ANNUAL REPORT 2014

ciberes

Centro de Investigación Biomédica en Red

Enfermedades Respiratorias

Índice

1. ORGANISATION 3
Letter from the Scientific Director 4
List of Groups and Institutions 5
Organisational Structure 7
Budget 10
CIBERES Staff 11
Scientific Production 12
2. SCIENTIFIC PROGRAMMES 17
Acute Lung Injury (ALI) 20
Asthma 22
Lung Cancer 24
Chronic Obstructive Pulmonary Disease (COPD) 27
Pathogen - Host Interactions 30
Pneumonia 33
Pulmonary Fibrosis 35
Sleep Apnea 38
Tuberculosis 40
3. TRANSVERSAL PROGRAMMES 43
Training Programme 44
Communication Programme 46
4. PLATFORMS 49
Pulmonary Biobank Consortium 50
Technology Transfer Platform 54
5. RESEARCH GROUPS 59

1. ORGANIZATION

Letter from the Scientific Director

Dr. Ferrán Barbé.
Scientific Director.
CIBERES.

It is an honour for me to present for the first time the annual report of the activities of the Centre de Investigación Biomédica en Red de Enfermedades Respiratorias (Respiratory Diseases CIBER).

In 2014, I received the responsibility of becoming the Scientific Director of the centre. I wanted to thanks and congratulate my predecessor first, Dr Alvar Agustí for his excellent work as Scientific Director. Under his command, CIBERES has strengthened as a nation and international centre of excellence in the research of respiratory diseases. The data presented in this report certifies the excellent trajectory followed, not only on an organisational level but also in regards to scientific results.

Secondly, I wanted to specifically thank all the team leaders and, in general, all the CIBEBRES researchers and personnel for the warm welcome they gave me. I am sure that under such a collaboration climate we will achieve new success. 2014 has involved the consolidation of our scientific organisation model. The Strategic Projects for the Corporate Research Programmes (CRPs) were evaluated externally and the good results of this evaluation endorse the work performed by our research programmes and group. Also, a new CRP proposal was externally evaluated last year. The excellence of said proposal allows us to announce that CIBERES now has a new CRP in Pulmonary Hypertension the strategic project of which will start up in 2016.

The scientific output indicators as they will be presented below have followed an upward line in 2014 and put CIBERES in a good position in the scientific institution rankings.

We have some passionate months ahead of us that will allow us to reorganise our scientific structure, taking advantage of the driving force of all that we have achieved, for the purpose of making it more flexible and efficient. We will incorporate new research groups and will focus on evaluating our practice and on improving some aspects in which we have a certain margin, such as finding external funding or internationalising our activity.

I would like to encourage all CIBERES members to continue with their work and with their enthusiasm for getting the results of the upcoming years to be at least as good as those presented in this 2014 activity report.

LIST OF GROUPS AND INSTITUTIONS

After the Resolution of July 28, 2006, whereby the ISCIII approved the initial list of applicants expressing interest (27 initial groups, 26 groups now resulting from the withdrawal of a group), and the Resolution of March 21, 2007 for incorporating new groups (7 groups), CIBERES was constituted in 2008 with 33 research groups. Subsequently, to execute the ISCIII call for proposals of March 12, 2008, in fiscal year 2009 a new research group joined CIBERES, which was then made up of a total of 34 research groups.

A clinical group joined in 2011 by means of an association agreement approved by the Board of Trustees in December 2011. There was no increase or decrease in the number of groups forming the CIBERES in 2014.

Therefore, as of 31 December 2013 CIBERES is made up of 34 full member research groups incorporated through the official ISCIII call for proposals and 1 associated group

Said groups bring together over 450 researchers, pneumologists, technicians and other specialists from universities, health and research centres carrying out the clinical, basic and translational research of the networking centre.

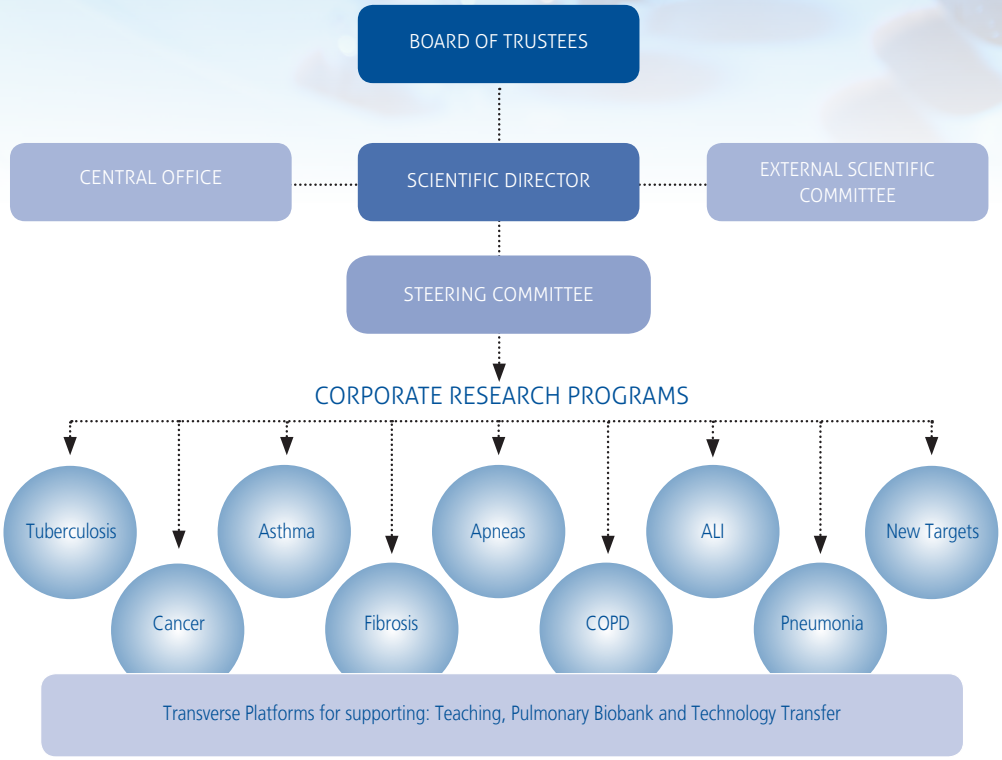
These 34+1 groups are geographically distributed according to the information contained in the following table.

REGIONS	Type of institution			TOTAL	%
	Research Center	Hospital	University		
Aragón	-	-	1	1	2,9%
Baleares	2	-	-	2	5,7%
Castilla-León	-	-	1	1	2,9%
Cataluña	1	11	1	13	37,1%
Extremadura	-	1	-	1	2,9%
Gran Canaria	-	1	-	1	2,9%
Madrid	6	5	2	13	37,1%
País Vasco	-	1	-	1	2,9%
Valencia	-	-	1	1	2,9%
Andalucía	-	1	-	1	2,9%
TOTAL	9	20	6	34	100,0%

Principal investigator	Workplace / Institution	Type of institution	City / Region	Year
Casals Carro Cristina	Univ- Complutense Madrid. Fac. de Biología.	Universidad	Madrid / Madrid	2006
García López, Ernesto	Centro de Investigaciones Biológicas / CSIC	Centro Invest.	Madrid / Madrid	2006
Gzlez. de la Campa, Adela	Centro Nacional de Microbiología / ISCIII	Centro Invest.	Majadahonda / Madrid	2006
González Mangado, Nicolás	Fundación Jiménez-Díaz-CAPIO. Servicio de Neumologia / IISFJD	Hospital	Madrid / Madrid	2006
Picado Vallés, Cesar	Hospital Clinic i Provincial. S. de Neumología.	Hospital	Barcelona / Cataluña	2006
Barberá Mir, Joan Albert	Hospital Clinic i Provincial. S. de Neumología.	Hospital	Barcelona / Cataluña	2006
del Pozo Adejón, Mª Victoria	Fundación Jiménez-Díaz-CAPIO. Servicio de Inmunología / IISFJD	Hospital	Madrid / Madrid	2006
Regueiro Comesaña, Verónica	Fundació d'Investigació Sanitaria de les Illes Balears. (FISIB)	Centro Invest.	Bunyola / Baleares	2006
Martín Montañés, Carlos	Universidad de Zaragoza, Fac. de Medicina.	Universidad	Zaragoza / Aragón	2006
Agustí García-Navarro, Alvar	Hospital Clinic i Provincial.	Hospital	Barcelona / Cataluña	2006
Monserrat Canal, Josep Mª	Hospital Clinic i Provincial.	Hospital	Barcelona / Cataluña	2006
Navajas Navarro, Daniel	Universidad de Barcelona, Fac. de Medicina	Universidad	Barcelona / Cataluña	2006
Morcillo Sánchez, Esteban J.	Universidad de Valencia, Facultad de Medicina.	Universidad	Valencia / Valencia	2006
Torres Martí, Antoni	Hospital Clinic i Provincial. S. de Neumología.	Hospital	Barcelona / Cataluña	2006
Masa Jiménez, Juan F.	Hsp. San Pedro de Alcántara / FUNDESALUD	Hospital	Cáceres / Extremadura	2006
Morell Botad, Ferran	Hsp. Gral. Vall d'Hebron / Inst. Catalá de Salut	Hospital	Barcelona / Cataluña	2006
Ausina Ruiz, Vicente	Hsp. Univ. Germans Trias i Pujol / FIIHGTP	Hospital	Barcelona / Cataluña	2006
Rello Condomines, Jordi	Hsp. Gral. Vall d'Hebron / Inst. Catalá de Salut	Hospital	Barcelona / Cataluña	2006
Liñares Louzao, Josefina	Hsp.Univ. de Bellvitge / Fundación IDIBELL	Hospital	L'Hospitalet de Llobregat / Cataluña	2006
Álvarez Martinez, Carlos	Hospital Universitario 12 de Octubre / SERMAS	Hospital	Madrid/ Madrid	2006
Gea Guiral, Joaquim	Hospital del Mar-IMIM / Consorci Mar Parc de Salut de Barcelona	Hospital	Barcelona / Cataluña	2006
Esteban de la Torre, Andrés	Hospital Universitario de Getafe / SERMAS	Hospital	Getafe / Madrid	2006
González Martínez Constancio	Universidad de Valladolid. Fac. de Medicina	Universidad	Valladolid / Castilla León	2006
Melero Fontdevila, José Antonio	Unidad de Investigación / ISCIII	Centro Invest.	Majadahonda / Madrid	2006
Pérez Trallero, Emilio	Hospital Donosti. Asoc. Instituto Biodonostia	Hospital	San Sebastián / Pais Vasco	2006
Bouza Santiago, Emilio	Hsp. Gral. Universitario Gregorio Marañón / SERMAS	Hospital	Madrid / Madrid	2007
Pérez Vizcaino, Francisco	Univ. Complutense de Madrid. Fac. Medicina	Universidad	Madrid / Madrid	2007
Villar Hernández, Jesús	Hsp. Gral. de Gran Canaria Dr. Negrin / Servicio Canario de Salud	Hospital	Las Palmas / Canarias	2007
Monsó Molas, Eduard	Hospital Universitario Germans Trias i Pujol / FIIHGTP	Hospital	Barcelona / Cataluña	2007
Ruiz-Cabello Osuna, Jesus Mª	Centro Nacional de Investigaciones Cardiovasculares (CNIC)	Centro Invest.	Madrid / Madrid	2007
Ortin Montón, Juan	Centro Nacional de Biotecnología / CSIC	Universidad	Cantoblanco / Madrid	2007
Blanch Torra, Lluis	Inst. Univ. Fundación Parc Taulí. Hospital de Sabadell. Corporación Sanitaria Parc Taulli	Hospital	Sabadell / Cataluña	2007
Menéndez Fernández, Margarita	Instituto Química Física Rocasolano / CSIC	Centro Invest.	Madrid / Madrid	2007
Barbé Illa, Ferrán E.	Hsp. Univ. Arnau de Vilanova / IRB Lleida	Centro Invest.	Lleida / Cataluña	2007
López-Campos, José Luis	FISEVI – Hospital Virgen del Rocío	Hospital	Sevilla / Andalucía	Vinc. 2011

ORGANIZATIONAL STRUCTURE

The Respiratory Diseases CIBER governing structure was organised in 2014 around four basic structures:



The **Board of Trustees**, presided by the Instituto de Salud Carlos III (ISCIII), is the highest governing and administration body of the Consortium, and in 2014 it represented the institutions forming the consortium.

The **Steering Committee**, which is responsible for the executive management of CIBERES, is formed by the following members, once the changes occurring in 2014 have been introduced:

STEERING COMMITTEE

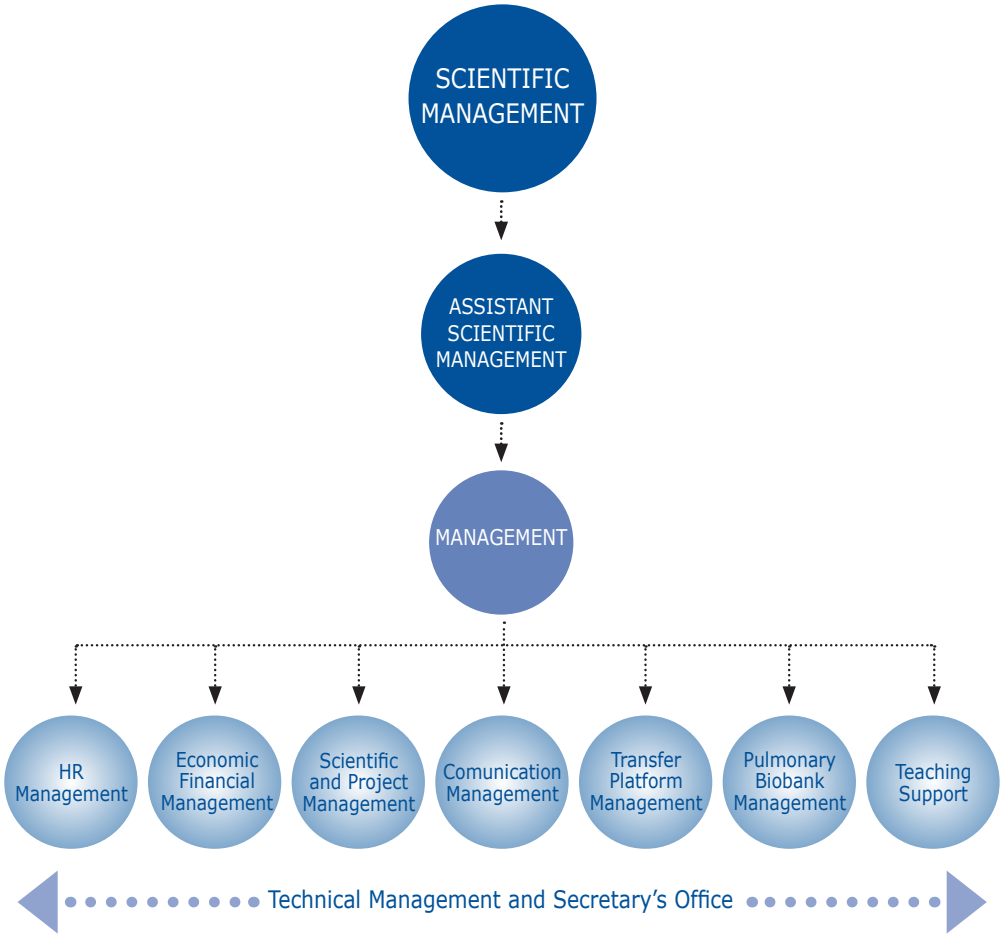
Position	Name
Scientific Director	Dr. Ferrán Barbé
Deputy Scientific Director (clinical field)	Dr. Joaquín Gea
Deputy Sicentific Director (basic field)	Dr. Cristina Casals
Manager	Dr. Manuel Sánchez
Teaching Coord.	Dr. Ana Obeso
Severe Asthma CRP Coord.	Dr. MªVictoria del Pozo
Cancer CRP Coord.	Dr. Eduard Monsó
Pulmonary Fibrosis CRP Coord.	Dr. María Molina
New Therapeutic Targets CRP Coord.	Dr. Junkal Garmendia
Acute Lung Injury CRP Coord.	Dr. Andres Esteban
Tuberculosis CRP Coord.	Dr. Vicenç Ausina
Pneumonia CRP Coord.	Dr. Antoni Torres
Sleep Apnea CRP Coord.	Dr. J.M. Montserrat
COPD CRP Coord.	Dr. Borja García-Cosío
Technology Transfer Plat. Coord.	Dr. Lluis Blanch
Scientific Programme Manager	D. Javier Muñoz

The **External Scientific Advisory Committee (ESAC)** is in charge of advising the Board of Trustees and the Steering Committee in the development of the research strategy. The new setup of the External Scientific Advisory Committee was approved by the Board of Trustees in June 2012, and comprises top-level researchers covering all the scientific areas identified in CIBERES:

EXTERNAL SCIENTIFIC ADVISORY COMMITTEE

Area	Name	Institution
EPOC	Prof. B. Celli	Tufts University of Boston (EEUU)
Cancer	Prof. J.R. Jett	Mayo Clinic Rochester of Minnesota (USA)
New Therapeutic Targets	Prof. H. Klenk	Philipps-Universität Marburg (Germany)
Tuberculosis	Dr. J.C. Palomino	Univestity of Ghent (Belgium)
Fibrosis	Dr. A. Pardo	Univesidad Nacioinal Autónoma de México (México)
Sleep Apneas	Dr. J. Kimoff	McGill University of Montreal (Canada)
Pneumonia	Prof. S. Ewig	Evangelisches Krakenhaus Herne-EVK of Herne (Germany)
Acute Lung Injury	Dr. T. Thompson	Harvard Medical School, Hayward, California (USA)
Asthma	Prof. R. Polosa	Università Degli Studi di Catania (Italy)

The **CIBER Technical Office** is led by CIBER Manager, Dr. Manuel Sánchez, who is responsible for the good operation and management of the Entity, and in 2014 it was located in the Instituto de Salud Carlos III. The structure of the operative administration and management is the following:



CONTACT:

- **Javier Muñoz Bravo**,Scientific Programme Manager. jmunoz@ciberes.org. Tel:+34 673799994
- **Cristina Broceño Corrales,** Technology Transfer Manager. cbroceno@ciberes.org Tel: +34 674097109.
- **Cristina Villena**, Coordinator Pulmonary Biobank Consortium. cvillena@ciberes.org, Tel. +34 871 205050 ext 64511

BUDGET

TOTAL 2014

REVENUE	**2.632.420,00**
ISCIII registered funds	2.632.420,00
EXPENSES	**2.672.662,93**
GROUPS through Programmes	934.425,97
RESEARCH PROGRAMMES	1.279.024,03
TOTAL RESEARCH	2.213.450,00
TRANSVERSAL PLATFORMS/ SERVICES	194.296,94
STEERING COMMITTEE	9.500,00
CENTRAL ADMINISTRATIVE OFFICE AND COMMUNICATION	159.648,88
TEACHING AND TRAINING	95.767,11
TOTAL CENTRAL SERVICES	459.212,93

STAFF CIBERES

	MEN			Total MEN
	Indefinite	Works and Services	Postdoctoral	
CIBERES	7	11	1	19
PhD	2	3	1	6
Degree Holder	4	3		7
Diploma Holder	1	1		2
Technician		4		4
Grand total	7	11	1	19

	WOMEN			Total WOMEN
	Indefinite	Works and Services	Postdoctoral	
CIBERES	24	33	1	58
PhD	7	10	1	18
Degree Holder	5	14		19
Diploma Holder	7	1		8
Technician	5	8		13
Grand total	24	33	1	58

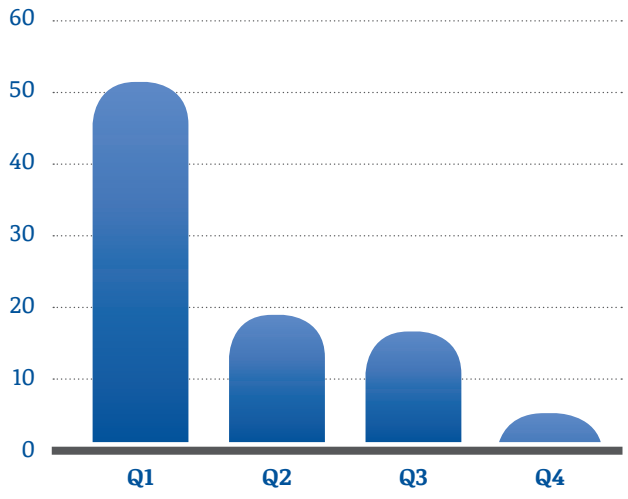
	Indefinite	Works and Services	Postdoctoral	Grand total
CIBERES	31	44	2	77
PhD	9	13	2	24
Degree Holder	9	17		26
Diploma Holder	8	2		10
Technician	5	12		17
Grand total	**31**	**44**	**2**	**77**

SCIENTIFIC PRODUCTION

In 2014 CIBERES publication results remained positive and were on an upward trend. The progressive increase in publications in which reference is made to CIBERES as a centre continues, and citations thereof increase[1].

YEAR 2014
No. Articles: 517
Total Impact Factor: 2.019,0980
Average Impact Factor: 4,2329
Total citations: 472
First autor %: 52,61%
Last author%: 58,41%
Corresponding author %: 50,29%

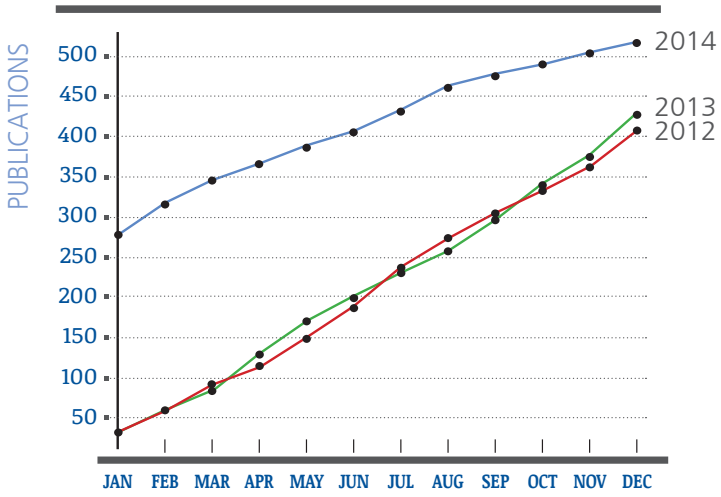
23.69% of the publications of 2014 are in the first decile, and their distribution by quartiles can be seen in the following table:



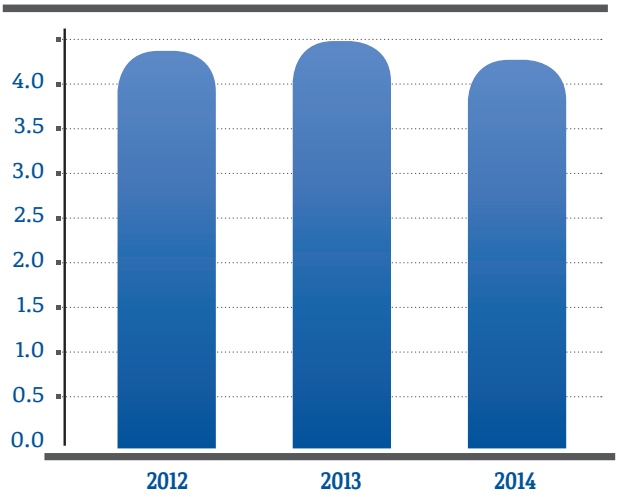
1. Intranet CIBER www.ciberisciii.es

The graphical evolution of CIBERES publications and of their citations and impact can be observed in the following graphs in which data from the years 2012 and 2014 is analyzed

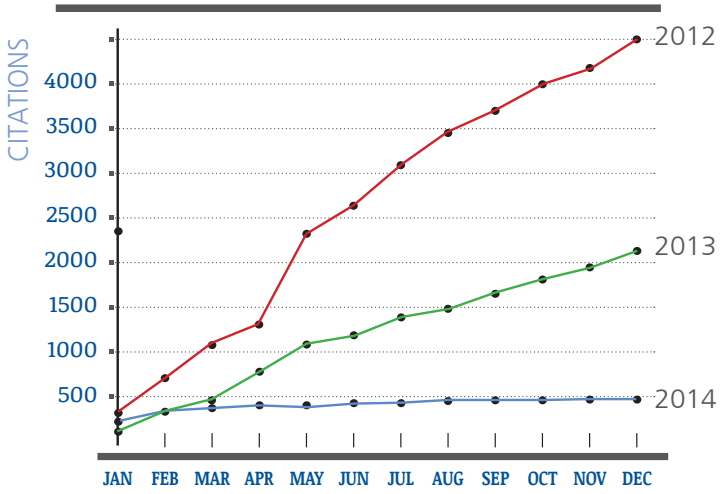
NO. ARTICLES EVOLUTION



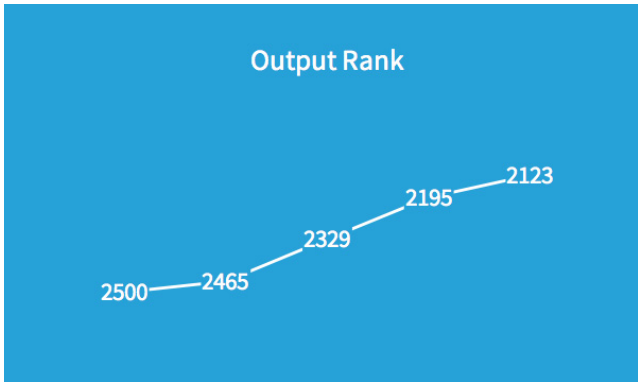
IMPACT FACTOR Average Total



ANUAL CITATIONS EVOLUTION



In relation to scientific production (Output) understood as the total number of documents published in indexed journals in SCOPUS, CIBERES production has increased in the years being evaluated. On a worldwide level, the institution went from 2465 in 2011 to 2123 in 2014[2].

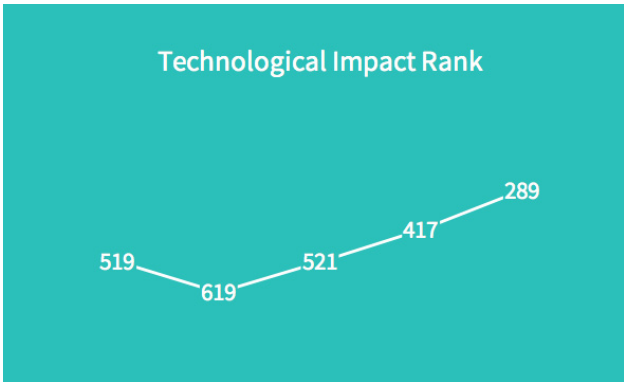


CIBERES continued in 2014 with a Normalised Impact Factor (NIF) greater than 2, which indicates that its publications are mentioned over 50% more than the worldwide average of institutions. An important piece of data about this indicator is that, as can be seen online on the web page www.scimagoir.com, CIBERES has maintained the highest NIF between 2010 and 2014 of all the CIBER subject areas, being in position 14 among Spanish research institutions in 2014.

Other relevant indicators of quality to be highlighted would be the excellence indicator, with leadership in which CIBERES has gone from worldwide position 1076 in 2011 to 854 in 2014[3].

2. Scimago Institutions Rankins www.scimagoir.com
3. Scimago Institutions Rankins www.scimagoir.com

In reference to rankings relating to innovation and technological impact, the citation of scientific publications of the centre in patent databases or directly in patents, it can be pointed out that CIBERES has improved its position in the Innovative Knowledge Rank from position 516 in 2011 to position 273 in 2014 and from position 619 to 289 in the Technological Impact Rank in the same period[4].



In summary and according to the Performance report on Spanish institutions in the Scimago Institutions Ranking (SIR) 2013, according to its excellence ratio CIBERES was Spanish scientific institution number 28 at the beginning of 2014.

The research activity of the 37 CIBERES member groups was very significant in 2014. It must be pointed out that all the groups participated in Corporate Research Programmes and participate in one or two of the (9) CIBERES strategic projects, so a significant portion of their activity is collaborative.

In addition to the 9 massive strategic projects, the groups have kept 260 research projects funded by both public and private entities active. In turn, the groups have participated in 105 clinical trials in 2014.

Finally, a key result in scientific production and internationalisation of CIBERES in 2014 has been the conclusion of participation of the Centre in two European projects. As the coordinator, CIBERES has developed the European project **Initial Training Network Pulmonary Imaging Network (P-NET)**, Ref: 264864, of FPVII-PEO-PLE-2010-ITN, funded by the European Union. Furthermore, as a partner CIBERES has participated in the project **Commhere: Communication of European Health Research, Health 2011.4.1-1**.

Understanding the importance of increasing participation as a Centre in Horizon Programme 2020 projects, CIBERES together with two other CIBER subject areas (CIBERER and CIBERBBN) participated in and achieved 2014 funding for developing a project to promote the participation of its groups in international projects within the **European Networks and Managers call for proposals**. Therefore, and for three years (2015-2017) a specific manager whose objective will be to promote research topics from the three subject areas involved, to seek partners and calls for proposals suitable for developing projects and starting up training activities intended for promoting internationalisation will be hired.

4. Scimago Institutions Rankins www.scimagoir.com

2. SCIENTIFIC PROGRAMMES

INTRODUCTION

Corporate Research Programmes (CRPs) are the corporate scientific work tool of CIBERES. A CRP is defined by a Strategic Project (SP) for research addressing a relevant health problem in the scope of respiratory diseases in a cooperative and comprehensive manner.

Strategic Projects (SPs) have been structured as work packets following the format of projects funded by the European Commission in the different framework research programmes and are clearly intended for transferring and translating results, therefore seeking the public investment to be returned to society as a whole.

As in previous years, for the 2014 fiscal year the CIBERES Steering Committee approved a budget item for each CRP. This budget item was managed by the Scientific Committee of each programme which has established the scientific priorities of each. The amount assigned to each CRP was variable and was calculated based on the interest expressed by CIBERES researchers in participating in each of said programmes and on the external evaluations received:

PCI	Budget 2014
Asma Grave	88.541,49€
Fibrosis Pulmonar	34.339,31€
EPOC	163.749,97€
Cáncer	97.559,60€
Lesión Pulmonar Aguda	251.275,66€
Síndrome de Apnea del Sueño	175.866,89€
Neumonía	254.656,02€
Tuberculosis	89.832,71€
Nuevas Dianas Terapeúticas	247.178,32€
TOTAL	**1.402.999,97€**

To assure the correct development of the SPs, CIBERES Scientific Management decided to subject the SPs to a new external follow-up evaluation at the beginning of 2014. The follow-up was performed in two phases. In a first phase, coordinators and managers of the job packets for each project were asked to complete an ad hoc form in which they were asked to provide comprehensive information about the development of the project and about the results obtained. In a second phase, the coordinators were asked to perform a presentation of the evolution of the project in its first 12 months of execution before a panel of 3 experts of recognised prestige in the field of biomedical research who had previously reviewed the forms completed in the preceding phase.

The experts making up the panel were:

Dr. Bartolome Celli. President of the CIBERES External Scientific Committee

Dr. Joaquín Arenas. Director of the Instituto de Investigación of Hospital 12 de Octubre.

Dr. Francisco Pozo. Consultant Researcher. Instituto de Investigación of Hospital 12 de Octubre.

After the presentations were made by the project coordinators the follow-up panel evaluated the information presented, assessing the following main criteria:

- Suitable development of the project according to the work plan. Percentage of milestones and deliverables reached.
- Taking into consideration (and making suitable modifications) of the recommendations made in the first evaluations by both the Agencia Nacional de Evaluación y Prospectiva (ANEP) and by the External Scientific Advisory Committee of CIBERES (ESAC).
- Development of suitable fundraising actions and economic viability of the project.
- Quality of the follow-up report presented.

After the evaluation, members of the panel wrote a report on each project in which both the evaluations of the criteria mentioned above and a set of recommendations for the better future development of projects was written.

In the process of developing SPs, a new CRP proposal which would have the objective of conducting research in the field of Pulmonary Hypertension was presented in 2014. Scientific Management gave the proposal a positive assessment and decided to send it for external evaluation by the ANEP and the ESAC, just as the remaining programmes had been evaluated. The proposal was evaluated under the same parameters used to evaluate the remaining SPs already underway, and both the ANEP, which considered it to be excellent and gave it a score of 48/50, and the ESAC gave a positive assessment of the proposal. For organisational and budgetary reasons it was decided that the CRP in Pulmonary Hypertension and its SP would officially start in CIBERES in January 2016. Meanwhile, this programme has been conducting dissemination and fund-raising activities with the support of CIBERES.

An introduction of each of the CRPs currently underway and their objectives as well as the main results obtained by said programmes up until the end of 2014 is schematically provided below.

Coordinator
Dr. Andrés Esteban

Early diagnosis and novel therapeutic strategies for acute lung injury

Having a strong scientific interest, the present ALI CRP is endowed with a clear translational relevance, aiming at solving questions of great social impact. Indeed, most citizens will eventually require in their lifetime an intensive care unit (ICU) admission. About one third of them require mechanical ventilation, of which over two thirds have acute respiratory failure as the admitting diagnosis. Common causes of acute respiratory failure are the conditions termed acute lung injury (ALI) and acute respiratory distress syndrome (ARDS). The social and economic impact of ALI and ARDS is documented by the high associated mortality rate -around 50%-, as well as the important sequelae of these patients, that often require prolonged rehabilitation treatment. This high mortality is comparable to the mortality of other conditions such as acute myocardial infarction, cancer or sepsis. However, funding from public or private agencies in this area is far from enough. This paradox implies a huge social and economic problem, given the severity of the disease, and the elevated cost of treatment, rehabilitation and work loss. The insufficient research in this field will not help solve these nationwide problems. Specifically, the present corporative research project (CRP) is designed to help solving the clinical and social problem of the early diagnosis and treatment of ALI.

Different groups of scientific excellence will participate in this research project, collaborating to accomplish a common objective: **how to diagnose earlier and treat better patients with ALI and ARDS in order to decrease their high morbidity and mortality**. Research questions include: (a) is there a specific diagnostic biomarker?; (b) which are the intracellular signalling pathways involved in the development and repair of ALI?; (c) which are the potential therapeutic targets based on involved pathways relevant to pathogenesis?; (d) can we define specific patient subgroups that could benefit from novel therapeutic approaches that will arise over the next 5 years?

The different research groups will collaborate with an integrated systems biology approach. Biological samples from participating patients with ALI and ARDS (i. e., serum, BAL fluid, etc.) will be collected for use in future investigations. These samples will be stored in and managed by the CIBERES' Biobank Platform.

The CRP is built on a limited number of WPs, defined to orchestrate in an efficient manner the different research areas, aiming at the common objective of diagnosis and treatment of ALI/ARDS.

