



6th Euro-Global Conference on

INFECTIOUS DISEASES

September 07-09, 2017 | Paris, France

Scientific Tracks & Abstracts Day 1

Euro Infectious Diseases 2017

Major Sessions:

Day 1 September 07, 2017

Viral Infectious Diseases | Bacterial Susceptibility & Resistance | Vaccines | Microbiology and Infectious Diseases | Emerging Infectious Diseases

Session Chair
Catherine Mullié
University of Lille, France

Session Introduction

Title: Development of five hyper-humanized antibodies neutralizing the Botulinum neurotoxins A, B and E: The European AntiBotABE project.

Arnaud Avril, Institut de Recherche Biomédicale des Armées (IRBA), France

Title: Phytotherapy from *Mentha piperita* L. modulates infection during experimental schistosomiasis

Fernanda de Freitas Anibal, Federal University of São Carlos, Brazil

Title: Molecular microbiology as a modern platform for rapid, specific, sensitive and unlimited detection of pathogenic microorganisms

Tereza Jancuskova, KitGen, Czech Republic

Title: Expression of major virulence genes of *Listeria monocytogenes* isolated from cattle, sheep and chicken

Naim Deniz AYAZ, Kirikkale University, Turkey

Title: Mediterranean Spotted Fever in Children of the Karak Province in South Jordan

Omar Nafi, Mutah University, Jordan

YRF: HIV care continuum outcomes: does Ethiopia meet the UNAIDS 90-90-90 targets?

Hailay Gesesew, Flinders University, Australia

Title: Seroprevalence of HIV, Hepatitis B and C viruses among antenatal clinic attendees of Secondary Healthcare facilities in Akoko area of Ondo State, Nigeria

Festus. A OLAJUBU, Adekunle Ajasin University, Nigeria

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Development of five hyper-humanized antibodies neutralizing the Botulinum neurotoxins A, B and E: The European AntiBotABE project

Arnaud Avril¹, Sebastian Miethe², Michel R Popoff³, Christelle Mazuet³, Christine Rasetti-escargueil⁴, Hannu Korkeala⁵, Dorothea Sesardic⁴, Thibaut Pelat⁶, and Michael Hus²

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Botulism is a naturally occurring disease, mainly caused by the ingestion of food contaminated by one of the 7 serotypes (A to G) of Botulinum neurotoxins (BoNTs). BoNT/A is the most lethal biological substance currently known, with a human 50% lethal dose estimated at 1 ng.kg⁻¹, and they are classified among the 6 major biological warfare agents. AntiBotABE, a European Framework, 7 funded projects aimed to develop 6 humanized IgGs, neutralizing BoNT serotypes A, B and E by targeting their heavy (HC) and light chains (LC). Six macaques were immunized with the recombinant LC or HC of BoNT/A, B or E, and their corresponding immune libraries were generated and screened by phage-display. After each panning, the most reactive scFv were isolated and their affinity measured. Inhibition or neutralization capacities were determined in vitro (SNAP25 or VAMP2 endopeptidasic assay) or ex vivo (mouse phrenic nerve-diaphragm assay). Neutralizing scFvs were identified for 5 of the 6 antigens. For each of the 5 libraries, the most efficient scFv was germline-humanized and expressed as full-length IgG. In the mouse bioassays, 3/5 IgGs alone and all IgGs in pairs, protected mice from paralysis or death after a challenge with the respective BoNT serotype. 1–5 Antibodies isolated during this project are potential lead candidates for further clinical development and we are looking for clinical development opportunity.

Biography

Arnaud Avril works for the French Armed Forces Biomedical Research Institute (IRBA), based in Paris area. He has a Master degree in Genetic and Immunology from Lyon University (France) and a PhD in Biotechnology applied to antibodies from the Grenoble-Alpes University (France). He is the Head of a team specialized in the research, development and engineering of recombinant antibodies against rare diseases for biodefense. He has developed germline-humanized recombinant antibodies starting from non-human primates immunized with non-toxic antigens. He has contributed to the development of several antibodies neutralizing botulinum neurotoxins, anthrax, ricin and Orthopoxvirus. He has also contributed to the development immuno-diagnostic assays for the rapid, convenient and cheap detection of biological agents, for armed forces, medical staff and first responders. He is involved as an expert on the clinical development of a recombinant antibody for anthrax therapy.

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Phytotherapy from *Mentha piperita* L. modulates infection during experimental schistosomiasis

Fernanda F Anibal¹, Karina A Feitosa¹, Maurício G Zaia¹, Silmara M Allegretti², Edson G Soares³ and Ana Afonso⁴¹Federal University of São Carlos, Brazil²UNICAMP, Brazil³FMRP-USP, Brazil⁴IHMT, Portugal

Schistosomiasis is a chronic parasitic disease promoted by the parasite of the genus *Schistosoma*, and Praziquantel (PZQ) is the only drug recommended by the World Health Organization, but there are reports of resistance, suggesting the importance of studying new compounds to treat this disease. In this work, we investigate the immunomodulatory and antiparasitic effects of Mentaliv (Apsen), from *Mentha piperita* L. during murine infection by *S. mansoni* (Sm). Experimental groups: Balb/c females, C, uninfected, SM, infected without treatment, Mentha 15 (50 mg/kg) infected with Sm (80 cercariae/animal), Mentha 60 (50 mg/kg), infected and treated daily for 60 days and PZQ, infected and treated with single dose (400 mg/kg) at the 43rd day after infection. The cell profile in the blood and serum IL-4 and IL-10 cytokines were analyzed. And the antiparasitic effect on egg count in the liver, intestine and granulomas, and comet assay for DNA modifications in worms recovered after treatments. Mentaliv phytotherapy has immunomodulatory and antiparasitic effects during murine infection of experimental schistosomiasis, by reducing serum levels of IL-4 and IL-10, and indirectly modulating negatively the blood eosinophils in the Mentha 60 group. In addition, there is an antiparasitic effect in these animals of the Mentha 60 group where there is a reduction in the number of eggs in the liver, intestine and in the hepatic granulomas. However, the absence of the genotoxic effect on Sm, suggests that other structures of the parasite other than DNA are being altered and thus contributing to the reduction of parasitic load. Thus, it is suggested that menthol and menton may be the main components of *Mentha piperita* L. with antiparasitic effect in this model.

