ANNUAL REPORT 2015

ciberes

Centro de Investigación Biomédica en Red

Enfermedades Respiratorias

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Centro de Investigación Biomédica en Red

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Scientific Director's Presentation

Dear researchers,

First of all please allow me to start this letter for presenting the Annual Report 2015 by thanking you for the great effort and commitment that you have put into CIBERES yet another year. All the good results that will be set forth in the following pages are due to your excellent work.

2015 was a vital year for CIBERES: first of all because we were assessed by the Comisión Técnica de Evaluación de Redes y CIBER (CTER) of the ISCIII and got the third highest mark of all the CIBER thematic areas. This good mark is a obviously a cause for celebration, but more important still, it shows us that there is room for improvement. Secondly, because our research programmes were evaluated by the ANEP with good results in general.

As a result of both assessments we proceeded to comprehensively restructure our scientific and governing organisation. We have gone from having nine scientific programmes to having three with ten lines of research and we have renewed our Management Committee, our Teaching Committee, our External Advisory Scientific Committee, which is now presided by Dr. David Gozal, and most of our coordinators in the Research Line. Our distribution of economic resources and our human resources and teaching policies will also be structured, in 2016 and more markedly in the following years, on the basis of the results of the assessments.

2015 gave us the chance to include a new group in the CIBERES; the group led by Dr. Francisco García Río at the Instituto de Investigación Sanitaria del Hospital Universitario La Paz (IdiPAZ). This group does research into the physiopathology of limitation of air flow, morbidity of cardiovascular sleep disorders, pathogenic mechanisms in asthma, tolerance of the innate immune system in respiratory diseases and characterisation of gene targets of the hypoxia-inducible factor (HIF) in intermittent and sustained hypoxia. We are sure that their joining us will allow new projects and intra, inter and extra-CIBER cooperation to be got under way, which will all result in the greater excellence of our scientific production.

Please let me finish with a very special remembrance of Dr. Constancio González, PI of group 24, Universidad de Valladolid, who died last June 2015. He was a master of dozens of doctors and an excellent scientist who leaves us a major legacy of knowledge and an example of good personal and professional practice. As a tribute to him, CIBERES has decided to grant a prize with his name to the best communication of a young researcher at the Annual Teaching Sessions.

Thank you once more for all your efforts and my best wishes for the coming year's work.

Dr. Ferran Barbé.

Scientific Director of CIBERES.

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Organization

Organizational Structure

The CIBERES is one of the eight thematic areas forming the Centro de Investigación Biomédica en Red (CIBER), a Spanish research consortium in the field of biomedical research with great scientific potential, under the Instituto de Salud Carlos III (ISCIII) – Ministry of the Economy and Competitiveness.

The Respiratory Disease area is made up of 34 research groups, keeping its independence as regards scientific management. Its organisational structure is based on the research groups belonging to this and its activity revolves around the Research Programmes and Transversal Programmes, with a coordinator for each Programme belonging to the Steering Committee. Scientific decisions are made by the Scientific Director, advised by said Steering Committee and the External Scientific Committee.

The Steering Committee is presided over by the Scientific Director and made up of the coordinators of the programmes and Managing Director of the CIBER.

The External Scientific Committee is a body for scientific support and advice, made up of relevant personalities in the field of health sciences standing out for their professional or scientific careers in line with the objectives of the thematic area.

The senior administrative bodies of the CIBERES are the Governing Body and the Permanent Commission, common for all the CIBER research areas.

The Governing Body is made up of three representatives of the ISCIII and by an institutional representative of each of the centres in the consortium. It is presided over by the Director of the ISCIII and meets every six months.

The Permanent Commission is an executive committee made up of the ISCIII and 8 members of the Governing Body, who can be renewed on an annual basis.

Both the operation and the purposes of the governing, support and advisory bodies are established in the statutes of the CIBER.

Members of the Steering Advisory Committee of CIBERES

NAME	POST HELD
Ferran Barbé	Scientific Director
Joaquim Gea	Assistant Scientific Director (clinical field)
Cristina Casals	Assistant Scientific Director (basic field)
Ana Obeso	Training Coordinator
Mª Victoria del Pozo	Severe Asthma PCI Coordinator
Eduard Monsó	Cancer PCI Coordinator
Maria Molina	Pulmonary Fibrosis PCI Coordinator
Junkal Garmendia	Host-Pathogen Interactions PCI Coordinator
Andrés Esteban	Acute Lung Injury PCI Coordinator
Vicenç Ausina	Tuberculosis PCI Coordinator
Antoni Torres	Pneumonia PCI Coordinator
Josep Maria Montserrat	Sleep Apnoea PCI Coordinator
Borja García-Cosío	Chronic Obstructive Pulmonary Disease (COPD) PCI Coordinator

NAME	POST HELD
Lluis Blanch	Technology Transfer Platform Coordinator
Germán Peces-Barba	Pulmonary Biobank Consortium Coordinator
Javier Muñoz	Manager of Scientific Programmes (Secretary of Management Committee)
Manuel Sánchez	Managing Director

Scientific Director Assistant: Roser Mias

External advisory Scientific Committee

NAME	INSTITUTION
David Gozal	President. Univ Chicago, USA
Francesco Blasi	Member. Univ. Milan, Italy
Antonio Azueto	Member. Univ. Texas, USA
Kenneth BM Reid	Member. Univ. Oxford, United Kingdom
Michael S. Niederman	Member. Weill Cornell University New York, USA
James R. Jett	Member. Professor of Medicine Emeritus, National Jewish Health. Minnesota, USA
Marc Humbert	Member. Centre National de Référence de l'Hypertension Pulmonaire Sévère. Paris, France
Bruno Crestaní	Member. Univ. Paris Diderot, France

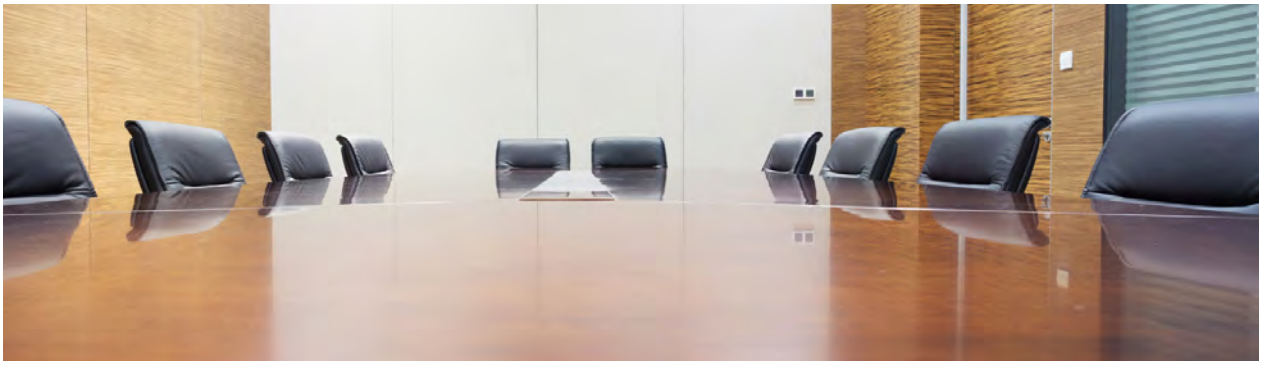
Scientific Management

NAME	POST
Javier Muñoz	Manager of Scientific Programmes
Cristina Broceño	Manager for Transfer Projects and Companies Collaboration
Cristina Villena	Coordinator of the Pulmonary Biobank Consortium

Contact: http://www.ciberes.org/en/about-us/contact

Technical Unit

Personnel list: http://www.ciberes.org/en/about-us/structure/head-office



Directory of Groups and Institutions

Group leader	Institution	Centre	Centre Prov.
Agusti García Navarro, Alvar	Fundación de Investigación Sanitaria de las Islas Baleares Ramon Llull	Fundación de Investigación Sanitaria de las Islas Baleares Ramon Llull	I. Balears
Álvarez Martínez, Carlos J.	Servicio Madrileño de Salud	Hospital Universitrio 12 de Octubre	Madrid
Ausina Ruiz, Vicente	Fundación Instituto de Investigación Germans Trias i Pujol	Hospital Germans Trias i Pujol	Barcelona
Barbé Illa, Ferran	Instituto de Investigación Biomédica de Lleida. Fundación Dr. Pifarre	Instituto de Investigación Biomedica de Lleida	Lleida
Barberá Mir, Joan Albert	Hospital Clínic de Barcelona	Hospital Clínic de Barcelona	Barcelona
Blanch Torra, Lluis	Corporación Sanitaria Parc Taulí	Corporación Sanitaria Parc Taulí	Barcelona
Bouza Santiago, Emilio	Servicio Madrileño de Salud	Hospital Gregorio Marañon	Madrid
Casals Carro, Cristina	Univ. Complutense de Madrid	Facultad de Biología	Madrid
Esteban de la Torre, Andrés	Servicio Madrileño de Salud	Hospital Universitario de Getafe	Madrid
García López, Ernesto	Agencia Estatal Consejo Superior de Investigaciónes Científicas	Centro de Investigaciónes Biológicas	Madrid
Gea Guiral, Joaquim	Consorci Mar Parc Salut de Barcelona	Hospital del Mar	Barcelona
González de la Campa, Adela	ISCIII	Centro Nacional de Microbiología	Madrid
González Mangado, Nicolás	Fundación Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Instituto de Investigación Sanitaria - Fundación Jimenez Diaz	Madrid
Liñares Louzao, Josefina	Fundación IDIBELL	Hospital Universitario de Bellvitge	Barcelona
Martín Montañés, Carlos	Universidad de Zaragoza	Universidad de Zaragoza	Zaragoza
Masa Jiménez, Juan Fernando	Fundación para la Formacion y la Investigación de los Profesionales de la Salud	Hospital San Pedro de Alcántara	Caceres
Melero Fontdevila, José Antonio	ISCIII	Unidad de Investigación	Madrid
Menéndez Fernández, Margarita	Agencia Estatal Consejo Superior de Investigaciónes Científicas	Instituto de Química Física Rocasolano	Madrid
Monsó Molas, Eduard	Corporación Sanitaria Parc Taulí	Corporacion Sanitaria Parc Taulí	Barcelona
Montserrat Canal, Josep Mª	Hospital Clínic de Barcelona	Hospital Clínic de Barcelona	Barcelona

Group leader	Institution	Centre	Centre Prov.
Morcillo Sánchez, Esteban Jesús	Universitat de València	Facultad de Medicina de Valencia	Valencia
Muñoz Gall, Xavier	Fundación Hospital Universitario Vall D´hebron - Institut de Recerca (VHIR)	Hospital Vall d'Hebron	Barcelona
Navajas Navarro, Daniel	Universidad de Barcelona	Facultad de Medicina	Barcelona
Obeso Caceres, Ana	Universidad de Valladolid	Facultad de Medicina	Valladolid
Ortín Montón, Juan	Agencia Estatal Consejo Superior de Investigaciónes Científicas	Centro Nacional de Biotecnologia	Madrid
Pérez Trallero, Emilio	Asociación Instituto Biodonostia	Hospital Donostia	Guipuzcoa
Pérez Vizcaíno, Francisco	Universidad Complutense de Madrid	Facultad de Medicina	Madrid
Picado Vallés, César	Hospital Clínic de Barcelona	Hospital Clínic de Barcelona	Barcelona
Del Pozo Abejón, Mª Victoria	Fundación Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Instituto de Investigación Sanitaria - Fundación Jiménez Díaz	Madrid
Regueiro Comesaña, Verónica	Fundación de Investigación Sanitaria de las Islas Baleares Ramon Llull	Hospital Universitario Son Espases	I. Balears
Relló Condomines, Jordi	Fundación Hospital Universitario Vall D´hebron - Institut de Recerca	Hospital Vall d'Hebron	Barcelona
Ruiz Cabello Osuna, Jesús	Fundación Centro Nacional de Investigaciónes Cardiovasculares	Fundación Centro Nacional de Investigaciónes Cardiovasculares	Madrid
Torres Martí, Antoni	Hospital Clínic de Barcelona	Hospital Clínic de Barcelona	Barcelona
Villar Hernández, Jesús	Fundación Canaria de Investigación Sanitaria	Hospital Universitario de Gran Canaria Dr. Negrin	Las Palmas

Budget

INCOME	5.036.177,26
NOMINAL ISCIII GRANT	2.572.420,00
INCOME FROM NEW GROUPS	60.000,00
AGREEMENTS AND CONTRACTS	628.284,19
SURPLUS	1.775.473,07

EXPENDITURE	2.988.188,12
GROUP	2.181.254,46
PROGRAMMES	35.544,92
TRAINING	77.932,33
TECHNICAL OFFICE	155.000,00
MANAGEMENT COMMITTEE	5.905,12
PLATFORMS	174.154,77
SCIENTIFIC SESSION, SECRETARIAT	14.498,67
COMPETITIVE P.	343.897,85

Personnel

Personnel contracted during the year as of 31st December, separating by categories:

Category	Permanent	Works and service	Post-doctoral	Main Total
Diploma holder	8	3		11
Doctor	9	10	7	26
Graduate	9	13		22
Technical	5	11		16
TOTAL	**31**	**37**	**7**	**75**

Significant Activities

Projects

The projects active in 2015 were as follows:

NATIONAL PROJECTS

Financing Agency: Instituto de Salud Carlos III

- Role of innate immune receptors in vascular alterations associated with acute lung damage (MS12/03304).
- Role of FAS-mediated apoptosis in damage of the pulmonary epithelium (PI12/02451).
- Identification of markers of very severe COPD activity in experimental models, and assessment of therapeutic intervention with soluble guanylate cyclase (PI13/00836).
- NATIONAL BIOBANKS NETWORK (PT13/00010).
- Molecular profile of cardiovascular risk in patients with obstructive sleep apnoea: Personalised predictive model (PI14/01266).

Financing Agency: Ministry of the Economy and Competitiveness:

- Juan de la Cierva Contract 2012 (JDC-2012-14801)
- Post-Doctoral Grant Contract 2013 (FPDI-2013-15598)

INTERNATIONAL EU PROGRAMMES

- FP7-COFUND Contract

Transfer

One of the CIBER's main aims is the transfer of research results into clinical practice, and one of the best tools existing for this purpose is technology transfer. The Unit managing this at the CIBER sets out to act as a bridge between our researchers and other agents in the Science and Technology System (companies, business associations, other research organisations, etc.) to make cooperation with these bodies more effective. This means that research results will be efficiently developed and can succeed in being applied. Work is done in several lines to this end:

- **Training in innovation management and continuous contact with our researchers to monitor their results.**

  In this respect, last year the first general session of the CIBER in training on technology transfer and innovation was held, on 26th February 2015 and where national experts took part sharing their knowledge in matters such as industrial property, business creation or publication in open access, etc.

- **Protection of their research results and management of cooperation with other agents, as vouched for by applications for patents and signing licensing contracts, amongst other agreements.**

  Hence, over 23 new patent applications were made and seven licensing agreements were signed at the CIBER in 2015.

- **The presentation of research results and technological capacities of our groups.**

  Among many other measures and only as an example, in 2015, several projects were presented at the II Foro de Innovación en Diagnóstico in Vitro – FENIN in Barcelona (December 2015).

- **Support for technology-based business creation stemming from CIBER groups.**

  The CIBER has since 2014 taken part in Epidisease (http://www.epidisease.com/es/) which it continued to support in 2015.

- **Other activities connected with innovation, public-private cooperation and industrial and intellectual property.**

  For example, the registration of the "community trademark" of the CIBER has been processed, or steps have been taken for registering intellectual property rights for audio-visual projects, amongst many others.

- **In this period CIBERES applied for one priority patent.**

Dissemination activities

In 2015 CIBER's Communication Department carried out different measures for dissemination and disclosure in order to improve the Centre's visibility, as well as publicising the research work done by the groups in its eight thematic areas.

We now detail the 2015 milestones in CIBERES Communication:

THE CIBERES IN THE MEDIA:

During the 2015 period 50 CIBER press releases were issued, nine of these from the CIBERES and four in cooperation between several CIBER areas.

Date	Themathic area	Title
January	SEVERAL CIBER	El CIBER pone en marcha tres proyectos de excelencia interdisciplinares financiados con casi 2 millones de euros por la AES
February	SEVERAL CIBER	Investigadores del CIBER identifican diversos factores de riesgo de sufrir cáncer
January	SEVERAL CIBER	El CIBER acerca su investigación al público de la mano de la improvisación teatral en #ImproCiencia
February	SEVERAL CIBER	Investigadores del CIBER identifican diversos factores de riesgo de sufrir cáncer
February	CIBERES	Un dispositivo muy simple para el diagnóstico de apneas del sueño posibilita su uso en atención primaria
February	CIBERES	El uso de antiinflamatorios reduce de forma significativa el fallo en el tratamiento en neumonía grave
February	CIBERES	CIBERES pone en marcha un nuevo programa de investigación en hipertensión pulmonar
April	CIBERES	CIBERES pone en marcha una base de datos de pacientes asmáticos en España
May	CIBERES	El CIBERES y la Fundación Contra la Pulmonary Hypertension colaborarán en la investigación
July	CIBERES	La ventilación no invasiva es un método eficaz para tratar insuficiencia respiratoria y apneas del sueño en pacientes con obesidad
July	CIBERES	El desarrollo normal de los pulmones en los primeros años de vida es clave para evitar la Enfermedad Pulmonar Obstructiva Crónica
September	CIBERES	Un análisis predictivo ayuda a personalizar el tratamiento de la apnea del sueño en pacientes con hipertensión
November	CIBERES	La vacuna candidata contra la tuberculosis, MTBVAC, muestra excelente seguridad y prometedora inmunogenicidad

270 appearances in the media were registered over this period:

CIBERES	NEWS	AUDIENCE
Internet	238	44.861.500
Press	32	3.240.000
CIBERES Total	**270**	**48.101.500**

NEW WEB PAGE OF THE CIBERES:

In November 2015 the new web page of the CIBERES was launched in order to have a common structure, image and contents manager for all the CIBER areas.

http://www.ciberes.org/en

CIBER NEWSLETTER

Over this period five CIBER newsletters were issued, including relevant contents on both the CIBERES and the other thematic areas. The digital newsletters were sent to around 4000 subscribers.

http://www.ciberisciii.es/comunicacion/boletines

SOCIAL NETWORKS

Main indicators of CIBERES's presence on Twitter:

UPDATES		FOLLOWERS		FOLLOWING		KLOUT (influence, values between 1 and 100)	
JANUARY	DECEMBER	JANUARY	DECEMBER	JANUARY	DECEMBER	JANUARY	DECEMBER
2242	2470	1.200	1500	285	293	45	43

CIBERES ANNUAL REPORT

The Communication area of the CIBER in cooperation with the CIBERES coordinated the content of the CIBERES report 2014 in Spanish/English, drawing up and disseminating 2 reports in interactive format (Flipbook) and PDF. These were distributed over the web page and Twitter account:

http://www.ciberisciii.es/en/press/annual-report

CIBER #IMPROCIENCIA SCIENCE WEEK

The #ImproCiencia dissemination event, arranged by the CIBER in the framework of the Madrid Science Week 2015, took place on 3rd November at the Nave 73 rooms in Madrid. The event combined science and theatre improvisation to give a light-hearted explanation of the biomedical research done by the CIBER in its eight thematic areas.

Games and improvisations were alternated with live connections with CIBER researchers during the event. Ferran Barbé, the Scientific Director from CIBERES, attended to present one of the research projects of the CIBERES on sleep apnoeas.

Scientific Production

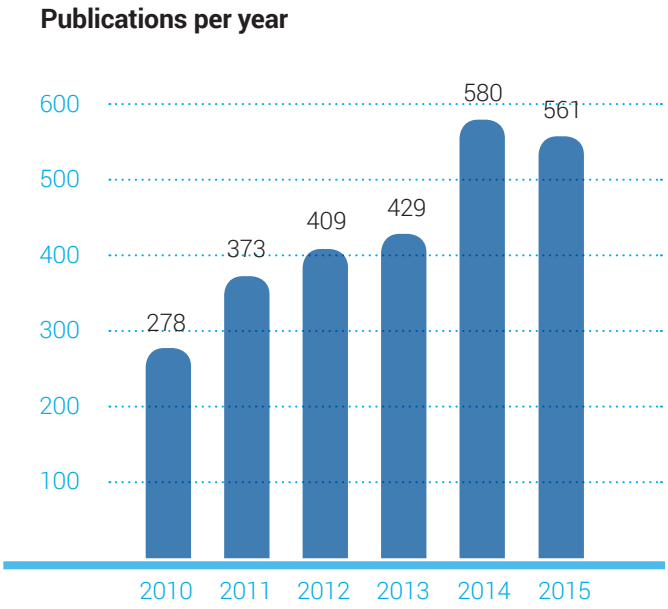
The graphic evolution of CIBERES publications can be seen from the following graphs in which the data from 2010 to 2015 is analysed

The publications are also detailed by group for this year, as well as the interCIBER and intraCIBER co-operation.

