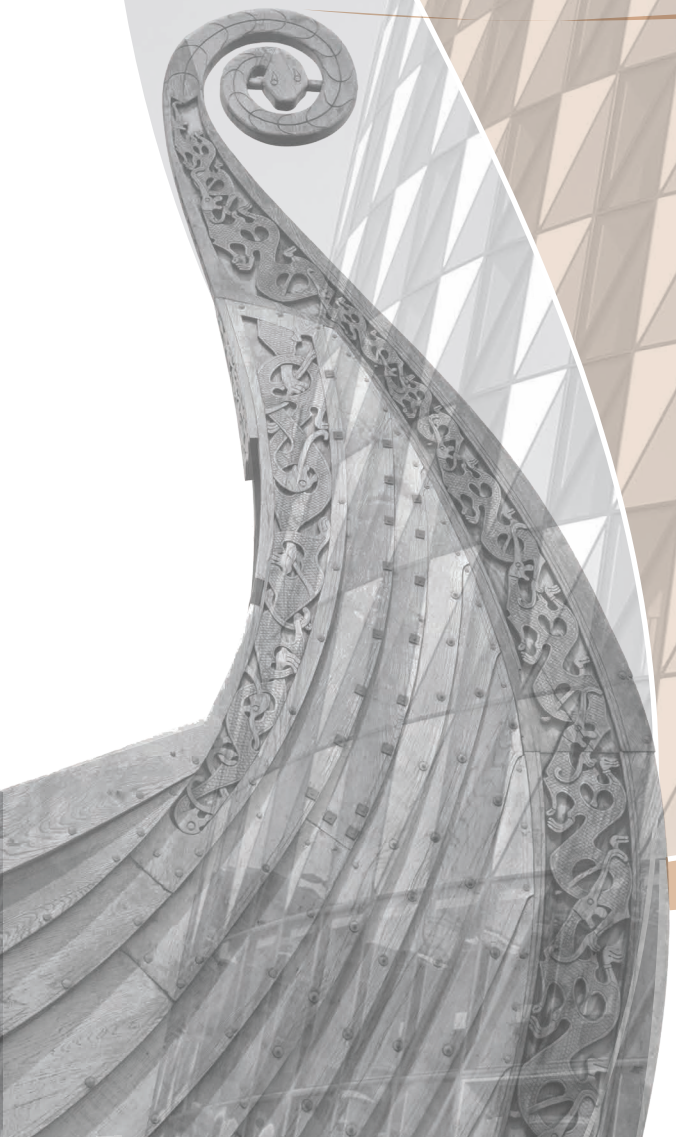
DAYS OF MOLECULAR MEDICINE 2016

Bugs to Beside to Biotech

Nobel Forum, Karolinska Institutet
Stockholm, Sweden, October 27-28, 2016



Organized by:

Days of Molecular Medicine Global Foundation

Karolinska Institutet

FONDATION IPSEN

DAYS OF MOLECULAR MEDICINE 2016

BUGS TO BESIDE TO BIOTECH

Nobel Forum, Karolinska Institutet
Stockholm, Sweden, October 27-28, 2016

Organized by:

Days of Molecular Medicine Global Foundation

Karolinska Institutet

FONDATION IPSEN

CONTENTS

WELCOME

Dear Participant,

On behalf of the DMM Global Foundation, Karolinska Institutet and Fondation IPSEN, we would like to welcome you to the 2016 DMM meeting

Bugs to Bedside to Biotech

The topic of DMM2016 is timely, as pandemics and "super bugs" have become global health problems that have dominated headlines on a daily basis. Hospital acquired infections, the rapid spread of the Zika virus, and appearance of infectives that are resistant to all known antibiotics, are raising concerns world-wide. At the same time, the technology to effectively combat this new generation of infectious diseases has never been more powerful.

In this regard, we are fortunate to have several of the leaders and pioneers in their respective fields to highlight new technologies and clinical advances that are on the forefront of combating infectious diseases affecting millions world-wide. While these infectious diseases continue to spread, the financial support for work in this arena has not kept pace with the growing threat to global public health. Our hope is that this meeting will promote new approaches, encourage partnerships between academia, non-profit and industry, and further identify the barriers that are hampering the funding of next generation infectious agents. We also hope to inspire a new cadre of young physicians and scientists from around the world to take up the challenge of developing biologically targeted therapy for unmet clinical needs.

We also would like to take this opportunity to thank our dedicated sponsors, who have helped make this meeting possible. We are most appreciative for your participation and support for DMM 2016.

We are thrilled that you have joined us and hope that you enjoy the outstanding list of speakers.

With very best wishes

Megan Donovan-Chien
Vice President, DMM Global Foundation

SPONSOR

Bactiguard®

THE 2016 MEETING

The DMM 2016 meeting, entitled "Bugs to Bedside to Biotech", will highlight the interface of new technologies to fight the next generation of infective agents and pandemics, as well as "superbugs" being created by over-treatment with antibiotics.

Research support and reimbursement for developing new therapeutic approaches to combat this growing problem has waned, creating clear financial disincentives for translational work in the area. Meanwhile, the sequencing of entire genomes of diverse infectious agents, the discovery of new anti-infectives from natural sources, and improved understanding of the intersection of the epidemiology of transmission and genetic susceptibility have combined to create unprecedented opportunities for the development of novel science-based clinical advances. In addition, new therapeutic platforms for vaccines, based on mRNA platforms, are moving forward for a host of target infectious diseases. The meeting is also designed to probe new approaches to allow access to these new technological advances for the communities most affected, which are often least able to cover the inherent costs of developing a new class of drugs.

The 2015 Nobel Prize in Physiology or Medicine celebrated discoveries of anti-infectives made many years ago, which have changed the lives of millions of children and adults worldwide. Our hope is that DMM 2016 will inspire continued work in this arena, harnessing novel technology and innovative partnerships among academia, pharma, non-profit organizations, and both developed and developing nations.

Organizers:

Karolinska Institutet *(Stockholm, Sweden)*, DMM Global Foundation *(Cambridge, USA)* in collaboration with the Fondation IPSEN *(Paris, France)*

Program Committee:

Hans-Gustaf LJUNGGREN *(Karolinska Institutet)*, Kenneth R. CHIEN *(Karolinska Institutet)*, Yves Christen *(Fondation IPSEN)*

Meeting Coordinators:

Megan DONOVAN-CHIEN *(DMMGF)*, Sara ALDÉN *(Karolinska Institutet)*, Céline COLOMBIER-MAFFRE *(Fondation IPSEN)*

MOST RECENT DMM MEETINGS

2006 • Inflammatory Pathways in Disease *(Stockholm, Sweden, May 24-27)*

2007 • Emerging Technologies in Cancer Biology *(Cambridge, USA, May 22-24)*

2008 • Molecular Medicine in Cognitive Dysfunction *(Stockholm, Sweden, April 17-18)*

2009 • Human Genetics, Stem Cells and Physiology:
The Future of Individualized Medicine *(Boston, USA, May 7-9)*

2010 • Systems biology approaches to cancer and metabolic disease
(Stockholm, Sweden, May 20-22)

2011 • Re-engineering regenerative medicine *(Hong Kong, China, November 10-12 - in collaboration with the University of Hong Kong and the support of the Croucher Foundation)*

2012 • From rare to care *(Vienna, Austria, October 8-10)*

2015 • Partnerships in Translational Science and Medicine
(Stckholm, Sweden, May 7-8)

THE DMM SERIES

Over the past 16 years, DMM has become one of the most prestigious international meetings dedicated to promoting translational science and molecular medicine. The meeting was initiated with the vision that medical research is the key to further understanding human biology and disease, which has increasingly become enabled by major leaps in core technology spanning the field of genetics, imaging, stem cell biology, and biotechnology. The meeting is designed to break new ground in a specific arena that is viewed as being timely as well as critical to translational science at the highest level, and is not intended to highlight a single disease area or technology.

The DMM Global Foundation

The DMM Global Foundation is a non-profit organization dedicated to forming a bridge between advances in molecular medicine and global cardiovascular health, through educational programs and research collaborations. Our primary focus is to promote global collaboration in the field of molecular medicine through the organization of conferences with other leading international institutions. A key to the success of these conferences is our dedication to support young physician-scientists, from all parts of the world, to participate in these conferences and to expand the international biomedical network to further advance global health issues. In addition, we are developing a Global Health initiative designed to identify, design, and catalyze promising research collaborations that uncover new scientific approaches to global cardiovascular health.

Karolinska Institutet

Karolinska Institutet is one of the world´s leading medical universities. Its vision is to significantly contribute to the improvement of human health. Karolinska Institutet accounts for over 40 per cent of the medical academic research conducted in Sweden and offers the country´s broadest range of education in medicine and health sciences. The Nobel Assembly at Karolinska Institutet selects the Nobel laureates in Physiology or Medicine.

Fondation IPSEN

Created in 1983 under the auspices of the Fondation de France, the Fondation IPSEN tracks progress in biomedical research with the continuing aim of highlighting fundamental advances. Staying away from passing trends, the ambition of the Fondation IPSEN is to identify emerging knowledge and new paradigms, and to foster the most promising interconnections between domains that have not previously been communicating. Because it was necessary to concentrate its efforts, the topics selected reflect some of the most important challenges for the current evolution of the world as well as of knowledge: the aging of populations; the spectacular development of neuroscience and its contribution to the understanding of cognitive mechanisms; the interactions between the great biological systems, such as the nervous and endocrine systems, and the medical challenges posed by the biomedical revolution, particularly in the science of cancer. Over the last 32 years, the Fondation IPSEN has organized over 250 meetings and produced several hundreds publications; more than 250 scientists and biomedical researchers have been awarded prizes and research grants.

