1938th Conference

Infectious Diseases & Neglacted tropical Diseases 2018

4th Annual Congress on **INFECTIOUS DISEASES**

&

5th International Conference on

NEGLECTED TROPICAL & INFECTIOUS DISEASES

August 29-30, 2018 | Boston, USA

Keynote Forum

Day 1

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Ivana Haluskova Balter

French society of Immunology, France

Innovative path to tackle neglected diseases : Restoring functionality of host immune system

Diseases neglected or omitted and neglected worth growing attention and new innovative immune/metabolic paths show real potential and overlapping approach to be undertaken. The fight against the Neglected Tropical Diseases receiving increased worldwide attention after the recent attribution of the 2015 Nobel Prize in Physiology or Medicine to William Campbell and Satoshi Ōmura for their development of a novel therapy against infections caused by roundworm parasites. Recently, WHO's efforts to address growing global AMR (27th Feb 2017) and it highlighted, in particular, the threat of gram-negative bacteria but initially "neglected" growing world urgency of tuberculosis – XDR/MDR and latent in particular. Based on recent works natural defenses to infection are mediated by intrinsic/innate and adaptive immune responses. While our understanding is considerable it is incomplete and emerging areas of research such as those related to the immune-metabolic axis are started to be appreciated. Macrophages play a frontline role in this process connecting immunity, infection and lipid biology, and collaterally are a central target for infection by a wide range of pathogens including viruses and bacteria, especially intracellular bacteria such as mycobacteria. Clinical manifestations of disease severity in the infected host are likely to pay tribute to perturbations of the metabolic-immune phenomena found in lymphocytes and myeloid cells. Historically and consistent with this notion, vitamin D based oxysterols have had a long association with promoting clinical improvements to patients infected with Mycobacterium tuberculosis. M. tuberculosis has invested considerable genomic real estate to encode enzymes capable of exploiting and catabolizing these host-derived immune metabolites (1) Similarly, it appears that L (Leishmania) parasites by decreasing membrane cholesterol during their intracellular life cycle may have altered the conformation of MHC-II molecules with direct bearing on the compromised agonist affinity leading to faster dissociation of cognate peptide from the peptide-MHC-II complex which could be corrected by liposomal cholesterol delivery. Several new paths to understanding host immune system interactions during L infection are looked at. Phagocytosis, a process known to be subverted by parasites like Leishmania (L). Indeed, the intracellular development of L amastigote relies on the biogenesis and dynamic remodeling of a phagolysosome, termed the parasitophorous vacuole. (2) It appears that L parasites by decreasing membrane cholesterol during their intracellular life cycle may have altered the conformation of MHC-II molecules with direct bearing on the compromised agonist affinity leading to faster dissociation of cognate peptide from the peptide-MHC-II complex which could be corrected by liposomal cholesterol delivery(4) Additionally or consequently CD8 T cells are driven to energy/exhaustion in human VL,

Notes:

which affect their ability to contribute to protective immune responses. (3) Effective approach capable of constraining the visceralizing parasites to the skin holds much promise as it would block colonization of the viscera, where these species are perfectly adapted for survival and subversion of the immune response. Based on recent works natural defenses to infection are mediated by intrinsic/innate and adaptive immune responses. Understanding the role of early metabolic mediators of inflammatory responses to infection, principles of immuno-metabolism will aid in the development of urgently needed HOST directed therapeutic, preventive (Vaccines) and diagnostic innovations knowing limitations of existing tools.

Biography

Haluskova Balter Ivana , MD,MBA, France, French/Slovak active medical professional specialised in infectious diseases, internal medicine covering various therapeutic axes, certified in Immunology and Pediatric, MBA in vaccinology. Lived multi-country medical "field "experience in Southeast Asia, West/Central/East Europe and Middle East. Speaking French, English, Russian, Italian, Czech, and Slovak with notion of Mandarin. Over 15 years of experience in pharmaceutical research and development for European and USA companies as Medical lead /Director of R&D in various therapeutic areas and as Scientific and Medical independent consultant for various academic and private stakeholders globally. Active member of French immunology society (SFI) administrative board and several international academic societies with focus on R&D innovation and partnership highlighting role immunology/immune-metabolism and genetics for innovative treatment, prevention and diagnostic. Member of advisory Health concern (India) and think tank group in order to attract attention to role of accessible medical care, education and awareness along with accurate diagnostic and innovative partnership in this area. Years of expertise to work globally but recently more focused on BRICS as Medical advisor for scientific partnership, bringing new innovative concepts alive and getting them endorsed.

