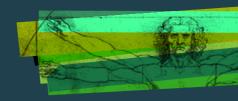
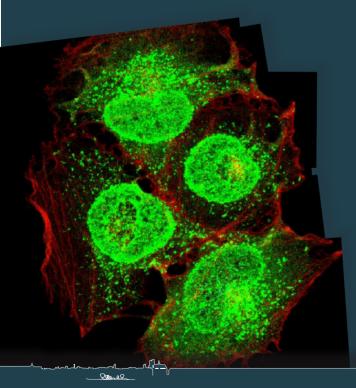
LE STUDIUM **CONFERENCES**

VIRTUAL MEETING | 2020



24-25 September 2020

Novel host- and Microbiota-directed strategies for treating respiratory infections



LOCATION

VIRTUAL MEETING

CONVENORS

Prof. Pieter Hiemstra

LE STUDIUM RESEARCH PROFESSOR / ARD 2020 BIOPHARMACEUTICALS **PROGRAMME**

FROM Leiden University Medical Center - NL

IN RESIDENCE AT Research Center for Respiratory Diseases (CEPR) / Inserm, University of Tours - FR

Dr Mustapha Si-Tahar

Research Center for Respiratory Diseases (CEPR) / Inserm, University of Tours - FR

Dr Antoine Guillon

Research Center for Respiratory Diseases (CEPR) / Inserm, Intensive Care Unit CHRU, University of Tours - FR



















CONVENORS

Prof. Pieter Hiemstra,

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Research Center for Respiratory Diseases (CEPR) / Inserm, Intensive Care Unit CHRU, University of Tours - FR

ORGANIZING COMMITTEE

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LE STUDIUM

CONFERENCES

VIRTUAL MEETING | 24-25 SEPTEMBER 2020

ABSTRACTS

Novel host- and microbiota-directed strategies for treating respiratory infections

EDITO

Created in 1996 on the CNRS campus in Orleans La Source, LE STUDIUM has evolved to become a multidisciplinary Loire Valley Institute for Advanced Studies (IAS), operating in the region Centre-Val de Loire of France. LE STUDIUM has its headquarters in the city centre of Orleans in a newly renovated 17th century building. The amazing facilities are shared with the University of Orleans. In 2014 new developments and programmes linked to the smart specialisation of the Centre-Val de Loire region came to strengthen existing IAS cooperative relationships with the local and the international community of researchers, developers and innovators.

LE STUDIUM IAS offers to internationally competitive senior research scientists the opportunity to discover and work in one of the IAS's affiliate laboratories from the University of Tours, the University of Orleans, National Institute of Applied Sciences (INSA) Centre Val de Loire and ESAD Orléans, as well as of nationally accredited research institutions located in the region Centre-Val de Loire (BRGM, CEA, CNRS, INSERM, INRA, IRSTEA). Our goal is to develop and nurture trans-disciplinary approaches as innovative tools for addressing some of the key scientific, socio-economic and cultural questions of the 21st century. We also encourage researchers' interactions with industry via the IAS's links with Poles of Competitiveness, Clusters, Technopoles, and Chambers of Commerce etc.

LE STUDIUM has attracted over two hundred LE STUDIUM RESEARCH FELLOWS and LE STUDIUM RESEARCH PROFESSORS for long term residencies. In addition to the contribution in their host laboratories, researchers are required to participate in the scientific life of the IAS through attendance at monthly interdisciplinary meetings called LE STUDIUM THURSDAYS and gathering members of the regional scientific community and industries.

For the period 2015-2021, LE STUDIUM operates with an additional award from the European Commission in the framework of the Marie Skłodowska-Curie Actions (MSCA) with the programme MSCA-COFUND for the mobility of experienced researchers. LE STUDIUM is also the official partner of the Ambition Research and Development 2020 (ARD 2020) initiated by the Region

Centre-Val de Loire, that supports the specialisation strategy around 5 main axes: biopharmaceuticals, renewable energies, cosmetics, environmental metrology and natural and cultural heritage.

Researchers are also invited and supported by the IAS to organise, during their residency and in collaboration with their host laboratory, a two-day LE STUDIUM CONFERENCE. It provides them with the opportunity to invite internationally renowned researchers to a cross-disciplinary conference, on a topical issue, to examine progress, discuss future studies and strategies to stimulate advances and practical applications in the chosen field. The invited participants are expected to attend for the duration of the conference and contribute to the intellectual exchange. Past experience has shown that these conditions facilitate the development or extension of existing collaborations and enable the creation of productive new research networks.

The present LE STUDIUM CONFERENCE named "Novel host- and microbiotadirected strategies for treating respiratory infections" is the 107th in a series started at the end of 2010 listed at the end of this booklet. It is organised in the framework of the Biopharmaceuticals Programme ARD2020.

