchers

Algar Algar; Francisco Javier Álvarez Kindelan; Antonio Ayala Montoro; José Baamonde Laborda; Carlos Cerezo Madueño; Francisco Espinosa Jimenez; Dionisio

**Post-Doctoral Researchers** Moreno Casado; Paula

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Carrasco Fuentes; Guadalupe Gonzalez Garcia; Francisco Javier Guaman Arcos; Hugo Dario Murillo Brito; Diego Alejandro



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**

#### Original

Garcia-Limones C, Lara-Chica M, Jimenez-Jimenez C, Perez M, Moreno P, Munoz E, Calzado MA.CHK2 stability is regulated by the E3 ubiquitin ligase SIAH2.Oncogene. 2016. 35(33):4289-301. IF:7,932 Q:1 D1

#### **In Collaboration**

Moreno P, Alvarez A, Carrasco G, Redel J, Guaman HD, Baamonde C, Algar FJ, Cerezo F, Salvatierra A.Lung transplantation for cystic fibrosis: differential characteristics and outcomes between children and adults. European Journal of Cardio-Thoracic Surgery.2016.49(5):1334-1343. IF:2,803 Q:2 D:5

Broncano J, Luna A, Sánchez-González J, Alvarez-Kindelan A, Bhalla S.Functional MR Imaging in Chest Malignancies. Magnetic Resonance Imaging Clinics of North America. 2016. 24(1):135-155. IF:1,854

Q:3

Freixinet Gilart J, Varela Simo G, Rodriguez Suarez P, Embun Flor R, Rivas de Andres JJ, de la Torre Bravos M, Molins Lopez-Rodo L, Ferrer JP, Elena JMI, Baschwitzh B, Lopez de Castro PE, Fibla Alfara JJ, Hernando Trancho F, Carvajal Carrasco A, Canalis A, Salvatierra Velazquez A, Canela Cardona M, Torres Lanzas J, Moreno Mata N.Benchmarking in Thoracic Surgery. Third Edition. Archivos de Bronconeumonia. 2016. 52(4):204-210. IF1771

Villar Alvarez F, Muguruza Trueba I, Belda Sanchis J, Molins Lopez-Rodo L, Rodriguez Suarez PM, Sanchez de Cos Escuin J, Barreiro E, Borrego Pintado MH, Disdier Vicente C, Flandes Aldeyturriaga J, Gamez Garcia P, Garrido Lopez P, Leon Atance P, Izquierdo Elena JM, Novoa Valentin N, Rivas de Andres JJ, Royo Crespo I, Salvatierra Velazquez A, Seijo Maceiras L, Solano Reina S, Aguiar Bujanda D, Avila Martinez RJ, de Granda Orive JI, de Higes Martinez E, Diaz-Hellin Gude V, Embun Flor R, Freixinet Gilarte JL, Garcia Jimenez MD, Hermoso Alarza F, Hernandez Sarmiento S, Honguero Martinez AF, Jimenez Ruiz CA, Lopez Sanz I, Mariscal de Alba A, Martinez Vallina P, Menal Munoz P, Perez LM, Garcia MEO,

Rombolda CA, Miguel Arregui IS, Somiedo Gutierrez MV, Trivino Ramirez AI, Trujillo Reyes JC, Vallejo C, Vaquero Lozano P, Varela Simo G, Zulueta JJ.Executive summary of the SEPAR recommendations for the diagnosis and treatment of non-small cell lung cancer. Archivos de Bronconeumonia. 2016. 52(7):378-388. IF:1,771 O:3

Alvarez FV, Trueba IM, Sanchis JB, Lopez-Rodo LM, Suarez PMR, Escuin JSD, Barreiro E, Pintado MHB, Vicente CD, Aldeyturriaga JF, Garcia PG, Lopez PG, Atance PL, Elena JMI, Valentin NMN, de Andres JJR, Crespo IR, Velazquez AS, Maceiras LMS, Reina SS, Bujanda DA, Martinez RJA, Orive JID, Martinez ED, Gude VDH, Flor RE, Gilart JLF, Jimenez MDG, Alarza FH, Sarmiento SH, Martinez AFH, Ruiz CAJ, Sanz IL, de Alba AM, Vallina PM, Munoz PM, Perez LM, Garcia MEO, Rombola CA, Arregui ISM, Gutierrez MDS, Ramirez AIT, Reyes JCT, Vallejo C, Lozano PV, Simo GV, Zulueta JJ.Recommendations of the Spanish Society of Pneumology and Thoracic Surgery on the diagnosis and treatment of non-small-cell lung cancer. Archivos de Bronconeumonia. 2016. 52:2-62.

IF:1,771 Q:3

#### **Research Funding**

#### Regional

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

Casado Moreno, P. Value of ex-vivo lung perfusion for optimising suboptimal lung grafts, thus expanding the pool of valid lung transplant donors.Funding agency: Fundación Mutua Madrileña.Reference: FMM16\_002.

#### **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



Q:3

# **GA2** • Comprehensive care nurses - a multidisciplinary perspective

# HIGHLIGHTS



# **Team Leader**

Principal Investigator María Aurora Rodríguez Borrego en1robom@uco.es PAIDI CTS-666 scientific group

#### Researchers

Bretones, José Miguel (Collaborator) Cuevas Pareja, Francisca (Collaborator) Gonçalves Nitschke, Rosane Muñoz Alonso, Adoración (Collaborator) Redondo Pedraza, Rosa (Collaborator) Ruiz Gándara, África

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

Florez Almonacid, Clara Inés Dios Guerra, Caridad Hidalgo Lopezosa, Pedro Guerra Martin, Dolores López Soto, Pablo Jesús Carmona Torres, Juan Manuel

# Pre-Doctoral Researchers (PhD Students y MSc Students)

Miñarro Del Moral, Rosa Luque Carrillo, Patricia Ruiz Cañete, Macarena Rodríguez Muñoz, Pedro Manuel Morales Cané, Ignacio Peinado Valeriano, Ángeles Fernández Luna, Jesús

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

Lopez-Soto PJ, Smolensky MH, Sackett-Lundeen LL, De Giorgi A, Rodriguez-Borrego MA, Manfredini R, Pelati C, Fabbian F. Temporal Patterns of In-Hospital Falls of Elderly Patients. Nursing Research. 2016. 65(6):435-445. IF:1,856 Q:1

Hidalgo-Lopezosa P, Hidalgo-Maestre M, Rodriguez-Borrego MA. Labor stimulation with oxytocin: effects on obstetrical and neonatal outcomes. Revista Latino-Americana de Enfermagem. 2016.24: Núm art e2744. IF:0,687 Q:4

Almonacid CIF, Ramos AJ, Rodriguez-Borrego MA. Level of anxiety versus self-care in the preoperative and postoperative periods of total laryngectomy patients. Revista Latino-Americana de Enfermagem. 2016. 24: Núm art e2707. IF:0,687 O:4

#### **Research Fundings**

#### 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

#### International

Rodríguez Borrego, M<sup>a</sup> 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. Reference: BIL/14/P2/089



# **GA3** • Pneumology

# HIGHLIGHTS



# **Team Leader**

Principal Investigator Bernabé Jurado Gámez bjg01co@hotmail.com PAIDI CTS-992 Scientifc Group

#### Researchers

Arenas de Larriva, Marisol Arenas Vacas, Antonio Pablo Entrenas Costa, Luis M Feu Collado, Nuria Gíl García, Francisco Luis Lama Martínez, Rafael Muñoz Cabrera, Luis Pascual Martínez, Natalia Redel Montero, Javier Santos Luna, Francisco Pre-Doctoral Researchers (PhD Students y MSc Students) Castillo Jurado, Montserrat Garcia Porcuna, Inmaculada



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

Ortea I, Rodriguez-Ariza A, Chicano-Galvez E, Arenas Vacas MS, Jurado Gamez B. Discovery of potential protein biomarkers of lung adenocarcinoma in bronchoalveolar lavage fluid by SWATH MS data-independent acquisition and targeted data extraction. Journal of Proteomics. 2016. 138:106-14. IF:3,867

Q:1

Peralbo-Molina A, Calderon-Santiago M, Priego-Capote F, Jurado-Gamez B, Luque de Castro MD. Identification of metabolomics panels for potential lung cancer screening by analysis of exhaled breath condensate. Journal of Breath Research. 2016.10(2): Núm art 2600. IF:4,177 Q:1

Peralbo-Molina A, Calderon-Santiago M, Priego-Capote F, Jurado-Gamez B, Luque de Castro MD. Metabolomics analysis of exhaled breath condensate for discrimination between lung cancer patients and risk factor individuals. Journal of Breath Research. 2016.10(1):16011-16011. IF:4,177

Q:1

Delgado-Povedano MD, Calderon-Santiago M, Priego-Capote F, Jurado-Gamez B, de Castro MDL.Recent advances in human sweat metabolomics for lung cancer screening. Metabolomics. 2016.12(11):Núm art 166. IF:3,661

Q:2

Jurado-Gamez B, Guglielmi O, Gude F, Buela-Casal G.Effects of continuous positive airway pressure treatment on cognitive functions in patients with severe obstructive sleep apnoea. Neurologia. 2016. 31(5):311-318. IF:1,79 Q:3

Guirao-Arrabal E, Santos F, Redel-Montero J, Vaquero JM, Cantisan S, Vidal E, Torre-Gimenez A, Rivero A, Torre-Cisneros J.Risk of tuberculosis after lung transplantation: the value of pretransplant chest computed tomography and the impact of mTOR inhibitors and azathioprine use.Transplant Infectious Disease. 2016.18(4):512-519. IF:1,459

Q:4

#### In Collaboration

Campos-Rodriguez F, Queipo-Corona C, Carmona-Bernal C, Jurado-Gamez B, Cordero-Guevara J, Reyes-Nunez N, Troncoso-Acevedo F, Abad-Fernandez A, Teran-Santos J, Caballero-Rodriguez J, Martin-Romero M, Encabo-Motino A, Sacristan-Bou L, Navarro-Esteva J, Somoza-Gonzalez M, Masa JF, Sanchez-Quiroga MA, Jara-Chinarro B, Orosa-Bertol B, Martinez-Garcia MA. Continuous Positive Airway Pressure Improves Quality of Life in Women with Obstructive Sleep Apnea A Randomized Controlled Trial. American Journal of Respiratory and Critical Care Medicine. 2016. 194(10):1286-1294. IF:13,118

Q:1 D1

Cosio BG, Soriano JB, Lopez-Campos JL, Calle-Rubio M, Soler-Cataluna JJ, de-Torres JP, Marin JM, Martinez-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. 2016.149(1):45-52. IF:5,94

Cosio BG, Soriano JB, Lopez-Campos JL, Calle M, Soler JJ, de-Torres JP, Marin JM, Martinez C, de Lucas P, Mir I, Peces-Barba G, Feu-Collado N, Solanes I, Alfageme I.Distributionand Outcomes of a Phenotype-Based Approach to Guide COPD Management: Results from the CHAIN Cohort. Plos One. 2016.11(9): Núm art e0160770. IF:3,057

Q:1

Plaza V, Fernandez-Rodriguez C, Melero C, Cosio Borja G, Entrenas LM, Perez de Llano L, Gutierrez-Pereyra F, Tarragona E, Palomino R, Lopez-Vina A. Validation of the 'Test of the Adherence to Inhalers' (TAI) for Asthma and COPD Patients. Journal of Aerosol Medicine and Pulmonary Drug Delivery. 2016. 29(2):142-152.

IF:3,041

Q:2

Plaza V, Lopez-Vina A, Entrenas LM, Fernandez-Rodriguez C, Melero C, Perez-Llano L, Gutierrez-Pereyra F, Tarragona E, Palomino R, Cosio BG.Differences in Adherence and Non-Adherence Behaviour Patterns to Inhaler Devices Between COPD and Asthma Patients. Copd-Journal of Chronic Obstructive Pulmonary Disease. 2016.13(5):547-54. IF:2,16

Q:3

Q:1

# **Research Funding**

#### Regional

Feu Collado, MN. Proyecto nº 6/2014. Fundación Neumosur. Proyecto Neumosur 6.

#### **Contracts with Companies**

Entrenas Costa, LM. Collaboration with Novartis. Funding agency: Novartis Farmacéutica SA. Reference: CCB.0060

#### **Clinical Trials**

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

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

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

2741.Prevalence of breathing disorders during sleep in patients with COP. DPI: Dr/a Feu Collado, María Nuria

3011.Retrospective observational study to evaluate the pharmaco-economic impact of omalizumab treatment in severe persistent allergic asthma in routine clinical practice in the autonomous communities of Andalusia and Extremadura.

PI: Dr/a Entrenas Costa, Luis Manuel.



