

4<sup>th</sup> World Congress on

# Infection Prevention and Control

November 28-29, 2016 Valencia, Spain

Keynote Forum

Day 1



*Infection Control 2016*

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## Indira T Kudva

United States Department of Agriculture-Agricultural Research Service, USA

### Targeting reservoirs to control human infections: A one health approach

Shiga toxin producing *Escherichia coli* (STEC) cause hemorrhagic colitis and potentially fatal extra-intestinal sequelae, such as the hemolytic uremic syndrome and thrombotic thrombocytopenic purpura in humans. Currently, treatment of human STEC disease is only symptomatic and supportive. Antibiotics are contraindicated owing to increased risk of sequelae; hence, diverse new STEC-specific management modalities are being investigated including those that target STEC bacteria, interfere with Shiga toxin (Stx) binding, neutralize Stx, inhibit Stx trafficking, modulate/interfere with host cellular responses to Stx, effect homeostasis of host microbiota (probiotics), and virulence factor-based vaccines. Because ruminants (cattle and sheep) are primary STEC reservoirs, several preharvest control strategies to reduce pathogen load and prevent STEC entry into the food chain are being implemented. These include: Water treatment, dietary strategies, water and feed additives, animal treatments and management and transportation practices. However, these strategies have variable or limited efficacy owing to diverse hosts/environments maintaining STEC on farms, further emphasizing the need for control measures that can be consistently employed. Hence, we are employing host specific studies and pathogen-directed systems-based approaches towards the development of such novel STEC-targeted modalities. These include, elucidating the “interactome” of STEC and the squamous epithelial cells constituting the rectoanal junction (the site of persistence in cattle) and evaluating O157 proteins expressed in the rumen (first compartment of the ruminant stomach). Proteins contributing to cell adherence and rumen survival are being investigated for inclusion in novel anti-adhesion/colonization therapies.

### Biography

Indira T Kudva is a Research Microbiologist and Lead Scientist at the National Animal Disease Center, USDA, Ames, Iowa. She has received her BSc in Zoology and MSc in Medical Microbiology degrees from India, PhD in Microbiology, Molecular Biology and Biochemistry from the University of Idaho and trained as a Postdoctoral Fellow at the University of Idaho, Massachusetts General Hospital and Harvard Medical School. She has over 25 years of experience in the field of microbiology, molecular biology and infectious diseases. She has 29 peer-reviewed publications, 3 invited reviews, 27 meeting abstracts, 18 invited talks, 8 funded grants and novel inventions (4 patent applications). She is also an adjunct Assistant Professor at the School of Veterinary Medicine, Iowa State University; the Executive Editor for the “*Virulence Mechanisms of Bacterial Pathogens*” book, 5<sup>th</sup> Edition, ASM press and is on the Editorial Boards of the *Applied and Environmental Microbiology* (ASM press) and the *SRL Proteomics and Bioinformatics* (SciRes Literature) journals.

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## P R Raghavan

Nanorx Inc, USA

### Controlling infectious diseases with Metadichol®

Metadichol® is a nano emulsion of long-chain alcohols found in many foods. It is commonly called Policosanol and is present in foods such as rice, sugar cane, wheat, peanuts. Metadichol® acts on Nuclear Vitamin D receptors (VDR) that are present in cells throughout the body to stimulate the immune system and inhibit a variety of disease processes, resulting from viral, bacterial and parasitic infections. Gene expression analysis will be presented. We tested Metadichol® *in vitro* against viruses and also against malaria, Tb and MRSA. It is the first of a class of unique nano emulsion molecules that are active against viruses, bacteria and parasites. In assays, Metadichol® showed no cytotoxicity and strongly inhibited cell death caused by each of the pathogen tested. Metadichol® is a safe and effective inhibitor of various pathogens in humans. Because it consists of natural components of common foods and has no known negative side effects, Metadichol® has the potential to serve as a novel, broad-spectrum antiviral treatment for viruses, bacteria and parasites that confront public health today.

### Biography

P R Raghavan is the CEO of Nanorx Inc, USA. He has completed his PhD in Organic Chemistry from Oregon State University (1979) and MS in Chemistry (1972) from IIT Mumbai, India. He has worked on drug discovery for over 25 years at Columbia University, Max-Planck Institute, Germany, Ciba-Geigy (now Novartis) and 'Boehringer Ingelheim'.

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## Stef Stienstra

Dutch Armed Forces/Royal Dutch Navy, Netherlands

### Drug delivery by tattooing to treat cutaneous leishmaniasis

**Background:** 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 or nodules on the skin, resulting from the infection of phagocytic cells located in the dermis. It often results into severe scar tissue in the skin. Most of the twelve million people infected with *Leishmania* worldwide are CL cases and 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 (OIPC) formulated as liposomes, particles known to be prone to macrophage ingestion. First it is shown that treatment of cultured *Leishmania* infected macrophages with OIPC 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 (OIPC) 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 tattoo 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.