We thank you for your participation and wish you an interesting and intellectually stimulating conference. Also, we hope that scientific exchanges and interactions taking place during this conference will bring opportunities to start a productive professional relationship with presenting research laboratories and LE STUDIUM Loire Valley Institute for Advanced Studies.

Yves-Michel GINOT

Chairman LE STUDIUM

INTRODUCTION

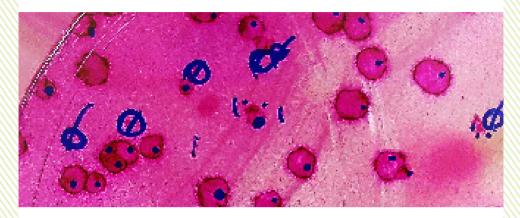
Respiratory infections ranked 4 in the WHO 2016 list of "Top 10 causes of death worldwide". There is an urgent need for improved treatment of respiratory infections, in view of the absence of affordable treatment, but also because of the absence of effective drugs for selected respiratory pathogens and the increase in microbial resistance to conventional antihiotic treatment

Recent insight into host defense mechanisms against respiratory infections and the respiratory microbiota have opened up new avenues for novel treatment strategies.

The aim of this Le Studium Conference is to bring together experts from a variety of countries to discuss the latest developments in the field, and to explore future opportunities for collaboration with the Horizon 2020 program or related EU programs.

> This international conference is organised in the framework of the BIOPHARMACEUTICALS ARD 2020 Programme.

ARD 2020 BIOPHARMACEUTICALS



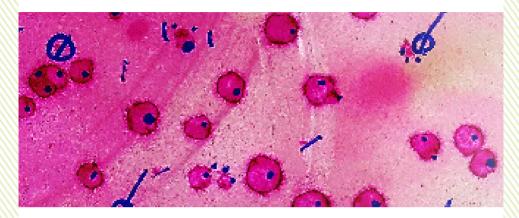
A drug is any substance or composition presented as having properties for treating, preventing or diagnosing disease in humans or animals. Whereas BIOPHARMACEUTICALS in the strict sense of the term, are molecules that have the characteristic of being produced from living organisms or their cellular components. These molecules are intermediate between chemical drugs and organisms' intrinsic biologics. The proportion of biopharmaceuticals in the drug market is constantly increasing and represents about 30% of the market.

The Centre-Val de Loire region is at the cutting edge of research in the pharmaceutical sector and has included the development of biopharmaceuticals into its smart specialisation strategy. The Regional Council supports research in this sector to facilitate innovative industrial development and partnerships for socioeconomic development beyond 2020.

The ARD 2020 Biopharmaceuticals programme aims to further develop and strengthen the Centre-Val de Loire region biopharmaceuticals industry by capitalising on the recognised capabilities of the multidisciplinary research teams from the regional research institutions in the view to:

- Develop a flagship research and development pole on biopharmaceuticals in the Centre-Val de Loire region.
- Configure the biopharmaceuticals field by inter-sectorial development and innovation in the pharmacy/health sectors through start-ups, SMEs (Small and Medium Enterprises) including established local and regional based multinational companies.
- Promote the transfer of technologies/competences to existing and new businesses
- Support the development of new competences for the sector.





The Biopharmaceuticals Programme creates a dynamic mobilizing actors in the pharmaceutical sector, from fundamental research to production, to jointly develop the biopharmaceutical treatments of tomorrow in the Centre-Val de Loire region. It focuses on the design and biosynthesis of biomolecules for preclinical and clinical development by including the search for synergies with conventional chemically synthesised drugs. A number of innovative projects including academic and industrial partnerships covering a wide spectrum of biological molecules and domains are directly financed to bring immediate outcomes: vaccines, therapeutic antibodies, nucleic acids, lipoproteins, bioproduction of medicines, etc...

Partners involved in the Biopharmaceuticals Programme are: University of Tours, University of Orléans, INRAE Val-de-Loire, CNRS, Inserm, Tours CHRU, LE STUDIUM, Polepharma IMT Group, MAbDesign, Bio3 Institute, Labex MAbImprove, ELISE Interreg.

In this programme, LE STUDIUM leads on the internationalization dynamic by providing expertise and services to recruit international experienced researchers and organizing actions and events to boost international scientific exchanges and collaborations.

