

2018

SCIENTIFIC REPORT

INCLIVA | VLC
Health Research Institute

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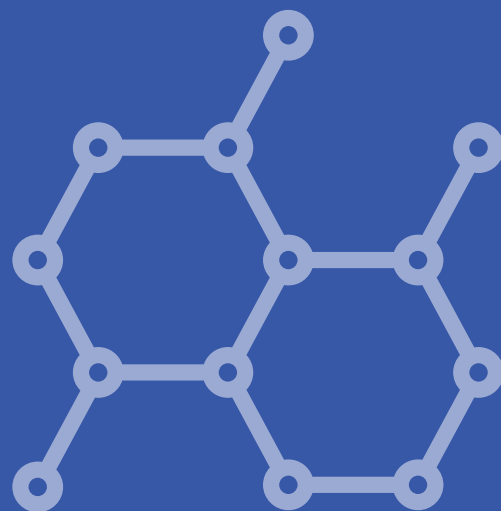
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Introduction

01





Andrés Cervantes

As an accredited biomedical research center, at INCLIVA Health Research Institute we take into consideration the biological complexity of life when planning research strategies, opting for integrative and multidisciplinary work methods.

We are proud to announce that this approach has enhanced research excellence at our institute in 2018, resulting in increased scientific production and a greater number of research projects and clinical trials developed in the entity.

Our researchers have submitted 550 articles which have earned over 3,800 impact factor points, continuing the upward trend observed in recent years. The quality of our published scientific production is also noteworthy: articles published in journals in the first and second quartiles of their respective categories accounted for 60% and 20% of total production, respectively. In this regard, we underscore an average impact factor per article of nearly seven points. During 2018 INCLIVA maintained almost 167 competitive projects active, and the participation in postgraduate programs has led to 52 doctoral theses defended, 11 of them with European mention.

In 2018, INCLIVA researchers have surpassed their fundraising record from Carlos III Health Institute; our research project grants have received 39% of the funds awarded to research centers in the Valencian Community. Our researchers have also been highly successful in European Union competitive tenders, obtaining over two and a half million euros of funding in the areas of cardiovascular and personalized medicine, aging, oncology, fragility and big data. Another highlight is our participation in international networks such as the Big Data Value Association (BDVA), the European Infrastructure for Translational Medicine (EATRIS) and the global Networking in Personalized Cancer Medicine (WIN) initiative. Likewise, we can confirm that this year for the first time INCLIVA will be the coordinating center of European project LEGACY, involving both European and Latin American countries.

Over this year we launched the Precision Medicine Platform, a new support platform for our researchers to develop and promote targeted therapies, and we have also continued to invest in research platforms, dedicating one and a half million euros to new technologies.

Additionally, our drug research ethics committee (CEIM) was the first to receive this accreditation in the Valencian Community, and was also among the first nationally. In fact, our CEIM has served as the benchmark committee in 29 studies since the new legislation was adopted in 2016, and throughout 2018 we have initiated 172 new clinical studies, with a total of 432 active this year.

Finally, as general and scientific director of INCLIVA I would like to thank all the people who form part of this institute, the board of trustees and the governing board, the external and internal scientific committees, the technical and management staff, and the researchers, without whose commitment, effort and creativity our institution's current strong growth and leading position would not be possible.

To better serve society we must continue to grow and generate quality research. Our knowledge, and the breakthroughs that result from it, must be translated as soon as possible to clinical practice to facilitate progress and sustainability in the public health system.







INCLIVA origin and structure

02



2.1. History

The *Hospital Clínico Universitario* of Valencia Research Foundation was constituted in the year 2000 as the first Valencian research foundation affiliated to a public hospital. Ten years later, various centers of excellence in biomedical research from the University of Valencia and IUIVI (Valencian Infertility Institute) joined the Foundation through the establishment of specific agreements, and thus INCLIVA Health Research Institute was created.

INCLIVA's main aims are to manage the biomedical research carried out by the *Hospital Clínico Universitario* of Valencia and its Health Department, and to encourage teaching and scientific activities, thus improving patient treatment and knowledge sharing.

In 2011 INCLIVA was accredited as a Health Research Institute by the Ministry of Science and Innovation (*Ministerio de Ciencia e Innovación*) thus obtaining preferential treatment from the Carlos III Health Institute (*Instituto de Salud Carlos III*), in recognition of its excellence in research.

On March 13, this accreditation as a Health Research Institute was renewed for a further five years.



2.2. Organizational structure

2.2.1. Government structure

The highest government body in the Foundation, the Board of Trustees is headed by the Regional Minister for Health of the Valencian Government. This body appoints a Board of Governors –headed by the Chief Executive Officer of the Health Department– the General Director, the Scientific Director and the Financial Director. These are guided by two Research Committees: the External Scientific Committee and the Internal Scientific Committee.

2.2.1.1 Board of Trustees

With a strong representation from the Valencian community, it is the highest collegiate body in the Institute and its function is to establish INCLIVA strategy and policies.

As at December 31st 2018, its members are as follows:

President:

- Ms. Ana Barceló Chico, Regional Minister for Health of the Valencian Government

Vice-president:

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

Board members by position:

- Ms. María Vicenta Mestre, Distinguished Dean of the University of Valencia
- Mr. Manuel Broseta, Social Council of the University of Valencia
- Mr. Juan López-Trigo, Cañada Blanch Foundation.
- Mr. Rafael Alcón, Bancaja Foundation
- Mr. José Noblejas, Valencia Chamber of Commerce
- Ms. Ana María Ávila, General Director of Research, Innovation,

Technology and Quality of the *Conselleria de Sanidad Universal y Salud Pública* of the Valencian Government

- Mr. Narcis Vázquez, Secretary of the *Conselleria de Sanidad Universal y Salud Pública* of the Valencian Government
- Mr. Martín Quirós, Valencian Council for Culture
- Mr. Francisco Javier Chorro, Distinguished Dean of the Faculty of Medicine
- Mr. Andrés Cervantes, INCLIVA General Director
- Mr. Carlos Simón, Scientific Director of the IGENOMIX Genetic Foundation for Life

Board members under own name:

- Mr. Carlos Pascual
- Mr. Joaquín Ortega
- Mr. Tomás Trenor
- Ms. Ana Lluch

The Scientific Director and Financial Director participate as nonvoting members.

2.2.1.2 Board of Governors

The Board of Governors executes and enforces the Board of Trustees agreements. Other duties are to prepare and approve activities and research project proposals and to decide on and allocate the budgetary means.

As at December 31st 2018, its members are as follows:

President:

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

Vice-president:

- Prof. Francisco Javier Chorro, Distinguished Dean of the Faculty of Medicine.

General Direction:

- Mr. Andrés Cervantes Ruipérez

Secretary General:

- Ms. Maite Sáenz González

Board members:

- Prof. Salvador Lluch, Department of Physiology, University of Valencia
- Mr. Manuel Alós Almiñana, Head of the Pharmacy Department, *Hospital Clínico Universitario* of Valencia

- Prof. Andrés Cervantes, Oncology Service
- Mr. Carlos Simón, Scientific Director of the IGENOMIX Genetic Foundation for Life
- Dr. Pascual Medina, Coordinator of Research Support Platform (UCIM), University of Valencia.
- Dr. Ana Sanmartín, Director of Primary Health Care, Health Service Department in Valencia *Clínico-Malvarrosa*
- Dr. Jorge Navarro, Medical Director, *Hospital Clínico Universitario* of Valencia
- Dr. Marina Soro, President of the Clinical Research Ethics Committee
- Dr. Ana María Ávila. General Director of Research, Innovation, Technology and Quality of the *Conselleria de Sanidad Universal y Salud Pública* (Universal and Public Health Department) of the Valencian Government

2.2.1.3 General and Scientific Director

The most senior person responsible for implementing scientific, economic and administrative policies is the Foundation's General Director.

Professor Andrés Cervantes Ruipérez is Professor of Medicine at the University of Valencia, Head of the Oncology Service of the University Clinical Hospital of Valencia and Director of the Cancer Area at the INCLIVA Health Research Institute.

His training as a resident medical intern took place at the *Hospital Clínico Universitario* of Valencia. After completing this residency he obtained a predoctoral fellowship at the Free University Hospital in Amsterdam, where he obtained his Doctorate in the laboratory of cellular pharmacology, with work on multidrug resistance.

His areas of interest and research are gastrointestinal and gynecological cancer, as well as phase I trials and new drug development.

As a clinical researcher in rectal cancer, he has published several papers on the quality of multidisciplinary work as well as on evaluating the quality of mesorectal surgery, how to optimize initial therapy choices and especially, how to treat cancer of the upper third of the rectum.

He is President of the Educational Steering Committee of ESMO (European Society of Medical Oncology) and since January 2014 he is also an Associate Editor in the gastrointestinal cancer section of the *Annals of Oncology* journal.

2.2.1.4 External Scientific Committee

The External Scientific Committee assesses the collegiate government bodies on research carried out and safeguards the quality of that research.

Its national and international members are appointed by the Board of Trustees, who chooses at least one expert in every INCLIVA priority area of research. It is constituted by well-known professionals renowned within the scientific community.

The composition of the External Scientific Committee as at December 31st 2018 is as follows:

President:

- Prof. Javier Díez. Professor of Medicine, University of Navarra. Director of the Cardiovascular Sciences Area, Applied Medical Research Center (CIMA), University of Navarra

Members:

- Prof. José Baselga. Physician in Chief of the Memorial Sloan-Kettering of New York (U.S.A.). Professor of Medicine, Autonomous University of Barcelona. Scientific Director of the Vall d'Hebrón Oncology Institute
- Prof. Nick S. Macklon. Professor in Obstetrics and Gynecology. Division of Developmental Origins of Adult Diseases (DOHaD). University of Southampton. Princess Anne Hospital. Coxford Road, Southampton (United Kingdom)
- Prof. Antonio Vidal-Puig. Professor in Molecular Nutrition and Metabolism. University of Cambridge. Honorary Consultant

in Metabolic Medicine. Metabolic research laboratories. Addenbrooke's Hospital, Cambridge (United Kingdom)

- Prof. Josep Taberner. Chief of Medical Oncology Department. Vall d'Hebrón Hospital, Barcelona
- Prof. José María Medina. Professor in Biochemistry and Molecular Biology. University of Salamanca. Castilla y León Neuroscience Institute (INCYL)
- Prof. Juan Carlos Lacal. Research Professor in Biomedical Research Institute (CSIC), Madrid
- Prof. Manuel Tena-Sempere. Professor in Cell Biology, Physiology, and Immunology Department. University of Córdoba

2.2.1.5 Internal Scientific Committee

INCLIVA's Internal Scientific Committee is advisory to the General Director and the Scientific Director, evaluating and supervising the scientific content of the research areas.

As at December 31st 2018, the Committee composition is as follows:

President:

- Dr. Andrés Cervantes Ruipérez

Members:

- Dr. Jorge Navarro Pérez
- Dr. Ana Sanmartín Almenar
- Dr. Julio Nuñez Villota

- Dr. Ana Lluch Hernández
- Dr. Josep Redón i Mas
- Dr. Mar Tormo Díaz
- Dr. María Jesús Sanz Ferrando
- Dr. Federico Pallardó Calatayud
- Dr. Vicente Bodí Peris

2.2.1.6 Ethical Committee in Clinical Research

The Ethical Committee in Clinical Research (ECCR) of the *Hospital Clínico Universitario* of Valencia is the independent body whose task is to safeguard the protection of the rights, security and welfare of the subjects taking part in a clinical trial or research project.

Among others tasks, this Committee assesses the protocol, the aptitude of the participating researchers, the adequacy of the center's facilities, and ensures the use and quality of the Fact Sheet for Patients in order to secure the informed consent.

The members of the ECCR in the *Hospital Clínico Universitario* of Valencia, dated December 31st 2018, are the following:

President:

- Dr. Marina Soro Domingo. Head of Section of the Anesthesiology and Reanimation Unit
- Dr. Julio Palmero Da Cruz. Head of the Radiology Department
- Prof. Joaquín Ortega Serrano. Head of the General Surgery Department

Vice-president:

- Dr. Cristina Gomis Gozalbo. Specialist of the Gynecology Department
- Dr. M^a Jesús Puchades Montesa. Specialist of the Nephrology Department
- Dr. M^a José Fabiá Valls. Specialist of the Internal Medicine Department

Secretary:

- Mr. Diego V. Cano Blanquer. Pharmacist
- Dr. Luis González Luján. Specialist in Primary Health Care
- Dr. Patricia Roselló Millet. Specialist of the Pediatrics Department

Substitute Secretary:

- Ms. M^a José Tarín Blasco. Graduate in Law
- Dr. Dra. Tania Fleitas Kanonnikoff. Specialist of the Oncology Department

Technical Secretary:

- Ms. Dolores Iglesias Ferri. Pharmacist
- Dr. José Alejandro Pérez Fidalgo. Specialist of the Oncology Department

Members:

- Prof. Esteban Morcillo Sánchez. Professor of Pharmacology
- Dr. Rafael Fernández-Delgado. Pediatrics Specialist
- Dr. Manuel Alós Almiñana. Head of the Pharmacy Department
- Dr. Antonio Peláez Hernández. Allergy Specialist
- Dr. José Luis Trillo Mata. Primary Health Care Pharmaceutics
- Dr. Francisco Dasí Fernández. Stabilized Miguel Servet Researcher
- Ms. M^a Ángeles Mora Plá. Nurse
- Ms. Vanesa Carretero López. Pharmacist
- Ms. Almudena Amaya Rubio. Nurse
- Dr. Ricardo Ruiz Granell. Head of Section of Cardiostimulation of Cardiology Department
- Mr. Luis Miguel Bayo Calaforra. Degree in Philosophy

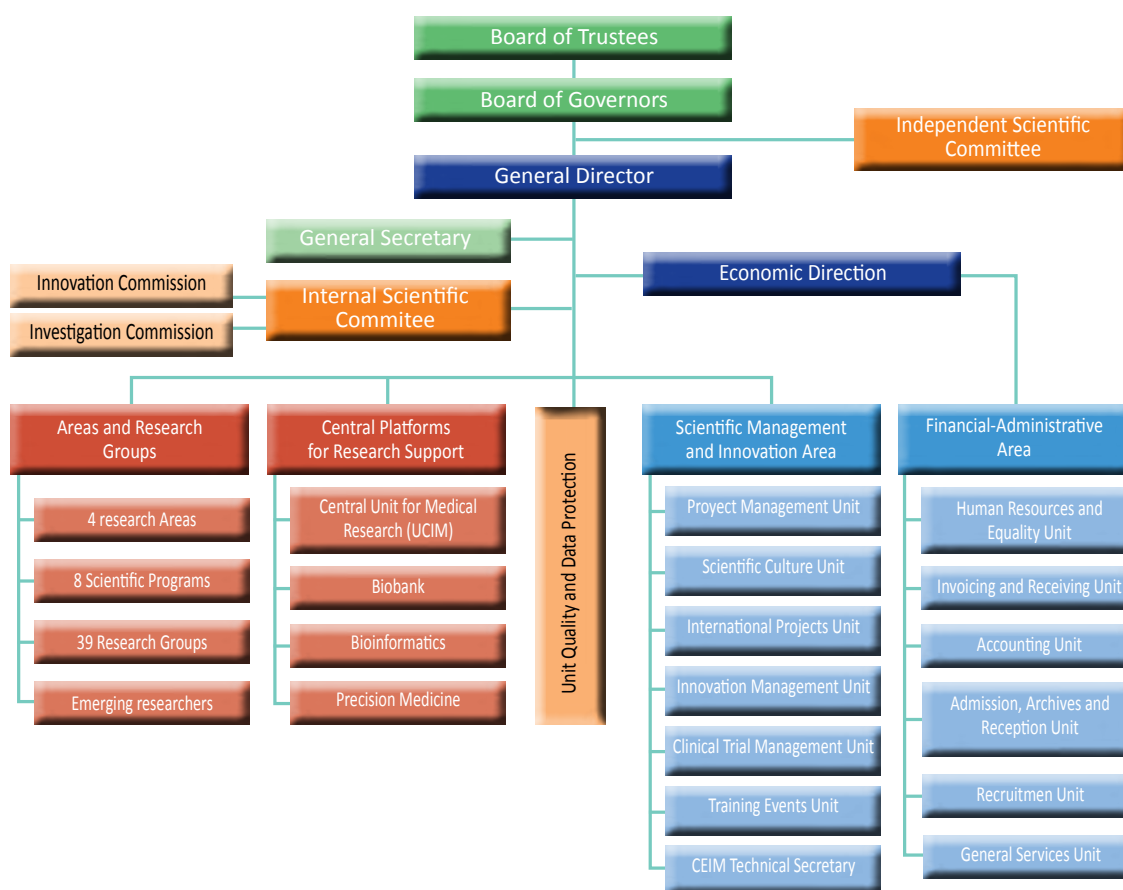


2.2.2. Management structure

The organizational chart, approved at the Board of Trustees held on December 4, is comprised of two sub-directorates, economic and scientific.

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

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



Administrative Area:

- Financial-Administrative Director: Mr. Vicente de Juan
- Financial-Administrative Subdirector: Ms. Consuelo López
- Human Resources and Equality Unit: Ms. Ruth Cano and Ms. Anabel Gil
- Invoicing and Receiving Unit: Ms. Vera Marín
- Accounting and Invoicing Unit: Ms. M^a José Rosalén
- Financial Unit: Ms. Consuelo López and Ms. Karen Iglesias
- Records Unit: Ms. Alicia Belenguer
- Purchasing Unit: Ms. Isabel Gomis
- General Services Unit: Cristina García
- Receptionists: Ms. Carmen Montagud, Mr. Julio Expósito

Scientific Management Area:

- Scientific Subdirector: Dr. Marta Peiró
- Project Management Unit: Ms. Mayca Román, Mr. Bernat Navarro
- Scientific Culture Unit: Mr. Justo Giner, Ms. Cristina García
- International projects Unit: Dr. Ana Ferrer, Dr. Javier Gámez
- Innovation Management Unit: Dr. Pedro Fernández
- Clinical Trials Management Unit: Ms. Dolores Iglesias, Ms. Maialen Llopis, Ms. Vanesa Carretero
- Clinical Trials Platform: Ms. Ana Portolés, Ms. Laura Silla,

Ms. Mireia Hernández, Mr. Bernat Navarro, Ms. Mercedes Peris

- Training Events Unit: Mr. Justo Giner, Ms. Cristina García
- CEIM Technical Secretary: Ms. Dolores Iglesias

Data Quality and Protection:

- Mr. Rafael Barajas

Secretary General:

- Head: Ms. Maite Saenz
- Technician: Ms. Lorena Munuera



➤ 2.3 Core facilities

In 2004 INCLIVA and the Central Service for Experimental Research Support (SCIE) of the University of Valencia signed a collaboration agreement aimed at enhancing cooperation between both institutions, with special emphasis on research projects and collective research activities. It gives *Hospital Clínico Universitario* of Valencia research staff access to and use of the Central Unit for Medical Research facilities as well as research stay opportunities.

The Central Unit for Medical Research (UCIM) was created thanks to FEDER funds in 1990. From its inception, it has received several grants from both University of Valencia and INCLIVA funds, as well as from external funds (*Comisión Interministerial de Ciencia y Tecnología, Generalitat Valenciana* and *Fondo de Investigaciones Sanitarias*).

In addition to these support units, INCLIVA has four additional platforms: the Biobank, the Bioinformatics Unit, the Precision Medicine Unit and the Cytogenetics Laboratory. The latter was created as such in 2013, through a Carlos III Health Institute (*Instituto de Salud Carlos III*) PROMIIS grant program to improve infrastructures.

These laboratories are supported by several research technicians and technical assistants included in the organization's structure thanks to diverse public grants or directly from the University budget.

The research support platforms are:

- Cell Culture Unit
- Flow Cytometric Unit
- Multigenic Analysis Unit
- Confocal Microscopy Unit
- Sequenom Platform
- Laboratory of Molecular Imaging and Metabolomics
- Animal Housing and Experimental Operating Theaters Unit
- Proteomics Unit
- Small Animals PET/CT Camera and Laboratory for Radioactive Isotopes
- Personal Autonomy, Dependence and Severe Mental Disorders Assessment Unit

INCLIVA Platforms are:

- Biobank
- Bioinformatics Unit
- Precision Medicine Unit
- Cytogenetics Laboratory







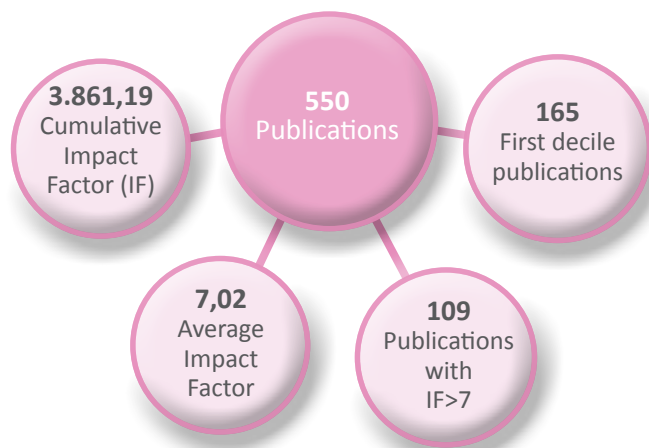
INCLIVA global analysis

03



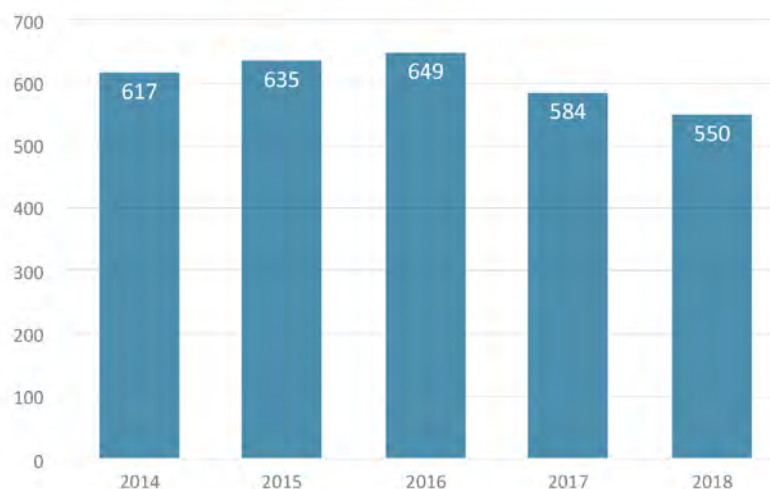
3.1 Scientific production global analysis

As in previous years, INCLIVA continued in 2018 with the upward trend in the quality of scientific production. Although the number of publications is lower than the previous year, the cumulative impact factor has increased (3.618 to 3.861), which translates into an average impact factor greater than in 2016 (6,19 to 7,02). This shows that the publications, despite being smaller in number, are of higher quality. The number of works indexed in the Medline database reached 550 in 2018.

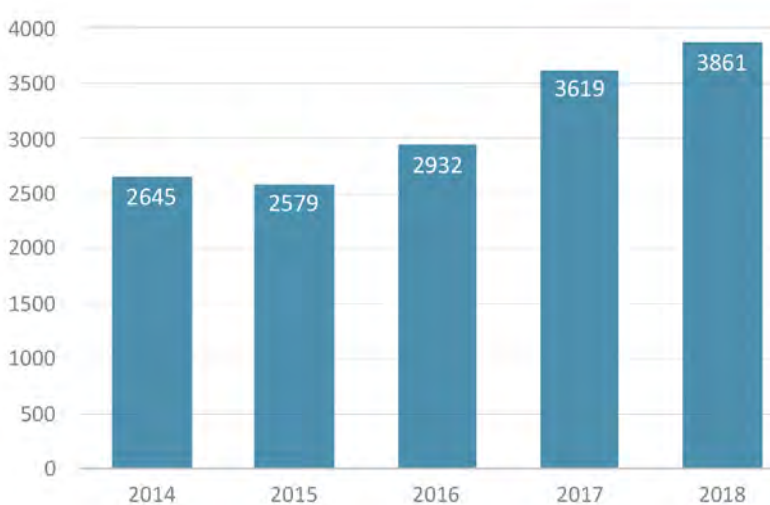


To show this trend, the following figures depict the number and quality of the published manuscripts expressed in terms of total and average impact factor.

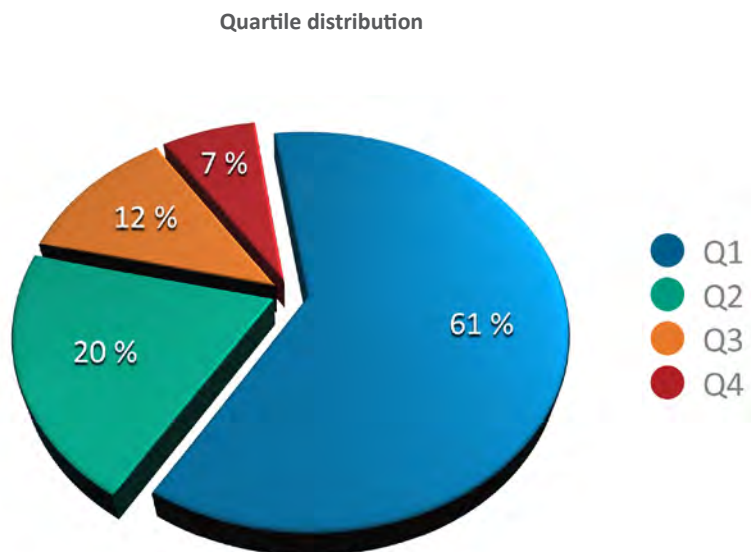
Publications indexed



Cumulative impact factor

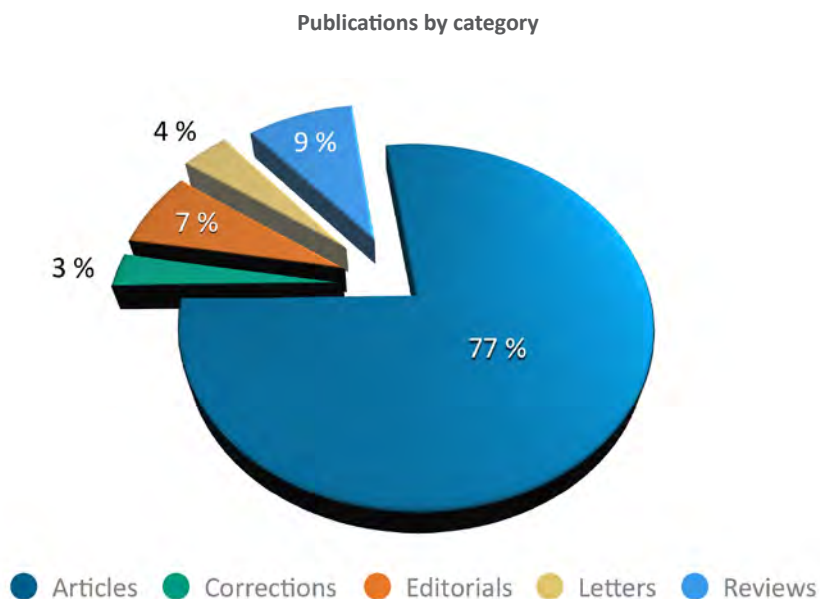


The distribution by quartiles within their thematic categories is shown below. In 2018, 80% of the papers that were published in indexed journals belong to the first and second quartiles of their corresponding thematic categories:

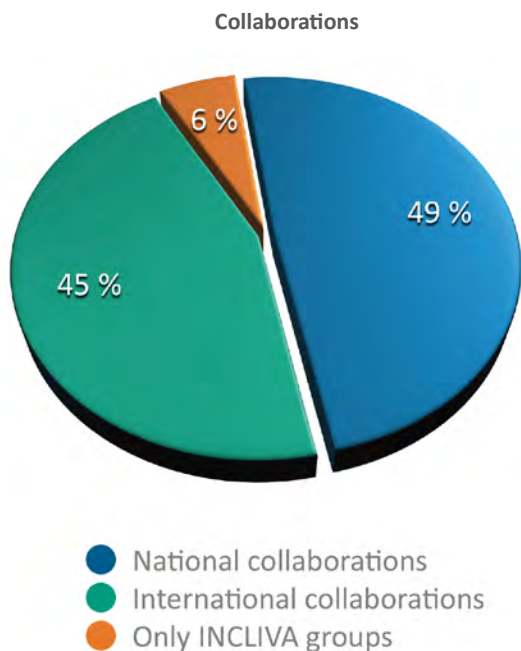


The number and percentage of scientific publications according to category are:

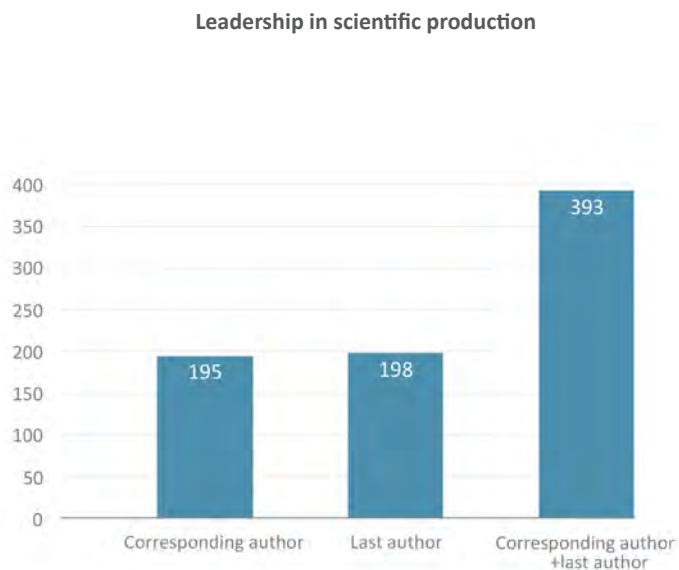
Category	Value
Articles	425
Corrections	16
Editorials	36
Letters	21
Reviews	52



One of the main success factors for a biomedical research institution has to do with its potential to establish high level scientific collaborations. The percentage of national and international collaborations which led to scientific output in 2018 is listed below.

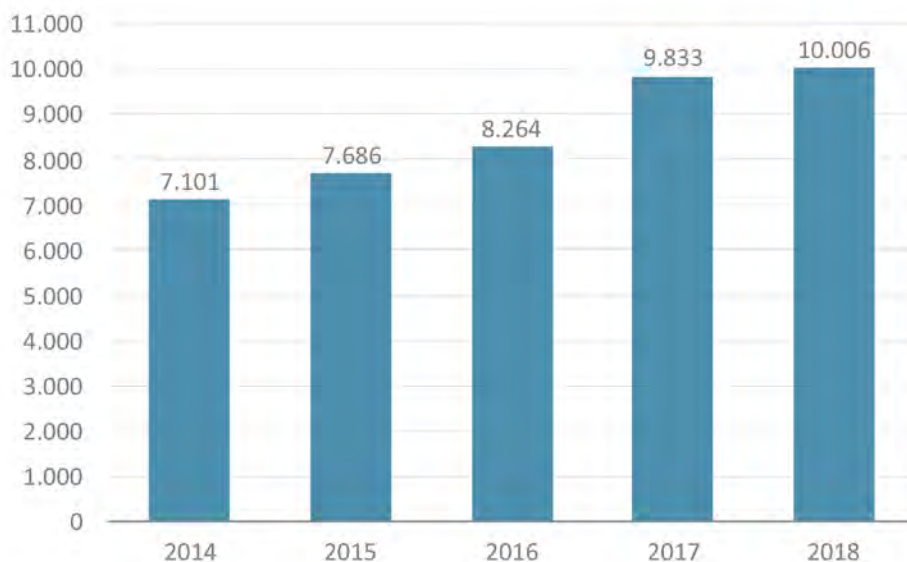


Another key performance indicator is the leadership role in scientific publications. The chart below shows the number of published articles in which INCLIVA researchers sign as last author, corresponding author or both at the same time.

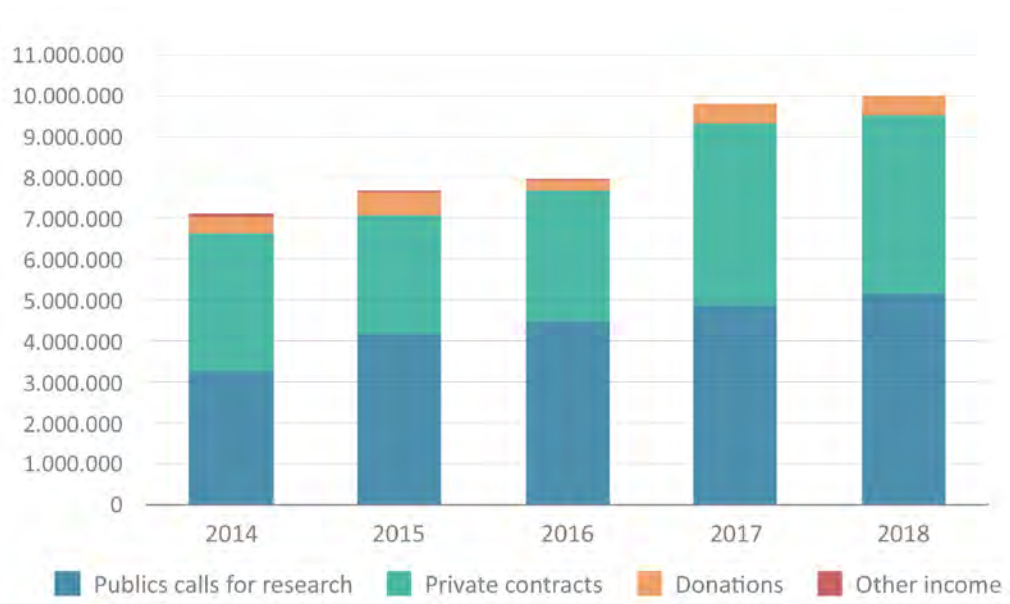


3.2. Financial resources

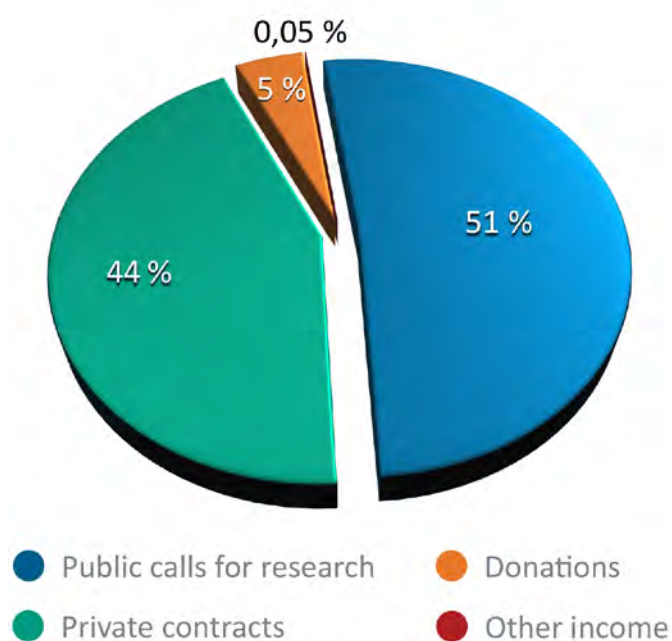
INCLIVA's funding during 2018 totaled €10,001,802.31. The funds raised from competitive sources were still higher than the average of recent years.



Funding source in the indicated period is shown below.



The remaining income corresponds to private sources of funding, clinical trial revenues and grants among others. The graph below shows this distribution of the year 2018.



The analysis of the income obtained by the Foundation in its last fiscal year (2018), classified according to its origin (funds of competitive origin, funds of non-competitive origin) is shown in the table. In the same way, with the same criteria, direct and indirect costs are explained.

Revenue	Non-competitive funding		Competitive funding		Total	
	Amount	Overheads	Amount	Overheads	Amount	Overheads
Grants	651,988.43	50,048.03	3,938,159.44	428,243.69	4,590,147.87	478,291.72
Donations	488,777.32	47,579.23			488,777.32	47,579.23
Turnover	4,373,661.69	702,914.27			4,373,661.69	702,914.27
Financial	4,275.30				4,275.30	
Extraordinary	1,241.96				1,241.96	
Capital Grants	458,878.84		89,094.63		547,973.47	
Overall Total	5,978,823.54	800,541.53	4,027,254.07	428,243.69	10,006,077.61	1,228,785.22

Also used as a source of information the Annual Accounts of 2018 approved by the Board of Trustees of the Foundation and audited by the General Intervention of the *Generalitat Valenciana* (through the audit firm BDO Auditores) the information of the expenses executed is provided, with the explanation of the use of the corresponding indirect costs.

Expenses 2018	Total	Applied Overheads
Cash funding	86,245.00	86,245.00
Supplies	1,308,316.00	67,787.00
Other functional expenses (activity)	1,144,627.00	73,500.00
Staff costs	5,411,757.00	669,724.22
Other functional expenses (structural)	327,720.00	327,720.00
Extraordinary expenses	3,809.00	3,809.00
Inventory item donation expenses	29,089.00	0.00
Repayment costs	739,963.00	0.00
Budget total expenses	9,051,526.00	1,228,785.22

Finally, this is the balance sheet of the foundation in official format, extracted from the Annual Accounts of 2018:

ASSETS			REPORT	FISCAL YEAR	FISCAL YEAR
			NOTES	2018	2017
A)	NON-CURRENT ASSETS			13,930,418.29	9,951,951.17
	I.	Intangible assets	Note 8	2,815,936.62	2,921,601.99
	2.	Concessions		2,714,513.78	2,804,735.60
	3.	Patents, licences, trademarks and similar		7,342.40	7,770.70
	5.	Software applications		94,080.44	109,095.69
	III.	Tangible fixed assets	Note 5	5,155,310.57	3,964,952.59
	2.	Technical facilities and other tangible fixed assets		5,155,310.57	3,964,952.59
	VI.	Long term financial investments	Note 10.1	5,959,171.10	3,065,396.59
	1.	Other government loans		3,117,003.90	2,232,137.87
	2.	Other loans from private entities		351,776.00	81,000.00
	3.	European Union loans		2,490,391.20	752,258.72
	5.	Other financial assets		0	0
B)	CURRENT ASSETS			14,055,922.03	10,719,557.73
	III.	Users and other accounts receivable from company activity	Note 11	2,250,827.10	3,359,547.04
	IV.	Trade and other accounts receivable	Note 10.1	4,156,528.30	4,304,487.45
	6.	Other government loans	Note 16	4,156,528.30	4,304,487.45
	VI.	Short term financial investments	Note 10.1	500,000.00	250,002.48
	5.	Other financial assets		500,000.00	250,002.48
	VII.	Short term accruals			
	VIII.	Cash and equivalent liquid assets		7,148,566.63	2,805,520.76
	1.	Liquidity	Note 10.1	7,148,566.63	2,805,520.76
TOTAL ASSETS (A + B)				27,986,340.32	20,671,508.90

LIABILITIES			REPORT	FISCAL YEAR	FISCAL YEAR
			NOTES	2018	2017
A)	NET WORTH			11,565,676.83	9,449,694.63
	A-1)	Equity		6,410,377.38	5,455,825.65
	I.	Endowments	Note 13	617,482.67	617,482.67
	II	Reserves		4,838,342.98	4,530,978.58
	2.	Other reserves		4,838,342.98	4,530,978.58
	III.	Previous year surplus		0	-429,337.42
	2.	Previous year negative surplus		0	-429,337.42
	IV.	Annual surplus		954,551.73	736,701.82
	A-3)	Grants, donations or gifts and legacies received	Note 21	5,155,299.45	3,993,868.98
B)	NON-CURRENT LIABILITIES			6,277,039.96	3,501,857.56
	II.	Long term debts	Note 21	6,277,039.96	3,501,857.56
	5.	Other financial liabilities		6,277,039.96	3,501,857.56
C)	CURRENT LIABILITIES			10,143,623.53	7,719,956.71
	II	Short term supplies	Note 18	171,714.54	390,103.95
	III.	Short term debts	Note 21	6,531,702.94	6,665,453.78
	5.	Other financial liabilities		6,531,702.94	6,665,453.78
	V.	Beneficiaries-Creditors	Note 12	1,469,891.39	21,310.12
	VI.	Trade creditors and other accounts payable		1,970,314.66	643,088.86
	1.	Suppliers	Note 10.2	56,962.66	49,591.11
	3.	Sundry creditors	Note 10.2	129,008.82	193,317.11
	6.	Other government debts	Note 16	1,765,990.99	374,996.65
	7.	Advances received for orders	Note 10.2	18,352.19	25,183.99
	VII.	Short term accruals		0	
TOTAL NET WORTH AND LIABILITIES (A + B + C)				27,986,340.32	20,671,508.90

3.3 Cooperative research networks

The Carlos III Health Institute (*Instituto de Salud Carlos III*) develops – through the General Subdirection of Networks and Centers for the Cooperative Research – the creation of stable research network structures such as RETICS (Thematic Networks of Cooperative Research) and CIBER (Network of Centres for Biomedical Research). INCLIVA participates in many of these research structures through its associated groups.

The following table shows the participation in scientific networks according to the prioritized research area, the center and its principal investigator.

CIBER

Research Area	INCLIVA PI	Scientific Network		Reference
Cardiovascular	Juan Francisco Ascaso Gimilio José Tomás Real Collado	CIBERdem		CB07/08/0018
	Empar Lurbe i Ferrer	CIBERobn		CB06/03/0039
	Francisco Javier Chorro Gascó	CIBERcv		CB16/11/00486
	Juan Sanchis Forés	CIBERcv		CB16/11/00420
Metabolism and Organ Damage	Guillermo Sáez Tormo	CIBERobn		CB12/03/30016
	Esteban Morcillo Sánchez	CIBERres		CB06/06/0027
	Federico V. Pallardó Calatayud	CIBERrer		CB06/07/0073
	Julio Sanjuán Arias	CIBERsam		CB07/09/006
	Rafael Tabarés Seisdedos	CIBERsam		CB07/09/0021
	Juan Vicente Esplugues Mota	CIBERehd		CB06/04/0071
	José Viña Ribes	CIBERfes		CB16/10/00435
Oncology	Andrés Cervantes Ruipérez	CIBERonc		CB16/12/00473
	Ana Lluch Hernández	CIBERonc		CB16/12/00481
	Rosa Noguera Salvá	CIBERonc		CB16/12/00484

3.4 Knowledge transfer activities

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

3.4.1 Knowledge transfer to the National Health System

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

The first twelve of these clinical practice guidelines are implemented in the IIS health centers:

Clinical guidelines	FI
19	127,532

- Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I; ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *European Heart Journal*. 2018; 39(33): 3021-3104. IF: 23,425
- Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I; Authors/Task Force Members. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *Journal of Hypertension*. 2018; 36(10): 1953-2041. IF: 4,092
- Lurbe E, Litwin M, Pall D, Seeman T, Stabouli S, Webb NJA, Wühl E; Working Group of the 2016 European Society of Hypertension Guidelines for the Management of High Blood Pressure in Children and Adolescents. Insights and implications of new blood pressure guidelines in children and adolescents. *Journal of Hypertension*. 2018; 36(7): 1456-1459. IF: 4,092
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- Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement D, Coca A, De Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen S, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder R, Shlyakhto E, Tsioufis K, Aboyans V, Desormais I. 2018 Practice Guidelines for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *Blood Press*. 2018; 27(6): 314-340. IF: 2,107
- Kotsis V, Jordan J, Micic D, Finer N, Leitner DR, Toplak H, Tokgozoglul L, Athyros V, Elisaf M, Filippatos TD, Redon J, Redon P, Antza C, Tsioufis K, Grassi G, Seravalle G, Coca A, Sierra C, Lurbe E, Stabouli S, Jelakovic B, Nilsson PM. Obesity and cardiovascular risk: a call for action from the European Society of Hypertension Working Group of Obesity, Diabetes and the High-risk Patient and European Association for the Study of Obesity: part A: mechanisms of obesity induced hypertension, diabetes and dyslipidemia and practice guidelines for treatment. *Journal of Hypertension*. 2018; 36(7): 1427-1440. IF: 4,092
- Yoshino T, Arnold D, Taniguchi H, Pentheroudakis G, Yamazaki K, Xu RH, Kim TW, Ismail F, Tan IB, Yeh KH, Grothey A, Zhang S, Ahn JB, Mastura MY, Chong D, Chen LT, Kopetz S, Eguchi-Nakajima T, Ebi H, Ohtsu A, Cervantes A, Muro K, Taberero J, Minami H, Ciardiello F, Douillard JY. Pan-Asian adapted ESMO consensus guidelines for the management of patients with metastatic colorectal cancer: a JSMO-ESMO initiative endorsed by CSCO, KACO, MOS, SSO and TOS. *Annals of Oncology*. 2018; 29(1): 44-70. IF: 13,926

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9. Roselló S, Blasco I, García Fabregat L, Cervantes A, Jordan K; ESMO Guidelines Committee. Management of infusion reactions to systemic anticancer therapy: ESMO Clinical Practice Guidelines. *Annals of Oncology*. 2018; 29(4): iv260. IF: 13,926
10. Glynne-Jones R, Wyrwicz L, Tiret E, Brown G, Rödel C, Cervantes A, Arnold D; ESMO Guidelines Committee. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. 2018; 29(4): iv263. IF: 13,926
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12. Giannini A, Russo E, Cano A, Chedraui P, Goulis DG, Lambrinouadaki I, Lopes P, Mishra G, Mueck A, Rees M, Senturk LM, Stevenson JC, Stute P, Tuomikoski P, Simoncini T. Current management of pelvic organ prolapse in aging women: EMAS clinical guide. *Maturitas*. 2018; 110: 118-123. IF: 3,315
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16. Afshari A, Ageno W, Ahmed A, Duranteau J, Faraoni D, Kozek-Langenecker S, Llau J, Nizard J, Solca M, Stensballe J, Thienpont E, Tsiridis E, Venclauskas L, Samama CM; ESA VTE Guidelines Task Force. European Guidelines on perioperative venous thromboembolism prophylaxis: Executive summary. *European Journal of Anaesthesiology*. 2018; 35(2): 77-83. IF: 3,958
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18. Chatwin M, Toussaint M, Gonçalves MR, Sheers N, Mellies U, Gonzales-Bermejo J, Sancho J, Fauroux B, Andersen T, Hov B, Nygren-Bonnier M, Lacombe M, Pernet K, Kampelmacher M, Devaux C, Kinnett K, Sheehan D, Rao F, Villanova M, Berlowitz D, Morrow BM. Airway clearance techniques in neuromuscular disorders: A state of the art review. *Respiratory Medicine*. 2018; 136: 98-110. IF: 3,23
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7

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Consensus documents	FI
4	10,668

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2. Oaknin A, Guarch R, Barretina P, Hardisson D, González-Martín A, Matías-Guiu X, Pérez-Fidalgo A, Vieites B, Romero I, Palacios J. Recommendations for biomarker testing in epithelial ovarian cancer: a National Consensus Statement

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- Oaknin A, Guarch R, Barretina P, Hardisson D, González-Martín A, Matías-Guiu X, Pérez-Fidalgo A, Vieites B, Romero I, Palacios J. Erratum to: Recommendations for biomarker testing in epithelial ovarian cancer: a National Consensus Statement by the Spanish Society of Pathology and the Spanish Society of Medical Oncology. *Clinical & Translational Oncology*. 2018; 20(3): 424. IF: 2,392
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Position statements	FI
1	4,287

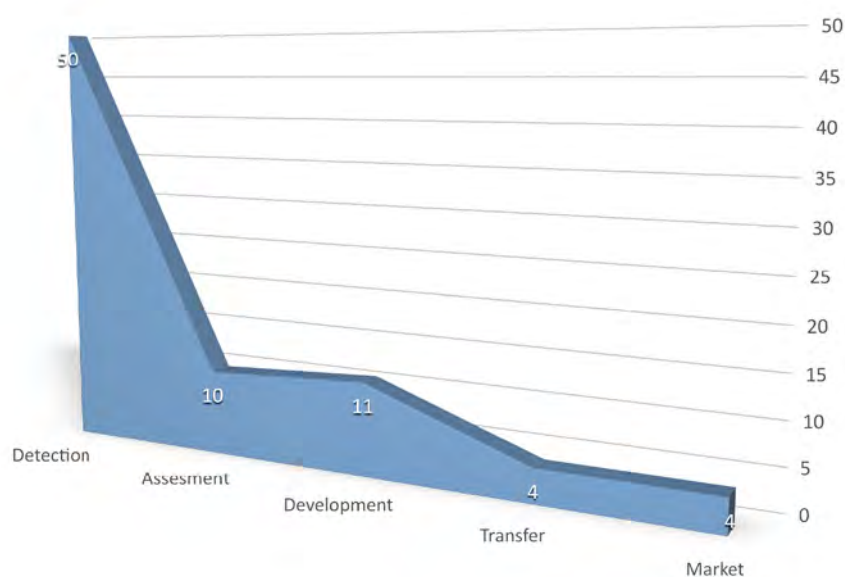
1. Dauden E, Blasco AJ, Bonanad C, Botella R, Carrascosa JM, González-Parra E, Jodar E, Joven B, Lázaro P, Olveira A, Quintero J, Rivera R. Position statement for the management of comorbidities in psoriasis. *Journal of the European Academy of Dermatology and Venereology*. 2018; 32(12): 2058-2073. IF: 4,287

3.4.2. Innovation and Knowledge transfer

One of the foundational reasons of INCLIVA is the translation of the research carried out into the society. Giving a medical need, researchers and clinicians use their knowledge to make ideas that through research and development can be taken in real products or processes that overcome this existing problem.

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

Plot of the INCLIVA innovation funnel in 2018



The breakdown of the INCLIVA innovation funnel in 2018 is the following:

	Detection	Assesment	Development	Transfer	Market
Organizational	6	0	0	0	0
ITC	2	1	3	0	0
Device	3	3	1	1	0
Imaging	0	0	1	0	0
Pharma	9	3	3	1	0
Bio	30	3	3	2	10
Total	50	10	11	4	4*

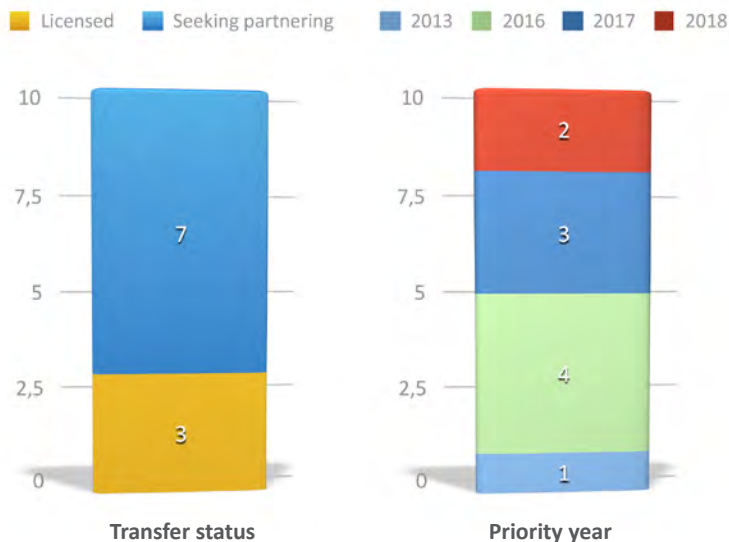
*10 ideas in the market, 4 achieved in 2018

3.4.2.1 Intellectual Assets

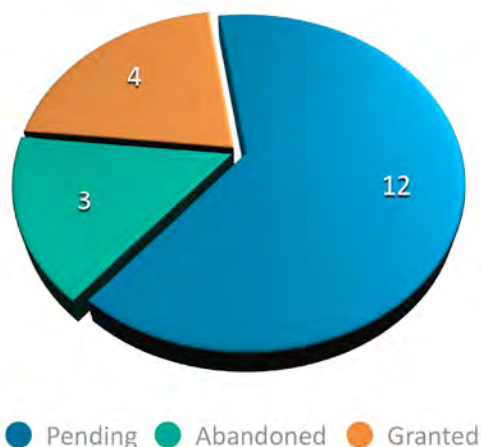
The protection of knowledge is the first step to move scientific findings and ideas from researchers to the industry and the most common way to protect technologies that are new, inventive and have industrial application are patents. Research institutions can exploit the patents they hold by licensing them to companies.

INCLIVA counts on 19 active patent applications in 2018 distributed in 10 active patent families (including 1 utility models). The next plot summarizes the main features of these protected inventions, such as their current situation in terms of either development or transfer status, as well as some legal aspects of the different applications that form this patent families.

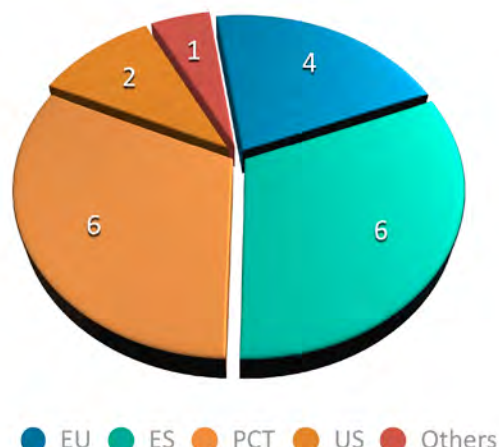
Patent families



Patent applications by legal status



Patent applications by territory



Of the previously mentioned patent applications, INCLIVA has filed or licensed the following ones in 2018:

Title: In vitro method for the prediction of response to chemotherapy in triple negative breast cancer patients

INCLIVA Inventors: Begoña Pineda, José Alejandro Pérez-Fidalgo, Pilar Eroles and Ana Lluch

Applicants: IDIBELL, ICREA, UV and INCLIVA

Application number: EP18382390.5

Priority Date: 2018/06/04

Territory: Europe

Title: Injectable material for regeneration of the articulate cartilage

INCLIVA Inventors: María Sancho-Tello and Carmen Carda

Applicants: UPV, CIBER, UV and INCLIVA

Application number: ES201830730

Priority Date: 2018/07/19

Territory: Spain

Title: Intramedullary fixation device

INCLIVA Inventors: Antonio Silvestre

Applicants: UPV, UV and INCLIVA

Application number: ES201631220

Priority Date: 2016/09/16. Licensed in 2018

Territory: USA, Europe, Spain and Brazil

Title: Device for the exo-prosthesisation of limbs and other percutaneous applications

INCLIVA Inventors: Antonio Silvestre

Applicants: UPV, UV and INCLIVA

Application number: ES201631218

Priority Date: 2016/09/16. Licensed in 2018

Territory: USA, Europe and Spain

Status: Licensed in 2018

3.4.2.2 Entrepreneurship

When the knowledge generated in INCLIVA is disruptive and the researches willing to exploit it by themselves, the knowledge transfer is direct, thanks to the creation of a new venture (also known as a spin-off or start-up) based on such knowledge with the support of INCLIVA.

INCLIVA counts with the following companies officially recognized as spin-offs:



Epidesase S.L.

Founding year: 2014

INCLIVA entrepreneurial team: Dr. José Luís García Giménez and Dr. Federico Pallardó



Sequencing Multiplex S.L.

Founding year: 2013

INCLIVA entrepreneurial team: Dr. Javier Chaves





Scientific activity

04



4.1 Scientific structure

INCLIVA articulates its research in 4 areas of research, 7 scientific programs and 3 platforms.



Areas of research constitute the basis on which to articulate the scientific work of the groups:

- Research area in oncology.
- Research area in cardiovascular.
- Research area in metabolism and organ damage.
- Research area in reproductive medicine.



Scientific programs are aimed at specific diseases from a translational perspective:

- Program in overweight and cardiovascular and renal risk.
- Program in myocardial ischemic damage.
- Program in rare diseases.
- Program in neurological impairment.
- Program in translational oncology.
- Program in reproductive medicine.
- Program in aging and its associated diseases.



Platforms are based on the provision of research services to the whole institute:

- Inflammation platform.
- Metabolomics platform.
- Genomics, epigenomics and transcriptomics platform.



4.2 Scientific translational programs

4.2.1 Overweight and cardiovascular and renal risk

Obesity and overweight is a field in which new strategies are developed both for prevention and treatment with the use of traditional resources and the new technologies. The present program is focused on the study of pathology on the first stages of obesity (overweight with or without metabolic syndrome) integrating different clinical and experimental research studies.

Coordinators:

Dr. Juan F. Ascaso and Dr. Josep Redon

INCLIVA research groups involved

Clinical groups:

- Research Group on the Study of Cardiometabolic and Renal Risk (Dr. Redón)
- Research Group on Cardiometabolic Risk (Dr. Ascaso)
- Research Group on the Study of Cardiovascular Risk in Children and Adolescents (Dr. Lurbe)
- Translational Research Group on Nutrition and Metabolism (Dr. Hernández)
- Cardiometabolic Research Group on Primary Care (Dr. Navarro)

Experimental groups:

- Research Group of the Genotyping and Genetic Diagnosis Unit (UGDG) (Dr. Chaves)
- Research Group on Endothelial Cells (Dr. Hermenegildo)
- Research Group on Inflammation (Dr. Morcillo y Dr. Sanz)
- Research Group on Molecular Imaging and Metabolomics (Dr. Monleón)

Objectives

- To deepen in the early alterations, mechanisms and biomarkers that contribute to the development of obesity, vascular and renal alterations as a complication, from its fetal, biological, genetic and environmental origins.
- To know potential signaling pathways susceptible to be therapeutic targets.
- Early application of new technologies for the prevention and treatment of obesity and vascular and renal alterations in overweight subjects.

Research lines

- To identify early vascular and renal changes in overweight subjects and in animal models.
- To study the state, mechanisms of vascular inflammation and endothelial injury in overweight and animal models.
- To analyze the relationship of “-omic” markers (genomic, epigenetic and metabolomic) with obesity and vascular and renal alterations in overweight and animal models.
- Interaction of biomarkers (biological, genomic and metabolic) and intervention in progression to obesity and vascular and renal complications.

4.2.2 Myocardial ischemic damage

The program focuses on the study of the pathophysiological mechanisms involved in myocardial ischemic damage, on its structural, functional and electrophysiological repercussions on the evaluation of diagnostic tools and markers and prognoses and on the study of new therapeutic approaches that may help to prevent their adverse consequences.

It is a truly and translational research program that capitalizes the synergies between clinical and experimental research groups and also includes specialists in cardiac imaging techniques and technological development experts. The multidisciplinary

approach extends the possibilities of collaboration between groups, strengthens those already existing and incorporates other groups into the activities of the program. Innovation through the development of analytical tools (imaging techniques such as cardiac magnetic resonance, cardiac electrical signals or cartographic techniques), allows the generalize of patents in the field of technological development.

Coordinator:

Dr. Francisco Javier Chorro Gascó

INCLIVA research groups involved

Clinical groups:

- Research Group on Clinical Cardiology (Dr. Sanchis, Dr. Nuñez)
- Group on Translational Research in Ischemic Heart Disease (Dr. Bodí)
- Research Group on Cardiac Experimental Electrophysiology (Dr. Chorro)

Experimental groups:

- Research Group on Aging and Physical Activity (Dr. José Viña)
- Research Group on Tissular Biochemistry (Dr. Juan Viña)
- Research Group on Inflammation (Dr. Morcillo and Dr. Sanz)
- Research Group on Endothelial Cells (Dr. Hermenegildo)
- Research Group on Molecular Imaging and Metabolomics (Dr. Monleón)

Others groups involved

Universidad Politécnica de Valencia (Prof. D. Moratal, Prof. J. Millet), *H. Clinic Barcelona* (Dr. Ortiz), *Heart Center Munich* (Dr. Husser), *ERESA* (Dr. López), *Universitat de Valencia*, *Fac. Físicas* (Prof. J. Guerrero), *Center for Arrhythmia Research* (University of Michigan, Prof. Jalife), *School of Engineering* (Univ. of California, Prof. Escobar).

Objectives

- Study of the pathophysiological mechanisms involved in myocardial ischemic damage and its structural, functional and electrophysiological repercussions.
- Evaluation of diagnostic and prognostic tools and markers.
- Evaluation of new therapeutic approaches.

- Study of the role played by: a) oxidative stress and its modifications in post-infarction damage; b) the vascular endothelial growth factor VEGF-A165b in microvascular obstruction, the deterioration of systolic function in the neoangiogenesis.
- Development of new diagnostic tools in cardiac magnetic resonance (MRI) for the detection of damage associated with ischemia / reperfusion and fibrosis.
- Evaluation of new prognostic and functional biomarkers in myocardial infarction from MRI, maximal O₂ consumption, metabolomics and the combined use of CA125, galectin-1 and galectin 3.
- Development and analysis of preventive measures against the adverse consequences of postinfarction damage (remodeling, heart failure, arrhythmias).

Research lines

- Clinical research: acute coronary syndromes, interventional cardiology, ventricular remodeling and heart failure.
- Translational research: regulation of post-infarction fibrosis; development of innovative tools for their characterization by MR after an infarct and study of new therapeutic approaches.
- Experimental study of arrhythmogenesis in the context of ischemia and myocardial damage. Influence of the substrate and the modulating mechanisms.
- Microimaging using RM. Metabolomics.
- Research of textures using RM.
- Analysis, using molecular biology and biochemical techniques of circulating metabolic factors associated with ischemic damage.
- Endothelial dysfunction.
- Microvascular obstruction.

• 4.2.3 Rare diseases

The main objectives of the program is to improve diagnosis and current treatments of rare diseases. To this end, we will proceed to identify and validate rare disease biomarkers for which we do not have effective diagnostic and / or prognostic indicators. On the other hand, new therapeutic strategies will be developed for the treatment of these diseases. Human and animal model samples will be used to understand the molecular basis of disease, to evaluate the activity of candidate drugs and to discover new biomarkers.

Basically, the program seeks to fill the gap between basic research and commercial development of diagnostic systems and treatments, so its aim is to transfer this knowledge to companies, in order to transform biomedical knowledge into products and services that improve the human health. With this objective contacts with biotechnology and pharmaceutical companies have been established. On the other hand, the program aims to disseminate its findings to society in order to get feedback about actual patients' needs.

Coordinator:

Dr. Federico Pallardó and Dr. Francisco Dasí

INCLIVA research groups involved

Clinical groups:

- Research Group on Respiratory Problems in Neuromuscular Diseases (Dr. Servera)

Experimental groups:

- Research Group on Cellular and Organic Physiopathology of Oxidative Stress (Dr. Pallardó)
- Research Group on Molecular Imaging and Metabolomics (Dr. Monleón)
- Research Group on Neurological Impairment (Dr. Montoliu)
- Research Group on Translational Genomics (Dr. Artero)

Objectives

- To improve diagnosis and current treatment of rare diseases.
- Identification and validation of rare diseases biomarkers for which, nowadays, no effective diagnostic and / or prognostic indicators are available.
- Development of new therapeutic strategies.

Research lines

- Study of the oxidative profile in rare diseases.
- Pathophysiology of alpha-1 antitrypsin deficiency and Primary Ciliary Dyskinesia Syndrome.
- Gene therapy for the treatment of rare respiratory diseases.
- Design and testing of new biomarkers and experimental treatments in animal models.
- Study by exploratory and directed metabolomics of altered metabolic clusters in rare diseases.

• **4.2.4 Neurological impairment**

Inflammation, which is associated with many chronic diseases (diabetes, liver cirrhosis, etc.), aging or major surgeries, leads to neuroinflammation and brain alterations that eventually lead to cognitive and functional impairment. This deterioration reduces the quality of life and increases the risk of accidents, falls, fractures and adverse consequences, which implies an increase in hospitalizations and the use of public resources.

Cognitive and functional impairment associated with aging and many chronic diseases is one of the most important challenges in order to improve the quality of life of the population and secure the sustainability of health systems. Early detection and treatment and prevention of cognitive and functional impairment would improve the quality of life of the elderly or with chronic diseases and reduce the demand for resources to the health system, improving its sustainability. Therefore, it is necessary to design new approaches to address these challenges, based on advances in knowledge on mechanisms, early diagnosis, prevention and treatment of cognitive and functional impairment.

Coordinator:

Dr. Carmina Montoliu and Dr. Vicente Felipo

INCLIVA research groups involved

Clinical groups:

- Research Group on the Study of Cardiometabolic and Renal Risk (Dr. Redón)
- Research Group on Cardiometabolic Risk (Dr. Ascaso)
- Research Group on Anesthesiology and Reanimation (Dr. Belda)

Experimental groups:

- Research Group on Neurological Impairment (Dr. Montoliu)
- Research Group on Inflammation (Dr. Morcillo and Dr. Sanz)
- Research Group on Aging and Physical Activity (Dr. José Viña)
- Research Group on Personal Autonomy, Dependence and Severe Mental Disorders (TMAP) (Dr. Tabarés)

Others groups involved

IPPC Neurobiology Research Group (Dr. Felipo), Cognitive Social Neuroscience Research Group from UV (Dr. Salvador), Hospital Neurorehabilitation Service NISA (Dr. Noe)

Objectives

- To characterize the alterations in inflammation, neuroinflammation, neurotransmission, brain function and structure

associated with the appearance of cognitive and functional impairment.

- To characterize in detail the cognitive and functional alterations.
- To identify biomarkers for the early detection of cognitive and functional impairment.
- To identify the mechanisms by which: a) peripheral inflammation leads to neuroinflammation; b) neuroinflammation leads to functional, structural and neurotransmission alterations in the brain; c) changes in the brain lead to cognitive and functional impairment.
- To identify therapeutic targets to reverse or prevent cognitive and functional impairment.
- To design and test new therapeutic procedures to reverse or prevent cognitive and functional impairment.

Research lines

- Characterization of cognitive and functional alterations.
- Cognitive impairment in diabetes.
- Cognitive impairment for major surgeries and anesthesia.
- Alzheimer’s and mild cognitive impairment.
- Cognitive and functional impairment in hyperammonemia and hepatic diseases.

• 4.2.5 Translational oncology

The translational oncology program called “Identification of oncogenic biomarkers: mechanisms and clinical implications, detection in non-invasive samples, omics analysis” tries to apply to the clinical practice the genomic screening in patients tumors.

Its main objective is to evaluate the dynamics of the disease through non-invasive biopsies in order to detect minimal residual disease, early onset of markers after surgery and patient response to different treatments.

The high heterogeneity of cancer results in inefficiency of treatments, even when they are directed against specific molecular targets. The low availability of tumor specimens makes genomic studies difficult.

In this sense, the use of liquid biopsies would facilitate the serial collection of samples to carry out molecular analysis and would guarantee a minimum risk for the patient. Thus improving the follow-up and allowing a dynamic understanding of the evolution of the genomic parameters of the patient.