Aims and objectives

1. **To identify genes/processes that are deregulated in preclinical models of ALI (assessed by functional genomics), or that constitute hits in genome-wide association studies being conducted.** To examine whether genetic variants of those genes are associated with acute lung injury (ALI) and the acute respiratory distress syndrome (ARDS) development and outcome (mortality or protection). To find new enigmatic genes that can explain the diversity of clinical presentation of ALI/ARDS, the response to current medical treatment, and the individual's genetic predisposition.
2. **To discover biomarkers of ALI** among the three most relevant families of markers (i.e., inflammation-cytokine, endothelial related and epithelial derived markers). Determine the utility of MRS and MS as biomarkers of ALI. To validate volatile organic compounds in airway fluid and exhaled breath samples collected by non-invasive or minimally invasive as biomarkers of ALI/ARDS. To determine specific biomarkers for the early detection of alterations in CNS function in ALI/ARDS at the local brain level (alterations in tissue architecture, and mapping of biological markers related to neuronal activation of early genes, apoptosis and inflammation); and to define their correlation with systemic biomarkers.

3. **To demonstrate a key role of TLR/NLR receptor activation in the pathogenesis of ALI**. These effects will be studied in animal models of ALI and in serum from patients with ALI, as well as in different cell types and in isolated ventilated perfused lung model.
4. **To define the relationship of asynchronies to clinically relevant outcomes in patients with ALI**, in order to define therapeutic targets based on ventilatory management and to define ventilatory management strategies
5. **To explore lung repair mechanisms that are initiated immediately following the insult** leading to ALI/ARDS (i.e. sepsis, VILI). To study interactions between initiating factors, structural pulmonary elements, and signalling pathways that are involved in lung repair.

   To define biochemical factors determining changes in surfactant function and structure in a rat model of ALI. To define mechanisms of alveolar repair, by means of stem cells, in decellularized lung scaffolds and in a lung-on-a-chip model. To use of adult stem cells in treatment.
6. **To spread knowledge and evidence providing new insights and training on acute lung injury mechanisms and lung repair.**

Main results until the end of 2014

- Location of new genes, genetic variants and microRNA for identifying the predisposition, underlying histological lesion and prognosis of the Acute Respiratory Distress Syndrome.
- First-time identification of the incidence in Spain and worldwide of the ARDS.
- New diagnostic criteria of ARDS, classifying it in three levels of severity (Berlin Definition, Consensus Conference).
- Description of the worldwide practice of the mechanical ventilation patterns in patients in the ICU, and in the different subgroups, according to the different pathologies that are a cause of acute respiratory failure.
- Design of a new continuous monitoring technique of critical patients.
- Design of a lung model from the extracellular matrix.
- Characterisation of the nanomechanics of the extracellular matrix of the lung by means of atomic force microscopy.

OTHER RELEVANT RESULTS OF THE CRP:

- Patent: Compuesto derivado de urea pirimidínica para el tratamiento de enfermedades inflamatorias. Application Number: P201031978.
- Patent: Uso de un compuesto químico derivado de un pirrol 1, 2, 3, 5-tetrasustituido en la preparación de un medicamento útil para el tratamiento de enfermedades inflamatorias que cursan con procesos apoptóticos celular. Application Number: P201131785.
- Patent: Marker for assessing the risk of developing acute kidney injury. Application/publication code: EP 12382393 .2
- Patent: Nanopartículas recubiertas de gelatina. Application/publication code: P201231038
- Better Care spin off CSPT: project for the analysis of digital respiratory signals.

ASTHMA

Coordinator

Dr. Mª Victoria Del Pozo

Mechanisms underlying genesis and evolution of asthma

Asthma represents a major health problem throughout the world. There has been an epidemic increase in global prevalence of asthma in the last decades with an estimated 300 million people affected worldwide. This is particularly relevant in the developed industrialized world, which has noted a tremendous increase in the prevalence of asthma over the last 50 years. Asthma currently affects 8-12% of the population in the developed world. Patients affected by this disease are recognized to have a poorer quality of life, reduced work productivity and school attendance and comorbidities associated. And, apart from individual suffering, because of their life-threatening of chronic course, these diseases present a high socioeconomic cost.

Asthma behaves as a spectrum of disorders initiated at different stages throughout life by a range of environmental factors interacting with a susceptible genetic background. At its simplest, asthma is divided into allergic (extrinsic) and no allergic (intrinsic) subtypes, but even within each of these 2 broad categories, there exists considerable heterogeneity with respect to underlying mechanisms, clinical and physiological manifestations, response to treatment, and natural history. The majority of asthma is associated with TH2-type T-lymphocyte-driven cell recruitment and mediator release involving mast cells, eosinophils, basophils, and macrophages that contribute to the chronic, subacute, and acute inflammatory responses.

During the last three decades an improved understanding of the pathophysiology underlying asthma, have led clinicians to shift their focus from managing acute attacks to achieving asthma control.

Severe asthma accounts for only 10% of patients with asthma, but it accounts for a considerable portion of the health care costs associated with the disease. Severe asthma patients are characterized by a poor quality of life, frequent hospitalisations and high risk of severe systemic side effects resulting from oral glucocorticoid therapy and/or high doses of inhaled glucocorticoids. All in all, these characteristics confer a relevant role to this group of patients when it comes to design a research programme aimed at achieving a better control of a disease that afflicts a progressively increasing number of patients.

Unmet needs in asthma are: The causes of the epidemic increase in asthma; Genetic susceptibility; The marginally understood interaction between environmental factors and immune system; Better subclassification of asthma: phenotypes; New agents acting on specific pathways in pathogenesis for the use as new therapeutic approaches; Better preclinical models for translation research; Better approaches in diagnosis and prediction of treatment responses and the monitoring of therapeutic effectiveness; Better tools to analysed complex data obtained; New and better biomarkers.

In our CRP project we will approach asthma as a trans-disciplinary research with expertise from clinical, epidemiological and biologist researchers to generate new therapeutic options based in a better diagnosis**. In our integrative we will tackle immunological, genetic and environmental factors leading to complex asthma phenotypes in order to identify, describe and validate immunological and molecular networks involved in the genesis and evolution of asthma.** To achieve our aims we propose to study retrospectively and prospectively two well defined cohorts.

Aims and objectives

In our project we will focus our interests on the following problems:

- Mechanisms underlying genesis and evolution of asthma.
- Characterization of asthma phenotypes
- Characterization of asthma severity and identification of the factors that are involved in asthma severity.
- New therapies for asthma.
- To identify novel biomarkers and pathways that can be translated into targets for therapeutic strategies.
- To generate and disseminate expertise and knowledge obtained from the consortium to transfer information to scientific community and society.

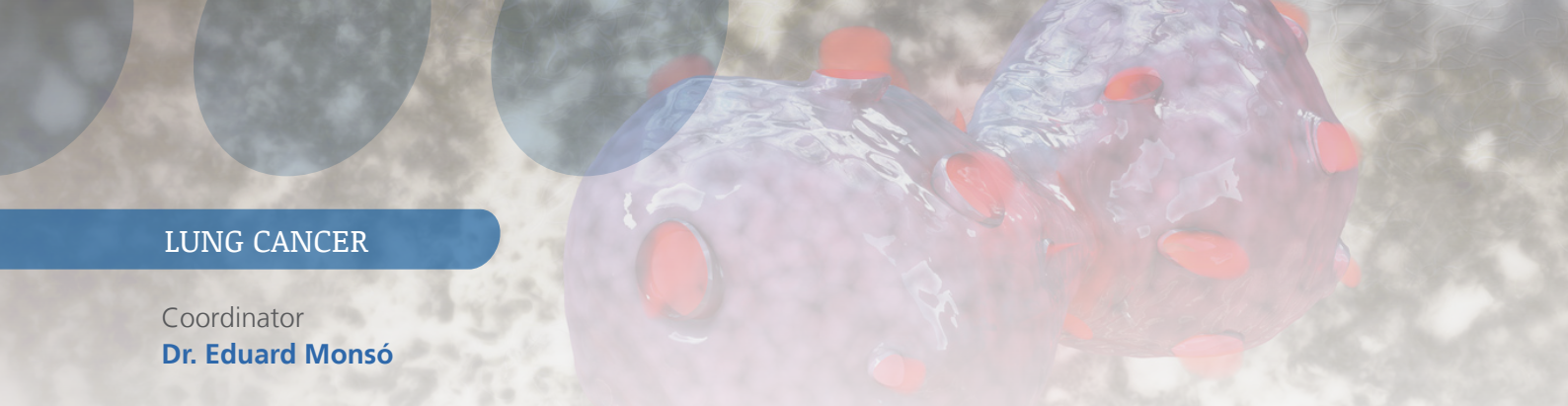
Main results until the end of 2014

CLINICAL GUIDELINES:

- Bousquet J, Schünemann HJ, Samolinski B, et al. World Health Organization Collaborating Center for Asthma and Rhinitis. Allergic Rhi- nitis and its Impact on Asthma (ARIA): achievements in 10 years and future needs. J Allergy Clin Immunol. 2012 Nov;130(5):1049-62.
- Montoro J, Del Cuvillo A, Mullol J, Molina X, Bartra J, Dávila I, Ferrer M, Jáuregui I, Sastre J, Valero A . Validation of the modified allergic rhinitis and its impact on asthma (ARIA) severity classification in allergic rhinitis children: the PEDRIAL study. Allergy. 2012 Nov;67(11):1437-42.
- Barranco P, Pérez-Francés C, Quirce S, Gómez-Torrijos E, Cárdenas R, Sánchez-García S, Rodríguez-Fernández F, Campo P, Olaguibel JM, Delgado J; Consensus document on the diagnosis of severe uncontrolled asthma. Severe Asthma Working Group of the SEAIC Asthma Committee. J Investig Allergol Clin Immunol. 2012; 22:460-75.
- Moscato G, Pala G, Barnig C, De Blay F, Del Giacco SR, Folletti I, Heffler E, Maestrelli P, Pauli G, Perfetti L, Quirce S, Sastre J, Siracusa A, Walusiak-Skorupa J, van Wjik RG. EAACI consensus statement for investigation of work-rela- ted asthma in non- specialized centres. Allergy. 2012 Apr;67(4):491-501.
- Van Kampen V, de Biay F, Folletti i, et all. EAACI position paper: skin prick testing in the diagnosis of occupational type I allergies. Allergy. Mayo de 2013;68(5):580-4.
- Siracusa A, de Biay F, Folletti i, et all. Asthma and exposure to cleaning products - a European Academy of Allergy and Clinical Immunology task force consensus statement. Allergy. Diciembre de 2013;68(12):1532-45.
- Canonica GW, Ansotegui iJ, Pawannkar R, et all. A WAO - ARIA - GA2LEN consensus document on molecular-based allergy diagnostics. World Allergy Organ J. 3 de octubre de 2013;6(1):17.

PATENT:

- ENGINEERED STEM CELLS AND THEIR THERA- PEUTIC USE Inventores: Josep Maria Aran, Itziar Martínez, María Jesús Cruz, Xavier Muñoz, Joan Ramón Masclans, Oriol Roca . No de solicitud: EP11382362 .9 Entidades titulares: IDIBELL / Institut de Recerca Vall d'Hebron / CIBER Enfermedades Respiratorias (CIBERES) . País de prioridad: España Fecha de prioridad: 24 de Noviembre de 2011 Países a los que se ha extendido: Europa Empresa/s que la están explotando: Histocell.



Coordinator
Dr. Eduard Monsó

Clinical and molecular characterization of early-stage lung cancer (lc).

LC is an important disease on account of its high incidence and severity, and on the level of associated mortality. In contrast to the response obtained with other solid tumours and despite an enormous research effort, the prognosis for LC has improved only slightly in recent decades, with a 5-year survival less than 15%.

The typology of LC is defined by anatomo-pathological criteria that initially differentiate LC as small cell carcinoma and NSCLC, with the latter further classified as adenocarcinoma, squamous cell carcinoma and large cell carcinoma. In a proportion of NSCLC cases this differentiation is not possible, with the carcinoma remaining as undifferentiated. Immunohistochemical markers can be used to clarify in part the situation, but uncertainty in the estimation of prognosis and response to treatment is high. The incorporation of prognostic molecular markers, such as epidermal growth factor receptor (EGFR) in tumour cells, which modulates a different therapeutic response when a mutation is present, has led to significant changes in treatment regimens used in NSCLC, which have been incorporated into clinical guidelines.

Early identification of the disease favours the use of therapeutic interventions associated with prolonged survival. The TNM system of staging according to the degree of extension of the primary tumour (T), lymph nodes (N) and metastasis (M) has been and is important, but is imprecise in relation to the prognosis and treatment selection. The percentage variation in survival with the TNM model is only 30%, with each patient's prognosis depending on poorly known determinants. In fact, in patients considered to have early-stage LC, there has barely been any reduction over the last 30 years in mortality and relapse. In cases that have been resected and staged as Ip, without evidence of lymph node or systemic metastases at baseline, very high rates (35-50%) of mortality or relapse are seen during follow-up. Moreover, despite the benefits seen with the use of platinum-based adjuvant chemotherapy in cases of advanced stages, the available data do not support the use of such treatment in patients with stage IA cancer and show very questionable results in patients with stage IB cancer. **It seems clear that TNM staging based on tumour extension conceals in its apparent homogeneity a considerable level of biological heterogeneity of the tumour or tumour-host relationship, which is evidenced in terms of prognosis and prediction.**

The inclusion of new predictive molecular variables to the staging of LC could be a promising approach to improve establishment of the prognosis and prediction of treatment response, in addition and complementarily to the TNM; such an approach could be easily incorporated into clinical practice guidelines and could enable alternative therapies to be defined beyond those currently in use. Numerous studies have addressed this problem, with inconclusive or contradictory outcomes. The cause resides in complexity and difficulty of the problem being studied, the methods used, studies with very specific scientific objectives, small case series, and results not validated in independent, external cohorts.

The SP-LC project within the CIBERES CRP aims to produce valid and useful knowledge from specific scientific objectives, avoiding the methodological problems that have placed in question the results of previous studies. The CRP also proposes, in addition to using the GCCP-II-IASLC Cohort, to generate a CIBERES Cohort, a case series of patients diagnosed with LC of squamous or adenocarcinoma cell lineage, and staged post-resection as I/IIp. Samples will include tumour tissue, non-tumorous pulmonary tissue, lymph nodes and peripheral blood, apart from the collection of clinicopathological characteristics of the patient at the time of treatment and following the evolution of patients included in the prospective cohort at two and five years following treatment, with information about disease-free time and survival. This will involve only those hospitals with a thoracic surgery unit and associated with SEPAR (N = 53).

The CIBERES SP-LC aims to create a cohort of patients diagnosed with LC by screening with LR-CT. An Early

COPD Cohort will be generated in the CIBERES Strategic Project on COPD. The objective of this work is to clinically and molecularly characterize patients with LC in this Cohort, to establish links between LC and COPD, and to verify molecular variables that differentiate cases identified by screening from cases diagnosed in clinical practice.

Aims and objectives

1. **To identify a set of clinico-molecular variables that improve the prognostic and predictive capacity of the TNM staging in LC.**

   Analysis of biological and molecular variables that have prognostic and/or predictive value with respect the therapeutic response, independently of TNM staging, in tumour samples, pulmonary tissue, lymph nodes and peripheral blood will include:

   - Epigenetics, according to the methylation pattern of chosen genes
   - Immunohistochemistry, determining alterations of the stroma.
   - Analysis of inflammation and oxidative stress, by measuring biomarker levels in tumour tissue and blood

2. **To validate in a population of smokers with COPD screening techniques developed for the general population, and to validate in the former population prognostic and predictive clinic-molecular variables.**

   The specific aims for this population are:

   - To create a high-performance cost-effective screening methodology for stage I/IIp LC.
   - To identify biological and molecular variables with potential prognostic and/or predictive value independently of the pathological TNM, in samples of tumour tissue, non-tumour lung tissue, lymph nodes and peripheral blood from patients with squamous/adenocarcinoma-type NSCLC, identified by a screening programme.
   - To identify biological variables associated with the early diagnosis of NSCLC by screening (Early-COPD Cohort), compared with the usual care clinical diagnosis (GCCP-II-IASLC and CIBERES Cohorts).
   - To study the potential correlation between the activity of molecular variables for COPD and LC.

Main results until the end of 2014

- Confirmation of the prognostic usefulness of the epigenetic analysis of tumour cells obtained by semi-invasive techniques and processes as a cell block.
- Definition of markers related to patient mortality in stages II and III, identified with this type of cytological approach.
- The Programme has successfully created a tumour tissue biobank containing tumour tissues from patients included in the International Association for the Study of Lung Cancer (IASLC) Cohort and in follow-up until 2016. It has over 250 samples available for the analysis of biological markers with potential prognostic capacity. Baseline clinical information of the patients included in this Cohort living in this territory was published by CIBERES researchers participating in the Programme (Sanchez of Cos J. Arch Bronconeumol [Barc] 2013) in 2013.

In the technological Innovations Line the Cancer CRP can show the following results:

- GUIBRO Project. Seventy-five (75) patients recruited with SPN, studied with ultra-fine bronchoscopy and radial EBUS. The preliminary results were presented in a correlative manner in conferences

of SEPAR, AEER (Asociación Española de Endoscopia Respiratoria), the World Association for Bronchology and Interventional Pulmonology (WABIP) and the ERS conference. The Robotics Group of the Facultad de Ingeniería Industrial of the Universitat Politècnica de Catalunya (UPC) has obtained from Amira© software (Visage Imaging) a 3D model with the possibility of navigation with a haptic device on a reconstruction of a real patient. The bases of this first phase were presented in worldwide robotics conferences.

- IBE-RM (Ibérica-Rapid Manufacturing) project. Collaboration with the Escuela Politécnica Superior de Mondragón and the Centro de Investigación de Lortek (Gipuzkoa) led to an online prosthesis design and parameterization system based on open software. In turn, the process for the analysis of a customised prosthesis was developed with the Facultat d'Ingenyeria of the Universitat de Girona. In parallel, in vitro bacteriological experiments of impregnation of silicone plates with silver.

PATENT:

- Procedimiento de generación de un recorrido para una broncoscopia virtual. Application/publication code: P20122230732

Coordinator
Dr. Borja G. Cosío

Defining biologic activity in copd: from the fragile patient to the early stage of the disease

It is necessary to study patients with early COPD for the understanding of **the natural history of the disease and for the design of therapeutic interventions with potential to modify its prognosis**. COPD is a highly prevalent disease affecting about 44 million people in Europe. In contrast to other major causes of death, its prevalence has been increasing in the past three decades. However, the natural history of COPD is still poorly understood, which limits the targets for intervention. The heterogeneous nature of COPD has led to the proposal that there might be different natural histories with different pathogenetic mechanisms in COPD. Indeed, the ECLIPSE study has shown that this accelerated loss of lung function is not present in 40% of patients diagnosed and treated for COPD. There are many questions about the natural history of the disease unresolved, such as the effect of lung development during childhood and adolescence on the future risk of COPD, the progression or activity of the disease from early stages, the role of bronchial hyperresponsiveness, the role of infection, among others. **The lack of a reliable animal model has contributed to maintain this problem. Also, little is known about the early stages of COPD because most patients are either never diagnosed or diagnosed at the age of sixty** when they already have moderate to severe disease. Furthermore the diagnosis of COPD is associated with a poorer quality of life and to a greater use of health resources.

There is a need for biomarkers of disease progression even in animal models. A number of attempts have been made in the last decade to obtain suitable biomarkers of COPD and its different associated conditions. However, only a general approach to this objective, with no really wide clinical applicability, has been achieved. The fact that only a limited number of molecules have been explored so far, especially in the area of inflammatory activity, may account for such a shortcoming. Despite these considerations, there are still interesting new possibilities such as those concerning lung injury, and the structure and metabolism of vascular and muscular tissues, among others. It is therefore necessary to identify biological markers of progression and of upmost importance to define and validate the concept of disease activity in COPD.

The role of COPD exacerbations and airway infection on disease activity is unknown.

COPD exacerbations are intermittent events occurring in the course of this disease. They speed the progression of the disease, reduce health-related quality of life and are associated with significant mortality, which can all translate into disease activity. The role of treatment on disease activity is unknown. A recent European audit showed that delivery of care based on the differences of resources revealed a huge inequality of care throughout Europe. As a consequence the outcome of COPD in terms of readmission rate and mortality within 90 days is alarming, and several factors have been identified. To study fragile patients cohorts in which these factors are present is required.

Infection and colonization of the tracheobronchial tree may be related to biological activity of the disease. Strong evidence implicates bacterial infection in the course and pathogenesis of COPD: (i) changes in the respiratory microbiome of COPD patients compared to healthy individuals have been reported; (ii) chronic and recurrent infection is associated to chronic bronchitis, to increased risk of exacerbation, and to accelerated loss of lung function, which may be translating into activity.; (iii) COPD infectious exacerbation is a frequent cause of death.

In this context, we hypothesize that COPD has different levels of activity that lead to different natural histories of the disease, ranging from the asymptomatic patient with preserved lung function along time with little or no exacerbations to the fragile symptomatic patient with accelerated loss of lung function

and frequent exacerbations. **The more fragile patients will show the most prominent markers of COPD activity that can be later applied to a cohort of early COPD patients in order to predict the type of progression**. Markers of activity can be identified in the clinical, biopathology, microbiology and imaging domains.

Aims and objectives

The main aim of this project is to demonstrate and define properly the concept of biologic activity in COPD as the undergoing mechanism that leads to differential evolution of disease, ranging from the low activity with low impact and low progression of disease to the high activity with high impact and rapid progression. As starting point, it is assumed that the fragile patients with more severe disease are those in which the disease is-or has been-more active. For that reason, this project plans to explore the concept of activity in a fragile COPD population from the clinical, microbiologic and experimental point of view as a first step, and subsequently apply the information obtained from them into a population at early stages of disease. Mechanistic studies in animal models of fragile, early COPD and microbial infection will help to probe the hypothesis generated from the clinical studies. To achieve this general goal, the following specific objectives will be pursued:

1- **To validate frailty criteria in relation to prognosis and evaluate the impact** of different Health Care approaches to management on disease activity by generating a fragile COPD cohort.

2- **To analyse clinical, imaging and biological** markers of activity as determinants of disease progression and severity in fragile COPD patients.

3- **To identify microbiology patterns or changes** within the pathogen or the host associated to disease progression in Fragile COPD patients.

4- To investigate potential markers of activity in animal models.

5- To integrate the previously identified markers of activity in fragile patients into a cohort of early COPD patients in order to **identify the patients with more active disease and faster progression**.

Main results until the end of 2014

Participation in the writing and editing of the review entitled "Global initiative for chronic obstructive lung disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease". It is the most important world reference for the clinical management of COPD. Accessible at the following address: www.goldcopd.org.

CLINICAL GUIDELINES AND RECOMMENDATIONS:

- Ram FS, Rodríguez-Roisin R, Granados-Navarrete A, García- Aymerich J, Barnes NC. WITHDRAWN: Antibioticsforexacerbations of chronic obstructive pulmonary disease. Documento publicado en la Cochrane Database Syst Rev. 2011; 1: CD004403.
- Luján M, Sogo A, Monsó E. Home Mechanical Ventilation - Monitoring Software: Measure More or Measure Better? Arch Bronconeumol. 2011 Dec 27. [Epub ahead of print]
- Informe: - AUDIPOC: Auditoría Clínica Nacional sobre - exacerbaciones de la EPOC en España. Proyecto coordinado. Subproyecto AUDIPOC Cataluña. E. Monso, Martínez-Rivera, C, Pozo P, Álvarez, C; Capelastegui, A; Hernández, C; Izquierdo, Jk. Haro, M, Antón, PA; Hernández, C; Rodríguez,E; Lloret, JA; Rodríguez, N; Rozadilla, J.

- Comercialización de la válvula ORYGEN Dual©, cuya propiedad intelectual pertenece a 2 miembros del CIBERES (M. Orozco- Levi & J. Gea, patente en 2010).
- Spin-off: Empresa LungOn destinada a comercializar la válvula de entrenamiento de músculos respiratorios que fue patentada por el Group 22 de CIBERES en el año 2011.

Coordinators
Dr. Juncal Garmendia & **Dr. José A. Melero**

Respiratory infections: from mechanisms to therapeutics

The main strategy for fighting infectious diseases has focused on targeting enzymes from pathogens with antibiotics. The rapid development of resistance shortens the life span of a therapeutic agent, leading to decreased interest of the industry to develop new agents because the costs are prohibitive compared to the economic potential of the drug. Moreover, there is an urgent need for specific antiviral therapies. Therefore, there is a need to develop effective therapeutics based on new targets/approaches and to develop efficient prophylactic measures. Importantly, the Spanish Research Plan and the next European research plan, Horizon 2020, consider respiratory infections and development of new therapies as a research priority.

The new project builds on the knowledge generated in the previous Research Programme. **It makes a major effort to analyse the transcriptome of alveolar macrophages infected with different pathogens**. Analysis of data is currently underway. Interesting results include the induction of antiviral responses by bacteria-infected macrophages and the activation of lipid metabolism in infected macrophages, independently of the pathogen used. These results open new avenues of research to fight infections. Collaborative efforts have also revealed new mechanisms of host-pathogen interaction and similarities between bacterial and viral strategies. Furthermore, the Programme has set up a microarray platform for the study of glycan-pathogen interactions that leads to the identification of some galectins interacting specifically with some pathogens. We also studied the lung surfactant modulation of the inflammatory response in airway epithelial cells infected by respiratory syncytial virus and other pathogens.

The project is divided into 6 work packages. Three of these are meant to pursue ambitious objectives at the forefront of research in infection biology. Importantly, one of these WPs aims to capitalize on the knowledge generated to develop new therapies. Therefore, the first pre-clinical studies have been planned.

ADDED VALUE

Our project focuses on important respiratory pathogens with different infection strategies. We employ an alveolar macrophage cell line as a common denominator in all our investigations, and we focus on common cell targets (pattern recognition receptors-mediated recognition, inflammatory responses, and IFN-induced defence responses) in order to reveal common schemes and principal differences of microbial infection strategies. These studies will allow the design of patient-customized therapeutic treatments. The project provides the required critical mass to carry out the research and developmental activities by joining leading scientists from important institutions in infection biology in Spain. Our work produces synergies based on:

- Distinct but complementary expertise of partners from the disciplines of microbiology, immunology, and cell biology.
- Common use of the established knock-out cells, reagents, and platforms.
- Indicator cell lines, tests and developed common reading systems with different pathogens.

The partners will work in a cooperative and supportive way. All WPs are set up in such a way that success is absolutely contingent on close interaction and collaboration.

Aims and objectives

In order to better understand how pathogens stimulate, inhibit, and manipulate host cell functions, we will analyse bacteria (K. pneumoniae, Haemophilus influenzae no tipable, S. pneumoniae, M. tuberculosis, S. aureus) and viruses (Influenza A viruses, paramyxoviruses, and respiratory syncytial virus) specified by various infection strategies. Analysis of pathways targeted by pathogens may reveal the strategies used to subvert immune responses and lead to the identification of the various Achilles heels of host defence. Although the immunomodulatory mechanisms used by viruses and bacteria may appear to be quite different, pathogens have to overcome the same host immune defences. Hence it is not surprising that there may be shared mechanisms. Consequently, the identification of a central core of systems implicated in host defence against several pathogens, which could be targeted for therapeutic manipulation, is an important goal of this project.

Our main hypothesis is that there is a common host response to infections associated with the clearance of the pathogen. In turn, pathogens try to counteract this response using conceptually similar but physically distinct processes. On the other hand, different signals (mediated by innate immune molecules and/or drugs) can tip the balance of this response, thereby affecting the outcome of the host-pathogen interaction.

The main objectives of our Programme are:

1. To **identify anti-immune strategies of different pathogens, focusing on their ability to modulate gene expression and hence cellular function via the manipulation of innate immune response.**
2. To **analyse the activation of pattern recognition receptors upon infection** with emphasis on these receptors launching IFN-dependent responses and controlling viral infections.
3. To **identify a set of IFN-dependent anti-infection determinants that might be common to viruses and bacteria.**
4. To **evaluate the impact of molecules of the innate immune system** (galectins and surfactant) on host-pathogen interactions.
5. To **uncover strategies to avoid intracellular killing**.

Main results until the end of 2014

- Discovery of neutralising antibodies against the pre-fusion conformation of the fusion (F) protein of the human respiratory syncytial virus (PNAS, 109, 3089-3094, 2012), which have shown great neutralising strength of this virus and represent most of the neutralising activity present in human sera.
- Pioneer analysis of the lipid A structure of the Gram-negative pathogen Klebsiella pneumoniae during an in vivo respiratory infection. It is the first study of this type that can be applied to other Gram-negative pathogens of clinical interest.
- Implementation of a new method for using bacteria microarrays as sensitive tools for exploring pathogen surface epitopes and recognition by host receptors (Campanero-Rhodes et al., RSC Advances 2015).
- Determination of the three-dimensional structure of ribonucleoproteins of the flu virus (Arranz et al., Science 338 1634, 2012).
- Identification of the attenuation and protection mechanism conferred by mutation in the *Mycobacterium tuberculosis* phoP gene (Solans *et al.*, Plos Pathogen 2014), the basis for the experimental vaccination MTBVAC, currently in clinical trial phase.

- Description of a mutation in the PhoP/R operon of M. tuberculosis involved in the species-specificity of the strains infecting animals and humans (Gonzalo-Asensio et al., PNAS2014).
- Development of new antimicrobials based on phage enzymes (Díaz-Martínez et al., Antimicrob. Agents Chemother 2013).
- Dissection of the therapeutic interference of the administration of the macrolide azithromycin in respiratory infection due to *Haemophilus influenzae*, a bacterial pathogen associated with the progression of COPD (Euba et al., Ant Agents Chemother, 2015).
- Dissection of the role of structures of bacterial surfaces (lipopolysaccharide and adhesins), and of an array of functions of the respiratory epithelium during infection due to *Haemophilus influenzae*, a pathogen associated with the progression of COPD (Morey *et al*., Microbiology 2011; López-Gómez *et al*., Microbiology 2012; Morey et al., Infect & Immunity 2013; Euba et al., PLoS One, 2015).
- First genomic study of the adaptive evolution of the pathogen *Haemophilus influenzae* in the respiratory system of a COPD patient which has disclosed a repertoire of new antimicrobial targets currently being studied (Garmendia *et al*., PLoS One, 2014).
- First study of the characterisation of the lifecycle of the pathogen *Staphylococcus aureus* in the alveolar macrophage.
- Demonstration of the antimicrobial effect of seconeolitsine on DNA topoisomerase I of *Staphylococcus aureus*.

Coordinator
Dr. Antoni Torres

Multidisciplinary translational research in respiratory tract infections.

Severe acute respiratory infection (SARI) is the leading global cause of morbidity and mortality from infectious diseases. Under this term, **we include severe community-acquired pneumonia (sCAP) and other community-acquired infections requiring admission to intensive care unit**. Severe community-acquired pneumonia (sCAP) is a current major health concern. Despite the introduction of antibiotic agents (1950s), the outcome of sCAP has shown little improvement in the past 3 decades and remains between 25% and 40% in patients admitted to the intensive care unit (ICU).

Hospital-acquired pneumonia (HAP) is currently the second most common nosocomial infection, and is associated with high mortality and morbidity. The presence of HAP increases hospital stay by an average of 7 to 9 days per patient and has been reported to produce an excess cost of more than $40,000 per patient. Incidence increases by as much as 6- to 20-fold in mechanically ventilated patients, and in this case we call these Ventilator-associated respiratory infections (VARI) such as pneumonia, tracheobronchitis and other bronchopulmonary infections.

At present, the emphasis in the field of SARI and VARI should be on effective prevention measures, rapid diagnosis techniques and adequate clinical management tools and treatment. **Our group intends to perform activities that will allow us to better understand the current epidemiology, patterns of care and treatment, and patient outcomes**. Furthermore we plan to undertake studies to improve the diagnosis of SARI/VARI (focusing on rapid tests and using biomarkers as selective predictors of respiratory infection) and **in terms of treatment we will prioritize optimizing the dosage of currently used antibiotics for respiratory infections and investigating the value of biomarkers for enhancing therapy** in SARI/VARI as well as finding new targets for S. pneumoniae. As DNA topoisomerases and choline-binding proteins fulfil this requirement, they are attractive targets for the treatment of pneumococcal diseases. Furthermore, we have done an initial screening of the Prestwick Chemical Library **finding six hits (not including known antibiotics)** that appear to inhibit the growth of S. pneumoniae at submillimolar concentrations. If the antimicrobial activity of all these compounds is confirmed, these hits would be tested using in vitro (planktonic or biofilm) and in vivo (animal models of infection)

We also plan to **approach emerging pathogens causing severe respiratory infections** or those that seem to complicate existing respiratory co-morbidities, such as *C. difficile*.

Finally, since this is major problem, we want to place a major emphasis on prevention and patient safety by investigating care-bundles in VARI.

Aims and objectives

The principal aims of this programme are:

1. To study the **risk, and prognosis factors of severe acute community-acquired and ICU-acquired respiratory infections in Spain, including biomarkers and genetic factors**.
2. To study risk, and **prognosis of community-acquired and hospital acquired respiratory infections in patients not admitted to the ICU in Spain, also including biomarkers.**
3. To study in depth the microbial etiology and resistances of all the populations mentioned above. In this objective we will include the investigation of new rapid molecular techniques.

4. To study whether the **implementation of educational programmes** and bundles may decrease the incidence of hospital-acquired pneumonia inside and outside the ICU.
5. To investigate the **best way to treat multiresistant microorganisms**.
6. To investigate the **epidemiology, virulence, inflammatory response and clinical outcomes of serotypes of S. pneumoniae causing invasive disease before and after the introduction of the new vaccine PVC 13**.
7. To investigate new **mechanisms of virulence, resistance and treatment of *S. pneumoniae***.
8. To use **our available animal models of severe pneumonia** (*P. aeruginosa, MR S. aureus* and *S. pneumoniae*) for translational research.
9. To develop **new clinical guidelines** for the management of community-acquired pneumonia, hospital-acquired pneumonia and ventilator-associated pneumonia.

Main results until the end of 2014

Between 2011 and 2014 papers have been published in high-impact factor journals and in the first decile the results of which will modify clinical practice. A large number of papers in the area of community-acquired pneumonia and Health Care Associated Pneumonia, in the area of VAP and HAP and major microbiological papers and papers on basic research in pneumococcus must be highlighted. In December 2014 a paper was published in the JAMA which is going to be fundamental in clinical practice (JAMA 2015 Feb 17;313(7):677-86). Furthermore, a new international clinical guideline (Clin Microbiol Infect. 2015 Jan 14) published by CIBERES members must be highlighted.

OTHER CLINICAL GUIDELINES:

- Guía multidisciplinar para la valoración pronostica, diagnóstico y tratamiento de la neumonía adquirida en la comunidad. Antoni Torres*, José Barberán, Miquel Falguera, Rosario Menéndez, Jesús Molina, Pedro Olaechea Y Alejandro Rodríguez, en nombre del Group de la Guía Multidisciplinar para el Manejo de la Neumonía Adquirida en la Comunidad; 1,2 Med Clin (Barc). 2013;140(5):223.e1–223.e19.
- A care bundle approach for prevención of ventilator-associated pneumonia. Rello J, Afonso E, Lisboa T et all. Investigadores del proyecto FADO. Clin Microbiol Infect. Abril de 2013; 19(4):363-9.