PROGRAMME

THURSDAY 24TH SEPTEMBER 2020

13h30 Opening of the conference

Sophie Gabillet: Le Studium Loire Valley Institute for Advanced Studies - France

Dr Mustapha Si-Tahar: Research Center for Respiratory Pathologies [CEPR], Tours - France

SESSION 1: NEW APPROACHES TO THE TREATMENT OF RESPIRATORY INFECTIONS

Chair: Mustapha Si-Tahar 14h00 Prof. Pieter Hiemstra

Antimicrobial Host Defence Peptides: Immunomodulatory Functions and Translational **Prospects**

14h30 Dr Nadia Naffakh

Antiviral potential of splicing regulatory molecules

15h00 Coffee break

SESSION 2: INNOVATIVE EXPERIMENTAL MODELS TO **COMBAT RESPIRATORY INFECTIONS**

Chair: Pieter Hiemstra

15h30 Dr Anne van der Does

Lung-on-chip technologies to study respiratory infections

16h00 Dr Rodrigo Guabiraba

Precision cut lung slices: a novel versatile tool to examine host-pathogen interactions in the chicken lung

16h30 Dr Guido Santos

Multi-level computational modeling as a tool to understand molecular mechanisms behind bacterial lung infection

17h00 Closure of day 1

FRIDAY 25TH SEPTEMBER 2020

SESSION 3: HOST METABOLISM AS A DRUGGABLE TARGET FOR TREATMENT OF RESPIRATORY INFECTIONS

Chair: Pieter Hiemstra

13h30 Dr Aurélie Crabbé

Host metabolites modulate bacterial susceptibility to antibiotics

14h00 Dr Mustapha Si-Tahar

Towards a metabolic anti-influenza therapy

SESSION 4: HOST AND MICROBIOTA-DERIVED INDUCERS OF HOST ANTIMICROBIAL DEFENCE

Chair: Mustapha Si-Tahar

14h30 Dr Raphaël Duivenvoorden

Trained Immunity as a novel therapeutic strategy

15h00 Prof. Mike Surette

The Good and the Bad of Commensal-Pathogen Interactions in the Airways

15h30 Coffee break

SESSION 5: HDT-BASED CLINICAL TRIALS AND PERSPECTIVES

Chair: Antoine Guillon

16h00 Dr Antoine Guillon

Flagellin-based antibacterial strategy and clinical perspectives

16h30 Prof. Adrian Martineau

Vitamin D in the prevention and treatment of respiratory infections

17h00 Prof. Kingston Mills

Local T cells and their subversion in protective immunity to infection in the respiratory tract

CONCLUSIONS AND CLOSURE

17h30 Prof. Pieter Hiemstra

Conclusions

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CONVENORS



Prof. Pieter Hiemstra

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Pieter Hiemstra is Professor of Respiratory Cell Biology and Immunology at the Department of Pulmonology of the Leiden University Medical Center (LUMC) in The Netherlands. His current research is focused on basic and translational research in COPD and lung cancer, with a specific interest in the role of airway and alveolar epithelial cells, host-microbe interactions and repair. His other activities include teaching and curriculum development for Biomedical Sciences and Medical students. He has organized a range of symposia and conferences, and is active in various national and international organizations. He is currently Section Editor Basic Science of the European Respiratory Journal. In 2018 and 2019 he worked for 5 months at the CEPR in Tours (Dr. M. Si-Tahar), based on a Le Studium Fellowship.

Antimicrobial Host Defence Peptides: Immunomodulatory Functions and Translational Prospects

Antimicrobial host defence peptides (AMPs) are effector molecules of the immune system. AMPs are considered as possible alternatives to conventional antibiotics for the treatment of respiratory infections, which is increasingly complicated by the problem of microbial antibiotic resistance. AMPs are also referred to as antimicrobial peptides and host defence peptides, and many AMPs were discovered based on their antimicrobial activity against a range of micro-organisms. However, they also display other activities that are relevant for host defence, including activities related to immune modulation and wound repair. Application of AMPs (and improved substitutes of these peptides) as a treatment for respiratory infections has been studied for some time, but they have not yet been introduced into the clinic. Direct administration of AMPs is complicated by e.g. cost of production and short half-life, and alternative strategies are considered. These include enhancement of their local production and activity. Nevertheless, there are a number of properties that make these peptides attractive candidates, including their broad-spectrum antimicrobial activity (possibly also including anti-SARS-CoV-2 activity), activity against multidrug resistant micro-organisms, and wide range of activities. In this presentation, recent developments in research on the role of these peptides in the lung, as well as their clinical use in novel therapies will be discussed.



Dr Mustapha Si-Tahar

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Mustapha Si-Tahar is the Director of the Research Center for Respiratory Diseases since 2012. In this academic laboratory, he is also the leader of the team entitled "Respiratory infection & Immunity". His main research goal is to understand how respiratory epithelial cells sense and respond to major pathogens, especially influenza viruses. M. Si-Tahar's research projects are also aimed at identifying innovative host-directed anti-infectious strategies, using complementary in vitro and in vivo models of lung infection. Prior to his current position, M. Si-Tahar supervised a research group at the Pasteur Institute in Paris (2001-2011) and he performed post-doctoral works (1997-2000) at Massachusetts General Hospital, HMS (Boston, USA) and Emory University (Atlanta, USA) on mucosal immune mechanisms

Towards a metabolic anti-influenza therapy

Influenza A virus (IAV) is the etiological agent of a contagious acute respiratory disease, which is associated with high morbidity and mortality. This virus also causes a considerable socioeconomic burden despite annual vaccination campaigns. To help design innovative antiviral therapies, it is essential to better understand IAV-host cells interaction. In that regard, recent studies revealed the interplay between metabolic and immune signaling pathways.

