

THE BARCELONA DEBATES ON THE HUMAN MICROBIOME 2017

FROM MICROBES TO MEDICINES

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THE BARCELONA DEBATES ON THE HUMAN MICROBIOME 2017 FROM MICROBES TO MEDICINES

June 29th and 30th, 2017

WELCOME

Dear Speakers and Participants,

It is our pleasure to welcome you for the meeting The Barcelona Debates on the Human Microbiome. From Microbes to Medicines. B·DEBATE, an initiative of Biocat and “la Caixa” Foundation, together with the IrsiCaixa AIDS Research Institute, the Vall d’Hebron Research Institute (VHIR), the University of Vic (UVic-UCC), and the Spanish National Cancer Research Centre (CNIO) made it possible.

The human microbiome is involved in a large variety of essential functions and its influence on human health and disease has long been evidenced. Understanding human-microbiome relationship and how it can be modulated is a challenge for preventive medicine and for the medical management of chronic diseases. Importantly, it also represents an opportunity for innovation for food and pharma industries. New sequencing technologies have revolutionized this field and have been crucial in characterizing and increasing our understanding of the human microbiome. Crucial advances have been made in the last months; however many important questions still remain open. While differences among healthy and diseased individuals in both microbial composition and functional pathways have been observed for many diseases, the mechanisms governing these associations are still mostly unknown.

Catalonia, a hub in biomedical research, has caught the wave of opportunity to explore the role of microbiome in human health.

At present, Catalan research centers are conducting cutting edge projects focused on the study of human microbiome. This is an evidence of the consolidation of the field in our region.

The Barcelona Debates on the Human Microbiome. From Microbes to Medicines, is the expression of this strategic commitment and the will to bring together international experts in the study of the microbiome.

With the participation of leading investigators in human microbiome research, we will discuss the more recent hypotheses and theories regarding the complex humanmicrobiome relationship and how it may be modulated for improving health and well-being. The invited talks and open debates will stimulate the discussion and will provide thoughts for future areas of research.

We encourage you to actively participate in the discussions and wish you a fruitful meeting over the next two days.

Yours sincerely,

IrsiCaixa, VHIR, UVic-UCC, CNIO and B·DEBATE

PROGRAM

Thursday, June 29th, 2017

8:15 Registration

8:30 Welcome

Jordi Portabella, La Caixa Foundation

Jordi Fàbrega, Director of Business Development, Biocat

Bonaventura Clotet, Director, IrsiCaixa AIDS Research Institute

9:00 **SESSION 1: HEALTHY EATING FOR HEALTHY AGING**

Chair: **José Manuel Fernández-Real**, University of Girona, Girona, Spain

The Microbiome in human aging

Ian Jeffery, University College Cork, Cork, Ireland

Eating well to age well: personalized diets for a healthy man-microbes symbiosis

Joël Doré, INRA, Paris, France

10:00 Discussion

10:30 Coffee break

11:00 **SESSION 2: DRUG - MICROBE INTERACTIONS**

Chair: **José Moltó**, Fight against AIDS Foundation, Barcelona, Spain

Extending the resolution of human gut microbiomics: drug-bug interactions

Peer Bork, EMBL, Heidelberg, Germany

Vaginal bacteria modify HIV tenofovir microbicide efficacy in African women

Nichole Klatt, University of Washington, Seattle, USA

12:00 Discussion

12:30 Lunch and poster viewing

13:30 **SESSION 3: THE MICROBIOME IN INFECTIOUS DISEASES**

Chair: **Darla Hazuda**, Merck, West Point, USA

Longitudinal microbiota changes following acute HIV infection

Roger Paredes, IrsiCaixa AIDS Research Institute, Barcelona, Spain

Bacteriome and Mycobiome Interactions Underscore Microbial Dysbiosis in Familial Crohn's Disease

Mahmoud Ghannoum, Center for Medical Mycology at Case Western Reserve University, Cleveland, USA

14:30 Discussion

15:00 SESSION 4: DIGESTIVE DISEASES

Chair: **Chaysavanh Manlchanh**, Vall d'Hebron Research Institute, Barcelona, Spain

Dangerous liaisons between gene and microbiota: the example of Card9 in IBD

Harry Sokol, Saint Antoine Hospital, Paris, France

The interplay between insulin resistance and fatty liver disease

José Manuel Fernández-Real, University of Girona, Girona, Spain

16:00 Discussion

16:30 Adjourn

Friday, June 30th, 2017

9:00 SESSION 5: BREAKFAST WITH EXPERTS

Experts: **Dusko Ehrlich**, Kings College London, UK

Joel Doré, INRA, Paris, France

Francisco Guarner, Vall d'Hebron Research Institute, Barcelona, Spain

B Cell Ontogeny and Stromal Regulation of Homeostatic Antibody Responses to Commensal Antigens in Humans

Sabrina Bascones, IMIM, Barcelona, Spain

Novel insight in the role of the gut microbiota in obesity: beyond composition, towards activity and functionality

Koen Venema, Maastricht University, Maastricht, The Netherlands

Gut microbiota determines increased circulating levels of succinate in human obesity

Carolina Serena, Health Institute Pere Virgili. Hospital Joan XXIII of Tarragona, Spain

9:30 SESSION 6: GETTING THE BIG PICTURE: FROM CITIZEN SCIENCE TO SYSTEMS BIOLOGY

Chairs: **Marc Noguera**, IrsiCaixa, Barcelona, Spain

Rosina Malagrida, IrsiCaixa, Barcelona, Spain

Stick out your tongue!: citizen-science to unveil the oral microbiome

Toni Gabaldón, Center for Genomic Regulation, Barcelona, Spain

Systems biology and model-based multi-omic analysis of the human microbiome

Elhanan Borenstein, University of Washington, Seattle, USA

10:30 Discussion

11:00 Coffee break

SESSION 7: GUT-BRAIN AXIS

Chair: **Agustín Ruiz**, Fundació ACE, Barcelona, Spain

11:30 The Brain Gut Microbiome System- Science and Potential Clinical Implications

Emeran A Mayer, David Geffen School of Medicine at UCLA, Los Angeles, USA

Gut Microbiota in Parkinson's Disease

Fillip Scheperjans, Helsinki University Hospital, Helsinki, Finland

12:30 Discussion

13:00 Lunch

14:00 **Special lecture: The human microbiome in medicine**
Dusko Ehrlich, King's College, London, UK

14:30 **SESSION 8: CANCER**

Chairs: **Núria Malats**, Spanish National Cancer Research Center - CNIO, Madrid, Spain
M. Luz Calle, Uvic-UCC, Vic, Spain

Gut microbiota and colon cancer: the carbohydrate link
Laurence Zitvogel, Gustave Roussy, Paris, France

Rational development of defined bacterial consortia drugs for cancer and cancer complications
Bernat Ollé, Vedanta Biosciences, Boston, USA

15:30 Discussion

16:00 **Meeting closure**
Francisco Guarner, Vall d'Hebron Research Institute, Barcelona, Spain

SCIENTIFIC COMMITTEE



Bonaventura Clotet, Director IrsiCaixa. Head of Infectious Diseases, Hospital Universitari Germans Trias i Pujol. **IrsiCaixa. UAB. UVIC-UCC** Badalona, Spain.

Bonaventura Clotet, Specialized in Internal Medicine and Infectious Diseases. PhD in Medical Sciences in 1981. He is Head of the Infectious Diseases department and Director of the Retrovirology Laboratory “IrsiCaixa” Foundation at the Hospital Universitari Germans Trias i Pujol since 1993. He is also President of the Foundation “Lluita contra la SIDA”, founded in 1992. Since 2006, he is co-director of the HIVACAT project for the development of the AIDS vaccine in Catalonia, Spain. Director of the Master in AIDS Pathogenesis and Treatment (Universitat Autònoma de Barcelona) since 2011. Dr. Clotet is member of the steering committee of EuroSIDA Scientific Advisory Board Member. He is the director of the Chair of AIDS and Related Diseases at the University of Vic (UVic), created in October 2013. In October 2012, he was awarded by the Catalan Government (Generalitat de Catalunya) with the Josep Trueta medal to Sanitary Merit for his contributions to the research in the HIV field. In April 2016, Clotet has been awarded with the 'Creu de St. Jordi' for being one of the most internationally renowned HIV researchers. Dr. Clotet has created 2 spin-offs from IrsiCaixa: AELIX Therapeutics (December 2015) for the development of a therapeutic vaccine for HIV infected patients and AlbaJuna Therapeutics (January 2016) for the development of an Immunoglobulin for curing & preventing HIV. More than 700 papers in international journals (Impact factor: >5.000 // H-index: 81)



Roger Paredes, HIV Physician at Hospital Germans Trias i Pujol and Head of the Microbial Genomics Group at the **IrsiCaixa AIDS Research Institute**, Barcelona, Spain.

Roger Paredes obtained an MD, PhD degree in Medicine and Surgery from the Autonomous University of Barcelona (UAB). He specialised in HIV resistance at the Brigham & Women’s Hospital in Boston and Harvard Medical School, being funded by a post-doctoral scholarship from “la Caixa”. He has demonstrated the clinical utility of new methods of sequencing HIV in both high- and low-income countries. He is a member of the WHO HIV Drug Resistance Strategy (ResNet) Steering Committee and of the International Antiviral Society-USA, which publishes an international annual update of drug resistance mutations in HIV-1. He is co-author of the Rega algorithm for interpreting resistance to antiretrovirals and is a virologist for the EuroSIDA European cohort. His group has led pioneering research into the role of the gut microbiome in the pathogenesis of HIV infection and chronic inflammation. He combines his research with a senior medical appointment at the HIV unit of the Germans Trias i Pujol University Hospital (Badalona).



Marc Noguera, Researcher, bioinformatics Lead. Microbial Genomics Group at the **IrsiCaixa AIDS Research Institute**, Badalona, Spain.

Background in Chemistry (Bsc in Chemistry, PhD in Computational Chemistry, Universitat Autònoma de Barcelona, Barcelona), Biochemistry (BSc in Biochemistry, Universitat Autònoma de Barcelona, Barcelona) and Computer Science (Computer Engineering, Universitat Oberta de Catalunya). He did his PhD in computational and theoretical chemistry and later switched to human and microbial genomics and bioinformatics. His research is mainly focused on human microbiome data analysis and HIV resistance from the computational perspective.



Francisco Guarner, Senior Investigator at **Vall d'Hebron Research Institute (VHIR)**, Barcelona, Spain.