PATENTS AND UTILITY MODELS:

- Inventors (by order of signature): Adela González de la Campa, María Teresa García Esteban, María Amparo Blázquez Ferrer. Title: "Uso de Seconeolitsina y N-Metil-Seconeolitsina para la fabricación de medicamentos" (Use of seconeolitsine and n-methyl-seconeolitsine for the manufacture of medicaments). Application no.: P200931186. Country of priority: Spain. Priority date: 17/December/2010. Proprietor: Instituto de Salud Carlos III, Universidad de Valencia and Consejo Superior de Investigaciones Científicas. Countries to which the patent is extended: International application according to the Patent Cooperation Treaty (PCT): PCT/ES2010/070808. Date: 23/June/2011

Coordinator
Dr. María Molina

Cell plasticity and microenvironment in lung fibrosis: looking for its regulation as a potential treatment

Idiopathic pulmonary Fibrosis (IPF) is the most lethal interstitial lung disease (ILD), with no effective treatment and a mean survival of 2-4 years from the diagnosis. The histological defined pattern is the usual interstitial pneumonia (UIP), characterized by the loss of epithelial structures, interstitial collagenized fibrosis, microscopic honeycombing, and focal areas of "fibroblast foci". The current pathogenic **hypothesis posited epithelial injury and impaired wound repair as the etiology of fibrosis**. The initial cause is unknown, but genetic factors have been found to be associated such as telomerase gene mutations, which imply an impaired cell turnover and aging. IPF is characterized by a reactive stroma surrounding the altered alveolar epithelial units that exhibits a spatial accumulation of fibroblasts and myofibroblasts. The imbalance between the increase of pro-fibrotic growth factors, such as transforming growth factor beta1 (TGF-□1), angiotensin-II (ANGII), or reactive oxygen species (ROS), and the decrease of anti-fibrotic mediators such as prostaglandin-E2 (PGE-2), enhance the perpetuation of the process. Despite advances in the knowledge of fibrotic pathogenesis, the complex and potentially therapeutically relevant relationship and interactions between the containing cells and ECM remain poorly understood.

CELL REGENERATING ANSWER TO TISSUE DAMAGE.

Pneumocyte loss is followed by attempted tissue regeneration and exaggerated release of molecular signals triggering fibroblast proliferation and migration. The increased activation of the Wnt-pathway signalling in IPF is directly related to abnormal myofibroblast activity and epithelial-mesenchymal transition (EMT). They have been a number of studies characterising population of stem cells in lung, as well as markers of EMT and MET and their implication in the fibrotic process. So far, though, LRSC's of whatever origin have not been characterized in human diseased lungs. On the other hand, in animal model, introduction of MSCs into the lungs ameliorates bleomycin injury since a BM-MSCs subpopulation provides protection from lung injury. These data **suggest that different MSCs subpopulations can significantly modulate the onset of a fibrogenic response**.

INTERSTITIAL HALLMARKS OF THE ALTERED WOUND HEALING IN IPF..

Progressive tissue distortion and hardening in fibrosis have been associated with abnormal wound healing. Thus, in normal physiological conditions our organism can repair epithelial injury by forming a provisional structure generated by ECM protein deposition, fibroblast proliferation and transient myofibroblast activation. Completion of injury repair is followed by degradation of the provisional ECM and apoptosis of myofibroblasts. In pathologic conditions, some glycoprotein ECM components remain increased, collagen I and III are not degraded; myofibroblasts evade apoptosis and develop dysfunctional repair mechanisms. The contributions of the different environmental alterations during dysfunctional repair to tissue scar are likely to depend on the particular disease and organ, and overall remain poorly understood. Our group has recently demonstrated abnormally high levels of ECM components in IPF lungs that are implicated in tissue remodelling (cell adhesion, fibroblast migration). Myofibroblasts are interstitial key effector cells in pulmonary fibrosis that can be derived from resident fibroblasts undergoing fibroblast-to-myofibroblast transformation (FMT), alveolar epithelial-to-mesenchymal transition (EMT), mesenchymal stem cells (MSCs) or even endothelial cells (EnMT). FMT is characterized by a dramatic increase in wound ECM components including collagens and glycoproteins. Extracellular microenvironment can regulate FMT and EMT. Based on these observations **it is tempting to speculate that there is a positive feedback loop between cell**

and extracellular-dependent microenvironment. Although EnMT has been less studied, it has been included as one of the different cellular process characteristics in the remodelling of pulmonary hypertension (PH)-associated IPF, together with endothelial dysfunction. PH in IPF portends a poor prognosis.

ADVANCED 3D CELL CULTURE MODEL FOR THE STUDY OF CELL-ECM PROTEIN INTERACTIONS

Traditional approaches to study IPF include conventional 2D culture systems, which lack essential components of the original tissue, and animal models that contain the full complexity of the tissue but lack the irreversible behaviour of IPF. There is wide evidence that cells grown in 3D cultures with appropriate ECM components retain many of their phenotypic characteristics, thereby behaving more closely to their in vivo conditions. **Our programme is working in a 3D culture model.**

Aims and objectives

1. **To study glycoprotein effect on primary human lung alveolar and mesenchymal cells** (migration, metabolism and differentiation) and the regulation of its synthesis in fibro-myofibroblasts .
2. To **evaluate the differences in cell behaviour and experimental results depending on telomere length and telomerase gene mutations**.
3. To **identify, characterize and assess, in vitro, the functional status and the regenerative/ reparative capacity of both hLRSC**, including lung-hMSCs and BM-hMSCs, from patients with IPF, compared to those obtained from subjects with normal lung function.
4. **Compare in these cells released factors related to signalling pathways** that induce proliferative and fibrogenic features of pulmonary target cells.
5. To **investigate the remodelling of those vascular structural cells from patients with PH complicating IPF**, and its possible regulation through some inhibitors.
6. To **study aquoporin system in lung fibrosis** and its modulation depending on the cell type and environmental growing conditions.

Main results until the end of 2014

In reference to CIBERES CRPs, the Pulmonary Fibrosis Programme highlights the following as its relevant results for the scientific and clinical community:

Interstitial pulmonary diseases constitute a group of rare or minority diseases affecting the interstitium and overall account for 15% of all respiratory diseases, being the most prevalent and lethal being idiopathic pulmonary fibrosis (IPF).

The incidence and prevalence of IPF has increased in recent years (3-6.8 /100000/year and 13-20/100000/ year, respectively), and other fibrosing pulmonary diseases have been detected which, although more slowly, also lead to respiratory failure and death of the patient. Mean survival media in IPF is 3-5 years from diagnosis and there is still no cure or treatment that allows stopping the progression of the disease. However, recent advancements in the knowledge on the pathogenesis of the disease and clinical trials conducted up until now, in which the coordinated Pulmonary Fibrosis programme has contributed, has led to the appearance of new anti-fibrotic treatments, nintedanib and Pirfenidone, which slow the progression of the disease and have completely modified the therapeutic approach of these patients (published clinical trial results, new drugs and therapeutic guidelines).

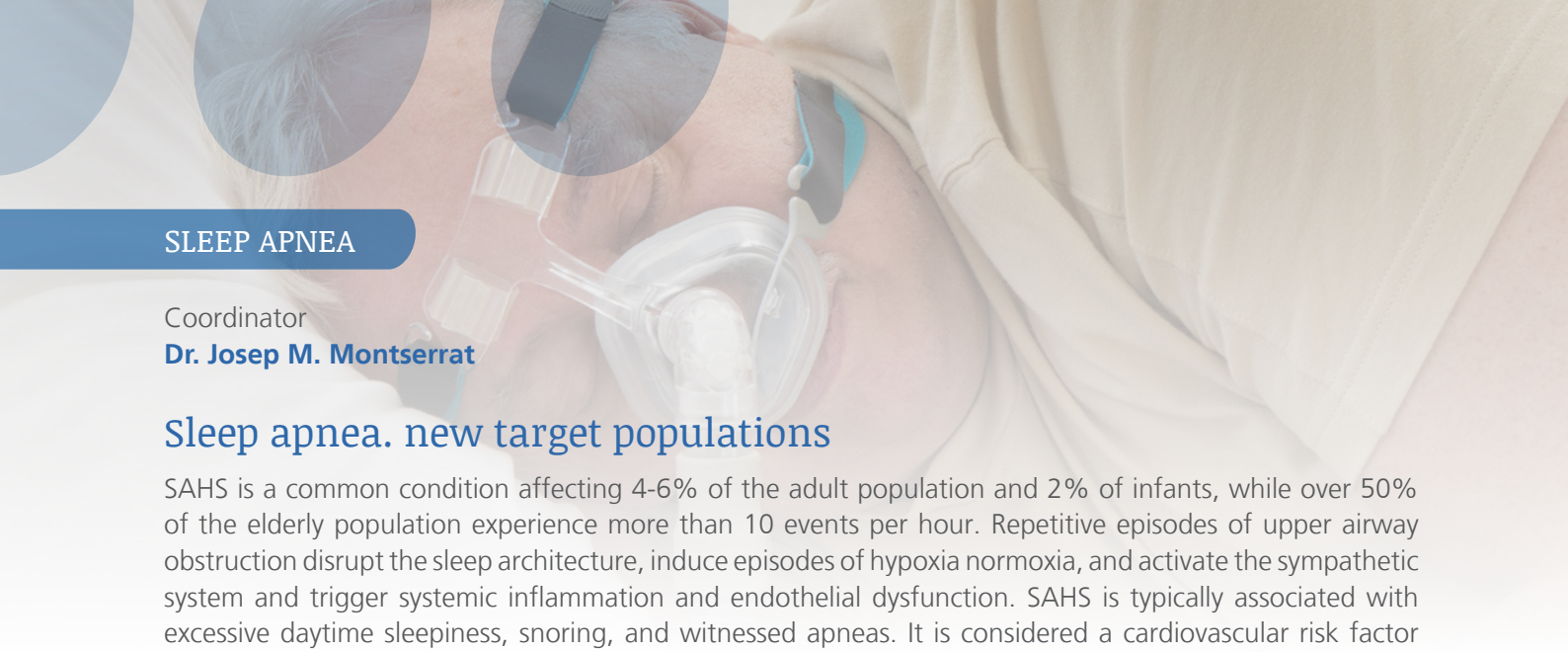
The objective of the current Pulmonary Fibrosis research SP is to understand some still unknown and relevant pathogenic aspects of pulmonary fibrogenesis associated with accelerated ageing as a predisposing factor in order to try to stop the progression or even prevent the development of the disease. Initial results have

demonstrated the role of specific extracellular matrix glycoproteins in fibroblast activity (fibroblast foci), such as tenascin-C, new fibrogenic pathways involved susceptible to being regulated and genetic aspects which can be regulated biologically (new anti-fibrotic approaches), which are reflected in references 10-26.

Furthermore, the Pulmonary Fibrosis programme has worked on technology transfer and innovation, as a result of which collaboration and transfer agreements have been entered into with other CIBERS (CIBER-BBN, CIBERER; 2012 CIBERES-CIBERBBN-SEPAR project, workshop 2013 CIBERER-CIBERES), and with technology transfer and innovation enterprises; Advanced Medical Projects (AMP, Madrid, Spain), Histocell (Bilbao, Spain) and bVentura (Mollet del Vallés, Barcelona, Spain). A patent on a new "medical device" in pulmonary fibrosis which is being evaluated has been drafted and filed (PCT/EP2015/050325).

OTHER RESULTS OF THE FIBROSIS CRP:

- Guía Española para el diagnóstico y tratamiento de FPI: Xaubet A, Ancoche A J, Bollo E, et al., Guidelines for the diagnosis and treatment of idiopathic pulmonary fibrosis. Sociedad Española de Neumología y Cirugía Torácica (SEPAR). Research Group on Diffuse Pulmonary Diseases. Arch Bronconeumol. August 2013; 49(8):343-53.37.



Coordinator
Dr. Josep M. Montserrat

Sleep apnea. new target populations

SAHS is a common condition affecting 4-6% of the adult population and 2% of infants, while over 50% of the elderly population experience more than 10 events per hour. Repetitive episodes of upper airway obstruction disrupt the sleep architecture, induce episodes of hypoxia normoxia, and activate the sympathetic system and trigger systemic inflammation and endothelial dysfunction. SAHS is typically associated with excessive daytime sleepiness, snoring, and witnessed apneas. It is considered a cardiovascular risk factor (hypertension) as it also induces metabolic deregulation. An incremental mortality has been described.

At this point in time the **whole research picture in Sleep Apneas is about to change in several very important ways**. In fact, some changes have occurred. Our data and those from other groups have now provided a good – or at least basic – guide to the management of most SAHS patients. Nevertheless, new works need to be done in a number of directions. Future research must embrace new mechanisms, clinical studies and technological approaches but also studies of transference to the health system to ensure cost-effective procedures, as well as transference to companies to ensure returns on research capital. Nowadays, a return on research capital is considered an essential component of a company's productivity and growth as well as Medicine 2 procedures are.

Furthermore, all the research to date has been performed on the adult population while other populations have been almost ignored. **The major aim of our new programme is to address this imbalance by investigating even more prevalent populations of SAHS, such as those associated with age (elderly or children), obesity such as the obesity hypoventilation syndrome, as well as other forms that have only recently come to light – such as cancer-related SAHS and acute coronary disease with SAHS**. All these topics could open up exciting new avenues of research.

The USA agency for Healthcare Research and Quality (AHRQ) (No. 12-EHC031-EF February 2012 published a list of recommendations with respect to future research needs. In our project we address many of these questions with some differences. **The research we have undertaken coincides with the recommendations of AHRQ especially those related to future research needs for the diagnosis and treatment of Obstructive Sleep Apnea (OSA)**. These recommendations reflect very closely not only our past research but also our current research in progress as well as the one proposed. **This programme tries to combine basic and clinical research together with cost-effectiveness, translational, transference and technological aspects to be able to produce return on the research capital invested as well as to use Medicine2 procedures**.

Key Questions need to be addressed:

1. Diagnosis

- Different diagnostic tests, subgroups of population or patients with different characteristics.
- How is phased testing working in sleep apnea diagnosis?. Role of new technologies.
- Long-term consequences and impact in the clinical management
- Studies facing clinical and basic aspects for the better understanding and the better management.
- To develop networks in order to detect better the patients (family and physicians among others).

2. Treatment

- Comparative effects of different sleep apnea treatments, depending on different characteristics (patient's personal characteristics, different physiological variables (SaO2), among others).
- Pre-treatment characteristics of patients and compliance.
- Interventions to improve compliance in different treatments. Role of telemedicine.
- To develop networks to improve management and control of sleep apnea and follow-up (nurses, family, physicians….)
- Non CPAP treatment of sleep apnea.

Aims and objectives

1. **Study the management and impact of sleep apnea in the new target populations mentioned above;**
2. **Develop new technologies to be applied in the diagnosis, treatment and follow up of patients with SAHS,**
3. **Work on transference protocols as well as a new cost-effective clinical protocols and**
4. **To start using the Medicine 2 system for working.**

Main results until the end of 2014

- Respiratory disorders during sleep have been associated for the first time with an increase in cancer incidence and mortality as well as with higher tumour aggressiveness.
- Refractory arterial hypertension is a growing health issue. The frequency of suffering SAHS in these patients is very high. The diagnosis and treatment of SAHS can significantly reduce blood pressure levels and will require a different clinical approach in managing these patients.
- Apnea models have been developed in completely original animals.
- Ample and validated development with new cost-effective strategies for managing SAHS that have changed clinical practice. These strategies also allow conducting sleep studies in rather uncommon environments (coronary units for example).

OTHER RESULTS OF THE APNEA CRP:

- Esquinas et Al. (2013). Rationale and Methodology of the Impact of Continuous Positive Airway Pressure on Patients With ACS and Nonsleepy OSA: The ISAACC Trial. Clinical cardiology, 36(9), OI:10,1002/clc.22166.
- Almendros I, Monserrat JM, Torres M, et all. Intermittent hypoxia increases melanoma metastasis to the lung in a mouse model of sleep apnea. Respir Physiol Neurbiol, 186 (2013) 303– 307.
- Campos-Rodriguez F, Martinez-García MA, Martinez M, Duran-Cantolla J, de La Peña M, Masdeu MJ, Gonzalez M, del Campo F, Gallego I, Marin JM, Barbe F, MontSerrAt JM, Farre R. Association between Obstructive Sleep Apnea and Cancer Incidence in a large multicenter Spanish Cohort. Am J Respir Crit Med, 2013; 187: 99-105.
- Almendros I, Wang Y, Becker l, Lennon Fe, ZHeng J, Coats Br, et all. Intermittent hipoxia-induced changes in tumor associated macrophages and tumor malignancy in a murine sleep apnea model. Submitted. Am J Respir Crit Care Med. 2014; 189: 593-601.
- Isetta V, León C, Torres M et all Telemedicine-based approach for obstructive sleep apnea management: building evidence. Interact J Med Res. 9 de febrero de 2014; 3(1):e6. doi: 10.2196/ ijmr.3060.

Coordinator
Dr. Vicente Ausina

New research and innovation on tuberculosis: basic research, prevention, drug regimens and diagnosis.

Tuberculosis (TB) is a major global health problem. Each year, there are around nine million new cases of TB, and close to two million deaths. All countries are affected, but 85% of cases occur in Africa (30%) and Asia (55%), while India and China alone represent 35% . TB is closely connected with HIV. People living with HIV, represent over 10% of annual TB cases, and are up to 37 times more likely to develop TB than people who are HIV-negative.

Yet TB is, in most instances, a curable disease. More than 90% of people with drug-susceptible TB can be cured in six months using combinations of first-line drugs. Treatment of multidrug-resistant TB (MDR-TB) is more challenging, requiring the use of second-line drugs that are more costly, cause more severe side-effects, and must be taken for up two years. Cure rates for MDR-TB are lower, typically ranging from 50% to 70%.

In 2006, the Stop TB Partnership launched the "Global Plan to Stop TB 2006-2015", a roadmap for scaling up prevention and treatment, for research and development, and for financing. By 2015, it is expected that we will have: point-of-care tests than can be used in health centres for diagnosing active TB, diagnosing latent TB infection and predicting the risk of progression to TB disease, and detecting drug resistance; a new, four-month TB treatment regimen for patients with drug-susceptible TB; at least one new drug on the marked for treatment of drug-resistant TB; a safer, higher-efficacy regimen for the treatment of latent TB infection; four new TB vaccine candidates in Phase III clinical trials for safety and efficacy. If no improvements in TB control are made, about 10 million people will die from TB by 2015.

This research programme is the result of evolution from previous versions of Corporate Research Programme on Tuberculosis since CIBERES consortium was established in 2006. **Some topics on the programme coincide with those listed in the "The Global Plan to Stop TB 2011-15".**

Aims and objectives

1. **Basic research. New approaches to the nature of latent tuberculosis infection (LTBI) and its treatment in experimental models.**

   LTBI affects one third of humanity, with the lack of clinical symptoms, in which case it may go unnoticed. However, approximately 10% of these cases develop into active disease. **The main problem is lack of understanding of the underlying mechanisms of the infection and the evolution of the active disease**. In spite of the classic theory to explain the origin and progression of LTBI, the data obtained in recent years have generated scientific doubts. On the other hand, to date, and despite the existence of very useful animal models to evaluate the different characteristics of the new therapeutic candidates, **the presence of a model that is able to faithfully imitate the infection and disease in humans has not been established**. An exception is, perhaps, the model in pigs, established by Cardona et al. Thus, research based on the development of animal experimental models plays an ever more essential role in terms of its importance for translation.

   In CIBERES researchers have been working in the field of basic research of latent tuberculosis infection since 1997. This work is essentially based on in an effort to determine its underlying mechanisms and novel a**nimal experimental models have been developed that can better imitate the infection and its progression into active disease** with the idea of being able

to use them in the assessment of new drug or vaccine candidates developed by other research groups, with which stable collaboration networks can be established to facilitate the evolution of these candidates into clinical development.

2. **Design and evaluation of new vaccine candidates against tuberculosis**

   The current BCG tuberculosis vaccine offers low protection against the respiratory forms of tuberculosis, among which are found the drug-resistant strains, as well as the high incidence of AIDS in third world countries and the difficulties in following treatment programmes, which makes a new, effective vaccine necessary to substitute the current BCG vaccine.

   Since 1999, our efforts have been invested in creating a new, attenuated tuberculosis vaccine, studying the test concepts and developing this new attenuated live vaccine. An attenuated vaccine has been created based on the double deletion of the genes phoP and fadD the **MTBVAC. The first vaccine based on attenuated M. tuberculosis satisfying the "Geneva consensus"** safety criteria for entry of new TB vaccines into clinical trials. Taken together, GMP production of freeze-dried MTBVAC and rigorous preclinical characterization from mouse to non-human primates provide the bases for entry into first-in-human clinical trials.

3. **Design and evaluation of new therapeutic strategies against tuberculosis (resistance, action and discovery of new drugs).**

   Anti-tuberculosis therapy constitutes one of the fundamental pillars in the battle against this disease. The success of the treatment can be compromised when the strains acquire resistance to any one of the drugs used in the treatment. Then the active drug arsenal against this disease is extremely limited. In addition various mechanisms of intrinsic drug resistance in M. tuberculosis could play a major role in favouring the acquisition of mutations that confer even greater levels of resistance.

   Based on these facts, **discovering new, active drugs against *M. tuberculosis* is one of the main priorities of tuberculosis research at a world level**. Insights have been made in the usefulness of efflux inhibitors have companion drugs in the therapy of tuberculosis.

4. **Design and evaluation of new diagnostic and molecular epidemiology methods in tuberculosis.**

   Effective control of TB is based on the rapid detection of M. tuberculosis, followed by the implementation of an adequate anti-tuberculosis therapy. As a result of several epidemiologic studies, new analytical challenges have been identified, for which a response must be given. Mainly, greater speed to obtain the genotypes, to identify the earliest transmission events, and thus facilitate the intervention is required. Likewise, the precision in identifying the transmission environment must be improved. CIBERES researchers have made important contributions in the diagnosis of latent TB infection and TB disease. Molecular techniques are essential tools to improve the control of tuberculosis. These techniques allow the strains to be differentiated from different clonal origins with greater efficiency.

Main results until the end of 2014

In the field of Tuberculosis, CIBERES highlights the following results:

- Development of a **new prophylactic tuberculosis vaccine (MTB VAC)** which can, in the near future, replace the current BCG vaccine. Phase I clinical trial was conducted in 2013 and phase II clinical trial is currently underway.
- Development and evaluation of a **new therapeutic tuberculosis vaccine (RUTI)**. Phase III clinical trials in South Africa have ended.

- In relation to this aspect, four patents have been generated (P200302551, P200602754, PCT/ES/2002/000381; PCT/ES/2007/070081) and the creation of two compagnies has been aided for the purpose of being able to market these vaccines.
- Other relevant achievements of the Programme to be highlighted according to the directives of the "Global Plan to Stop Tuberculosis 2006-2015" include the following:
  - Contribution of new knowledge about the intrinsic resistance mechanisms of *M. tuberculosis*, particularly in relation to "efflux pumps".
  - Development of new *M. tuberculosis* molecular typing techniques which allow faster and more efficient genotyping for epidemiological purposes.
  - Development of new experimental animal models to measure the virulence of *M. tuberculosis* strains that have led to papers written through the collaboration of several groups in the Programme.
  - Relevant contributions have also been made in the evaluation of new immunological techniques in the diagnosis of latent tuberculosis infection which have generated joint publications with different groups of CIBERES and other international groups. As a result of this work, several researchers of the Tuberculosis CRP have had very active participation active in drawing up clinical guidelines for the use of these new diagnostic tests for latent tuberculosis infection.
  - The inter-group collaboration work within the tuberculosis programme, in collaboration with CIBERES, has generated a prominent transfer action (new *M. tuberculosis* molecular typing methodology) which has been worked on to generate a new patent.

3. TRANSVERSAL PROGRAMMES

TRAINING PROGRAMME

Coordinator: **Dr. Ana Obeso**
Teaching Secretary: **D. Gonzalo Bajaneta**

The primary objectives of the training and teaching programme are:

- To promote the acquisition of integrated clinical-basic knowledge among CIBERES researchers to provide a translational approach to the scientific objectives.
- To boost interest for research in respiratory diseases among younger people undergoing training within the field of Biomedicine so that they can nurture future CIBERES research teams, as well as attract those who are the most talented.
- To facilitate interaction and mobility of staff between the teams integrated in CIBERES to improve their technical abilities and scientific capacitya.

Three action programmes were established to achieve these objectives, and their activity in 2014 included:

Research Staff Training Programme

RESEARCH INITIATION GRANTS

This programme was considerably successful in CIBERES because of the interest in the call for grant proposals and because of the results obtained. The grants can be used as aid to young researchers to begin their training. For 1 year, they are a part of a research project funded by official bodies comprised within one of the research groups forming part of CIBERES.

The intention is that in that year, the grant holders can access an official research staff training (RST) programme and be linked to the CIBERES group. 66% of the grant money is provided by the CIBERES training and teaching programme and 33% of it is provided by the group actually receiving the grant holder.

Like in previous years, according to budget availabilities, 5 grant contracts awarded at the end of 2013 were carried out in 2014. In the last month of 2014, 5 calls for grant proposals (8th call for proposals) were held again.

According to the recommendations of the External Scientific Committee, in 2010 mechanisms for evaluation of the results of this programme were implemented both by the CIBERES training committee and by the beneficiaries of this programme. These mechanisms for evaluation were maintained in 2014.

Improvement and Mobility Programme:

There are currently 3 lines of action:

- Co-funding registration fees (generally for 3rd cycle university courses). Modules of up to 500 Euros/module.
- Travel expenses for attending training courses or activities outside of one's place of residence. Modules of up to 500 Euros/module.
- Co-funding stays in another city for learning techniques. Modules of up to 1200 Euros.

In 2014, 24 applications were received and 17 of them were funded.

Programme to Promote interest in Respiratory Research

RESEARCH STAFF TRAINING CONFERENCE

In 2014 the 7th Training Conference was held in Valladolid on 16-17 October at the Palacio de Congresos Conde Ansúrez.

This year there was a new feature in the programme which included a space dedicated to innovation, where several researchers participated in "innovation capsules", which are short sessions lasting only a few minutes in which the innovative projects being carried out are explained.

The conference had the institutional support of CIBER with the presence of the manager in the conference inauguration and of CIBERES with the presence of its Scientific Director. As usual, the conference was attended by many groups that sent 44 junior researchers in addition to a significant presence of senior researchers, with 10 senior speakers between the plenary sessions and the innovation session. As regards junior speakers, they presented 10 oral communications and 34 poster presentations. Furthermore, 3 "uva de oro" awards were given to the best communications.

In 2014 the organizational logistics of the Conference were handled by teaching coordination office, continuing with its aim to reduce conference cost, and this was achieved for the most part.

This conference is held every year, so the eighth instalment of said conference is expected to be held also in Valladolid in the fall of 2014.

Other Teaching Activities:

AGREEMENT WITH THE UNIVERSITAT DE BARCELONA AND THE UNIVERSITAT POMPEU FABRA TO DEVELOP THE RESPIRATORY MEDICINE MASTERS PROGRAMME.

By means of this agreement, CIBERES assigns a budget item intended for co-funding up to 30% of the amount of the registration for students belonging to any of the CIBERES groups. Registration co-funding is expected to be maintained. For next year, the Masters Programme will fundamentally be virtual, so this will make it easier for students located in different Spanish cities to attend. At the end of the course how the Masters Programme activities are developed will be assessed with a view to continuing with co-funding.

The following aid was granted in the 2013-2014 course:

Student	Grop	IP
Carmen Ángela Centeno Clemente	Group 30	Eduard Monsó
Izaskun Bilbao Luri	Group 31	Jesús Ruiz-Cabello

Communication results for this period:

Press Releases:

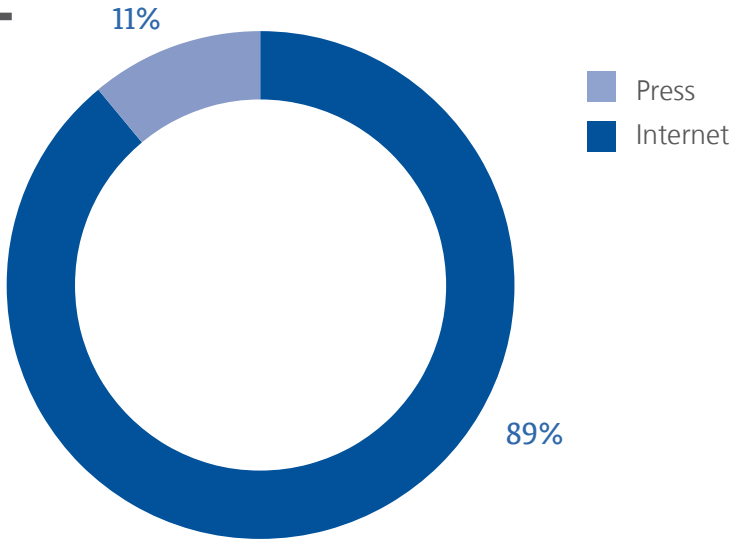
- Investigadores de la Universidad de Zaragoza contribuyen al desarrollo de nuevos fármacos contra la tuberculosis 26/01/2014
- El Doctor Ferran Barbé, nuevo director científico del CIBER de Enfermedades Respiratorias 07/04/2014
- Descubierta la mutación por la que diferentes bacterias de la tuberculosis se especializan en la infección de humanos o de ganado 21/06/2014
- Investigan en pulmones bioartificiales como alternativa a la escasez de órganos para trasplantes 03/07/2014
- Proponen el uso de unas nuevas nanopartículas para imagen médica en diagnóstico y tratamiento en EPOC 15/10/2014
- El Congreso Nacional de Biobancos abordará los retos de la medicina personalizada en Palma de Mallorca 11/11/2014
- Alvar Agustí entre los 10 investigadores biomédicos más citados. 24/11/2014

Hits in the media

Total number of hits: 457 (89% internet and 11% press)
Audience: 93% internet and 7% press
Most noteworthy hits in the media:

Date	Owner/Topic Addressed	Cited Member	No. Hits
26/01/2014	Desarrollan una nueva familia de antibióticos contra la tuberculosis	Jose Antonio Ainsa	67
15/01/2014	Mortalidad por EPOC disminuye un 26% en Europa	José Luis López-Campos	64
22/07/2014	Descubierta la mutación que especializa a las bacterias de la tuberculosis	Jesús Gonzalo-Asensio	43
17/09/2014	Nanotecnología para crear antibióticos más eficaces	Jose Antonio Ainsa	25
11/06/2014	Avalan la eficacia de la MTBVAC como vacuna de tuberculosis	Carlos Martín	22

HITS IN THE MEDIA



Twitter Statistics

https://twitter.com/ciberes

	January 2014	December 2014
Updates	1894	2213
Followers	861	1.180
Klout (level of influence, value between 1 & 100)	42	44

2013 Annual Reports

(Spanish/English version) (pdf and interactive)
http://www.ciberisciii.es/comunicacion/memorias-anuales;
http://www.ciberes.org/attachments/Memorias/2013/FlipES-Cast/Maq-CIBERES-DEF-SC.html

Bimonthly CIBER Newsletters

This includes the 4 most important pieces of CIBERERS news during this period.
http://www.ciberisciii.es/comunicacion/boletines

Participation in the Semana de la Ciencia. Activity: TapaConCiencia.

In the TapaConCiencia activity organised during the Semana de la Ciencia, 8 research projects were presented corresponding to the subject areas of the CIBER that served as an inspiration to chef Jorge Cuellar to design 8 elaborate "tapas".

Darío García de Viedma (Respiratory Diseases CIBER and Hospital Gregorio Marañón) presented the usage of 'molecular detectives' to investigate the transmission of tuberculosis strains.

The act was covered by more than 20 mainstream and specialised media outlets.

http://www.ciberes.org/index.php?option=com_noticias&view=noticia&noticia_id=1745&Itemid=19

News update on the CIBERES webpage

ciberes.org

CIBERES Scientific Conference

Like in previous years, the 8th CIBERES conference took place in Madrid in the Escuela Nacional de Sanidad del ISCIII on 3-4 July. The main researchers from the CIBERES research groups as well as other researchers from the groups met at this conference.

In this conference, it is important to highlight that the CIBERES researchers presented, among others, new breakthroughs in the candidate tuberculosis vaccine MTBVAC, the use of biomarkers to improve lung cancer treatment, and the relationship between apnea and cancer.

In turn, Dr, Ferran Barbé, Scientific Director of CIBERES, stressed the importance of incorporating the objectives of the European programme Horizon 2020 to the function of the centre. He also reviewed the CIBERES transversal means, such as the Technology Transfer Platform which has 12 patents and 4 more currently pending, as well as the Pulmonary Biobank Platform which has about 30,000 samples from about 1,200 patients.

4. PLATFORMS

PULMONARY BIOBANK CONSORTIUM

Scientific Director: **Dr. Germán Peces-Barba**
Coordinator: **Cristina Villena, PhD**

Objectives

The general objectives of the Pulmonary Biobank Consortium (PBC) according to its 2012-2017 Strategic Plan approved by the PBP Steering Committee on 28 June 2012 are:

1. **RESEARCH**: to cover the needs of researchers with PBP resources to promote translational research in respiratory pathologies.
2. **QUALITY:** To consolidate the quality in pre- and post- sample acquisition processes to minimise artefacts and variations between batches of samples.
3. **COOPERATION:** To collaborate and integrate the PBC with similar cooperative structures.

2014 Actions

To reach these objectives the following action lines were addressed in 2014:

INVENTORY ADAPTATION

Currently, samples and data have been registered from about 1,700 patients with an average of 320 cases per year, as seen in Figure 1. Since 2013 because of budget limitations, the incorporation of new cases has been restricted to those that comply with a series of strategic requirements.

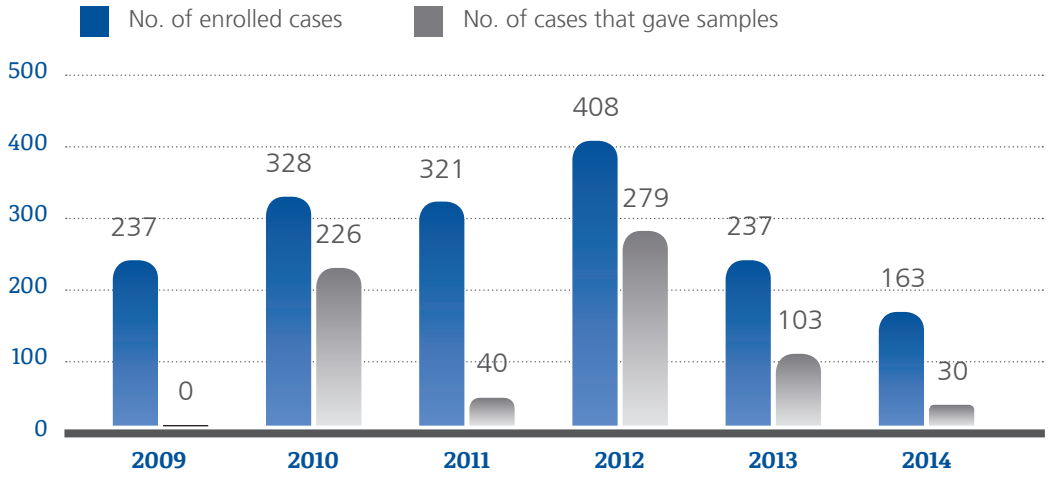


Figure 1. Number of patients enlisted annually (black) and number of cases for which samples have been sent for applications requesting favourably resolved samples

After periodic analyses of the existing inventory, resources to obtain strategic and/or highly demanded samples have continued to be enhanced and focused. This is the case of healthy lungs coming from organ donors, highly diseased or difficult to access lungs coming from pulmonary explants, and other respiratory samples such as last stages of diseases, bronchoalveolar lavage, sputum, etc.