Publications:

Nº of affiliated publications 2015	
Total publications	**561**
First quartile	303
First decile	143

EVOLUTION OF CIBERES PUBLICATIONS 2010-2015



MOST RELEVANT CIBERES PUBLICATIONS IN 2015 BY IMPACT FACTOR

Publication	Impact Factor
LANGE P., CELLI B., AGUSTI A., JENSEN G.B., DIVO M., FANER R. ET AL. Lung-function trajectories leading to chronic obstructive pulmonary disease. New England Journal of Medicine. 2015; 373 (2):111-122.	55,8730
GALIE N., BARBERA J.A., FROST A.E., GHOFRANI H.-A., HOEPER M.M., MCLAUGHLIN V.V. ET AL. Initial use of ambrisentan plus tadalafil in pulmonary arterial hypertension. New England Journal of Medicine. 2015; 373 (9):834-844.	55,8730
WOODRUFF P.G., AGUSTI A., ROCHE N., SINGH D., MARTINEZ F.J. Current concepts in targeting chronic obstructive pulmonary disease pharmacotherapy: Making progress towards personalised management. The Lancet. 2015; 385(9979):1789-1798.	45,2170
PRINA E., RANZANI O.T., TORRES A. Community-acquired pneumonia. The Lancet. 2015; 386(9998):1097-1108.	45,2170

Publication	Impact Factor
MARTINEZ FJ, CALVERLEY PM, GOEHRING UM, BROSE M, FABBRI LM, RABE KF ET AL. Effect of roflumilast on exacerbations in patients with severe chronic obstructive pulmonary disease uncontrolled by combination therapy (REACT): a multicentre randomised controlled trial.Lancet. 2015.	45,2170
HOLGATE S., AGUSTI A., STRIETER R.M., ANDERSON G.P., FOGEL R., BEL E. ET AL. Drug development for airway diseases: Looking forward. Nature Reviews Drug Discovery. 2015; 14(6):367-368.	41,9080
CASARES L, VINCENT R, ZALVIDEA D, CAMPILLO N, NAVAJAS D, ARROYO M ET AL. Hydraulic fracture during epithelial stretching.Nature materials. 2015; 14(3).	36,5030
TORRES A., SIBILA O., FERRER M., POLVERINO E., MENENDEZ R., MENSA J. ET AL. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: A randomized clinical trial. JAMA - Journal of the American Medical Association. 2015; 313(7):677-686.	35,2890
SANCHEZ-DE-LA-TORRE M., KHALYFA A., SANCHEZ-DE-LA-TORRE A., MARTINEZ-ALONSO M., MARTINEZ-GARCIA M.A., BARCELO A. ET AL. Precision Medicine in Patients With Resistant Hypertension and Obstructive Sleep Apnea Blood Pressure Response to Continuous Positive Airway Pressure Treatment. Journal of the American College of Cardiology. 2015; 66(9):1023-1032.	16,5030
CILLONIZ C., ALBERT R.K., LIAPIKOU A., GABARRUS A., RANGEL E., BELLO S. ET AL. The effect of macrolide resistance on the presentation and outcome of patients hospitalized for streptococcus pneumoniae pneumonia. American Journal of Respiratory and Critical Care Medicine. 2015; 191(11):1265-1272.	12,9960

PUBLICATIONS PER GROUP 2015

Group	Nombre IP	Total	Q1	D1
1	C. Casals	2	2	0
2	E. García	13	11	6
4	N. González	14	6	3
5	C. Picado	21	7	6
6	J.A. Barberá	41	22	13
7	V. Pozo	17	6	5
8	V. Regueiro	9	8	1
9	C. Martín	11	9	4
10	A. Agustí	55	33	27
11	J.M. Monserrat	19	12	7
12	D. Navajas	29	20	12
13	E. Morcillo	7	2	1
14	A. Torres	49	25	13
15	J.F. Masa	15	9	4
16	X. Muñoz	62	20	10
17	V. Ausina	19	8	3
18	J. Rello	37	25	8
19	F. Liñares	25	18	7
21	C. Álvarez	24	15	4
22	J. Gea	36	19	12
23	A. Esteban	14	9	2
24	A. Obeso	5	1	1
26	E. Pérez Trallero	4	4	1
27	E. Bouza	44	29	15

28	F. Pérez Vizcaino	5	5	2
29	J. Villar	29	24	10
30	E. Monsó	24	9	5
31	J Ruiz Cabello	9	7	2
32	J. Ortín	13	7	2
33	L. Blanch	34	15	2
34	M. Menéndez	6	6	2
35	F. Barbé	27	13	12

COOPERATION:

No. of intraCIBER publications 2015: **161**

No. of interCIBER publications 2015: **87**

Patents:

APPLIED FOR:

System for integrating the filtrate/concentration and detection of biological samples by immunological methods on porous surfaces. Dr. Noemí Parrega (Dr. Monsó's group). (CSIC 75% /IGTP 17.5% /CIBER 6% / UAB 2.5%). Integrated filter holder in which mechanical filtration of the samples is carried out to concentrate the biological material on the filtration membrane and a culture is made in order to perform microbiological detection by methods based on biomolecule affinity, keeping its watertightness during concentration and detection.

PATENTS EXTENDED TO PCT IN 2015:

- "Method for predicting response to continuous positive air pressure treatment" Dr. Manuel Sánchez de la Torre (Group Dr. Barbé) (IRB Lleida 53,85%/ CIBER 38,46%/ Fundación Hospital la Fe 7,69%).
- "Micellar nanoparticles containing antitumoralglycosides" . DR. Hugo Groult (Group Dr. Ruiz-Cabello) CNIC 67%/ CIBER 33%.
- "Methods and systems for providing oxygen to a patient". Dra. Molina y Dr. Rossell (Groups Dr. Picado Y Dr. Monsó). IDIBELL57,5%/ UAB 37,5%/ CIBERES 5%.
- "Bimodal fluorophore-labeled liposomes and associated methods and systems". Dr. Carlos Pérez –Medina (Group Dr. Ruiz-Cabello) MSKCC (50%), Mount Sinai (35%), and CIBER 7.5%/ CNIC (7.5%).

Guías clínicas:

- ESCMID guideline for the diagnosis and treatment of biofilm infections 2014.
- A clinical clasification of the acute respiratory distress syndrome for predicting outcome and guiding medical therapy.
- Nebulized Antibiotic Treatment of Respiratory Infections in Critically Ill Mechanically Ventilated Patients.
- Clinical Practice Guide of the Study Group in Mycobacteria Infections (GEIM) of the Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC).
- Consensus statement from the 2014 International Microdialysis Forum.
- Spanish consensus on the prevention and treatment of Pseudomonas aeruginosa bronchial infections in cystic fibrosis patients.
- SEPAR protocol for control and follow-up of home respiratory therapies. Syndrome of sleep apnoea-hypopnea.
- MACVIA-ARIA sentinel Network for Allergic Rhinitis, MASK-Rhinitis. The new generation guideline implementation.
- Member of the GOLD Board of Directors.
- SEPAR regulation on muscular dysfunction of patients with chronic obstructive pulmonary disease.

3

Scientific Programmes

Asthma

COORDINATOR: DR. Mª VICTORIA DEL POZO

The Corporate Research Programme (PCI) for asthma has got under way a study of cohorts of asthmatic patients in Spain (Project MEGA) which will enable more effective research into this disease. Asthma affects three million people in Spain and constitutes a worldwide health problem.

The MEGA project combines research groups with extensive experience in asthma, allergy, genetics, genomics, proteomics and immunology. This cooperation contributes the work done by a critical mass of researchers who are applying their knowledge for better understanding of the molecular mechanisms involved in the start and progression of a chronic inflammatory disease such as asthma. To this end researchers in the project have designed a database and established a common methodology for collecting biological samples. This database of the Asthma PCI, in which seven nationwide hospital centres are currently taking part, is already set up and data of over 100 patients have been included in the six months for which it has been operating.

This includes demographic data, clinical data, data on control of the disease, use of medication or of family background, as well as the results of the analytical tests carried out on those affected. It is intended to carry out follow-up of the patients for at least the four years for which the study lasts, although our intention is for those affected, and thus the evolution of their disease, to go on being studied for longer than that.

Thanks to the cooperation of the seven groups from different hospitals, resources can be optimised, thus shortening the time taken to transfer the results to healthcare practice, This will ultimately enable an improvement in the health of asthmatic patients and increase their quality of life and well-being.

Accomplishments	Impact
Identification and characterisation of phenotypic markers of asthma.	Better diagnosis, treatment of patients and possible personalised treatments.
Becoming a worldwide leader in research into occupational asthma: study of epidemiological, immunological aspects and prevalence of occupational asthma.	These studies have enabled learning about the mechanism and prevalence of occupational pathology in the Spanish population, which has enabled better diagnosis and treatment of affected patients.
Study on sputum induction applied to respiratory diseases.	Incorporation as a clinical trial in different hospitals.

Lung Cancer

COORDINATOR: DR. EDUARD MONSÓ

The 2013-2015 Strategic Project of the Corporate Research Programme (PCI) on Lung Cancer (LC) involved the creation of three cohorts, two of these with initial LC identified by the health system and a third cohort for screening individuals with a risk of LC. In 2015 the follow-up was completed three years after the first initial LC cohort, thus creating a repository of 253 paraffin-embedded samples of lung cancer in stages I-IIp at the CIBERES Pulmonary Biobank Consortium. These samples have been analysed by a panel of Pathologists, which has selected 233 samples for molecular analysis. Tissue Microarrays (TMAs) were prepared with these samples and nucleic acids were extracted. The analysis of their biological markers is currently being carried out. The inclusion of patients in the second cohort of initial LC is active and covers clinical information, tumoural tissue, non-tumoural tissue and fresh blood, at the 9 centres taking part. The third screening cohort was started in 2014 and has already included 200 individuals, operating on the patients with pulmonary nodules compatible with LC.

The first joint publication of the PCI for lung cancer in which the methodology of the strategic project is described was published in 2015 (Eduard Monsó, Luis M. Montuenga, Julio Sánchez de Cos, Cristina Villena and by the Lung Cancer Cooperative Group CIBERES-RTICC-SEPAR-Pulmonary Biobank Consortium. Biological Marker Analysis as Part of The CIBERES-RTIC Cancer-SEPAR Strategic Project on Lung Cancer. Arch Bronconeumol. 2015 Sep;51 (9):462-7). This will be followed in 2016 by those that are generated from the analysis of molecular markers which are currently being carried out on patients in the first cohort, with the aim of identifying survival markers three years from diagnosis. The analysis of the second initial cancer cohort will be started in the second half of 2016, and those of the screening cohort in 2017, a period in which it is estimated that the number of cases operated on will be enough to obtain clinically significant results.

Chronic Obstructive Pulmonary Disease (COPD)

COORDINATOR: DR. BORJA GARCÍA-COSÍO

ACCOMPLISHMENTS IN 2015:

1. Activity of the disease and care in fragile patients. We have generated the DELICATO cohort of patients with advanced COPD and performed a clinical audit of 1440 cases in 40 Spanish hospitals 530 of these patients are included in the BIOME- POC-CIBERES biomarkers cohort.

2. Markers of activity in COPD. Everything is ready to carry out the determinations on human and animal samples, after having obtained the biological samples from different studies, cohorts of fragile COPD (BIOMCOPD), of early starting COPD (Early-COPD) and from the animal models performed.

   In the microbiological sphere we have defined the markers associated with COPD after completing a systematic analysis of the respiratory microbiome existing in two cohorts of COPD in a stable situation and undergoing exacerbation and we have identified the interferences existing between the bacterial pathogeny and the therapeutic response during infection. We have described the structure of the bacterial and viral microbiomes present in the stable and exacerbation situations, in the presence or absence of P. Aeruginosa and finally we have identified the phenotypes of NT Haemophilus influenzae and its relations with pathogenicity in COPD.

3. Potential markers of activity in animal models of fragile and early-starting COPD. We concluded the experiments for characterising a murine model of early starting COPD by controlled exposure to tobacco smoke and at the present time the data collected on morphometry, image, function, transcriptomics and proteomics is being processed. As regards the fragile COPD model, we have developed severe pulmonary hypertension in the murine model of hypoxia and SU5416. We have also shown that the models of acute hypoxia and/or hypercapnia in rats develop lesions and signs of regeneration of the respiratory muscles and of the extremities and that the model of right-sided heart failure is associated with oxidative muscular stress.

   The therapeutic trials were completed with guanylate cyclase stimulators in a model of exposure to tobacco in guinea pigs, as well as LGF treatment in a previously established murine model of emphysema.

   We have prepared a protocol for functionalisation of nanoparticles for dual application, PET and magnetic resonance (Patent WO2014006254 A1), of potential application in the diagnosis and treatment of COPD.

4. Characterisation and determinants of activity in COPD. We completed the design of the Early-COPD cohort and the recruitment started in January 2015, with the participation of pneumologists and primary healthcare doctors. Until now 140 cases have been recruited. We have closed a cooperation agreement with the scientific committee of the PESA study to include new variables facilitating the study of the start of COPD. The PESA study is carried out by the CNIC on a cohort of over 3500 employees of the Banco Santander to study the evolution of factors of cardiovascular risk.

Pulmonary Fibrosis

COORDINATOR: DR. MARÍA MOLINA

In 2015 the Pulmonary Fibrosis Programme completed the corporate research programme entitled "Cell plasticity and microenvironment in lung fibrosis: looking for its regulation as a potential treatment". The most significant achievements involved were:

17 "PEER REVIEWED" PUBLICATIONS GENERATED, HIGHLIGHTING THE FOLLOWING:

- V. Vicens et al. Resp. Research. Fibroblasts viability and phenotype changes into glycated stiffened three dimensional collagen matrices. 2015;16:82, which establishes a new model of three-dimensional in vitro pro-fibrotic culture which comes closer to human tissue complexity in the study of pulmonary fibrosis.
- Milara J, et al. Roflumilast prevents the metabolic effects of bleomycin-induced fibrosis in a murin model. PLoS One. 2015;10:e0133453, where the preventive effects of pulmonary damage achieved with roflumilast are determined.
- Bonella F, et al. European IPF Patient Charter: unmet needs and a call to action for healthcare policymakers. Eur Respir J. ERJ-01204-2015. In press, which stipulates minimum healthcare, therapeutic and research levels to be obtained in IPF in the European framework of Rare Diseases.

TRANSFER AND INNOVATION:

a) Utility model (V. Vicens et al),

b) Patent applied for: PCT application number PCT/EP2015/050325.

CIBERES-IDIBELL+CIBERBBN-UAB.

c) Work in cooperation with biotech company Advanced Medical Project (AMP, Antonio Molina) for transfer, through which outside financing has been obtained to carry out part of the studies included in the corporate project and in future proposals (2016-2018).

STRENGTHENING INTERCIBER RELATIONS: CIBERES-CIBERER-CIBERBBN. As a result of this the 2nd CIBERES-CIBERER Workshop was held on Telomeric Regulation in IPF. Hospitalet de Llobregat (Barcelona), 4th December 2015.

INTERNATIONALISATION: application for Starting Grant from CIBERES, ERC 2015-2016, participation in the strategic international forum on rare diseases for IPF (Bonella F, et al), along with the IPF relatives and patients' association (AFEFPI).

IPF COHORT: telomere shortening and its regulation. In December 2015 financing was obtained for development of the IPF cohort, collecting samples to be biobanked at the CIBERES Biobank Platform. This is the first cohort of these characteristics for this rare respiratory disease nationwide and one of the few held abroad.

Pulmonary Hypertension

COORDINATOR: DR. ALBERT BARBERÀ

Experimental in vitro and in vivo models of the disease have been prepared. For the in vitro models culture of endothelial cells of patients with pulmonary hypertension have been used, obtained both from pulmonary arteries and from peripheral blood. Endothelial cell lines were also obtained from the pulmonary arteries in pulmonary endarterectomy surgery in patients with chronic thromboembolic pulmonary hypertension (CTEPH). These cell lines are available for studies of response to drugs and have been used in studies intended to evaluate the antiproliferative potential of certain drugs.

Experimental in vivo models were prepared. At the present time there are experimental models of pulmonary arterial hypertension (PAH) (monocrotaline in rats, SU5416 and hypoxia in rats and mice), CTEPH (injection of microspheres in suckling piglets) and of pulmonary hypertension associated with respiratory diseases (exposure to tobacco and hypoxia in guinea pigs, bleomycin in rats). These experimental models are being used in different studies in the Programme.

The Spanish Pulmonary Hypertension Biobank has been got under way. It already has samples of 250 patients with PAH or CTEPH stored in this. This Biobank has entered into a cooperation agreement with the Registro Español de Pulmonary Hypertension (REHAP) for those biological samples to be linked with the clinical information available in said register. This relationship between a biological repository and a nationwide registry, something unique in the field of pulmonary hypertension, gives great value to this collection with a view to its use in different projects.

Cooperation with the CIBERES pulmonary biobank platform has also been arranged to promote the collection of lung explants from patients with pulmonary hypertension who have been given a lung transplant. 20 cases have already been included. This collection is also of great value as it provides researchers with lung tissue of patients with advanced pulmonary hypertension.

The Programme takes part in the REHAP national registry and in HPTEC international registry, which in 2015 made known the long-term evolution of patients with CTEPH and the favourable impact of pulmonary endarterecomy surgery for survival (Circulation 2016 pii:115.016522. Int J Cardiol 2016;203:938-44). We took part in an international multi-centre study intended to evaluate a new strategy for treatment in HAP, based on the use of treatment combined with two drugs from the beginning (N Engl J Med 2015;373:834-844), proving that this strategy improves the long-term clinical results is modifying the therapeutic approach to said patients.

Different studies within the Programme have been given financing from the State Plan for Scientific and Technical Research and Innovation; the Strategic Health Plan of the ISCiii; the State R+D+i Programme Oriented towards Society's Challenges and from the Marie Sklodowska-Curie Innovative Training Networks actions, EU Programme H2020.

CIBERES has set up a cooperation agreement with the Fundación Contra la Pulmonary Hypertension for fostering research into this disease in Spain.

Acute Lung Injury

COORDINATOR: **DR. ANDRÉS ESTEBAN**

The following should be mentioned among this year's major achievements of the Corporate Research Programme (PCI) for Acute Lung Injury:

We have considerably improved knowledge of the epidemiology of both mechanical ventilation in general and of patients with ARDS. Two of the groups in the PCI thus continue to exploit the two prospectively collected databases existing in this respect in the world.

From the progression point in the diagnosis of ARDS, a phenotype associated with the presence of ARDS with Diffuse Alveolar Damage as opposed to the ones which have another alteration such as pneumonia has been described for the first time. Since we have a huge base of tissues from 700 clinical autopsies, we have been able to use the gold standard of histological findings and thus be able to establish the different groups of ARDS.

We have also carried out functional studies using luciferase in vitro and EMSA in the characterisation of polymorphisms and its association with vulnerability to developing ARDS in three candidate genes: PI3 (peptidase inhibitor 3), S1PR3 (sphingosine 1- phosphate receptor 3) and GADD45a (growth arrest DNA damage inducible alpha). At the same time, we have found the presence of microRNA 27a associated with the presence of ARDS with hyaline membranes. Lastly, we have studied the presence of proteins in the alveolar cell attachment as a marker of the increase in permeability and thus of Acute Lung injury, as well as the measurement of Tryptase as a marker of the development of pulmonary fibrosis induced by acute lung injury induced by sepsis. To this end we have included 500 patients with severe sepsis and ALI/ARDS admitted to the Intensive Care Units of 20 Spanish hospitals. We are now analysing this valuable database.

We have developed an important model by means of intravital microscopy imaging, to monitor the migration in the vessels and, through these, of previously marked monocytes. The model used was that of haemorrhage and reperfusion in mice in order to have a situation of transfusion-related acute lung injury (TRALI). At the same time, we have worked on acquiring images of lungs using PET and TAC, particularly for evaluating pulmonary oedema.

After developing the programme for monitoring asynchronies between the ventilator and the patient we proceeded to quantify and associate these with the most important outcomes, such as duration of the mechanical ventilation, failure of disconnection and mortality.

In the area of cell signals and therapeutic targets we analysed the cell activation of DAMP and the potential therapeutic benefits, as well as the possibility of acid sphingomyelin derived from ceramide in order to induce the production of inflammatory mediators and pulmonary vascular dysfunction.

In the area of tissue repair we have managed to develop an animal model in the mouse, in which we analysed the local response after intratracheal installation of stem cells in a decellularised lung scaffold and we verified the effect in hypoxia and hyperoxia conditions of the lung. We also analysed the resulting differentiation with different mechanical stimuli.

Pneumonia

COORDINATOR: DR. ANTONI TORRES

PUBLICATIONS

- Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: a randomized clinical trial. Torres A, Sibila O, Ferrer M, Polverino E, Menendez R, Mensa J, Gabarrús A, Sellarés J, Restrepo MI, Anzueto A, Niederman MS, Agustí C. JAMA. 2015 Feb 17;313(7):677-86
- Genome-wide association study of survival from sepsis due to pneumonia: an observational cohort study. Rautanen A, Mills TC, Gordon AC, Hutton P, Steffens M, Nuamah R, Chiche JD, Parks T, Chapman SJ, Davenport EE, Elliott KS, Bion J, Lichtner P, Meitinger T, Wienker TF, Caulfield MJ, Mein C, Bloos F, Bobek I, Cotogni P, Sramek V, Sarapuu S, Kobilay M, Ranieri VM, Rello J, Sirgo G, Weiss YG, Russwurm S, Schneider EM, Reinhart K, Holloway PA, Knight JC, Garrard CS, Russell JA, Walley KR, Stüber F, Hill AV, Hinds CJ; ESICM/ECCRN GenOSept Investigators. Lancet Respir Med. 2015 Jan;3(1):53-60.
- Ercibengoa M, Bell M, Marimón JM, Humrighouse B, Klenk HP, Schumann P, Pérez -Trallero E. Nocardia donostiensis sp. nov. , isolated from human respiratory specimens. Antonie Van Leeuwenhoek 2016 (aceptado para publicación).

STUDIES

- The VAP Gravity-Trial was completed with the inclusion of 400 patients. This study aims to reduce the incidence of pneumonia acquired during mechanical ventilation.
- The enrolment of patients in the NEUMONAC study was completed with the inclusion of 1900 patients from a multi-centre study which set out to learn about the pneumococcal disease in Spain, risk factors, serotypes and prognosis.

PROJECTS

- Co-leader de Combatting Bacterial Resistance in Europe - Molecules Against Gram Negative Infections. (COMBACTE-MAGNET). CE_IMI-13_11th_2stg
- European project I-MOVE+, H2020. Case study and negative control for assessment of the effectiveness of the anti-influenza vaccination as opposed to hospitalisation in cases of severe acute respiratory infection (SARI) confirmed of influenza, in persons over 64 years of age in Spain. Dr. Gustavo Cilla. Servicio de Microbiología Clínica, Hospital Donostia, San Sebastián, Spain. CIBERES 26. Grant Agreement: 634446.

THESIS:

- Pneumonia in the Intensive Care Unit associated or not with mechanical ventilation: characteristics and factors of hospital mortality. Doctorand: Carmen Alicia San José Arribas. Directors: Dr. Antoni Torres Martí, Dr. Miquel Ferrer, Universidad de Valladolid. Mark: Outstanding, April 2015.
- Assessment of non-pharmacological strategies for preventing nosocomial respiratory infections in a porcine model of mechanical ventilation. Doctorand: Néstor Alejandro Luque Chipana. Directors: Dr. Antoni Torres Martí, Dr. Miquel Ferrer. Facultad de Medicina.
- U. Barcelona.
- Systemic Inflammatory response in pneumonia acquired in the community. Clinical relevance and prognostic impact. Doctorand: Raquel Martínez Tomás. Directors: Antoni Torres Martí and Rosario Menéndez. Facultad de Medicina de Barcelona.
- J. Riera, based on different articles, particularly: Ventilator-associated respiratory infection following lung transplantation. Riera J, Caralt B, López I, Augustin S, Roman A, Gavalda J, Rello J; Vall d'Hebron Lung Transplant Study Group. Eur Respir J. 2015 Mar;45(3):726-37.
- Carmen Puig (June, 2015; Mención internacional) "Non-typeable Haemophilus influen- zae: colonization, infection and biofilm formation". Universitat de Barcelona. Biomedicine Doctorate Programme. Directors: Carmen Ardanuy and Sara Martí.