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Notes:

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Stef Stienstra

Royal Dutch Navy, The Netherlands

Drug delivery by tattooing to treat cutaneous leishmaniasis

Leishmaniasis is a vector-borne disease that is caused by obligate intra-macrophage protozoa of the Leishmania species. Leishmaniasis can cause different clinical syndromes, including cutaneous leishmaniasis (CL), in which the patient generally presents with one or several ulcers (s) or nodule(s) on the skin, resulting from the infection of phagocytic cells located in the dermis. It often results in severe scar tissue in the skin. Most of the twelve million people infected with Leishmania worldwide are CL cases, a 1.5 million new cases occur annually.

Objective: WHO has a program to develop new treatments for cutaneous leishmaniasis. This study establishes a proof-of-concept that a tattoo device can target intra-dermal drug delivery against cutaneous leishmaniasis (CL).

Methods: The selected drug is oleylphosphocholine (OLPC) formulated as liposomes, particles known to be prone to macrophage ingestion. First is shown that treatment of cultured Leishmania-infected macrophages with OLPC-liposomes results in a direct dose-dependent killing of intracellular parasites. Based on this, *in vivo* efficacy is demonstrated using a 10-day tattooing-mediated treatment in mice infected with *L major* and *L Mexicana*. In both models, this regimen results in rapid clinical recovery with complete regression of skin lesions by Day 28. Parasite counts and histopathology examination confirm high treatment efficacy at the parasitic level. Low amount of drug required for tattooing combined with fast clinical recovery may have a positive impact on CL patient management.

Results: This first example of tattoo-mediated drug delivery could open to new therapeutic interventions in the treatment of skin diseases. This study demonstrates that the use of a tattoo instrument for drug delivery is possible in the treatment of cutaneous leishmaniasis and that this method can successfully eliminate intracellular parasites at the site of infection. After showing that the selected drug oleylphosphocholine (OLPC) formulated as liposomes could efficiently reach intracellular parasites when in contact with infected macrophages, the activity of the drug was compared *in vivo* in mouse models of Old (*L major*) and New World (*L Mexicana*) leishmaniasis. Three routes of administrations of the same drug formulation were investigated: systemic (IP) administration, topical administration as a drop, and administration via the tattooing instrument. Evaluation parameters included clinical (lesion sizes) and parasitological parameters (burdens) using quantitative and qualitative methods. In all experiments, the tattooing delivery procedure was the most efficacious at both the clinical and parasitological levels.

Biography

Dr. Stef Stienstra works internationally for several medical and biotech companies as the scientific advisory board member and is also an active reserve-officer of the Royal Dutch Navy in his rank as Commander (OF4). For the Dutch Armed Forces, he is CBRN specialist with the focus on (micro)biological and chemical threats and medical- and environmental functional specialist within the 1st CMI (Civil-Military Interaction) Battalion of the Dutch Armed Forces. For Expertise France he is now managing an EU CBRN CoE public health project in West Africa. He is visiting professor for the University of Rome Tor Vergata in Italy for the CBRN Masters Course and lecturer for the NATO School in Oberammergau in Germany and the Joint NATO CBRN-Defense Center of Excellence in Vyskov in the Czech Republic. In his civilian position, he is at this moment developing with MT-Derm in Berlin (Germany) a novel intradermal vaccination technology as well as a new therapy for cutaneous leishmaniasis for which he has won a Canadian 'Grand Challenge' grant. With Hemanua in Dublin (Ireland) he has developed an innovative blood separation unit, which is also suitable to produce convalescent plasma for Ebola Virus Disease therapy. He has finished both his studies in Medicine and in Biochemistry in The Netherlands with a doctorate and has extensive practical experience in cell biology, immuno-hematology, infectious diseases, biodefense, and transfusion medicine. His natural business acumen and negotiation competence help to initiate new successful businesses, often generated by unexpected combinations of technologies.