In this line a new hospital centre has been added to the PBC (Hospital Universitario Vall d'Hebron) with a high number of pulmonary transplants per year, for the incorporation of a higher number of explanted lungs. The collaboration agreement between entities was signed and equipment and formation were provided for this new centre.

QUALITY

For the purpose of assuring compliance with CIBERES PBP objectives, the ISO 9001:2008 management and quality system was implemented in 2011, being certified in 2012. In 2014, the organisational structure was modified as a result of the new CIBER structure and at the beginning of 2015 the certificate for the entire platform was renovated.

The quality management system forces establishing objective compliance indicators for each of the processes of the PBP. Figure 2 shows its most relevant activity:

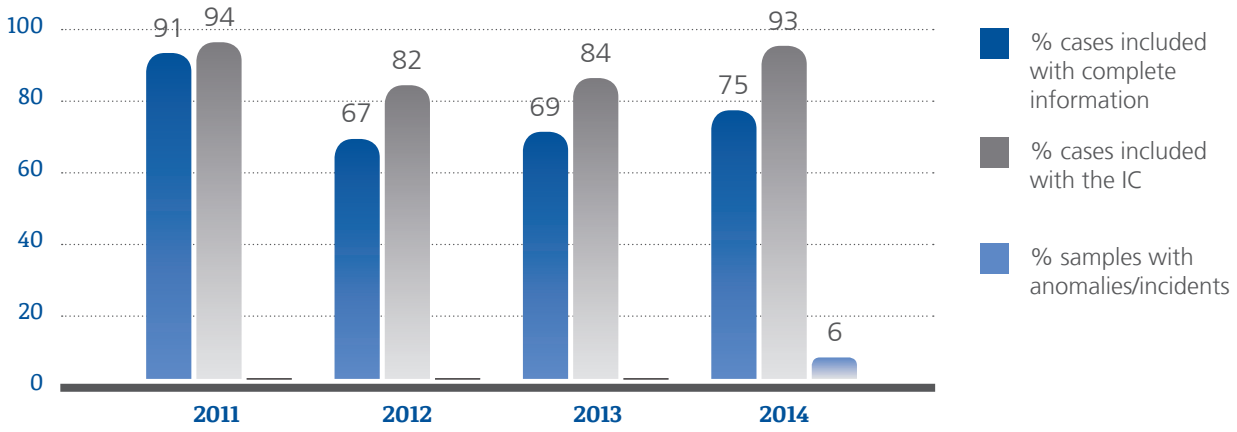


Figure 2. Percentage of newly registered cases in the PBP with complete clinical information (blue), with a record of the informed consent of the patient (in red) and since 2014 the number of samples with processing or storage incidents or anomalies is also evaluated (in green)

Its activity is registered in the National Biobank Registry in the ISCIII (B.0000471), overcoming yearly audits and external evaluations. All its functioning is consensual and is done by means of standard operating procedures, as well as its management board and advisory committee (External Scientific and External Ethical) that oversee all the activities of the platform.

The Steering Committee advises the director on the planning and decision making that affects the PBC as a whole, and the Advisory Committees are independent, advisory and interdisciplinary bodies formed by expert members of the implicated disciplines that are not linked to CIBERES, the basic function of which are to oversee the scientific suitability and quality in the use of samples managed by the PBC.

INTEGRATION WITH OTHER STRUCTURES AND ORGANISATIONS TO PERFORM SYNERGISTIC AND MUTUAL BENEFICIAL ACTIVITIES.

Several agreements have been signed with different entities for taking specific sample collections with specific pathologies:

- Creation of a prospective multicentre sample and data collection from patients with pulmonary thromboembolism, sponsored by the Integrated Pulmonary Thromboembolism Research Project of the **Sociedad Española de Neumología y Cirugía Torácica (SEPAR)**.
- Creation of a prospective and retrospective multicentre sample and data collection from patients in **stages I and II of lung cancer, sponsored by the CIBERES Lung Cancer Corporate Research Programme** and funded by **SEPAR-FIS-CIBERES**.

The incorporation of 20 more hospitals on a national level national for collecting blood products from patients who have suffered pulmonary thromboembolism and 2 hospitals for the prospective incorporation of lung cancer sample has been worked on in 2014.

COOPERATION WITH SIMILAR INITIATIVES AND INSTITUTIONS IN THE FIELD THAT ALLOW IMPROVING THE PUBLIC SERVICE OF THE PBP TO THE SCIENTIFIC COMMUNITY FOR MORE EFFECTIVE TRANSLATIONAL RESEARCH.

The Pulmonary Biobank ConsortiumCIBERES (PBC) is currently a member of the following cooperative structures:

NATIONALLY:

- Member of the National Biobank Network Platform of the ISCIII of AES 2013-2016.
  - – Actively participating in the Quality Management Systems work group since 2014.
  - – Member of the National Biobank Network Platform Steering Committee of the ISCIII since 2014.
  - – Coordinating together with Fundación Cien since the end of 2014 the line of work called "Quality and development of new methods for processing and storing tissues" of Programme 3: Research, Development and Innovation.

INTERNATIONALLY:

- *International Society for Biological and Environmental Repositories (ISBER).*
  - – Participation in the Marketing and Promotion Committee.
  - – Participation in the BioSpecimen Science work group.
- *European, Middle Eastern & African Society for Biopreservation & Biobanking (ESBB).*
  - – Participation in the rare pathologies work group.

ACTIONS FOR STRENGTHENING COOPERATION WITH OTHER ENTITIES

- Organisation by CIBERES of the 5th National Biobank Conference in the coordination headquarters on 12-14 November 2014 under the slogan: MEDICINA PERSONALIZADA Y BIOBANCOS. This is an annual event that brings together all national biobanks (www.uibcongres.org/biobancos2014)
- The first draft agreement was signed with the National Biobank Network Platform-ISCIII to organise the 5th National Biobank Conference, which will serve as a draft agreement for future events of the network.
- Member of the organising committee of the 6th National Biobank Conference, Lleida, 18-20 November 2015.

EXPOSURE

Internal and external exposure of the PBC is one of the most important actions for the purpose of the scientific community learning about its services and favouring the interrelation with other entities and companies. In addition to the specific web page describing PBP activity (www.biobancopulmonar.ciberes.org), the presence of triptychs and posters at scientific and technological events, as well as the inclusion in national and international networks or catalogues (www.redbiobancos.es; www.bbmri-lpc-biobanks.eu; www.trans-hit.com; Catálogo de Servicios Tecnológicos de I+D+i en Ciencias de la Salud de las Illes Balears; www.biobancos.isciii.es), in 2014 we have participated in:

Training Activities:

- University Master's degree in Translational Medicine (Universidad de Barcelona).
- University Master's degree in Health Law (Universitat de les Illes Balears).
- Course on "Good Clinical Practice" accredited by the National Health System, Mallorca 2014.
- CIBERES Training Conference, Valladolid 2014.
- CIBERES Scientific Conference, Madrid 2014.
- Training Workshop on "Clinical Data and Research", Mallorca 2014.

Scientific Publications:

- Monsó E, Montuenga LM, Sánchez of Cos J, Villena C; for the Collaborative Lung Cancer Group CIBERES-RTICC-SEPAR-**Pulmonary Biobank Platform**. Biological Marker Analysis as Part of The CIBERES-RTIC Cancer-SEPAR Strategic Project on Lung Cancer.Arch Bronconeumol.2015 Jan 19.

Presentations at Conferences:

- Diez años de Biobanco VIH del Hospital GM RED IRIS (Madrid, 2014).
- ESBB's 2014 Annual Conference (Leipzig, Germany 2014).
- 5th National Biobank Conference (Palma 2014).
- 66th ANNUAL MEETING OF THE SOCIEDAD ESPAÑOLA DE NEUROLOGÍA.

Awards:

- Received travel allowance to conduct Research from Hospital Universitario Son Espases to attend ESBB's 2014 Annual Conference (Leipzig, Germany 2014).

Coordinator: **Dr. Lluis Blanch**
Manager: **Dr. Cristina Broceño**

The Technology Development and Transfer Platform (PDTT-CIBERES) is a transversal instrument of CIBERES **the primary purpose of which is to boost technological research and development activity of our groups in the field of respiratory medicine and to focus results on translation to clinical practice and transfer to companies**. The PDTT is a unified path for channelling technology transfer and innovation offers and demands for CIBERES.

The **objectives** of the PDTT are:

- To promote innovation and transfer in CIBERES.
- To increase the projection and exposure of the technological activities of CIBERES.
- To ensure an operative, fast and effective response of the entire transfer process to researchers and to CIBERES.
- To protect the Intellectual Property Rights of CIBERES and its researchers.
- To achieve good coordination and communication between the different CIBERES transfer/innovation agents.

2014 PDTT Action Summary

Within its capabilities, the PDTT carries out all the actions necessary for promoting innovation and transfer of CIBERES results. The actions are grouped by lines of action. The following has been done throughout 2014:

Promoting innovation in CIBERES

- **Promoting innovation among researchers.** By means of individual interviews and in presentations of the PDTT on innovation at Scientific Conference July 2014 (discussion concerning innovation and providing services from PDTT in CIBERES) and the annual CIBERES Training Workshop in October (Conference of the ITEMAS Platform Coordinator: Manuel Desco, short presentations on 3 transfer projects funded by CIBERES and a round table with 5 innovative CIBERES/CIBERBBN researchers with a discussion concerning questions about innovation).
- **Continuous counselling in relation to intellectual property and transfer for hired and associated researchers.**
- **Managing 2012 joint CIBERES-BBN-SEPAR multidisciplinary projects.**
- **New call for proposals for joint multidisciplinary CIBERES-CIBERBBN-SEPAR2014 transfer projects.** Call for proposals, reception of proposals, evaluation, resolution and management of documents in coordination with CIBERBBN and SEPAR management. The call for proposals this year has given joint funding to 3 multidisciplinary projects that CIBERES groups lead or participate in.

Nº	acronym	IP Coordinador	endow-ment
1	MICROCOPD "3D analysis of vascular architecture in emphysematous lungs using microcomputed tomography (microCT)"	JOAN ALBERT BARBERÀ	15.000 €
2	PVI-ANS-NCOG "Effects of an early neurocognitive intervention on patient-ventilator interaction and stress in critically ill patients receiving mechanical ventilation"	LLUIS BLANCH	15.000 €
3	TARMAC "New tools for the diagnosis and treatment of respiratory infectious diseases: pH-responsive matryoshka nanoparticles for an efficient and controlled intracellular delivery of oral antibiotics and gated nanoparticles for the detection of pathogenic microorganisms showing intracellular persistence"	MANUEL ARRUEBO	15.000 €

- **CIBERES intellectual property management**

ASSESSMENT OF IDEAS

In 2014 the PDTT **evaluated 3 ideas in collaboration** with the majority co-owning institutions. For all 3, interest was evaluated and the information and protection process was managed together with patent co-owners, inventors and agents.

PATENT MANAGEMENT

Throughout 2014, **5 new patents** listing CIBERES as a co-owner as well as a new PCT extension were filed, and all the **steps required for the 15 patents listing CIBERES as a co-owner were taken**. This year there were 2 abandonments due to the lack of interest by companies to take over the development and maintenance of these ideas beyond the PCT extension. Furthermore, **1 transfer agreement** for one of our patents in which we are listed as a co-owner has been **signed** and another **collaboration and transfer agreement has been negotiated** with a company which ultimately declined due to a change in direction of the company's business. Related agreements: **6 co-ownership agreements, 2 licensing agreements, 5 inventor agreements, 2 collaboration agreements, 2 assignment agreements, 2 agreements relating to a name change from CIBERES to CIBER and over 20 CIBER power of attorney for extensions and changes of agents.**

CIBERES patent and intellectual property management **furthermore includes**: Petitions and evaluation of budgets, reports, information to involved parties and agents, communication with co-owners, inventors and agents, patent extensions, timely follow-up, corrections, payment management and applications. Drafting and managing specific agreements relating to: inventors, co-ownership, assignment, non-disclosure, collaboration, closing reports…

All the current patents in which CIBER/ES is listed as an owner and in force throughout 2014 to present are shown in the following table:

Fecha y número solicitud prioritaria	Título invención	Group CIBERES	Titulares	Extensiones	Lidera transfer.	Estado
16/12/2009 P200931177 PCT/ES2010/070836	Detección de Streptococcus pneumoniae mediante genosensores magneto-amperométricos empleando cebadores y sondas específicos del gen lytA	2	CSIC 50%/UCM 26% /CIBERES 24%	PCT/ES2010/070836 19/12/10	CSIC	Vigente. Licenciado a Alphasip fecha 19/12/2012
17/12/2009 P200931186 PCT/ ES10/070808	Uso de Seconeolitsina y N-Metil-Seconeolitsina para la fabricación de medicamentos	3	ISCIII 50%/U. Valencia 40% CSIC 5%/CIBERES	PCT/ES10/070808 03/12/2010	ISCIII	Abandon.
08/11/2011 P201131785 PCT/ ES2012/070767	Uso de un compuesto químico derivado de un pirrol 1,2,3,5- tetrasustituídos en la elaboración de un medicamento útil para el tratamiento de enfermedades inflamatorias que cursan con procesos apoptóticos celulares	29	CIBERES50%/U. La Laguna 25% / Sistema Canario Salud 25%	PCT/ES2012/070767 31/10/2012	CIBERES	Abandon.
24/11/2011 EP11382362 PCT/ ES2012/070823	"Engineered stem cells and theyr therapeutic use"	16	IDIBELL50% / FUVall de Hebron 37,5%/ CIBERES12,5%	PCT/ES2012/070823 23/11/2012	IDIBELL	Vigente. Licencia Histocell 4/12/2012
31/12/2012 P201232075 PCT/ ES2013/070909	Compuestos ciclopentanonas , procedimiento de obtención y su uso en la preparación de un medicamento útil para el tratamiento de enfermedades inflamatorias que cursan con procesos apoptóticos y fibróticos celulares.	29	CIBERES50%/U.La Laguna 16,67% / Sistema Canario Salud 16,67%/ CSIC 16,67%	PCT/ES2013/070909 20/12/ 2013	CIBERES	Vigente
15/06/2012 P201200640 PCT/ ES2013/000145	Micobacterias inactivadas para su uso por vía oral en la prevención de la tuberculosis	17	Inst. germans Tries i Pujol (IGTP) 66,7%/ CIBERES 33,3%	PCT/ES2013/000145 13/06/2013	IGTP	Vigente. Licencia a Manremyc.
28/05/2013 P201330777PCT/ ES2014/070429	Enzibióticos bactericidas mejorados frente a neumococo y otras bacterias	34 / 2	CSIC 90%/ CIBERES10%	PCT/ES2014/070429	CSIC	Vigente.
10/01/2014 EP14382007 PCT/ EP2015/050325 10/01/2015	"Methods and systems for providing oxygen to a patient"	5 / 30	IDIBELL57,5%/ UAB 37,5%/ CIBER 5%	PCT/EP2015/050325 10/01/2015	IDIBELL	Vigente
17/03/2014 EP14382093. PCT/EP2015/055544 17/03/2015	"Micellar nanoparticles containing antitumoralglycosides"	31	CNIC 67%/ CIBER 33%	PCT/EP2015/055544 17/03/2015	CNIC	Vigente
EP14382286.4 25/07/14	"Methods and agents related to lung diseases"	23	CIBER 66,7%/ FIB Hospital Universitario de Getafe 33,3%		CIBERES	Vigente
U.S. Provisional Patent Application No. 62/004,174. 28/05/2014	"Bimodal fluorophore-labeled liposomes and associated methods and systems"	31	MSKCC (50%), Mount Sinai (35%), and CIBER 7.5%/ CNIC (7.5%).	PCT Soon	MSKCC	Vigente
EP14382533.9 18/12/2014	"Method for predicting response to continuous positive air pressure treatment"	35	IRB Lleida 53,85%/ CIBER 38,46%/ Fundación Hospital la Fe 7,69%		IRB Lleida	Vigente

- For the purpose of improving exposure of our technology offer, the transfer space on our CIBERES web as well as the **space dedicated to the CIBERES technology offer in which there are currently 8 technology offers** of CIBERES ideas are constantly updated. These documents have been drafted by PDTT for the CIBERES web page and for being sent to companies. They present ideas that are co-owned by CIBERES and for patents of CIBERES groups. Furthermore, specific documents of these offers have been prepared for dissemination to the Europe Enterprise Network (EEN).
- This documentation was required in order to **be presented to specific companies in the area**, which have been sought and actively contacted concerning the presented product. At least 10 companies were contacted in relation to every transfer patent managed by PDTT CIBERES.
- For the purpose of assuring an operative response in the protection and transfer process, the PDTT has also been responsible for **drafting and/or reviewing and managing non-disclosure agreements, collaboration agreements** and **licensing agreements**, as well as reports for specific questions sent by companies, among others.
- In 2014, the PDTT has furthermore made contact and exchanged information relating to a technology offer with other platforms interested in the transfer, as is the case of the **KTT-CEDARS-SINAI** office and the National Network for the discovery of new antibiotics **(AD-SP)**.

Promoting CIBERES innovation outside CIBERES

Besides disseminating the CIBERES technology offer directly to companies, the PDTT works to promote the ideas and the capabilities of our work programmes and of our investigators and groups. Some of the work done throughout 2014 includes:

- **CIBERES as a collaborator in the ITEMAS Platform.** Participation in the ITEMAS Assessment Work Group.
- **Drafting and preparing CIBERES documentation to be presented in meetings, to companies and other entities.** PDTT posters, PDTT CIBERES dossiers, technology offer and objectives of the Corporate Programmes.
- **Sending notifications relating to company/innovation to the CIBERES/CIBER web page.**
- **"CIBERE's networking"**. Presenting CIBERES, its offer and its capabilities (co-owned by CIBERES or CIBERES groups) in Forums, to companies, to entities that support innovation, to networks, at informative meetings and in specific training courses, as well as to generate contacts and agreements with institutions of interest for CIBERES transfer.

Establishing CIBERE's systematic processes in innovation and transfer

To constantly improve the transparency of processes in the CIBERES transfer/innovation area, and their efficacy and to therefore generate trust and a feeling of proximity to these subjects among CIBERES investigators and the consortium entities, the PDTT **has established processes in recent years, such as the drafting of a CIBERES Intellectual Property Regulation and the design of methods under ISO9001 specific for the evaluation and management of protecting ideas.**

Throughout 2014, 8 of the 9 CIBERs have merged in a central office. PDTT followed this same line, **contributing to the CIBER unification process in the Transfer Area**. In November 2014 the concept of a Transfer Manager was incorporated into CIBER, and from this time on PDTT has maintained close communication with the person in this position, sending all the information required about the work done by CIBERES transfer. **PDTT currently works closely with CIBER transfer**.

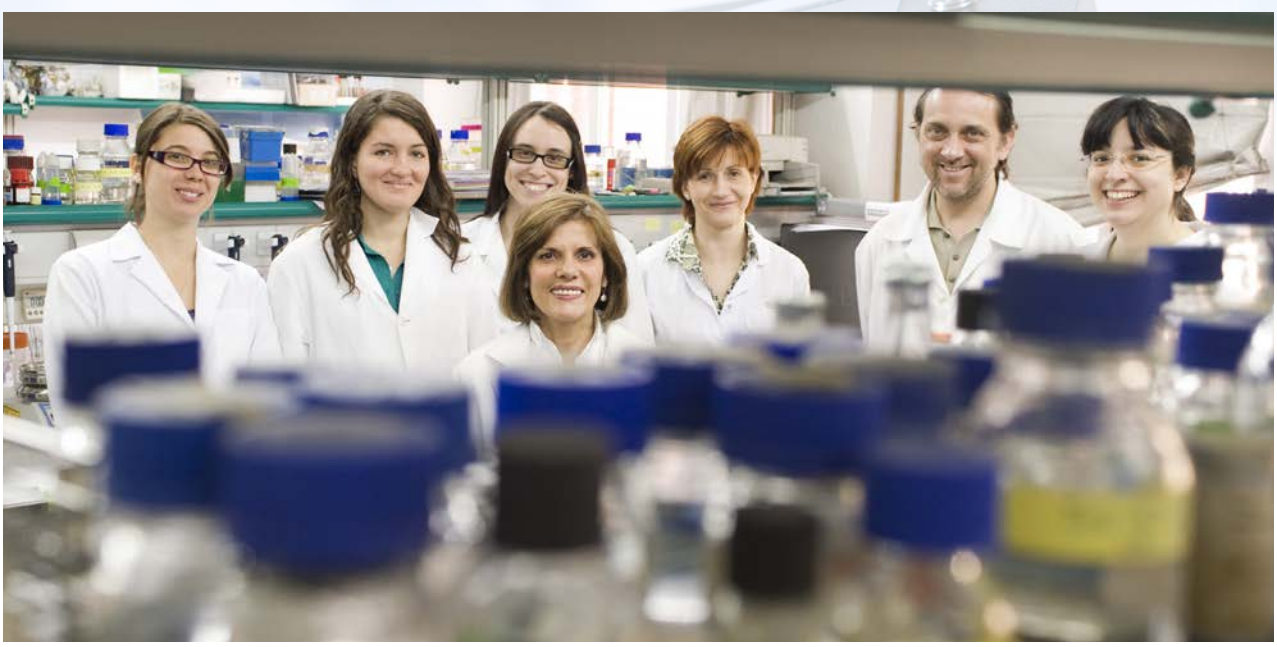
Other tasks in establishing a systematic process in PDTT CIBERES this year was:

- **Annual meeting and timely consultation provided with the CIBERES Innovation Committee**. To discuss topics relating to innovation and transfer in CIBERES, to advise Scientific Management and establish processes. Furthermore, the members are evaluators of the proposals for transfer projects funded by CIBERES, always under a non-disclosure agreement and certifying that there is no conflict of interests.
- **Drafting, delivering, negotiating and correcting model documents** to enforce legal compliance in the framework of the CIBERES. Non-disclosure agreements, inventor agreements, co-ownership agreements, collaboration agreements with companies, consortium agreements, assignment agreements, licensing agreements…
- From the beginning, the CIBERES Innovation Committee has identified as a priority the need to provide CIBERES with a manager or **a service that will activate participation of CIBERES groups in European and international calls for proposals** aimed at knowledge transfer to the health care market. This year, CIBERES has participated in the Networks and Managers call for proposals sponsored by MINECO together with CIBERBBN and CIBERER for the purpose of obtaining funds for hiring a manager for what will be the Research Internationalisation Support Platform (RSP).The project has been granted and after May 2015 we will have a new manager dedicated exclusively to this task for the 3 CIBER areas involved. The PDTT belongs to the work group linked to this project in relation to **the improvement of the economic return of the effort made by CIBER_BBN/ER/RES**. PDTT has participated in this process until now and will continue participating from the RSP in the future.
- Drafting **PDTT reports and action plans**, PDTT presentations, executive summaries, minutes, etc.
- Space in the **CIBER intranet open to attached and hired CIBERES staff contains both the CIBERES technology offer** and model documents required for CIBER/ES transfer, PDTT dissemination, information and operation documentation.

5. RESEARCH GROUPS

Group 1

Programme: Host-Pathogen Interactions/ Acute Lung Injury (ALI)



Lead Researcher: Casals Carro, Cristina

Group members

STAFF MEMBERS: Cañadas Benito, Olga | García-Fojeda García-Valdecasas, María Belén

ASSOCIATED MEMBERS: Coya Raboso, Juan Manuel | Egido Martín, Virginia | Monsalve Hernando, Carmen | Muñoz Minutti, Carlos Arturo | Saenz Martínez, Alejandra |

Main lines of research

The respiratory epithelium has evolved to produce a complicated network of extracellular membranes, called lung surfactant, that are essential for breathing and, ultimately, survival. Lung surfactant not only protects the lung against alveolar collapse during the breathing cycle but is involved in host defense. The manner in which surfactant components might participate in successful elimination of microorganisms without triggering excessive inflammatory response in the alveolus is still poorly understood. How biophysical surfactant properties and host defense mechanisms can be interdependent is also unknown.

The focus of our group is to understand how surfactant lipids and proteins exert their action. We study:

- The molecular mechanisms by which surfactant components control unnecessary tissue inflammation, using cell culture models of inflammation and infection (CRP on Host-Pathogen Interactions).
- The potential molecular interactions between surfactant protein A (SP-A) and antimicrobial peptides present in the alveolar fluid (SP-BN, LL37, and beta-defensins) that might facilitate (or block) antimicrobial actions (CRP on Host-Pathogen Interactions).
- Surfactant membranes' mechanisms of resistance to inactivation by factors which increase in the alveolar fluid during infection and inflammation (CRP on Host-Pathogen Interactions).
- Molecular interactions between alveolar protein SP-A and nanoparticles (CRP on New Therapies to Treat Respiratory Diseases).

- The high-stretch ventilation impact in the alveolar space and in particular on the composition, structure, and functional activity of lung surfactant (CRP on Acute Lung Injury).
- Benefits of intratracheal treatment of natural and synthetic surfactants as well as anti-inflammatory agents in acute lung injury induced by mechanical ventilation (CRP on Acute Lung Injury).

This research has direct relevance for the development of new therapies for inflammatory and infectious lung diseases.

Most relevant scientific articles

- Izquierdo-Garcia J.L., Naz S., Nin N., Rojas Y., Erazo M., Martinez-Caro L. et al. A metabolomic approach to the pathogenesis of ventilator-induced lung injury. Anesthesiology. 2014;120(3):694-702.
- Martínez-Florensa M., Consuegra-Fernández M., Martínez V.G., Canadas O., Armiger-Borras N., Bonet-Rosello L. et al. Targeting of key pathogenic factors from gram-positive bacteria by the soluble ectodomain of the scavenger-like lymphocyte receptor CD6. Journal of Infectious Diseases. 2014;209(7):1077-1086.

Institution: Universidad Complutense de Madrid
Contact: Facultad de Biología · Ciudad Universitaria, S/N. 28040 Madrid
Tel.: (+34) 91 394 42 61 · E.mail: ccasalsc@ucm.es · Web: http://pendientedemigracion.ucm.es/info/respira/

Group 2

Programme: Pneumonia / Host-Pathogen Interactions

Lead Researcher: García López, Ernesto

Group members

STAFF MEMBERS: Ruiz García, Susana

ASSOCIATED MEMBERS: Díez Martinez, Roberto | Domenech Lucas, Mirian | García González, Pedro | Moscoso Naya, Miriam | Ramos Sevillano, Elisa | Yuste Lobo, José Enrique

Main lines of research

The development of invasive pneumococcal disease is preceded by the establishment of the "carrier state", this is, the colonization of the human nasopharynx by *Streptococcus pneumoniae* (pneumococcus). Pneumococcal carriage takes place through the establishment of a still largely unknown, host-pathogen interplay as well as by interactions with other bacteria colonizing the same habitat, such as non-typeable pneumococci, other streptococci of the mitis group, or pathogens like *Haemophilus influenzae*. Most of these interactions involve bacterial surface proteins on one hand, and cellular receptors and host defense mechanisms on the other. Cell wall hydrolases (CWHs) are surface proteins produced by the pneumococcus that are directly involved in virulence. Thus, LytB and LytC are essential in nasopharyngeal colonization and help to avoid host immunity, while LytA triggers the release of other virulence factors, like the potent toxin pneumolysin and the neuraminidase and plays an important role in pathogenesis by releasing cell wall fragments that are markedly pro-inflammatory. All these CWHs are involved in biofilm formation. The role(s) in colonization of LytA and pneumolysin will be studied using biofilms (either mono or multispecies), cell cultures, and a mouse model of nasopharyngeal colonization. Besides, the impact of risky behaviors like smoking that facilitates bacterial colonization of the lungs and that contributes to the acute exacerbations in patients with chronic obstructive pulmonary disease will also be examined. Finally, one of the main aims of the present project is to develop prophylactic and therapeutic approaches to fight pneumococcal colonization. This will be performed using CWHs (*enzybiotics*) like Cpl-7 (a phage-coded enzyme of great antibacterial potential), and novel drugs including several choline analogs and ceragenins. As for other objectives of this project, the efficacy of enzybiotics and novel drugs will be tested in vitro (planktonic as well as biofilm cultures) and in animal models of infection.

Most relevant scientific articles

- Ardanuy C., De La Campa A.G., Garcia E., Fenoll A., Calatayud L., Cercenado E. et al. Spread of streptococcus pneumoniae serotype 8-st63 multidrug-resistant recombinant clone, Spain. Emerging Infectious Diseases. 2014;20(11):1848-1856.
- Domenech M., Araujo-Bazan L., Garcia E., Moscoso M.. In vitro biofilm formation by Streptococcus pneumoniae as a predictor of post-vaccination emerging serotypes colonizing the human nasopharynx. Environmental Microbiology. 2014;16(4):1193-1201.
- Moscoso M., Esteban-Torres M., Menendez M., Garcia E.. In vitro bactericidal and bacteriolytic activity of ceragenin CSA-13 against planktonic cultures and biofilms of Streptococcus pneumoniae and other pathogenic streptococci. PLoS ONE. 2014;9(7):-.
- Martin-Galiano A.J., Yuste J., Cercenado M.I., de la Campa A.G.. Inspecting the potential physiological and biomedical value of 44 conserved uncharacterised proteins of Streptococcus pneumoniae. BMC Genomics. 2014;15(1):-.
- Dinjaski N., Fernandez-Gutierrez M., Selvam S., Parra-Ruiz F.J., Lehman S.M., San Roman J. et al. PHACOS, a functionalized bacterial polyester with bactericidal activity against methicillin-resistant Staphylococcus aureus. Biomaterials. 2014;35(1):14-24.

Highlights

- The 2nd DropSens Award (The International DropSens Award to the Best Research Work in Applied Electroanalytical Chemistry). Awarded during the 15th International Conference on Electroanalysis (ESEAC). Malmö (Sweden). 11-15 June 2014. Authors: A. Sotillo, J. Mingorance (IdiPAZ); J.L. García, P. García, E. García (CIB-CSIC/CIBERES); Y. Belacortu, D. Olea, M. Roncalés, V. Escamilla, B. Garcinuño (Alphasip); S. Campuzano, M. de Pablos, B. Esteban-Fernández, M. Pedrero, J.M. Pingarrón (UCM).
- Patent: García, P., Menéndez, M., García, E., Díez-Martínez, R. y de Paz, H. 2013. Enzibióticos bactericidas mejorados frente a neumococo y otras bacterias. No. P201330777. Ampliación de 18 meses mediante solicitud PCT No. PCT/ES2014/070429.
- Preparation and characterization of a bacterial polymer with bactericidal properties against methicillin-resistant staphylococci.
- We have shown that Ceragenina CSA-13, a novel antibiotic, shows bacteriolytic and bactericidal activity against pneumococci and other pathogenic streptococci grown in biofilms or planctonic cultures.
- Identification of novel therapeutic targets in the human pathogen *Streptococcus pneumoniae*.

Institution: Agencia Estatal Consejo Superior de Investigaciones Científicas
Contact: Centro de Investigaciones Biologicas · C/ Ramiro de Maeztu, 9. 28040 Madrid
Tel.: (+34) 91 837 31 12 · E.mail: e.garcia@cib.csic.es
Web: http://www.cib.csic.es/es/Group.php?idGroup=7

Group 3

Programme: Pneumonia

Lead Researcher: González de la Campa, Adela

Group members

STAFF MEMBERS: Tirado Vélez, José Manuel

ASSOCIATED MEMBERS: Amblar Esteban, Mónica | Ferrándiz Avellano, María José | Martín Galiano, Antonio Javier

Main lines of research

- Molecular basis of antimicrobial action in pathogenic bacteria, mainly in Streptococcus pneumoniaee.
- Molecullar studies of the fluoroquinolone targets (DNA gyrase and DNA topoisomerase IV).
- Studies on the organization of the genome in supercoiling domains and their role in global transcription.
- Effect of fluoroquinolone treatment in the global transcription.
- Role of the S. pneumoniae small RNAs in gene expression.
- Characterization of new antimicrobial targets.
- DNA topoisomerase I as a new antibiotic target.
- Characterization of new virulence factors.

Most relevant scientific articles

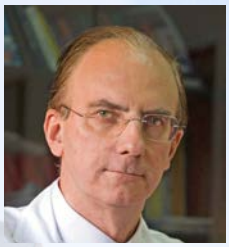
- Ferrandiz M.-J., De La Campa A.G.. The fluoroquinolone levofloxacin triggers the transcriptional activation of iron transport genes that contribute to cell death in streptococcus pneumoniae. Antimicrobial Agents and Chemotherapy. 2014;58(1):247-257.
- Martin-Galiano A.J., Yuste J., Cercenado M.I., de la Campa A.G.. Inspecting the potential physiological and biomedical value of 44 conserved uncharacterised proteins of Streptococcus pneumoniae. BMC Genomics. 2014;15(1):-.
- Ardanuy C., De La Campa A.G., Garcia E., Fenoll A., Calatayud L., Cercenado E. et al. Spread of streptococcus pneumoniae serotype 8-st63 multidrug-resistant recombinant clone, Spain. Emerging Infectious Diseases. 2014;20(11):1848-1856.
- Lopez E., Domenech A., Ferrandiz M.-J., Frias M.J., Ardanuy C., Ramirez M. et al. Induction of prophages by fluoroquinolones in Streptococcus pneumoniae: Implications for emergence of resistance in genetically-related clones. PLoS ONE. 2014;9(4):-.
- Domenech A., Tirado-Velez J.M., Fenoll A., Ardanuy C., Yuste J., Linares J. et al. Fluoroquinolone-resistant pneumococci: Dynamics of serotypes and clones in Spain in 2012 compared with those from 2002 and 2006. Antimicrobial Agents and Chemotherapy. 2014;58(4):2393-2399.