**Limitations:** The used tattoo device, used routinely for permanent makeup procedures is not yet optimal for quantitative drug delivery.

### Biography

Stef Stienstra is a strategic and creative Consultant in Biomedical Science with a parallel career as a Commander of the Reserve of the Royal Dutch Navy. For the Dutch Armed Forces he has responsibility for the counter measures in CBNRE threats and (medical) consequence management both in a military and a civilian (terrorism) setting. In his civil career he works internationally as a Consultant or as Scientific Supervisory Board Member for several medical and biotech *companies*, merely involved in biodefense. He is also a Visiting Professor for Punjab University in Pakistan and Rhein-Waal University in Germany. He has completed his studies in Medicine and in Biochemistry at the University of Groningen in Netherlands and has extensive practical experience in cell biology, immuno-hematology, biodefense and transfusion medicine.

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## Lia Monica Junie

University of Medicine and Pharmacy, Romania

### Polymerase chain reaction in the detection of the methicillin-resistant *staphylococci*

**Background:** Methicillin resistant strains of *Staphylococcus aureus* (MRSA) were identified shortly upon the introduction of methicillin into the clinical practice. Rapid detection of MRSA is desirable.

**Methods:** *S. aureus* strains were isolated from hospitalized patients, including intensive care wards and other units. The identification of the *S. aureus* strains was made by phenotypic methods and automated methods (Vitek2Compact BioMerieux). The *MecA* gene of the clinical isolates detection has been unfold by PCR. The PBP2' latex agglutination test, Cefoxitin E-test and Oxacillin MIC as phenotypic methods of MRSA detection are evaluated and compared with the *mecA* detection by PCR, as the standard method to identify the MRSA strains.

**Results:** 57.5% of the isolated strains from different pathological products were MRSA and 42.5% were MSSA. The PBP2' latex agglutination test detected PBP2a in 55.3% of the tested strains leading to a sensitivity of 96.3% using *mecA* gene detection. Most of the MRSA isolates were multi-resistant to antibiotics, being resistant to  $\beta$ -lactamins, Aminoglycosides, Macrolides and Ciprofloxacin.

**Conclusions:** Molecular methods which detect the *mecA* gene are replacing the Oxacillin MIC method as the reference one. The comparison of the phenotypic methods with PCR reveals that among the first of them, PBP2a latex has a high sensitivity (97.9%), being used as an alternative phenotypic method for the MRSA detection. Following the resistance profiles of the strains, identified by these methods, we observe the existence among them of some different clones that reveal the importance of the correct identification of the MRSA strains for the infection therapy and its prophylaxis.

### Biography

Lia Monica Junie is an MD, Ph D, Professor, Head Microbiology Department, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj Napoca, Romania. She is a Coordinator of resident doctor's in the Laboratory Medicine specialty and Leadership PhD doctor's thesis in Medicine field. She is a Board Member of European professional Societies ESCMID (ESGCP Study Groups), Society of Chemotherapy, Scientia Parasitologica Pro Vita and is a Reviewer of international reviews, Member of International organizations, Director/Coordinator in research projects. She has more than 63 papers published in full in international journals and is an editorial board member of national reviews. She is an Organizer/President, Keynote, Invited Speaker and Chair of International and National Congresses.

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Day 2



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## Maria Paula Ramalho Bajanca-Lavado

National Institute of Health, Portugal

### Ampicillin resistance mechanisms in clinical *Haemophilus influenzae*

*Haemophilus influenzae* remains a key etiological agent of upper and lower respiratory tract infections. Two major mechanisms are involved in ampicillin (AMP) resistance:  $\beta$ -lactam hydrolysis due to  $\beta$ -lactamase production (TEM-1 or ROB-1) and decreased affinity of penicillin-binding protein 3 (PBP3) for  $\beta$ -lactam antibiotics as a result of *ftsI* gene mutations encoding PBP3. Isolates exhibiting this latter resistant mechanism are termed  $\beta$ -lactamase-non-producing ampicillin-resistant (BLNAR), while isolates with both resistant mechanisms are defined as  $\beta$ -lactamase-positive amoxicillin-clavulanic acid-resistant (BLPACR). A variety of amino acid (AA) substitutions within the transpeptidase domain of PBP3 are mainly responsible for resistance. According to specific substitutions, these isolates have been classified in one of three mutational groups: I-III. Group II was further divided into subgroups IIa-IId. More recently, a new group was described, "III-like" with additionally AA substitutions to the ones described in group III. Decreased ampicillin susceptibility have been associated to group I and II, while group III is normally associated with high resistance levels to ampicillin. Isolates with the non-enzymatic resistance mechanisms have been described and emerging worldwide. In this context, we aimed to characterize ampicillin resistance mechanisms in clinical *H. influenzae* strains isolated in Portugal. Amplification and sequencing of *ftsI* gene was performed in 568 clinical *H. influenzae* isolates. Analysis of mutations characterized 61% of isolates as gBLNAR or gBLPACR. Most of the strains were included in group II (85%) with predominance of IIb (61%). Rare isolates were of group I and no isolate was classified in group III, although few strains were of group III-like. Our results are indicative of wide dissemination of a non-enzymatic resistance mechanism to  $\beta$ -lactams among *H. influenzae* isolates circulating in our country, probably due to inappropriate use of oral antibiotics, which is a matter of concern. A better understanding of this issue may help to establish adequate therapeutic and preventive measures to avoid selection or dissemination of such strains.