Dr. Francisco Guarner graduated in Medicine at the University of Barcelona in 1973, trained Gastroenterology and Hepatology at Hospital Clinic (Barcelona); obtained PhD degree at University of Navarra (Spain). He was Research Fellow at Royal Free Hospital (London, UK), King's College Hospital (London, UK), and Wellcome Research Laboratories (Beckenham, UK). He is Senior Researcher at the Digestive System Research Unit, Vall d'Hebron Institut de Recerca (Barcelona, Spain). Member of the Steering Committee of the International Human Microbiome Consortium (www.human-microbiome.org), past member of the Board of Directors on the International Scientific Association for Probiotics and Prebiotics (www.isapp.net), current President of the Board of the Spanish Society for Probiotics and Prebiotics (www.sepyp.es), Member of the Guidelines Committee of World Gastroenterology Organisation (www.worldgastroenterology.org), and co-author of 295 publications on original research or reviews (Web of Science); holds an h-index of 50.



Chaysavanh Manichanh, Research investigator, head of the Metagenomics Lab, Department of Physiology and Physiopathology, **Vall d'Hebron Research Institute (VHIR)**, Barcelona, Spain.

Since 2002, Dr. Chaysavanh Manichanh is using meta-omic approaches to study the human microbiome associated with disorders. In 2006, Chaysavanh joined the VHIR institute in Barcelona as principal investigator to pursue her line of research on Human Microbiome. She has collaborated with the MetaHIT and the IHMS consortia to build a comprehensive gene catalogue from the human gut microbiome and to develop standard operating procedures (SOPs) and protocols in order to optimize data comparisons in the human microbiome field. With this experience and her double expertise in molecular microbiology (PhD University Paris VI, 2001) and in bioinformatics (Degree at Pasteur Institute, Paris 2000), she is leading at VHIR a multidisciplinary research group to develop molecular, cellular as well as bioinformatics tools to understand the role of the microbiome in human health and disease. <https://sites.google.com/site/manichanhlab/home>



Fernando Azpiroz, Chief of the Department of Digestive Diseases, **University Hospital Vall d'Hebron**, and Professor of Medicine, **Autonomous University of Barcelona**, Barcelona, Spain.

Dr. Azpiroz is currently Chief of the Department of Digestive Diseases, University Hospital Vall d'Hebron, and Professor of Medicine, Autonomous University of Barcelona, Spain. Dr. Azpiroz clinical practice develops in a large referral unit, and specifically focusses on functional gut disorders. His research program investigates the origin of gastrointestinal sensations, either pleasant or unpleasant (symptoms), which involves the control mechanisms of gut motility, sensitivity and contents. Dr. Azpiroz has been distinguished with the 1999 Janssen Award for Clinical Research in Digestive Diseases, the Fourth Research Award of the International Group for the Study of Gastrointestinal Motility, the 2003 Research Scientist Award of the Functional Brain Gut Research Group, and the Senior Investigator-Clinical Science Award of the International Foundation for Functional Gastrointestinal Disorder. At present Dr Azpiroz serves as Chairman of the Microbiota & Health Section, European Society of Neurogastroenterology and Motility and is a member of the Board of Directors, Rome Foundation for the Study of Functional Gastrointestinal Disorders.



M. Luz Calle, Head of the Bioinformatics and Medical Statistics Group, Systems Biology Department, **University of Vic – Central University of Catalonia (UVic-UCC)**, Vic, Spain.

Professor of Biostatistics and Bioinformatics at the Systems Biology Department, University of Vic – Central University of Catalonia. Background in Mathematics (BSc Mathematics, Universitat de Barcelona and PhD in Mathematics, Universitat Politècnica de Catalunya). Chair of the Master of Sciences in Omics Data Analysis, UVic-UCC. Group leader of the Bioinformatics and Medical Statistics Group of the University of Vic (consolidated group 2014SGR-596). Former President of the Spanish Region of the International Biometrics Society (2012-2013) and Vice-president (2014). Her main research areas are statistical genetics, omics data analysis and survival analysis. She works on the development of new methods for biomarker discovery, identification of genetic risk profiles and construction of dynamic prediction and prognostic models of disease evolution. She is also interested in statistical methods for integration of multi-omics data and compositional data approaches in metagenomics. She is member of several scientific societies: BiostatNet-Spanish National Network in Biostatistics, Catalan Statistical Society, Spanish Society of Statistics and Operational Research, International Biometric Society, International Genetic Epidemiology Society.



Núria Malats, Principal Investigator of the Genetic & Molecular Epidemiology Group at the **Spanish National Cancer Research Centre (CNIO)**, Madrid, Spain

Dr. Núria Malats is currently the head of the Genetic and Molecular Epidemiology Group at the Spanish National Cancer Research Centre (CNIO), Madrid, Spain. She has a broad expertise in these fields of research by focusing mainly on pancreas and bladder cancer. She coordinates several large national and international studies integrating different levels of information, including omics data, in both disease development and progression. She has over 250 publications and is external reviewer of national and international funding agencies and first rank scientific journals. Dr. Malats chaired the EUPancreas COST Action (BM1204), is a board member of the International Pancreatic Cancer Case Control Consortium (PanC4), and the chair of the Research Work Stream of Pancreatic Cancer Europe (PCE) multistakeholder platform.



Toni Gabaldón, ICREA Research Professor and Head of the comparative genomics group, at **Centre for Genomic Regulation (CRG)**, Barcelona, Spain.

Biochemist by training (University of Valencia, Spain, 1997), Toni Gabaldón performed a PhD in comparative genomics in The Radboud university (Nijmegen, The Netherlands) in 2005, and an EMBO-funded postdoc in 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 focused in 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 or the ERC Starting Grant. He currently leads a citizen science project focused on the oral microbiome of thousands of Spanish teenagers (Saca La Lengua, Stick out your tongue), which was awarded with the Diario Medico « Best Idea of the Year » prize in 2015.



Peer Bork, Senior group leader, Joint Head of Unit, and Strategic Head of Bioinformatics, EMBL, Heidelberg, Germany.

Professor Peer Bork is senior group leader and joint head of the Structural and Computational Biology unit at EMBL, a European research organization with headquarters in Heidelberg, where he also serves as strategic head of bioinformatics. Dr. Bork received his PhD in Biochemistry (1990) and his Habilitation in Theoretical Biophysics (1995). He works in various areas of computational and systems biology with a focus on function prediction, comparative analysis and data integration. He is an ERC investigator, has published more than 500 research articles, among them more than 60 in *Nature*, *Science* or *Cell* and is one of the most highly cited researchers in life sciences, with an H-factor of 162. He is on the editorial board of a number of journals including *Science* and functions as senior editor of the journal *Molecular Systems Biology*. Dr. Bork co-founded five successful biotech companies, two of which went public. More than 35 of his former associates now hold professorships or other group leader positions in prominent institutions all over the world. He received the "Nature award for creative mentoring" for his achievements in nurturing and stimulating young scientists and was recipient of several other prizes, including the prestigious "Royal Society and Académie des Sciences Microsoft award".



Stanislav Dusko Ehrlich, Director Emeritus at Institut National de la Recherche Agronomique (INRA) and PI of the Metagenopolis project, Jouy en Josas, France. And Director of Centre for Host Microbiome Interaction, King's College, London, UK.

Stanislav Dusko EHRlich was trained in Organic Chemistry at the University of Zagreb, Croatia and obtained PhD degree in Biochemistry at the University Paris VII, France. He was a research associate of Dr. Joshua Lederberg, Nobel Prize winner, in the Department of Genetics, Stanford University Medical School, California. He founded and directed Microbial Genetics Research Unit and the Microbiology Division at the National Institute for Agricultural Research (INRA) and coordinated the MetaHIT project. He authored or co-authored 350 publications in peer-reviewed scientific journals, 60 book chapters and 14 patents and holds an H index of 75. He is member of the Croatian Academy of Sciences and Arts, French Academy of Agriculture, the European Molecular Biology Organisation, the American Academy of Microbiology and the European Academy of Microbiology. He is Research Director Emeritus at INRA, where he is the PI of the Metagenopolis project and Professor at King's College London, where he is Director of the Centre for Host Microbiome Interactions. He is Laureate of the Excellence in the Agricultural Research of INRA and of the Grand Prix Scientifique Del Duca de l'Institut de France, Chevalier de l'Ordre de Mérite et de la Légion d'Honneur.



José-Manuel Fernández-Real, Chief of Section at Institut d'Investigació Biomèdica de Girona (IdIBGi) and CIBERobn, Girona, Spain.

Dr. Fernández-Real received his M.D. and Ph.D. degrees from University of Barcelona, Spain. Since then, he has been researching in chronic inflammation, iron metabolism and insulin resistance. He has published 389 articles indexed in PubMed, of which 102 as first author and 118 as last author (corresponding author). He is Principal Investigator of >20 competitive National and International competitive Projects (continuously since 1993) and is a former member of the Editorial Board of *Diabetes Care* and *Clinical Chemistry*, among others. He was among the very first authors to propose chronic low grade inflammation in the pathophysiology of type 2 diabetes, obesity and insulin resistance and iron stores as a component of the metabolic syndrome. The interplay of the microbiota with all these elements is also an important line of research. He has been recently invited to talk about his research in the Annual Meeting of the American Diabetes Association (San Francisco 2015), the Endocrine Society (Boston 2016) and the American Society of Nutrition (San Diego 2016), in addition to invited conferences in meetings from European Association for the study of Diabetes (Lisbon 2011), Endocrinology (Budapest 2012), Obesity (Sofia 2014) and Nutrition (Prague 2016). He is currently Associate Professor in the Faculty of Medicine (University of Girona), Director of Research in the Department of Endocrinology, and Scientific Director of the "Fat Bank", a nation-wide Biobank specialized in adipose tissue samples. He is Principal Investigator and member of the Steering Committee of the CIBERobn, a Network of Excellence in the Research of Obesity in Spain.

DETAILED PROGRAM AND INVITED SPEAKERS

Thursday, June 29th, 2017

Session 1: Healthy eating for healthy aging



José Manuel Fernández-Real, Chief of Section at Institut d'Investigació Biomèdica de Girona (IdIBGi) and CIBERobn, Girona, Spain.

(See his CV at the Scientific Committee section)



Ian Jeffery, SFI Principal Investigator, APC Microbiome Institute/Microbiology Dept., UCC, Cork, Ireland.

Ian Jeffery is a Principal Investigator at University College Cork, Ireland. His main research themes are investigation of the role of the gut microbiota in Rheumatoid Arthritis, ageing and IBS. He is also involved in a number of collaborations and the NuAge consortium that examine the composition and function of the gut microbiota, its reaction to habitual diet, and its relationship to health and functional gastrointestinal disorders. The aim of these investigations is to understand how the gut microbiota affects

the immune system and initiates/contributes to the presentation or aggravation of disease such as Rheumatoid Arthritis. His research also involves the development of bioinformatic pipelines for the determination of Co-abundance Groups and the integration of omic datasets. As well as this he is also interested in the relationship between Co-abundant taxa within the microbiota and the associated combined functions of these groups. The Principal Investigator position is funded by a prestigious Science Foundation Ireland starting investigator Research grant (SIRG).