Highlights

PROJECTS

- We have characterized a global transcriptomic response of Streptococcus pneumoniae under fluoroquinolone treatment. Such a response has revealed an increase in the reactive oxygen species that contribute to levofloxacin lethality. These effects occur mainly by the activation of an iron transport. The possibility to increase fluoroquinolones efficacy by elevating the levels of intracellular iron remains open.
- We have performed the functional identification of 44 hypothetical proteins of S. pneumoniae. A new antibacterial target has been identified. Five proteins seemed to be virulence factors.
- We have performed an epidemiological study of fluoroquinolone resistance in S. pneumoniae of year 2012 and compared the data with our previous studies of 2002 and 2006. Fluoroquinolone-resistance has been stabilized in 2.3%, even when levofloxacin consumption has increased. We have detected changes both in serotypes and in genotypes distributions as a consequence of vaccination.
- We have detected the spread of a pre-existent multi-drug resistant clone, 8-ST63. This clone has been originated by the acquisition of the capsular genes of serotype 8 from clone 8-ST53. The new clone 8-ST63 has been identified as a cause of invasive disease in Spain. An increase in fluoroquinolone resistance would occur by the expansion of these kinds of clones.
- We have characterized the induction of bacteriophages by fluoroquinolones in S. pneumoniae. Resistant isolates carried less functional prophages than the susceptible ones. Two isogenic strains, one lysogen and the other non-lysogen were treated with subinhibitory fluoroquinolone concentrations. Resistant mutants only emerged in the non-lysogen strain. These results are compatible with the lysis of lysogenic isolates receiving fluoroquinolones before the development of resistance and explain the inverse relation between presence of inducible prophages and fluoroquinolone resistance.

Institution: Instituto de Salud Carlos III
Contact: Centro Nacional de Microbiología · Campus Majadahonda.
Ctra.Majadahonda-Pozuelo km 2.200. Madrid. · Phone: (+34) 91 822 39 44 · E.mail: agcampa@isciii.es



Group 4

Programme: Sleep Apnea-Hypopnea Syndrome (SAHS)/ Lung Cancer

Lead Researcher: González Mangado, Nicolás

Group members

STAFF MEMBERS: Fernández Arias, José | Pérez Rial, Sandra

ASSOCIATED MEMBERS: Fernández Ormaechea, Itziar | Peces Barba Romero, Germán | Rodríguez Nieto, María Jesús | Seijo Maceiras, Luis Miguel | Suárez Sipmann, Fernando | Villar Álvarez, Felipe

Main lines of research

- **CRP of Sleep Apnea:** OSA as a risk factor for cardiovascular morbidity and mortality, OSA as a risk factor for cancer and SAHS in women.
- **CRP of cancer:** Early detection program in subjects at high risk for emphysema or lung function impairment. Risk of each individual as his smoking habit and personal and family history. Influence of associated diseases, especially chronic obstructive pulmonary disease (COPD) and emphysema over the risk of developing lung cancer and its prognosis. Genetic and molecular factors that determine the risk profile of each individual.
- **CRP of COPD:** Susceptibility to the development of lung injury and its evolution up to present the well established disease in animal models. Identification of the key biomarkers in the development and progression of the disease and its translation to the clinic. Cohorts of COPD patients with early onset and with late-stage severe COPD. New therapeutic targets based on the utilization of growth factors in experimental models of disease and in endoscopic implantation in patients of spirals and valves for the treatment of emphysema.

Most relevant scientific articles

- Tusman G., Groisman I., Fiolo F.E., Scandurra A., Arca J.M., Krumrick G. et al. Noninvasive monitoring of lung recruitment maneuvers in morbidly obese patients: The role of pulse oximetry and volumetric capnography. Anesthesia and Analgesia. 2014;118(1):137-144.
- Perez-Rial S., del Puerto-Nevado L., Giron-Martinez A., Terron-Exposito R., Diaz-Gil J.J., Gonzalez-Mangado N. et al. Liver growth factor treatment reverses emphysema previously established in a cigarette smoke exposure mouse model. American Journal of Physiology - Lung Cellular and Molecular Physiology. 2014;307(9):L718-L726.
- Giron-Martinez A., Perez-Rial S., Terron-Exposito R., Diaz-Gil J.J., Gonzalez-Mangado N., Peces-Barba G.. Proliferative activity of liver growth factor is associated with an improvement of cigarette smoke-induced emphysema in mice. PLoS ONE. 2014;9(11):-.
- De Torres J.P., Marin J.M., Martinez-Gonzalez C., De Lucas-Ramos P., Mir-Viladrich I., Cosio B. et al. Clinical application of the COPD assessment test: Longitudinal data from the COPD history assessment in Spain (CHAIN) Cohort. Chest. 2014;146(1):111-122.
- Masa J.F., Duran-Cantolla J., Capote F., Cabello M., Abad J., Garcia-Rio F. et al. Effectiveness of home single-channel nasal pressure for sleep apnea diagnosis. Sleep. 2014;37(12):1953-1961B.

Highlights

CURRENT PROJECTS

• PI12 /0133 "Association between sleep-disordered breathing and growth rate of cutaneous melanoma." Collaborating Investigator: N. González-Mangado. AES 2013-2016 • PI13/01909 "Identification of activity markers since the beginning of COPD in experimental models and therapeutic assessment with growth factor LGF". Principal Investigator: G. Peces-Barba. AES 2013-2016 • NANOCOPD "Bioorthogonal nanoparticles for COPD Theranostics". Principal Investigator: G. Peces-Barba. Multidisciplinary collaborative projects CIBERBBN-SEPAR-CIBERES • SEPAR # 39 "Effect of CPAP treatment in women with OSA. Multicenter, randomized, controlled trial." Collaborating Investigator: N. González-Mangado. Grants for Research SEPAR • SEPAR#139 "Role of the liver growth factor (LGF) like regenerative experimental lung emphysema". Principal Investigator: S. Pérez-Rial. Grants for Research SEPAR • SEPAR # 250 "Reference values for the parameters of maximum oxygen consumption, acidosis threshold, ventilatory reserve and cardiac reserve in the Spanish population of European ancestors (VARCO)". Collaborating Investigator: M. J. Rodriguez-Nieto. Grants for Research SEPAR • NMD2012 "Identification of novel pathogenic mechanisms, triggered by activation of arginase in patients with stable COPD exacerbated in association with bronchiectasis phase." Principal Investigator: F. Villar-Alvarez. Neumomadrid • NMD2014 "Evaluation of lung damage caused by the electronic cigarette". Principal Investigator: N. González-Mangado. Neumomadrid.

HIGHLIGHTS RESULTS

• Lung recruitment in morbidly obese patients could be effectively monitored by combining noninvasive pulse oximetry and VCap. SpO2, the elimination of CO2, and Bohr's dead space. • Liver Growth Factor (LGF) treatment normalizes the physiological/morphological parameters and levels of various systemic inflammatory biomarkers in a chronic cigarette smoke exposure AKR/J model, which may have important therapeutic implications for subjects with stable COPD. • One-year longitudinal data show variability in COPD Assessment Test (CAT) scores among patients with stable COPD similar to modified Medical Research Council (mMRC) scale score, which is the best predictor of 1-year CAT changes. • Effectiveness of home single-channel nasal pressure for sleep apnea diagnosis.

Institution: Instituto de Investigación Sanitaria - Fundación Jiménez Díaz
Contact: Instituto de Investigacion Sanitaria - Fundacion Jiménez Díaz
Avda. Reyes Católicos, 2. Madrid · Phone: (+34) 91 550 49 12 · E.mail: ngonzalez@fjd.es
http://www.fjd.es/es/cartera-servicios/especialidades-medicas/neumologia

Group 5
Programme: Asthma

Lead Researcher: Picado Vallés, César

Group members

STAFF MEMBERS: Planas Cerezales, Lourdes | Vennera Trunzo, María del Carmen.

ASSOCIATED MEMBERS: Alobid, Isam | Fernández Bertolín, Laura | Fuentes Prado, Mireya | Guilemany Toste, José María | Martínez Antón, Asunción | Molina Molina, María | Mullol Miret, Joaquim | Muñoz Cano, Rosa | Pérez González, María | Pujols Tarres, Laura | Roca Ferrer, Jordi | Serrano Mollar, Ana María | Valero Santiago, Antonio | Xaubet Mir, Antonio.

Main lines of research

- Study of the links between upper airway diseases (rhinitis, rhinosinusitis and nasal polyps) and lower airway diseases (asthma, chronic obstructive pulmonary disease and bronchiectasis). Relationship between chronic rhinosinusitis and asthma severity.
- Study of the alterations in the regulation of glucocorticoid receptor in the reduced response to glucocorticoids (glucocorticoid resistance) in inflammatory airway diseases (chronic rhinosinusitis, nasal polyposis and asthma).
- Study of the role of the cyclooxygenase pathaway of arachidonic acid metabolism in the pathophysiology of airway inflammation (chronic rhinosinusitis, asthma), and in the airways remodelling and lung fibrosis.
- Study of the mechanisms involved in non-steroidal antiinflammatory drugs intolerance in asthma.
- Severe asthma: study of the efficacy of the new biologic therapies (omalizumab).
- New therapies: 6.1 In asthma (agonists of EP2 receptor of prostaglandin E2). 6.2 Transplantation of type II alveolar cells in the treatment of lung fibrosis.

Most relevant scientific articles

- Alobid I., Benitez P., Cardelus S., De Borja Callejas F., Lehrer-Coriat E., Pujols L. et al. Oral plus nasal corticosteroids improve smell, nasal congestion, and inflammation in sino-nasal polyposis. Laryngoscope. 2014;124(1):50-56.
- De Borja Callejas F., Martinez-Anton A., Alobid I., Fuentes M., Cortijo J., Picado C. et al. Reconstituted human upper airway epithelium as 3-D in vitro model for nasal polyposis. PLoS ONE. 2014;9(6):-.
- Colom A., Galgoczy R., Almendros I., Xaubet A., Farre R., Alcaraz J.. Oxygen diffusion and consumption in extracellular matrix gels: Implications for designing three-dimensional cultures. Journal of Biomedical Materials Research - Part A. 2014;102(8):2776-2784.
- Guillamat-Prats R., Gay-Jordi G., Xaubet A., Peinado V.I., Serrano-Mollar A.. Alveolar Type II cell transplantation restores pulmonary surfactant protein levels in lung fibrosis. Journal of Heart and Lung Transplantation. 2014;33(7):758-765.
- Torres-Atencio I., Ainsua-Enrich E., De Mora F., Picado C., Martin M.. Prostaglandin E2 prevents hyperosmolar-induced human mast cell activation through prostanoid receptors EP2 and EP4 . PLoS ONE. 2014;9(10):-.

Highlights

- Two works of the group resulted in the optimization of techniques useful for the studies using tridimensional cellular structures and for in vitro reconstruction of airway mucosa with all structural components. These methodologies are important because will allow to carry out mechanistic studies which could be extrapolated to in vivo scenarios.
- Experimental demonstration that transplantation of type II alveolar cells improve interstitial lung disease by promoting the recovery of the capacity to produce surfactant. This experimental study has been performed in parallel with a clinical trial with this new cellular therapy in humans.
- Physical exercise can precipitate bronchospasm in asthma patients. Bronchoconstriction appears to be due to the increase in the osmolarity of the liquid present in the apical part of airway epithelium buy still partially known mechanisms. Prostaglandin E2 prevents exercise-induced bronchospasm when administered prior to exercise. The mechanisms by which prostaglandin E2 abrogates bronchoconstriction remain to be elucidated. One study of the group demonstrated that prostaglandin E2 stabilizes mast cells exposed to an osmotic challenge and prevents mast cells degranulation. This finding can account for the preventive effect of prostaglandin E of exercise-induced bronchoconstriction.
- Our group is one of the partners of the Integrated Care Pathway for Airway Disease (AIRWAY-ICP), which is one of the programs of the Global Alliance Against Chronic Respiratory Diseases.

Institution: Hospital Clínico y Provincial de Barcelona
Contact: Hospital Clinico y Provincial de Barcelona. C/ Villarroel, 170. 08036 Barcelona
Phone: (+34) 93 451 09 93 · E.mail: cpicado@ub.edu

Group 6

Programme: Cáncer de Pulmón / EPOC

Lead Researcher: Barberà Mir, Joan Albert

Group members

STAFF MEMBERS: Peinado Cabre, Víctor Ivo | Torralba García, Yolanda

ASSOCIATED MEMBERS: Bastos Simmersbach, Ricardo | Blanco Vich, Isabel | Burgos Rincón, Felipe | Gómez Yeron, Federico Pablo | Hernández Carcereny, Carmen | Ramírez Ruz, Josep | Ribas Solà, Jesús | Roca Torrent, Josep | Rodríguez Roisin, Roberto | Tura Ceide, Olga | Zavala Zegarra, Elizabeth

Main lines of research

- Pulmonary Hypertension:
  - o Biopathology, role of progenitor cells in the injury and repair.
  - o Identification of new biomarkers and therapeutic targets. Experimental models.
- COPD:
  - o Physical activity, cellular biogenetic and systemic effects.
  - o Gas exchange abnormalities.
  - o Biopathology of pulmonary vascular changes.
- Healthcare continuity and information technology and communication in chronic respiratory diseases:
  - o Quality control model of forced spirometry supported by information and comunication technologies (ICT).
  - o Early detection of sleep breathing disorders with ICT support.

Most relevant scientific articles

- Zock J.-P., Rodriguez-Trigo G., Rodriguez-Rodriguez E., Souto-Alonso A., Espinosa A., Pozo-Rodriguez F. et al. Evaluation of the persistence of functional and biological respiratory health effects in clean-up workers 6years after the Prestige oil spill. Environment International. 2014;62:72-77.
- Ramon M.A., Gimeno-Santos E., Ferrer J., Balcells E., Rodriguez E., De Batlle J. et al. Hospital admissions and exercise capacity decline in patients with COPD. European Respiratory Journal. 2014;43(4):1018-1027.
- Weissmann N., Lobo B., Pichl A., Parajuli N., Seimetz M., Puig-Pey R. et al. Stimulation of soluble guanylate cyclase prevents cigarette smoke-induced pulmonary hypertension and emphysema. American Journal of Respiratory and Critical Care Medicine. 2014;189(11):1359-1373.
- Sanchez-Salcedo P., Divo M., Casanova C., Pinto-Plata V., De-Torres J.P., Cote C. et al. Disease progression in young patients with COPD: Rethinking the Fletcher and Peto model. European Respiratory Journal. 2014;44(2):324-331.
- Magnussen H., Disse B., Rodriguez-Roisin R., Kirsten A., Watz H., Tetzlaff K. et al. Withdrawal of inhaled glucocorticoids and exacerbations of COPD. New England Journal of Medicine. 2014;371(14):1285-1294.

Highlights

Approval of the Corporate Program of Research in Pulmonary Hypertension

Institution: Hospital Clínico y Provincial de Barcelona
Contact: Servicio de Neumología · Hospital Clínic i Provincial de Barcelona · Subterraneo Esc. 4b
Phone: (+34) 93 227 57 47 · E.mail: jbarbera@clinic.ub.es

Group 7

Programme: Asthma

Lead Researcher: Del Pozo Abejón, Mª Victoria

Group members

STAFF MEMBERS: González Guerra, Andrés | Mazzeo, Carla Silvana

ASSOCIATED MEMBERS: Barranco Sanz, Pilar | Cardaba Olombrada, Blanca | Fernández Nieto, María del Mar | Lahoz Navarro, Carlos | Quirce Gancedo, Santiago | Sastre Domínguez, Joaquín

Main lines of research

- Mechanism underlying to genesis and evolution of asthma.
- Characterization of asthma phenotypes.
- Characterization of asthma severity and identification of the factors that are involved in asthma severity.
- New therapies in asthma.
- Eosinophils.
- Exosomes and asthma.

Most relevant scientific articles

- Sander I., Rihs H.-P., Doekes G., Quirce S., Krop E., Rozynek P. et al. Component-resolved diagnosis of baker's allergy based on specific IgE to recombinant wheat flour proteins. Journal of Allergy and Clinical Immunology. 2014;:-.
- Mazzeo C., Canas J.A., Zafra M.P., Marco A.R., Fernandez-Nieto M., Sanz V. et al. Exosome secretion by eosinophils: Apossible role in asthma pathogenesis. Journal of Allergy and Clinical Immunology. 2014;:-.
- Vandenplas O., Suojalehto H., Aasen T.B., Baur X., Burge P.S., De Blay F. et al. Specific inhalation challenge in the diagnosis of occupational asthma: Consensus statement. European Respiratory Journal. 2014;43(6):1573-1587.
- Raulf M., Buters J., Chapman M., Cecchi L., De Blay F., Doekes G. et al. Monitoring of occupational and environmental aeroallergens - EAACI Position Paper: Concerted action of the EAACI IG occupational allergy and aerobiology & air pollution. Allergy: European Journal of Allergy and Clinical Immunology. 2014;69(10):1280-1299.
- Moscato G., Pala G., Cullinan P., Folletti I., Gerth Van Wijk R., Pignatti P. et al. EAACI position paper on assessment of cough in the workplace. Allergy: European Journal of Allergy and Clinical Immunology. 2014;69(3):292-304.

Institution: Instituto de Investigación Sanitaria - Fundación Jiménez Díaz
Contact: Instituto de Investigacion Sanitaria Fundación Jiménez Díaz (IIS-FJD)
Edificio Investigación. 4a Planta. Avda. Reyes Católicos, 2, 28040 Madrid · Phone: (+34) 91 550 48 91
E.mail: vpozo@fjd.es

Group 8

Programme: Host-Pathogen Interactions

Lead Researcher: Regueiro Comesaña, Verónica

Group members

STAFF MEMBERS: Euba Rementería, Begoña | Martinez Moliner, Verónica

ASSOCIATED MEMBERS: Garmendia García, Juncal | Llobet Brossa, Enrique | Moranta Mesquida, David

Main lines of research

The main goal of our group is to study the immune response of hosts to face pathogenic microorganisms, and decipher the molecular mechanisms that regulate the interaction between host and pathogen. Thus, we study host response mechanisms, resistance and evasion systems developed by pathogens.

- Molecular dissection of host cellular systems involved in the immune response to front pathogens.
- Analysis of Klebsiella pneumoniae adaptations to survive in the lung.
- Analysis of antimicrobial peptide resistance mechanisms.
- Molecular mechanisms of bacterial infection associated to COPD exacerbation.
- Identification and preclinical evaluation of novel host-directed therapies to treat respiratory infection by the bacterial pathogen nontypable Haemophilus influenzae.
- Molecular evolution and human host adaptation of the bacterial pathogen nontypable Haemophilus influenzae.

Most relevant scientific articles

- Garmendia J., Viadas C., Calatayud L., Mell J.C., Marti-Lliteras P., Euba B. et al. Characterization of nontypable Haemophilus influenzae isolates recovered from adult patients with underlying chronic lung disease reveals genotypic and phenotypic traits associated with persistent infection. PLoS ONE. 2014;9(5):-.
- Lery L.M.S., Frangeul L., Tomas A., Passet V., Almeida A.S., Bialek-Davenet S. et al. Comparative analysis of Klebsiella pneumoniae genomes identifies a phospholipase D family protein as a novel virulence factor. BMC Biology. 2014;12:-.
- Puig C., Domenech A., Garmendia J., Langereis J.D., Mayer P., Calatayud L. et al. Increased biofilm formation by nontypeable Haemophilus influenzae isolates from patients with invasive disease or otitis media versus strains recovered from cases of respiratory infections. Applied and Environmental Microbiology. 2014;80(22):7088-7095.
- Mell JC, Sinha S, Balashov S, Viadas C, Grassa CJ, Ehrlich GD et al. Complete Genome Sequence of Haemophilus influenzae Strain 375 from the Middle Ear of a Pediatric Patient with Otitis Media.Genome announcements. 2014;2(6).

Highlights

Our group has become a worldwide reference for lipid A analysis since we have been able to analyze, for the first time, the Lipid A structure from a pathogen during infection without isolating or enriching the organism. This achievement opens the door not only to consider new therapeutic targets but also to study how pathogens present them self to the host. For instance, and as a proof of principle, we have developed a bacterial glycome based microchip that enables us to identify different pathogens according to specific membrane structures (Ringer-Rhodes et al., Advances RSC, 2015,5,7173-7181).

We currently apply our progresses in lipid A analysis at the Hospital Universitary Son Espases, which is Balearic's reference hospital, to clarify how distinct respiratory pathogens (i.e. Pseudomonas aeruginosa, and Haemophilus influenzae) modify their membrane structures in order to colonize permanently the lung becoming a chronic pathogen.

Finally, it is worth to point out that all these advances on Lipid A analysis has allowed us to collaborate with several national and international research groups focused on the study of antibiotics resistance mechanisms of multi resistant pathogens (Beceiro et al, Antimicrob Agents Chemother, 2011;. Conde-Alvarez et al, PLoS Pathog, 2012;. Reinés et al, PLoS Pathog. , 2012; De Majumdar et al, PLoS Pathog, 2015), as has done it to participate in various national (SEPAR 068/2011; SEPAR 054/2011; SAF2012-39841) and international projects (INBIONET FP7-PEOPLE-2012-ITN).

Institution: Fundación de Investigacion Sanitaria de las Islas Baleares Ramon Llull (FISIB)
Contact: Fundación de Investigación Sanitaria de las Islas Baleares Ramon Llull (FISIB)
Ctra. Sóller km. 12. Recinto Hospital Joan March. 07110 Bunyola (Mallorca)
Phone: (+34) 971 011 780 · E.mail: regueiro@caubet-cimera.es · Website: www.caubet-cimera.es

Group 9

Programme: Tuberculosis (TB)/ Host-Pathogen Interactions

Lead Researcher: Martín Montañés, Carlos

Group members

STAFF MEMBERS: Cebollada Solanas, Alberto | Lampreave Carrillo, Carlos

ASSOCIATED MEMBERS: Aguiló Anento, Ignacio | Ainsa Claver, José Antonio | Alonso Ezcurra, María Henar | Arbues Arribas, Ainhoa | Dias Rodrigues, Liliana Isabel | Gavin Benavent, Patricia | Gómez Aguirre, Ana Belen | Gómez Lus, Rafael | Gonzalo Asensio, Jesús | Gracia Díaz, Begoña | Ibarz Bosqued, Daniel | Iglesias Gozalo, María José | Lafoz Pueyo, Carmen | Lezcano Carrera, María Antonia | Lucía Quintana, Ainhoa | Millán Lou, María Isabel | Otal Gil, Isabel | Pico Marco, Ana | Revillo Pinilla, María José | Rubio Calvo, María Carmen | Samper Blasco, Sofía Luisa | Solans Bernad, Luis | Villellas Arilla, María Cristina | Vitoria Agreda, Mª Asunción

Main lines of research

Our Research Group of Mycobacterial Genetics has been working since 1992 in four lines of research financed by European and national investigation funds and that has permitted it to acquire an internationally recognized prestige. These lines of research include: Construction of New Vaccines against Tuberculosis • Molecular Epidemiology of Tuberculosis & Transposition and Latency of M. tuberculosis • Molecular Bases of the Resistance of mycobacteria.

The objectives of our group are to study the complexity of M. tuberculosis in a multidisciplinary focus and our group is coordinated with other national and international groups. More concretely we focus our research in: Genes implicated in the pathogenicity and virulence of M. tuberculosis • Molecular epidemiology of tuberculosis, risk factors of transmission, and differences between strains of major epidemiological importance and the mechanism of slow growth of the Koch bacillus • Mechanisms of resistance.

Active Projects:

- Line 1: NEW TBVAC 241745 FP7 Discovery and preclinical testing of new vaccine candidates for tuberculosis. European Union Organization. Chief Researcher and Coordinator: Carlos Martín Montañes "http://www.tbvi.eu/projects/newtbvac.html/ 2010- 2014 Coordinator Dr Jelle Thole NL. • BIO2011-23555 BIO2011-23555 Project: "Study of the mechanisms of protection of MTBVAC and its potential use as recombinant polyvalent vaccine." MCyT/DGI/FEDER Organization. 2012-2014. Chief Researcher and Coordinator: Carlos Martín • INNPACTO: Ref. IPT-2012-0327-090000 Ministerio de Economía y Competitividad "Vacuna Inactivada contra la tuberculosis en base a una cepa modificada genéticamente – .Universidad de Zaragoza, IP: Carlos Martín, Universidad Complutense y la empresa BIOFABRI.
- Line 2: Polimorfismos genómicos y transcriptómicos en M. tuberculosis complex y su significado en clínica. IP: Sofía Samper. Number of researchers: 10; FIS, Instituto de Salud Carlos III. 2013- 2015.

• Study of the impact of RD8 on the regulation of ESAT-6 secretion in Mycobacterium bovis and Mycobacterium africanum.SecRegulTBC. REFBIO. 2013- 2014 • Antimicrobial resistance, virulence and new therapies in bacterial human pathogens. REFBIO 2013- 2014 • Network: European reference laboratory network for tuberculosis (ERLTB-Net) - to strengthen TB diagnosis, drug susceptibility testing and coordination at European Union level. Ref: GRANT/2013/003. ECDC. Fecha inicio: 2014.

- Line 3: MM4TB More Medicines for Tuberculosis. European Union Organization Chief Researcher and Coordinator: José Antonio Ainsa. 2011-2014 • NAREB - Nanotherapeutics for antibiotic resistant emerging bacterial pathogens European Union. 2014- 2018.

Most relevant scientific articles

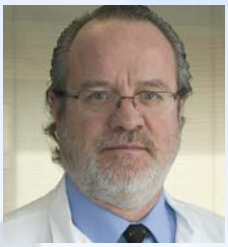
- Lee R.E., Hurdle J.G., Liu J., Bruhn D.F., Matt T., Scherman M.S. et al. Spectinamides: A new class of semisynthetic antituberculosis agents that overcome native drug efflux. Nature Medicine. 2014;20(2):152-158.
- Gonzalo-Asensio J., Malaga W., Pawlik A., Astarie-Dequeker C., Passemar C., Moreau F. et al. Evolutionary history of tuberculosis shaped by conserved mutations in the PhoPR virulence regulator. Proceedings of the National Academy of Sciences of the United States of America. 2014;111(31):11491-11496.
- Solans L., Gonzalo-Asensio J., Sala C., Benjak A., Uplekar S., Rougemont J. et al. The PhoP-Dependent ncRNA Mcr7 Modulates the TAT Secretion System in Mycobacterium tuberculosis. PLoS Pathogens. 2014;10(5):-.
- Aguiló N., Uranga S., Marinova D., Martin C., Pardo J.. Bim is a crucial regulator of apoptosis induced by Mycobacterium tuberculosis. Cell Death and Disease. 2014;5(7):-.
- Allix-Beguec C., Wahl C., Hanekom M., Nikolayevskyy V., Drobniewski F., Maeda S. et al. Proposal of a consensus set of hypervariable mycobacterial interspersed repetitive-unit-variable-number tandem-repeat loci for subtyping of mycobacterium tuberculosis Beijing isolates. Journal of Clinical Microbiology. 2014;52(1):164-172.

Highlights

ACTIVE PROJECTS IN 2014

• MM4TB More Medicines for Tuberculosis. European Union Organization. Chief Researcher and Coordinator: José Antonio Ainsa • NAREB Nanotherapeutics for antibiotic resistant emerging bacterial pathogens. European Union Organization. Chief Researcher and Coordinator: José Antonio Ainsa • BIO2011-23555 Project: "Study of the mechanisms of protection of MTBVAC and its potential use as recombinant polyvalent vaccine." MCyT/DGI/FEDER Organization 2012-2014 Chief Researcher and Coordinator: Carlos Martín • INNPACTO: Ref. IPT-2012-0327-090000. Vacuna Inactivada contra la tuberculosis en base a una cepa modificada genéticamente Ministerio de Economía y Competitividad Organization. Universidad de Zaragoza, Universidad Complutense and Biofabri. Chief Researcher and Coordination: Carlos Martín • Polimorfismos genómicos y transcriptómicos en M. tuberculosis complex y su significado en clínica. FIS, Instituto de Salud Carlos III Organization Chief Researcher and Coordination: Sofía Samper • Study of the impact of RD8 on the regulation of ESAT-6 secretion in Mycobacterium bovis and Mycobacterium africanum. SecRegulTBC. REFBIO Organization Chief Researcher and Coordination: Sofía Samper • Patent Number P2014/30421 2014/03/25. Spain.Inventors: Carlos Martin, Brigitte Gicquel, Luis Solans, Nacho Aguilo, Santiago Uranga Title: Triple mutant of Mycobacterium tuberculosis Complex erp-, phoP- Y DIM Zaragoza University • Clinical Trials: "Dose-Escalation Study to Evaluate the Safety and Immunogenicity of MTBVAC Vaccine in Comparison With BCG Vaccine." ClinicalTrials.gov Identifier: NCT02013245

Institution: Universidad de Zaragoza
Contact: Universidad de Zaragoza. C/ Pedro Cerbuna, 12. 50009 Zaragoza
Phone: (+34) 976 761 759 · E.mail: carlos@unizar.es · Website: genmico.unizar.es



Group 10

Programme: Chronic Obstructive Pulmonary Disease (COPD)/Pulmonary Fibrosis

Lead Researcher: Agustí García-Navarro, Àlvar

Group members

STAFF MEMBERS: Iglesias Coma, Amanda | Sunyer Dequiogiovanni, Gemma.

ASSOCIATED MEMBERS: Barceló Martín, Bernardino | Faner Canet, María Rosa | Ferrer Balaguer, Joana Maria | García-Cosío Piqueras, Francisco de Borja | López Zamora, Meritxell | Molins López Rodo, Laureano | Noguera Bennaser, Francisca Ana | Pons de Ves, Jaime | Ríos Olivencia, Ángel | Sala Llinas, Ernest | Sauleda Roig, Jaume | Sibila Vidal, Oriol | Soler Cataluña, Juan José | Valera Felices, José Luis

Main lines of research

- Line called "Natural History" which seeks to deepen into the different clinical , pathophysiological and structural aspects of COPD, with emphasis on discovering predictors of evolution.
- Line called "Pathobiology" focuses on aspects related to the origin or cause of the disease and the changes at the molecular and cellular level, including the initial effects of tobacco to subsequent inflammatory immune mechanisms and remodelling.
- Thirdly, the study of "Systemic effects and polimorbility" of COPD wants to identify mechanisms of extra pulmonary entity and its clinical consequences . Basically, this line goes to the cardiovascular effects and skeletal muscle.
- Line "Exacerbations" refers to the phenomenon of exacerbation of COPD, from its causes to the consequences of behaviour in the evolution of the disease.

Most relevant scientific articles

- Faner R., Gonzalez N., Cruz T., Kalko S.G., Agusti A.. Systemic inflammatory response to smoking in chronic obstructive pulmonary disease: Evidence of a gender effect. PLoS ONE. 2014;9(5):-.
- Grosdidier S., Ferrer A., Faner R., Pinero J., Roca J., Cosio B. et al. Network medicine analysis of COPD multimorbidities. Respiratory Research. 2014;15(1):-.
- McDonald M.-L.N., Cho M.H., Sorheim I.-C., Lutz S.M., Castaldi P.J., Lomas D.A. et al. Common genetic variants associated with resting oxygenation in chronic obstructive pulmonary disease. American Journal of Respiratory Cell and Molecular Biology. 2014;51(5):678-687.
- Diez D., Agusti A., Wheelock C.E.. Network analysis in the investigation of chronic respiratory diseases. From basics to application. American journal of respiratory and critical care medicine. 2014;190(9):981-988.
- Vestbo J, Agusti A, Wouters EF, Bakke P, Calverley PM, Celli B et al. Should we view chronic obstructive pulmonary disease differently after ECLIPSE? A clinical perspective from the study team.American journal of respiratory and critical care medicine. 2014;189(9):1022-30.

Highlights

During 2014 the group 10 of CIBERES has achieved the following results:

- systems biology has been applied to COPD in order to describe the molecular networks that are common to the frequent COPD comorbidities.
- we have descried that the systemic inflammatory response to smoke is different in patients with COPD than in normal lung function smokers and that it also varies according to the gender.
- the group has been involved in the COPD associated biomarker discovery and phenotyping in the context of the ECLIPSE study.

On reference to new projects, the group has initiated a study funded by the SEPAR (PI065/2013) whose PI is Alvar Agusti. The group is involved in the projects of the COPD PCI and during this year the active projects funded by ISCiii, Recercaixa, SEPAR and FUCAP have been developed as initially planned.

On reference to clinical guidelines, the group leader Dr. Agusti is member of the GOLD board (Global Initiative for Chronic Obstructive Lung Disease) that in year 2014 published the Clinical Guidelines for the Asthma, COPD and Asthma – COPD Overlap Syndrome (ACOS)(http://www.goldcopd.org/).

Institution: Fundación de Investigación Sanitaria de las Islas Baleares Ramon Llull (FISIB)
Contact: Tel.: (+34) 93 227 17 01 · E.mail: alvar.agusti@clinic.ub.es · Website: www.isciii.es

Group 11

Programme: Sleep Apnea-Hypopnea Syndrome (SAHS)

Lead Researcher: Montserrat Canal, Josep Mª

Group members

STAFF MEMBERS: Torres López, Marta.

ASSOCIATED MEMBERS: Arboix Damunt, Adria | Ballester Rodes, Eugenio | Dalmases Cleries, Mireia | De Pablo Rabasso, Juan | Embid López, Cristina | Hernández Plaza, Lourdes | Martinez García, Miguel Ángel | Mayos Pérez, Mercedes | Monasterio Ponsa, Carmen | Morello Castro, Antonio | Parra Ordaz, Olga | Salamero Baro, Manuel | Salord Oleo, Neus | Uriarte Díaz, Juan José | Vilaseca González, Isabel

Main lines of research

- Respiratory Sleep disorders, apnoea and cancer. Since 2011 the group was working group in this area that has been seminal with two lines of research clinical and basic . There are a number of published clinical and basic work.
- Sleep disorders and aging . For the group this aspect is considered essential because in the near future the elderly will be 20 % of the population and the number of apneas of them is usually much higher. Perhaps the diagnostic and therapeutic procedures in this patients would be different and more cost-efective procedures are neded. This studies are performed in human and in murine.
- The group has another important goal. Specifically and as apneas are considered a systemic disease attempts to assess the effect of apnea in other organs. A first study already published in JAMA assesses the relationship between apnea and high blood pressure. Currently another line has already finished part (murine model) and is the effect of apneas on fertility. Now , will begin the human studies. In the future other organs such as liver, aspects of intestinal flora, etc.will be studied.
- Telemedicine and very specifically in the development of a virtual laboratory where all sleep studies and patient care will be performed outside of the hospital. In addition programs with nurses are on going to improve CPAP compliance.
- Finally mechanical ventilation in the direction of the appropriate titration and monitoring are priorities. Also in this context, the group works with companies to assess various devices.

Most relevant scientific articles

- Dalmases M., Torres M., Marquez-Kisinousky L., Almendros I., Planas A.M., Embid C. et al. Brain tissue hypoxia and oxidative stress induced by obstructive apneas is different in young and aged rats. Sleep. 2014;37(7):1249-1256.
- Guerrero A., Embid C., Isetta V., Farre R., Duran-Cantolla J., Parra O. et al. Management of sleep apnea without high pretest probability or with comorbidities by three nights of portable sleep monitoring. Sleep. 2014;37(8):1363-1373.
- Masa J.F., Duran-Cantolla J., Capote F., Cabello M., Abad J., Garcia-Rio F. et al. Effectiveness of home single-channel nasal pressure for sleep apnea diagnosis. Sleep. 2014;37(12):1953-1961B.
- Moreno-Indias I, Torres M, Montserrat JM, Sanchez-Alcoholado L, Cardona F, Tinahones FJ et al. Intermittent hypoxia alters gut microbiota diversity in a mouse model of sleep apnoea.The European respiratory journal. 2014;.
- Martinez-Garcia M.-A., Martorell-Calatayud A., Nagore E., Valero I., Selma M.J., Chiner E. et al. Association between sleep disordered breathing and aggressiveness markers of malignant cutaneous melanoma. European Respiratory Journal. 2014;43(6):1661-1668.