This point of view benefits the National Health System as a whole since it allows the application of more specific treatments to patients, thus avoiding those that would have been less effective, reducing hospitalization and improving life expectancy and quality thereof. It could also prevent generalized treatments, secondary toxicities and rapid treatment adequacy responses.

Finally, it would improve the inclusion of patients in clinical trials which are stratified by molecular mutations.

Coordinator:

Dr. Andrés Cervantes

INCLIVA research groups involved

Clinical groups:

- Research Group on Colorectal Cancer and New Therapeutic Developments in Solid Tumours (Dr. Cervantes)
- Research Group on Breast Cancer Biology (Dr. Lluch)
- Translational Research Group on Pediatric Solid Tumours (Dr. Navarro)

Experimental groups:

- Research Group of the Genotyping and Genetic Diagnosis Unit (UGDG) (Dr. Chaves)
- Research Group on Cellular and Organic Physiopathology of Oxidative Stress (Dr. Pallardó)

Objectives

- To obtain a large database of genetic material (viable cells, DNA, RNA, serum / plasma) from tumors (solid and haematological). Implementing the clinical database for data management and data crossing. (Hospital, biobank, PROS-UPV).
- Molecular characterization of tumor biopsies using high throughput platforms (Sequenom, NGS).

- To improve inclusion of patients in clinical trials.
- To establish a routine for obtaining liquid biopsies in order to evaluate the detection of biomarkers as disease follow-up, minimal residual disease, early onset and response to treatment. (biobank, BEAMing PCR, NGS).
- To develop functional assays (modified cell lines, patient cell lines, xenografts) to evaluate mechanisms of disease.
- Incorporation of molecular results into clinical decision making.

Research lines

- Development of new therapeutic agents through Phase I clinical trials (first-in-human).
- Development of non-invasive early diagnostic methods and monitoring of therapeutic effects.
- Application of methodologies for clinical and molecular characterization of solid tumors and response to treatment (analysis of gene expression profiles, microRNAs, methylation).
- Translational studies for the identification of mechanisms of resistance to targeted therapies.

• 4.2.6 Reproductive medicine

This program comprises two main lines:

1. Role of maternal miRNAs in the transmission of obesity and type 2 diabetes to the embryo:

Obesity and type 2 diabetes are increasingly important public health problems whose prevalence cannot be explained only by genetic and / or environmental factors, so the hypothesis of the program lies in the existence of an embryonic epigenetic regulation of maternal origin in these diseases. Preliminary data reveals that miRNAs secreted by the maternal endometrium to the endometrial fluid are internalized by the embryo, leading to a transcriptional and functional modification and increasing its adhesion to the endometrium during its implantation. In this sense, the program goal is to explore if this new epigenetic mechanism of maternal origin could explain the origin of the development of certain adult-onset diseases such as obesity and type 2 diabetes.

2. Study of adult stem cells in human endometrium:

Use of autologous bone marrow stem cells by prior mobilization and collection of Peripheral Blood Progenitor Cells (PPSCs) and subsequent apheresis and transplantation of these cells in order to regenerate the endometrium de novo in patients undergoing assisted reproductive therapy (ART). The results of this study would allow a new therapeutic approach for the treatment of Asherman's Syndrome and endometrial atrophy, which currently lack of specific treatment.

Coordinator:

Dr. Carlos Simón

INCLIVA research groups involved

Clinical groups:

- Translational Research Group on Nutrition and Metabolism (Dr. Hernández)
- Research Group on Hematopoietic Transplantation (Dr. Solano)
- Research Group on Women Health (Dr. Cano)
- Research Group on the Study of Cardiovascular Risk in Children and Adolescents (Dr. Lurbe)

Experimental groups:

- Research Group on Stem Cells Applied to Reproduction, Embryo Viability and Endometrial Receptivity (Dr. Simón)
- Research Group on Reproductive Pathology (Dr. Remohí)

Objectives

- To advance in the understanding of the mechanisms that regulate maternal-fetal communication and that may be involved in the implantation of the embryo in the maternal uterus and to be able to understand the embryonic / fetal origin of adult diseases such as obesity and type II diabetes.
- To regenerate uterine function in patients suffering from en-

dometrial atrophy and / or Asherman's Syndrome through cell therapy.

- The creation of an in vitro model to obtain germ cells by direct reprogramming of human somatic cells.

Research lines

- Role of maternal miRNAs in the transmission of obesity and type 2 diabetes to the embryo.
- Use of autologous bone marrow stem cells in order to regenerate the endometrium in patients with Asherman Syndrome and endometrial atrophy undergoing assisted reproductive therapy (ART).
- Identification of the main regulating genes of the development of the germinal line in humans, as well as of the experimental conditions that allow obtaining of germinal cells in vitro.

• 4.2.7 Aging and its associated diseases

This program has the priority of improving the quality of life of the elderly and promoting longevity as much as possible. Aging population it's a challenge for current health systems since the population over 65 years old contributes, in a very significant percentage, to health expenditure. As life expectancy increases, so do the diseases associated with aging.

In this context, the concept of "healthspan" (quality of life) has emerged. The program is formed by many researchers and health professionals who consider that efforts to extend life at the expense of causing a severe physical or psychic disability are undesirable and, on the contrary, they should focus on lengthening the part of life during which we are able to maintain autonomy, independence, productivity and well-being.

A central guiding idea in this program is that people who achieve exceptional longevity (i.e. centenarians) serve as a model of satisfactory aging. On the other hand, it is considered that the most problematic expression of the population aging is the clinical condition of the frailty since an important part of the collective of older people presents criteria of frailty. Approximately one-fourth of people over the age of 85 are estimated to be fragile. Frailty is a geriatric syndrome characterized by increased vulnerability to external aggressions as a result of an alteration in the physiological reserves of multiple systems, leading to difficulties in maintaining homeostasis. The program tries to identify specific molecular targets to be able to intervene in a concrete and rational way to improve the quality of life of the elderly.

For this, INCLIVA has an enormous advantage because of the great integration that exists, by proximity and interests, between the *Hospital Clínico Universitario de Valencia* and the Faculty of Medicine of the University of Valencia. This framework allows intense collaboration between basic research groups, that develop possible biomarkers associated with healthy aging, frailty or diseases associated with aging and clinical research groups that, on the one hand, provide samples of the subjects and, on the other hand, can transfer to the patient those results that have been interesting at the bench.

In addition to this, in INCLIVA has registered the first and only Spanish Group for the Study of Centenaries, which has research groups working in this field distributed in different Spanish communities.

Coordinator:

Dr. José Viña

INCLIVA research groups involved

Clinical groups:

- Research Group on the Study of Cardiometabolic and Renal Risk (Dr. Redón)
- Research Group on Oxidative Pathology (Dr. Sáez)
- Cardiometabolic Research Group on Primary Care (Dr. Navarro)
- Research Group on Clinical Cardiology (Dr. Sanchís)
- Research Group on Women Health (Dr. Cano)
- Group on Translational Research in Ischemic Heart Disease (Dr. Bodí)

Experimental groups:

- Research Group on Aging and Physical Activity (Dr. José Viña)
- Research Group on Inflammation (Dr. Morcillo and Dr. Sanz)

- Research Group on Genetics of Osteoporosis (Dr. García)
- Research Group on Neurological Impairment (Dr. Montoliu)
- Research Group on Endothelial Cells (Dr. Hermenegildo)
- Research Group on Cellular and Organic Physiopathology of Oxidative Stress (Dr. Pallardó)

Objectives

- Determination of parameters of oxidative stress and inflammation associated with healthy aging, frailty and diseases associated with healthy aging, frailty and others associated diseases (mainly cardiovascular and neurodegenerative).
- Determination of genetic biomarkers (microRNAs, mRNAs and SNPs) associated with healthy aging and frailty and others associated diseases (mainly cardiovascular and neurodegenerative).
- Determination of epigenetic biomarkers associated with healthy aging, frailty and others associated diseases (mainly cardiovascular and neurodegenerative).

- Determination of metabolic biomarkers associated with healthy aging, frailty and others associated diseases (mainly cardiovascular and neurodegenerative).
- Physical exercise protocols for the prevention of frailty and others associated diseases.
- Impairment of other biomarkers associated with healthy aging, frailty and others associated diseases.

Research lines

- Oxidative stress, associated inflammation and healthy aging.
- Genetics and healthy aging.
- Epigenetics and healthy aging.
- Metabolomics and healthy aging.
- Exercise and healthy aging.

4.3. Research areas

INCLIVA Health Research Institute has four research areas in order to organize its scientific activity. Despite their independence, they have a common objective: meeting health needs and improving R&D&i system.

Their main aim is to establish a common reference framework to promote collaboration between INCLIVA attached researchers.

Each of the lines counts on the participation of one or several advisers from the External Scientific Committee. These lines are led by the following coordinators:

Cardiovascular Area

- Coordinator: Dr. Francisco Javier Chorro Gascó
- Mission: to contribute to the study of different aspects of cardiovascular disease (CVD) from its origins to its consequences.

Oncology Area

- Coordinator: Dr. Andrés Cervantes Ruipérez
- Mission: to contribute to the study of different aspects of oncological diseases, at the stage of diagnosis and molecular characterization and selection of specific molecular targets of therapeutic interest.

Metabolism and Organic Damage Area

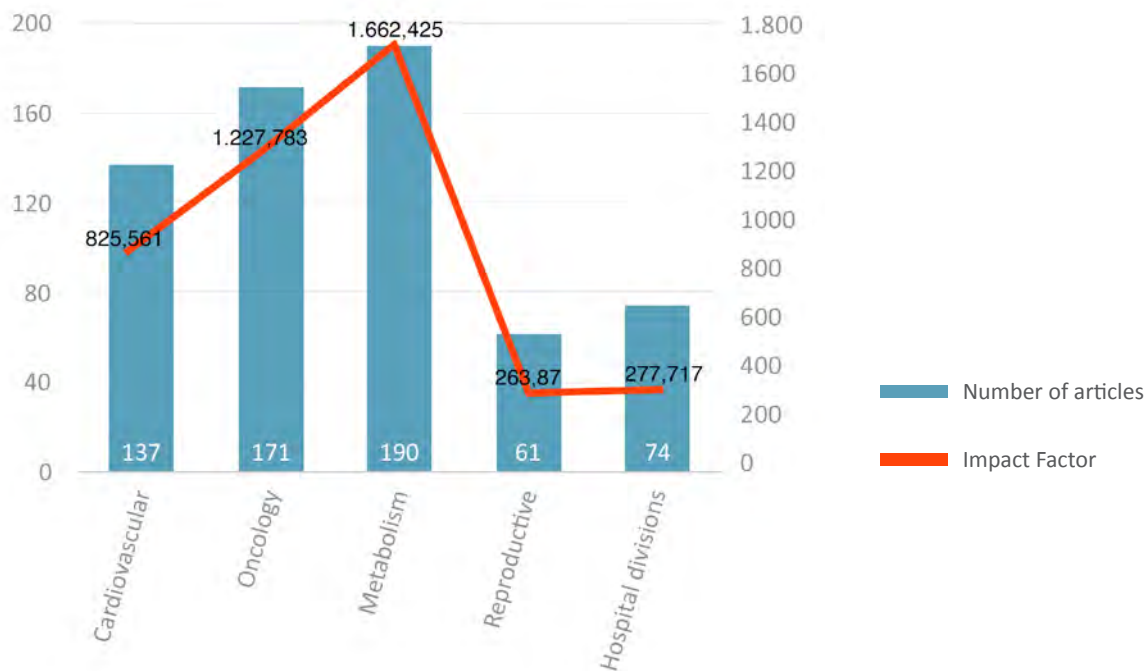
- Coordinator: Dr. José Viña Ribes
- Mission: to contribute to the study of the etiology, pathophysiology and diagnosis mechanisms or treatment of various metabolic diseases; or those that generate organ damage as a fundamental link of its trigger action.

Reproductive Medicine Area

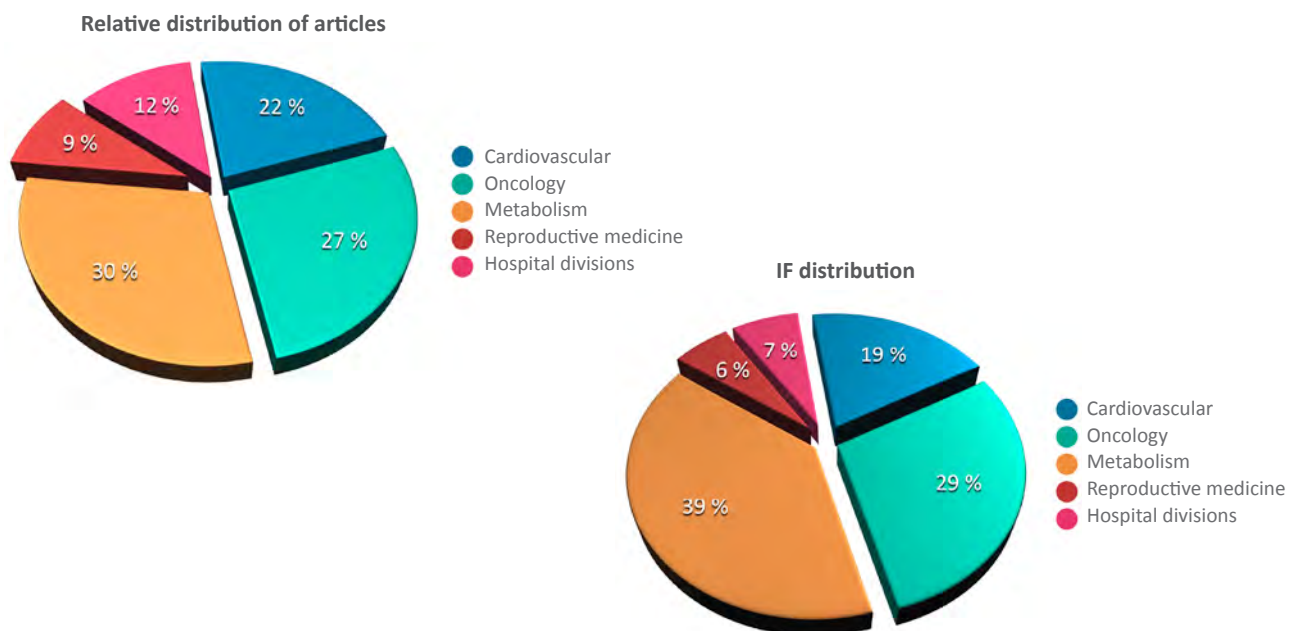
- Coordinator: Dr. Carlos Simón Vallés
- Mission: to advance in knowledge of human reproduction for translational application, improving the efficiency of assisted reproduction treatment and reducing adverse effects.

• Scientific production analysis by research area

The following charts and figures summarize the main scientific activity indicators of the four areas of research and the other divisions from *Hospital Clínico de Valencia*.

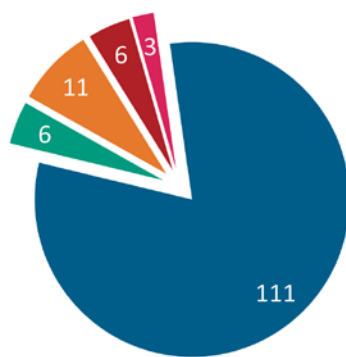
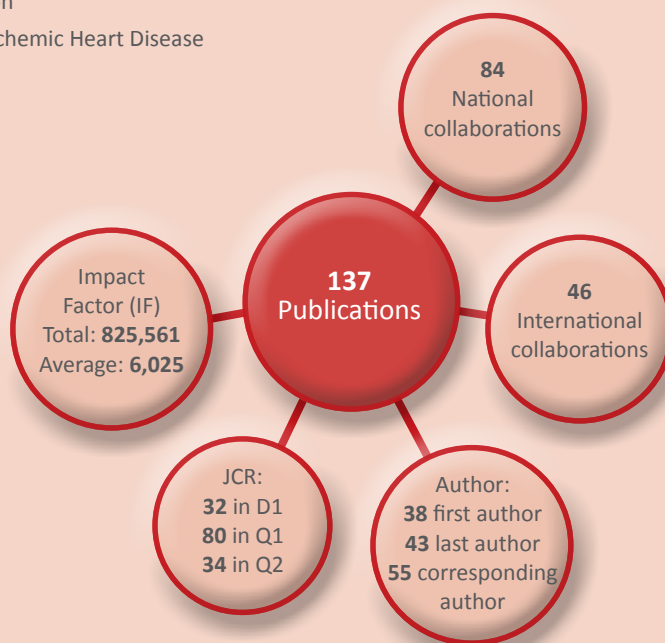


Since there are some scientific articles which are shared by two or more areas, it is worth mentioning that the sum of publications by area exceeds INCLIVA's total scientific output. Additionally, the next tables shows scientific publications distribution by area in terms of number of articles and impact factor.



4.3.1 Cardiovascular Area

Research Group on Cardiometabolic Risk	54
Genotyping and Genetic Diagnosis Unit (UGDG)	57
Research Group on Cardiac Experimental Electrophysiology	60
Research Group on Endothelial Cells (LINCE)	63
Research Group on Clinical Cardiology	66
Research Group on the Study of Cardiovascular Risk in Children and Adolescents	70
Cardiometabolic Research Group on Primary Care	74
Research Group on the Study of Cardiometabolic and Renal Risk	76
Research Group on Vascular Function	80
Research Group on Pediatric Nutrition	82
Group on Translational Research in Ischemic Heart Disease	85



● Original articles ● Letters ● Editorial ● Reviews ● Corrections

Research Group on Cardiometabolic Risk Consolidated group

Team involved in



Group members

Principal investigator

Juan Francisco Ascaso Gimilio
University

José Tomás Real Collado
Hospital. University

Collaborating researchers

Rafael Carmena Rodríguez. University
Francisco Javier Ampudia Blasco. Hospital
Miguel Civera Andrés. Hospital
Marta Peiró Signes. INCLIVA. CIBERdem
Esther Benito Casado. CIBERdem
Miriam Moriana Hernández. Hospital

Technicians

Blanca Alabadí Pardiñes. INCLIVA

Emerging researchers

Sergio Martínez Hervás. Hospital
Ana Bárbara García García. CIBERdem

	R1	R2	R3	R4	STAFF
Researchers by categories	1	3	2	3	2



Strategic aims

- In terms of scientific activity of the research group during 2018 we wish to emphasize the continuity of three competitive and multidisciplinary research projects led by the Dr. Ascaso and Dr. Real. The project led by Dr. Ascaso, entitled “Immunopharmacological modulation of the systemic inflammation associated to metabolic disorders. Search for new therapeutic targets and synthesis of novel drugs”, studies the role of shaft CCL11/CCR3 in systemic inflammation associated with Familial Hypercholesterolemia and its immune modulation by oral lipid overload, as well as the study of the role of the axis CXCL16/CXCR6 in Ang-II-induced Endothelial dysfunction in subjects with metabolic syndrome.
- On the other hand, the main objective the project “Study of new inflammatory and angiogenic mechanisms associated to severe morbid obesity: Role of CXCR3 axis and nuclear receptors RORs” led by Dr. Real, is to explore the CXCR3 axis and RORs receptors in patients with severe morbid obesity or without diabetes undergoing a gastric bypass.

Main lines of research

- Pharmacological modulation of the immune system as a key target in the prevention of cardiovascular disease associated with metabolic disorders. Synthesis of novel drugs: This line of research focuses on the study of the different mediators and immunological mechanisms involved in cardiovascular disease associated with metabolic disorders.
- Identification of epigenetic markers related to insulin resistance or diabetes in morbid obesity. In this line of research we focus on evaluating the role of genetic markers related to IR or diabetes in morbid obesity. Specifically, it aims to understand and analyze the role of the DNA methylation pattern of adipose, hepatic and peripheral blood tissues (lymphomonocytes) in relation to IR or diabetes.
- Identification of the genetic causes of complex diseases with high cardiovascular risk, especially in the case of type 2 diabetes (DM2). Our hypothesis is that numerous low frequency genetic markers are responsible for an important part of the genetic component of this disease and other complex diseases. Thus, our interest is to identify rare genetic variations with a high effect on risk / protection against the development of DM2.
- Study of inflammatory axes related to IR, diabetes and its implication as therapeutic targets: In this line of research we focus on the study of the role of the inflammatory axis CXCR3 and its ligands, chemokines that are characterized by showing chemotactic and proliferative responses of different leukocyte subpopulations and angiostatic activity in the vascular endothelium, in human obesity.
- Role of inflammatory processes associated with diabetes in the stability of atheromatous plaque and hepatic steatosis and study of the potential use of therapeutic strategies. This line of research aims to study molecular mechanisms that potentially connect these metabolic alterations, such as chronic inflammation, investigating the effect of the inflammatory mediator LIGHT in type 2 diabetes mellitus, fatty liver and atherosclerosis, as well as molecular mechanisms underlying.

Other research lines:

- Study of the neuroendocrine axes involved in obesity, RI and diabetes.
- Study of a new protein involved in IR in morbid obesity.
- Neurodegeneration in diabetes.



Emerging researcher

Sergio Martínez Hervás

The line of research is based on cardiovascular risk, essentially on insulin resistance and diabetes, familial combined hyperlipidemia, inflammation, vitamin D, and atherosclerosis, just like new markers of cardiovascular risk.



Emerging researcher

Ana Bárbara García García

The research focuses mainly on DM2, one of the most frequent diseases of Western societies. On the other hand, another line of research is the identification of new genes responsible for abetalipoproteinemia with exome sequencing.

• PUBLICATIONS

Number of articles	IF	Average IF
13	69,088	5,314
National collaborations	International collaborations	Corresponding author
6	5	4

SELECTED PUBLICATIONS

1. D'Erasmo L, Minicocci I, Nicolucci A, Pintus P, Roeters Van Lennepe JE, Masana L, Mata P, Sánchez-Hernández RM, Prieto-Matos P, Real JT, Ascaso JF, Lafuente EE, Pocovi M, Fuentes FJ, Muntoni S, Bertolini S, Sirtori C, Calabresi L, Pavanello C, Averna M, Cefalu AB, Noto D, Pacifico AA, Pes GM, Harada-Shiba M, Manzato E, Zambon S, Zambon A, Vogt A, Scardapane M, Sjouke B, Fellin R, Arca M. Autosomal recessive hypercholesterolemia: long-term cardiovascular outcomes. *Journal of the American College of Cardiology*. 2018; 71(3): 279 - 288. IF: 16,834
2. Collado A, Marques P, Escudero P, Rius C, Domingo E, Martínez-Hervás S, Real JT, Ascaso JF, Piqueras L, Sanz MJ. Functional role of endothelial CXCL16/CXCR6-platelet-leucocyte axis in angiotensin II-associated metabolic disorders. *Cardiovascular Research*. 2018; 114(13): 1764 - 1775. IF: 6,290
3. Collado A, Marques P, Domingo E, Perello E, González-Navarro H, Martínez-Hervás S, Real JT, Piqueras L, Ascaso JF, Sanz MJ. Novel Immune Features of the Systemic Inflammation Associated with Primary Hypercholesterolemia: Changes in Cytokine/Chemokine Profile, Increased Platelet and Leukocyte Activation. *Journal of Clinical Medicine*. 2018; 8(1). IF: 5,583
4. Hueso L, Ortega R, Sellés F, Wu-Xiong NY, Ortega J, Civera M, Ascaso JF, Sanz MJ, Real JT, Piqueras L. Upregulation of angiostatic chemokines IP-10/CXCL10 and I-TAC/CXCL11 in human obesity and their implication for adipose tissue angiogenesis. *International Journal of Obesity*. 2018; 42(8): 1406 - 1417. IF: 5,151
5. Carratala A, Martínez-Hervás S, Rodríguez-Borja E, Benito E, Real JT, Saez GT, Carmena R, Ascaso JF. PAI-1 levels are related to insulin resistance and carotid atherosclerosis in subjects with familial combined hyperlipidemia. *Journal of Investigative Medicine*. 2018; 66(1): 17 - 21. IF: 2,029

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI15/00082

Title: *Estudio de nuevos mecanismos inflamatorios y angiogénicos asociados a la obesidad grave mórbida: papel del eje CXCR3 y los receptores nucleares RORs*

Principal Investigator: Laura Piqueras and José Tomás Real

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total budget: 154.577€

Reference: CB07/08/0018

Title: *CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERdem)*

Principal Investigator: Juan Francisco Ascaso Gimilio and José Tomás Real Collado

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2008-

Total budget: 154.577€

Reference: SAF2017-89714-R

Title: *Modulación farmacológica del sistema inmune como diana clave en la prevención de la enfermedad cardiovascular asociada a desordenes metabólicos. Síntesis de fármacos novedosos*

Principal Investigator: María Jesús Sanz Ferrando and Juan Francisco Ascaso Gimilio

Funding Body: *Ministerio de Economía y Competitividad*

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

Duration: 2017-2020

Presupuesto total: 205.700€

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



Group members

Principal investigator

Felipe Javier Chaves Martínez. INCLIVA

Collaborating researchers

Jesús Rodríguez Díaz. University
José Miguel Juanes Tébar. INCLIVA

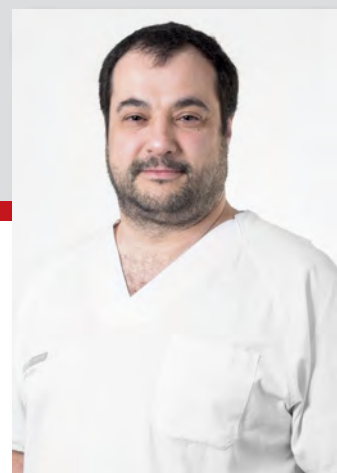
Post-doctoral researchers

Irene Andrés Blasco. INCLIVA

Technicians

Sebastián Blesa Luján. INCLIVA
Azahara M^a Fuentes Trillo. INCLIVA

	R1	R2	R3	R4	STAFF
Researchers by categories	2	1	1	1	1
Researchers financed by competitive public calls or networks	2	-	-	-	-



Strategic aims

- To identify genetic causes of complex diseases with high cardiovascular risk, especially of type 2 diabetes.
- To identify genetic causes of some rare diseases (Abeta, ATA and hereditary forms of hypercholesterolemias not caused by known genes).
- Study the genetic factors and the human microbiota, associated with the infection of the enterovirus rotavirus and norovirus.
- To identify alterations of methylation and hydroxymethylation in relation to the development of type 2 diabetes and its potential use as biomarkers.
- Study of environmental factors involved in the development of diseases of high cardiovascular risk, especially type 2 diabetes and associated organic damage.

Main lines of research

- Identification of frequent and rare functional variants involved in high cardiovascular risk disease development via exome sequence research and verification in population studies.
- Genotyping and/or sequencing of complete rotavirus and norovirus genomes. Human genotype study of FUT2 and FUT3 genes related to viral genotypes and their relationship with intestinal microbiota.
- Candidate gene and exome studies to identify genes involved in these diseases. Functional, population and family studies to demonstrate these roles.
- Analysis of methylated and hydroxymethylated regions in the genome in patients with specific phenotypes at baseline compared with phenotypes present five years later, as pertains to type 2 diabetes.
- Population studies on different aspects involved in high cardiovascular risk disease development.
- Monitoring and molecular characterization of chronic lymphocytic leukaemia and study of molecular markers.
- Identification of relationships between different genes, essential metals and pollutants in relation to diseases with high cardiovascular risk.

• PUBLICATIONS

Number of articles	IF	Average IF
15	70,181	4,678

National collaborations	International collaborations	Corresponding author
10	4	3

SELECTED PUBLICATIONS

1. Riffo-Campos AL, Fuentes-Trillo A, Tang WY, Soriano Z, De Marco G, Rentero-Garrido P, Adam-Felici V, Lendinez-Tortajada V, Francesconi K, Goessler W, Ladd-Acosta C, Leon-Latre M, Casasnovas JA, Chaves FJ, Navas-Acien A, Guallar E, Tellez-Plaza M. In silico epigenetics of metal exposure and subclinical atherosclerosis in middle aged men: pilot results from the Aragon Workers Health Study. *Philosophical Transactions of the Royal Society B-Biological Sciences*. 2018; 373(1748). IF: 5,666
2. Olivares D, Perez-Hernandez J, Forner MJ, Perez-Soriano C, Tormos MC, Saez GT, Chaves FJ, Redon J, Cortes R. Urinary levels of sirtuin-1 associated with disease activity in lupus nephritis. *Clinical Science*. 2018; 132(5): 569 - 579. IF: 5,220
3. Casino P, Gozalbo-Rovira R, Rodríguez-Díaz J, Banerjee S, Boutaud A, Rubio V, Hudson BG, Saus J, Cervera J, Marina A. Structures of collagen IV globular domains: insight into associated pathologies, folding and network assembly. *IUCrJ*. 2018; 5(Pt 6): 765 - 779. IF: 6,544
4. Monedero V, Collado MC, Rodríguez-Díaz J. Therapeutic opportunities in intestinal microbiota-virus interactions. *Trends in Biotechnology*. 2018; 36(7): 645 - 648. IF: 13,578
5. Grau-Perez M, Navas-Acien A, Galan-Chilet I, Briongos-Figuero LS, Morchon-Simon D, Bermudez JD, Crainiceanu CM, de Marco G, Rentero-Garrido P, Garcia-Barrera T, Gomez-Ariza

JL, Casanovas JA, Martin-Escudero JC, Redon J, Chaves FJ, Tellez-Plaza M. Arsenic exposure, diabetes-related genes and diabetes prevalence in a general population from Spain. *Environmental Pollution*. 2018; 235: 948 - 955. IF: 4,358

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI17/00544

Title: *Identificación de variantes genéticas protectoras frente al desarrollo de diabetes tipo 2 en octogenarios*

Principal Investigator: Felipe Javier Chaves Martínez

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 196.020€

Reference: CM1406

Title: *Epigenetic Chemical Biology (EPICHEM)*

Principal Investigator: María Téllez Plaza

Funding Body: *European Commission*

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

Duration: 2015 - 2019

Title: *Clonal evolution and molecular monitoring in chronic lymphocytic leukemia under selective pressure of therapy: impact on clinical outcome*

Principal Investigator: María José Terol Castera

Funding Body: *Gilead (Fellowship Program)*

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

Duration: 2018-2019

Total budget: 35.000€

Reference: AGL2017-84165-C2-2-R

Title: *Descifrando las interacciones entre la microbiota intestinal/virus entéricos/hospedador: bases para proteger frente a la diarrea viral*

Principal Investigator: Jesús Rodríguez Díaz

Funding Body: *Ministerio de Economía y Competitividad*

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

Duration: 2018-2020

Total budget: 133.100€

Title: *Metagenomics to identify viral indicators in the produce chain*

Principal Investigator: Jesús Rodríguez Díaz, Gloria Sánchez Moragas

Funding Body: *CPS Centre For Produce Safety (USA)*

Beneficiary Institution: *Instituto de Agroquímica y Tecnología de Alimentos (CSIC) y Universidad de Valencia*

Duration: 2018-2019

Total budget: 226.070,25€

Title: *Creació d'una infraestructura de producció, purificació i caracterització de proteïnes d'interés biomèdic i biotecnològic*

Principal Investigator: Jesús Rodríguez Díaz

Funding Body: *FEDER/Generalitat Valenciana*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2018-2020

Total budget: 430.414€

• THESIS

Thesis title: *Perfil de micro ARNs exosomales asociados a daño glomerular en pacientes hipertensos con microalbuminuria*

Doctoral candidate: Javier Pérez Hernández

Director(s): Raquel Cortés Vergaz, Felipe Javier Chaves, Josep Redón i Mas

Date of the defense: 15/02/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Desarrollo de un sistema de detección de mutaciones somáticas de interés clínico mediante secuenciación masiva en muestras oncológicas*

Doctoral candidate: Enrique Seda García

Director(s): Benjamín Sarriá Chust, M^a del Rosario Abellán Sánchez, Sebastián Blesa Luján

Date of the defense: 24/05/2018

Grade: *Sobresaliente "cum laude"*

Research Group on Cardiac Experimental Electrophysiology
Consolidated group

Team involved in



Group members

Principal investigator

Francisco Javier Chorro Gascó
Hospital. University

PhD researchers

Patricia Genovés Martínez. CIBER
Óscar Julián Arias Mutis. CIBER

Collaborating researchers

Luis Such Belenguer. University
Antonio M. Alberola Aguilar. University
Luis Such Miquel. University
Isabel Trapero Gimeno. University
Manuel Zarzoso Muñoz. University
Germán Parra Giraldo. INCLIVA
Irene del Canto Serrano. INCLIVA



	R1	R2	R3	R4	STAFF
Researchers by categories	2	5	-	3	-
Researchers financed by competitive public calls or networks	2	1	-	-	-

Strategic aims

- Publication of the results obtained on using the 1,4-benzothiazepine derivative JTV-519 to modify the proarrhythmic manifestations of mechanoelectric feedback and continuation of the programmed experimental series to analyze the effects of KN-93, carvedilol and analogues, late Na⁺ current inhibitors and the Nitric Oxide carrier S-nitrosoglutathione.
- Continuation of the analysis of the effects of modifications of the basic electrophysiological properties on the processes involved in the induction and maintenance of ventricular fibrillation.
- Analysis of the electrophysiological effects of chronic physical exercise and its protective effect against arrhythmias, the influence of the cardiac nervous system and mitochondrial oxidative stress and the involvement of the IKATP current.
- Development of instruments for recording, processing and analysing cardiac electrophysiological signals obtained with mapping systems.
- Progressive development of the experimental series aimed to study the mechanisms involved in the deterioration of the systolic function, fibrosis and the inducibility of arrhythmias in a chronic model of infarction.
- Progressive development of an experimental model of metabolic syndrome to analyze the electrophysiological modifications and the inducibility of cardiac arrhythmias.

Main lines of research

- Myocardial stretching: analysis of electrophysiological changes induced by mechanical stretching. Autocrine/paracrine influences and study of protective actions by means of drugs.
- Clinical and basic research on heart failure: role of calcium homeostasis in arrhythmogenesis. Study on the effects of drugs acting on intracellular Ca²⁺ dynamics.
- Analysis of the effects of modifications in basic electrophysiological properties on the processes involved in induction and maintenance of ventricular fibrillation.
- Study of electrophysiological effects of chronic physical activity by: a) analysis of the protection against arrhythmias or scientific activity facilitation of its reversion; b) study of the influence of heart's nervous system and mitochondrial oxidative stress; and c) analysis of the effects on the electrical instability induced by myocardial ischemia and the implication of IKATP current.
- Development and extension of tools for the registration, processing and analysing of cardiac electrophysiological signals based on multielectrodes and optical mapping systems able to analyze voltage and calcium signals.
- Study of mechanisms involved in the deterioration of the systolic function, fibrosis and the inducibility of arrhythmias in a chronic model of infarction.
- Study of electrophysiological modifications and inducibility of cardiac arrhythmias in an experimental model of metabolic syndrome.

• PUBLICATIONS

Number of articles	IF	Average IF
15	86,273	5,751
National collaborations	International collaborations	Corresponding author
9	4	4

SELECTED PUBLICATIONS

1. Núñez J, Bayés-Genís A, Zannad F, Rossignol P, Núñez E, Bodí V, Miñana G, Santas E, Chorro FJ, Mollar A, Carratalá A, Navarro J, Górriz JL, Lupón J, Husser O, Metra M, Sanchis J. Long-term potassium monitoring and dynamics in heart failure and risk of mortality. *Circulation*. 2018; 137(13): 1320 - 1330. IF: 18,880
2. Ponce-Balbuena D, Guerrero-Serna G, Valdivia CR, Caballero R, Diez-Guerra FJ, Jiménez-Vázquez EN, Ramírez RJ, Monteiro da Rocha A, Herron TJ, Campbell KF, Willis BC, Alvarado FJ, Zarzoso M, Kaur K, Pérez-Hernández M, Matamoros M, Valdivia HH, Delpón E, Jalife J. Cardiac Kir2.1 and Na V 1.5

channels traffic together to the sarcolemma to control excitability. *Circulation Research*. 2018; 122(11): 1501 - 1516. IF: 15,211

3. Marchio P, Guerra-Ojeda S, Vila JM, Aldasoro M, Valles SL, Soler C, Mauricio MD. Chronic exercise impairs nitric oxide pathway in rabbit carotid and femoral arteries. *Journal of Physiology-London*. 2018; 596(18): 4361 - 4374. IF: 4,540
4. Such-Miquel L, Brines L, Alberola AM, Zarzoso M, Chorro FJ, Guerrero J, Parra G, Gallego N, Soler C, Del Canto I, Guill A, Such L. Effect of chronic exercise on myocardial electrophysiological heterogeneity and stability. Role of intrinsic cholinergic neurons: a study in the isolated rabbit heart. *PLoS One*. 2018; 13(12): e0209085. IF: 2,766
5. Rios-Navarro C, Gavara J, Vidal V, Bonanad C, Racugno P, Bayes-Genis A, Miñana G, Husser O, Oltra R, Nuñez J, Chorro FJ, Bodi V, Ruiz-Sauri A. Characterization and implications of the dynamics of eosinophils in blood and in the infarcted myocardium after coronary reperfusion. *PLoS One*. 2018; 13(10): e0206344. IF: 2,766

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: CB16/11/00486

Title: CIBER Cardiovascular (CIBERcv)

Principal Investigator: Francisco Javier Chorro Gascó

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2017-

Reference: PI15/01408

Title: Efectos de la inhibición de la desacetilación de las histonas en el remodelado post-infarto del sustrato arritmogénico

Principal Investigator: Francisco Javier Chorro Gascó

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2018

Total Budget: 93.170€

Reference: PIE15/00013

Title: A multidisciplinary project to advance in basic mechanisms, diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction

Principal Investigator: Vicente Bodí Peris (Francisco Javier Chorro as collaborating researcher)

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2018

Total Budget: 589.050€

Reference: PROMETEOII/2018/078

Title: Mecanismos protectores frente a la muerte cardiaca súbita de causa arrítmica

Principal Investigator: Francisco Javier Chorro Gascó

Funding Body: Conselleria de Educación, Cultura y Deporte

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2018-2021

Total budget: 275.859,02€

• THESIS

Thesis title: Aplicación del kinesio taping en el corsé estabilizador, en mujeres con incontinencia urinaria de esfuerzo

Doctoral candidate: Laura Fuentes Aparicio

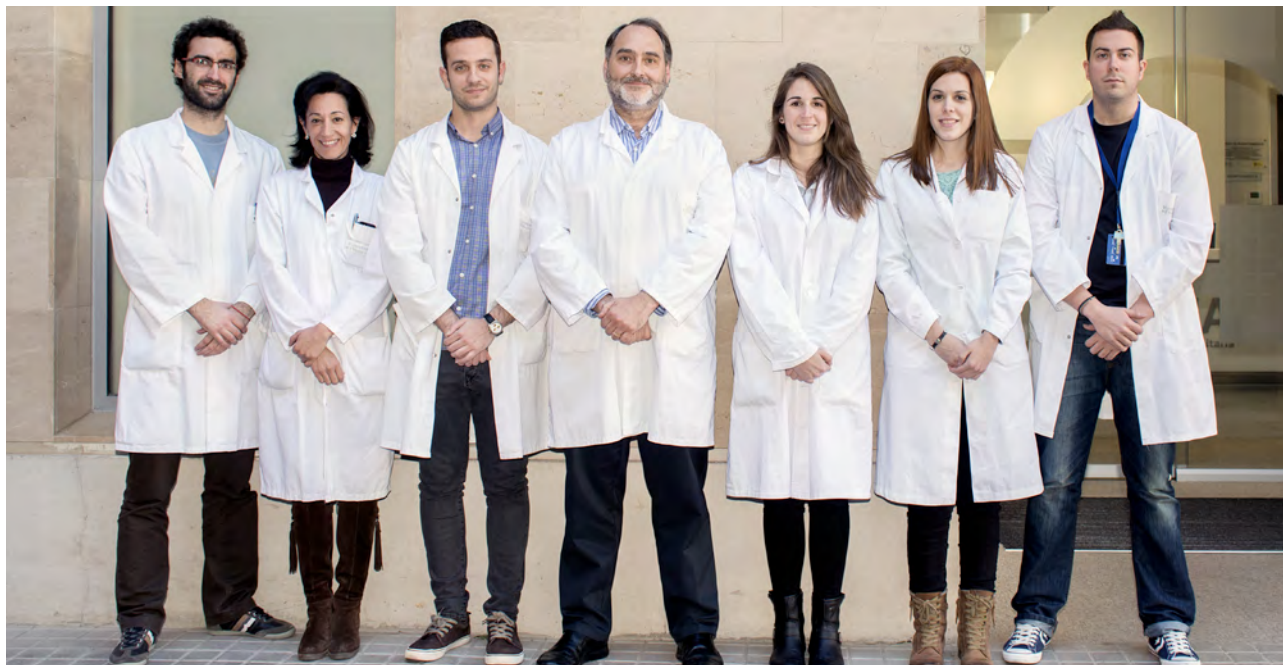
Director(s): Celedonia Igual Camacho, Laura López Bueno

Date of the defense: 19/04/2018

Grade: Sobresaliente "cum laude"

Research Group on Endothelial Cells (LINCE)
Consolidated group

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



Group members

Principal investigator

Carlos Hermenegildo Caudevilla
University

Emerging researcher

Susana Novella del Campo. University

Collaborating researchers

Elena Monsalve Villalba. University

PhD researchers

Daniel Bernardo Pérez Cremades. University
Ana Mompeón Campos. University



	R1	R2	R3	R4	STAFF
Researchers by categories	1	3	-	1	-

Strategic aims

- To analyze the levels of selected miRNA of acute myocardial infarction patients included in the studies of P116/00229.
- To analyze the role of estrogen receptors on the regulation of miRNA by estradiol.
- To collaborate with Rare Diseases group on the histone effects on endothelial cell function and to publish a first paper on this topic.
- To incorporate new pre and postdoctoral researchers to our group.

Main lines of research

- Gender differences in cardiovascular area.
- Vascular effects of sex hormones.
- Identification of new hormone-regulated signaling pathways in endothelium.
- Identification and characterization of miRNA regulated by estradiol in endothelium.
- Interaction of sex hormones with pro-atherogenic factors.
- Determination of circulating endothelial progenitor cells and their link with hormone treatment.



Emerging Researcher

Susana Novella del Campo

The research focuses on the study of endothelial dysfunction associated with aging and lack of stress. We also studied the regulatory role of miRNAs associated with acute coronary syndrome and estrogen-dependent vascular function and aging.

• PUBLICATIONS

Number of articles	IF	Average IF
4	19,231	4,807

National collaborations	International collaborations	Corresponding author
3	-	4

SELECTED PUBLICATIONS

1. Ibañez-Cabellos JS, Aguado C, Pérez-Cremades D, García-Giménez JL, Bueno-Betí C, García-López EM, Romá-Mateo C, Novella S, Hermenegildo C, Pallardó FV. Extracellular histones activate autophagy and apoptosis via mTOR signaling in human endothelial cells. *Biochimica et Biophysica Acta*. 2018; 1864(10): 3234 - 3246. IF: 5,108
2. Vidal-Gómez X, Pérez-Cremades D, Mompeón A, Dantas AP,

Novella S, Hermenegildo C. MicroRNA as crucial regulators of gene expression in estradiol-treated human endothelial cells. *Cellular Physiology and Biochemistry*. 2018; 45(5): 1878 - 1892. IF: 5,500

3. Pérez-Cremades D, Mompeón A, Vidal-Gómez X, Hermenegildo C, Novella S. miRNA as a new regulatory mechanism of estrogen vascular action. *International Journal of Molecular Sciences*. 2018; 19(2): pii: E473. IF: 3,687
4. Perez-Cremades D, Mompeon A, Vidal-Gomez X, Hermenegildo C, Novella S. Role of miRNA in the regulatory mechanisms of estrogens in cardiovascular ageing. *Oxidative Medicine and Cellular Longevity*. 2018: 6082387. IF: 4,936

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: COST Action CA17129

Title: *Catalysing transcriptomics research in cardiovascular disease*

Principal Investigator: Yvan Devaux (Susana Novella as collaborating researcher)

Funding body: *European Commission*

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

Duration: 2018-2022

Reference: COST Action BM1402

Title: *Development of a European network for preclinical testing of interventions in mouse models of age and age-related diseases (MouseAGE)*

Principal Investigator: Ilaria Bellantuono (Susana Novella as collaborating researcher)

Funding body: European Commission

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

Duration: 2014-2018

Reference: PI16/00229

Title: *Perfil plasmático de miRNA en infarto agudo de miocardio: relación con la evolución clínica en pacientes y con la función cardiovascular y posible terapia con micropartículas en ratones*

Principal Investigator: Carlos Hermenegildo Caudevilla

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2017-2019

Total Budget: 138.450€

Reference: 13-TESDIVE-COSTERO-MEDINA-2017-A

Title: *Nuevas terapias dirigidas a la eliminación selectiva de células senescentes en el tratamiento de la disfunción vascular asociada al envejecimiento*

Principal Investigator: Ana Costero Nieto, Pascual Medina Besó (Susana Novella and Carlos Hermenegildo as collaborating researchers)

Funding body: *Fundación Investigación Hospital Clínico Universitario de Valencia and Universidad de Valencia*

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

Duration: 2018

Total Budget: 4.000€

• THESIS

Thesis title: *Efecto de las ciclooxigenasas en la biodisponibilidad del óxido nítrico en la respuesta vascular al tromboxano α_2 en un modelo murino de envejecimiento y menopausia*

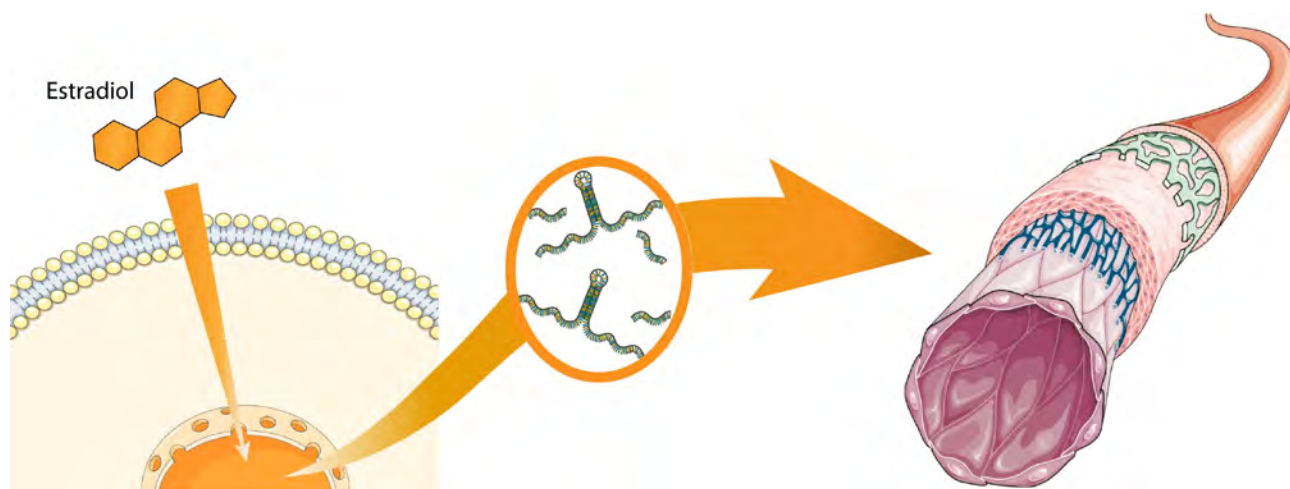
Doctoral candidate: Xavier Vidal Gómez

Director(s): Susana Novella del Campo, Carlos Hermenegildo Caudevilla, Pascual Medina Besó

Date of the defense: 20/12/2018

Grade: *Sobresaliente "cum laude"*

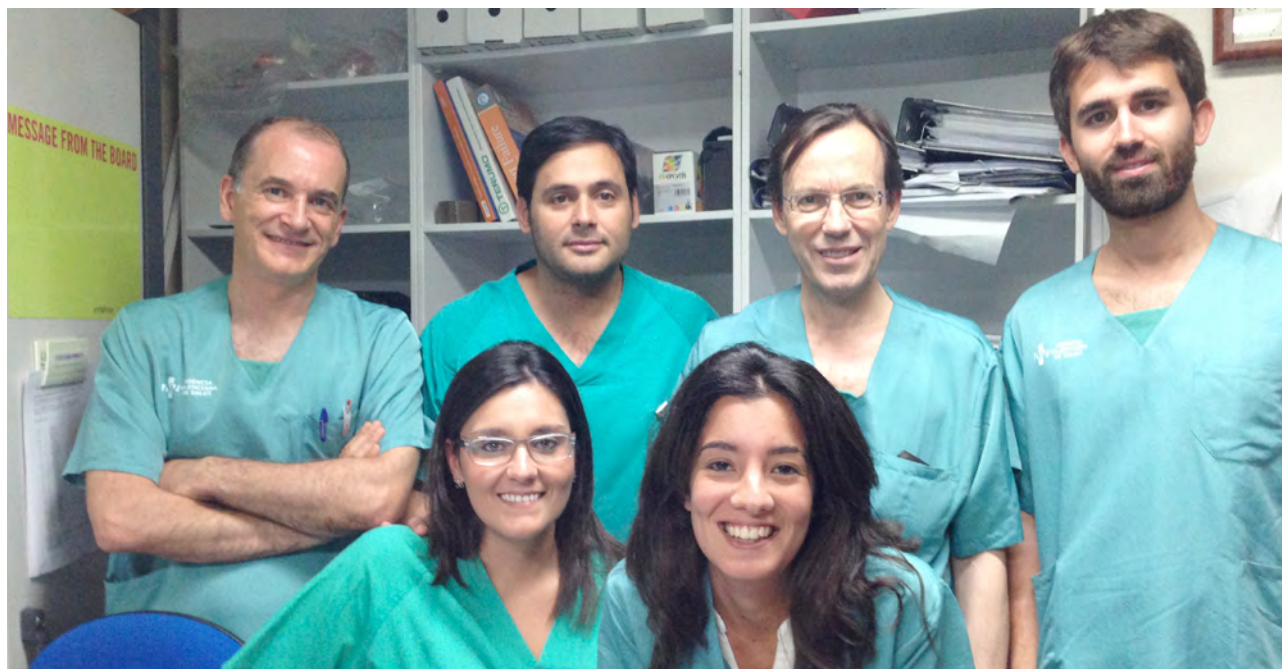
Quality recognition/Award: Extraordinary PhD program and European PhD



miRNAs are Regulatory Mechanisms of Estrogen Vascular Actions (from Int. J. Mol. Sci. 2018, 19, 473)

Research Group on Clinical Cardiology
Consolidated group

Team involved in



Group members

Principal investigator

Juan Sanchis Forés
Hospital. University

Collaborating researchers

Vicente Ruiz Ros. Hospital. University
Sergio García Blas. Hospital
Ernesto Valero Picher. Hospital
Gemma Miñana Escrivá. Hospital
Rafael de la Espriella Juan. Hospital
Vicente Pernias Escrig. INCLIVA
Enrique Santas Olmeda. Hospital

PhD researchers

Clara Sastre Arbona. CIBER
Anna Mollar Fernández. INCLIVA

Emerging researcher

Julio Núñez Villota. Hospital

Technicians

José Manuel Civera Gómez. INCLIVA
Adriana Conesa Bona. INCLIVA
Agustín Fernández Cisnal. Hospital
Amparo Villaescusa Capilla. INCLIVA



	R1	R2	R3	R4	STAFF
Researchers by categories	4	4	1	1	5
Researchers financed by competitive public calls or networks	1	-	-	-	-

Strategic aims

- Publication of manuscripts in high IF journals.
- CIBER Cardiovascular.
- Development of FIS projects.

Main lines of research

- Research line in heart failure:
 - Beta Blocker Treatment Withdrawal in Patients with Heart Failure with Preserved Systolic Function and Evidence of Chronotropic Incompetence.
 - Short-term effects of dapagliflozin on peak oxygen consumption in type 2 diabetic patients with heart failure with reduced systolic function.
- Research line in acute coronary syndrome: Randomized comparison between invasive and conservative strategies in frail elderly patients with non-ST-segment elevation myocardial infarction (MOSCA-FRAIL).
- Investigation line in interventional cardiology: Effect of changes in antigen carbohydrate 125 levels before percutaneous aortic valve prosthesis implant on prognosis after implantation.



Emerging Researcher

Julio Núñez Villota

The research team has focused on the development of new clinical tools to improve diagnosis, risk stratification and treatment of patients with ischemic heart disease and heart failure. More specifically, we focus on identifying new biomarkers and therapeutic strategies. We have already carried out several independent clinical trials and have undergone numerous observational studies (potential utility of peritoneal dialysis for patients with advanced heart failure, the development of new algorithms for the monitoring of patients and the development of a new multi-marker approach for the stratification of the risk).

• PUBLICATIONS

Number of articles	IF	Average IF
49	300,827	6,139
National collaborations	International collaborations	Corresponding author
37	11	17

SELECTED PUBLICATIONS

1. Núñez J, Bayés-Genís A, Zannad F, Rossignol P, Núñez E, Bodí V, Miñana G, Santas E, Chorro FJ, Mollar A, Carratalá A, Navarro J, Górriz JL, Lupón J, Husser O, Metra M, Sanchis J. Long-term potassium monitoring and dynamics in heart failure and risk of mortality. *Circulation*. 2018; 137(13): 1320 - 1330. IF: 18,880
2. Fernández-Avilés F, Sanz-Ruiz R, Bogaert J, Casado Plasencia A, Gilaberte I, Belmans A, Fernández-Santos ME, Charron D, Mulet M, Yotti R, Palacios I, Luque M, Sádaba R, San Román JA, Larman M, Sánchez PL, Sanchis J, Jiménez MF, Claus P, Al-Daccak R, Lombardo E, Abad JL, DelaRosa O, Corcóstegui L, Bermejo J, Janssens S. Safety and efficacy of intracoronary infusion of allogeneic human cardiac stem cells in patients with ST-segment elevation myocardial infarction and left ventricular dysfunction. *Circulation Research*. 2018; 123(5): 579 - 589. IF: 15,211
3. Ware JS, Amor-Salamanca A, Tayal U, Govind R, Serrano I, Salazar-Mendiguchía J, García-Pinilla JM, Pascual-Figal DA, Nuñez J, Guzzo-Merello G, Gonzalez-Vioque E, Bardaji A, Manito N, López-Garrido MA, Padron-Barthe L, Edwards E, Whiffin N, Walsh R, Buchan RJ, Midwinter W, Wilk A, Prasad S, Pantazis A, Baski J, O'Regan DP, Alonso-Pulpon L, Cook SA, Lara-Pezzi E, Barton PJ, Garcia-Pavia P. Genetic etiology for

alcohol-induced cardiac toxicity. *Journal of the American College of Cardiology*. 2018; 71(20): 2293 - 2302. IF: 16,834

4. Bayés-Genís A, Lupón J, Núñez J. No urgent need for revisiting kalaemia guidelines: rebuttal. *European Journal of Heart Failure*. 2018; 20(9): 1256. IF: 10,683
5. Lupón J, Gavidia-Bovadilla G, Ferrer E, de Antonio M, Perra-Lluna A, López-Ayerbe J, Domingo M, Núñez J, Zamora E, Moliner P, Díaz-Ruata P, Santesmases J, Bayés-Genís A. Dynamic trajectories of left ventricular ejection fraction in heart failure. *Journal of the American College of Cardiology*. 2018; 72(6): 591 - 601. IF: 16,834

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI17/01426

Title: *Retirada del tratamiento betabloqueante en pacientes con insuficiencia cardíaca con función sistólica preservada e incompetencia cronotrópica. Efecto sobre la capacidad funcional*

Principal Investigator: Julio Núñez Villota

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 127.050€

Reference: PI17/01736

Title: *Comparación aleatoria entre las estrategias invasivas y conservadoras en pacientes ancianos frágiles con infarto de miocardio sin elevación del segmento ST (MOSCA-FRIL)*

Principal Investigator: Gemma Miñana Escrivá

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 70.180€

Reference: PI15/00837

Title: *Comparación aleatoria entre un estrategia de intervención sobre fragilidad frente a la estrategia habitual en pacientes frágiles después de un infarto agudo de miocardio*

Principal Investigator: Juan Sanchis Forés

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico*

Universitario de Valencia

Duration: 2016-2018

Total budget: 36.300€

Reference: PIE15/00013

Title: *A multidisciplinary project to advance in basic mechanisms, diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction*

Principal Investigator: Vicente Bodí Peris (Juan Sanchis and Julio Núñez as collaborating researchers)

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total Budget: 589.050€

Reference: RTC-2016-4684-1 DeVaDip

Title: *Desarrollo de una nueva técnica de evaluación del tejido adiposo intramuscular mediante densitometría de doble energía*

Principal Investigator: Josep Redon i Mas and Juan Sanchis Forés

Funding Body: *Ministerio de Economía y Competitividad*

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

Duration: 2016-2018

Total budget: 386.775€

Reference: CB16/11/00420

Title: *Incorporación nuevos grupos al Consorcio CIBER (CIBER-cv)*

Principal Investigator: Juan Sanchis Forés

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-

Title: *Changes in myocardial iron content following administration of intravenous iron – Myocardial-IRON*

Principal Investigator: Julio Núñez Villota

Funding Body: *Vifor International AG*

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

Duration: 2017-2018

Total budget: 100.000€

- **THESIS**

Thesis title: *Utilidad de la electroestimulación muscular funcional y el entrenamiento de la musculatura inspiratoria en pacientes con insuficiencia*

Doctoral candidate: Eloy Domínguez Mafé

Director(s): Patricia Palau Sampio, Julio Núñez Villota

Date of the defense: 06/07/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Implementación de una intervención multidisciplinar orientada al autocuidado en una unidad de insuficiencia cardíaca hospitalaria*

Doctoral candidate: Rosa Fonfría Vivas

Director(s): Lorenzo Fácila Rubio, Vicente Ruiz Ros

Date of the defense: 15/11/2018

Grade: *Sobresaliente "cum laude"*



Research Group on the Study of Cardiovascular Risk in Children and Adolescents
Consolidated group

Team involved in



Group members

Principal investigator

Empar Lurbe i Ferrer
 University

José Miguel Calderón Terol. INCLIVA
 Gonzalo Collantes Pablo. INCLIVA
 Irene Cuenca Ortolá. INCLIVA

Collaborating researchers

Isabel Torró Doménech. University
 Julio Álvarez Pitti. University
 Francisco Aguilar Bacallado. University
 Nuria García Carbonell. University
 Pau Redón Lurbe. CIBERObn

Administrative assistant

Christine Deutsch. INCLIVA

Technician

Francisco Ponce Zanón. CIBERObn
 Carlos Planells Palop. INCLIVA



	R1	R2	R3	R4	STAFF
Researchers by categories	1	2	2	1	6
Researchers financed by competitive public calls or networks	-	1	-	-	1

Strategic aims

- The iPEDITEC Unit brings healthcare workers into daily contact with engineers developing software for signal capture through mobile devices. Studying the psychological parameters that facilitate personalized therapy has been a priority aim during 2018, resulting in improved treatment of obese pediatric patients in the Unit.
- The PAIDO Program is focused on personalized medical care extended through initiatives involving family, educators, nutritionists, physical education teachers and other social agents. Treatment goes beyond the hospital setting to include the child's environment and personal sphere and is supported by state-of the art artificial intelligence technologies.
- To improve the knowledge of fetal life and postnatal growth on the development of cardiometabolic risk factors early in life. The KITE cohort is a prospective study starting at birth and assessing the determinants of cardiometabolic risk factors in the first decades of life. Omics data from umbilical cord are available and the analysis of the interaction between clinical data and omics may help to introduce actions in critical periods of life and the potential contribution to reduce cardiometabolic disease later in life. Dr. Lurbe is the coordinator of the new document of the European Guidelines on Arterial Hypertension in Children and Adolescents.

Main lines of research

- New technologies applied to the detection of congenital heart diseases and sepsis in asymptomatic newborn babies.
- Childhood obesity: new insights in the personalized treatment: study of the cardiorespiratory capacity.
- New technologies applied to the treatment of obesity: physical exercise preventing and treating obesity.
- Arterial hypertension in children and adolescents.
- Cardiovascular and renal risk in diabetes.
- Early origins of cardiometabolic risk factors assessed in a prospective study starting at birth (Cohort KITE).
- Obese mothers: influence of breast feeding in the offspring during the first year of life.

• PUBLICATIONS

Number of articles	IF	Average IF
10	55,689	5,568

National collaborations	International collaborations	Corresponding author
2	6	4

SELECTED PUBLICATIONS

1. Lurbe E, Aguilar F, Álvarez J, Redon P, Torró MI, Redon J. Determinants of cardiometabolic risk factors in the first decade of life: a longitudinal study starting at birth. *Hypertension*. 2018; 71(3): 437 - 443. IF: 6,823
2. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I, ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *European Heart Journal*. 2018; 39(33): 3021 - 3104. IF: 23,425
3. Kotsis V, Jordan J, Micic D, Finer N, Leitner DR, Toplak H, Tokgozoglu L, Athyros V, Elisaf M, Filippatos TD, Redon J, Redon P, Antza C, Tsioufis K, Grassi G, Seravalle G, Coca A, Sierra C, Lurbe E, Stabouli S, Jelakovic B, Nilsson PM. Obesity and cardiovascular risk: a call for action from the European Society of Hypertension Working Group of Obesity, Diabetes and the High-risk Patient and European Association for the Study of Obesity: part A: mechanisms of obesity induced hypertension, diabetes and dyslipidemia and practice guidelines for treatment. *Journal of Hypertension*. 2018; 36(7): 1427 - 1440. IF: 4,092
4. Lurbe E, Torro MI, Alvarez-Pitti J, Redon J, Borghi C, Redon P. Uric acid is linked to cardiometabolic risk factors in overweight and obese youths. *Journal of Hypertension*. 2018;

36(9): 1840 - 1846. IF: 4,092

5. Lurbe E, Litwin M, Pall D, Seeman T, Stabouli S, Webb NJA, Wühl E, Working Group of the 2016 European Society of Hypertension Guidelines for the Management of High Blood Pressure in Children and Adolescents. Insights and implications of new blood pressure guidelines in children and adolescents. *Journal of Hypertension*. 2018; 36(7): 1456 - 1459. IF: 4,092

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI17/01517

Title: *Programación fetal y desarrollo postnatal en hijos de madres obesas: modulación por la alimentación en el primer año de vida*

Principal Investigator: Empar Lurbe i Ferrer

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 170.005€

Reference: PI14/01781

Title: *Impacto del peso al nacer y la ganancia ponderal postnatal en la disfunción endotelial e inflamación vascular*

Principal Investigator: Empar Lurbe i Ferrer

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2015-2018

Total budget: 93.500€

Reference: EAT4HEALTHYLIFE

Title: *Obesity and abnormal eating behavior across the lifespan. A cross sectional and longitudinal approach of environmental and neurobiological factors*

Principal Investigator: Fernando Fernández Aranda (Empar Lurbe, Julio Álvarez, Pau Redón as collaborating researchers)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Consorcio Hospital General Universitario de Valencia*

Duration: 2018-2020

Total budget: 69.220€

Reference: CB06/03/0039

Title: *CIBER de Fisiopatología de la Obesidad y Nutrición (CIBERObn)*

Principal Investigator: Empar Lurbe i Ferrer

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2006-

Total Budget (2018): 85.000€

Reference: PROMETEO/2016/084

Title: *Innovación tecnológica en la evaluación del sistema nervioso simpático en adolescentes y adultos jóvenes obesos: papel en la estratificación del riesgo e intervención terapéutica*

Principal Investigator: Josep Redón i Mas

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

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

Duration: 2016-2019

Total budget: 246.190€

Reference: 12-NEO9TEC-CALPE-LURBE-2017-B

Title: *Diagnóstico precoz de la sepsis neonatal mediante la monitorización de la variabilidad cardiaca*

Principal Investigator: J Calpe and Empar Lurbe i Ferrer

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

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

Duration: 2018

Total budget: 9.500€

Reference: PRV00229

Title: *Innovando en el tratamiento de la obesidad infantil: desarrollo de una plataforma y su implantación en la clínica*

Principal Investigator: Julio Álvarez Pitti

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

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

Duration: 2017-2018

Total budget: 10.000€

Reference: PAIDO

Title: *Marchando con mi pediatra Paido. Programa PAIDO*

Principal Investigator: María Isabel Torró Doménech and Julio Álvarez Pitti

Funding Body: *Consorcio Hospital General Universitario de Valencia and Ayuntamiento de Valencia*

Beneficiary Institution: *Consorcio Hospital General Universitario de Valencia*

Duration: 2016 -



Logo of the KITE cohort: Impact of intrauterine life and postnatal gain in the development of cardiometabolic risk factors in the first two decades of life



Logo of the Program of comprehensive attention to childhood obesity (PAIDO), NAOS Strategy Award in 2011

Cardiometabolic Research Group on Primary Care
Consolidated group



Group members

Principal investigator

Jorge Navarro Pérez. Hospital

Collaborating researchers

- Álvaro Bonet Plá. Clínico-Malvarrosa Health Department
- Victoria Gosalbes Soler. Clínico-Malvarrosa Health Department
- Nidia Ruiz Varea. Clínico-Malvarrosa Health Department
- Pilar Roca Navarro. Clínico-Malvarrosa Health Department. University
- José Sanfélix-Genovés. Clínico-Malvarrosa Health Department
- José Luis Trillo Mata. Clínico-Malvarrosa Health Department
- Ruth Usó Talamantes. Clínico-Malvarrosa Health Department



	R1	R2	R3	R4	STAFF
Researchers by categories	-	3	3	1	-

Strategic aims

- Consolidation of various lines of cardiometabolic research.
- Consolidation of a network of partners in the area of primary care.

Main lines of research

- Cardiovascular population studies (ESCARVAL).
- Studies monitoring cardiovascular risk factors (ADAMPA).
- Population studies on fractures prevention.