### Biography

Maria Paula Ramalho Bajanca-Lavado has completed her PhD in Biomedical Science, specialty Microbiology and is responsible for the *Haemophilus influenzae* Reference Laboratory, Department of Infectious Diseases, National Institute of Health in Lisbon, Portugal. She has published several scientific publications in peer-review journals, along with other scientific productions, including invited lectures, oral communications and posters presented in international conferences. Her research is focused at *H. influenzae* infections, in different clinical and epidemiological aspects.

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## Stef Stienstra

*Dutch Armed Forces/Royal Dutch Navy, Netherlands*

### The threat of zoonotic diseases and Ebola virus disease specifically

Public health systems are not always prepared for huge outbreaks of infectious diseases. Although in past several public health institutes were prominent surveyors of infectious diseases and very active in the mitigation of infectious diseases both in and outside their country of origin, like the French Institute Pasteur, Dutch Tropeninstituut and many others Institutes, the investments in worldwide public health was in the last decennia far less compared to curative healthcare. With the recent Ebola Virus Disease outbreak in West Africa we see now a new wave of growing interest in investing in Worldwide Public Health to prevent spreading of highly contagious disease outbreaks. Zoonotic diseases are the most dangerous for outbreaks as the population does not have natural nor artificial (from vaccination) immune response to new emerging diseases. The Ebola Virus Disease outbreak in 2014 in West Africa is such an example. As the new strain of the Ebola Virus in West Africa has a longer incubation time and is only slightly less lethal compared other Ebola Virus strains, the threat of spreading among the population is far bigger. Especially when the epidemic enters denser populated areas. The mitigation of a highly infectious and deadly disease outbreak has several aspects for which most public health systems in the world are not trained well enough. NGO's helping to fight the outbreak are often also better trained in curative treatments and have less experience with biological (bioweapon) threats for which the military are trained for. The UNMEER mission is unique in this. It is a setting in which military and civilian actors cooperate in fighting a biological threat. Protection is essential for health workers and smart systems have to be developed to prevent further spreading of the disease. But it is unfortunately not only the biosafety, which has to be considered, but also the biosecurity, as misuse of extremely dangerous strains of microorganisms cannot be excluded. Several zoonotic infectious diseases, like anthrax, small pox and also the hemorrhagic fevers like Ebola Virus Disease are listed as potential bioweapons. With this extra threat in mind both biosafety and biosecurity has to be implemented in all measures to fight outbreaks of highly infectious diseases, as we are now doing in West Africa. Several international and national organizations invest now in improving public healthcare in Africa to mitigate the global threat of the spreading of infectious diseases by the increasing international travel.

### Biography

Stef Stienstra is a strategic and creative Consultant in Biomedical Science with a parallel career as a Commander of the Reserve of the Royal Dutch Navy. For the Dutch Armed Forces he has responsibility for the counter measures in CBNRe threats and (medical) consequence management both in a military and a civilian (terrorism) setting. In his civil career he works internationally as a Consultant or as Scientific Supervisory Board Member for several medical and biotech companies, merely involved in biodefense. He is also a Visiting Professor for Punjab University in Pakistan and Rhein-Waal University in Germany. He has completed his studies in Medicine and in Biochemistry at the University of Groningen in Netherlands and has extensive practical experience in cell biology, immuno-hematology, biodefense and transfusion medicine.