Highlights

Group 11 operates in the Hospital Clinic of Barcelona (HCB) (Coordinator Dr Josep M. Montserrat, HCB Senior Consultant, director of the Sleep Unit and Professor University of Barcelona (UB). The group includes sleep units from the following Hospitals in Barcelona: Sagrat Cor, San Pablo, Bellvitge and La Fe from Valencia. The group's activities are divided into five components: basic, clinical and technological aspects; collaboration with the COST-European Group Action; and own group activities.

- Basic aspects on collaboration with Professor Daniel Navajas's (UB) group. We have jointly developed animal models of sleep apnea (supported by FIS 11/01892. Papers more representatives (R), Torres 2014 SLEEP, Dalmases SLEEP 2014).
- Clinical aspects, in collaboration with PII Group of SEPAR (previously directed by Dr Montserrat). This collaboration has enabled to perform the large multicenter studies of the Spanish sleep group. Papers (R), Masa et al. Sleep 2014 and the ones led by the members of our group Martinez-Garcia et al. SLEEP MED 2014, Martinez-Garcia et al. ERJ 2014) (Supported by Dr Masa FIS PI 13/02638, and SEPAR.
- Regarding the technological studies, we have developed a platform for patient care (technology knowledge transfer and visits by videoconference (collaboration with Dr. Isetta, Biomedical engineer, Dr Navajas group) (Paper (R) Isetta. Interact J Med Res. 2014)(Supported by FIS PI14/0041 and SEPAR special grant).
- In the context of the European Group the most important publications have been related to European database (Kent ERJ 2014).
- Finally, the group is analyzing the relation between apnea and cancer, or obesity or aging (Support FUCAP and SOCAP. Paper (R): Salord JCSM 2014 and Dalmses Sleep 2014)

The group is currently working on developing a Virtual Sleep Unit and col.laborate wit Esteve-Teijin, Respironics and SIBEL.

Institution: Hospital Clínico y Provincial de Barcelona
Contact: Hospital Clinico y Provincial de Barcelona · Villarroel, 170. Barcelona
Phone: (+34) 93 227 92 14 · E.mail: jmmontserrat@ub.edu

Group 12

Programme: Sleep Apnea-Hypopnea Syndrome (SAHS)/ Acute Lung Injury (ALI)

Lead Researcher: Navajas Navarro, Daniel

Group members

STAFF MEMBERS: Polo Tortola, Maeba.

ASSOCIATED MEMBERS: Alcaraz Casademunt, Jordi | Campillo Agullo, Noelia | Carreas Palau, Alba | Farré Ventura, Ramon | Isseta, Valentina | Luque González, Tomas Alberto | Melo Herráiz, Esther | Rodríguez Lazaro, Miguel Angel | Rotger Estapé, Maria del Mar | Trepat Guixer, Xavier

Main lines of research

- Pathophysiology of sleep apnea and acute lung injury in patients and animal models.
- Tissue engineering and regenerative medicine in respiratory diseases.
- Nanotechnologies and lab-on-a-chip for the study and characterization of the mechanical behavior of cells and tissue systems.
- Instrumentation for diagnostic, therapeutic and monitoring of sleep apnea and acute lung injury.

Most relevant scientific articles

- Almendros I., Wang Y., Becker L., Lennon F.E., Zheng J., Coats B.R. et al. Intermittent hypoxia-induced changes in tumor-associated macrophages and tumor malignancy in a mouse model of sleep apnea. American Journal of Respiratory and Critical Care Medicine. 2014;189(5):593-601.
- Isetta V., Leon C., Torres M., Embid C., Roca J., Navajas D. et al. Telemedicine-based approach for obstructive sleep apnea management: Building evidence. Journal of Medical Internet Research. 2014;16(2).
- Andreu I., Luque T., Sancho A., Pelacho B., Iglesias-Garcia O., Melo E. et al. Heterogeneous micromechanical properties of the extracellular matrix in healthy and infarcted hearts. Acta Biomaterialia. 2014;10(7):3235-3242.
- Martínez-García M.-A., Martorell-Calatayud A., Nagore E., Valero I., Selma M.J., Chiner E. et al. Association between sleep disordered breathing and aggressiveness markers of malignant cutaneous melanoma. European Respiratory Journal. 2014;43(6):1661-1668.
- Moreno-Indias I, Torres M, Montserrat JM, Sanchez-Alcoholado L, Cardona F, Tinahones FJ et al. Intermittent hypoxia alters gut microbiota diversity in a mouse model of sleep apnoea.The European respiratory journal. 2014.

Highlights

The research activity of the group has an interdisciplinary and translational character, integrating basic and clinical aspects. In 2014 the research has focused mainly on the corporate programs "Sleep Apnea-Hypopnea Syndrome" (SAHS) and "Acute Lung Injury" (ALI). In the first program we have obtained very significant achievements in the study of the relationship between cancer and SAHS. We have established that there is increased cancer mortality in patients with SAHS, that SAHS enhances human malignant melanoma and we have shown that the immune system plays an important role in cancer-related SAHS. We have also shown that telemetric tools are useful for diagnosing and home monitoring of SAHS. We have developed research contracts with companies to improve instrumentation equipment for SAHS therapy. In animal models we have determined that age induces significant changes in brain response to apneas and male fertility is greatly reduced by the intermittent hypoxia of SAHS. In ALI we have used tissue engineering tools to advance the understanding of the basic mechanisms of lung regeneration/repair. Using nano- and micro-technologies we first described local changes in rigidity of the extracellular matrix in normal and fibrotic lungs. These results will allow understanding cell-matrix interaction in lung regeneration. We have characterized the local viscoelasticity of normal and fibrotic cardiac tissue, which is relevant to understand cardiac remodeling in pulmonary hypertension. We have also studied the mechanical changes induced in pulmonary extracellular matrix by freezing/thawing and sterilization of the lung tissue. We also described for the first time that the partial pressure of oxygen enhances physiological differentiation of stem cells into lung epithelial phenotypes, being relevant for the optimization of lung regeneration.

Institution: Universidad de Barcelona
Contact: Facultad de Medicina. Universidad de Barcelona · C/ Casanova, 143. 08036 Barcelona
Phone: (+34) 93 402 45 15 · E.mail: dnavajas@ub.edu · Website: www.ub.edu/biofisica

Group 13

Programme: Host-Pathogen Interactions / Pulmonary Fibrosis

Lead Researcher: Morcillo Sánchez, Esteban J.

Group members

STAFF MEMBERS: Serrano Gimeno, Adela.

ASSOCIATED MEMBERS: Almudever Folch, Patricia | Cerda Nicolás, Miguel | Cortijo Gimeno, Julio | Juan Samper, Gustavo | Mata Roig, Manuel

Main lines of research

- COPD human and animal models: pharmacological modulation.
- Pulmonary fibrosis: human and animal models: pharmacological modulation.
- Pulmonary hypertension-associated pulmonary idiopathic fibrosis.
- In vitro models of corticoid-resistance on relevant to COPD.

Most relevant scientific articles

- Milara J., Lluch J., Almudever P., Freire J., Xiaozhong Q., Cortijo J.. Roflumilast N-oxide reverses corticosteroid resistance in neutrophils from patients with chronic obstructive pulmonary disease. Journal of Allergy and Clinical Immunology. 2014;134(2).
- Milara J., Peiro T., Armengot M., Frias S., Morell A., Serrano A. et al. Mucin 1 downregulation associates with corticosteroid resistance in chronic rhinosinusitis with nasal polyps. Journal of Allergy and Clinical Immunology. 2014.
- Moreno L., Moral-Sanz J., Morales-Cano D., Barreira B., Moreno E., Ferrarini A. et al. Ceramide mediates acute oxygen aensing in vascular tissues. Antioxidants and Redox Signaling. 2014;20(1):1-14.
- Pastor-Clerigues A., Marti-Bonmati E., Milara J., Almudever P., Cortijo J.. Anti-inflammatory and anti-fibrotic profile of fish oil emulsions used in parenteral nutrition-associated liver disease. PLoS ONE. 2014;9(12).
- De Borja Callejas F., Martinez-Anton A., Alobid I., Fuentes M., Cortijo J., Picado C. et al. Reconstituted human upper airway epithelium as 3-D in vitro model for nasal polyposis. PLoS ONE. 2014;9(6).

Institution: Universidad de Valencia
Contact: Facultad de Medicina de Valencia · Avda. Vicente Blasco Ibañez, 13. 46010 Valencia
Phone: (+34) 96 386 46 22 · E.mail: esteban.morcillo@uv.es

Group 14

Programme: Pneumonia

Lead Researcher: Torres Martí, Antoni

Group members

STAFF MEMBERS: Cilloniz Campos, Catia | Fernández Barat, Laia | Li Bassi Li Bassi, Gianluigi | Sancho Roset, Elisabeth.

ASSOCIATED MEMBERS: Agustí García Navarro, Carlos | Almirall Pujol, Jorge | Badia Jobal, Juan Ramon | Bello Dronda, Salvador | Falguera Sacrest, Miquel | Ferrer Monreal, Miguel | Martínez Olondris, Pilar | Menéndez Villanueva, Rosario | Polverino, Eva | Ramírez Galleymore, Paula | Sellares Torres, Jacobo | Sirvent Calvera, José María | Soler Porcar, Nestor | Soy Muner, Dolores

Main lines of research

- Animal Model.
- Community-acquired pneumonia (CAP).
- Bronchiectasis non associated to Cystic Fibrosis (BQ-noFQ), Cystic Fibrosis (CF) and immune deficiencies.
- Exacerbations of Chronic Obstructive Pulmonary Disease (COPD).
- Ventilator associated-pneumonia.

Most relevant scientific articles

- Di Pasquale M., Ferrer M., Esperatti M., Crisafulli E., Giunta V., Li Bassi G. et al. Assessment of severity of ICU-acquired pneumonia and association with etiology. Critical Care Medicine. 2014;42(2):303-312.
- Li Bassi G., Rigol M., Marti J.-D., Saucedo L., Ranzani O.T., Roca I. et al. A novel porcine model of ventilator-associated pneumonia caused by oropharyngeal challenge with pseudomonas aeruginosa. Anesthesiology. 2014;120(5):1205-1215.
- Cilloniz C., Torres A., Polverino E., Gabarrus A., Amaro R., Moreno E. et al. Community-acquired lung respiratory infections in HIV-infected patients: Microbial aetiology and outcome. European Respiratory Journal. 2014;43(6):1698-1708.
- Bello S., Minchole E., Fandos S., Lasierra A.B., Ruiz M.A., Simon A.L. et al. Inflammatory response in mixed viral-bacterial community-acquired pneumonia. BMC Pulmonary Medicine. 2014;14(1).
- Li Bassi G., Marti J.D., Saucedo L., Rigol M., Roca I., Cabanas M. et al. Gravity predominates over ventilatory pattern in the prevention of ventilator-associated pneumonia. Critical Care Medicine. 2014;42(9).

Highlights

- First of all it is necessary to stand out have managed reproduce an animal model of serious pneumonia in porks ventilated mechanically for S. pneumoniae serotipo 19 ª. This model is going to be very important in next year for translational studies.
- We have signed and closed 4 contracts with international industries for studies in our animal model of S. aeruginosa and MRSA (Medimmune, Cardeas, Theravance and Cubist).
- We have obtained a Juan de la Cierva-Ciber contract for Dr. Catia Cillóniz, member of the group. Dr. Gianluigi Li Bassi, member of the group as well, is continuing with his Juan de la Cierva-Ciber contract.
- Our group has been qualified as the first one of 34 groups of the Ciber of Respiratory of last 3 years.
- Dr Antoni Torres, chief of the group, has been honored by the ICREA Acadèmia 2014 Program for excellence in research in the area "Life & Medical Sciences" by the University of Barcelona.

Institution: Hospital Clínico y Provincial de Barcelona
Contact: Hospital Clínic i Provincial de Barcelona. C/ Villarroel, 170. 08036 BARCELONA
Phone: (+34) 93 227 55 49 · E.mail: atorres@ub.edu · Website: www.idibapsrespiratoryresearch.org

Group 15

Programme: Sleep Apnea-Hypopnea Syndrome (SAHS)

Lead Researcher: Masa Jiménez, Juan Fernando

Group members

STAFF MEMBERS: Iglesias Román, María Vanessa | Pereira Solís, Ricardo

ASSOCIATED MEMBERS: Corral Peñafiel, Jaime | Disdier de Vicente, Carlos | Gallego Domínguez, Rocío | Gomez de Terreros Caro, Francisco Javier | Riesco Miranda, Juan Antonio | Rubio González, Manuela | Sánchez Escuín, Julio | Terán Santos, Joaquín

Main lines of research

- Respiratory disorders and sleep apneas during sleep.
- Noninvasive ventilation treatment in acute and chronic settings.
- Lung cancer diagnosis and treatment.
- Telematic diagnosis in respiratory medicine.
- Tobacco quit and treatment.

Most relevant scientific articles

- Masa J.F., Duran-Cantolla J., Capote F., Cabello M., Abad J., Garcia-Rio F. et al. Effectiveness of home single-channel nasal pressure for sleep apnea diagnosis. Sleep. 2014;37(12):1953-1961B.
- Guerrero A., Embid C., Isetta V., Farre R., Duran-Cantolla J., Parra O. et al. Management of sleep apnea without high pretest probability or with comorbidities by three nights of portable sleep monitoring. Sleep. 2014;37(8):1363-1373.
- Alonso-Alvarez M.L., Cordero-Guevara J.A., Teran-Santos J., Gonzalez-Martinez M., Jurado-Luque M.J., Corral-Penafiel J. et al. Obstructive sleep apnea in obese community-dwelling children: The NANOS study. Sleep. 2014;37(5):943-949.
- Sánchez de Cos Escuin J., Abal Arca J., Melchor Iniguez R., Miravet Sorribes L., Nunez Ares A., Hernandez Hernandez J.R. et al. Tumor, node and metastasis classification of lung cancer - M1a versus M1b - Analysis of M descriptors and other prognostic factors. Lung Cancer. 2014;84(2):182-189.
- Casanova C., Marin J.M., Martinez-Gonzalez C., de Lucas-Ramos P., Mir-Viladrich I., Cosio B. et al. New GOLD classification: Longitudinal data on group assignment. Respiratory Research. 2014;15(1).

Highlights

The group's activity has focused on the completion of two clinical guidelines and implementation and dissemination of projects:

- Validity and cost effectiveness of a single channel expert system in the diagnosis of the SAHS. FIS, SEPAR. Code: PI050445. Dissemination: two published articles (2014 and 2015).
- Efficiency at medium and long-term noninvasive ventilation in obesity syndrome hypoventilation. (Pickwicks) SEPAR, FIS PS09 / 00510. Dissemination first phase (2 months): An article under review and another in execution. Running second phase (36 months follow-up).
- Cost-effectiveness of home respiratory management polygraphy (hrp management) SEPAR, Neumosur and Fundesalud. Execution.
- Cost-effectiveness and of an oversimplified efectiveness system for the management of patients with high probability of sleep apnea in primary care. FIS PI13 / 02638. Execution.
- Spanish record of patients in Ricu (REPUCRI); Project 116 | 2012 SEPAR. Running and dissemination: an article review and two running.
- A multi-centre, randomized study to assess the effects of adaptive servo ventilation on survival and frequency of cardiovascular hospital admissions in patients with heart failure and sleep apnea. Canadian institutes of health research and Philips. Execution.
- Prevalence of Shahs in obese children. importance of hormonal factors (nanos) PRI09A138; SEPAR; Spread: 2 items in 2014 and two running. Sleep apnea.
- The European Database (Esada). Cost EU action. In implementation and dissemination. Two articles in 2014.
- Apnea syndrome -hypopnea (SAHS) as a risk factor for the development of acute myocardial infarction. fis pi 10/02763. execution.
- Utility of basic curves in COPD patients in synchrony. fis. execution.
- Sleep disorders association between respiratory and growth rate of cutaneous melanoma. fis pii2 / 01363 and separ. execution.
- Effect of treatment with in women with cpap sleep apnea obstructive. multicenter, randomized, controlled study. FIS PI13 / 00743 and SEPAR. Execution.

Institution: Fund. para la Formación y la Investigación de los Profesionales de la Salud (FUNDESALUD)
Contact: Hospital San Pedro de Alcantara. Avda. Pablo Naranjo, s/n. 10003 Cáceres
Phone: (+34) 927 256 204 · E.mail: fmasa@separ.es

Group 16
Programme: Asthma

Lead Researcher: Morell Brotad, Ferrán

Group members

STAFF MEMBERS: Ollé Monge, Marta | Sánchez Ortiz, Mónica.

ASSOCIATED MEMBERS: Álvarez Fernández, Antonio | Bravo Masgoret, Carlos | Cruz Carmona, Maria Jesus | De Gracía Roldán, Javier | Ferrer Sancho, Jaime | Genover Llimona, María Teresa | Gómez Olles, Susana | Lloberes Canadell, Patricia | Martí Beltran, Sergi | Miravitlles Fernández, Marc | Monforte Torres, Víctor | Muñoz Gall, Javier | Orriols Martínez, Ramón | Roca Gas, Oriol | Rodríguez González, Esther | Roman Broto, Antonio | Romero Santo Tomas, Odile | Ruano Burgos, Laura | Sampol Rubio, Gabriel | Untoria Corral, María Dolores | Vendrell Relat, Montserrat

Main lines of research

The PCI on asthma has started the MEGA project (Mechanism underlying to genesis and evolution of asthma) with the aim to examine the mechanism underlying to genesis and evolution of asthma in a well defined cohort. Using an integrate approximation, MEGA will identify, describe and validate immunological and molecular networks involved in the genesis and evolution of asthma. This project will devise, operate and exploit a carefully integrated network of collaborative studies designed to understand the mechanism underlying to the asthma genesis and evolution. The knowledge generated by this project will be translated into therapeutic strategies designed to address the current epidemic of asthma in the world.

The Group is also working in the evolution of occupational asthma in order to know if cessation of exposure really improve prognosis (paper submitted):

Muñoz X, Viladrich M, Manso L, del Pozo V, Quirce S, Cruz MJ, Carmona F, Sánchez-Pla A, Sastre J. Evolution of occupational asthma: does cessation of exposure really improve prognosis?. Under Review.

However, the group has published in 2013 more than 50 scientific articles which more than half are collaborative. This is because, the clinical and basic research activity of the group 16 is mainly focused on areas of inflammation and repair, respiratory failure and tissue hypoxia, and there is complementarily and interrelatedness of these areas for the study of diseases such as asthma COPD, pulmonary fibrosis, infections, transplant, pulmonary hypertension and sleep-disordered breathing. For this reason, the Group is also collaborating with other Corporate Research Programs such us COPD, Sleep Disorders and others (see publications of the Group).

Most relevant scientific articles

- Gathmann B., Mahlaoui N., Gerard L., Oksenhendler E., Warnatz K., Schulze I. et al. Clinical picture and treatment of 2212 patients with common variable immunodeficiency. Journal of Allergy and Clinical Immunology. 2014;134(1).
- Roberts J.A., Paul S.K., Akova M., Bassetti M., De Waele J.J., Dimopoulos G. et al. DALI: Defining antibiotic levels in intensive care unit patients: Are current ß-lactam antibiotic doses sufficient for critically ill patients?. Clinical Infectious Diseases. 2014;58(8):1072-1083.
- Ramon M.A., Gimeno-Santos E., Ferrer J., Balcells E., Rodriguez E., De Batlle J. et al. Hospital admissions and exercise capacity decline in patients with COPD. European Respiratory Journal. 2014;43(4):1018-1027.
- Vandenplas O., Suojalehto H., Aasen T.B., Baur X., Burge P.S., De Blay F. et al. Specific inhalation challenge in the diagnosis of occupational asthma: Consensus statement. European Respiratory Journal. 2014;43(6):1573-1587.
- Welte T., Miravitlles M.. Viral, bacterial or both? Regardless, we need to treat infection in copd. European Respiratory Journal. 2014;44(1):11-12.

Institution: Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)
Contact: Hospital Universitario Vall d'Hebron. Pº Vall d'Hebron, 119. 08035 Barcelona
Phone: (+34) 93 489 40 48 · E.mail: fmorell@vhebron.net · Web: www.vhir.org

Group 17

Programme: Tuberculosis / Host-Pathogen Interactions

Lead Researcher: Ausina Ruiz, Vicente

Group members

STAFF MEMBERS: Iglesias Coma, Amanda

ASSOCIATED MEMBERS: Cardona Iglesias, Pere Joan | Domínguez Benítez, José Antonio | Giménez Pérez, Montserrat | Jordana Lluch, Elena | Latorre Moreno, Irene | Prat Aymerich, Cristina | Ruíz Manzano, Juan | Vilaplana Massaguer, Cristina

Main lines of research

- Development and evaluation of new experimental animal models in tuberculosis.
- New approaches to the nature, diagnosis and treatment of latent tuberculosis.
- New vaccines against tuberculosis.
- Antituberculosis drugs: resistance, action and evaluation of new drugs.
- New diagnostic methods and molecular epidemiology of tuberculosis.
- New molecular approaches to epidemiological, pathogenic and diagnostic of the respiratory infections caused by respiratory virus, Haemophilus influenzae and Mycoplasma pneumonia.
- Characterization of intracellular life stage of Staphylococcus aureus. Involvement in treatment and outcome of staphylococcal infections.
- Design and evaluation of a novel inpedimetric immunosensor for diagnosis of sepsis of respiratory origin.
- Improving the diagnosis of bloodstream Infections: PCR coupled with mass spectrometry.
- Multiplexed determination of pathogenic bacteria in sepsis by novel magneto-nanohollows immunoassays.

Most relevant scientific articles

- Stolz D., Kostikas K., Blasi F., Boersma W., Milenkovic B., Lacoma A. et al. Adrenomedullin refines mortality prediction by the BODE index in COPD: The BODE-A index. European Respiratory Journal. 2014;43(2):397-408.
- Cardona P.-J., Vilaplana C.. Multiple consecutive infections might explain the lack of protection by bcg. PLoS ONE. 2014;9(4).
- Latorre I., Diaz J., Mialdea I., Serra-Vidal M., Altet N., Prat C. et al. IP-10 is an accurate biomarker for the diagnosis of tuberculosis in children. Journal of Infection. 2014.
- Stolz D., Boersma W., Blasi F., Louis R., Milenkovic B., Kostikas K. et al. Exertional hypoxemia in stable COPD is common and predicted by circulating proadrenomedullin. Chest. 2014;146(2):328-338.
- Serra-Vidal M., Latorre I., Franken K., Diaz J., de Souza-Galvao M., Casas I. et al. Immunogenicity of 60 novel latency-related antigens of Mycobacterium tuberculosis. Frontiers in Microbiology. 2014;5(SEP).

Highlights

Following the WHO priorities stated in the "Global Plan to Stop TB 2006-2015", over the last few years researchers belonging to group 17 within CIBERES have generated considerable scientific knowledge, with an emphasis on joint publications involving groups form different Programs and collaborations with other national and international groups in the context of the pathogenesis, prevention, diagnosis and treatment of tuberculosis. The researchers of this group have continued investigating new prophylactic and therapeutic vaccines against tuberculosis, and have also developed new experimental animal models that better reproduce infection and disease in humans. Studies have also been carried out that provide new insights into the resistance of *M.tuberculosis* and multi-drug resistant TB. New procedures have been developed and evaluated for the molecular typing of *M.tuberculosis* for epidemiological purposes. New immunological techniques to diagnose latent tuberculosis infection have also been evaluated. As a result of this work, the researchers have actively participated in the development of clinical guidelines for the use of new diagnostic tests (interferon-gamma release assays-IGRAs) for latent tuberculosis infection.

Group 17 members have also developed several research projects related to other respiratory pathogens: *S.aureus, M.pneumoniae, S.pneumoniae, H.influenzae* and respiratory viruses. One line of research in which the group has been active in recent years is the assessment of the importance of the inflammatory response in respiratory tract infections. The main objective is to identify and describe pathogen and host factors that modulate clinical outcome.

Researchers belonging to group 17 are currently involved in five projects funded by the EU in the FP7 framework, and in several research projects funded by national agencies (FIS, Ministry of Economy and others), the industry and the Administration. We have also developed scientific collaboration with other CIBER (CIBER-BBN, CIBERESP, and others).

The research activities of the group have recently generated six new patents and created a *spin-off* with the aim of commercializing a new probiotic that may allow treatment shortening in latent tuberculosis infections.

Institution: Fundación Instituto de Investigación Germans Trias i Pujol
Contact: Hospital Universitario Germans Trias i Pujol · Carretera Canyet, 08916 Badalona, Barcelona
Phone: (+34) 93 497 88 94 · E.mail: vausina.germanstrias@gencat.cat
Webs: http://www.gencat.cat/ics/germanstrias/web_micro/
http://unitatdetuberculosiexperimental.wordpress.com/

Group 18

Programme: CPOD / Pneumonia

Lead Researcher: Rello Condomines, Jordi

Group members

STAFF MEMBERS: Pérez Is, Laura

ASSOCIATED MEMBERS: Bodi Saera, María Amparo | Boque Oliva, María del Carmen | Canalis Arrayas, Emilio | Gallego Díaz, Miguel | Lujan Torne, Manel | Mendoza Asensi, Diego | Palomar Martínez, Mercedes | Pobo Peris, Angel | Riera del Brio, Jordi | Rodríguez Oviedo, Alejandro | Sandiumenge Camps, Alberto | Sole Violan, Jordi | Vidaur Tello, Loreto

Main lines of research

- Etiology, pathogenesis and treatment of pneumonia associated with mechanical ventilation.
- Eitology, pathogenesis and treatment of Chronic Obstructive Pulmonar Disease (COPD).
- Use of antimicrobials in Intensive Care Units.
- Serious community-acquired pneumonia: diagnosis, treatment and prevention.
- Sepsis in the critical patient.
- Lung transplant.

Most relevant scientific articles

- Rodriguez A., Claverias L., Marin J., Magret M., Rosich S., Bodi M. et al. Regional oxygen saturation index (rSO2) in brachioradialis and deltoid muscle. Correlation and prognosis in patients with respiratory sepsis. Medicina Intensiva. 2014.
- Trefler S., Rodriguez A., Martin-Loeches I., Sanchez V., Marin J., Llaurado M. et al. Oxidative stress in immunocompetent patients with severe community-acquired pneumonia. A pilot study. Medicina Intensiva. 2014;38(2):73-82.
- Pedro-Botet M.L., Burgos J., Lujan M., Gimenez M., Rello J., Planes A. et al. Impact of the 2009 *influenza A* H1N1 pandemic on invasive pneumococcal disease in adults. Scandinavian Journal of Infectious Diseases. 2014;46(3):185-192.
- Salva S., Duran N., Rodriguez V., Nieto L., Serra J., Rello J. et al. Clostridium difficile in the ICU: Study of the incidence, recurrence, clinical characteristics and complications in a University Hospital. Medicina Intensiva. 2014;38(3):140-145.
- Ferrer Aguero J.M., Millan S., Rodriguez de Castro F., Martin-Loeches I., Sole Violan J.. Community acquired pneumonia: Genetic variants influencing systemic inflammation. Medicina Intensiva. 2014;38(5):315-323.

Highlights

FUNDED PROJECTS

- Clinical Research / Innovation in Pneumonia & Sepsis (CRIPS) (GRC). PI: Rello, J. Financial entity: AGAUR.
- Project iROOT: Biomarkers associated to ICU readmission for lung organ transplant. PI: Rello, J. Financial entity: Fondo de Investigación Sanitaria.
- Nebulizated treatment with antibiotic combinations in murine models of respiratory infection caused by multiresistent P. aeruginosa. neb-PaR project. PI: Gavaldà, J. Financial entity: Fondo de Investigación Sanitaria.
- "Impact of Aggressive Empiric Antibiotic Therapy and Duration of Therapy on the Emergence of Antimicrobial Resistance during the Treatment of Hospitalized Subjects with Pneumonia Requiring Mechanical Ventilation". PI: Rello, J. Financial entity: National Institute of Health (NIH).
- Acute respiratory failure (primary draft disfunction and pneumonia vs. rechazo) in UCI postoperatory of pulmonar transplantation (UCI-TRASP). PI: Rello, J. Financial entity: Fondo de Investigación Sanitaria.
- Mecanic ventilation in patients: quality of life related to health and sensitive results to nursery intervention (CUVE project). PI: Riera, MA. Financial entity: Fondo de Investigación Sanitaria.
- Sampling Antibiotics in Renal Replacement Therapy (SMARRT). PI: Rello, J.
- Implementing strategic bundles for infection prevention and management (IMPLEMENT). PI: Palomar, M; Rello, J. Financial entity: Executive Agency for Health Consumers (EAHC).
- Psychosocial impact of the alive donnor transplant donation process. PI: Pont, T. Financial entity: Fondo de Investigación Sanitaria.
- Achieving Comprehensive Coordination in ORgan Donation throughout the European Union (ACCORD). Hospital Study on end-of-life care and deceased donation in the European Union. PI: Pont, T. Financial entity: European Comission.
- European multicentric study. Hospital Study on End-of life care and deceased donation in the European Union (Accord). PI: Pont, T.
- Multicentric study on end-of-life care on neurologic patient with Central Nerous System injury and organ donation in Spain. PI: Pont, T.

Institution: Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR)
Contact: Hospital Universitario Vall d'Hebron. Paseo Vall d'Hebron, 119-129. 08035 Barcelona
Phone: (+34) 93 274 62 09 · E.mail: jrello@crips.es

Group 19

Programme: Pneumonia / COPD

Lead Researcher: Liñares Louzao, Josefina

Group members

STAFF MEMBERS: Cubero González, Meritxell | Moreno Cano, Francisco Javier

ASSOCIATED MEMBERS: Ardanuy Tisaire, María Carmen | Ayats Ardite, Josefina | Calatayud Samper, Laura | Domenech Pena, Arnau | Dorca Sargatal, Jordi | García Somoza, María Dolores | Grau Garriga, Inmaculada | Martí Martí, Sara | Niubo Bosch, Jordi | Pallares Giner, Román | Puig Pitarch, Carmen | Santos Pérez, Salud | Tubau Quintana, María Fe

Main lines of research

- Clinical and molecular epidemiology of invasive and non-invasive pneumococcal diseases.
- Study of bacterial resistance mechanisms and mobile elements harboring resistance determinants.
- Molecular typing and population dynamics of microorganisms causing respiratory infections (Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Pseudomonas aeruginosa, Klebsiella pneumoniae, Streptococcus pyogenes, Staphylococcus aureus).
- Bacterial diversity analysis of respiratory samples from patients with chronic obstructive pulmonary disease. Traditional culture-based vs culture-independent (microbiome) techniques.
- Biofilm formation by microorganisms causing respiratory tract infections. Bacterial genotypes persistence.

Most relevant scientific articles

- Ardanuy C., De La Campa A.G., Garcia E., Fenoll A., Calatayud L., Cercenado E. et al. Spread of streptococcus pneumoniae serotype 8-st63 multidrug-resistant recombinant clone, Spain. Emerging Infectious Diseases. 2014;20(11):1848-1856.
- Puig C., Domenech A., Garmendia J., Langereis J.D., Mayer P., Calatayud L. et al. Increased biofilm formation by nontypeable Haemophilus influenzae isolates from patients with invasive disease or otitis media versus strains recovered from cases of respiratory infections. Applied and Environmental Microbiology. 2014;80(22):7088-7095.
- Domenech A., Ardanuy C., Tercero A., Garcia-Somoza D., Santos S., Linares J.. Dynamics of the pneumococcal population causing acute exacerbations in COPD patients in a Barcelona hospital (2009-12): Comparison with 2001-04 and 2005-08 periods. Journal of Antimicrobial Chemotherapy. 2014;69(4):932-939.
- Domenech A., Ardanuy C., Grau I., Calatayud L., Pallares R., Fenoll A. et al. Evolution and genetic diversity of the Spain23F-ST81 clone causing adult invasive pneumococcal disease in Barcelona (1990-2012). Journal of Antimicrobial Chemotherapy. 2014;69(4):924-931.
- Puig C., Marti S., Hermans P.W.M., de Jonge M.I., Ardanuy C., Linares J. et al. Incorporation of phosphorylcholine into the lipooligosaccharide of nontypeable haemophilus influenzae does not correlate with the level of biofilm formation in vitro. Infection and Immunity. 2014;82(4):1591-1599.

Highlights

- The Corporate Research Program on Pneumonia:

  PI11/00763 "Multicenter study of adult invasive pneumococcal disease(IPD): epidemiology and molecular characterization of pneumococcal clones in the 13 Valent Conjugate Vaccine era. This study analyze the impact of PCV13 vaccination in the incidence of adult IPD, serotype/genotype distributions and antimicrobial resistance of Streptococcus pneumoniae. The emerging clones and capsular switching were also studied. The mechanisms of resistance to penicillin, macrolides and quinolones and the genetic diversity of neumococcal surface proteins, which are vaccine candidates, were characterized. Results. A total of 1558 IPD episodes (949 in the pre-PCV13 period (2008-2009) and 609 in the PCV13 period (2012-2013). An overall decrease in the incidence of IPD was observed from 12,25 to 7,8/100.000h, associated with a decrease in the IPD due to PCV13 serotypes and related clones. The serotype 5 was associated with outbreaks of IPD, mainly in the Barcelona area. A new recombinant and multiresistent clone of serotype 8 (ST63) was detected. The Sp1992 protein has two alleles, the large one is associated with invasive disease. The decrease in the adult IPD was related with herd protection after PCV13 introduction for children in 2010. New emerging and recombinant clones and changes in the clonal composition of PCV13 serotypes recommend the future surveillance of IPD. The pneumococcal protein SP1992 could be a good candidate to protein based vaccine due to the association with invasive clones. PI11/01106 "Usefulness of a rule based on PIRO model for categorizing hospitalized adults with community-acquired pneumonia".