• PUBLICATIONS

Number of articles	IF	Average IF
7	32,953	4,707
National collaborations	International collaborations	Corresponding author
5	2	1

SELECTED PUBLICATIONS

1. Navarro-Pérez J, Orozco-Beltran D, Gil-Guillen V, Pallares V, Valls F, Fernandez A, Perez-Navarro AM, Sanchis C, Dominguez-Lucas A, Martin-Moreno JM, Redon J, Tellez-Plaza M; ESCARVAL STUDY GROUP. Mortality and cardiovascular disease burden of uncontrolled diabetes in a registry-based cohort: the ESCARVAL-risk study. *BMC Cardiovascular Disorders*. 2018; 18(1): 180. IF: 1,812
2. Brotons Cuixart C, Alemán Sánchez JJ, Banegas Banegas JR, Fondón León C, Lobos-Bejarano JM, Martín Rioboó E, Navarro Pérez J, Orozco-Beltrán D, Villar Álvarez F; Grupo de Prevención Cardiovascular del PAPPs. Recomendaciones preventivas cardiovasculares. Actualización PAPPs 2018. *Atención Primaria*. 2018; 50(1): 4 - 28. IF: 1,148
3. Sanfélix-Genovés J, Rodríguez-Bernal CL, Marco-Moreno I, Martínez-Ibañez P, Martínez-Ibañez L, Bóveda-García M, Barreira-Franch I, Calleja-Del Ser M, Borrás-Moreno G, Avelino-Hidalgo E, Escrig-Veses M, Lauriano M, Giménez-Loreiro M, Bellot-Pujalte L, García-Sempere A, Peiró S, Sanfélix-Gimeno G; ADAMPA group. Rationale and design of a pragmatic clinical trial to assess the impact of self-monitoring blood pressure at home and self-titration of antihypertensive medication in poorly controlled hypertension: the

ADAMPA study protocol. *BMC Family Practice*. 2018; 19(1): 160. IF: 2,032

4. Núñez J, Bayés-Genís A, Zannad F, Rossignol P, Núñez E, Bodí V, Miñana G, Santas E, Chorro FJ, Mollar A, Carratalá A, Navarro J, Górriz JL, Lupón J, Husser O, Metra M, Sanchis J. Long-term potassium monitoring and dynamics in heart failure and risk of mortality. *Circulation*. 2018; 137(13): 1320 - 1330. IF: 18,880

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI16/02130

Title: *Impacto de la auto-medición y el auto-ajuste de la medicación antihipertensiva en el control de la hipertensión arterial. Un ensayo clínico pragmático: estudio ADAMPA*

Principal Investigator: José Sanfélix Genovés

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2019

Total Budget: 86.515€



Research Group on the Study of Cardiometabolic and Renal Risk

Consolidated group



Group members

Principal investigator

Josep Redón i Mas. Hospital. University

Collaborating researchers

M^a José García-Fuster González-Alegre. Hospital

M^a José Galindo Puerto. Hospital

M^a José Forner Giner. Hospital

Gernot Helmut Pichler. INCLIVA

María José Fabiá Valls. Hospital

Raquel Cortés Vergaz. INCLIVA

Ana Ferrer Albero. INCLIVA

Javier Gámez Payá. INCLIVA

Estela Selma Soriano. INCLIVA

Javier Pérez Hernández. INCLIVA

Ana Ortega Gutiérrez. INCLIVA

PhD researchers

José Luis Holgado Sánchez. INCLIVA

Cristina López Zumel. INCLIVA

Carlos Sánchez Sánchez. INCLIVA

Adrián Ruiz Hernández. Hospital

Elena Solaz Moreno. Hospital

Emerging researchers

Fernando Martínez García. INCLIVA

María Téllez Plaza. INCLIVA

Technicians

Óscar Calaforra Juan. CIBERobn

Noemí Dolz Gilba. INCLIVA

Antonio Fernández Giménez. INCLIVA

Alexandra Eugenia Muñoz Oliver. INCLIVA

María Inmaculada Saurí Ferrer. INCLIVA

	R1	R2	R3	R4	STAFF
Researchers by categories	5	11	2	1	5
Researchers financed by competitive public calls or networks	2	1	-	-	1



Strategic aims

- To start-up the laboratory for the analysis of podocytes (identification, cultivation and phenotyping) and its derivatives: micro-RNA, exosomes.
- The integration of metabolomics and genomics in the study of factors related to the development of kidney damage.
- Development of studies for noninvasive hemodynamic characterization in vascular pathology.
- Analysis of morbidity and mortality linked to the presence of hypertension and renal injury.
- Development of in vitro studies of platelet and leukocyte adhesion in venous thromboembolism.
- Genetic studies related to obesity and overweight and venous thromboembolism.
- Development of phase III and IV clinical trials.

Main lines of research

- Mechanisms of development of renal damage associated with hypertension with special emphasis on the podocyte damage.
- Impact of cardiovascular risk factors and renal function in absolute morbidity and mortality in high-risk population and in the general population.
- Inflammation and oxidative stress in the development of cardiovascular disease.
- Genomics, proteomics and metabolomics of early cardiometabolic and renal disorders.
- Impact of environmental toxins (metals) in cardiometabolic risk.
- Identification of polymorphisms and related to the control of BMI and waist circumference and the risk of obesity genes.
- Venous thrombosis in young patients: factors associated with its development.
- The relationship between risk of venous thromboembolic disease and arteriosclerosis.



Emerging Researcher

Fernando Martínez García

During the last year we have focused our research activity on the mechanisms involved in the development of microalbuminuria and kidney damage in hypertensive patients. We are also studying the role of new imaging techniques for

the early diagnosis of atherosclerosis and the potential value of markers of vascular rigidity for risk prediction. And we are conducting some collaborative studies on the metabolic syndrome and insulin resistance.



Emerging Researcher

María Téllez Plaza

Our lines of interest are focused on the health consequences of widespread exposure to environmental toxicants. Her research has built experience in population-based studies of chronic cardiovascular effects of cadmium, arsenic and other toxic metals. An important area of work involves the development of data analysis methods that can be applied to the study of environmental epigenetic effects.

• PUBLICATIONS

Number of articles	IF	Average IF
34	203,1	5,973
National collaborations	International collaborations	Corresponding author
10	22	7

SELECTED PUBLICATIONS

1. Böhm M, Schumacher H, Teo KK, Lonn E, Mahfoud F, Mann JFE, Mancía G, Redon J, Schmieder R, Weber M, Sliwa K, Williams B, Yusuf S. Achieved diastolic blood pressure and pulse pressure at target systolic blood pressure (120-140 mmHg) and cardiovascular outcomes in high-risk patients: results from ONTARGET and TRANSCEND trials. *European Heart Journal*. 2018; 39(33): 3105 - 3114. IF: 23,425
2. Furio E, García-Fuster MJ, Redon J, Marques P, Ortega R, Sanz MJ, Piqueras L. CX3CR1/CX3CL1 axis mediates platelet-leukocyte adhesion to arterial endothelium in younger patients with a history of idiopathic deep vein thrombosis. *Thrombosis and Haemostasis*. 2018; 118(3): 562 - 571. IF: 4,952
3. Lurbe E, Aguilar F, Álvarez J, Redon P, Torrón MI, Redon J. Determinants of cardiometabolic risk factors in the first decade of life: a longitudinal study starting at birth. *Hypertension*. 2018; 71(3): 437 - 443. IF: 6,823
4. Pichler G, Amigo N, Tellez-Plaza M, Pardo-Cea MA, Dominguez-Lucas A, Marrachelli VG, Monleon D, Martin-Escudero JC, Ascaso JF, Chaves FJ, Carmena R, Redon J. LDL particle size and composition and incident cardiovascular disease in a South-European population: the Horta-Liposcale Follow-up Study. *International Journal of Cardiology*. 2018; 264: 172 - 178. IF: 4,034
5. Orkin C, Molina JM, Negro E, Arribas JR, Gathe J, Eron JJ, Van Landuyt E, Lathouwers E, Hufkens V, Petrovic R, Vanveggel S, Opsomer M, EMERALD study group. Efficacy and safety of switching from boosted protease inhibitors plus emtricitabine and tenofovir disoproxil fumarate regimens to single-tablet darunavir, cobicistat, emtricitabine, and tenofovir alafenamide at 48 weeks in adults with virologically suppressed HIV-1 (EMERALD): a phase 3, randomised, non-inferiority trial. *Lancet HIV*. 2018; 5(1): e23 - e34. IF: 11,355

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: 779780 - BodyPass

Title: *API-ecosystem for cross-sectorial exchange of 3D personal data*

Principal Investigator: Josep Redón i Mas

Funding body: *European Commission*

Beneficiary institution: *Fundación Investigación Hospital Clínico*

Universitario de Valencia

Duration: 2018-2020

Total budget: 351.937,50€

Reference: 780495 - BigMedilytics

Title: *Big Data for Medical Analytics*

Principal Investigator: Josep Redón i Mas

Funding body: *European Commission*

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

Duration: 2018-2021

Total budget: 1.062.136,25€

Reference: 785815 - BigData@Heart

Title: *Big Data for Better Hearts*

Action: *IMI2 Call 7 Topic 7 «Increase access and use of high quality data to improve clinical outcomes in heart failure (HF), atrial fibrillation (AF), and acute coronary syndrome (ACS) patients», under the Big Data for Better Outcomes programme*

Principal Investigator: Josep Redón i Mas

Funding body: *European Commission*

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

Duration: 2017-2022

Total budget: 386.250€ (Contribution EC: 100%)

Reference: 724099 - ADVANTAGE

Title: *Managing Frailty. A comprehensive approach to promote a disability-free advanced age in Europe: the ADVANTAGE initiative*

Principal Investigator: Josep Redón i Mas

Funding body: *European Commission (3rd Health Program)*

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

Duration: 2016-2019

Total budget: 130.005€

Reference: COST Action CM1406

Title: *Epigenetic Chemical Biology (EPICHEM)*

Principal Investigator: María Téllez Plaza

Funding Body: *European Commission*

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

Duration: 2015-2019

Reference: PI17/02217

Title: *Modelos predictivos en insuficiencia cardíaca con FE*

preservada-intermedia a partir de información de los registros electrónicos de salud. Valor aditivo de marcadores de metabólica

Principal Investigator: Fernando Martínez García

Funding body: Instituto de Salud Carlos III

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2018-2020

Total budget: 24.200€

Reference: PI16/01402

Title: *Estudio experimental in vivo e in vitro y la aplicación clínica del impacto de las proteínas del complejo Rhabphilin-Rab en el desarrollo del daño renal y cardiovascular*

Principal Investigator: Josep Redón i Mas

Funding body: Instituto de Salud Carlos III

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2017-2019

Total budget: 194.205€

Reference: PI15/00071

Title: *Metales y arteriosclerosis subclínica: papel de la variación genética y epigenética en genes candidatos*

Principal Investigator: María Téllez Plaza

Funding body: Instituto de Salud Carlos III

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2018

Total budget: 195.415€

Reference: PT17/0005/0017

Title: *Biobank Platform*

Principal Investigator: Josep Redón Mas

Funding body: Instituto de Salud Carlos III

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2018-2020

Total budget: 104.775€

Reference: PT17/0005/0017

Title: *Innovation Platform*

Principal Investigator: Josep Redón i Mas

Funding body: Instituto de Salud Carlos III

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2018-2020

Total budget: 104.775€

Reference: RTC-2016-4684-1 DeVaDip

Title: *Desarrollo de una nueva técnica de evaluación del tejido adiposo intramuscular mediante densitometría de doble energía*

Principal Investigator: Josep Redon i Mas and Juan Sanchis Forés

Funding Body: Ministerio de Economía y Competitividad

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2018

Total budget: 386.775€

Reference: PROMETEO/2016/084

Title: *Innovación tecnológica en la evaluación del sistema nervioso simpático en adolescentes y jóvenes obesos*

Principal Investigator: Josep Redón i Mas

Funding Body: Conselleria de Educación, Cultura y Deporte

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2019

Total budget: 246.190€

Title: *Concentraciones genéticamente elevadas de metales, metilación del DNA y el síndrome coronario agudo: un estudio epidemiológico de aleatorización*

Principal Investigator: María Téllez Plaza

Funding Body: Fundación Astra Zéneca - III Convocatoria Jóvenes Investigadores

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2017-2018

Total budget: 20.000€

• THESIS

Thesis title: *Perfil de micro ARNs exosomales asociados a daño glomerular en pacientes hipertensos con microalbuminuria*

Doctoral candidate: Javier Pérez Hernández

Director(s): Josep Redón i Mas, Raquel Cortés Vergaz, Felipe Javier Chaves Martínez

Date of the defense: 14/02/2018

Grade: Sobresaliente "cum laude"

➤ **Research Group on Vascular Function**
Consolidated group



Group members

Principal investigator

José M^a Vila Salinas
University

Collaborating researchers

Martín Aldasoro Celaya. University
M^a Dolores Mauricio Aviñó. University



	R1	R2	R3	R4	STAFF
Researchers by categories	-	1	-	2	-

Strategic aims

- Vascular changes associated with different pathologies.
- Regulation of blood flow.

Main lines of research

- Characterization of alterations in the control of vascular tone and endothelial function induced by aging.
- The effects of exercise training on the vascular response.
- Vascular and extravascular effects of ranolazine.
- Improvement of insulin vascular effects by ranolazine.
- Vascular effects of nanoparticles.

• PUBLICATIONS

Number of articles	IF	Average IF
2	9,476	4,738

National collaborations	International collaborations	Corresponding author
2	-	-

SELECTED PUBLICATIONS

1. Marchio P, Guerra-Ojeda S, Vila JM, Aldasoro M, Valles SL, Soler C, Mauricio MD. Chronic exercise impairs nitric oxide pathway in rabbit carotid and femoral arteries. *Journal of Physiology-London*. 2018; 596(18): 4361 - 4374. IF: 4,540
2. Mauricio MD, Guerra-Ojeda S, Marchio P, Valles SL, Aldasoro M, Escribano-Lopez I, Herance JR, Rocha M, Vila JM, Victor VM. Nanoparticles in medicine: a focus on vascular oxidative stress. *Oxidative Medicine and Cellular Longevity*. 2018: 6231482. IF: 4,936

Research Group on Pediatric Nutrition
Consolidated group



Group members

Principal investigator

Cecilia Martínez Costa
Hospital. University

Collaborating researchers

Francisco Núñez Gómez. Hospital
M^a Carmen Collado Amores. IATA-CSIC
Javier Buesa Gómez. Hospital. University
M^a Ángeles Montal Navarro. Hospital
Pablo García Molina. University
Evelin Balaguer López. Hospital
Elena Crehuá Gaudiza. Hospital

Julia Sánchez Zahonero. Hospital
Inmaculada Tarazona Casany. Hospital
Javier Estañ Capell. Hospital
Laura Martínez Rodríguez. Hospital

PhD researchers

Ana Paula Grattarola. INCLIVA



	R1	R2	R3	R4	STAFF
Researchers by categories	2	3	5	1	2
Researchers financed by competitive public calls or networks	-	1	-	-	-

Strategic aims

- Cardiovascular area:
Study of metabolome, epigenetic markers and microbiome in obese children with/without insulin resistance before and after personalized nutritional intervention and physical exercise.
- Area of human milk:
Characterization of mother-infant microbiome in term and preterm infants.
- Area of hospital malnutrition and artificial nutrition:
Validation of the pediatric screening tools for detecting the risk of malnutrition linked to chronic disease and pediatric hospitalization.

Main lines of research

- Cardiovascular area:
 - Study of early markers of vascular damage in dyslipidemic obese children by Doppler ultrasonography to establish a correlation with insulin resistance and other metabolic markers.
 - Monitoring exercise and energy consumption in obese schoolchildren and teenagers to adjust nutritional intervention.
- Area of human milk:
 - Analysis of defensive factors against norovirus infections and its relationship with histo-blood group antigens and FUT genotype.
 - Analysis of mother-fetal microbiome and cold preservation methods.
- Area of hospital malnutrition and artificial nutrition:
 - Screening procedures for detecting the risk of malnutrition linked to chronic disease and pediatric hospitalization.
 - Multicenter study of acceptance and quality of life in children treated with home enteral nutrition.

• PUBLICATIONS

Number of articles	IF	Average IF
11	55,762	5,069
National collaborations	International collaborations	Corresponding author
7	4	5

SELECTED PUBLICATIONS

1. Boix-Amorós A, Martínez-Costa C, Querol A, Collado MC, Mira A. Author Correction: multiple approaches detect the presence of fungi in human breastmilk samples from healthy mothers. *Scientific Reports*. 2018; 8(1): 16829. IF: 4,122
2. García-Molina P, Balaguer López E, Verdú J, Nolasco A, García Fernández FP. Cross-cultural adaptation, reliability and validity of the Spanish version of the Neonatal Skin Risk Assessment Scale. *Journal of Nursing Management*. 2018; 26(6): 744 - 756. IF: 1,912
3. Gómez-Gallego C, Morales JM, Monleón D, du Toit E, Kumar H, Linderborg KM, Zhang Y, Yang B, Isolauri E, Salminen S, Collado MC. Human breast milk NMR metabolomic profile across specific geographical locations and its association with the milk microbiota. *Nutrients*. 2018; 10(10): pii: E1355. IF: 4,196
4. Beeckman D, Van den Bussche K, Alves P, Arnold Long MC, Beele H, Ciprandi G, Coyer F, de Groot T, De Meyer D, Deschepper E, Dunk AM, Fourie A, García-Molina P, Gray M, Iblasi A, Jelnes R, Johansen E, Karadag A, Leblanc K, Kis Dadara Z, Meaume S, Pokorna A, Romanelli M, Ruppert S, Schoonhoven L, Smet S, Smith C, Steininger A, Stockmayr M, Van Damme N, Voegeli D, Van Hecke A, Verhaeghe S, Woo K, Kottner J. Towards an international language for incontinence-associated dermatitis (IAD): design and evaluation of psychometric properties of the Ghent Global IAD Categorization Tool (GLOBIAD) in 30 countries. *British Journal of Dermatology*. 2018; 178(6): 1331 - 1340. IF: 6,129
5. van Beek J, de Graaf M, Al-Hello H, Allen DJ, Ambert-Balay

K, Botteldoorn N, Brytting M, Buesa J, Cabrerizo M, Chan M, Cloak F, Di Bartolo I, Guix S, Hewitt J, Iritani N, Jin M, John R, Lederer I, Mans J, Martella V, Maunula L, McAllister G, Niendorf S, Niesters HG, Podkolzin AT, Poljsak-Prijatelj M, Rasmussen LD, Reuter G, Tuite G, Kroneman A, Vennema H, Koopmans MPG, NoroNet. Molecular surveillance of norovirus, 2005-16: an epidemiological analysis of data collected from the NoroNet network. *Lancet Infectious Diseases*. 2018; 18(5): 545 - 553. IF: 25,148

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: MAMI

Title: MAMI - *The Power of Maternal Microbes on Infant Health*

Principal Investigator: M^a Carmen Collado Amores (Cecilia Martínez Costa as collaborating researcher)

Funding body: *European Commission*

Beneficiary institution: *Consejo Superior de Investigaciones Científicas*

Duration: 2015-2020

Total budget: 1.499.978,43€

Reference: INTIMIC-085

Title: *Maternal obesity and cognitive dysfunction in the offspring: cause effect-role of the GUT MicrobiOME and early dietary prevention*

Principal Investigator: Patricia Lozzo (Consuelo Borrás, Daniel Monleón, Vannina González, José Manuel Morales as collaborating researchers)

Funding Body: *JPI HDHL. European Commission*

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

Duration: 2017-2020

Total Budget: 778.240€

Reference: PCIN-2017117

Title: *Obesidad materna y disfunción cognitiva en la descendencia: papel causa-efecto de la microbiota intestinal y prevención dietética temprana*

Principal Investigator: Consuelo Borrás Blasco

Funding body: *Ministerio de Economía y Competitividad*

Beneficiary institution: *Universidad de Valencia*

Duration: 2017-2020

Total budget: 143.000€

• THESIS

Thesis title: *Epidemiología de las bronquitis sibilantes y el asma en los primeros 6 años: resultados de la cohorte de Alzira (Valencia)*

Doctoral candidate: María Julia Alfonso Diego

Director(s): Santiago Pérez Tarazona, Francisco Javier Estañ Capell, Ricardo Bou Monterde

Date of the defense: 06/07/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Valoración de los niveles materno-fetales de 25-oh vitamina D y grado de mineralización ósea del recién nacido*

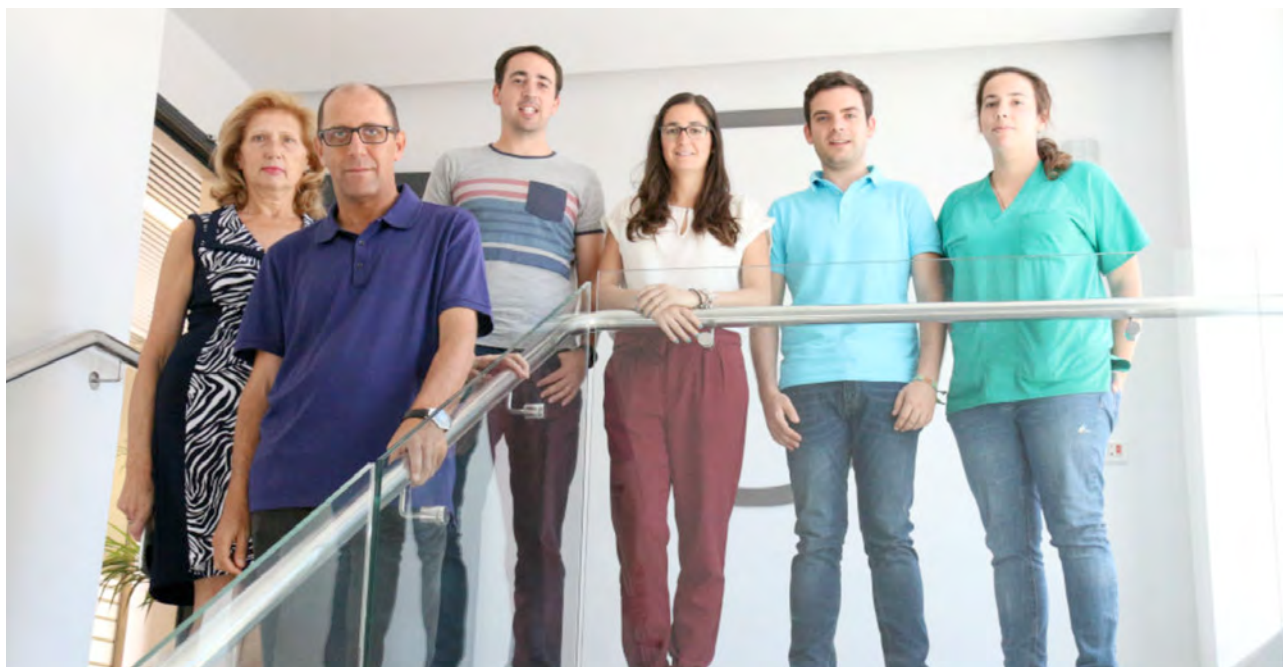
Doctoral candidate: Irene Ruiz Alcántara

Director(s): Jaime Fons Moreno, Francisco Javier Estañ Capell, Susana Ferrando Monleón

Date of the defense: 21/12/2018

Grade: *Sobresaliente "cum laude"*

Group on Translational Research in Ischemic Heart Disease
Consolidated group



Group members

Principal investigator

Vicente Bodí Peris
Hospital. University

PhD researcher

César Ríos Navarro. INCLIVA
José Gavara Doñate. INCLIVA

Collaborating researchers

Clara Bonanad Lozano. Hospital
Amparo Ruiz Saurí. University
Paolo Racugno. Hospital
Ana Díaz Cuevas. University
Víctor Marcos Garcés. Hospital
Mauricio José Pellicer Bañuls. Hospital

Technicians

Elena de Dios Lluch. CIBER
Nerea Pérez Solé. INCLIVA



	R1	R2	R3	R4	STAFF
Researchers by categories	4	2	1	1	3
Researchers financed by competitive public calls or networks	-	-	-	-	1

Strategic aims

- From our research experience from the last years in the clinical and experimental field related to ischemic cardiopathy, our current goal is to focus into a translational approach.
- In 2018 we continued dilucidating the physiological role of the immune dysregulation as well as the macroscopic, microscopic and molecular changes in the fibrotic process after a myocardial infarction by using a swine model. Moreover, we have started clarifying the implication of angiogenesis and new angiogenic biomarkers in the recovery of the microvasculature after a myocardial infarction in animal models and in patients.
- We have also developed new tools to study patients with ST-segment elevation myocardial infarction using cardiac magnetic resonance imaging.

Main lines of research

- Prospective registry of patients with first ST-segment elevation myocardial infarction studied with cardiac magnetic resonance imaging.
- Multicenter registry of patients with myocardial ischemia studied with stress cardiac magnetic resonance imaging.
- Porcine and mice model of experimental myocardial ischemia and myocardial infarction. To achieve a better understanding of the pathophysiology of ischemia, necrosis, fibrosis, angiogenesis, and reperfusion injury and test new novel therapeutic avenues.
- Involvement in several large international multicenter clinical trials in the field of acute coronary syndromes.

• PUBLICATIONS

Number of articles	IF	Average IF
22	179,37	8,153

National collaborations	International collaborations	Corresponding author
14	6	7

SELECTED PUBLICATIONS

1. Gavara J, Rodriguez-Palomares JF, Valente F, Monmeneu JV, Lopez-Lereu MP, Bonanad C, Ferreira-Gonzalez I, Garcia Del Blanco B, Rodriguez-Garcia J, Mutuberria M, de Dios E, Rios-Navarro C, Perez-Sole N, Racugno P, Paya A, Minana G, Canoves J, Pellicer M, Lopez-Fornas FJ, Barrabes J, Evangelista A, Nunez J, Chorro FJ, Garcia-Dorado D, Bodi V. Prognostic value of strain by tissue tracking cardiac magnetic resonance after ST-segment elevation myocardial infarction. *JACC Cardiovascular Imaging*. 2018; 11(10): 1448 - 1457. IF: 10,247
2. Rios-Navarro C, Gavara J, Vidal V, Bonanad C, Racugno P, Bayés-Genís A, Miñana G, Husser O, Oltra R, Nuñez J, Chorro FJ, Bodi V, Ruiz-Sauri A. Characterization and implications of the dynamics of eosinophils in blood and in the infarcted myocardium after coronary reperfusion. *PLoS One*. 2018; 13(10): e0206344. IF: 2,766
3. Miñana G, Núñez J, Bayés-Genís A, Revuelta-López E, Ríos-Navarro C, Núñez E, Chorro FJ, López-Lereu MP, Monmeneu JV, Lupón J, Bodí V. ST2 and left ventricular remodeling after ST-segment elevation myocardial infarction: a cardiac magnetic resonance study. *International Journal of Cardiology*. 2018; 270: 336 - 342. IF: 4,034
4. Larroza A, López-Lereu MP, Monmeneu JV, Gavara J, Chorro FJ, Bodí V, Moratal D. Texture analysis of cardiac cine magnetic resonance imaging to detect nonviable segments in patients with chronic myocardial infarction. *Medical Physics*. 2018; 45(4): 1471 - 1480. IF: 2,884
5. Núñez J, Bayés-Genís A, Zannad F, Rossignol P, Núñez E, Bodí V, Miñana G, Santas E, Chorro FJ, Mollar A, Carratalá A, Navarro J, Górriz JL, Lupón J, Husser O, Metra M, Sanchis J. Long-term potassium monitoring and dynamics in heart failure and risk of mortality. *Circulation*. 2018; 137(13): 1320 - 1330. IF: 18,880

• **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: PI17/01836

Title: *Estudio multidisciplinar de la obstrucción microvascular y su reparación tras un infarto agudo de miocardio: de la arteria coronaria a la microcirculación. Foco en el factor VEGF-A165b*

Principal Investigator: Vicente Bodí Peris

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2018-2020

Total Budget: 99.220€

Reference: PIE15/00013

Title: *A multidisciplinary project to advance in basic mechanisms, diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction*

Principal Investigator: Vicente Bodí Peris

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2018

Total Budget: 589.050€

Title: *Estudio multidisciplinar de la dinámica, mecanismos básicos, diagnóstico y exploración de nuevas oportunidades terapéuticas en la obstrucción microvascular tras infarto agudo de miocardio*

Principal Investigator: Clara Bonanad Lozano

Funding Body: Conselleria de Educación, Cultura y Deporte

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2018-2019

Total Budget: 15.000€

Title: *Dinámica e implicación de la isoforma anti-angiogénica VEGF-A165b en la fisiopatología tras un infarto agudo de miocardio: estudio en pacientes y en un modelo murino de infarto reperfundido*

Principal Investigator: Clara Bonanad Lozano

Funding Body: Sociedad Española de Cardiología

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2018-2019

Total Budget: 20.000€

• **THESIS**

Thesis title: *Estudio de la obstrucción microvascular y el proceso de fibrosis en el infarto de miocardio reperfundido*

Doctoral candidate: Arantxa Hervás Lorente

Director(s): Vicente Bodí Peris, Amparo Ruiz Saurí

Date of the defense: 21/02/2018

Grade: Sobresaliente "cum laude"

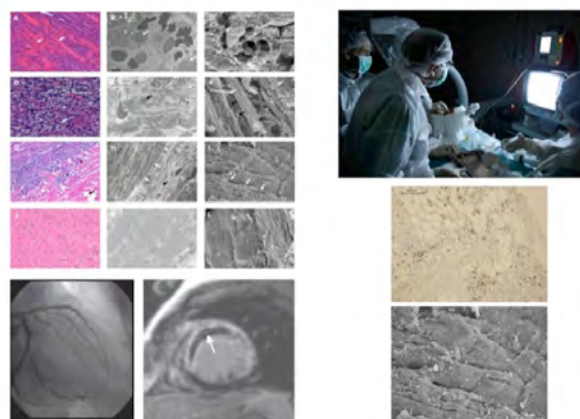
Thesis title: *Evaluación de biopolímeros como superficie de regeneración de tejido dérmico y cardíaco*

Doctoral candidate: Delia Castellano Izquierdo

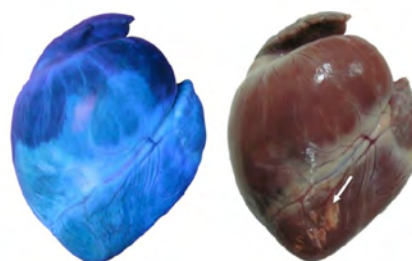
Director(s): Pilar Sepulveda Sanchís, Amparo Ruiz Saurí

Date of the defense: 17/07/2018

Grade: Sobresaliente "cum laude"



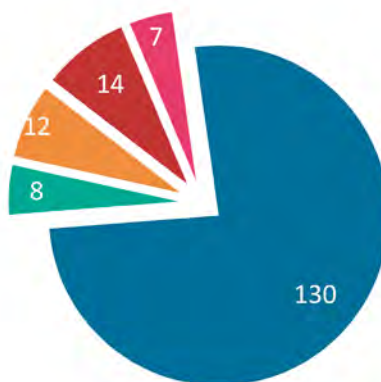
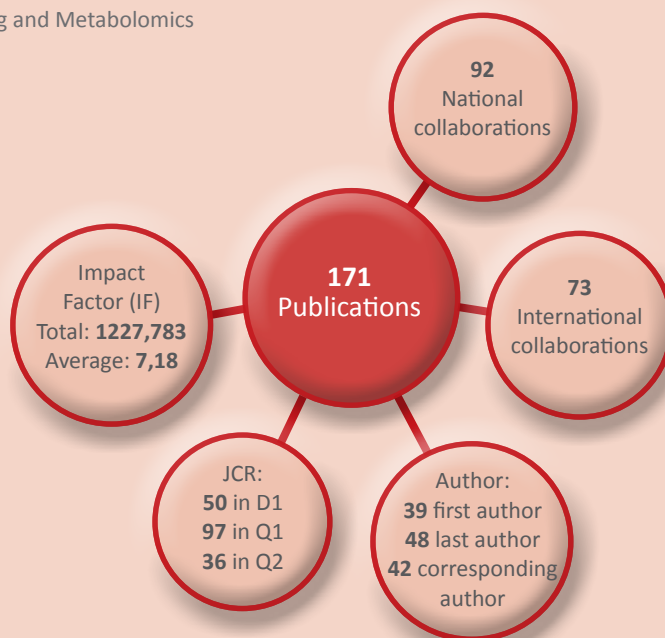
Samples obtained in patients with acute myocardial infarction and in an in vivo model of myocardial infarction. The inflammatory process and the degree of fibrosis can be studied at different levels: macroscopic, microscopic, cellular, gene expression and protein and by magnetic resonance microimaging.



The group has developed a model of acute myocardial infarction in which a transient occlusion is induced in the left anterior descending artery. With these samples, events that occur in the pathophysiology of myocardial regeneration after a heart attack can be simulated.

4.3.2 Oncology Area

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● Original articles ● Letters ● Editorial ● Reviews ● Corrections



Research Group on Histopathology and Tissue Engineering

Consolidated group



Group members

Principal investigator

Carmen Carda Batalla. University

Collaborating researchers

Amando Peydró Olaya. University
 Amparo Ruiz Saurí. University
 María Sancho-Tello Valls. University
 José Javier Martín de Llano. University
 Manuel Mata Roig. University
 Lara Milián Medina. University
 Teresa Sagrado Vives. University
 Miguel Armengot Carceller. University
 Carlos Tejerina Botella. Hospital
 Miguel Puche Torres. Hospital
 Mari Fe Mínguez Rey. Hospital
 Genaro Galán Gil. Hospital
 Antonio Silvestre Muñoz. Hospital
 Francisco Forriol Brocal. Hospital

Antonio Fons Font. University
 Rosa María Cibrián Ortiz de Anda. University
 Santiago Peydró Tomas. University
 Javier Zurriaga Carda. Hospital

PhD researchers

Esperanza Núñez Benito. University
 María Oliver Ferrándiz. University
 Javier Alcácer Fernández-Coronado. University
 Rubén Salvador Clavell. University
 Ignacio Peregrín Nevado. Hospital
 Giovanna Foschini Martínez. Hospital



	R1	R2	R3	R4	STAFF
Researchers by categories	5	3	13	2	2

Strategic aims

- The group obtained funding to continue working on to the line of Tissue Engineering: cartilage and bone regeneration techniques and their application in tracheal pathology.

Main lines of research

Regenerative Medicine:

- Study of articular cartilage regeneration.
- Study of bone regeneration.
- Study of the use of dental pulp cells as precursors in regenerative therapies.
- Study of regeneration of dental and periodontal tissues.

Histopathology:

- Study of ciliary pathology.
- Study of recurrent myocardial infarction and its determinants.
- Study of vascularization in renal tumors.

• PUBLICATIONS

Number of articles	IF	Average IF
15	50,906	3,393

National collaborations	International collaborations	Corresponding author
12	2	1

SELECTED PUBLICATIONS

1. Romero-Gavilan F, Araújo-Gomes N, Sánchez-Pérez AM, García-Arnáez I, Elortza F, Azkargorta M, Martín de Llano JJ, Carda C, Gurruchaga M, Suay J, Goñi I. Bioactive potential of silica coatings and its effect on the adhesion of proteins to titanium implants. *Colloids and Surfaces B: Biointerfaces*. 2018; 162: 316 - 325. IF: 3,997
2. Mérida S, Sancho-Tello M, Almansa I, Desco C, Peris C, Moreno ML, Villar VM, Navea A, Bosch-Morell F. Bevacizumab diminishes inflammation in an acute endotoxin-induced uveitis model. *Frontiers in Pharmacology*. 2018; 9: 649. IF: 3,831
3. Araújo-Gomes N, Romero-Gavilán F, García-Arnáez I, Martínez-Ramos C, Sánchez-Pérez AM, Azkargorta M, Elortza F, Martín de Llano JJ, Gurruchaga M, Goñi I, Suay J. Osseointegration mechanisms: a proteomic approach. *Journal of Biological Inorganic Chemistry*. 2018; 23(3): 459 - 470, 2018. IF: 2,952
4. Araújo-Gomes N, Romero-Gavilán F, Lara-Sáez I, Elortza F,

Azkargorta M, Iloro I, Martínez-Ibañez M, Martín de Llano JJ, Gurruchaga M, Goñi I, Suay J, Sánchez-Pérez AM. Silica-gelatin hybrid sol-gel coatings: a proteomic study with biocompatibility implications. *Journal of Tissue Engineering and Regenerative Medicine*. 2018; 12(7): 1769 - 1779. IF: 4,089

5. Pleguezuelos-Villa M, Mir-Palomo S, Díez-Sales O, Vila Buso O, Ruiz Sauri A, Nacher A. A novel ultradeformable liposomes of Naringin for anti-inflammatory therapy. *Colloids and Surfaces B: Biointerfaces*. 162: 265 - 270. IF: 3,997

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI16/01315

Title: *Sustitutos traqueales epitelizados generados por ingeniería tisular*

Principal Investigator: Manuel Mata Roig and Miguel Armentgot Carceller

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2019

Total Budget: 68.365€

Title: *Cell-free approach for articular cartilage regeneration using autologous and synthetic microspheres as supporting biomaterial (JOINTCART)*

Principal Investigator: José Luis Gómez Ribelles (Carmen Carda, María SanchoTello, Manuel Mata, José Javier Martín de Llano, Lara Milián as collaborating researchers)

Funding Body: Ministerio de Economía y Competitividad

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia and Universidad de Valencia

Duration: 2018-2021

Total Budget: 59.241,25€

Reference: MAT2016-76039-C4-2-R

Title: Diferenciación condrogénica de células cultivadas en interfases eléctricamente activas

Principal Investigator: María Sancho-Tello Valls and Carmen Carda Batalla

Funding Body: Ministerio de Economía y Competitividad

Beneficiary Institution: Universidad de Valencia

Duration: 2017-2019

Total Budget: 151.250€

Reference: SAF2017-85806-R

Title: Mecanismos reguladores de la inflamación y su resolución en enfermedades crónicas articulares y de la piel

Principal Investigator: M^a Carmen Montesinos Mezquita, M^a Luisa Ferrándiz Manglano (Antonio Silvestre Muñoz as collaborating researcher)

Funding Body: Ministerio de Economía y Competitividad

Beneficiary Institution: Universidad de Valencia

Duration: 2018-2020

Total Budget: 182.246€

Reference: INNVAL 10/18/017

Title: Validación mecánica inicial de un nuevo sistema de fijación intramedular para prótesis e internacionalización de la patente

Principal Investigator: José Albelda Vitoria (Antonio Silvestre Muñoz as collaborating researcher)

Funding Body: Agencia Valenciana de la Innovación-AVI Generalitat Valenciana

Beneficiary Institution: Universidad Politécnica de Valencia

Duration: 2018-2019

Total Budget: 60.549€

• THESIS

Thesis title: Estudio de la obstrucción microvascular y el proceso de fibrosis en el infarto de miocardio reperfundido

Doctoral candidate: Arantxa Hervás Lorente

Director(s): Vicente Bodí Peris, Amparo Ruiz Saurí

Date of the defense: 21/02/2018

Grade: Sobresaliente "cum laude"

Thesis title: Soportes tridimensionales biodegradables basados en micropartículas para la regeneración del cartílago articular

Doctoral candidate: Javier Zurriaga Carda

Director(s): Carmen Carda Batalla, Antonio Silvestre Muñoz, María Sancho-Tello Valls

Date of the defense: 23/02/2018

Grade: Sobresaliente "cum laude"

Thesis title: Evaluación de biopolímeros como superficie de regeneración de tejido dérmico y cardíaco

Doctoral candidate: Delia Castellano Izquierdo

Director(s): Pilar Sepulveda Sanchís, Amparo Ruiz Saurí

Date of the defense: 17/07/2018

Grade: Sobresaliente "cum laude"

Thesis title: Estudio del estrés oxidativo en el epitelio nasal cilado de pacientes con discinesia ciliar primaria

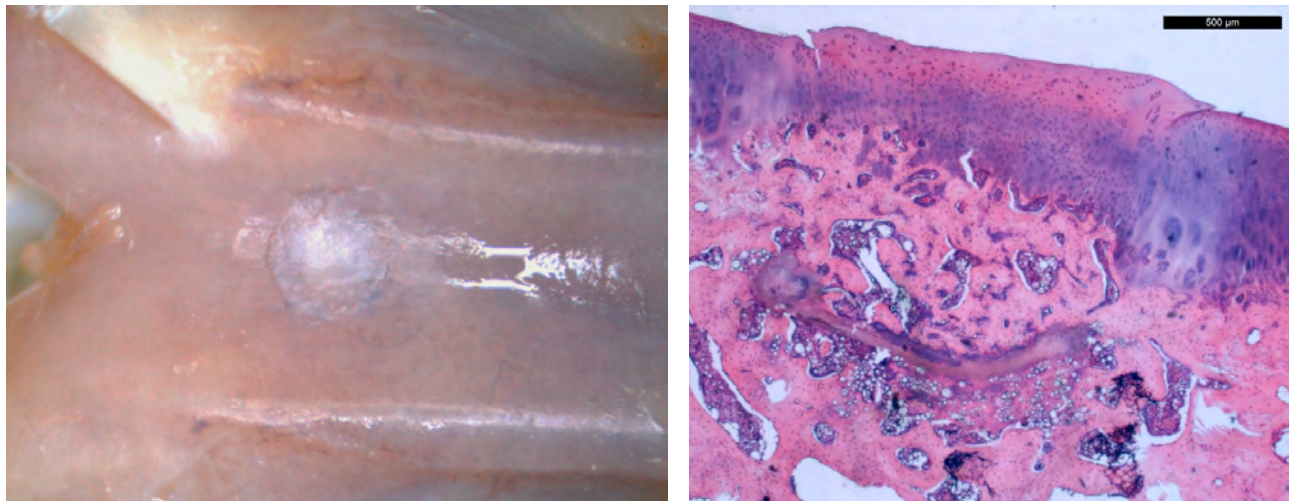
Doctoral candidate: Ana Reula Martín

Director(s): Miguel Armengot Carceller, Amparo Escribano Montaner, Francisco José Dasí Fernández

Date of the defense: 22/11/2018

Grade: Sobresaliente "cum laude"

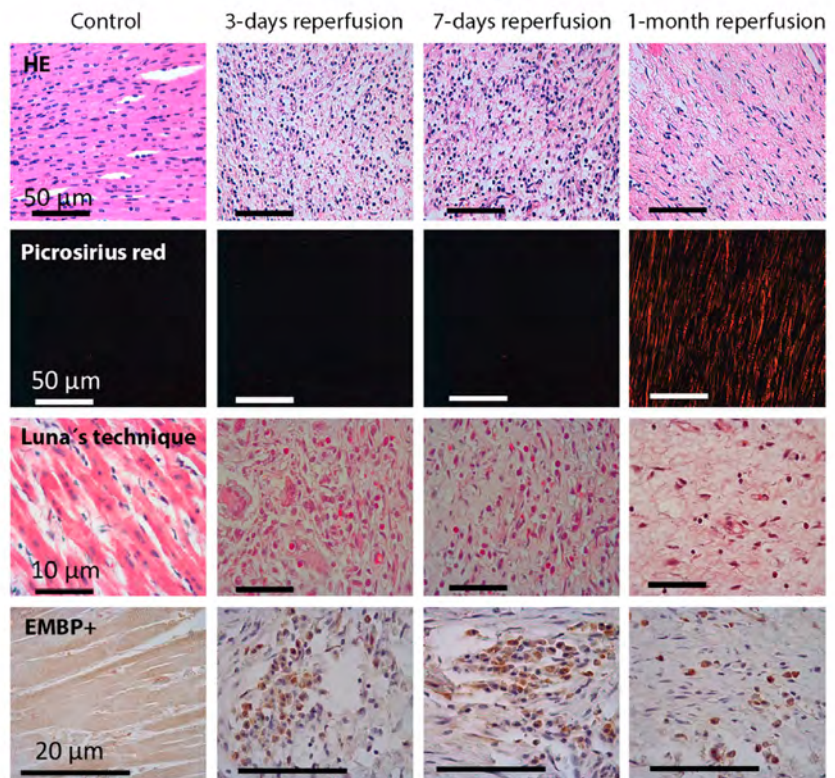
Quality recognition/Award: European PhD



Articular cartilage regeneration *in vivo*.

(a) Macroscopic visualization of the regenerated cartilage three months after implantation of microspheres covered by a membrane.
(b) Microscopic view of an experimental sample showing the regenerated cartilage and the remaining microspheres and membrane located in subchondral bone (*); arrows show the limit of the practiced cartilage defect.

Fig 3. Eosinophil mobilization into the infarcted myocardium in a controlled swine model of reperfused myocardial infarction (MI). (A) Representative images from infarcted tissue isolated from control and three MI groups (90-min of ischemia followed by 3-days, 7-days, and 1-month reperfusion) stained with hematoxylin-eosin (HE) (first panel). The presence of eosinophils was revealed by staining myocardial samples with Luna's technique, specific for eosinophil granules (second panel) and with the eosinophil-specific protein eosinophil major basic protein (EMBP) (third panel). (B) Quantification of eosinophil cells in the myocardial tissue. Images from the infarcted area isolated from the four independent groups were quantified with Image-Pro Plus analysis software. Scoring was performed by a blinded observer unaware of the experimental group. (C) The expression of eosinophil peroxidase (EPO) in the infarcted myocardium at different times of the ischemia and reperfusion process. Data



(mean±SD, n≥4) were analysed by one-way ANOVA analysis followed by Bonferroni test. *P<0.05, ** P<0.01 vs. control.

Research Group on Central Nervous System Tumors
Consolidated group



Group members

Principal investigator

Miguel Cerdá Nicolás
Hospital. University

PhD researchers

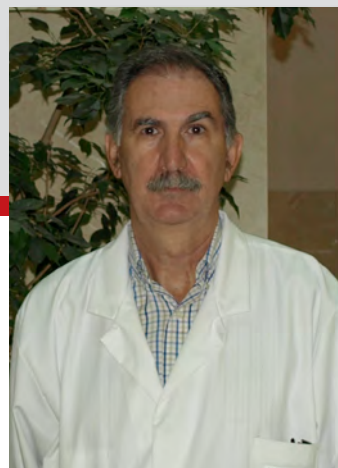
Lisandra Muñoz Hidalgo. University

Collaborating researchers

Rosario Gil Benso. University
Concepción López Ginés. University
Teresa San Miguel Díez. University
Pablo Cerdá Durán. University
Pedro Roldán Badía. University
Javier Megías Vericat. University

Technicians

Ana María Clari Pérez. University
Lara Navarro Cerveró. University



	R1	R2	R3	R4	STAFF
Researchers by categories	-	4	3	1	2

Strategic aims

- Clinical-pathological study of 40 patients affected by primary glioblastoma according to established protocol. Sample collection (formaldehyde, freezing, collection in culture medium) was performed, tissue matrices of the 40 tumors and neuropathological, immunohistochemical and FISH analysis of the matrices were performed according to established methodology:
 - Short-cell cultures and their viability analysis have been performed. Analysis by FISH of EGFR status and freezing of the different passes according to established methodology.
 - The study of the proteomic analysis of the 40 tumors (frozen samples) by Western Blott according to established methodology has been completed.
 - A cell line has been established from a primary culture of glioblastoma. Morphological, genetic and behavioral analysis in vitro (generation of neurospheres, functional migration profiles) have been completed.
- Experimental study:
 - Spheres (neurospheres) have been elaborated from different cell lines and cell cultures of glioblastoma, characterizing and analyzing their behavior.
 - Analysis of cultures subjected to silencing and overexpression by transfection of miRNAs by the lipofection method.
 - Analysis of cell cultures in hypoxia situation, analyzing their characteristics and behavior before silencing and overexpression by transfection of selected miRNAs in hypoxia situation and in the different amplification status of the EGFR.
 - The pilot study of viability and effectiveness of xenotransplantation in nude mice has been completed with the achievement of neoplasias under study.

Main lines of research

- Primary GBM. Amplification status of EGFR and angiogenic/infiltrative phenotype. Molecular networks responsible for tumor modulation and reprogramming processes.
- Role of microRNA in the regulation of EGFR-dependent signalling pathways in high-grade astrocytic gliomas.
- Development of a model for analyzing the modulation of microRNA gene activity in cell cultures of primary GBM and GBM cell lines.
- Development of a model of population analysis and spatial distribution of these neoplasias.
- Metabolomics and microvascular environment characterization of aggressive human glioma by DCE-MRI and genetic study of biopsies.

• PUBLICATIONS

Number of articles	IF	Average IF
1	3,520	3,520

National collaborations	International collaborations	Corresponding author
-	1	-

SELECTED PUBLICATIONS

1. Martínez A, Bono C, Megías J, Yáñez A, Gozalbo D, Gil ML. Systemic candidiasis and TLR2 agonist exposure impact the antifungal response of hematopoietic stem and progenitor

cells. *Frontiers in Cellular and Infection Microbiology*. 2018; 8: 309. IF: 3,520

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PROMETEOII/2015/007

Title: *Papel de los microRNA en la regulación de las vías de señalización dependientes de EGFR en "gliomas astrocitarios de alto grado". Desarrollo de un modelo poblacional de análisis poblacional y de distribución espacial de estas neoplasias*

Principal Investigator: Miguel Cerdá Nicolás

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

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

Duration: 2015-2018

Total Budget: 186.400€



Research Group of Innovative Diagnostic and Therapeutical Developments in Solid Tumours - InDeST
Consolidated group

Team involved in

ciberonc



Group members

Principal investigator

Andrés Cervantes Ruipérez. Hospital. University

Collaborating researchers

Susana Roselló Keranen. Hospital
Maidar Ibarrola Villava. INCLIVA
Josefa Castillo Aliaga. University
Ana Isabel Gil Tébar. INCLIVA
María Peña Chilet. INCLIVA
Jose A. Pérez Fidalgo. Hospital
Amelia Insa Mollá. Hospital
Sheila Zúñiga Trejos. INCLIVA

PhD researchers

Marisol Huerta Álvaro. Hospital
Noelia Tarazona Llaveró. INCLIVA
Gema Bruixola Campos. Hospital
María Carolina Martínez Ciarpaglini. Hospital
Valentina Gambardella. Hospital
Sara Oltra Sanchis. INCLIVA
Marta Llorca Cardeñosa. INCLIVA
Fernanda Gutiérrez Bravo. INCLIVA
Jorge Martín Aranda. CIBER
Federica Papaccio. ESMO
Roberto Tebar Martínez. INCLIVA

Technicians

Cristina Mongort Sanchis. INCLIVA
Francisca Carrasco Bailén. CIBER
Ana Ferrer Martínez. CIBER

Emerging researchers

Gloria Ribas Despuig. INCLIVA
Joan Climent Bataller. INCLIVA
Desamparados Roda Pérez. Hospital
Tania Fleitas Kanonnikoff. Hospital

Nurses

Inma Blasco Blasco. INCLIVA
Celia Martínez Ridaura. INCLIVA
Luna Porta Campos. INCLIVA

Administrative assistant

Gabriela Pérez Garrity. INCLIVA
Elena Jiménez Martí. INCLIVA
Julia Peláez Sánchez. INCLIVA
Jessica Fraile. INCLIVA
Enrique Castelló Moreno. INCLIVA
Ana Vercher Grau. INCLIVA

	R1	R2	R3	R4	STAFF
Researchers by categories	9	13	-	1	13
Researchers financed by competitive public calls or networks	5	4	-	-	1

**Emerging researcher***Gloria Ribas Despuig*

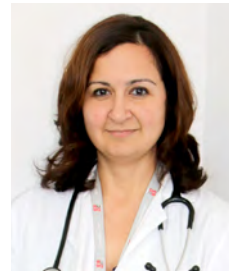
Our scientific interests are based on both the study of genetic susceptibility to complex diseases, such as melanoma, as well as the understanding of genomic deregulation in solid tumors, specially breast cancer in young women. We are also involved in the characterization of genetics and epigenetic alterations that play a role in gastric cancer, specifically in the positive subgroups of Epstein Bar virus and instability.

**Emerging Researcher***Desamparados Roda Pérez*

Our interest is focused in personalized medicine and new drug development with the main objective of identifying new biomarkers of response to targeted agents in advanced solid tumors. We are also focused in a new multiomic characterization of colorectal tumors, using a mathematical model specially in advanced rectal cancers.

**Emerging Researcher***Joan Climent Bataller*

Our research area focuses on exploiting "Systems" approaches for the understanding of cancer susceptibility and its sub-phenotype relationship. The main experience focuses on breast cancer research and covers the use of novel mathematical tools for the comprehensive analysis of gene and gene expression data, with the purpose of optimizing responses to targeted pharmacological treatment.

**Emerging Researcher***Tania Fleitas Kanonnikoff*

Our scientific interests are based on the understanding of the tumor immune microenvironment of Gastric Cancer and the mechanisms of tumor resistance. Moreover, we are also focused on understanding the different GC profiles from EU and Latin-America population through a multi-omic approach thanks to an international collaboration.

Strategic aims

- Our group aims to improve the patient's life through the development of new diagnostic and therapeutic methods. In addition to this main goal, we intend to implement strategies to facilitate the development of precision medicine in solid tumors with innovative therapeutic approaches and provide knowledge on how to approach precision medicine in colorectal and gastric cancer from different points such as molecular classification, the use of predictive biomarkers and new therapeutic approaches.

Main lines of research

- To develop first-in-human Phase I trials of antineoplastic agents with innovative designs.
- To develop liquid biopsies (ctDNA, cmicroRNAs) for early diagnosis, monitoring and the prediction of therapeutic effects in patients with gastro-intestinal malignancies.
- To use the latest technologies to improve our knowledge of the molecular and genetic causes of cancer.
- To implement the use of organoids (3D cell cultures) from patients as functional models, in order to understand the underlying causes of tumorigenesis and to test the appropriateness of the treatments.

• PUBLICATIONS

Number of articles	IF	Average IF
43	406,576	9,455
National collaborations	International collaborations	Corresponding author
11	28	11

• SELECTED PUBLICATIONS

- Dickler MN, Saura C, Richards DA, Krop IE, Cervantes A, Beardard PL, Patel MR, Pusztai L, Oliveira M, Cardenas AK, Cui N, Wilson TR, Stout TJ, Wei MC, Hsu JY, Baselga J. Phase II Study of Taselisib (GDC-0032) in combination with Fulvestrant in patients with HER2-Negative, hormone receptor-positive advanced breast cancer. *Clinical Cancer Research*. 2018; 24(18): 4380 - 4387. IF: 10,199
- Roselló S, Frasson M, García-Granero E, Roda D, Jordá E, Navarro S, Campos S, Esclápez P, García-Botello S, Flor B, Espí A, Masciocchi C, Valentini V, Cervantes A. Integrating downstaging in the risk assessment of patients with locally advanced rectal cancer treated with neoadjuvant chemoradiotherapy: validation of Valentini's Nomograms and the neoadjuvant rectal score. *Clinical Colorectal Cancer*. 2018; 17(2): 104 - 112.e2. IF: 3,861
- Jordan K, Aapro M, Kaasa S, Ripamonti CI, Scotté F, Strasser F, Young A, Bruera E, Herrstedt J, Keefe D, Laird B, Walsh D, Douillard JY, Cervantes A. European Society for Medical Oncology (ESMO) position paper on supportive and palliative care. *Annals of Oncology*. 2018; 29(1): 36 - 43. IF: 13,926
- Sobrero A, Grothey A, Iveson T, Labianca R, Yoshino T, Taieb J, Maughan T, Buyse M, André T, Meyerhardt J, Shields AF, Souglakos I, Douillard JY, Cervantes A. The hard road to data interpretation: 3 or 6 months of adjuvant chemotherapy for patients with stage III colon cancer?. *Annals of Oncology*. 2018; 29(5): 1099 - 1107. IF: 13,926
- Vogel A, Cervantes A, Chau I, Daniele B, Llovet J, Meyer T, Nault JC, Neumann U, Ricke J, Sangro B, Schirmacher P, Verslype C, Zech CJ, Arnold D, Martinelli E, ESMO Guidelines Committee. Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. 2018; 29(4): iv238 - iv255. IF: 13,926

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: IntraColor

Title: INTRACOLOR - Translational research on human tumour heterogeneity to overcome recurrence and resistance to therapy

Principal Investigator: Andrés Cervantes Ruipérez

Funding Body: European Commission (ERANET)

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2018

Total Budget: 29.645€

Reference: MoTriColor

Title: Molecularly guided trials with specific treatment strategies in patients with advanced newly molecular defined subtypes of colorectal cancer (MoTriColor)

Principal Investigator: Josep Tabernero (Andrés Cervantes as collaborating researcher)

Funding Body: European Commission (H2020)

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2015-2019

Total budget: 271.424€

Reference: PINV15-156

Title: Proyecto multicéntrico de determinación del perfil mutacional de pacientes con cáncer de tumores sólidos para guiar la estrategia terapéutica hacia una medicina personalizada

Principal Investigator: Andrés Cervantes Ruipérez

Funding Body: CONACYT Paraguay

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2017-2018

Total Budget: 56.000€

Reference: PINV15-149

Title: Proyecto multicéntrico de formación multidisciplinar en cáncer y aplicación de la Historia Clínica Electrónica (HCE) con el fin de integrar los datos clínico-moleculares y orientar la estrategia terapéutica

Principal Investigator: Tania Fleitas Kanonnikoff

Funding Body: CONACYT Paraguay

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2017-2018

Total Budget: 24.660€

Reference: PI16/00393

Title: *De la genómica del cáncer a la inmuno-oncología. Búsqueda de biomarcadores de respuesta a la inmunoterapia anti-PD1/PDL1 en cáncer mediante una aproximación de biología de sistemas*

Principal Investigator: Joan Climent Bataller

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2019

Total Budget: 98.615€

Reference: PI16/00395

Title: *Caracterización genómica y funcional del cáncer gástrico VEB+/IMS+*

Principal Investigator: Gloria Ribas Despuig

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2019

Total Budget: 98.615€

Reference: PI15/02180

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

Principal Investigator: Andrés Cervantes Ruipérez

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total budget: 80.465€

Reference: PT17/0017/0003

Title: *Clinical Research and Trials Platform*

Principal Investigator: Andrés Cervantes Ruipérez

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2020

Total budget: 266.475€

Reference: CB16/12/00473

Title: *Centro de Investigación Biomédica en Red Cáncer (CIBERonc)*

Principal Investigator: Andrés Cervantes Ruipérez

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-

Reference: INNACC00/18/001

Title: *Acciones complementarias de impulse y fortalecimiento de la innovación*

Principal Investigator: Andrés Cervantes Ruipérez

Funding Body: *AVI (Agencia Valenciana de Innovación) – Generalitat Valenciana*

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

Duration: 2018

Title: *Estudio de los factores pronósticos y predictores de resistencia a tratamientos diana en cáncer colorrectal derecho e izquierdo utilizando organoides como modelo preclínico de enfermedad*

Principal Investigator: Andrés Cervantes Ruipérez

Funding Body: *Fundación Merck Salud*

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

Duration: 2017-2018

Total Budget: 30.000€

Title: *Papel de la vía p53-Aurora kinasa en la resistencia a platino e inhibidores del PARP en cáncer de mama triple negativo y cáncer seroso de ovario de alto grado*

Principal Investigator: Alejandro Pérez Fidalgo

Funding Body: *Sociedad Española de Oncología Médica (SEOM)*

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

Duration: 2018-2019

Title: *Nuevos biomarcadores en cáncer de recto: relevancia del perfil inmunológico en el pronóstico de la enfermedad*

Principal Investigator: Desamparados Roda Pérez

Funding Body: *Sociedad Española de Oncología Médica (SEOM)*

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

Duration: 2017-2018

Total Budget: 30.000€

- **THESIS**

Thesis Title: *Mecanismos de resistencia primaria y secundaria a tratamiento antiher2 en cáncer gástrico HER2 positivo*

Doctoral candidate: Valentina Gambardella

Director(s): Andrés Cervantes Ruipérez, Josefa Castillo Aliaga

Date of the defense: 13/03/2018

Grade: *Sobresaliente "cum laude"*

Quality recognition/Award: European PhD

Thesis Title: *Expresión de microRNAs en las zonas de transición epitelio mesenquimal en el carcinoma colorrectal como factor inmunomodulador y pronóstico. Estudio clínico patológico*

Doctoral candidate: María Carolina Martínez Ciarpaglini

Director(s): Andrés Cervantes Ruipérez, Samuel Navarro Fos, Antonio Ferrández Izquierdo

Date of the defense: 30/10/2018

Grade: *Sobresaliente "cum laude"*

Thesis Title: *Nueva localización y función de la calpaína 2 en el nucleolo de células de cáncer colorrectal en la biogénesis ribosomal: efecto del estado de KRAS*

Doctoral candidate: Marcelino Telechea Fernández

Director(s): Andrés Cervantes Ruipérez, Elena Ruiz García-Trevijano

Date of the defense: 09/11/2018

Grade: *Sobresaliente "cum laude"*



Research Group on Breast Cancer Biology

Consolidated group

Team involved in

ciberonc



Group members

Principal investigator

Ana Lluch Hernández. Hospital. University

Collaborating researchers

Begoña Bermejo De Las Heras. Hospital

Octavio Burgues Gasión. Hospital

Estela Contel Martín. INCLIVA

Isabel Catoira Domenech. INCLIVA

Patricia Martínez Belenguer. INCLIVA

Antonio Millet Serrano. Hospital

Begoña Pineda Merlo. INCLIVA

Eduardo Tormo Martín. CIBERONC

María Teresa Martínez Martínez. Hospital

Cristina Hernando Meliá. Hospital

Marcos Adrianzen Vargas. Hospital

Gemma Bellver Lobato. Hospital

Elvira Buch Villa. Hospital

Juan Miguel Cejalvo Andújar. Hospital

Ana Julve Parreño. Hospital

Liria Terrádez Mas. Hospital

Emerging researchers

Isabel Chirivella González. Hospital

Pilar Eroles Asensio. INCLIVA

PhD researchers

Paula Cabello Navarro. INCLIVA

Anna Adam-Artigues. INCLIVA

Iris Garrido Cano. INCLIVA

Birlipta Pattanayak. INCLIVA

Technician

Elisa Alonso Yuste. INCLIVA

Administrative assistant

Yolanda De La Cruz Robles. INCLIVA

	R1	R2	R3	R4	STAFF
Researchers by categories	7	10	2	1	5
Researchers financed by competitive public calls or networks	4	2	-	-	-



Strategic aims

Resistance to treatments:

- Evaluation of the recent insights into the development of preclinical trastuzumab-resistant HER2+ breast cancer models.

Metastatic setting:

- Identification of MSK1 as regulator of luminal cell differentiation and metastatic dormancy in ER+ breast cancer.
- Multicenter phase II study of lurbinectedin in BRCA-mutated and unselected metastatic advanced breast cancer and biomarker assessment substudy .
- Analysis of postmastectomy radiation therapy in women with T1-T2 tumors and 1 to 3 positive lymph nodes.

ER+ breast cancer:

- Evaluation of the outcomes of single versus double hormone receptor-positive breast cancer.
- Description that the ER+ breast cancers resistant to prolonged neoadjuvant letrozole exhibit an E2F4 transcriptional program sensitive to CDK4/6 inhibitors.
- Design of adjuvant endocrine therapy for premenopausal breast cancer.

Breast cancer in very young women:

- Identification of miR124-2 as a survival biomarker by methylation deregulation of its promoters.
- Review of breast cancer in pregnant patients.

Prognostic and prediction:

- Prognostic role for the derived neutrophil-to-lymphocyte ratio in early breast cancer.
- Evaluation of the pathologic complete response rate to neoadjuvant chemotherapy in triple negative breast cancer subtypes.
- Study of the incidence, characteristics, and prevention of the alopecia following adjuvant docetaxel.

Main lines of research

- Study of methylation as a prognostic and predictive factor of neoadjuvant treatment in triple negative breast cancer.
- Evaluation of microRNAs and mRNAs differentially expressed after chemotherapy treatment.
- Involvement of miRNAs in breast cancer processes.
- Role of tumor heterogeneity and dynamic reprogramming of tumor cell resistance to anti-HER2 therapy.
- Evaluation of the involvement of stem cells and epithelial mesenchymal transition in the mechanisms of resistance to treatment in HER2 + breast cancer.
- Primary and secondary resistance in HER2 + breast cancer: search for new treatments.
- Interaction between estrogen receptors, tumor angiogenesis and breast cancer metabolism.
- Molecular and Clinical characterization of breast tumors from very young women.



Emerging Researcher

Isabel Chirivella González

The research line suggests a possible relation between mammographic density, as a genetic susceptibility marker and the risk to suffer breast cancer in women with a mutation in BRCA (hereditary breast cancer). We also have a project to evaluate a set of endometrial cancer risk markers in Lynch syndrome patients.



Emerging Researcher

Pilar Eroles Asensio

The lines of research aim at deepening the knowledge of some of the molecular subtypes of breast cancer, especially HER2+ and triple negative, through studies of expression and epigenetic changes (microRNAs, methylation) to decipher the possible mechanisms of resistance to current treatments. We intend to develop new strategies for diagnostic

and therapeutic intervention to reverse the identified resistance, based on combinations with other biologic agents and the use of predictive biomarkers of resistance.