# **GA4** • Endocrinology and Nutrition. Insulin resistance, diabetes and metabolism

HIGHLIGHTS



# **Team Leader**

Principal Investigator María Ángeles Gálvez Moreno mariaa.galvez.sspa@juntadeandalucia.es

#### **Researchers**

Alhambra Expósito, María Rosa Bellido Muñoz, Enrique Berral de la Rosa, Francisco José Calañas Continente, Alfonso Corpas Jiménez, Mª Sierra Gutiérrez Alcántara, Carmen Molina Puertas, Mª José Palomares Ortega, Rafael Vigara Madueño, Remedios

Post-Doctoral Researchers Romero Jimenez, Magdalena Herrera Martínez, Aura Dulcinea Pre-Doctoral Researchers (PhD Students y MSc Students) Escandell Morales, Juan Manuel Fernández Bedmar, Zahira Noemi

Other members of the Group (Others Researchers, Nursing, Technical, and Administrative Staff) Torres Roldán, María del Rosario



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 Productions**

#### **Publications**

#### Original

Ibanez-Costa A, Rivero-Cortes E, Vazquez-Borrego MC, Gahete MD, Jimenez-Reina L, Venegas-Moreno E, de la Riva A, Arraez MA, Gonzalez-Molero I, Schmid HA, Maraver-Selfa S, Gavilan-Villarejo I, Garcia-Arnes JA, Japon MA, Soto-Moreno A, Galvez MA, Luque RM, Castano JP. Octreotide and pasireotide (dis)similarly inhibit pituitary tumor cells in vitro. Journal of Endocrinology. 2016. 231(2):135-145. IF:4,498 Q:1

Navarro-Valverde C, Sosa-Henriquez M, Alhambra-Exposito MR, Quesada-Gomez JM.Vitamin D-3 and calcidiol are not equipotent. Journal of Steroid Biochemistry and Molecular Biology. 2016. 164:205-208. IF:3,985

Moreno-Fernandez J, Gomez FJ, Moreno MAG, Castano JP. Clinical Efficacy of Two Different Methods to Initiate Sensor-Augmented Insulin Pumps: A Randomized Controlled Trial. Journal of Diabetes Research. 2016. (2016):Núm art 4171789. IF:2,431 Q:3

Vallejo Casas JA, Mena Bares LM, Galvez Moreno MA, Moreno Ortega E, Marlowe RJ, Maza Muret FR, Albala Gonzalez MD.Thyroid remnant ablation success and disease outcome in stage III or IV differentiated thyroid carcinoma: recombinant human thyrotropin versus thyroid hormone withdrawal. Quarterly Journal of Nuclear Medicine and Molecular Imaging. 2016. 60(2):163-171. IF:2,413

Q:2

Moreno-Moreno P, Alhambra-Exposito MR, Herrera-Martinez AD, Palomares-Ortega R, Zurera-Tendero L, Herrero JJE, Galvez-Moreno MA. Arterial Calcium Stimulation with Hepatic Venous Sampling in the Localization Diagnosis of Endogenous Hyperinsulinism. International Journal of Endocrinology. 2016. 2016: Núm art 4581094. IF:2,376

Q:3

Luque RM, Ibanez-Costa A, Sanchez-Tejada L, Rivero-Cortes E, Robledo M, Madrazo-Atutxa A, Mora M, Alvarez CV, Lucas-Morante T, Alvarez-Escola C, Fajardo C, Castano L, Gaztambide S, Venegas-Moreno E, Soto-Moreno A, Galvez MA, Salvador J, Valassi E, Webb SM, Pico A, Puig-Domingo M, Gilabert M, Bernabeu I, Marazuela M, Leal-Cerro A, Castano JP. The Molecular Registry of Pituitary Adenomas (REMAH): A bet of Spanish Endocrinology for the future of individualized medicine and translational research. Endocrinologia y Nutricion. 2016. 63(6):274-284. IE:0

#### **In Collaboration**

Lecube A, de Hollanda A, Calanas A, Vilarrasa N, Rubio M, Breton I, Goday A, Vidal J, Iglesias P, Fernandez-Soto ML, Pellitero S, de Cos A, Morales M, Campos C, Masmiquel L, Tinahones F, Pujante P, Garcia-Luna P, Bueno M, Camara R, Bandres O, Caixas A. Trends in Bariatric Surgery in Spain in the Twenty-First Century: Baseline Results and 1-Month Follow Up of the RICIBA, a National Registry. Obesity Surgery. 2016. 26(8):1836-1842. IF:3,346 Q:1



Q:2

Vilarrasa N, Goday A, Rubio MA, Caixas A, Pellitero S, Ciudin A, Calanas A, Botella JI, Breton I, Morales MJ, Diaz-Fernandez MJ, Garcia-Luna PP, Lecube A.Hyperinsulinemic Hypoglycemia after Bariatric Surgery: Diagnosis and Management Experience from a Spanish Multicenter Registry. Obesity Facts. 2016. 9(1):41-51. IF:2,4 Q:3

Puig-Domingo M, Soto A, Venegas E, Vilchez R, Blanco C, Cordido F, Lucas T, Marazuela M, Casany R, Cuatrecasas G, Fajardo C, Galvez MA, Maraver S, Martin T, Romero E, Paja M, Pico A, Bernabeu I, Resmini E. Use of lanreotide in combination with cabergoline or pegvisomant in patients with acromegaly in the clinical practice: The ACROCOMB study. Endocrinologia y Nutricion. 2016. 63(8):397-408. IF:1.314 Q:4

#### **Contracts with Companies**

Gálvez Moreno, MA. Development of advanced fats. Funding agency: Aceites Del Sur-Coosur S.A. Reference: ITC-20151323

Gálvez Moreno, MA. Agreement with JYC. Funding agency: JYC Ediciones Medicas. Reference: PSS.0163

Calañas Continente A. Agreement with Nutri. Funding agency: Nutricia Nutricia. Reference: CCB.0116

#### **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

\*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

0303/15. Intravenous versus subcutaneous basal insulin in diabetic non-critical hospitalized patients receiving total parenteral nutrition

PI: Dr/a Molina Puerta, MJ

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 TouieoR compared to d insulins PI: Dr/a Gálvez Moreno, MA

3216.An open-label study to assess the safe-

ty and efficacy of COR-003 (2S,4R- ketoconazole) in the treatment of endogenous Cushing's Syndrome. Pl: Dr/a Galvez Moreno, MA

3043.Study to assess blood-sugar monitoring in patients receiving enteral nutrition in routine clinical practice. Novadi-Control StudyPI: Dr/a Molina Puerta, MJ

3164.International multi-centre observational study to assess the efficacy in daily clinical practice of lanreotide autogel 120 mg during a prolonged dosage period (over 4 weeks), for the treatment of acromegaly: SOMAC Study. PI: Dr/a Galvez Moreno, MA



Escalada J, Orozco-Beltran D, Morillas C, Alvarez-Guisasola F, Gomez-Peralta F, Mata-Cases M, Palomares R, Iglesias R, Carratala-Munuera C.Attitudes towards insulin initiation in type 2 diabetes patients among healthcare providers: A survey research. Diabetes Research and Clinical Practice. 2016.122:46-53. IF:3,045 Q:2

# **GA5** • Study of growth. Endocrinology and Child Nutrition

# HIGHLIGHTS



# **Team Leader**

Principal Investigator Ramón Cañete Estrada em1caesr@uco.es PAIDI CTS-329 Scientific Group

#### Researchers

Cañete Vázquez, Mª Dolores Gómez Guzmán, Elena Guzmán Cabañas, Juana Mª Jimenez Reina, Luis Martos Estepa, Rosario Mata Rodríguez, Cristina Parraga Quiles, Mª José Ruiz González, Mª Dolores Tofe Valera, Inés Torres Borrego, Javier Valle Jiménez, Miguel Vázquez Rueda, Fernando Post-Doctoral Researchers García Martínez, Elena



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

Pastor-Villaescusa B, Caballero-Villarraso J, Canete MD, Hoyos R, Maldonado J, Bueno G, Leis R, Gil A, Canete R, Aguilera CM. Evaluation of differential effects of metformin treatment in obese children according to pubertal stage and genetic variations: study protocol for a randomized controlled trial. Trials. 2016. 17: Núm art 323.

IF:1,859 Q:3

Torres-Borrego J, Tortajada-Girbes M.Factors that increase wheezing risk in nursing infants in the first year of life. Allergologia et Immunopathologia. 2016. 44(5):391-392. IF:1,689 0:4

Girela-Lopez E, Ruz-Caracuel I, Beltran C, Jimena I, Leiva-Cepas F, Jimenez-Reina L, Pena J.Histological Changes in Skeletal Muscle During Death by Drowning: An Experimental Study. American Journal of Forensic Medicine and Pathology. 2016. 37(2):118-26. IF:0,795 Q:4

Murcia-Pascual FJ, Gracia-Rodriguez R, Vazquez-Rueda F, Pereira PL, Esteban RMP. Testicular and paratesticular tumors in children. Archivos Españoles de Urologia. 2016. 69:691-697. IF:0,307

#### Q:4

#### **In Collaboration**

Gómez-Chaparro Moreno JL, Rodríguez Torronteras A, Ruiz González MD, Izquierdo Palomares L, Bonilla Valverde D, Ruiz Laguna J, Delgado Rubio A, López-Barea J. The beta-glucosidase assay: a new diagnostic tool for necrotizing enterocolitis. Sensitivity, specificity, and predictive values. European Journal of Pediatrics. 2016. 175(7):931-941. IF: 1,791 Q:2

Corripio R, Soriano-Guillen L, Herrero FJ, Canete R, Castro-Feijoo L, Escribano A, Espino R, Labarta JI, Argente J. Changes in Body Mass Index in Girls with Idiopathic Central Precocious Puberty under Gonadotropin-Releasing Hormone Analogue Therapy: The Spanish Registry. Hormone Research in Paediatrics. 2016. 86(3):154-160. IF:1,661 Q:4

Plaza AM, Ibanez MDP, Sanchez-Solis M, Bosque-Garcia M, Cabero MJ, Corzo JL, Garcia-Hernandez G, de la Hoz B, Korta-Murua J, Sanchez-Salguero C, Torres-Borrego J, Tortajada-Girbes M, Valverde-Molina J, Zapatero L, Nieto A. Consensus-based approach for severe paediatric asthma in routine clinical practice. Anales de Pediatria. 2016. 84(2):122-122. IF:0,773 Q:4

# **Clinical Trials**

0291/11. A randomized, multicenter, blind trial with topiramato vs. placebo for the treatment of newborns with perinatal asphyxia treated with moderate whole-body hypothermia. PI: Dr/a Guzman Cabañas, JM.

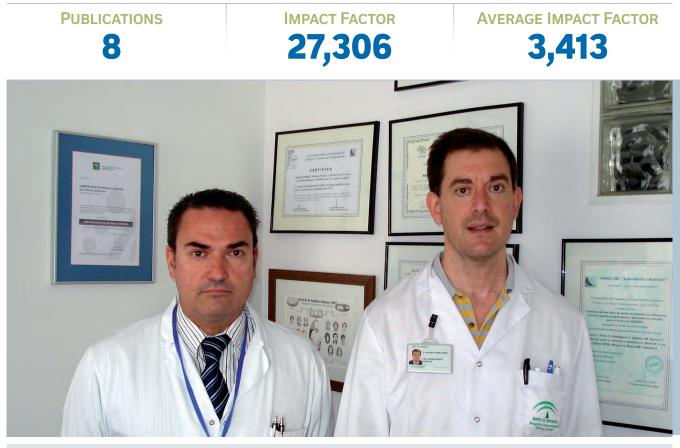
2876. Observational cross-sectional study to assess the quality of life of patients with a diagnosis of seasonal allergic rhinitis or rhinoconjunctivitis with or without asthma caused by pollen olive or olive more grasses treated with immunotherapy PI: Dr/a Torres Borrego, J.

2079.Observational, non-interventional, multi-centre, multi-national study of patients with atypical hemolytic-uremic syndrome (AHUS Registry) PI: Dr/a: García Martínez, E. 3013. Tolerance to the introduction of a formula based on highly hydrolised whey proteins enriched with Lactobacillus fermentum (Damira-Pro1®) in children with allergy to cow's milk protein.

PI: Dr/a Torres Borrego, J.

# **GA6** • Clinical Analysis

HIGHLIGHTS



### **Team Leader**

Principal Investigator Fernando Rodríguez Cantalejo fernando.rodriguez.c.sspa@juntadeandalucia.es

#### Researchers

Caballero Villarraso, Javier Martínez Peinado, Antonio Molero Payan, Rafael

### **Scientific Activity**

Our group is currently developing two lines of research related to the assessment of the diagnostic accuracy of new technologies. On the one hand, we are assessing the diagnostic efficacy of the methodologies used for prenatal diagnosis of aneuploidy such as 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**

New methodologies; chorionic villus sampling; prenatal screening; karyotype; POCT.