PROGRAM

THURSDAY, OCTOBER 27

9:00 - 9:10 am

Welcome Remarks

Karin DAHLMAN-WRIGHT *(Acting Vice-Chancellor, Karolinska Institutet)*
and **Kenneth CHIEN** *(Professor, Karolinska Institutet)*

9:10 - 10:00 am

Keynote

Peter PIOT *(Director, London School of Hygiene & Tropical Medicine)*
AIDS and Ebola: Game changers for global health and R&D

Session I

Global Trends and Burdens

Chairs: **Yves CHRISTEN** *(Chairman, IPSEN Fondation)* and **Orla SMITH** *(Managing Editor, AAAS/Science Translational Medicine)*

10:00 - 10:40 am

Gabriel LEUNG *(Dean, Li Ka Shing Faculty of Medicine, University of Hong Kong)*
Frontiers of influenza research for a common secure future

10:40 - 11:00 am

Break

11:00 - 11:40 am

Renato SANTANA *(Professor, Federal University of Rio de Janeiro)*
Risk factors associated to neurodevelopmental malformations in neonates during Zika outbreak in Brazil

11:40 - 12:20 pm

Ian WILSON *(Chairman, Department of Integrative Structural and Computational Biology, The Scripps Research Institute)*
Global Trends and Burdens: New insights into recognition of HIV-1 by broadly neutralizing antibodies

12:20 - 1:20 pm

Lunch

Session II

New Technology

Chairs: **Susan JONES** *(Senior Editor, Nature Biotechnology)* and **Jan ANDERSSON** *(Professor of Infectious Diseases, Karolinska Institutet)*

1:20 - 2:00 pm — **Marie-Paule KIENY** *(Assistant Director-General, Health Systems and Innovation, World Health Organization)*
From Ebola to Zika : development of health technologies to prevent epidemics

2:00 - 2:40 pm — **Kim LEWIS** *(Director, Antimicrobial Discovery Center, Northeastern University)*
The Quest for New Antibiotics

2:40 – 3:20 pm — **Michel C. NUSSENZWEIG** *(Professor, Rockefeller University)*
The HIV Vaccine Problem

3:20 - 3:40 pm — Break

3:40 - 4:20 pm — **Pascale COSSART** *(Head, Bacteria-Cell Interactions Unit, Institut Pasteur)*
The infection by Listeria : new insights in the intestinal phase

6:00 - 8:00 pm — Speakers Dinner

FRIDAY, OCTOBER 28

Session III

Population Studies

Chairs: **Hans-Gustaf LJUNGGREN** *(Professor, Karolinska Institutet)* and **Rui-Ping XIAO** *(Director, Institute of Molecular Medicine, Peking University; Associate Editor, New England Journal of Medicine)*

9:00- 9:40 am — **Jean-Laurent CASANOVA** *(Professor, Rockefeller University)*
Toward a genetic theory of childhood infectious diseases

9:40- 10:20 am — **Martin J. BLASER** *(Professor of Medicine, Professor of Microbiology, and Director of the Human Microbiome Program, NYU School of Medicine)*
Antibiotic perturbation of the early-life microbiome affects metabolic and immunologic development

10:20- 11:00 am — **Janelle AYRES** *(Assistant Professor, Salk Institute)*
The concept of disease tolerance in host-microbiota interactions

11:00-11:20 am — Break

11:20 - 12:00 pm	**Mats WAHLGREN** *(Professor, Karolinska Institutet)* Successful development of an adjunctive drug against severe Plasmodium falciparum malaria
12:00 - 12:40 pm	**Jean-Marc ROLAIN** *(Professor of Microbiology, Faculté de Médecine et de Pharmacie France, Marseille)* Superbugs: Plasmid Mediated Colistin Resistance and Animal to Human Transmission
12:40 - 1:40 pm	Lunch

Session IV

Biotechnology and Pharma

Chairs: **Ken CHIEN** *(Professor, Karolinska Institutet)* and **Julie STACEY** *(US Editor-in-Chief, EBioMedicine)*

1:40 - 2:20 pm	**Michael CALDERWOOD** *(Professor, Geisel School of Medicine, Dartmouth College)* The Good, the Bad and the Ugly: HAI public reporting and pay-for-performance in US hospitals
2:20 - 3:00 pm	**Gregg ALTON** *(Executive Vice President, Corporate and Medical Affairs, Gilead Sciences)* Delivering access to innovative medicines – the journey to hepatitis C elimination
3:00 - 3:40 pm	**Mariola FOTIN-MLECZEK** *(Chief Scientific Officer, CureVac AG)* Next generation RNA vaccines
3:40 - 4:20 pm	**Patrick JAULT** *(Director of Anesthesiology, Percy Military Instruction Hospital)* Bacteriophages: When the past illuminates the future!

Closing Remarks

Reception

SPEAKER ABSTRACTS

Peter PIOT

Director
London School of Hygiene and Tropical Medicine (LSHTM)
London, UK

Baron Peter Piot CMG MD PhD is the Director of the London School of Hygiene & Tropical Medicine, and the Handa Professor of Global Health. He was the founding Executive Director of UNAIDS and Under Secretary-General of the United Nations (1995-2008), and was an Associate Director of the Global Programme on AIDS of the World Health Organization.

A clinician and microbiologist by training, he co-discovered the Ebola virus in Zaire in 1976, and subsequently led pioneering research on HIV/AIDS, women's health and infectious diseases in Africa. He has held academic positions at the Institute of Tropical Medicine, Antwerp; the University of Nairobi; the University of Washington,

Seattle; Imperial College London, and the College de France, Paris, and was a Senior Fellow at the Bill & Melinda Gates Foundation. He is a member of the US National Academy of Medicine, the National Academy of Medicine of France, and the Royal Academy of Medicine of his native Belgium, and is a fellow of the UK Academy of Medical Sciences and the Royal College of Physicians. He is a past president of the International AIDS Society and of the King Baudouin Foundation. In 1995 he was made a baron by King Albert II of Belgium.

Professor Piot has received numerous awards for his research and service, including the Canada Gairdner Global Health Award (2015), the Robert Koch Gold Medal (2015), the Prince Mahidol Award for Public Health (2014), and the Hideyo Noguchi Africa Prize for Medical Research (2013), the F. Calderone Medal (2003), and was named a 2014 TIME Person of the Year (The Ebola Fighters). He has published over 580 scientific articles and 16 books, including his memoir, "No Time to Lose".

NOTES

AIDS and Ebola: Game changers for global health and R&D

HIV infection emerged as a pandemic in the early 1980s and has caused the death of over 30 million people. Thanks to major investments in research, rapid translation of innovation, activism, political leadership and specific financing mechanisms such as the Global Fund, significant progress has been made in the fight against AIDS resulting in a major decline in new HIV infections (now 2 million new infections per year) and deaths (now 1.1 million). However the end of the epidemic is not in sight as yet and there is still no vaccine. Major obstacles to further reduce the burden of HIV/AIDS will be discussed.

The AIDS response brought for the first time a health issue to the top political, economic and security agendas in the world, was driven by human rights, and grounded in scientific evidence and multi-disciplinary action. Global access to new medicines still under patent has been uniquely achieved for millions of people I low and middle income countries. The AIDS movement contributed greatly to the emergence of global health as an area of enquiry and action around the Millennium.

The 2014-2015 Ebola epidemic in West Africa was unprecedented in local and global impact. As pointed by several panels, this crisis was a wake up call to the lack of preparedness and response to outbreaks, exposing fault lines in national capacity and global governance. It also dramatically illustrated that the current R&D system is not fit for purpose when it comes to developing vaccines, therapeutics and diagnostics for infectious diseases affecting low and middle income countries where there is often no market incentive.

Epidemics of new and old pathogens will continue to emerge, usually as zoonoses, and it will be crucial that reforms for national and global epidemic preparedness and R&D are implemented without delay.

Gabriel LEUNG

Dean
Li Ka Shing Faculty of Medicine, The University of Hong Kong
Hong Kong, China

Gabriel Leung became the fortieth Dean of Medicine at the University of Hong Kong in 2013. Leung, a clinician and a respected public health authority, concurrently holds the Chair of Public Health Medicine. Previously he was Professor and Head of Community Medicine at the University and served as Hong Kong's first Under Secretary for Food and Health and fifth Director of the Chief Executive's Office in government.

Born in Hong Kong, Leung received his early education locally and in the UK. He read medicine at Western Ontario and completed family medicine residency training in Toronto. He earned his master's from Harvard and research doctorate from HKU.

Leung is one of Asia's leading epidemiologists, having authored more than 400 scholarly papers and edited numerous journals. His research defined the epidemiology of two novel viral epidemics, namely SARS-CoV in 2003 and influenza A(H7N9) in 2013. While in government, he led Hong Kong's policy response against the 2009 influenza A(H1N1) pandemic. More recently he has worked on the epidemiology and control of Hand, Foot and Mouth Disease in China.

Leung directs the WHO Collaborating Centre for Infectious Disease Epidemiology and Control. He was inaugural Chair of the Asia Pacific Observatory on Health Systems and Policies during 2010-4. He regularly advises national and international agencies including the World Health Organisation, World Bank, Asian Development Bank and the Chinese Center for Disease Control and Prevention.

After the West African Ebola crisis, he has served on the Commission on a Global Health Risk Framework for the Future led by the US National Academy of Medicine and the Harvard-LSHTM Independent Panel on the Global Response to Ebola, and was an expert reviewer for the United Nations Secretary-General High-level Panel on the Global Response to Health Crises.