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Eugenie Bergogne

Paris University, France

Pharmacotherapeutics of anti-infectives in the respiratory tract

Antibiotic levels in tissues and fluids of the respiratory tract have been seen as significant for therapeutic efficacy: Using appropriately chosen drugs in localized infections due to pathogenic microorganisms, concept of "tissue pharmacokinetics" has become controversial, taking into account multiple factors limiting the significance of antibiotic tissue kinetics and "high tissue antibiotic levels". Multiple anatomic sites constitute human respiratory tract and can be diversely infected. Some have been explored in terms of antibiotic local concentrations, like bronchial secretions; many data on a variety of antibiotic local levels have been published: but inflammatory conditions, purulence, edema influencing the variable permeability of tissue barriers to drugs tested are factors leading to a doubtful value of data established. Similarly in terms of concentrations in pulmonary tissues and fluids, collected directly from lungs, or in surgical conditions or exploratory conditions, local transfer of antibiotics through lung membranes, alveolar structures, levels of antibiotics can be reached. In respiratory tract infected sites the potential antibiotic distal course of antibiotics has been explored, with however methodological and interpretive remaining questions, and potential therapeutic efficacy. Other pharmacotherapeutic models have been used such as Epithelial lining fluid (ELF), Alveolar Macrophages (AM), Bronchoalveolar lavage (BAL), reflecting the potential improvement in the respiratory tract infections: in most respiratory tract infected sites the potential antibiotic distal course of antibiotics has been explored with interpretive remaining questions.

Biography

Deanna Mulvihill has her expertise in evaluation and passion for improving the health and wellbeing. Her open and contextual evaluation model based on responsive constructivists creates new pathways for improving healthcare. She has built this model after years of experience in research, evaluation, teaching, and administration both in hospital and education institutions. The foundation is based on fourth-generation evaluation (Guba & Lincoln, 1989) which is a methodology that utilizes the previous generations of evaluation: measurement, description and judgment. It allows for value-pluralism. This approach is responsive to all stakeholders and has a different way of focusing.

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Notes:

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Peter F Billingsley

Sanaria Inc. for the International PfSPZ Consortium, USA

PfSPZ vaccines: Developing a malaria vaccine to prevent infection, protect individuals and eliminate malaria in areas with intense transmission

Cases and deaths caused by malaria worldwide increased in 2016. Prevalence of *Plasmodium falciparum* (Pf) by RDT was ~11% in 2-14-year olds on Bioko Island, Equatorial Guinea (EG) in 2017 compared to ~45% in 2004. Between 2004 and 2017, a national and international team supported by a technical advisory group instituted intense malaria control measures funded by one of the largest per capita investments in malaria control in the world. Consistent with prevalence reduction, malaria related mortality was reduced by ~85% and the EIR and basic case reproduction number (R_0) by >90%. However, the prevalence as measured by RDT has remained stable recently (14% and 11% in 2012 and 2016), and qPCR studies in EG indicate prevalence is 3-fold higher. This situation is common in Africa. New tools are needed to move toward an R_0 <1 and elimination. R_0 has two components, vectorial capacity of mosquitoes and the chance an individual bitten by an infected mosquito will transmit: the majority of investment in malaria control is aimed at reducing vectorial capacity. Case management and other treatment strategies reduce the chance an exposed individual will transmit in the short term. A vaccine with significant efficacy against infection could have an enormous additional impact on the probability an exposed individual can transmit, directly protecting many and indirectly protecting many more through herd immunity if administered to an entire community. PfSPZ Vaccine induced sterile protection for 6 months against intense Pf transmission in 3 clinical trials in Mali and Burkina Faso. Protection by time to event and proportional analyses reached 52% and 38% respectively, opening the possibility of mass vaccination programs to regionally eliminate Pf. The results of clinical trials including >5,000 injections to >2,000 subjects of PfSPZ products and plans for Phase 3 and 4 trials and elimination campaigns will be presented.

Biography

Peter F. Billingsley PhD is Vice President of International Projects and Strategy at Sanaria Inc. He has over 25 years' experience working on malaria, in particular the biology of transmission of malaria through the mosquito from the molecular level in the laboratory right through to the ecology and epidemiology of transmission. He was awarded a prestigious Royal Society University Research Fellowship in 1988 which he held at Imperial College and then later was senior lecturer, head of Zoology and director of post-graduate studies for life sciences at the University of Aberdeen in Scotland. At Sanaria, Dr. Billingsley has been part of the core team taking the PfSPZ Vaccine and PfSPZ Challenge from R&D right through to major clinical trials in USA, Africa and Europe. Until recently, he was Senior Director of Quality Systems at Sanaria and retains a functional QA role with respect to international site visits and training, while stilll acting as PI on grants for vaccine R&D.