Q:1

Q:1

Q:3

Q:4

#### **Scientific Production**

#### **Publications**

#### **In Collaboration**

Perez-Martinez P, Alcala-Diaz JF, Kabagambe EK, Garcia-Rios A, Tsai MY, Delgado-Lista J, Kolovou G, Straka RJ, Gomez-Delgado F, Hopkins PN, Marin C, Borecki I, Yubero-Serrano EM, Hixson JE, Camargo A, Province MA, Lopez-Moreno J, Rodriguez-Cantalejo F, Tinahones FJ, Mikhailidis DP, Perez-Jimenez F, Arnett DK, Ordovas JM, Lopez-Miranda J. Assessment of postprandial triglycerides in clinical practice: Validation in a general population and coronary heart disease patients. Journal of Clinical Lipidology. 2016. 10(5):1163-1171. IF:4,906 Q:1 D1

Leon-Acuna A, Alcala-Diaz JF, Delgado-Lista J, Torres-Pena JD, Lopez-Moreno J, Camargo A, Garcia-Rios A, Marin C, Gomez-Delgado F, Caballero J, Van-Ommen B, Malagon MM, Perez-Martinez P, Lopez-Miranda J. Hepatic insulin resistance both in prediabetic and diabetic patients determines postprandial lipoprotein metabolism: from the CORDIOPREV study. Cardiovascular Diabetology. 2016.15: Núm art 68. IF:4,534 Q-1

Delgado-Lista J, Perez-Martinez P, Garcia-Rios A, Alcala-Diaz JF, Perez-Caballero AI, Gomez-Delgado F, Fuentes F, Quintana-Navarro G, Lopez-Segura F, Ortiz-Morales AM, Delgado-Casado N, Yubero-Serrano EM, Camargo A, Marin C, Rodriguez-Cantalejo F, Gomez-Luna P, Ordovas JM, Lopez-Miranda J, Perez-Jimenez F.CORonary Diet Intervention with Olive oil and cardiovascular PREVention study (the CORDIOPREV study): Rationale, methods, and baseline characteristics: A clinical trial comparing the efficacy of a Mediterranean diet rich in olive oil versus a low-fat diet. American Heart JournaL.2016.177:42-50. IF:4,332 Q:1

Yubero-Serrano EM, Delgado-Lista J, Alcala-Diaz JF, Garcia-Rios A, Perez-Caballero AI, Blanco-Rojo R, Gomez-Delgado F, Marin C, Tinahones FJ, Caballero J, Ordovas JM, van Ommen B, Perez-Jimenez F, Perez-Martinez P, Lopez-Miranda J. A dysregulation of glucose metabolism control is associated with carotid atherosclerosis in patients with coronary heart disease (CORDIOPREV-DIAB study). Atherosclerosis. 2016. 253:178-185. IF:3,942



2016

Q:1

Rangel-Zuniga OA, Corina A, Lucena-Porras B, Cruz-Teno C, Gomez-Delgado F, Jimenez-Lucena R, Alcala-Diaz JF, Haro-Mariscal C, Yubero-Serrano EM, Delgado-Lista J, Lopez-Moreno J, Rodriguez-Cantalejo F, Camargo A, Tinahones FJ, Ordovas JM, Lopez-Miranda J, Perez-Martinez P. TNFA gene variants related to the inflammatory status and its association with cellular aging: From the COR-DIOPREV study. Experimental Gerontology. 2016. 83:56-62. IF:3,35

Talavera-Garcia E, Delgado-Lista J, Garcia-Rios A, Delgado-Casado N, Gomez-Luna P, Gomez-Garduno A, Gomez-Delgado F, Alcala-Diaz JF, Yubero-Serrano E, Marin C, Perez-Caballero AI, Fuentes-Jimenez FJ, Camargo A, Rodriguez-Cantalejo F, Tinahones FJ, Ordovas JM, Perez-Jimenez F, Perez-Martinez P, Lopez-Miranda J. Influence of Obesity and Metabolic Disease on Carotid Atherosclerosis in Patients with Coronary Artery Disease (CordioPrev Study). Plos One. 2016. 11(4):Núm art e0153096. IF:3,057

Pastor-Villaescusa B, Caballero-Villarraso J, Canete MD, Hoyos R, Maldonado J, Bueno G, Leis R, Gil A, Canete R, Aguilera CM. Evaluation of differential effects of metformin treatment in obese children according to pubertal stage and genetic variations: study protocol for a randomized controlled trial. Trials. 2016. 17: Núm art 323. IF:1,859

Nobre-Carvalho A, Caballero-Villarraso J, Grande-Perez P, Siles-Cadilla J. Cauda equina syndrome in elderly patient. European Geriatric Medicine. 2016. 7(5):459-461. IF:1,326

# **GA8** • Radiology

# HIGHLIGHTS

# PUBLICATIONS



**AVERAGE IMPACT FACTOR** 



#### **Team Leader**

**Principal Investigator** Daniel López Ruiz danieljlruiz@gmail.com

#### Researchers

Álvarez Benito, Marina Benito Ysamat, Alberto Cano Sánchez, Antonio Cara García, María Delgado Acosta, Fernando García Ortega, María José García-Revillo García, José Izquierdo Palomares, Lucia Nuria Muñoz Carrasco, Rafaela Roldán Romero, Elisa Santos Romero, Ana Luz Ysamat Marfa, Roser Other members of the Group (Nursing, Technical, and Administrative Staff) Amate Rivas, Cristina



### **Scientific Activity**

Continuous advances in diagnostic imaging techniques have allowed physician to make highly accurate diagnoses, perform a close follow-up of the evolution of the disease, and assess TJE response of a large number of nosologic entities to a range of drugs and therapies. The collaboration of the Diagnostic Radiology Unit has allowed to assess the effect of new drugs on the evolution of a large number of neoplasms, 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**

#### In Collaboration

Martinez-Galdamez M, Perez S, Vega A, Ruiz P, Caniego JL, Barcena E, Saura P, Mendez JC, Delgado F, Ortega-Gutierrez S, Romance A, Diaz T, Gonzalez E, Gil A, Murias E, Vega P. Endovascular treatment of intracranial aneurysms using the Pipeline Flex embolization device: a case series of 30 consecutive patients. Journal of Neurointerventional Surgery. 2016. 8(4):396-401. IF:2,959

Q:2

#### **Resercher Funding**

#### National

Álvarez Benito, M. Comparación de la Mamografía Digital con la Tomosintesis en Programas de detección Precoz de Cáncer de Mama. Comparison of Digital Mammography with Tomosynthesis in Early Breast Cancer Detection Programs Funding Agency: Sociedad Española de Radiología Médica. Reference: Seram14.001

\*In Collaborations with others IMIBIC's Group: \*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

#### **Contracts with Companies**

López Ruíz, DJ. Oncoexpert. Funding agency: Intra Sistemas SA. Reference: INTER.0003/3

#### **Clinical Trials**

2802.Pilot endovascular recanalization study of stroke beyond 8 hours from the selected start via imaging techniques PI: Dr/a Delgado Acosta, F. 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, J.

\*3118. Efficacy and safety of intra-arterial administration of rexmyelocel t to treat critical limb ischemia in subjects with diabetes mellitus: a multicenter, randomized, double-blind, placebo controlled trial.

PI: Dr/a García-Revillo García, J.



# **GA9** • Cardiology Cardiovascular

# HIGHLIGHTS





#### **Team Leader**

Principal Investigator Ignacio Muñoz Carvajal ignacio.munoz.carvajal.sspa@juntadeandalucia.es PAIDI TEP-226 PRINIA Scientific Group (Collaborator)

#### Researchers

Alados Arboledas, Pedro Jose Arias Dachary, Francisco Javier Blazquez Ruiz, Maria Del Valle Canis López, Miguel Casares Mediavilla, Jaime Guillermo Chacón Quevedo, Antonio Fernández Carbonell, Azahara Garcia-Revillo Garcia, Jose Hervas Sotomayor, Daniela Jiménez Castilla, Agustina Jurado Morata, Aurea Maiorano Iuliano, Pasquale Merino Cejas, Carlos Manuel Moya González, Javier Ortega Lopera, Bibián Pernía Orena, Isabel Turegano Cisneros, José María Zurita Martinez, Federico

Pre-Doctoral Researchers (PhD Students y MSc Students) Conejero Jurado, Maria Teresa Valencia Núñez, Diana

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

Canales Ruiz, Rafael Recio Rufián, Manuel Riballo Cortes, Raquel Romero Mata, Noelia M<sup>a</sup> Romero Morales, María del Carmen

#### **Research Funding**

#### International

Muñoz Carvajal, I. STARS-Empowering Patients by Professional Stress Avoidance and Recovery Services.Funding agency: European Commission. Reference: PM-12-2016-002

#### **Contracts with Companies**

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. Pl: Dr/a Muñoz Carvajal, I.

3276. European multi-centre registry to assess outcomes in patients undergoing coronary artery bypass graft surgery: treatment of vascular conduits with DuraGraft<sup>®</sup>, a novel endothelial damage inhibitor. PI: Dr/a Muñoz Carvajal, I.

3128. Acute study on extravascular defibrillation, electrostimulation and electrograms. ASD2. Pl: Dr/a Muñoz Carvajal, I.



# **GA10** • Nuclear Medicine

# HIGHLIGHTS



#### **Team Leader**

**Principal Investigator** Juan Antonio Vallejo Casas jantonio.vallejo.sspa@juntadeandalucia.es

#### **Researchers**

Carmona Asenjo, Elvira Maza Muret, Francisco Roberto Mena Bares, Luisa

**Pre-Doctoral Researchers (PhD** Students y MSc Students) Guiote Moreno, María Victoria Rodríguez Caceres, Esther

Other members of the Group (Nursing, Technical, and Administrative Staff) Lesmes Porras, M del Carmen Moreno Ortega, Estefenía Martin Ruiz, Antonio Rojas Arroyo, Anahi



### **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

Vallejo Casas JA, Mena Bares LM, Galvez Moreno MA, Moreno Ortega E, Marlowe RJ, Maza Muret FR, Albala Gonzalez MD.Thyroid remnant ablation success and disease outcome in stage III or IV differentiated thyroid carcinoma: recombinant human thyrotropin versus thyroid hormone withdrawal. Quarterly Journal of Nuclear Medicine and Molecular Imaging. 2016. 60(2):163-171. IF:2,413 Q:2



# **GA11 • Learning and Artificial Neural** Networks-AYRNA

HIGHLIGHTS



#### **Team Leader**

Principal Investigator Cesar Hervás Martínez chervas@uco.es PAIDI TIC-148 Scientific Group

#### **Researchers**

Becerra Alonso, David Carbonero Ruz, Mariano Cruz Ramírez, Manuel De la Paz Marín, Mónica Fernández Caballero, Juan Carlos Fernández Navarro, Francisco García Alonso, Carlos Gutiérrez, Pedro Antonio Martínez Estudillo, Alfonso Carlos Martínez Estudillo, Francisco José Pérez Ortiz, María Sánchez Monedero, Javier Torres Jiménez, Mercedes Pre-Doctoral Researchers (PhD Students y MSc Students) Dorado Moreno, Manuel Durán Rosal, Antonio M



### **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

Perez-Ortiz M, Gutierrez PA, Tino P, Hervas-Martinez C.Oversampling the Minority Class in the Feature Space. IEEE Transactions on Neural Networks and Learning Systems. 2016. 27(9):1947-1961. IF:4,854 Q:1 D1

Saez A, Sanchez-Monedero J, Gutierrez PA, Hervas-Martinez C.Machine Learning Methods for Binary and Multiclass Classification of Melanoma Thickness From Dermoscopic Images. IEEE Transactions on Medical Imaging. 2016. 35(4):1036-1045. IF:3,756 Q:1 D1

Perez-Ortiz M, Manuel Pena J, Gutierrez PA, Torres-Sanchez J, Hervas-Martinez C, Lopez-Granados F.Selecting patterns and features for between- and within-crop-row weed mapping using UAV-imagery. Expert Systems With Applications. 2016. 47:85-94. IF:2,981 Q:1 D:1

Gutierrez PA, Perez-Ortiz M, Sanchez-Monedero J, Fernandez-Navarro F, Hervas-Martinez C.Ordinal Regression Methods: Survey and Experimental Study. IEEE Transactions on Knowledge and Data Engineering. 2016. 28(1):127-146. IF:2,476 O:1

Perez-Ortiz M, Jimenez-Fernandez S, Gutierrez PA, Alexandre E, Hervas-Martinez C, Salcedo-Sanz S. A Review of Classification Problems and Algorithms in Renewable Energy Applications. Energies. 2016.9(8): Núm art 607. IF:2,077 Q:2

Dorado-Moreno M, Sianes A, Hervas-Martinez C .From outside to hyper-globalisation: an Artificial Neural Network ordinal classifier applied to measure the extent of globalisation. Quality & Quantity. 2016. 50(2):549-576. IF:0,867 Q:3

Duran-Rosal AM, Dorado-Moreno M, Gutierrez PA, Hervas-Martinez C. On the Use of the Beta Distribution for a Hybrid Time Series Segmentation Algorithm. Advances in Artificial Intelligence, Caepia 2016. 2016. 9868:418-427. IF:0

Dorado-Moreno M, Perez-Ortiz M, Ayllon-Teran MD, Gutierrez PA, Hervas-Martinez C. Ordinal Evolutionary Artificial Neural Networks for Solving an Imbalanced Liver Transplantation Problem. Hybrid Artificial Intelligent Systems. 2016. 9648:451-462. IF:0

Dorado-Moreno M, Duran-Rosal AM, Guijo-Rubio D, Gutierrez PA, Prieto L, Salcedo-Sanz S, Hervas-Martinez C. Multiclass Prediction of Wind Power Ramp Events Combining Reservoir Computing and Support Vector Machines. Advances in Artificial Intelligence, Caepia 2016. 2016. 9868:300-309. IF:0

#### **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



# **GH** • Other scientific Contributions from the Hospital divisions

# **Anesthesia Unit**

#### **Research Funding**

Galán Cabezas, A. Improved patient wellbeing and safety in management procedures using collaborative systems. m-LISTABLE. . Funding agency: Ministry of Economy and Competitiveness (MINECO). Reference: RTC-2016-5149\_001

Herrador Montiel, I. RELIEF - Recovering Life wellbeing through pain self-management techniques involving ICTs.Funding Agency: European Comission. Refernece: PHC-27-2015-001

#### **Contracts with Companies**

Herrador Montiel, I. Grünenthal Agreement Funding Agency:GRÜNENTHAL PHARMA, S.A.Reference:PSS.0159

#### **Clinical Trials**

\*3219. One-arm, open-label, multi-centric phase IIIb study to evaluate the effectiveness, safety, tolerability, ease of use and use of Zalviso resources in the management of moderate-to-severe acute postoperative pain. PI: Dr/a Herrador Montiel, Inmaculada 3188. Evaluation of the quality of life and satisfaction of the patient with breakthrough pain associated with chronic neuropathic pain. Economic impact assessed through quality of life. CANDI study.