The Microbiome in human aging

The increase in life expectancy has resulted in an ever-increasing number of elderly individuals who are faced with unique age-related challenges when it comes to maintenance of their health and consequently their living independence. Clinical issues such as inflamm-aging, sarcopenia and depression are particularly noteworthy in this regard. The association between unhealthy diets and all-cause mortality is established but the importance of the role of the gut microbiota has only recently been widely recognized. To date, the largest gut microbiome study in an elderly population has been the ELDERMET study which showed that the intestinal microbiota composition is associated with long-term diet and the health status of the elderly individuals. This presentation will define what constitutes age-related changes of the gut microbial system. It will discuss the role of composition and diversity of the microbiota in age-related health loss. We will link these microbiota changes with age related dietary changes and other factors contributing to these changes.



Joël Doré, Scientific Director of the Industrial Demonstrator MetaGenoPolis at MetaGenoPolis, French National Institute for Agricultural Research, Paris, France.

Research Director at INRA, Joël is Scientific Director of MetaGenoPolis, a Unit of the Micalis Institute "Food and Gut Microbiology for Human Health" and member of the Scientific Council of Paris-Sud University Medical School. Joël joined INRA in 1983 and received his PhD from the University of Illinois at Urbana-Champaign, USA, in 1988. He trained as gut microbial ecologist and developed expertise in intestinal metagenomics towards diagnostic and prognostic applications as well as a window into microbe-host crosstalk. He aims to contribute to a better understanding of the intestinal ecosystem in order to support therapeutic choices in the medical area, as well as science-based recommendations in health nutrition. Joël Doré chairs the gutmicrobiotaforhealth.com scientific web-platform and is scientific advisor to the Healthtech startup MaaT Pharma.

Eating well to age well: personalized diets for a healthy man-microbes symbiosis.

During the first months of life, the newborn develops as an intimate symbiosis between human cells and complex microbial communities that colonize the skin, intestinal contents and all mucosal surfaces of the body. As any cell, our microbial symbionts are recognized as 'self' by our immune system and homeostasis of symbiosis is essential for the maintenance of health and wellbeing. With a rich diversity of species and on average 25 times more genes than the human genome, the intestinal microbiota contributes major functions that pertain to host nutrition, physiology and ensure protection from colonization by environmental microbes. An alteration of the intestinal microbiota, hence of man-microbes symbiosis, has been documented for a broad range of immune-mediated, chronic disorders. The latter have all increased in incidence over the past 60 years, to a point where one in four persons of the world population is affected today. After 25 years of exploration of dysbiosis in chronic conditions, we have come to realize that it corresponds to an alteration of man-microbes symbiosis. Imposed over 2 to 3 generations, nutritional transition, exposure to environmental xenobiotics, as well as major changes in perinatal management and environment all combined drastic effects on man-microbes symbiosis. In this context, we generated preliminary evidence that alternative stable states derived from critical transitions may be a basic feature of altered man-microbes symbiosis and could characterize major diseases of modern societies. Specific nutrients (fibers, polyphenols) and live microbes (probiotics, microbiotherapy preparations) would be bioactives of choice to restore symbiosis or prevent the onset or aggravation of chronic diseases. The current context hence calls for an urgent change in paradigm towards preventive nutrition and clinical management addressed to man as a true man-microbes symbiosis.

Session 2: Drug - Microbe interactions



José Moltó Marhuenda, Consultant physician. MD, PhD at **Lluita contra la sida Foundation**, Barcelona, Spain.

Dr. José Moltó received his degree in Medicine from the University of Alicante in 1996, and his Doctor of Medicine Degree from the Universitat Autònoma de Barcelona in 2008. He completed a residency at Hospital General Universitari in Elche (Alicante). He joined the Fight against AIDS Foundation, in Barcelona, in 2002. He has been working as a physician assistant, taking care of HIV-infected patients, as well as a clinical researcher, with special focus on Clinical Pharmacology of antiretroviral treatment.

Chair of the **SESSION 2**



Peer Book, Senior group leader, Joint Head of Unit, and Strategic Head of Bioinformatics, **EMBL**, Heidelberg, Germany.

(See his CV at the Scientific Committee section)

Extending the resolution of human gut microbiomics: drug-bug interactions

Our knowledge of the human gut microbiome and its role for human health and well-being are constantly increasing. While a healthy gut microbiome is still not clearly defined, an increasing number of diseases is being associated with dysbiosis of the microbiome, as deduced from metagenomics studies. I will illustrate the respective diagnostic potential using microbial markers for colorectal cancer as an example (Zeller et al., *Mol.Sys.Biol.*, 2014). Such metagenome-wide association (MWAS) studies are powerful, but currently still suffer from insufficient resolutions at several levels, such as (i) limited taxonomic resolution (species at best), (ii) the inability to infer causality, and (iii) indirect and thus misleading associations due to hidden confounding factors. An example for the latter is drug treatment as we could show recently for the drug metformin and type 2 diabetes after disentangling drug treatment signals from disease phenotypes (Forslund et al., *Nature* 2015). By now a number of drugs have been associated with gut microbiome alterations using MWAS studies, but causality and direct interactions can still not be inferred. To increase the resolution in this respect, several groups at EMBL established together an in vitro microbiome project based on culturing human gut microbiota individually and as sub-communities using a variety of defined media. It enabled us, for example, to screen of >1000 marketed drugs against each of 40 human gut bacteria, implying that at least 24% of all drugs directed against human cells inhibit at least one gut microbial strain. We are starting now to also increase the taxonomic resolution by looking at conspecific strains. This is paralleled by efforts to utilise single nucleotide variants (SNVs) in metagenomic data (Schloissnig et al., *Nature* 2013, Zhu et al., *Genome Biol.* 2015). One application is the monitoring of donor and recipient strains after faecal microbiota transplantation (FMT) that performs remarkably well in patients with recurrent *C.difficile* infections, but appears to work less efficient for other conditions such as ulcerative colitis. Using single nucleotide variation, we can show how donor strains can colonise for at

least three months in the recipient, often in coexistence with indigenous strains (Li et al., Science 2016). Thus, the increase of taxonomic resolution empowers MWAS studies for more fine-grained hypotheses, which can now be also explored in vitro, allowing more efficient use of animal models.



Nichole Klatt, Associate professor at **University of Washington, Department of Pharmaceutics**, Seattle, United States.

The complex interactions between the microbiome, the epithelial barrier, immune cells and drug metabolism are critical for protection from disease. The focus of the Klatt lab is to understand mechanisms underlying mucosal dysfunction, microbiome dysbiosis, drug metabolism, and altered immunity in mucosal tissues (mainly gastrointestinal and female reproductive tracts), and how these defects contribute to HIV transmission and pathogenesis. Our ultimate goal is to improve prevention and treatment strategies for HIV infection. Nikki Klatt is an associate professor in the department of Pharmaceutics at the University of Washington, and adjunct assistant professor in the programs in Pathobiology in the school of global health and the molecular and cellular biology graduate program. Nikki is also director of the mucosal immunology core of the Washington National Primate Research Center. Nikki received her PhD in Immunology and Molecular Pathogenesis from Emory University in Atlanta, GA in 2009, and she also studied as a visiting fellow at the University of Pennsylvania in Philadelphia, PA from 2006-2008. She completed her postdoctoral training at the NIH in 2012, in the Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases in Bethesda, MD.

Vaginal bacteria modify HIV tenofovir microbicide efficacy in African women

Antiretroviral-based strategies for HIV prevention have shown inconsistent results in women. We investigated whether vaginal microbiota modulated tenofovir gel microbicide efficacy in the CAPRISA-004 trial. Two major vaginal bacterial community types were identified in 688 women profiled; one dominated by *Lactobacillus* (59.2%), and the other where *Gardnerella vaginalis* predominated with other anaerobic bacteria (40.8%). Tenofovir reduced HIV incidence by 61% ($P=0.013$) in *Lactobacillus*-dominant women but only 18% ($P=0.644$) in women with non-*Lactobacillus* bacteria - a three-fold difference in efficacy. Detectible mucosal tenofovir was lower in non-*Lactobacillus* women, negatively correlating with *G. vaginalis* and other anaerobic bacteria, which depleted tenofovir by metabolism more rapidly than target cells convert to pharmacologically active drug. This study provides new evidence linking vaginal bacteria to microbicide efficacy through tenofovir depletion via bacterial metabolism.

Session 3: The microbiome in infectious diseases



Daria Hazuda, Vice President, Infectious Disease & Vaccines, CSO Cambridge Exploratory Science Center, **Merck**, West Point, PA, USA.

Daria Hazuda, Ph.D., trained as a biochemist at the State University of New York at Stony Brook, N.Y. After completing her postdoctoral research fellowship in the department of Immunology at Smith Kline, she joined the antiviral group as a Senior Research Biochemist at Merck in 1989. Daria is currently Vice President of Infectious Disease and Vaccines at Merck Research Labs and Chief Scientific Officer of MRL Cambridge. Daria has over 20 years of experience in drug discovery and development with more than one hundred-eighty publications focused primarily on antiviral research in the fields of HIV and HCV. She led the research efforts that identified the first-in class HIV integrase inhibitor Isentress which was awarded the Prix Galien in 2008 and was responsible for pioneering work on HCV drug resistance enabling the discovery of agents with improved spectrum and efficacy including the NS5A inhibitor Elbasvir and the NS3 inhibitor Grazoprevir. Daria has been recognized with the Bernie Field Lecture Award, the David Barry DART Achievement Award for HIV Drug Development and is a Fellow of the American Society of Microbiology. Daria is on the editorial board of the ACS Journal on Anti-infectives Research and the Journal of Viral Eradication. She is currently on the Scientific Program Advisory Council of the American Foundation for Aids Research (AMFAR) and The Forum for HCV Collaborative Research and a past member of NIH Aids Research Advisory Committee (ARAC) and the NCI Basic Sciences Board of Scientific Counselors (2010-2015).

Chair of the **SESSION 3**



Roger Paredes, HIV Physician at **Hospital Germans Trias i Pujol** and Head of the Microbial Genomics Group at the **IrsiCaixa AIDS Research Institute**, Barcelona, Spain.