Host-Pathogen Interactions

COORDINATOR: DR. JUNKAL GARMENDIA

In 2015 our work focussed on analysing the molecular mechanisms used by a panel of respiratory pathogens of great healthcare relevance for manipulating host functions in their own benefit and evading the immune system. This information has enabled identifying host-pathogen interactions, as well as designing and evaluating new antimicrobial agents. To sum up:

1. In the fight against multi-resistant bacteria we proved the in vitro and in vivo bactericide effectiveness of auranofin (a drug against rheumatoid arthritis), dendrimers of esters of bicyclic amines and new chimeric endolysins based on endolysins of Streptococcus pneumoniae phages (G2 and 34).
2. We assessed a panel of strains of Staphylococcus aureus isolated from patients subject to mechanic ventilation in an alveolar macrophage model of infection, displaying differences in the intracellular dynamics of the infection, and established systems for detection of virulence factors of S. aureus in clinical samples and of evaluation of the intracellular activity of drugs encapsulated in nanoparticles (G17).
3. We determined the synergic microbicide action of proteins SP-BN and SP-A, present in the alveolar fluid, against Klebsiella pneumoniae (Kpn), and showed that its therapeutic administration reduces infection and boosts immune response against Kpn. We determined the immune-modulator role of SP-A in classic and alternative activation of alveolar macrophages (G1).
4. We characterised the PhoP- WhiB6 transcriptional network in the context of the expression and secretion of ESAT-6 in M. tuberculosis, identified a new non-coding antisense RNA to gene ideR, and optimised a system for quantifying c-di-AMP in M. tuberculosis, which shows a greater production of c-di-AMP associated with phoP (G9) mutation.
5. We determined the immune-modulation effect of anionic phospholipids on alveolar macrophages and pneumocytes in the presence of bacterial lipopolysaccharide, syncytial respiratory virus or Haemophilus influenzae (Hi) (G1, 19, 32).
6. We developed design microarrays for the study of receptors on the surface of live bacteria used in the characterisation of Hi glycosylation profiles and their recognition by lectins of the immune system (G19 and 34).
7. We characterised that a small amount of large deletions of the segments of the viral genoma in the influenza virus virions constitutes a factor of pathogenicity for the human population (G32).
8. We determined the atomic structure of protein F of the human metapneumovirus in its post-fusion conformation, displaying a high degree of homology with protein F of the human syncytial respiratory virus. In view of the cross-reactivity between both proteins, we obtained chimerical proteins to induce an immune response against the two virus (G32).
9. We provided the first evidence of Hi adaptation in vivo, defining for Hi an intracellular niche in the human respiratory epithelium and a panel of strategies of cell subversion used by the bacteria to access this niche; we displayed the antimicrobial potential of pharmacological interference of eukaryotic targets and took part in the first study to define the effect of glucocorticoids in the Hi transcriptome during lung infection (G19).

Sleep Apnoeas Syndrome

COORDINATOR: DR. JOSEP Mª MONTSERRAT

There have been two basic objectives of the programme in 2015:

1. Study and impact of the obstructive sleep apnoea syndrome (OSA) in special and little-studied populations (ischaemic cardiopathy, elderly subjects, obesity hypoventilation and cancer) to personalise the handling and treatment in these groups, which represent a public health, social and even economic problem. All of this has been done on a translational basis.
2. Technological studies with the aim of optimising the treatment and follow-up of the patients.

The most transcendent results with greatest impact are the following.

1. OSA and cardiovascular pathology. a) Development of an international patent to predictively detect which patients with OSA and resistant hypertension are going to respond positively to CPAP, reducing their blood pressure. b) Multi-centre study on OSA and acute coronary pathology. This is a seminal study with lengthy development as regards patients and duration. c) Basic studies in murine models confirming the role of hypoxia in vascular lesion and remodelling.
2. OSA and elderly patients. Original works have been carried out on murine and clinical models which prove that in elderly subjects the presence of OSA with a high apnoea index gives rise to the manifestation of anatomical-pathological cerebral symptoms and anomalies. This is a highly relevant study due to the growing demographic problem in which a large percentage of the European population will be senescent in the near future.
3. Cancer and OSA. A totally seminal work has been performed relating cancer and OSA. The results of clinical studies and on animal models confirm their interaction, generating a major impact on the international scientific community.
4. Obesity, as a currently transcendent problem and its relationship with OSA and hyper-ventilation. The clinical and basic data enable clearing up and personalising the need for treatment in these groups of patients.

As regards the technological aspects, the most important contributions involve:

1. New simplified diagnostic methodologies at the patient's home.
2. Creation of networks between the different care levels to deal with patients with the aim of tackling treatment of a complex, chronic and frequently-found illness, such as OSA.
3. Development of TIC platforms for follow-up of patients. All these contributions are carried out with the main aim of performing comprehensive cost-effective measures and for transfer to the healthcare system.

Finally, specific mechanisms have been analysed in the programme to describe the relationship between OSA and associated pathology by means of: parabiotic models, analysis of exhaled gases, immunological aspects of OSA, perinatal hyperoxia and postnatal damage, relationship between OSA, ventilation, hypoxia biomarkers, and the relationship in animal models of hypoxia and pulmonary hypertension and their improvement with drugs. Other contributions have been the creation of a spinoff, cooperation with companies and several national protocols and clinical guides.

Tuberculosis

COORDINATOR: DR. VICENÇ AUSINA

In the context of study of immunity in tuberculosis (TB) and the development of new antiTB vaccinations, we have joined two Consortiums financed by the EU (H2020) in cooperation with forty universities and research centres. This activity means the consolidation of a translational line of research enabling demonstrating in humans the findings obtained in basic science and which has a great internationalisation component (participation in the Africa-Europe Host-Directed Therapies International Consortium) and innovation (Contract with Manremyc SL; Archivel Technologies SL.; Fundació IrsiCaixa; Fundació Idibell-Bellvitge).

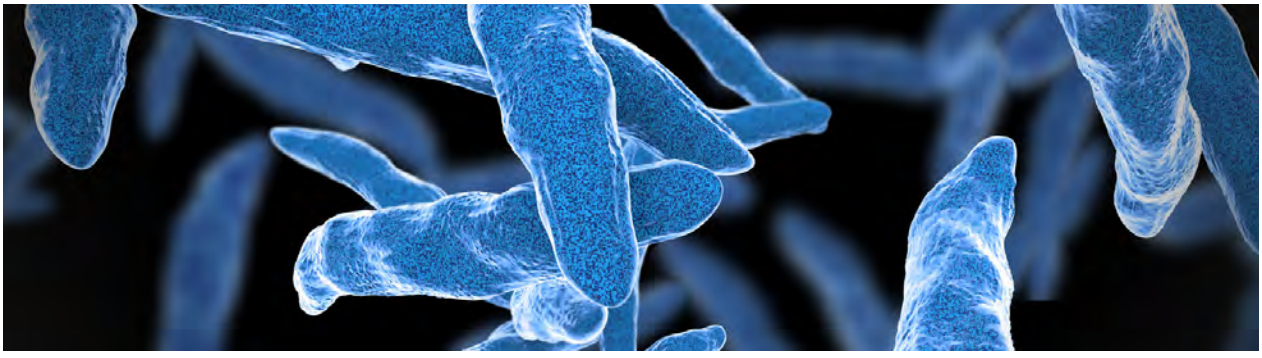
The results of safety and immunogenicity obtained in the first clinical test in healthy adults in Lausanne (Switzerland) have been published. The reliability of this data supports progress in the clinical development of the MTBVAC application in tuberculosis-endemic countries with a high incidence of disease. In this respect Phase 1b of the MTBVAC safety and immunogenicity assay on new-born babies in South Africa has been approved.

Progress has been made in the characterisation of the impact of eflux pumps in the intrinsic resistance to new candidates for antiTB drugs in development identified by our European contributors after phenotypic screenings. The study of the metabolism of nucleic acids and control of oxidative stress has been started as new targets for anti-tuberculosis agents. Some combinations of drugs maintaining their activity against M. tuberculosis (MTB) when encapsulated in nanoparticles of different kinds have been identified.

An analysis has been made of the strains of MTB with greatest prevalence and/or active transmission in Aragon, characterising the appearance of genomic changes due to evolutionary processes. New strategies for surveillance of the transmission of MTB risk strains, based on allele-specific PCRs directed at specific strain SNPs have been developed. Approximations of complete genome sequencing have been applied to analyse the clonal complexity which MTB infection can acquire both between patients and throughout transmission chains.

We have started the development of new methods based on nanoparticles for detecting MTB in clinical samples. A metabolomic pattern in urine has been identified which differentiates patients with tuberculosis from healthy individuals or ones with other breathing infections. The characteristics of tuberculosis in paediatric age caused both by MTB and by other non-tuberculosis mycobacteria have been studied, identifying glycopeptidolipids which enable differentiating between both. We have finally identified new MTB latency antigens which enable characterising the specific immune response of infected individuals and the sick.

New molecular platforms for detecting resistances to anti-tuberculosis drugs have been developed, optimised and assessed. The detection of resistances and identification of lineages with phylogenetic ends have been got under way by means of massive sequencing technologies.



4

Transversal Programmes

Training Programme

COORDINATOR: DR. ANA OBESO

The main objectives of the teaching programme continued to be:

- To promote the acquisition of clinical-basic intergrade knowledge by CIBERES researchers, so as to facilitate a translational approach to scientific objectives.
- To foster interest for research in respiratory diseases among young people in their training stage in the field of Biomedicine, so that they can form part of CIBERES research teams, attracting the ones with greatest talent.
- To facilitate interaction and mobility of personnel among CIBERES groups in order to improve their technical skills and scientific capacity.

In 2015 the activity was focussed on two programmes:

Programme for training research personnel

GRANTS FOR INITIATION TO RESEARCH

This programme was a considerable success at the CIBERES, both through the interest of the call and because of the results obtained. The grants are intended to act as assistance for young researchers to start their training for one year, by joining a research project financed by official bodies, at one of the research groups forming part of the CIBERES.

The intention is that during this year the beneficiaries should be able to gain access to an official research personnel training programme (-Spanish "FPI"), staying in the CIBERES group. The grants are 66% co-financed by the training and teaching programme of the CIBERES and 33% by the actual receiving group.

As in previous years, in accordance with the budget possibilities, five contracts for grants were implemented in 2015, awarded in late 2014.

Improvement and mobility group

Three lines of action were implemented in 2015:

- Co-financing of enrolment dues (generally 3rd university cycle courses). Modules of up to 500 euros per module.
- Travel pools for attending training courses or activities away from the place of residence. Modules of up to 500 euros per module.
- Co-financing of stays in another city for learning techniques. Modules of up to 1200 euros.

In 2015 ten applications were financed in this line of action.

Programme for fostering interest in respiratory research

TRAINING EVENTS FOR RESEARCH PERSONNEL

On 15th and 16th October 2015 the 8th Training Event was held in Valladolid, at the Palacio de Congresos Conde Ansúrez.

The CIBERES Training Events set out to make known the research lines, the research work done and the available resources of the different CIBERES groups, as well as to foster interrelations between younger researchers, attempting to establish bonds and interactions between clinical and basic researchers. As a novelty at this 2015 edition some new ideas were brought in about preparing proposals for European projects from an interdisciplinary and cooperative standpoint with CIBERBBN and CIBERER.

42 junior CIBERES researchers took part and there was also a major presence of senior researchers.

3 awards for the best oral communications and a special "Dr. Constancio González" award for the oral communication getting most votes were granted.

Internationalisation Programme

COORDINATOR: DR. CRISTINA RODRÍGUEZ

Last 11th May 2015 the CIBER programme for supporting internationalisation was set up, as a joint initiative of the areas of Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Rare Diseases (CIBERER) and Respiratory Diseases (CIBERES), of the Centro de Investigación Biomédica en Red (CIBER). Its purpose is to reinforce and coordinate endeavours intended to promote its researchers' participation in European programmes and to create a common structure for encouraging internationalisation and leadership of research and innovation in these three thematic areas.

Over these first six months of its action the platform has focussed its work on establishing a relationship of trust with the research groups. This started by holding bilateral interviews with the groups and the area leaders to get first-hand information on the research done and the internationalisation potential of the CIBER groups. The platform has also created profiles of specific area capacities so as to have a simple and comprehensive document acting as an introductory letter for the research done at the CIBER. This could be used at the different events for seeking partners. Likewise, the CIBER register of different tools for seeking existing partners has been completed (Cordis, IMI…).

As regards improving CIBER's international visibility, the CIBER has worked hard by attending over sixteen events (including conferences, infodays and partner-seeking events). One of the greatest accomplishments in this field was CIBER's invitation by CDTI to form part of the CDTI-SOST Manager Specialisation Course (CDTI, Brussels, BE). This course is intended to boost the international presence of invited organisations by substantially improving their international network of contacts and knowledge on H2020 programmes. The platform also placed special stress on establishing smooth relations with the different national representatives, national points of contact by means of specific meetings, acting as a point of encounter on an institutional level.

The platform has also given awareness-raising talks on the relevance of internationalisation as part of the area conferences. The success of these events can be seen in the form of a significant increase in the number of enquiries from researchers: (twenty specific enquiries, six requests for support for presentation, six requests for partnering, and six requests for valuing research proposals). This means the platform is already seen as an effective tool for aid and a reference point for settling doubts involving international programmes.

In the field of backing for submission of proposals, the platform has drawn up specific material providing support for writing and managing proposals. This year a practical drafting guide has been drafted, entitled "How to write a European Proposal" as well as a practical guide for management and the "Quick guide for third parties" in order to provide researchers with understandable and reliable consultation material. As part of the support material the platform has also drawn up models and specific templates for managing and applying for H2020 proposals. These include the budget calculator, models of hour sheets, letters for acceptance of participation in proposals, support letters, CIBER profile for European proposals as a partner and as third party and different forms for compiling all the data required for submitting a proposal. This material is intended to facilitate the process of submitting proposals for all our researchers. Thanks to this, in these six months of 2015 the CIBER has submitted four new proposals (three of these coordinated) while expressions of interest for the submission of ten new proposals have been received. In this area it should also be stressed that CIBER has received five new contacts from research groups or companies with the aim of reaching agreements for joint submission of proposals in the H2020 framework. For the time being two of these contacts have materialised in actual presentation of two H2020 proposals.

5

Platforms

Pulmonary Biobank Consortium

PBP SCIENTIFIC DIRECTOR: DR. GERMÁN PECES-BARBA · COORDINATOR: DR. CRISTINA VILLENA

Most relevant accomplishments in 2015

The certification of the Pulmonary Biobank Consortium (PBP) Quality Management System to ISO 9001:2008 standard was renewed for the 2015-2018 period. The Hospital Universitario Vall d'Hebron (HVH) joined after passing the first internal audit.

Samples of lung explants were also collected at the HVH. In 2015 27 new explants were collected (19 at the Hospital Universitario Doce de Octubre and 8 at the HVH).

Samples were also received from 126 new cases of conventional surgery and 9 new healthy lungs from donations of organs.

Samples from 621 patients were supplied to internal CIBER research projects (including a Biotech company in cooperation with the Pulmonary Fibrosis PCI).

Cooperation with the Lung Cancer PCI for carrying out the strategic project on a retrospective cohort of patients, and getting under way the prospective collection. As a result of the work the following were published:

- Monsó E, Montuenga LM, Sánchez de Cos J, Villena C; por el Group Colaborativo en Lung Cancer CIBERES-RTICC-SEPAR-Plataforma Biobanco Pulmonar. Biológical Marker Analysis as Part of the CIBERES-RTIC Cancer-SEPAR Strategic Project on Lung Cancer. Arch Bronconeumol. 2015 Sep;51(9):462-467.

Cooperation in the objectives undertaken with the Red Nacional de Biobancos Platform of the AES 2013 (PRNB), participating in its 5 work programmes.

- Member of the PRNB Management Committee

- Co-coordination of the R+D+i line in Human Tissue (Programme 3: Research, Development and Innovation). This group has already presented the following works:

- Villena C, Artiga MJ, Bermudo R, Buesa A, Caballero R, Del Agua C, Escámez T, Fraga M, Gelpí E, Marquina I, Novoa I, Piñero E, Pérez L, Rejón JD, Ruiz M, Segura A, Ventura C, Vieiro P, Zazo S, Peiró-Chova L y Rábano A. Últimos avances en la evaluación de la calidad de los tejidos archivados en los biobancos. Congreso Nacional de Biobancos, 2015, Lleida. Comunicación. Premio a la mejor comunicación en "I+D+i en biobancos".
- Rábano A, Artiga MJ, Bermudo R, Buesa A, Caballero R, Del Agua C, Escámez T, Fraga M, Gelpí E, Marquina I, Novoa I, Piñero E, Pérez L, Rejón JD, Ruiz M, Segura A, Ventura C, Vieiro P, Zazo S , Peiró-Chova L y Villena C. Aplicación del estado del arte en calidad de muestras de tejido a la actividad de los biobancos. Congreso Nacional de Biobancos, 2015, Lleida. Comunicación.

- Coordination of the work group on Respiratory Diseases (Programme 1: Strategic Collections).

- Co-Coordination of the LEGAL line and participation in the ETHICS line (Programme 4: ELSI).

- Participation in other lines:

- Quality Management System (Programme 2: Management of services).
- Harmonisation of the Database (Programme 3).

- Member of the organising Committee and Scientific Committee of the National Biobanks Congress 2015, Lérida (programme 5).

The PBP was given an outstanding mark for its contribution to the accomplishment of objectives of programmes 1, 3, 4 and 5, and optimum in programme 2.

The Integrated Research Projected on Pulmonary Thromboembolism SEPAR (OSIRIS) was got under way.

Participation in:

Participation in international consortiums
International Society for Biological and Environmental Repositories (ISBER)
European, Middle Eastern & African Society for Biopreservation & Biobanking (ESBB)
Global Biobank Directory (Specimen Central)
Included in the Biobanking and Biomolecular Resources Research Infrastructure Catalogue
Cooperating with Trans-Hit Biomarkers

Participation in training activities

Name of the activity	Organising institution
Master in Healthcare Law (60 EC)	UNIVERSIDAD DE LAS ISLAS BALEARES (UIB)
University Master Course in Biobanks and use of Human Biological Samples in Research (60 EC)	UNIVERSITAT CATÒLICA DE VALÈNCIA
Master in Translational Medicine (60 EC)	UNIVERSITAT DE BARCELONA Y HOSPITAL CLÍNIC (IDIBAPS)
Course on "Good Clinical Practice"	ESCUELA BALEAR DE ADMINISTRACIÓN PÚBLICA (EBAP) - HOSPITAL SON LLÁTZER
CIBERES Training Days	CIBERES
National Biobanks Congress	IRB-LLEIDA Y PLATAFORMA RED NACIONAL DE BIOBANCOS (CNIO)

Technology Development and Transfer Platform (PDTT)

COORDINATOR: DR. LLUIS BLANCH · MANAGER: DR. CRISTINA BROCEÑO

The PDTT's work attempts to foster innovation in the CIBERES environment by facilitating the operability, speed and effectiveness of innovative projects. We coordinate all the agents required in biomedical innovation projects. The PDTT acts as a 'single window' between these and CIBERES researchers.

Principales hitos conseguidos en 2015

CIBERES INTERNAL INNOVATION PROMOTION

- Consultancy for over 70 cases of transfer projects for CIBERES researchers. Protection of inventions, agreements, cooperation...
- Coordination in management of CIBERES innovation projects with CIBER central office (transfer, legal, projects, personnel departments, etc.).
- Training and promotion of innovation at CIBERES. Individual meetings with researchers and round table entitled ""Present and future of innovation and transfer at CIBER(ES)" at CIBERES Scientific Conference.
- Drafting and management of signatures. Over 26 documents connected with transfer (cooperation, MTA, confidentiality, inventors, assignment, co-ownership...).
- Assessment of CIBERES ideas, management of 11 active patents, 1 new priority application, 5 PCT extensions and 3 patents abandoned.
- Active participation in the incorporation and

management of the Platform for Assistance for Internationalisation (PAI) CIBER(ER-BBN-ES) for promoting the internationalisation of innovative CIBERES projects.

CIBERES INNOVATION PROMOTION OUTSIDE CIBERES

- Drawing up a list of "CIBERES capacities and services" based on meetings with most of the groups.
- Channelling interests of companies, research centres or other CIBER areas to CIBERES researchers and vice-versa.
- Drafting and disseminating CIBERES technology offer on the CIBER/ES web site, Europe Enterprise Network (EEN), events (2nd Forum of entrepreneurs in in vitro diagnosis (FENIN), MEDICA2016...), sent directly to businesses (over 10 per project) and contributors (CEDARS-SINAI, FENIN, ITEMAS...).
- Improving the CIBER/ES innovation network. Presentation of CIBER/ES to networks involved in healthcare innovation. Biomedical Research Technology Platforms, ITEMAS, IMI2, CDTI...
- Contributing to proper external and internal communication of CIBERES Innovation Projects. CIBERES contact for the CIBER communication department, management of CIBER/ES web texts and CIBER/ES intranet.

ESTABLISHMENT OF SYSTEMATICS FOR PROCEDURES IN INNOVATION AND TRANSFER AT CIBER/ES.

- Drafting model agreements for CIBER in coordination with the transfer and legal Departments of CIBER (MTAs, confidentiality, licence, co-ownership, cooperation ...).
- Along with one of the work groups of ITE- MAS, preparation of the "Valorisation of technology" section in ITEMAS Good Practices in Innovation.
- Improving transparency and access to documents required for innovation processes. Creation and constant updating of the technology transfer file on CIBER/ES intranet (minutes of the CIBERES innovation committee, procedures, model documents ...).
- Facilitating coordination in innovation strategy for all CIBER areas. Meeting of the CIBERES innovation committee with CIBER transfer coordinator for harmonising different aspects in the strategy for promotion and management of innovation. Assignment of all the material generated until that time from the PDTT.