In this communication, I will present evidence that IAV alters lung tissues metabolism and I will show its functional consequence. Remarkably, we recently identified one metabolite that accumulates in the airways of IAV-infected hosts and which exhibits a potent antiviral activity, as assessed using both in vitro and in vivo approaches. I will also present the underlying inhibiting molecular mechanism that involves a specific post-translational modification process and an inhibition of IAV replication cycle. Hence, my presentation will highlight metabolites as novel components of the lung antiviral arsenal.



Dr Antoine Guillon

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Antoine Guillon, 42 y.o., M.D. Ph.D is a critical care physician of the intensive care unit of Tours with research activities in the Research Center for Respiratory Diseases, INSERM U1100. He earned a Ph.D. degree in innate lung immunity and his training included a postdoctoral research fellowship in the Pulmonary Center – Boston University (USA). He is member of the CRICS-TRIGGERSEP network (pluridisciplinary experts gathering research projects in sepsis therapeutic approaches with an international expertise). AG published more than 80 articles, mostly focused on respiratory infections.

Flagellin-based antibacterial strategy and clinical perspectives

Bacterial pneumonia is a leading cause of morbidity and mortality worldwide. Antibiotics constitute the standard of care but are faced with the emergence of antimicrobial resistance and the curative failure. Targeting the innate immune system is an underexploited area of drug discovery for infectious diseases. The JC Sirard's research team (Lille, Fr) has demonstrated that the respiratory tract administration of a Toll-like receptor 5 agonist (the immunomodulatory flagellin) activates innate immunity in the lung airway epithelium and enhances the therapeutic outcome (relative to low doses of antibiotic alone) in the context of pneumonia caused by antibiotic-susceptible S. pneumoniae, in the mouse. The presentation will describe a European consortium (FAIR project) which plans to bridge experimental data to human trial by developing a TLR-agonist as nebulized adjunct therapy approach. If this adjunct therapy approach can ultimately be translated into humans and extended to other bacterial pathogens (especially antibiotic-resistant bacteria) and various classes of antibiotics, the treatment of pneumonia would be transformed.

SPEAKERS



Dr Aurélie Crabbé

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Aurélie Crabbé is an assistant professor at the Laboratory of Pharmaceutical Microbiology, Ghent University, Belgium (UGhent). Her main research interests are (i) to understand how the microenvironment at the host-pathogen interface drives the efficacy of antimicrobials in the respiratory tract, and (ii) to explore beneficial properties of the lung microbiota. In vivo-like three-dimensional models of lung epithelium are central tools in this research. Prior to her current position, A. Crabbé received an Odysseus II fellowship of the Research Foundation Flanders at UGhent (2014-2019), and she conducted postdoctoral studies at Arizona State University [2010-2014). She obtained a PhD in Bioscience Engineering (2009) and a MSc in Biomedical Sciences (2006) at the Vrije Universiteit Brussel.

Host metabolites modulate bacterial susceptibility to antibiotics

Antibiotic susceptibility of bacterial pathogens is typically evaluated using in vitro assays that do not consider the complex host microenvironment. This may help explaining a significant discrepancy between antibiotic efficacy in vitro and in vivo for chronic lung infections, with some antibiotics being effective in vitro but not in vivo or vice versa. We previously demonstrated that lung epithelial cells enhance the activity of aminoglycoside antibiotics against the opportunistic pathogen Pseudomonas aeruginosa, yet the mechanism behind was unknown. I will present mechanistic insights on how lung epithelial cells stimulate aminoglycoside activity. To this end, an in vivo-like 3-D lung epithelial cell model was used. We report that conditioned medium of 3-D lung cells, containing secreted but not cellular components, potentiated the bactericidal activity of aminoglycosides against P. aeruginosa, including resistant clinical isolates, and several other pathogens. We found that 3-D lung cells secreted endogenous metabolites that modulate aminoglycoside activity, and provide evidence on the mode of action. Our findings reveal a cross-talk between host and bacterial metabolic pathways, that influence downstream activity of antibiotics. Understanding the underlying basis of the discrepancy between the activity of antibiotics in vitro and in vivo may lead to improved diagnostic approaches and pave the way towards novel means to stimulate antibiotic activity.