NOTES

Frontiers of influenza research for a common secure future

Drawing on real-life examples from past influenza outbreaks, particularly 2009 H1N1pdm and 2013 H7N9, this talk will highlight the state of the science in influenza preparedness research, in mitigation of annual epidemics, the next pandemic and newly emerging outbreaks otherwise. It will draw on the multiple disciplines of ecology, evolutionary biology, virology, epidemiology, and mathematical sciences. A "One Health" approach that recognises the zoonotic driver of epidemics will be emphasised. Particular attention will focus on the multiple strands of global health initiatives contributing to the common goal of health and human security against influenza and its sequelae.

Renato SANTANA

Professor
Federal University of Rio de Janeiro
Rio De Janeiro, Brazil

I am an Associate Professor at Federal University of Rio de Janeiro, Brazil with a broad background in virology and cell biology, with specific training and expertise in arboviruses including Zika, Dengue and Chikungunya virus. My research includes the interaction of virus-host factors that contribute to neuropathogenesis including the immune response and cellular restriction factors as antiviral response. I also worked developing several antiviral against HIV, Dengue and more recently Zika virus. I have been the PI or co-Investigator on several grants funded by Brazilian (CNPq, FAPERJ and CAPPES) and international (CFAR) agencies. We are the first group to isolate and sequence the whole genome of Zika associated to neonate microcephaly. We also published several articles regarding the clinical and molecular diagnose of Zika infection in pregnant woman through ultrasonography, magnetic resonance, NAT and deep sequencing. We published important articles in journals such Science, Lancet, NEJM and Cell describing the clinical manifestations of Zika infection, immuneactivation and neuron permissiveness to virus infection. I also mentored undergraduate and PhD students in several virology related projects. I have worked in several projects mapping cellular factors that are important for HIV replication including APOBEC proteins that can hypermutate virus genome blocking virus replication. I also investigated the cellular proteins that are important for virus release including ESCRT machinery. These results are very important to screening for new targets to develop possible antivirals against HIV. In the past I worked as consultant of Center of Disease Control (CDC) in the PEPFAR program in HIV/AIDS in African countries such as Angola and Mozambique, visiting the countries many times and helping in the HIV diagnostic and treatment.

NOTES

Risk factors associated to neurodevelopmental malformations in neonates during Zika outbreak in Brazil

The recent larger outbreaks of Zika virus (ZKV) in Brazil has raised concern that ZKV infection during pregnancy could cause severe neurodevelopmental malformations in the fetus, including microcephaly. We have performed ZKV diagnostics in Campina Grande (Brazil) which has the second highest incidence of ZKV infection and microcephaly cases. We first isolate and sequence the whole genome of ZKV from the amniotic fluid of fetal microcephaly cases. We expanded our analysis by following 600 pregnant women with suspected ZKV infection with 10% confirmed cases. We identified 11 cases showing signs of brain lesions during fetal USG images confirming microcephaly. Brain damage was confirmed with intrauterine ultrasound and MRI that showed, in all cases, neurological impairment including, cerebral volume reduction, ventriculomegaly, cerebellar hypoplasia, hydrocephaly and arthrogryposis. The mechanisms by which ZKV causes fetal abnormalities are unknown. We believe that both viral and host factors are important to characterize the disease outcome and severity. Virus diversity was analyzed by deep sequencing of ZKV positive tissues obtained from post-mortem cases. The phylogenetic analyses showed an intra-host variation between ZKV sequences in the envelope domain I of different post-mortem tissues that may be implicated in viral tropism to brain tissues. To investigate the cellular pathways associated to neuropathogenesis we performed transcriptome analysis of post-mortem brain tissues from neonates with microcephaly. Our analysis showed altered gene expression in several pathways related to extracellular matrix organization, glycolysis, ionotropic glutamate receptor pathway, cadherin signaling pathway and synaptic vesicle trafficking. All these pathways are congruent with our previous histopathological analysis showing calcification, gliosis and neuronal migration impairment. We also report a remarkable increase of the inflammatory cytokines IL-6, IL-8, MCP-1 and G-CSF in the amniotic fluid of ZKV positive pregnant women with neonate microcephaly, suggesting that immuneactivation could also interfere with the fetal development.

Ian WILSON

Chairman
Department of Integrative Structural and Computational Biology, The Scripps Research Institute
La Jolla, USA

Dr. Ian A. Wilson received his B.Sc. in Biochemistry from the University of Edinburgh, D. Phil. in Molecular Biophysics from Oxford University, and did postdoctoral research on influenza virus at Harvard University. Dr. Wilson has been a Professor at The Scripps Research Institute since 1982 and is Hansen Prof. of Structural Biology and Chair of the Department of Integrative Structural and Computational Biology. His laboratory focuses on the immune system and on microbial pathogens and, in particular, on how viruses are recognized by the adaptive and innate immune systems. His laboratory has determined crystal structures of many different antibodies (>250) with a variety of antigens, as well as MHC class I and class II, CD1, T cell receptors, cytokine receptors, Toll-like receptors (TLRs), variable lymphocyte receptors (VLRs) and other key pattern recognition receptors. His current focus is on how microbial pathogens are neutralized by human broadly neutralizing antibodies, particularly for HIV-1, influenza virus, and HCV. His lab also recently determined crystal structures of the HIV-1 gp140 envelope glycoprotein and the HCV E2 surface glycoprotein. The goal of these projects is to define the sites of vulnerability (epitopes) on these viral pathogens to aid in structure-based design of new vaccines and therapeutics. Dr. Wilson's lab is also investigating how avian and other zoonotic influenza viruses adapt to human hosts and cross the species barrier by changing their receptor specificity. Dr. Wilson also directs the Joint Center for Structural Genomics (JCSG) that has pioneered new methods for high throughput structural studies, including x-ray and NMR. Since its inception in 2000, the JCSG has determined over 1600 novel structures that, in particular, explore the expanding protein universe and the human gut microbiome. The JCSG was one of four high-throughput production centers in NIH NIGMS PSI:Biology. Dr. Wilson is a Fellow of the Royal Society, Corresponding Fellow of the Royal Society of Edinburgh, Member of the American Academy of Arts and Sciences, Foreign Associate of the National Academy of Sciences USA, Honorary Fellow of Corpus Christi College, Oxford, and was awarded a D.Sc. from Oxford University 2000. He is on the Statistical Board of Reviewing Editors for Science, on the Editorial Board of Cell, and on the Board of Directors for Keystone Symposia. He has published more than 680 papers.

NOTES

Global Trends and Burdens: New insights into recognition of HIV-1 by broadly neutralizing antibodies

The discovery and isolation of highly potent, broadly neutralizing antibodies (bnAbs) that recognize highly diverse HIV-1 isolates and subtypes has opened up tremendous opportunities for understanding of how the immune system can combat HIV-1. These human bnAbs have now been found to target a surprising number of sites of

vulnerability on the HIV Envelope glycoprotein (Env). Structural characterization by X- ray and EM continues has identified a number of novel epitopes on the HIV-1 Env trimer and the full extent of their interactions with antibodies. These bnAbs possess unique features that enable them to penetrate the dense glycan shield surrounding Env, bind epitopes that consist of glycans and protein segments, and promiscuously adapt to variation in the glycans. We have identified their mode of binding and neutralization and how such antibodies evolve to acquire potency and breadth. Elucidation and characterization of these bnAbs in the context of the Env trimer has provided valuable insights for structure-assisted HIV vaccine design.

This work was supported by NIH grants UM1 AI100663 (the Scripps Center for HIV/AIDS Vaccine Immunology and Immunogen Design (CHAVI-ID), P01 AI110657 (HIVRAD), R01 AI084817, the International AIDS Vaccine Initiative (IAVI) and the Collaboration for AIDS Vaccine Discovery (CAVD).

Marie-Paule KIENY

Assistant Director-General
Health Systems and Innovation, World Health Organization
Geneva, Switzerland

Dr Marie-Paule Kieny was appointed Assistant Director-General at the World Health Organization (WHO) in October 2010 and is now leading the Health Systems and Innovation cluster. Prior to this, Dr Kieny directed the WHO Initiative for Vaccine Research since its inception in 2001. Major successes under her leadership were the development and licensing of new vaccines against meningitis and against pandemic influenza in developing countries through pioneering the transfer of technology and know-how. During 2015-2016, Dr Kieny led WHO's Ebola research activities. She is currently in charge of Zika Research & Development (R&D) in WHO as well as of the preparation of an R&D Blueprint to accelerate global research preparedness for future outbreaks.

Before coming to WHO, Dr Kieny held top research positions in the public and private sectors of her home country, France. The positions included Assistant Scientific Director of Transgene S.A. from 1981 to 1988, and Director of Research and Head of the Hepatitis C Virus Molecular Virology Group at the Institute of Virology, Institut national de la santé et de la recherche médicale (INSERM) from 1999 to 2000.

She received her PhD in Microbiology from the University of Montpellier in 1980, where she was also awarded a University Diploma in Economics, and her Diplôme d'Habilitation à Diriger des Recherches from the University of Strasbourg in 1995.

NOTES

From Ebola to Zika : development of health technologies to prevent epidemics

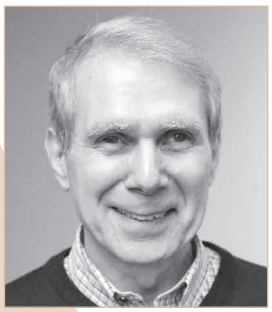
The epidemic of Ebola in West Africa, and more recently the Zika epidemic in Latin America, showed that the world is unable to develop effective interventions in a timely manner for control of severe emerging infectious diseases using current approaches to vaccine, drug and diagnostics development.