(See his CV at the Scientific Committee section)

Longitudinal microbiota changes following acute HIV infection

HIV-1 infection damages the intestinal mucosal barrier and gut-associated lymphoid tissues (GALT) enabling translocation of bacterial products to regional lymph nodes and systemic circulation. It also induces inflammation of the mesenteric fat and promotes extensive deregulation of local immune responses. In all, this leads to chronic inflammation and immune activation, which are only partially restored with ART. Immune activation hinders immune reconstitution, diminishes the efficacy of HIV-1 preventive and curative strategies, fosters immune senescence and, at the mucosal level, is a major risk factor for HIV-1 transmission. Nevertheless, the nature, determinants and mechanisms underlying gut microbiome changes during HIV-1 infection are not well understood. Using whole metagenome shotgun sequencing of fecal microbial DNA we previously showed that HIV-1-induced immune deficiency is strongly linked to reduced microbial gene richness and results in stark compositional and functional shifts in the gut microbiome. However, longitudinal studies are needed to understand when is gut dysbiosis instituted during the course of HIV infection and under which circumstances and, more importantly, whether it can be recovered or not. Here, we will present microbiome data from a cohort of acutely HIV-1 infected subjects in Mozambique and will compare it with that of HIV-negative controls and chronically HIV-1 infected subjects receiving ART or not.



Mahmoud Ghannoum, Professor and Director, Center for Medical Mycology at Case Western Reserve University, Cleveland, USA.

Dr Mahmoud Ghannoum received MSc in Medicinal Chemistry and PhD in Microbial Physiology from University of Technology in England, and an MBA from the Weatherhead School of Management at Case. Presently he is a tenured Professor and Director of the Center for Medical Mycology, Case Western Reserve University and University Hospitals Case Medical Center (UH) where he established a multidisciplinary disciplinary Center of Excellence that combines basic and translational research investigating microbes from the test tube to the bedside. He is also a fellow of the Infectious Disease Society of America and past President of the Medical Mycological Society of the Americas (MMSA). In 2016, Dr Ghannoum received the Rohda Benham Award presented for his continuous outstanding and meritorious contributions to medical mycology from the Medical Mycological Society of the Americas and he also received the Freedom to Discover Award from Bristol-Myers Squibb for his work on microbial biofilms. In 2017, he was inducted as a fellow of the American Academy of Microbiology.

Bacteriome and Mycobiome Interactions Underscore Microbial Dysbiosis In Familial Crohn's Disease

Crohn's disease (CD) results from a complex interplay between host genetic factors and endogenous microbial communities. In the current study, we used Ion Torrent sequencing to characterize the gut bacterial microbiota (bacteriome) and fungal community (mycobiome) in patients with CD and their non-diseased first degree relatives (NCDR) in 9 familial clusters living in Northern France/Belgium, and in healthy individuals from 4 families living in the same area (non-CD unrelated, NCDU). Principal components analysis, diversity, and abundance analyses were conducted and CD-associated inter- and intra-kingdom microbial correlations determined. Significant microbial interactions were identified and validated using single- and mixed-species biofilms. CD and NCDR groups clustered together in the mycobiome, but not in bacteriome. Microbiota of familial (CD, NCDR) samples were distinct from that of non-familial (NCDU) samples. Abundance of *Serratia marcescens* (SM), *Escherichia coli* (EC) was elevated in CD patients, while that of beneficial bacteria was decreased. Abundance of the fungus *Candida tropicalis* (CT) was significantly higher in CD compared to NCDR ($P = .003$), and positively correlated with levels of anti-*Saccharomyces cerevisiae* antibody (ASCA). Abundance of CT was positively correlated with SM and EC, suggesting these organisms interact in the gut. The mass and thickness of Triple species (CT+SM+EC) biofilm were significantly higher than single and double species biofilm. CT biofilms comprised of blastospores, while double and triple species biofilms were enriched in hyphae. SM used fimbriae to co-aggregate or attach with CT/EC, while EC closely apposed with CT. Specific inter-kingdom microbial interactions may be key determinants in CD.

Session 4: Digestive diseases



Chaysavanh Manichanh, Research investigator, head of the Metagenomics Lab, Department of Physiology and Physiopathology, **Vall d'Hebron Research Institute (VHIR)**, Barcelona, Spain.

(See her CV at the Scientific Committee section)

Chair of the **SESSION 4**



Harry Sokol, Professor of Gastroenterology at **APHP, UPMC, INSERM, INRA**, Paris, France.

Harry Sokol, is Professor in the Gastroenterology department of the Saint Antoine Hospital (APHP, Paris, France) and is the head of Avenir Team, Gut Microbiota and Immunity lab (INSERM U1157/UMR CNRS 7203, UPMC, Paris). Following a MD degree in Gastroenterology and a PhD in Microbiology, he spent 2 years in Ramnik Xavier's lab as postdoctoral research Fellow (Massachusetts General Hospital and Harvard Medical School, Boston, USA). Harry Sokol is an internationally recognized expert in IBD and in gut microbiota fields. He published over 120 papers on these topics and is reviewer for several major peer review journals (including Gut, Gastroenterology, Mucosal Immunology, ISME journal, Nature Methods, Science Translational Medicine and Nature). He received several awards including the French Medical Academy Award in 2009 and a rising star award from the United European Gastroenterology Federation in 2013. His work on the role of the gut microbiota in IBD pathogenesis led to landmark papers describing the IBD-associated dysbiosis (imbalance in gut microbiota composition) and the role of the pivotal commensal bacteria *Faecalibacterium prausnitzii* in gut homeostasis and in IBD. Currently, his work focuses on deciphering the gut microbiota-host interactions in health and diseases (particularly IBD), including viruses and fungi, in order to better understand their pathogenesis and develop innovative treatments. Harry Sokol is now exploring particularly the role of the microbiota in tryptophan metabolism for which he is recipient of an ERC starting grant (2017-2021). Beside basic science work, he is also involved in translational research and notably coordinates two French randomized control trial evaluating fecal microbiota transplantation in Crohn's disease and ulcerative colitis.

Dangerous liaisons between gene and microbiota: the example of Card9 in IBD

Complex interactions between the host and the gut microbiota govern intestinal homeostasis but remain poorly understood. Here we reveal a relationship between gut microbiota and caspase recruitment domain family member 9 (CARD9), a susceptibility gene for inflammatory bowel disease (IBD) that functions in the immune response against microorganisms. CARD9 promotes recovery from colitis by promoting interleukin (IL)-22 production, and *Card9(-/-)* mice are more susceptible to colitis. The microbiota is altered in *Card9(-/-)* mice, and transfer of the microbiota from *Card9(-/-)* to wild-type, germ-free recipients increases their susceptibility to colitis. The microbiota from *Card9(-/-)* mice fails to metabolize tryptophan into metabolites that act as aryl hydrocarbon receptor (AHR) ligands. Intestinal inflammation is attenuated after inoculation of mice with three *Lactobacillus* strains capable of metabolizing tryptophan or by treatment with an AHR agonist. Reduced production of AHR ligands is also observed in the microbiota from individuals with IBD, particularly in those with CARD9 risk alleles associated with IBD. Our findings reveal that host genes affect the composition and function of the gut microbiota, altering the production of microbial metabolites and intestinal inflammation.



José-Manuel Fernández-Real, Chief of Section, **Institut d'Investigació Biomèdica de Girona (IdIBGi)** and **CIBERobn**, Girona, Spain.

(See his CV at the Scientific Committee section)

The interplay between insulin resistance and fatty liver disease

The past decade has witnessed an impressive increase in the appreciation of the importance of inflammation in insulin resistance and non-alcoholic steatohepatitis, with much attention focused on the role of innate and adaptive immune cells. Relatively little is known about the potential triggers of inflammation. The balance between different inflammatory factors and anti-inflammatory systemic level should be explored to better understand the different eukaryote and prokaryote biological processes involved in a complex phenotype such as insulin resistance. Gut microbiota composition could constitute a critical modulating factor. The study of the key roles of the immune system and its interactions with the gut

microbiota reconciles the most well known features of insulin resistance and inflammation. Systems biology approaches will possibly illuminate transgenomic cross-talk between the metagenome and the host genome and how these influences on host systemic biochemistry affects systemic insulin action. Iron could also constitute an important confounder in all these interactions.

Friday, June 30th, 2017

Session 5: Breakfast with experts



Stanislav Dusko Ehrlich, Director Emeritus at **Institut National de la Recherche Agronomique** (INRA) and PI of the Metagenopolis project, Jouy en Josas, France. And Director of Centre for Host Microbiome Interaction, **King's College**, London, UK.

(See his CV at the Scientific Committee section)

Expert



Joël Doré, Scientific Director of the Industrial Demonstrator MetaGenoPolis at **MetaGenoPolis, French National Institute for Agricultural Research**, Paris, France.

(See his CV at the Session 2)

Expert



Francisco Guarner, Senior Investigator at **Vall d'Hebron Research Institute (VHIR)**, Barcelona, Spain.

(See his CV at the Scientific Committee section)

Expert

Oral presentation of the 3 best communications

B Cell Ontogeny and Stromal Regulation of Homeostatic Antibody Responses to Commensal Antigens in Humans.

Sabrina Bascones, Giuliana Magri, Marc Pybus, Jordi Sintes and Andrea Cerutti

The spleen contains a unique subset of innate-like marginal zone (MZ) B cells that rapidly mount protective antibody responses to invasive encapsulated bacteria. Here we show that human splenic MZ B cells also mount homeostatic antibody responses to commensal antigens undergoing systemic translocation from mucosal surfaces. This humoral response decreased upon splenectomy and correlated with splenic capture of commensal antigens and with the generation of MZ B cell-derived plasmablasts and plasma cells following GC-independent and -dependent pathways. Remarkably, commensal antigens targeted marginal reticular cells (MRCs) in addition to macrophages. Besides canonical stromal properties, MRCs expressed macrophage-like immunoactivating functions that promoted robust MZ B cell responses to microbial ligands. These responses required both contact-dependent and contact-independent signals from MRCs, including MAdCAM-1 and VCAM-1 adhesion molecules as well as cytokines such as BAFF and APRIL, respectively. Thus, MRCs may function as stromal activator cells that

integrate the innate and adaptive arms of the splenic immune system to orchestrate a secondary line of systemic defense against commensal antigens of mucosal origin.

Novel insight in the role of the gut microbiota in obesity: beyond composition, towards activity and functionality.

Koen Venema

It has become evident in the last few years that the microbial activity contributes to obesity, but the exact mechanisms are still unclear. Some researchers blame the microbiota to increase bodyweight, due to the extraction of energy in the form of short-chain fatty acids (SCFA) which become available to the host. However, these SCFA also have an anti-inflammatory effect, induce satiety hormones, and affect systemic metabolism, potentially leading to a reduction in bodyweight.

This contribution will highlight some recent results obtained using a validated in vitro model of the colon:

i) in terms of energy extraction by microbiotas originating from obese and lean volunteers, using established prebiotics, but also novel substrates derived from waste-streams of fruit and vegetables.

ii) an example of modification of a dietary fiber by the gut microbiota, which subsequently modulates its interaction with the host's immune system.

iii) interventions using pro- and/or prebiotics in (pre)diabetic and healthy children. Using molecular tools we show that the microbiota composition of these groups is different. Some of the interventions in the diabetic children lead to a shift of the microbiota towards those of the healthy children.