Dr Raphaël Duivenvoorden

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Raphaël Duivenvoorden (born 1980 in Leiden, The Netherlands) is a medical doctor at the Radboud University Medical Center in Nijmegen, The Netherlands. He studied medicine in Amsterdam, The Netherlands, and received is PhD from the University of Amsterdam in 2013. During his PhD he worked at the Icahn Medical School at Mount Sinai in New York where he returned as a post-doctoral researcher. He completed his specialist training in nephrology in the Amsterdam University Medical Center in 2017. He currently works as an Internist-Nephrologist at the Radboud university medical center in Nijmegen, The Netherlands, and is affiliated with the Icahn Medical School at Mount Sinai, New York as an Adjunct Assistant Professor. He leads a research group that focuses on the therapeutic modulation of innate immune responses and the development of nanotherapeutics for the targeting innate immune cells.

Trained Immunity as a Novel Therapeutic Strategy

Innate immune cells form a vital first line of defense against pathogens, and their activation upon recognition of pathogens is rapid and non-specific. For a long time it has been assumed that innate immune cells do not develop immunological memory. However, over the past years this view has been challenged. A new concept has emerged, referred to as trained immunity. Upon stimulation of innate immune cells, long-term functional and epigenetic reprogramming can occur. Although the cells return to a non-activated state after the initial stimulus, they develop an enhanced secondary response to a subsequent non-specific stimulus. This shows that the innate immune system exhibits adaptive characteristics, which may have evolved to provide greater protection against reinfection. In this presentation we will reflect on the concept and underlying immunological mechanisms of trained immunity and discuss how trained immunity can be utilized as a therapeutic strategy to prevent infection and potentially treat other immune related diseases



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Biologist with a PhD in Immunopharmacology (Mauro Teixeira's lab, UFMG, Brazil). Post-doctoral training in Mucosal Immunology and Host-Pathogen interactions (Eddy Liew's lab, Glasgow, UK). INRAE Research Scientist (CR) with a major interest in leukocyte biology and avian immunology. At the INRAE, I aim to understand the chicken inflammatory response to respiratory pathogens, with a focus on the intestinal microbiota and the gut-lung axis. I am also interested in investigating early mediators on inflammation, with a great interest on cytokines, lipids and vascular peptides.

Precision cut lung slices: a novel versatile tool to examine host-pathogen interactions in the chicken lung

The avian respiratory tract is a common entry route for many pathogens and an important delivery route for vaccination in the poultry industry. Immune responses in the avian lung have mostly been studied in vivo due to the lack of robust, relevant in vitro and ex vivo models mimicking the mucosal microenvironment. Various principles of microbial infection including pathogen tropism, replication, spread, and innate antimicrobial host responses can readily be studied in suitable cell or tissue culture models. Precision-cut lung slices (PCLS) have the major advantages of maintaining the 3-dimensional architecture of the lung and includes heterogeneous cell populations. PCLS have been obtained from a number of mammalian species and from chicken embryos. However, as the embryonic lung is physiologically undifferentiated and immunologically immature, it is less suitable to examine complex host-pathogen interactions including antimicrobial responses. Together with our partners from the Roslin Institute (Edinburgh, UK), we have recently established the first protocols for preparing and culturing PCLS from immunological mature chickens (chPCLS) and for assessing avian influenza infection and the innate immune response. Further analyses will be focused on revealing virulence-associated infection and/ or host response patterns in chPCLS, which may help to improve our understanding of avian influenza pathogenesis and/or avian influenza virus pathotype evolution in gallinaceous poultry.



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Adrian Martineau is Professor of Respiratory Infection and Immunity at Queen Mary University of London. He is a respiratory physician with a research interest in the effects of vitamin D on human health. His work combines laboratory investigation, clinical trials and meta-analysis investigating the potential for vitamin D supplementation to prevent and treat respiratory disease. He also leads the COVIDENCE UK study (www.qmul.ac.uk/covidence), a n=12,000 national cohort study investigating modifiable risk factors for COVID-19. Adrian's research is funded by the MRC, NIHR and NIH among others.

Vitamin D in the prevention and treatment of respiratory infections

Vitamin D is best known for its effects on calcium homeostasis, but a growing body of evidence shows that it also has extensive immunomodulatory actions. In this talk I will describe the effects of vitamin D metabolites on host responses to respiratory pathogens, before going on to review results of clinical trials that have evaluated a potential role for vitamin D in the prevention and treatment of acute respiratory infections and tuberculosis. The potential for vitamin D to reduce incidence and severity of COVID-19 will also be discussed



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Kingston Mills is Professor of Experimental Immunology and Director of The Trinity Biomedical Sciences Institute at Trinity College Dublin. He is a graduate of TCD and trained at as a Postdoctoral Fellow at University College London and the National Institute for Medical Research, Mill Hill (now the Crick Institute), London, before joining the Scientific Staff of NIBSC, Herts, UK. He returned to Ireland in 1993 to take up an academic position at National University of Ireland, Maynooth. He was appointed to a Personal Chair at Trinity College Dublin in 2001 and was Head of the School of Biochemistry and Immunology from 2008-2011. He heads an active research team focusing on T cells in infection and autoimmunity.