Indeed, market-driven models for R&D do not cater for medical technologies for diseases that are sporadic or unpredictable, especially when they occur in countries with low investment in health infrastructure and delivery. The challenge becomes even greater when faced with a wholly new disease such as SARS, MERS and Nipah virus infection, which are just three examples of diseases that have emerged at the human-animal interface in the last two decades.

The international community needs to invest to improve our collective ability to respond to new threats and to prepare itself with a novel R&D paradigm to address future epidemics. An efficient response during an infectious disease epidemic requires R&D preparedness – work done between epidemics to fill knowledge gaps, identify potentially useful candidate medical products and other interventions, and to ensure the timely availability of such when an epidemic occurs. Moreover, an efficient research and development response during an epidemic relies on the existence of the right conditions – or an enabling environment – to facilitate timely and efficient action. This means that there must be, for example, a system in place for coordinated action, and broad agreement on data and sample sharing. The WHO R&D Blueprint is a global strategy and preparedness plan to ensure that targeted research and development can strengthen the emergency response by bringing medical technologies to populations in need during epidemics. In particular, the Blueprint aims to reduce the time between the declaration of an international public health emergency and the availability of effective tests, vaccines and medicines that can be used to save lives and avert crisis.

Kim LEWIS

Director
Antimicrobial Discovery Center, Northeastern University
Boston, USA



Kim Lewis is a University Distinguished Professor and Director, Antimicrobial Discovery Center at Northeastern University in Boston, and a Fellow of the American Society of Microbiology.
He obtained his Ph.D. in Biochemistry from Moscow University in 1980, and has been on the Faculty of MIT, University of Maryland, and Tufts University prior to coming to Northeastern.
Dr. Lewis has authored over 100 papers and is an inventor on several patents. His more notable findings include the development of general methods to grow previously uncultured bacteria that make up >99% of biodiversity on the planet, the discovery of the culprit of recalcitrant biofilm infections, drug-tolerant persister cells; antimicrobials for sterilizing biofilm infections and killing M. tuberculosis, *and the discovery of teixobactin which is largely free of resistance development.*
Dr. Lewis presented over 100 invited talks. Dr. Lewis has been a permanent member of the Drug Discovery and Drug Resistance NIH Study Section, and Chair of two NIH Study Sections on Drug Discovery. Dr. Lewis has served as a panelist and contributor to the National Academies Institute of Medicine reports on antibiotic resistance in 2010, 2011 and 2014, and the European Academies Science Advisory Meeting in 2014. Dr. Lewis is a member of Faculty 1000, a world-wide panel of experts evaluating research advancements. He is a recipient of the MIT C.E. Reed Faculty Initiative Award for an innovative research project (1992), is a recipient of the NIH Director's Transformative Grant (2009), and a recipient of the Lyme Research Alliance award in 2014.
Apart from his work in Academia, Dr. Lewis has served as a consultant to the Pharmaceutical Industry, The Biotech, and is a founder of two Biotech Companies, NovoBiotic Pharmaceuticals, and Arietis Corporation.

NOTES

The Quest for New Antibiotics

Our ability to discover novel compounds has diminished, and pathogens acquire and spread resistance largely unchecked, leading to a human health crisis. The main source of antibiotics – soil actinomycetes – has been overmined. The problem is compounded by the presence of dormant persister cells tolerant to killing by all antibiotics. As a result, chronic osteomyelitis or infections of patients with cystic fibrosis can be untreatable. The majority of environmental microorganisms, 99%, are uncultured. We developed approaches to grow uncultured bacteria and find that this "microbial dark matter" harbors novel antimicrobials. Lassomycin produced by a soil actinomycetes kills persisters of Mycobacteria by forcing the ClpC1 chaperone to hydrolyze ATP. Teixobactin, made by a β-proteobacterium, evolved to be essentially free of resistance. These examples suggest that mining uncultured bacteria holds the promise of reviving natural product antibiotic discovery.

Michel C. NUSSENZWEIG

Professor
Laboratory of Molecular Immunology, The Rockefeller University
New York, USA

Michel C. Nussenzweig is the Zanvil A. Cohn and Ralph M. Steinman Professor and head of the laboratory of Molecular Immunology at The Rockefeller University. He is also an Investigator of the Howard Hughes Medical Institute. Nussenzweig received a B.A. degree from New York University College of Arts and Sciences in 1975. He earned a Ph.D. from The Rockefeller University in 1981 for work with Ralph M. Steinman on mouse dendritic cells. Nussenzweig received an M.D. from New York University School of Medicine in 1982 and completed his internship, and residency in Medicine, and fellowship in Infectious Diseases at Massachusetts General Hospital in 1985. From 1986 to 1989, he was a postdoctoral fellow in genetics in the Harvard Medical School laboratory of Philip Leder. He returned to Rockefeller as an independent Assistant Professor in 1990 and was promoted to Professor in 1996. Nussenzweig is responsible for key insights into dendritic and B cell function. With Steinman, he opened the field of antigen presentation by DCs by discovering that they capture, process and present antigens to initiate immunity. He produced the first DC-monoclonal antibody that was essential in establishing the role of DCs in immune responses and cloned the first endocytic receptor expressed by DCs. In his own laboratory he used these reagents to develop a method to deliver antigens to DCs in vivo, *leading to the discoveries that in steady state, DCs maintain peripheral tolerance and that different DC subsets have distinct antigen processing capacities. Nussenzweig also resolved the long-standing problem of how DCs are related to and diverge from other myeloid cells including monocytes during development in the bone marrow. In 2011, after Steinman's untimely death, Nussenzweig delivered the Nobel lecture in Steinman's place.*

Antibodies are the essential protective elements of nearly all vaccines. In the last several years' antibodies have also become important therapeutic agents in treating inflammation and cancer. Nussenzweig's research is on the development and function of antibodies and on the B-lymphocytes that produce them. He developed robust and scalable methods for the cloning of antibody genes from single human B cells. He first applied this approach to define how tolerance develops in normal individuals. Nussenzweig made a ground-breaking advance in the area of HIV-1 research when he applied his single cell antibody cloning methods to elucidate the development of HIV-1 antibodies. He discovered that broad and potent antibodies to HIV-1 are highly somatically mutated and proposed that this property could explain why it has been so difficult to elicit such antibodies by immunization. This fundamental insight has led to new approaches to HIV-1 vaccine development including the use of multiple sequential immunogens to elicit broadly neutralizing antibodies. His work on anti-HIV-1 antibodies, and that of others that rapidly adopted his methods, led to the discovery of naturally arising anti-HIV antibodies that were orders of magnitude more potent than previously known antibodies. Moreover, they revealed novel targets of HIV-1 vulnerability. The new antibodies neutralized up to 95% of all HIV-1 strains individually, and nearly all known strains when combined even at very low concentrations. Nussenzweig and his colleagues established that these antibodies both prevent and control chronic infection in humanized mice and in macaques. He then confirmed the pre-clinical studies in phase 1 clinical trials in humans. His clinical experiments established that broadly neutralizing antibodies are a safe and effective against HIV-1 in humans and set the stage for ongoing large-scale passive prevention trials.

Nussenzweig is a fellow of the American Academy of Arts and Sciences, the Brazilian Academy of Sciences, the Spanish Royal Academy, a member of the National Academy of Medicine USA, and the National Academy of Sciences USA. Among other prizes he is the recipient of the 2016 Robert Koch Award.

NOTES

The HIV Vaccine Problem

Abstract to be provided

Pascale COSSART

Head
Bacteria-Cell Interactions Unit, Institut Pasteur
Paris, France

Pascale Cossart, after studying chemistry in Lille (France) obtained a master degree at Georgetown University, Washington, DC. Back in France, she obtained her PhD in Paris in the Institut Pasteur where she is still now, heading the "Bacteria-Cell Interactions" unit which is also an Inserm and an INRA unit. After studying DNA-protein interactions, in E. coli, *she started in 1986, to study the molecular and cellular basis of host-pathogen interactions taking as a model system the bacterial pathogen* Listeria monocytogenes *which now appears as one of the best documented bacterium. Pascale Cossart pioneered the field of Cellular Microbiology. Her series of discoveries in Cellular Microbiology and Infection Biology in a broader sense have led to novel concepts in fundamental Microbiology, in Cell Biology, Innate Immunity and more recently in Epigenetics.*

Pascale Cossart's contributions have been recognized by a number of awards, including the Robert Koch Prize(2007), the Louis Jeantet Prize for Medicine(2008), the Balzan Prize(2013). She is a member of the French Academy of Science(2002), a foreign member of the National Academy of Science (NAS) (2009), of the German Leopoldina(2001), of the Royal Society(2010) and National Academy of Medicine (NAM, ex IOM) 2014. She is Secrétaire Perpetuel of the French Académie des Sciences since January 2016.

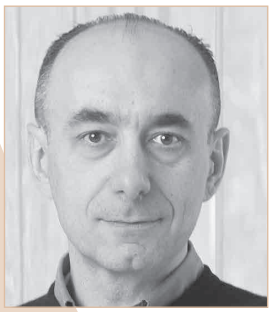
NOTES

The infection by Listeria : new insights in the intestinal phase

The bacterial pathogen *Listeria monocytogenes* is responsible for gastroenteritis, meningitis and abortions. Crossing of the intestinal barrier is critical for infection and has been the focus of my laboratory for many years. This phase of the infection can only occur if the bacterium reaches the intestine. We had published several years ago that a bile salt hydrolase is required for survival/persistence in the intestine. We now show that some strains of *Listeria* which happen to be those involved in epidemics and only those, encode a bacteriocin which affects the composition of the intestinal microbiota and favors infection. These results reinforce the emerging view that interaction of an enteropathogen with the microbiota is critical for a productive infection.