6

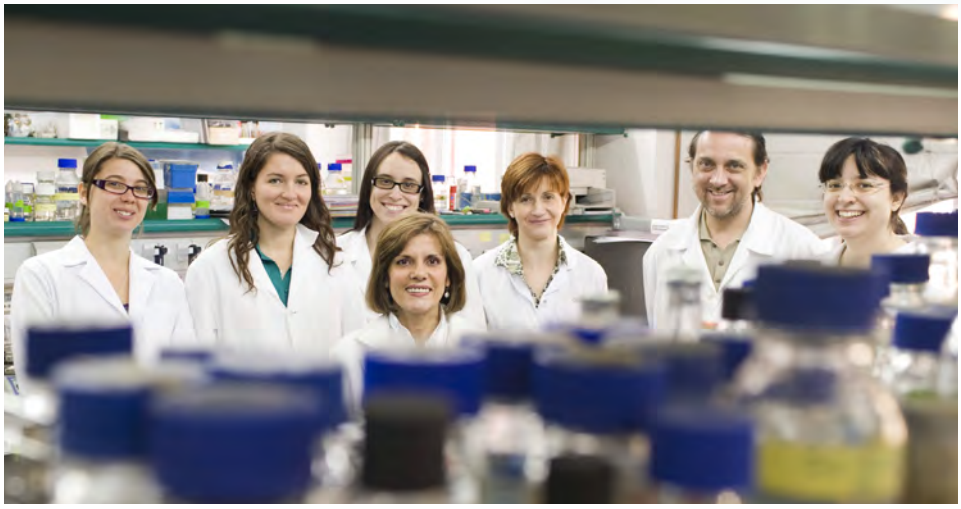
Research Groups

Group 1

Programme: Host-Pathogen Interactions / Acute Lung Injury

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 | Sáenz 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:

1. The molecular mechanisms by which surfactant components control unnecessary tissue inflammation, using cell culture models of inflammation and infection (CRP on Host-Pathogen Interactions).
2. 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).
3. Surfactant membranes' mechanisms of resistance to inactivation by factors which increase in the alveolar fluid during infection and inflammation (CRP on Host-Pathogen Interactions).
4. Molecular interactions between alveolar protein SP-A and nanoparticles (CRP on New Therapies to Treat Respiratory Diseases).
5. 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).
6. 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

COYA J.M., AKINBI H.T., SAENZ A., YANG L., WEAVER T.E., CASALS C.. Natural anti-infective pulmonary proteins: In vivo cooperative action of surfactant protein SP-A and the lung antimicrobial peptide SP-BN. Journal of Immunology. 2015;195(4):1628-1636.

SAENZ A., PRESTO J., LARA P., AKINYI-OLOO L., GARCÍA-FOJEDA B., NILSSON I. ET AL. Folding and intramembraneous BRICHOS binding of the prosurfactant protein C transmembrane segment. Journal of Biológical Chemistry. 2015;290(28):17628-17641.

Highlights

RELEVANT RESEARCH PROJECT: SAF2012-32728 (2013-2015) Lung surfactant as protector and modulator of lung infection and inflammation. Funded by the Spanish Ministry of Economy and Competitiveness. Principal Investigator: Cristina Casals.

RELEVANT RESULTS:

Line 1: We demonstrated that (i) anionic phospholipids exert an immunomodulatory effect on alveolar macrophages and pneumocytes in the presence of LPS, respiratory syncytial virus, or H. influenzae; and (ii) SP-A enhances IL-4-induced macrophage proliferation and alternative activation, revealing an important role in respiratory diseases with high levels of IL-4, such as asthma or pulmonary fibrosis.

Line 2: We demonstrated that (i) SP-A and SP-BN, present in the alveolar fluid, exhibit a synergic microbicidal activity against K. pneumoniae K2; and (ii) the therapeutic co-administration of both proteins reduces infection and enhances immune response in a mouse model of K. pneumoniae K2 infection.

Line 3: We demonstrated that beta-glucans, the major structural components of the cell wall of many pathogenic fungi, inhibit the surface activity of pulmonary surfactant. This effect is prevented by the binding of SP-A to beta-glucan.

Line 4: We demonstrated that the interaction of SP-A with different nanoparticles that can be used as theranostic systems alters the nanomaterial biodistribution, favoring, in some cases, their retention in the lung.

DOCTORAL THESIS: 25/02/2015. Juan Manuel Coya Raboso. "Synergic activity of surfactant protein A (SP-A) and antimicrobial peptides in defense of the lung against infection". Complutense University of Madrid. Doctoral Program: Biochemistry, Molecular Biology and Biomedicine ("Mention of Excellence" by the Ministry of Science and Education). Evaluation: Excellent "cum laude". Director: Dr. Cristina Casals and Alejandra Sáenz.

INTERNATIONAL COLLABORATION: 1) Prof. Dr. Timothy Weaver, Cincinnati Children's Hospital (Ohio, USA); 2) Prof. Dr. Jan Johansson, Karolinska Institute (Stockholm Sweden); 3) Prof. Dr. Claus-Michael Lehr, Saarland University (Saarbrücken, Germany); 4) Prof. Dr. Judith E. Allen, University of Edinburgh (U.K.).

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Group 2

Programme: Pneumonia / Host-Pathogen Interactions

Lead Researcher: García López, Ernesto

Group members

STAFF MEMBERS: Ruiz García, Susana.

ASSOCIATED MEMBERS: Díez Martínez, Roberto | Doménech 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

DOMENECH M., RUIZ S., MOSCOSO M., GARCÍA E.. In vitro biofilm development of Streptococcus pneumoniae and formation of choline-binding protein-DNA complexes. Environmental Microbiology Reports. 2015;7(5):715-727.

DE GRACIA RETAMOSA M., DIEZ-MARTÍNEZ R., MAESTRO B., GARCÍA-FERNÁNDEZ E., DE WAAL B., MEIJER E.W. ET AL. Aromatic Esters of Bicyclic Amines as Antimicrobials against Streptococcus pneumoniae. Angewandte Chemie - International Edition. 2015;54(46):13673-13677.

RICO-LASTRES P., DIEZ-MARTÍNEZ R., IGLESIAS-BEXIGA M., BUSTAMANTE N., ALDRIDGE C., HESEK D. ET AL. Substrate recognition and catalysis by LytB, a pneumococcal peptidoglycan hydrolase involved in virulence. Scientific Reports. 2015;5:-.

RAMOS-SEVILLANO E., URZAINQUI A., CAMPUZANO S., MOSCOSO M., GONZÁLEZ-CAMACHO F., DOMENECH M. ET AL. Pleiotropic effects of cell wall amidase LytA on Streptococcus pneumoniae sensitivity to the host immune response. Infection and Immunity. 2015;83(2):591-603.

AGUINAGALDE L, DÍEZ-MARTÍNEZ R, YUSTE J, ROYO I, GIL C, LASA Í ET AL. Auranofin efficacy against MDR Streptococcus pneumoniae and Staphylococcus aureus infections.The Journal of antimicrobial chemotherapy. 2015;70(9):2608-17.

Highlights

1) In late 2015, the patent Application No. 13/516,617 and entitled "DETECTION OF *STREPTOCOCCUS PNEUMONIAE* THROUGH MAGNETO-AMPEROMETRIC GENOSENSORS EMPLOYING SPECIFIC PRIMERS ANO PROBES FOR THE LYTA GENE" has been approved by the United States Patent and Trademark Office.

2) Streptococcus pneumoniae are usually found as asymptomatic colonizers of the upper respiratoru tract in humans. In addition, this bacterium is endowed with a high virulnce potential and is one of the most common etiological agents of respiratory and life-threatening infections. Dr. Pedro García from our group is one of the invited contributors to the book "*Streptococcus pneumoniae:* Molecular mechanisms of host-pathogen interactions" (2015; Academic Press; ISBN: 978-0-12-410530-0) that provides a comprehensive overview of our existing knowledge on *S. pneumoniae* disease pathogenesis.

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Group 4

Programme: Sleep Apnoeas Syndrome / Lung Cancer / COPD

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

Masa J.F., Corral J., Alonso M.L., Ordax E., Troncoso M.F., González M. et al. Efficacy of different treatment alternatives for obesity hypoventilation syndrome: Pickwick study. American Journal of Respiratory and Critical Care Medicine. 2015;192(1):86-95.

MASA J.F., DURAN-CANTOLLA J., CAPOTE F., CABELLO M., ABAD J., GARCÍA-RIO F. ET AL. Efficacy of home single-channel nasal pressure for recommending continuous positive airway pressure treatment in sleep apnea. Sleep. 2015;38(1):13-21.

SÁNCHEZ-SALCEDO P., WILSON D.O., DE-TORRES J.P., WEISSFELD J.L., BERTO J., CAMPO A. ET AL. Improving selection criteria for lung cancer screening: The potential role of emphysema. American Journal of Respiratory and Critical Care Medicine. 2015;191(8):924-931.

CASANOVA C, MARIN JM, MARTÍNEZ-GONZÁLEZ C, DE LUCAS-RAMOS P, MIR-VILADRICH I, COSIO B ET AL. Differential effect of mMRC dyspnea, CAT and CCQ for symptom evaluation within the new GOLD staging and mortality in COPD.Chest. 2015.

FERRANDO C., SUAREZ-SIPMANN F., GUTIERREZ A., TUSMAN G., CARBONELL J., GARCÍA M. ET AL. Adjusting tidal volume to stress index in an open lung condition optimizes ventilation and prevents overdistension in an experimental model of lung injury and reduced chest wall compliance. Critical Care. 2015;19(1).

Highlights

The Sleep-Apnea area, has been working on projects multicentric lines of great interest within the CIBERES program (ADVENT-HF Trial, association between sleep-disordered breathing and growth rate of cutaneous melanoma, effect of CPAP treatment in women with Obstructive sleep apnea, et.). It has participated in teaching, directing and organizing the Morfeo Project-SEPAR. It has also helped to guide respiratory therapy in the SEPAR protocol control and monitoring of home respiratory therapies (in the apnea-hypopnea and the home mechanical ventilation).

COPD group participates in the recruitment of cases (46-BIOMCOPD, 90-DELICATO, 31-EarlyCOPD). In the experimental laboratory, we have concluded the results of the therapeutic response to the administration of LGF in the experimental emphysema and complete animal exposure groups referred to in PI13 / 01909 project. We are at the stage of data analysis PET-CT, echocardiography, lung function and blood and tissue samples. Transcriptomics is completed and is now under proteomic analysis led pending validation in samples of lung BIOMCOPD biobank and cohort.

The area of Cancer continues its participation in the retrospective and prospective cohort of lung cancer linked to IASLC and maintains a growing share in the recruitment of the cohort screening for lung cancer with 300 patients enrolled and 3 cancers diagnosed. It has also expanded our involvement in collaboration with the sleeping area to include the study of sleep-disordered breathing in our cohort both screening and lung cancer patients with promising results. We have also participated in the new guide SEPAR as authors section on cancer screening.

Institution: Fundación Instituto de Investigación Sanitaria - Fundación Jiménez Díaz
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Website: http://www.fjd.es/es/cartera-servicios/especialidades-medicas/neumologia

Group 5

Programme: Asthma / Fibrosis

Lead Researcher: Picado Vallés, César

Group members

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

ASSOCIATED MEMBERS: Alobid, Isam | Fernández Bertolin, Laura | Fuentes Prado, Mireya | Guilemany Toste, José Mª | Martínez Antón, Asunción | Molina Molina, Maria | Mullol Miret, Joaquim | Muñoz Cano, Rosa | Pérez González, María | Pujols Tarres, Laura | Roca Ferrer, Jordi | Serrano Mollar, Ana Mª | 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

FERNÁNDEZ-BERTOLIN L., MULLOL J., FUENTES-PRADO M., ROCA-FERRER J., ALOBID I., PICADO C. ET AL. Effect of lipopolysaccharide on glucocorticoid receptor function in control nasal mucosa fibroblasts and in fibroblasts from patients with chronic rhinosinusitis with nasal polyps and asthma. PLoS ONE. 2015;10(5).

SERRA-PAGES M., TORRES R., PLAZA J., HERRERIAS A., COSTA-FARRE C., MARCO A. ET AL. Activation of the Prostaglandin E2 receptor EP2 prevents house dust mite-induced airway hyperresponsiveness and inflammation by restraining mast cells' activity. Clinical and Experimental Allergy. 2015;45(10):1590-1600.

DE BORJA CALLEJAS F., MARTÍNEZ-ANTON A., PICADO C., ALOBID I., PUJOLS L., VALERO A. ET AL. Corticosteroid treatment regulates mucosal remodeling in chronic rhinosinusitis with nasal polyps. Laryngoscope. 2015;125(5):E158-E167.

DE GARIBAY G.R., HERRANZ C., LLORENTE A., BONI J., SERRA-MUSACH J., MATEO F. ET AL. Lymphangioleiomyomatosis biomarkers linked to lung metastatic potential and cell stemness. PLoS ONE. 2015;10(7).

AINSUA-ENRICH E., SERRANO-CANDELAS E., ALVAREZ-ERRICO D., PICADO C., SAYOS J., RIVERA J. ET AL. The adaptor 3BP2 is required for KIT receptor expression and human mast cell survival. Journal of Immunology. 2015;194(9):4309-4318.

Highlights

MAIN RESEARCH RESULTS: 1. We have demonstrated that bacterial infeccions can reduce the ability of corticosteroids to regulate the expression of antiinflammatory genes (MKP-1, GILTZ). 2. We have demonstrated that agonists of EP2 receptor of prostaglandin E2 exert antiinflammatory effects throught the stabilization of mast cells, preventing their degranulation and the release of proinflammatory mast cell products. 3. We have demonstrated that corticosteroids modify the remodelling process present in the airways of inflammatory respiratory diseases by repearing the damaged epithelium and regulating the expression of matrix metalloproteinases MMP-1, MMP-2 and MMP-9, as well as the expression of the tissue inhibitor of metalloproteases type I (TIMP-1). 4. Our study have revealed novel lymphnagioleimyomatosis (LAM) markers linked to breast cancer metastasis to the lung, which in turn might guide the assessment of new therapies for LAM. 5 We have reported that the protein 3BP2 regulates human mast cell survivla by conrolling KIT receptor expression, suggesting its potential as a therapeutic target in mast-cell-mediated inflammatory diseases.

CLINICAL GUIDELINES: Members of the research team have participated in the implementation of an International Clinical Guideline: MACVIA-Aria sentinel Network for allergic rhinitis, MASK-Rhinitis. The new generation guideline implementation. Allergy 2015:70:1372-92).

RESEARCH PROJECTS: 5 active projects financed by official agencies with PIs who are members of the research team. One colaborative project with another CIBER, CIBERBBN.

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Contact: Villarroel, 170. 08036 Barcelona · Tel.: 93 451 09 93 · E.mail: cpicado@ub.edu

Group 6

Programme: Pulmonary Hypertension / COPD / Lung Cancer

Lead Researcher: Barberá 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 Solá, Jesús | Roca Torrent, Josep | Rodríguez Roisin, Roberto | Tura Ceide, Olga | Zavala Zegarra, Elizabeth.

Main lines of research

PULMONARY HYPERTENSION

- Biopathology, role of progenitor cells in the injury and repair.
- Identification of new biomarkers and therapeutic targets. Experimental models.

COPD

- Physical activity, cellular biogenetic and systemic effects.
- Gas exchange abnormalities.
- Biopathology of pulmonary vascular changes.

HEALTHCARE CONTINUITY AND INFORMATION TECHNOLOGY AND COMMUNICATION IN CHRONIC RESPIRATORY DISEASES:

- Quality control model of forced spirometry supported by information and comunication technologies (ICT)
- Early detection of sleep breathing disorders with ICT support.

Most relevant scientific articles

GALIE N., BARBERA J.A., FROST A.E., GHOFRANI H.-A., HOEPER M.M., MCLAUGHLIN V.V. ET AL. Initial use of ambrisentan plus tadalafil in pulmonary arterial hypertension. New England Journal of Medicine. 2015;373(9):834-844.

GALIÈ N, HUMBERT M, VACHIERY JL, GIBBS S, LANG I, TORBICKI A ET AL. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT).The European respiratory journal. 2015;46(4):903-75.

DOMINGUEZ-FANDOS D., VALDES C., FERRER E., PUIG-PEY R., BLANCO I., TURA-CEIDE O. ET AL. Sildenafil in a cigarette smoke-induced model of COPD in the Guinea-pig. European Respiratory Journal. 2015;46(2):346-354.

AGUSTI A., ANTO J.M., AUFFRAY C., BARBE F., BARREIRO E., DORCA J. ET AL. Personalized respiratory medicine: Exploring the horizon, addressing the issues: Summary of a BRN-AJRCCM workshop held in Barcelona on June 12, 2014. American Journal of Respiratory and Critical Care Medicine. 2015;191(4):391-401.

MOLINA R, MARRADES RM, AUGÉ JM, ESCUDERO JM, VIÑOLAS N, REGUART N ET AL. Assessment of a Combined Panel of Six Serum Tumor Markers for Lung Cancer.American journal of respiratory and critical care medicine. 2015;.

Highlights

The group has led the implementation of the CIBERES Research Line on Pulmonary Hypertension. Within this line is worth mentioning the participation in an international multicenter clinical trial aimed at evaluating a new strategy for treatment of pulmonary hypertension with combined initial therapy (New Engl J Med. 2015. 373: 834-844). The group has also contributed to the preparation of the new european guidelines for the treatment of pulmonary hypertension and a guideline on chronic thromboembolic pulmonary hypertension, in the program of Action and Monitoring Guidelines developed jointly by the Spanish College of Physicians and the Ministry of Health. The group is also involved in a collaborative project with industry on network management of patients with rare diseases, using pulmonary hypertension as a use case, funded by the National Program of Research, Development and Innovation Oriented to the Challenges of the Society.

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Web: http://www.idibaps.org/research/604/physiopathological-mechanisms-of-respiratory-illnesses

Group 7

Programme: Asthma

Lead Researcher: Del Pozo Abejón, María Victoria

Group members

STAFF MEMBERS: Romero García, Álvaro | Sastre Turrión, Beatriz Sara.

ASSOCIATED MEMBERS: Cardaba Olombrada, Blanca | Fernández Nieto, María del Mar | Lahoz Navarro, Carlos | 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

MAZZEO C., CANAS J.A., ZAFRA M.P., ROJAS MARCO A., FERNÁNDEZ-NIETO M., SANZ V. ET AL. Exosome secretion by eosinophils: A possible role in asthma pathogenesis. Journal of Allergy and Clinical Immunology. 2015;135(6):1603-1613.

YUCESOY B., KAUFMAN K.M., LUMMUS Z.L., WEIRAUCH M.T., ZHANG G., CARTIER A. ET AL. Genome-wide association study identifies novel loci associated with diisocyanate-induced occupational asthma. Toxicological Sciences. 2015;146(1):192-201.

BOBOLEA I., BARRANCO P., DEL POZO V., ROMERO D., SANZ V.L., OPEZ-CARRASCO V. ET AL. Erratum: Sputum periostin in patients with different severe asthma phenotypes. (Allergy 2015; 70: (540-546)). Allergy: European Journal of Allergy and Clinical Immunology. 2015;70(7):886.

GAMEZ C., ZAFRA M.P., SANZ V., MAZZEO C., IBANEZ M.D., SASTRE J. ET AL. Simulated gastrointestinal digestion reduces the allergic reactivity of shrimp extract proteins and tropomyosin. Food Chemistry. 2015;173:475-481.

ZAFRA M.P., CANAS J.A., MAZZEO C., GAMEZ C., SANZ V., FERNÁNDEZ-NIETO M. ET AL. SOCS3 silencing attenuates eosinophil functions in asthma patients. International Journal of Molecular Sciences. 2015;16(3):5434-5451.

Highlights

Several competitive grants have been gained during 2015: Exosomes and miRNAs in asthma: phenotypes/endotypes biomarkers and likey therapeutic tools an mRNA engineered mesenqhymal stromal cells: a new generation of cell therapy for inflammatory diseases.

Dr. Joaquin Sastre is the actual president of Spanish Society of Allergy and Clinic Immunology (SEAIC).

In the last EAACI congress two work were awarded as best Poster in the Junior Member and Affiliates

(JMA) Poster Session asd best Poster in General Session.

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Group 8

Programme: Host-Pathogen Interactions

Lead Researcher: Regueiro Comesaña, Verónica

Group members

ASSOCIATED MEMBERS: González Nicolau, Maria del Mar | Llobet Brossa, Enrique | Martí Lliteras, Juan Pablo | 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

CAMPANERO-RHODES M.A., LLOBET E., BENGOECHEA J.A., SOLIS D.. Bacteria microarrays as sensitive tools for exploring pathogen surface epitopes and recognition by host receptors. RSC Advances. 2015;5(10):7173-7181.

TOMAS A., LERY L., REGUEIRO V., PÉREZ-GUTIERREZ C., MARTÍNEZ V., MORANTA D. ET AL. Functional genomic screen identifies klebsiella pneumoniae factors implicated in blocking nuclear factor κB (NF-κB) signaling. Journal of Biológical Chemistry. 2015;290(27):16678-16697.

CANO V., MARCH C., INSUA J.L., AGUILO N., LLOBET E., MORANTA D. ET AL. Klebsiella pneumoniae survives within macrophages by avoiding delivery to lysosomes. Cellular Microbiology. 2015;17(11):1537-1560.

LLOBET E., MARTÍNEZ-MOLINER V., MORANTA D., DAHLSTROM K.M., REGUEIRO V., TOMASA A. ET AL. Deciphering tissue-induced Klebsiella pneumoniae lipid a structure. Proceedings of the National Academy of Sciences of the United States of America. 2015;112(46):E6369-E6378.

EUBA B., MOLERES J., SEGURA V., VIADAS C., MOREY P., MORANTA D. ET AL. Genome expression profiling-based identification and administration efficacy of host-directed antimicrobial drugs against respiratory infection by non-typeable Haemophilus influenzae. Antimicrobial Agents and Chemotherapy. 2015;59(12):7581-7592.

Highlights

Our laboratory has developed a new method to purify and identify lipid A structure from a pathogen in vivo, directly from site of infection; without a subculture and/or enrichment step. This new method allowed us to identify that K. pneumoniae (KP) expresses a modified 2'-hydroxilated lipid A. This modification is dependent on the activation of the oxygenase enzyme LpxO, in a phoPQ dependent manner (which is a KP two component system). The LpxO is ultimately responsible for the 2'-hydroxylation of lipid A. This hydroxylated lipid A has lower immunogenicity than the non-hydroxylated structure that presents KP in a normal laboratory culture medium. In addition, this lipid A structure expressed during a lung infection confers to KP increased resistance to antimicrobial peptides present in lung; but further to colistin, which is one of the last options for treating infections caused by multiresistant KP strains. Deleting lpxO gene, or inhibiting LpxO expression by deleting some of the genes controlling its expression, reduces or completely removes the 2'-hydroxylation from lipid A and increases KP sensibility to colistin. We have analyzed a clinical isolates collection with KP strains resistant to multiple antibiotics and some of them resistant to colistin. These results suggest LpxO enzyme as a new therapeutic target to consider when dealing with KP strains resistant to colistin.