Local T cells and their subversion in protective immunity to infection in the respiratory tract

Respiratory infection with Bordetella pertussis causes whooping cough. The infection is controlled by innate immune responses, but complete bacterial clearance from the respiratory tract and protection against re-infection is mediated largely by Th1 and Th17 cells. However the bacteria has evolved sophisticated immune subversion strategies to subvert these responses Antigenspecific regulatory T (Treg) cells that secrete IL-10 are induced in the respiratory tract during B. pertussis infection and suppress protective T cell responses. Pertussis disease can be prevented in children by immunization with acellular pertussis (aP) vaccines. However, aP vaccines fail to prevent nasal colonization and transmission of B. pertussis and may enhance infection in the nasal mucosae. This may be due to activation of immune checkpoints or Treq cells. aP vaccine fail to induce Th1 or Th17 cells or respiratory tissue resident memory T (TRM) cells that maintain long term immunity in the respiratory tract. We found that blocking IL-10 during immunization restores the induction of Th1 and Th17 responses and enhances efficacy of an aP vaccine. Furthermore, we have demonstrated that immunization with an aP vaccine formulated with a novel adjuvant combination, comprising TLR2 and STING agonists, induces Th1- and Th17-type TRM cells in the lung and nasal tissue, especially when delivered by nasal route, and this confers long-term protection against nasal colonization as well as lung infection.



Dr Nadia Naffakh

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The major focus of my research group in the recent years has been to explore how the influenza virus RNA polymerase interacts and cooperates with host cell components, to control the synthesis, processing, and trafficking of the viral mRNAs and genomic RNAs. We assume that these interactions represent potential targets for the development of therapeutic antiviral drugs. Also at stake is a better understanding of the mechanisms through which the viral RNA polymerase determines the virulence and zoonotic potential of influenza viruses. I

am currently a senior scientist at the Centre National de la Recherche Scientifique and head of the RNA Biology

Antiviral potential of splicing regulatory molecules

and Influenza Virus unit at the Institut Pasteur in Paris.

Alternative splicing (AS) expands the diversity of proteins that can be expressed from a given pre-mRNA and modulates the stability and translation of mRNAs. There is growing evidence that viruses can co-opt splicing factors and/or modulate cellular AS events to favor viral replication and evade antiviral responses. Splicing regulatory molecules have a potential for host-directed therapy of viral infections, especially so in the case of acute respiratory infections as a local and short-course treatment can be considered.

In the case of influenza A viruses (IAVs), we and others have identified cellular factors that regulate splicing of the NS1 and M1 viral mRNAs, and have used RNAseq to characterize viral-induced alterations of the cellular AS landscape. Based on our findings that the human RED-SMU1 complex regulates splicing of the viral NS1 mRNA, we carried out the biochemical and structural characterization of RED-SMU1. Our structural data provided the rationale to screen in silico a set of small compounds for binding at the RED-SMU1 interface. We thereby identified two compounds that disrupt the RED-SMU1 complex, inhibit NS1 mRNA splicing a, inhibits viral replication at micromolar concentrations, whilst preserving cell viability. Overall, our data demonstrate the potential of destabilizing the RED-SMU1 complex as a novel antiviral therapy, which could be active against a wide range of IAVs and be less likely to select for resistance mutants.



Dr Guido Santos Universidad de La Laguna

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Professor of Biochemistry and Molecular Biology at the University of La Laguna. Background on Biology and specialized with the Master in Biomedicine. Research expertise on biomedicine, focusing on molecular and cellular processes explaining diseases. Focused on the paradigm of systems biology, through computational and bioinformatics methodologies, especially through the use of mathematical modeling and simulation based approach. Three years of experience in the Department of Dermatology of the University Hospital of Erlangen in Germany on the topic of lung inflammation.

Specially attracted on popular science. Participation in a multitude of initiatives and projects related to popular science such as talks, radio programs, articles, expositions, scientific cafes, research projects for high school students, among other things. Proudly finalist on the International scientific stand-up contest FameLab in 2016 in Spain.

Multi-level computational modeling as a tool to understand molecular mechanisms behind bacterial lung infection

Pneumonia is one of the most prevalent infectious diseases worldwide, whose main cause is the pathogen Streptococcus pneumoniae. This is an opportunistic disease affecting the most to sensitive groups (infants, elderly and immunosuppressed people). In these patients the inflammatory response generated in the lungs is the main risk factor that happens in the very first days of infection. Under this situation the main goal is finding therapeutical or preventive strategies that are able to cut the inflammatory response as soon as possible.