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Eugenie Bergogne Berezin

Paris University, France

Chronicle of EBOLA epidemics (2017): The return of EBOLA

2014,17,01, an Editorial entitled "Planetary viral extension" underlined the insufficient attention of Occidental Countries to the 20 EBOLA epidemics within 30 years, with 9936 cases and 4877 deaths. Guinea, Liberia, Sierra Leone were the most contaminated populations. Starting in Guinea WHO announced 2000 deaths. A French investigation published in 2007 had described a blaze-off epidemics only in 1995 in Kinshasa West with 250 deaths. Since then a brutal development of the disease extremely contagious has gained a rapid geographical extension in all Sub-Saharan Africa, Zaire, Soudan as well as West African countries. A worldwide interest in the disease (the journal TIME in 2014 "now arriving the deadly Ebola virus lands in America" (death was waiting for the traveler). Four major analyzes: (a) Epidemiology: including local surveillance, containment measures, WHO and journals of instant information. (b) Measures Since 2007: CDC-Mobile laboratories, surveillance of suspects or alerts or probable (febrile or hemorrhagic or deaths cases) (immediately notified). (c) The office of "rumors" (news) (WHO: gloves, javel, mosquitos). Ebola is transmitted directly by contact, imposing the "salut EBOLA" (EBOLA fistful). (d) Funerals major source of contamination with traditional cleaning, embalms in close contact with the body and family members. Containment, surveillance, education, hygiene, medical personnel are current. WHO "Staff at the outbreak sites see evidence that the nimbers of reported cases and deaths underestimate the magnitude of the outbreak."

Biography

Eugenie Bergogne-Berezin is a Professor of Clinical Microbiology at University Diderot, Paris. She has studied MD in Medicine and PhD in Sciences in the early 1970s. She is a Chief of Department of Clinical Microbiology and research group, University Bichat Claude-Bernard and developed research on Acinetobacter spp., (nosocomial pathogen, pathogenicity, resistance), pharmacology of antibiotics, tissue distribution (lungs, brain, bronchi), research on intestinal ecology, jejunal flora and bacterial adhesion. She is an Adviser to pharmaceutical companies, expert in pharmacology-toxicology for the Ministry of Health, expert for international journals. She has developed a journal Antibiotics, (Elsevier). She has published 6 medical books, many chapters in international infectious diseases books, 200 articles in scientific journals.

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Royal Dutch Navy, The Netherlands

Investing in public health gives especially in low income countries extremely impressive returns

The implementation of the International Health Regulation (IHR) of WHO in 2005 for worldwide public health systems is already in its second extension phase. At the 2012 deadline, only 16% of the countries were fully prepared to detect and respond to pandemics. In 2014 the Ebola Virus Disease outbreak in West Africa was another indicator that WHO's IHR has to be taken seriously. Especially the biosecurity part of IHR is not fully in place yet for most developing countries, which makes the world vulnerable for bioterrorism. According to the World Bank, the returns from investing in public health are extremely impressive and is not a high-risk venture as with a rapid mortality decline many 'value life years' (VLYs) are gained. For low- and middle-income countries typically about a quarter of the growth in full income resulted from VLYs gained and supports not only the local economy but also the world economy. Therefore several international programs help to prepare low- and middle-income countries to mitigate outbreaks of infectious diseases. EU CBRN CoE initiatives and the US CBEP, DTRA, CTR, GEIS, DIMO, USAID, PEPFAR and several other programs are involved in establishing public health systems and give local healthcare workers training in both disease outbreak mitigation and biosecurity. Zoonotic diseases are the most dangerous for outbreaks as the population does not have natural or artificial (from vaccination) immune response to new emerging diseases. Zoonotic diseases are often neglected in the first instance in developing countries. The recent Ebola Virus Disease outbreak in West Africa was such an example. Still, there is hope to find fast and supportive therapies with proper blood bank facilities in place. The therapy with immunoglobulins obtained from plasma donations from survivors is a relatively cheap and effective therapy. International there was some criticism of this method, as for this therapy it is extremely important that the convalescent plasma has to be safe for other blood transmissible diseases. But as it is feasible with other convalescent plasma therapies, the necessary safety tests can be done in the laboratories, which are installed for the outbreak diagnosis. Convalescent plasma can be obtained from a donor, who has survived the disease, with a novel hollow fiber blood separation technology. This results in an immunoglobulin concentration, which does not need for its production any sophisticated infrastructure. This patented and recently developed disposable device is developed in cooperation with the Irish Blood Transfusion Service. Dr. Stef Stienstra works internationally for several medical and biotech companies as the scientific advisory board member and is also an active reserve-officer of the Royal Dutch Navy in his rank as Commander (OF4). For the Dutch Armed Forces, he is CBRN specialist with the focus on (micro)biological and chemical threats and medical- and environmental functional specialist within the 1st CMI (Civil-Military Interaction) Battalion of the Dutch Armed Forces. For Expertise France he is now managing an EU CBRN CoE public health project in West Africa. He is visiting professor for the University of Rome Tor Vergata in Italy for the CBRN Masters Course and lecturer for the NATO School in Oberammergau in Germany and the Joint NATO CBRN-Defense Center