Lipid A analysis directly from infection site has also revealed that KP differentially modulates the lipid A structure depending on the organ that is infecting. These results highlight the ability of pathogens to change their lipid A structure depending on occupied niches; which in turn reinforces the need to explore new antimicrobial therapies, more specific to bacterial strain causing infection, and also to the specific organ that is infected.

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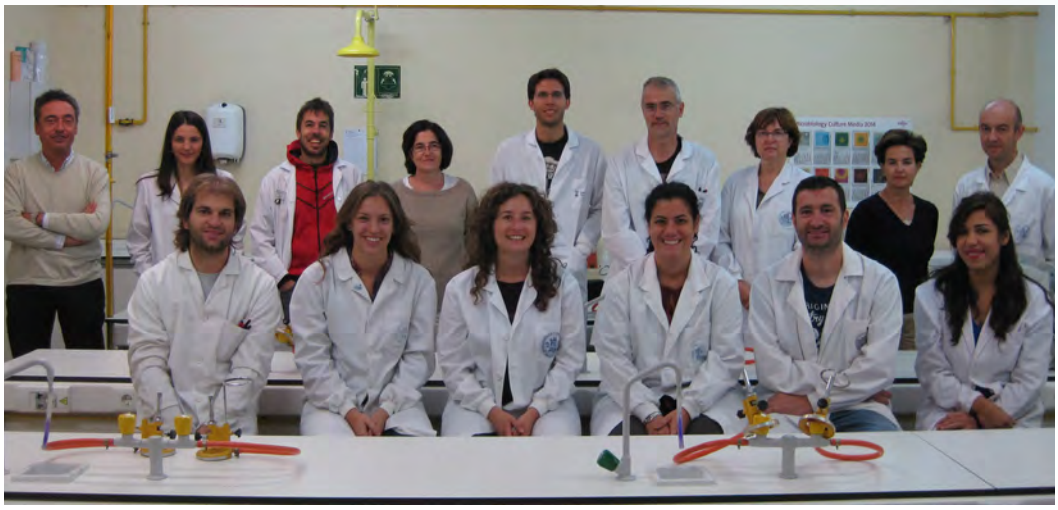
Group 9

Programme: Tuberculosis / 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 | Días Rodrigues, Liliana Isabel | Gavín Benavent, Patricia | Gómez Aguirre, Ana Belén | Gómez Lus, Rafael | Gonzalo Asensio, Jesús | Gracia Díaz, Begoña | Ibarz Bosqued, Daniel | Iglesias Gozalo, MªJosé | Lafoz Pueyo, Carmen | Lezcano Carrera, Mª Antonia | Lucía Quintana, Ainhoa | Otal Gil, Isabel | Picó Marco, Ana | Revillo Pinilla, Mª José | Rubio Calvo, Mª Carmen | Samper Blasco, Sofía Luisa | Vitoria Agreda, Mª Asunción.

Main lines of research

Our Research Group on Mycobacterial Genetics has been working since 1992 in three lines of research funded by European and national research grants, being recognized as a leading group at the international level. Our current research interests are:

- Construction of New Vaccines against Tuberculosis, focusing on genes implicated in the pathogenicity and virulence of M. tuberculosis. PI Carlos Martín.
- Molecular Epidemiology of Tuberculosis & Transposition and Latency of M. tuberculosis focusing on the study of risk factors of transmission, and differences between strains of major epidemiological importance and the mechanism of slow growth of the Koch bacillus.PI Sofía Samper.
- Molecular Bases of Drug Resistance in Mycobacteria, focusing on the contribution of efflux pumps to intrinsic drug resistance and in the discovery of novel antituberculosis compounds. PI José Antonio Ainsa

Altogether, our commitment is to study the complexity of M. tuberculosis by using a multidisciplinary approach and to work in coordination with other national and international research groups.

Active Projects:

Line 1: • TBVAC H2020 643381 - H2020-PHC-2014 "Advancing novel and promising TB vaccine candidates from discovery to preclinical and early Clinical development" 2015-18 • BIO2014-52580-P "Innovando MTBVAC como vacuna contra la tuberculosis y nuevas aplicaciones terapéuticas en cáncer". 2015-18. • INNPACTO: Ref. IPT-2012-0327-090000 "Vacu-

na Inactivada contra tuberculosis en base a una cepa modificada genéticamente". 2013-16

Line 2: • Polimorfismos genómicos y transcriptómicos en M. tuberculosis complex y su significado en clínica. IP: Sofía Samper. Number of researchers: 10; FIS 12/1970, Instituto de Salud Carlos III. 2013-15. • Study of the impact of RD8 on the regulation of ESAT-6 secretion in M. bovis and M. africanum.SecRegulTBC. REFBIO. 2013-14 • Antimicrobial resistance, virulence and new therapies in bacterial human pathogens. REFBIO 2013-14 • 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: • MM4TBMore Medicines for Tuberculosis. European Union FP7. 2011-14 • NAREB - Nanotherapeutics for antibiotic resistant emerging bacterial pathogens. European Union FP7. 2014-18 • SAF-2013-48971-C2-2-R. Aplicaciones biomédicas de AS-48, una proteína con amplio espectro de actividad antimicrobiana. 2014-16.

Most relevant scientific articles

SPERTINI F., AUDRAN R., CHAKOUR R., KAROUI O., STEINER-MONARD V., THIERRY A.-C. ET AL. Safety of human immunisation with a live-attenuated Mycobacterium tuberculosis vaccine: A randomised, double-blind, controlled phase I trial. The Lancet Respiratory Medicine. 2015;:-.

IGLESIAS M.-J., MARTÍN C.. Editorial commentary: Nonspecific beneficial effects of BCG vaccination in high-income countries, should we extend recommendation of BCG vaccination?. Clinical Infectious Diseases. 2015;60(11):1620-1621.

BROSET E., MARTÍN C., GONZALO-ASENSIO J.. Evolutionary landscape of the mycobacterium tuberculosis complex from the viewpoint of phoPR: Implications for virulence regulation and application to vaccine development. mBio. 2015;6(5):-.

BAILO R., BHATT A., AINSA J.A.. Lipid transport in Mycobacterium tuberculosis and its implications in virulence and drug development. Biochemical Pharmacology. 2015;96(3):159-167.

MILLAN-LOU M.I., OTAL I., MONFORTE M.L., VITORIA M.A., REVILLO M.J., MARTÍN C. ET AL. In Vivo IS6110 profile changes in a Mycobacterium tuberculosis strain as determined by tracking over 14 years. Journal of Clinical Microbiology. 2015;53(7):2359-2361.

Highlights

In 2015 we started the European project TBVAC H2020 "Advancing novel and promising TB vaccine candidates from discovery to preclinical and early Clinical development" in collaboration with 40 International Universities and Research Centers. Safety and Immunogenicity of the first Clinical trial in human with MTBVAC in healthy adults in Lausanne Switzerland, has been published in December 2015 (Spertini et al Lancet Respir Med. 2015 Dec;3(12):953-62.). Excellent safety and strong immunogenicity data, support advanced clinical development in high-burden tuberculosis endemic countries. In September 2015 South African authorities have approved Phase 1b in neonates in South Africa.

In line 2, the analysis of the more transmitted strains in our population and monitoring these strains over time, including the genomic changes as marks of evolution, using different techniques has been done. We have studied tuberculosis and other mycobacteria disease in children. We have started using mass sequencing to detect resistance and phylogeny of the M. tuberculosis complex. We collaborated in the development for rapid techniques for detecting resistance to drugs of first and second line.

In line 3, we have progressed in the characterisation of the impact of efflux pumps in intrinsic drug resistance of M. tuberculosis against new candidate drugs in development, that have been identified by our European collaborators through phenotypic screenings. We have started the study of novel drug targets (implicated in the metabolism of nucleic acids and control of oxidative stress response) for developing new antituberculosis agents. We have identified several combinations of drugs that do not decrease their antimicrobial activity upon encapsulation on nanoparticles of diverse chemical origins.

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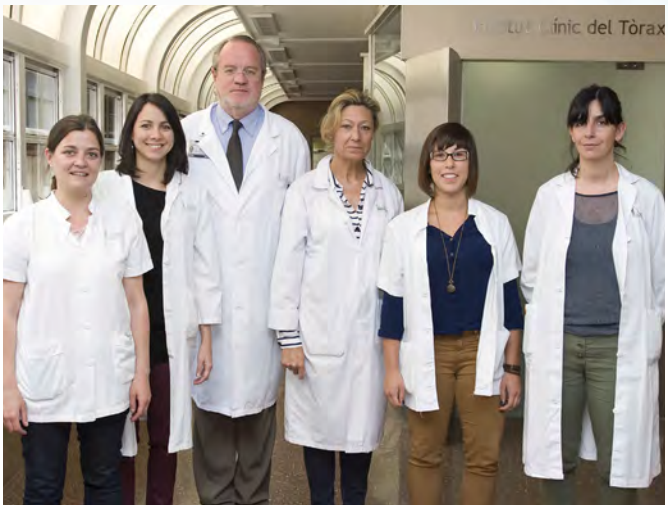
Group 10

Programme: COPD / Fibrosis

Lead Researcher: Agustí García-Navarro, Àlvar

Group members



STAFF MEMBERS: Faner Canet, Maria Rosa | Iglesias Coma, Amanda | Sunyer Dequiogiovanni, Gemma.

ASSOCIATED MEMBERS: Barceló Martín, Bernardino | Cruz Santacruz, Tamara | Ferrer Balaguer, Joana Maria | García-Cosío Piqueras, Francisco de Borja | López Giraldo, Alejandra | López Zamora, Meritxell | Molins López Rodó, 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

MOLINA R, MARRADES RM, AUGÉ JM, ESCUDERO JM, VIÑOLAS N, REGUART N ET AL. Assessment of a Combined Panel of Six Serum Tumor Markers for Lung Cancer.American journal of respiratory and critical care medicine. 2015;.

FANER R., GUTIERREZ-SACRISTAN A., CASTRO-ACOSTA A., GROSDIDIER S., GAN W., SÁNCHEZ-MAYOR M. ET AL. Molecular and clinical diseasome of comorbidities in exacerbated COPD patients. European Respiratory Journal. 2015;46(4):1001-1010.

LANGE P., CELLI B., AGUSTI A., JENSEN G.B., DIVO M., FANER R. ET AL. Lung-function trajectories leading to chronic obstructive pulmonary disease. New England Journal of Medicine. 2015;373(2):111-122.

HOLGATE S., AGUSTI A., STRIETER R.M., ANDERSON G.P., FOGEL R., BEL E. ET AL. Drug development for airway diseases: Looking forward. Nature Reviews Drug Discovery. 2015;14(6):367-368.

WOODRUFF P.G., AGUSTI A., ROCHE N., SINGH D., MARTÍNEZ F.J.. Current concepts in targeting chronic obstructive pulmonary disease pharmacotherapy: Making progress towards personalised management. The Lancet. 2015;385(9979):1789-1798.

Highlights

During 2015, the group 10 has produced the following main results:

- The line of the natural history of COPD has shown that COPD can develop not only as a result of deterioration in lung function associated with smoking, but also as a consequence of poor lung development. The results of this study have been published in the NEJM.
- Network medicine applied to the study of COPD comorbidities, has shown the common molecular pathways between several COPD comorbidities in exacerbated COPD patients, results have been published in ERJ.
- Work on the identification of biomarkers associated to lung cancer has been published in AJRCCM.

In terms of projects the group has initiated a new one funded by the ISCIII (PI15 / 00799) with co-IPs Alvar Agusti / Rosa Faner. The group continued the participation in the projects of the COPD PCI and continued with active projects funded in previous years by SEPAR and FUCAP.

As for clinical guidelines, the group leader Dr. Alvar Agustí is a member of the scientific committee of GOLD (Global Initiative for Chronic Obstructive Lung Disease).

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Group 11

Programme: Sleep Apnoeas Syndrome

Lead Researcher: Montserrat Canal, Josep Maria

Group members

STAFF MEMBERS: Isseta, Valentina | Torres López, Marta.

ASSOCIATED MEMBERS: Arboix Damunt, Adrià | Ballester Rodes, Eugenio | Dalmases Cleries, Mireia | De Pablo Rabasso, Juan | Embid López, Cristina | Hernández Plaza, Lourdes | Martínez García, Miguel Ángel | Mayos Pérez, Mercedes | Monasterio Ponsa, Carmen | Morello Castro, Antonio | Parra Ordaz, Olga | Salamero Baró, 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

ISETTA V., NEGRIN M.A., MONASTERIO C., MASA J.F., FEU N., ALVAREZ A. ET AL. A Bayesian cost-effectiveness analysis of a telemedicine-based strategy for the management of sleep apnoea: A multicentre randomised controlled trial. Thorax. 2015;70(11):1054-1061.

CARRERA H.L., MARCUS C.L., MCDONOUGH J.M., MORERA J.C.O., HUANG J., FARRE R. ET AL. Negative expiratory pressure technique: An Awake test to measure upper airway collapsibility in adolescents. Sleep. 2015;38(11):1783-1791.

DALMASES M., SOLE-PADULLES C., TORRES M., EMBID C., NUNEZ M.D., MARTÍNEZ-GARCÍA M.A. ET AL. Effect of CPAP on cognition, brain function, and structure among elderly patients with OSA a randomized pilot study. Chest. 2015;148(5):1214-1223.

MASA J.F., DURAN-CANTOLLA J., CAPOTE F., CABELLO M., ABAD J., GARCÍA-RIO F. ET AL. Efficacy of home single-channel nasal pressure for recommending continuous positive airway pressure treatment in sleep apnea. Sleep. 2015;38(1):13-21.

FARRE R, MARTÍNEZ-GARCÍA MA, CAMPOS-RODRÍGUEZ F, MONTSERRAT JM. A Step Forward for Better Interpreting the Apnea-Hypopnea Index.Sleep. 2015;38(12):1839-40.

Highlights

We work in 3 areas:

A) Basic studies in collaboration with Dr. Navajas group. We analyze apneas mechanisms. In this case, we study completely new aspects: the collapsibility of the upper airway (UAW) in Marfan syndrome, aspects of the microbiome and sleep apnea (OSA) and also parabiotics models in models of hypoxia / normoxia. Marta Torres, PhD in biology, works very closely. The findings are seminal and open up remarkable perspectives on OSA pathogenesis.

B) Multicenter, together with the Spanish group of sleep. Specifically, OSA and elderly (15-20 % of the population) as well as technologies used for the diagnosis. According to these studies it can be said that in elderly patients the presence of OSA with high index of sleep apnea (IAH) leads to brain anatomical and pathological symptoms and anomalies. Both improve with CPAP. These are some of the former studies randomized in the literature. Finally it has been found that in patients with an increased risk of suffering OSA the simplified systems are worth.

C) One aspect on which we has worked harder during 2015 are the information technologies. Specifically, on the development of a virtual dream where most patients are diagnosed with household simple equipment with telematics data , interviews by video conference and monitoring of treatment with CPAP by data transmission besides being able to modify the settings of the equipment from distance. This has been made possible by support from the FIS , SEPAR , SOCAP and specialized industry. The ultimate goal is to change the model of care for these patients to be more cost effective through networking and ICT technology. Several publications confirm the feasibility of the project.

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Group 12

Programme: Sleep Apnoeas Syndrome / Acute Lung Injury

Lead Researcher: Navajas Navarro, Daniel

Group members

STAFF MEMBERS: Polo Tórtola, Maeba.

ASSOCIATED MEMBERS: Alcaraz Casademunt, Jordi | Almendros López, Isaac | Campillo Agullo, Noelia | Carreras Palau, Alba | Farré Ventura, Ramon | Luque González, Tomás Alberto | Melo Herraiz, Esther | Rodríguez Lazaro, Miguel Ángel | Rotger Estapé, Mª del Mar.

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

MORENO-INDIAS I, TORRES M, MONTSERRAT JM, SÁNCHEZ-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. 2015;.

TORRES M., ROJAS M., CAMPILLO N., CARDENES N., MONTSERRAT J.M., NAVAJAS D. ET AL. Parabiotic model for differentiating local and systemic effects of continuous and intermittent hypoxia. Journal of Applied Physiology. 2015;118(1):42-47.

VIZOSO M., PUIG M., CARMONA F.J., MAQUEDA M., VELASQUEZ A., GÓMEZ A. ET AL. Aberrant DNA methylation in non-small cell lung cancer-associated fibroblasts. Carcinogenesis. 2015;36(12):1453-1463.

CASARES L, VINCENT R, ZALVIDEA D, CAMPILLO N, NAVAJAS D, ARROYO M ET AL. Hydraulic fracture during epithelial stretching.Nature materials. 2015;14(3):343-51.

KOSMALSKA A.J., CASARES L., ELOSEGUI-ARTOLA A., THOTTACHERRY J.J., MORENO-VICENTE R., GONZÁLEZ-TARRAGO V. ET AL. Physical principles of membrane remodelling during cell mechanoadaptation. Nature Communications. 2015;6:-.

Highlights

Obstructive Sleep Apnea (OSA) is a very prevalent disease characterized by patient exposure to intermittent hypoxic events. We have addressed the basic mechanisms involved in the consequences of this disease. We have established and validated a parabiotic mouse model, two animals sharing circulation by surgical union through the skin, and confirmed the hypothesis that when one of the parabionts breathes room air and the other one is subjected to hypoxic air, both mice share systemic circulation but remain normoxic and hypoxic, respectively. This novel model is useful to investigate the effects of local and systemic intermittent hypoxia. In another study in mice we proved for the first time that intermittent hypoxia modifies the microenvironment oxygenation and the microbiota in the gut. Evidence of altered fecal microbiota composition and diversity suggests that physiological interplays between host and gut microbiota could be deregulated in OSA.

Acute lung injury is a severe disease associated with disruption of the alveolar epithelial cell monolayer. The underlying mechanisms of alveolar barrier damage and repair remain poor known. The origin of fracture in epithelial cell sheets subject to stretch is commonly attributed to excess tension in the cells' cytoskeleton, in the plasma membrane, or in cell-cell contacts. We showed a new poroelastic mechanism involved in the disruption of epithelial cell monolayer subjected to stretch. We also showed that the 3D remodelling of the cell membrane during cell mechanoadaptation can be explained by a purely mechanical process generating different types of membrane invaginations that can repeatedly store and release large fractions of cell membrane. Once formed, cells reabsorb the invaginations through an active process with duration of the order of minutes.

Lung Cancer is the leading cause of cancer-related deaths worldwide. Our current knowledge of the aberrant genomic DNA methylation in tumor-associated fibroblasts (TAFs) is very scarce. We therefore conducted genome-wide DNA methylation profiling on lung TAFs and paired control fibroblasts. Our findings shed light on the unique origin and molecular alterations underlying the aberrant phenotype of lung TAFs, and identify a stromal biomarker with potential clinical relevance.

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Group 13

Programme: Host-Pathogen Interactions / Fibrosis / Pulmonary Hypertension

Lead Researcher: Morcillo Sánchez, Esteban Jesús

Group members

ASSOCIATED MEMBERS: Armengot Carceller, Miguel | Cerdá Nicolás, Miguel | Cortijo Gimeno, Julio | Juan Samper, Gustavo | Mata Roig, Manuel | Milara Paya, Javier | Serrano Gimeno, Adela.

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., 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. 2015;135(2):470-476.

SARRION I., MILIAN L., JUAN G., RAMON M., FUREST I., CARDA C. ET AL. Role of circulating miRNAs as biomarkers in idiopathic pulmonary arterial hypertension: Possible relevance of miR-23a. Oxidative Medicine and Cellular Longevity. 2015;2015:-.

LORENZO M.-J., MORET I., SARRIA B., CASES E., CORTIJO J., MENDEZ R. ET AL. Lung inflammatory pattern and antibiotic treatment in pneumonia. Respiratory Research. 2015;16(1):-.

MILARA J., MORELL A., BALLESTER B., SANZ C., FREIRE J., QIAN X. ET AL. Roflumilast improves corticosteroid resistance COPD bronchial epithelial cells stimulated with toll like receptor 3 agonist. Respiratory Research. 2015;16(1):-.

MILARA J., MORCILLO E., MONLEON D., TENOR H., CORTIJO J.. Roflumilast prevents the metabolic Effects of bleomycin-induced fibrosis in a murine model. PLoS ONE. 2015;10(7)

Highlights

Multidisciplinary team specializing in basic and translational pharmacology applied to the respiratory system; with a multitude of public research projects and more than 10 private projects with the pharmaceutical industry developed during 2015.

In addition to the good annual rate of scientific publications; contributions in national and international congresses, and teaching activities for the group members.

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Group 14

Programme: Pneumonia

Lead Researcher: Torres Martí, Antoni

Group members

STAFF MEMBERS: Cilloniz Campos, Catia | Fernández Barat, Laia | Polverino, Eva | Sancho Roset, Elisabeth.

ASSOCIATED MEMBERS: Agustí García Navarro, Carlos | Almirall Pujol, Jorge | Badía Jobal, Juan Ramón | Bello Dronda, Salvador | Bodi Saera, María Amparo | Falguera Sacrest, Miquel | Ferrer Monreal, Miguel | Guerrero Molina, Laura | Martínez Olondris, Pilar | Menéndez Villanueva, Rosario | Ramírez Galleymore, Paula | Rodríguez Oviedo, Alejandro | 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

TORRES A., SIBILA O., FERRER M., POLVERINO E., MENENDEZ R., MENSA J. ET AL. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: A randomized clinical trial. JAMA - Journal of the American Medical Association. 2015;313(7):677-686.

PRINA E., RANZANI O.T., TORRES A.. Community-acquired pneumonia. The Lancet. 2015;386(9998):1097-1108.

RINAUDO M., FERRER M., TERRANEO S., DE ROSA F., PERALTA R., FERNÁNDEZ-BARAT L. ET AL. Impact of COPD in the outcome of ICU - Acquired pneumonia with and without previous intubation. Chest. 2015;147(6):1530-1538.

BASSI G.L., LUQUE N., MARTI J.D., XIOL E.A., PASQUALE M.D., GIUNTA V. ET AL. Endotracheal tubes for critically ill patients: An in vivo analysis of associated tracheal injury , mucociliary clearance, and sealing effi cacy. Chest. 2015;147(5):1327-1335.