In order to identify possible molecular targets to focus on this early phase of infection we propose a computational approach to simulate the very first stages of the pneumococcal infection happening in a single alveolus. In vivo experiments at this level are unpracticable with the current technology, which makes in silico strategies the best approach. We created a multi-level mathematical model that combines the intracellular signalling pathways and the cellular interactions that play a role during the early stages of pneumococcal alveolar infection. By systematic perturbations of the model we obtained a high number of solutions that we analysed. The results of the analysis of the simulations predict two main processes that could control the establishment of the infection in the alveolus. Bacterial proliferation and bacterial adherence together can predict the evolution of the early phases of the pneumococcal infection.



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Michael Surette (PhD, University of Western Ontario,1991) joined the University of Calgary in 1998 in the Department of Microbiology and Infectious Diseases. In 2010 he moved to McMaster University and is currently Professor and Canada Research Chair Interdisciplinary Microbiome Research in the Departments of Medicine, and Biochemistry. He is also director of the Farncombe Genomics Facility and a Fellow of the American Academy of Microbiology. Dr. Surette's research addresses the human microbiome of the respiratory and gastrointestinal tracts in health and disease, combining culture-based approaches with next generation sequencing. The lab has a focus on the microbiology of chronic airway diseases and the role of the microbiome in modulating susceptibility to respiratory infections.

The Good and the Bad of Commensal-Pathogen Interactions in the Airways

The airways are colonized by a complex microbiota that varies in composition and density spatially throughout the respiratory tract, as well as temporally through the life-course. While the lower respiratory tract has traditionally been considered sterile in healthy individuals, it is now clear that the lower airways are continuously seeded with microbiota from oral and upper respiratory tract. This may represent a transient community that is cleared and reseeded in healthy individuals; however, it is clear that in chronic airway disease, members of this commensal microbiota thrive in the lower airways. Here they are often in the presence of the pathogens traditionally associated with chronic lung infections. These may simply represent opportunistic colonizers with little contribution to disease, or they may contribute to disease as part of polymicrobial infections, or more directly as pathogens themselves. The pathogenic potential of many commensal microbiota is under appreciated. Conversely, the commensal microbiota plays an integral role in colonization resistance, and the ability of commensal microbiota to inhibit the growth of common pathogens is widespread. The dichotomy in 'good vs bad' behaviour of commensal microbiota is often a 'strain' rather than species specific property. While the complexity of these commensal-pathogen Interactions pose a challenge in standard diagnostic and microbiome profiling approaches to respiratory disease, they do represent opportunities for novel interventions in managing chronic airway disease and reducing susceptibility to respiratory infections in vulnerable populations.



Dr Anne van der Does

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Anne van der Does, Ph.D. is a Senior Researcher in the Department of Pulmonology at the Leiden University Medical Center, Leiden, the Netherlands. Her work is focused on host-microbe interactions in chronic inflammatory lung diseases, with specific focus on host defence proteins and peptides. She was awarded a Marie Curie fellowship twice, of which the second included a one-year visit to Emulate Inc. -a pioneer in Organs-on-Chip technology- to study host-microbiome interactions using their Airway Lung-Chip platform. Dr. van der Does has published in peer-review journals including the European Respiratory Journal.

Dr. van der Does received her Ph.D. from the Department of Infectious Diseases at the LUMC before completing

a 4-year postdoc at the Karolinska Institute, in Stockholm, Sweden.

Lung-on-chip technologies to study respiratory infections

With advances brought on by Organ-on-Chip technology, a new level of cell culture complexity was introduced allowing research into human cellular cross-talk combined with mechanical cues, in a controlled microenvironment. This added level of complexity is especially relevant for organs where biomechanics play a significant role, such as in the lungs. So far limited knowledge is available on how (altered) breathing biomechanics affect human lung cell biology and cross-talk between cell types since studying the role of breathing biomechanics is problematic in standard in vitro cell cultures. Alternatively animal models could be used in this respect, however besides the ethical arguments, these models cannot be considered very relevant in comparison to humans as the altered bifurcation of rodent lungs alters air flow dynamics and airway epithelial cell biology is furthermore significantly different compared to humans. Organ-on-chip technology has provided designs that are more suitable for mimicking lung tissue biology by integrating tissue-tissue interface and including breathing biomechanics such as stretch and airflow. In this presentation I will discuss how Organ-on-chip technology can provide new insights into host-microbe interactions in the lung.

