

The microbiome in respiratory medicine

June, 2nd 2016
WORKSHOP
MARIE CURIE ROOM
(attendance by invitation)

June, 3rd 2016
SYMPOSIUM
AUDITORI
(attendance by registration)

Barcelona Biomedical Research Park (PRBB)
c/ Aiguader 88, Barcelona

Main Partners:

With the collaboration of:

Welcome

The microbiome in respiratory medicine

Dear Guests and Participants,

It is our pleasure to welcome you to the meeting “The Microbiome in Respiratory Medicine”, co-organized by the Barcelona Respiratory Network (BRN) and the Center for Genomic Regulation (CRG), and endorsed by the European Respiratory Society (ERS).

In recent years the use of culture-independent microbiological techniques has enabled tremendous growth in understanding how large amounts of microbiological organisms: bacteria, fungi and viruses, collectively known as the microbiome, coexist in intimate contact with different body surfaces, both in health and disease. The lung is not an exception to this phenomenon, and this fact has challenged the previous belief that the healthy lung was sterile. Understanding the nature of the relationship between the lung microbiome and the respiratory epithelial surfaces that are in close contact with it, appears as one of the more promising research fields in respiratory medicine.

Today, a large body of evidence supports the concept that dysregulation of host-microbiota crosstalk at body surfaces may underlie chronic inflammatory disorders. As a consequence, from the clinical point of view, there is a growing interest in determining the potential value of the airway microbiome composition as a prognostic marker, or even as an indicator for monitoring airway disease progression that eventually could prompt specific therapeutic interventions. However, before this can be implemented, several challenges have to be considered such as: 1) the harmonization of methodologies for airway sampling and sample processing, 2) the understanding of the broader interactions of the microbiome components and how they impact the lung disease pathogenesis and 3) the functional characterization of the respiratory microbiome using proteomic, transcriptomic, metabolomic and animal models. These and other relevant questions about this exciting field have to be addressed in this meeting.

We would like to thank you for joining us at this meeting dedicated to this highly important topic and we hope that you will find it exciting and interesting. We encourage you to actively participate in the scientific discussions.

Yours faithfully,

Jordi Dorca,
President,
Fundació BRN

Eduard Monsó
Chairman,
Fundació BRN

Toni Gabaldón
Group Leader,
Centre for Genomic Regulation



Scientific agenda

June, 2nd 2016
WORKSHOP
MARIE CURIE ROOM

Certainties and uncertainties in the respiratory microbiome

14:00h

Welcome and introduction

Welcome, Goals and Round Presentations.

Organizing committee.

Introduction:

The respiratory microbiome: a new frontier in medicine.

Eduard Monsó, Sabadell, Spain.

14:30h

Block 1: Bioinformatic challenges

Bioinformatic challenges:

16S rRNA analyses.

Vicente Pérez Brocal, Valencia, Spain.

“Sala La Lengua”:

Study of human mouth microbiome as a large citizen science project.

Julia Ponomarenko, Barcelona, Spain.

General discussion.

15:15h

Block 2: Respiratory microbiome

The Promises and Challenges of the Study of the Lung Microbiome.

Gary Huffnagle, Ann Arbor, USA.

Microbiome in COPD:

Pitfalls and Progress.

Sanjay Sethi, Buffalo, USA.

Microbial dysbiosis in bronchiectasis and cystic fibrosis.

James Chalmers, Dundee, UK.

Respiratory microbiome in IPF:

Pathogenesis, Progression and Exacerbations.

Philip Molyneaux, London, UK.

Plasticity of the pulmonary microbiota over the spectrum of inflammation to immunosuppression.

Eric Bernasconi, Lausanne, Switzerland.

17:00h

Coffee Break

17:30h

Block 3: Lessons from other human systems

Meta-omics used to study the gut microbiota: from the bench to the computer.

Chaysavanh Manichanh, Barcelona, Spain.

The gut microbiome in HIV infection.

Roger Paredes, Barcelona, Spain.

General discussion.

18:15h

Round discussion: Specific challenges on lung microbiome research

Eduard Monsó, Sabadell, Spain.

19:15h

Closing Remarks

Scientific agenda

June, 3rd 2016
SYMPOSIUM
AUDITORI

The microbiome in respiratory medicine

8:30h

Welcome and introduction

Welcome to the Symposium.
Jordi Dorca, L'Hospitalet de Llobregat, Spain.

**The respiratory microbiome:
a new frontier in medicine.**
Eduard Monsó, Sabadell, Spain.

9:00h

**Block 1: Understanding
the microbiome**

Chairs: Oriol Sibila, Pilar Francino

**Understanding the microbiome:
How can we determine/analyse it?
Technical issues.**
Vicente Pérez Brocal, Valencia, Spain.

“Sala La Lengua”:

**Study of human mouth microbiome
as a large citizen science project.**
Julia Ponomarenko, Barcelona, Spain.

10:00h

**Block 2: Lung microbiome:
were we are - airway diseases**

*Chairs: Rosa Faner,
Marian Garcia-Núñez*

**The Dynamics of the Lung Microbiome
during Health and Disease.**
Gary Huffnagle, Ann Arbor, USA.

**Microbiome in COPD:
Pitfalls and Progress.**
Sanjay Sethi, Buffalo, USA.

**Microbial dysbiosis in bronchiectasis
and cystic fibrosis.**
James Chalmers, Dundee, UK.

11:30h

Coffee Break

12:00h

**Block 3: Lung microbiome:
were we are - airway diseases**

Chairs: Julia Ponomarenko, Jordi Dorca

**Respiratory microbiome in IPF:
Pathogenesis, Progression
and Exacerbations.**

Philip Molyneaux, London, UK.

**Host-microbe interplay sets the lower
airway microenvironment in lung
transplantation.**

Eric Bernasconi, Lausanne, Switzerland.

13:00h

**Block 4: Lessons from other
microbiomes**

*Chairs: Vicente Pérez Brocal,
Eduard Monsó.*

**Lesson from the human gut
microbiome.**

*Chaysavanh Manichanh, Barcelona,
Spain.*

The gut microbiome in HIV infection.

Roger Paredes, Barcelona, Spain.

14:00h

**General discussion,
wrap-up and next steps.**

Jordi Dorca, Eduard Monsó

Invited Speakers, Scientific Committee & Chairs



Eduard Monsó

Scientific Leader
of the Meeting
& Invited Speaker

Hospital Universitari del Parc Taulí,
Sabadell, Spain.

Dr. Eduard Monsó graduated in Medicine from the Universitat de Barcelona in 1981, and attained his Ph.D. Degree in Medicine at the Universitat Autònoma de Barcelona in 1987. He finished his training in Respiratory Medicine in 1985, and worked after his degree at the Institut Català de la Salut. He is currently Head of the Department of Respiratory Diseases at the Hospital Universitari del Parc Taulí de Sabadell and professor at the Universitat Autònoma de Barcelona. His research interests have focused on COPD, bronchial infections, lung cancer, endoscopy techniques, respiratory epidemiology, occupational lung diseases and telemedicine. He is currently Head of the Research Group in Respiratory Diseases Metropolitana Nord de Barcelona (RESPINORD-BCN), part of Centro de Investigación Biomédica en Red de Enfermedades Respiratorias – Ciberes - Instituto de Salud Carlos III. Dr. Eduard Monsó is author of 150 published research papers.



Àlvar Agustí

Member Scientific
Committee

Hospital Clínic,
Barcelona, Spain.

Prof. Alvar Agustí is currently Director of the Respiratory Institute at Hospital Clínic in Barcelona (www.hospitalclinic.org), and Associate Professor of Medicine at the University of Barcelona. His main research interests include COPD and sleep disorders. He has published more than 400 papers in peer-reviewed journals (H-Index 62) and has made over 40 contributions to books. He is regularly invited to speak at international conferences and symposia. He is a member of several professional societies, including the American Thoracic Society, and the European Respiratory Society (ERS), in which he has been a Member of its Executive Committee. He has a seat at the Royal Academy of Medicine of the Balearic Islands, he is an Honorary Fellow of the Royal College of Physicians of Edinburgh (FRCP), a Fellow of the European Respiratory Society (FERS) and a member of the Scientific Committee and the Board of Directors of GOLD (www.goldcopd.org).