CILLONIZ C., ALBERT R.K., LIAPIKOU A., GABARRUS A., RANGEL E., BELLO S. ET AL. The effect of macrolide resistance on the presentation and outcome of patients hospitalized for streptococcus pneumoniae pneumonia. American Journal of Respiratory and Critical Care Medicine. 2015;191(11):1265-1272.

Highlights

It has been completed and published a clinical trial randomized double-blind administration of corticosteroids in severe community-acquired pneumonia. The results demonstrate the beneficial effect of corticosteroids in reducing treatment failure. These results can be reviewed in more detail in the publication : JAMA - Journal of the American Medical Association. 2015;313(7):677-686.

We have been asked to write a review on the Community acquired pneumonia in the Lancet Journal (The Lancet.2015;386(9998):1097-1108)

It has ended Gravity-VAP Trial study comparing the semi-recumbent position vs. lateral decubitus position rendelenburg for the prevention of pneumonia associated with artificial ventilation. It's planned to publish the results for 2016.

We have developed an animal model of streptococcus pneumoniae in mechanically ventilated pigs for more than 72 hours. Specifically it was used serotype 19A. These results were presented as an Abstract at the last Congress of the European Respiratory Society and in the SEPAR.

Many contracts have been signed with the following industries for studies in Animal Model: Mediimmune, Cardeas, Arsanis and Theravance.

They were presented 3 doctoral thesis of group members or researcher sassociated with it in the 2015.

The IP of the group is co-leader of the European Project WP4A COMBACTE MAGNET.

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Group 15

Programme: Sleep Apnoeas Syndrome

Lead Researcher: Masa Jiménez, Juan Fernando

Group members

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

ASSOCIATED MEMBERS: Alonso Alvarez, María Luz | Corral Peñafiel, Jaime | Disdier de Vicente, Carlos | Gallego Domínguez, Rocío | Gómez de Terreros Caro, Francisco Javier | Riesco Miranda, Juan Antonio | Rubio González, Manuela | Sánchez Escuin, 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., CORRAL J., ALONSO M.L., ORDAX E., TRONCOSO M.F., GONZÁLEZ M. ET AL. Efficacy of different treatment alternatives for obesity hypoventilation syndrome: Pickwick study. American Journal of Respiratory and Critical Care Medicine. 2015;192(1):86-95.

SÁNCHEZ-DE-LA-TORRE M., KHALYFA A., SÁNCHEZ-DE-LA-TORRE A., MARTÍNEZ-ALONSO M., MARTÍNEZ-GARCÍA M.A., BARCELO A. ET AL. Precision Medicine in Patients With Resistant Hypertension and Obstructive Sleep Apnea Blood Pressure Response to Continuous Positive Airway Pressure Treatment. Journal of the American College of Cardiology. 2015;66(9):1023-1032.

ISETTA V., NEGRIN M.A., MONASTERIO C., MASA J.F., FEU N., ALVAREZ A. ET AL. A Bayesian cost-effectiveness analysis of a telemedicine-based strategy for the management of sleep apnoea: A multicentre randomised controlled trial. Thorax. 2015;70(11):1054-1061.

SÁNCHEZ-DE-LA-TORRE M., NADAL N., CORTIJO A., MASA J.F., DURAN-CANTOLLA J., VALLS J. ET AL. Role of primary care in the follow-up of patients with obstructive sleep apnoea undergoing CPAP treatment: A randomised controlled trial. Thorax. 2015;70(4):346-352.

MASA J.F., DURAN-CANTOLLA J., CAPOTE F., CABELLO M., ABAD J., GARCÍA-RIO F. ET AL. Efficacy of home single-channel nasal pressure for recommending continuous positive airway pressure treatment in sleep apnea. Sleep. 2015;38(1):13-21.

Highlights

PROJECTS DIRECTED BY OUR GROUP

(projects in collaboration excluded) (€ 1,000,000).

1. Efficiency at medium /long-term niv in OHS. (pickwicks). FIS, VITALAIR. • 2. Cost-effectiveness of home respiratory polygraphy management (HRP) SEPAR, NEUMOSUR, VITALAIR and FUNDESALUD. • 3. Effectiveness and cost-efectiveness of an oversimplified system for the management of patients with high osa probability in primary care. FIS, PRI, SEPAR, SEAR, NEUMOSUR • 4. Telemedicine platform in COPD (E-NEUMO). CRONEX 3.0. NEUMOSUR. SEPAR. SEAR. TELEFÓNICA EHEALTH. • 5. Effect of CPAP in the deterioration of renal function in early stages of chronic kidney disease (RENAS). FIS, FIS, SEAR, NEUMOSUR. • 6. Evolution of SAHS in children in a clinical cohort of children studied in the sleep unit. Approach to the natural history of disease. (atlantis). FIS. • 7. SAHS in obese and non-obese children, implications. Junta de castilla y león.

TRANSFER

Collaboration with VitalAire (HRP and Pickwicks projects) of 280,000 €.

INTERNALIZATION

• "OHS: definition, diagnosis, pathophysiology and management" coordinator. ERS Monograph. • Respiratory Intensive Care Assembly membership in the ERS. • Task Force ERS member: Technical Standards for the Scoring of Respiratory Events using Type III Devices for the Diagnosis of Sleep Disordered Breathing. • ADVENT-HF TRIAL. (Canadian institute of health research & Philips-Respironics). • THE EUROPEAN SLEEP APNEA DATABASE (ESADA). (EU Cost action).

INNOVATION

1) Implementation of telematics spirometry in Extremadura. 2) Development and validation of a telematic platform for COPD patients. 3) Development and validation of a system of tele estetoscopia. 4) Spectral analysis and artificial intelligence in sleep studies in children.

TRAINING

1. Thesis: HIF-2 a cellular response to hypoxia. Isabel Escauriaza

2. Courses:

- Organization of the VIII International Symposium on Non Invasive Ventilation. November 12-15. Cáceres.
- Organization of Sleep Course. University Hospital Burgos, Spain. 4th to 7th May.

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E.mail: fmasa@separ.es

Group 16

Programme: Asthma

Lead Researcher: Muñoz Gall, Xavier

Group members

STAFF MEMBERS: Ojanguren Arranz, Íñigo.

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

Main lines of research

The activity of basic and clinical research of the group focuses mainly in areas of inflammation and repair, respiratory failure and tissue hypoxia, and there is complementarity and interrelation of these areas for the study of diseases such as asthma, COPD, pulmonary fibrosis, infections, transplants, pulmonary hypertension and sleep-disordered breathing (SDB).

Specifically, within the research in asthma the group is working in the MEGA project aimed at increasing knowledge about the molecular mechanisms of asthma as well as to study the parameters that can determine long-term changes in the patient's condition and treatments that can influence the progression of the disease. In short, the group aims to better understand the natural history of disease in order to reduce its incidence. We believe that the key to a better understanding of asthma is to carry out an integrated approach, in which immunological, genetic and environmental factors that define the relevant characteristics of the disease are analyzed.

In the line of pulmonary fibrosis, our studies have shown that it is possible to determine the causes of this disease in half of the cases after the completion of a clinical study in depth. The group has shown that a major cause of idiopathic pulmonary fibrosis is exposure to minimal but persistent antigen quantities. Ultimately, it is the disease called hypersensitivity pneumonitis crónica. In this research the group has a murine model of hypersensitivity pneumonitis that will be significant in the near future to see the effect of different treatments as well as to study the pathophysiological pathways of this disease.

Our center is currently one of the 7 hospitals in the country where lung transplants are performed and one of the most active in this field, which places it in one of the top European and world level. With the unique opportunity generated by the lung transplant program at our hospital, the group is actively working on the inclusion of samples in the CibeRes biobank.

Most relevant scientific articles

ROCA O., MASCLANS J.R.. High-flow nasal cannula oxygen therapy: Innovative strategies for traditional procedures. Critical Care Medicine. 2015;43(3):707-708.

MIRAVITLLES M., LLOR C.. Are C-reactive protein levels associated with bacteria in COPD exacerbations?. European Respiratory Journal. 2015;45(5):1514-1515.

DONAIRE-GONZÁLEZ D, GIMENO-SANTOS E, BALCELLS E, DE BATLLE J, RAMON MA, RODRÍGUEZ E ET AL. Benefits of physical activity on COPD hospitalisation depend on intensity. The European respiratory journal. 2015;46(5):1281-9.

PÉREZ-TERAN P., ROCA O., RODRÍGUEZ-PALOMARES J., SACANELL J., LEAL S., SOLE J. ET AL. Influence of right ventricular function on the development of primary graft dysfunction after lung transplantation. Journal of Heart and Lung Transplantation. 2015;34(11):1423-1429.

ISETTA V., NEGRIN M.A., MONASTERIO C., MASA J.F., FEU N., ALVAREZ A. ET AL. A Bayesian cost-effectiveness analysis of a telemedicine-based strategy for the management of sleep apnoea: A multicentre randomised controlled trial. Thorax. 2015;70(11):1054-1061.

Highlights

The group has get funding from the Instituto de Salud Carlos III (PI15 / 01900) for the completion of MEGA project, a collaborative project in the research area of asthma that aims to generate a cohort of patients with asthma that encompasses the possibility of access to clinical, physiological, molecular and genetic in patients with various degrees of severity, and can help establish the different pathophysiological pathways that cause or influence the varied expression of this disease and to know what percentage of patients may develop into the appearance bronchiectasis and / or bronchial obstruction fixed, and what factors predispose or condition this evolution.

It has also launched a project in collaboration with the Public Health Service of Barcelona aimed at determining the prevalence of sensitization to avian or fungal proteins in different work areas: Organizations of bird control, and workers in parks and gardens. For the development of this project the group also receives funding from the Instituto de Salud Carlos III (PI15 / 01954).

It has published a clinical guideline establishing a national consensus for the prevention and treatment of bronchial infection by Pseudomonas aeruginosa in patients with cystic fibrosis (PubMed No. 25614377). Likewise, the group has participated in the development of an international position paper about the research in COPD (Am J Respir Crit Care Med Vol 191, Iss 7 pp e4-e27).

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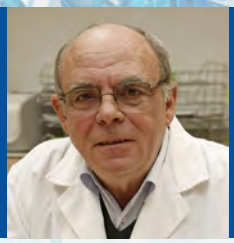
Group 17

Programme: Tuberculosis / Host-Pathogen Interactions

Lead Researcher: Ausina Ruiz, Vicente



Group members

STAFF MEMBERS: Lacoma de la Torre, Alicia | Latorre Rueda, Irene.

ASSOCIATED MEMBERS: Cardona Iglesias, Pere Joan | Domínguez Benítez, José Antonio | Giménez Pérez, Montserrat | Jordana Lluch, Elena | Molina Moya, Bárbara | Prat Aymerich, Cristina | Ruiz 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

GÓMEZ-PASTRANA D., DOMINGUEZ J.. Diagnosis of tuberculosis in children using mycobacteria-specific cytokine responses: Are there reasons for hope?. American Journal of Respiratory and Critical Care Medicine. 2015;192(4):409-410.

LATORRE I., LEIDINGER P., BACKES C., DOMINGUEZ J., DE SOUZA-GALVAO M.L., MALDONADO J. ET AL. A novel whole-blood miRNA signature for a rapid diagnosis of pulmonary tuberculosis. European Respiratory Journal. 2015;45(4):1173-1176.

MOLINA-MOYA B., LACOMA A., PRAT C., PIMKINA E., DIAZ J., GARCÍA-SIERRA N. ET AL. Diagnostic accuracy study of multiplex PCR for detecting tuberculosis drug resistance. Journal of Infection. 2015;71(2):220-230.

CARDONA P.-J.. The key role of exudative lesions and their encapsulation: Lessons learned from the pathology of human pulmonary tuberculosis. Frontiers in Microbiology. 2015;6(JUN).

JORDANA-LLUCH E., GIMENEZ M., DOLORES QUESADA M., RIVAYA B., MARCO C., JESÚS DOMINGUEZ M. ET AL. Evaluation of the broad-range PCR/ESI-MS technology in blood specimens for the molecular diagnosis of bloodstream Infections. PLoS ONE. 2015;10(10)

Highlights

Following the WHO priorities stated in the "Global Plan to Stop TB post 2015 global TB strategy", 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, MINECO, others), the industry and the Administration. We have also developed scientific collaboration with other CIBER.

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.

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Group 18

Programme: COPD / Pneumonia

Lead Researcher: Rello Condomines, Jordi

Group members

STAFF MEMBERS: Pérez Is, Laura.

ASSOCIATED MEMBERS: Boque Oliva, María del Carmen | Canalis Arrayas, Emilio | Gallego Díaz, Miguel | Luján Torne, Manel | Mendoza Asensi, Diego | Palomar Martínez, Mercedes | Riera del Brío, Jordi | Sandiumenge Camps, Alberto | Solé Violan, Jordi | Vidaur Tello, Loreto.

CONTRIBUTORS: Mazo Torre, Cristopher.

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

RELLO J., RIERA J., SERRANO R.. What's new in ventilator-associated pneumonia?. Intensive Care Medicine. 2015;41(11):1954-1956.

MARTÍN-LOECHES I., POVOA P., RODRÍGUEZ A., CURCIO D., SUAREZ D., MIRA J.-P. ET AL. Incidence and prognosis of ventilator-associated tracheobronchitis (TAVeM): A multicentre, prospective, observational study. The Lancet Respiratory Medicine. 2015.

DEMOULE A., RELLO J.. High flow oxygen cannula: the other side of the moon. Intensive Care Medicine. 2015;41(9):1673-1675.

BURGOS J., LUJAN M., LARROSA M.N., PEDRO-BOTET M.L., FONTANALS D., QUESADA M.D. ET AL. The problem of early mortality in pneumococcal pneumonia: A study of risk factors. European Respiratory Journal. 2015;46(2):561-564.

RAUTANEN A., MILLS T.C., GORDON A.C., HUTTON P., STEFFENS M., NUAMAH R. ET AL. Genome-wide association study of survival from sepsis due to pneumonia: An observational cohort study. The Lancet Respiratory Medicine. 2015;3(1):53-60.

Institution: Fund. Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR) · Hospital Vall d'Hebron
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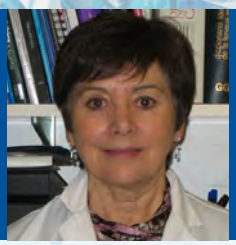
Group 19

Programme: Pneumonia / COPD / Host-Pathogen Interactions

Lead Researcher: Liñares Louzao, Josefina



Group members

STAFF MEMBERS: Cubero González, Meritxell | Euba Rementería, Begoña | Martí Martí, Sara | Moreno Cano, Francisco Javier.

ASSOCIATED MEMBERS: Ardanuy Tisaire, María Carmen | Ayats Ardite, Josefina | Calatayud Samper, Laura | García Somoza, María Dolores | Garmendia García, Juncal | Grau Garriga, Inmaculada | Niubo Bosch, Jordi | Pallarés 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

PUIG C., TIRADO-VELEZ J.M., CALATAYUD L., TUBAU F., GARMENDIA J., ARDANUY C. ET AL. Molecular characterization of fluoroquinolone resistance in nontypeable haemophilus influenzae clinical isolates. Antimicrobial Agents and Chemotherapy. 2015;59(1):461-466.

EARL C.S., KEONG T.W., AN S.-Q., MURDOCH S., MCCARTHY Y., GARMENDIA J. ET AL. Haemophilus influenzae responds to glucocorticoids used in asthma therapy by modulation of biofilm formation and antibiotic resistance. EMBO Molecular Medicine. 2015;7(8):1018-1033.

CUBERO M., GRAU I., TUBAU F., PALLARES R., DOMINGUEZ M.A., LINARES J. ET AL. Hypervirulent Klebsiella pneumoniae clones causing bacteraemia in adults in a teaching hospital in Barcelona, Spain (2007-2013). Clinical Microbiology and Infection. 2015;:-.

AGUINAGALDE L, DÍEZ-MARTÍNEZ R, YUSTE J, ROYO I, GIL C, LASA Í ET AL. Auranofin efficacy against MDR Streptococcus pneumoniae and Staphylococcus aureus infections.The Journal of antimicrobial chemotherapy. 2015;70(9):2608-17.

LLOBET E., MARTÍNEZ-MOLINER V., MORANTA D., DAHLSTROM K.M., REGUEIRO V., TOMASA A. ET AL. Deciphering tissue-induced Klebsiella pneumoniae lipid a structure. Proceedings of the National Academy of Sciences of the United States of America. 2015;112(46):E6369-E6378.

Highlights

1. The pneumococcal clonal complex (CC) 156 is one of the major CC causing invasive pneumocccal disease. We analyzed the evolution of CC156 by whole genome sequencing throughout 25 years in our area. This is a new approach in the analysis of pneumococcal evolution that allow us to describe subclones with recombination events and antibiotic-multiresistance.

2. We described a novel typing method for S.pneumoniae using selected surface proteins. After screening the allelic dispersion of 97 outer protein families in 19 complete pneumococcal genomes, 116 non-redundant surfotypes were identified. In order to establish a relationship between surfogroup and pathogenicity, the surfotypes of 95 clinical isolates with different serogroup/serotype combinations were analysed. We found a significant correlation between surfotype and pathogenic behaviour (primary invasive, opportunistic invasive and non-invasive). (Collaboration with Group-3- CIBERes)

3. We analysed the frequency and the clinical and molecular epidemiology of Klebsiella pneumoniae bacteraemia isolates obtained over a 7-year period (2007–2013) in HUB. Fifty-three of 878 Kpneumoniae invasive isolates (5.4%) showed a hypermucoviscous phenotype. Patients with magA+ and/or rmpA+ Klebsiella pneumoniae bacteraemia more frequently had pyogenic liver abscesses and pneumonia than patients without hypermucoviscosity genes.

4. The use of *in vitro* and *in vivo* model systems allowed us to compare Azithromycin's effects on infection by an Azithromycin-susceptible and an Azithromycin-resistant NT-H. influenzae clinical isolate and to establish associations between Azithromycin efficacy, dose, bacterial MIC, and bactericidal and immunomodulatory properties.

5. Using a mouse model of infection, we show that corticosteroid treatment promotes *H. influenzae* persistence. The corticosteroid-responsive genes showed elevated expression in *H.influenzae* within sputum from patients undergoing steroid treatment. Addition of corticosteroid to H.influenzae led to alteration in biofilm formation and enhanced resistance to azithromycin.

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Group 21

Programme: COPD / Lung Cancer / Fibrosis / Pulmonary Hypertension

Lead Researcher: Álvarez Martínez, Carlos José

Group members

STAFF MEMBERS: Castro Acosta, Ady Angelica | Fernández González, Saúl.

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

POZO-RODRÍGUEZ F, CASTRO-ACOSTA A, ALVAREZ CJ, LÓPEZ-CAMPOS JL, FORTE A, LÓPEZ-QUILEZ A ET AL. Determinants of between-hospital variations in outcomes for patients admitted with COPD exacerbations: findings from a nationwide clinical audit (AUDIPOC) in Spain.International journal of clinical practice. 2015;.

FANER R., GUTIERREZ-SACRISTAN A., CASTRO-ACOSTA A., GROSDIDIER S., GAN W., SÁNCHEZ-MAYOR M. ET AL. Molecular and clinical diseasome of comorbidities in exacerbated COPD patients. European Respiratory Journal. 2015;46(4):1001-1010.

PAESMANS M., GARCÍA C., WONG C.-Y.O., PATZ E.F., KOMAKI R., ESCHMANN S. ET AL. Primary tumour standardised uptake value is prognostic in nonsmall cell lung cancer: A multivariate pooled analysis of individual data. European Respiratory Journal. 2015;46(6):1751-1761.

GALIÈ N, HUMBERT M, VACHIERY JL, GIBBS S, LANG I, TORBICKI A ET AL. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). The European respiratory journal. 2015;46(4):903-75.

SÁNCHEZ-DE-LA-TORRE M., KHALYFA A., SÁNCHEZ-DE-LA-TORRE A., MARTÍNEZ-ALONSO M., MARTÍNEZ-GARCÍA M.A., BARCELO A. ET AL. Precision Medicine in Patients With Resistant Hypertension and Obstructive Sleep Apnea Blood Pressure Response to Continuous Positive Airway Pressure Treatment. Journal of the American College of Cardiology. 2015;66(9):1023-1032.

Highlights

The Group 21 CIBERES-imas12 Respiratory Disease, has updated its working hypothesis, and incorporated new lines of research and projects to traditional bronchogenic cancer and COPD.

Scientific focus: Study of determinants of health conditions in patients with respiratory diseases and clinical implications for the evaluation and update of action, identification of biomarkers (diagnostic, prognostic and therapeutic), new therapeutic options, quality improvement and optimization assistance protocols .

Main lines and task in 2015:

LUNG AND PLEURA CANCER: To identified a set of clinical-molecular variables that improve the prognostic and predictive TNM and clinical translation of results.

-Collaboration generation and initial analysis of database knowledge clinical molecular lung cancer stages I and IIs.

-Generation and maintenance Cohort resected cancer early.

COPD: To studied clinical, biological, microbiological, radiological, functional determinants of progression and severity. To evaluated the impact of different health care approaches in the management of disease activity.

-Participation COPD study EARLY (Determinants of the onset and progression of COPD in young adults) and BIOMCOPD (biomarkers and personalized clinical profiles in Chronic Obstructive Pulmonary Disease).

-Coordination DELICATO study (local Design and Implementation of clinical audits in different types of OLD).

-Updating and publishing new results CEPA (Spanish Cohort advanced COPD).

-Further analysis and publication AUDIPOC Spain AUDIPOC Europe 2008 and 2011.

-Participation planning next European Auditing.

PULMONARY HYPERTENSION: To established complementary network of research to identify new markers of activity and new therapeutic targets on Lung Hypertension, with clinical vocation.

-Participation EMPATHY project (New Markers and Therapeutic Targets for the Diagnosis and Treatment of Pulmonary Hypertension)

LUNG TRANSPLANT: To Collaborate with BIOBANK CIBERES

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E.mail: carlosjose.alvarez@salud.madrid.org · Web: http://imas12.h12o.es/index.php/areas-de-investigacion

Group 22

Programme: COPD / Lung Cancer / Pulmonary Hypertension

Lead Researcher: Gea Guiral, Joaquim

Group members

STAFF MEMBERS: 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 | Puig Vilanova, Ester | 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

MASA J.F., DURAN-CANTOLLA J., CAPOTE F., CABELLO M., ABAD J., GARCÍA-RIO F. ET AL. Efficacy of home single-channel nasal pressure for recommending continuous positive airway pressure treatment in sleep apnea. Sleep. 2015;38(1):13-21.