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## Naim Deniz Ayaz

Kirikkale University, Turkey

### *Listeria monocytogenes* risk in poultry meat and usage of bacteriophages as a biocontrol agent

Poultry are playing a significant role in human food-borne infections because they are frequent vehicles of some human pathogens. In order not to take hygienic precautions, contaminations with pathogenic microorganisms such as *Listeria* may be occurred and consumption of such poultry meat and meat products can cause food-borne illnesses. *L. monocytogenes* is a zoonotic food-borne bacteria that leads to a variety of serious infections in humans such as encephalitis, meningitis, abortion and septicemia and those suffering with listeriosis occurs in approximately 30% mortality. Epidemiologic studies have revealed that a significant proportion of cases of listeriosis caused by contaminated foods. Consumption of poultry meat is increasing in the world. Related with the production technology, cross contamination risk is very high during processing, so it is important to control *L. monocytogenes* in poultry meat. Rapidly growing bacterial resistance to antibiotics and need for development of alternative methods, increasing interest in using bacteriophages in treatment or as biocontrol agents in foods nowadays. Bacteriophages can be applied to living tissues without causing any harm due to their highly selective toxicity. This is the most important advantage when they compared with antibiotics and antiseptics. The use of specific virulent bacteriophages for *L. monocytogenes* in order to reduce *L. monocytogenes* load in foods before, during and after slaughter processes emerges as an another method. It is reported that the usage of specific virulent bacteriophages to *L. monocytogenes* as a biocontrol agent of *L. monocytogenes* in foods, do not cause any side effects in humans.

### Biography

Naim Deniz Ayaz is an Associate Professor of the Department of Food Hygiene and Technology at Kirikkale University, Faculty of Veterinary Medicine. He has received his PhD in Food Hygiene and Technology from the Ankara University in 2008. He is the Vice Dean and Executive Board Member of Kirikkale University, Faculty of Veterinary Medicine; an Expert of the Biosafety Clearing-House Mechanism of Turkey; a Research and Advisory Board Member of the National Red Meat Council and an Editorial Board Member of several scientific journals. His main research interests are food microbiology, characterization of food-borne pathogens, bacteriophages, biocontrol of pathogens and bacterial antibiotic resistance.

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## Aziz Alami Chentoufi

King Fahad Medical City, KSA

### Novel vaccination approach against HSV type-1 and type-2 infections

Herpes simplex virus type 1 and type 2 (HSV-1 and HSV-2) infections would be controlled by the development of an effective vaccine. However, in spite of several clinical trials, starting as early as 1920s, no vaccine has been proven sufficiently safe and efficient to warrant commercial development. Recently, great advances in cellular and molecular immunology understanding have stimulated creative approaches in controlling herpes infections and diseases. Before moving towards novel vaccine strategy, it is required to answer the important questions: Why past herpes vaccines were unsuccessful? Why the majority of HSV seropositive individuals naturally control HSV infections and exhibit few or no recurrent herpetic disease, while few others have frequent herpes clinical episodes? We recently discovered that HSV-1 symptomatic and asymptomatic individuals develop distinct immunity to viral epitopes recognized by CD4+ and CD8+ T cells. These epitopes (protective vs. pathologic) have provided a solid foundation for the development of novel herpes epitope based vaccine strategy. In this presentation, I will provide an overview of past clinical vaccine trials and outline current progress towards developing a new generation “asymptomatic” clinical herpes vaccines and discuss future mucosal “asymptomatic” prime boost vaccines that could optimize the protective immunity.

### Biography

Aziz Alami Chentoufi is a Consultant and Head of Immunology/Serology/HLA section at Pathology and Clinical Laboratory Medicine, King Fahad Medical City (KFMC). He is also an Assistant Professor of Immunology at Faculty of Medicine, King Saud Ibn AbdulAziz University. He is the Chairperson of Research Committee of PCLMA-KFMC. He is the Diplomate of the American Board of Medical laboratory Immunology D(ABMLI), Fellow of the Association of Clinical Sciences (FACSc), accredited by the European Society of Translational Medicine (PCTM) and Fellow of the Academy of translational Medicine (FacadTM). He received his Ph.D. in Biomedical Sciences (Tolerance induction to xenogenic and allogenic antigens using monoclonal antibody anti-IgM and anti-IgD) from the University Catholic of Louvain, Brussels, Belgium in 1999. He has done postdoctoral fellowship at McGill University, Montreal, Canada from 1999 to 2004 where he worked on immunogenetic of type 1 Diabetes and gene therapy for graft versus host disease then he was appointed as specialist at the University of California Irvine-Medical Center, Irvine, California, USA in 2006 where he was a key investigator in the development of mucosal vaccine against herpes simplex virus type 1 and 2. He is an independent Immunologist with a national and international reputation in vaccine development against both infectious and autoimmune diseases. He is well-integrated into the scientific community within the United States as well as Europe and Saudi Arabia and he is actively involved in a number of professional societies including American Society of Histocompatibility and Immunogenetic (ASHI), Association of Clinical Scientist, Canadian Society of Immunology and The Federation of Clinical Immunology Societies (FOCIS). He is PI and Co-PI in a number of research grant proposals and associate editor in many scientific journals and has more than 50 publications in high impact factor journals.

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