Eric Bernasconi

Invited Speaker

University Hospital of Lausanne,
Lausanne, Switzerland.

Holding a PhD in molecular virology, I have been trained since 1999 as a mucosal immunologist in the Division of Immunology of the University Hospital of Lausanne, Switzerland, where I studied the ability of gut-derived micro-organisms to modulate epithelial permeability and allergic responses. I then joined, in 2005, the Division of Gastroenterology, where my focus was on innate cell activation during colitis, and the critical role of macrophages in wound healing. Since 2011, my studies as Research associate in the Division of Respiratory Medicine directed by LP Nicod (Head of Division) and BJ Marsland (Head of Research), also at the University Hospital of Lausanne, have allowed me to bring these different topics together. Specifically, we assess the extent to which variations in the pulmonary microbiota composition are associated with underlying immunological changes, and how such variations may impact upon lung function within the transplantation context.



Jerónimo Carnés

Member Scientific
Committee

Laboratoris LETI, SL,
Barcelona, Spain.

Dr Jerónimo Carnés, PhD is a Doctor in Animal Physiology. He qualified in Biological Sciences in Madrid, Spain in 1994. He started to work on Immunology and Allergy in 1995. From that point onwards, he has collaborated, designed and directed research projects in different fields, including Immunology, Allergy and, more recently, Vaccines for parasitic diseases. Currently he is the R&D Director of the Immunology and Allergy Business Unit at Laboratorios LETI S.L, Spain. In this period he has developed and launched the best-selling product of the company for the treatment of allergenic diseases and he has participated in the design, development and registration of different molecules in Germany and recently in the EMA. He has published more than 90 peer-review articles in different scientific journals, is the author of 2 patents and has been speaker in more than 50 national and international conferences. He is currently involved in different research projects for the development of Immunotherapy for the treatment of allergic diseases and the research and development of vaccines for parasitic infectious diseases.



James Chalmers

Invited Speaker

University of Dundee,
Dundee, UK.

Dr James Chalmers is Senior Lecturer and Honorary Consultant at the University of Dundee. His research is focused on understanding interactions between bacteria and neutrophilic inflammation in the lung, with a particular focus on bronchiectasis, COPD and cystic fibrosis. He is chair of the European Bronchiectasis Registry (EMBARC), an initiative of the European Union and European Respiratory Society to accelerate research and clinical trials in non-CF bronchiectasis. He is associate editor of the European Respiratory Journal and a member of the international advisory board of the Lancet Respiratory Medicine. He has published more than 120 papers with an H index of 30. He is chair of the European Bronchiectasis guidelines group, which will produce clinical practice guidelines for bronchiectasis towards the end of 2016. He is also involved in continuing medical education and is the secretary of the European Board for Accreditation in Pneumology, and is active in the European Respiratory Society and American Thoracic Society.



Jordi Dorca

Member Scientific
Committee & Chair

Hospital Universitari de Bellvitge,
L'Hospitalet de Llobregat, Spain.

Jordi Dorca is currently Chief of the Respiratory Department at the Hospital Universitari de Bellvitge, located in the Barcelona area. He is Professor of Medicine at the University of Barcelona and Coordinator of the Respiratory Diseases Research Group at the Institut d'Investigació Biomèdica de Bellvitge (IDIBELL). His main research interests are focused on the epidemiology, diagnosis and treatment of different kinds of respiratory infections. He has published more than 110 papers in peer-reviewed journals with a combined IF of 511 and a h-index of 29. He is also a member of several scientific societies. Currently, he is the president of Barcelona Respiratory Network.

Invited Speakers, Scientific Committee & Chairs



Rosa Faner

Member Scientific
Committee & Chair

CIBER Enfermedades Respiratorias,
Barcelona, Spain.

Maria Rosa Faner is a Post-Doctoral researcher at the CIBER Respiratory Diseases group 10 (Hospital Clínic, Barcelona). She has a degree in Biological Sciences (Universitat Autònoma de Barcelona, 2001) and a PhD in Immunology (Universitat Autònoma de Barcelona, 2006). She has been PI of 5 projects funded by competitive agencies, author of 26 papers in international peer-reviewed journals with a total IF of 196.7, H index of 12, 351 citations and author of 3 patents.

Her main contributions to the research in the respiratory diseases described the pulmonary immune response deregulation observed patients with COPD using unbiased omics and network medicine methods, the genetic basis of observed multimorbidity, and the gender differences in the systemic response to smoke.



Pilar Francino

Chair

Fundación para el Fomento
de la Investigación Sanitaria y Biomédica,
Valencia, Spain.

M. P. Francino studied Biology at the National University of Mexico and then pursued graduate studies at the University of Rochester (New York), where she obtained her Ph.D. degree working on analyses of rates and patterns of DNA sequence evolution in bacteria and primates. Next, she conducted postdoctoral research in bacterial genetics as an EMBO Fellow at the University of Paris. After that, she served as a Research Scientist at the U.S. Department of Energy Joint Genome Institute for five years, and was Head of their Evolutionary Genomics Program from 2007 to 2009. Since 2009, she has been a Senior Scientist at the Genomics and Health Department of FISABIO-Public Health in Valencia, and the Head of the Department since 2012. Her current research focuses on the metagenomic analysis of human microbiome communities, in particular on understanding the development of the gut microbiota in infants. Work in her research group studies this process by analyzing the taxonomic composition, coding capabilities and gene expression patterns of the gut microbial community at different stages during infancy, as well as the relationships of these features with infant health.



Toni Gabaldón

Member Scientific
Committee

Centre for Genomic Regulation,
Barcelona, Spain.

A biochemist by training (University of Valencia, Spain, 1997), Toni Gabaldón carried out a PhD in comparative genomics at The Radboud university (Nijmegen, The Netherlands) in 2005, and an EMBO-funded postdoc at the CIPF center (Valencia, Spain). In 2008 he started his own group at the Centre for Genomic Regulation (Barcelona, Spain). Gabaldón has always used an evolutionary perspective to address different biological questions. His research is not only focused on understanding how complex biological systems work, but also how they have come to be as they are. Over his career he has been awarded prestigious grants and awards such as the ICREA professorship and the ERC Starting Grant.



Marian Garcia-Nuñez
Chair

CIBER Enfermedades Respiratorias,
Sabadell, Spain.

PhD in Biology. Postdoctoral Researcher of the CIBER in Respiratory Diseases for the Instituto de Salud Carlos III (chief researcher: Dr. Eduard Monsó). Lead researcher of the “Lung Microbiome and Respiratory Community-acquired Infections Group” from the Institut d’Investigació i Innovació Parc Taulí (I3PT), Barcelona. Member of RESPINORD group (2014SGR801) financed by the Generalitat de Catalunya (Catalan Regional Government). Her main research areas are focused on the role of lung microbiome in COPD and cystic fibrosis diseases; development of new tools and screening strategies of bacterial molecular typing; and improvement in the diagnosis of respiratory diseases, particularly in the field of Legionnaires’ disease.



Gary B. Huffnagle
Invited Speaker

University of Michigan,
Ann Arbor, USA.

Gary B. Huffnagle, PhD received his PhD in immunology from the University of Texas Southwestern Medical School. He holds faculty appointments (Professor) in Internal Medicine, Microbiology & Immunology, and Molecular Cellular & Developmental Biology, as well as an endowed professorship in the Mary H. Weiser Food Allergy Center at the University of Michigan. He was elected to the American Academy of Microbiology of the American Society for Microbiology in 2013 and has been a frequent reviewer for the NIH (USA). The overall goals of his current research are to identify and delineate the interactions between the microbiome (lung and gut) and the immune system. Using animal models, clinical samples and in vitro assays, his laboratory is investigating host-microbiome interactions in the control of pulmonary inflammation, allergic responses and infectious disease. Over the past decade, his laboratory has developed expertise in applying high-throughput sequencing and gene expression technologies to biological processes and disease, including bacterial genomics and the microbiome.



Chaysavanh Manichanh
Invited Speaker

Vall d’Hebron Research Institute,
Barcelona, Spain.