2020

Dr Emilio Maria Sanfilippo & Xavier Rodier FAIR Heritage: Digital Methods, Scholarly Editing and Tools for Cultural and Natural Heritage

17-18 June 2020

Dr Margriet Hoogvliet & Prof. Chiara Lastraioli Spatial Humanities and Urban Experiences During the Long Fifteenth Century

11 Mai 2020

Dr Thimmalapura Marulappa Vishwanatha & Dr Vincent Aucagne Dr Thimmalapura Marulappa Vishwanatha & Dr Vincent Aucagne 27-29 January 2020

Dr Arunabh Ghosh & Prof. Fouad Ghamouss

Towards Futuristic Energy Storage; paving its way through Supercapacitors, Li-ion batteries and beyond

22-24 January 2020

2019

Dr Eric Robert, Dr Jean-Michel Pouvesle & Dr Catherine Grillon International Meeting on Plasma Cosmetic Science

25-27 November 2019

Prof. Richard Freedman & Prof. Philippe Vendrix

Counterpoints: Renaissance Music and Scholarly Debate in the Digital Domain

14-16 November 2019

Prof. Manuela Simoni, Dr Frédéric Jean-Alphonse, Dr Pascale Crépieux & Dr Eric Reiter Targeting GPCR to generate life, preserve the environment and improve animal breeding: technological and pharmaco logical challenges

16-18 October 2019

Prof. Akkihebbal Ravishankara & Dr Abdelwahid Mellouki Climate, air quality and health: longterm goals and near-term actions

Dr Wolfram Kloppmann
N and P cycling in catchments: How
can isotopes guide water resources
management?

18 June 2019

Dr Carmen Díaz Orozco & Dr Brigitte Natanson **Forging glances**.

Images and visual cultures in XIXth century Latin America

28-29 May 2019

Dr Marcelo Lorenzo & Prof. Claudio Lazzari New avenues for the behavioral manipulation of disease vectors

21-23 May 2019

Prof. Yiming Chen & Prof. Driss Boutat 2019 International Conference on Fractional Calculus Theory and Applications (ICFCTA 2019)

25-26 April 2019

Prof. Temenuga Trifonova & Prof. Raphaële Bertho On the Ruins and Margins of European Identity in Cinema: European Identity in the Era of Mass Migration

2-3 April 2019

Dr Patrizia Carmassi & Prof. Jean-Patrice Boudet Time and Science in the Liber Floridus of Lambert of Saint-Omer

27-28 March 2019

Dr Vincent Courdavault & Prof. Nathalie Guivarc'h

Refactoring Monoterpenoid Indole Alkaloid Biosynthesis in Microbial Cell Factories (MIAMI)

5-6 February 2019

Dr Denis Reis de Assis & Prof. Hélène Blasco Induced Pluripotent Stem Cells (iPSCs): From Disease Models to Mini-Organs

28-30 January 2019

2018

Prof. Igor Lima Maldonado & Prof. Christophe Destrieux Frontiers in Connectivity: Exploring and Dissecting the Cerebral White Matter 5-6 December 2018

Dr Marius Secula, Prof. Christine Vautrin-Ul & Dr Benoît Cagnon Water micropollutants: from detection to removal 26-28 November 2018

Prof. Guoxian Chen & Prof. Magali Ribot Balance laws in fluid mechanics. geophysics, biology (theory,

computation, and application)

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Dr Volodymyr Sukach & Prof. Isabelle Gillaizeau Progress in Organofluorine Chemistry 15-17 October 2018

Jens Christian Moesgaard, Prof. Marc Bompaire, Bruno Foucray & Dr Guillaume Sarah Coins and currency in the 10th and 11th centuries: issuing authorities, political powers, economic influences 11-12 October 2018

Dr Norinne Lacerda-Queiroz & Dr Valérie Quesniaux Malaria - Current status and challenges 27-28 September 2018

Dr Renaud Adam & Prof. Chiara Lastraioli Lost in Renaissance

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Prof. Abdelwahid Mellouki & Dr Véronique Daële The 6th Sino-French Joint Workshop on Atmospheric Environment

10-12 September 2018

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Prof. Graeme Boone & Prof. Philippe Vendrix Affective horizons of 'song' in the long fifteenth century

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Prof. Bilal Haider Abbasi, Prof. Nathalie Guivarc'h & Dr Christophe Hano Modern aspects of Plant in Vitro Technology

27 June 2018

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Prof. Vladimir Shishov & Dr Philippe Rozenberg Wood formation and tree adaptation to climate

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Dr Ján Žabka & Dr Christelle Briois Advances in Space Mass Spectronometry for the Search of **Extraterrestrial Signs of Life**

16-18 May 2018

Dr Massimiliano Traversino Di Cristo & Prof. Paul-Alexis Mellet From Wittenberg to Rome, and Beyond Giordano Bruno: Will, Power, and Being Law, Philosophy, and Theology in the Early Modern Era 26-27 April 2018

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Dr Kristina Dianashvili & Dr Éva Jakab Tóth Is Multimodal Imaging an Invention with a Future? The Input of Chemistry

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10-12 June 2010

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