• PUBLICATIONS

Number of articles	IF	Average IF
22	235,078	10,684
National collaborations	International collaborations	Corresponding author
9	13	2

SELECTED PUBLICATIONS

- Pernas S, Martin M, Kaufman PA, Gil-Martin M, Gomez Pardo P, Lopez-Tarruella S, Manso L, Ciruelos E, Perez-Fidalgo JA, Hernando C, Ademuyiwa FO, Weilbaecher K, Mayer I, Pluard TJ, Martinez Garcia M, Vahdat L, Perez-Garcia J, Wach A, Barker D, Fung S, Romagnoli B, Cortes J. Balixafortide plus eribulin in HER2-negative metastatic breast cancer: a phase 1, single-arm, dose-escalation trial. *Lancet Oncology*. 2018; 19(6): 812 - 824. IF: 36,418
- Gianni L, Mansutti M, Anton A, Calvo L, Bisagni G, Bermejo B, Semiglazov V, Thill M, Chacon JI, Chan A, Morales S, Alvarez I, Plazaola A, Zambetti M, Redfern AD, Dittrich C, Dent RA, Magazzù D, De Fato R, Valagussa P, Tusquets I. Comparing Neoadjuvant Nab-paclitaxel vs Paclitaxel both followed by anthracycline regimens in women with ERBB2/HER2-Negative breast cancer-The Evaluating Treatment with Neoadjuvant Abraxane (ETNA) Trial: a randomized phase 3 clinical trial. *JAMA Oncology*. 2018; 4(3): 302 - 308. IF: 20,871
- Colleoni M, Luo W, Karlsson P, Chirgwin J, Aebi S, Jerusalem G, Neven P, Hitre E. Extended adjuvant intermittent letrozole versus continuous letrozole in postmenopausal women with breast cancer (SOLE): a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncology*. 2018; 19(1): 127 - 138. IF: 36,418
- Cruz C, Llop-Guevara A, Garber JE, Arun BK, Pérez Fidalgo JA, Lluch A, Telli ML, Fernández C, Kahatt C, Galmarini CM, Soto-Matos A, Alfaro V, Pérez de la Haza A, Domchek SM, Antolin S, Vahdat L, Tung NM, Lopez R, Arribas J, Vivancos A, Baselga J, Serra V, Balmaña J, Isakoff SJ. Multicenter phase ii study of Lurbinectedin in BRCA-Mutated and unselected metastatic advanced breast cancer and biomarker assessment substudy. *Journal of Clinical Oncology*. 2018; 36(31): 3134 - 3143. IF: 26,303
- Gawrzak S, Rinaldi L, Gregorio S, Arenas EJ, Salvador F, Urosevic J, Figueras-Puig C, Rojo F, Del Barco Barrantes I, Cejalvo JM, Palafox M, Guiu M, Berenguer-Llargo A, Symeonidi A, Bellmunt A, Kalafatovic D, Arnal-Estapé A, Fernández E, Müllauer B, Groeneveld R, Slobodnyuk K, Stephan-Otto Attolini C, Saura C, Arribas J, Cortes J, Rovira A, Muñoz M, Lluch A, Serra V, Albanell J, Prat A, Nebreda AR, Benitah SA, Gomis RR. MSK1 regulates luminal cell differentiation and metastatic dormancy in ER + breast cancer. *Nature Cell Biology*. 2018; 20(2): 211 - 221. IF: 19,064

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: COST Action CA15204

Title: *European Platform for Outcomes Research into Perioperative Interventions during Surgery for Cancer*

Principal Investigator: Pilar Eroles Asensio

Funding Body: *European Commission*

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

Duration: 2016-2020

Reference: PI15/01617

Title: *Papel de la heterogeneidad tumoral y la reprogramación dinámica de la célula tumoral en la resistencia a anticuerpos antiHER2 en cáncer de mama HER2 positivo*

Principal Investigator: Ana Lluch Hernández

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total Budget: 182.407,50€

Reference: CB16/12/00453

Title: *CIBER Cáncer de mama (CIBERonc)*

Principal Investigator: Ana Lluch Hernández

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-

Reference: IMIDTA/2016/75

Title: *Brecan Risk: Nuevo sistema de estratificación de riesgo y detección precoz basados en marcadores moleculares en cáncer de mama*

Principal Investigator: Ana Lluch Hernández

Funding Body: *Instituto para la Acreditación y Evaluación de las Prácticas Sanitarias (INACEPS)*

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

Duration: 2017-2018

Total Budget: 37.524€

Title: *Análisis del papel de la vía aurora kinasa-p53 como potencial marcador predictivo y dianas terapéuticas en cáncer de mama triple negativo*

Principal Investigator: Begoña Pineda Merlo

Funding Body: *Fundación de la Mutua Madrileña*

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

Duration: 2018-2019

Title: *Papel de la vía p53-Aurora kinasa en la resistencia a platino e inhibidores del PARP en cáncer de mama triple negativo y cáncer seroso de ovario de alto grado*

Principal Investigator: Alejandro Pérez Fidalgo

Funding Body: *Sociedad Española de Oncología Médica*

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

Duration: 2018-2019

• THESIS

Thesis title: *Nuevas vías moleculares implicadas en los mecanismos de resistencia primaria y adquirida en cáncer de mama HER2 positivo*

Doctoral candidate: Juan Miguel Cejalvo Andújar

Director(s): Ana Lluch Hernández, Pilar Eroles Asensio, José Alejandro Pérez Fidalgo

Date of the defense: 13/03/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Identificación de TRIM29 localizado en la región cromosómica 11q23.3 como biomarcador de resistencia a doxorubicina y proliferación celular en cáncer de mama triple negativo*

Doctoral candidate: Raimundo Cervera Vidal

Director(s): Joan Climent Bataller, Ana Lluch Hernández

Date of the defense: 29/06/2018

Grade: *Sobresaliente "cum laude"*

➤ **Research Group on Skin Cancer**
Consolidated group



Group members

Principal investigator

José Carlos Monteagudo Castro
Hospital. University

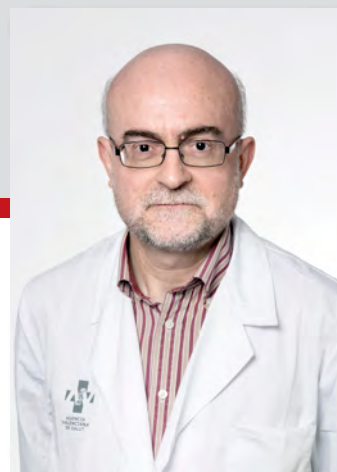
Collaborating researchers

David Ramos Soler. Hospital. University
José M^a Martín Hernández. Hospital
Liria Terrádez Más. Hospital
Inés Escandell González. Hospital
Jaime Agustí Martínez. Hospital

Anaïs Moscardó Navarro. Hospital
Bárbara Vázquez Fernández. Hospital

PhD researchers

Beatriz Sánchez Sendra. University
José Francisco González Muñoz. INCLIVA



	R1	R2	R3	R4	STAFF
Researchers by categories	4	1	2	1	2

Strategic aims

- Transcriptomic identification of miRNA-205 target genes potentially involved in metastasis and survival of cutaneous malignant melanoma.
- Search for a genetic and/or epigenetic signature which permit a more precise diagnosis and prediction of the metastatic potential of ambiguous melanocytic lesions, and particularly of spitzoid tumors.
- Identification of circulating miRNAs which may serve as prognostic and/or staging biomarkers in patients with primary cutaneous melanoma.

Main lines of research

- Prognostic value of intratumoral and circulating microRNAs in melanoma tumor progression and clinical outcome.
- Improvement by circulating biomarkers of melanoma staging schedule at the time of diagnosis.
- Machine learning in the study of whole slide digitized images of spitzoid melanocytic tumors for diagnosis and prognosis improvement.
- Evaluation of long- and short-term morphological changes in melanocytic nevi in a digitized dermoscopic unit.

• PUBLICATIONS

Number of articles	IF	Average IF
18	39,907	2,217

National collaborations	International collaborations	Corresponding author
13	4	7

SELECTED PUBLICATIONS

1. Zaballos P, Gómez-Martín I, Martín JM, Bañuls J. Dermoscopy of adnexal tumors. *Dermatologic Clinics*. 2018; 36(4): 397 - 412. IF: 3,214
2. Roig J, Saiz ML, Galiano A, Trelis M, Cantalapiedra F, Monteagudo C, Giner E, Giner RM, Recio MC, Bernal D, Sánchez-Madrid F, Marcilla A. Extracellular vesicles from the helminth *fasciola hepatica* prevent DSS-induced acute ulcerative colitis in a t-lymphocyte independent mode. *Frontiers in Microbiology*. 2018; 9: 1036. IF: 4,019
3. Sánchez-Sendra B, Martínez-Ciarpaglini C, González-Muñoz JF, Murgui A, Terrádez L, Monteagudo C. Downregulation of intratumoral expression of miR-205, miR-200c and miR-125b in primary human cutaneous melanomas predicts shorter survival. *Scientific Reports*. 2018; 8(1): 17076. IF: 4,122
4. Martínez-Ciarpaglini C, Agustí J, Alvarez E, Hueso L, Terrádez

L, Monteagudo C. h-caldesmon immunoreactivity in atypical fibroxanthoma: implications for the differential diagnosis. *Pathology*. 2018; 50(3): 358 - 361. IF: 3,068

5. Cerrillo E, Moret I, Iborra M, Ramos D, Busó E, Tortosa L, Sáez-González E, Nos P, Beltrán B. Alpha-defensins (a-Def5) in Crohn's disease: decrease of ileal a-Def 5 via permanent methylation and increase in plasma a-Def 1-3 concentrations offering biomarker utility. *Clinical and Experimental Immunology*. 2018; 192(1): 120 - 128. IF: 3,542

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI17/02019

Title: *Estudio del valor del patrón de metilación y variaciones del número de copias del genoma para determinar el grado de malignidad en los tumores melanocíticos de potencial maligno incierto*

Principal Investigator: José Carlos Monteagudo Castro

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total Budget: 99.220€

Reference: PROMETEOII/2015/009

Title: *Análisis transcriptómico y proteómico de los cambios condicionados por miRNAs en el melanoma cutáneo: identificación de nuevos biomarcadores proteicos con significación pronóstica*

Principal Investigator: José Carlos Monteagudo Castro

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

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

Duration: 2015-2018

Total Budget: 167.010€

- **THESIS**

Thesis Title: *Valor pronóstico de la presencia de un componente tumoral indiferenciado ("tumor budding") en pacientes con carcinoma vesical músculo-invasivo*

Doctoral candidate: Laura Lorenzo Soriano

Director(s): David Ramos Soler

Date of the defense: 09/11/2018

Grade: *Sobresaliente "cum laude"*

Translational Research Group on Pediatric Solid Tumors
Consolidated group

Team involved in
ciberonc



Group members

Principal investigator

Samuel Navarro Fos
Hospital. University

Collaborating researchers

Rosa Noguera Salvá. University
Antonio Llombart Bosch. University
Ana Pilar Berbegall Beltrán. CIBERONC
Irene Tadeo Cervera. University
Esther Gamero Sandemetrio. CIBERONC
M^a Amparo López Carrasco. INCLIVA
Aitor Carretero Martínez. INCLIVA
Víctor Zúñiga Zaragoza. Generalitat Cataluña

PhD researcher

Susana Martín Vañó. INCLIVA
Maite Blanquer Maceiras. CIBERONC
Ezequiel Monferrer Garzarán. INCLIVA
Rebeca Brugos Panadero. INCLIVA



	R1	R2	R3	R4	STAFF
Researchers by categories	3	6	-	3	1
Researchers financed by competitive public calls or networks	1	2	-	-	-

Strategic aims

- Genomic heterogeneity in neuroblastoma (NB), especially in MYCN amplification.
- Xenotransplant models of NB.
- Importance of extracellular matrix and vascularization in NB.
- Morphological and molecular analysis of neuroblastic and malignant infantile skeletal tumours.

Main lines of research

- Genetic analysis in neuroblastoma. At the European level we participate in the establishment of a uniform nomenclature, and standard practices and quality validation studies, essential to obtain and maintain high quality in genetic results used for therapeutic stratification.
- Identification of new genetic factors with prognostic value in neuroblastic and malignant infantile skeletal tumors.
- Histopathologic studies of the expression of diagnostic and prognostic markers in solid pediatric tumors.
- Tumor microenvironments in neuroblastoma – research findings.
- Preclinical models. Obtaining and characterizing cell lines in vivo and in vitro from fresh neuroblastic and malignant infantile skeleton tumor material.

• PUBLICATIONS

Number of articles	IF	Average IF
15	61,554	4,103
National collaborations	International collaborations	Corresponding author
5	10	4

SELECTED PUBLICATIONS

1. Tadeo I, Gamero-Sandemetro E, Berbegall AP, Gironella M, Ritort F, Cañete A, Bueno G, Navarro S, Noguera R. Lymph microvascularization as a prognostic indicator in neuroblastoma. *Oncotarget*. 2018; 9(40): 26157 - 26170. IF: 5,168
2. Gambera S, Abarrategi A, Rodríguez-Milla MA, Mulero F, Menéndez ST, Rodríguez R, Navarro S, García-Castro J. Role of activator protein-1 complex on the phenotype of human osteosarcomas generated from mesenchymal stem cells. *Stem Cells*. 2018; 36(10): 1487 - 1500. IF: 5,587
3. Berbegall Beltran A, Bogen D, Pötschger U, Beiske K, Bown N, Combaret V, Defferrari R, Jeison M, Mazzocco K, Varesio L, Vicha A, Ash S, Castel V, Coze C, Ladenstein R, Owens C, Papadakis V, Ruud E, Amann G, Sementa A, Navarro Fos S, Ambros P, Noguera Salva R, Ambros I. Heterogeneous MYCN amplification in neuroblastoma: a SIOP Europe Neuroblastoma Study. *British Journal of Cancer*. 2018; 118(11): 1502 - 1512. IF: 5,922
4. Braekeveldt N, von Stedingk K, Fransson S, Martinez-Monleon A, Lindgren D, Axelson H, Levander F, Willfors J, Hansson K, Øra I, Backman T, Börjesson A, Beckman S, Esfandyari J, Berbegall AP, Noguera R, Karlsson J, Koster J, Martinsson T, Gisselsson D, Pålman S, Bexell D. Patient-derived xenograft models reveal intratumor heterogeneity and temporal stability in neuroblastoma. *Cancer Research*. 2018; 78(20): 5958 - 5969. IF: 9,130
5. Depuydt P, Boeva V, Hocking TD, Cannoodt R, Ambros IM, Ambros PF, Asgharzadeh S, Attiyeh EF, Combaret V, Defferrari R, Fischer M, Hero B, Hogarty MD, Irwin MS, Koster J, Kreissman S, Ladenstein R, Lapouble E, Laureys G, London WB, Mazzocco K, Nakagawara A, Noguera R, Ohira M, Park JR, Pötschger U, Theissen J, Tonini GP, Valteau-Couanet D, Varesio L, Versteeg R, Speleman F, Maris JM, Schleiermacher G, De Preter K. Genomic amplifications and distal 6q loss: novel markers for poor survival in high-risk neuroblastoma patients. *JNCI-Journal of the National Cancer Institute*. 2018; 110 (10): 1084 - 1093. IF: 11,238

• **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: PI17/01558

Title: *Identificación y validación de nuevas terapias, modelos preclínicos y marcadores de respuesta*

Principal Investigator: Rosa Noguera Salvá

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 123.420€

Reference: PI14/01008

Title: *Estudio de la biotensegridad en los tumores neuroblásticos*

Principal Investigator: Rosa Noguera Salvá

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2015-2018

Total budget: 122.815€

Reference: CB16/12/00484

Title: *Centro de Investigación Biomédica en Red Cáncer (CIBER-Ronc)*

Principal Investigator: Rosa Noguera Salvá

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Universidad de Valencia*

Duration: 2017-

Reference: FAECC2015

Title: *Búsqueda de dianas terapéuticas en los puntos de contacto de la célula tumoral en el neuroblastoma infantil con su matriz extracelular*

Principal Investigator: Rosa Noguera Salvá

Funding Body: *Asociación Española Contra el Cáncer (AECC)*

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

Duration: 2015-2018

Total budget: 150.000€

Title: *Espacio intercelular: Bioimagen microscópica*

Principal Investigator: Rosa Noguera Salvá

Funding body: *Fundación Neuroblastoma*

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

Duration: 2017-2018

Total budget: 50.000€

Title: *Identification and validation of targeted and immune therapies, preclinical models and markers of therapeutic response in peripheral neuroblastic tumours*

Principal Investigator: Rosa Noguera Salvá

Funding body: *Asociación de familiares y amigos de pacientes con Neuroblastoma*

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

Duration: 2017-2019

Total budget: 203.000€

Title: *Impacto de las alteraciones en número de copias en el pronóstico de los pacientes de Sarcoma de Ewing. Validación prospectiva de las alteraciones en cr 1q y cr 16q como biomarcadores*

Principal Investigator: Rosa Noguera Salvá

Funding body: *Fundación CRIS*

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

Duration: 2017-2018

Total budget: 60.000€

• **THESIS**

Thesis title: *Análisis microscópico digital del infiltrado inmune en neuroblastoma. Impacto pronóstico*

Doctoral candidate: Víctor Zúñiga Zaragoza

Director(s): Rosa Noguera Salvá

Date of the defense: 22/10/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Expresión de microRNAs en las zonas de transición epitelio mesenquimal en el carcinoma colorrectal como factor inmunomodulador y pronóstico. Estudio clínico patológico*

Doctoral candidate: María Carolina Martínez Ciarpaglini

Director(s): Andrés Cervantes Ruipérez, Samuel Navarro Fos, Antonio Ferrández Izquierdo

Date of the defense: 30/10/2018

Grade: *Sobresaliente "cum laude"*

Research Group on Hematopoietic Transplantation
Consolidated group



Group members

Principal investigator

Carlos Solano Vercet
 Hospital. University

Eliseo Alejandro Albert Vicent. Hospital
 Rafael Hernani Morales. Hospital
 Ana Miralles. Whitehead

Collaborating researchers

María José Remigia Pellicer. Hospital
 Rosa Goterris Viciedo. Hospital
 David Navarro Ortega. Hospital. University
 Joana Hernández Martín. INCLIVA
 Paula Amat Martínez. Hospital
 Estela Giménez Quiles. Hospital
 Ariadna Pérez Martínez. Hospital

Technicians

Iván Martín Castillo. INCLIVA
 Eva Villamón Ribate. INCLIVA



	R1	R2	R3	R4	STAFF
Researchers by categories	3	5	-	2	3
Researchers financed by competitive public calls or networks	-	-	-	-	1

Strategic aims

- Translational research on biology and treatment of graft-versus-host disease after allogeneic transplantation of hematopoietic progenitor cells.
- Infection and immune reconstitution after haematopoietic transplant.
- Creation of a Multidisciplinary Unit of Advanced Therapies-CART in *Hospital Clínico Universitario de Valencia* - INCLIVA.

Main lines of research

- Translational research on complications of allogeneic hematopoietic transplantation: graft-versus-host disease.
- Infection and immune reconstitution after hematopoietic transplantation.
- Translational research of alloreactivity in the context of new modalities of allogeneic transplantation from compatible and incompatible alternative donors (haploidentical transplant).
- Clinical application of gene and cellular therapy using CAR-T and other immune effector cells.

• PUBLICATIONS

Number of articles	IF	Average IF
23	133,233	5,792

National collaborations	International collaborations	Corresponding author
14	7	13

SELECTED PUBLICATIONS

1. Winston DJ, Mullane KM, Cornely OA, Boeckh MJ, Brown JW, Pergam SA, Trociukas I, Zák P, Craig MD, Papanicolaou GA, Velez JD, Panse J, Hurtado K, Fernsler DA, Stek JE, Pang L, Su SC, Zhao Y, Chan ISF, Kaplan SS, Parrino J, Lee I, Popmihajlov Z, Annunziato PW, Arvin A, V212 Protocol 001 Trial Team. Inactivated varicella zoster vaccine in autologous haemopoietic stem-cell transplant recipients: an international, multi-centre, randomised, double-blind, placebo-controlled trial. *Lancet*. 2018; 391(10135): 2116 - 2127. IF: 53,254
2. Piñana JL, Perez-Pitarch A, Guglieri-Lopez B, Giménez E, Hernandez-Boluda JC, Terol MJ, Ferriols-Lisart R, Solano C, Navarro D. Sirolimus exposure and the occurrence of cytomegalovirus DNAemia after allogeneic hematopoietic stem cell transplantation. *American Journal of Transplantation*. 2018; 18(12): 2885 - 2894. IF: 4,497
3. Giménez E, Solano C, Vinuesa V, Hernández-Boluda JC, Albert E, Pérez A, Piñana JL, Navarro D. Cytomegalovirus DNAemia burden and mortality following allogeneic hema-

topoietic stem cell transplantation: an area under a curve-based investigational approach. *Clinical Infectious Diseases*. 2018; 67(5): 805 - 807. IF: 9,117

4. Aguilar G, Navarro D. The culpability of respiratory viruses in pneumonia-related acute respiratory failure: the jury is still out. *Chest*. 2018; 154(1): 223 - 223. IF: 7,652
5. Solano C, Talaya A, Giménez E, Albert E, Piñana JL, Hernández-Boluda JC, Pérez A, Navarro D. Refractory cytomegalovirus DNAemia after allogeneic hematopoietic stem cell transplantation: when should genotypic drug resistance testing be requested?. *Bone Marrow Transplantation*. 2018; 53(6): 787 - 790. IF: 4,497

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI17/01097

Title: *Score integrado de factores inmunológicos y genotípicos de predicción del riesgo y evolución de la infección por CMV en pacientes con trasplante renal*

Principal Investigator: María José Remigia Pellicer

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 32.670€

Reference: PI15/01396

Title: *Inmunobiología de la aloreactividad NK en el trasplante de progenitores hematopoyéticos haploidenticos asociado al uso de ciclofosfamida post-trasplante*

Principal Investigator: Carlos Solano Vercet

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total budget: 116.765€

Reference: PI15/00090

Title: *Inmunobiología de la infección por el citomegalovirus en el trasplante alogénico de precursores hematopoyéticos haploidentico asociado al uso de ciclofosfamida postrasplante*

Principal Investigator: David Navarro Ortega

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total budget: 98.615€

Title: *Inmunobiología de la alo-reactividad NK en el trasplante de progenitores hematopoyéticos haploidenticos asociado al uso de ciclofosfamida post-trasplante*

Principal Investigator: Carlos Solano Vercet

Funding Body: Janssen - Cilag S.A.

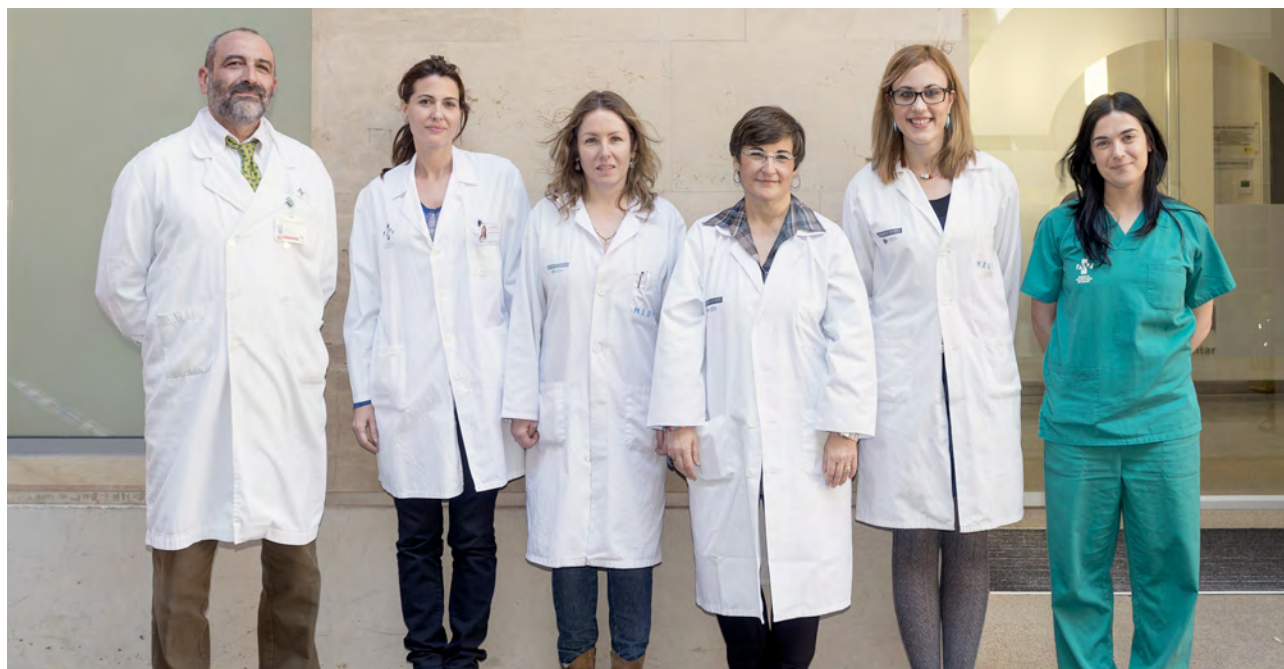
Program: Research Fellowship Program

Fellow: Eva Villamón Ribate

Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2018

Research Group on Lymphoproliferative Disorders
Consolidated group



Group members

Principal investigator

M^a José Terol Casterá
Hospital. University

Alicia Serrano Alcalá. INCLIVA
Mercedes Bou Moreno. INCLIVA
Verónica García Oliver. INCLIVA

Collaborating researchers

Antonio Ferrández Izquierdo. Hospital. University
Ana Isabel Teruel Casaús. Hospital
Edelmira Martí Sáez. Hospital
Lucía Brines Sinerol. INCLIVA
Blanca Ferrer Lores. Hospital



	R1	R2	R3	R4	STAFF
Researchers by categories	-	2	1	1	5

Strategic aims

- During the year 2018, we were able to deepen the knowledge of the role of the NOTCH1 / FBXW7 / PI3K / PTEN / AKT signaling pathway in the progression of Chronic Lymphocytic Leukemia B (CLL-B) to advanced forms. Thus, in the cell lines and in the patient's primary cells, we observed a variation in the number of gene copies by both FISH and PCRq in the NOTCH1, FBXW7 and PTEN genes, with an inverse relationship between NOTCH1 and FBXW7 / PTEN.
- A second objective has been to analyze the clinical significance of the rearrangements of myc, bcl-2 and bcl-6 in diffuse large cell lymphoma. We have been able to verify that patients with concomitant c-myc and bcl-2 protein expression present a worse prognosis in terms of SLP and Sg than the rest.
- Thirdly, during 2018, the study of the mutational status of IgVH in CLL and its prognostic impact in a wide series of patients has been implemented. New molecular markers (mutations TP53, BIRC3, MYD88, NOTCH1 and SF3B1) have also been studied in CLL by new generation sequencing techniques. In addition, we have continued the collaboration in the GENOMA CLL sequencing project, with a clinical-evolutionary update.
- Finally, we have expanded our participation in clinical research projects in CLL, refractory lymphomas and multiple myeloma, both with the incorporation of new drugs and in the design and development of new therapeutic options.

Main lines of research

- Analysis of the interactions of CLL cells with their cellular microenvironment: further study of the intracellular mechanisms triggered by VEGF. Analysis of the possible correlation with CXCR4/CCR7 cytokines pathway. Transactivation mechanisms of the aforementioned receptors.
- Role of the NOTCH1 / FBXW7 / PI3K / PTEN / AKT signaling pathway in the progression of Chronic Lymphocytic Leukemia B (CLL -B) to advanced forms: pathway molecular profile analysis in 100 patients with CLL-B of primary cells obtained at diagnosis and at the time of the progression, analyzing for this, the presence of mutations and number of copies of DNA, gene expression, FISH and (RT-PCR).
- Study of the rearrangements of bcl-2, bcl-6 and myc in diffuse large cell lymphoma: clinical significance and correlation with immunohistochemical expression using FISH and IHQ techniques.
- Study of new molecular markers (mutations of IgVH, TP53, BIRC3, MYD88, NOTCH1 and SF3B1) in CLL: conventional versus NGS techniques. Implication in clonal evolution associated with tumor progression.
- New therapeutic options for CLL/MM patients who are resistant to chemoimmunotherapy.

• PUBLICATIONS

Number of articles	IF	Average IF
13	239,992	18,460
National collaborations	International collaborations	Corresponding author
8	5	-

SELECTED PUBLICATIONS

1. Sabater L, Muñoz E, Roselló S, Dorcaratto D, Garcés-Albir M, Huerta M, Roda D, Gómez-Mateo MC, Ferrández-Izquierdo A, Darder A, Cervantes A. Borderline resectable pancreatic cancer. Challenges and controversies. *Cancer Treatment Reviews*. 2018; 68: 124 - 135. IF: 8,122
2. De Chiara F, Heebøll S, Marrone G, Montoliu C, Hamilton-Dutoit S, Ferrandez A, Andreola F, Rombouts K, Grønbaek H, Felipe V, Gracia-Sancho J, Mookerjee RP, Vilstrup H, Jalan R, Thomsen KL. Urea cycle dysregulation in non-alcoholic fatty liver disease. *Journal of Hepatology*. 2018; 69(4): 905 - 915. IF: 14,911
3. Rodríguez-Otero P, Mateos MV, Martínez-López J, Martín-Calvo N, Hernández MT, Ocio EM, Rosiñol L, Martínez R, Teruel AI, Gutiérrez NC, Bargay J, Bengoechea E, González Y, de Oteyza JP, Gironella M, Encinas C, Martín J, Cabrera C, Palomera L, de Arriba F, Cedena MT, Paiva B, Puig N, Oriol A, Bladé J, Lahuerta JJ, San Miguel JF. Early myeloma-related

death in elderly patients: development of a clinical prognostic score and evaluation of response sustainability role. *Leukemia*. 2018; 32(11): 2427 - 2434. IF: 10,023

4. Connors JM, Jurczak W, Straus DJ, Ansell SM, Kim WS, Gallamini A, Younes A, Alekseev S, Illés Á, Picardi M, Lech-Ma-randa E, Oki Y, Feldman T, Smolewski P, Savage KJ, Bartlett NL, Walewski J, Chen R, Ramchandren R, Zinzani PL, Cunningham D, Rosta A, Josephson NC, Song E, Sachs J, Liu R, Jolin HA, Huebner D, Radford J, ECHELON-1 Study Group. Brentuximab Vedotin with Chemotherapy for Stage III or IV Hodgkin's Lymphoma. *New England Journal of Medicine*. 2018; 378(4): 331 - 344. IF: 79,258
5. Morschhauser F, Fowler NH, Feugier P, Bouabdallah R, Tilly H, Palomba ML, Fruchart C, Libby EN, Casasnovas RO, Flinn IW, Haioun C, Maisonneuve H, Ysebaert L, Bartlett NL, Bouabdallah K, Brice P, Ribrag V, Daguindau N, Le Gouill S, Pica GM, Martin Garcia-Sancho A, López-Guillermo A, Larouche JF, Ando K, Gomes da Silva M, André M, Zachée P, Sehn LH, Tobinai K, Cartron G, Liu D, Wang J, Xerri L, Salles GA, RELEVANCE Trial Investigators. Rituximab plus Lenalidomide in advanced untreated follicular lymphoma. *New England Journal of Medicine*. 2018; 379(10): 934 - 947. IF: 79,258

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI14/02018

Title: *Papel de la vía de señalización NOTCH1/FBXW7/PI3K/PTEN/AKT en la progresión de la Leucemia Linfocítica Crónica B (LLC-B) a formas avanzadas*

Principal Investigator: M^a José Terol Casterá

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2015-2018

Total Budget: 81.070€

Title: *Impacto clínico de la evolución clonal y monitorización molecular en pacientes con leucemia linfocítica crónica subsidiarios de tratamiento*

Principal Investigator: M^a José Terol Casterá

Funding Body: *Gilead Sciences Fellowship Programme*

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

Duration: 2018-2019

Title: *Estudio de nuevos marcadores moleculares (mutaciones IgVH, TP53, BIRC3, MYD88, NOTCH1 y SF3B1) en la Leucemia Linfática Crónica-B (LLC-B): técnicas convencionales versus NGS (Next Generation Sequencing). Implicación en la evolución clonal asociada a la progresión tumoral*

Principal Investigator: Blanca Ferrer Lores

Funding Body: *Sociedad Española de Hematología y Hemoterapia*

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

Duration: 2016-2018

• THESIS

Thesis title: *Expresión de microRNAs en las zonas de transición epitelio mesenquimal en el carcinoma colorectal como factor inmunomodulador y pronóstico. Estudio clínico patológico*

Doctoral candidate: María Carolina Martínez Ciarpaglini

Director(s): Andrés Cervantes Ruipérez, Samuel Navarro Fos, Antonio Ferrández Izquierdo

Date of the defense: 30/10/2018

Grade: *Sobresaliente "cum laude"*

Research Group on Myeloid Neoplasms
Consolidated group



Group members

Principal investigator

Mar Tormo Díaz
Hospital. University

Emerging researcher

Juan Carlos Hernández Boluda. Hospital

Collaborating researchers

Blanca Navarro Cubells. Hospital
Marisa Calabuig Muñoz. Hospital
Montserrat Gómez Calafaz. Hospital
Elena Fernández Pons. Hospital



	R1	R2	R3	R4	STAFF
Researchers by categories	2	2	-	1	1

Strategic aims

- Assess the effect of imiquimod on proliferation and differentiation of bone marrow cells of patients with myelodysplastic syndrome (MDS) or acute myeloid leukaemia (AML).
- Analyse the impact of genetic mutations and epigenetic regulation on response to hypomethylating drug azacitidine.
- Analyze curcumin (cur) activity combined with azacitidine in myeloid cell lines and samples from MDS and AML patients.
- NGS molecular characterization in patients with essential thrombocythemia or polycythemia vera developing resistance to hydroxycarbamide.
- Develop prognostic model for myelofibrosis secondary to ET and PV. Spanish Myelofibrosis (MF) Registry study.
- Study treatment discontinuation in chronic myeloid leukaemia (CML). Spanish LMC group (GELMC) study.

Main lines of research

- Study of mechanisms involved in leukemic transformation in myeloproliferative neoplasms.
- Studies on molecular biomarker mutations in response to myelodysplastic syndromes (MDS) and AML treated with hypomethylating agents.
- In vitro studies of Curcumin, a histone deacetylase inhibitor and apoptosis inducer, in combination with azacitidine in MDS and AML.
- Effect of imiquimod on bone marrow cell proliferation and differentiation in myelodysplastic syndrome or acute myeloid leukaemia patients.
- Collaborative studies with the CETLAM group (LMA, SMD), PETHEMA (LLA, LMA), the Spanish Philadelphia-negative chronic myeloproliferative disorders group (GEMFIN), the Spanish LMC group (GELMC) and the Spanish SMD group (GESMD).



Emerging Researcher

Juan Carlos Hernández Boluda

Our research is focused on the molecular mechanisms involved in the progression of the chronic myeloproliferative neoplasms from the chronic phase to the leukemic phase.

Amigo ML, Martí-Tutusa JM, García-Guiñón A, Bargay J, Sampol A, Salameo O, Font L, Talarn C, Hoyos M, Díaz-Beyá M, Garrido A, Navarro B, Nomdèdeu J, Sierra J, Tormo M. Bone marrow VEGFC expression is associated with multilineage dysplasia and several prognostic markers in adult acute myeloid leukemia, but not with survival. *Leukemia & Lymphoma*. 2018; 59(10): 2383 - 2393. IF: 2,644

• PUBLICATIONS

Number of articles	IF	Average IF
25	116,279	4,651
National collaborations	International collaborations	Corresponding author
21	3	5

SELECTED PUBLICATIONS

1. Guillem V, Calabuig M, Brunet S, Esteve J, Escoda L, Gallardo D, Ribera JM, Queipo de Llano MP, Arnan M, Pedro C,

2. Hernández-Boluda JC, Pereira A, Pastor-Galán I, Alvarez-Larrán A, Savchuk A, Puerta JM, Sánchez-Pina JM, Collado R, Díaz-González A, Angona A, Sagüés M, García-Gutiérrez V, Boqué C, Osorio S, Vallansot R, Palomera L, Mendizábal A, Casado LF, Pérez-Encinas M, Pérez-López R, Ferrer-Marín F, Sánchez-Guijo F, García C, Heras NL, López-Lorenzo JL, Cervantes F, Steegmann JL, Grupo Español de Leucemia Mieloide Crónica (GELMC). Feasibility of treatment discontinuation in chronic myeloid leukemia in clinical practice: results from a nationwide series of 236 patients. *Blood Cancer Journal*. 2018; 8(10): 91. IF: 8,125
3. Hernández-Boluda JC, Pereira A, Correa JG, Alvarez-Larrán A, Ferrer-Marín F, Raya JM, Martínez-López J, Velez P, Pérez-Encinas M, Estrada N, García-Gutiérrez V, Fox ML, Payer A,

Kerguelen A, Cuevas B, Durán MA, Ramírez MJ, Gómez-Casares MT, Mata-Vázquez MI, Mora E, Gómez M, Cervantes F. Prognostic risk models for transplant decision-making in myelofibrosis. *Annals of Hematology*. 2018; 97(5): 813 - 820. IF: 2,845

4. Hernández-Boluda JC, Pereira A, Correa JG, Alvarez-Larrán A, Ferrer-Marín F, Raya JM, Martínez-López J, Pérez-Encinas M, Estrada N, Velez P, Fox ML, García-Gutiérrez V, Payer A, Kerguelen A, Cuevas B, Durán MA, Ramírez MJ, Gómez-Casares MT, Mata-Vázquez MI, Mora E, Martínez-Valverde C, Gómez M, Cervantes F. Performance of the myelofibrosis secondary to PV and ET-prognostic model (MYSEC-PM) in a series of 262 patients from the Spanish registry of myelofibrosis. *Leukemia*. 32(2): 553 - 555. IF: 10,023
5. Martín I, Navarro B, Villamón E, Solano C, Serrano A, Calabuig M, Amat P, Domingo F, Abellán R, García F, Olivares MD, Chaves FJ, Tormo M, Hernández-Boluda JC. Therapy-related acute myeloid leukemia developing 14 years after allogeneic hematopoietic stem cell transplantation, from a persistent R882H-DNMT3A mutated clone of patient origin. *Experimental and Molecular Pathology*. 2018; 105(1): 139 - 143. IF: 2,566

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI13/00636

Title: *Role of the RUNX1/CBF-beta/p300/HIPK2 complex in the leukemic progression of the chronic myeloproliferative neoplasms*

Principal Investigator: Juan Carlos Hernández Boluda

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2014-2018

Total Budget: 79.860€

Reference: INT00038

Title: *Evaluación del efecto del imiquimod en la proliferación y diferenciación de células procedentes de médula ósea de pacientes con síndrome mielodisplásico o leucemia mieloide aguda*

Principal Investigator: Mar Tormo Díaz

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

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

Duration: 2018

Total Budget: 6.200€

Reference: GLD16/00047

Title: *Molecular characterisation with NGS of patients with essential thrombocythaemia or polycythaemia vera who develop resistance to hydroxycarbamide according to the European LeukemiaNet criteria*

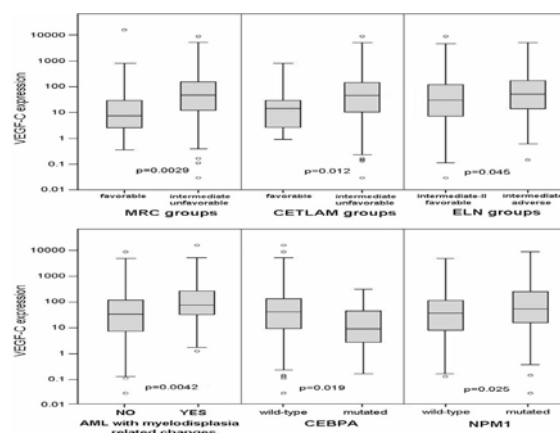
Principal Investigator: José V. Cervera Zamora

Funding Body: Gilead Fellowship Program

Beneficiary Institution: *Instituto de Investigación Sanitaria del Hospital Universitario y Politécnico La Fe*

Duration: 2018-2019

Total Budget: 49.657€



Box-plot diagram of VEGFC gene expression in AML according to cytogenetic prognostic factors (MRC, CETLAM, and ELN group criteria), myelodysplasia related alterations, and molecular markers (CEBPA and NPM1 gene mutations).

Research Group on Epigenetics and Chromatin
Consolidated group

<http://www.bioeticaweb.com/byline/luis-franco-vera/>



Group members

Principal investigator

Luis Franco Vera
University

Collaborating researchers

Gerardo López Rodas. University
Josefa Castillo Aliaga. INCLIVA
Francisco Gimeno Valiente. INCLIVA



	R1	R2	R3	R4	STAFF
Researchers by categories	1	1	1	1	-

Strategic aims

- The selection between KRAS alternative splicing isoforms 4A (apoptotic) and 4B (anti-apoptotic) in CRC-derived cell lines, depends on histone post-translational modifications (PTM).
- Overexpression of EPDR1 in CRC patients is associated with the TNM staging parameters, especially T and M and correlate with invasiveness and dissemination of tumour cells.
- ZNF518B is overexpressed in CRC tumour tissues and favours tumour cell dissemination. The expression of the gene is governed by chromatin structure at the promoter and epigenetic mechanisms.
- Members of the group have collaborated with the Prof. Cervantes' group in the analysis of anti-HER2 drug resistance in gastric cancer and with Prof. González-Bosch group (IATA-UV) in the study of the epigenetics of resistance to response to *Botrytis cinerea*.

Main lines of research

- Exploring the role of ZNF518B and EPDR1 genes in human colorectal cancer: A translational approach. The research is aimed at: a) Immunochemical detection of EPDR1 in patients. b) Expression of total ZNF518B, of its splicing isoforms and of those of EPDR1. c) Mechanisms involved in EPDR1-driven invasiveness. d) Analysis of the in vivo the effects of EPDR1 on tumour growth and dissemination. e) Regulation of EPDR1 and ZNF518B expression. f) Search for the target genes of ZNF518B as a transcriptional factor.
- Epigenetic changes in acute pancreatitis. Analysis of the role of S-adenosymethionine in the epigenetic regulation of the inflammatory cascade in acute pancreatitis.
- Role of EPDR1 in bladder cancer. We will go on analysing the expression of the gene in tumour and adjacent tissues and studying the role of DNA methylation in the expression of the gene.

• PUBLICATIONS

Number of articles	IF	Average IF
2	8,157	4,078

National collaborations	International collaborations	Corresponding author
1	1	1

SELECTED PUBLICATIONS

1. Riffo-Campos AL, Gimeno-Valiente F, Rodríguez FM, Cervantes A, López-Rodas G, Franco L, Castillo J. Role of epigenetic factors in the selection of the alternative splicing isoforms of human *KRAS* in colorectal cancer cell lines. *Oncotarget*. 2018; 9(29): 20578 - 20589. IF: 5,168
2. Crespo-Salvador O, Escamilla-Aguilar M, López-Cruz J, López-Rodas G, González-Bosch C. Determination of histone

epigenetic marks in *Arabidopsis* and tomato genes in the early response to *Botrytis cinerea*. *Plant Cell Reports*. 2018; 37(1): 153 - 166. IF: 2,989

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: SAF2015-71208-R

Title: *Papel de la señalización redox, beta-arrestina 2 y nucleosomas extracelulares en la pancreatitis aguda*

Principal Investigator: Juan Sastre (Luis Franco as collaborating researcher)

Funding body: *Ministerio de Economía y Competitividad*

Beneficiary institution: *Universidad de Valencia*

Duration: 2016 - 2019

Total budget: 254.100€

Reference: UV-INV_AE17-708563

Title: *EPDR1 y ZNF518B en cáncer colorrectal: Mecanismos de actuación y potencial aplicación en diagnóstico y terapia*

Principal Investigator: Gerardo López-Rodas

Funding body: Universidad de Valencia

Beneficiary institution: Universidad de Valencia

Duration: 2018

Total budget: 12.000€

• **THESIS**

Thesis title: *Mecanismos de resistencia primaria y secundaria a tratamiento antiher2 en cáncer gástrico her2 positivo*

Doctoral candidate: Valentina Gambardella

Director(s): Andrés Cervantes Ruiz, Josefa Castillo Aliaga

Date of the defense: 13/03/2018

Grade: *Sobresaliente "cum laude"*

Quality recognition/Award: European PhD

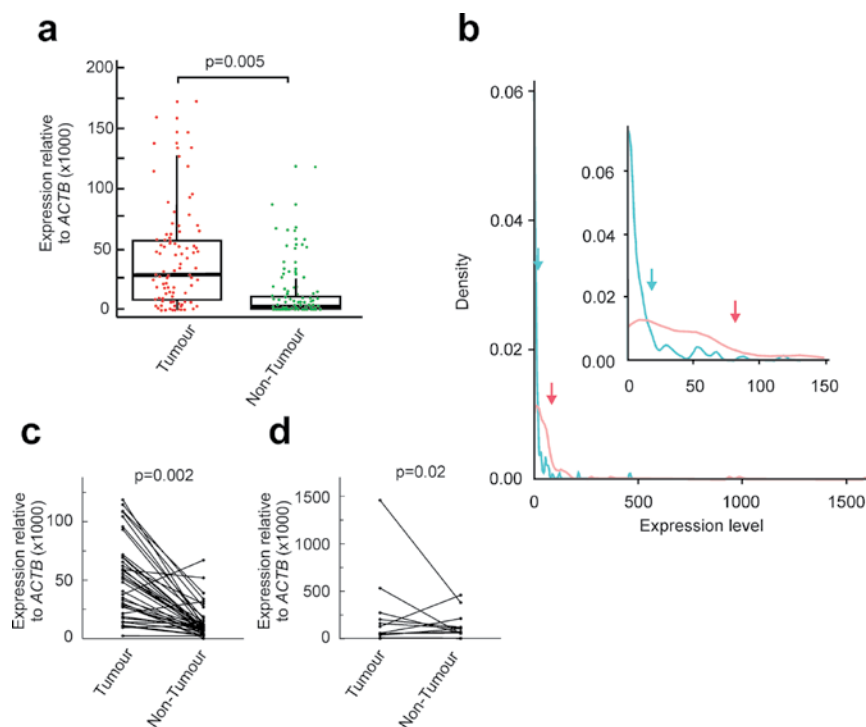


Figure 1. Expression of total EPDR1 in a cohort of 101 CRC patients from our University Hospital

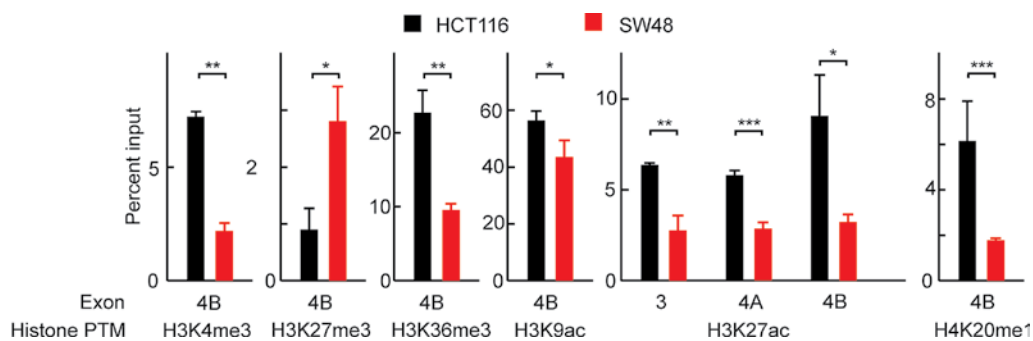
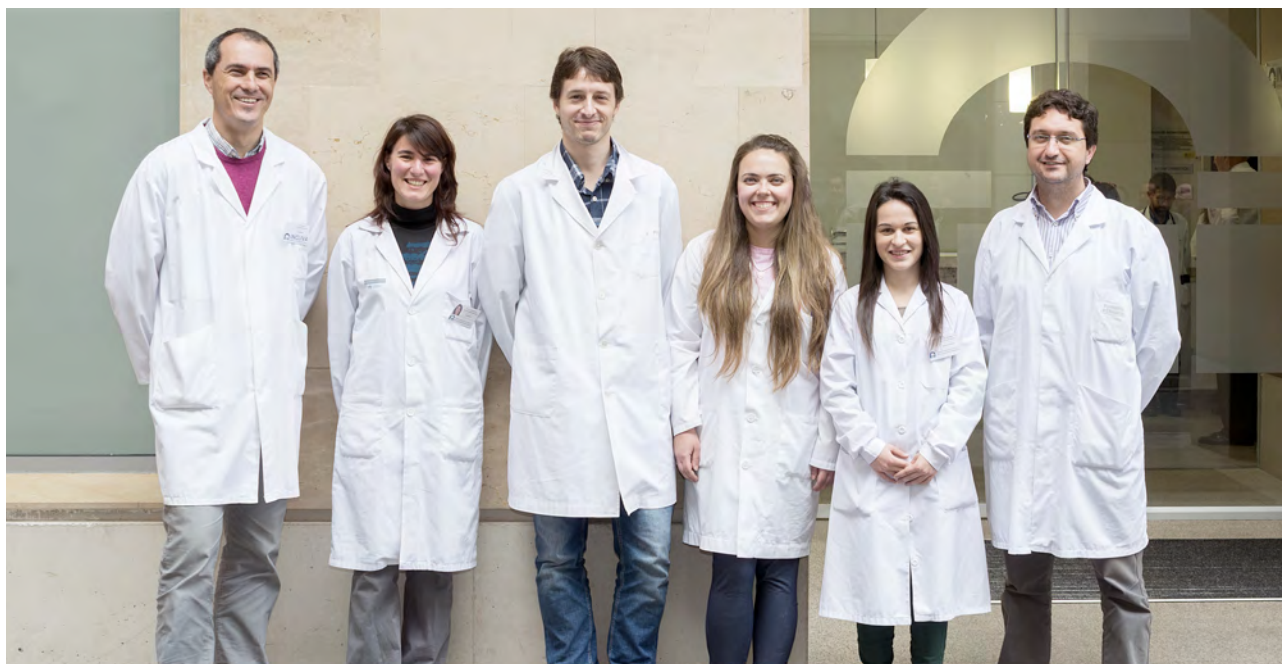


Figure 2. Nuc-ChIP analysis of histone epigenetic modifications in nucleosomes located over the exons 3, 4A and 4B

Research Group on Molecular Imaging and Metabolomics
Emerging group



Group members

Principal investigator

Daniel Monleón Salvadó
University

PhD researchers

Mercedes Pardo Tendero. INCLIVA

Collaborating researchers

Vannina González Marrachelli. University
Antonio Pellín Carcelén. University
Itziar Pérez Terol. INCLIVA
María Martín Grau. INCLIVA

Technicians

José Manuel Morales Tatay. University



	R1	R2	R3	R4	STAFF
Researchers by categories	1	2	-	1	3
Researchers financed by competitive public calls or networks	1	-	-	-	-

Strategic aims

- Identify new metabolomic markers of tumor aggressiveness in breast cancer.
- Identify new markers of myocardial infarction.
- Identify new metabolomic cardiovascular risk markers based on the microbiota-host interaction.

Main lines of research

- Tumor metabolism through metabolic profiles in biopsies, biofluids and cells (breast cancer, glioblastoma multiforme, prostate, bladder).
- Metabolic profiles in the progression of cardiometabolic risk modulated by the microbiota-host interaction.
- Metabolic profiles of healthy aging vs frailty.
- MRI microimaging study of porcine cardiac tissue samples to develop new detection methods.

• PUBLICATIONS

Number of articles	IF	Average IF
8	29,795	3,724

National collaborations	International collaborations	Corresponding author
5	3	0

SELECTED PUBLICATIONS

1. Zhang ZY, Monleon D, Verhamme P, Staessen JA. Branched-Chain amino acids as critical switches in health and disease. Hypertension. 2018; 72(5): 1012 - 1022. IF: 6,823
2. Gómez-Gallego C, Morales JM, Monleón D, du Toit E, Kumar H, Linderborg KM, Zhang Y, Yang B, Isolauri E, Salminen S, Collado MC. Human breast milk NMR metabolomic profile across specific geographical locations and its association with the milk microbiota. Nutrients. 2018; 10(10): pii: E1355. IF: 4,196
3. Burguete P, Morales JM, Fernández L, El Haskouri J, Latorre J, Guillem C, Pérez-Pla F, Cros A, Beltrán D, Beltrán A, Amorós P. Layered-expanded mesostructured silicas: generalized synthesis and functionalization. Nanomaterials. 2018; 8(10): pii: E817. IF: 3,504
4. Sanguinetti E, Collado MC, Marrachelli VG, Monleon D, Selma-Royo M, Pardo-Tendero MM, Burchielli S, Iozzo P. Microbiome-metabolome signatures in mice genetically prone to develop dementia, fed a normal or fatty diet. Scientific Reports. 2018; 8(1): 4907. IF: 4,122

5. García-Villaescusa A, Morales-Tatay JM, Monleón-Salvadó D, González-Darder JM, Bellot-Arcis C, Montiel-Company JM, Almerich-Silla JM. Using NMR in saliva to identify possible biomarkers of glioblastoma and chronic periodontitis. PLoS One. 2018; 13(2): e0188710. IF: 2,766

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: INTIMIC-085

Title: *Maternal obesity and cognitive dysfunction in the offspring: cause effect role of the GUT MicrobiOME and early dietary prevention*

Principal Investigator: Consuelo Borrás Blasco (Daniel Monleón, Vannina González, José Manuel Morales as collaborating researchers)

Funding Body: JPI HDHL. European Commission

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

Duration: 2017-2020

Total Budget: 778.240€

Reference: PIE15/00013

Title: *A multidisciplinary Project to advance in basic mechanisms, diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction*

Principal Investigator: Vicente Bodí Peris (Daniel Monleón as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total Budget: 589.050€

Reference: PCIN-2017-117

Title: *Obesidad materna y disfunción cognitiva en la descendencia: papel causa-efecto de la microbiota intestinal y prevención dietética temprana*

Investigador principal: Consuelo Borrás Blasco (Daniel Monleón, Vannina González, José Manuel Morales as collaborating researchers)

Funding Body: *Ministerio de Economía y Competitividad*

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

Duration: 2017-2020

Total Budget: 143.000€

Reference: GV/2018/111

Title: *Nuevos nanomateriales como agentes de contraste en IRM y desarrollo de la plataforma de RMN para estudios biomédicos mediante histología correlativa*

Investigador principal: José Manuel Morales Tatay

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

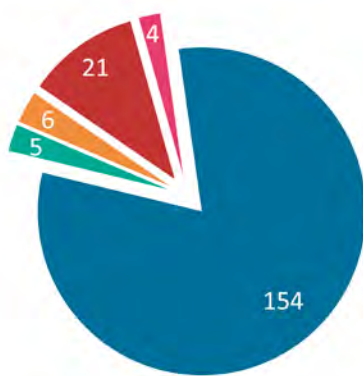
Beneficiary Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2018-2019

Total Budget: 9.500€

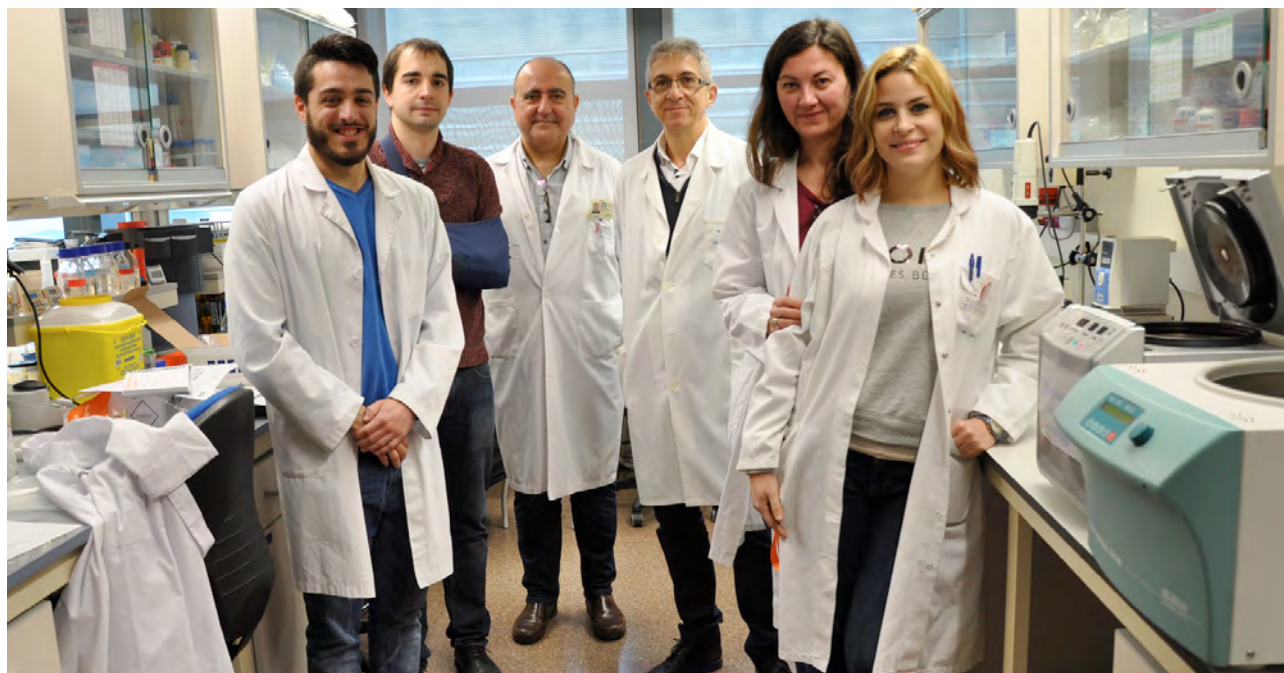
4.3.3 Metabolism and organic damage area

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● Original articles ● Letters ● Editorial ● Reviews ● Corrections

Research Group on Genetics of Osteoporosis
Consolidated group



Group members

Principal investigator

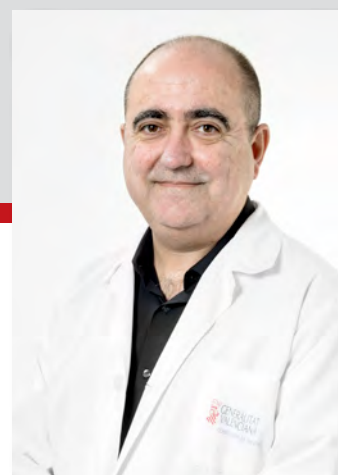
Miguel Ángel García Pérez
 University

PhD researchers

Álvaro Acebrón Fabregat. Hospital
 Clara María Pertusa Viñuales. INCLIVA

Collaborating researchers

Rosa María Aliaga Corachán. University
 Damián Mifsut Miedes. Hospital



	R1	R2	R3	R4	STAFF
Researchers by categories	2	-	1	1	1
Researchers financed by competitive public calls or networks	1	-	-	-	-

Strategic aims

During 2018 our group has continued the association studies of candidate genes and polymorphisms with bone phenotypes. Specifically, this time we have focused mainly on genes related to the metabolism of arginine and certain epigenetic mechanisms. Likewise, we continue the search for biomarkers (miRNAs) in bone fracture and we have initiated a new line that seeks to establish the role of arginine metabolism with bone phenotypes (fragility fracture and bone mass).

In addition, we have collaborated in a national study on vitamin D and have continued our usual collaboration in aspects related to fertility.

Main lines of research

- Identification of genes and polymorphisms associated with bone phenotypes, mainly related to epigenetic mechanisms and to the metabolism of arginine.
- Identification of genes and miRNAs differentially expressed in bone fracture due to fragility.
- Functional characterization by genetic and epigenetic techniques of polymorphisms associated with bone phenotypes.
- Identification of genetic, biochemical and cytomic biomarkers in patients with the Idic15.

• PUBLICATIONS

Number of articles	IF	Average IF
1	3,315	3,315

National collaborations	International collaborations	Corresponding author
1	-	-

SELECTED PUBLICATIONS

1. Pineda-Moncusí M, Garcia-Perez MA, Rial A, Casamayor G, Cos ML, Servitja S, Tusquets I, Diez-Perez A, Cano A, Garcia-Giralt N, Nogues X. Vitamin D levels in Mediterranean breast cancer patients compared with those in healthy women. *Maturitas*. 2018; 116: 83 - 88. IF: 3,315

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: FOCUS

Title: *Frailty management Optimisation through EIP AHA Commitments and Utilisation of Stakeholders input*

Principal Investigator: Antonio Cano Sánchez (Miguel Ángel García Pérez as collaborating researcher)

Funding body: *European Commission - DG SANTE*

Beneficiary institution: *Universidad de Valencia*

Duration: 2015-2018

Total budget: 2.379.633€

Reference: PI17/01875

Title: *Osteoporosis y fractura ósea: identificación de genes asociados y evaluación del papel del metabolismo de la arginina*

Principal Investigator: Miguel Ángel García Pérez

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 99.220€

**Translational Research Group on Nutrition and Metabolism**
Consolidated group

Team involved in

ciberehd**Group members****Principal investigator**

Antonio Hernández Mijares. University

Collaborating researchers

Milagros Rocha Barajas. Hospital Dr. Peset - FISABIO

Víctor Manuel Víctor González. Hospital Dr. Peset. University

Juan Vicente Esplugues Mota. Hospital Dr. Peset. University

Carlos Morillas Ariño. Hospital Dr. Peset. University

Eva Solá Izquierdo. Hospital Dr. Peset. University

Celia Bañuls Morant. Hospital. Hospital Dr. Peset - FISABIO

Ana Jover Fernández. Hospital Dr. Peset

Marcelino Gómez Balaguer. Hospital Dr. Peset

Nadezda Apostolova Atanasovska. University

Silvia Veses Martín. Hospital Dr. Peset. University - FISABIO

Susana Rovira Llopis. Hospital Dr. Peset. University - FISABIO

Iciar Castro de la Vega. Hospital Dr. Peset - FISABIO

Noelia Díaz Morales. Hospital Dr. Peset - FISABIO

Sandra López Doménech. Hospital Dr. Peset - FISABIO

Irene Escribano López. Hospital Dr. Peset - FISABIO

Aránzazu Martínez de Marañón Peris. Hospital Dr. Peset - FISABIO

Francesca Iannantuoni. Hospital Dr. Peset - FISABIO

Zaida Abad Jiménez. Hospital Dr. Peset - FISABIO

Rosa Falcón Tapiador. Hospital Dr. Peset - FISABIO



	R1	R2	R3	R4	STAFF
Researchers by categories	7	6	4	2	1

Strategic aims

- To evaluate whether metformin treatment might modulate ER stress, autophagy, and oxidative stress in leukocytes of type 2 diabetic (T2D) patients.
- To determine if metformin treatment protects T2D patient leukocytes from oxidative stress by regulating ROS production and antioxidant enzyme expression.
- To assess whether metformin modulates leukocyte-endothelium interactions and adhesion molecule expression in T2D patients.
- To evaluate the relationship between testosterone levels, metabolic parameters, mitochondrial function, adhesion molecules and leukocyte-endothelium in T2D patients.
- To evaluate whether metabolic profile influences ER and oxidative stress in an obese population with/without comorbidities.
- To evaluate the effect of pinitol on peripheral blood mononuclear cells (PBMCs) and visceral (VAT) and subcutaneous adipose tissues (SAT) in human obese subjects, focusing on the involvement of endoplasmic reticulum (ER) stress and sirtuin 1 (SIRT1).
- To evaluate whether the presence of metabolic syndrome in polycystic ovary syndrome patients can influence endoplasmic reticulum (ER) and oxidative stress and leukocyte - endothelium interactions.
- To determine the prevalence of nutritional risk and malnutrition, and the type and degree of malnutrition in outpatient, hospitalized and institutionalized populations in a health department.

Main lines of research

- Prevalence of nutritional risk and malnutrition.
- Diabetes mellitus and cardiovascular risk.
- Obesity, inflammation and endothelial dysfunction.
- Polycystic ovary syndrome and insulin resistance.
- Dyslipidemia and residual cardiovascular risk.
- Functional foods and their influence on cardiovascular risk factors.
- Endoplasmic reticulum stress, mitochondrial dysfunction and oxidative stress.
- Characterization of new cellular mechanisms of antiretroviral hepatotoxicity.

• PUBLICATIONS

Number of articles	IF	Average IF
24	154,112	6,421

National collaborations	International collaborations	Corresponding author
21	2	0

SELECTED PUBLICATIONS

1. Diaz-Morales N, Iannantuoni F, Escribano-Lopez I, Bañuls C, Rovira-Llopis S, Sola E, Rocha M, Hernandez-Mijares A, Victor VM. Does metformin modulate endoplasmic reticulum stress and autophagy in type 2 diabetic peripheral blood mononuclear cells?. *Antioxidants & Redox Signaling*. 2018; 28(17): 1562 - 1569. IF: 6,530
2. Rovira-Llopis S, Apostolova N, Bañuls C, Muntané J, Rocha M, Victor VM. Mitochondria, the NLRP3 inflammasome, and sirtuins in Type 2 Diabetes: new therapeutic targets. *Antioxidants & Redox Signaling*. 2018; 29(8): 749 - 791. IF: 6,530
3. Rovira-Llopis S, Escribano-Lopez I, Diaz-Morales N, Iannantuoni F, Lopez-Domenech S, Andújar I, Jover A, Pantoja J, Pallardo LM, Bañuls C, Victor VM. Downregulation of miR-31 in diabetic nephropathy and its relationship with inflammation. *Cellular Physiology and Biochemistry*. 2018; 50(3): 1005 - 1014. IF: 5,500

4. Diaz-Morales N, Lopez-Domenech S, Iannantuoni F, Lopez-Gallardo E, Sola E, Morillas C, Rocha M, Ruiz-Pesini E, Victor VM. Mitochondrial DNA Haplogroup JT is related to impaired glycaemic control and renal function in type 2 diabetic patients. *Journal of Clinical Medicine*. 2018; 7(8): pii: E220. IF: 5,583
5. Hernandez AF, Green JB, Janmohamed S, D'Agostino RB, Granger CB, Jones NP, Leiter LA, Rosenberg AE, Sigmon KN, Somerville MC, Thorpe KM, McMurray JJV, Del Prato S, Harmony Outcomes committees and investigators. Albiglutide and cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease (Harmony Outcomes): a double-blind, randomised placebo-controlled trial. *Lancet*. 2018; 392(10157): 1519 - 1529. IF: 53,254

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI16/01083

Title: *Estudio de la dinámica mitocondrial, el inflammasoma y su relación con las complicaciones cardiovasculares en la diabetes tipo 2: implicaciones fisiopatológicas y clínicas*

Principal Investigator: Víctor Manuel Víctor González

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO)*

Duration: 2017-2019

Total budget: 147.015€

Reference: PI16/00301

Title: *Papel de la autofagia y el inflammasoma en la fisiopatología de la obesidad: efecto de la pérdida de peso y posibles implicaciones terapéuticas*

Principal Investigator: Milagros Rocha Barajas

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO)*

Duration: 2017-2019

Total budget: 92.565€

Reference: PI15/01424

Title: *Prevalencia de desnutrición en el medio hospitalario y ambulatorio. Mecanismos moleculares asociados a la desnu-*

trición: estrés oxidativo, inflamación y estrés de retículo endoplasmático

Principal Investigator: Antonio Hernández Mijares

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO)*

Duration: 2016-2018

Total budget: 86.515€

Reference: SAF2015-67678-R

Title: *Estudio del mecanismo responsable de la toxicidad vascular de Abacavir: papel del sistema purinérgico sobre la interacción leucocito/endotelio/plaqueta*

Principal Investigator: Juan Vicente Esplugues Mota and Ángeles Álvarez Ribelles

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2016-2018

Total budget: 169.400€

Reference: CB06/04/0071

Title: *CIBER de Enfermedades Hepáticas y Digestivas (CIBERehd)*

Principal Investigator: Juan Vicente Esplugues Mota

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2007-

Reference: PROMETEOII/2018/141

Title: *Farmacología del Tracto Hepato-Digestivo*

Principal Investigator: Antonio Hernández Mijares

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

Beneficiary Institution: *Universidad de Valencia*

Duration: 2018-2021

Total budget: 280.407,5€

• THESIS

Thesis title: *Estudio de la enfermedad periodontal y la respuesta al tratamiento periodontal no-quirúrgico en pacientes obesos no-diabéticos: influencia del perfil metabólico y de la pérdida de peso*

Doctoral candidate: María Teresa Martínez Herrera

Director(s): Francisco Javier Silvestre Donat, Milagros Rocha Barajas, Antonio Hernandez Mijares

Date of the defense: 22/06/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio de la implicación del receptor p2x7 en los efectos proinflamatorios de abacavir*

Doctoral candidate: Víctor Collado Díaz

Director(s): Ángeles Alvarez Ribelles, Juan Vicente Esplugues Mota

Date of the defense: 19/07/2018

Grade: *Sobresaliente "cum laude"*

Quality recognition/Award: European PhD

Thesis title: *Estudio de prevalencia de desnutrición en el Departamento de Salud Valencia-Doctor Peset. Comparación de tres herramientas de cribado nutricional. Mecanismos moleculares asociados a la desnutrición: estrés oxidativo, inflamación y estrés de retículo endoplasmático*

Doctoral candidate: Silvia Veses Martín

Director(s): Antonio Hernández Mijares, Celia Bañuls Morant

Date of the defense: 17/12/2018

Grade: *Sobresaliente "cum laude"*

Research Group on Neurological Impairment
Consolidated group



Group members

Principal investigator

Carmina Montoliu Félix. INCLIVA

Researchers

Amparo Uriós Lluch. INCLIVA
 Andrea Cabrera Pastor. INCLIVA

Collaborating researchers

Isabel Pascual-Moreno. Hospital
 Amparo Escudero García. Hospital
 Joan Tosca Cuquerella. Hospital
 Cristina Montón Rodríguez. Hospital
 José Ballester Fayos. Hospital
 Paloma Lluch García. Hospital
 Paula Cases Bergón. Hospital
 Nicolás Peñaranda Sarmiento. Hospital
 Rut Victorio Muñoz. Hospital
 José Luis León Guijarro. Hospital
 Roberto Aliaga Méndez. Hospital

PhD researcher

Juan José Gallego Roig. INCLIVA
 Raquel García García. Unidad Mixta INCLIVA-CIPF
 Mika Aiko. Hospital
 María Pilar Ballester Ferrer. Hospital
 David Martí Aguado. Hospital

Collaborating staff nursing

Pilar Aguilar Santaisabel. Hospital
 María Jesús Campa Santiago. Hospital
 Nuria Casasús Moya. Hospital

Technician staff

Laura Puchades Lanza. INCLIVA
 Consuelo Miguel Moreno. Hospital



	R1	R2	R3	R4	STAFF
Researchers by categories	4	9	5	1	5
Researchers financed by competitive public calls or networks	2	2	-	-	-

Strategic aims

- To better characterize the neuropsychological alterations in attention, coordination, perception, spatial and working memory and other aspects of cognitive and motor function in patients with MHE.
- To characterize the alterations in sleep in patients with MHE.
- To analyze the contribution of oxidative and nitrosative stress and of inflammation to MHE and to specific neuropsychological alterations.
- To study by fMRI:
 - The pattern of activation of brain areas while performing tests of attention and “mismatch negativity”.
 - The neuronal connectivity of the default mode network.
 - The cerebral mechanisms of alterations in cognitive and motor tasks in patients with MHE.