Institution: Fundación IDIBELL
Contact: Fundación IDIBELL- Hospital Universitario de Bellvitge.
Phone: (+34) 93 260 79 30 · E.mail: fina.linares@bellvitgehospital.cat

Group 21

Programme: COPD / Lung Cancer / Pulmonary Fibrosis

Lead Researcher: Álvarez Martínez, Carlos

Group members

STAFF MEMBERS: Castro Acosta, Ady Angelica | Fernandez Gonzalez, Saul

ASSOCIATED MEMBERS: Díaz de Atauri Rodríguez de los Rios, María Josefa | Enguita Valls, Ana Belén | Gámez García, Antonio Pablo | García Lujan, Ricardo | Gómez Sánchez, Miguel Ángel | Rami Porta, Ramón | Villena Garrido, María Victoria

Main lines of research

- Line NEOPLASIAS TORÁCCICAS LUNG CANCER AND PLEURA: Identify a set of clinical-molecular variables that improve the prognostic and predictive capacity of TNM and clinical translation of these results.
- Line CHRONIC OBSTRUCTIVE PULMONARY DISEASE: To study the clinical, biological, microbiological, radiological, functional determinants of progression and severity. Evaluate new endoscopic treatment in obstructive airway disease and the impact of different approaches to health care in the management of disease activity.
- Line PULMONARY HYPERTENSION (HP): Establish a network of groups with complementary capabilities of research aimed at identifying new markers for assessing disease activity and new therapeutic targets for the treatment of pulmonary hypertension following a strategy of translational research, with the ultimate aim of contributing to alleviate and cure the disease.
- Line INSTERSTICIALES DISEASES AND FIBROSIS: Create a record of well-characterized patients, and incorporate new treatments in their care, measuring the impact on quality of life, progression and prevention of exacerbations.
- Line SAHS & NO INVASIVE VENTILATION (NIV): Develop new ways of simplified diagnosis, deepen treatment indications and establish new indications for NIV outside the critical care units. Investigate the causes of failure of NIV and asynchrony.
- Line RESEARCH IN LUNG TRANSPLANTATION: Advance knowledge of the causes of rejection and infection and diagnosis, and expand the selection criteria organ donor and recipient.

Most relevant scientific articles

- Alvarez Martinez C.J., Bastarrika Aleman G., Disdier Vicente C., Fernandez Villar A., Hernandez Hernandez J.R., Maldonado Suarez A. et al. Guideline on management of solitary pulmonary nodule. Archivos de Bronconeumologia. 2014;50(7):285-293.
- Villena Garrido V., Cases Viedma E., Fernández Villar A., de Pablo Gafas A., Perez Rodríguez E., Porcel Perez J.M. et al. Recommendations of diagnosis and treatment of pleural effusion. Update. Archivos de Bronconeumologia. 2014;50(6):235-249.
- De leyn P., Dooms C., Kuzdzal J., Lardinois D., Passlick B., Rami-Porta R. et al. Revised ests guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer. European Journal of Cardiothoracic Surgery. 2014;45(5):787-798.
- Lopez-Campos J.L., Hartl S., Pozo-Rodríguez F., Roberts C.M.. Variability of hospital resources for acute care of COPD patients: The European COPD Audit. European Respiratory Journal. 2014;43(3):754-762.
- Zock J.-P., Rodríguez-Trigo G., Rodríguez-Rodríguez E., Souto-Alonso A., Espinosa A., Pozo-Rodriguez F. et al. Evaluation of the persistence of functional and biological respiratory health effects in clean-up workers 6years after the Prestige oil spill. Environment International. 2014;62:72-77.

Highlights

The group 21 CIBERES has added new lines of research and projects.

Working hypothesis: The study of the determinants of health conditions in respiratory patients and clinical implications of these findings, supports the evaluation and updating of action protocols, the identification of biomarkers (diagnostic, prognostic and therapeutic) new treatments, improve quality and optimizes assistance.

2014 highlights:

- The creation of advanced COPD patient's knowledge database for the study of the clinical course COPD, phenotypic feature, healthcare system's burden , treatments, readmissions, mortality, Comorbidoma and inflammasome (E. CEPA).
- The creation of databases of knowledge with clinical information and hospitals's resources and organization for periodic evaluation of management and clinical impact. (E. AUDIPOCs Spain and EUROPE).
- Preparation of early lung Cancer cohort to identify clinical and molecular variables that improve the prognostic and predictive ability of the TNM classification, Participation in the coordination, management and analysis of database-related knowledge and participation in the study's pathologists panel for centralized biomarker determinations (PE Lung Cancer).
- Participation in the construction and coordination of the Spanish record of pulmonary hypertension: REHAP.
- Participation of the spirometry and bronchial hyperresponsiveness in asthma nonspecific SEPAR guidelines.
- Coordination of the management of solitary pulmonary nodule SEPAR guidelines.
- Research proyects in course:

  a) New Markers and Therapeutic Targets for the Diagnosis and Treatment of Pulmonary Hypertension (EMPATHY, PE Pulmonary Hypertension).

  b) Determinants of the onset and progression of COPD in young adults (EARLY COPD).

  c) Biomarkers and customized clinical profiles in Chronic Obstructive Pulmonary Disease (BIOMEPOC).

  d) Local Design and Implementation of clinical audits in different types of OLD (DELICATO).

  e) Clinical and Molecular stratification of Lung Cancer Stage I and II (PE Lung Cancer).

Institution: Servicio Madrileño de Salud
Contact: Hospital Univ. 12 de Octubre · Av de Córdoba S/N · C. de Actividades Ambulatorias I+12 · 6ª Planta Bloque D, Pasillo, 1. 28041Madrid · Phone: (+34) 91 779 28 68
E.mail: carlosjose.alvarez@salud.madrid.org
Web: http://www.ciberes.org/index.php?option=com_personal&view=personal&Group_id=21&Itemid=77

Group 22

Programme: Chronic Obstructive Pulmonary Disease (COPD)

Lead Researcher: Gea Guiral, Joaquim

Group members

STAFF MEMBERS: Capllonch Amer, Gabriela | Casadevall Fusté, Carme

ASSOCIATED MEMBERS: Admetllo Papiol, Mireia | Balcells Vilarnau, Eva | Barreiro Portela, Esther | Curull Serrano, Víctor | Domínguez Álvarez, Marisol | Ferrer Monreal, Antonio | Galdiz Iturri, Juan Bautista | Horcajada Gallego, Juan Pablo | Martínez Llorens, Juana María | Orozco Levi, Mauricio | Rodríguez, Diego Agustín

Main lines of research

- Respiratory and limb muscle abnormalities in respiratory diseases.
- Fenotyping in COPD.
- Pulmonary abnormalities in COPD and lung cancer.
- Pulmonary Hypertension.

Most relevant scientific articles

- Barreiro E.. Protein carbonylation and muscle function in COPD and other conditions. Mass Spectrometry Reviews. 2014;33 (3):219-236.
- Balch W.E., Sznajder J.I., Budinger S., Finley D., Laposky A.D., Cuervo A.M. et al. Malfolded protein structure and proteostasis in lung diseases. American Journal of Respiratory and Critical Care Medicine. 2014;189 (1):96-103.
- Barreiro E., Criner G.J.. Update in chronic obstructive pulmonary disease 2013. American Journal of Respiratory and Critical Care Medicine. 2014;189 (11):1337-1344.
- Ramon M.A., Gimeno-Santos E., Ferrer J., Balcells E., Rodriguez E., De Batlle J. et al. Hospital admissions and exercise capacity decline in patients with COPD. European Respiratory Journal. 2014;43 (4):1018-1027.
- De Torres J.P., Marin J.M., Martinez-Gonzalez C., De Lucas-Ramos P., Mir-Viladrich I., Cosio B. et al. Clinical application of the COPD assessment test: Longitudinal data from the COPD history assessment in Spain (CHAIN) Cohort. Chest. 2014;146 (1):111-122.

Highlights

In the last year our group has evolved to incorporate a greater number of postdoctoral investigators and researchers in training, adding more translational components to our activities. The group has also increased connections with other national and international groups in fields related to our main objective: the study of muscle involvement in respiratory diseases. As a result, production has increased in quantity and quality (35 Originals in indexed journals, several editorials, reviews and one Statement of two international scientific societies, 2 PhD theses, etc). In the same period members of the group have presented 38 communications and given 28 invited lectures (18 at international meetings). The group has been rated as Excellent by the external scientific committee of CIBERES, and our group leader is the Clinical Deputy Director of this network of excellence. Moreover, different members of the group continue to be integrated in the editorial board of different journals including Am J Respir Crit Care Med, J Appl Physiol, and Arch Bronconeumol (the Editor in Chief of the last journal is a member our group) and are reviewers of a total of 12 indexed journals, and 5 national and international agencies, including different programmes of the European Commission, agencies from the UK, the Netherlands and France, as well as FIS and Plan Nacional. As for resources, we have obtained different competitive grants (10 ongoing projects) and have increased significantly the number of clinical trials (15 ongoing trials, 6 of them initiated in 2014). With regard to research teaching, the group leader continues as the dean of the Faculty of Health and Life Sciences (Universitat Pompeu Fabra), coordinates a Master on Clinical Research in Respiratory Diseases and is a member of the Ph.D. program committee at the above mentioned university. Finally, our group has been actively involved in the genesis of the Barcelona Respiratory Network Foundation, an initiative which integrates academic researchers and industrial companies related to respiratory health.

Institution: Consorci Mar Parc Salut de Barcelona
Contact: Hospital del Mar. Pº Marítimo, 25-29. Barcelona · Tel.: (+34) 93 248 35 48
E.mail: jgea@parcdesalutmar.cat
Websites: www.imim.es / www.upf.edu / www.brn.cat / www.parcdesalutmar.cat

Group 23

Programme: Acute Lung Injury (ALI)

Lead Researcher: Esteban de la Torre, Andrés

Group members

STAFF MEMBERS: Ferruelo Alonso, Antonio José | Herrero Hernández, Raquel

ASSOCIATED MEMBERS: Arias Rivera, Susana | De la Cal López, Miguel Ángel | De Paula Ruiz, Marta | Frutos Vivar, Fernando | Lorente Balanza, Jose Ángel | Martínez Caro, Leticia | Peñuelas Rodriguez, Óscar | Rojas Vega, Yeny | Tejerina Álvarez, Eva Esther

Main lines of research

- Acute Respiratory Distress Syndrome.
  Clinical studies. Experimental studies.
- Mechanical Ventilation.
  Epidemiology. Weaning.
- Selectic Digestive Descontamination.
  Clinical and experimental.

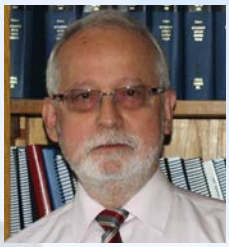
Most relevant scientific articles

- Beloncle F., Lorente J.A., Esteban A., Brochard L.. Update in acute lung injury and mechanical ventilation 2013. American Journal of Respiratory and Critical Care Medicine. 2014;189(10):1187-1193.
- Brown A.O., Mann B., Gao G., Hankins J.S., Humann J., Giardina J. et al. Streptococcus pneumoniae Translocates into the Myocardium and Forms Unique Microlesions That Disrupt Cardiac Function. PLoS Pathogens. 2014;10(9).
- Izquierdo-Garcia J.L., Naz S., Nin N., Rojas Y., Erazo M., Martinez-Caro L. et al. A metabolomic approach to the pathogenesis of ventilator-induced lung injury. Anesthesiology. 2014;120(3):694-702.
- Frutos-Vivar F., Esteban A.. Our paper 20 years later: how has withdrawal from mechanical ventilation changed?. Intensive Care Medicine. 2014;40(10):1449-1459.
- Chacon-Cabrera A., Rojas Y., Martinez-Caro L., Vila-Ubach M., Nin N., Ferruelo A. et al. Influence of mechanical ventilation and sepsis on redox balance in diaphragm, myocardium, limb muscles, and lungs. Translational Research. 2014;164(6):477-495.

Highlights

- We have implemented a procedure to collect fresh lung tissue from deceased patients. This is a complex action as it implies the presence of the investigators at the autopsy to collect fresh tissue for storage at -80°. We already have 40 cases . This tissue is available for genetic studies, and will allow the definition of the genetic phenotype of DAD.
- We have identified by massive sequencing (NGS) a miRNA (miRNA 27a-5p) as a biomarker of DAD in an animal model. We are currently studying the effects of its interference in various models (cells undergoing stretch, ex vivo lung ventilation, in vivo model of VILI) (PI 12/2898).
- The role of Fas ligand and the subsequent activation of the inflammation and the apoptosis pathways in alveolocapillary permeability and edema formation is being investigated. Also, the role of Fs ligand in the integrity of intercellular tight junctions, and the relationship with alveolocapillary hyperpermeability is under current investigation (PI 12/02451).
- We have participated as part of the Steering Committee in the to date largest epidemiological study on acute respiratory failure (Lung Safe Study). The study recruited 31000 patients from all over the world under the auspices of the ESICM.
- We have reported in an animal model for the first time the metabolomic pattern that characterizes Acute Lung Injury. Also, in patients with ARDS due to H1N1 influenza virus we have reported the characteristic metabolomic pattern by NMR (PI 11/02791) (Anesthesiology 2014;120(3):694-702).
- In a pioneer study, we have reported the myocardial lesions in patients with pneumococcal sepsis that may explain arrhythmias and heart failure under these conditions. This was carried out by the autopsy tissue samples from our group in collaboration with the University of Texas (PloS Pathog. 2014 Sep 18;10(9).

Institution: Servicio Madrileño de Salud
Contact: Hospital Univ. de Getafe · Ctra. Toledo km. 12,5. 28905 Getafe, Madrid.
Phone: (+34) 91 683 49 82 · E.mail: aesteban@ucigetafe.com · Web: www.ciberes.org



Group 24

Programme: Acute Lung Injury (ALI) / Sleep Apnea-Hypopnea Syndrome (SAHS)

Lead Researcher: González Martínez, Constancio

Group members

STAFF MEMBERS: Gordillo Cano, Ana | Olea Fraile, Elena

ASSOCIATED MEMBERS: Agapito Serrano, María Teresa | Castañeda Casado, Javier | Gallego Martín, Teresa | Gómez Niño, Angela | Obeso Cáceres, Ana | Quintero Coca, Miguel | Ramírez Arroyo, María | Rigual Bonastre, Ricardo Jaime | Rocher Martín, Asunción | Yubero Benito, Sara

Main lines of research

- Oxygen sensing mechanisms in the carotid body arterial chemoreceptors.
- Mechanisms of the hypoxic damage: reactive oxygen species.
- Animal models of intermittent and sustained hypoxia.
- Biomarkers of the hypoxic damage.
- Pulmonary hypertension.

Most relevant scientific articles

- Davidsen P.K., Herbert J.M., Antczak P., Clarke K., Ferrer E., Peinado V.I. et al. A systems biology approach reveals a link between systemic cytokines and skeletal muscle energy metabolism in a rodent smoking model and human COPD. Genome Medicine. 2014;6(8).
- Gonzalez C., Conde S.V., Gallego-Martin T., Olea E., Gonzalez-Obeso E., Ramirez M. et al. Fernando de castro and the discovery of the arterial chemoreceptors. Frontiers in Neuroanatomy. 2014;8(MAY).
- Olea E., Agapito M.T., Gallego-Martin T., Rocher A., Gomez-Nino A., Obeso A. et al. Intermittent hypoxia and diet-induced obesity: Effects on oxidative status, sympathetic tone, plasma glucose and insulin levels, and arterial pressure. Journal of Applied Physiology. 2014;117(7):706-719.
- Conde S.V., Sacramento J.F., Guarino M.P., Gonzalez C., Obeso A., Diogo L.N. et al. Carotid body, insulin and metabolic diseases: Unravelling the links. Frontiers in Physiology. 2014;5(OCT).

Institution: Universidad de Valladolid
Contact: Facultad de Medicina de Valladolid. c/ Ramón y Cajal, 7. 47005 Valladolid
Phone: (+34) 983 423 089 · E.mail: constanc@ibgm.uva.es

Group 25

Programme: Host-Pathogen Interactions

Lead Researcher: Melero Fontdevila, José Antonio

Group members

STAFF MEMBERS: González Sanz, Rubén | Vázquez Alcaraz, Mónica.

ASSOCIATED MEMBERS: Cano Morato, Olga | Delgado Romero, María Teresa | García Barreno, Blanca | Herránz Sánchez, Cristina | Llorente Rodríguez, María Teresa | Magro de la Plaza, Margarita | Martínez González, Isidoro | Mas Lloret, Vicente | Palomo Sanz, Concepción | Trento Trento, María Alfonsina

Main lines of research

Our group has been working for more than 30 years with respiratory viruses of human relevance such as respiratory syncytial virus (RSV), metapneumovirus (MPV) and influenza virus. One of the main aspects of our research has been the antigenic, immunogenic and structural characterization of some of the viral gene products, as well as the virus-host cells interactions.

On the one hand, we have presently focused our studies on the RSV and MNV fusion glicoproteins. These proteins are the main targets of the neutralizing and protective antibodies. Thus, we are carrying out an extensive and detailed analysis of the different conformations adopted by these proteins during the process of membrane fusion and the mechanisms by which neutralizing antibodies interfere with that process. These studies are essential for the development of safe and effective vaccines, which are currently lacking.

On the other hand, we are developing methods to uncover antigenic differences between hemagglutinins (HAs) from different influenza virus strains. The new methods are allowing us to unveil antigenic differences that were undetected by traditional methods, such as the hemagglutination inhibition (HI) assay. In addition, amino acid changes associated to the noted antigenic differences could be identified. Thus, the new methods will allow a more detailed study of the antigenic evolution of human influenza virus.

Finally, we are also interested in the regulation of the intracellular signaling cascade associated to the antiviral response triggered in RSV infected cells. Fine modulation of these routes is essential not only to control virus

replication but also to control the inflammatory response. The activity of many of the proteins participating in the signaling cascade is influenced by post-translational modifications, such as covalent linkage of ubiquitine or other tags (ISG15). Our results show that the expression of certain genes involved in the innate immune response, as well as RSV replication are regulated by these processes of ubiquitination and ISGylation.

Most relevant scientific articles

- Díez-Domingo J., Perez-Yarza E.G., Melero J.A., Sanchez-Luna M., Aguilar M.D., Blasco A.J. et al. Social, economic, and health impact of the respiratory syncytial virus: A systematic search. BMC Infectious Diseases. 2014;:544.
- Swanson K.A., Balabanis K., Xie Y., Aggarwal Y., Palomo C., Mas V. et al. A monomeric uncleaved respiratory syncytial virus F antigen retains prefusion-specific neutralizing epitopes. Journal of Virology. 2014;88(20):11802-11810.
- García-Barreno B., Delgado T., Benito S., Casas I., Pozo F., Melero J.A.. Exploring the antigenic relatedness of influenza virus haemagglutinins with strain-specific polyclonal antibodies. Journal of General Virology. 2014;95:2140-2145.
- Palomo C., Mas V., Vazquez M., Cano O., Luque D., Terron M.C. et al. Polyclonal and monoclonal antibodies specific for the six-helix bundle of the human respiratory syncytial virus fusion glycoprotein as probes of the protein post-fusion conformation. Virology. 2014;460-461(1):119-127.
- García-Barreno B., Delgado T., Benito S., Casas I., Pozo F., Cuevas M.T. et al. Characterization of an enhanced antigenic change in the pandemic 2009 H1N1 influenza virus haemagglutinin. Journal of General Virology. 2014;95(PART 5):1033-1042.

Highlights

ACTIVE RESEARCH PROJECTS IN 2014

- Title: Membrane fusión mediated by the pneumovirus F protein and conformation specific antibodies: two new paradigms for clinical intervention against these viruses. Funding agency: Plan Nacional de I+D+i. Duration: January 2013-December 2015. Budget: 339.300 €.
- Title: Regulation by deubiquitinases of the inflammatory response induced by human respiratory syncytial virus. Funding agency: FIS. Duration: January 2012-December 2015. Budget: 86.212,50.

MOST RELEVANT RESEARCH RESULTS ACHIEVED IN 2014

- Design and development of new methods for the antigenic characterization of the influenza virus haemagglutinin (HA) with strain specific polyclonal antibodies and mapping of relevant antigenic sites.
- Design and development of new methods for the isolation of postfusion specific monoclonal antibodies directed against the Pneumovirinae fusion protein.
- Identification and characterization of a new monomeric form of the Pneumovirinae fusion protein.
- Demonstration of the ISG15 antiviral effect at early stages of human respiratory syncytial virus (HRSV) replication through covalent binding to target proteins (ISGylation). Furthermore, ISG15 accumulation and correlation with virus load in nasopharyngeal washes from infected children, suggesting that ISG15 may also have an anti-HRSV effect in vivo.
- Demonstration of HRSV induced DNA degradation and cell senescence in vitro (A549 cells) and in vivo, respiratory epithelium of mice.

Institution: Instituto de Salud Carlos III

Contact: C. Nacional de Microbiologia. Campus Majadahonda. Ctra. Majadahonda -Pozuelo km 2.200. 28220 Majadahonda, Madrid · Phone: (+34) 91 822 39 08 · E.mail: jmelero@isciii.es

Group 26

Programme: Pneumonia

Lead Researcher: Pérez Trallero, Emilio

Group members

STAFF MEMBERS: Esnal Lasarte, Olatz | Moreiro Olondris, Esther | Tamayo Oya, Esther

ASSOCIATED MEMBERS: Alonso Asencor, Marta | Cilla Eguiluz, Carlos Gustavo | Ercibengoa Arana, María | González Pérez Yarza, Eduardo | Marimón Ortiz de Zarate, Jose María | Montes Ros, Milagrosa | Vicente Anza, Diego

Main lines of research

RESPIRATORY INFECTION:

Main objective: to study the epidemiology of respiratory infections.

STREPTOCOCCUS PNEUMONIAE INFECTION.

- Pneumococcal invasive infection in paediatric and adult populations: incidence, serotypes and genotypes.
- Non-invasive pneumococcal infection: otitis media and conjunctivitis. Serotypes and genotypes. Antibiotic resistance.
- Studies on vaccines. Impact of the 13 -valent conjugate vaccine. Comparison with the 7-valent vaccine. Influence of childhood vaccination with the new 13-valent vaccine on invasive infection and nasopharyngeal carriage in the first years of life.
- Design of new pneumococcal typing techniques.
- Determine the evolution of S. pneumoniae antibiotic resistance over time: new serotypes causing infection and genetic resistance determinants; influence of antibiotic consumption in resistance; spread of multi-resistant clones after the introduction of conjugate vaccines.
- To confirm the replacement of the "resistant serotypes" as a result of the commercialization of 13-valent conjugate vaccine in 2010.
- Influence of childhood vaccination on antibiotic resistance in adults.

STREPTOCOCCUS PYOGENES INFECTION.

- Incidence and characterization of strains causing invasive disease.

- Incidence and characterization of S. pyogenes strains causing non-invasive disease: otitis, pharyngitis, and other skin and soft tissue infections.
- S. pyogenes pneumonia. Clinical and epidemiological aspects.
- Phenotypic and genotypic characterization of S. pyogenes isolates.
- Study of antibiotic susceptibility. S. pyogenes mechanisms of resistance to macrolides, tetracyclines and fluoroquinolones.

RESPIRATORY INFECTION CAUSED BY VIRUS.

- Influenza-virus infections. Genetic characterizations of seasonal strains.
- Microbiological characterization of emerging respiratory viruses: influenza pandemic H1N1 and H3N2 virus, human metapneumovirus, bocavirus. Diagnosis and epidemiology of their infections.
- Epidemiology of non- influenza viruses causing ILI. Seasonality, hospitalization and incidence distributed by age groups.
- Value or significance of viral infections in exacerbations of COPD.
- Characteristics of mixed infections by two or more respiratory virus and between viruses and bacteria in pneumonia.

Most relevant scientific articles

- Tamayo E., Montes M., Garcia-Arenzana J.M., Perez-Trallero E.. Streptococcus pyogenes emm-types in northern Spain; population dynamics over a 7-year period. Journal of Infection. 2014;68(1):50-57.
- Fernandez-Reyes M., Vicente D., Gomariz M., Esnal O., Landa J., Onate E. et al. High rate of fecal carriage of extended-spectrum-ß-lactamase-producing Escherichia coli in healthy children in Gipuzkoa, northern Spain. Antimicrobial Agents and Chemotherapy. 2014;58(3):1822-1824.
- Montes M., Tamayo E., Mojica C., Garcia-Arenzana J.M., Esnal O., Perez-Trallero E.. What causes decreased erythromycin resistance in Streptococcus pyogenes? Dynamics of four clones in a southern European region from 2005 to 2012. Journal of Antimicrobial Chemotherapy. 2014;69(6):1474-1482.
- Marhuenda C., Barcelo C., Fuentes I., Guillen G., Cano I., Lopez M. et al. Urokinase versus VATS for treatment of empyema: A randomized multicenter clinical trial. Pediatrics. 2014;134(5):e1301-e1307.
- Perez-Trallero E., Esnal O., Marimon J.M.. Progressive decrease in the potential usefulness of meningococcal serogroup B vaccine (4CMenB, Bexsero®) in Gipuzkoa, Northern Spain. PLoS ONE. 2014;9(12).

Highlights

The group has also participated during 2014 in two research projects related to industry:

- "Strategic research and technological development in biomedical applications nanoglicotecnology and mass spectrometry surfaces for clinical diagnosis and food security." within the program of strategic research projects of the Department of Economic Development and Competitiveness of the Basque Government. This project is coordinated by the CIC biomaGUNE of San Sebastián and achieved competitive funding in 2014 and 2015 in the Etortek call.
- "Easy-PCR lab: preindustrial development of new clinical diagnostic applications as a platform to launch a new business initiative based on easy-PCR technology," led by Gaiker Foundation , at Zamudio Technology Park, Bizkaia. The project objective is to develop a molecular diagnostic kit that can be manufactured at industrial scale with commercial applications in the clinical diagnostics market.

Institution: Asociación Instituto Biodonostia
Contact: Hospital Donostia · Pº Dr. Beguiristain, s/n. 20080 San Sebastián, Guipúzcoa
Phone: (+34) 94 300 71 53 · E.mail: mikcrobiol@terra.com

Group 27

Programme: Pneumonia

Lead Researcher: Bouza Santiago, Emilio

Group members

STAFF MEMBERS: Herránz Martín, Marta | Iglesias Arribas, Cristina | Pérez García, Laura | Rodríguez Sánchez, Belén

ASSOCIATED MEMBERS: Alcalá Hernández, Luis | Alonso Martínez, María | Barrio Gutiérrez, José María | Cercenado Mansilla, Emilia | Fernández del Rey, Rocío | García de Viedma del Alamo, Darío | Guinea Ortega, Jesús Vicente | Hortal Iglesias, Francisco Javier | Marín Arriaza, María de las Mercedes | Martín Rabadan Caballero, Pablo | Muñoz García, Patricia | Peláez Rasilla, Teresa | Pérez Granda, María Jesús | Rodríguez Creixems, Marta | Ruiz Serrano, María Jesús

Main lines of research

- Serious lower respiratory tract infection.
- Infection caused by bacteremia and catheter-related infection.
- Infection in immunocompromised patients and transplant patients.
- Hospital-acquired systemic mycoses.
- C. difficile.
- Tuberculosis and diseases caused by mycobacteria.

Most relevant scientific articles

- Ardanuy C., De La Campa A.G., Garcia E., Fenoll A., Calatayud L., Cercenado E. et al. Spread of streptococcus pneumoniae serotype 8-st63 multidrug-resistant recombinant clone, Spain. Emerging Infectious Diseases. 2014;20(11):1848-1856.
- Perez-Lago L., Comas I., Navarro Y., Gonzalez-Candelas F., Herranz M., Bouza E. et al. Whole Genome Sequencing Analysis of Intrapatient Microevolution in Mycobacterium tuberculosis: Potential Impact on the Inference of Tuberculosis Transmission. Journal of Infectious Diseases. 2014;209(1):98-108.
- Munoz P., Ceron I., Valerio M., Palomo J., Villa A., Eworo A. et al. Invasive aspergillosis among heart transplant recipients: A 24-year perspective. Journal of Heart and Lung Transplantation. 2014;33(3):278-288.
- Kestler M., Munoz P., Rodriguez-Creixems M., Rotger A., Jimenez-Requena F., Mari A. et al. Role of 18F-FDG PET in patients with infectious endocarditis. Journal of Nuclear Medicine. 2014;55(7):1093-1098.
- Ceron I., Munoz P., Marin M., Segado A., Roda J., Valerio M. et al. Efficacy of daptomycin in the treatment of enterococcal endocarditis: A 5 year comparison with conventional therapy. Journal of Antimicrobial Chemotherapy. 2014;69(6):1669-1674.

Institution: Servicio Madrileño de Salud
Contact: Hospital Gregorio Marañón · C/ Ibiza 43, 28009 Madrid · Phone: (+34) 91 586 84 53
E.mail: micro.hgugm@gmail.com

Group 28

Programme: Acute Lung Injury (ALI)

Lead Researcher: Pérez Vizcaíno, Francisco

Group members

STAFF MEMBERS: Barreira Barba, Bianca | Martínez Ramas, Andrea | Moreno Gutiérrez, Laura.

ASSOCIATED MEMBERS: Cogolludo Torralba, Ángel Luis | Morales Cano, Daniel

Main lines of research

Pulmonary hypertension is a condition characterized by increased pulmonary vascular resistance with a complex and not well characterized pathophysiology. Our interest is mainly focused on the mechanisms involved in pulmonary vasodilation and inhibition of cell proliferation in order to identify and design new drugs that are potentially useful in the treatment of pulmonary hypertension.

Acute lung injury (ALI) or its more severe form, acute respiratory distress syndrome (ARDS) is characterized by pulmonary edema and alveolar collapse leading to severe arterial hypoxemia. Although the protective ventilatory support strategies have improved the prognosis of patients, the associated mortality remains unacceptably high. Our interest is to characterizie the pulmonary vascular inflammatory response associated with acute lung injury and the identification of therapeutic targets to improve prognosis in these patients.

Our research work is focused in analyzing different signaling pathways involved in these pathologies: 1) Sphingolipids, components of the plasma membrane of all eukaryotic cells whose hydrolysis products (ceramides and sphingosine) play a key role in various signal transduction pathways. 2) Innate immunity receptors and danger-associated molecular patterns.

Most relevant scientific articles

- Moreno L., Moral-Sanz J., Morales-Cano D., Barreira B., Moreno E., Ferrarini A. et al. Ceramide mediates acute oxygen aensing in vascular tissues. Antioxidants and Redox Signaling. 2014;20(1):1-14.
- Morales-Cano D., Menendez C., Moreno E., Moral-Sanz J., Barreira B., Galindo P. et al. The flavonoid quercetin reverses pulmonary hypertension in rats. PLoS ONE. 2014;9(12).
- Gomez-Guzman M., Jimenez R., Romero M., Sanchez M., Zarzuelo M.J., Gomez-Morales M. et al. Chronic hydroxychloroquine improves endothelial dysfunction and protects kidney in a mouse model of systemic lupus erythematosus. Hypertension. 2014;64(2):330-337.
- Oliveras A., Roura-Ferrer M., Sole L., De La Cruz A., Prieto A., Etxebarria A. et al. Functional assembly of Kv7.1/Kv7.5 channels with emerging properties on vascular muscle physiology. Arteriosclerosis, Thrombosis, and Vascular Biology. 2014;34(7):1522-1530.
- Quintela A.M., Jimenez R., Piqueras L., Gomez-Guzman M., Haro J., Zarzuelo M.J. et al. PPARβ activation restores the high glucose-induced impairment of insulin signalling in endothelial cells. British Journal of Pharmacology. 2014;171(12):3089-3102.

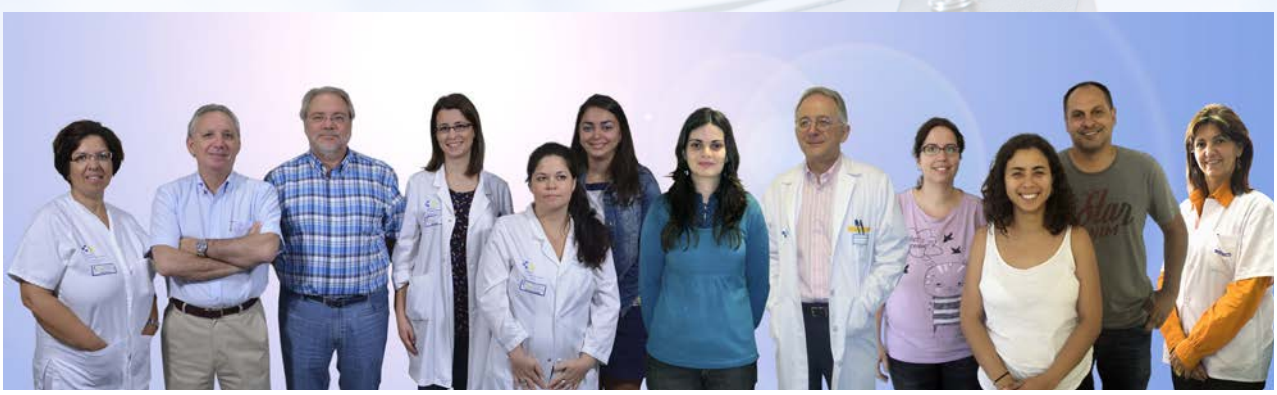
Highlights

- 2012-15. New vasodilators for pulmonary hypertension. Funding: Ministry of Science and Innovation (CICYT (SAF2011- 28150) PI: F. Pérez-Vizcaíno.
- 2011-2014. SAF2010-22066-C02-02Efectos cardiovasculares de agonistas de los receptores activados por proliferador de peroxisomas (PPAR)beta/delta en modelos de diabetes experimental.PI: A. Cogolludo.
- 2013-2015. CP12/03304. Papel de los receptores de inmunidad innata en las alteraciones vasculares asociadas a daño pulmonar e hipertensión pulmonar. Implicación de patrones moleculares endógenos asociados a peligro. PI: L. Moreno.
- New Corporative Program on Pulmonary Hypertension within the CIBERES.

Institution: Universidad Complutense de Madrid
Contact: Facultad de Medicina. Pza. Ramón y Cajal, s/n. Ciudad Universitaria. 28040 Madrid
Phone: (+34) 91 394 14 77 · E.mail: fperez@med.ucm.es
Web: http://www.ucm.es/farmacologia/farmacologia-vascular-factores-vasoactivos

Group 29

Programme: Acute Lung Injury (ALI)



Lead Researcher: Villar Hernández, Jesús

Group members

STAFF MEMBERS: Cabrera Benítez, Nuria Esther | Ramos Nuez, Angela María.

ASSOCIATED MEMBERS: Acosta Herrera, Marialbert | Blanco Varela, Jesús | Corrales Moreno, Almudena | Del Pino Yanes, María del Mar | Flores Infante, Carlos Alberto | Pérez Méndez, Lina Inmaculada | Valladares Parrilla, Francisco

Main lines of research

- Epidemiology and Stratification of the Acute Respiratory Distress Syndrome (ARDS).
- Genetic Susceptibility to the Acute Respiratory Distress Syndrome.
- Ventilator-Induced Lung Injury (VILI).
- Cellular and Molecular Mechanisms of Lung Repair.
- Searching from common genetic activation and signalling pathways among ARDS, Asthma and Pulmonary Fibrosis.

Most relevant scientific articles

- Villar J, Cabrera-Benítez NE, Ramos-Nuez A, Flores C, García-Hernández S, Valladares F et al. Early activation of pro-fibrotic WNT5A in sepsis-induced acute lung injury.Critical care (London, England). 2014;18(5):568.
- Rodriguez-Gonzalez R., Martin-Barrasa J.L., Ramos-Nuez A., Canas-Pedrosa A.M., Martinez-Saavedra M.T., Garcia-Bello M.A. et al. Multiple system organ response induced by Hyperoxia in a clinically relevant animal model of sepsis. Shock. 2014;42(2):148-153.
- Cabrera-Benitez N.E., Laffey J.G., Parotto M., Spieth P.M., Villar J., Zhang H. et al. Mechanical ventilation-associated lung fibrosis in acute respiratory distress syndrome: A significant contributor to poor outcome. Anesthesiology. 2014;121(1):189-198.
- Tejera P., O'Mahony D.S., Owen C.A., Wei Y., Wang Z., Gupta K. et al. Functional characterization of polymorphisms in the peptidase inhibitor 3 (Elafin) gene and validation of their contribution to risk of acute respiratory distress syndrome. American Journal of Respiratory Cell and Molecular Biology. 2014;51(2):262-272.