Chaysavanh Manichanh, PhD (University Pierre et Marie-Curie, Paris, 2001) is a research scientist and head of the Metagenomics Lab in the Department of Physiology and Physiopathology (Vall d’Hebron Research Institute, Barcelona). Since 2002, she has been using meta-omics approaches to study the human microbiome associated with human diseases. She has collaborated with the European MetaHIT consortium in building a comprehensive gene catalogue from the human gut microbiome and has participated in the International Human Microbiome Standards (IHMS) project that seeks to coordinate the development of standard operating procedures (SOPs) and protocols to optimize data comparisons in the human microbiome field. With her group, she develops molecular as well as bioinformatics tools to characterize the human microbiome associated with different human disorders (<https://sites.google.com/site/manichanhlab/>).

Invited Speakers, Scientific Committee & Chairs



Philip Molyneaux
Invited Speaker

Royal Brompton Hospital
London, UK.

Dr Philip Molyneaux qualified from Guy's, King's and St Thomas' School of Medicine in 2004, where he completed an intercalated BSc. in Molecular Genetics. He undertook his clinical training at Guy's and St Thomas' and went on to attain an NIHR Academic Clinical Fellow position in Respiratory medicine at Imperial College. He spent the next two years training at St Mary's Hospital and working with Professors Cookson, Moffatt and Johnston studying the respiratory microbiome in COPD.

Moving to the Royal Brompton Hospital he went on to complete a PhD examining the host response and microbial flora in Idiopathic Pulmonary Fibrosis (IPF) as part of the Prospective Study of Fibrosis In the Lung Endpoints (PROFILE) study with Dr Toby Maher. His ongoing work concentrates on delineating the host microbe interaction in fibrotic lung disease.



Roger Paredes
Invited Speaker

IRSiCaixa AIDS Research Institute,
Barcelona, Spain.

Dr. Roger Paredes, MD, PhD, leads the Microbial Genomics Group at the irsiCaixa AIDS Research Institute and is attending HIV physician at the HIV Unit, Hospital Universitari Germans Trias i Pujol in Barcelona, Catalonia, Spain. He's assistant professor in infectious diseases at the Universitat Autònoma de Barcelona (UAB) and Lecturer in the Chair on AIDS and Related Diseases, UVIC-UCC. His team has made seminal contributions to the current understanding of the clinical relevance of minority drug-resistant HIV and X4 viruses on antiretroviral treatment outcomes and HIV disease progression. He's now using next-generation genomics to characterize the role of the human microbiome on HIV disease, chronic inflammation and aging. Dr. Paredes is clinical virologist for several European HIV cohorts (EuroSIDA), advisor to the WHO HIV ResNet group and member of the organizing committee of the first International Workshop on Microbiome in HIV Pathogenesis, Prevention and Treatment, held annually in Bethesda, MD.



Vicente Pérez Brocal
Invited Speaker
& Chair

Fundación para el Fomento
de la Investigación Sanitaria y Biomédica,
Valencia, Spain.

I got my degree in Biology, at the University of Valencia in 2001, where I did my PhD research project in the program 'Biodiversity and Evolutionary Biology' from 2002 to 2006. I worked on bacterial genome reduction and minimal genomes. I sequenced the smallest bacterial genome at that time, that of *Buchnera aphidicola*, the primary endosymbiont from the cedar aphid. Next, I worked as a postdoctoral researcher at the London School of Hygiene and Tropical Medicine at the University of London, from 2006 to 2009. My topic there was the genetic evolution of mitochondrial and related organelles during the transition from an aerobic to a strictly anaerobic lifestyle working on *Blastocystis*. Next, I held a 'Sara Borrell' contract at the 'Genomics and Health Area' at the FISABIO (Valencia), from 2010 to 2014 to work on Metagenomics of microbial and viral communities associated to inflammatory bowel disease and other pathologies affecting the gastrointestinal tract. Since then, I have also collaborated with groups of Barcelona (respiratory microbiome and virome), Madrid (celiac disease virome), Italy (fermenting bacteria), Girona (gut microbiota-brain relationship) etc., with a contract at the FISABIO.



Julia Ponomarenko

Invited Speaker
& Chair

Centre for Genomic Regulation,
Barcelona, Spain.

Dr. Julia Ponomarenko is Head of the Bioinformatics Unit at the CRG, Barcelona, Spain. After obtaining in 2002 the PhD in computational biology, Julia moved to the San Diego Supercomputer Center, University of California San Diego (UCSD), where until 2015 she was the US NIH Principal Investigator. Dr. Ponomarenko is one of the primary developers of the Immune Epitope Database (IEDB.org), a \$35M NIAID/NIH contract. In 2014, she received the US National Science Foundation RAPID award for studies of the immunity against the Ebola virus epitope. Dr. Ponomarenko's research interests include NGS data analysis, immunoinformatics, structural genomics, transcriptomics, systems biology, development of biological databases and bioinformatics software.



Sanjay Sethi

Invited Speaker

University of Buffalo,
Buffalo, USA.

Sanjay Sethi, MD, FACP, is a Professor in the Department of Medicine at the University of Buffalo at the State University of New York (SUNY) in Buffalo, NY. He is Chief of the Division of Pulmonary/Critical Care/Sleep Medicine, Assistant Vice President for Health Sciences and Director of the Clinical Research office at the University at Buffalo. Dr Sethi's main research interests include chronic obstructive pulmonary disease (COPD) and respiratory infections, focused on the specific areas of exacerbations, new therapeutics and innate lung defense in COPD. Dr Sethi has co-authored more than a 180 research articles, reviews and book chapters in many peer-reviewed medical journals. He is a member of the editorial board for several pulmonary journals. He was a member of the lung cellular, molecular, and immunobiology study section of the National Institutes of Health (NIH) and the Pulmonary study section of the VA, and is an ad hoc reviewer for several North American and European research funding agencies. Dr. Sethi is currently active in several professional organizations including the American Thoracic Society where he has chaired the Clinical Problems program committee, and is chair for the Clinical Problems Assembly.



Oriol Sibila

Member Scientific
Committee & Chair

Hospital de la Santa Creu i Sant Pau,
Barcelona, Spain.

Medical Doctor. Pulmonary Disease Specialist since 2004. PhD Cum Laude at University of Barcelona (UB) in 2008. Research Fellow at University of Texas Health Science Center at San Antonio (UTHSCSA), San Antonio, TX (2011-2012). Pulmonologist staff at Hospital de la Santa Creu i Sant Pau, Barcelona since 2009. Clinical Associate Professor of Autonomia University of Barcelona (UAB).

Honors: Best young Investigator Award by Spanish Society of Pneumology (SEPAR) at 2009. Early-Career Peer Recognition Award by Assembly of Microbiology, Tuberculosis and Pulmonary Infections (MTPI) of the American Thoracic Society at 2016. Principal investigator of one active grant supported by Spanish Government focused on the study of microbiome in COPD. More than 30 international publications in the last 5 years.

WORKSHOP



The respiratory microbiome: a new frontier in medicine

Eduard Monsó
Sabadell, Spain.

Bronchial colonization by potentially pathogenic bacteria is common in stable chronic obstructive pulmonary disease (COPD), and in about a half of patients positive cultures for *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis* are found during stability periods. However available culture techniques are not suitable for the identification of an important part of the bacterial flora inhabitant of the respiratory mucosa. Most bacteria present do not grow adequately on commonly used selective cultures, and are masked by the presence of other faster-growing bacteria. Through independent culture techniques, such as amplification and sequencing, it is possible to determine the composition of bronchial microbiome, both bronchial and viral, defining the relationships between the colonizing flora and MPOC. The use of these techniques in bronchial secretions has shown the existence of a diverse microbiome in COPD, and a predominant presence of bacteria from the phylum Proteobacteria, Firmicutes, Actinobacteria and Bacteroidetes. The bacterial flora observed in patients with COPD alters the pattern of continuity observed in the oropharynx and the bronchial tree of normal subjects, through a partial disappearance of microorganisms common in the healthy population. The magnitude of these changes parallels the severity of the disease, with a relative increase in the proportion of Proteobacteria in severe patients, inversely correlated with the decrease of Firmicutes in advanced COPD. Thus, the bacterial diversity in the respiratory tract appears to be clearly higher in the healthy subject and the patient with mild-moderate COPD, to be replaced in severe COPD by a narrow range of microorganisms, with a high proportion of potentially pathogenic bacteria. In patients with severe COPD, frequent colonization by *Pseudomonas aeruginosa* does not determine a change in the bronchial flora as a whole, which has a similar spectrum in all patients with advanced disease, independently of their colonizing patterns.