Main lines of research

- Identification of peripheral biomarkers for MHE. Identification of metabolites useful for early diagnosis of minimal hepatic encephalopathy. Search of peripheral parameters related with inflammation as possible indicators of the presence of MHE.
- Detailed characterization of the neurological alterations in attention, coordination, perception, spatial and working memory and other aspects of cognitive and motor function in patients with MHE using a wide battery of psychometric tests.
- Identification of alterations in cerebral function using structural and functional magnetic resonance imaging (including edema, cerebral atrophy, alterations in neuronal tracts structure and connectivity) in patients with liver cirrhosis and MHE. Analysis of their utility in the diagnosis of minimal hepatic encephalopathy.
- Identification of alterations in cerebral function using neurophysiological tools (EEG, cerebral cartography, ...) in patients with liver cirrhosis and MHE. Analysis of their utility in the diagnosis of minimal hepatic encephalopathy.
- Study of alterations in sleep patterns and quality in patients with liver cirrhosis with or without minimal hepatic encephalopathy.
- Analysis of synergistic effect between hyperammonemia and inflammation in the induction of cognitive and motor impairment in MHE.
- Characterization of the changes in the immunophenotype associated to the appearance of minimal hepatic encephalopathy in cirrhotic patients. Diagnostic implications.

• PUBLICATIONS

Number of articles	IF	Average IF
12	56,265	4,688
National collaborations	International collaborations	Corresponding author
6	5	3

SELECTED PUBLICATIONS

1. Balzano, T, Forteza J, Molina P, Giner J, Monzó A, Urios A, Montoliu C, Felipo V. The cerebellum of patients with steatohepatitis shows lymphocyte infiltration, microglial activation and loss of purkinje and granular neurons. Scientific Reports. 2018. 14; 8(1): 3004. IF: 4,122
2. García-García R, Cruz-Gómez AJ, Urios A, Mangas-Losada A, Forn C, Escudero-García D, Kosenko E, Torregrosa I, Tosca J, Giner-Durán R, Serra MA, Avila C, Belloch V, Felipo V, Montoliu C. Learning and memory impairments in patients with minimal hepatic encephalopathy are associated with structural and functional connectivity alterations in hippocampus. Scientific Reports. 2018; 8(1): 9664. IF: 4,122
3. Balzano T, Forteza J, Borreda I, Molina P, Giner J, Leone P, Urios A, Montoliu C, Felipo V. Histological features of cerebellar neuropathology in patients with alcoholic and non-alcoholic steatohepatitis. Journal of Neuropathology and Experimental Neurology. 2018; 77(9): 837 - 845. IF: 3,490

4. De Chiara F, Heebøll S, Marrone G, Montoliu C, Hamilton-Dutoit S, Garcia-Torres ML, Andreola F, Rombouts K, Grønbaek H, Felipe V, Mookerjee R, Jalan R, Thomsen KL. Urea cycle enzyme expression and function are reversibly modified in non-alcoholic fatty liver disease. *Journal of Hepatology*. 2018; 69(4): 905 - 915. IF: 14,911
5. Giménez-Garzó C, Urios A, Agustí A, Mangas-Losada A, García-García R, Escudero-García D, Kosenko E, Ordoño JF, Tosca J, Giner-Durán R, Serra MA, Felipe V, Montoliu C. Cirrhotic patients with minimal hepatic encephalopathy have increased capacity to eliminate superoxide and peroxynitrite in lymphocytes, associated with cognitive impairment. *Free Radical Research*. 2018; 52(1): 118 - 133. IF: 3,830

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI18/00150

Title: *Caracterización de las alteraciones neurológicas y cerebrales en pacientes con encefalopatía hepática mínima. Contribución de la inflamación. Implicaciones diagnósticas y terapéuticas*

Principal Investigator: Carmina Montoliu Félix

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 171.820€

Reference: PI15/00035

Title: *Caracterización de las alteraciones neurológicas en pacientes con encefalopatía hepática mínima y de las alteraciones cerebrales responsables. Contribución del estrés oxidativo y la inflamación*

Principal Investigator: Carmina Montoliu Félix

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total budget: 159.115€

Reference: PROMETEO/2018/051

Title: *Mecanismos moleculares y cerebrales de las alteraciones cognitivas y motoras en hiperamonemia y encefalopatía hepática. Implicaciones terapéuticas y diagnósticas*

Principal Investigator: Vicente Felipe Orts (Carmina Montoliu Félix as collaborating researcher)

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

Beneficiary institution: *Centro de Investigación Príncipe Felipe (CIPF)*

Duration: 2018-2021

Total budget: 289.194,57€

Title: *Estudio descriptivo de los movimientos oculares mediante OSCANNTM y su valor en la asistencia diagnóstica en encefalopatía hepática mínima*

Principal Investigator: Carmina Montoliu Félix

Funding body: *AURA Innovative Robotics SL*

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

Duration: 2017-2019

Total budget: 10.000€

• THESIS

Thesis title: *Efectos de la hiperamonemia y la encefalopatía hepática sobre la conectividad neuronal en cerebro de pacientes cirróticos y modelos animales. Implicaciones terapéuticas*

Doctoral candidate: Raquel García García

Director(s): Carmina Montoliu Félix, Cristina Forn Frías, Vicente Felipe Orts

Date of the defense: 25/10/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Efectos del sorafenib, un inhibidor tirosina quinasa, en el control del tono vascular*

Doctoral candidate: Isabel Pérez Monzó

Director(s): Pascual Medina Bessó, Gloria Segarra Irlles, Paloma LLuch García

Date of the defense: 24/04/2018

Grade: *Sobresaliente "cum laude"*

Figure 1

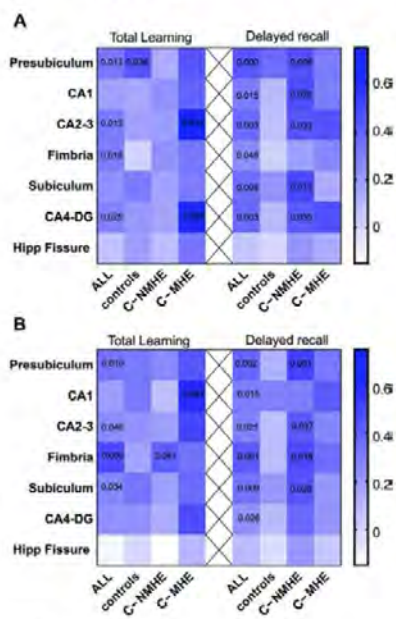


Figure 2

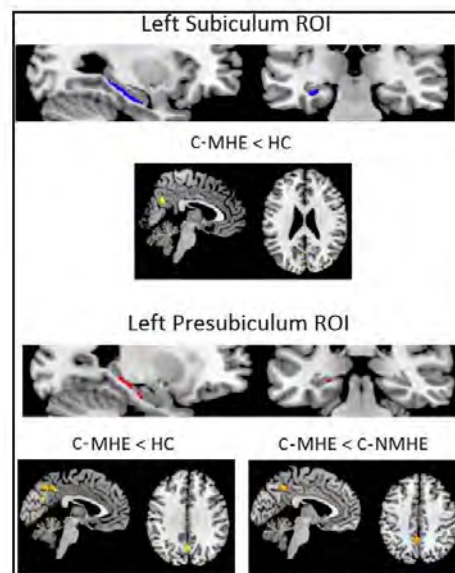


Figure 3

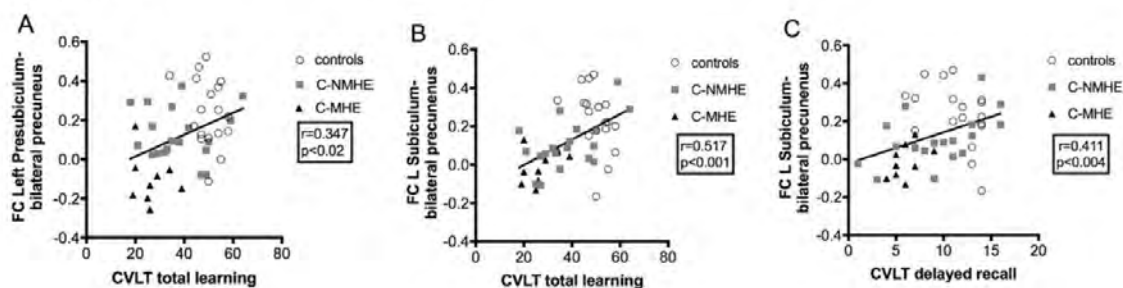


Figure 1. Correlational heat map depicting the relationship between different hippocampal subfield volumes of the left (A) and right (B) hemispheres and total learning and delayed recall in CVLT (California Verbal Learning Test).

Figure 2. Significant differences in subiculum and presubiculum functional connectivity (FC) between groups in the ANCOVA design (including gender as nuisance covariate).

Figure 3. Correlations between CVLT parameters and functional connectivity (FC) in controls, cirrhotic patients without (C-NMHE) and with MHE (C-MHE).

(A) positive correlations between CVLT total learning and FC between the left presubiculum and bilateral precuneus; (B) positive correlations between CVLT total learning and FC between left subiculum and bilateral precuneus; (C) positive correlations between CVLT delayed recall and FC between left subiculum and bilateral precuneus. CVLT, California Verbal Learning Test; MHE, minimal hepatic encephalopathy.

Research Group on Inflammation
Consolidated group

Team involved in
ciberes



Group members

Principal investigator

Esteban Morcillo Sánchez. University
María Jesús Sanz Ferrando. University

Elena Domingo Pérez. University
Andrea Herrero Cervera. INCLIVA

Emerging researchers

Laura Piqueras Ruiz. INCLIVA
Herminia González Navarro. INCLIVA
Nuria Cabedo Escrig. INCLIVA

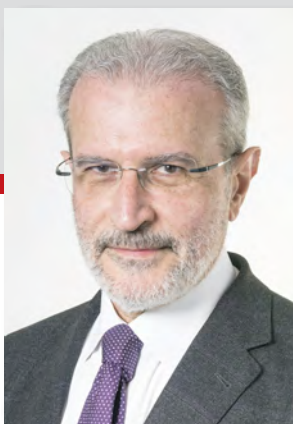
Technicians

Ángela Vinué Visús. INCLIVA
Francisca Sellés Sorli. INCLIVA
Laura Vila Dasí. INCLIVA

PhD researchers

Aida Collado Sánchez. University
Patrice Gomes Marques. INCLIVA

	R1	R2	R3	R4	STAFF
Researchers by categories	3	4	-	2	3
Researchers financed by competitive public calls or networks	1	3	-	-	2



Strategic aims

- Study of membrane tethered mucin MUC1 deficiency in steroid resistance scenario of chronic pulmonary inflammation and oxidative stress.
- Study of JAK2 signaling in lung fibrosis, pulmonary vascular remodeling and pulmonary hypertension.
- Study of the anti-inflammatory effects of selective inhibitors of phosphodiesterase type 4 isoforms, in particular PDE4B and PDE4D inhibitors.
- Study of the role of CXCL16/CXCR6 axis in the cardiovascular disease associated to metabolic syndrome and abdominal aortic aneurysm (AAA).
- Study of the systemic inflammation associated to Primary Hypercholesterolemia.
- Study of the CCL11/CCR3 axis in Primary Hypercholesterolemia and atherosclerosis.
- Study of the impact of PCSK9 blockade in the systemic inflammation associated to Familial Hypercholesterolemia.
- Synthesis of new dual PPAR α / γ agonists and pharmacology study in ob/ob mice.
- Study of the role of CXCR3 axis in obesity.
- Study of SGLT-2 inhibitors in abdominal aortic aneurysm (AAA).
- Study of the role of the inflammatory axis LIGHT(TNFSF14)/Lymphotoxin β receptor, in the biochemical, cellular and genetic mechanisms of atherosclerosis and insulin.

Main lines of research

- Pharmacological modulation of chronic inflammation and remodeling in the context of chronic obstructive pulmonary disease, asthma and idiopathic pulmonary fibrosis.
- Study of the vascular inflammation induced by different risk factors of atherosclerosis: metabolic syndrome, primary and familial hypercholesterolemia. Effect of PCSK9 inhibitors in the systemic inflammation associated to familial hypercholesterolemia.
- Synthesis of new dual PPAR α / γ agonists to be used in the control of cardiometabolic disorders.
- Study of the role of CXCR3 axis and nuclear ROR receptors in human obesity.
- Study of new anti-angiogenic mediators in acute myocardial infarct.
- Study of the CDKN2A/B genes and the LIGHT cytokine in the atherosclerosis associated with insulin resistance.



Emerging Researcher

Laura Piqueras Ruiz

The preclinical research focuses on the understanding of the molecular and cellular mechanisms that underlie the development and progression of the aneurysm. We are also exploring the effect of several nuclear receptors, X retinoid receptor (RXR), peroxisome proliferator activating receptors (PPAR) and vitamin D receptor ligands (VDR) in the development of AAA. We are also interested in characterizing the new molecular mechanism associated with the

formation of aneurysms in animal models and human samples. Additionally, we are investigating the role of several nuclear receptors on inflammation and angiogenesis associated to obesity.



Emerging Researcher

Herminia González Navarro

The research is focused in the study of the molecular mechanisms of the diabetes mellitus (DM) and its effect on atherosclerosis, the main cause of cardiovascular disease. To perform these studies we employ genetically-modified mice that develop metabolic alterations such as diabe-

tes, insulin resistance, fatty liver disease (another related metabolic disease) and atherosclerosis. To translate our findings into the human pathology we also perform investigations in human subjects and in human cell cultures. Specifically our research lines are focused in the understanding of one main mechanism connecting these metabolic diseases, the unbalanced interplay of the different immune cellular subsets. Recently, we have observed that either genetic inactivation of some key inflammatory mediators or inhibition of intracellular signaling-cascades in mice and human cells, restore the immune cell homeostasis and decreases disease progression. These studies will allow us to identify novel therapeutic targets based on immune cell modulation to treat metabolic diseases.



Emerging Researcher

Nuria Cabedo Escrig

The research lines include the synthesis and pharmacological studies of biologically active molecules with both natural and synthetic origin in the field of the medicinal chemistry. We search the development of new drugs focused mainly on therapeutic targets such as peroxisome proliferator activating receptors (PPAR) and liver X receptors (LXR), dopaminergic receptors, mitochondrial respiratory chain inhibitors as new anti-inflammatory, antidiabetic, anti-obesity and cytotoxic agents in order to treat cardiometabolic disorders and neurological diseases.

• PUBLICATIONS

Number of articles	IF	Average IF
12	75,31	6,275

National collaborations	International collaborations	Corresponding author
6	4	5

SELECTED PUBLICATIONS

1. Furio E, García-Fuster MJ, Redon J, Marques P, Ortega R, Sanz MJ, Piqueras L. CX3CR1/CX3CL1 AXIS mediates platelet-leukocyte adhesion to arterial endothelium in younger patients with a history of idiopathic deep vein thrombosis. *Thrombosis and Haemostasis*. 2018; 118: 562 - 571. IF: 4,952
2. Collado A, Marques P, Escudero P, Rius C, Domingo E, Martínez-Hervás S, Real JT, Ascaso JF, Piqueras L, Sanz MJ. Functional role of endothelial CXCL16/CXCR6-platelet-leukocyte axis in Angiotensin II-associated metabolic disorders. *Cardiovascular Research*. 2018; 114: 1764 - 1775. IF: 6,290
3. Ferrando C, Soro M, Unzueta C, Suarez-Sipmann F, Canet J, Librero J, Pozo N, Peiró S, Llombart A, León I, India I, Aldecoa C, Díaz-Cambronero O, Pestaña D, Redondo FJ, Garutti I, Balust J, García JI, Ibáñez M, Granell M, Rodríguez A, Gallego L, de la Matta M, Gonzalez R, Brunelli A, García J, Rovira L, Barrios F, Torres V, Hernández S, Gracia E, Giné M, García M, García N, Miguel L, Sánchez S, Piñero P, Pujol R, García-Del-Valle S, Valdivia J, Hernández MJ, Padrón O, Colás A, Puig J, Azparren G, Tusman G, Villar J, Belda J; Individualized Perioperative Open-lung VEntilation (iPROVE) Network. Individualised perioperative open-lung approach versus standard protective ventilation in abdominal surgery (iPROVE): a randomised controlled trial. *Lancet Respiratory Medicine*. 2018; 6(3): 193 - 203. IF: 21,466
4. Milara J, Ballester B, Morell A, Ortiz JL, Escrivá J, Fernández E, Perez-Vizcaino F, Cogolludo A, Pastor E, Artigues E, Morcillo E, Cortijo J. JAK2 mediates lung fibrosis, pulmonary vascular remodelling and hypertension in idiopathic pulmonary fibrosis: an experimental study. *Thorax*. 2018; 73(6): 519 - 529. IF: 9,655
5. Hueso L, Ortega R, Sellés F, Wu-Xiong NY, Ortega J, Civera M, Ascaso JF, Sanz MJ Real JT, Piqueras L. Upregulation of angiostatic chemokines IP-10/CXCL10 and I-TAC/CXCL11 in human obesity and their implication for adipose tissue angiogenesis. *International Journal of Obesity*. 2018; 42: 1406 - 1417. IF: 5,151

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: COST Action CA15135

Title: *Multi-target paradigm for innovative ligand identification in the drug discovery process (MuTaLig)*

Principal Investigator: Stefano Alcaro (Nuria Cabedo as Management Committee substitute)

Funding Body: *European Commission*

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

Duration: 2016-2020

Title: *The William Harvey International Translational Research Academy (WHRI-ACADEMY)*

Principal Investigator: Márta Korbonits (María Jesús Sanz as collaborating researcher)

Funding Body: *FP7 Marie Curie Actions*

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

Duration: 2015-

Total budget: 6,5 million€

Reference: COST Action BM1402

Title: *Development of a European network for preclinical testing of interventions in mouse models of age and age-related diseases (MouseAGE)*

Principal Investigator: Ilaria Bellantuono (Herminia González as collaborating researcher)

Funding Body: *European Commission*

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

Duration: 2014-2018

Reference: PI16/00091

Title: *Papel de los procesos inflamatorios asociados a la diabetes en la estabilidad de la placa de ateroma y estudio del uso potencial de estrategias terapéuticas*

Principal Investigator: Herminia González Navarro

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2019

Total Budget: 122.815€

Reference: PI15/00082

Title: *Estudio de nuevos mecanismos inflamatorios y angiogénicos asociados a la obesidad grave mórbida: papel del eje CXCR3 y los receptores nucleares RORs*

Principal Investigator: Laura Piqueras Ruiz

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total Budget: 154.577€

Reference: PIE15/00013

Title: *A multidisciplinary project to advance in basic mechanisms, diagnosis, prediction, and prevention of cardiac damage*

in reperfused acute myocardial infarction

Principal Investigator: Vicente Bodí Peris (Laura Piqueras as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total Budget: 589.050€

Reference: CP15/00150

Title: *Synthesis and pharmacological evaluation of new dual PPARalpha/gamma agonists as new therapeutic tools in the control of cardiometabolic disorders*

Principal Investigator: Nuria Cabedo Escrig

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total budget: 121.500€

Reference: CB07/08/0018

Title: *CIBER de Diabetes y de Enfermedades Metabólicas asociadas (CIBERdem)*

Principal Investigator: Juan Francisco Ascaso Gimilio and José Tomás Real Collado

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2008-

Total budget: 154.577€

Reference: CB06/06/0027

Title: *CIBER Enfermedades Respiratorias (CIBERes)*

Principal Investigator: Esteban Morcillo Sánchez

Fundingbody: *Instituto de Salud Carlos III*

Beneficiary institution: *Universidad de Valencia*

Duration: 2007-

Reference: CB07/08/0043

Title: *CIBER de Diabetes y de Enfermedades Metabólicas asociadas (CIBERdem)*

Principal Investigator: Deborah J Burks

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Universidad de Valencia*

Duration: 2007-

Reference: SAF2017-89714-R

Title: *Modulación farmacológica del sistema inmune como diana clave en la prevención de la enfermedad cardiovascular asociada a desórdenes metabólicos. Síntesis de fármacos novedosos*

Principal Investigator: Juan Francisco Ascaso and María Jesús Sanz Ferrando

Funding body: *Ministerio de Economía y Competitividad*

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

Duration: 2018-2020

Total budget: 205.700€

Reference: SAF2015-65368-R

Title: *Modulación farmacológica de la señalización inflamación-remodelado por inhibidores isoforma-selectivos de PDE4 y comparadores en modelos humanos in vitro relevantes en EPOC*

Principal Investigator: Esteban Morcillo Sánchez

Funding body: *Ministerio de Economía y Competitividad*

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

Duration: 2016-2018

Total budget: 181.500€

Reference: SAF2014-57845-R

Title: *Modulación inmunofarmacológica de la inflamación sistémica asociada a desórdenes metabólicos. Búsqueda de nuevas dianas terapéuticas y síntesis de fármacos novedosos*

Principal Investigator: María Jesús Sanz Ferrando and Juan Francisco Ascaso Gimilio

Funding Body: *Ministerio de Economía y Competitividad*

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

Duration: 2015-2018

Total Budget: 302.500€

Reference: APOTIP/2018/02

Title: *Desarrollo preclínico de un nuevo tratamiento para la aterosclerosis*

Principal Investigator: Herminia González Navarro

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

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

Duration: 2018-2019

Total budget: 27.000€

Title: *Role of the cytokine LIGHT (TNFSF14) in the development of insulin resistance and fatty liver disease*

Principal Investigator: Herminia González Navarro

Funding Body: *European Foundation for the Study of Diabetes*

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

Duration: 2016-2018

Total budget: 70.000€

Reference: 3251-17

Title: *Desarrollo preclínico de un nuevo tratamiento para la aterosclerosis*

Principal Investigator: Herminia González Navarro

Funding Body: *Fundación para la Innovación y Prospectiva en Salud en España (FIPSE)*

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

Duration: 2018

Total budget: 30.000€

Reference: Proyecto Paula

Title: *Estudio del papel del locus Ink4/Arf en la funcionalidad de las células β en un modelo murino de diabetes*

Principal Investigator: Herminia González Navarro

Funding Body: *Proyecto Paula*

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

Duration: 2013-2018

Total budget: 108.472,03€

Research Group on Oxidative Pathology
Consolidated group

Team involved in
ciberobn



Group members

Principal investigator

Guillermo Sáez Tormo
University

Collaborating researchers

Antonio Iradi Casal. University
Leticia Bagán Debón. University
Nuria Estañ Capell. University
Pedro Gargallo Bayo. University



	R1	R2	R3	R4	STAFF
Researchers by categories	3	0	1	1	-

Strategic aims

- To study the role of Mediterranean diet and the individual effect of olive oil and dietary polyphenols on hemodynamics, endothelial function, abdominal adiposity and gene expression in patients at high cardiovascular risk has been studied.
- To monitor the morbidly obese patients in terms of anthropometric changes, metabolic and oxidative stress markers before and after dietary intervention, exercise and bariatric surgery.
- To analyze in gastric carcinoma patients the role of DNA damage and different markers of oxidative stress in order to validate the modified base 8-oxo-dG as a possible tumor marker at high cardiovascular risk.

Main lines of research

- Study of the role of OS as a physiopathological mechanism of cardiometabolic diseases.
- Study of DNA damage and repair signaling routes in patients with cardiovascular evolution pathologies, in order to identify grades of expression in different genes.
- Study of OS role in the pathology of neoplastic diseases, as well as the possible validation of their molecular oxidative products as clinical markers.

• PUBLICATIONS

Number of articles	IF	Average IF
6	95,794	15,966
National collaborations	International collaborations	Corresponding author
2	2	1

SELECTED PUBLICATIONS

1. Carratala A, Martínez-Hervas S, Rodríguez-Borja E, Benito E, Real JT, Saez GT, Carmena R, Ascaso JF. PAI-1 levels are related to insulin resistance and carotid atherosclerosis in subjects with familial combined hyperlipidemia. *Journal of Investigative Medicine*. 2018; 66(1): 17 - 21. IF: 2,029
2. Corella D, Ramírez-Sabio JB, Coltell O, Ortega-Azorín C, Estruch R, Martínez-González MA, Salas-Salvado J, Sorlí JV, Castañer O, Arós F, García-Corte FJ, Serra-Majem L, Gómez-Gracia E, Fiol M, Pintó X, Saez GT, Toledo E, Basora J, Fitó M, Cofán M, Ros E, Ordovas JM. Effects of the Ser326Cys polymorphism in the DNA Repair OGG1 gene on cancer, cardiovascular, and all-cause mortality in the PREDIMED Study: modulation by diet. *Journal of the Academy of Nutrition and Dietetics*. 2018; 118(4): 589 - 605. IF: 4,021
3. Estruch R, Ros E, Salas-Salvado J, Covas MI, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pintó X, Basora J, Muñoz

MA, Sorlí JV, Martínez JA, Fitó M, Gea A, Hernán MA, Martínez-González MA, PREDIMED Study Investigators. Primary prevention of cardiovascular disease with a mediterranean diet supplemented with extra-virgin olive oil or nuts. *New England Journal of Medicine*. 2018; 378(25): e34. IF: 79,258

4. Gargallo P, Colado JC, Jueas A, Hernando-Espinilla A, Estañ-Capell N, Monzó-Beltran L, García-Pérez P, Cauli O, Sáez GT. The effect of moderate- versus high-intensity resistance training on systemic redox state and DNA damage in healthy older women. *Biological Research for Nursing*. 2018; 20(2): 205 - 217. IF: 1,579
5. Olivares D, Perez-Hernandez J, Forner MJ, Perez-Soriano C, Tormos MC, Saez GT, Chaves FJ, Redon J, Cortes R. Urinary levels of sirtuin-1 associated with disease activity in lupus nephritis. *Clinical Science*. 2018; 132(5): 569 - 579. IF: 5,220

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: CB12/03/30016

Title: *CIBER de la Obesidad y Nutrición (CIBERObn)*

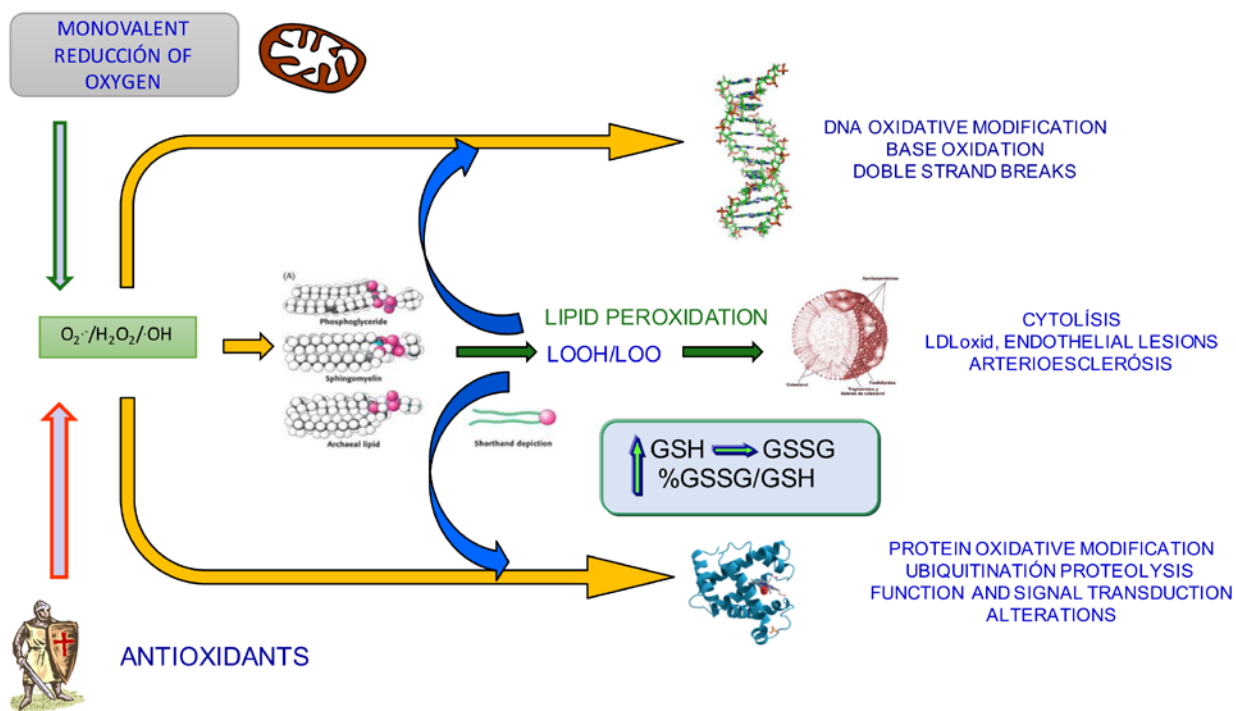
Principal Investigator: Guillermo Sáez Tormo

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2013-

Molecular Interactions of Reactive Oxygen Species



➤ **Research Group on Psychiatry and Neurodegenerative Diseases**
Consolidated group

Team involved in
cibersam
Centro de Investigación Biomédica En Red
de Salud Mental



Group members

Principal investigator

Julio Sanjuán Arias. Hospital. University

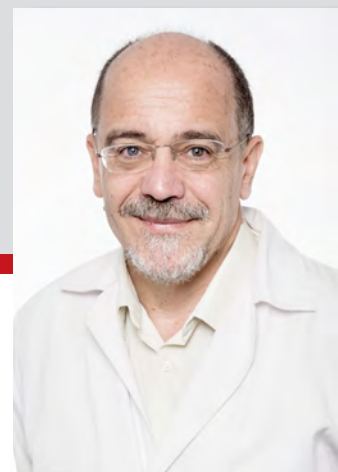
Collaborating researchers

José Carlos González Piqueras. Hospital
Eduardo Jesús Aguilar García-Iturrospe. Hospital. University
Esther Lorente Rovira. Hospital
María José Escartí Fabra. Hospital
María Dolores Moltó Ruiz. University
Marien Gadea Domenech. University
Gracián García Martí. CIBERSAM
Javier Gilabert Juan. University
Juan Nacher Roselló. University
Francisco Olucha Bordonau. University
Carlos Cañete Nicolás. Hospital

Miguel Hernández Viadel. Hospital. University
José Vicente Llorens Llorens. University
Pablo Calap Quintana. University
Noelia Sebastía Ortega. University
Javier González Fernández. University
Ramón Guirado Guillén. University
Blanca Llàcer Iborra. CIBERSAM

PhD researchers

Pablo Soldevila Matías. INCLIVA



	R1	R2	R3	R4	STAFF
Researchers by categories	2	3	11	1	3
Researchers financed by competitive public calls or networks	1	-	1	-	2

Strategic aims

- Elaboration of a mobile application associated to the Clinical Records to improve adherence to the treatment of patients with first episode psychosis.
- Publication of Results of Gene –Environmental interaction First Episode Psychosis projects.
- Development of new techniques to diagnosis psychosis by fMRI and machine learning approach.
- Development of animal models in severe mental disorder and neurodegenerative diseases.
- Models of Prediction of Response in First Psychotic Episodes.

Main lines of research

- Identifying risk polymorphisms in psychosis and affective disorders.
- Epigenetic studies (functional expression) of candidate genes in psychosis and mental illness.
- Study on animal models in serious mental illness.
- Generating models of neurodegenerative diseases (Friedreich Ataxia) on invertebrate animals (Drosophila).
- Study of mutations in monogenic neurodegenerative diseases.
- Identifying genetic and environmental risk factors in affective and psychotic disorders.
- Identifying abnormal patterns in neuroimaging (morphometry, functional, spectroscopy) in psychotic patients.
- Design and coordination of clinical, genetic and neuroimage data bases oriented to performing multicenter projects.
- Development of interactive systems for improving therapeutic adherence.
- Study on the efficiency of psycho-social intervention techniques in serious mental illness.

• PUBLICATIONS

Number of articles	IF	Average IF
17	74,496	4,382
National collaborations	International collaborations	Corresponding author
8	8	5

SELECTED PUBLICATIONS

1. Rotheneichner P, Belles M, Benedetti B, König R, Dannehl D, Kreutzer C, Zaubmair P, Engelhardt M, Aigner L, Nacher J, Couillard-Despres S. Cellular plasticity in the adult murine piriform cortex: continuous maturation of dormant precursors into excitatory neurons. *Cerebral Cortex*. 2018; 28(7): 2610 - 2621. IF: 6,308
2. Aguilar EJ, Corripio I, García-Martí G, Grasa E, Martí-Bonmatí L, Gómez-Ansón B, Sanjuán J, Núñez-Marín F, Lorente-Rovira E, Escartí MJ, Brabban A, Turkington D. Emotional fMR auditory paradigm demonstrates normalization of limbic hyperactivity after cognitive behavior therapy for auditory hallucinations. *Schizophrenia Research*. 2018; 193: 304 - 312. IF: 3,958
3. Gassó P, Mas S, Bioque M, Cabrera B, Lobo A, González-Pinto A, Díaz-Caneja CM, Corripio I, Vieta E, Castro-Fornieles J, Sarró S, Mané A, Sanjuan J, Llerena A, Lafuente A, Saiz-Ruiz J, Bernardo M, PEPs Group. Impact of NTRK2, DRD2 and ACE polymorphisms on prolactin levels in antipsychotic-treated patients with first-episode psychosis. *Journal of Psychopharmacology*. 2018; 32(6): 702 - 710. IF: 4,738
4. Perez-Rando M, Castillo-Gomez E, Bueno-Fernandez C, Nacher J. The TrkB agonist 7,8-dihydroxyflavone changes the structural dynamics of neocortical pyramidal neurons and improves object recognition in mice. *Brain Structure & Function*. 2018; 223(5): 2393 - 2408. IF: 4,231
5. Jongasma HE, Gayer-Anderson C, Lasalvia A, Quattrone D, Mulè A, Szöke A, Selten JP, Turner C, Arango C, Tarricone I, Berardi D, Tortelli A, Llorca PM, de Haan L, Bobes J, Bernardo M, Sanjuán J, Santos JL, Arrojo M, Del-Ben CM, Menezes PR, Velthorst E, Murray RM, Rutten BP, Jones PB, van Os J, Morgan C, Kirkbride JB, European Network of National Schizophrenia Networks Studying Gene-Environment In. Treated incidence of psychotic disorders in the multinational EU-GEI Study. *JAMA Psychiatry*. 2018; 75(1): 36 - 46. IF: 16,642

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI17/00402

Title: *Resonancia magnética funcional y expresión génica como predictores en primeros episodios psicóticos*

Principal Investigator: Julio Sanjuán Arias

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 110.231€

Reference: PI14/00044

Title: *Eficacia del entrenamiento metacognitivo individualizado (EMC+) en personas con psicosis de reciente evolución*

Principal Investigator: Susana Ochoa (Esther Lorente and Ana Luengo as collaborating researchers)

Funding body: *Ministerio de Ciencia e Innovación*

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

Duration: 2015-2018

Total budget: 92.565€

Reference: CB07/09/006

Title: *CIBER de Investigación en Salud Mental (CIBERsam)*

Principal Investigator: Julio Sanjuán Arias

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Universidad de Valencia*

Duration: 2008-

Reference: SAM16PE07

Title: *Cohorte CIBERSAM de casos con primer episodio psicótico y controles*

Principal Investigator: David Fraguas (Julio Sanjuán Arias as collaborating researcher)

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *CIBER de Investigación en Salud Mental (CIBERsam)*

Duration: 2016-2018

Total budget: 499.720€

Reference: SAF2015-68436-R

Title: *Plasticity of perisomatic inhibition on pyramidal neurons of the prefrontal cortex: impact of peripubertal stress and implication in psychiatric disorder*

Principal Investigator: Juan Salvador Nacher Roselló

Funding body: *Ministerio de Economía y Competitividad*

Beneficiary institution: *Universidad de Valencia*

Duration: 2016-2019

Total budget: 193.600€

Reference: INNVAL10/18/003

Title: *Nueva Técnica para el Diagnóstico individualizado de Psicosis, basada en aprendizaje automático ("machine learning"), a partir de datos de RMf*

Principal Investigator: Julio Sanjuán Arias

Funding Body: *AVI (Agencia Valenciana de Innovación) – Generalitat Valenciana*

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

Duration: 2018

Total budget: 48.000€

Reference: PROMETEO/2016/082

Title: *Investigación de marcadores biológicos y nuevas estrategias terapéuticas en la Psicosis*

Principal Investigator: Julio Sanjuán Arias

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

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

Duration: 2016-2019

Total budget: 179.940€

Title: *Identification of genetic factors involved on FXN transcriptional silencing mediated by the GAA repeat expansion*

Principal Investigator: M^a Dolores Moltó Ruiz

Funding Body: *Friedreich's Ataxia Research Alliance (FARA)*

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

Duration: 2016-2019

Total budget: 154.575,59€

Title: *Inhibidores de fosfodiesterasas como tratamiento para la Ataxia de Friedreich*

Principal Investigator: Pilar González Cabo (M^a Dolores Moltó Ruiz as collaborating researcher)

Funding Body: *Fundación Ramón Areces*

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

Duration: 2017-2019

Total budget: 119.700€

- **THESIS**

Thesis title: *Modelos de Ataxia de Friedreich en drosophila: identificación de candidatos terapéuticos y caracterización de un modelo portador de las repeticiones GAA*

Doctoral candidate: Pablo Calap Quintana

Director(s): M^a Dolores Moltó Ruiz, José Vicente Llorens Llorens

Date of the defense: 15/10/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Papel del sistema relaxina3/rxfp3 en la memoria espacial y comportamiento social*

Doctoral candidate: Héctor Albert Gascó

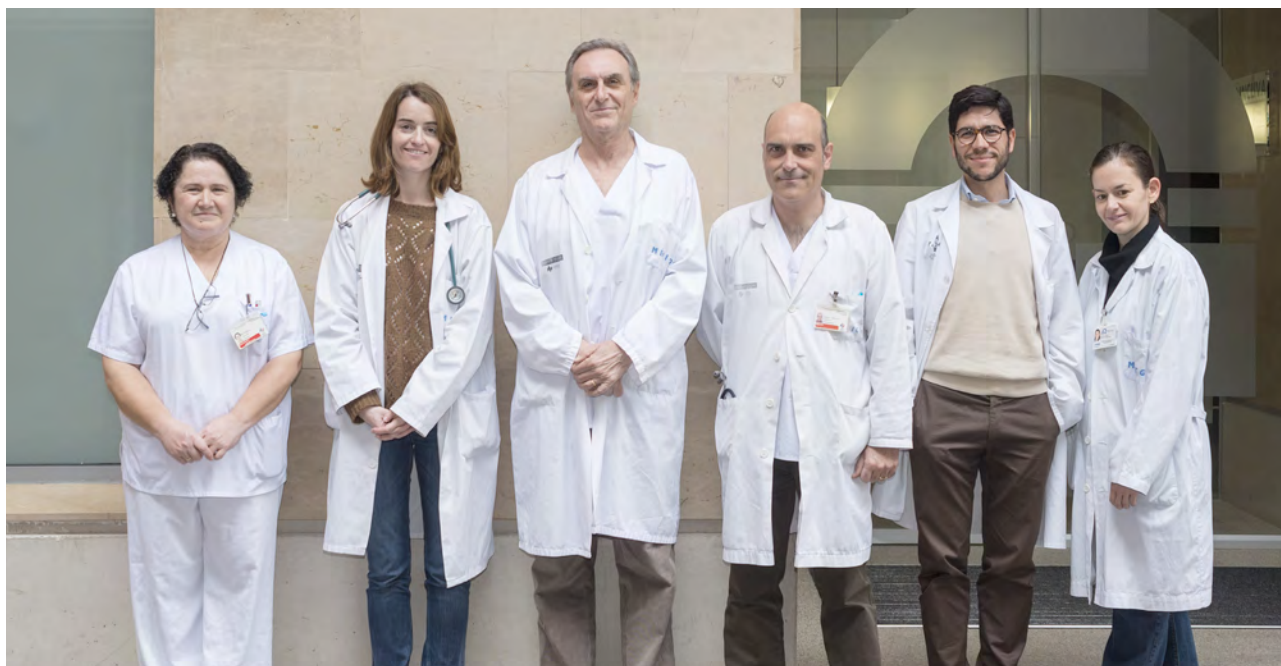
Director(s): Ana María Sánchez Pérez, Francisco Olucha Bordonau

Date of the defense: 29/10/2018

Grade: *Sobresaliente "cum laude"*

Quality recognition/Award: European PhD

Research Group on respiratory problems of neuromuscular diseases and lung damage Consolidated group



Group members

Principal investigator

Emilio Servera Pieras
Hospital. University

- M^a Luisa Briones Urtiaga. Hospital
- M^a Jesús Zafra Pirés. Hospital
- María Belén Safont Muñoz. Hospital
- M^a Cruz González Villaescusa. Hospital
- Enric Burés Sales. Hospital
- Nuria Garrido Zafra. Hospital
- Jaime Signes-Costa Miñana. Hospital
- Santos Ferrer Espinosa. INCLIVA

Collaborating researchers

- Jesús Sancho Chinesta. Hospital
- María Pilar Barreto Martín. University
- José Luís Díaz Cordobés. University
- Pilar Bañuls Polo. Hospital
- Manuela Marín González. Hospital



	R1	R2	R3	R4	STAFF
Researchers by categories	4	1	5	1	3

Strategic aims

- To evaluate the usefulness of non invasive ventilation in the weaning process of patients with chronic critical disorders and those with prolonged mechanical ventilation in Respiratory Care Units.
- To analyze physiology of cough in patients with amyotrophic lateral sclerosis (ALS) during mechanically assisted cough, with high frequency oscillations.
- To study the effect of bulbar type of ALS among the efficacy of coughing , mechanically assisted with in-exhuflation, through high frequency oscillations in ALS patients.
- To identify the predictive factors for complicated grief in relatives of severe respiratory patients.
- To study clinical tools to evaluate front-temporal dementia to ALS patients.
- To find effective non-pharmacological treatments to improve dysnea in patients with chronic respiratory failure.

Main lines of research

- Study of long term utility of mechanically assisted cough with in-exhuflation, through high frequency oscillations, in ALS patients.
- Study of the efficacy of mechanically assisted cough with in-exhuflation, through high frequency oscillations, during acute respiratory infections, in ALS patients.
- Study of long term utility of mechanically assisted cough with in-exhuflation, through high frequency oscillations, in ALS patients and mechanical ventilation trough tracheotomy.
- Study of physio-pathology of assisted cough with in-exhuflation, through high frequency oscillations, in ALS patients.
- Study of the effect of bulbar alteration in survival of ALS patients and non invasive mechanical ventilation.
- Study of the physio-pathology in the failure of non invasive mechanical ventilation in ALS patients.
- Study of treatment with quinidine/dextromethorphan in the delay of failure of non invasive management of respiratory problems in ALS patients.
- To improve knowledge in the staging of patients with neuromuscular diseases to anticipate decisions and to adjust respiratory therapeutic measures.
- To improve knowledge in technical assistance and replacement of the respiratory muscles in neuromuscular diseases, particularly to the life-prolonging without adding suffering.
- To improve knowledge in the management of the psycho-emotional needs in patients with COPD and incapacitating dyspnea and their caregivers.
- To improve knowledge about the role of genetic polymorphisms in the predisposition, severity and susceptibility to bacteremia in community-acquired pneumonia.
- To evaluate the efficiency of the management of dyspnea.
- To assess cognitive / behavioral signs associated with neuromuscular dementia patients and their involvement in the decision-making process.
- To evaluate the prevalence of stressful life events, different styles of attachment and the proportion of adaptive and problem duels present in relatives of patients at the end of life.
- Cardiac morphological changes in patients with sleep respiratory disorders and ischemic heart disease: response to CPAP treatment.
- Effects of e-liquids (propylene glycol (PG), diethylene glycol (DG), and nicotine) from electronic cigarettes in human cell cultures: Human umbilical vein endothelial cells (HUVEC) and adenocarcinomic human alveolar basal epithelial cells (A549).
- Efficacy of a tobacco treatment program about severe exacerbation in smokers with a moderate or severe COPD.
- Evaluation of CPAP on kidney function in patients with early-stage renal disease and sleep apnea syndrome (RENAS study).

- Characterization of asthmatic patients: new bio-markers (perioistine and protein CC16) and their relationship with the severity of bronchial asthma.
- Study of genetic variability in the susceptibility and severity of pneumonia.
- Efficiency of an integrated program for COPD patients with frequent hospital admissions.
- Open label multicentric study of RCP1063 oral in recurrent multiple sclerosis (MS).
- Randomized, double-blind, multicentric, parallel groups, controlled with placebo and variable duration, to evaluate efficacy and safety of Sponimod (BAF312) in patients with secondary MS, followed by an open extension treatment of BAF312.

• PUBLICATIONS

Number of articles	IF	Average IF
7	32,124	4,589

National collaborations	International collaborations	Corresponding author
4	3	-

SELECTED PUBLICATIONS

1. Vinuesa V, Borrás R, Briones ML, Clari MÁ, Cresencio V, Giménez E, Muñoz C, Oltra R, Servera E, Scheelje T, Tornero C, Navarro D. Performance of a highly sensitive mycobacterium tuberculosis complex real-time PCR assay for diagnosis of pulmonary tuberculosis in a low-prevalence setting: a prospective intervention study. *Journal of Clinical Microbiology*. 2018; 56(5): pii: e00116 - 18. IF: 4,054
2. Chatwin M, Toussaint M, Gonçalves MR, Sheers N, Mellies U, Gonzales-Bermejo J, Sancho J, Fauroux B, Andersen T, Hov B, Nygren-Bonnier M, Lacombe M, Pernet K, Kampelmacher M, Devaux C, Kinnett K, Sheehan D, Rao F, Villanova M, Berlowitz D, Morrow BM. Airway clearance techniques in neuromuscular disorders: a state of the art review. *Respiratory Medicine*. 2018; 136: 98 - 110. IF: 3,230
3. Toussaint M, Chatwin M, Gonzales J, Berlowitz DJ, ENMC Respiratory Therapy Consortium. 228th ENMC International Workshop: airway clearance techniques in neuromuscular disorders Naarden, The Netherlands, 3-5 March, 2017. *Neuromuscular Disorders*. 2018; 28(3): 289 - 298. IF: 2,487
4. Moreno G, Rodríguez A, Reyes LF, Gomez J, Sole-Violan J, Díaz E, Bodí M1, Trefler S, Guardiola J, Yébenes JC, Soriano A, Garnacho-Montero J, Socias L, Del Valle Ortíz M, Corregio E, Marín-Corral J, Vallverdú-Vidal M, Restrepo MI, Torres A, Martín-Loeches I; GETGAG Study Group. Corticosteroid

treatment in critically ill patients with severe influenza pneumonia: a propensity score matching study. *Intensive Care Medicine*. 2018; 44(9): 1470 - 1482. IF: 15,008

5. García-Villaescusa A, Morales-Tatay J, Monleón-Salvado D, González-Darder J, Bellot-Arcis C, Montiel-Company J, Almerich-Silla J. Using NMR in saliva to identify possible biomarkers of glioblastoma and chronic periodontitis. *Plos One*. 13(2):e0188710. IF: 2,766

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI15/00137

Title: *Efecto de la CPAP en el deterioro de la función renal en estadios tempranos de enfermedad renal crónica*

Principal Investigator: Jaime Coral Peñafiel

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación para la Formación y la Investigación de los profesionales de la salud (FUNDESALUD)*

Duration: 2016-2018

Total budget: 134.915€

Title: *Valoración de la demencia frontotemporal y su repercusión en el proceso de toma de decisiones terapéuticas en pacientes con esclerosis lateral amiotrófica*

Principal Investigator: Emilio Servera Pieras

Funding Body: *Sociedad Valenciana de Neumología/Fundación de Neumología de la Comunidad Valenciana*

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

Duration: 2016-2018

Total budget: 12.000€

Title: *Eficacia de un programa intensivo de tratamiento del ta-*

baquismo sobre las exacerbaciones graves de pacientes fumadores con EPOC moderada-severa

Principal Investigator: Jaime Signes-Costa

Funding Body: *Sociedad Española de Neumología y Cirugía Torácica*

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

Duration: 2016-2018

Total budget: 12.000€

Reference: MI-E WAVEFORMS ALS Study

Title: *Estudio sobre la influencia de la efectividad de los pico flujo de tos del análisis de las gráficas generadas por la tos asistida mecánicamente en los pacientes con esclerosis lateral amiotrófica en situación clínica estable*

Principal Investigator: Jesús Sancho Chinesta

Funding body: *Sociedad Española de Neumología y Cirugía Torácica (SEPAR) and Asociación Latinoamericana del Tórax (ALAT)*

Beneficiary institution: *Hospital Clínico Universitario de Valencia*

Duration: 2017-2018

Total budget: 6.000€

Title: *Efecto de VitaBreath para la recuperación tras el ejercicio en EPOC grave y muy grave*

Principal Investigator: Emilio Servera Pieras

Funding body: Philips- Respiroics

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

Duration: 2017-2019

• **THESIS**

Thesis title: *Beneficios de un programa de soporte para familiares de pacientes al final de la vida: estudio multicéntrico*

Doctoral candidate: Ana Lucila Soto Rubio

Director(s): Pilar Barreto Martín, M^a Antonia Pérez Marín

Date of the defense: 09/07/2018

Grade: *Sobresaliente "cum laude"*

Quality recognition/Award: European PhD

Research Group on Tissular Biochemistry

Consolidated group



Group members

Principal investigator

Juan R. Viña
University

Collaborating researchers

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

Technicians

Concha García de Mier. University

Emerging researcher

Rosa Zaragoza Colom. University



	R1	R2	R3	R4	STAFF
Researchers by categories	1	1	4	-	1

Strategic aims

- Calpains, activated in the mammary gland during involution can be implicated in cell anchoring loss. The isoform-specific function of CAPN1 and -2 was explored in two models of cell-adhesion disruption: mice mammary gland during involution and breast cancer cell lines.
- Role of calpains in cancer cells, CAPNs appear in the nucleolar compartment, having a role in ribosomal biogenesis.
- Vitamin A deficiency impairs lung basement membrane and alters lung parenchyma. Our goal was to elicit several proteins responsible for this alteration.

Main lines of research

- The mammary gland as a physiological model for the study of programmed cell death.
- Mammalian tissues metabolism and its regulation.
- Role of calpains in proliferation of cancer cells: Colon cancer cell lines.
- Vitamin A deficiency induces oxidative stress in several tissues including lung and liver.



Emerging Researcher

Rosa Zaragozá Colom

The research has been focused on the pathways that regulate mammary gland involution after the pregnancy/lactation cycle and how these pathways become deregulated in breast cancer. Over the past years,

our group has unveiled the role of calpains, calcium-dependent proteases, in the mammary tissue. We have demonstrated a dual role for calpains during involution, controlling programmed cell death of epithelial cells and adipocyte redifferentiation. Moreover, in breast cancer cell lines, calpains are involved in adhesion and cell migration. In the near future we will try to elucidate new functions of these proteases according to their subcellular localization.

• PUBLICATIONS

Number of articles	IF	Average IF
3	14,532	4,844

National collaborations	International collaborations	Corresponding author
3	0	3

SELECTED PUBLICATIONS

1. Timoneda J, Rodríguez-Fernández L, Zaragozá R, Marín MP, Cabezuelo MT, Torres L, Viña JR, Barber T. Vitamin A deficiency and the lung. *Nutrients*. 2018; 10(9): pii: E1132. IF: 4,196
2. Telechea-Fernández M, Rodríguez-Fernández L, García C, Zaragozá R, Viña JR, Cervantes A, García-Trevijano ER. Correction: New localization and function of calpain-2 in nucleoli of colorectal cancer cells in ribosomal biogenesis: effect of KRAS status. *Oncotarget*. 2018; 9(26): 18664. IF: 5,168
3. Telechea-Fernández M, Rodríguez-Fernández L, García C, Zaragozá R, Viña J, Cervantes A, García-Trevijano ER. New localization and function of calpain-2 in nucleoli of colorectal cancer cells in ribosomal biogenesis: effect of KRAS status. *Oncotarget*. 2018; 9(10): 9100 - 9113. IF: 5,168

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PROMETEOII/2018/167

Title: *Estudios tridimensionales de ductos mamarios para determinar el papel de las calpáinas en la remodelación del tejido mamario. Implicaciones biomédicas*

Principal Investigator: Juan Viña Ribes

Funding Body: Conselleria de Educación, Cultura y Deporte

Beneficiary Institution: Universidad de Valencia

Duration: 2018-2021

Total Budget: 201.920,20€

- **THESIS**

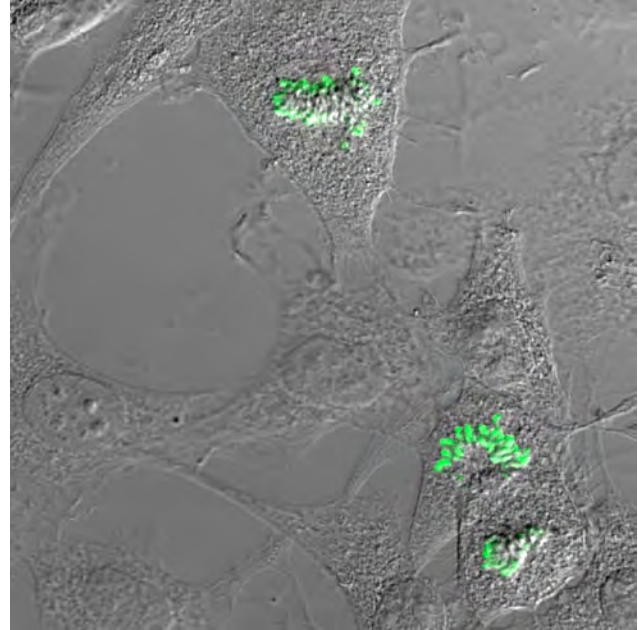
Thesis title: *Nueva localización y función de la calpaína 2 en el nucleolo de células de cáncer colorrectal en la biogénesis ribosomal: efecto del estado de KRAS*

Doctoral candidate: Marcelino Telechea Fernández

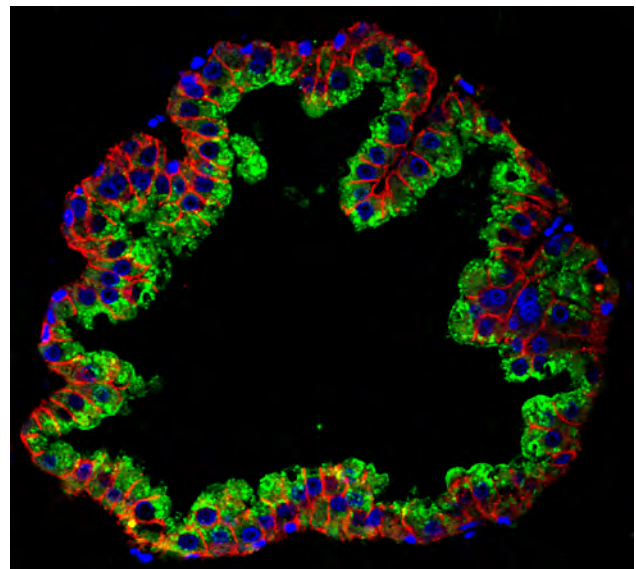
Director(s): Andrés Cervantes Ruipérez, Elena Ruiz García-Trevijano

Date of the defense: 09/11/2018

Grade: *Sobresaliente "cum laude"*



Nuclear distribution of CAPN1 (Green) in the nuclei of MCF-7 cells.



Mammary duct from control lactating mice. Immunofluorescence staining shows distribution of E-cadherin (red) along the cell junctions and CAPN1 (green) at the apical side of epithelial cells.

Research Group on Aging and Physical Activity Consolidated group

Team involved in



Group members

Principal investigator

José Viña Ribes. University

Collaborating researchers

- Gloria Olaso González. University
- José Viña Almunia. University
- Marta Inglés de la Torre. University
- Consolación García Lucerga. University
- Eva Serna García. University
- Cristina Amézcuca García. CIBER
- Mónica Cebrian Pinar. INCLIVA

PhD researchers

- Cristina Mas Bargues. University
- Andrea Salvador Pascual. University
- Paloma Monllor Taltavull. University

- Coralie Arc-Chagnaud. University
- Mar Dromant Jarque. CIBER
- Lucía Gimeno Mallench. INCLIVA
- Adrián Marcel De la Rosa González. University

Emerging researchers

- Consuelo Borrás Blasco. University
- M^a Carmen Gómez Cabrera. University
- Ana Lloret Alcañíz. University
- Juan Gambini Buchón. University



	R1	R2	R3	R4	STAFF
Researchers by categories	5	11	-	1	2

Strategic aims

- Prevented of neuronal death in Alzheimer's by Glutaminase Inhibition.
- Identification of exercise training as a drug to treat age associated frailty.
- Testing that G6PD protects from oxidative damage and improves healthspan in mice.
- Reductive stress: a new concept in Alzheimer's disease.

Main lines of research

- Aging: identification of genes associated with aging, particularly genes that are specific in centenary people. Implication of the estrogens and phytoestrogens in the prevention of age-related damage.
- Physical activity: identification of the molecular mechanisms by which physical activity is good for health. Identification of the mechanisms by which physical activity and antioxidant supplements help preventing primary and secondary sarcopenia in both human and animal studies. Identification of the best exercise intervention to delay and to treat frailty in humans.
- Physiopathology of the Alzheimer's disease: identification of the mechanisms by which free radicals, originators of the oxidative stress are used to unleash cell signals that lead to cell death in Alzheimer disease.



Emerging Researcher

Consuelo Borrás Blasco

The research focuses on stem cells and their optimization for the use of them, or their derived exosomes, in the regeneration of different tissues. We have studied the role of oxygen concentration in different parameters such as proliferation, pluripotency, senescence or apoptosis in the culture of human dental pulp stem cells (hDPSC) observing that the properties of stem cells are better maintained under physiological oxygen concentrations. The step we have taken now is to study if there is a beneficial effect of the addition of exosomes from "young" stem cells to "old" stem cells.



Emerging Researcher

María Carmen Gómez Cabrera

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



Emerging Researcher

Ana Lloret Alcañiz

Our main line of research has been the role of oxidative stress in Alzheimer's disease. Our group elucidated the importance of mitochondria in the generation of oxidants by their direct interaction with the amyloid peptide of Alzheimer. In recent years, we have focused on the study of the molecular changes produced by the toxicity of beta-amyloid.



Emerging Researcher

Juan Gambini Buchón. University

The main aim is mainly focused on nutrition, ageing, and longevity manipulation.

• PUBLICATIONS

Number of articles	IF	Average IF
16	117,001	7,312
National collaborations	International collaborations	Corresponding author
7	8	3

SELECTED PUBLICATIONS

1. Pagano AF, Brioché T, Arc-Chagnaud C, Demangel R, Chopard A, Py G. Short-term disuse promotes fatty acid infiltration into skeletal muscle. *Journal of Cachexia Sarcopenia and Muscle*. 2018; 9(2): 335 - 347. IF: 12,511
2. Ferrando B, Gomez-Cabrera MC, Salvador-Pascual A, Puchades C, Derbré F, Gratas-Delamarche A, Laparre L, Olaso-Gonzalez G, Cerda M, Viosca E, Alabajos A, Sebastián V, Alberich-Bayarri A, García-Castro F, Viña J. Allopurinol partially prevents disuse muscle atrophy in mice and humans. *Scientific Reports*. 2018; 8(1): 3549. IF: 4,122
3. Martínez de Toda I, Garrido A, Vida C, Gomez-Cabrera MC, Viña J, De la Fuente M. Frailty quantified by the Valencia score as a potential predictor of lifespan in mice. *Journals of Gerontology Series A-Biological Sciences and Medical Sciences*. 2018; 73(10): 1323 - 1329. IF: 4,902
4. GBD 2017 Mortality Collaborators. Global, regional, and national age-sex-specific mortality and life expectancy, 1950-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018; 392(10159): 1684 - 1735. IF: 53,254
5. Viña J, Borrás C, Gomez-Cabrera MC. A free radical theory of frailty. *Free Radical Biology and Medicine*. 2018; 124: 358 - 363. IF: 6,020

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: INTIMIC-085

Title: *Maternal obesity and cognitive dysfunction in the offspring: cause-effect role of the GUT Microbiome and early dietary prevention*

Principal Investigator: Patricia Lozzo (Consuelo Borrás as collaborating researcher)

Funding Body: *European Commission*

Beneficiary Institution: *Universitat de València*

Duration: 2017-2020

Total Budget: 778.240€

Reference: 724099-ADVANTAGE

Title: *Managing Frailty. A comprehensive approach to promote a disability-free advanced age in Europe: the ADVANTAGE initiative*

Principal Investigator: José Viña Ribes

Funding Body: *HP-JA. European Commission*

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

Duration: 2016-2019

Total budget: 130.005€

Reference: CA15203 MITOEAGLE

Title: *Evolution-Age-Gender-Lifestyle-Environment: mitochondrial fitness mapping*

Principal Investigator: Erich Gnaiger (Consuelo Borrás as collaborating researcher)

Funding Body: *European Commission*

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

Duration: 2016-2020

Reference: FRAIOMIC

Title: *Utility of OMIC-Based biomarkers in characterizing older individuals at risk for frailty, its progression to disability and general consequences to health and well-being - The Frailomic Initiative*

Principal Investigator: José Viña Ribes

Funding body: *European Commission*

Beneficiary institution: *Universidad de Valencia*

Duration: 2013-2018

Total budget: 596.520€

Reference: PIE15/00013

Title: *A multidisciplinary Project to advance in basic mechanisms, diagnosis, prediction, and prevention of cardiac damage in reperfused acute myocardial infarction*

Principal Investigator: Vicente Bodí Peris (José Viña as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2016-2018

Total Budget: 589.050€

Reference: CB16/10/00435

Title: *CIBER de Fragilidad y envejecimiento (CIBERfes)*

Principal Investigator: José Viña Ribes

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2017-

Reference: PCIN-2017-117

Title: *Obesidad materna y disfunción cognitiva en la descendencia: papel causa-efecto de la microbiota intestinal y prevención dietética temprana*

Principal Investigator: Consuelo Borrás Blasco

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2017-2020

Total Budget: 143.000€

Reference: SAF 2016-75508-R

Title: *Envejecimiento cerebral: protección contra el daño asociado al mismo y su aplicación a la enfermedad de Alzheimer*

Principal Investigator: José Viña Ribes

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2016-2019

Total budget: 140.000€

Reference: GV/2018/067

Title: *Estudio de posibles huellas genéticas de envejecimiento saludable en descendientes de centenarios*

Principal Investigator: Marta Inglés de la Torre

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

Beneficiary Institution: *Universidad de Valencia*

Duration: 2018-2019

Total Budget: 12.040€

Reference: PROMETEOII/2014/056

Title: *Señalización por radicales libres de oxígeno en células madre: importancia en medicina regenerativa*

Principal Investigator: José Viña Ribes

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

Beneficiary Institution: *Universidad de Valencia*

Duration: 2014-2018

Total Budget: 122.535€

Reference: POCTEP 0348_CIE_6_E

Title: *Estudio de la fragilidad cognitiva y su transición a la demencia mediante un conjunto de biomarcadores en sangre periférica. Intervención con genisteína*

Principal Investigator: José Viña Ribes

Funding Body: *Fundación General del Consejo Superior de Investigaciones Científicas (FGCSIC)*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2018-2019

Total Budget: 39.940€

• THESIS

Thesis title: *Programa de ejercicio multicomponente para prevenir la fragilidad, y para la mejora cognitiva, emocional y social en ancianos frágiles*

Doctoral candidate: Helena Pilar Cabo Plaza

Director(s): Francisco José Tarazona Santabalbina, M^a Carmen Gómez Cabrera, José Viña Ribes

Date of the defense: 21/03/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Activación del metabolismo energético del ratón mediante el tratamiento con resveratrol o genisteína*

Doctoral candidate: Lucía Gimeno Mallench

Director(s): José Viña Ribes, Consuelo Borrás Blasco, Juan Gambini Buchón

Date of the defense: 17/07/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *El envejecimiento del envejecimiento: un estudio sobre personas nonagenarias y centenarias en Valencia*

Doctoral candidate: Victoria Córdoba Castillo

Director(s): Sacramento Pinazo Hernandis, Jose Viña Ribes

Date of the defense: 21/09/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Funciones protectoras de los astrocitos en la inflamación y el estrés oxidativo cerebral*

Doctoral candidate: Adrán Jordá Vallés

Director(s): Martín Aldasoro Celaya, María Dolores Mauricio Aviñó, Lilian Soraya Valles Martín

Date of the defense: 15/10/2018

Grade: *Sobresaliente "cum laude"*

Research Group on Anesthesiology and Reanimation
Consolidated group

<http://www.anestesiaticlinicovaencia.org/>



Group members

Principal investigator

Francisco Javier Belda Nácher. Hospital. University

Collaborating researchers

Marina Soro Domingo. Hospital
Gerardo Aguilar Aguilar. Hospital
Carlos Ferrando Ortolá. Hospital
José García de la Asunción. Hospital
Beatriz Garrigues Olivé. Hospital
Rafael Badenes Quiles. Hospital
Armando Maruenda Paulino. Hospital
María Luisa García Pérez. Hospital
Carlos Tornero Tornero. Hospital
Benigno Escamilla Cañete. Hospital
María Luisa Laredo Alcázar. Hospital
Blanca Arocas Chicote. Hospital
José Antonio Carbonell López. Hospital
Pedro Charco Mora. Hospital

Mario de Fez Barberá. Hospital
Mar Garzando Civera. Hospital
Andrea Gutiérrez Valcárcel. Hospital
M^{re} José Parra González. Hospital
Ernesto Pastor Martínez. Hospital
Ana Mugarra Llopis. Hospital
Laura Reviriego Agudo. Hospital
Estefanía Gracia Ferrándiz. Hospital
Cristina Crisán Ovidiu. Hospital
Antonio Guillen Bañuelos. Hospital
Rosa Herrera Castro. Hospital
Jorge Orduña Valls. Hospital



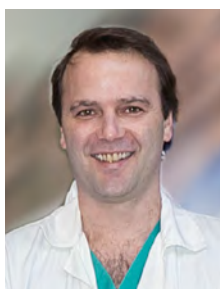
	R1	R2	R3	R4	STAFF
Researchers by categories	5	7	5	2	8

Strategic aims

- The effects of advanced monitoring on hemodynamic management in critically ill patients.
- Open lung approach for the acute respiratory distress syndrome.
- Stratification and outcome of acute respiratory distress syndrome.
- Recommendations on invasive candidiasis in patients with complicated intra-abdominal infection and surgical patients with ICU extended stay.
- Pharmacokinetics of anidulafungin during venovenous extracorporeal membrane oxygenation.