PI: Dr/a Herrador Montiel, Inmaculada

2934. Epidemiological study to estimate the prevalence and evaluate the severity, approach and organizational structures used for the management of acute post-operative pain after major surgery in admitted patients in Spain.

PI: Dr/a Herrador Montiel, Inmaculada

# **Cardiology Unit**



#### **Scientific Production**

#### Publications

#### Original

Q:1

Anguita Sanchez M, Bertomeu Martinez V, Cequier Fillat A.Degree of Anticoagulation Control in Patients With Atrial Fibrillation in Spain: Need to Minimize Biases and Contextualize Results. Response by Anguita Sanchez et al..Revista Espanola De Cardiologia.2016.69(3):356-356. IF:4,596 Q:1

Anguita Sanchez M, Bertomeu Martinez V, Cequier Fillat A.Heart Failure, Nonvalvular Atrial Fibrillation and Anticoagulation Control With Vitamin K Antagonists.Revista Espanola De Cardiologia.2016.69(1):75-76. IF:4,596 Journal.2016.46(5):583-589. IF:1,526 Q:2

Anguita-Sanchez M, Marco-Vera P, Alonso-Moreno FJ, Arribas-Ynsaurriaga F, Gallego-Cullere J, Honorato-Perez J, Suarez-Fernandez C.Perception of physicians on factors that influence the choice of a dicoumarin or a new oral anticoagulant in patients with non-valvular atrial fibrillation.Atencion Primaria.2016.48(8):527-534. IE:1.098

Q:3

#### In Collaboration

Regueiro A, Linke A, Latib A, Ihlemann N, Urena M, Walther T, Husser O, Herrmann HC, Nombela-Franco L, Cheema AN, Le Breton H,Stortecky S, Kapadia S, Bartorelli AL, Sinning JM, Amat-Santos I, Munoz-Garcia A, Lerakis S, Gutiérrez-Ibanes E, Abdel-Wahab M, T.Association Between Transcatheter Aortic Valve Replacement and Subsequent Infective Endocarditis and In-Hospital Death.Jama (The Journal Of American Medical Association).2016.310(10):1083-1092. IF:37,684 Q:1 D1

Rodriguez-Padial L, Bertomeu V, Elola FJ, Anguita M, Fernandez Lozano I, Silva L, Hidalgo R, Iniguez A.Quality Improvement Strategy of the Spanish Society of Cardiology: The RE-CALCAR Registry..Journal Of The American College Of Cardiology.2016.68(10):1140-2. IF:17,759 Q:1 D1

Delgado JF, Alonso-Pulpon L, Mirabet S, Almenar L, Villa FP, Gonzalez-Vilchez F, Palomo J, Blasco T, Garcia-Cosio MD, Gonzalez-Costello J, de la Fuente L, Rabago G, Lage E, Pascual D, Molina BD, Arizon JM, Muniz J, Crespo-Leiro MG.Cancer Incidence in Heart Transplant Recipients With Previous Neoplasia History.American Journal Of Transplantation.2016.16(5):1569-1578. IF:5,669

Q:1 D1

Gonzalez Saldivar H, Figueiras-Graillet LM, Anguita M, Marin F, Bertomeu V, Roldan I, Ruiz M, Muniz J, Martinez-Selles M.Oral anticoagulation in octogenarians with atrial fibrillation..International Journal Of Cardiology.2016.223():87-90. IF:4,638 Q:12

Comin-Colet J, Anguita M, Formiga F, Almenar L, Crespo-Leiro MG, Manzano L, Muniz J, Chaves J, de Frutos T, Enjuanes C.Health-related Quality of Life of Patients With Chronic Systolic Heart Failure in Spain: Results of the VIDA-IC Study.Revista Espanola De Cardiologia.2016.69(3):256-271. IF:4,596

Q:12

Roldan Rabadan I, Anguita Sanchez M, Marin F, Angustias Quesada M, Camacho Siles J, Peinado R, Bertomeu V, Cequier Fillat A, Badimon L, Muniz J.Current Antiarrhythmic Therapy for Nonvalvular Atrial Fibrillation in Spain. Data From the FANTASIIA Registry.Revista Espanola De Cardiologia.2016.69(1):54-60. IF:4,596 Q:1 2

Esteve-Pastor MA, Garcia-Fernandez A, Macias M, Sogorb F, Valdes M, Roldan V, Muniz J, Badimon L, Roldan I, Bertomeu-Martinez V, Cequier A, Lip GYH, Anguita M, Marin F.Is the ORBIT Bleeding Risk Score Superior to the HAS-BLED Score in Anticoagulated Atrial Fibrillation Patients?.Circulation Journal.2016.80(10):2102-2108.

Esteve-Pastor MA, Marin F, Bertomeu-Martinez V, Roldan-Rabadan I, Cequier-Fillat A, Badimon L, Muniz-Garcia J, Valdes M, Anguita-Sanchez M.Do physicians correctly calculate thromboembolic risk scores? A comparison of concordance between manual and computer-based calculation of CHADS(2) and CHA(2)DS(2)-VASc scores.Internal Medicine

IF:4,124 Q:1 3

Gonzalez-Saldivar H, Rodriguez-Pascual C, de la Morena G, Fernandez-Golfin C, Amoros C, Baquero Alonso M, Martinez Dolz L, Ariza Sole A, Guzman-Martinez G, Gomez-Doblas JJ, Arribas Jimenez A, Fuentes ME, Galian Gay L, Ruiz Ortiz M, Avanzas P, Abu-Assi E, Comparison of 1-Year Outcome in Patients With Severe Aorta Stenosis Treated Conservatively or by Aortic Valve Replacement or by Percutaneous Transcatheter Aortic Valve Implantation (Data from a Multicenter Spanish Registry).American Journal Of Cardiology.2016.118(2):244-250. IF:3,154 Q:2 4

Jonkman NH, Westland H, Groenwold RHH, Agren S, Anguita M, Blue L, de la Porte PW-FBA, Dewalt DA, Hebert PL, Heisler M, Jaarsma T, Kempen GIJM, Leventhal ME, Lok DJA, Martensson J, Muniz J, Otsu H, Peters-Klimm F, Rich MW, Riegel B, Stromberg A, Tsuyuki RT.What Are Effective Program Characteristics of Self-Management Interventions in Patients With Heart Failure? An Individual Patient Data Meta-analysis.Journal Of Cardiac Failure.2016.22(11):861-871. IE:3.259

Q:2 4

Moreno-Arribas J, Bertomeu-Gonzalez V, Anguita-Sanchez M, Cequier A, Muniz J, Castillo J, Sanchis J, Roldan I, Marin F, Bertomeu-Martinez V.Choice of New Oral Anticoagulant Agents Versus Vitamin K Antagonists in Atrial Fibrillation: FANTASIIA Study.Journal Of Cardiovascular Pharmacology And Therapeutics.2016.21(2):150-156. IF:2,538

Q:2

Gamez JM, Ripoll T, Barrios V, Anguita M, Pedreira M, Madariaga I.The clinical profile of women with stable ischaemic heart disease in Spain. More effort is needed in secondary prevention. SIRENA study.Revista Clinica Espanola.2016.216(1):1-7. IF:0,76

Q:3

#### **Clinical Trials**

\*3327. A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Assess the Efficacy and Safety of Omecamtiv Mecarbil on Mortality and Morbidity in Subjects With Chronic Heart Failure With Reduced Ejection Fraction (GALACTIC-HF)

PI: Dr/a Arizon Del Prado, José María

0063/14.A prospective, multicenter, double-blind, randomized, placebo-controlled, parallel group, 12-week study to evaluate the safety and tolerability of macitentan in subjects with combined pre- and post-capillary pulmonary hypertension (CpcPH) due to left vent PI: Dr/a Arizon Del Prado, José María

0146/13. A Multicenter, Randomized, Double-blind, Placebo-controlled Phase III Study to Evaluate the Efficacy, Safety and Tolerability of Serelaxin When Added to Standard Therapy in Acute Heart Failure Patients. PI: Dr/a Arizon Del Prado, José María

2602. An observational and cross-sectional study to evaluate the sociodemographic and clinical characteristics of patients treated with rivaroxaban in the usual clinical practice of hematologists, cardiologists and internists throughout Spain

PI: Dr/a Ruiz Ortiz, Martin

2594. Global review of long-term oral antithrombotic therapy in patients with atrial fibrillation (Phase II/III EU/ESA Member States) PI: Dr/a López Granados, Amador

1568.Monitoring resycronization in cardiac patients

PI: Dr/a Arizon Del Prado , José María

2816. Internacional registry to assess medical practise with longitudinal observation for trearment of heart failure PI: Dr/a Arizon Del Prado , José María

2881. An observational study to evaluate the relationship between CMV infection and the survival and evaluation of graft vascular disease in a cohort of transplanted cardiac patients: 8 years of follow-up. EVICARD study. Pl: Dr/a Arizon Del Prado , José María

2218. Impact of the genotype and phenotype of Staphylococcus aureus on clinical characteristics and evolution of infective endocarditis.

PI: Dr/a Anguita Sánchez, Manuel

2174. "Fantasia" Study: Influence of the type of adequacy of oral anti-coagulation on the incidence of thromboembolic and hemorrhagic events in an unselected Spanish population of patients with non-valvular atrial fibrillation. Pl: Dr/a Anguita Sánchez, Manuel

2615. Long-term general register of atrial fibrillation. EORP Register

PI: Dr/a Anguita Sánchez, Manuel

2931 .Epidemiological study to evaluate the management, quality of life and therapeutic adherence of patients with stable coronary disease. "AVANCE II" STUDY. PI: Dr/a López Aguilera, Jose

# Department of the Subdirectorate of Information and Communication Technologies



#### **Scientific Production**

#### **Publications**

#### Original

Delgado-Osuna JA, Lozano M, Garcia-Martinez C.An alternative artificial bee colony algorithm with destructive-constructive neighbourhood operator for the problem of composing medical crews.Information Sciences.2016.326():215-226. IF:3,364 Q:1 D1



# **General and Digestive Surgery Unit**



### **Scientific Production**

#### Publications

#### Original

Garcia-Cabezas S, Rodriguez-Linan M, Otero-Romero AM, Bueno-Serrano CM, Gomez-Barbadillo J, Palacios-Eito A.Response to treatment and interval to surgery after preoperative short-course radiotherapy in rectal cancer.Cirugia Espanola.2016.94(8):460-466. IF:1,00 Q:3

Macias I.Massive upper gastrointestinal bleeding due to splenoportal axis thrombosis in a patient with a tested JAK2 mutation: A case report and review literature..International Journal Of Surgery Case Reports.2016.28:93-96. IF:0

#### **In Collaborations**

Calvo Rodriguez R, Montero Perez FJ, Garcia Olid A, Gallardo Valverde JM, Calderon de la Barca JM, Jimenez Murillo LM.Value of plasma C-reactive protein and lactate dehydrogenase levels in the diagnosis of intestinal obstruction in an emergency department.Anales Sistema Sanitario Navarra.2016.39(1):115-122. IF:0,783 Q:4 **Clinical Trials** 

\* 3119. A multicenter, randomized, placebo-controlled, double-blind study to evaluate the efficacy and tolerability of 2% diltiazem hydrochloride in the treatment of chronic anal fissure, and open-label extension of 24 weeks. Pl: Dr/a Gallardo Valverde, José María

2601. Surgical strategy in the cylindrical abdominoperineal amputation of the rectum due to cancer. Lithotomy vs prone-jackknife position. Multicenter randomized prospective study. PI: Dr/a Gómez Barbadillo, José

2810. Evaluation of the quality of life and satisfaction of an elderly patient with chronic pain and irruptive pain, under treatment with opioids. SAND study.