The study of the bacterial flora in COPD exacerbations have shown increases in specific bacterial genera in most patients, which include, in most cases, one or more potentially pathogenic species. These increases in many cases are not identified by culture, a finding that has confirmed the insufficient sensitivity of conventional techniques for identifying causative pathogens in COPD. This approach have shown that the bacterial pattern in exacerbations from patients colonized by *Pseudomonas aeruginosa*, when identified from independent culture techniques, are similar to patterns found in non-colonized patients. This supports the hypothesis that microorganisms causing exacerbations in *Pseudomonas*-colonized COPD patients are not different from the pathogens related to bronchial infections in non-colonized patients, and the colonizing role of *Pseudomonas aeruginosa* continues, both in stability periods and in exacerbations. These findings from microbiome analysis have potential implications for recommendations in therapeutic guidelines. One additional advantage of the identification of the composition of respiratory microbiome by culture-independent techniques in respiratory samples is the characterization of the functional features of the bacterial genome, through metagenomics. This approach has shown that in COPD exacerbations the functional activity of the background flora may change, in spite of the absence of changes in their composition, with increases in the abundance of genes involved in carbohydrate metabolism and carcinogenesis, and parallel decreases in genes related to cell growth and catabolism. Thus, the introduction of microbiological identification techniques not based on culture has demonstrated that the diversity of bacterial flora is reduced with advanced COPD, with an overrepresentation of potentially pathogenic microorganisms. In exacerbations, 16S rRNA gene sequencing have identified causal pathogenic bacteria not recovered through cultures, and functional changes in bacterial flora with potential clinical significance.

Certainties and uncertainties in the respiratory microbiome



Bioinformatic challenges: 16S rRNA analyses

Vicente Pérez Brocal
Valencia, Spain.

In order to answer our questions regarding the diversity of the microbiome harboured in complex ecosystems such as that of the human respiratory tract, we require the development of a series of computational software to help us untangle its composition, abundance and diversity, based on the 16S rRNA. However, bioinformatic tools alone are not enough to tackle the challenges arising from the increasingly demanding biomedical research. Thus, researchers must contemplate an appropriate conceptual framework in order to achieve a proper use of those tools. In summary, being able to pose

the right questions and accordingly, carrying out the appropriate workflow using the available bioinformatic tools may be as challenging and is, at least, as important as the tools we use themselves. Therefore, features such as the awareness of the relevance that the detection of shortcomings has in currently existing 16S rRNA-based databases, the presence of chimeras and other bioinformatic challenges, rather than the automatic application of a particular software or even pipeline, represent aspects that must be emphasized.



“Sala La Lengua”: Study of human mouth microbiome as a large citizen science project

Julia Ponomarenko
Barcelona, Spain.

Sala La Lengua is a citizen science project studying the human mouth microbiome. Bacterial profiles of over 1500 school children across Spain were obtained using 16S rRNA sequencing and analyzed in relation to their diet,

mouth hygiene, geographic area and other environmental characteristics and lifestyle. In my talk I will discuss the results of the project and also bioinformatics challenges we have encountered undertaking the project.

WORKSHOP



The Promises and Challenges of the Study of the Lung Microbiome

Gary Huffnagle
Ann Arbor, USA.

The identification and confirmation that the lungs are not sterile during health has begun to change views of the role of indigenous bacteria in lung health and disease. However, the airways are a challenging site to sample and repeated sampling by bronchoscopy is not ethically feasible in a healthy population or in most diseased individuals. Despite the theoretical possibility of bronchoscope contamination by nasal or oral microbiome during insertion, this has not proven to be an issue. Contamination is usually below the limits of detection for culture-independent sequencing-based assays. Rather,

the issue that has emerged is that sequencing of low biomass samples can generate spurious signals. This underscores the critical need for proper technical controls in sequence-based analyses of the low bacterial biomass of the airways during health (and even some diseases) in order to separate “signal from noise.” The emerging concept of the lung microbiome is of that of a tidal ecosystem in which immigration, elimination and regional growth conditions are the primary factors that determine the composition of the lung microbiome.



Microbiome in COPD: Pitfalls and Progress

Sanjay Sethi
Buffalo, USA.

Microbiome studies of respiratory secretions have provided exciting new observations regarding the bacterial causation of exacerbations of COPD, and the impact of treatment of the exacerbation on the airway microbiome. Bacterial exacerbations likely represent abrupt major changes in the microbiome with resultant large increases in airway and systemic inflammation. Microbiome studies could lead to discovery of new pathogens that have been difficult to obtain with standard culture techniques. The Vicious Circle Hypothesis embodies the likely contribution of an altered microbiome to COPD progression, with an unhealthy microbiome driving the inflammatory process in stable COPD. While studies with conventional microbiology found potential pathogenic bacteria to be virtually absent in bronchoscopic samples in healthy controls, smoking and development of COPD was associated with 35–50% incidence of isolation of pathogenic bacteria. In contrast, recent microbiome

studies have found no or minor differences from controls in smokers and COPD. These contradictory findings could be explained by the extreme sensitivity of the microbiome technique to upper airway contamination. Several challenges need to be tackled to fully utilize the benefits of microbiome research in COPD. Paramount is the issue of upper airway and environmental contamination of lower airway samples. Significant concentration thresholds in microbiome data need to be defined. The microbiome differs in sputum, bronchoalveolar lavage and lung parenchyma samples obtained from patients with COPD. Determination as to which of the various new microbes that will be identified in microbiome studies are pathogenic is still unclear, especially for unculturable pathogens. Though various obstacles need to be surmounted, ultimately lung microbiome studies will provide new insights in to how infection contributes to COPD.

Certainties and uncertainties in the respiratory microbiome



Microbial dysbiosis in bronchiectasis and cystic fibrosis.

*James Chalmers
Dundee, UK.*

Bacterial infection is central to our understanding of the pathophysiology of bronchiectasis and cystic fibrosis. Traditional culture based microbiology techniques have revealed the importance of well characterised pathogens such as *Haemophilus influenzae*, *Pseudomonas aeruginosa* and *Moraxella catarrhalis* in bronchiectasis, and *Staphylococcus aureus* and *Burkholderia cepacia* in cystic fibrosis among many others. The management of these diseases and drug development efforts have been largely devoted to antimicrobial therapies targeting these pathogens. *P. aeruginosa* represents a special case, having been shown to impact prognosis in both diseases and being both frequently multidrug resistant and difficult to eradicate.

The availability of next generation sequencing technologies and particularly characterisation of the bacterial lung microbiome are causing an evolution in our understanding of the disease. Previously unrecognised organisms

are found to dominate the microbiome in some patients, while studies characterising the airway microbiome following antibiotic treatment show remarkable resistance of bacterial communities to change. The addition of fungi, viruses and *Mycobacteria* adds to the complexity of understanding the host/pathogen interaction in these polymicrobial lung diseases.

Key questions still need to be addressed with regard to the microbiome in bronchiectasis and CF, including the extent to which sequencing provides clinical information beyond that provided by culture, whether antibiotic treatment can be targeted based on microbiota profiles, and whether prognostic information can be gained. Finally, it is important to determine if the microbiome can be used to evaluate therapeutic response or give insights into adverse effects of antibiotics such as emerging of new pathogens or loss of bacterial diversity. I will discuss all of these issues during the meeting.



Respiratory microbiome in IPF: Pathogenesis, Progression and Exacerbations

*Philip Molyneaux
London, UK.*

The recent characterization of the respiratory microbiome in idiopathic pulmonary fibrosis (IPF) has suggested that an increased bacterial burden, and presence of specific organisms, could drive disease progression. This strengthens the epidemiological argument that environmental factors may be integral to the pathogenesis of IPF in genetically susceptible individuals. However, there remain a number of unanswered questions regarding the role of the microbiome in IPF including the effect of the MUC5B polymorphism and the optimal sampling modality to study a parenchymal disease process.

We will review the current understanding of the microbiome in fibrotic lung disease, and explore the evidence supporting the role of the microbiome in the pathogenesis and progression of IPF. We will then discuss how an understanding of the microbiome may help us to gain further insights into currently “non-infective” acute exacerbations of IPF.