• Villar J., Muros M., Cabrera-Benitez N.E., Valladares F., Lopez-Hernandez M., Flores C. et al. Soluble platelet-endothelial cell adhesion molecule-1, a biomarker of ventilator-induced lung injury. Critical Care. 2014;18(2).

Highlights

PROJECTS

- PI13/0119: Randomized Study of Neurally Adjusted Ventilation Assisted in patients with Acute Respiratory Failure. ISCIII. IP: Jesus Villar.
- PI2012 FMM: Randomized Study to evaluate the effectiveness of dexamethasone in patients with ARDS. Mutua Madrileña Foundation. IP: Jesus Villar.
- REB11 -024: Practice Pattern Variation in Mechanical Ventilation in Critically discontinuing Ill. Ministry of Research, Canada. IP: Karen Burns & Jesus Villar.
- PI11/0623: Genetic susceptibility to asthma. ISCIII. IP: Carlos Flores.
- REGPOT FP7- 2012 -2013- 1: IMBRAIN: Improvement of Biomedical Research and Innovation in the Canary Islands. CORDIS.
- NAVA in patients with Acute Respiratory Failure. MAQUET. IP: Jesus Villar.
- PI- 0279-2012: Identification of genetic mechanisms and characterization of functional networks with Systems Biology in hypersensitivity reactions to non-steroid anti-inflammatories Junta de Andalucía. Co- IP: Carlos Flores.

POST-GRADUATES FELLOWSHIP

- CD11/00104: Post- Doctoral Sara Borrel. ISCIII.
- FI11/00074: Predoctoral Training Health Research. ISCIII.
- FI12/00493: Predoctoral Training Health Research. ISCIII.

PATENTS

- BOPI Publication Award Patent 16/05/2013, P201031978.
- Title or Certificate of Invention Patent ES2385443 07/11/2013, P201031978.
- BOPI Publication Report of the state of the art 19/06/2013, P201131785
- BOPI Publication resumption general award patent procedure IET 19/06/2013, P201131785.

CLINICAL GUIDELINES

- Assessing the quality of studies supporting genetic susceptibility and outcomes of ARDS. Front Genet 2014; 5:20.

OTHER CONSIDERATIONS:

- Jesus Villar: Referee for New England Journal of Medicine , American Journal of Respiratory and Critical Care Medicine, Critical Care Medicine, Intensive Care Medicine, Critical Care, Minerva Anestesiologica.
- Jesus Villar: Member, Editorial Board of Intensive Care Monitor.
- Carlos Flores: Member, Editorial Board of ISRN Pulmonology, Clinical Antiallergy antiinflamatory & Drugs.

Institution: Servicio Canario de Salud
Contact: Hospital Universitario de Gran Canaria Dr. Negrín
Barranco de la Ballena, s/n. 35010 Las Palmas de Gran Canaria. Tel.: (+34) 928 449 413
E.mail: jesus.villar54@gmail.com · Web: http://www.ciberes.org/

Group 30

Programme: Lung Cancer / COPD / Pneumonia

Lead Researcher: Monsó Molas, Eduard

Group members

STAFF MEMBERS: Garcia Nuñez, Mª Angeles | Millares Costas, Laura | Parraga Niño, Noemi | Setó Gort, Laia

ASSOCIATED MEMBERS: Andreo García, Felipe Cristobal | Castella Fernández, Eva | Cubero de Frutos, Noelia | García Olive, Ignasi | Llatjos Sanuy, María | López Alujes, Pedro Enrique | Marín Tapia, Alicia | Martínez Rivera, Carlos | Mateu Pruñonosa, Lourdes | Modol Deltell, Josep Maria | Morera Prat, José | Pedro Botet Montoya, María Luisa | Pomares Amigo, Xavier | Rosell Gratacos, Antoni | Sabria Leal, Miguel | Sopena Galindo, Nieves | Vigil Giménez, Laura

Main lines of research

- CRP Lung Cancer: the group coordinates the Strategic RCP on Lung Cancer (2013-2015). Three cohorts of lung early stage (I / IIp) cancer have been created, with obtaining clinical information and follow-up samples and tumor and non-tumor lung tissue and peripheral blood, registered in the CIBERES Pulmonar Biobank Consortium.
- CRP COPD: the Group participates in the RCP including patients in a cohort of iniatial COPD diagnosis (Early - Cohort COPD) and in a severe COPD cohort with fragility characteristics of frequent exacerbations. The group performs the analysis of bronchial inflammatory response and the study of bronchial microbiology.
- CRP Pneumonia: the Group is the partner of RCP participating in the register of invasive pneumococcal disease and the analysis of early mortality determinants in bacteremic pneumococcal pneumonia. The Group is leading a multicenter project focused on nosocomial pneumonia outside the Intensive Care Unit. The Group maintains a study on clinical and molecular aspects of Legionellosis, including the prospective registry of new cases. In environmental health, the Group studies the disinfection effects and consequences of different measures applied on water supplies, and acts as a reference center for Legionella molecular typing.

Most relevant scientific articles

- Garcia-Nunez M., Millares L., Pomares X., Ferrari R., Perez-Brocal V., Gallego M. et al. Severity-related changes of bronchial microbiome in chronic obstructive pulmonary disease. Journal of Clinical Microbiology. 2014;52(12):4217-4223.
- Pedro-Botet M.L., Burgos J., Lujan M., Gimenez M., Rello J., Planes A. et al. Impact of the 2009 *influenza A* H1N1 pandemic on invasive pneumococcal disease in adults. Scandinavian Journal of Infectious Diseases. 2014;46(3):185-192.
- Sanchez de Cos Escuin J., Abal Arca J., Melchor Iniguez R., Miravet Sorribes L., Nunez Ares A., Hernandez Hernandez J.R. et al. Tumor, node and metastasis classification of lung cancer - M1a versus M1b - Analysis of M descriptors and other prognostic factors. Lung Cancer. 2014;84(2):182-189.
- Garcia-Olive I., Sanz-Santos J., Centeno C., Andreo F., Munoz-Ferrer A., Serra P. et al. Results of bronchial artery embolization for the treatment of hemoptysis caused by neoplasm. Journal of Vascular and Interventional Radiology. 2014;25(2):221-228.
- Millares L., Ferrari R., Gallego M., Garcia-Nunez M., Perez-Brocal V., Espasa M. et al. Bronchial microbiome of severe COPD patients colonised by Pseudomonas aeruginosa. European Journal of Clinical Microbiology and Infectious Diseases. 2014;33(7):1101-1111.

Highlights

CRP Lung Cancer; Coordination of the CRP and creation of a tumour tissue biobank containing tumour tissues from patients staged I and II, with more than 200 samples in 2014. .

Collaboration with IASLC and RETIC-Cancer in order to incorporate staging molecular variables.

Members of the group has registrered two EU patents (EP14382007:METHODS AND SYSTEMS FOR PROVIDING OXYGEN TO A PATIENT) and (EP14382315.1:ROCESS FOR MANUFACTURING A CUSTOMIZABLE MEDICAL DEVICE AND DEVICED OBTAINED BY SAID PROCESS).

CRP COPD: Consolidation of bronchial microbiome analysis in collaboration with FISABIO-CIBERESP.

The severity of COPD is associated with a loss of bronchial diversity. Exacerbation of chronic colonized COPD patients is attributable to different pathogens from colonizers.

Collaboration in the inclusion of patients in the Early-COPD and fragile-COPD cohorts. The group performed microbiome analysis and bronquial inflammatory determinations.

CRP Pneumonia, the group leads a multicenter study about invasive pneumococal disease (IPD) and has designed a intervention Project in order to determine the incidence of hospital-acquired pneumonia.

A close relationship betwen Influenza A H1N1 and IPD was observed. The influenza may be associated with significant changes in the individual characteristic of IPD patients and the serotype and virulence of S.pneuniae which emerge in the evolution and mortality of the disease.

The variables associated with the premature mortality of patients with IPD are different that those associated with later-mortality.

Development of biosensors to detect pathogens in collaboration with CNM-UAB.

A high diversity of Legionella types has been described and the group has been stablished as a legionella typing reference laboratory in Catalonia (agreement ASP).

The group has been the chair of the 2nd ESGLI congress.

Finally, the group has maintained its two spin-offs AQUALAB and ADBRONCHUS.

Institution: Corporación Sanitaria Parc Taulí
Contact: E.mail: emonso@tauli.cat

Group 31

Programme: COPD

Lead Researcher: Ruiz-Cabello Osuna, Jesús

Group members

STAFF MEMBERS: Pérez Medina, Carlos | Pérez Sánchez, José Manuel

ASSOCIATED MEMBERS: Benito Vicente, Marina | Bilbao Luri, Izaskun | Herranz Rabanal, Fernando | Pellico Saez, Juan | Rodríguez Ramírez de Arellano, Ignacio | Villa Valverde, Palmira

Main lines of research

The group is integrated in the Advanced Imaging Unit (AIU) that was established in the Spanish National Centre for Cardiovascular Imaging in early 2012. It is a multidisciplinary group focused in developing new imaging applications and molecular imaging developments that will expand the molecular and cellular knowledge of the different cardiovascular and pulmonary diseases. With this aim our research is focused on 1) Cardiovascular and Pulmonary Imaging 2) Nanomedicine and radiochemistry and 3) Metabolomics. The group offers the scientific community state of the art imaging technologies including five modalities: MRI, X-ray CT, nuclear imaging (PET), ultrasound (echocardiography) and optical (bi and tri-dimensional luminescence and fluorescence). In the field of Nanomedicine the group encompasses a nanotechnology and organic chemistry laboratory in which we develop new nanoparticles, molecular probes and biofunctionalization techniques for the diagnosis and treatment of different cardiovascular and pulmonary diseases. Currently our group produces multifunctional nanoparticles for all imaging techniques available at our institution, like Iron Oxide, liposomes, Up-converting Nanophosphors and Gold Nanoparticles, all of them functionalized with different cardiovascular and pulmonary biomarkers. Additionally, a new 68Ga (and from beginning of 2014) 89Zr radiochemistry laboratory is fully operative to provide specific PET radiotracers for nuclear imaging. Finally, the group also has a long experience in the application of metabolic analysis to the study of different pathologies, by the use of Magnetic Resonance Spectroscopy and Mass Spectrometry and different statistical tools developed within the group. Our research projects range from technical developments and chemistry advances to in vitro studies and tracking biological processes in vivo.

Most relevant scientific articles

- Sreeramkumar V., Adrover J.M., Ballesteros I., Cuartero M.I., Rossaint J., Bilbao I. et al. Neutrophils scan for activated platelets to initiate inflammation. Science. 2014;346(6214):1234-1238.
- Izquierdo-Garcia J.L., Naz S., Nin N., Rojas Y., Erazo M., Martinez-Caro L. et al. A metabolomic approach to the pathogenesis of ventilator-induced lung injury. Anesthesiology. 2014;120(3):694-702.
- Bujak R., Garcia-Alvarez A., Ruperez F.J., Nuno-Ayala M., Garcia A., Ruiz-Cabello J. et al. Metabolomics reveals metabolite changes in acute pulmonary embolism. Journal of Proteome Research. 2014;13(2):805-816.
- Perez-Medina C., Abdel-Atti D., Zhang Y., Longo V.A., Irwin C.P., Binderup T. et al. A modular labeling strategy for in vivo PET and near-infrared fluorescence imaging of nanoparticle tumor targeting. Journal of Nuclear Medicine. 2014;55(10):1706-1711.
- Zafra M.P., Mazzeo C., Gamez C., Marco A.R., De Zulueta A., Sanz V. et al. Gene silencing of SOCS3 by siRNA intranasal delivery inhibits asthma phenotype in mice. PLoS ONE. 2014;9(3).

Institution: Fundación Centro Nacional de Investigaciones Cardiovasculares

Contact: Centro Nacional de Investigaciones Cardiovasculares

C/ Melchor Fernández Almagro, 3. 28029 Madrid · Phone: (+34) 91 453 12 00 -Ext. 4150

E.mail: ruizcabe@cnic.es · Web: http://www.cnic.es/es/unidades/imagen/index.php

Group 32

Programme: (SAHS) / (ALI)

Lead Researcher: Ortín Montón, Juan

Group members

STAFF MEMBERS: Marcos Villar, Laura | Pazo Fernández, Alejandra.

ASSOCIATED MEMBERS: Chávez González, Juan Pablo | Coloma Ciudad, Rocío | De Lucas Arias, Susana | Falcón Escalona, Ana | Landeras Bueno, Sara | Llompart Vázquez, Catalina María | Nieto Martín, Amelia | Peredo Hernández, Joan | Pérez Cidoncha, María Teresa | Rodríguez Rodríguez, Paloma | Soledad Ver, Lorena

Main lines of research

- Structure-function studies on the influenza virus RNA polymerase.
- Virus counteraction to the interferon response after infection.
- Mechanism of influenza virus interaction with the host cell.

Most relevant scientific articles

- Perez-Gonzalez A., Pazo A., Navajas R., Ciordia S., Rodriguez-Frandsen A., Nieto A.. HCLE/C14orf166 associates with DDX1-HSPC117-FAM98B in a novel transcription-dependent shuttling RNATransporting complex. PLoS ONE. 2014;9(3).
- Perez-Cidoncha M., Killip M.J., Asensio V.J., Fernandez Y., Bengoechea J.A., Randall R.E. et al. Generation of replication-proficient influenza virus NS1 point mutants with interferon-hyperinducer phenotype. PLoS ONE. 2014;9(6).
- Peredo J., Villace P., Ortin J., De Lucas S.. Human Staufen1 associates to MiRNAs involved in neuronal cell differentiation and is required for correct dendritic formation. PLoS ONE. 2014;9(11).
- Garcia-Barreno B., Delgado T., Benito S., Casas I., Pozo F., Cuevas M.T. et al. Characterization of an enhanced antigenic change in the pandemic 2009 H1N1 influenza virus haemagglutinin. Journal of General Virology. 2014;95(PART 5):1033-1042.

Institution: Agencia Estatal Consejo Superior de Investigaciones Científicas
Contact: Centro Nacional de Biotecnologia · C/ Darwin, 3. Universidad Autónoma de Madrid. Cantoblanco. Dpto de Biología Molecular y Celular. 28049 Madrid
Phone: (+34) 91 585 45 57 · E.mail: jortin@cnb.csic.es

Group 33

Programme: Acute Lung Injury / Pneumonia

Lead Researcher: Blanch Torra, Lluís

Group members

STAFF MEMBERS: Broceño Corrales, Cristina | Guillamat Prats, Raquel | Montanyà Castells, Jaume.

ASSOCIATED MEMBERS: Artigas Raventos, Antonio | Fernández Fernández, Rafael | Ferrer Roca, Ricard | López Aguilar, Josefina | Martí Sistac, Octavi | Martín Loeches Carrondo, Ignacio Esteban | Martínez Perez, Melcior | Muñiz Albaiceta, Guillermo | Ochagavia Calvo, Ana | Sales López, Bernat | Valles Daunis, Jorge | Villagra García, Ana Mª.

Main lines of research

The main lines of research in our group are part of the two Corporate Research Programs in which we participate: 1. Acute Lung Injury: Early Diagnosis and Novel Therapeutic Strategies for Acute Lung Injury (EDIT-ALI) Project. 2. Pneumonia: Multidisciplinary Translational Research Project in Respiratory Tract Infections (MARTIN).

- New techniques for monitoring in critically ill patients:
- Non-invasive monitoring of tissue oxygenation and exhaled air.
- Software for computed interpretation of physiological variations.
- Experimental models (animals and cell cultures) for the characterization of new mechanisms involved in acute lung injury, specific treatments and prevention. (CIBERES Groups 23, 29 and 33).
- Clinical and Experimental Approach of the brain-lung axis during mechanical ventilation: molecular alterations, neuropsychological / psychopathological squeals and neurocognitive prevention through rehabilitation (CIBERES Groups 29 and 33; GTC-I3A CIBER BBN and SEPAR).
- Prognostic classification of the Acute respiratory distress syndrome.
- Epidemiology of pneumonia associated with mechanical ventilation (CIBERES Groups 14 and 33).

Most relevant scientific articles

- Gruartmoner G., Mesquida J., Masip J., Martinez M.L., Villagra A., Baigorri F. et al. Thenar oxygen saturation during weaning from mechanical ventilation: An observational study. European Respiratory Journal. 2014;43(1):213-220.
- Valles J., Martin-Loeches I., Torres A., Diaz E., Seijas I., Lopez M.J. et al. Epidemiology, antibiotic therapy and clinical outcomes of healthcare-associated pneumonia in critically ill patients: A Spanish cohort study. Intensive Care Medicine. 2014;40(4):572-581.
- Bos L.D.J., Martin-Loeches I., Kastelijn J.B., Gili G., Espasa M., Povoa P. et al. The volatile metabolic fingerprint of ventilator-associated pneumonia. Intensive Care Medicine. 2014;40(5):761-762.
- Villar J., Fernandez R.L., Ambros A., Parra L., Blanco J., Dominguez-Berrot A.M. et al. A Clinical Classification of the Acute Respiratory Distress Syndrome for Predicting Outcome and Guiding Medical Therapy. Critical Care Medicine. 2014.
- Aguirre A., Lopez-Alonso I., Gonzalez-Lopez A., Amado-Rodriguez L., Batalla-Solis E., Astudillo A. et al. Defective autophagy impairs ATF3 activity and worsens lung injury during endotoxemia. Journal of Molecular Medicine. 2014;92(6):665-676.

Highlights

Our goal is to improve knowledge of respiratory diseases in critically ill patients using a multidisciplinary and translational approach. Our projects are aimed at transferring to society and market developments that can help improve the health and wealth generation. We have patents and a spin-off. We cooperate with national / international networks in innovation and in clinical studies.

NOTABLE RESULTS

- Development of translational projects funded under the Strategic Action Program of Health (AES):
- PI13/02204: Influence of persistent patient/ventilator uncoupling in cognitive and psychopathological alterations in critically ill patients: Multicenter clinical and mechanistic study. (Groups CIBERES 29 y 33).
- PI13/02189. Translational research in fragile patients undergoing mechanical ventilation: From experimental models to therapeutic opportunities.
- PI12/02548 Transplantation of alveolar type II cells in experimental models of Acute Lung Injury (Groups CIBERES 23 y 33).
- PI10/00393. Finalization of the project: Mechanisms of pulmonary fibrosis induced by mechanical ventilation and possible therapeutic targets (Groups CIBERES 29 y 33).

FUNDED PROJECTS IN THE CONTEXT OF CRITICAL PATIENT MONITORING

- EU THALEA. "Telemonitoring and Telemedicine for Hospitals Assisted by ICT for Life saving co-morbid patients in Europe As part of a Patient personalised care program of the EU".
- EU-Egypt cooperation to improve monitoring of critically ill patients.
- CIBERES-SEPAR-CIBERBBN Cooperation: Effects of an early neurocognitive intervention on patient-ventilator interaction and stress in critically ill patients receiving mechanical ventilation.
- Agreement with a Pharmaceutical Company. Effect of Antithrombin in an in vitro model of Acute Lung Injury.
- Patent: Method and system for managing related-patient parameters provided by a monitoring device.
- Multicenter clinical trials in the field of mechanical ventilation-associated pneumonia.
- Publication of Clinical Guidelines: "Defining a framework for training clinicians in respiratory critical care".

Institution: Corporación Sanitaria Parc Taulí

Contact: Centre de Crítics. Corporacion Sanitaria Parc Tauli · Parc Taulí, S/N · 08208 Sabadell, Barcelona
Phone: (+34) 93 723 10 10 ext. 22229 · E.mail: lblanch@tauli.cat

Group 34

Programme: Host-Pathogen Interactions

Lead Researcher: Menéndez Fernández, Margarita

Group members

STAFF MEMBERS: Bustamante Spuch, Noemí | Iglesias Bexiga, Manuel Alberto.

ASSOCIATED MEMBERS: Álvarez Pérez, Mónica | Campanero Rhodes, María Asunción | Kalograiaki, Ioanna | López Merino, Lara | Rico Lastres, Palma | Solís Sánchez, María Dolores

Main lines of research

The group activity focuses on in-depth characterization of structure/function relationships in biomolecules and molecular recognition processes, with emphasis in i) bacterial virulent factors, ii) host-pathogen interactions, iii) search and characterization of new antimicrobials, and iv) development of new designer's microarrays.

Most relevant scientific articles

- Ruiz F.M., Scholz B.A., Buzamet E., Kopitz J., Andre S., Menendez M. et al. Natural single amino acid polymorphism (F19Y) in human galectin-8: Detection of structural alterations and increased growth-regulatory activity on tumor cells. FEBS Journal. 2014;281(5):1446-1464.
- Solis D., Bovin N.V., Davis A.P., Jimenez-Barbero J., Romero A., Roy R. et al. A guide into glycosciences: How chemistry, biochemistry and biology cooperate to crack the sugar code. Biochimica et Biophysica Acta - General Subjects. 2014.
- Moscoso M., Esteban-Torres M., Menendez M., Garcia E.. In vitro bactericidal and bacteriolytic activity of ceragenin CSA-13 against planktonic cultures and biofilms of Streptococcus pneumoniae and other pathogenic streptococci. PLoS ONE. 2014;9(7).

Highlights

- The antimicrobial activity of ceragenin CSA-13 in planktonic cultures and biofilms of pathogenic streptococci, including multidrug-resistant Streptococcus pneumoniae, has been established in collaboration with Group 2 of CIBERES (Dr. E. García) (PMID:25006964).
- We have engineered and characterized a new chimeric lysin (Cpl-711) whose exogenous killing activity against Strepcotococcus pneumoniae surpasses those of the more potent enzybiotics against this pathogen, in collaboration with Group 2. Results have been validated in vitro and in vivo (PMID:25733585).
- A new methodology for generation and validation of bacteria microarrys and their application to the study of epitopes on the pathogen's surface and interactions with host receptors has been implemented using Klebsiella pneumoniae as bacterial model (DOI 10.1039/C4RA14570d), in cooperation with Group 8 of CIBERES (Dr. V. Regueiro). The same approach, used also to explore the glycosilation profiles of Haemophilus influenzae no tipable wild-type and several mutants in association with Dr. J. Garmendia (Group 8 of CIBERES), has started to be employed with a large series of pathogens.
- New structure-function relationships have been identified on different lectins of the innate immune system, like galectins 3 and 4, and the macrophage galactose binding lectin (hMGL). The effect of SNPs on human galectin 8 was also studied.

The activity has generated five publications (two in press), several communications to scientific congresses and specialized workshops. The international extension of one patent has been applied for, and there are four doctoral thesis in progress.

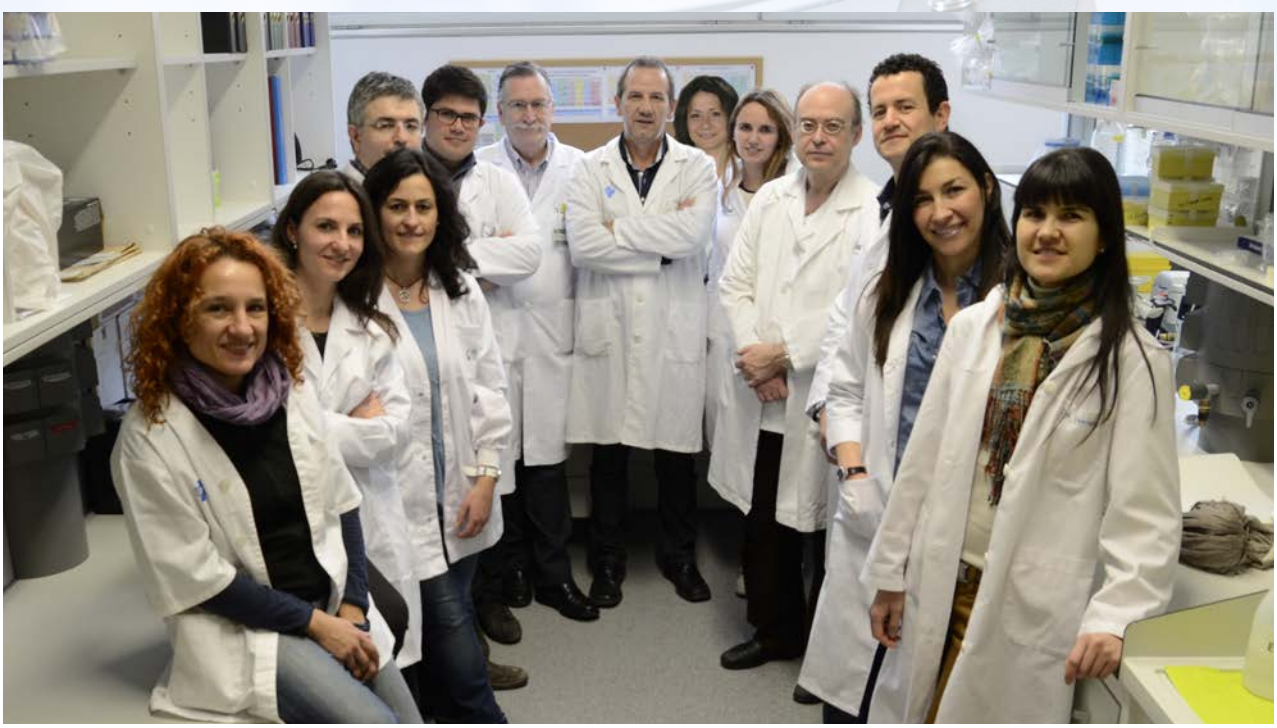
PROJECTS

- 2011-2014. Glycomics by High-throughput Integrated Technologies (UE; FP7-HEALTH-2010-260600).
- 2011-2015. Dynamic interactive nanosystems (EU; FP7-ITN-GA:289003).
- 2012-2016. The Sugar Code: from (bio)chemical concept to clinics (UE; FP7-PEOPLE-2012-ITN-317297).
- 2012-2015. Bioinformatics Integrative platform for structure-based drug discovery BIPPED2 (CAM; S2010/BMD-2457).
- 2013-2015. Exploring exogenous and endogenous factors as tools for the control of infectious and immune processes MINECO; BFU2012-36825).

Institution: Agencia Estatal Consejo Superior De Investigaciones Científicas
Contact: Inst. de Química Física Rocasolano · C/ Serrano, 119. Madrid · Phone: (+34) 91 561 94 00
E.mail: mmenendez@iqfr.csic.es

Group 35

Programme: Sleep Apnea-Hypopnea Syndrome (SAHS)



Lead Researcher: Barbé Illa, Ferrán

Group members

STAFF MEMBERS: Forner Vicente, Marta | Inglés Borda, Sandra | Muñoz Bravo, Javier | Sánchez De la Torre, Manuel.

ASSOCIATED MEMBERS: Alonso Fernández, Alberto | Barceló Bennassar, Antonia | Carrera Lamarca, Miguel | Carrizo Sierra, Santiago | De la Peña Bravo, Mónica | Duran Cantolla, Joaquín José | Egea Santaolalla, Carlos Javier | Esquinas López, Cristina | Gómez Falguera, Silvia | Marín Trigo, José María | Martínez Alonso, Montserrat | Martínez Null, Cristina | Mediano San Andres, Olga | Pifarre Teixido, Ricardo | Rubio Aramendi, Ramón | Sánchez de la Torre, Alicia | Vicente González, Eugenio | Vila Justribo, Manuel

Main lines of research

Sleep disorders breathing:

- Evaluation of new diagnostic and treatment methods.
- Pathogenesis of cardiovascular and metabolic complications.
- Thecnologic development.

Most relevant scientific articles

- Masa JF, Duran-Cantolla J, Capote F, et al. Effectiveness of home single-channel nasal pressure for sleep apnea diagnosis. Sleep. 2014 Dec 1;37(12):1953-61. doi: 10.5665/sleep.4248. PubMed PMID: 25325484; PubMed Central PMCID: PMC4237536.
- Guerrero A, Embid C, Isetta V, et al. Management of sleep apnea without high pretest probability or with comorbidities by three nights of portable sleep monitoring. Sleep. 2014 Aug 1;37(8):1363-73. doi: 10.5665/sleep.3932. PubMed PMID: 25083017; PubMed Central PMCID: PMC4096206.
- Bratton DJ, Stradling JR, Barbé F, et al. Effect of CPAP on blood pressure in patients with minimally symptomatic obstructive sleep apnoea: a meta-analysis using individual patient data from four randomised controlled trials. Thorax. 2014 Dec;69(12):1128-35. doi: 10.1136/thoraxjnl-2013-204993. Epub 2014 Jun 19. PubMed PMID: 24947425; PubMed Central PMCID: PMC4251445.
- Muniesa MJ, Huerva V, Sánchez-de-la-Torre M, et al. The relationship between floppy eyelid syndrome and obstructive sleep apnoea. Br J Ophthalmol. 2013 Nov;97(11):1387-90. doi: 10.1136/bjophthalmol-2012-303051. Epub 2013 Apr 12. PubMed PMID: 23584721.
- Alonso-Álvarez ML, Cordero-Guevara JA, Terán-Santos J, Gonzalez-Martinez M, Jurado-Luque MJ, Corral-Peñafiel J, Duran-Cantolla J, Kheirandish-Gozal L, Gozal D. Obstructive sleep apnea in obese community-dwelling children: the NANOS study. Sleep. 2014 May 1;37(5):943-9. doi: 10.5665/sleep.3666. PubMed PMID: 24790273; PubMed Central PMCID: PMC3985101.

Highlights

PATENT APPLICATION

Aplication. Number: P3158EP00

Title: Method for predicting response to continuous positive air pressure treatment.

Inventors: F Barbé, M Sánchez-de-la-Torre, D Gozal, A Khalyfa, A Sánchez-de-la-Torre, MA Martinez-García.

Date: 18 December 2014.

- Inauguracón Curso Académico 2013/2014. "Conferencia Magistral". Universidad de Vic/Complejo Hospitalario de Vic. 03 de Octubre de 2013.
- Hacia la Medicina Personalizada en EPOC. VII Jornadas Científicas del CIBERES. Madrid 20-21 de Junio de 2013.

Institution: Instituto de Investigacion Biomédica de Lleida. Fundación Dr. Pifarre

Contact: Instituto de Investigación Biomédica de Lleida · Avda. Alcalde Rovira Roure, 80. 25198 Lleida
Phone: (+34) 973 705 372 · E.mail: febarbe.lleida.ics@gencat.cat
http://www.ciberes.org/index.php?option=com_ personal&view=personal&Group_id=35&Itemid=77

Group Vinculado 1

Programme: Chronic Obstructive Pulmonary Disease (COPD) / Pulmonary Fibrosis

Lead Researcher: López-Campos Bodinau, José L.

Group members

ASSOCIATED MEMBERS: Barrot Cortes, Emilia | Calero Acuña, Carmen | Echevarría Irusta, Miriam | Montes Worboys, Ana | Moreno Mata, Nicolas | Ortega Ruiz, Francisco | Ortega Sáenz, Patricia | Otero Candelera, Remedios | Quintana Gallego, Esther | Rodríguez Panadero, Francisco | Rodríguez Portal, José Antonio

Main lines of research

- COPD.
- Interstitial lung disease.
- Pulmonary circulation.
- Cystic fibrosis.
- Sleep respiratory disorders.

Most relevant scientific articles

- Lopez-Campos J.L., Ruiz-Ramos M., Soriano J.B.. Mortality trends in chronic obstructive pulmonary disease in Europe, 1994-2010: A joinpoint regression analysis. The Lancet Respiratory Medicine. 2014;2(1):54-62.
- Lopez-Campos J.L., Hartl S., Pozo-Rodriguez F., Roberts C.M.. Variability of hospital resources for acute care of COPD patients: The European COPD Audit. European Respiratory Journal. 2014;43(3):754-762.
- Serna A., Galan-Cobo A., Rodrigues C., Sanchez-Gomar I., Toledo-Aral J.J., Moura T.F. et al. Functional Inhibition of Aquaporin-3 With a Gold-Based Compound Induces Blockage of Cell Proliferation. Journal of Cellular Physiology. 2014;229(11):1787-1801.
- Spruit M.A., Pitta F., Garvey C., ZuWallack R.L., Roberts C.M., Collins E.G. et al. Differences in content and organisational aspects of pulmonary rehabilitation programmes. European Respiratory Journal. 2014;43(5):1326-1337.
- De Torres J.P., Marin J.M., Martinez-Gonzalez C., De Lucas-Ramos P., Mir-Viladrich I., Cosio B. et al. Clinical application of the COPD assessment test: Longitudinal data from the COPD history assessment in Spain (CHAIN) Cohort. Chest. 2014;146(1):111-122.

Highlights

2014 has been a year of intense research has been supported by the aforementioned publications and some more that have come during 2015. Our group participates CIBERES two corporate research programs and actively participate in the new program being created on pulmonary hypertension.

In the PCI COPD has two main lines. 1) In the line of translational research, the team has made progress in implementing its project FIS PI12 / 01576 which is in its second year of implementation. This project studies the production of inflammatory mediators by cells of the respiratory completing the limitations of our previous projects: including more specific mediators of the main pathogenic pathways of COPD (apoptosis, oxidation-antioxidation imbalance, imbalance proteasasantiproteasas and local inflammation) including vascular cells and subjecting these cells to stimulation and inhibition, to evaluate biological pathway which is more relevant in the production of this inflammation, and its output compared to the liver. The group is developing another project on the importance of inflammation in the pulmonary vasculature.

2) The evaluative line, the group has secured funding in collaboration with the group 21 for the DELICATO project is the work package 1 of one of the Corporate Research Projects CIBERES in COPD. DELICATO is the continuation of AUDIPOC project, outpatient evaluation and implementation of improvements in hospitalization. This project identifies fragile for subsequent program work packages patients.

In him PCI pulmonary fibrosis, our group works in collaboration with the group of Dr. Maria Molina on inflammatory mediators in idiopathic pulmonary fibrosis.

During 2014 we also participated in the creation of PCI pulmonary hypertension providing a node to the network with clinical and research interest and experience in this field.

Institution: Fundación Pública Andaluza para la Gestion de la Investigacion en Salud de Sevilla
Contact: Hospital Universitario Virgen del Rocío · Avda. Manuel Siurot, s/n. 41013 Sevilla
Phone: (+34) 955 013 164 · E.mail: lcampos@separ.es

ciberes

Centro de Investigación Biomédica en Red

Enfermedades Respiratorias

MINISTERIO DE ECONOMIA Y COMPETITIVIDAD

Instituto de Salud Carlos III

ciber

Centro de Investigación Biomédica en Red (CIBER)
Instituto de Salud Carlos III
C/ Monforte de Lemos 3-5. Pabellón 11
28029 Madrid
www.ciberisciii.es