Jean-Laurent CASANOVA

Professor
Laboratory of Human Genetics of Infectious Diseases, The Rockfeller University
New York, USA



Dr. Jean-Laurent Casanova received his M.D. from the University of Paris Descartes in 1987 and his Ph.D. in immunology from the University of Paris Pierre and Marie Curie in 1992. After completing a residency in pediatrics and a clinical fellowship in pediatric immunology-hematology, he was appointed a professor of pediatrics at the Necker Medical School in Paris. There, with Dr. Abel, he cofounded and codirected the Laboratory of Human Genetics of Infectious Diseases in 1999. He was appointed professor at Rockefeller in 2008 and named a Howard Hughes Medical Institute investigator in 2014.

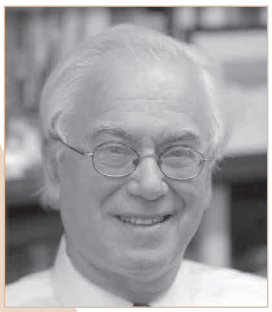
NOTES

Toward a genetic theory of childhood infectious diseases

The hypothesis that inborn errors of immunity underlie infectious diseases is gaining experimental support. However, the apparent modes of inheritance of predisposition or resistance differ considerably between diseases and between studies. A coherent genetic architecture of infectious diseases is lacking. We suggest here that life-threatening infectious diseases in childhood, occurring in the course of primary infection, result mostly from individually rare but collectively diverse single-gene variations of variable clinical penetrance, whereas the genetic component of predisposition to secondary or reactivation infections in adults is more complex. This model is consistent with (i) the high incidence of most infectious diseases in early childhood, followed by a steady decline, (ii) theoretical modeling of the impact of monogenic or polygenic predisposition on the incidence distribution of infectious diseases before reproductive age, (iii) available molecular evidence from both monogenic and complex genetics of infectious diseases in children and adults, (iv) current knowledge of immunity to primary and secondary or latent infections, (v) the state of the art in the clinical genetics of non-infectious pediatric and adult diseases, and (vi) evolutionary data for the genes underlying single-gene and complex disease risk. With the recent advent of new-generation deep resequencing, this model of single-gene variations underlying severe pediatric infectious diseases is experimentally testable.

Martin J. BLASER

Professor of Medicine, Professor of Microbiology, and Director of the Human Microbiome Program
NYU School of Medicine
New York, USA



Martin J. Blaser is the Muriel and George Singer Professor of Medicine, Professor of Microbiology, and Director of the Human Microbiome Program at the NYU School of Medicine. He served as Chair of the Department of Medicine at NYU from 2000-2012. A physician and microbiologist, Dr. Blaser is interested in understanding the relationships we have with our persistently colonizing bacteria. His work over 30 years focused on particular organisms, including Campylobacter *species and* Helicobacter pylori, *which also are model systems for understanding the interactions of residential bacteria with their human hosts. Over the last 15 years, he has been actively studying the relationship of the human microbiome with health and with such important diseases as asthma, obesity, diabetes, and allergies. Over the course of his career, Dr. Blaser has served as the advisor for a large number of students, post-doctoral fellows, and junior faculty. He served as President of the Infectious Diseases Society of America, Chair of the Board of Scientific Counselors of the National Cancer Institute, Chair of the Advisory Board for Clinical Research of the National Institutes of Health, and on the Scientific Advisory Board of the Doris Duke Charitable Foundation. He was elected to the National Academy of Medicine and the American Academy for Arts and Sciences. He holds 25 U.S. patents relating to his research, and has authored over 540 original articles. Recently, he wrote "Missing Microbes", a book targeted to general audiences. He now is serving as the Chair of the Presidential Advisory Council for Combating Antibiotic-Resistant Bacteria.*

NOTES

Antibiotic perturbation of the early-life microbiome affects metabolic and immunologic development

There is increasing evidence that indicates that the composition of the human microbiome is not accidental, but has largely been inherited at least during primate evolution, and probably longer. Such conservation is consistent with the notion of mutual benefit during the long-period of co-evolution. Early life, following the transfer of microbes from mothers to their babies, is likely the critical time. We have been examining the assembly of the microbiota in human children and in mice, and assessing the effects of perturbations on its formation. In particular, murine models have focused on early life exposures and their effects on microbiome, metabolism, and immunological development. We have found that there are early life windows in which microbiome perturbations, even if transient, can have long-term developmental effects. We have been assessing the reversibility of these phenomena. Ecological models suggest that the actual microbial networks are important in defining the microbial context of the symbiosis, and are an emergent property that affects host development.

Janelle AYRES

Assistant Professor
Nomis Center for Immunobiology and Microbial Pathogenesis,
Salk Institute for Biological Studies
La Jolla, USA

Janelle Ayres completed her PhD at Stanford University School of Medicine and her post doctoral studies at University of California, Berkeley before joining the Salk Institute on Faculty in the Nomis Center for Immunobiology and Microbial Pathogenesis. In a new approach to therapeutics, Janelle Ayres studies how the body controls and repairs the collateral damage generated during infectious and non-infectious diseases - a strategy called tolerance. She is taking an innovative approach grounded in mathematical and evolutionary predictions that uses the beneficial microbes that inhabit our digestive system for damage-control therapeutics. In pivotal work, Janelle showed that those damage-control mechanisms are just as important as an animal's immune system in surviving infection. Janelle's ultimate goal is to develop treatments for infectious and non-infectious diseases (such as pathologies associated with cancer and aging) without the need for antibiotics. She is the recipient of several awards including the Searle Scholar Award, the DARPA Young Faculty Award, a Ray Thomas Edward Foundation Award and a Senior Scholar Award from the Crohn's and Colitis Foundation.

NOTES

The concept of disease tolerance in host-microbiota interactions

Animal defenses against microbes are most often thought of as a function of the immune system, the primary function of which is to sense and kill microbes through the execution of resistance mechanisms. We have been at the forefront of characterizing a distinct defense response called disease tolerance that enables the host to endure physiological damage that occurs during microbial interactions without having a negative effect on microbial fitness. I will discuss our recent advances understanding how beneficial microbes of the intestinal microbiota have evolved mechanisms to promote tolerance defenses in their host by focusing on infection-induced muscle wasting pathology.

Mats WAHLGREN

Professor
Department of Microbiology, Tumor and Cell Biology,
Karolinska Institutet
Stockholm, Sweden

Mats Wahlgren is professor of infectious disease control, with an emphasis on clinical parasitology. Professor Wahlgren received his medical degree from Karolinska Institutet and a DTM&H from the Mahidol University in Bangkok, Thailand, in 1979. In 1981, Mats Wahlgren began his career in the field of molecular pathogenesis of malaria with doctoral studies that led to a PhD degree in 1986. He is a member of the Nobel Assembly for Physiology or Medicine at KI. Mats Wahlgren was appointed associate professor at KI in 1990 and spent the next years at DNAX Research Institute/Stanford University in Palo Alto in the laboratory of Dr. Russell Howard. Wahlgren was subsequently appointed professor of parasitology in 1993 and has since served as chairman of the Department of Microbiology, Tumor and Cell Biology at KI, director of the Multilateral Initiative on Malaria, program director for the Infection and Vaccinology Program, president of the Swedish Society of Tropical Medicine and vice-dean of research at Karolinska Institutet.

Professor Wahlgren identified the cell-phenomenon known as rosetting (adhesion of uninfected erythrocytes around infected ones) during his thesis work and later studied the association between rosetting and severity from P. falciparum *(Carlson* et al. Lancet *1989). He and his colleagues unveiled the molecular details of the interaction between the rosetting-ligand (PfEMP1) and its receptors on endothelial and red blood cells, the details of* var *gene switching involved in the expression PfEMP1 (Chen* et al. Nature, *1998) and discovered the role of heparan sulfate as a receptor in rosetting-binding to red blood- and to endothelial cells. This led to the creation of a novel drug named sevuparin together with Dilafortette AB. Recently, the RIFINs were identified as important co-receptors in the rosetting (Goel* et al. Nature Med, *2015).*

Wahlgren is one of the co-founders of the Dilafor AB and Dilaforette AB biotech companies committed to the development of carbohydrate-based therapy for conditions including severe malaria and sickle-cell crisis. Dilaforette AB recently completed a Phase I/II clinical study with sevuparin in malaria with Oxford University/Mahidol University. Results are important. A clinical Phase II study with sevuparin is presently ongoing in sickle-cell crisis patients. Wahlgren is the inventor of several patents.

Professor Wahlgren received the Axel Hirsch Prize 2016, a Fogarty Award from NIH, was named Carl Harford Visiting Professor at Washington University, St. Louis, USA and has received the title of «Excellent scientist» from the Swedish Research Council, a Distinguished Professor Award from KI, and a Söderberg professorship from the Royal Academy of Sciences.