WORKSHOP



Plasticity of the pulmonary microbiota over the spectrum of inflammation to immunosuppression

Eric Bernasconi
Lausanne, Switzerland.

The composition of a « core » pulmonary microbiota community in healthy subjects starts to emerge, with interactions between community members and functional redundancy believed to reinforce resistance to disturbance or support a return to community equilibrium, after being disturbed. However, in a range of disease states and treatment regimens, the magnitude and/or duration of disturbance in lower airways microenvironment is sufficient to trigger profound changes in community composition. Considering that the lower airways represent an ecosystem shared by the microbiota and host immune cells, e.g. alveolar macrophages, substantial disturbance in local conditions may be expected to impact upon both of these components in parallel. Accordingly, acute pneumonia or exacerbation in COPD, both eliciting strong type 1 host inflammatory responses, were reported to be typically associated with the outgrowth of Firmicutes or Gammaproteobacteria (e.g. *Staphylococcus aureus* and *Pseudomonas aeruginosa*, respectively).

In addition, the relative abundance of the Bacteroidetes genus *Prevotella*, associated with the healthy state in combination with *Streptococcus* and *Veillonella*, was strongly reduced in inflammation, suggesting these latter taxa do not adapt to the same microenvironmental conditions as the aforementioned pathogens. In a marked contrast, we found *Prevotella*, *Streptococcus* and *Veillonella* co-occurring and dominating in a large set of lung transplant recipients, reaching levels that exceeded the reported values for healthy subjects. In this setting, characterized by an abnormally low baseline inflammatory status due to constant exposure to immunosuppressive drugs aiming at controlling immune responses to the allograft, *Staphylococcus* and *Pseudomonas* were poorly represented, except in overt infection. Overall, the composition of the pulmonary microbiota appears to vary in concert with host inflammatory status over a range of clinical conditions, that reflect contrasting alterations in lower airways microenvironment.

Certainties and uncertainties in the respiratory microbiome



Meta-omics used to study the gut microbiota: from the bench to the computer

Chaysavanh Manichanh
Barcelona, Spain.

Functions of the gut microbiota affects many aspects of our systems physiology, ranging from processing and harvesting of nutrients from our diets, to shaping the features of our innate and adaptive immune system. Any factors that disturb this mutualism could result in diseases. Over the last decade, the limitations of culture-based methods have been overcome thanks to Next Generation Sequencing techniques, allowing us to understand the microbial gut community in greater depth through the study of microbial genes or full genomes, called metagenomics. To catalyse the field, the NIH and the European Commission launched, in 2008, the Human Microbiome and the MetaHIT Projects, respectively. These initiatives have

allowed a deep characterization of the human gut microbiome in health and disease states. The human GI-tract harbours one of the most complex and abundant microbial ecosystems colonised by more than 100 trillion microorganisms, and the number of microbial genes is about 100 times higher than that of our own genes. Although stable across ages, the composition and functions of the microbiome may be influenced by a number of factors including genetics, mode of delivery, age, diet, geographic location and medical treatments. Alteration in the microbiome structure and function has been linked to inflammatory, functional and metabolic disorders such as IBD, IBS and obesity.



The gut microbiome in HIV infection

Roger Paredes
Barcelona, Spain.

The human intestinal microbiota is essential for human health and well-being and is driven by genetic, lifestyle and environmental factors. The precise effects of HIV-1 on the gut microbiome are unclear. Initial cross-sectional studies provided contradictory associations between microbial richness and HIV serostatus and suggested shifts from *Bacteroides* to *Prevotella* predominance following HIV-1 infection, which have not been found in animal models or in studies matched for HIV-1 transmission groups. We demonstrate in two independent cohorts of HIV-1-infected subjects and HIV-1-negative controls in Europe that gay men often have a distinct composition of the human fecal microbiota, with increased microbial

richness and diversity and enrichment in the *Prevotella* enterotype. This is independent of HIV-1 status, and with only a limited contribution of diet effects. After accounting for sexual orientation, however, HIV-1 infection remains associated with reduced bacterial richness, more so in subjects with suboptimal CD4+ T-cell count recovery under antiretroviral therapy. Our findings indicate that all studies of HIV-microbiota relationships should carefully investigate possible confounding or effect modification by sexual orientation, injection drug use, and demographics. They also suggest interventions on gut bacterial richness as possible novel avenues to improve HIV-1-associated immune dysfunction.

SYMPOSIUM



The respiratory microbiome: a new frontier in medicine

Eduard Monsó
Sabadell, Spain.

Bronchial colonization by potentially pathogenic bacteria is common in stable chronic obstructive pulmonary disease (COPD), and in about a half of patients positive cultures for *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis* are found during stability periods. However available culture techniques are not suitable for the identification of an important part of the bacterial flora inhabitant of the respiratory mucosa. Most bacteria present do not grow adequately on commonly used selective cultures, and are masked by the presence of other faster-growing bacteria. Through independent culture techniques, such as amplification and sequencing, it is possible to determine the composition of bronchial microbiome, both bronchial and viral, defining the relationships between the colonizing flora and MPOC. The use of these techniques in bronchial secretions has shown the existence of a diverse microbiome in COPD, and a predominant presence of bacteria from the phylum Proteobacteria, Firmicutes, Actinobacteria and Bacteroidetes. The bacterial flora observed in patients with COPD alters the pattern of continuity observed in the oropharynx and the bronchial tree of normal subjects, through a partial disappearance of microorganisms common in the healthy population. The magnitude of these changes parallels the severity of the disease, with a relative increase in the proportion of Proteobacteria in severe patients, inversely correlated with the decrease of Firmicutes in advanced COPD. Thus, the bacterial diversity in the respiratory tract appears to be clearly higher in the healthy subject and the patient with mild-moderate COPD, to be replaced in severe COPD by a narrow range of microorganisms, with a high proportion of potentially pathogenic bacteria. In patients with severe COPD, frequent colonization by *Pseudomonas aeruginosa* does not determine a change in the bronchial flora as a whole, which has a similar spectrum in all patients with advanced disease, independently of their colonizing patterns.

The study of the bacterial flora in COPD exacerbations have shown increases in specific bacterial genera in most patients, which include, in most cases, one or more potentially pathogenic species. These increases in many cases are not identified by culture, a finding that has confirmed the insufficient sensitivity of conventional techniques for identifying causative pathogens in COPD. This approach have shown that the bacterial pattern in exacerbations from patients colonized by *Pseudomonas aeruginosa*, when identified from independent culture techniques, are similar to patterns found in non-colonized patients. This supports the hypothesis that microorganisms causing exacerbations in *Pseudomonas*-colonized COPD patients are not different from the pathogens related to bronchial infections in non-colonized patients, and the colonizing role of *Pseudomonas aeruginosa* continues, both in stability periods and in exacerbations. These findings from microbiome analysis have potential implications for recommendations in therapeutic guidelines. One additional advantage of the identification of the composition of respiratory microbiome by culture-independent techniques in respiratory samples is the characterization of the functional features of the bacterial genome, through metagenomics. This approach has shown that in COPD exacerbations the functional activity of the background flora may change, in spite of the absence of changes in their composition, with increases in the abundance of genes involved in carbohydrate metabolism and carcinogenesis, and parallel decreases in genes related to cell growth and catabolism. Thus, the introduction of microbiological identification techniques not based on culture has demonstrated that the diversity of bacterial flora is reduced with advanced COPD, with an overrepresentation of potentially pathogenic microorganisms. In exacerbations, 16S rRNA gene sequencing have identified causal pathogenic bacteria not recovered through cultures, and functional changes in bacterial flora with potential clinical significance.

The microbiome in respiratory medicine



Understanding the microbiome: How can we determine/analyse it? Technical issues

Vicente Pérez Brocal
Valencia, Spain.

The microbiome harboured in the human respiratory tract represents a complex ecosystem, consisting of more than 600 species, and subject to environmental fluctuations and changes. Determining the diversity of such an elusive community has been a permanent challenge for researchers until the advent of metagenomics contributed to circumvent it. However, these culture-independent approaches are not exempt from limitations, not only in the experimental steps, but also during the bioinformatic analyses arising from the huge amount of data generated. Those have to be suitably processed in order to extract proper conclusions, therefore avoiding erroneous interpretations of the results. Here, the relevance of choosing an appropriate database is

set out. Moreover, after outlining the initial processing steps, the problems of chimeras and their removal are addressed. Finally, other shortcomings of the metagenomic approach are also tackled and suggestions to avoid them in order to reliably assign taxonomy are suggested. The main conclusion is that there are still technical issues associated with the biological limitations inherent to the data themselves and the databases that bioinformatic tools alone cannot easily discriminate, despite our efforts. Therefore, we must be cautious when it comes to drawing conclusions, since results represent usually a trade-off between their accuracy and the necessity to present them unambiguously.