Clearly these examples need to be corroborated in clinical studies, but the results provided by the validated in vitro model show promise for the development of strategies to combat overweight and obesity.

Gut microbiota determines increased circulating levels of succinate in human obesity.

Carolina Serena, Victoria Ceperuelo-Mallafré, Noelia Keiran, Maribel Queipo, Rosa Bernal, Francisco Tinahones, Jose Manuel Fernández Real, Joan Vendrell and Sonia Fernández-Veledo

Background Metabolic sensors and gut microbiota are well-recognized biological drivers of obesity and type 2 diabetes mellitus (T2DM). Succinate, a tricarboxylic acid metabolite, is a novel mediator in local stress situations including hypoxia and inflammation, both important stimuli for metabolic dysfunction in obesity-related disorders. Notably, a relevant source of extracellular circulating succinate might be attributed to intestinal efflux driven by specific microbiota as a natural metabolic end product of some bacteria. Modifications in gut microbiota are highly valued as a potential treatment for obesity.

Session 6: Getting the big picture: from citizen science to systems biology



Marc Noguera, Researcher, bioinformatics Lead. Microbial Genomics Group at the **IrsiCaixa AIDS Research Institute**, Badalona, Spain.

(See his CV at the Scientific Committee section)

Chair of the **SESSION 6**



Rosina Malagrida, Head of Living Lab for Health at **IrsiCaixa**, Barcelona, Spain.

Rosina Malagrida has a degree in chemistry from the University of Barcelona, Spain, a master's in science communication from Imperial College London, UK (with a scholarship from "la Caixa" Foundation) and has run a programme for Strategic Communication at the business school ESADE. She is specialised in Responsible Research and Innovation (RRI), and in particular in communication, multistakeholder engagement, participatory governance, community based research and educational programmes and her interest focuses on facilitating spaces for collaboration between health research and society. Currently, she is the head of the Living Lab for Health Research at IrsiCaixa in Barcelona, where she is in charge of: 1) training organizations, HE and secondary students on competences for RRI, 2) facilitating the participation of patients in shaping the R&I of the institution, 3) running participatory processes where different stakeholders can participate in R&I and in R&I decision making and 4) assessing organisations on how to implement RRI. These tasks are implemented with the support of several EC funded projects, in which Malagrida is IP: a) deputy coordinator of the EC project RRI Tools, to promote RRI in Europe (just finalised), b) EnRRICH, to better promote research in response to societal needs through HE research projects, c) Inpires, to promote RRI and open science in collaboration among different stakeholders with the aim to co-decide Health R&I policies, and d) CRISH, to facilitate training on patient experience in RRI in several hospitals around Europe. Finally, Malagrida also coordinates the European educational portal Xplore Health, and a programme for outreach and prevention of HIV/AIDS. Malagrida previously worked at the Barcelona Science Park, where she was communication director, and at the science museums of London and Barcelona, developing exhibitions, experimental workshops, fairs, debates and 4 EC projects, such as Xplore Health or Nanopinion.

Chair of the **SESSION 6**



Toni Gabaldón, ICREA Research Professor and Head of the comparative genomics group, at **Centre for Genomic Regulation (CRG)**, Barcelona, Spain.

(See his CV at the Scientific Committee section)

Stick out your tongue!: citizen-science to unveil the oral microbiome

Developments in sequencing technologies have enabled us to study the human microbiome, a complex system of microbial life that lives on us and plays important roles in our health and disease. 'Stick out your Tongue' is the first citizen-science project performed at the CRG, whose aim is to study the microbes that inhabit our mouth, one of the most heavily colonized sites of our body and an entry point to the digestive and respiratory tracks. In this talk, I will provide an introduction to the fascinating world of the microbiome, show our recent results of the 'Stick out your Tongue' project, and discuss the intricacies of science performed hand-in-hand with the citizens.



Elhanan Borenstein, Associate Professor of Genome Sciences, **University of Washington**, Seattle, USA.

Elhanan Borenstein is an associate professor of Genome Sciences at the University of Washington, with an adjunct position in the Department of Computer Science and engineering. He is also an external professor at the Santa Fe Institute for complexity science. Dr. Borenstein received his PhD in computer science from Tel-Aviv University, Israel, and held a joint postdoctoral fellowship at the Department of Biology in Stanford and at the Santa Fe Institute. He also has extensive professional experience in the hi-tech industry, where he held top management positions in several hi-tech companies. Dr. Borenstein integrates metagenomic data with methods inspired by systems biology, network theory, machine-learning, and statistical inference to develop a variety of computational methods for studying the human microbiome. His work focuses on reconstructing predictive, systems-level models of the human microbiome and on integrative, multi-meta-omic analysis, aiming to provide a better principled understanding of the microbiome and its role in human health. Dr. Borenstein is the recipient of various awards including the Alfred P. Sloan Fellowship and the NIH New Innovator Award. Homepage: <http://elbo.gs.washington.edu/>.

Systems biology and model-based multi-omic analysis of the human microbiome

The human microbiome – the diverse ensemble of microorganisms that populate the human body – represents a vastly complex ecosystem that is tightly linked to our health. Multiple molecular assays now enable high-throughput profiling of this system, providing large-scale and comprehensive characterization of its ecology, functional capacity, and metabolic activity. To date, however, analyses of such multi-omic data typically focus on statistical associations, often ignoring extensive prior knowledge of the mechanisms, dependencies, and regularities linking these various facets of the microbiome. In this talk, I will highlight the pressing need for the development of predictive systems-level models of the microbiome and of model-based methods for integrating and analyzing microbiome multi-omic data. I will further introduce several novel computational frameworks for linking taxonomic, genomic, metagenomic, and metabolomic information about the microbiome. Combined, such frameworks lead to an improved comprehensive, multi-scale, and mechanistic understanding of the microbiome in health and disease, informing efforts for personalized microbiome-based therapy.

Session 7: Gut-Brain axis



Agustín Ruiz, Research Director at the **Neuroscience Center. Institut Català de Neurosciences Aplicades**, Barcelona, Spain.

Dr. Agustin Ruiz Laza is currently the Director of Research of Fundació ACE. Barcelona Alzheimer Treatment & Research Center (Barcelona, Spain). Born in Utrera, Sevilla, Spain (August 10th, 1969). He graduated in Medicine and Surgery and has a Ph.D. in Molecular and Cellular Biology from the University of Seville. For eight year he conducted research work at the Department of Medical Genetics and Prenatal Diagnosis in the Hospital Universitario Virgen del Rocío, Sevilla (1993-2001). There he received the Extraordinary Doctoral Award at the University of Seville (2000) for his thesis. He then co-promoted and co-founded four biotech companies receiving awards for best 50K Business Idea and Best Business Plan in the field of Biotechnology, Instituto Internacional San Telmo. The result of this activity with their partners received the award for business excellence in the area of Innovation of the Government of Andalusia (2008). Agustin Ruiz has published 144 articles in indexed journals such as JAMA, Lancet Neurol., J. Exp. Med., Nature, Nature series, among others. He is co-author of several patents related to the molecular diagnosis of complex diseases and bioinformatics tools for genomic research. He has received funding for >35 projects granted by regional, national and European competitive agencies. He participated in the writing of several chapters of scientific books and reviews in national magazines. His scientific interest is focused on the application of genomic technologies in medicine. He has participated in the identification of numerous genetic factors linked to different diseases and in the identification of 14 genes associated with Alzheimer's disease. Ruiz is the co-founder of the Dementia Genetics Spanish Consortium (DEGESCO). Currently, he is coordinating the EU Innovative Medicine Initiative (IMI) ADAPTED project (www.imi-adapted.eu) and the GR@ACE project conducting GWAS using samples from 14000 Spanish individuals.

Chair of the **SESSION 7**



Emeran A Mayer, Professor and Center Director at the **University of California Los Angeles (UCLA)**, Los Angeles, USA.

Emeran A Mayer is a Gastroenterologist, Neuroscientist and Professor in the Departments of Medicine, Physiology and Psychiatry at the David Geffen School of Medicine at UCLA. He is the Executive Director of the G Oppenheimer Center for Neurobiology of Stress & Resilience and the co-director of the CURE: Digestive Diseases Research Center at UCLA. As one of the pioneers and leading researchers in the role of mind-brain-gut interactions in health and chronic disease, he has made major scientific contributions to the area of basic and translational enteric neurobiology with wide-ranging applications in clinical GI diseases and disorders. He has published more than 300 scientific papers (h-factor 95), and co edited 3 books. He is the recipient of the 2016 Paul D McLean award from the American Psychosomatic Society and the Distinguished Mentor Award from the American Gastroenterological Association. In addition to his ongoing research in chronic visceral pain, his most recent work in the area of brain gut interactions has focused on the role of the gut microbiota in influencing different aspects of the brain gut axis, including inflammatory bowel disorders, food addiction in obesity, autism spectrum disorders, and gastrointestinal symptoms in Irritable Bowel Syndrome and Dr. Mayer has been interviewed on National Public Radio, PBS and by many national and international media outlets including the Los AngelesTimes, Atlantic magazine, Time and Newsweek Magazine and National Geographic Explorer. He has spoken at UCLA TEDx on the Mysterious Origins of Gut Feelings in 2015, and his book *The Mind Gut Connection* has been published by Harper&Collins in July of 2016 and has been translated into 10 languages.

The Brain Gut Microbiome System- Science and Potential Clinical Implications

Preclinical studies published during the past decade have clearly established an important role of the gut microbiota in behavior and in the modulation of key components of the gut brain axis, including brain structure and function. However, there is limited evidence from studies in human subjects to demonstrate a causative role of gut microbiota brain interactions in health and disease. Our group has published the first evidence that perturbation of the gut microbiome in healthy individuals can lead to altered brain responses to emotional stimuli. This effect was likely mediated by alterations in gut microbial metabolites, as no effect of the probiotic intervention on gut microbial composition was observed. A number of clinical studies have identified associations of altered gut microbial composition (“dysbiosis”) with clinical symptoms of patients with major depressive disorder, Parkinson’s disease, hepatic encephalopathy, and autism spectrum disorders. To date, the human evidence for a possible role of a dysbiotic state is strongest for major depressive disorder. For example, fecal microbial transfer from depressed patients into germfree mice can result in depression-like behaviors in mouse recipients. Associations of gut microbial composition and metabolites with brain parameters have also been shown in patients with irritable bowel syndrome and in healthy subjects. We have been using multimodal brain imaging of healthy human subjects and disease populations (irritable bowel syndrome, obesity) to identify correlations between a multitude of structural and functional brain parameters with gut microbial composition and microbial metabolites. Early results demonstrate cross sectional correlations between gut microbial composition and grey and white matter changes primarily within sensory processing regions of the brain. In ongoing studies, we are looking at the involvement of gut microbiota and their metabolites in brain changes in mediating the therapeutic effects of bariatric surgery in obesity, and of mind based therapies (cognitive behavioral therapy, mindfulness based stress reduction) in chronic visceral pain. In summary, there is growing evidence from human studies that gut dybiosis may play a role in brain gut disorders, including IBS and depression. However, longitudinal and interventional studies demonstrating causality are required to confirm these initial findings.