NOTES

Successful development of an adjunctive drug against severe *Plasmodium falciparum* malaria

High parasitemia and excessive sequestration of infected erythrocytes (IE) are typical features of severe *P. falciparum* malaria. Sequestration involves binding of IE to the host receptor heparan sulphate that also partakes in merozoite invasion. Sevuparin was developed by Dilaforette AB from heparin given the fact that heparan sulfate and heparin are close to identical and with the assumption that sevuparin would work as a decoy receptor during a malaria infection. The potentially harmful anticoagulant activities of heparin were eliminated by periodate treatment and a successful clinical Phase I study in healthy volunteers with sevuparin was completed in 2009. I report the results of a Phase I/II study in patients with uncomplicated *falciparum* malaria. Sevuparin was found to be safe and well tolerated when given in intravenous infusions as adjunct therapy to malaria patients treated with atovaquone/ proguanil (Malanil). Further, we found that the number of ring-stage IE to be significantly decreased already one hour after the first infusion of sevuparin while the parasites continued to expand in control patients not given the drug ($p<0.05$). This is in line with the capacity of sevuparin to block merozoite invasion into red blood cells. The data also revealed a potentially, clinically meaningful anti-sequestration effect since higher numbers of mature IE appeared in the circulating blood of treated patients compared to controls ($p<0.05$). These effects are consistent with previous *in vitro r*esults as sevuparin has been found to disrupt rosettes and also to reverse already established sequestration in animals *in vivo*. In conclusion, sevuparin inhibits merozoite invasion and reverses *in vivo* sequestration of IE in humans with uncomplicated *P. falciparum* malaria.

References:

1. Vogt AM, Pettersson F, Moll K, Jonsson C, Normark J, Ribacke U, Egwang TG, Ekre HP, Spillmann D, Chen Q, Wahlgren M. Release of sequestered malaria parasites upon injection of a glycosaminoglycan. PLoS Pathog. Sep; 2 (9):e100 doi:10.1371/journal.ppat. 0020100 (comments: see Nature, 443, 12 Oct, p 607, 2006), 2006
2. Wahlgren M. Tackle Severe Malaria. Comment in: Perspectives: The missing pieces. Nature. 2012 Apr 25;484(7395):S2 3. doi: 10.1038/484S22a

Jean-Marc ROLAIN

Professor of Microbiology
Unité de Recherche sur les Maladies Infectieuses et Tropicales Emergen, Aix Marseille Université
Marseille, France

Biosketch to be provided

NOTES

Superbugs: Plasmid Mediated Colistin Resistance and Animal to Human Transmission

Abstract to be provided

Michael CALDERWOOD

Professor
Geisel School of Medicine, Dartmouth College
Hanover, Germany

Michael S. Calderwood, MD MPH is the Regional Hospital Epidemiologist at Dartmouth-Hitchcock Medical Center, a hospital staff physician in the Section of Infectious Disease and International Health, and an Assistant Professor of Medicine at the Geisel School of Medicine at Dartmouth College. Prior to this, he was an Assistant Professor of Medicine at Harvard Medical School and a faculty member in the Division of Infectious Diseases at Brigham and Women's Hospital in Boston, MA where he served as the Assistant Hospital Epidemiologist and the Associate Director of Antimicrobial Stewardship. Dr. Calderwood has clinical and research expertise in hospital epidemiology, infection prevention, and antimicrobial stewardship. His primary research has involved collaboration with the U.S. Centers for Disease Control and Prevention (CDC), the Centers for Medicine and Medicaid Services (CMS), and the Agency for Healthcare Research and Quality (AHRQ). He has led multicenter and national studies seeking to improve the accuracy and validity of publicly reported data on healthcare associated infections, while also working to understand the effects of pay-for-reporting and pay-for-performance programs on hospital quality metrics in U.S. hospitals.»

NOTES

The Good, the Bad and the Ugly: HAI public reporting and pay-for-performance in US hospitals

Dr. Calderwood will review the evolution of public reporting and pay-for-performance measures targeting healthcare-associated infections in US hospitals. He will discuss the move from a focus on structure, to a targeting of process measures, and eventually to a reliance on outcome measures. He will discuss current hospital quality metrics, the advantages and disadvantages of various metrics, and the recognized limitations in assessing quality of care in the US health care system. From the perspective of a hospital epidemiologist, he will review how efforts to reward quality rather than volume have led to incentives to adopt evidence-based medicine for the prevention of healthcare-associated infections. At the same time, he will raise concerns about data limitations which focus quality assessment on larger hospitals, difficulties in differentiating true aberrant performance from random variation, and the need for better risk adjustment when comparing outcomes across hospitals. Finally, with the explosion of different quality metrics, rapidly available on-line data, and demands for data transparency, Dr. Calderwood will reflect on how these data are being used and how to respond when different metrics provide discordant assessments of quality.

Gregg ALTON

Executive Vice President
Commercial and Access Operations ALA,
Corporate and Medical Affairs, Gilead Sciences

Gregg Alton joined Gilead Sciences in 1999. From 2000 to 2009 he served as General Counsel. In his current role, Mr. Alton is responsible for commercial and access operations in Asia, Latin America and Africa, government affairs and policy, public affairs and medical affairs. Prior to joining Gilead, Mr. Alton was an attorney at the law firm of Cooley Godward, LLP, where he specialized in mergers and acquisitions, corporate partnerships and corporate finance transactions for healthcare and information technology companies. Mr. Alton has led the expansion of Gilead's access initiatives, which make the company's HIV and hepatitis C medicines available at significantly reduced prices in the developing world. Through these programs, Gilead's medicines now reach more than 10 million people in developing nations. A key component of Gilead's efforts has been providing licenses to Indian, South African and Chinese manufacturers to produce and distribute generic versions of Gilead's antiretrovirals and groundbreaking hepatitis C therapies in the developing countries most seriously affected by the HIV and HCV epidemics. Under Mr. Alton's leadership, Gilead became the first innovator pharmaceutical company to join the Medicines Patent Pool (MPP), granting the MPP licensing rights for the company's HIV medicines. Gilead also works to increase global access to treatments for other life-threatening diseases, including visceral leishmaniasis.

Mr. Alton speaks frequently at international scientific conferences and policy forums about HIV/AIDS and viral hepatitis research and development, and global health policy issues related to treatment access, including financing, delivery and intellectual property. Mr. Alton is a member of the boards of the AIDS Institute and the Boys and Girls Clubs of Oakland. He is also a member of the U.S. Government's Industry Trade Advisory Committee on Intellectual Property Rights, the advisory boards of UCSF Global Health Group, USC Schaeffer Center for Health Policy and Economics, Pharmozyme, Inc. and the Dean's Advisory Council at Stanford Law School. In addition, he serves on Partners In Health's Board of Trustees. Mr. Alton received a bachelor's degree in legal studies from the University of California at Berkeley, and holds a JD from Stanford University.

NOTES

Delivering access to innovative medicines – the journey to hepatitis C elimination

Hepatitis C (HCV) is one of the most urgent health priorities worldwide, which the World Health Organization (WHO) estimates affects more than 130 million people. Until recently, treatment options for hepatitis C were limited to medicines which had a long duration of therapy, significant side effects and only offered a limited chance of a cure. The discovery and availability of direct-acting antivirals (DAAs) such as sofosbuvir have transformed the treatment of HCV. DAA regimens can now cure most people with HCV in 8 to 12 weeks and with fewer side effects than prior therapies.

Gilead believes these therapies should be available to all people who can benefit from them, regardless of where they live or their economic status. The company has therefore put principles in place with programs that address countries with a high burden of disease. Because Egypt has the highest HCV prevalence in the world, it was among the first countries where we applied these principles for HCV. Working with the country's Ministry of Health, we are supporting the implementation of an ambitious national HCV treatment program, providing affordable medication through public health services and supporting clinical education across the country. Through programs like this, and other innovative projects around the world, we are working to support the WHO's target to eliminate HCV by 2030.

Mariola FOTIN-MLECZEK

Chief Scientific Officer
CureVac AG
Tübingen, Germany

Mariola Fotin-Mleczek studied biology at the University of Stuttgart with focus on genetics, cellular biology and immunology. In her PhD at the Institute of Cell Biology and Immunology at the University of Stuttgart, she dedicated herself to study the crosstalk between TNF receptors 1 and 2 by the induction of the programmed cell death apoptosis. The results of her work contributed significantly to the better understanding of the interaction between TNF receptors. During her postdoc time at the Intrafacultary Institute of the Eberhard Karl University of Tübingen she worked on the cell-penetrating peptides, a potent tool to introduce desired cargo into the cells. Together with colleagues from neighboring disciplines, she explained in detail the mechanism, by which specific short peptides are able to cross cellular membranes and bring pro- apoptotic peptide into the tumor cells, forcing them into the programmed cell death.

She joined CureVac 2006 and was responsible for the preclinical development of mRNA based RNActive technology with the goal to enter first in men clinical studies in tumor patients. In the course of the preclinical development she was responsible for the elucidation of mechanism of action of mRNA-based vaccines. She was critically involved in the number of scientific publications and patents in the field of mRNA-based therapeutics. 2013 she took over the responsibility for the research at CureVac as Chief Scientific Officer. At the moment she coordinates the research of around 50 employees and together with her colleagues in the board of directors refines the strategy of CureVac.

Mariola Fotin-Mleczek holds 25 patents among others in the field of formulation and cancer immunotherapy.

NOTES

Next generation RNA vaccines

Over decades, messenger RNA (mRNA) has been regarded as being unsuited for medical applications because of its perceived instability and difficult handling. CureVac recognized the huge potential of mRNA molecule very early and since the year 2000 develops different technology platforms, based on engineered, optimized mRNA, supporting high expression of encoded protein and adjustable formulation allowing different administrations.

Whereas CureVac's RNActive® technology was developed to induce immune response against encoded antigens, the RNArt® platform focuses on the expression of therapeutic proteins without raising an immune response.

Pre-clinical experiments demonstrate that RNActive® vaccines can be used for multiple approaches and induce balanced and boostable effector and memory immune responses. Moreover, mRNA-based vaccines were demonstrated to protect different species against infections with multiple pathogens. Even in humans, RNActive® vaccines were immunogenic and well tolerated, which makes them a potent and universal platform for therapeutic and prophylactic vaccines.