PI: Dr/a Collazo Chao, Eliseo

2811. Epidemiological study to evaluate the prevalence of breakthrough pain in patients with chronic pain secondary to chronic low back pain. COLUMBUS study. Pl: Dr/a Collazo Chao, Eliseo

# **Maxillofacial Surgery Unit**



### **Scientific Production**

#### **Publications**

#### Original

Heredero S, Solivera J, Garcia B, Dean A.Osteomyocutaneous peroneal artery perforator flap for reconstruction of the skull base. British Journal Of Oral & Maxillofacial Surgery.2016.54(1):99-101. IF:1,237 Q:3

# **Plastic Surgery Unit**



### **Scientific Production**

#### Publications

#### Original

Alonso PE, Rioja LF.Solanidine and tomatidine trigger scar pruritus.Burns.2016.42(3):535-40. IF:1,904 Q:4



# **Dermatology Unit**



#### **Scientific Production**

#### **Publications**

#### Original

Fernandez-Crehuet P, Vano-Galvan S, Martorell-Calatayud A, Arias-Santiago S, Grimalt R, Camacho-Martinez FM.Clinical and trichoscopic characteristics of temporal triangular alopecia: A multicenter study.Journal Of The American Academy Of Dermatology.2016.75(3):634-637. IF:5,621 Q:1 D1

Fernandez-Crehuet P, Ruiz-Villaverde R. Yellowish Papules on the Palms After Water Immersion.. Mayo Clinic Proceedings .2016.91(8):1149-50. IF:5,92 Q:1 Fernandez-Crehuet P, Ruiz-Villaverde R.Dermoscopic features of aquagenic syringeal acrokeratoderma.International Journal Of Dermatology.2016.55(7):E407-E408. IF:1,415 Q:3

Reifs CMA, Salido-Vallejo R.Dermatofibrosarcoma protuberans with fibrosarcomatous transformation.Anais Brasileiros De Dermatologia.2016.(91):5700-701. IF:0,88

Q:4

#### **In Collaboration**

Martinez-Peinado C, Ruiz-Villaverde R, Galan-Gutierrez M, de Victoria JMM.Linear Multiple Epithelioid Hemangioma Associated With a Quiescent Vascular Malformation.Actas Dermo-Sifiliograficas.2016.107(10):862-863. IF:0

# **Pharmacy Unit**



#### **Scientific Production**

#### **Publications**

#### Original

Jurado I, Maestre JM, Velarde P, Ocampo-Martinez C, Fernandez I, Isla Tejera B, del Prado JR.Stock management in hospital pharmacy using chance-constrained model predictive control.Computers In Biology And Medicine.2016.72():248-255. IF:1,521 Q:2

## In Collaboration

Hernandez-Cruz B, Marquez-Saavedra E, Caliz-Caliz R, Navarro-Sarabia F.Comparative effectiveness of treatment with the first TNF antagonist in monotherapy, the first TNF antagonist plus one conventional synthetic disease-modifying antirheumatic drug, and the first TNF antagonist plus two or more conventional synthetic diseas.Arthritis Research & Therapy.2016. 18(1):259. IF:3.979

Q:1

#### **Contracts with Companies**

Del Prado Llergo, JR.ROCHE Agreement. Funding Agency: ROCHE FARMA, S.A. Reference: CCB.0129

Del Prado Llergo, JR.ROCHE Agreement. Funding Agency: ROCHE FARMA, S.A.Reference: CCB.0090

Del Prado Llergo, JR.ROCHE Agreement. Funding Agency: ROCHE FARMA, S.A.Reference: CCB.0077

Del Prado Llergo, JR.TEVA Agreement. Funding Agency: TEVA PHARMA, SLU.Reference: CCB.0106

Del Prado Llergo, JR. BOEHRINGER Agreement. Funding Agency: BOEHRINGER INGEL-HEIM ESPAÑA, S.A..Reference: CCB.0086

Del Prado Llergo, JR. MERCK SHARP Agreement. Funding Agency: MERCK SHARP & DOHME DE ESPAÑA SA. Reference: CCB.0027

Del Prado Llergo, JR.Gilead Agreement Funding Agency:GILEAD SCIENCES, S.L. Reference:PSS.0160

Del Prado Llergo, JR.Novartis Agreement. Funding Agency:NOVARTIS FARMACEUTICA, S.A.Reference:PSS.0149

Del Prado Llergo, JR.Sanofi Agreement.Funding Agency:SANOFI-AVENTIS, S.A. Reference:PSS.0139

Del Prado Llergo, JR. Consultoria Agreement. Funding Agency: CONSULTORIA DE EVEN-TOS MT GLOBAL. Reference: PSS.0037

Del Prado Llergo, JR. Gilead Agreement.Funding Agency: GILEAD SCIENCES, S.L. Reference:PSS.0083 Del Prado Llergo, JR. Astellas Agreement. Funding Agency: ASTELLAS PHARMA, S.A. Reference:PSS.0093

Del Prado Llergo, JR.Janssen Agreement. Funding Agency: JANSSEN-CILAG, S.A. Reference: PSS.0089

Del Prado Llergo, JR.Novartis Agreement. Funding Agency:NOVARTIS FARMACEUTICA, S.A.Reference:PSS.0150

Del Prado Llergo, JR. Merck Agreement.Funding Agency: MERCK SERONO, S.A.Reference: PSS.0100

Del Prado Llergo, JR. Hospira Agreement. Funding Agency: HOSPIRA PRODUCTOS FAR-MACÉUTICOS Y HOSPITALARIOS S.L.U.Reference:PSS.0046

Del Prado Llergo, JR. Janssen Agreement. Funding Agency:JANSSEN-CILAG, S.A. Reference:PSS.0047

Del Prado Llergo, JR.Novartis Agreement. Funding Agency:NOVARTIS FARMACEUTICA, S.A.Reference: PSS.0087

Del Prado Llergo, JR.Janssen Agreement .Funding Agency:JANSSEN-CILAG, S.A. Reference:PSS.0073

#### **Clinical Trials**

3072. The prospective study of clinical toxicity with different formulations of docetaxel. Pl: Dr/a Gago Sanchez, Ana Isabel

3130.Impact of the PROVAUR stewardship program on linezolid resistance in a tertiary university hospital: A before-after interventional study

PI: Dr/a García Martinez, Lucrecia



# **Medical Physics and Radiological Protection Unit**



#### **Scientific Production**

#### **Publications**

#### **In Collaboration**

Ruiz-Cruces R, Vano E, Carrera-Magarino F, Moreno-Rodriguez F, Soler-Cantos MM, Canis-Lopez M, Hernandez-Armas J, Diaz-Romero FJ, Rosales-Espizua F, Fernandez-Soto JM, Sanchez-Casanueva R, Martin-Palanca A, Perez-Martinez M, Gil-Agudo A, Zarca-Diaz MA, Pa.Diagnostic reference levels and complexity indices in interventional radiology: a national programme.European Radiology.2016. (26):124268-4276. IF:3,64 O:1

# **Gynecology & Obstetrics Unit**



### **Scientific Production**

#### Publications

#### Original

Lara-Dominguez MD, Arjona-Berral JE, Dios-Palomares R, Castelo-Branco C.Outpatient hysteroscopic polypectomy: bipolar energy system (Versapoint (R) versus diode laser randomized clinical trial.Gynecological Endocrinology.2016.32(3):196-200. IF:1,413 Q:4

Lorente Gonzalez J, Rios Castillo JE, Pomares Toro E, Romero Nieto MI, Castelo-Branco C, Arjona Berral JE.Essure a novel option for the treatment of hydrosalpinx: a case series and literature review..Gynecological Endocrinology.2016.32(2):166-70. IF:1,413

Q:4

#### **Contract with Companies**

Arjona Berral, JA. Johnson Agreement. Funding Agency: JOHNSON & JOHNSON S.A Reference:

Guisado López, R.Medtronic Agreement. Funding Agency: MEDTRONIC IBERICA, S.A. Reference: PSS.0151

Guisado López, R.Takeda Agreement.Funding Agency: TAKEDA FARMACEUTICA ESPAÑA S.A. Reference: PSS.0148

Guisado López, R Takeda Agreement.Funding Agency:TAKEDA FARMACEUTICA ESPAÑA S.A. Reference: PSS.0097

Guisado López, R. Takeda Agreement.Funding Agency:TAKEDA FARMACEUTICA ESPAÑA S.A.Reference:PSS.0049

#### **Clinical Trials**

0284/14. Phase III multicenter, international, randomized, double-blind, double-simulated, parallel-group, active-comparator-controlled, placebo-controlled clinical trial to assess the analgesic efficacy and safety of ibuprofen arginine/tramadol 400.

PI: Dr/a Arjona Berral, José Eduardo

0253/13. A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Elagolix in Subjects With Moderate to Severe Endometriosis-Associated Pain. Pl: Dr/a Arjona Berral, José Eduardo 0033/14. Extension Study to Evaluate the Long-Term Safety and Efficacy of Elagolix in Subjects With Moderate to Severe Endometriosis-Associated Pain.

PI: Dr/a Arjona Berral, José Eduardo

\*3146. Comparison of the effect of a combination of myo-inositol: D-chiro-inositol with a low proportion of D-chiro-inositol (40:1) versus a combination with a higher proportion of D-chiro-inositol (3.6:1) on oocyte quality . PI: Dr/a Lorente González, Juan

2003. Protocol for clinical study, use of transvaginal ultrasound to confirm placement of Essure® microinserts in women: demonstration of efficacy.

PI: Dr/a Arjona Berral, José Eduardo

2885 Effectiveness of induction methods in IUGR fetuses.

PI: Dr/a Duro Gómez, Jorge

2887. Effectiveness of intravaginal Misoprostol (25 mg) and intracervical double balloon as methods of induction of childbirth in postterm pregnancies.

Pl: Dr/a Duro Gómez, Jorge

2447. An international multi-center clinical study to evaluate the safety and efficacy of the Essure health product (Model ESS505) to prevent pregnancy in women seeking permanent contraception.

PI: Dr/a Arjona Berral, José Eduardo

# **Digestive Unit**



### **Scientific Production**

#### **Publications**

#### In Collaboration

Calleja JL, Delgado S, del Val A, Hervas A, Larraona JL, Teran A, Cucala M, Mearin F.Ferric carboxymaltose reduces transfusions and hospital stay in patients with colon cancer and anemia.International Journal Of Colorectal Disease.2016.31(3):543-551. IF:2,383 **Clinical Trials** 

2600. Treatment with ligation without resection of the short segment of Barrett's esophagus. PI: Dr/a Antonio Naranjo Rodríguez

2242. Comparative prospective randomized multi-centric study of the endoscopic treatment of stenosis in Crohn's disease: Self-expanding metal prosthesis vs. balloon dilatation. PI: Dr/a Antonio Naranjo Rodríguez

# **Immunology & Allergy Unit**

#### **Scientific Production**

#### **Contracts with Companies**

Santamaria Ossorio, M. Clinic Agreement Funding Agency: CLINICORD, S.L. Reference: CCB.0002

#### **Clinical Trials**

0.3

\*3040.A Multi-center, Open-label, Single-arm Trial to Evalue Efficacy, Pharmacokinetics, and Safetyand Tolerability of IGSC 20% in Subjets with Primary Immunodeficiency. PI: Dr/a Santamaria Ossorio, Manuel 2927. PID-RSV study: etymological study on the incidence of acute respiratory infections (ARI) caused by respiratory syncytial virus (RSV) requiring hospitalization in pediatric populations with primary immunodecifience (PID)

PI: Dr/a Santamaria Ossorio, Manuel

# **Infectious Diseases Unit**

#### **Scientific Production**

#### **Publications**

#### Original

2853 . Epidemiologia y eficacia de tratamiento con fosfomicina en la infeccion del tracto urinario causada por Klebsiella pneumoniae resistente a carbapenemas y colistina. Estudio KAPECOR-ITU. Pl: Dr/a Rodríguez Gómez, Jorge

# **Intensive Medicine Unit**



# **Scientific Production**

Publications

#### In Collaboration

Tejedor Fernandez M, Ferrer Higueras MJ, Tejedor Benitez R.Patient safety, clinical outcomes, and efficiency in the emergency department. Emergencias.2016.28(3):141-142. IF:2,917 Q:1

Minambres E, Perez-Villares JM, Terceros-Almanza L, Duenas-Jurado JM, Zabalegui A, Misis M, Bouza MT, Ballesteros MA, Coll E.An intensive lung donor treatment protocol does not have negative influence on other grafts: a multicentre study.European Journal Of Cardio-Thoracic Surgery.2016.49(6):1719-1724. IF:2,803 Q:2 Llompart-Pou JA, Chico-Fernandez M, Sanchez-Casado M, Alberdi-Odriozola F, Guerrero-Lopez F, Mayor-Garcia MD, Gonzalez-Robledo J, Ballesteros-Sanz MA, Herran-Mongei R, Leon-Lopez R, Lopez-Amork L, Bueno-Gonzalez A.Age-related injury patterns in Spanish trauma ICU patients. Results from the RETRAUCI.Injury-International Journal Of The Care Of The Injured.2016.47():S61-S65. IF:1,91

Q:3

#### **Clinical Trials**

2685. Antiplatelet treatment in acute coronary syndrome. PI: Dr/a Alonso Muñoz. Gema



# **Internal Medicine Unit**

# **Scientific Production**

#### **Clinical Trials**

2767. Multicentric observational study to determine the profile and management of antithrombotic treatment of patients with non-valvular atrial fibrillation who are attended by the internal medicine services of Spanish hospitals. PI: Dr/a Jurado Porcel, Ana

# **Emergencies Unit**



### **Scientific Production**

**Publications** 

#### Original

Calvo-Rodriguez R, Gallardo-Valverde J M, Montero-Perez FJ, Baena-Delgado E, Jimenez-Murillo L.Utility of biomarkers in abdominal pain management.Emergencias.2016.28(3):185-192. IF:2,917 Q:1 Calvo Rodriguez R, Montero Perez FJ, Garcia Olid A, Gallardo Valverde JM, Calderon de la Barca JM, Jimenez Murillo LM.Value of plasma C-reactive protein and lactate dehydrogenase levels in the diagnosis of intestinal obstruction in an emergency department.Anales Sistema Sanitario Navarra.2016.39(1):115-122. IF:0,783 Q:4

#### **In Collaboration**

Carbajosa V, Martin-Sanchez FJ, Llorens P, Herrero P, Jacob J, Alquezar A, Perez-Dura MJ, Alonso H, Garrido JM, Torres-Murillo J, Lopez-Grima MI, Pinera P, Fernandez C, Miro O.Factors associated with short stays for patients admitted with acute heart failure.Emergencias.2016.28(6):366-374. IF:2,917 O:1

Torres-Degayon V, Montero-Perez FJ, Torres-Murillo JM, Faus-Dader MJ, Baena-Parejo MI, Calleja-Hernandez MA.Medication-related negative outcomes in patients with permanent atrial fibrillation attended in a hospital emergency department.Emergencias.2016.28(2):75-82. IF:2,917

Q:1

#### **Clinical Trials**

\*3270. Study Design and Rationale of A Multicenter, Open-Labeled, Randomized Controlled Trial Comparing MIdazolam Versus MOrphine in Acute Pulmonary Edema: MIMO Trial PI: Dr/a Calvo Rodriguez, Rafael