AGUSTI A., ANTO J.M., AUFFRAY C., BARBE F., BARREIRO E., DORCA J. ET AL. Personalized respiratory medicine: Exploring the horizon, addressing the issues: Summary of a BRN-AJRCCM workshop held in Barcelona on June 12, 2014. American Journal of Respiratory and Critical Care Medicine. 2015;191(4):391-401.

BARREIRO E., SZNAJDER J.I., NADER G.A., BUDINGER G.R.S.. Muscle dysfunction in patients with lung diseases a growing epidemic. American Journal of Respiratory and Critical Care Medicine. 2015;191(6):616-619.

GUERRA S., HALONEN M., VASQUEZ M.M., SPANGENBERG A., STERN D.A., MORGAN W.J. ET AL. Relation between circulating CC16 concentrations, lung function, and development of chronic obstructive pulmonary disease across the lifespan: A prospective study. The Lancet Respiratory Medicine. 2015;3(8):613-620.

MESSAGGI-SARTOR M., GUILLEN-SOLA A., DEPOLO M., DUARTE E., RODRÍGUEZ D.A., BARRERA M.-C. ET AL. Inspiratory and expiratory muscle training in subacute stroke. Neurology. 2015;85(7):564-572.

Highlights

Our group has continued its evolution, incorporating new pre-doctoral, postdoctoral and Senior researchers. Collaborations with groups of CIBERBBN are still very active, and a mixed unit has been constituted. The group has also maintained its national and international collaborations, and is preparing a project for the 2020 European initiative. With regard to production, it has remained high and stable [32 originals, several reviews, different chapters of a SEPAR clinical guidelines, and 2 doctoral theses]. In addition, we have presented numerous communications at international conferences, and eight invited lectures (6 international). Some of our researchers are members of the editorial boards of journals such as Am J Respir Crit Care Med (highest IF in our field), J Appl Physiol and Arch Bronconeumol (the Editor in Chief is a member of the group), and are also reviewers for 12 indexed journals and 5 agencies, including the European Commission, and some UK, the Netherlands and France foundations, as well as for the FIS and the Plan Nacional programs. In terms of resources we have obtained different competitive grants (6 active projects, including one from the Plan Nacional and one FIS) and 17 ongoing clinical trials (10 of them started in 2015). In educational activities related to research, the group leader continues as member of the UPF doctoral program and one researcher is the director of a inter-university Master in respiratory research. Group members are also continuing their activities in national and international research networks of excellence, like the Barcelona Respiratory Network (BRN). As a result of all of this, the group has been ranked in the highest tertile of the CIBERES (6th out of 34 groups), confirming its qualification as “excellent” given by the external scientific committee. From an institutional perspective, the head of the group has been the CIBERES deputy director.

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Group 23

Programme: Acute Lung Injury

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, José Angel | Martínez Caro, Leticia | Peñuelas Rodríguez, 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

LORENTE J.A., BALLEN-BARRAGAN A., HERRERO R., ESTEBAN A.. Acute respiratory distress syndrome: Does histology matter?. Critical Care. 2015;19(1):-.

MARTÍNEZ-CARO L., NIN N., SÁNCHEZ-RODRÍGUEZ C., FERRUELO A., EL ASSAR M., DE PAULA M. ET AL. Inhibition of nitro-oxidative stress attenuates pulmonary and systemic injury induced by high-tidal volume mechanical ventilation. Shock. 2015;44(1):36-43.

COUDROY R., JAMET A., PENUELAS O., THILLE A.W.. Use of Type III procollagen measurement as predictor of lung fibroproliferation in ARDS: early measurement for earlier antifibroproliferative therapy?. Intensive Care Medicine. 2015;41(6):1159-1160.

SUTHERASAN Y., PENUELAS O., MURIEL A., VARGAS M., FRUTOS-VIVAR F., BRUNETTI I. ET AL. Management and outcome of mechanically ventilated patients after cardiac arrest. Critical Care. 2015;19(1):-.

MURIEL A., PENUELAS O., FRUTOS-VIVAR F., ARROLIGA A.C., ABRAIRA V., THILLE A.W. ET AL. Impact of sedation and analgesia during noninvasive positive pressure ventilation on outcome: a marginal structural model causal analysis. Intensive Care Medicine. 2015;41(9):1586-1600.

Highlights

In the line of ARDS, we have worked at four levels. At the cellular level with the model of stretch of alveolar cells, analyzing the response of inflammatory mediators, microRNAs and cell-binding proteins. At the level of our ex-vivo rat model, we analyzed association of the microRNA to 27, as well as after his inhibiting. At the vivo level, with the model of VILI, we analyzed the inhibition of nitro-oxidative stress on pulmonary and vascular injury. At the human level, we have analyzed, along with the Group at the University of Poitiers Type III procolagen as a predictor of fribroproliferacion in the lung in the ARDS.

One of the most important findings of our group, has been the description of a fenotype that is characteristic of patients with clinical criteria for ARDS and histological pattern of Diffuse Alveolar Damage. The mechanical ventilation line has led to results more relevant analysis of the effect of sedation in the evolution of the ventilation not invasive, the evolution of patients with mechanical ventilation after a cardiac arrest , and the incidence and outcome of the acquired muscle weakness in ICU, in patients with mechanical ventilation. This line, in a wide international cooperation, remains very active. At this moment we have two manuscripts under review (ability to predict prolonged mechanical ventilation, and the effect of hypercapnia on the outcome of patients with VM).

In the line of prevention of respiratory infections, we have studied in a model of rat in vivo with selective digestive decontamination, the effect of this in animals with and without harmful mechanical ventilation. This study has been the thesis of a member of the Group (Yeny Rojas) which has been read in January 2016.

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Group 24

Programme: Sleep Apnoeas Syndrome / Pulmonary Hypertension

Lead Researcher: Obeso Cáceres, Ana

Group members

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

ASSOCIATED MEMBERS: Agapito Serrano, María Teresa | Gallego Martín, Teresa | Gómez Niño, Ángela | 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 chronic hypoxia and obesity.
- Biomarkers of the hypoxic damage.
- Chronic intermittent hypoxia and spontaneous tumorigenesis.
- Pulmonary hypertension.

Most relevant scientific articles

PRIETO-LLORET J., RAMÍREZ M., OLEA E., MORAL-SANZ J., COGOLLUDO A., CASTANEDA J. ET AL. Hypoxic pulmonary vasoconstriction, carotid body function and erythropoietin production in adult rats perinatally exposed to hyperoxia. Journal of Physiology. 2015;593(11):2459-2477.

OLEA E., RIBEIRO M.J., GALLEGO-MARTÍN T., YUBERO S., RIGUAL R., MASA J.F. ET AL. The carotid body does not mediate the acute ventilatory effects of leptin. Advances in Experimental Medicine and Biology. 2015;860:379-385.

SACRAMENTO J.F., GONZÁLEZ C., GONZÁLEZ-MARTÍN M.C., CONDE S.V.. Adenosine Receptor Blockade by Caffeine Inhibits Carotid Sinus Nerve Chemosensory Activity in Chronic Intermittent Hypoxic Animals. Advances in Experimental Medicine and Biology. 2015;860:133-137.

SACRAMENTO J.F., RIBEIRO M.J., YUBERO S., MELO B.F., OBESO A., GUARINO M.P. ET AL. Disclosing caffeine action on insulin sensitivity: Effects on rat skeletal muscle. European Journal of Pharmaceutical Sciences. 2015;70:107-116.

Highlights

FINANCIAL SUPPORT OBTAINED

BFU2012-37459. Ministerio de Economía y Competitividad. DGICYT (2012-2014). Project title: Physiopathologicl mechanisms of the cardiovascular alterations encountered in the obstructive sleep apnea: foundations for therapeuctic designs. Budget: 222.300€. PI. Constancio Gonzalez / Asuncion Rocher since July 2015.

Asociación Española Contra el Cancer (A predoctoral Fellowship in Oncology) (2013-2015). Given to the Proyect entitled: Obstructive Sleep Apnoea Syndrome and Cancer. Budget: 56.000€. IP del Proyecto. Constancio Gonzalez / Ana Obeso since July 2015.

FELLOWSHIP RECIPIENT: TERESA GALLEGO MARTÍN

1. Adult animals that have been exposed to perinatal hyperoxia, showing loss of hypoxic pulmonary vasoconstriction, associated with early postnatal oxidative damage that can be corrected with dietary antioxidant. Perinatal hyperoxia damage the function of the carotid body chemoreceptors which is not prevented by antioxidant diet. Plasma levels of erythropoietin increased by hypoxia are unaffected by perinatal hyperoxia. These facts may be relevant in clinical situations such as chronic obstructive diseases and general anesthesia.
2. Given that leptin is a hormone primarily produced by adipose tissue and plays an important role in the control of food intake and energy expenditure, and is involved in obesity and breathing disorders such as OSA and recently it has been involved in ventilation control, we have confirmed that leptin produces stimulation of ventilation, checking that the ventilatory response is not mediated by chemoreceptors of the carotid body, even though they have receptors for leptin.
3. We demonstrate that adenosine contributes to fix CSN basal activity during CIH, being also involved in hypoxic CB chemotransduction. Adenosine participes in CB sensitization in CB during CIH.
4. Caffeine is a nonselective adenosine receptor antagonist, which are involved in the regulation of glucose metabolism in skeletal muscle and in adipose tissue inhibit lipolysis (obesity). We have seen that: caffeine administered acutely decreases insulin sensitivity in skeletal muscle in a dose dependent manner, an effect that is mediated by adenosine receptors A1 and A2b; also significantly it reduces GLUT4 expression, but not AMPkinasa expression in skeletal muscle.

Institution: Universidad de Valladolid · **Contact:** Facultad de Medicina · c/ Ramón y Cajal, 7. 47005 Valladolid
Tel.: 983 423 089 · E.mail: aobeso@ibgm.uva.es

Group 26

Programme: Pneumonia

Lead Researcher: Pérez Trallero, Emilio

Group members

STAFF MEMBERS: Esnal Lasarte, Olatz | Tamayo Oya, Esther.

ASSOCIATED MEMBERS: Alonso Asencor, Marta | Cilla Eguiluz, Carlos Gustavo | Ercibengoa Arana, María | González Pérez Yarza, Eduardo | Marimón Ortiz de Zarate, José Mª | 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

COSME A., LIZASOAN J., MONTES M., TAMAYO E., ALONSO H., MENDARTE U. ET AL. Antimicrobial Susceptibility-Guided Therapy Versus Empirical Concomitant Therapy for Eradication of Helicobacter pylori in a Region with High Rate of Clarithromycin Resistance. Helicobacter. 2015;:-.

MARIMON J.M., MORALES M., CILLA G., VICENTE D., PÉREZ-TRALLERO E.. Detection of bacteria and viruses in the pleural effusion of children and adults with community-acquired pneumonia. Future Microbiology. 2015;10(6):909-915.

PÉREZ-YARZA E.G., MORENO-GALDO A., RAMILO O., RUBI T., ESCRIBANO A., TORRES A. ET AL. Risk factors for bronchiolitis, recurrent wheezing, and related hospitalization in preterm infants during the first year of life. Pediatric Allergy and Immunology. 2015;26(8):797-804.

CARBONELL-ESTRANY X, PÉREZ-YARZA EG, GARCÍA LS, GUZMÁN CABAÑAS JM, BÒRIA EV, ATIENZA BB ET AL. Long-Term Burden and Respiratory Effects of Respiratory Syncytial Virus Hospitalization in Preterm Infants-The SPRING Study.PloS one. 2015;10(5):e0125422.

Highlights

MAIN PROJECTS

During 2015 we began a collaboration with the European project from the I-MOVE (Influenza - Monitoring Vaccine Effectiveness) network within the Horizon 2020 framework entitled: "Study of cases and controls to assess the effectiveness of influenza vaccine against hospitalization in people over 64 years in Spain" (Grant Agreement: 634,446, PI: GCE).

As a result of Project FIS PI13/01708 ("*Streptococcus pneumoniae* serotyping by multiplex-PCR and reverse hybridization strip"), two prototypes have been validated, being the second one ready for marketing.

TRAINING

The group has a University Professor (EPT) and a Titular Professor who during 2015 was accredited by ANECA University Professor (EGPY).

MFR developed for 6 months a research program in the center Max von Pettenkofer-Institute, University Research Institute.

PHD AND MASTER PROGRAMS

During 2015, it was imparted the VI Master of the University of the Basque Country (UPV / EHU), in an academic course of 40-hour entitled: "Preventive Interventions for Communicable Diseases. EPT organized and gave classes with the participation as teachers of another 5 members of the group (EPT, JMM, MMR, GCE, DVA).

Group members have participated in three doctoral programs at the University of the Basque Country. Programs: Medicine and Surgery (EPT and EGPZ); Research in Biomedicine (EGPY); Preventive Medicine and Public Health (EPT, JMM, MMR, GCE, DVA).

OUTSTANDING RESULTS

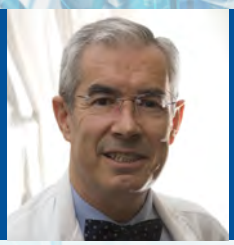
As a result of our research in the "Multidisciplinary translational research in respiratory tract infections-MARTIN project", within the Corporate Research Program on Pneumonia, our group has discovered and described in 2015 a new species of *Nocardia* (Ercibengoa M, Bell M, Marimon JM, Humrighouse B, Klenk HP, Schumann P, E. Perez –Trallero. N *Nocardia donostiensis* sp. nov. , isolated from human respiratory specimens. Antonie van Leeuwenhoek 2016 [accepted for publication]).

Institution: Asociación Instituto Biodonostia · **Contact:** Hospital Donostia · Paseo Dr. Beguiristain, s/n. 20014 San Sebastián · Tel.: 943 007 153 · E.mail: mikcrobiol@terra.com

Group 27

Programme: Pneumonia / Tuberculosis

Lead Researcher: Bouza Santiago, Emilio



Group members

STAFF MEMBERS: Herranz Martín, Marta | Iglesias Arribas, Cristina.

ASSOCIATED MEMBERS: Alcalá Hernández, Luis | Barrio Gutiérrez, José María | Cercenado Mansilla, Emilia | Fernández del Rey, Rocío | García de Viedma Del Alamo, Dario | Guinea Ortega, Jesús Vicente | Hortal Iglesias, Francisco Javier | Marín Arriaza, María de las Mercedes | Martín Rabadán 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

DE EGEA V., MUNOZ P., VALERIO M., DE ALARCON A., LEPE J.A., MIRO J.M. ET AL. Characteristics and outcome of Streptococcus pneumoniae endocarditis in the XXI century: A systematic review of 111 cases (2000-2013). Medicine (United States). 2015;94(39):e1562-.

GONZÁLEZ-DEL VECCHIO M., CATALAN P., DE EGEA V., RODRÍGUEZ-BORLADO A., MARTOS C., PADILLA B. ET AL. An algorithm to diagnose influenza infection: evaluating the clinical importance and impact on hospital costs of screening with rapid antigen detection tests. European Journal of Clinical Microbiology and Infectious Diseases. 2015;34(6):1081-1085.

BUNSOW E., GONZÁLEZ-DEL VECCHIO M., SÁNCHEZ C., MUNOZ P., BURILLO A., BOUZA E.. Improved sepsis alert with a telephone call from the clinical microbiology laboratory a clinical trial. Medicine (United States). 2015;94(39):e1454

MARCOS-ZAMBRANO L.J., ESCRIBANO P., SANGUINETTI M., GÓMEZ G. DE LA PEDROSA E., DE CAROLIS E., VELLA A. ET AL. Clusters of patients with candidaemia due to genotypes of Candida albicans and Candida parapsilosis: Differences in frequency between hospitals. Clinical Microbiology and Infection. 2015;21(7):677-683.

MARTÍNEZ-JIMENEZ M.C., MUNOZ P., VALERIO M., ALONSO R., MARTOS C., GUINEA J. ET AL. Candida biomarkers in patients with candidaemia and bacteraemia. Journal of Antimicrobial Chemotherapy. 2015;70(8):2354-2361.

Highlights

During the year 2015, our group has been working in different aspects of respiratory infections. I will summarize some of the achievements, excluding those occurring in the field of tuberculosis that will be report edelswhere.

Field of pneumococcal and other respiratory bacterial infections.

We described the present situation of Endocarditis caused by Streptococcus pneumonia, an uncommon but devatastating complication of pneumococcal pneumonia. We depicted criteria for suspicion and management. Characteristics and Outcome of Streptococcus pneumoniae Endocarditis. Medicine. 2015 Sep;94(39):e1562.

We participated in important practice Guidelines

- Executive summary of the diagnosis and treatment of bacteremia and endocarditis due to Staphylococcus aureus. A clinical guideline From the Spanish Society of Clinical Microbiology and Infectious Diseases (SEIMC). EnfermInfeccMicrobiolClin. 2015 Nov;33(9):626-32.
- Managing skin and soft-tissue infection and nosocomial pneumonia caused by MRSA: a 2014 follow-up survey. Int J AntimicrobAgents. 2015 Apr 24;45 Suppl 1:S1-14.
- We participated in assessing the value of scores to screen patients with pneumonia caused by MDR microorganisms Individualizingrisk of multidrug-resistantpathogens in community-onset pneumonia. PLoSOne. 2015 Apr 10;10.

In the field of viral respiratory infections.

We remained active in the field of Influenza improving the value of present diagnostic algorythms. An algorithm to diagnose influenza infection. Eur J ClinMicrobiolInfectDis.2015 Jun;34(6):1081-5. PMID: 25620782.

To the field of sepsis in general, and particularly to contributions to sepsis alert in hospitals.

We demonstrate the alert and knowledge situation in general hospitals and the value of Blood Cultures Request as an alarm sign for sepsis. Medicine (Baltimore). 2015 Sep;94(39):e1454.

In the field of mycotic infections.

We kept very active in the implementation and evaluation of Antifungal steward ship programs, being in the field one of the leading study groups.

We incorporated a new species of Aspergillus to the scientific knowledge and also improved the diagnostic interpretation of Aspergillus isolation in respiratory samples.

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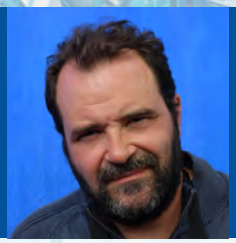
Group 28

Programme: Acute Lung Injury / Pulmonary Hypertension
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. 3) microRNAs.

Most relevant scientific articles

PRIETO-LLORET J., RAMÍREZ M., OLEA E., MORAL-SANZ J., COGOLLUDO A., CASTANEDA J. ET AL. Hypoxic pulmonary vasoconstriction, carotid body function and erythropoietin production in adult rats perinatally exposed to hyperoxia. Journal of Physiology. 2015;593(11):2459-2477.

MORALES-CANO D., MORENO L., BARREIRA B., PANDOLFI R., CHAMORRO V., JIMENEZ R. ET AL. Kv7 channels critically determine coronary artery reactivity: Left-right differences and down-regulation by hyperglycaemia. Cardiovascular Research. 2015;106(1):98-108.

TORAL M., ROMERO M., JIMENEZ R., MAHMOUD A.M., BARROSO E., GÓMEZ-GUZMAN M. ET AL. Carnitine palmitoyltransferase-1 up-regulation by PPAR-β/δ prevents lipid-induced endothelial dysfunction. Clinical Science. 2015;129(9):823-837.

JIMENEZ R., LÓPEZ-SEPULVEDA R., ROMERO M., TORAL M., COGOLLUDO A., PÉREZ-VIZCAINO F. ET AL. Quercetin and its metabolites inhibit the membrane NADPH oxidase activity in vascular smooth muscle cells from normotensive and spontaneously hypertensive rats. Food and Function. 2015;6(2):409-414.

TORAL M., GÓMEZ-GUZMAN M., JIMENEZ R., ROMERO M., ZARZUELO M.J., UTRILLA M.P. ET AL. Chronic peroxisome proliferator-activated receptorβ/δ agonist GW0742 prevents hypertension, vascular inflammatory and oxidative status, and endothelial dysfunction in diet-induced obesity. Journal of Hypertension. 2015;33(9):1831-1844.

Highlights

PROJECT FUNDED: Micrornas involved in pulmonary vascular dysfunction: pathohysiological and therapeutic implications. SAF2014- 55399R (01/01/2015-31/12/2016) 110.000 €.

PROJECT FUNDED: Therapeutic potential of exosomes derived from mesenquimal cells an endothelial progenitor cells in bronchopulmonart displasia and pulmonary hypertension.

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

Group 29

Programme: Acute Lung Injury

Lead Researcher: Villar Hernández, Jesús

Group members

STAFF MEMBERS: 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 Mendez, 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 for common genetic activation and signalling pathways among ARDS, Asthma and Pulmonary Fibrosis.

Most relevant scientific articles

VILLAR J., FERNÁNDEZ 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. 2015;43(2):346-353.

CABRERA-BENITEZ N.E., VALLADARES F., GARCÍA-HERNANDEZ S., RAMOS-NUEZ A., MARTÍN-BARRASA J.L., MARTÍNEZ-SAAVEDRA M.-T. ET AL. Altered profile of circulating endothelial-derived microparticles in ventilator-induced lung injury. Critical Care Medicine. 2015;43(12):e551-e559.

ACOSTA-HERRERA M., PINO-YANES M., BLANCO J., BALLESTEROS J.C., AMBROS A., CORRALES A. ET AL. Common variants of NFE2L2 gene predisposes to acute respiratory distress syndrome in patients with severe sepsis. Critical Care. 2015.

ACOSTA-HERRERA M., LORENZO-DIAZ F., PINO-YANES M., CORRALES A., VALLADARES F., KLASSERT T.E. ET AL. Lung transcriptomics during protective ventilatory support in sepsis-induced acute lung injury. PLoS ONE. 2015;10(7).

VILLAR J., CABRERA-BENITEZ N.E., VALLADARES F., GARCÍA-HERNANDEZ S., RAMOS-NUEZ, MARTÍN-BARRASA J.L. ET AL. Tryptase is involved in the development of early ventilator-induced pulmonary fibrosis in sepsis-induced lung injury. Critical Care. 2015;19(1).

Highlights

PROJECTS:

PI13/0119: Randomized Study "NAVA in patients with Acute Respiratory Failure". ISCIII. IP: Jesus Villar. • PI2012 FMM: Randomized Study "Evaluate 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. • REGPOTFP7-2012-2013-1: IMBRAIN: Improvement of Biomedical Research and Innovation in 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-steroids. Junta Andalucía. Co-IP: Carlos Flores. • PI14-00844: Implicaciones de la susceptibilidad genética y alteraciones del microbioma en la patogénesis del ARDS. ISCIII. IP: Carlos Flores.