Filip Scheperjans, Neurologist at **Helsinki University Hospital**, Helsinki, Finland.

Filip Scheperjans, MD, PhD, studied medicine at the University of Düsseldorf (Germany) and gained international experience as a visiting student in London, New York and Helsinki. His doctoral thesis under Prof. Karl Zilles (C & O Vogt Institute for Brain Research, University of Düsseldorf and Institute of Medicine, Research Center Jülich, Germany) was concerned with the cytoarchitectonical and neurochemical anatomy of the human parietal lobe. He received the award for the best thesis of the medical faculty of the University of Düsseldorf in 2008. Now living in Finland he works as attending neurologist and clinical researcher at the Department of Neurology of Helsinki University Hospital. He has been involved in several international multicenter trials related to acute stroke treatment. His main research interests are movement disorders and acute neurology including stroke, status epilepticus and neuroimaging. Currently, his main focus is on the role of microbiota in Parkinson’s disease and his group was the first to demonstrate microbiome community structure alterations in Parkinson’s disease. For his groundbreaking work in this field he was awarded the Uschi Tschabitscher Prize for Young Neurologists by the European Academy of Neurology in 2014.

Gut Microbiota in Parkinson’s Disease

In Parkinson’s Disease (PD), the neuropathology extends beyond the brain involving essentially the whole autonomic nervous system and olfactory structures. Accordingly, PD patients suffer from a broad range of non-motor symptoms, in particular gastrointestinal dysfunction and hyposmia, frequently years before emergence of motor symptoms. PD patients

show alpha-synuclein deposits and neurodegeneration in the enteric nervous system as well as breakdown of the mucosal barrier, bacterial invasion, and mucosal inflammation in the colon. Pathological forms of alpha-synuclein may show prion-like spreading and neuron-to-neuron transmission and can be transported from the gut to the brain via axonal transport through the vagal nerve. It has been proposed that local inflammation in the gut mucosa and / or olfactory structures in PD could be a precipitating event leading to alpha-synuclein toxicity. Gut bacteria do not only affect gut physiology, but there is also an intense bidirectional interaction with the brain influencing neuronal activity, behavior, as well as levels of neurotransmitter receptors, neurotrophic factors, and inflammation. According to one hypothesis, gut microbiota could be implicated in the initiation of inflammation and protein misfolding in PD. Recently, gut microbiome alterations in PD subjects and a connection between gut microbiota and akinetic-rigid symptoms have been described. This talk will give an overview of recent findings regarding the gut-microbiota-brain axis in PD and how this may reshape our understanding of disease etiology and pathogenesis and could lead to new therapeutic approaches.

Special lecture: The human microbiome in medicine



Stanislav Dusko Ehrlich, Director Emeritus at **Institut National de la Recherche Agronomique (INRA)** and PI of the Metagenopolis project, Jouy en Josas, France. And Director of Centre for Host Microbiome Interaction, **King's College**, London, UK.

(See his CV at the Scientific Committee section)

Abstract not available

Session 8: Cancer



Núria Malats, Principal Investigator of the Genetic & Molecular Epidemiology Group at the **Spanish National Cancer Research Centre (CNIO)**, Madrid, Spain

(See her CV at the Scientific Committee section)

Chair of the **SESSION 8**



M. Luz Calle, Head of the Bioinformatics and Medical Statistics Group, Systems Biology Department, **University of Vic – Central University of Catalonia (UVic-UCC)**, Vic, Spain.

(See her CV at the Scientific Committee section)

Chair of the **SESSION 8**



Laurence Zitvogel, PUPH at **Gustave Roussy**, Paris, France.

Pr L. Zitvogel, MD (clinical oncology), PhD (tumor immunology), PU-PH Faculty Paris Sud, University Paris XI (Clinical Biology), graduated in Medical Oncology from the School of Medicine of the University of Paris in 1992. She started her scientific career when she was at the University of Pittsburgh in the USA in Michael Lotze's laboratory. She became Research Director at Institut National de la Santé et Recherche Médicale U1015, and Scientific Director of the Immuno-Oncology program at Gustave Roussy, the largest cancer Center in Europe. She has been actively contributing to the field of cancer immunology and immunotherapy, and she brought together basic and translational research, including the design of cancer therapies through combined animal studies and Phase I/II patient trials. Her expertise is mainly dendritic cell and innate effector biology and relevance during tumour development as well as exosome-based vaccine designs. She pioneered the concept of immunogenic cell death and showed that chemotherapy, radiotherapy and inhibitors of tyrosine kinase mediate their tumoricidal activity, at least partly through the immune system. Her team discovered the critical role and impact of gut microbiota in cancer immunosurveillance and therapies. She was the recipient of many awards including the National Academy of Medicine, the Translation Research INSERM Prize, the ASCO-SITC and the Brupbacher Awards 2017.

Gut microbiota and colon cancer: the carbohydrate link

The tumor microenvironment is influenced by anticancer therapies, and even more so by those affecting the gut homeostasis. We reported that a deviated repertoire of the intestinal microbiome called « dysbiosis », caused by broad spectrum antibiotics compromised the efficacy of cyclophosphamide (CTX), an immunomodulatory alkylating agent exerting cytotoxic effects against cancer (Viaud, Science, 2013). Lately, we reported the importance of the gut microbiota in the efficacy of ipilimumab, a human monoclonal antibody targeting CTLA-4 (Vetizou, Science, 2015). Mechanisms underlying this gut-cancer axis in these two therapeutic contexts are different. CTX is responsible for disrupting the gut barrier integrity as well as intestinal homeostasis, allowing a NOD1/2-dependent translocation of several Gram-positive bacteria into secondary lymphoid organs. CTX breaks the intestinal tolerance towards the intestinal microbiota and leads to immunization of the host against some bacterial strains. We identified a Gram positive bacteria, *Enterococcus hirae*, which markedly modulates the intestinal and systemic immunity through the elicitation of bacterial-specific Th1 and pathogenic Th17 cells. Moreover, we have shown that *E. hirae* is capable of enhancing tumor-specific CD4+ and CD8+ T cell responses against candidate tumor antigens. Finally, *E. hirae* specific-memory Th1 immune responses selectively predicted longer progression-free survival in advanced lung or ovarian cancer patients treated with immunotherapy and chemotherapy (platinum salts- or CTX-based chemotherapy). Altogether, *E. hirae* represents a valuable probiotic against cancer, an oncomicrobiotic ameliorating the efficacy of the most common alkylating immunomodulatory compound. Other oncomicrobiotics discovered in the context of PD1 blockade in lung and kidney cancers will be presented at this meeting.



Bernat Ollé, CEO, **Vedanta Biosciences**, Cambridge, MA, USA.

Dr. Olle is a co-founder and Chief Executive Officer of Vedanta Biosciences. Dr. Olle is also a venture partner at PureTech Health. He has been a member of the founding teams of several companies of the PureTech portfolio and has served as a member of the Board of Directors of Vedanta Biosciences and Follica Biosciences. In 2013 Dr. Olle was named "Innovator of the Year" in MIT Technology Review Spain's "Innovators under 35" awards, and in 2015 he was awarded the Princess of Girona business award by the King of Spain. He completed his doctoral work at the Chemical Engineering Department at MIT, where he developed a novel method for large scale bacterial culture. During his graduate work, Dr. Olle was awarded the "la Caixa" fellowship. Dr. Olle received his B.Eng. in Chemical Engineering from Universitat Rovira i Virgili, Spain, his M.S. and PhD in Chemical Engineering Practice from MIT, and his MBA from the MIT Sloan School of Management. He has published his work in journals including Nature and Nature Biotechnology.

Systems biology and model-based multi-omic analysis of the human microbiome

The human microbiome – the diverse ensemble of microorganisms that populate the human body – represents a vastly complex ecosystem that is tightly linked to our health. Multiple molecular assays now enable high-throughput profiling of this system, providing large-scale and comprehensive characterization of its ecology, functional capacity, and metabolic activity. To date, however, analyses of such multi-omic data typically focus on statistical associations, often ignoring extensive prior knowledge of the mechanisms, dependencies, and regularities linking these various facets of the microbiome. In this talk, I will highlight the pressing need for the development of predictive systems-level models of the microbiome and of model-based methods for integrating and analyzing microbiome multi-omic data. I will further introduce several novel computational frameworks for linking taxonomic, genomic, metagenomic, and metabolomic information about the microbiome. Combined, such frameworks lead to an improved comprehensive, multi-scale, and mechanistic understanding of the microbiome in health and disease, informing efforts for personalized microbiome-based therapy.

POSTERS

1. Human Secretory IgM Emerges from Plasma Cells Clonally Related to Gut Memory B Cells and Targets Highly Diverse Commensals Dually Coated by Secretory IgA

Giuliana Magri, Laura Comerma, Marc Pybus, Jordi Sintes and Andrea Cerutti

Secretory immunoglobulin A (SIgA) enhances host-microbiota symbiosis, whereas SIgM remains poorly understood. We found that gut IgM+ plasma cells (PCs) were more abundant in humans than mice and clonally related to a large repertoire of memory IgM+ B cells disseminated throughout the intestine but rare in systemic lymphoid organs. Besides sharing a gut-specific signature with memory IgA+ B cells, memory IgM+ B cells interrelated with some IgA+ clonotypes and switched to IgA in response to T cell-independent or T cell-dependent signals. These signals induced abundant IgM, which recognized mucus-embedded commensals as SIgM from clonally affiliated PCs did. Unlike its murine counterpart, human SIgM recognized bacteria dually coated by SIgA that were characterized by increased richness and diversity compared to IgA-only-coated or uncoated bacteria. Thus, SIgM may emerge from pre-existing memory rather than newly activated naïve IgM+ B cells and could help SIgA to anchor highly diverse commensal communities to mucus.