2905. Retrospective observational study of actual use in practice and treatment outcomes of patients treated with tolvaptan for hyponatremia due to SIADH (SAMPLE) PI: Dr/a Berlango Jiménez, Antonio

# **Microbiology Unit**



#### **Scientific Production**

#### **Publications**

#### **In Collaboration**

Delgado-Valverde M, Torres E, Valiente-Mendez A, Almirante B, Gomez-Zorrilla S, Borrell N, Corzo JE, Gurgui M, Almela M, Garcia-Alvarez L, Fontecoba-Sanchez MC, Martinez-Martinez L, Canton R, Praena J, Causse M, Gutierrez-Gutierrez B, Roberts JA, Farkas A.Impact of the MIC of piperacillin/tazobactam on the outcome for patients with bacteraemia due to Enterobacteriaceae: the Bacteraemia-MIC project.Journal Of Antimicrobial Chemotherapy.2016.71(2):521-530. IF:4,919 Q:1

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# **Nephrology Unit**

# **Scientific Production**

#### **Clinical Trials**

1715. Study to assess humoral immunity and its impact on survival functionality of graft in patients with a kidney transplant in Spain in e. PI: Dr/a Del Castillo Caba, Domingo

# **Neurology Unit**



### **Scientific Production**

#### **Publications**

#### **In Collaboration**

Munoz I, Hernandez MS, Santos S, Jurado C, Ruiz L, Toribio E, Sotelo EM, Guerrero AL, Molina V, Uribe F, Cuadrado ML.Personality traits in patients with cluster headache: a comparison with migraine patients.Journal Of Headache And Pain.2016.17:25 IF:3,497 Q:1

Sepulveda M, Armangue T, Sola-Valls N, Arrambide G, Meca-Lallana JE, Oreja-Guevara C, Mendibe M, de Arcaya AA, Aladro Y, Casanova B, Olascoaga J, Jimenez-Huete A, Fernandez-Fournier M, Ramio-Torrenta L, Cobo-Calvo A, Vinals M, de Andres C, Meca-Lallana V.Neuromyelitis optica spectrum disorders Comparison according to the phenotype and serostatus.Neurology-Neuroimmunology & Neuroinflammation.2016.3(3):-. IE:0

#### **Clinical Trials**

\*3067.A randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of sage-547 injection in the treatment of subjects with super-refractory status epilepticus

Pl: Dr/a Estévez María, José Carlos

0255/13. Phase II, multicenter, open, controlled and randomized clinical trial to evaluate the effectiveness of intra-arterial infusion of autologous bone marrow mononuclear cells in patients with ischemic stroke. PI: Dr/a Valverde Moyano, Roberto

2347. A 24-month prospective observational study to describe the regular long-term use of BOTOX for the symptomatic treatment of adults with chronic migraine and to measure the use of health resources and outcomes. Pl: Dr/a Jurado Cobo, Carmen

2569. An observational prospective study to evaluate the effectiveness of injections of botulinum toxin type A (BoNT-A) in patients with spasticity of upper and/or lower limbs after a stroke, in the early phase of spastic development.

PI: Dr/a Ochoa Sepúlveda, Juan José

2855. Impact of eslicarbazepine acetate on lipid metabolism and vascular risk factors. PI: Dr/a Estévez María, José Carlos

# **Neurosurgery Unit**



#### **Scientific Production**

#### Publications

#### **In Collaboration**

Heredero S, Solivera J, Garcia B, Dean A.Osteomyocutaneous peroneal artery perforator flap for reconstruction of the skull base. British Journal Of Oral & Maxillofacial Surgery.2016.54(1):99-101. IF:1,237 Q:3

#### **Research Fundings**

Solivera Vela, J. Diagnosis and post-operative forecast of human gliomas using a new interactomic approach. Funding agency: Regional Ministry of Health and Social Policy (CISPS). Reference: PI-0143-2016



# **Preventive Medicine Unit**



### **Scientific Production**

#### **Publications**

#### Original

Guzman-Herrador B, Molina CD, Allam MF, Navajas RFC.Independent risk factors associated with hospital-acquired pneumonia in an adult ICU: 4-year prospective cohort study in a university reference hospital.Journal Of Public Health.2016.38(2):378-383. IF:1,527 O:3

# **Pneumology Unit**



#### **Scientific Production**

**Publications** 

#### In Collaboration

Lopez-Campos JL, Abad Arranz M, Calero-Acuna C, Romero-Valero F, Ayerbe-Garcia R, Hidalgo-Molina A, Aguilar-Perez-Grovas RI, Garcia-Gil F, Casas-Maldonado F, Caballero-Ballesteros L, Sanchez-Palop M, Perez-Tejero D, Segado A, Calvo-Bonachera J, Hernandez-. Guideline Adherence in Outpatient Clinics for Chronic Obstructive Pulmonary Disease: Results from a Clinical Audit.Plos One.2016.11(3):-. IF:3,057 Q:1

Lopez-Campos JL, Abad Arranz M, Calero Acuna C, Romero Valero F, Ayerbe Garcia R, Hidalgo Molina A, Aguilar Perez-Grovas RI, Garcia Gil F, Casas Maldonado F, Caballero Ballesteros L, Sanchez Palop M, Perez-Tejero D, Segado A, Calvo Bonachera J, Hernandez .Determinants for changing the treatment of COPD: a regression analysis from a clinical audit.International Journal Of Chronic Obstructive Pulmonary Disease.2016.11():1171-1178. IF:3,046 Q:2

Cordovilla R, Bollo de Miguel E, Nunez Ares A, Cosano Povedano FJ, Herraez Ortega I, Jimenez Merchan R.Diagnosis and Treatment of Hemoptysis.Archivos De Bronconeumologia.2016.52(7):368-377. IF:1,771 Q:3

#### **Contracts with Companies**

Lorente González, J. Merck Agreement Funging Agency: MERCK, S.L.U. Reference:C-CB.0081

Vaquero Barrios, J.Astellas Agreement.Funging Agency: ASTELLAS PHARMA, S.A. Reference:CCB.0066

# **Oncology Unit**

#### **Scientific Production**

#### **Clinical Trials**

2701.Evaluation of prognostic factors and treatment regimes for metastatic gastric adenocarcinoma in clinical practice. Pl: Dr/a Serrano Blanch, Raquel \*3068 .Phase II study to evaluate the efficacy of sunitinib retreatment in patients with advanced or metastatic well-differentiated (G1/2) pancreatic neuroendocrine tumors (pNET) who have already failed prior sunitinib therapy. PI: Dr/a Serrano Blanch, Raquel



# **Onco-radiotherapy Unit**



#### **Scientific Production**

#### **Publications**

#### Original

Garcia-Cabezas S, Rodriguez-Linan M, Otero-Romero AM, Bueno-Serrano CM, Gomez-Barbadillo J, Palacios-Eito A.Response to treatment and interval to surgery after preoperative short-course radiotherapy in rectal cancer.Cirugia Espanola.2016.94(8):460-466. IF:1,00 0:3

#### **Contracts with Companies**

Palacios Eito, A.Elekta Agreement. Funging Agency: eLEKTA MEDICAL, S.A. Reference: CCB.0117 Palacios Eito, A.Janssen Agreement. Funding Agency: JANSSEN-CILAG, S.A. Reference: PSS.0133

Palacios Eito, A.Janssen Agreement.Funding Agency: JANSSEN-CILAG, S.A. Reference:PSS.0134

#### **Clinical Trials**

2901 Measurement of the impact of radiation therapy with combined or non-hormonal therapy on quality of life in clinical practice in localized prostate cancer. VEPIC-ORT- study PI: Dr/a Palacios Eito, Amalia

2637.OPTimizing Irradiation through Molecular Assessment of Lymph node PI: Dr/a Espinosa Calvo, María

# **Radiotherapy Unit**



#### **Scientific Production**

#### **Publications**

#### Original

Valle-Alonso J, Rudski-Ricondo L, Fonseca J, Lopez-Sanchez A, Lopera-Lopera E.Thalamic stroke secondary to vertebral dissection after doing yoga.Revista De Neurologia. 2016.62(6):286-287. IF:0,684

# Q:4

#### In Collaboration

Ruiz-Cruces R, Vano E, Carrera-Magarino F, More-

no-Rodriguez F, Soler-Cantos MM, Canis-Lopez M, Hernandez-Armas J, Diaz-Romero FJ, Rosales-Espizua F, Fernandez-Soto JM, Sanchez-Casanueva R, Martin-Palanca A, Perez-Martinez M, Gil-Agudo A, Zarca-Diaz MA, Pa.Diagnostic reference levels and complexity indices in interventional radiology: a national programme.European Radiology.2016. (26):124268-4276. IF:3,64

Q:1

#### **Clinical Trials**

2925 .A Phase III Clinical Trial of Intra-arterial TheraSphere® in the Treatment of Patients With Unresectable Hepatocellula. Pl: Dr/a Zurera Tendero, Luis

# **Ophthalmology Unit**

#### **Scientific Production**

#### **Research Funding**

Gallardo Galera JM. Improved patient wellbeing and safety in management procedures using collaborative systems. m-LISTABLE. . Funding agency: Ministry of Economy and Competitiveness (MINECO). Reference: RTC-2016-5149\_001

Gallardo Galera JM. Network for the prevention, early detection, treatment and rehabilitation of ocular pathologies. Funding agency: Institute Carlos III Health (ISCIII).Reference: RD16/0008/0018

#### **Contracts with Companies**

Gallardo Galera JM Carlson Agreement. Funding Agency:CARLSON WAGONLIT ESPAÑA S.L.Reference:QUERATOCO2016

#### **Clinical Trials**

0260/12. Phase IV, open, randomized, 3-arm, multi-center, 12-month clinical trial to evaluate the efficacy and safety of two treatment regimes, bimonthly or flexible PRN individually tailored to the treat-and-extend regime. PI: Dr/a Caballos Castilla, Rafael

0360/14. The Efficacy and Safety of Bimatoprost SR in Patients With Open-angle Glaucoma or Ocular Hypertension. Pl: Dr/a Giménez Gómez, Rafael

0184/11. Multicenter clinical trial for the evaluation of the safety and feasibility of an allogeneic tissue engineering drug (human artificial nanostructured cornea) in patients with advanced trophic-type corneal ulcers. PI: Dr/a Gallardo Galera, José María

0236/13. Evaluation of THE safety of Monoprost (latanoprost without preservative) compared to Lumigan 0.01% and Lumigan 0.03% in the Emergency Unit, in patients with primary open-angle glaucoma or ocular hypertension, stabilized with Lumigan 0.01%. PI: Dr/a Giménez Gómez, Rafael



# **Pathological Anatomy Unit**

### **Scientific Production**

#### **Contracts with Companies**

Medina Pérez M.Roche Agreement, Funding agency: ROCHE FARMA, S.A.Reference: CCB.0112

Medina Pérez M. Astrazeneca Agreement. Funding agency: ASTRAZENECA FARMACEU-TICA SPAIN S.A.

# **Pediatrics Unit**

### **Scientific Production**

#### **Clinical Trials**

\*3215 A Phase 1, open-label, single-dose, non-randomized study to evaluate pharmacokinetics and pharmacodynamics of edoxaban in pediatric patients.

Pl: Dr/a Tejero Hernández, María Ángeles

\*2718 Effects of probiotic supplementation during the neonatal period on pre-term infants.

Pl: Dr/a De La Camara Morano, Carmen

# **Psychiatry Unit**



### **Scientific Production**

#### Publications

#### Original

Luque-Luque R, Chauca-Chauca GM, Alonso-Lobato P, Jaen-Moreno MJ.Depersonalisation and schizophrenia: Comparative study of initial and multiple episodes of schizophrenia.Revista De Psiquiatria Y Salud Mental.2016.9(3):143-149. IF:1,65 Q:3

#### **In Collaboration**

Garcia-Portilla MP, Garcia-Alvarez L, Sarramea F, Galvan G, Diaz-Mesa E, Bobes-Bascaran T, Al-Halabi S, Elizagarate E, Iglesias C, Saiz Martinez PA, Bobes J.It is feasible and effective to help patients with severe mental disorders to quit smoking: An ecological pragmatic clinical trial with transdermal nicotine patches and varenicline.Schizophrenia Research.2016.176(42431):272-280. IF:4,453 Q:1

Lubeiro A, Rueda C, Hernandez JA, Sanz J, Sarramea F, Molina V.Identification of two clusters within schizophrenia with different structural, functional and clinical characteristics.Progress In Neuro-Psychopharmacology & Biological Psychiatry.2016.64():79-86. IF:4.361

Q:1

#### **Research Funding**

Sarramea F. Efficacy in patients with severe mental disorders of an intensive motivational interventional programme offering individualized information on respiratory damage for smoking cessation. Funding agency: Institute Carlos III Health (ISCIII). Reference: PI16/00802

#### **Contracts with Companies**

Prada Carrasco, C. Janssen Agreement.Funging Agency: JANSSEN-CILAG, S.A.Reference:

#### CCB.0113 03

Luque Luque, R. Janssen Agreement.Funging Agency: JANSSEN-CILAG, S.A.Reference: CCB.0007

#### **Clinical Trials**

\*3330.An Open-label Long-term Extension Safety Study of Intranasal Esketamine in Treatment-resistant Depression. PI: Dr/a Prados Ojeda, Juan Luis