CONTRACTS FOR RESEARCH PERSONNEL

CD11/00104: Post- Doctoral Sara Borrel. • FI11/00074: Predoctoral Training Health Research • FI12/00493: Predoctoral Training Health Research. • CD13/00304: Post- Doctoral Sara Borrel.

PATENTS

Title/Certificate Invention Patent ES2385443, P201031978. • Title/Certificate Invention Patent ES2408281, P201131785 • Title/Certificate Invention Patent ES2481990, P201232075 • Patent Application: P201531475 "Method to determine geographical origin of a subject"

INTERNATIONAL COLLABORATION:

Arthur Slutsky: Keenan Research Center for Biomedical Science, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto. • Robert Kacmarek: Department Respiratory Care, Massachusetts General Hospital, Boston. • Joe Garcia: Arizona Health Sciences Center, University of Arizona, Tucson. • Shwu-Fan Ma: Section Pulmonary and Critical Care Medicine, University Chicago, Illinois.

OTHER CONSIDERATIONS:

Jesus Villar:Referee for New England Journal Medicine, AJRCC, Critical Care Medicine, Intensive Care Medicine, Critical Care, Minerva Anestesiologica • Jesus Villar:Member, Editorial Board Intensive Care Monitor, Faculty 1000. • Carlos Flores:Member, Editorial Board of ISRN Pulmonology, Clinical Antiallergy antiinflamatory Drugs.

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Group 30

Programme: Lung Cancer / COPD / Pneumonia
Lead Researcher: Monsó Molas, Eduard

Group members

STAFF MEMBERS: García Núñez, Mª Ángeles | Millares Costas, Laura | Parraga Niño, Noemí | Setó Gort, Laia.

ASSOCIATED MEMBERS: Andreo García, Felipe Cristobal | Castellà Fernández, Eva | Cubero de Frutos, Noelia | García Olive, Ignasi | Llatjos Sanuy, Maria | López Alujes, Pedro Enrique | Marín Tapia, Alicia | Martínez Rivera, Carlos | Mateu Pruñonosa, Lourdes | Modol Deltell, Josep Mª | Morera Prat, José | Pedro Botet Montoya, Mª 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 has coordinated the Strategic CRP on Lung Cancer (2013-2015). The main objectives are the clinical and molecular characterization of lung early stage cancer. 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 CRP including patients in a cohort of initial 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 CRP 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 ICU (NNPNV) (NEUNOS14) about the incidence of this complication in hospitals in our area.
- 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; evaluates the Legionella molecular typing techniques.
- CRP Pulmonary Hypertension: The group participates in the CRP which will be executed in 2016.

Most relevant scientific articles

SANZ-SANTOS J., SERRA M., GALLEGO M., MONTON C., COSIO B., SAULEDA J. ET AL. Determinants of false-negative results in non-small-cell lung cancer staging by endobronchial ultrasound-guided needle aspiration. European Journal of Cardio-thoracic Surgery. 2015;47(4):642-647.

BURGOS J., LUJAN M., LARROSA M.N., PEDRO-BOTET M.L., FONTANALS D., QUESADA M.D. ET AL. The problem of early mortality in pneumococcal pneumonia: A study of risk factors. European Respiratory Journal. 2015;46(2):561-564.

MILLARES L., PÉREZ-BROCAL V., FERRARI R., GALLEGO M., POMARES X., GARCÍA-NUNEZ M. ET AL. Functional metagenomics of the bronchial microbiome in COPD. PLoS ONE. 2015;10(12).

MILLARES L., SERRA M., ANDREO F., SANZ-SANTOS J., MONTON C., GRIMAU C. ET AL. Assessment of methylation status of locoregional lymph nodes in lung cancer using EBUS-NA. Clinical and Experimental Metastasis. 2015;32(7):637-646.

POMARES X., MONTON C., BARE M., PONT M., ESTIRADO C., GEA J. ET AL. Emergency Hospital Care for Exacerbation of COPD: Is Inhaled Maintenance Therapy Modified?. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2015.

Highlights

Coordination of the Lung Cancer CRP (2013-15).

The Group is PI in the Integrated Research Projects of Cancer and Interventional Bronchology_ SEPAR, coordinating the management of clinical information from the participating cohorts and the collection and processing of biological samples.

Cooperation agreements with Cancer RETIC_ ISCIII and the company AMADIX for innovation in oncology diagnostic tools.

Epigenetic analyses are feasible in EBUS-NA cell blocks and may identify methylation patterns associated with worse prognosis. Methylation of p16 and APC genes in NSCLC patients was associated with advanced staging and lower 6-month survival. Continuity of the project in the Lung Cancer CRP 2016-2018.

COPD CRP, the group has maintained the research on respiratory microbiology and the relationship with the disease. Functional changes during exacerbation have been described by shotgun sequencing. These changes are associated to Carbohydrate metabolism and Cancer and Cell growth and Death, with potentially significance in the natural history of COPD patients suffering frequent exacerbations, when COPD risk factor for lung cancer.

Group PI in the multicentric and coordinated IP PI15 / 00167 project “Respiratory Microbiome in COPD”, to start in 2016, and workpackage in the CRP_COPD.

PI of the NEUNOS14 project. The 1st phase is completed. The incidence of nosocomial pneumonia and characterization of patients affected has been described before implementing preventive action. The 2nd phase has been initiated.

Cooperation agreement with the Agencia de Salud Pública de Cataluña that certifies the group as a reference center for typing Legionella in Catalonia.

Patent P201531409 and cooperation agreeement with GAS Natural Fenosa company for extensión thereorf.

The group has took part in the preparation of Pulmonary Hypertension CRP, to run from 2016, as a research line, assuming responsibilities in the work packages to be developed.

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Group 31

Programme: COPD

Lead Researcher: Ruiz Cabello Osuna, Jesús

Group members

STAFF MEMBERS: Santos Oviedo, Arnoldo de Jesús.

ASSOCIATED MEMBERS: Benito Vicente, Marina | Bilbao Luri, Izaskun | Herranz Rabanal, Fernando | Izquierdo García, José Luís | Lechuga Vieco, Ana Victoria | Pellico Sáez, 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

GROULT H., RUIZ-CABELLO J., PELLICO J., LECHUGA-VIECO A.V., BHAVESH R., ZAMAI M. ET AL. Parallel multifunctionalization of nanoparticles: A one-step modular approach for in vivo imaging. Bioconjugate Chemistry. 2015;26(1):153-160.

GONZÁLEZ-VALDES I., HIDALGO I., BUJARRABAL A., LARA-PEZZI E., PADRON-BARTHE L., GARCÍA-PAVIA P. ET AL. Bmi1 limits dilated cardiomyopathy and heart failure by inhibiting cardiac senescence. Nature Communications. 2015;6.

SALINAS B., RUIZ-CABELLO J., LECHUGA-VIECO A.V., BENITO M., HERRANZ F.. Surface-Functionalized Nanoparticles by Olefin Metathesis: A Chemoselective Approach for in Vivo Characterization of Atherosclerosis Plaque. Chemistry - A European Journal. 2015;21(29):10450-10456.

PÉREZ-MEDINA C., TANG J., ABDEL-ATTI D., HOGSTAD B., MERAD M., FISHER E.A. ET AL. PET imaging of tumor-associated macrophages with ⁸⁹Zr-labeled high-density lipoprotein nanoparticles. Journal of Nuclear Medicine. 2015;56(8):1272-1277.

ALCOCER-GÓMEZ E., ULECIA-MORON C., MARIN-AGUILAR F., RYBKINA T., CASAS-BARQUERO N., RUIZ-CABELLO J. ET AL. Stress-Induced Depressive Behaviors Require a Functional NLRP3 Inflammasome. Molecular Neurobiology. 2015.

Highlights

Throughout 2015, the Group 31, led by Dr. Ruiz-Cabello has participated in seven competitive projects funded by several agencies (ISCIII; Mineco and EU Comission), focused mainly on COPD, ALI, pulmonary hypertension, atherosclerosis and Nanomedicine. Along these this year we have just begun two, one funded by the Spanish Ministry of Economy for the early detection of pulmonary hypertension using advanced image methods (SAF2014-58920-R) and another, funded by the Carlos III Institute of Health to study the effect of HIF-1 inhibition on atherosclerosis progression (PI14-01427), that will be also relevant in the context of Pulmonary Hypertension. For the development of these projects and publications the group has continued to work actively with other national and international CIBER groups. We have worked with the Tuberculosis Research program, especially for the processing, measuring and analyse of urine samples from this disease in collaboration with the group of Dr. Vicente Ausina 17 (Cristina Prat and Jose A. Dominguez). This project has been funded by SEPAR.

In the area of training and formation, the group presented a doctoral thesis, which was defended by the international student Hugo Groult on 15 July 2015 at the Complutense University of Madrid, awarded with the cum laude excellence mark. This thesis summarizes part of work done with the European project Pinet coordinated by CIBERES. We have attended a total of 5 international meetings, an abstract, presented by Juan Pellico, was selected as the best oral presentation at the European Molecular Imaging Meeting in Tübigen (Germany). Finally, we actively participate in the management of CIBERES, as members of the Committee on teaching and since December 2015 as deputy director of CIBERES.

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Group 32

Programme: Host-Pathogen Interactions

Lead Researcher: Ortín Montón, Juan

Group members

STAFF MEMBERS: González Sanz, Rubén | Marcos Villar, Laura | Pazo Fernández, Alejandra | Vázquez Alcaraz, Mónica.

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

Main lines of research

- Mechanism of influenza virus interaction with the host cell.
- Mecahnisms of pathogeinicity of influenza virus.
- Study of human respiratory syncityal virus and metapneuomovirus glycoproteins.

Most relevant scientific articles

Falcon A., Cuevas M.T., Rodríguez-Frandsen A., Reyes N., Pozo F., Moreno S. et al. CCR5 deficiency predisposes to fatal outcome in influenza virus infection. Journal of General Virology. 2015;96(8):2074-2078.

Ortin J., Martín-Benito J.. The RNA synthesis machinery of negative-stranded RNA viruses. Virology. 2015;479-480:532-544.

Gilman M.S.A., Moin S.M., Mas V., Chen M., Patel N.K., Kramer K. et al. Characterization of a Prefusion-Specific Antibody That Recognizes a Quaternary, Cleavage-Dependent Epitope on the RSV Fusion Glycoprotein. PLoS Pathogens. 2015;11(7).

Ver LS, Marcos-Villar L, Landeras-Bueno S, Nieto A, Ortín J. The Cellular Factor NXP2/MORC3 Is a Positive Regulator of Influenza Virus Multiplication.Journal of virology. 2015;89(19):10023-30.

Trento A, Ábrego L, Rodríguez-Fernández R, González-Sánchez MI, González-Martínez F, Delfraro A et al. Conservation of G-Protein Epitopes in Respiratory Syncytial Virus (Group A) Despite Broad Genetic Diversity: Is Antibody Selection Involved in Virus Evolution?. Journal of virology. 2015;89(15):7776-85.

Highlights

Influenza virus establishes a complex network of interactions with the host cell, accordingly it is known that its pathogenicity depends on a large number of virus-host interactions. This suggests that efficient replication of influenza viruses is based on a set of virus-host cell interactions in which there are two factors involved; the viral pathogenicity determinants and the genetic determinants of the host.

We have characterized some cellular factors that interact with influenza virus proteins and modulate its replicative cycle such as the cellular factor NXP2 / MORC3, which is a positive modulator of viral replication in cultured cells. On the other hand we have characterized a risk factor for the human population, the chemokine receptor CCR5, whose presence in homozygous of a deleted form, increases very significantly the fatality rate by influenza virus infection.

Progress has also been attained in understanding of the F glycoprotein of human respiratory syncytial virus (hRSV) and human metapneumovirus (hMPV), two highly related viruses at the clinic and genetic level. The hMPV F protein was purified to homogeneity in its postfusion conformation, allowing crystallization and determination of its atomic structure. Comparison of this structure with those of other paramyxovirus F proteins revealed many similarities with that of hRSV F but more differences with its counterparts of two other paramyxoviruses (PIV3 and NDV).

Despite crossreactivity of hRSV and hMPV F glycoproteins with a monoclonal antibody, polyclonal sera raised against either protein failed to exhibit crossreactivity. This prompted us the design of chimeric F proteins that could be used as “universal” vaccine against the *Pneumovirinae*.

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Group 33

Programme: Acute Lung Injury / Pneumonia
Lead Researcher: Blanch Torra, Lluis

Group members

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

ASSOCIATED MEMBERS: Artigas Raventos, Antonio | Fernández Fernández, Rafael | Ferrer Roca, Ricard | López Aguilar, Josefina | Martín Loeches Carrondo, Ignacio Esteban | Martínez Pérez, Melcior | Ochagavia Calvo, Ana | Sales López, Bernat | Valles Daunis, Jorge | Villagra García, Ana María

Main lines of research

The main research lines of our group combine preclinical and clinical studies from a translational perspective and are focused into two main areas:

- Acute Lung Injury: Early diagnosis, pathophysiology and new therapeutic strategies in acute lung injury (CIBERES Groups 23, 29 and 33)
- Pneumonia: Project of Translational Multidisciplinary Research in Respiratory Tract Infections. (CIBERES Groups 14 and 33).

We are interested in the characterization of molecular, cellular and physiological changes related to the development of acute lung injury, as well as the impact on other organs or systems and the development of new therapeutic strategies.

LINES:

1. monitoring of critically ill patients: Non-invasive monitoring • Development of software for continuous monitoring of critically ill patients on mechanical ventilation (MV). Processing and storing digital signals from monitoring equipment or ventilators. • Software for interpretation, analysis and multimodal-multichannel physiological-diagnosed computerized interpretation of biomedical signals.
2. Development of experimental models (animals and cell cultures) for the characterization of new mechanisms involved in acute lung injury (ALI) and prevention strategies. (CIBERES Groups 23, 29 and 33).
3. Development of new therapeutic strategies for ALI and ARDS management: Pharmacological treatment (systemic or inhaled) by administering anticoagulants, heparin, AT-III, thrombomodulin in animal and cell culture models. • Cell therapy based on local instillation of mesenquimal stem cells or type II alveolar cells in animal models of ALI.
4. clinical and experimental approach of the axis brain-lung during mechanical ventilation (CIBERES Groups 29 and 33; GTC I3A CIBER-BBN and SEPAR): Molecular alterations in brain and lung • Characterization

of neuropsychological / psychopathology alterations and cognitive assessment • Integrity of the autonomic nervous system during VM collaboration with CIBER-BBN-SEPAR. • Feasibility, safety and efficacy of neurocognitive rehabilitation in patients with VM.

5. Study of the patient-ventilator interaction during VM: Impact of asynchronies • Characterization of asynchronies • Parameters involved • Consequences of poor patient interaction / ventilator

Most relevant scientific articles

GARCÍA-PRIETO E., LÓPEZ-AGUILAR J., PARRA-RUIZ D., AMADO-RODRÍGUEZ L., LÓPEZ-ALONSO I., BLAZQUEZ-PRIETO J. ET AL. Impact of Recruitment on Static and Dynamic Lung Strain in Acute Respiratory Distress Syndrome. Anesthesiology. 2015

QUILEZ M.E., RODRÍGUEZ-GONZÁLEZ R., TURON M., FERNÁNDEZ-GONZALO S., VILLAR J., KACMAREK R.M. ET AL. Moderate peep after tracheal lipopolysaccharide instillation prevents inflammation and modifies the pattern of brain neuronal activation. Shock. 2015;44(6):601-608.

MURIAS G., DE HARO C., BLANCH L.. Does this ventilated patient have asynchronies? Recognizing reverse triggering and entrainment at the bedside. Intensive Care Medicine. 2015;:1-4.

MARTÍN-LOECHES I., POVOA P., RODRÍGUEZ A., CURCIO D., SUAREZ D., MIRA J.-P. ET AL. Incidence and prognosis of ventilator-associated tracheobronchitis (TAVeM): A multicentre, prospective, observational study. The Lancet Respiratory Medicine. 2015

BLANCH L, VILLAGRA A, SALES B, MONTANYA J, LUCANGELO U, LUJÁN M ET AL. Asynchronies during mechanical ventilation are associated with mortality.Intensive care medicine. 2015

Highlights

Our goal is to raise awareness 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 help to improve health and generate wealth. We have patents and a spin-off. We cooperate with national / international networks and innovation in clinical studies.

NOTABLE RESULTS Development of translational projects funded under AES Program: PI15 / 02204. Immunomodulatory cell therapy in sepsis. ISCIII (2016-2018) • PI13 / 02204: Influence of persistent decoupling patient/ventilator in cognitive and psychopathological alterations in critically ill patients: multicenter clinical and mechanistic study. (CIBERES Groups 29-33) • PI13 / 02189. Translational research in the fragile patient undergoing MV: In experimental models therapeutic opportunities. • PI12 / 02548 transplantation of alveolar type II cells in experimental models of ALI (CIBERES Groups 23-33).

International projects funded in context of monitoring of critically ill patients: EU THALEA I and II "Telemonitoring and Telemedicine for Hospitals Assisted by ICT for Life saving co-morbid Patients in Europe As part of a Personalised Patient Care Program of the EU" • EU-Egypt partnership for improved monitoring of critically ill patients. • Collaborative CIBERES-SEPAR-CIBERBBN: Effects of an early neurocognitive intervention on patient-ventilator interaction and stress in critically ill Patients receiving MV.

OTHER ACHIEVEMENTS: Global Sepsis Award in the category for non-governmental Organizations, health care provider groups and patient advocacy groups (A Artigas) • ESICM established investigator award Cell therapies for the treatment of ALI in an experimental model (A Artigas) • Grant Taulí Excellence: Development of an experimental model of controlled asynchronies to analyse the mechanisms involved in the cognitive or psychopathology in patients ventilated. (2015-2016) IP: J Lopez-Aguilar • Agreement with Grífols. Effect of Antithrombin in an in vitro model of ALI • Grant for research initiation CIBERES 2015 • Development of multi-center clinical trials in the field of pneumonia associated with MV.

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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:

1. bacterial virulent factors.
2. host-pathogen interactions.
3. search and characterization of new antimicrobials, and
4. development of new designer's microarrays.

Most relevant scientific articles

DIEZ-MARTÍNEZ R., DE PAZ H.D., GARCÍA-FERNÁNDEZ E., BUSTAMANTE N., EULER C.W., FISCHETTI V.A. ET AL. A novel chimeric phage lysin with high in vitro and in vivo bactericidal activity against Streptococcus pneumoniae. Journal of Antimicrobial Chemotherapy. 2015;70(6):1763-1773.

RICO-LASTRES P., DIEZ-MARTÍNEZ R., IGLESIAS-BEXIGA M., BUSTAMANTE N., ALDRIDGE C., HESEK D. ET AL. Substrate recognition and catalysis by LytB, a pneumococcal peptidoglycan hydrolase involved in virulence. Scientific Reports. 2015;5.

CAMPANERO-RHODES M.A., LLOBET E., BENGOECHEA J.A., SOLIS D.. Bacteria microarrays as sensitive tools for exploring pathogen surface epitopes and recognition by host receptors. RSC Advances. 2015;5(10):7173-7181.

SINGH A.K., BERBIS M.A., BALLMANN M.Z., KILCOYNE M., MENENDEZ M., NGUYEN T.H. ET AL. Structure and sialyllactose binding of the carboxy-terminal head domain of the fibre from a siadenovirus, Turkey adenovirus 3. PLoS ONE. 2015;10(9).

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. 2015;1850(1):186-235.

Highlights

RESULTS

- The glycosylation patterns and recognition by several lectins of the innate immune system of nontypeable *Haemophilus influenzae* (NTHi) strain 375, a panel of isogenic mutants expressing sequentially truncated lipooligosaccharide and other clinical isolates of this bacterium have been characterized, in collaboration with Dr. J. Garmendia (Group 8 of CIBERES). A similar study using *S. pneumoniae*, as Gram+ model bacterium, and related species, has been initiated, in collaboration with group 2 of CIBERES (Dr. E. García). In addition, bacteria microarrays have been proved to be useful for the detection of receptors on the pneumococcal surface.
- New designer microarrays have been developed for the study of receptors on the surface of live bacteria, using as model bacterium the E. coli strain UTI89, which expresses the best characterized bacterial adhesin, FimH.
- New bacteriolytic enzymes active against *S. pneumoniae*, *S. pyogenes* and other Gram-positive pathogens have been developed and characterized, in a colaboration with Group 2 of CIBERES.
- Identification of a new family of compounds that inhibit the activity of the major pneumococcal autolytic enzyme, LytA, and have also antimicrobial activity, by means of high-through put screening of chemical libraries of compounds.

INTERNATIONAL AND NATIONAL ACTIVE PROJECTS:

- 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).
- 2012-2016. 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).

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Group 35

Programme: Sleep Apnoeas Syndrome

Lead Researcher: Barbé Illa, Ferran

Group members

STAFF MEMBERS: Forner Vicente, Marta | Ingles Borda, Sandra | Mias Carballal, María Rosario | Muñoz Bravo, Javier | Sánchez de la Torre, Manuel | Villena Portella, Cristina.

ASSOCIATED MEMBERS: Alonso Fernández, Alberto | Barceló Bennássar, Antonia | Carrizo Sierra, Santiago | De la Peña Bravo, Monica | Durán Cantolla, Joaquín José | Egea Santaolalla, Carlos Javier | Esquinas López, Cristina | Gómez Falguera, Silvia | Marin Trigo, José María | Martínez Alonso, Montserrat | Mediano San Andrés, Olga | Sánchez de la Torre, Alicia.

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

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Highlights

Group 35 of the Centre for Biomedical Network Research on Respiratory Diseases (CIBER) is led by Dr. Ferran Barbé. Group 35 focuses its research on the study of the Sleep Apnea Syndrome (OSAS). In 2015 Group 35 was responsible for 32 original publications. It also received funding for competitive development for 14 new research projects calls and started participating in 4 new clinical trials. These projects aim to understand the underlying causes of the pathological manifestation associated with SAHS, and the development and adaptation of treatments for patients with this pathology. It has also developed the first international patent for identifying, through predictive measures and by analyzing microRNAs in plasma, if a patient with resistant hypertension and OSA will respond to treatment with CPAP which, in turn, lowers their blood pressure . They have also participated in the development of several transfer contract of a specific device for the diagnosis of OSA, and form part of a new spin-off as well. Moreover, Group 35 is responsible for developing clinical guidelines for the control and monitoring of respiratory therapies in Spain. Last but not least, two awards have been received and the group has been invited to participate in more than 20 international and national conferences.

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