“Sala La Lengua”: Study of human mouth microbiome as a large citizen science project

Julia Ponomarenko
Barcelona, Spain.

Sala La Lengua is a citizen science project studying the human mouth microbiome. Bacterial profiles of over 1500 school children across Spain were obtained using 16S rRNA sequencing and analyzed in relation to their diet,

mouth hygiene, geographic area and other environmental characteristics and lifestyle. In my talk I will discuss the results of the project and also bioinformatics challenges we have encountered undertaking the project.

SYMPOSIUM



The Dynamics of the Lung Microbiome during Health and Disease

Gary Huffnagle
Ann Arbor, USA.

The macro- and micro-anatomic features of the lungs are very much distinct from that of the gastrointestinal tract. The factors that regulate microbial residence, growth and metabolism in the lungs will, therefore, be very different from those in the GI tract. In the past decade, culture-independent techniques of microbial identification have revealed a previously unappreciated complexity to the microbial ecosystem of the lungs. Numerous studies have shown that the airways are not sterile and the composition of the lung microbiome is determined by the balance of three factors: (1) microbial immigration into the airways from the nose, mouth and air, (2)

elimination of microbes from the airways, and (3) the relative reproduction rates of its community members, as determined by regional growth conditions. Any change in the microbiome - within an individual or across disease states - must be due to some perturbation in these factors. Thus, the microbiome of the lungs can significantly change during disease, which has potential significant implications for respiratory disease pathogenesis and therapeutic interventions.



Microbiome in COPD: Pitfalls and Progress

Sanjay Sethi
Buffalo, USA.

Microbiome studies of respiratory secretions have provided exciting new observations regarding the bacterial causation of exacerbations of COPD, and the impact of treatment of the exacerbation on the airway microbiome. Bacterial exacerbations likely represent abrupt major changes in the microbiome with resultant large increases in airway and systemic inflammation. Microbiome studies could lead to discovery of new pathogens that have been difficult to obtain with standard culture techniques. The Vicious Circle Hypothesis embodies the likely contribution of an altered microbiome to COPD progression, with an unhealthy microbiome driving the inflammatory process in stable COPD. While studies with conventional microbiology found potential pathogenic bacteria to be virtually absent in bronchoscopic samples in healthy controls, smoking and development of COPD was associated with 35–50% incidence of isolation of pathogenic bacteria. In contrast, recent microbiome

studies have found no or minor differences from controls in smokers and COPD. These contradictory findings could be explained by the extreme sensitivity of the microbiome technique to upper airway contamination. Several challenges need to be tackled to fully utilize the benefits of microbiome research in COPD. Paramount is the issue of upper airway and environmental contamination of lower airway samples. Significant concentration thresholds in microbiome data need to be defined. The microbiome differs in sputum, bronchoalveolar lavage and lung parenchyma samples obtained from patients with COPD. Determination as to which of the various new microbes that will be identified in microbiome studies are pathogenic is still unclear, especially for unculturable pathogens. Though various obstacles need to be surmounted, ultimately lung microbiome studies will provide new insights in to how infection contributes to COPD.

The microbiome in respiratory medicine



Microbial dysbiosis in bronchiectasis and cystic fibrosis.

*James Chalmers
Dundee, UK.*

Bacterial infection is central to our understanding of the pathophysiology of bronchiectasis and cystic fibrosis. Traditional culture based microbiology techniques have revealed the importance of well characterised pathogens such as *Haemophilus influenzae*, *Pseudomonas aeruginosa* and *Moraxella catarrhalis* in bronchiectasis, and *Staphylococcus aureus* and *Burkholderia cepacia* in cystic fibrosis among many others. The management of these diseases and drug development efforts have been largely devoted to antimicrobial therapies targeting these pathogens. *P. aeruginosa* represents a special case, having been shown to impact prognosis in both diseases and being both frequently multidrug resistant and difficult to eradicate.

The availability of next generation sequencing technologies and particularly characterisation of the bacterial lung microbiome are causing an evolution in our understanding of the disease. Previously unrecognised organisms

are found to dominate the microbiome in some patients, while studies characterising the airway microbiome following antibiotic treatment show remarkable resistance of bacterial communities to change. The addition of fungi, viruses and *Mycobacteria* adds to the complexity of understanding the host/pathogen interaction in these polymicrobial lung diseases.

Key questions still need to be addressed with regard to the microbiome in bronchiectasis and CF, including the extent to which sequencing provides clinical information beyond that provided by culture, whether antibiotic treatment can be targeted based on microbiota profiles, and whether prognostic information can be gained. Finally, it is important to determine if the microbiome can be used to evaluate therapeutic response or give insights into adverse effects of antibiotics such as emerging of new pathogens or loss of bacterial diversity. I will discuss all of these issues during the meeting.



Respiratory microbiome in IPF: Pathogenesis, Progression and Exacerbations

*Philip Molyneaux
London, UK.*

The recent characterization of the respiratory microbiome in idiopathic pulmonary fibrosis (IPF) has suggested that an increased bacterial burden, and presence of specific organisms, could drive disease progression. This strengthens the epidemiological argument that environmental factors may be integral to the pathogenesis of IPF in genetically susceptible individuals. However, there remain a number of unanswered questions regarding the role of the microbiome in IPF including the effect of the MUC5B polymorphism and the optimal sampling modality to study a parenchymal disease process.

We will review the current understanding of the microbiome in fibrotic lung disease, and explore the evidence supporting the role of the microbiome in the pathogenesis and progression of IPF. We will then discuss how an understanding of the microbiome may help us to gain further insights into currently “non-infective” acute exacerbations of IPF.

SYMPOSIUM



Host-microbe interplay sets the lower airway microenvironment in lung transplantation

Eric Bernasconi
Lausanne, Switzerland.

The lower airways can be considered as an ecosystem, whose equilibrium post-transplantation conditions graft survival. Due to long-term use of immunosuppressive and antibiotic therapy, the transplanted lung offers particular microenvironmental conditions. Despite prophylactic and therapeutic regimens, strong disturbance in local conditions may be observed. In particular, inflammatory episodes are elicited, most often by lower airway infections and during the first months post-transplant. Later, the onset of bronchiolitis obliterans syndrome, a clinical manifestation of chronic lung allograft dysfunction (CLAD) associated with obstructive fibrotic airway remodeling, has also been linked to host-microbe interactions, through pathogen-driven inflammatory triggers and/or impaired host innate responses affecting bacterial clearance. Hence, a concept of growing interest suggests that host-microbe interactions in lower airways are involved in controlling resistance to disturbance, or supporting a return to equilibrium. Correspondingly, microbiota dysbiosis may reflect a substantial disturbance in local conditions. Our

work allowed us to determine the microbiota composition based on 16S ribosomal RNA analysis in a total of 203 bronchoalveolar lavages obtained from 112 patients, up to 12 months post-lung transplantation. Host cellular gene expression profiles were characterized in parallel, by quantifying expression of a set of genes involved in prototypic macrophage functions. We found that the characteristics of the pulmonary microbiota align with distinct innate cell gene expression profiles. While a non-polarized activation was associated with bacterial communities consisting of a balance between pro-inflammatory (e.g. *Staphylococcus* and *Pseudomonas*) and low stimulatory (e.g. *Prevotella* and *Streptococcus*) bacteria, “inflammatory” and “remodeling” profiles were linked to bacterial dysbiosis. Mechanistic assays provided direct evidence that bacterial dysbiosis could lead to inflammatory or remodeling profiles in macrophages, while a balanced microbial community maintained homeostasis. We conclude that host-microbe interactions determine the lower airway microenvironment post-lung transplantation, and consequently could impact upon graft survival.

The microbiome in respiratory medicine



Lesson from the human gut microbiome

Chaysavanh Manichanh
Barcelona, Spain.