Comparably pre-clinical experiments with the RNArt® platform demonstrated that the application of optimized mRNA can boost the serum levels of erythropoietin without an activation of an immune system and consistently leads to long-lasting biologically-relevant effects, even in large animals. An important field of protein therapy is passive immunization with recombinant antibodies against threats, such as infectious diseases or intoxication. Up to this point we showed that a single injection of mRNA immediately leads to high neutralizing antibody titers, sufficient to provide fast protection to animals in lethal challenge situations.

Taken together CureVac holds the key to define a new class of drugs based on mRNA, which gives the body the information to cure itself.

Patrick JAULT

Director of Anesthesiology
Percy Military Instruction Hospital
Clamart, France

Engaged in the French military health service at 18 yo. He was graduated in 1999 as general practitioner by university of Lyon and as anesthesiologist and critical care in 2007 by the university of Pierre et Marie Curie (Paris V). Skilled in field medicine, he was deployed in Kosovo, Gabon, Afghanistan, Mali and Ivory Coast. He is experienced in collective hygiene issues and life threatening trauma care. He is qualified in tropical diseases, management of infectious diseases in critical care, ultrasound management of critical disorders and medical information.

In 2008, he was affected in the Burn unit in the military teaching Hospital PERCY in Clamart, France. In 2009, he was involved in a NATO group in charge of publication of recommendations about burn cares on the battlefield. This group was leaded by a Belgium team, who suggested the use of bacteriophages to prevent development of MDR infections in burn patients. In 2010, The first part of the project PACOBURN was funded by a military grant. It was the pre-clinical part of the project. As phages were never used in Western Europe, we decided to use phages in a topical application. It is a common application route in burn wounds infections. Since 2010 to 2013, we developed our network of clinical sites in the 3 countries involved in the clinical trial. He led discussions about harmonization of clinical practices between all centers, and the choice of the topical treatment in the control arm.

Patrick JAULT is the coordinator of the PHAGOBURN project. He's in charge of the right fit between medical needs, biothec constraints and regulatory requests. In a very close but independent collaboration with PHERECYDES-PHARMA, sponsor of the project, he advised the design of pre-clinical and clinical study and collaborated in all the discussions with the 3 national regulators agencies (French, Belgium and Swiss) and with supervision by the European Medicine Agency.

In 2013, the clinical trial was launched. The first two years were dedicated to biotech production of phages in a GMP environment and qualification of the production chain by the ANSM (Agence Nationale de Sécurité du Médicament et des Produits de Santé) the French agency for the safety of drugs. The first patient was included in July 2015, after the agreement of the 3 European agencies.

After 27 years of duty, Dr Patrick JAULT resigned from the army. He is now anesthetist in a private clinic in Paris. He is still the scientific coordinator of the project and stay active in the future development of phage therapy. He is expert for the French agency in the special scientific committee for phage therapy created in march 2016. He is married with 3 kids. He was honored by the highest French national rewards: knight of Légion d'honneur, Knight of ordre National du mérite, Citation with Military Cross.

NOTES

Bacteriophages: When the past illuminates the future!

Antibiotic resistance has become in few years a major public health issue. WHO estimates that by 2050 infectious diseases will be the leading cause of death worldwide. Despite many policies of prudent use of antibiotics, the incidence of infection by MDR bacteria is still increasing. Therefore, it becomes necessary to find innovative therapeutic alternatives.

Bacteriophages are environmental virus capable of lysing targeted bacteria. They represent the largest biomass on earth. They are highly specific of their bacterial receptor. After phage has bound the bacterial wall it injects its genetic material into bacteria and turns bacterial biosynthesis to his advantage to produce new virions. The concentration of virions increases fast and sharply until the bacterial wall rupture and the release of new virions. New virions propagate from host to host spreading the bacterial infections. This lysis occurs within minutes after infection.

PHAGOBURN expects to bring a proof of concept for an old empirical therapy used in eastern Europe for one century and abandoned in western Europe for the benefit of antibiotics. The project is funded by European Commission (3,8 Millions Euros) and has begun in June 2013. It is a controlled, multicentric, randomized, double blinded trial. The main objective is the comparison of time in the reduction of bacterial burden between the topical application of a cocktail of phages and the topical application of silver sulfadiazine. The cocktails are association of natural lytic phages against *Pseudomonas aeruginosa* and *Escherichia coli*. The first part of the project drove to the bio-production of 2 cocktails of bacteriophages in a GMP-like environment. PP0121 is composed of 13 different bacteriophages active against *Escherichia coli* and PP1131 has 12 different bacteriophages active against *Pseudomonas aeruginosa*. The Belgian, the Swiss and the French health authorities authorized the first human inclusion in July 2015 in one of the eleven centers engaged in the study. Stability of phages in a cocktail is a common issue. We decided to suspend since January to May 2016. This period was necessary to prove the good stability of cocktails over time. After 6 months 15 patients have been included, only one in the *E coli* arm. Due to this too small number of, we decided to continue inclusions only in the *Pseudomonas aeruginosa* arm. Inclusions have restarted in May 2016.

SPEAKER & CHAIR LIST

ALTON Gregg
Corporate and Medical Affairs, Gilead Sciences

ANDERSSON Jan
Unit for Infection and Dermatology, Karolinska Institutet
Stockholm, Sweden
Jan.Andersson@ki.se

AYRES Janelle S.
Nomis Center for Immunobiology and Microbial Pathogenesis, Salk Institute for Biological Studies
La Jolla, USA
jayres@salk.edu

BLASER Martin J.
Departments of Medicine and Microbiology, NYU School of Medicine
New York, USA
martin.blaser@nyumc.org

CALDERWOOD Michael
Department of Medicine, Geisel School of Medicine, Darmouth College
Hanover, Germany
Michael.Calderwood@Dartmouth.edu

CASANOVA Jean-Laurent
Laboratory of Human Genetics of Infectious Diseases, The Rockfeller University
New York, USA
Jean-Laurent.Casanova@rockefeller.edu

CHIEN Kenneth R.
Department of Cell & Molecular Biology & Medicine, Karolinska Institutet
Stockholm, Sweden
kenneth.chien@ki.se

CHRISTEN Yves
Fondation IPSEN
Boulogne-Billancourt, France
yves.christen@ipsen.com

COSSART Pascale
Inserm U604 ´Interactions Bactéries-Cellules´, Institut Pasteur
Paris, France
pascale.cossart@pasteur.fr

DAHLMAN-WRIGHT Karin
Karolinska Institutet
Stockholm, Sweden
Karin.Dahlman-Wright@ki.se

FOTIN-MLECZEK Mariola
CureVac AG
Tübingen, Germany

JAULT Patrick
Percy Military Instruction Hospital
Clamart, France

JONES Susan
Nature Biotechnology, Nature Publishing Group
London, UK
s.jones@nature.com

KIENY Marie-Paule
Health Systems and Innovation, World Health Organization
Geneva, Switzerland

LEUNG Gabriel M.
Division of Community Medicine and Public Health Practice, Li Ka Shing Faculty of Medicine, The University of Hong Kong
Hong Kong, China
deanmed@hku.hk

LEWIS Kim
Antimicrobial Discovery Center, Northeastern University
Boston, USA
k.lewis@neu.edu

LJUNGGREN Hans-Gustaf
Human NK Cells in Health and Disease Group, Karolinska Institutet
Stockholm, Sweden
hans-gustaf.ljunggren@ki.se

NUSSENZWEIG Michel C.
Laboratory of Molecular Immunology, The Rockefeller University
New York, USA
Michel.Nussenzweig@rockefeller.edu

PIOT Peter
London School of Hygiene and Tropical Medicine (LSHTM)
London, UK
director@lshtm.ac.uk

ROLAIN Jean-Marc
U1095 URMITE - Unité de Recherche sur les Maladies Infectieuses et Tropicales Emergentes, Aix Marseille Université
Marseille, France
jm.rolain@medecine.univ-mrs.fr

SANTANA DE AGUIAR Renato
Federal University of Rio de Janeiro
Rio De Janeiro, Brazil
santanarnt@gmail.com

SMITH Orla M.
Editorial Department, AAAS/ Science Translational Medicine
Washington, USA
osmith@aaas.org

STACEY Julie
EBioMedicine, Elsevier – Journals

WAHLGREN Mats
Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet
Stockholm, Sweden
Mats.Wahlgren@ki.se

WILSON Ian A.
Department of Integrative Structural and Computational Biology, The Scripps Research Institute
La Jolla, USA
wilson@scripps.edu

XIAO Rui-Ping
Laboratory of Signal Transduction, Institute of Molecular Medicine, Peking University
Beijing, China
xiaor@grc.nia.nih.gov

PARTICIPANT LIST

FLODSTRÖM TULLBERG Malin
Department of Medicine - Huddinge, Karolinska Institutet
Stockholm, Sweden
malin.flodstrom-tullberg@ki.se

PALANICHAMY Elanchelian
Bioscience and Nutrition, Karolinska Institutet
Stockholm, Sweden
elanchelian@mail.com

ADLHOCH Cornelia
Surveillance, European Centre for Disease Prevention and Control (ECDC)
Solna, Sweden
cornelia.adlhoch@ecdc.europa.eu

AKUFFO Hannah
Research Cooperation, MTC, Sida and Karolinska Institutet
Stockholm, Sweden
Hannah.Akuffo@Sida.se

AL FARSI Hissa
Laboratory Medicine, Karolinska Institutet
Stockholm, Sweden
hissa.al.farsi@ki.se

ANDERSSON Yasmin
Drug Discovery and Development, SciLife Lab
Solna, Sweden
yasmin.andersson@scilifelab.se