\*3272.A randomized, double-blind, multicenter, active-controlled study to evaluate the efficacy, safety, and tolerability of flexible doses of intranasal esketamine plus an oral antidepressant in adult subjects with treatment-resistant depression. PI: Dr/a Prados Ojeda, Juan Luis

\*3273. A randomized, double-blind, multicenter, active-controlled study of intranasal esketamine plus an oral antidepressant for relapse prevention in treatment-resistant depression. PI: Dr/a Prados Ojeda, Juan Luis

2904. Cross-sectional, multi-centric, observational study to describe the functional capacity of patients with schizophrenia treated with Paliperidone Palmitate for at least six months. PICTURE

PI: Dr/a Alcala Partera, Jose Angel

# **Rehabilitation Unit**

### **Scientific Production**

#### **Contracts with Companies**

Mayordomo Riera, F. Ams Agreement.Funding Agency: AMS CENTRO MEDICO DE EJERCI-CIO SL. Reference: ITC-20151244

Mayordomo Riera, F. Magtel Agreement.Funding Agency: MAGTEL OPERACIONES S.L.U. Reference:ITC-20151115

#### **Clinical Trials**

3005. Effectiveness of a Homebased Cardiac Rehabilitation Program of Mixed Surveillance Using NUUBO Monitoring Vest in Patients With Ischemic Heart Disease at Moderate Cardiovascular Risk PI: Dr/a Heredia Torres, Ángela

# **Quality Unit**



### **Scientific Production**

#### **Publications**

#### Original

Tejedor Fernandez M, Ferrer Higueras MJ, Tejedor Benitez R.Patient safety, clinical outcomes, and efficiency in the emergency department.Emergencias.2016.28(3):141-142. IF:2,917 Q:1

#### **Research Funding**

Jimber Del Rio, M. EPP - eHealth - European Procurers Platform - eHealth - Transforming the market for eHealth Solutions.Funding Agency; European Comssion. Reference: ICT-35-2014-002

# **Orthopaedics Unit**



#### **Scientific Production**

#### **Publications**

#### Original

Carlos Minarro J, Urbano-Luque MT, Quevedo-Reinoso R, Lopez-Pulido MJ, Fernandez-Gonzalez A, Delgado-Martinez AD.ls obesity related with periprosthetic fractures around the knee?.International Orthopaedics.2016.40(8):1583-1586. IF:2,387 Q:2

Natividad-Pedreno M, Nunez-Chia A, Cobo-Valenzuela N, Alcantara-Martos T, Carrascal MT, Delgado-Martinez AD.Effect of cefazolin and cefuroxime on fracture healing in rats.Injury-International Journal Of The Care Of The Injured.2016.47():S3-S6. IF:1,91 Q:3

#### **Clinical Trials**

3041. Multicenter Register of Treatment of Scoliosis Patients in Andalusia. Pl: Dr/a Fuentes Caparros, Simón

2543. Spanish register of osteoporotic femoral fractures.PI: Dr/a Carpintero, Pedro



# **Urology Unit**



### **Scientific Production**

#### **Publications**

#### In Collaboration

Cienfuegos JA, Rotellar F, Salguero J, Ruiz-Canela M, Nunez-Cordoba JM, Sola I, Benito A, Marti-Cruchaga P, Zozaya G, Pardo F, Hernandez-Lizoain JL.A single institution's 21-year experience with surgically resected pancreatic neuroendocrine tumors: an analysis of survival and prognostic factors. Revista Espanola De Enfermedades Digestivas.2016.108(11):689-696. IF:1,455 Q:4





# Facts & Figures

# 9. Facts & Figures

# 9.1 Research Activity

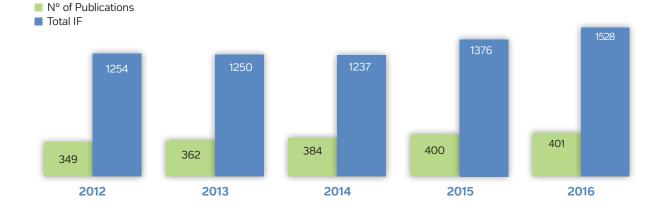
### 9.1.1 Publications

The scientific activities carried out by researchers in their respective groups have led to the following global production:

The following graph shows the evolution of IF over the past five years:

### **Evolution in the last 5 years**

	N° of Publications	Total IF	Average IF
2012	349	1254	3,593
2013	362	1250	3,453
2014	384	1237	3,221
2015	400	1376	3,439
2016	401	1528	3,810



Of note, more than half of these publications appeared in journals within the first quartile, and of those, 15,46% in the first decile, which underscores the growing rates of scientific quality of the published papers. Regarding the authorship of the works, 57,90% of the published articles have an IMIBIC researcher at the first/ last author and corresponding author, whereas the remaining 39,20 % corresponds to co-authorships in the frame of collaborative research projects.

### Distribution of publications per quartiles and first decile

50,12%	20,95%	28,93%
QUARTILE 1	QUARTILE 2	QUARTILE 3/4
15,46%		
DECILE 1		



	N° Of Publications	Total IF	Average IF	%
Q1	201	1135,644	5,650	50,12%
Q2	84	227,3727	2,707	20,95%
Q3+Q4	116	165,027	1,423	28,93%
	N° Of Publications	Total IF	Average IF	%
D1	62	491,559	7,92837097	15,46%

### Distribution of national and international journals

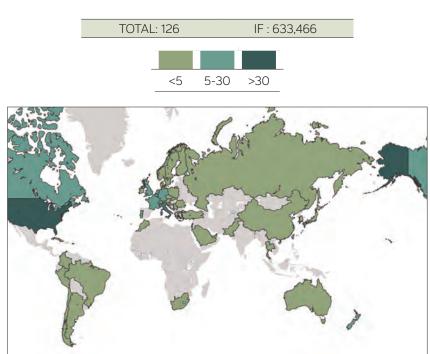
	N° Of Publications	Total IF	Average IF
National	69	133,836	1,940
International	332	1394,208	4,199

Regarding the affiliation of the authors, the papers published in collaboration with groups from other research centers are shown in the **table** below:

### Distribution of affiliation of the authors

	Total IF	No. of publications	%
Distribution of affiliation of the authors - International Groups	633,466	126	31%
Distribution of affiliation of the authors - National Groups	606,751	178	44%
Distribution of affiliation of the authors - Local Groups	287,827	97	24%
	1528,044	401	100%
Distribution of affiliation of the authors - Among IMIBIC Groups	328,971	88	22%

# **International Collaborations**





# 9.1.2 Research projects & networks

# Ongoing Projects in 2016

NATIONAL	INTERNATIONAL	REGIONAL
110	15	82

National Projects	No. of ongoing projects
Institute of Health Carlos III (ISCIII)	54
Ministry of Economy and Competitiveness (MINECO)	31
Ministry of Education, Culture and Sport (MECD)	1
Private Entities	24
Regional Projects	
FIBICO. Research Programme	26
Regional Ministry of Healt (CS)	22
Regional Ministry of Economy, Innovation, Science and Employment (CEICE).	15
Andalusian Progress and Health Foundation (FPS).	8
Private Entities	11
International Projects	
European Commission	12
Icahn School Of Medicine Mount Sinai	1
Academy Of Finland	1
Private Entities	1

### **Granted Projects & Networks in 2016**

NATIONAL	INTERNATIONAL	REGIONAL
46	4	34

National	No. of granted projects
Institute of Health Carlos III (ISCIII)	18
Ministry of Economy and Competitiveness (MINECO)	18
Ministry of Education, Culture and Sport (MECD)	1
Private Entities	9
Regional	
FIBICO. Research Programme	18
Regional Ministry of Health (CS)	14
Private Entities	2
International	
European Commission	2
Icahn School Of Medicine Mount Sinai	1
Foundation For Research In Rheumatology	1



### **Outgoing Humans Resources in 2016**

SENIOR RESEARCHERS	23
POST-MIR RESEARCHERS	5
POSTDOCTORAL RESEARCHERS	3
PREDOCTORAL RESEARCHERS	5
SUPPORT STAFF	21
Total	57

SENIOR RESEARCHERS	
Nicolas Monarde -Andalusian Health Service	6
Miguel Servet Programme II	5
Juan Rodés Programme	1
Juan de la Cierva Programme	1
Strengthening of research activity Programme - (ISCIII) - SNS	4
Strengthening of research activity Programme - Regional Ministry of Health (CS)	6
POSTDOCTORAL RESEARCHERS	
	1

SAS Postdoctoral Programme	1
Sara Borrell	1
Marie Curie	1
POST-MIR RESEARCHER	
Río Hortega Programme	5
PREDOCTORAL RESEARCHERS	
PFIS	1
FPU	1
I-PFIS	1
Research Programme FEHH	1
Predoctoral Programme Ministry of Economy and Competitiveness (MINECO)	1

SUPPORT STAFF	
Ministry of Economy and Competitiveness (MINECO)	14
Institute of Health Carlos III (ISCIII) - GIS	1
Andalusian Health Service	6
Total	57



### 9.1.3 Clinical Trials

### **Ongoing Clinical Trials in 2016**

\*Classified according to the Trial Phase & Study Observational

PHASE I	PHASE II	PHASE III	PHASE IV	MEDICAL ADVICE	Study Observational	
3	79	167	20	14	141	Total 424

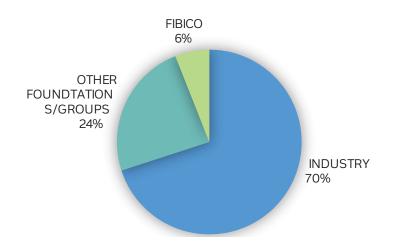
### Funding (M€)

**Clinical trials** 

PHASE I	PHASE II	PHASE III	PHASE IV	MEDICAL ADVICE	TOTAL
12,18 €	297,57 €	1.316,46 €	99,01€	4,98 €	1.730,18 €

### **Clinical Trials classified according to promoter**

		424
6%	FIBICO	27
24%	OTHER FOUNDTATIONS/GROUPS	102
70%	INDUSTRY	295



### **Clinical Trials Submitted to CEIC in 2016**

Clinical Trials	12
Observational Studies	51
Research Projects	150
TFGs	77
PAS Amendments	30
TOTAL	320



9.1.4. Media

Website imibic.org



### **Social Media**



SINGLE USERS **114.276** 

# FREQUENT USERS **149.193**

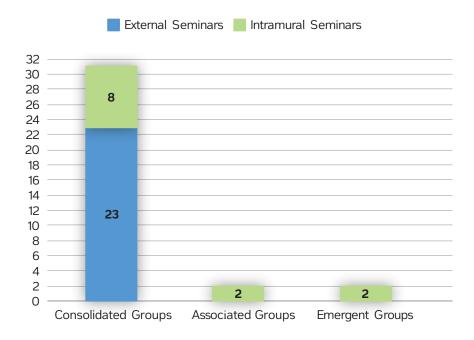
### Awards

The Instituto Andaluz de la Juventud award



### 9.1.5. Training Activities

### 9.1.5.1. IMIBIC Scientific Seminars



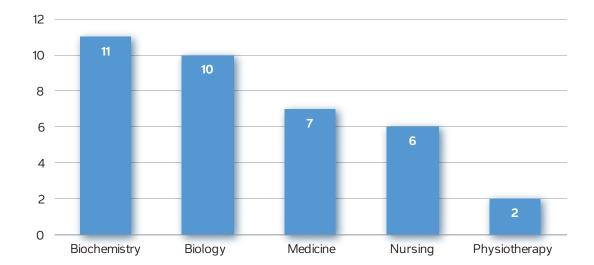


IMIBIC Groups	<b>External Seminars</b>	Intramural Seminars
Consolidated Groups	23	8
Associated Groups		2
Emergent Groups		2
Total:	23	12

### 9.1.5.2. Master's Degrees (2015-16)

The Master's Degree final projects "NO IMIBIC" refer to those supervised by researchers from the University of Cordoba or Reina Sofia University Hospital (Córdoba) that are not associated to the IMIBIC.