Functions of the gut microbiota affects many aspects of our systems physiology, ranging from processing and harvesting of nutrients from our diets, to shaping the features of our innate and adaptive immune system. Any factors that disturb this mutualism could result in diseases. Over the last decade, the limitations of culture-based methods have been overcome thanks to Next Generation Sequencing techniques, allowing us to understand the microbial gut community in greater depth through the study of microbial genes or full genomes, called metagenomics. To catalyse the field, the NIH and the European Commission launched, in 2008, the Human Microbiome and the MetaHIT Projects, respectively. These initiatives

have allowed a deep characterization of the human gut microbiome in health and disease states. The human GI-tract harbours one of the most complex and abundant microbial ecosystems colonised by more than 100 trillion microorganisms, and the number of microbial genes is about 100 times higher than that of our own genes. Although stable across ages, the composition and functions of the microbiome may be influenced by a number of factors including genetics, mode of delivery, age, diet, geographic location and medical treatments. Alteration in the microbiome structure and function has been linked to inflammatory, functional and metabolic disorders such as IBD, IBS and obesity.



The gut microbiome in HIV infection

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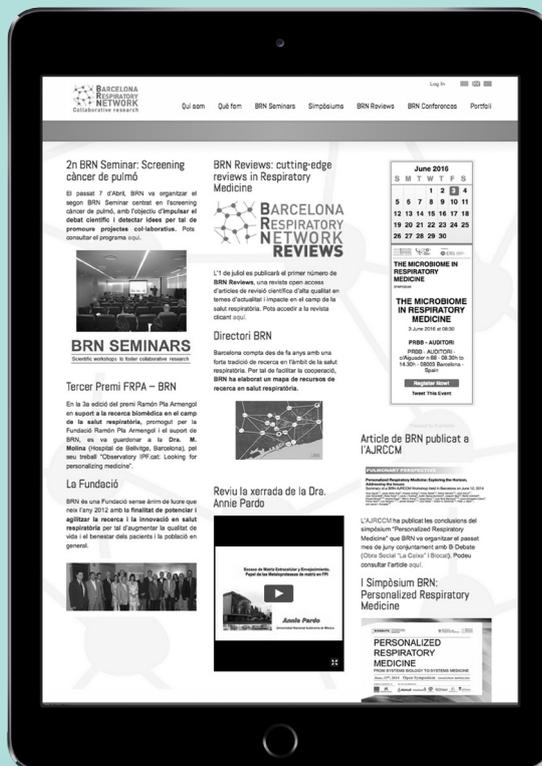
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Outcomes

Intended publication of a position paper on the topic of “The Microbiome in Respiratory Medicine” in the European Respiratory Journal. <http://erj.ersjournals.com/>

On the BRN website, you will find all the necessary information related to the holding of the meeting. That includes videos of the talks, abstracts of the presentations, speaker’s CVs, images, scientific documents, press documentation and other related materials. We invite you to visit it on <http://brn.cat/microbiome2016/>

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PULMONARY PERSPECTIVE

Personalized Respiratory Medicine: Exploring the Horizon, Addressing the Issues Summary of a BRN-AJRCCM Workshop Held in Barcelona on June 12, 2014

Alvar Agustí^{1,2}, Josep Maria Antó³, Charles Auffray⁴, Ferran Barba^{5,6}, Esther Barreiro^{7,8}, Jordi Dorca⁹, Joan Escarabell¹⁰, Rosa Fievet¹¹, Liana J. Furberg¹², Judith Garcia-Aymerich¹³, Joaquin Gasol¹⁴, Bertil Lindmark¹⁵, Eduard Monsó¹⁶, Vicente Plaza¹⁷, Miki A. Puhari¹⁸, Josep Roca¹⁹, Juan Ruiz-Manzano²⁰, Laura Sampieri-Corom¹, Ferran Sanz²¹, Luis Serrano^{22,23}, James Sharpe^{24,25}, Oriol Sibila²⁶, Edwin K. Silberman²⁷, Peter J. Stenk²⁸, and Jozsef S. Szepiet²⁹

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and main respiratory aspects. epidemiology, bioinformatics, and network/systems medicine; (3) the bottlenecks and opportunities identified by some currently ongoing projects; and (4) the implications for the individual, the healthcare system and the pharmaceutical industry. The authors hope that, although it is not a systematic review on the subject, this document can be a useful reference for researchers, clinicians, healthcare managers, policy-makers, and industry parties interested in personalized respiratory medicine.

and the AJRCCM in June 2014. As such, this manuscript is not a systematic review on the topic but rather a potentially useful reference for

all form November 21, 2014) of unrestricted grants from Amgen, Astra-Zeneca, Chiesi, GSK, Menarini, and Novartis, C.A., and of Bioware for the PRECISION of respiratory disease outcomes, grant agreement 481110215; the Department of Allergy, grant agreement FP7 no. 264207; and C.A. by the HPC Knowledge Management Service, grant agreement no. 115446; J.A., J.C., J.L., J.S., and J.S. acknowledge support of the Spanish Ministry of Science and Innovation, grant FIS 10/2004, and FUDAP 2011 and 2012; E.K.S. by NIH grants P01 HL05539 and P01 HL046206, S01HL110652-01A, HL110273, and P01HL110273, J.E. by the Master Plan of I.I.I.S. by HL-46129, HL-85234, and HL-71643.

and to Alvar Agustí, M.D., Thon Institute, Hospital Clinic, Vilanova 170, 08035 Barcelona, Spain.

DOI: 10.1164/rccm.2014.03.0515

Received December 22, 2014

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BARCELONA RESPIRATORY NETWORK Collaborative research

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Personalized Respiratory Medicine – 2014

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On June 12-13, 2014, BRN organized its first international meeting "Personalized Respiratory Medicine: Exploring the Horizon."

With the support of B Octave (Bozell and "La Caixa" Foundation) and the American Journal of Respiratory and Critical Care Medicine (AJRCCM), the meeting consisted of a scientific workshop (12th June 2014) followed by an open symposium (13th June 2014).

Please do not hesitate to download the detailed agenda or the complete program here.

The workshop brought together around 20 global scientific leaders from different disciplines (genomics, systems biology, epidemiology, clinical research, translational) with the aim to debate the state of the art in the field of personalized respiratory medicine, identifying priorities and future opportunities for the next decade. The conclusions drawn from the workshop will be published after peer review in the American Journal of Respiratory and Critical Care Medicine, the journal with the highest global impact in respiratory health.

The open symposium aimed to provide a broad, non-specialized view of the topic to a larger audience and solve deeper into how to tackle the challenge of personalized respiratory medicine. Below you will find complete information for each presentation of the symposium.

BARCELONA RESPIRATORY NETWORK Collaborative research

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04. Systems Epidemiology
05. Introduction to Network Medicine
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07. US-COPD
08. A Pharma Industry Perspective
09. Individual Risk Stratification
10. Implications for the Health Care System
11. Revolutionizing healthcare management
12. Meeting Program

Edwin K. Silberman, M.D., Ph.D.
Channing Division of Network Medicine, Pulmonary and Critical Care Medicine, Brigham and Women's Hospital, Boston, Massachusetts

Introduction to Network Medicine

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BRIGHAM AND WOMEN'S HOSPITAL
BOSTON
HARVARD MEDICAL SCHOOL

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Talk 1
Historical and ethical aspects

Talk 2
Systems Biology

Talk 4
Systems Epidemiology

Talk 5
Introduction to network Medicine

Talk 7

Talk 8

Organizers



Barcelona Respiratory Network (BRN) is a network of different institutions based in Barcelona that seeks to promote cutting-edge translational research in Respiratory Health. Founded in 2012 as a non-profit organization, its Board of Trustees is composed of researchers from prestigious university hospitals and research centres in the field of respiratory health, pharmaceutical & healthcare companies, and civil society organizations. Therefore, BRN is a clear example of private-public partnership. BRN's mission is to strengthen and streamline research and innovation in the field of respiratory health, in order to improve the quality of life and well-being of patients and the population in general. BRN encompasses the basic, preclinical, and clinical research performed in the field of respiratory health by 7 major tertiary hospitals (H. Clinic, H. Bellvitge, H. Sant Pau, H. Mar, H. Germans Trias i Pujol, H. Parc Taulí, H. Arnau de Vilanova), an epidemiological research centre (CREAL) and 7 companies (Aldo-Unión, Astra Zeneca, Boehringer Ingelheim, Esteve, Esteve-Teijin, Ferrer, Leti and Linde Medicinal). BRN members hold a high degree of expertise in COPD,