BÅLÖW Ros-Mari
Unit for Research Cooperation, Swedish International Development Cooperation Agency (SIDA)
Stockholm, Sweden
ros-mari.balow@sida.se

BEJARANO Maria Teresa
Unit for Research Cooperation, Sida and Karolinska Institutet
Stockholm, Sweden
maria-teresa.bejarano@sida.se

BERGMAN Peter
Department of Laboratory Medicine, Karolinska Institutet
Stockholm, Sweden
peter.bergman@ki.se

BERGSTEN Helena
Center for Infectious Medicine, Department of Medicine, Karolinska Institutet / Karolinska University Hospital - Huddinge
Solna, Sweden
helena.bergsten@ki.se

BLIXT Martin
Department of Medical Cell Biology, Uppsala University
Uppsala, Sweden
martin.blixt@mcb.uu.se

BUJILA Ioana
Molecular Biosciences, Stockholm University
Stockholm, Sweden
ioana.bujila@gmail.com

CAI Yanling
Department of Pharmacy, Uppsala University
Uppsala, Sweden
yanling.cai@farmaci.uu.se

CHIODI Francesca
Microbiology, Tumor and Cell Biology (MTC), Karolinska Institutet
Stockholm, Sweden
francesca.chiodi@ki.se

CHIODI Francesca
Microbiology, Tumor and Cell Biology (MTC), Karolinska Institutet
Stockholm, Sweden
francesca.chiodi@ki.se

DANIELS Robert
Biochemistry and Biophysics, Stockholm University
Stockholm, Sweden
robertd@dbb.su.se

DANIELSSON Niklas
Surveillance and Response, European Centre for Disease Prevention and Control (ECDC)
Stockholm, Sweden
niklas.danielsson@ecdc.europa.eu

DIAS Joana
Department of Medicine, Karolinska Institutet
Stockholm, Sweden
joana.dias@ki.se

DIEHL Johanna
Faculty Office and International Relations, Karolinska Institutet
Stockholm, Sweden
johanna.diehl@ki.se

DYAR Oliver James
Department of Public Health Sciences, Karolinska Institutet
Stockholm, Sweden
oliver.dyar@ki.se

EDFELDT Gabriella
Department of Medicine - Solna, Karolinska Institutet
Stockholm, Sweden
gabriella.edfeldt@ki.se

ERIKSSON Anneli
Department of Public Health Science, Karolinska Institutet
Stockholm, Sweden
anneli.eriksson@ki.se

FEYISSA Yonas Bekele
Microbiology, Tumor and Cell Biology (MTC), Karolinska Institutet
Stockholm, Sweden
yonas.bekele.feyissa@ki.se

GORIN Jean-Baptiste
Department of Medicine - Huddinge, Karolinska Institutet
Stockholm, Sweden
jean-baptiste.gorin@ki.se

GUSTAFSSON Anders
Department of Dental Medicine, Karolinska Institutet
Stockholm, Sweden
anders.gustafsson@ki.se

HAGMAIER Kathrin
Eurosurveillance, European Centre for Disease Prevention and Control (ECDC)
Solna, Sweden
Kathrin.Hagmaier@ecdc.europa.eu

INTURI Raviteja
Department of Medical Biochemistry and Microbiology, Uppsala University
Uppsala, Sweden
raviteja.inturi@imbim.uu.se

IRWIN Rachel
Department of Public Health Science, Karolinska Institutet
Stockholm, Sweden
rachel.irwin@ki.se

JANSA Josep
Epidemic Intelligence and Response, European Centre for Disease Prevention and Control (ECDC)
Stockholm, Sweden
Josep.jansa@ecdc.europa.eu

KASTENG Frida
Department of Public Health Sciences, Karolinska Institutet
Stockholm, Sweden
frida.kasteng@ki.se

LASSITER David
Department of Molecular Medicine and Surgery, Karolinska Institutet
Stockholm, Sweden
david.gray.lassiter@ki.se

LI Meishan
Department of Physiology and Pharmacology, Karolinska Institutet
Stockholm, Sweden
meishan.li@ki.se

LINDHE Örjan
Sales, Olink Proteomics
Uppsala, Sweden
orjan.lindhe@olink.com

LINDQVIST Maria
Department of Women's and Children's Health, Karolinska Institutet
Stockholm, Sweden
maria.lindqvist@ki.se

LUNDMARK Frida
Stockholm Medical Biobank, Stockholm County Council
Stockholm, Sweden
frida.lundmark@sll.se

LUNDMARK Frida
Stockholm County Council, Stockholm Medical Biobanks
Stockholm, Sweden
frida.lundmark@sll.se

MAGNUSSON Magnus
Directorate, Capital4Development (Capital4D.com)
magnus.magnusson@capital4d.com

MOLL Markus
Center for Infectious Medicine, Department of Medicine - Huddinge, Karolinska Institutet
Stockholm, Sweden
markus.moll@ki.se

MOLL Markus
Center for Infectious Medicine, Department of Medicine - Huddinge, Karolinska Institutet
Stockholm, Sweden
markus.moll@ki.se

MUN Kwangchol
Department of Medical Biochemistry and Microbiology, Uppsala University
Uppsala, Sweden
kwangchol.mun@imbim.uu.se

NASI Aikaterini
Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet
Stockholm, Sweden
aikaterini.nasi@ki.se

NEEDHAM Howard
Office of the Chief Scientist, (OCS), European Centre for Disease Prevention and Control (ECDC)
Solna, Sweden
howard.needham@ecdc.europa.eu

NORDENSTEDT Helena
Department of Public Health Science, Karolinska Institutet
Stockholm, Sweden
helena.nordenstedt@ki.se

NOWAK Piotr
Department of Medicine - Huddinge, Karolinska Institutet
Stockholm, Sweden
Piotr.Nowak@ki.se

NY Sofia
Department of Laboratory Medicine, Karolinska Institutet
Stockholm, Sweden
sofia.ny@folkhalsomyndigheten.se

OHRLANDER Marie
Governmental Affairs, GIlead Sciences
Solna, Sweden
marie.ohrlander@gilead.com

PENTTINEN Pasi
Office of the Chief Scientist (OCS), European Centre for Disease Prevention and Control (ECDC)
Solna, Sweden
Pasi.Penttinen@ecdc.europa.eu

PEUCKERT Christiane
Department of Neuroscience, Uppsala University
Uppsala, Sweden
c.peuckert@neuro.uu.se

PINTOR Otto
Laboratory Medicine, Stem Cell Laboratory, Karolinska University Hospital
Stockholm, Sweden
pintor@kth.se

ROSALES KLINTZ Senia
Department of Public Health Sciences, Karolinska Institutet
Stockholm, Sweden
senia.rosales-klintz@ki.se

SALIBA Erika
Department of Public Health Sciences, Karolinska Institutet
Stockholm, Sweden
erika.saliba@ki.se

SANDBERG Johan
Department of Medicine, Karolinska Institutet
Stockholm, Sweden
johan.sandberg@ki.se

SAXELIN Elina
Healthcare/Mental Health, Swedish Association of Local Authorities and Regions (SKL)
Bromma, Sweden
elinasaxelin@gmail.com

SELVAM Apoorva
Biomedical Sciences, Humanitas University
Milano, Italy
selvamapoorva@gmail.com

SIVAKUMAR Ishwarya
Biomedical Sciences, Humanitas University
London, UK
i.sivakumar1996@gmail.com

SKOGLUND Göran
Medical Affairs, Gilead Sciences
Solna, Sweden
goran.skoglund@gilead.com

SOLA RIERA Carles
Department of Medicine - Huddinge, Karolinska Institutet
Stockholm, Sweden
carles.sola.riera@ki.se

SÖNNERBORG Anders
Unit of Infectious Diseases, Department of Medicine - Huddinge, Karolinska Institutet
Stockholm, Sweden
anders.sonnerborg@ki.se

SOOP Teresa
Unit for Research Cooperation, Swedish International Development Cooperation Agency (SIDA)
Stockholm, Sweden
teresa.soop@sida.se

STEFFENS Ines
Eurosurveillance Editorial Office, European Centre for Disease Prevention and Control (ECDC)
Solna, Sweden
ines.steffens@ecdc.europa.eu

SU Guobin
Department of Public Health Sciences, Karolinska Institutet
Stockholm, Sweden
guobin.su@ki.se

SWEDBERG Göte
Medical Biochemistry and Microbiology, Uppsala University
Uppsala, Sweden
gote.swedberg@imbim.uu.se

TIRADO Veronika
Department of Public Health Sciences, Karolinska Institutet
Stockholm,
veronika.tirado@ki.se

TJERNLUND Annelie
Department of Medicine - Solna, Karolinska Institutet
Stockholm, Sweden
annelie.tjernlund@ki.se

TOMSON Göran
Department of Learning, Informatics, Management and Ethics, Karolinska Institutet
Stockholm, Sweden
Goran.Tomson@ki.se

VÅGESJÖ Evelina
Department of Medical Cell Biology, Uppsala University
Uppsala, Sweden
evelina.vagesjo@mcb.uu.se

VOSS Matthias
Department of Medicine - Huddinge, HERM, Karolinska Institutet
Stockholm, Sweden
matthias.voss@ki.se

WILSON Karen
Eurosurveillance, European Centre for Disease Prevention and Control (ECDC)
Solna, Sweden
Karen.Wilson@ecdc.europa.eu

ZUCS Phillip
Surveillance and Response Support, European Centre for Disease Prevention and Control (ECDC)
Solna, Sweden
phillip.zucs@ecdc.europa.eu

NOTES

Days of Molecular Medicine
Global Foundation

Karolinska Institutet

FONDATION IPSEN