2. Study of the microbiota composition in adult celiac disease.

Simona Panelli, Rachele Ciccocioppo, Annalisa Schiepatti, Elena Betti, Carmelisa Lombardo, Federico Biagi and Enrica Capelli

Celiac Disease (CD) is an autoimmune, inflammatory disorder of the small intestine that involves a complex interplay between genetic and environmental factors. Gluten is the key, but not the unique, environmental trigger of CD in genetically predisposed individuals. However, it remains a mystery why the frequency of susceptibility alleles in the general population is about 30% (considering only the “celiac 1” locus, i.e., the HLA region and its “risk” molecules DQ2/DQ8) while only 1-3% of individuals will develop CD. To explain this and other discrepancies, the existence of additional environmental factors with a role in pathogenesis and clinical picture has to be supposed. Among these, a relevant role for imbalances (“dysbiosis”) in the gut microbiota has been repeatedly invoked in the last years. In detail, such dysbiosis would result in the expansion of proinflammatory gut pathobionts, together with the parallel decline of anti-inflammatory mutualistic bacteria. This, in turn, would lead to a perturbation of the physiological roles normally played by the microbiota in the gut ecosystem

Our ongoing project, funded by “Associazione Italiana Celiachia” (AIC), specifically addresses these poorly understood aspects. The general aims of our project are to obtain a comparative metagenomic picture of the salivary, duodenal and fecal microbiota composition in four categories of adult CD patients (10 potential, 10 refractory, 20 active neo-diagnosed, 20 treated patients under gluten-free diet) vs. non-CD controls (n=20, suffering of functional dyspepsia). This allows to address the following questions: (i) does the eventual dysbiosis anticipate or follows the development of enteropathy?; (ii) does the gluten-free diet restore a normal composition of the microbiota?; (iii) is there any difference between active and complicated conditions, i.e.: are microbiota changes larger in complicated patients? In our poster, we will present some of these preliminary findings.

3. Identification of relevant microbiome balances using compositional data analysis.

Javier Rivera-Pinto, Juan José Egozcue, Vera Pawlowsky-Glahn, Roger Paredes, Marc Noguera-Julian and M. Luz Calle

Microbiome abundance data from DNA throughput sequencing technologies is summarized in a matrix of counts (OTU table) corresponding to the number of reads per sample for different taxa. Raw abundances and the total counts per sample are not informative themselves since they depend on technical issues related to DNA sequencing. This kind of data is mathematically known as compositional data and their analysis requires from specific statistical approaches. Information of interest, carried by compositional data, is relative, and is contained in the ratios between the parts of the composition. For this reason, the analysis of microbiome data for differential abundance testing is still challenging.

We propose to perform microbiome relative abundance testing by identifying two groups of taxa whose relative abundance is associated with the phenotype of interest. This corresponds to the notion of balance between two parts of a composition, which is a central concept in compositional data theory and is defined as a value proportional to the ratio between the geometric means of two disjoint groups of variables.

Because there are intractable many possible balances defined by two groups of taxa in a microbiome study, we propose an iterative greedy algorithm for searching the most relevant balance. That is, given a response variable Y (either numeric or dichotomous), the algorithm selects the two groups of taxa whose balance is most associated with Y, after adjusting for possible confounding variables.

The proposed algorithm is applied to an HIV-microbiome study conducted at IrsiCaixa AIDS research institute, in Barcelona, Catalonia, Spain. We identify microbiome balances associated with HIV infection and inflammation parameters, such as sCD14. This can be useful in order to define microbiome biomarkers for classifying individuals according to disease status and to analyze their evolution among the different stages of the infection.

4. New single nucleotide polymorphisms to distinguish between adherent-invasive E.Coli (AIEC) and non-AIEC strains from the human intestine

Carla Camprubí-Font, Mireia López-Siles, Meritxell Ferrer-Guixeras, Laura Niubó-Carulla, Carles Abellà-Ametller, Jesús Garcia-Gil and Margarita Martinez-Medina

Crohn's disease (CD) is an idiopathic inflammatory bowel disease in which variations of the intestinal microbiome have been reported. In particular, it has been described an increase in proinflammatory species, such as *Escherichia coli*. Notably, higher abundance of the adherent-invasive *E. coli* (AIEC) pathotype in CD patients than in healthy controls has also been outlined. A relation between this pathotype and CD pathogenesis has been supported. So far, some of the molecular mechanisms of the AIEC phenotype have been resolved, however, no specific genetic differences for this pathotype have been found. The aim of this study was to look for a signature sequence that could easily differentiate an AIEC from a non-AIEC strain.

We focused our attention on single nucleotide polymorphisms (SNPs) identified by comparative genomics between three AIEC/non-AIEC strain pairs.

A total yield of 5209 gene clusters were obtained, 3327 of which were detected in the six strains and none was found to be common in the three AIEC strains, not even exclusively in two of them. Comparative genomics identified 18 SNPs between the strains of the D-phylogroup pair, 17 in the B2-pair and 30 in the B1-pair that met the selection criteria. Of those, 24 SNPs (found in 13 genes) were confirmed and further analysed in the strain collection. Three of the SNPs-encompassing genes were related with adhesion/invasion and two with stress tolerance. Three SNPs resulted in differential nucleotide distribution between AIEC and non-AIEC strains ($p < 0.016$). These SNPs also presented association with adhesion and invasion strain capacities ($p < 0.006$). Interestingly, one of these polymorphisms can predict the AIEC phenotype with a 71% of global success ($p = 0.008$). No differences according to pathotype were reported in the prevalence of previously AIEC-related genes, nor in point mutations frequency.

Our study corroborates the absence of AIEC-specific genetic markers widely distributed across all AIEC strains. Nonetheless, three SNPs putatively involved with the AIEC phenotype have been described and one of them could be applied in AIEC screening.

5. Development of an in vitro co-culture model colonized with characteristic small intestinal microbiota.

Radu Ghemis, Elisabet Fernandez, Montse Bosch, Àngels Díaz-Ramos and Lourdes Gombau

Evaluation of efficacy and safety data on the intestinal absorption of active ingredients can provide the basis for the assurance of a high level of protection of human health and consumer interest in relation to drugs and food. In vitro intestinal models based on the Caco-2 cell system are a well characterized tool widely used to evaluate the ability of nutrients and chemicals to cross the intestinal barrier, as well as to study their transport mechanisms.

Along the last 5 years, however, the ability of the gut microbiome to modify dietary nutrients/drugs metabolism and brain signalling has emerged as a key feature of host-microbe relationships in the small and large intestine. Consequently, the inclusion of gut microbiota in the intestinal models is clue for more representative and confident in vitro assays. To circumvent this problem, here we show the development of a coculture system for intestinal Caco-2 cells and the consortium of microorganisms most representative of the small intestine. In this model, Caco-2 cells were cultured and differentiated on Transwell inserts for 21 days and thereafter bacteria were applied apically to the Caco-2 cell monolayer. Cell viability was tested after 2 and 4-h colonization and bacterial-cell extracts recovered for real-time quantitative PCR (qPCR) to measure putative changes in bacterial population. Results indicated that cell viability is not compromised by bacterial colonization after these time incubation periods. In addition, bacterial strains grew differently when grown on cells that on their culture media, suggesting that a symbiotic interaction may exist between them. Overall data indicate that we have developed an in vitro model that could more realistically mimic the intestine in vivo conditions and that could be useful to study the molecular crosstalk that may induce metabolic changes in the host and microbial cells either under health or disease.

6. Using MinION® to characterize dog skin microbiota through full-length 16S rRNA gene sequencing approach.

Anna Cuscó, Joaquim Viñes, Sara D'Andreano, Francesca Riva, Anita M. Oberbauer, Juan F. Medrano, Joaquim Casellas, Armand Sánchez Bonastre and Olga Francino

Skin microbiota is usually characterized by sequencing 16S rRNA V1-V2 hypervariable regions. It is the best approach when working with short-read sequencers, however it has two main pitfalls: (1) fails to classify sequences at lower taxonomic levels, such as species; and (2) V1-V2 primers tend to overestimate and underestimate certain taxa.

Here we aim to assess the potential of long-read Nanopore sequencing in complex microbiota samples using the full-length 16S rRNA (1,500bp). First set-up step was performed using a staggered mock community and then a pool of several skin microbiota samples previously sequenced by Ion Torrent PGM.

Mock community analyses revealed that aligners like LAST recover all the information when using the proper database. On the other hand RDP taxonomy classifier, which is the most commonly used in microbial ecology, fails more times in classifying nanopore reads.

Skin microbiota diversity retrieved by Nanopore is similar to that found with Ion Torrent PGM. Moreover, biological replicates in skin microbiota led to similar results, even with different primer sets (V1-V8 and V1-V9). 1D reads still have an elevated error rate, so the new upcoming 1D2 kit is needed to improve accuracy.

To sum up, single-molecule sequencing with Nanopore can obtain qualitative data and also quantitative data to assess microbiota on complex samples.

7. Fecal microbiota characterization of hypercholesterolemic subjects.

Ana Belen Granado-Serrano, Meritxell Martin-Gari, Victoria Estrada Pujol, Virginia Sanchez, Manuel Portero-Otín and Jose Ce Serrano

Recent evidence suggests that microbiota may be considered as an environmental factor that contributes to the development of metabolic disorders such as cardiovascular diseases. Among them, hypercholesterolemia, has gain the interest of health and scientific community, since it may be modulated by diet. In the same context, gut microbiota has been suggested to affect and/or regulate lipid metabolism through several mechanisms, which include lipid absorption modulation, SFCA synthesis and chronic inflammation onset. Nevertheless, to date, it is unclear the characteristics of the gut microbiota, independent of dietary habits, that may affect the blood lipid profile. The overall microbial structure and alpha-diversity was similar in controls and hypercholesterolemic patients, but the latter had lower relative abundance of Anaeroplasmia (mean 0.002% (SD 0.006) and Haemophilus genus (0.041% (SD 0.138)) than healthy controls (0.219% (SD 0.458) and 0.078% (SD 0.166) respectively) and higher relative abundance of Odoribacter (0.51% (SD 0.783) vs 0.158% (SD 0.114)) and Ruminococcus. (2.325% (SD 2.095) vs 1.119% (SD 1.559)). Accordingly, Spearman's correlation analysis revealed that Haemophilus associated negatively with total cholesterol levels, triglycerides and ratio cholesterol/HDL-C, and positively with LDL particle size, while Odoribacter associated positively with the ratio Cholesterol/HDL-C. Dietary habits assessments showed that hypercholesterolemic patients ingested lower dietary fibre per day than healthy controls. However, only Ruminococcus abundance seemed to be associated to fibre intake.

In conclusion, the abundance of the genera Anaeroplasmia, Haemophilus, Odoribacter and Ruminococcus could be associated with lipid profile which differ between hypercholesterolemic and normocholesterolemic individuals, although only the three formers do it independently of the dietary habits.

8. Usefulness of mucosa-associated Akkermansia muciniphila and Faecalibacterium prausnitzii co-abundance to discriminate between inflammatory bowel diseases with shared disease location.