Asthma, Pulmonary Hypertension, Mechanical Ventilation, Interstitial Lung Diseases, and Sleep Apnea, among other respiratory research topics. BRN has recently launched two initiatives such as:

BRN Reviews: an official journal of Barcelona Respiratory Network. An online, open access, quarterly journal that publishes cutting-edge, high quality, internationally authored reviews on timely topics in respiratory medicine, with an emphasis on their translational aspects. More information at: <http://www.brnreviews.com/>

BRN Seminars: thematic scientific meetings specifically created to foster scientific debate, to share the latest advances and ideas and to explore opportunities for new collaborative projects in the field of respiratory health. BRN Seminars are open to all interested researchers, either clinical, basic or involved in industrial research. More information at: <http://brn.cat/brn-seminars/>
For more information, please do not hesitate to contact us at info@brn.cat or visit <http://brn.cat/en/>

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The Centre for Genomic Regulation (CRG) is an innovative centre for basic research created in December 2000 by an initiative of the former Department of Universities, Research and Information Society (DURSI) of the Catalan Government. CRG is legally constituted as a non-profit foundation with the participation of the Catalan Government through the Economy and Business Department, the Health Department, the Pompeu Fabra University (UPF) and the Spanish Ministry of Economy & Competitiveness (MINECO). On this basis, CRG performs as a full member of the Barcelona Biomedical Research Park (PRBB), one of the scientific parks in the city, which is physically connected to the Hospital del Mar.

CRG believes in the fundamental value of scientific knowledge and that the medicine and biotechnology of the future depends on the ground-breaking science of today. As an essential platform to achieve that, CRG offers its scientists a cutting-edge environment that allows them to focus on top-level interdisciplinary research into the complexity of life.

Since 1st July 2015, CRG has integrated the National Centre for Genomic Analysis (CNAG-CRG). CNAG-CRG was created to carry out projects in DNA sequencing and analysis in collaboration with local researchers from Catalonia and Spain as well as with international researchers, to ensure Spanish competitiveness in the strategic area of genomics.

Visit <http://www.crg.eu/> for more information.

Endorsers



ERS EUROPEAN
RESPIRATORY
SOCIETY
every breath counts

The European Respiratory Society (ERS; www.ersnet.org) is an international organisation that brings together physicians, healthcare professionals, scientists and other experts working in respiratory medicine. We are one of the leading medical organisations in the respiratory field, with a growing membership representing over 140 countries worldwide.

Our mission is to promote lung health in order to alleviate suffering from disease and drive standards for respiratory medicine globally. Science, education and advocacy are at the core of everything we do.

ciberes

Centro de Investigación Biomédica en Red
Enfermedades Respiratorias

Biomedical Research Networking Center (CIBER) is a Public Research Consortium created in 2006 under the leadership of the Carlos III Health Institute (ISCIII, the main Public Research Entity responsible of funding, managing and carrying out biomedical research in Spain), to promote research excellence and build a critical mass of researchers in the field of Biomedicine and Health Sciences. Organized in 8 research areas including Bioengineering, Biomaterials and Nanomedicine (CIBERBBN), Mental Health (CIBERSAM), Hepatic Diseases (CIBEREHD), Diabetes and Metabolic Diseases (CIBERDEM), Rare Diseases (CIBERER), Respiratory Diseases (CIBERES), Public Health and Epidemiology (CIBERESP) and, Obesity and Metabolic Diseases (CIBEROBN), CIBER is the largest Research Network in Spain.

CIBER numbers with more than 830 dedicated employees and 4,000 associated researchers integrated in 399 leading-edge research groups. Thanks to its network structure, CIBER is capable of bringing together more than 92 different associated institutions including Hospitals, Research Centers, Technology Centers, Private Institutions and Universities selected to join CIBER consortium on the basis of their excellence.

CIBERES is the area of CIBER devoted to respiratory diseases, with 10 specific research lines regarding, Lung Cancer, Acute lung Injury (ALI), Asthma, Chronic Obstructive Pulmonary Disease (COPD), Pathogen-Host Interaction, Pneumonia, Pulmonary Fibrosis, Sleep Apnea, Tuberculosis and Pulmonary Hypertension. CIBERES brings together 33 leading-edge Spanish research groups in the area of respiratory diseases selected on the basis of scientific excellence.



Sociedad Española
de **Neumología**
y **Cirugía Torácica**
SEPAR

The Spanish Society of Pneumology and Thoracic Surgery (SEPAR) is the scientific society bringing together more than 3,600 respiratory health professionals in Spain, including pulmonologists, thoracic surgeons, and other specialists, both national and

international, who all share common interests. The SEPAR goal is to work on scientific projects that advance pulmonology and thoracic surgery and to perform respiratory health initiatives that positively impact society.

Main Partners



GRUPO
MENARINI

www.menarini.es

Menarini is an international pharmaceutical group with over 125 years of history that is present in over 100 countries around the world. Grupo Menarini España is one of the strategic subsidiaries of the group, with a production of more than 60 million units of medicines per year and employs about 700 workers. Based in Badalona,

with an area of 15,000 m², it includes the production plant and one of the six R&D centres that Menarini International Group has in Europe. Menarini, present in Spain for 55 years, ranks among the top 20 pharmaceutical companies in the Spanish sector.



Glaxo Smith Kline (GSK) is one of the world's leading research-based pharmaceutical and healthcare companies – is committed to improving the quality of human life by enabling people to do more, feel better and live longer.

Ramón Pla Armengol
FUNDACIÓN PRIVADA

Ramón Pla Armengol Private Foundation was created in 2011 and has among its objectives the promotion and support research in Pulmonology and a biennial award recognizing researchers in respiratory diseases with special contribution to medical innovation. Dr. Ramón Pla Armengol (1880-1956) was a specialist in tuberculosis, researcher and entrepreneur who brought together the preponderance of immunological processes in the tuberculosis etio-pathogenesis and, based on that,

generated two treatments that were developed at the Institut Ravetllat-Pla (Barcelona). Doctor of Medicine, author of several papers in national and international journals, director of the "Academy Laboratory Annals of Medical Sciences of Catalonia", was also cofounder of the Sindicat de Metges de Catalunya (Union of Doctors in Catalonia).

Collaborators



AstraZeneca's mission is to make a meaningful difference to healthcare through great medicines. AstraZeneca's vision is to be a global biopharmaceutical business delivering great medicines to patients through innovative science and excellence in development and commercialization. Everything they do at AstraZeneca is driven by its commitment to improving the lives of patients. Whether that's working to reach more

people with their medicines, or applying their science skills to developing the next generation of treatments, or collaborating with others in the fight against disease – everything centers on understanding and meeting the needs of people facing serious health challenges. They focus primarily on cancer, cardiovascular / metabolic disease and respiratory, inflammatory and autoimmune disease.



Chiesi Farmaceutici is a multinational pharmaceutical company based in Parma (Italy) created in 1935 and R&D oriented, investing the 18% of its turnover in the last years. It has a strong presence in Europe and worldwide (United States, Brazil, Mexico, Pakistan, China, Russia).



Laboratorios LETI, SL Unipersonal (LETI) is a biopharmaceutical research company founded in Barcelona in 1919. Today the company is one of the first four World Laboratories in the field of allergen based immunotherapy. In addition immunology, preventive medicine and biological products are key pillars of the Company. The headquarters is located in Barcelona and its Industrial Plant and Research

Laboratory are located in Tres Cantos (Madrid), where individualized allergy vaccines are produced. The Company has subsidiaries in Germany, Portugal and the United States, and exclusive distributors in several countries of Europe, Latin America and Africa. LETI invests between 15-20% of its turnover in R&D. LETI collaborates with research centers, universities and hospitals in numerous countries.



Novartis is a world-leading healthcare company that operates in 140 countries, with global headquarters in Basel, Switzerland and with more than 135,000 associates. Novartis mission is to care

and cure and for that his objective is to discover, develop and successfully market innovative products to prevent and cure diseases, to ease suffering, and to enhance quality of life.

With the support of:



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