Main lines of research

- Oxidative stress and protection of organs in ischemia-reperfusion surgery.
- Study of hyperglycemia and aldose reductase-mediated mitochondrial dysfunction and apoptosis in platelets in critical patients.
- Ventilatory and pharmacological strategies to decrease organ damage in the lungs associated with mechanical ventilation in healthy and injured lungs.
- Development of hemodynamic monitoring and its application in the field of patients undergoing surgery or admitted to critical care units.
- Study and development of methods of detection of infections, especially fungal and virological, and how to prevent them.
- Study and development of therapeutic drug monitoring (TDM) to describe antimicrobials pharmacokinetics (PK) and determination of minimum inhibitory concentration (MIC).
- Development of new strategies and drugs for pain treatment.



Emerging Researcher

Carlos Ferrando Ortola

Some of the ongoing research lines in our group are: a) Role of anaesthetics in the inflammatory response in anaesthesia and critical care patients. b) Strategies to optimize and individualize intraoperative ventilatory management (precision medicine). c) Role of the perioperative ventilatory strategies in postoperative complications. d) Role of perioperative supplemental oxygen in postoperative complications.

• PUBLICATIONS

Number of articles	IF	Average IF
21	104,877	4,994
National collaborations	International collaborations	Corresponding author
2	14	8

SELECTED PUBLICATIONS

1. Abbott TEF, Ahmad T, Phull MK, Fowler AJ, Hewson R, Biccard BM, Chew MS, Gillies M, Pearse RM, International Surgical Outcomes Study (ISOS) group. The surgical safety checklist and patient outcomes after surgery: a prospective observational cohort study, systematic review and meta-analysis. *British Journal of Anaesthesia*. 2018; 120(1): 146 - 155. IF: 6,499
2. Ferrando C, Soro M, Unzueta C, Suarez-Sipmann F, Canet J, Librero J, Pozo N, Peiró S, Llombart A, León I, India I, Aldecoa C, Díaz-Cambronero O, Pestaña D, Redondo FJ, Garutti I, Balust J, García JI, Ibáñez M, Granell M, Rodríguez A, Gallego L, de la Matta M, Gonzalez R, Brunelli A, García J, Rovira L, Barrios F, Torres V, Hernández S, Gracia E, Giné M, García M, García N, Miguel L, Sánchez S, Piñeiro P, Pujol R, García-Del-Valle S, Valdivia J, Hernández MJ, Padrón O, Colás A, Puig J, Azparren G, Tusman G, Villar J, Belda J, Individualized Perioperative Open-lung Ventilation (iPROVE) Network. Individualised perioperative open-lung approach versus standard protective ventilation in abdominal surgery (iPROVE):

a randomised controlled trial. *Lancet Respiratory Medicine*. 2018; 6(3): 193 - 203. IF: 21,466

3. Villar J, Martínez D, Mosteiro F, Ambrós A, Añón JM, Ferrando C, Soler JA, Montiel R, Vidal A, Conesa-Cayuela LA, Blanco J, Arrojo R, Solano R, Capilla L, Del Campo R, Civantos B, Fernández MM, Aldecoa C, Parra L, Gutiérrez A, Martínez-Jiménez C, González-Martín JM, Fernández RL, Kacmarek RM, Stratification and Outcome of Acute Respiratory Distress Syndrome (STANDARDS) Ne. Is Overall Mortality the Right Composite Endpoint in Clinical Trials of Acute Respiratory Distress Syndrome?. *Critical Care Medicine*. 2018; 46(6): 892 - 899. IF: 6,630
4. Coburn M, Sanders RD, Maze M, Nguyễn-Pascal ML, Rex S, Garrigues B, Carbonell JA, Garcia-Perez ML, Stevanovic A, Kienbaum P, Neukirchen M, Schaefer MS, Borghi B, van Oven H, Tognù A, Al Tmimi L, Eyrolle L, Langeron O, Capdevila X, Arnold GM, Schaller M, Rossaint R, HIPELD Study Investigators. The hip fracture surgery in elderly patients (HIPELD) study to evaluate xenon anaesthesia for the prevention of postoperative delirium: a multicentre, randomized clinical trial. *British Journal of Anaesthesia*. 2018; 120(1): 127 - 137. IF: 6,499
5. Pérez-Pitarch A, Ferriols-Lisart R, Aguilar G, Ezquer-Garín C, Belda FJ, Guglieri-López B. Dosing of caspofungin based on a pharmacokinetic/pharmacodynamic index for the treatment of invasive fungal infections in critically ill patients on continuous venovenous haemodiafiltration. *International Journal of Antimicrobial Agents*. 2018; 51(1): 115 - 121. IF: 4,253

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: COST Action CA15204

Title: *European platform for outcomes research into perioperative interventions during surgery for cancer*

Principal Investigator: Pilar Eroles Asensio and Carlos Ferrando Ortola

Funding body: *European Commission*

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

Duration: 2016-2020

Research Group on Translational Genomics
Consolidated group



Group members

Principal investigator

Rubén D. Artero Allepez
University

Technicians

Águeda Blázquez Bernal. University
Irene González Martínez. University

Collaborating researchers

Manuel Pérez Alonso. University
M^a Beatriz Llamusí Troisi. University
Juan M. Fernández Costa. University
Ariadna Bargiela Schönbrunn. University

https://twitter.com/GenomicsLab_UV
<http://medicina-genomica.blogspot.com/es/>
<https://twitter.com/MPAlonso>
<http://www.uv.es/gt/>
<https://twitter.com/selmasoriano>

PhD researchers

Estefanía Cerro Herreros. University
Estela Selma Soriano. University
María Sabater Arcís. University
Sarah Overby. University
Jorge Patricio Espinosa Espinosa. University



	R1	R2	R3	R4	STAFF
Researchers by categories	4	4	-	2	2
Researchers financed by competitive public calls or networks	2	-	-	-	2

Strategic aims

- We have accomplished the goal of publishing significant scientific studies based on the ongoing strategic research lines. Briefly, publication of results demonstrating the therapeutic potential of several molecules (miRNAs and chemical-based) on the improvement of key muscular myotonic dystrophy (DM) disease phenotypes, in parallel with the publication of the first in time Drosophila model simulating cardiac phenotypes displayed by DM patients. In addition, publication of proof of concept results in additional rare diseases (new therapeutic target in SMA and gene modifier in Huntington disease). Moreover, we have put the basis for the establishment of a start-up (Arthex) for developing of the promising molecules with therapeutic potential in DM discovered.

Main lines of research

- Using miRNAs as therapeutic targets in myotonic dystrophy (DM).
- Discovery, development, and repurposing of drugs for the treatment of DM.
- Study of the molecular causes of muscle atrophy, heart dysfunction, and CNS degeneration in DM.
- Study of the molecular mechanisms associated with spinal muscular atrophy and search for potential therapies.
- Understanding human podocyte function through Drosophila nephrocytes.
- Drosophila modeling of limb girdle muscular dystrophy subtype 1F (LGMD1F).

• PUBLICATIONS

Number of articles	IF	Average IF
8	57,395	7,174
National collaborations	International collaborations	Corresponding author
2	3	6

SELECTED PUBLICATIONS

1. Overby SJ, Cerro-Herreros E, Llamusi B, Artero R. RNA-mediated therapies in myotonic dystrophy. *Drug Discovery Today*. 2018; 23(12): 2013 - 2022. IF: 6,848
2. Chakraborty M, Llamusi B, Artero R. Modeling of myotonic dystrophy cardiac phenotypes in Drosophila. *Frontiers in Neurology*. 2018; 9: 473. IF: 3,508
3. Cerro-Herreros E, Sabater-Arcis M, Fernandez-Costa JM, Moreno N, Perez-Alonso M, Llamusi B, Artero R. miR-23b and miR-218 silencing increase Muscblind-like expression and alleviate myotonic dystrophy phenotypes in mammalian models. *Nature Communications*. 2018; 9(1): 2482. IF: 12,353
4. Garcia-Lopez A, Tessaro F, Jonker HRA, Wacker A, Richter C, Comte A, Berntenis N, Schmucki R, Hatje K, Petermann

O, Chiriano G, Perozzo R, Sciarra D, Konieczny P, Faustino I, Fournet G, Orozco M, Artero R, Metzger F, Ebeling M, Goekjian P, Joseph B, Schwalbe H, Scapozza L. Targeting RNA structure in SMN2 reverses spinal muscular atrophy molecular phenotypes. *Nature Communications*. 2018; 9(1): 2032. IF: 12,353

5. Sellier C, Cerro-Herreros E, Blatter M, Freyermuth F, Gaucherot A, Ruffenach F, Sarkar P, Puymirat J, Udd B, Day JW, Meola G, Bassez G, Fujimura H, Takahashi MP, Schoser B, Furling D, Artero R, Allain FHT, Llamusi B, Charlet-Berguerand N. rbFOX1/MBNL1 competition for CCUG RNA repeats binding contributes to myotonic dystrophy type 1/type 2 differences. *Nature Communications*. 2018; 9(1): 2009. IF: 12,353

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI17/00352

Title: *Modulación terapéutica de los genes MBNL como tratamientos innovadores para distrofia miotónica*

Principal Investigator: Manuel Pérez Alonso and Beatriz Llamusi Troísi

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Clínico*

Universitario de Valencia

Duration: 2018-2020

Total budget: 75.020€

Reference: SAF2015-64500-R

Title: *Modulación terapéutica de la expresión de genes patogénicos en Distrofia Miotónica: prueba de concepto*

Principal Investigator: Rubén Artero Allepuz

Funding Body: *Ministerio de Economía y Competitividad*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2016-2018

Total budget: 145.000€

Reference: PROMETEO II/2014/067

Title: *Aproximaciones genéticas para el estudio de patologías humanas y del desarrollo en Drosophila*

Principal Investigator: Nuria Paricio Ortiz (Rubén Artero as collaborating researcher)

Funding Body: *Conselleria de Educación Cultura y Deporte*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2014-2018

Total budget: 91.965€

Reference: 2017/0435

Title: *Therapeutic modulation of MBNL1-2 gene expression in myotonic dystrophy*

Principal Investigator: Rubén Artero Allepuz

Funding body: *Fundació Bancària La Caixa (Caixa Impulse)*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2017-2019

Total budget: 45.000€

Reference: HR17-00268

Title: *TATAMI (Therapeutic Targeting of MiRNAs) therapeutic targeting of mbnl micrnas as innovative treatments for myotonic dystrophy*

Principal Investigator: Rubén Artero Allepuz

Funding Body: *Fundació Bancària La Caixa*

Beneficiary Institution: *Consortium (Leader: Universidad de Valencia)*

Duration: 2018-2021

Total budget: 997.023€

Title: *A Spinal muscular atrophy Drosophila model for in vivo drug discovery*

Principal Investigator: Rubén Artero Allepuz

Funding Body: *SMA Europe*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2016-2018

Total budget: 121.500€

Reference: 2014/063

Title: *Characterization of novel suppressors of neurodegeneration in myotonic dystrophy type1*

Principal Investigator: Manuel Pérez Alonso

Funding body: *Fundación La Marató de TV3*

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

Duration: 2015-2018

Total budget: 125.125€

Reference: 3100-17

Title: *Desarrollo preclínico de un nuevo tratamiento para la aterosclerosis*

Principal Investigator: Beatriz Llamusí Troísi

Funding body: *Fundación para la Innovación y Prospectiva en Salud en España (FIPSE)*

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

Duration: 2018

Total budget: 30.000€

• THESIS

Thesis title: *A spinal muscular atrophy reporter system for in vivo drug discovery in Drosophila melanogaster*

Doctoral candidate: Piotr Konieczny

Director(s): Rubén Artero Allepuz

Date of the defense: 21/09/2018

Grade: *Sobresaliente "cum laude"*

Quality recognition/Award: Extraordinary PhD program

Thesis title: *Generation and characterization of Drosophila models of cardiac dysfunction in myotonic dystrophy*

Doctoral candidate: Mouli Chakraborty

Director(s): Rubén Artero Allepuz, Beatriz Llamusí Troísi

Date of the defense: 06/07/2018

Grade: *Sobresaliente "cum laude"*

Quality recognition/Award: Extraordinary PhD program

Thesis title: *Utilización de microRNAs como dianas terapéuticas en Distrofia Miotónica*

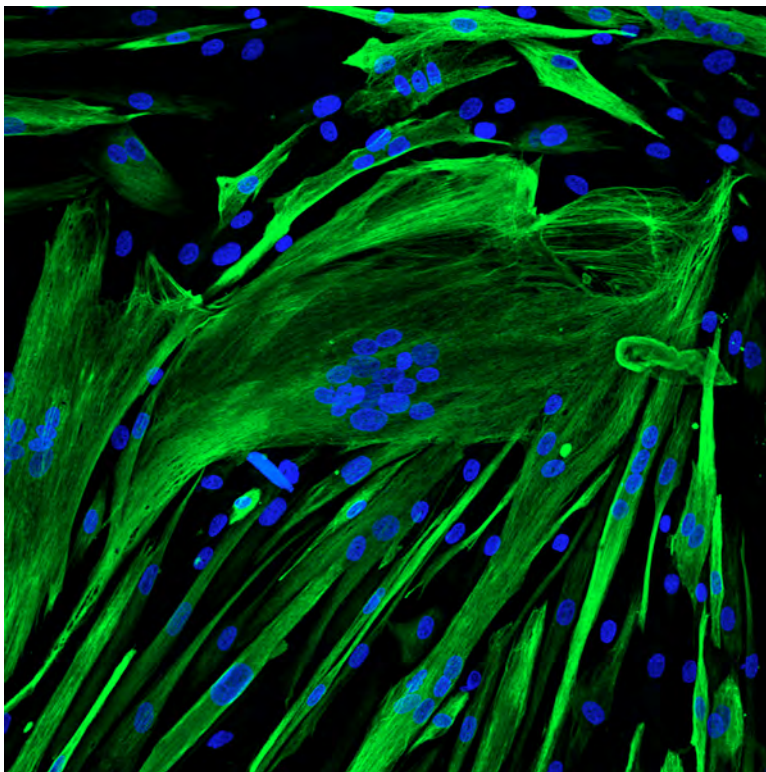
Doctoral candidate: Estefanía Cerro Herreros

Director(s): Rubén Artero Allepuz, Beatriz Llamusi Troisi

Date of the defense: 27/07/2018

Grade: *Sobresaliente "cum laude"*

Quality recognition/Award: Extraordinary PhD program



Confocal microscopy image where we detected the MBNL1 protein (green staining-MBNL1 antibody) and the nucleus (blue staining-DAPI) in human myoblasts.

Research Group on General and Digestive Surgery
Consolidated group



Group members

Principal investigator

Joaquín Ortega Serrano
 Hospital. University

Roberto Martí Obiol. Hospital
 Julio Calvete Chornet. Hospital
 Elena Martí Cuñat. Hospital
 Marina Garcés Albir. Hospital
 Estefanía García Botello. Hospital
 Raquel Alfonso Ballester. Hospital
 Dimitri Dorcaratto. Hospital

Collaborating researchers

Luis Sabater Ortí. Hospital. University
 Alejandro Espí Macías. Hospital. University
 Elena Muñoz Forner. Hospital
 José Martín Arévalo. Hospital
 David Moro Valdezate. Hospital
 Vicente Plá Martín. Hospital
 Norberto Cassinello Fernández. Hospital
 Fernando López Mozos. Hospital



	R1	R2	R3	R4	STAFF
Researchers by categories	1	12	2	1	-

Strategic aims

- Incorporation of the retroperitoneoscopy as a new surgical technique for the department, as a treatment of adrenal tumors.
- Development of the clinical pathway for thyroidectomy.
- International edition of a book on esophageal cancer: "Esophageal cancer: symptoms, management and prognosis".
- Completion of the national multicenter trial on the differences between the pancreato-gastrostomy and pancreato-jejunostomy in cephalic pancreaticoduodenectomy technique.

Main lines of research

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

• PUBLICATIONS

Number of articles	IF	Average IF
14	43,999	3,142

National collaborations	International collaborations	Corresponding author
7	7	5

SELECTED PUBLICATIONS

1. Sabater L, Muñoz E, Roselló S, Dorcaratto D, Garcés-Albir M, Huerta M, Roda D, Gómez-Mateo MC, Ferrández-Izquierdo A, Darder A, Cervantes A. Borderline resectable pancreatic cancer. Challenges and controversies. *Cancer Treatment Reviews*. 2018; 68: 124 - 135. IF: 8,122
2. Pellino G, Frasson M, García-Granero A, Granero-Castro P, Ramos Rodríguez JL, Flor-Lorente B, Bargallo Berzosa J, Alonso Hernández N, Labrador Vallverdú FJ, Parra Baños PA, Ais Conde G, Garcia-Granero E, ANACO Study Group. Predictors of complications and mortality following left colectomy with primary stapled anastomosis for cancer: results of a multicentric study with 1111 patients. *Colorectal Disease*. 2018; 20(11): 986 - 995. IF: 2,778
3. Royo-Aznar A, Moro-Valdezate D, Martín-Arévalo J, Pla-Martí V, García-Botello S, Espín-Basany E, Espí-Macías A. Reversal of Hartmann's procedure: a single-centre experience of 533 consecutive cases. *Colorectal Disease*. 2018; 20(7): 631 - 638. IF: 2,778
4. García-Granero Á, Sánchez-Guillén L, Fletcher-Sanfeliu D, Sancho-Muriel J, Alvarez-Sarrado E, Pellino G, Delgado-Moraleda JJ, Sabater Ortí L, Valverde-Navarro AA, Frasson M. Surgical anatomy of D3 lymphadenectomy in right colon cancer, gastrocolic trunk of Henle and surgical trunk of Gillot - a video vignette. *Colorectal Disease*. 2018; 20(10): 935 - 936. IF: 2,778
5. Hueso L, Ortega R, Sellés F, Wu-Xiong NY, Ortega J, Civera M, Ascaso JF, Sanz MJ, Real JT, Piqueras L. Upregulation of angiostatic chemokines IP-10/CXCL10 and I-TAC/CXCL11 in human obesity and their implication for adipose tissue angiogenesis. *International Journal of Obesity*. 2018; 42(8): 1406 - 1417. IF: 5,151

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI16/01465

Title: *Impacto de la diseminación de las CTCs durante la duo-*

denopancreatectomía cefálica en la aparición de metástasis y supervivencia en pacientes con tumores de páncreas y periampulares

Principal Investigator: Javier Padillo (Elena Muñoz and Marina Garcés as collaborating researchers)

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia and Hospital Virgen del Rocío de Sevilla

Duration: 2017-2019

Total budget: 80.465€

Reference: PI15/02180

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

Principal Investigator: Andrés Cervantes Ruipérez (Alejandro Espí as collaborating researcher)

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2018

Total budget: 80.465€

Reference: PI15/00076

Title: Duodenopancreatectomía cefálica en tumores de páncreas y periampulares: abordaje inicial de la arteria mesentérica superior versus abordaje clásico. Estudio prospectivo, aleatorizado y multicéntrico

Principal Investigator: Luis Sabater Ortí

Funding Body: Instituto de Salud Carlos III

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2016-2018

Total budget: 56.265€

Reference: AMD-CPA-2016-01

Title: Estudio para el desarrollo y validación de una huella genética para el diagnóstico de cáncer de páncreas y lesiones precursoras

Principal Investigator: Luis Sabater Ortí

Funding Body: AMADIX

Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2017-2018

• THESIS

Thesis title: Estándares de calidad de la cirugía de las metástasis hepáticas del cáncer de colon

Doctoral candidate: Manuel José Bellver Oliver

Director(s): Luis Sabater Ortí, Javier Escrig Sos, Fernando Rottellar Sastre

Date of the defense: 13/07/2018

Grade: Sobresaliente "cum laude"

Thesis title: Estudio de la eficacia de la plicatura del tendón cantal lateral con anclaje en y en el síndrome del ojo seco evaporativo

Doctoral candidate: Leticia Ortega Evangelio

Director(s): Joaquín Ortega Serrano, Juan Miguel Tomás Torrent

Date of the defense: 09/11/2018

Grade: Sobresaliente "cum laude"

Research Group on Personal Autonomy, Dependence and Severe Mental Disorders (TMAP)
Consolidated group

Team involved in



Group members

Principal investigator

Rafael Tabarés Seisdedos
University

Jaume Forés Martos. CIBER
Diego Macías Saint-Geroms. CIBER
Salvador Martínez Pérez. University. Hospital
Mikel Munárriz Ferrandis. University
Jose Salazar Fraile. CIBER

Collaborating researchers

Gabriel Selva Vera. University. Hospital
Manuel Gómez Beneyto. University
Patricia Correa Ghisays. CIBER
Inmaculada Fuentes Durá. University
Ferrán Catalá López. University
Vicente Balanzá Martínez. University
Constanza San Martín Valenzuel. University

Technician

Víctor Mestre Salvador. University



	R1	R2	R3	R4	STAFF
Researchers by categories	2	7	2	2	1
Researchers financed by competitive public calls or networks	1	-	-	-	-

Strategic aims

- Project on “Comorbidity between Cancer and Central Nervous System Disorders”, which aims to synthesize epidemiological evidence and assess the validity of associations between central nervous system disorders and the risk of developing or dying from cancer. It is a collaborative meta-analysis in 5 countries (Spain, Canada, Australia, United Kingdom and the United States) coordinated by the University of Valencia/CIBERSAM.
- “The Global Burden of Disease Study” is the largest international collaborative project on the epidemiology of diseases, injuries and risk factors at the global, national and regional levels.
- Projects in advanced methods of systematic reviews and meta-analyses, including the publication in PLoS One interested in the identification of endophenotypes, as well as biomarkers of neuroprogression and clinical staging in bipolar and psychotic disorders.
- Various papers and editorials have been published on methodological quality, biases and conflicts of interest in mental health research, public health and health economics.

Main lines of research

- Study of neurocognitive endophenotypes in schizophrenia and bipolar disorder.
- Study of pharmacological strategies for improving cognitive function in bipolar disorder.
- Epidemiology and disability associated with TMG.
- Identification of biomarkers in TMG.
- Study of the direct and reverse comorbidity in TMG in relation to cancer and diabetes.
- Development and efficacy study of psychoeducation and neurocognitive therapy and functional rehabilitation for people with SMI.
- Establishment of a clinical staging system (ClinicalStaging) applied to bipolar disorder by the combination of biomarkers, neurocognitive and functional performance.
- Global Burden of Disease studies.
- Systematic revisions and web meta-analysis.
- Nutritional Psychiatry.
- Stigma in Sanitary Professionals (#VALMSE project).

• PUBLICATIONS

Number of articles	IF	Average IF
45	866,475	19,255
National collaborations	International collaborations	Corresponding author
14	31	5

SELECTED PUBLICATIONS

1. GBD 2016 Lifetime Risk of Stroke Collaborators (Tabarés-Seisdedos R, Catalá-López F). Global, regional, and country-specific lifetime risks of stroke, 1990 and 2016. *New England Journal of Medicine*. 379(25): 2429 - 2437. IF: 79,258
2. Global Burden of Disease 2016 Injury Collaborators (Tabarés-Seisdedos R). Global mortality from firearms, 1990-2016. *JAMA-Journal of the American Medical Association*. 2018; 320(8): 792 - 814. IF: 47,661
3. Global Burden of Disease Cancer Collaboration (Tabarés-Seisdedos R, Catalá-López F). Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2016: a systematic analysis for the Global Burden of Disease Study. *JAMA Oncology*. 2018; 4(11): 1553 - 1568. IF: 20,871
4. GBD 2017 SDG Collaborators (Tabarés-Seisdedos R). Measuring progress from 1990 to 2017 and projecting attainment

to 2030 of the health-related sustainable development goals for 195 countries and territories: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018; 392(10159): 2091 - 2138. IF: 53,254

5. Global Burden of Cardiovascular Diseases Collaboration (Catalá-López F, Tabarés-Seisdedos R). The burden of cardiovascular diseases among US States, 1990-2016. *JAMA Cardiology*. 2018; 3(5): 375 - 389. IF: 10,133

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI17/00719

Title: *Identificación de biomarcadores epigenéticos periféricos asociados con el déficit neurocognitivo en personas con trastorno bipolar, depresión, esquizofrenia y diabetes tipo 2*

Principal Investigator: Rafael Tabarés Seisdedos

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 105.270€

Reference: CB07/09/0021

Title: *CIBER de Enfermedades Mentales (CIBERsam)*

Principal Investigator: Rafael Tabarés Seisdedos

Funding Body: *Instituto de Salud Carlos III*

Beneficiary institution: *CIBERSAM*

Duration: 2015-

Reference: PROMETEOII/2015/021

Title: *INverse and direct CANCER comorbidity in people with Central Nervous System disorders: from drug repurposing to effective strategies for cancer prevention (INCANCER/CNSd)*

Principal Investigator: Rafael Tabarés Seisdedos

Funding Body: *Conselleria de Educación Cultura y Deporte*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2015-2018

Total budget: 212.400€

Reference: *Programme Erasmus+ KA2 -Cooperation for innovation and the Exchange of Good Practices KA203 – Strategic Partnerships for higher education*

Title: *Development of innovative training solutions in the field of functional evaluation aimed at updating of the curricula of health sciences schools- TEACH project (2018-2020)*

Principal Investigator: Rafael Tabarés Seisdedos

Funding Body: *Universidad de Valencia*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2018-2020

• THESIS

Thesis title: *Desregulación del estado redox en modelos de depleción aguda de genes implicados en la disqueratosis congénita*

Doctoral candidate: José Santiago Ibáñez Cabellos

Director(s): Rafael Tabarés Seisdedos, José Luis García Giménez, Gisselle Pérez Machado, Federico Pallardó Calatayud

Date of the defense: 13/06/2018

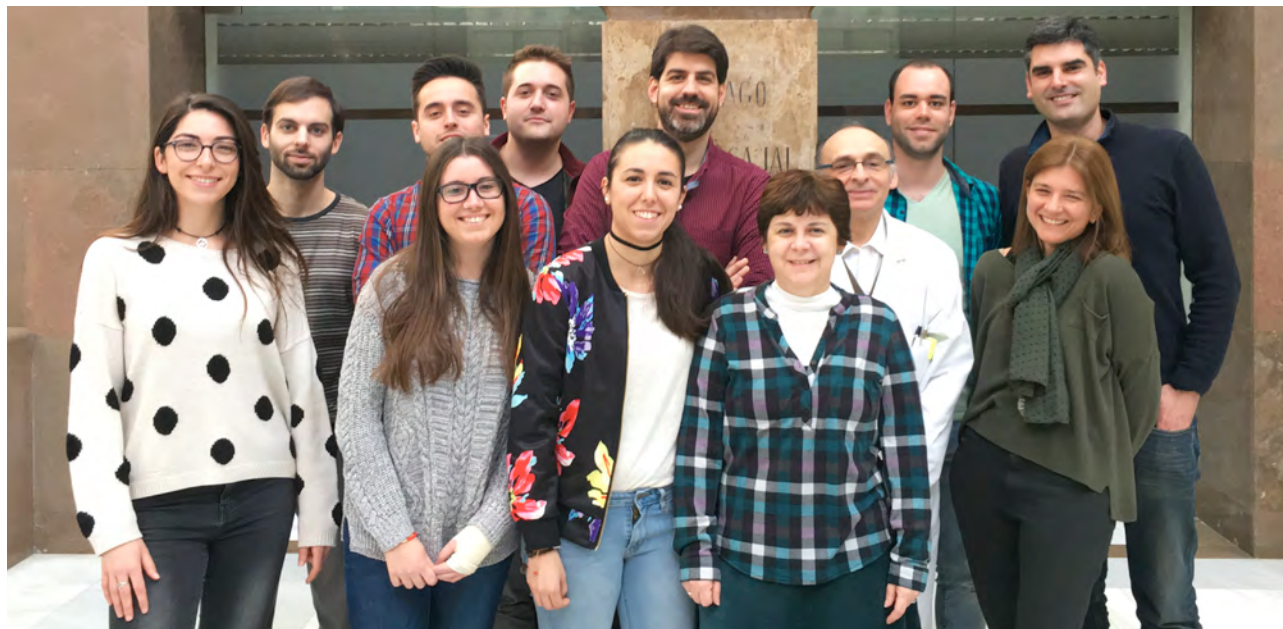
Grade: *Sobresaliente "cum laude"*

Quality recognition/Award: European PhD



Research Group on Cellular and Organic Physiopathology of Oxidative Stress
Consolidated group

Team involved in



Group members

Principal investigator

Federico V. Pallardó Calatayud. University

Collaborating researchers

Amparo Gimeno Monrós. University

Carlos Romá Mateo. University

Pilar González Cabo. CIBERer

José Manuel Torres Ibáñez. University

Pablo Calap Quintana. CIBERer

José Santiago Ibáñez Cabellos. University

Marta Seco Cervera. University

María Mercedes Navarro. University

PhD researchers

Jesús Beltrán García. INCLIVA

Laura Rodríguez Robles. CIBERer

Emerging researchers

José Luis García Giménez. CIBERer

Francisco Dasí Fernández. INCLIVA

Pre-doctoral researchers

Lucía Bañuls Soto. INCLIVA

María Magallón Serrano. INCLIVA

Daniel Pellicer Roig. INCLIVA

Selene Valero Moreno. University



	R1	R2	R3	R4	STAFF
Researchers by categories	7	4	4	1	1
Researchers financed by competitive public calls or networks	3	4	1	-	-

Strategic aims

- Among the scientific activity of the research group, remarkable achievements are the extension to PCT phase of the European patent “Mass spectrometry-based methods for the detection of circulating histones H3 and H2B in plasma from sepsis or septic shock (ss) patients” (PCT/EP2017/078362). Related to this patent, the technology was selected to participate in the mentorship program from FIPSE and MIT Idea2 global.
- In reference to acquisition of budget and resources, funding from the following programs and grants has been obtained: VLC-Bioclinic 2017 (2 projects), Plan Nacional I+D+i del MINECO (1 project, 2016-2019), AES 2016 (2 projects, 2017-2019), Fundación Ramón Areces (1 project, 2017-2019), AES 2017 (1 project, 2018-2019).
- Regarding teaching and outreach activities, the group has maintained the teaching of the subject “Enfermedades raras”, from the Grade on Medicine’s study plan at the University of Valencia and in the master course in Biomedical Research; and also in the “Máster de enfermedades raras”, directed by Dr. Pallardó, at the same University. Besides, it was organized, in collaboration with the Escuela Valenciana de Estudios de la Salud and the CIBERER, the 2nd edition of the on-line course “Introducción a las EE.RR: investigación y atención clínica” addressed to residents of medical specialties from the Valencian public health system.
- Within the framework of the Alliance for translational research in rare diseases of the Comunitat Valenciana, Dr. Pallardó has coordinated the joint application for FEDER funding for acquisition of research infrastructure. As result of that, our group have coordinated de acquisition of equipments for more than € 500.000 for the research on epigenetics and personalized medicine in rare diseases.

Main lines of research

- Pathophysiology of Friedreich’s ataxia and other neuromuscular diseases.
- Study of oxidative stress and mechanisms of DNA repair in different progeroid syndromes and genodermatosis.
- Epigenetic regulation in the pathophysiology of rare diseases.



Emerging Researcher

José Luis García Giménez

We aim to understand the role of epigenetics in the phenotypic variability of rare diseases (eg, Friedreich’s ataxia, dyskeratosis congenita and adolescent idiopathic scoliosis). Furthermore, we collaborate with clinicians of Intensive Care Unit to study the role of circulating histones in the physiopathology of sepsis and septic shock. Our challenge is to identify epigenetic biomarkers (DNA methylation, microRNAs, and post-translational modifications of histones) to design new potential tools for diagnostic and prognostic and improve precision medicine.



Emerging Researcher

Francisco Dasí Hernández

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

• PUBLICATIONS

Number of articles	IF	Average IF
6	26,939	4,48
National collaborations	International collaborations	Corresponding author
6	-	5

SELECTED PUBLICATIONS

1. Ibáñez-Cabellos JS, Pérez-Machado G, Seco-Cervera M, Berenguer-Pascual E, García-Giménez JL, Pallardó FV. Acute telomerase components depletion triggers oxidative stress as an early event previous to telomeric shortening. *Redox Biology*. 2018; 14: 398 - 408. IF: 7,126
2. Seco-Cervera M, González-Rodríguez D, Ibáñez-Cabellos JS, Peiró-Chova L, Pallardó FV, García-Giménez JL. Small RNA-seq analysis of circulating miRNAs to identify phenotypic variability in Friedreich's ataxia patients. *Scientific Data*. 2018; 5: 180021. IF: 5,305
3. García-Giménez JL, Rubio-Belmar PA, Peiró-Chova L, Hervás D, González-Rodríguez D, Ibáñez-Cabellos JS, Bas-Hermida P, Mena-Mollá S, García-López EM, Pallardó FV, Bas T. Circulating miRNAs as diagnostic biomarkers for adolescent idiopathic scoliosis. *Scientific Reports*. 2018; 8(1): 2646. IF: 4,122
4. Ibáñez-Cabellos JS, Aguado C, Pérez-Cremades D, García-Giménez JL, Bueno-Betí C, García-López EM, Romá-Mateo C, Novella S, Hermenegildo C, Pallardó FV. Extracellular histones activate autophagy and apoptosis via mTOR signaling in human endothelial cells. *Biochimica et Biophysica Acta*. 2018; 1864(10): 3234 - 3246. IF: 5,108
5. Micó-Martínez P, García-Giménez JL, Seco-Cervera M, López-Roldán A, Almiñana-Pastor PJ, Alpiste-Illueca F, Pallardó FV. miR-1226 detection in GCF as potential biomarker of chronic periodontitis: a pilot study. *Medicina Oral Patología Oral y Cirugía Bucal*. 2018; 23(3): e308 - e314. IF: 1,671

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: COST Action BM1407

Title: *Translational Research in primary ciliary dyskinesia – bench, bedside, and population perspectives (BEAT-PCD)*

Principal Investigator: Jane Lucas, Antonio Moreno and Miguel Armengot (Amparo Escribano y Francisco Dasí as collaborating researchers)

Funding Body: *European Commission*

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

Duration: 2016-2019

Reference: COST Action CA16125

Title: *European network for translational research in children's and adult interstitial lung disease*

Principal Investigator: Antonio Moreno (Amparo Escribano and Francisco Dasí as collaborating researchers)

Funding Body: *European Commission*

Beneficiary institution: *University of Southampton (UK)*

Duration: 2016-2019

Reference: DTS17/00132

Title: *Kit multiplex para la detección simultánea de biomarcadores de diagnóstico y pronóstico de sepsis y shock séptico por espectrometría de masas*

Principal Investigator: Federico Pallardó Calatayud

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2019

Total budget: 78.210€

Reference: PI17/01250

Title: *Estudio del efecto de la hipoxia en la degranulación, producción de citoquinas y perfil oxidativo de neutrófilos de pacientes con déficit de alfa-1 antitripsina*

Principal Investigator: Francisco Dasí Fernández

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 99.220€

Reference: PI16/01031

Title: *Respuestas epigenéticas a cambios en el entorno redox nuclear. Posibles dianas terapéuticas en enfermedades raras*

Principal Investigator: Federico Pallardó Calatayud

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2019

Total budget: 105.875€

Reference: PI16/01036

Title: *Epigenética e inmunosupresión. Uso de las histonas circulares y sus modificaciones posttraduccionales como biomarcadores de diagnóstico y pronóstico en sepsis y shock séptico*

Principal Investigator: José Luis García Giménez

Funding Body: Instituto de Salud Carlos III
Beneficiary Institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2017-2019
Total budget: 87.725€

Reference: CB06/07/0073
Title: CIBER de Enfermedades Raras (CIBERer)
Principal Investigator: Federico Vicente Pallardó Calatayud
Funding body: Instituto de Salud Carlos III
Beneficiary institution: Universidad de Valencia
Duration: 2007-

Reference: SAF 2015-66625-R
Title: El paisaje de la biología axonal y las membranas asociadas a mitocondria en las enfermedades neurogenéticas
Principal Investigator: Pilar González Cabo
Funding body: Ministerio de Economía y Competitividad
Beneficiary institution: CIBER de Enfermedades Raras (CIBERer), Fundació Sant Joan de Déu
Duration: 2016-2019
Total budget: 411.400€

Reference: BFU2015-68366-R
Title: Papel de la señalización por MAP quinasas y la dinámica mitocondria en reprogramación y transdiferenciación celular
Principal Investigator: José Manuel Torres Ibáñez
Funding Body: Ministerio de Economía y Competitividad
Beneficiary Institution: Universidad de Valencia
Duration: 2016 -2018
Total budget: 110.000€

Reference: PROMETEOII/2014/056
Title: Señalización por radicales libres de oxígeno en células madre: importancia en medicina regenerativa
Principal Investigator: José Viña Ribes (Federico Pallardó and José Luis García-Giménez as collaborating researcher)
Funding Body: Conselleria de Educación, Cultura y Deporte
Beneficiary Institution: Universidad de Valencia
Duration: 2014-2018
Total budget: 122.535€

Title: Inhibidores de fosfodiesterasas como tratamiento para la Ataxia de Friedreich
Principal Investigator: Pilar González Cabo
Funding Body: Fundación Ramón Areces

Beneficiary Institution: CIBER de Enfermedades Raras (CIBERer)
Duration: 2017-2019
Total budget: 119.700€

Title: Caracterización del estrés oxidativo en pacientes con enfermedades pulmonares intersticiales de la infancia
Principal investigator: Amparo Escribano Montaner and Francisco Dasí Fernández
Funding body: Servicio de Pediatría/UVEG/Unidad 60 INCLIVA. Enfermedades Raras Respiratorias
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2017-2020
Total budget: 6.000€

Title: Estudio del estrés oxidativo en pacientes con osteonecrosis femoral idiopática
Principal Investigator: Antonio Silvestre Muñoz, Francisco Dasí Fernández
Funding Body: Servicio de Traumatología y Cirugía Ortopédica/UVEG/Unidad 60 INCLIVA. Enfermedades Raras Respiratorias
Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia
Duration: 2018-2021
Total budget: 6.000€

Title: Relationship between physical activity, sedentary life and quality of life in children and adolescents with cystic fibrosis
Principal Investigator: Alexandra Valencia Peris
Funding Body: Universidad de Valencia
Beneficiary institution: Universidad de Valencia
Duration: 2017-2018

Title: Psychosocial and adaptive factors in the family of the paediatric patients with chronic respiratory problems
Principal Investigator: Inmaculada Montoya Castilla
Funding Body: Federación Española de Asociaciones de Terapia Familiar (FEATF)
Beneficiary institution: Universidad de Valencia
Duration: 2017-2018

Title: Relationship between physical activity, sedentary life and quality of life in children and adolescents with cystic fibrosis
Principal Investigator: Alexandra Valencia Peris
Funding Body: Universidad de Valencia
Beneficiary institution: Universidad de Valencia
Duration: 2017-2018

Title: Edición génica del gen *SERPINA1* mediante el uso de CRISPR/Cas9 en monocitos de pacientes con déficit de alfa-1 antitripsina

Principal Investigator: Francisco Dasí Fernández

Funding Body: Sociedad Española de Neumología y Cirugía Torácica (SEPAR)

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2017-2019

Total budget: 12.000€

Title: Estudio del perfil de miRNAs circulantes en pacientes con déficit de alfa-1 antitripsina (DAAT). Implicaciones diagnósticas, pronósticas y terapéuticas

Principal Investigator: Amparo Escribano (Francisco Dasí as collaborating researcher)

Funding body: Asociación Española de Pediatría

Beneficiary institution: Fundación Investigación Hospital Clínico Universitario de Valencia

Duration: 2014-2020

Total budget: 30.000€

• THESIS

Thesis title: Desregulación del estado redox en modelos de depleción aguda de genes implicados en la disqueratosis congénita

Doctoral candidate: José Santiago Ibáñez Cabellos

Director(s): Rafael Tabarés Seisdedos, José Luis García Giménez, Gisselle Pérez Machado, Federico Pallardó Calatayud

Date of the defense: 13/06/2018

Grade: Sobresaliente "cum laude"

Quality recognition/Award: European PhD

Thesis title: Estudio del estrés oxidativo en el epitelio nasal ciliado de pacientes con discinesia ciliar primaria

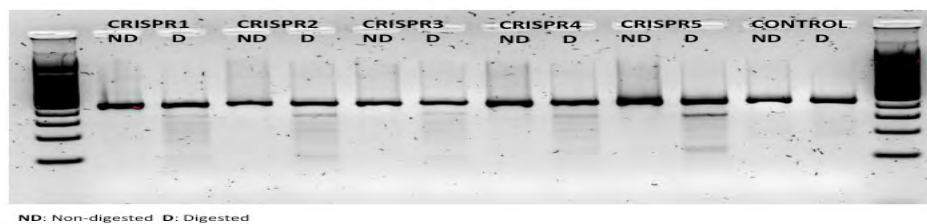
Doctoral candidate: Ana Reula Martín

Director(s): Miguel Armengot Carceller, Amparo Escribano Montaner, Francisco Jose Dasí Fernández

Date of the defense: 22/11/2018

Grade: Sobresaliente "cum laude"

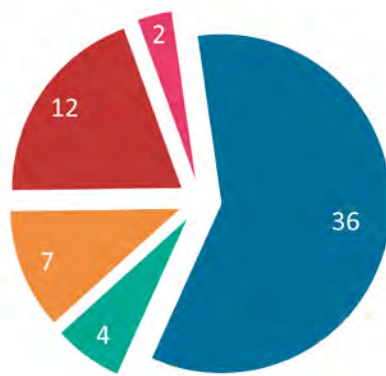
Quality recognition/Award: European PhD



Gene editing *SERPINA1* gene in cells of patients with DAAT by CRISPR / Cas9

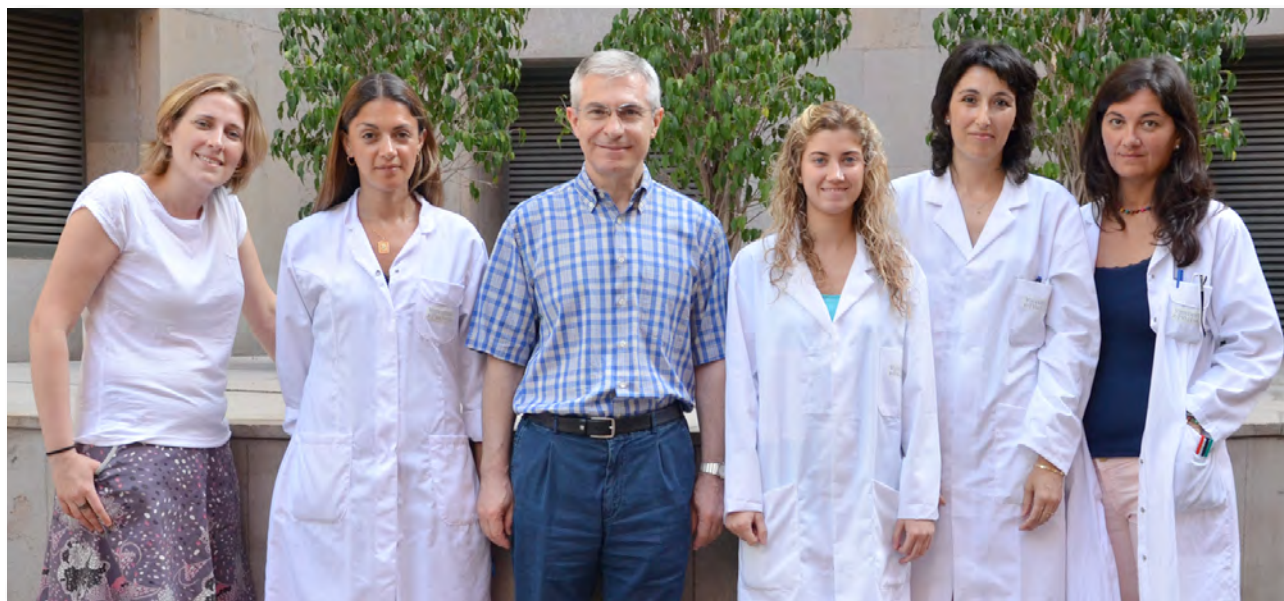
4.3.4 Reproductive medicine area

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Research Group on Reproductive Pathology	187



● Original articles ● Letters ● Editorial ● Reviews ● Corrections

Research Group on Women Health
Consolidated group



Group members

Principal investigator

Antonio Cano Sánchez
University

Emerging researcher

Raúl Gómez Gallego. INCLIVA

Collaborating researchers

Juan José Tarín Folgado. University
Ana Martínez Aspas. Hospital
Juan José Hidalgo Mora. Hospital
Gemma Arribas Ferriol. Hospital



	R1	R2	R3	R4	STAFF
Researchers by categories	1	3	1	1	-
Researchers financed by competitive public calls or networks	-	1	-	-	-

Strategic aims

- The group is positioned in the field of healthy ageing, with special interest to frailty, where it has collaborated in the support of INCLIVA in the project ADVANTAGE. We have collaborated to position the reference site of the Valencia Region within EIP-PAHA, the partnership of the European Commission. Moreover, we have participated in the application to different European projects with groups from different European countries, including an application to the Maire Curie grants.

Main lines of research

- In healthy ageing in the female we are continuing our interest on osteoporosis but also have added frailty and functional decline. The group is consolidating the CARMEN cohort (see the EIP-PAHA commitment tracker, https://ec.europa.eu/eip/ageing/commitments-tracker/a3/integrated-care-and-ict-reduce-frailty-and-chronic-diseases-ageing-women_en).
- With regard to endometriosis:
 - To analyze the role of microRNA and vascularization regulators and pain mechanisms. Role of the TNF cytokine family
 - To analyze the initial atherogenesis and selective estrogen receptor modulators



Emerging Researcher

Raúl Gómez Gallego

The lines of research have focused on the dissection of how the deregulation of the angiogenic component is related to the onset and maintenance of gynecological disorders such as endometriosis, ovarian hyperstimulation syndrome, recurrent miscarriage or preeclampsia. We are also interested in developing tests for the early non-invasive diagnosis of endometriosis through combined analysis of multiple biomarkers simultaneously.

• PUBLICATIONS

Number of articles	IF	Average IF
17	52,232	3,072

National collaborations	International collaborations	Corresponding author
8	8	9

SELECTED PUBLICATIONS

1. Gwyther H, Bobrowicz-Campos E, Luis Alves Apóstolo J, Marcucci M, Cano A, Holland C. A realist review to understand the efficacy and outcomes of interventions designed to minimise, reverse or prevent the progression of frailty. *Health Psychology Review*. 2018; 12(4): 382 - 404. IF: 8,597
2. Cano A, Chedraui P, Goulis DG, Lopes P, Mishra G, Mueck A, Senturk LM, Simoncini T, Stevenson JC, Stute P, Tuomikoski P, Rees M, Lambrinoudaki I. Calcium in the prevention of postmenopausal osteoporosis: EMAS clinical guide. *Maturitas*. 2018; 107: 7 - 12. IF: 3,315
3. Cano A, Dargent G, Carriazo A, López-Samaniego L, Apostolo J, Campos E, Holland C, Varela-Nieto I, Luz Sánchez-Sánchez M, Illario M, Iaccarino G, Roller RE, Goossens E, Vollenbroek-Hutten M, Pais S, Schena F, Musian D, Alvino S, Maggio M, Liotta G, Ussai S, Orfila F, O’Caoimh R, Paul C, Pazzi S, Romano V, Obbia P. Tackling frailty and functional decline: Background of the action group A3 of the European innovation partnership for active and healthy ageing. *Maturitas*. 2018; 115: 69 - 73. IF: 3,315
4. Buigues A, Ferrero H, Martínez J, Pellicer N, Pellicer A, Gómez R. Evaluation of PAI-1 in endometriosis using a homologous immunocompetent mouse model. *Biology of Reproduction*. 2018; 99(2): 326 - 335. IF: 3,184
5. Ferrero H, Díaz-Gimeno P, Sebastián-León P, Faus A, Gómez R, Pellicer A. Dysregulated genes and their functional pathways in luteinized granulosa cells from PCOS patients after cabergoline treatment. *Reproduction*. 2018; 155(4): 373 - 381. IF: 3,086

- **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: 777500- IMI-PainCare

Title: *Improving the care of patients suffering from acute or chronic pain*

Principal Investigator: Raúl Gomez Gallego

Funding body: *European Commission*

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

Duration: 2018-2022

Total budget: 257.066,25€

Reference: FOCUS

Title: *Frailty management Optimisation through EIP AHA Commitments and Utilisation of Stakeholders input*

Principal Investigator: Antonio Cano Sánchez (Miguel Ángel García Pérez as collaborating researcher)

Funding body: *European Commission - DG SANTE*

Beneficiary institution: *Universidad de Valencia*

Duration: 2015-2018

Total budget: 2.379.633€

Reference: PI17/02329

Title: *Papel de los agonistas dopaminérgicos en el dolor e infertilidad asociados a endometriosis en modelos animales de nueva generación*

Principal Investigator: Raúl Gómez Gallego

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 111.320€

Title: *Global multivariant analysis of putative biomarkers identified through a combined multi-technical approach for the early non-invasive detection of endometriosis*

Principal Investigator: Raúl Gómez Gallego

Funding body: *The Endometriosis Foundation of America*

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

Duration: 2017-2018

Total budget: 12.500€

- **THESIS**

Thesis title: *Establecimiento y optimización de modelo murino de la patología ginecológica endometriosis utilizando xenografts de endometrio humano*

Doctoral candidate: Paula Calvo Hoyas

Director(s): Antonio Pellicer Martínez, Raúl Gómez Gallego

Date of the defense: 04/09/2018

Grade: *Sobresaliente "cum laude"*

Research Group on Stem Cells Applied to Reproduction, Embryo Viability and Endometrial Receptivity Consolidated group



Group members

Principal investigator

Carlos Simón Vallés
University

Collaborating researchers

Tamara Garrido Gómez. IGENOMIX Foundation
Hortensia Ferrero Cháfer. INCLIVA
Diana Valbuena Perilla. IGENOMIX Foundation
David Blesa Jarque. IGENOMIX Foundation
Carmen García Pascual. IGENOMIX Foundation
Inmaculada Moreno Gimeno. IGENOMIX Foundation
M^a Paz Moreno Murciano. INCLIVA
Carmen Rubio Lluesa. IGENOMIX Foundation

Emerging researchers

Felipe Vilella Mitjana. INCLIVA

PhD researchers

Nuria Balaguer Cuenca. IGENOMIX Foundation
Iolanda García Grau. University
Irene Corachán García. INCLIVA
David Bolumar Recuero. University
Claudia Abellán Orihuela. INCLIVA

Technician

Roberto Alonso Valero. IGENOMIX Foundation



	R1	R2	R3	R4	STAFF
Researchers by categories	4	7	2	1	2
Researchers financed by competitive public calls or networks	1	3	-	-	-

Strategic aims

- Our activity predominantly involves research in the field of Reproductive Medicine, with a particular focus on the fields of regenerative medicine concerning the endometrium and genomic studies on embryonic viability and endometrial receptivity, as well as other factors that cause infertility.
- One of our aims is to advance in the understanding of the mechanisms that regulate maternal-fetal communication and that may be involved in the implantation and subsequent development of adult diseases such as obesity and type II diabetes.
- Creation of an in vitro model to obtain germ cells through direct reprogramming of human somatic cells, to provide the ultimate solution for the treatment of infertility.

Main lines of research

- Adult stem cells in the human endometrium: we have identified the existence of human endometrial stem cells, and we have demonstrated the therapeutic potential of autologous bone marrow CD133+ stem cells in the treatment of non-curable endometrial pathologies such as Asherman's syndrome or endometrial atrophy.
- The embryo viability: nowadays the selection of embryo is based solely on morphological parameters, which doesn't guarantee its genetic viability. We aim to develop a non-invasive approach based on molecular techniques to identify euploid embryos.
- Study of endometrial receptivity: we discovered the transcriptomic signatura of human endometrial receptivity. Now, we are focus on a new minimally invasive procedure using single-cell analysis.
- The endometrial microbiome in human reproduction: our research group has described the existence of the endometrial microbiome and its clinical implications on the reproductive outcome. We investigate the impact of uterine microbiome dysbiosis and its clinical impact.
- Artificial gametes: creation of artificial gametes by transdifferentiating human somatic cells.
- The maternal implication in the origin of pre-eclampsia: our research has provided evidence that endometrial decidualization resistance is implicated in the origin of this disease. This finding offers a new perspective based on the maternal contribution to gestation, aiming to develop a tool that will diagnose pre-eclampsia.
- Molecular diagnosis of myometrial tumors: our previous work has demonstrated the genomic differential characterization of myomas and leiomyosarcomas. We aim to shift the diagnostic and therapeutic focus of uterine leiomyomas and leiomyosarcomas through genomic characterization.



Emerging Researcher

Felip Vilella Mitjana

The research line of Endometrial Receptivity is based on the study of endometrial secretions, specifically the endometrial fluid. We use secretomic and genomic approach so we can describe new molecules that can be correlated with the days of the menstrual cycle and may be involved in obtaining the window of implantation period, opening a new field of study for the analysis of the changes in the

endometrium during the menstrual cycle and the cross-talk between the embryo and the endometrium.

• PUBLICATIONS

Number of articles	IF	Average IF
21	113,07	5,38
National collaborations	International collaborations	Corresponding author
4	14	7

SELECTED PUBLICATIONS

1. Von Grothusen C, Lalitkumar PG, Ruiz-Alonso M, Boggavara-pu NR, Navarro R, Miravet-Valenciano J, Gemzell-Danielsson K, Simon C. Effect of mifepristone on the transcriptomic signature of endometrial receptivity. *Human Reproduction*. 2018; 33(10): 1889 - 1897. IF: 4,99
2. Vera-Rodriguez M, Diez-Juan A, Jimenez-Almazan J, Martinez S, Navarro R, Peinado V, Mercader A, Meseguer M, Blesa D, Moreno I, Valbuena D, Rubio C, Simon C. Origin and composition of cell-free DNA in spent medium from human embryo culture during preimplantation development. *Human Reproduction*. 2018; 33(4): 745 - 756. IF: 4,99
3. Moreno I, Cicinelli E, Garcia-Grau I, Gonzalez-Monfort M, Bau D, Vilella F, De Ziegler D, Resta L, Valbuena D, Simon C. The diagnosis of chronic endometritis in infertile asymptomatic women: a comparative study of histology, microbial cultures, hysteroscopy, and molecular microbiology. *American Journal of Obstetrics and Gynecology*. 2018; 218(6): 602.e1 - 602.e16. IF: 5,732
4. Suhorutshenko M, Kukushkina V, Velthut-Meikas A, Altmäe S, Peters M, Mägi R, Krjutškov K, Koel M, Codoñer FM, Martínez-Blanch JF, Vilella F, Simón C, Salumets A, Laisk T. Endometrial receptivity revisited: endometrial transcriptome adjusted for tissue cellular heterogeneity. *Human Reproduction*. 2018; 33(11): 2074 - 2086. IF: 4,99
5. Herraiz S, Buigues A, Díaz-García C, Romeu M, Martínez S, Gómez-Seguí I, Simón C, Hsueh AJ, Pellicer A. Fertility rescue and ovarian follicle growth promotion by bone marrow stem cell infusion. *Fertility and Sterility*. 2018; 109(5): 908 - 918.e2. IF: 4,803

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI18/00957

Title: *Función del ADN y ARN contenido en vesículas extracelulares secretadas por el endometrio humano sobre el embrión pre-implantatorio*

Principal Investigator: Felipe Vilella Mitjana

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2019-2021

Total budget: 135.520€

Reference: PI17/00931

Title: *Influencia de los disruptores endocrinos sobre la receptividad endometrial humana y su relación con el fallo de implantación y la endometriosis*

Principal Investigator: Francisco Domínguez Hernández

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 62.920€

Reference: PI17/01039

Title: *Identificación de factores regenerativos en medicina reproductiva y su aplicación como futura herramienta terapéutica para la reparación del endometrio*

Principal Investigator: Irene Cervelló Alcaraz

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 99.220€

Reference: BFU 2015-72131-EXP

Title: *Criptocromos, la inexplicable presencia de sensores de luz en la oscuridad que conectan el embrión temprano con el cosmos*

Principal Investigator: Carlos Simón Vallés

Funding Body: *Ministerio de Economía, Industria y Competitividad*

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

Duration: 2016-2019

Total budget: 60.000€

Reference: SAF2015-67154-R

Title: *Regulación transcriptómica materna del embrión pre-implantatorio. Nuevo mecanismo para el estudio del origen de enfermedades complejas del adulto: obesidad y/o exposición tabaco*

Principal Investigator: Carlos Simón Vallés

Funding Body: *Ministerio de Economía, Industria y Competitividad*

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

Duration: 2016-2018

Total budget: 169.400€

Reference: PROMETEU/2018/161

Title: *Medicina regenerativa del útero humano: desde la terapia celular a la creación del órgano mediante bioingeniería*

Principal Investigator: Carlos Simón Vallés

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

Beneficiary institution: *Universidad de Valencia*

Duration: 2018-2021

Total budget: 297.066,67€

Reference: ACIF/2016/024

Title: *Estudio de los miRNAs secretados al líquido endometrial y su papel en la regulación del embrión en los primeros estadios de desarrollo*

Principal Investigator: Felipe Vilella Mitjana

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

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

Duration: 2016-2019

Total budget: 66.578,40€

• THESIS

Thesis title: *Analysis of miRNAs in endometrial fluid as a tool for non-invasive diagnosis of endometrial receptivity*

Doctoral candidate: Alessia Grasso

Director(s): Felipe Vilella Mitjana, Carlos Simón Vallés

Date of the defense: 20/02/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Identification of specific somatic stem cell markers in the human endometrium and mechanisms of the bone marrow for endometrial regeneration*

Doctoral candidate: Nuria López Pérez

Director(s): Irene Cervelló Alcaraz, Jose Bellver Pradas

Date of the defense: 24/07/2018

Grade: *Sobresaliente "cum laude"*

Quality recognition/Award: European PhD

Thesis title: *Molecular alterations in eutopic endometrium of women with endometriosis and implications in its diagnostic*

Doctoral candidate: Júlia Vallvé Juanico

Director(s): Antonio Gil Moreno, Xavier Santamaría Costa, Joaquima Navarro Ferreté

Grade: *Sobresaliente "cum laude"*

Quality recognition/Award: European PhD

Thesis title: *Importancia del estudio cromosómico de los restos abortivos mediante técnicas de secuenciación masiva (NGS) y arrays de CGH para un adecuado consejo reproductivo*

Doctoral candidate: Nasser Al-Asmar Piñar

Director(s): Carmen Rubio Lluesa, Jose Remohí Giménez, Carlos Simón Vallés, Mercedes Costell Roselló

Date of the defense: 09/11/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Mejora en la detección de aneuploidías y especificidad del diagnóstico genético preimplantacional en biopsias de blastómero y de trofoectodermo en embriones humanos*

Doctoral candidate: Pere Mir Pardo

Director(s): Carmen Rubio Lluesa, Carlos Simón Vallés

Date of the defense: 18/04/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Bioengineering strategies of the uterus towards improving current investigative models and female reproductive health*

Doctoral candidate: Hannes Marcus Campo

Director(s): Antonio Pellicer Martínez, Irene Cervelló Alcaraz

Date of the defense: 21/11/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Expresión, localización y estudio funcional de pgr-mc1 en el endometrio humano a lo largo del ciclo menstrual*

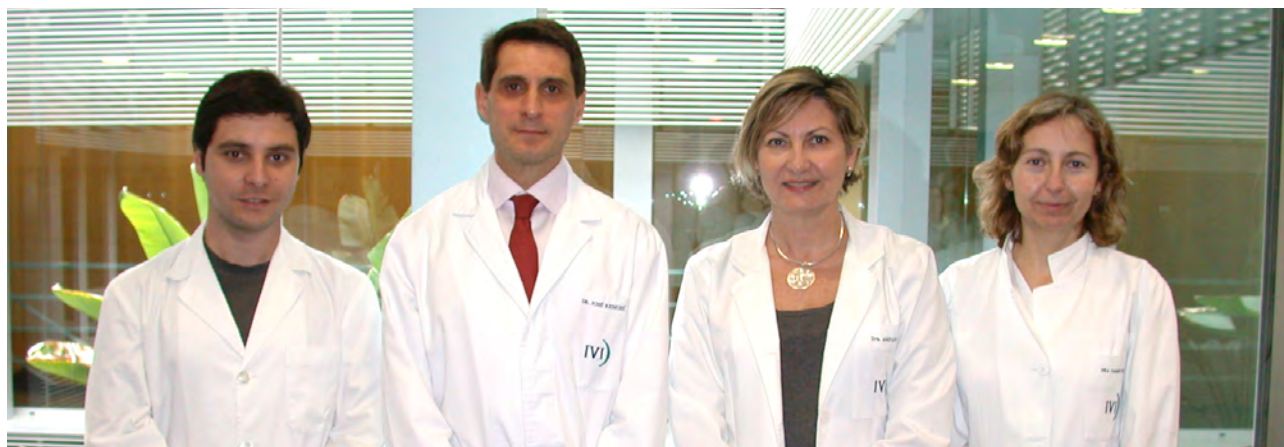
Doctoral candidate: Stefania Salsano

Director(s): Francisco Domínguez Hernández, Carlos Simón Vallés

Date of the defense: 27/11/2018

Grade: *Sobresaliente "cum laude"*

Research Group on Reproductive Pathology
Consolidated group



Group members

Principal investigator

José Remohí Giménez
IVI. University

Collaborating researchers

Amparo Ruiz Jorro. IVI
Jaime Ferro Camargo. IVI
Rocío Rivera Egea. IVI
José María de los Santos Molina. IVI
Tamara Viloría Samochín. IVI
M^a del Carmen Vidal Martínez. IVI
Juan Giles Jiménez. IVI
M^a José Escribá Pérez. IVI
Arancha Galán Rivas. IVI
Amparo Mercader Bayarri. IVI
María José de los Santos Molina. IVI
Ernesto Bosch Aparicio. IVI
Pilar Alamá Faubel. IVI
Patricia Díaz Gimeno. IVI
José Bellver Pradas. IVI
Elena Labarta Demur. IVI

Emerging researchers

Irene Cervelló Alcaraz. IVI
Francisco Domínguez Hernández. INCLIVA
Nicolás Garrido Puchalt. IVI
Marcos Meseguer Escrivá. IVI

PhD students

Hannes Marcus Campo. INCLIVA
Anna Buigues Monfort. UV
Silvia Pérez Deben. UV
Sara López. INCLIVA

Technicians

Alicia Quiñonero Villora. IVI
María Amparo Faus Esteve. IVI



	R1	R2	R3	R4	STAFF
Researchers by categories	3	17	4	1	2
Researchers financed by competitive public calls or networks	3	-	1	-	-

Strategic aims

- To study of the causes of infertility and the pathologies of woman, from a holistic perspective, including aspects of the laboratory, as well as surgical and immunological. To study of the physiology and biology of the elements involved in human reproduction as well as tissue bioengineering, and the technological and procedural development of the area of assisted human reproduction.
- To discover embryonic and endometrial quality biomarkers, as well as the development of statistical and bioinformatic analysis and methods that allow a practical advance in the knowledge of the area, from different perspectives.

Main lines of research

- Biomarkers, genomic medicine, statistics and massive data analysis in assisted human reproduction.
- Reproductive biology and bioengineering in assisted human reproduction.
- Infertility and reproductive pathology.



Emerging Researcher

Irene Cervelló Alcaraz

Research is based on the identification, characterization and isolation of Somatic Stem Cells in the endometrium. Endometrial Stem Cells have been identified in human and murine models, the regenerative potential of these cells has been proven and there

is an ongoing research on the existence of Lgr5 marker in the endometrial tissue. Moreover, the work is also focused on essential processes based on the regenerative medicine related with the porcine and human uterus.