Mireia López-Siles, Núria Enrich-Capó, Xavier Aldeguer, Míriam Sàbat-Mir, L. Jesús García Gil and Margarita Martínez-Medina

Differential diagnosis in inflammatory bowel disease (IBD) is essential to give adequate clinical management, therapeutic strategies and prognosis. Inclusion of gut bacterial biomarkers specific of each entity as strategy to optimise standard diagnostic approaches has gain interest lately. *F. prausnitzii* and its phylogroups have been reported as useful biomarkers to classify some IBD subtypes. However, discrimination is still limited between conditions that overlap in location of inflammation. Notably, alterations in the mucus layer have been shown in IBD patients, particularly affecting mucus thickness and composition in ulcerative colitis (UC) patients. It can be hypothesised that the inclusion of other bacterial species that inhabit the mucus and previously associated to gut health, such as *Akkermansia muciniphila*, could assist to achieve greater discrimination values between IBD, and its usefulness in diagnosis merits further investigation.

This study aims to determine the amount of these two species in healthy individuals and patients with IBD in order to assess their capability to discriminate between conditions.

Lower levels of both species were found in subjects with CD compared with H subjects ($p \leq 0.002$). Despite the high dispersion of data, we observed that UC patients tend to feature a reduction in *F. prausnitzii* counts whereas *A. muciniphila* load was increased in comparison to H. Concerning disease subtypes, patients with CD of ileal involvement presented the lowest levels of both *F. prausnitzii* phylogroups. In contrast, UC patients, regardless of disease location, were characterised by higher abundances of *A. muciniphila* when compared to CD subjects, including those with colonic involvement. The index combining *A. muciniphila* and *F. prausnitzii* phylogroup II counts was the best biomarker to discriminate between IBD (AUC=0.748, Specificity=74.19%, Sensitivity=78.26%). Over a 74% of CD patients were characterised by a low *A. muciniphila* –low *F. prausnitzii* phylogroup II load, which can be used to discriminate this group of subjects from those with UC. This index also was the best to discriminate between colonic CD and all UC subtypes (AUC>0.75).

Differences in *A. muciniphila* have been found between IBD patients, and its quantification in conjunction to *F. prausnitzii* phylogroups may help to differentiate patients with CD involving the colon from those with UC.

9. Human microbiome data: from fundamental research to practical exploitation.

Tamara Meleshko, Viktoriia Bati, Olga Levchuk, Roman Rukavchuk, Volodymyr Drobnych and Nadiya Boyko

The human microbiome is unique to each person, and the ratio of commensals covering the mucosal sites is highly flexible in biodiversity and function. Still, it remains unclear how to use these data to fix the balance between health and disease.

It might be an important issue to understand all the mechanisms by which the microbiota modulates/affects our health and apply it at least in two closely related areas of personalized approaches: 1) in the treatment of patients and 2) selection of the correct individual methods of prevention of various [noncommunicable, “chromatin”] diseases connected with the human microbiome disturbances. This is also valuable data for practical implementation in all the other aspects of P4 medicine.

In our previous studies on different mouse models we showed the molecular mechanism by which the different gut commensal representatives modulate local immune response at mucosal sites in a strain/species specific manner.

Recently we were able to analyze in vitro the effects of individual commensal bacteria on monocyte derived human dendritic cells (moDCs)-mediated inflammation and effector T-lymphocyte priming conditions mimicking the unique intestinal microenvironment. Human moDCs expressing PPAR γ also regulate the cell surface expression of type I and II CD1 glycoprotein receptors as well as mucosa-associated CD103 protein differently in the absence or presence of ATRA, when ATRA is provide tolerogenic effect. In other words making possible (enabling) the pro- and anti-inflammatory reprogramming of this population of immune cells.

We observed the strong Pierson correlation between microbial, immune and biochemical parameters specific for the patients with obesity, diabetes type 2 and CVD as early biomarkers for the individual health state. We also formulated the personalized diet using the algorithm developed by us and tested its efficacy in limited clinical trials for the treatment of patients of diabetes type 2 (DT2).

Finally, we had started to build the information system (IS), geographic information system (GIS), for personalized nutrition' calculation aimed to regulate the saliva/gut microbiota ratio, biodiversity and functionality-directed GM correction (GMC). This was done via consumption of food products specific to the individual.

10. Siropins, novel serine protease inhibitors from gut microbiota acting on human proteases involved in inflammatory bowel diseases.

Hela Mkaouar, Nizar Akermi, Vincent Mariaule, Samira Boudebouze, Nicolas Pons, Josan Marquez, Ali Gargouri, Emmanuelle Maguin and Moez Rhimi

In eukaryotes, serpins constitute a wide family of protease inhibitors regulating many physiological pathways. Many studies have stressed the key role of these inhibitors in several human physiopathologies including mainly the inflammatory bowel diseases (IBD). Unlike eukaryotic serpins, prokaryotic ones remain poorly studied and current information about their functions are very limited. Our project is focused on the investigation of the therapeutic potential of serpin from human gut microbiota. Here we report the purification and the biochemical characterization of two novel serpins originated from *Eubacterium siraum*, a human gastro-intestinal tract commensal bacteria. These proteins called Siropins, efficiently inhibit two human proteases reported to be associated with IBD. To the best of our knowledge, it is the first bacterial serpins showing an attractive inhibition of fecal proteases recovered from a mice group with chemically induced inflammation. Altogether our data highlight the interesting potential of Siropins, and serpins from the human gut microbiota in general, to be used as new alternative to face inflammatory diseases.

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www.human-microbiome.org

www.metahit.eu

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www.gutmicrobiotawatch.org/en/home

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OUTCOMES

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B-Debate sees debate as a powerful, effective way to generate new knowledge. The debates are top-notch international scientific meetings featuring a selection of experts of renowned international prestige and scientists that work in Barcelona and Catalonia, moderated by scientific leaders. Since 2009 B-Debate has invited about 1200 recognized speakers and over 7.000 attendees. B-Debate seeks out answers to the challenges and needs of society in the field of life sciences, taking into account the complex, ever-changing conditions of this global world. The debates foster the integration of different disciplines of science and deal with such diverse topics as ageing, new therapeutic approaches to various diseases, innovative technology to improve knowledge of the human genome, food resources, new tools to integrate knowledge management, clinical genomics, neurosciences, climate change, and new energy sources, among others. The knowledge and results obtained through these events is spread throughout both the scientific community and general society through the various **B-Debate** channels and instruments.

More info: www.bdebate.org



The **IrsiCaixa AIDS Research Institute** is an internationally recognized organization. Its aim is to do research on HIV/AIDS and related diseases, their prevention and treatments, with the ultimate goal of eradicating the pandemic. It was founded in 1995 as a private non-profit foundation promoted by the Obra Social “la Caixa” and the Health Department of the Generalitat de Catalunya. IrsiCaixa scientific research takes place in coordination with the most prestigious international research centers and its publications have one of the highest impact factors in its field. More than 60 professionals devoted to research, academic training and public engagement work in collaboration with health care professionals and more than 3.000 patients.

IrsiCaixa research lines include the study of the microbiome and its influence on the development of the disease and the effectiveness of treatments. The Institute also participates in clinical trials to evaluate new therapeutic strategies and collaborates with developing countries to help in the fight against the global pandemic.

More info: www.irsicaixa.es/en

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UVic-UCC is a public university under private management. It's committed to economic and social development of the surrounding region and Catalonia, through teaching, research and knowledge transfer, imbued with a distinctive European and international vocation. There is twenty-one research groups, three research and knowledge transfer centres and nine research chairs carry forward UVic-UCC research activity, with the aim of generating knowledge and transferring it to society. The universal scope of UVic-UCC science and training builds on the present-day reality of Catalan society – with the Catalan language as its shared symbol of identity – and Europe as a unifying force. UVic-UCC considers international exchange programmes and internships abroad to be essential, and promotes joint academic and research projects with other universities and institutions.

More info: www.uvic.cat/en



Vall d'Hebron Institute of Research (VHIR) is a public sector institution that promotes and develops the research, innovation and biosanitary teaching of the Vall d'Hebron Barcelona Hospital Campus. Through the excellence of its research, they identify and apply new solutions to the health problems of society and contribute to spread them around the world. The research activities of the centre are divided into 8 different areas and over 60 research groups. One of them is the Physiology and Pathophysiology of the Digestive Tract group, that studies, among other research lines, the microbiome.

More info: www.vhir.org/index.asp?Idioma=en



The Spanish National Cancer Research Centre (CNIO) is one of the world's leading cancer research centres. Almost 400 researchers at the forefront of global science, strive to better understand the underlying mechanisms of cancer and to find ways to combat it. The ultimate goal of the CNIO is to advance knowledge and foster translation of scientific breakthroughs into novel and more effective ways to prevent, diagnose and treat cancer. As a comprehensive Cancer Centre, the CNIO integrates both basic and translational research. We also have an active innovation programme that guarantees the transfer of knowledge, from our scientific discoveries to the market and bedside and to society as soon as possible.

More info: www.cnio.es/ing/index.asp



Germans Trias i Pujol Hospital is a public center that provides high-quality healthcare to the 800,000 people living in the Barcelonès Nord and the Maresme, as well as some citizens of other Catalan territories in the case of certain pathologies, in which the hospital is Reference for up to 1,200,000 inhabitants. The hospital is managed by the Northern Metropolitan Territorial Management of the Catalan Health Institute (ICS), which is also responsible for primary care in the Barcelonès Nord, Maresme, Vallès Oriental and Vallès Occidental. Germans Trias is at the same time a basic general hospital for more than 200,000 people in Badalona and several municipalities in the surrounding area. All this is possible thanks to the intense and skilled work of some 2,500 healthcare professionals and non-healthcare workers.

More info: www.hospitalgermanstrias.cat

CosmoCaixa offers interactive, enjoyable science and an open door for anyone who is eager to learn and understand and who never stops wondering why things are the way they are. **CosmoCaixa Barcelona** boasts the Geological Wall and the Amazon Flooded Forest, which features more than 100 plant and animal species that convince visitors they have been transported from the Mediterranean to the very heart of the tropical jungle. In addition to its permanent facilities and its open areas, CosmoCaixa offers a scientific and educational programme that includes exhibitions, workshops, conferences, courses and debates involving experts from all over the world.

More info: obrasocial.lacaixa.es

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More info: www.mandarinoriental.com/barcelona/



For more than a century, **MSD**, a leading global biopharmaceutical company, has been inventing for life, bringing forward medicines and vaccines for the world's most challenging diseases. MSD is a trade name of Merck & Co., Inc., with headquarters in Kenilworth, N.J., U.S.A. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, MSD continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit www.msd.com and connect with us on [Twitter](#), [LinkedIn](#) and [YouTube](#).

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