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Ivana Haluskova Balter

French Society of Immunology, France

Tackling neglected diseases in current context

The fight against the Neglected Tropical Diseases receiving increased worldwide attention after the recent attribution of the 2015 Nobel Prize in Physiology or Medicine to William Campbell and Satoshi Ōmura for their development of a novel therapy against infections caused by roundworm parasites. Neglected Tropical Diseases (NTDs) known to be a diverse and growing group of communicable diseases that prevail in tropical and subtropical conditions in 149 countries affect more than one billion people and cost developing economies billions of dollars every year. Populations living in poverty, without adequate sanitation and in close contact with infectious vectors and domestic animals and livestock are those worst affected. Despite encouraging progress, millions of people still need free high-quality treatments and millions more still need care and treatment for human dog-mediated rabies, echinococcosis, leishmaniasis and other neglected tropical diseases seemingly difficult to treat. Neglected tropical diseases program in global manner encompass biology of parasites and their vectors. Its research program addresses global public health concerns in terms of disease prevention, control and antiparasitic treatment. Along with understanding of the dynamic interactions between these microorganisms and their hosts, identifying the fundamental bases of parasitism and transmission by vectors, host invasion mechanisms, and determine parasite factors underlying virulence and pathology of these organisms. From scientific point of view, tackling infectious and tropical disease encompass various aspects including like transmission mechanisms, virulence factors, pathogens reservoirs, host immune response working transversally through epidemiology , microbiology, genetics and genomics, cell biology, biochemistry and bioinformatics and imaging. Apart vector born diseases like Dengue and Zika recent research in France look particularly on three key eukaryotic pathogens responsible for severe parasitic diseases that have a significant health and economic impact and affect most of the world's population: *Plasmodium* the causative agent of malaria, *Leishmania* – the agent of leishmaniasis, and Trypanosoma brucei – responsible for sleeping sickness. The Anopheles mosquito, which is the vector of Plasmodium and a number of arboviruses, is being studied along with the tsetse fly, the vector of African trypanosomiasis. Fundamental research on *in vitro* and *in vivo* models – including field work in Africa, Asia, South America – with applied research on resistance to antimalarial drugs and on the discovery of new antiparasitic drugs include exploration of traditional medicine and methods like reverse pharmacology.Accurate diagnostic and surveillance with better understanding of genetic and immunologic background of host specific response and pathogen evolution drives adapted vaccine research but also preventive interventions. As one of examples to illustrate it, global mapping of resistance to artemisinin (the KARMA study driven by Institut Pasteur in Paris and the Institut

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Pasteur in Cambodia and members of Institut Pasteur International Network) monitoring risk of spread of artemisine resistance from Asia to Africa using discovery of kelch(K13)–propeller domains as the primary determinant of artemisinin resistance. Immunology is relatively new science about composition, functions, reaction of immune system. Host immune system co-evolute with pathogens and commensal microbiota given individual genetic predispositions and variability and remains along with neuroendocrine system one of the key to maintain homeostasis of organism. Knowledge in immunology is growing and providing clinically valuable solutions across various for diagnostic, preventive (innovative vaccination) and treatment strategies including neglected and tropical diseases. Based on works natural defences to infection are mediated by intrinsic/innate and adaptive immune responses. Understanding the role of early metabolic mediators of inflammatory responses to infection and principles of immuno-metabolism expect to help in the development of urgently needed host directed therapeutic, preventive (vaccines) and diagnostic innovations knowing limitations of existing tools.

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