Emerging Researcher

Francisco Domínguez Hernández

The main lines focus on research in molecular biology of the implantation and search for biomarkers of endometrial receptivity and embryonic competence. He was the Scientific Director of Embryomics, a technological

company dedicated to the development of non-invasive diagnosis of chromosomal abnormalities in pre-implantation embryos using metabolomic techniques.



Emerging Researcher

Nicolás Garrido Puchalt

In this research line about male fertility, factors related to sperm physiology are intended to be discovered, and sperm selection techniques in order to improve reproductive results are

being evaluated.



Emerging Researcher

Marcos Meseguer Escrivá

The group is a pioneer in the introduction and development of time-lapse technology, this technique allows the analysis of embryos without using an invasive technique. It represents an important conceptual advance in

the evaluation of quality by measuring the processes of embryonic development against the embryonic stages. Parallel projects are being carried out with new hardware lapse technologies such as Auxogyn-Eeva and Geri-Genia. Our research focuses on oxygen consumption, oxidative profile and embryonic protein secretions.

• **PUBLICATIONS**

Number of articles	IF	Average IF
30	130,722	4,357
National collaborations	International collaborations	Corresponding author
11	18	11

SELECTED PUBLICATIONS

1. Sebastian-Leon P, Garrido N, Remohí J, Pellicer A, Diaz-Gimeno P. Asynchronous and pathological windows of implantation: two causes of recurrent implantation failure. *Human Reproduction*. 2018; 33(4): 626 - 635. IF: 4,990
2. Lawrenz B, Labarta E, Fatemi H, Bosch E. Premature progesterone elevation: targets and rescue strategies. *Fertility and Sterility*. 2018; 109(4): 577 - 582. IF: 4,803
3. Alviggi C, Conforti A, Esteves SC, Andersen CY, Bosch E, Bühler K, Ferraretti AP, De Placido G, Mollo A, Fischer R, Humaidan P; International Collaborative Group for the Study of r-hLH (iCOS-LH). Recombinant luteinizing hormone supplementation in assisted reproductive technology: a systematic review. *Fertility and Sterility*. 2018; 109(4): 644 - 664. IF: 4,803
4. Santamaría X, Mas A, Cervelló I, Taylor H, Simon C. Uterine stem cells: from basic research to advanced cell therapies. *Human Reproduction Update*. 2018; 24(6): 673 - 693. IF: 11,852
5. Cobo A, García-Velasco J, Domingo J, Pellicer A, Remohí J. Elective and Onco-fertility preservation: factors related to IVF outcomes. *Human Reproduction*. 2018; 33(12): 2222 - 2231. IF: 4,990

• **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: PI17/00931

Title: *Influencia de los disruptores endocrinos sobre la receptividad endometrial humana y su relación con el fallo de implantación y la endometriosis*

Principal Investigator: Francisco Domínguez Hernández

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 52.000€

Reference: PI17/01039

Title: *Identificación de factores regenerativos en medicina reproductiva y su aplicación como futura herramienta terapéutica para la reparación del endometrio*

Principal Investigator: Irene Cervelló Alcaraz

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 82.000€

Reference: PI16/00687

Title: *Diagnóstico genético ovocitario por análisis del primer corpúsculo polar*

Principal Investigator: M^a José Escribá Pérez

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2019

Total budget: 97.405€

Reference: PI15/00312

Title: *Combined treatment of Vitamin D with aGnRH on uterine fibroids growth*

Principal Investigator: Antonio Pellicer Martínez

Funding body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Hospital Universitario y Politécnico La Fe*

Duration: 2016-2018

Total budget: 189.365€

Reference: PROMETEO/2018/137

Title: *Regenerative factors and bioengineering in reproductive medicine. Its application as a future therapeutic tool for ovarian function recovery and endometrium repair*

Principal Investigator: Antonio Pellicer Martínez

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

Beneficiary Institution: *Universidad de Valencia*

Duration: 2018-2021

Total budget: 334.394€

Reference: GV/2018/151

Title: *Bases moleculares del estrés a largo plazo como causa del*

fallo de implantación embrionaria

Principal Investigator: Patricia Díaz Gimeno

Funding body: Conselleria de Educación, Cultura y Deporte

Beneficiary Institution: Fundación IVI

Duration: 2018-2019

Total budget: 16.000€

Title: Nueva estrategia para estimar la calidad embrionaria y el éxito de las embrio-transferencias por evaluación y selección automática

Principal Investigator: Marcos Meseguer Escrivá

Funding body: Sociedad Española de Fertilidad

Beneficiary Institution: Fundación IVI

Duration: 2018-2020

Total budget: 15.000€

• THESIS

Thesis title: Identification of specific somatic stem cell markers in the human endometrium and mechanisms of the bone marrow for endometrial regeneration

Doctoral candidate: Nuria López Pérez

Director(s): Irene Cervelló Alcaraz, Jose Bellver Pradas

Date of the defense: 24/07/2018

Grade: Sobresaliente "cum laude"

Quality recognition/Award: European PhD

Thesis title: Importancia del estudio cromosómico de los restos abortivos mediante técnicas de secuenciación masiva (NGS) y arrays de CGH para un adecuado consejo reproductivo

Doctoral candidate: Nasser Al-Asmar Piñar

Director(s): Carmen Rubio Llusa, Jose Remohí Giménez, Carlos Simón Vallés, Mercedes Costell Roselló

Date of the defense: 09/11/2018

Grade: Sobresaliente "cum laude"

Thesis title: Bioengineering strategies of the uterus towards improving current investigative models and female reproductive health

Doctoral candidate: Hannes Marcus Campo

Director(s): Antonio Pellicer Martínez, Irene Cervelló Alcaraz

Date of the defense: 21/11/2018

Grade: Sobresaliente "cum laude"

Thesis title: Expresión, localización y estudio funcional de pgr-mc1 en el endometrio humano a lo largo del ciclo menstrual

Doctoral candidate: Stefania Salsano

Director(s): Francisco Domínguez Hernández, Carlos Simón Vallés

Date of the defense: 27/11/2018

Grade: Sobresaliente "cum laude"

Thesis title: Utilidad de PLA2G2A, CD84 y ubiquitina en el diagnóstico de las muestras de semen y en la selección de espermatozoides

Doctoral candidate: Nerea Sota Echarri

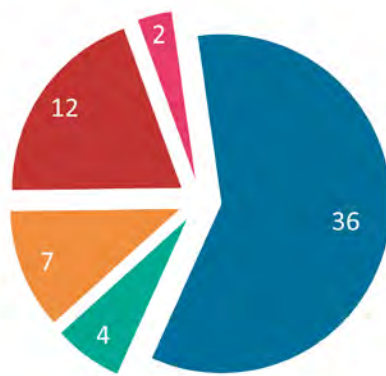
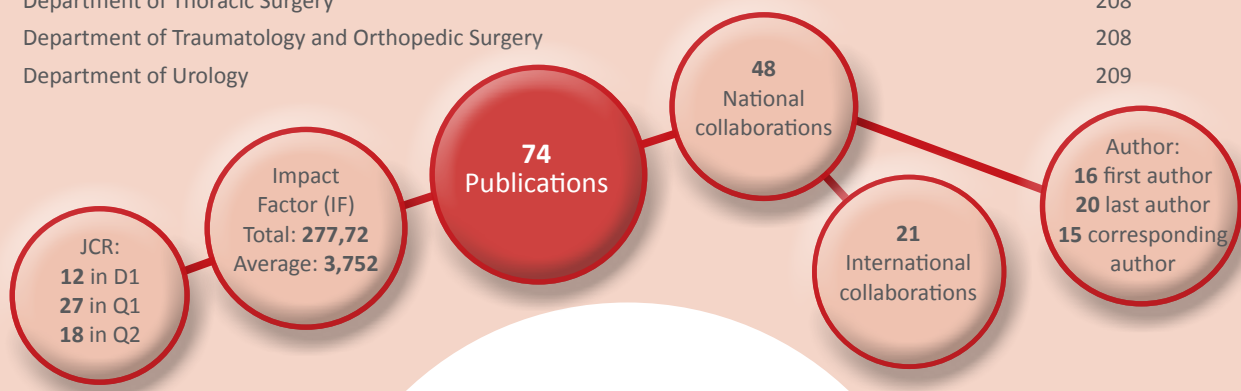
Director(s): Nicolás Garrido Puchalt, Marcos Meseguer Escrivá

Date of the defense: 03/12/2018

Grade: Sobresaliente "cum laude"

4.4 Hospital divisions research area

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● Original articles ● Letters ● Editorial ● Reviews ● Corrections

4.4 Other scientific contributions from the Hospital Divisions and the *Valencia Clínico-Malvarrosa* Health Department

Arrhythmia and Cardiac Pacing Unit

Strategic aims

- Our Unit has received the Excellence Credit in the Program “Atrial Fibrillation Ablation” from the Spanish Society of Cardiology.
- The multicentre project “Left atrial geometry and outcome in atrial fibrillation ablation, LAGO-AF” has been concluded. First results have been published.

Main lines of research

- Collaboration in the national prospective observational study on Crioballoon ablation of atrial fibrillation (RECABA).
- Leading and Collaboration in the registry on sleep alterations in patients with pacemakers.
- Leading a multicenter prospective study on ablation of typical atrial flutter without radioscopy and guided by electrogram amplitudes.

• PUBLICATIONS

Number of articles	IF	Average IF
1	8,336	8,336

National collaborations	International collaborations	Corresponding author
1	-	-

SELECTED PUBLICATIONS

1. Bisbal F, Alarcón F, Ferrero-de-Loma-Osorio A, González-Ferrer JJ, Alonso C, Pachón M, Tizón H, Cabanas-Grandío P, Sanchez M, Benito E, Teis A, Ruiz-Granell R, Pérez-Villacastín J, Viñolas X, Arias MA, Vallés E, García-Campo E, Fernández-Lozano I, Villuendas R, Mont L. Left atrial geometry and outcome of atrial fibrillation ablation: results from the multicentre LAGO-AF study. *European Heart Journal-Cardiovascular Imaging*. 2018; 19(9): 1002 - 1009. IF: 8,336



Department of Biochemistry and Clinical Analysis

Strategic aims

- Implementation of the GestPet on-line laboratory communication system with the Primary Care physicians of the Clinical-Malvarrosa Department: the tool helps the efficient use of the laboratory.

Main lines of research

- Group-specific: managing laboratory test requests and patient safety through electronic requests.
- Laboratory Service staff research is carried out in collaboration with the following clinical research groups: Clinical Cardiology (ischemic heart disease and heart failure), Cardiometabolic Risk and Diabetes (lipid metabolism and insulin resistance), Clinical Hematology (Minimal Residual Disease), Infant Gastroenterology (Inflammatory Bowel Disease), Public Health and Digestive System (Stratification of the priority of colonoscopy using the SOH test in the Colorectal Cancer Screening Program).

• PUBLICATIONS

Number of articles	IF	Average IF
8	37,230	4,654
National collaborations	International collaborations	Corresponding author
6	1	2

SELECTED PUBLICATIONS

- Rodríguez-Borja E, Corchon-Peyrallo A, Diaz-Gimenez M, Carratala-Calvo A. Computer physician order entry (CPOE) as a strategy to estimate laboratory activity and costs associated with cancer clinical trials. *Biochemia Medica*. 2018; 28(3): 30706. IF: 3,653
- Núñez J, Bayés-Genís A, Zannad F, Rossignol P, Núñez E, Bodí V, Miñana G, Santas E, Chorro FJ, Mollar A, Carratalá A, Navarro J, Górriz JL, Lupón J, Husser O, Metra M, Sanchis J. Long-term potassium monitoring and dynamics in heart failure and risk of mortality. *Circulation*. 2018; 137(13): 1320 - 1330. IF: 18,880
- Rodríguez-Borja E, Corchon-Peyrallo A, Barba-Serrano E, Villalba Martínez C, Carratala Calvo A. Send hold clinical decision support rules improvement to reduce unnecessary testing of vitamins A, E, K, B1, B2, B3, B6 and C. *Clinical Chemistry and Laboratory Medicine*. 2018; 56(7): 1063 - 1070. IF: 3,556
- Fernández-Julián E, Pérez-Carbonell T, Marco R, Pellicer V, Rodríguez-Borja E, Marco J. Impact of an oral appliance on obstructive sleep apnea severity, quality of life, and biomarkers. *Laryngoscope*. 2018; 128(7): 1720 - 1726. IF: 2,442
- Martín I, Navarro B, Villamón E, Solano C, Serrano A, Calabuig M, Amat P, Domingo F, Abellán R, García F, Olivares MD, Chaves FJ, Tormo M, Hernández-Boluda JC. Therapy-related acute myeloid leukemia developing 14 years after allogeneic hematopoietic stem cell transplantation, from a persistent R882H-DNMT3A mutated clone of patient origin. *Experimental and Molecular Pathology*. 2018; 105(1): 139 - 143. IF: 2,566

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI16/00393

Title: *De la genómica del cáncer a la inmuno-oncología. Búsqueda de biomarcadores de respuesta a la inmunoterapia anti PD1/PDL1 en cáncer mediante una aproximación de biología de sistemas*

Principal Investigator: Joan Climent Bataller (Ana Cuesta Peredo as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2019

Total budget: 98.615€

Reference: PI14/00959

Title: *Comparación aleatoria entre un estrategia de intervención sobre fragilidad frente a la estrategia habitual en pacientes frágiles después de un infarto agudo de miocardio*

Principal Investigator: Juan Sanchis Forés (Enrique Rodríguez Borja as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2015-2018

Total budget: 36.300€

Reference: PI14/02018

Title: *Papel de la vía de señalización NOTCH1/FBXW7/PI3K/PTEN/AKT en la progresión de la Leucemia Linfocítica Crónica B (LLC-B) a formas avanzadas*

Principal Investigator: M^a José Terol Casterá (Ana Cuesta Peredo as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2015-2018

Total budget: 81.070€

Title: *Aplicación de la técnica de hibridación genómica comparada mediante arrays (array-CGH) al estudio de retraso mental, reordenamientos cromosómicos en cáncer, diagnóstico prenatal y preimplantacional*

Principal Investigator: Ana Cuesta Peredo (Ana Ruiz Quilez as

collaborating researcher)

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

Beneficiary Institution: *Hospital Clínico Universitario de Valencia*

Duration: 2018

Total budget: 15.000€

Title: *Implantación y gestión del registro de los resultados de las gasometrías que se realizan en distintos Servicios del Hospital Clínico en el Sistema Informático del Laboratorio (SIL)*

Principal Investigator: Arturo Carratalá Calvo (Elena Vidal Miñana as collaborating researcher)

Funding Body: *Radiometer*

Beneficiary Institution: *Hospital Clínico Universitario de Valencia*

Duration: 2018

Total budget: 15.000€

Department of Cardiovascular Surgery

• PUBLICATIONS

Number of articles	IF	Average IF
1	4,880	4,880
National collaborations	International collaborations	Corresponding author
1	-	-

Original articles

1. Fletcher-Sanfeliu D, García-Granero A, Rueda Muñoz C, Martín-González I. Type I thoracoabdominal aortic aneurysm: intercostal reimplantation by the snake technique. *Journal of Thoracic and Cardiovascular Surgery*. 2018; 155(4): 1399 - 1400. IF: 4,880

Department of Dermatology

Strategic aims

- To continue making a biobank of melanoma patients.

Main lines of research

- Melanocytic tumors. Malignant Melanoma: study of cytokines involved in tumor growth.
- Hemangiomas.
- Contact dermatitis.
- Alopecia.
- Psoriasis: application of new molecules in treatment.

• PUBLICATIONS

Number of articles	IF	Average IF
7	12,712	1,816
National collaborations	International collaborations	Corresponding author
5	2	1

SELECTED PUBLICATIONS

1. Silva Díaz E, Estébanez Corrales A, Miralles Palmero A, Martín Hernández JM. Enfermedad de Riga-Fede. *Anales de Pediatría*. 2018; 89(6): 389 - 390. IF: 1,318
2. Martín JM, Mateo E, Ramón D. Spontaneous regression of a recalcitrant wart after bivalent papillomavirus vaccination. *Journal of Pediatrics*. 2018; 194: 259 - 259.e1. IF: 3,667
3. Martín JM, Cuesta A, Velasco R, Herrero A, Ramón D, Monteagudo C. Two-year-old girl with tuberous xanthomas. *Journal of Clinical Pathology*. 2018; 71(10): 860 - 862. IF: 2,894
4. Fernández-Flores A, Bermúdez CF, Molina I, Saus C, Monteagudo C, Cassarino DC. Pigmented deposits in the skin. *American Journal of Dermatopathology*. 2018; 40(5): 307 - 328. IF: 1,210

5. Martín JM, Torres C, Cordero P, Sánchez S, Terradez L, Ramón D. Bascule syndrome associated with syncopal episodes. *Pediatric Dermatology*. 2018; 35(2): e142-e143. IF: 1,041

• PUBLICATIONS

Number of articles	IF	Average IF
7	17,688	2,526
National collaborations	International collaborations	Corresponding author
4	1	2

Department of Digestive Medicine

Strategic aims

- Update of protocols and clinical guidelines of the Department.
- It has been possible to consolidate the relationship of the Unit of Inflammatory Bowel Disease of our Department with the network of National Units, through collaborative studies that have been published in international journals. The group has also consolidated motility and pancreas research in the national and international area through consensus guides that have been published.

Main lines of research

- On the section of gastroenterology, to continue the studies on digestive hemorrhage, acute pancreatitis, inflammatory bowel disease, motion sickness and digestive benign anorectal pathology.
- On the hepatology division to continue the analysis of hepatic encephalopathy, the nonalcoholic, epidemiological, therapeutic and immunoprophylaxis on Hepatitis Virus steatohepatitis. Also hepatocellular damage and nitric oxide and liver tumors.
- About endoscopy division: study on the therapeutic dilatation, the ecoendoscopy diagnostics and therapeutics, ampulectomia, diverticulotomy of Zencker and digestive prostheses.

SELECTED PUBLICATIONS

1. Sebastian S, Black C, Pugliese D, Armuzzi A, Sahnan K, Elkady SM, Katsanos KH, Christodoulou DK, Selinger C, Maconi G, Fearnhead NS, Kopylov U, Davidov Y, Bosca-Watts MM, Ellul P, Muscat M, Karmiris K, Hart AL, Danese S, Ben-Horin S, Fiorino G. The role of multimodal treatment in Crohn's disease patients with perianal fistula: a multicentre retrospective cohort study. *Alimentary Pharmacology & Therapeutics*. 2018; 48(9): 941 - 950. IF: 7,357
2. Bosca-Watts MM, Minguez M, Planelles D, Navarro S, Rodriguez A, Santiago J, Tosca J, Mora F. HLA-DQ: celiac disease vs inflammatory bowel disease. *World Journal of Gastroenterology*. 2018; 24(1): 96 - 103. IF: 3,300
3. Bosca-Watts MM, Minguez M, Planelles D, Navarro S, Rodriguez A, Santiago J, Tosca J, Mora F. HLA-DQ: celiac disease vs inflammatory bowel disease. *World Journal of Gastroenterology*. 2018; 24(1): 96 - 103. IF: 3,300
4. Ballester Ferré MP, Boscá-Watts MM, Mínguez Pérez M. Crohn's disease. *Medicina Clinica*. 2018; 151(1): 26 - 33. IF: 1,168
5. Barreiro-de Acosta M, Marín-Jiménez I, Panadero A, Guardiola J, Cañas M, Gobbo Montoya M, Modino Y, Alcaín G, Bosca-Watts MM, Calvet X, Casellas F, Chaparro M, Fernández Salazar L, Ferreiro-Iglesias R, Ginard D, Iborra M, Manceñido N, Mañosa M, Merino O, Rivero M, Roncero O, Sempere L, Vega P, Zabana Y, Mínguez M, Nos P, Gisbert JP. Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU) and the Association of Crohn's Disease and Ulcerative Colitis Patients (ACCU) in the management of psychological problems in Inflammatory Bowel Disease patients. *Gastroenterologia y Hepatologia*. 2018; 41(2): 118 - 127. IF: 1,078

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Title: *Implantación del sistema de gestión de la calidad en la actividad desarrollada por la Unidad de Enfermedad Inflamatoria Intestinal en el Servicio de Medicina Digestiva*

Principal Investigator: Miguel Mínguez Pérez

Funding Body: Janssen - Cilag S.A.

Program: Research Fellowship Program

Fellow: Laura Puchades Lanza

Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2018

Department of Intensive Medicine

Main lines of research

- Histones and septic shock.
- UCI Epidemiology. Multiresistant bacteria surveillance.
- Serious flu.
- Genetics in severe NAC.
- Quality of life of UCI (Mindfulness).

• PUBLICATIONS

Number of articles	IF	Average IF
4	10,436	2,609
National collaborations	International collaborations	Corresponding author
1	3	-

SELECTED PUBLICATIONS

1. Garnacho-Montero J, León-Moya C, Gutiérrez-Pizarraya A, Arenzana-Seis. Clinical characteristics, evolution, and

treatment-related risk factors for mortality among immunosuppressed patients with influenza A (H1N1) virus admitted to the intensive care unit. *Journal of Critical Care*. 2018; 48:172-177. IF: 2,872

2. Marin-Corral J, Climent C, Muñoz R, Samper M, Dot I, Vilà C, Masclans JR, Rodríguez A, Martín-Loeches I, Álvarez-Lerma F, en representación del Grupo de Trabajo H1N1 GETGAG SEMICYUC. Patients with influenza A (H1N1) pdm09 admitted to the ICU. Impact of the recommendations of the SEMICYUC. *Medicina Intensiva*. 2018; 42(8):473-481. IF: 1,755
3. Marin-Corral J, Climent C, Muñoz R, Samper M, Dot I, Vilà C, Masclans JR, Rodríguez A, Martín-Loeches I, Álvarez-Lerma F, en representación del Grupo de Trabajo H1N1 GETGAG SEMICYUC. Relationship between acute kidney injury and serum procalcitonin (PCT) concentration in critically ill patients with influenza infection. *Medicina Intensiva*. 2018; 42(7): 399-408. IF: 1,755
4. Vinuesa V, Borrás R, Briones ML, Clari MÁ, Crescencio V, Giménez E, Muñoz C, Oltra R, Servera E, Scheelje T, Tornero C, Navarro D. Performance of a highly sensitive mycobacterium tuberculosis complex real-time PCR assay for diagnosis of pulmonary tuberculosis in a low-prevalence setting: a prospective intervention Study. *Journal of Clinical Microbiology*. 2018; 56(5). pii: e00116-18. IF: 4,054

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI16/01036

Title: *Epigenética e inmunosupresión. Uso de las histonas circulantes y sus modificaciones post-traduccionales como biomarcadores de diagnóstico y pronóstico en sepsis y shock séptico*

Principal Investigator: José Luis García Giménez (Nieves Carbonell as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2019

Total budget: 87.725€

Reference: DTS17/00132

Title: *Kit multiplex para la detección simultánea de biomarcadores de diagnóstico y pronóstico de sepsis y shock séptico por espectrometría de masas*

Principal Investigator: Federico Vicente Pallardó Calatayud (Nieves Carbonell as collaborating researcher)

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2018

Total budget: 78.210€

Reference: 2018/8

Title: *DUCIAM: Transformación digital de la UCI del Hospital Clínico de Valencia para el diagnóstico y pronóstico de pacientes con Infarto Agudo de Miocardio*

Principal Investigator: M^a Luisa Blasco Cortés

Funding Body: *Convocatoria de ayudas para actividades preparatorias de proyectos coordinados entre institutos tecnológicos de REDIT e investigadores y profesionales del Instituto de Investigación Sanitaria INCLIVA*

Beneficiary Institution: *ITI*

Duration: 2018

Total budget: 3.000€

Reference: 03-CaViPro-Galiana-Blasco-2017-A

Title: *Diagnóstico y tratamiento de la calidad de vida de los profesionales de cuidados intensivos y paliativos: eficacia de intervenciones basadas en mindfulness*

Principal Investigator: M^a Luisa Blasco Cortés, Laura Galiana Llinares

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

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

Duration: 2018-2019

Total budget: 2.500€

Department of Maxillofacial Surgery

Strategic aims

- Innovation in personalised prosthesis for maxillofacial reconstruction.
- Translational research project for the development of implants with high added value through additive manufacturing.

Main lines of research

- Cost-effectiveness analysis on the management of oral surgery processes in patients with severe dependence and / or plurypathological chronicles with comorbidities. Proposal for a new organizational model of care.
- Radiological evaluation of predictive factors of access to pterygopalatine fossa.
- Research on materials involved in bone regeneration.
- Project: Mandibular Condylar Hyperplasia: Impact of Bone SPECT on Therapeutic Decision. Proposal of a decision algorithm.

RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: NervBiotube

Title: *Dispositivo reabsorbible (microtubo) con extremos auto-bioadhesivos para reparación de lesiones con defecto en nervios periféricos*

Principal Investigator: Miguel Puche Torres

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

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

-AIMPLAS

Duration: 2017-2018

Total budget: 3.000€

Department of Microbiology

Strategic aims

- We have identified rotavirus and norovirus genotypes infecting populations studied in Valencia during recent years.
- We have characterized the most common phenotypes of histo-blood antigens (secretory, Lewis and ABO antigens) in children infected with rotavirus.
- Isolation in culture of human enteroids from norovirus strains.

Main lines of research

- Phylogenetic analysis of polymerase and capsid genes sequences of norovirus strains in patients with acute gastroenteritis and chronic infections in immunocompromised patients.
- Study of association between histo-blood antigens (HBGA) of patients infected with different rotavirus and norovirus genotypes.
- Anti-adhesive effect of human milk oligosaccharides against rotavirus and norovirus.
- Human norovirus replication in enteroids.

• PUBLICATIONS

Number of articles	IF	Average IF
4	34,351	8,587
National collaborations	International collaborations	Corresponding author
2	2	-

SELECTED PUBLICATIONS

1. Monedero V, Buesa J, Rodríguez-Díaz J. The Interactions between Host Glycobiology, Bacterial Microbiota, and Viruses in the Gut. *Viruses-Basel*. 2018; 10(2). IF: 3,761
2. Huntley D, Mollar A, Buesa J, Rodríguez S, Giménez E, Sanchez J, Núñez J, Navarro D. Are pathogenic intestinal bacteria present in stool specimens from patients with chronic heart failure?. *Diagnostic Microbiology and Infectious Disease*. 2018; 91(2):141-143. IF: 2,341

3. Harvala H, Broberg E, Benschop K, Berginc N, Ladhani S, Susi P, Christiansen C, McKenna J, Allen D, Makiello P, McAllister G, Carmen M, Zakikhany K, Dyrdak R, Nielsen X, Madsen T, Paul J, Moore C, von Eije K, Piralla A, Carlier M, Vanoverschelde L, Poelman R, Anton A, López-Labrador FX, Pellegrinelli L, Keeren K, Maier M, Cassidy H, Derdas S, Savolainen-Kopra C, Diedrich S, Nordbø S, Buesa J, Bailly JL, Baldanti F, MacAdam A, Mirand A, Dudman S, Schuffenecker I, Kadambari S, Neyts J, Griffiths MJ, Richter J, Margaretto C, Govind S, Morley U, Adams O, Krokstad S, Dean J, Pons-Salort M, Prochazka B, Cabrerizo M, Majumdar M, Nebbia G, Wiewel M, Cottrell S, Coyle P, Martin J, Moore C, Midgley S, Horby P, Wolthers K, Simmonds P, Niesters H, Fischer TK. Recommendations for enterovirus diagnostics and characterisation within and beyond Europe. *Journal of Clinical Virology*. 2018; 101: 11-17. IF: 3,101
4. Van Beek J, de Graaf M, Al-Hello H, Allen DJ, Ambert-Balay K, Botteldoorn N, Brytting M, Buesa J, Cabrerizo M, Chan M, Cloak F, Di Bartolo I, Guix S, Hewitt J, Iritani N, Jin M, John R, Lederer I, Mans J, Martella V, Maunula L, McAllister G, Niendorf S, Niesters HG, Podkolzin AT, Poljsak-Prijatelj M, Rasmussen LD, Reuter G, Tuite G, Kroneman A, Vennema H, Koopmans MPG; 2018. NoroNet. Molecular surveillance of norovirus, 2005-16: an epidemiological analysis of data collected from the NoroNet network. *Lancet Infectious Diseases*. 18(5):545-553. IF: 25,148

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI16/01471

Title: *Diversidad genética y antigénica de norovirus humanos: estudio de anticuerpos séricos protectores y de la inmunidad celular en ratones y en pacientes infectados*

Principal Investigator: F. Javier Buesa Gómez

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2017-2019

Total budget: 68.365€

Reference: EuroRotaNet

Title: *Rotavirus surveillance in Europe: Determining the diversity of cocirculating rotavirus strains in consecutive rotavirus seasons*

Principal Investigator: Miren Iturriza Gómara (University of Liverpool)

Funding Body: *directed by Health Protection Agency, funded by Sanofi Pasteur, Glaxo Smith Kline Biologicals, sponsored by World Health Organization*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2007-2018

Total budget: 229.000€

Reference: IDIFEDER/2018/056

Title: *Creació d'una infraestructura de producció, purificació i caracterització de proteïnes d'interès biomèdic i biotecnològic*

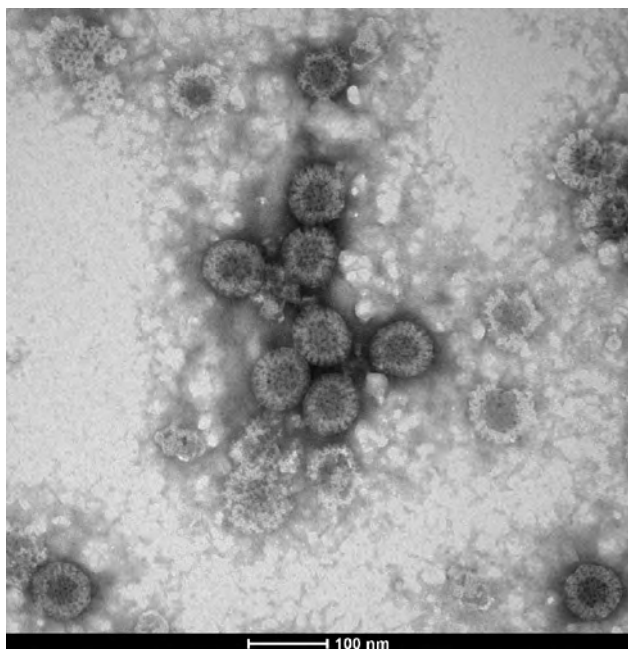
Principal Investigator: Jesús Rodríguez Díaz

Funding Body: *Conselleria d' Educació, Investigació, Cultura i Esports. Generalitat Valenciana*

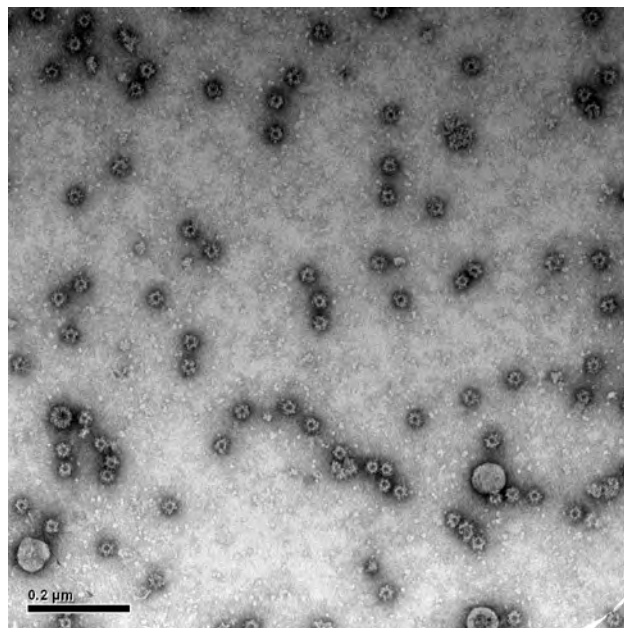
Beneficiary Institution: *Universidad de Valencia*

Duration: 2018 - 2020

Total budget: 431.414€



1. Rotavirus electron microscope image



2. Human norovirus pseudovirus particles synthesized in vitro

Department of Nephrology

Strategic aims

- To work together with cardiology Department in order to explore new developments in treatment of cardio-renal syndrome by peritoneal dialysis.
- Diabetic kidney disease: risk factors and progression. Diabetic kidney disease in dialysis patients.
- To analyze risk factors for developing hyperkalemia and the adherence to the current treatments.
- To establish the picture of the renal problems detected in Oncology and Hematology patients: kidney damage in the onco-hematologic patients.
- To analyze the incidence of acute kidney injury in hospitalized patients.

Main lines of research

- Treatment of cardio-renal syndrome by peritoneal dialysis
- Diabetic kidney disease and chronic kidney disease: risk factors and progression and proteinuria development.

Diabetic kidney disease in dialysis patients.

- Hyperkalemia and chronic kidney disease.
- Onco-nephrology: kidney damage in the oncologic patient.
- Biomarkers of acute kidney injury.

• PUBLICATIONS

Number of articles	IF	Average IF
10	42,688	4,268

National collaborations	International collaborations	Corresponding author
5	5	1

SELECTED PUBLICATIONS

1. Navarro-González JF, Sánchez-Niño MD, Donate-Correa J, Martín-Núñez E, Ferri C, Pérez-Delgado N, Górriz JL, Martínez-Castelao A, Ortiz A, Mora-Fernández C. Effects of pentoxifylline on soluble klotho concentrations and renal tubular cell expression in diabetic kidney disease. *Diabetes Care*. 2018; 41(8): 1817 - 1820. IF: 13,397
2. Brück K, Jager KJ, Zoccali C, Bello AK, Minutolo R, Ioannou K, Verbeke F, Völzke H, Arnlöv J, Leonardis D, Ferraro PM, Brenner H, Caplin B, Kalra PA, Wanner C, Castelao AM, Górriz JL, Hallan S, Rothenbacher D, Gibertoni D, De Nicola L, Heinze G, Van Biesen W, Stel VS, European CKD Burden Consortium. Different rates of progression and mortality in patients with chronic kidney disease at outpatient nephrology clinics across Europe. *Kidney International*. 2018; 93(6): 1432 - 1441. IF: 8,429
3. Molina P, Vizcaino B, Molina MD, Beltrán S, González-Moya M, Mora A, Castro-Alonso C, Kanter J, Ávila AI, Górriz JL, Estañ N, Pallardó LM, Fouque D, Carrero JJ. The effect of high-volume online haemodiafiltration on nutritional status and body composition: the ProtEin Stores prEservaTion (PESET) study. *Nephrology Dialysis Transplantation*. 2018; 33(7): 1223 - 1235. IF: 4,600
4. García-García R, Cruz-Gómez AJ, Urios A, Mangas-Losada A, Forn C, Escudero-García D, Kosenko E, Torregrosa I, Tosca J, Giner-Durán R, Serra MA, Avila C, Belloch V, Felipe V, Montoliu C. Learning and memory impairments in patients with minimal hepatic encephalopathy are associated with structural and functional connectivity alterations in hippocampus. *Scientific Reports*. 2018; 8(1): 9664. IF: 4,122
5. Núñez J, Palau P, Domínguez E, Mollar A, Núñez E, Ramón JM, Miñana G, Santas E, Fácila L, Górriz JL, Sanchis J, Bayés-Genís A. Early effects of empagliflozin on exercise tolerance in patients with heart failure: a pilot study. *Clinical Cardiology*. 2018; 41(4): 476 - 480. IF: 2,733

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: ESR- 17-13201

Title: *Severe hyperkalemia in the emergency room: retrospective study and analysis of risk factors, comorbidities, treatments given and subsequent changes and clinical evolution. Detection of areas of improvement*

Principal Investigator: Jose Luis Górriz Teruel

Funding Body: AstraZeneca

Beneficiary Institution: *Hospital Clínico Universitario de Valencia and Hospital Universitario Dr Peset*

Duration: 2018

Total Budget: 6.000€

Department of Neurology

• PUBLICATIONS

Number of articles	IF	Average IF
8	21,777	2,722

National collaborations	International collaborations	Corresponding author
6	2	0

SELECTED PUBLICATIONS

1. Alcalá C, Gascón F, Pérez-Miralles F, Gil-Perotín S, Navarré A, Boscá I, Coret F, Casanova B. Efficacy and safety of rituximab in relapsing and progressive multiple sclerosis: a hospital-based study. *Journal of Neurology*. 2018; 265(7): 1690 -

1697. IF: 3,783

2. Gil-Perotin S, Castillo-Villalba J, Carreres-Polo J, Navarré-Gimeno A, Mallada-Frechín J, Pérez-Miralles F, Gascón F, Alcalá-Vicente C, Cubas-Nuñez L, Casanova-Estruch B. Progressive demyelination in the presence of serum myelin oligodendrocyte glycoprotein-igg: a case report. *Frontiers in Neurology*. 2018; 9: 340. IF: 3,508
3. Bottiroli S, Allena M, Sances G, De Icco R, Avenali M, Fadic R, Katsarava Z, Lainez MJ, Goicochea MT, Jensen RH, Nappi G, Tassorelli C; Comoestas Consortium. Changes in anxiety and depression symptoms associated to the outcome of MOH: a post-hoc analysis of the Comoestas Project. *Cephalalgia*. 2018; 38(4): 646 - 654. IF: 3,882
4. Ramos ML, García-Cabo C, Leira R, Domínguez C, Pozo-Rosich P, Vila C, Laínez MJ, Pascual J. Comorbidity between idiopathic overactive bladder and chronic migraine. *Cephalalgia*. 2018; 38(3): 581 - 584. IF: 3,882
5. Casanova B, Lacruz L, Villar ML, Domínguez JA, Gadea MC, Gascón F, Mallada J, Hervás D, Simó-Castelló M, Álvarez-Cermeño JC, Calles C, Olascoaga J, Ramió-Torrentà L, Alcalá C, Cervelló A, Boscá I, Pérez-Miralles FC, Coret F. Different clinical response to interferon beta and glatiramer acetate related to the presence of oligoclonal IgM bands in CSF in multiple sclerosis patients. *Neurological Sciences*. 2018; 39(8): 1423 - 1430. IF: 2,285

- rathyroidism and not conclusive pre-surgical scintigraphy.
- Sentinel node detection in breast cancer after neoadjuvant chemotherapy.

Main lines of research

- Radioembolization of hepatocarcinoma by resin microspheres labeled with 90-Yttrium.
- Assessment of cardiac sympathetic nerve activity by 123I-MIBG scintigraphy in heart failure patients.
- Evaluation of left ventricular dyssynchrony by Gated SPECT myocardial perfusion in patients with cardiac resynchronization therapy.
- Sentinel lymph node detection in breast cancer in patients with previous mammary surgery.
- Evaluation of screws loosening and other complications after lumbar spinal fusion surgery by bone SPECT.
- Diagnosis and follow-up of hyperplasia of the mandibular condyles by bone SPECT.

• PUBLICATIONS

Number of articles	IF	Average IF
2	2,404	1,202
National collaborations	International collaborations	Corresponding author
2	-	1

SELECTED PUBLICATIONS

1. Ruano Pérez R, Rebollo Aguirre AC, García-Talavera San Miguel P, Díaz Expósito R, Vidal-Sicart S, Cordero García JM, Carrera Salazar D, Rioja Martín ME, Grupo de Trabajo de Cirugía Radioguiada de la SEMNIM. Review of the role of the sentinel node biopsy in neoadjuvant chemotherapy in women with breast cancer and negative or positive axillary node at diagnosis. *Revista Espanola de Medicina Nuclear e Imagen Molecular*. 2018; 37(1): 63 - 70. IF: 1,202
2. Casás Tormo I, Grupo de Trabajo de Cardiología Nuclear de la Sociedad Española de Medicina Nuclear. Wider scope for nuclear cardiology. *Revista Espanola de Medicina Nuclear e Imagen Molecular*. 2018; 37(3): 139 - 140. IF: 1,202

Department of Nuclear Medicine

Strategic aims

- Dosimetric assessment in patients with hyperthyroidism treated with 131-Iodine.
- Cardiac sympathetic nerve activity by 123I-MIBG scintigraphy in heart failure patients.
- Evaluation of left ventricular dyssynchrony by Gated SPECT myocardial perfusion in the evaluation of cardiac resynchronization therapy.
- Radioguided surgery by intraoperative scintigraphy with portable gamma camera in patients with primary hyperpa-

Department of Ophthalmology

Strategic aims

- Study of retinochoroidal vascularization via techniques of OCT angiography, a new technology under development. The majority of Spanish-authored publications on OCT angiography appearing in ophthalmological journals correspond to research from the Hospital Clínico of Valencia group.

Main lines of research

- OCT for quantitative analysis of the retinal ganglion cell layer in patients with multiple sclerosis: correlation with the degree of disability and cerebral atrophy in magnetic resonance.
- Analysis of filtration blebs after glaucoma surgery using anterior pole OCT.

• PUBLICATIONS

Number of articles	IF	Average IF
1	6,669	6,669

National collaborations	International collaborations	Corresponding author
-	1	-

SELECTED PUBLICATIONS

1. De Moraes CG, Mansouri K, Liebmann JM, Ritch R, Triggerfish Consortium. Association between 24-hour intraocular pressure monitored with contact lens sensor and visual field progress; on in older adults with glaucoma. *JAMA Ophthalmology*. 136(7): 779 - 785. IF: 6,669

Department of Otorhinolaryngology

Strategic aims

- Osseointegrated implants.
- Cochlear Implants.
- Otoneurology.

Main lines of research

- Osseointegrated Implants: results of new implants with hydroxyapatite.
- Cochlear Implants: result of unilateral IC.
- Otoneurology: vHIT in cochlear implants.

• PUBLICATIONS

Number of articles	IF	Average IF
2	3,988	1,994

National collaborations	International collaborations	Corresponding author
2	-	2

SELECTED PUBLICATIONS

1. Fernández-Julián E, Pérez-Carbonell T, Marco R, Pellicer V, Rodríguez-Borja E, Marco J. Impact of an oral appliance on obstructive sleep apnea severity, quality of life, and biomarkers. *Laryngoscope*. 2018; 128(7): 1720 - 1726. IF: 2,442
2. Marco Pitarch R, Selva García M, Puertas Cuesta J, Marco Algarra J, Fernández Julian E, Fons Font A. Effectiveness of a mandibular advancement device in obstructive sleep apnea patients: a prospective clinical trial. *European Archives of Oto-Rhino-Laryngology*. 2018; 275(7): 1903 - 1911. IF: 1,546

Department of Pediatrics

• PUBLICATIONS

Number of articles	IF	Average IF
7	21,697	3,099

National collaborations	International collaborations	Corresponding author
4	3	2

SELECTED PUBLICATIONS

- García-Molina P, Balaguer López E, Verdú J, Nolasco A, García Fernández FP. Cross-cultural adaptation, reliability and validity of the Spanish version of the Neonatal Skin Risk Assessment Scale. *Journal of Nursing Management*. 2018; 26(6): 744 - 756. FI: 1,912
- García-Molina P, Balaguer-López E, García-Fernández FP, Ferrera-Fernández MLÁ, Blasco JM, Verdú J. Pressure ulcers' incidence, preventive measures, and risk factors in neonatal intensive care and intermediate care units. *International Wound Journal*. 2018; 15(4): 571 - 579. IF: 2,380
- Griese M, Seidl E, Hengst M, Reu S, Rock H, Anthony G, Kiper N, Emiralioğlu N, Snijders D, Goldbeck L, Leidl R, Ley-Zaporozhan J, Krüger-Stollfuss I, Kammer B, Wesselak T, Eismann C, Schams A, Neuner D, MacLean M, Nicholson AG, Lauren M, Clement A, Epaud R, de Blic J, Ashworth M, Aurora P, Calder A, Wetzke M, Kappler M, Cunningham S, Schwerk N, Bush A; the other chILD-EU collaborators. International management platform for children's interstitial lung disease (chILD-EU). *Thorax*. 2018; 73: 231 - 239. IF: 9,655
- Matamala N, Lara B, Gomez-Mariano G, Martínez S, Retana D, Fernandez T, Silvestre RA, Belmonte I, Rodriguez-Frias F, Vilar M, Sáez R, Iturbe I, Castillo S, Molina-Molina M, Texido A, Tirado-Conde G, Lopez-Campos JL, Posada M, Blanco I, Janciauskiene S, Martinez-Delgado B. Characterization of Novel Missense Variants of SERPINA1 Gene Causing Alpha-1 Antitrypsin Deficiency. *American Journal of Respiratory Cell and Molecular Biology*. 2018; 58: 706 - 716. IF: 3,785
- Escribano Montaner A, García de Lomas J, Villa Asensi JR, Asensio de la Cruz O, de la Serna Blázquez O, Santiago Buruchaga M, Mondéjar López P, Torrent Vernetta A, Feng Y, Van Dyke MK, Reyes J, Garcia-Corbeira P, Talarico CA; EPI-Strep-064 study group. Bacteria from bronchoalveolar lavage fluid from children with suspected chronic lower respiratory tract infection: results from a multi-center, cross-sectional study in Spain. *European Journal of Pediatrics*. 2018; 177: 181 - 192. IF: 2,242

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI16/01233

Title: *Caracterización molecular de la discinesia ciliar primaria*

Principal Investigator: Antonio Moreno (Amparo Escribano Montaner as collaborator researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación de Investigación Vall d'Hebrón*

Duration: 2017-2019

Total Budget: 110.715€

Reference: PI15/00466

Title: *Estudio multicéntrico de la estructura poblacional de Staphylococcus aureus, su relación con el microbioma, colonización patogénica por P. aeruginosa y situación clínica en fibrosis quística*

Principal Investigator: Rafael Cantón Moreno (Amparo Escribano Montaner as collaborator researcher)

Funding Body: *Instituto de Salud Carlos III*

Beneficiary Institution: *Fundación Investigación Biomédica Ramón y Cajal*

Duration: 2016-2018

Total Budget: 196.927,50€

Title: *Molecular characterization of primary ciliary dyskinesia*

Principal Investigator: Antonio Moreno

Funding Body: *Sociedad Española de Neumología Pediátrica "Senior"*

Beneficiary institution: *Hospital Vall d'Hebrón*

Duration: 2016-2019

Total budget: 10.000€

Title: *Caracterización del perfil oxidativo en células epiteliales nasales de pacientes con Discinesia Ciliar Primaria*

Principal Investigator: Amparo Escribano Montaner

Funding body: *Sociedad Española de Neumología Pediátrica and Sociedad Valenciana Neumología*

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

Duration: 2015-2018

Total budget: 10.000€

Title: *Estudio del efecto de la hipoxia en la degranulación, en la producción de citoquinas y en el perfil oxidativo de los neutrófilos de pacientes con déficit de alfa-1 antitripsina*

Principal Investigator: Amparo Escribano Montaner

Funding Body: *Sociedad Valenciana de Neumología*

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

Duration: 2017-2020

Total budget: 12.000€

Title: *Diseño y desarrollo de un método basado en CRISPR/Cas9 para la reparación del gen de la alfa-1-antitripsina*

Principal Investigator: Amparo Escribano Montaner

Funding Body: *Sociedad Valenciana de Neumología*

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

Duration: 2016-2019

Total budget: 12.000€

Title: *Caracterización del perfil oxidativo en células epiteliales nasales de pacientes con Discinesia Ciliar Primaria*

Principal Investigator: Amparo Escribano Montaner

Funding body: *Sociedad Valenciana Neumología*

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

Duration: 2015-2018

Total budget: 12.000€

• THESIS

Thesis title: *Valoración de los niveles materno-fetales de 25-oh vitamina D y grado de mineralización ósea del recién nacido*

Doctoral candidate: Irene Ruiz Alcántara

Director(s): Jaime Fons Moreno, Francisco Javier Estañ Capell, Susana Ferrando Monleón

Date of the defense: 21/12/2018

Grade: *Sobresaliente "cum laude"*

Department of Pharmacy

Strategic aims

- Implementation of a new therapeutic drug monitoring system in a clinical analytical laboratory for pharmacokinetic control of antibiotic, antifungal and antineoplastic agents in the hospitalized patient, with the aim of optimal and rational use of pharmacological treatment.
- Study of pharmacokinetics of caspofungin in patients under hemodiafiltration. Study approved by the Agencia Española del Medicamento y Productos Sanitarios with code MER-CAS-2013-01.
- Observational Study of population pharmacokinetic model of voriconazole in allogeneic stem cell transplantation. Study approved by the Agencia Española del medicamento y Productos Sanitarios with code CSV-VOR-2014-01.
- Study of pharmacokinetics of Ceftolozane in critical patients. Study pending of approval by the Agencia Española del Medicamento y Productos Sanitarios with code CEFT-TCRR-2017.
- Study of Physico-chemical stability of a new mycophenolate mofetil intravenous solution in polypropylene infusion bag at different storage conditions.
- Study of Physico-chemical stability of a new ophthalmic eyedrop formulation at different storage conditions.

Main lines of research

- Implementation of a new therapeutic drug monitoring system in a clinical analytical laboratory for pharmacokinetic control of antibiotic, antifungal and antineoplastic agents in the hospitalized patient, with the aim of optimal and rational use of pharmacological treatment.
- Study of pharmacokinetics of caspofungin in patients under hemodiafiltration. Study approved by the Agencia Española del Medicamento y Productos Sanitarios with code MER-CAS-2013-01.
- Observational Study of population pharmacokinetic model of voriconazole in allogeneic stem cell transplantation. Study approved by the *Agencia Española del Medicamen-*

to y Productos Sanitarios with code CSV-VOR-2014-01.

- Study of pharmacokinetics of Ceftolozane in critical patients. Study pending of approval by the *Agencia Española del Medicamento y Productos Sanitarios* with code CEFT-TCRR-2017.
- Study of Physico-chemical stability of a new mycophenolate mofetil intravenous solution in polypropylene infusion bag at different storage conditions.
- Study of Physico-chemical stability of a new ophthalmic eyedrop formulation at different storage conditions.
- Dosing of caspofungin based on a pharmacokinetic/pharmacodynamic index for the treatment of invasive fungal infections in critically ill patients on continuous venovenous haemodiafiltration.
- Cost effectiveness analysis of direct-acting antiviral therapy for treatment-of patients with chronic HCV infection.

• PUBLICATIONS

Number of articles	IF	Average IF
3	13,224	4,408
National collaborations	International collaborations	Corresponding author
2	-	-

SELECTED PUBLICATIONS

1. Piñana JL, Perez-Pitarch A, Guglieri-Lopez B, Giménez E, Hernandez-Boluda JC, Terol MJ, Ferriols-Lisart R, Solano C, Navarro D. Sirolimus exposure and the occurrence of cytomegalovirus DNAemia after allogeneic hematopoietic stem cell transplantation. *American Journal of Transplantation*.2018; 18(12): 2885 - 2894. IF: 6,493
2. Pérez-Pitarch A, Ferriols-Lisart R, Aguilar G, Ezquer-Garín C, Belda FJ, Guglieri-López B. Dosing of caspofungin based on a pharmacokinetic/pharmacodynamic index for the treatment of invasive fungal infections in critically ill patients on continuous venovenous haemodiafiltration. *International Journal of Antimicrobial Agents*. 2018; 51(1): 115 - 121. IF: 4,253
3. Ezquer-Garín C, Ferriols-Lisart R, Alós-Almiñana M, Aguilar-

Aguilar G, Belda-Nacher JF, Carbonell JA. Validated HPLC-UV detection method for the simultaneous determination of ceftolozane and tazobactam in human plasma. *Bioanalysis*. 2018; 10(7): 461 - 473. IF: 2,478

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Title: *Estudio de estabilidad en mezclas intravenosas y compatibilidad química asociada al uso de sistemas cerrados de transferencia de medicamentos*

Principal Investigator: Raquel Ferriols Lisart

Funding Body: Janssen - Cilag S.A.

Program: Research Fellowship Program

Fellow: Carlos Ezquer Garín

Institution: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Duration: 2018

• THESIS

Thesis title: *Prevención secundaria tras infarto agudo de miocardio con elevación del segmento ST: factores de riesgo y consecuencias clínicas de la falta de tratamiento farmacológico*

Doctoral candidate: Ana María Padilla López

Director(s): Manuel Alós Almiñana, José Esteban Peris Ribera

Date of the defense: 06/06/2018

Grade: *Sobresaliente "cum laude"*

Department of Pneumology

Strategic aims

- Efficacy of a tobacco treatment program about severe exacerbation in smokers with a moderate or severe COPD.
- To assess cognitive / behavioral signs associated with neuromuscular dementia patients and their involvement in the decision-making process.

Main lines of research

- Study of long term utility of mechanically assisted cough with in-exhufation, through high frequency oscillations, in ALS patients.
- Study of the efficacy of mechanically assisted cough with in-exhufation, through high frequency oscillations, during acute respiratory infections, in ALS patients.
- Study of long term utility of mechanically assisted cough with in-exhufation, through high frequency oscillations, in ALS patients and mechanical ventilation trough tracheotomy.
- Study of physio-pathology of assisted cough with in-exhufation, through high frequency oscillations, in ALS patients.
- Study of the effect of bulbar alteration in survival of ALS patients and non invasive mechanical ventilation.
- Study of the physio-pathology in the failure of non invasive mechanical ventilation in ALS patients.
- Study of treatment with quinidine/dextromethorphan in the delay of failure of non invasive management of respiratory problems in ALS patients.
- To improve knowledge in the staging of patients with neuromuscular diseases to anticipate decisions and to adjust respiratory therapeutic measures.
- To improve knowledge in technical assistance and replacement of the respiratory muscles in neuromuscular diseases, particularly to the life-prolonging without adding suffering.
- To improve knowledge in the management of the psycho-emotional needs in patients with COPD and incapacitating dyspnea and their caregivers.
- To improve knowledge about the role of genetic polymorphisms in the predisposition, severity and susceptibility to bacteremia in community-acquired pneumonia.
- To evaluate the efficiency of the management of dyspnea.
- To evaluate the prevalence of stressful life events, different styles of attachment and the proportion of adaptive and problem duels present in relatives of patients at the end of life.
- Cardiac morphological changes in patients with sleep respiratory disorders and ischemic heart disease: response to CPAP treatment.
- Effects of e-liquids (propylene glycol (PG), diethylene glycol (DG), and nicotine) from electronic cigarettes in

human cell cultures: Human umbilical vein endothelial cells (HUVEC) and adenocarcinomic human alveolar basal epithelial cells (A549).

- Efficacy of a tobacco treatment program about severe exacerbation in smokers with a moderate or severe COPD.
- Evaluation of CPAP on kidney function in patients with early-stage renal disease and sleep apnea syndrome (RENAS study).
- Characterization of asthmatic patients: new bio-markers (periostine and protein CC16) and their relationship with the severity of bronchial asthma.
- Study of genetic variability in the susceptibility and severity of pneumonia.
- Efficiency of an integrated program for COPD patients with frequent hospital admissions.
- Open label multicentric study of RCP1063 oral in recurrent multiple sclerosis (MS).
- Randomized, double-blind, multicentric, parallel groups, controlled with placebo and variable duration, to evaluate efficacy and safety of Sponimod (BAF312) in patients with secondary MS, followed by an open extension treatment of BAF312.
- To assess cognitive / behavioral signs associated with OSA patients.
- Study about effectiveness of peak cough flows generated by mechanical in-exsufflation using waveforms analysis y amyotrophic lateral sclerosis patients (MI-E waveforms ALS study).

• PUBLICATIONS

Number of articles	IF	Average IF
1	2,633	2,633
National collaborations	International collaborations	Corresponding author
-	1	1

SELECTED PUBLICATIONS

1. Carrión Valero F, Paulos Dos Santos S, Celli BR. Smoking In COPD patients: a new clinical phenotype?. Archivos de Bronconeumología. 2018; 54(5): 249 - 250. IF: 2,633

Department of Preventive Medicine

• THESIS

Thesis title: *La actividad física como promotora de salud en personas mayores*

Doctoral candidate: Javier Guillem Saiz

Director(s): Carmen Saiz Sánchez

Date of the defense: 21/05/2018

Grade: *Sobresaliente "cum laude"*

Thesis title: *Estudio epidemiológico de encuestas y escalas en el tratamiento multicomponente sobre un colectivo de pacientes fumadores de la Comunidad Valenciana*

Doctoral candidate: Yang Wang

Director(s): Carmen Saiz Sánchez

Date of the defense: 04/05/2018

Grade: *Sobresaliente "cum laude"*

Department of Psychiatry

• PUBLICATIONS

Number of articles	IF	Average IF
1	3,786	3,786

National collaborations	International collaborations	Corresponding author
-	1	1

SELECTED PUBLICATIONS

1. Cano-Vindel A, Muñoz-Navarro R, Medrano LA, Ruiz-Rodríguez P, González-Blanch C, Gómez-Castillo MD, Capafons A, Chacón F, Santolaya F, PsicAP Research Group. A computerized version of the Patient Health Questionnaire-4 as an ultra-brief screening tool to detect emotional disorders in

primary care. *Journal of Affective Disorders*. 2018; 234: 247 - 255. IF: 3,786

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PI14/00044

Title: *Eficacia del entrenamiento metacognitivo individualizado (EMC+) en personas con psicosis de reciente evolución*

Principal Investigator: Susana Ochoa (Esther Lorente and Ana Luengo as collaborating researcher)

Funding body: *Instituto de Salud Carlos III*

Beneficiary institution: *Fundación para la investigación y docencia Sant Joan de Déu*

Duration: 2015-2018

Total budget: 92.565€

Department of Radiologic Diagnosis

Main lines of research

- To participate in clinical trials with Hematology and Oncology Departments by performing CT and / or biopsies to check inclusion of patients in new chemotherapy treatments.
- To evaluate cerebral reperfusion syndrome after treatment of carotid stenosis by stent.
- To study gastric pre-oesophagectomy conditioning to reduce the incidence of dehiscence of sutured anastomoses.

• THESIS

Thesis title: *Tomografía computerizada de doble energía en patología pulmonar*

Doctoral candidate: Víctor González Pérez

Director(s): David Moratal Pérez, Estanislao Arana Fernández De Moya, Delfina Dualde Beltrán

Date of the defense: 21/09/2018

Grade: *Sobresaliente "cum laude"*

Department of Thoracic Surgery

Strategic aims

- Tracheal tissue bioengineering.

Main lines of research

- Tracheal tissue bioengineering.
- Rare diseases.
- Endoscopic VATS resections.
- Fast track pulmonary surgery and ERAS project.

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: SAF2015-65368-R

Title: *Modulación farmacológica de la señalización inflamación-remodelado por inhibidores isoforma-selectivos de PDE4 y comparadores en modelos humanos in vitro relevantes en EPOC*

Principal Investigator: Esteban Morcillo Sánchez (Genaro Galán Gil as collaborating researcher)

Funding body: *Ministerio de Economía y Competitividad*

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

Duration: 2016-2018

Total budget: 181.500€

Reference: PROMETEO/2017/023

Title: *Modulación del eje óxido nítrico-guánilato ciclasa soluble-GMPC como nueva diana farmacológica para el tratamiento del asma y la enfermedad pulmonar obstructiva crónica (EPOC)*

Principal Investigator: Julio Cortijo Gimeno (Genaro Galán Gil as collaborating researcher)

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

Beneficiary institution: *Universidad de Valencia*

Duration: 2017-2021

Total budget: 315.728€

Department of Traumatology and Orthopedic Surgery

Strategic aims

- Non-invasive image in orthopedics.
- Mechanisms of inflammation and oxidative stress in bone pathologies.
- New systems of fixation of prostheses applied to Traumatology.

Main lines of research

- Cellular oxidative stress and its relationship with idiopathic femoral osteonecrosis.
- Sequentiality of muscle contraction: importance in early detection of lumbopelvic, cervical and shoulder girdle dysfunction.
- Diagnosis and monitoring of the diabetic foot using infrared thermography.
- Cellular mechanisms to regulate inflammatory response in chronic inflammatory diseases.
- Protection strategies against osteoarticular deterioration.
- Robotics for precision in orthopedic reconstructive surgery.
- Rehabilitation to improve outcomes after total knee arthroplasty prospective randomized study.
- Local mechanical stimulation of mesenchymal cells for osteogenic and chondrogenic differentiation in regenerative medicine.

• PUBLICATIONS

Number of articles	IF	Average IF
2	6,449	3,224
National collaborations	International collaborations	Corresponding author
2	-	-

SELECTED PUBLICATIONS

1. Gil-Santos L, Monleón-Pradas M, Gomar-Sancho F, Más-Estellés J. Positioning of the cross-stitch on the modified

Kessler core tendon suture. *Journal of the Mechanical Behavior of Biomedical Materials*. 2018; 80: 27 - 32. IF: 3,239

- García-Rellán JE, Sánchez-Alepuz E, Mudarra-García J. Increased fatigue of the biceps after tenotomy of the long head of biceps tendon. *Knee Surgery Sports Traumatology Arthroscopy*. 2018; 26(12): 3826 - 3831. IF: 3,210

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: AICO/2017/122

Title: *Protocolo de diagnóstico y seguimiento del pie diabético mediante termografía infrarroja*

Principal Investigator: Rosa M^a Cibrián-Ortiz de Anda (Laura Pino Almero, María Fe Mínguez Rey as collaboratin researchers)

Funding Body: *Generalitat Valenciana*

Beneficiary Institution: *Universidad de Valencia*

Duration: 2017-2018

Department of Urology

Strategic aims

- To finish the line of research related to metabolomics in prostate cancer.
- To consolidate a new research line in relation to metabolomics in bladder cancer.
- Open a new research line in liquid biopsy for bladder cancer.

Main lines of research

- Usefulness of microRNAs in blood and urine in the diagnosis and prognosis of bladder cancer.
- Testosterone deficiency syndrome in the aging male and its relation to erectile dysfunction.
- Metabolic analysis of urine in patients with prostate and bladder cancer.
- Liquid biopsy for bladder cancer.

• PUBLICATIONS

Number of articles	IF	Average IF
4	5,999	1,499
National collaborations	International collaborations	Corresponding author
3	1	3

SELECTED PUBLICATIONS

- March-Villalba JA, Panach-Navarrete J, Herrero-Cervera MJ, Aliño-Pellicer S, Martínez-Jabaloyas JM. hTERT mRNA expression in urine as a useful diagnostic tool in bladder cancer. Comparison with cytology and NMP22 BladderCheck Test[®]. *Actas Urologicas Espanolas*. 2018; 42(8): 524 - 530. IF: 1,260
- Panach-Navarrete J, Valls-González L, Sánchez-Cano E, Medina-González M, Castelló-Porcar A, Martínez-Jabaloyas JM. Comparison of three different antibiotic protocols in transurethral resection of bladder tumour and the possible infectious risk factors: a non-randomized, prospective study. *CUAJ-Canadian Urological Association Journal*. 2018; 12(11): E466 - E674. IF: 1,179
- Panach-Navarrete J, Valls-González L, Medina-González M, Martínez-Jabaloyas JM. Holmium laser endoureterotomy with the lovaco technique for the treatment of ureterointestinal stenosis: step by step. *Urology*. 2018; 120: 263. IF: 2,300
- Arlandis S, Morán E, Martínez-Cuenca E, Bonillo MÁ, Martínez-García R, Rosier P. Adaptation to Spanish of the ICS Good Urodynamic Practices. *Actas Urologicas Espanolas*. 2018; 42(10): 625 - 631. IF: 1,260

• 4.5 Other scientific contributions from scientific platforms

4.5.1 Biobank

Team

Principal Investigator

Antonio Ferrández Izquierdo
Hospital. University

Collaborating researchers:

Lorena Peiró Chova. INCLIVA

Technicians

Olga Bahamonde Ponce. INCLIVA
Marta Belda Moscardó. INCLIVA
Ángela Bañuls Alemany. INCLIVA

biobanco@incliva.es

ACTIVITIES DEVELOPED

Incorporation of samples in pre-existing collections within the biobank regime:

Oncological Node:

- Collection of solid tumors: 130 new cases
- Collection of peripheral blood and derivative products in patients suffering from breast cancer: 870 new sample donations
- Collections of peripheral blood and derivative products in patients suffering from lung cancer: 212 new sample donation
- Collection of peripheral blood and derivative products in patients suffering from melanoma: 88 new cases
- Collection of peripheral blood and derivative products in patients suffering from gastrointestinal: 911 new sample donations
- Collection of peripheral blood and derivative products in patients suffering from head and neck tumors: 80 sample donations
- Collections of peripheral blood and derivative products in patients suffering from brain tumors: 9 sample donations
- Collections of peripheral blood and derivative products in patients suffering from gynecological tumors: 4 sample donations

Immunological Diseases Node:

- Collection of peripheral blood and derivative products in patients suffering from Systemic Lupus Erythematosus or other autoimmune diseases: 11 new cases

Cardiovascular Node:

- Collections from the cardiovascular node: 11 new cases

Other collections:

- Collection sepsis gravis and septic shock: 18 new sample donations
- Collection of peripheral blood and derivative products in patients suffering from Multiple Esclerosis: no new cases
- Collection of peripheral blood and derivative products in standard population: 15 new cases

Incorporation of new collections within the biobank regime:

- Hiperaldosteronismo, New Collection of peripheral blood and derivative products from the cardiovascular node

In summary, 2445 new sample donations have been received and 9347 samples have been processed in 2018 at INCLIVA Biobank facilities.

In addition, the Biobank has surplus diagnostic samples from the HCUV Pathology and Hematology service that may be used in research provided they have the corresponding Biobank Informed Consent.

Incorporation of new collections within the biobank regime (since 2018 the management of these collections is considered as a biobank activity):

The collections are outside the organizational structure of the

biobank that are generated in the scope of projects and / or private clinical trials. The biobank manages the storage and custody of the samples, as well as the processing of the same in some cases.