### A. Master's Degree in Translational Biomedical Research

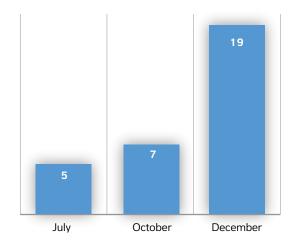


# Background of enrolled student

Master's degree in Translational Biomedical Research		
Biochemistry	11	
Biology	10	
Medicine	7	
Nursing	6	
Physiotherapy	2	
Total	36	

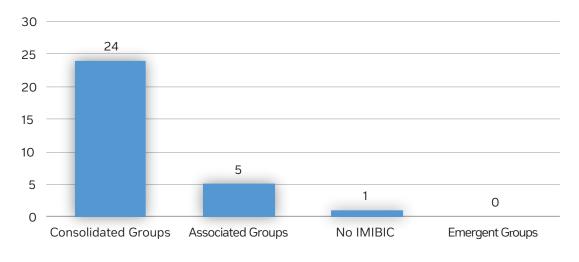


### Master's Degree final projects presented in each call



Call	July	October	December	Total MPs presented 15/16
No. of Students enrolled in the Ma <b>s</b> ters's Degree in Translational Biomedical Research	5	7	19	31

### Master's Degree final projects supervised by researchers from IMIBIC groups 15/16

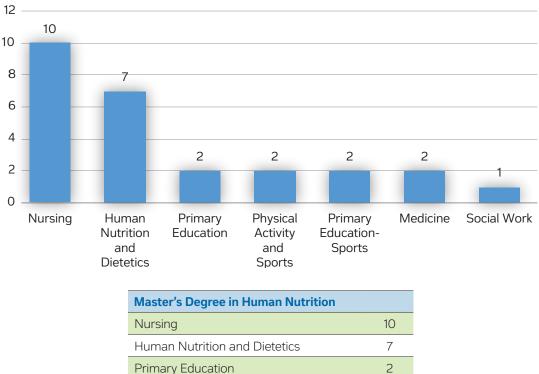


IMIBIC Groups	Master's Degree in Translational Biomedical Research
Consolidated Groups	24
Associated Groups	5
NO IMIBIC	1
Emergent Groups	



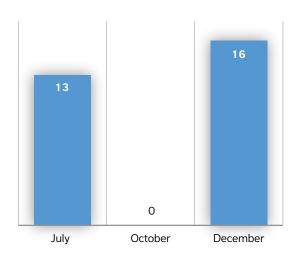
### **B. Master's Degree in Human Nutrition**

### **Background of enrolled student**



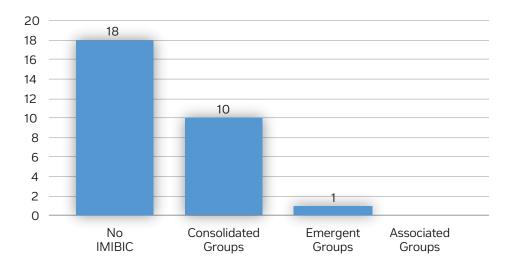
Master's Degree in Human Nutrition	
Nursing	10
Human Nutrition and Dietetics	7
Primary Education	2
Physical Activity and Sports	2
Primary Education-Sports	2
Medicine	2
Social Work	1

### Master's Degree final projects presented in each call



Call	July	October	December	Total MPs presented 15/16
No. of Students enrolled in the Ma <b>s</b> ters's Degree in Human Nutrition	13	0	16	29

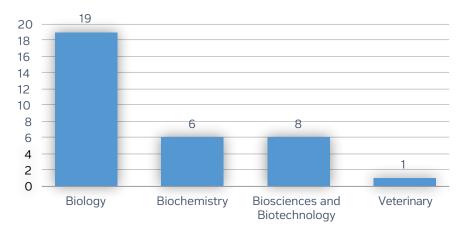
### Master's Degree final projects supervised by researchers from IMIBIC groups 15/16



IMIBIC Groups	Master's Degree in Human Nutrition
No IMIBIC	18
Consolidated Groups	10
Emergent Group	1
Associated Groups	

# C. Master's Degree in Biotechnology

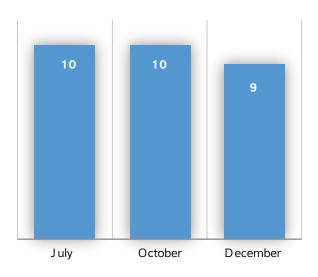
# Background of enrolled student



Master's Degree in Biotechnology	
Biology	19
Biochemistry	6
Biosciences and Biotechnology	1
Veterinary	1

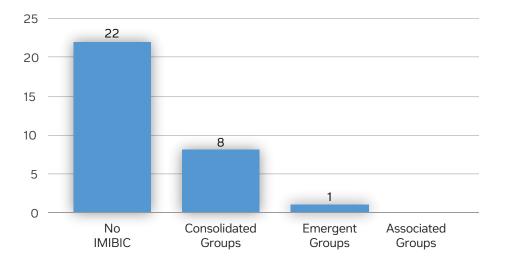


# Master's Degree final projects presented in each call



Call	July	October	December	Total MPs presented 15/16
No. of Students enrolled in the Ma <b>s</b> ters's Degree in Biotechnology	10	10	9	29

# Master's Degree final projects supervised by researchers from IMIBIC groups 15/16

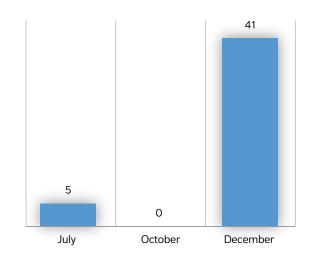


IMIBIC Groups	Master's Degree in Biotechnology
No IMIBIC	22
Consolidated Groups	8
Emergent Groups	1
Associated Groups	



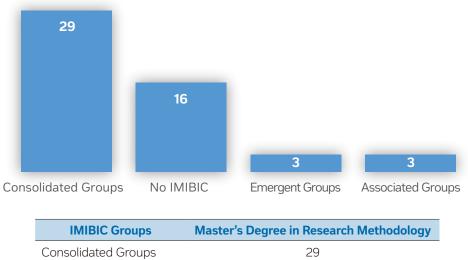
# D. Master's Degree in Research Methodology

Master's Degree final projects presented in each call



Call	July	October	December	Total MPs presented 15/16
No. of Students enrolled in the Maters's Degree in Research Methodology	5	0	41	46

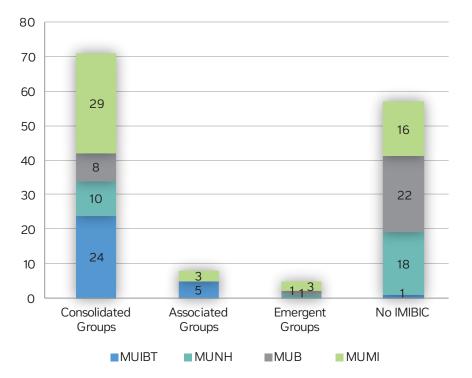
## Master's Degree final projects supervised by researchers from IMIBIC groups 15/16



Consolidated Groups	29	
NO IMIBIC	16	
Emergent Groups	3	
Associated Groups	3	



## Summary Master's Work end Supervise/Directed for IMIBIC Group



Grupo IMIBIC	MUIBT	MUNH	MUB	MUMI
Consolidated Groups	24	10	8	29
Associated Groups	5			3
Emergent Groups		1	1	3
NO IMIBIC	1	18	22	16

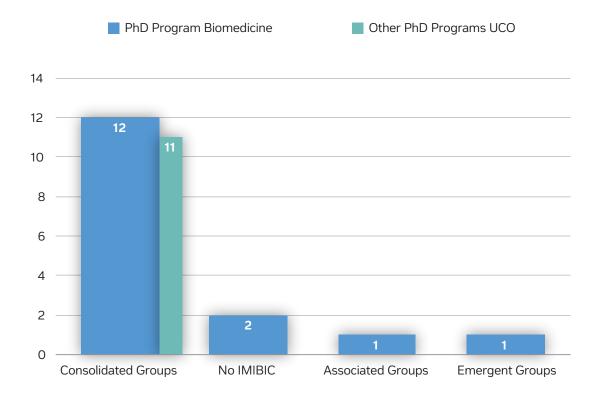
# **Doctoral Programme in Biomedicine**

#### Results of the Doctoral Programme in Biomedicine during the academic year 2015/16:

<b>Doctoral Programme in Biomedicine</b>	
Number of new admissions	55
Total number of students in the PhD programme	149
Foreign students	10
Part-time enrolled students	37
Number of Thesis defended	16
Supervisors of Thesis defended	26
Percent of PHD students drop-out	6%
Cum Laude	89,36%



## Doctoral theses supervised by researchers from IMIBIC groups



IMIBIC Groups	Number of Thesis defended	Other PhD Programs UCO
Consolidated Groups	12	11
NO IMIBIC	2	
Associated Groups	1	
Emergent Groups	1	





# **10. Knowledge Transfer**

IMIBIC is aware that one of the key issue to the institute is to promote that the results of research as well as the ideas generated, have a direct impact on improving patient care and, therefore, on their health. Thus, IMIBIC has the commitment to encouraging its researchers to take an innovative culture within the Institute from a global perspective, with the specific objective that this innovation affect directly or indirectly to the quality of patient care as well as improving the praxis of professionals who belong to the Institution.

During 2016, one of the priority challenge from the Innovation Management area has been to promote the Technology Innovation area. Main emphasis was set to include the participation of the Technology Innovation area in the research projects where application of technologies was needed. Their participation in research and innovation projects has increased during 2016, as more researchers became aware of the importance of ICTs and data analysis applied to their research projects.

In this context, the Innovation Department has carried out the following activities during 2016:

- 1. 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 established on this platform: Entrepreneurship and Innovative Public Procurement. Furthermore, Innovation Management area and it is collaborating actively on their activities.
- 2. The Innovation Management area has started the implementation of a management quality system according to the ISO 166.002:2014 standard.
- 3. With the purpose of promote an innovation culture, the Innovation Department, several presentation took place in different Medical Services to the hospital, allowing us to get more than 120 contacts with healthcare professionals and researchers. 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.

- 4. Annual trade fairs meeting and conferences were attended, with the purpose of networking with company representatives and with other research centers allowing to establish links with them and enabling future collaboration between entities:
  - a. BIOSPAIN 28<sup>th</sup>-30<sup>th</sup> September, BILBAO, (Spain).
  - b.Workshop "Open Market Consultation" of the PCP (Pre Commercial Procurement) project Relief. 14<sup>th</sup> December, Córdoba (Spain).
  - c. Convention ITEMAS 2016, 3<sup>rd</sup> 4<sup>th</sup> October, Santiago (Spain).
  - d. 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.
- 5. The Innovation Management area is participating in one European project, which 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. Furthermore, they collaborated in a PCP (Pre Commercial Procurement) project on the field of chronic pain management that started in 2016. Also they had collaborated in the consortium creation of another PCP (Pre Commercial Procurement) project on the field of stress reduction and measurement management that was requested and got funded during 2016. This PCP project will start in 2017.
- 6. Participation in FIPSE call "Feasibility studies for Healthcare Innovations". Three projects were presented to this call and one of them obtained funding. This call will help to do the validation and feasibility studies needed to achieve successfully the transfer the project to the market and finally one of them was funded.
- 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 4 RETOS projects, 3 DTS projects and 4 INNTERCONECTA projects. Finally, 2 RETOS and 1 DTS projects had been funding during 2016.
- 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. Specifically, during 2016, the Innovation Department has carried out meetings with Indra, Magtel, Roche and Philips.

9. Related with start ups promotion, Innovation Management area had been supporting two important projects, in areas of regenerative medicine and surgical robotics, negotiating with investors and looking for additional funds for their development.

Evolution of Results	2011	2012	2013	2014	2015	2016
Patents	6	8	13	11	14	9
PCTs	2	3	3	4	7	6
Licenses	0	4	4	2	2	0
Companies	1	2	0	1	0	0

As a result of all the activities above described, the following results were obtained:

#### Industrial and intellectual property patents

During 2016, a total of 15 industrial property patents were applied for:

Title	Registry type	Owner Entity
MicroRNA as biomarker and diagnostics of lung cancer.	National Patent	SAS, UCO
Circulating microRNAs as biomarkers of Primary Antiphospholipid Syn- drome.	National Patent	SAS, UCO
Identification of solanacea pruritogena using cutaneous application of its alcaloids.	National Patent	SAS
Biomarkers for the screening and diagnosis of Prostate Cancer.	National Patent	SAS, UCO
Non-invasive Cancer diagnosis method.	National Patent	SAS, UCO
Decompressive Craniectomy device	National Patent	SAS
Method for obtaining useful data for predicting and forecasting of the de- velopment of interferon-induced thrombocytopenia.	PCT	SAS, UCO
Robotic Surgical System and Method for managing a Robotic Surgical System.	PCT	SAS, UCO, TECNALIA, UMA
Laparoscopic Extractor	PCT	SAS
Derivatives of retinoic acid for the treatment of cholestasis.	PCT	SAS, CIBER, UCO
Using the GOAT enzyme levels as a marker of prostate cancer. "Ghrelin -O - acyltransferase (GOAT) and its uses."	PCT	SAS, UCO
Biomarkers in exhaled breath condensate for the diagnosis, classification and monitoring of lung cancer.	PCT	SAS, UCO
Method and kit for predicting or forecasting response to antiangiogenic.	National Phases	SAS, UCO



# Goals for 2017

# **11. Goals for 2017**

	Objective for 2017	
1	Foster and consolidate institutional integration with regard to human resources (See Plan Integración _ OE.1 actions 5 to 7), and enhance access to the ser- vices provided by institutions to their professionals.	Achieve
2	Develop strategies to improve the quality and num- ber of scientific publications and the status of IMIBIC researchers as lead authors.	≥ 27% articles in first decile
3	Promote and improve clinical research at IMIBIC, fos- tering the development, quality and efficiency of inde- pendent clinical research projects.	≥ 10 trials with IMIBIC as pro- moter
4	Strengthen and improve IMIBIC's self-sustainability, optimising the management of its own resources by obtaining more European funding and competitive state funding, and by fostering partnerships with the business sector.	Structural income ≥ 2.3 million € Private/public income ≥ 46%
5	Develop a strategy for incorporating new clinical and university groups, and for promoting existing groups.	2 new groups (at least one emerging group) 1 group promoted
6	Attract more research talent and promote profession- al development.	Active competitively-funded HR > 8% of 2016 value Number of new emerging re-
		searchers -> 3
7	Foster, arrange and consolidate international allianc- es and cooperative ventures.	Apply for > 24 projects
8	Promote and enhance the protection of the knowl- edge generated and the transfer of technology to the business sector.	>20% patents in exploitation
9	Assure the quality of the service provided by UCAIBs and Institute management units and promote trans- versal innovation through them.	User satisfaction $\ge 85\%$
10	Develop and implement an action plan for promoting research by residents.	70%
11	Develop and implement an action plan for promoting primary research and research in nursing.	70%









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