- Study immunity in breast cancer and Olaparib. Collaboration and delivery of SP tubes (original sample) to the project: Role of tumor heterogeneity and dynamic reprogramming of the tumor cell in resistance to anti-HER2 antibodies in HER2 positive breast cancer. PI15 / 01617; PI15 / 00146
- MAMI study. Temporary custody of samples of the project: ERC-European Research Council, Horizon 2020 Program: European Project MAMI, the power of maternal microbes for infant health. ERC Starting Grant ref. 639226
- Amadix Studio. Processing, conservation and shipment of processed samples for the PancreaDIX study: study for the development and validation of a genetic fingerprint for the diagnosis of pancreatic cancer and precursor lesions. AMD-CPA-2016-01
- I-Prove Study: Sampling of samples for the study: Reduction of postoperative complications and hospital stay with an individualized perioperative strategy of pulmonary protection ventilation. A comparative, prospective, multicenter, randomized and controlled study. IPROVE. NCT02158923
- Cronotrial study. Processing, conservation and shipment of processed samples for the CRONOTRIAL study: Exploratory study for the determination of ctDNA in blood samples of patients treated for breast cancer in follow-up and without evidence of recurrence
- RENAS study. Processing, conservation and shipment of processed samples for this study: effect of CPAP on the deterioration of renal function in early stages of chronic kidney disease. 195/2015
- Rolando Studio. Processing, conservation and shipment of samples for translational study within the framework of the ROLANDO trial: Multicenter and uncontrolled phase II clinical trial to evaluate the safety and efficacy of the combination of Olaparib and Pegylated Liposomal Doxorubicin (DLP) in patients with peritoneal carcinoma Primary ovarian and resistant platinum fallopian tubes. GEICO-1601 ROLANDO
- Custody of samples for the OPTIMBIOMA study. Optimization of antibiotic treatment in hematopoietic allotransplant recipients: impact on intestinal microbiota and clinical outcomes. PI16/02010

Transfer of samples

Project	Ref./Agency	Principal Researcher /Institution	Samples
BBI_03/2016; <i>Enfermedad mínima residual en cánceres colorrectales de alto riesgo resecaados. Valor de las biopsias líquidas en el seguimiento y análisis de la heterogeneidad tumoral</i>	PI15/02180, <i>Instituto de Salud Carlos III</i>	Andrés Cervantes, HCUV/ INCLIVA	Gastrointestinal tumors: plasma and tissue. 659 aliquots
BBI_13/2016. <i>Biomarcadores de respuesta a los inhibidores de tirosina quinasa mediante fenotipado metabólico de biopsias líquidas de pacientes con adenocarcinoma pulmonar con mutaciones</i>	IIS La Fe 2015/0345	Óscar Juan Vidal, Biomarkers & Precision Medicine Unit, <i>Hospital Universitario y Politécnico La Fe</i>	Collections of peripheral blood and derivative products in patients suffering from lung cancer: serum 79 aliquots

<p>BBI_05/2017.</p> <p><i>Biomarcadores de respuesta a los inhibidores de tirosina quinasa mediante fenotipado metabólico de biopsias líquidas de pacientes con adenocarcinoma pulmonar con mutaciones</i></p>	<p>IIS La Fe 2015/0345</p>	<p>Óscar Juan Vidal, Biomarkers & Precision Medicine Unit, <i>Hospital Universitario y Politécnico La Fe</i></p>	<p>Collections of peripheral blood and derivative products in patients suffering from lung cancer: 252 slides FFPE</p>
<p>BBI_09/2017.</p> <p><i>Diagnóstico y estratificación de pacientes de lupus eritematoso sistémico mediante espectrometría de masas dirigida a la detección de histonas circulantes</i></p>	<p>Programa VLC-BIOCLINIC 2017</p>	<p>Carlos Romá, <i>Universidad de Valencia</i></p>	<p>Systemic Lupus Erythematosus or other autoimmune diseases : plasma;</p> <p>Standar population: plasma</p> <p>22 aliquots</p>
<p>BBI_01/2018.</p> <p><i>Estudio de polimorfismos en pacientes con cáncer de mama que reciben esquemas con docetaxel como predictores de respuesta y toxicidad</i></p>	<p>INCLIVA</p>	<p>Begoña Bermejo, HCUV/INCLIVA</p>	<p>Collection of peripheral blood and derivative products in patients suffering from breast cancer:</p> <p>DNA</p> <p>48 aliquots</p>
<p>BBI_02/2018. (adenda BBI_06/2017)</p> <p>Epigenética e inmunosupresión. Uso de las histonas circulantes y sus modificaciones posttraduccionales como biomarcadores de diagnóstico y pronóstico en sepsis y shock séptico</p>	<p>PI16/01036 <i>Ministerio de Economía y Competitividad</i></p>	<p>José Luis García Giménez, CIBERER - <i>Universidad de Valencia</i></p>	<p>Collection sepsis gravis and septic shock: DNA</p> <p>19 aliquots</p>
<p>BBI_03/2018.</p> <p><i>Metabolomics based detction of early stage cancers with an upgrade to other technologies</i></p>	<p>Universal Diagnostics SL (UDX) UDXP001-G</p>	<p>Kristi Kruusmaa, Universal Diagnostics SL (UDX)</p>	<p>Collection of solid tumors:</p> <p>OCT tissues.</p> <p>Collection of peripheral blood and derivative products in patients suffering from gastrointestinal: plasma</p> <p>136 aliquots</p>

BBI_04/2018. <i>Estudio del efecto de la hemólisis en el perfil de miARNs en el plasma sanguíneo</i>	Epidisease SL (spin-off INCLIVA)	Jose Luis García Giménez, CIBER- Epidisease SL (spin-off de INCLIVA)	Standar population: plasma 18 aliquots
BBI_05/2018. <i>Exploring mechanisms of resistance in adult and pediatric T-cell acute lymphoblastic leukemia</i>	GC16173697BIGA	Josep María Ribera, (<i>Hospital Germans Trias i Pujol</i>), Eulàlia Genescà (<i>Fundación Josep Carreras</i>)	Samples from the Hematology service. Acute lymphoblastic leukemia (LMA, LLA, LPA): DNA and RNA. 22 aliquots
BBI_06/2018. Posible asociación de hongos con el cáncer de próstata	BOLCSISP00085 FISABIO	Álex Mira Obrador, <i>Fundación FISABIO</i>	Collection of solid tumors: prostate cancer . Frozen prostate tissue. 28 aliquots
BBI_07/2018. Detection of epidermal growth factor receptor (EGFR) T790M mutation by ultrasensitive PCR assay before treatment with tyrosine-kinase inhibitors (TKI) and assessment of the role of T790M mutation to predict resistance mechanism at progression in stage IV non-small cell lung cancer (NSCLC) patients	2016/0129 ESR16 11899	Óscar Juan Vidal, Biomarkers & Precision Medicine Unit, <i>Hospital Universitario y Politécnico La Fe</i>	gDNA FFPE tissue from lung cancer patients. 53 aliquots
BBI_08/2018. (adenda II BBI_06/2017) <i>Epigenética e inmunosupresión. Uso de las histonas circulantes y sus modificaciones posttraduccionales como biomarcadores de diagnóstico y pronóstico en sepsis y shock séptico</i>	PI16/01036 <i>Ministerio de Economía y Competitividad</i>	Jose Luis García Giménez, CIBERER- <i>Universidad de Valencia</i>	Collection sepsis gravis and septic shock: PBMCs. Standar population: PBMCs. 14 aliquots
BBI_09/2018. <i>Genomic and epigenomic biomarkers of response to nivolumab in non-small cell lung cancer</i>	2016/0372 CA-209-684	Óscar Juan Vidal, Biomarkers & Precision Medicine Unit, <i>Hospital Universitario y Politécnico La Fe</i>	Paraffin-embedding (FFPE) lung tumor tissue 77 aliquots

BBI_10/2018. <i>Kit multiplex para la detección simultánea de biomarcadores de diagnóstico y pronóstico de sepsis y shock séptico por espectrometría de masas</i>	DTS17/00132 Ministerio de Economía y Competitividad	Federico Pallardó Calatayud, Universidad de Valencia	Collection sepsis gravis and septic shock: plasma and urine. 33 aliquots
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In summary, 1460 aliquots have been provided in 2018 to respond to these sample requests.

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PT17/0005/0017

Title: *Biobank Platform*

Principal Investigator: Josep Redón i Mas

Funding body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total budget: 104.775€

• PUBLICATIONS

2018 scientific articles derived from the use of samples or services provided by the biobank:

Original articles

1. Sánchez-Sendra B, Martínez-Ciarpaglini C, González-Muñoz JF, Murgui A, Terrádez L, Monteagudo C. Downregulation

of intratumoral expression of miR-205, miR-200c and miR-125b in primary human cutaneous melanomas predicts shorter survival. *Scientific Reports*. 2018; 8(1): 17076. IF: 4,122

2. Pero-Gascon R, Sanz-Nebot V, Berezovski MV, Benavente F. Analysis of Circulating microRNAs and Their Post-Transcriptional Modifications in Cancer Serum by On-Line Solid-Phase Extraction–Capillary Electrophoresis–Mass Spectrometry. *Analytical Chemistry*. 2018; 90(11): 6618 - 6625. IF: 6,042
3. García-Giménez JL, Rubio-Belmar PA, Peiró-Chova L, Hervás D, González-Rodríguez D, Ibañez-Cabellos JS, Bas T. Circulating miRNAs as diagnostic biomarkers for adolescent idiopathic scoliosis. *Scientific Report*. 2018; 8(1): 2646. IF: 4,122
4. Seco-Cervera M, González-Rodríguez D, Ibañez-Cabellos JS, Peiró-Chova L, Pallardó FV, García-Giménez JL. Small RNA-seq analysis of circulating miRNAs to identify phenotypic variability in Friedreich's ataxia patients. *Scientific Data*. 2018; 5: 180021. IF: 5,305

4.5.2 Oncology Phase I Oncology Clinical Trials Unit

Team

Principal investigator

Andres Cervantes Ruipérez. Hospital. University

Medical doctors

Jose A. Pérez Fidalgo. Hospital

Susana Roselló Keranen. Hospital

Cristina Herrando Meliá. Hospital

Marisol Huerta Álvaro. Hospital

Gema Bruixola Campos. Hospital

Desamparados Roda Pérez. Hospital

Valentina Gambardella. Hospital

Nurses

Inma Blasco Blasco. INCLIVA

Celia Martínez Ridaura. INCLIVA

Luna Porta Campos. INCLIVA

Data Managers

Julia Peláez Sánchez. INCLIVA

Ana Vercher Grau. INCLIVA

Administrative assistant

Enrique Castelló Moreno. INCLIVA

INCLIVA is the only hospital in Valencia performing Phase I cancer clinical trials, and one of the few in Spain. Phase I trials are those in which a substance or product is tested in humans for the first time.

INCLIVA is conducting, through the Oncology and Hematology Department, 158 clinical trials, 86 of them related to treatment in the early stages of testing (33 phase I or “first in human” and 53 phase II). INCLIVA’s new facilities provide a full floor and a half specifically dedicated to host the unit.

The unit aims to develop and select new drugs through clinical trials and to perform studies related to the pathogenesis, prognosis and new experimental therapies in solid tumors.

FUNCTIONS:

The unit implements early clinical trials with experimental agents in the field of Oncology.

EQUIPMENTS:

- -80° C Freezer
- -20° C Freezer
- Refrigerated desktop centrifuge
- Scientific refrigerator
- Conventional fridge
- Defibrillator
- Electrocardiographic equipment
- 7 monitors (blood pressure, heart rate and O2 saturation)
- 7 double medication infusion pumps
- 7 heads gases (oxygen and vacuum)

LOCATION:

The following facilities are located on the second floor:

- Reception and waiting room
- 2 Consulting rooms
- Staff room
- Meeting room
- Therapy room

The third floor hosts the following facilities

- Clinical trials office
- Monitoring room
- Clinical trials archives

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PT17/0017/0003

Title: *Clinical Research and Trials Platform*

Principal Investigator: Andrés Cervantes Ruipérez

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2017-2020

Total budget: 266.475€

4.5.3. Innovation Platform ITEMAS

Team

Principal investigator

Josep Redón i Mas. Hospital. University

Collaborating researchers:

Pedro Fernández Nohales. INCLIVA

Rafael Barajas Cenobio. INCLIVA

Justo Giner García. INCLIVA

Indicators in 2018	
National collaborations managed by the UAI that have been formalized through agreements	10
International collaborations managed by the UAI that have been formalized through agreements	2
Training activities, for IIS personnel, aimed at increasing competencies for the effective transfer of research results to healthcare practice	4
External diffusion events	12
Actions with companies to promote the innovation portfolio of the IIS	108
Projects requested to competitive national calls for innovation / knowledge transfer	12
Projects awarded through competitive external calls for innovation / knowledge transfer	8 (440.000€)
Projects financed by internal innovation calls	3 (12.000€)

• RESEARCH PROJECTS AND GRANTS FOR RESEARCH

Reference: PT17/0005/0017

Title: *Innovation Platform ITEMAS-ISCI*

Principal Investigator: Josep Redón i Mas

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total Budget: 104.775€

Reference: GIS17/00014

Title: *Contract for management of research*

Principal Investigator: Pedro Fernández Nohales

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020

Total Budget: 80.598€

Title: *Banco de Patentes GVA*

Principal Investigator: Andrés Cervantes Ruipérez

Funding Body: *Generalitat Valenciana*

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

Duration: 2018

Total Budget: 10.000€

Reference: INNACC00/18/001

Title: *Complementary actions to foster innovation*

Principal Investigator: Andrés Cervantes Ruipérez

Funding Body: *Agencia Valenciana de la Innovación*

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

Duration: 2018

Total Budget: 9.299,98€

4.5.4. Spanish Clinical Research Network (SCReN), Clinical Research and Clinical Trials of the Clinical Trials Platform (UICEC INCLIVA)

Team

Principal investigator

Andrés Cervantes Ruipérez. Hospital. University

Associated Members

Julio Núñez Villota. Hospital. INCLIVA

Marta Peiró Signes. INCLIVA

María Carmen Román. INCLIVA

Dolores Iglesias Ferri. INCLIVA

Inmaculada Blasco Blasco. INCLIVA

Hired Members

Ana Portolés Monzón. INCLIVA

Mireia Hernández Hernández. INCLIVA

Laura Silla Mira. INCLIVA

Bernat Navarro Aguir. INCLIVA

Mercedes Peris Costa. INCLIVA

UICEC participates in all activities related with the correct development of observational studies and clinical trials, in accordance with the applicable legal regulations and the standards of good clinical practice.

Currently, the portfolio of services includes, among others, the following activities:

1. Methodological and regulatory advice: collaboration tasks in the drafting of the protocol, CRF, Patient Information Sheet and Informed Consent and all documentation necessary for the correct development of the study in accordance with applicable regulations.
2. Start-up activities: in this phase the unit collaborate with of economic viability evaluation; identification and selection of participating sites; submission to national and local authorities and Ethics Committee); contract management with the participating sites; monitoring plan; master file creation.
3. Development activities: project management activities, notifications; processing of amendments and reports; home visits; maintenance of file and monitoring visits.
4. Completion and closure activities: closing visits; resolution of queries, elaboration of final reports.

ACTIVITIES DEVELOPED

During 2018, UICEC had collaborated with the development of the following clinical trials and observational studies:

• CLINICAL TRIALS

Study: ESR-17-13447(DAPA-HF)

Title: *Short-term effects of Dapagliflozin on Peak VO2 in patients with heart failure with reduced ejection fraction and type 2 diabetes*

EUCTRACT: 2018-002614-12

Sponsor: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Phase: IV

Study: BBLOQ-2017

EUCTRACT: 2017-005077-39

Title: *Betablockers withdrawal in patients with heart failure with preserved ejection fraction and chronotropic incompetence: effect on functional capacity and life quality*

Sponsor: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Phase: IV

Study: ADAMPA

Title: *Impact of self-measurement of blood pressure and self-adjustment of antihypertensive medication in the control of hypertension and adherence to treatment. A pragmatic, randomized, controlled clinical trial (ADAMPA Study)*

EUCTRACT: 2016-003986-25

Sponsor: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Phase: Low intervention clinical trial

Study: X16082

Title: Phase Ib/II trial to evaluate safety and efficacy of oral ixazomib in combination with sirolimus and tacrolimus in the prophylaxis of chronic graft-versus-host disease

EUCRACT: 2016-002503-26

Sponsor: Fundación Pública Andaluza para la Gestión en Salud de Sevilla (FISEVI)

Phase: Ib/II

Study: CECUM

Title: Efficacy of high-dose corticosteroid pulses added to conventional oral corticosteroid course in comparison with monotherapy oral corticosteroid course for moderate flares of ulcerative colitis: a randomized multicentre clinical trial

EUCRACT: 2016-001170-15

Sponsor: Grupo Español de Trabajo en Enfermedad de Crohn y Colitis ulcerosa (GETECCU)

Phase: IV

Study: MYOCARDIAL-IRON

Title: Changes in myocardial iron content following administration of intravenous iron

EUCRACT: 2016-004194-40

Sponsor: Fundación Investigación Hospital Clínico Universitario de Valencia

Phase: IV

Study: SECURE

Title: Secondary prevention of cardiovascular disease in the elderly

EUCRACT: 2015-002868-17

Sponsor: Fundación Centro Nacional de Investigaciones Cardiovasculares, Instituto de Salud Carlos III (CNIC)

Phase: III

Study: EXIT

Title: Suspension of anti-tnf treatment in patients with intestinal inflammatory disease: multicenter, prospective and randomized clinical trial

EUCRACT: 2015-001410-10

Sponsor: Fundación de Investigación Biomédica Hospital Universitario de la Princesa

Phase: IV

Study: Forest

Title: Randomized, multicenter, open, controlled clinical trial,

in phase III, to evaluate the efficacy of phosphomycin vs meropenem or ceftriaxone in the directed treatment of bacteremic urinary infection by multiresistant Escheriquia Coli

EUCRACT: 2013-002922-21

Sponsor: Fundación Pública Andaluza para la Gestión en Salud de Sevilla (FISEVI)

Phase: III

Study: STARMEN01-2013

Title: Sequential therapy with tacrolimus and rituximab in primary membranous nephropathy (STARMEN STUDY): European Multicentre and Open-Label Controlled Randomized Trial to evaluate the Efficacy of Sequential Treatment with Tacrolimus-Rituximab versus Steroids plus Cyclophosphamide in patients with Primary Membranous Nephropathy

EUCRACT: 2013-000226-55

Sponsor: Fundación para la Investigación Biomédica Hospital 12 de Octubre

Phase: III

Study: CSAI

Title: Randomized, masked, placebo-controlled study the effects of intralesional Adalimumab in intestinal stenosis of patients with Crohn's Disease (CSAI Study)

EUCRACT: 2012-001723-12

Sponsor: Fundació Clínic per a la Recerca Biomèdica

Phase: III

Study: RAPIDO

Title: Randomized Multicentre Phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in primary high risk rectal cancer compared to standard chemoradiotherapy and surgery and optional adjuvant chemotherapy

EUCRACT: 2010-023957-12

Sponsor: UMCG, Groningen, The Netherlands

Phase: III

Study: IGR2009/1593

Title: Intergroup trial for children or adolescents with B-cell NHL or B-AL: evaluation of rituximab efficacy and safety in high risk patients

EUCRACT: 2010-019224-31

Sponsor: Institut Gustave Roussy

Phase: II/III

Study: Lines

Title: *European Low and Intermediate Risk Neuroblastoma*

EUCRACT: 2010-021396-81

Sponsor: *Fundación para la Investigación Hospital Universitario y Politécnico La Fe*

Phase: III

Study: SCOT Study

Title: *Short course oncology therapy – a study of adjuvant chemotherapy in colorectal cancer*

EUCRACT: 2007-003957-10

Sponsor: *Greater Glasgow Health Board/University of Glasgow (GU)*

Phase: III

Study: CETUPANC

Title: *Impact of the dissemination of the circulating tumor cells (CTCS) during the cephal duopenopancreatotomy at the appearance of metastasis and survival in patients with tumors of pancreas and periampulars (CETUPANC Study)*

Sponsor: *Fundación Pública Andaluza para la Gestión en Salud de Sevilla (FISEVI)*

Phase: Intervention clinical trial

Study: MOSCA FRAIL

Title: *Randomized comparison between the invasive and conservative strategies in elderly frail patients with non-ST elevation myocardial infarction: The MOSCA-FRAIL Clinical Trial*

Sponsor: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Phase: Intervention clinical trial

Study: DUOPAM-EPAM

Title: *Duodenopancreatotomy in pancreatic and periampular tumors: initial approach of the superior mesenteric artery versus classic approach. Prospective, randomized, multicenter study*

Sponsor: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Phase: Intervention clinical trial

• **OBSERVATIONAL STUDIES**

Study: DNO-IBR-2018-01

Title: *Virology and immunology of cytomegalovirus (CMV) in-*

fection in patients with hematological malignancies in the time of new biotherapies

Sponsor: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Phase: EPA-AS

Study: TMK-RAM-2018-01

Title: *Macrophages associated with tumor, tumor angiogenesis and resistance to therapies in diffuse gastric cancer mesenchymal phenotype*

Sponsor: *Tania Fleitas Kanonnikoff*

Phase: EPA-AS

Study: FIS-BAZ-2012-01

Title: *Action of bazedoxifen about bone metabolism and the risk factors cardiovascular*

Sponsor: *Antonio Cano Sánchez*

Phase: EPA-SP

Study: JSC-TAB-2015-01

Title: *Effectiveness of an intensive smoking treatment program on the serious exacerbations of smoking patients with moderate-severe EPOC*

Sponsor: *Jaime Signes Costa*

Phase: EPA-SP

Study: INC-ACO-2013-01

Title: *Prospective observational study of the perioperative management of direct oral anticoagulants (DOAC)*

Sponsor: *Fundación Investigación Hospital Clínico Universitario de Valencia*

Phase: EPA-AS

• **PUBLICATIONS**

1. Iveson TJ, Kerr RS, Saunders MP, Cassidy J, Hollander NH, Tabernero J, Haydon A, Glimelius B, Harkin A, Allan K, McQueen J, Scudder C, Boyd KA, Briggs A, Waterston A, Medley L, Wilson C, Ellis R, Essapen S, Dhadda AS, Harrison M, Falk S, Raouf S, Rees C, Olesen RK, Propper D, Bridgewater J, Azzabi A, Farrugia D, Webb A, Cunningham D, Hickish T, Weaver A, Gollins S, Wasan HS, Paul J. 3 versus 6 months of adjuvant oxaliplatin-fluoropyrimidine combination therapy for colorectal cancer (SCOT): an international, randomised, phase 3, non-inferiority trial. *Lancet Oncology*. 2018; 19(4): 562 - 578. IF: 36,418

2. Miñana G, Cardells I, Palau P, Llàcer P, Fàcila L, Almenar L, López-Lereu MP, Monmeneu JV, Amiguet M, González J, Serrano A, Montagud V, López-Vilella R, Valero E, García-Blas S, Bodí V, de la Espriella-Juan R, Sanchis J, Chorro FJ, Bayés-Genís A, Núñez J, Myocardial-IRON Investigators. Changes in myocardial iron content following administration of intravenous iron (Myocardial-IRON): Study design. *Clinical Cardiology*. 2018; 41(6): 729 - 735. IF: 2,733
3. Sanfèlix-Genovés J, Rodríguez-Bernal CL, Marco-Moreno I, Martínez-Ibáñez P, Martínez-Ibáñez L, Bóveda-García M, Barreira-Franch I, Calleja-Del Ser M, Borrás-Moreno G, Avelino-Hidalgo E, Escrig-Veses M, Lauriano M, Giménez-Loreiro M, Bellot-Pujalte L, García-Sempere A, Peiró S, Sanfèlix-Gimeno G, ADAMPA group. Rationale and design of a pragmatic clinical trial to assess the impact of self-monitoring blood pressure at home and self-titration of antihypertensive medication in poorly controlled hypertension: the ADAMPA study protocol. *BMC Family Practice*. 2018; 19(1): 160. IF: 2,032
4. Sabater L, Muñoz E, Roselló S, Dorcaratto D, Garcés-Albira M, Huerta M, Roda D, Gómez-Mateo MC, Ferrández-Izquierdo A, Darder A, Cervantes A. Borderline resectable pancreatic cancer. Challenges and controversies. *Cancer Treatments Reviews*. 2018; 68: 124-135. IF: 8,122

- **RESEARCH PROJECTS AND GRANTS FOR RESEARCH**

Reference: PT17/0017/0003

Title: *Spanish Clinical Research Network (SCReN)*

Principal Investigator: Andrés Cervantes Rui Pérez

Funding Body: *Instituto de Salud Carlos III*

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

Duration: 2018-2020





Clinical trials and other studies

05



5.1. Clinical Research Ethics Committee (ECCR) Activity

Ethics Committee for investigation with medicinal products are an independent board with a multidisciplinary composition whose main purpose is to oversee the protection of the rights, safety and well-being of subjects participating in clinical studies and biomedical research projects.

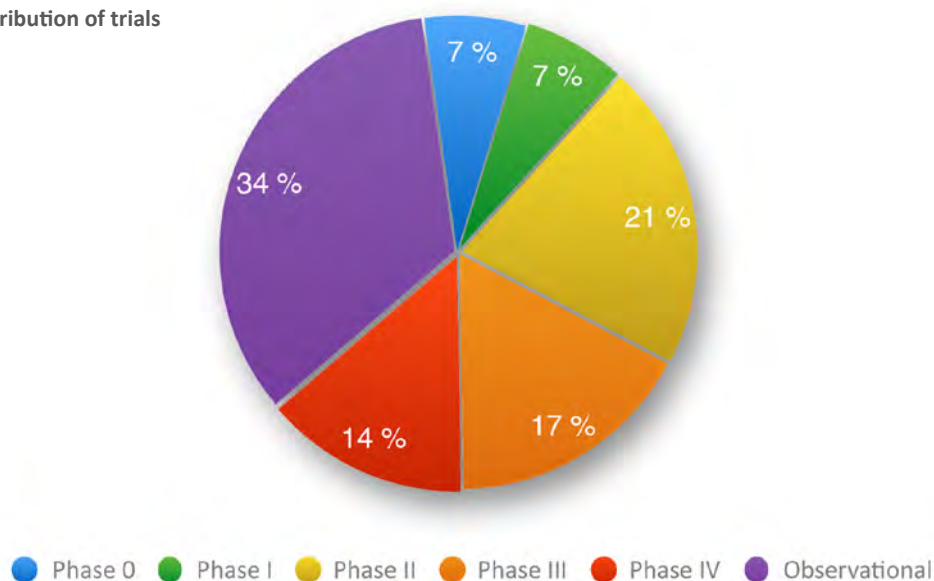
On January 2018, ended the period that the Clinical Research Ethical Committees (ECCR) had to be accredited as CEIm. On January 30th, 2018, the CEIm of the *Hospital Clínico Universitario de Valencia* received the accreditation by the General Department of Pharmacy and Medical Devices of *Conselleria de Sanitat i Salut Pública*.

As a result of its activity along 2018, the CEIm has processed a total of 29 studies (clinical trials and observational studies): 21 positively valued and 8 are pending of approval.

The following table shows the number of clinical trials and other studies according to their typology.

Types of clinical study	Number
Observational Studies	10
PHASE 0	2
PHASE I	2
PHASE II	6
PHASE III	5
PHASE IV	4
TOTAL	29

Distribution of trials



Distribution of clinical studies depending on the department where they are performed is as follows:

SERVICE	Number
Anesthesia and Reanimation	4
Cardiology	2
Digestive Medicine	2
Gynaecology	1
Haematology	1
Internal Medicine	2
Nephrology	1
Neurology	1
Oncology	8
Paediatrics	1
Primary Care	1
Respiratory Diseases	1
Tutelage	4
TOTAL	29

5.2. Clinical research activity performed by Valencia Clínico-Malvarrosa Health Department

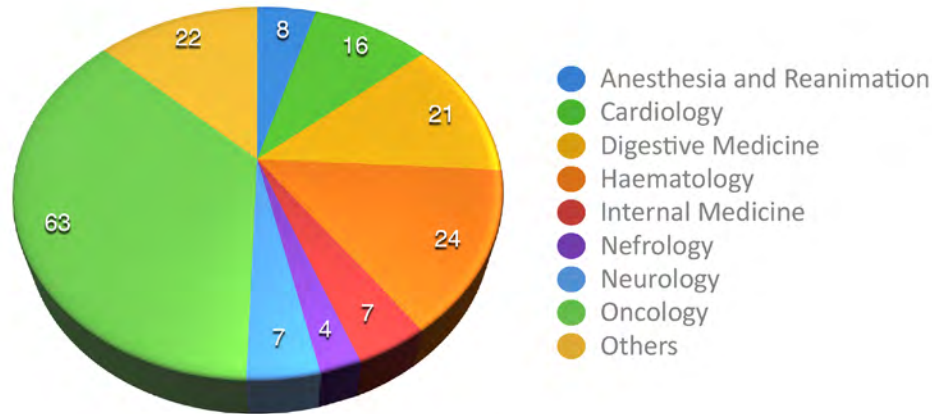
5.2.1. Activity during 2018

INCLIVA Health Research Institute manages the clinical studies (trials, observational studies, and research projects) carried out by the *Hospital Clínico Universitario de Valencia* and the Valencia Clínico-Malvarrosa Health Department researchers.

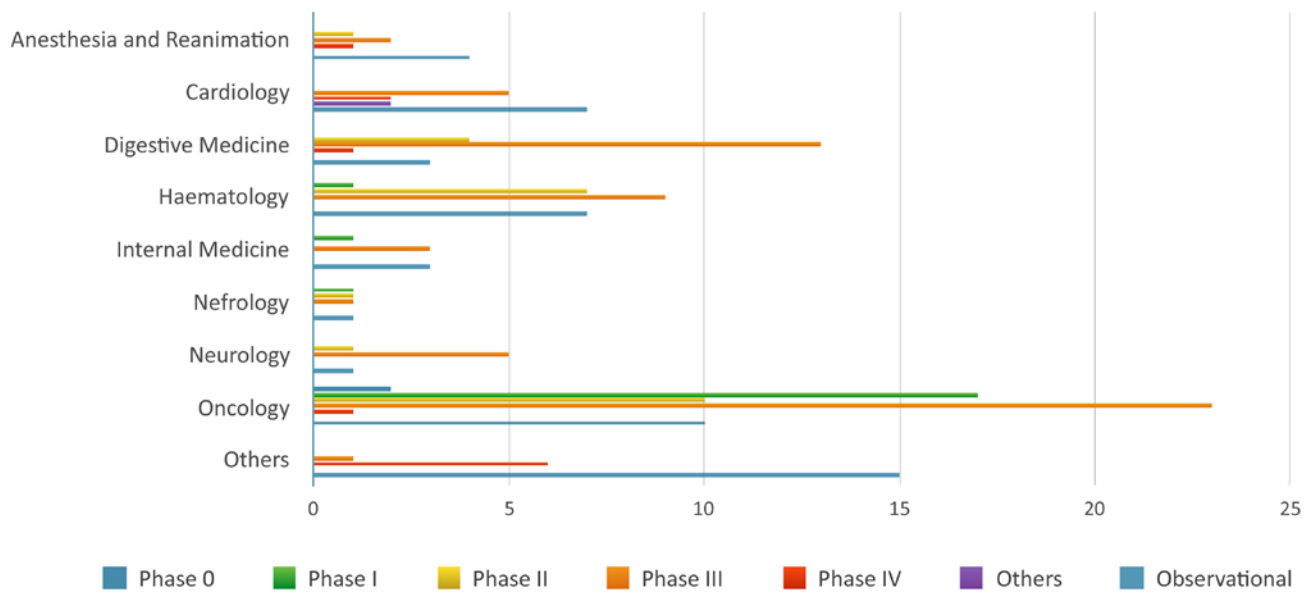
As a result of its activity along 2018, the INCLIVA has managed a total of 172 studies (clinical trials and observational studies).

The distribution of these trials by phase is: Phase 0:2, Phase I: 20, Phase II: 25, Phase III: 67, Phase IV: 5, Observational studies: 51, others: 2. The following table shows the number of clinical trials and other studies according to their phase and department.

	Phase 0	Phase I	Phase II	Phase III	Phase IV	Others	Observational	TOTAL
Anesthesia and Reanimation	-	-	1	2	1	-	4	8
Cardiology	-	-	-	5	2	2	7	16
Digestive Medicine	-	-	4	13	1	-	3	21
Haematology	-	1	7	9	-	-	7	24
Internal Medicine	-	1	-	3	-	-	3	7
Nephrology	-	1	1	1	-	-	1	4
Neurology	-	-	1	5	-	-	1	7
Oncology	2	17	10	23	1	-	10	63
Others	-	-	1	6	-	-	15	22
TOTAL	2	20	25	67	5	2	51	172



The Department of Medical Oncology leads the number of trials assted to INCLIVA. It is followed by the departments of Haematology, Digestive Medicine and Cardiology. These four services make over 70 % of the total processed trials.

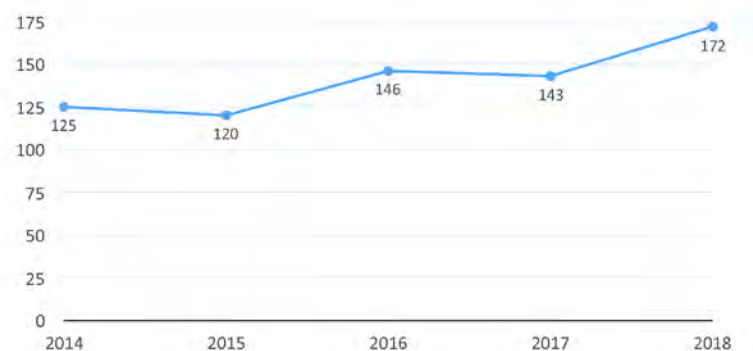


Regarding the distribution of studies per promoter, 49 trials are considered Independent Clinical Research (trials from associations, groups, foundations, and private individuals), 8 of which have been promoted by researchers from the *Hospital Clínico Universitario de Valencia* and INCLIVA and the rest of them have been promoted by the pharmaceutical industry.

PROMOTOR	Nº
HOSPITAL CLÍNICO UNIVERSITARIO DE VALENCIA RESEARCHERS AND INCLIVA	8
INDEPENDENT CLINICAL RESEARCH	41
COMERCIAL RESEARCH	123

5.2.2 Assessment activity during last 5 years

The table below shows that the number of studies processed yearly remains close to a hundred.

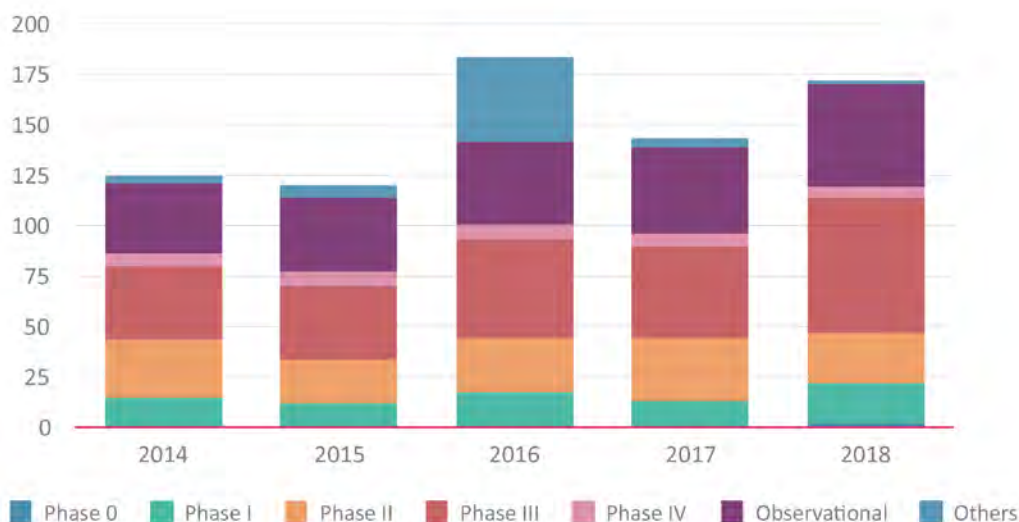


Year	Processed studies
2014	125
2015	120
2016	146
2017	143
2018	172

One of INCLIVA's main goals is to develop clinical research at its early stages, thus contributing to translational research that moves scientific knowledge from bench to bedside. With this regard, during the period 2014-2018, Phase I and Phase II trials are prioritized and its number remains stable as shown in the table and graph below.

PHASE	2014	2015	2016	2017	2018
Phase 0	-	-	-	-	2
Phase I	14	12	17	13	20
Phase II	29	21	27	31	25
Phase III	37	37	49	46	67
Phase IV	6	7	7	6	5
Observational	35	37	42	43	51
Others	4	6	4	4	2

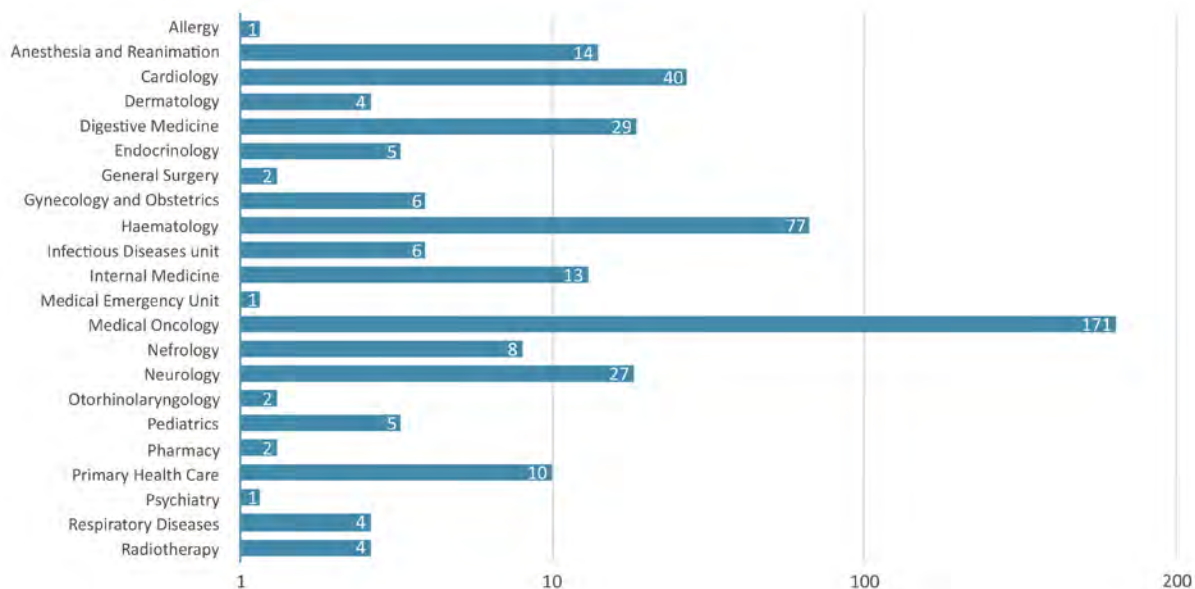
Evolution of clinical trial distribution by phase



5.2.3. Ongoing studies

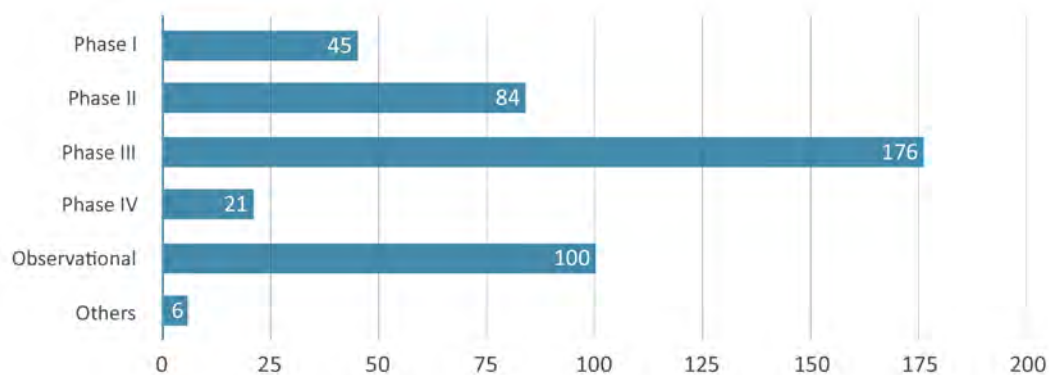
During 2018, 432 studies have been active. The distribution of clinical trials per department analyzed below uses a semilogarithmic scale due to the great difference between the Department of Medical Oncology and the rest of the Departments.

Allergy	1
Anesthesia and Reanimation	14
Cardiology	40
Dermatology	4
Digestive Medicine	29
Endocrinology	5
General Surgery	2
Gynecology and Obstetrics	6
Haematology	77
Infectious Diseases unit	6
Internal Medicine	13
Medical Emergency Unit	1
Medical Oncology	171
Nefrology	8
Neurology	27
Otorhinolaryngology	2
Pediatrics	5
Pharmacy	2
Primary Health Care	10
Psychiatry	1
Respiratory Diseases	4
Radiotherapy	4
TOTAL	432



The distribution of ongoing trials and other studies according to typology is as follows:

Phase I	45
Phase II	84
Phase III	176
Phase IV	21
Observational	100
Other	6

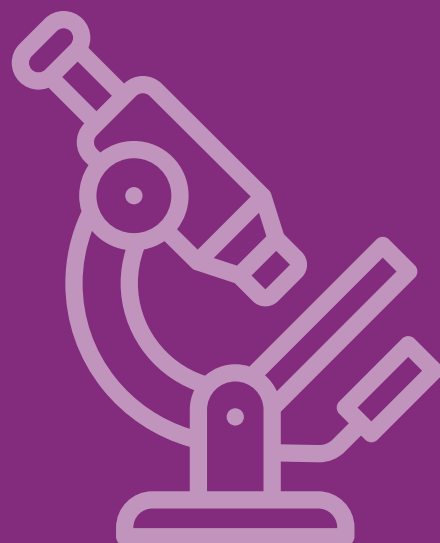






Initiatives for research promotion

06



6.1. Grants for secondments in centers of excellence

To allow researchers to acquire new knowledge for clinical and research techniques, INCLIVA promotes every year its Grants for research secondments in centers of excellence.

Since the establishment of this scholarship program, over 115 professionals have visited national and foreign centers. In 2018 the average number of awards was 15, 10 of them to international centers and 5 to national ones.

The awarded researchers and the assigned training centers in 2018 are shown in the following table:

Adam Artigues, Anna Icahn School of Medicine at Mount Sinai, United States	Hueso Soler, Luisa María Karolinska Institutet, Sweden
Ballester Ferré, María Pilar University of Pittsburgh Medical Center, United States	Martínez Castro, Sara Sant Joan de Déu Barcelona, Spain
Díaz Bóveda, Rosalía Hospital de Basurto, Bilbao, Spain	Muñoz Hidalgo, Lisandra Instituto de Recerca Vall D'Hebrón, Spain
Dudenko Lozenko, Darya St. George's Hospital/Clinica IVI, United Kingdom	Piñana Plaza, Carlos Hospital Clinic de Barcelona, Spain
Giménez Quiles, Estela Berenice Lausanne University Hospital, Switzerland	Trapero Gimeno, Isabel Centre of Molecular Medicine, Karolinska Institutet, Sweden
Gimeno Valiente, Francisco Gastrointestinal Cancer Biology and Genomics Institute Cancer Research, United Kingdom	Serrano Alcalá, Alicia Institute of Applied Biosciences, Thessaloniki, Greece
Gómez Cabrera, M ^a Carmen National Institute of Aging, United States	Garcés Albir, Marina Azienda Ospedaliero-Universitaria Pisana, Italy
González D'Gregorio, Jessika Hospital General Universitario Gregorio Marañón, Spain	

6.2 Training and Teaching Activities

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

The number of internal secondments in 2018 was 8 which represent an aggregate of 25,5 months of training during the period. A total of 15 stays outside of INCLIVA were carried out by researchers.

The Institute has kept on developing, along the year, its annual training program. The courses, seminars and educational conferences that have been developed during the year 2018 are the following:

Courses (17)

- *Curso IV Workshop Internacional de Ecografía y Resonancia Anorrectal*
- *Curso de anatomía quirúrgica aplicada: Accesos vasculares periféricos*
- *Curso de anatomía quirúrgica aplicada: Aorta integral*
- *Curso de Vaciamiento Axilar y primeros pasos en Oncoplastia de Mama*
- *Curso de anatomía quirúrgica aplicada hepato-bilio-pancreática. 7ª Edición.*
- *Workshops Thyroidectomies for Benign Cases (2 editions)*
- *Advanced course Thoracic surgery: Vats technique Procedure*
- *12th Hands-on Course on Neurosurgical Approaches: endoscopy and microsurgery in the ventricular system and skull base*
- *Advanced course in Hernia surgery: TEP, TAPP & IPOM*
- *V Workshop Cirugía Laparoscópica Colorrectal Avanzada*
- *II Curso de Autorización e Inspección de Actividades de Tejidos y Células*
- *IV Curso Avanzado de Educación Terapéutica en Diabetes*
- *Curso catéter venoso central inserción periférica PICC*
- *Curso de formación Semana de la Resincronización*
- *Fundamental Critical Care Support Course*
- *Curso de Patología Infecciosa*

INCLIVA Seminars (2)

- *Seminario OncoINCLIVA: Cáncer de páncreas e inflamación: "of mice and men"*
- *Seminario INCLIVA - Dr. Ignacio Hernández Medrano*

Workshops (19)

- *III Jornada Científica de Residentes del Hospital Clínico Universitario de Valencia*
- *First Spanish Meeting on Oligonucleotide Therapeutics (SMOT1)*
- *I Jornada de Investigación Clínica Traslacional post-ESMO 2018*
- *III Jornada de investigación en prediabetes, diabetes y enfermedad cardiovascular*
- *Jornada jóvenes investigadores en enfermedades raras*
- *Jornada de Valoración Funcional pacientes hematológicos de edad avanzada*
- *10ª Jornada Valenciana "Tabaquismo y Respiración": Tabaquismo y Enfermedades Infecciosas*
- *Avances en el tratamiento activo y de soporte en neoplasias hematológicas*
- *7ª Jornada de Actualización en Vacunas Hospital Malvarrosa*
- *I Reunión sobre enfermedades hereditarias renales*
- *Jornada sobre vasculopatía periférica en el paciente diabético. Actualización para residentes.*
- *I Jornadas anatomo-clínicas en Síndromes Linfoproliferativos*
- *Jornada sobre Vasculopatía Periférica en el paciente diabético.*
- *Actualización para residentes*
- *Manejo del paciente con diabetes y dislipemia*
- *I Jornadas de Actualización en Obstetricia*
- *Jornada cirugía de cadera*
- *Jornada "¿Cómo prevenimos las Lesiones relacionadas con la dependencia?"*
- *La investigación sanitaria con perspectiva de género*
- *Jornada "Sanitat i investigació: el futur és dona"*

Other activities in which INCLIVA participates (8)

- *Foro de debate en enfermedades infecciosas*
- *VII Reunión formativa en Diálisis Peritoneal para residentes de nefrología "Acercándonos a la Diálisis Peritoneal"*
- *Formación Clínica Especializada en la Unidad de Neuroinmunología y Esclerosis Múltiple de Hospital Clínico Universitario de Valencia*
- *Programa Docente Unidad de Insuficiencia Cardíaca*
- *Formación en Cirugía Bariátrica Laparoscópica (Fase 4 y 5 SECO)*
- *Programa formativo "Lymphoproliferative Diseases and Hematopoietic Progenitor Cell"*
- *Transplantation specialized program of Clinical Excellence*
- *I Congreso sobre actualización en Trastorno Mental Grave: Una visión multidisciplinar*



Communication

07



7.1. Highlights

January

- A study by Dr. María Téllez suggests that the reduction in environmental exposure to lead and cadmium over recent decades has helped reduce cardiovascular mortality by up to 30%.
- INCLIVA anaesthesia research group participates in an international multicentre trial comparing the results of two different care strategies for patients with acute respiratory distress syndrome.

February

- Dr. Alejandro Pérez-Fidalgo coordinates a new clinical trial to halt ovarian cancer.
- INCLIVA and AINIA research genistein as a functional food for Alzheimer's prevention.

March

- INCLIVA and Asociación NEN sign a collaborative agreement to combat neuroblastoma.
- The INCLIVA Anesthesia Research Group participate in a multicentre observational study in which the surgical Check-List is shown to reduce surgery-associated deaths and complications.

April

- INCLIVA takes part in the Big Data BigMedilytics European project to improve healthcare.
- Cecilia Martínez Costa, coordinator of INCLIVA's Paediatric Nutrition Research Group has helped draw up new World Health Organization (WHO) guidelines addressing excess overweight and obesity in young children.

May

- INCLIVA researchers demonstrate that changes in urinary levels of the enzyme Sirtuina-1 are associated with disease activity in lupus nephritis.
- Inauguration of the Breccanrisk project, a stratification method to classify women by breast cancer risk, developed by ASCIRES and INCLIVA in partnership with CNIO, CEGEN, UPV and funded by IVACE.

June

- INCLIVA researchers find evidence of a new type of neuroplasticity in adults.
- INCLIVA collaborates in neurological impairment diagnosis in different disorders through eye movement analysis with OSCANN desk technology.
- The second meeting of Joint Action ADVANTAGE stakeholders addresses the need for a new approach to social and healthcare systems to meet frailty and disability needs in the elderly.

July

- Productive oncology teleconferences held between researchers from Spain and Paraguay developing a multicentre, multidisciplinary training project in cancer and Electronic Medical Records (EMR).
- EpiDisease spin-off to receive €344,000 from the Botín Foundation Mind the Gap program.

> August

- INCLIVA and Hospital Clínico Universitario of Valencia, founding members of the Clinical and Translational Diabetes Group (CTD).

> September

- Science takes to the streets for European Researchers Night with workshops and experimental shows in the Plaza del Ayuntamiento (main square) of Valencia.
- INCLIVA teams up with NELA BioDynamics in research and innovation in orthopaedic and traumatological surgery.

> October

- Early diagnosis, research and tailored treatments: three cornerstones of successful breast cancer treatment.

> November

- INCLIVA Metabolic Diseases Laboratory research a molecule used in cancer treatment to improve the most severe cases of atherosclerosis.
- Breakthrough discovery of how specific cell genes affect cellular transformation in others.

> December

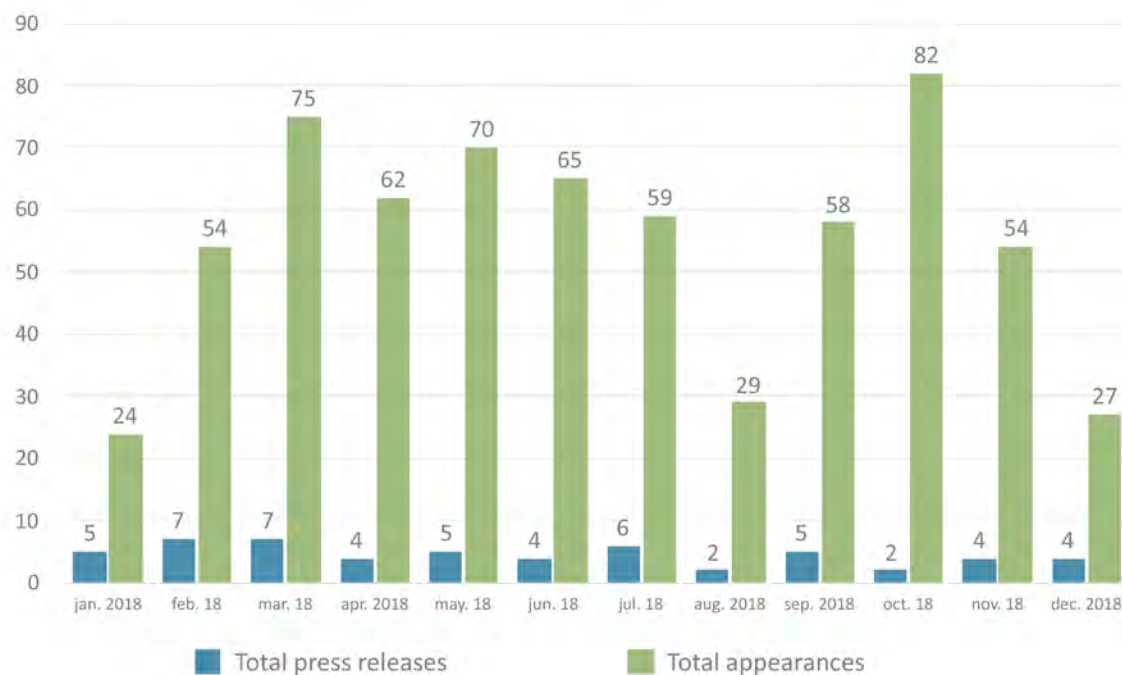
- Dr. Josep Redón, named one the world's most highly cited researchers by Clarivate Analytics.
- INCLIVA skin cancer research group study identifies prognostic biomarkers in patients with highly aggressive skin cancer.
- INCLIVA and *Hospital Clínico de Valencia* researchers led by Dr. Vicente Bodí conduct a study finding an association between left ventricular deformation as measured by resonance and prognosis in myocardial infarction patients.



7.2. Communication Indicators 2018

Press office




During 2018, INCLIVA issued a total of 96 press releases on the Web, of which 55 were sent to the media, with a total of 659 press appearances, around 86 percent digital and 14 percent in print.



	jan-18	feb-18	mar-18	apr-18	may-18	jun-18	jul-18	aug-18	sep-18	oct-18	nov-18	dec-18
Total press releases	5	7	7	4	5	4	6	2	5	2	4	4
Total media appearances	24	54	75	62	70	65	59	29	58	82	54	27
General Media	19	45	63	46	55	48	49	20	42	60	38	23
Specialized media	5	9	12	16	15	17	10	9	16	22	16	4
Total	53	115	157	128	145	134	124	60	121	166	112	58

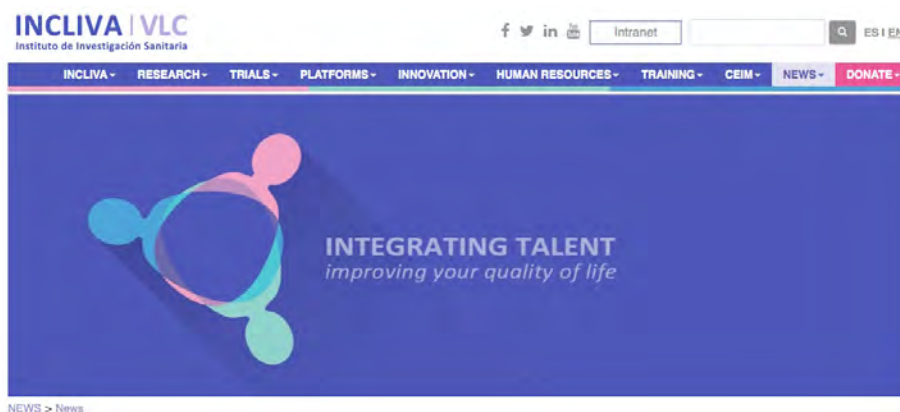
The most extensive media attention was generated by the oncology area together with the Transversal Program of Translational Oncology, while Dr. Ana Lluch is the researcher who appeared most frequently in the media.

Social Media engagement rates 2018

2018					
	Users	Impressions	Interactions	Posts	Average
	3,573	1,689,073	87,279	592	49
	2,318	444,573	14,889	562	47
	2,493	247,172	8,735	421	35
		2,380,818	110,903	1,575	

INCLIVA Website

- Website users: 62,977
- Website Visits: 272,670
- Website Sessions: 127,552



Educational Outreach

In 2018 INCLIVA launched a pilot educational outreach project aimed at raising awareness of the importance of research and how it improves quality of life, in addition to boosting the visibility of women in science and inspiring scientific vocation. The activity's direct target audience is school children aged between eight and thirteen.

The project is a bidirectional initiative, in which INCLIVA welcomes visits from schools and our researchers visit schools to give talks.

To this end between February and May this year Doctors Gloria Ribas, Pilar Eroles, Pilar González Cabo, Pepa Castillo and Ana Lluch, all INCLIVA researchers, visited 10 schools in which 731 children participated.



During the same period the Biobank and UCIM and INCLIVA laboratories received visits from six schools including 429 schoolchildren in total.

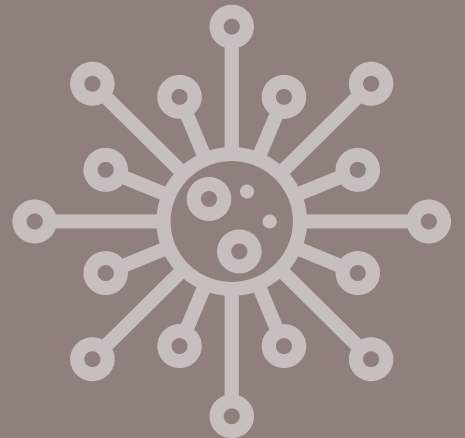






INCLIVA
social initiatives

08



INCLIVA's mission is "to contribute to improve citizen health and quality of life"; therefore, in addition to our own research projects, the institute is also involved in and committed to initiatives promoted by individuals close to someone ill.

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

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

8.1 Philanthropic projects

PROYECTO PAULA

This project was set up in 2011 by Cristina Ponce, when her 8 year old daughter Paula was diagnosed with type 1 diabetes mellitus, a disease that completely destroyed her insulin-producing cells.

Proyecto Paula focuses on raising public and private funds and resources, to research diabetes and to find a cure for Paula and other people with this illness.

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

Since its inception, *Proyecto Paula* has contributed more than €16,064.



FUNDACION LE CADÓ

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

Fundación Le Cadó collaborates with INCLIVA in funding the research project "Study of breast cancer in young women under 35 years," conducted by Dr. Gloria Ribas. It also involves other researchers such as Dr. Isabel Chirivella (a genetic diagnosis specialist physician) and Ms. Carmen Peña Chilet, the entire team led by the oncologist Dr. Ana Lluch.

Almost €25,000 has been donated for the project so far.



NICO CONTRA EL CÁNCER

The movement “Nico contra el cáncer” was formed in November 2015 in Ourense, after Nicolas Rodriguez Leal came home following a surgical intervention at the Hospital La Paz in Madrid.

The movement is led by his mother and aunts as an activity under the umbrella of the *Asociación NEN*, whose main objective is to finance research projects on childhood cancer, and more specifically solid tumors.

In 2018 €57,000 has been donated for this project.



FUNDACION NEOBLASTOMA

The Neuroblastoma Foundation, created in 2017, funds research on neuroblastoma, a particularly aggressive type of childhood cancer that affects the nervous system. Survival figures have not improved in recent years. The Neuroblastoma foundation informs families about existing treatments, and brings together families of sick children, motivating them to raise funds for research through numerous campaigns. The funds are destined to research projects and clinical trials in Spanish laboratories and hospitals.

In 2018 €30,000 has been donated for this project.



ASOCIACIÓN NACIONAL DE ALPHA 1

The Alfa-1 Spain Association defends the interests of patients affected by the Deficit, their families and their caregivers, and promotes the research and training of health personnel who treat these patients. The defense of early diagnosis, access to available medical treatments and the daily support of patients and newly diagnosed, are its foundational tasks.

In 2018 the Association has contributed €5,684 to collaborate investigating this disease.



➤ **8.2 Social initiatives - updates**

INCLIVA presents the Palleter-Erudito Falla with a banner for its solidarity project “Plantar la Esperanza (Planting Hope)”.

The Falla Palleter-Erudito Orellana has received an Incliva banner in acknowledgment of its contribution to research, presented by Dr. Lluch in a ceremony attended by the vice



president of Valencia regional council, María Josep Amigó, and the Solidarity award granted by Canal 7.

Valencia Mayor Joan Ribó and president of the Generalitat (regional government) Ximo Puig, who also visited the Falla, form part of the long list of authorities and representatives from Valencia's civic, business and political spheres who have given their support to the 'Plantar la Esperanza' project.

The committee organized a full program of activities including workshops, readings, games, informative seminars and other ideas aimed at destigmatizing and normalizing the disease, supporting breast cancer patients, their families and the general public, and raising awareness of the importance of research. All these activities, free and open to the public, were organised with the support of Valencia provincial council.

The most symbolic event was held on Saturday 10 March, with a traditional "Plantà al tombe" (erecting the Falla monument by hand) in which 200 women affected by cancer took part, using ropes to raise the 10-meter-high monument, made in traditional wood by Manolo García, which represents *The Palleter* (a historical character who inspired people to join forces against the French in the War of Independence), who oversees the fight against cancer from above.

There are several ways to contribute open to individuals, organizations and institutions within the framework of the 'Plantar la Esperanza' project. Supporters can make donations on the website (<http://plantarlaesperanza.es/dona-ahora/>), buy the charity calendar for which Víctor Cucart has photographed well-known women affected by the disease, purchase other fundraising merchandise, or sign the petition to modify the Patronage Law.

Spain is one of the countries with highest quality research, but there is a lack of funding and legislation does not facilitate donations: tax relief is limited to 15% for individuals and 25% for legal entities, in sharp contrast to the situation in other countries such as Germany, where they are up to 100% deductible.

A message of hope

"There's really no need to be afraid of cancer nowadays, because in most cases it can be controlled. Nearly 70% can be cured with the right approach, a percentage that rises in cases such as breast cancer, where 85% is already reached, compared to 60% three decades ago. These outcomes have been achieved owing to improvements in diagnostic and treatment methods, all thanks to research". Dr. **Ana Lluch**, principal investigator of **Incliva's Breast Cancer Biology Group**, conveyed this message in

the talk held inside the Palleter-Erudito Orellana Falla marquee. The framework of the philanthropic project 'Plantar la Esperanza', puts women who currently have or have experienced breast cancer and their families in the spotlight, and this ceremony gives special meaning to its this Falla's 50th anniversary.

The medical statistics revealed by Dr. Lluch indicate that one in eight women will suffer from breast cancer during their life. Currently, about 1,800 new cases are detected each year in the Valencian Community: around 27,000 in Spain and more than 300,000 across Europe. 'Plantar la Esperanza' aims to help raise awareness about the importance of research and its findings results, raise greater public and private support to conduct it, and foment a culture of patronage as well as laws that favor research.

As the principal investigator of the **Incliva Breast Cancer Biology Group**, recognized as the best oncologist in Spain according to the first **Healthcare Reputation Monitor (Monitor de Reputación Sanitaria, MRS)**, she explains that treatments have evolved and are less aggressive. *"In 70% of operations, only the tumour is removed, and if it is necessary to remove the gland, this is immediately reconstructed. Neither is it necessary to treat all women with chemotherapy; only 30% of breast cancer patients currently receive it. Thanks to the genomic method, the study of biology and tumour alterations informs us which patients need chemotherapy or not after surgery. The rest receive hormonal or biological treatments, without side effects. We can make the best decisions based on each tumour and each patient. In the case of 15% of patients who are not cured, there are also important advances in chronic disease which extend hope and quality of life. Thanks to research, in the future we will be able to cure many more patients."*

Nowadays cancer is the primary cause of death; when asked about incidence of the disease, Dr. Lluch answers *"On one hand, our environment has changed a lot, and external factors can play a part; but above all, it owes to an increase in life expectancy. Whereas in 1900 expectancy was 34 years for men and 36 years for women, now it is 84 years for men and 87 for women. The longer people live, the more likely they are to get cancer, because with age cells also divide more and acquire alterations and genomic mutations."*

Nonetheless, as she clarifies *"although prevalence is increasing, mortality has plummeted since the 1990s owing to two factors: screening campaigns and new treatments. Early diagnosis allows us to detect tumours in an earlier, smaller*

phase. We can attribute the 6-8% decrease in mortality to the success of these campaigns”.

Many of Dr. Lluch’s research group projects and clinical trials

are centred on Triple negative breast cancer “because there is still so much to discover, and this cancer accounts for between 12% and 15% of all breast cancer cases”.

8.3 Private charitable donations and acknowledgments

On behalf of INCLIVA, we want to thank all the people who have helped our research through their donations, for their support and solidarity. For us, this collaboration means much more than an economic contribution: it is the encouragement we need to keep investigating and working in research.

Private donations

Susana Aguilar Aguilar, Vicente Ayala Crespo, María Antonia Belloch Burguera, María Blasco Felip, Esteban Borreda Bolinches, Francisco Botella Aparicio, Rafael Pascual Caballer Molina, Guillermo Caballero De Luján, Juana Carmen Campos Yeste, Nicolás Carrión Domínguez, Amparo Reyes Castelló Gómez, María Luisa Ebrí Méndez, Elba Ferrer Gil, Marta García Janini Pastor, Nuria Gelonch Soler, Enrique Gimeno Calabuig, Alicia Martínez Espinosa, María Herminia Muñoz Torregrosa, María Paz Perez Sangüesa, Jorge Iván Rodríguez Gonzalez, Rosalía Sánchez Rilla, Antonia Serrano Monedero.

Corporative donations

Abbvie Spain SLU, Associació de Familiars i Amics Pacients amb Neuroblastoma, Asociación Alfa-1 de España, Asociación de Afectados de Cáncer Asac de Segorbe, Asociación de Amas de Casa y Consumidores Tyrius- Foios, Asociación de Mujeres y Hombres afectados de Cáncer de Mama, Asociación La Virgen de los Dolores, Asociación Tiradas contra el Cáncer Memorial Vicente Estellés, Asociación Valenciana de Investigaciones Inmunoalergológicas, B. Braun Medical SA, Bayer Hispania SL, Biomed SA, Biotronik Spain SA, Doctaforum Servicios, Fresenius Kabi España SA, Fundación Bancaria Caixa Déstalvis i Pensions de Barcelona, Fundación Lecadó, Fundación Neuroblastoma, Fundación Patrimonio Benéfico Marqués de Dos Aguas, GE Healthcare Biosciences SA, Gedeon Richter Iberica SAU, Gimnasio Femenino Eixample SL, Junta Asociada Provincial de Valencia de la Asociación Española Contra el Cáncer, Laboratorios Farmacéuticos Rovi SA, Laboratorios Gebro Pharma SA, Laboratorios Servier SL, Logimed SLU, Medtronic Ibérica SA, N&N Consultores SL, OPC Congress SL, Philips Iberica SAU, Prosmédica Valencia SL, Radiometer Iberica SL, Roche Farma SA, Roxall Medicina España SA, Sanlucar Fruit SL, Sofpromed Investigación Clínica SLU, SQR Medical Resources SLU, Torse SA, Variocana Asociación Interna de Reiki y Terapias Alternativas, Vifor Fresenius Medical Care Renal Pharma España SLU, Vifor Pharma España SL.



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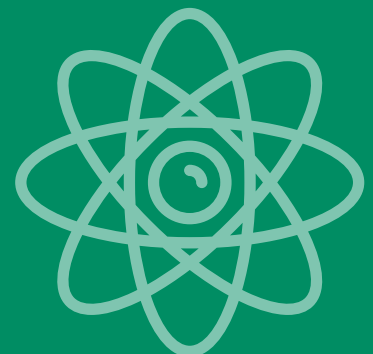
TARGET.....

Risk assessment.....



List of scientific publications

09



List of 550 scientific publications derived from the activity of the IIS

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