Biography

Fernanda F Anibal has completed her PhD from University of São Paulo, Brazil in Basic and Applied Immunology. She is a Principal Investigator at Laboratory of Inflammation and Infectious Diseases (Federal University of São Carlos) seeks new tools for the treatment, prevention and diagnostics for infectious diseases. Currently, they are working with two plants and six enzymes and their effects against Schistosomiasis mansoni, leishmaniasis and toxocariasis, about the treatment of the infectious diseases. Their group studies effects of plants (extracts) and their isolated fractions to evaluate the anti-parasitic and anti-inflammatory effects and for infectious disease prevention, moreover have been working on the evaluation of the proteins of the parasite that has been potential to induce immune responses that decrease the parasite burden.

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Molecular microbiology as a modern platform for rapid, specific, sensitive and unlimited detection of pathogenic microorganisms

Tereza Jancuskova

KitGen , czech republic

Molecular microbiology is a novel concept that opens fascinating possibilities in the pathogen detection. Many microorganisms are fastidious or uncultivable; their cultivation time is unacceptably long; are of high epidemiological importance; or require sophisticated cultivation conditions. Molecular techniques allow for quantitative detection of microorganisms based solely on the presence of their unique DNA or RNA sequences. Molecular microbiology enables to identify causative infectious agents even in those situations when standard cultivation-based microbiology fails. Since 2006, we have developed over 500 single and multiplex quantitative Real-Time PCR assays to detect pathogenic and opportunistic infectious agents relevant for both human and veterinary clinical settings. We have implemented pandetection approach to detect bacteria and fungi based on Sanger sequencing. For the most challenging biological samples (gut microbiome) we have also developed a pandetection strategy based on Next Generation Sequencing (NGS). Using this combined approach, we can identify microbial agents with the widest detection range possible (pandetection), quantify the load of individual microorganisms in the sample and provide the clinician with the result within hours (Real-Time PCR), or 2-3 days maximum (Sanger sequencing or NGS). Over the past 10 years, we have diagnosed more than 30,000 biological samples, originating from both human and veterinary patients. They covered hyperacute clinical settings (sepsis), chronic and underdiagnosed diseases, and emerging zoonoses (our finding of a novel zoonotic agent *Candidatus, Neoehrlichia Mikurensis* transmissible by a tick bite, with unexpected Central and Western European geographic occurrence).

Biography

Tereza Jancuskova has completed her Graduation from Charles University in Prague, Czech Republic in 2008. She has continued her PhD studies at the Third Medical Faculty, Charles University in Prague, specializing in Genetics, Molecular Biology and Virology. She has received her PhD degree in 2015. She has extensive expertise in Molecular Haemato-Oncology and Molecular Genetics, both in human and veterinary medicine.

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Expression of major virulens genes of *Listeria monocytogenes* isolated from cattle, sheep and chicken

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Statement of the Problem: *Listeria monocytogenes* is a zoonotic food-borne bacteria that leads to a variety serious infections in humans such as encephalitis, meningitis, abortion and septicemia. Most *L. monocytogenes* strains can cause high morbidity and mortality depending on their virulence, however some strains don't cause any infections in mammals due to absence of their virulence factors. *L. monocytogenes* provides its pathogenicity with virulence factors such as *hlyA*, *actA*, *inlA*, *inlB*, *inlC*, *inlJ*, *plcA*, *plcB* genes and *vip*, *fbpA* and *fri* which are recently reported. The presence of these genes is just as important as the expression levels that play an important role on its pathogenicity. Therefore, this study was aimed to detect the important virulence genes and expression levels of *L. monocytogenes* isolated from cattle, sheep carcasses and chicken (broiler) neck skin samples during slaughtering in Turkey. Methodology & Theoretical Orientation: In the study 31 *L. monocytogenes* isolated from 5 cattle, 3 sheep carcasses and 10 chicken neck skin samples were analyzed by real time RT-PCR for the presence and expression levels of major virulence genes including *hlyA*, *actA*, *inlA*, *inlB*, *inlC*, *inlJ*, *plcA*, *plcB*, *vip*, *fbpA* and *fri*. In the study *spoG* was used as house-keeping gene. Findings: According to the real time RT-PCR, *hlyA*, *actA*, *inlA*, *inlB*, *inlC*, *inlJ*, *plcA*, *plcB*, *fbpA* and *fri* genes were detected from all the isolates. However 5 isolate were not harbor *vip* gene. Six virulence genes were up regulated in a chicken isolate that has the highest virulence potential compared with the other *L. monocytogenes* isolates. Conclusion & Significance: Most of the *L. monocytogenes* isolates harbored all the 11 virulence genes. Some were up regulated, some were down and some were expressed as same as the house-keeping gene. Genetically, most virulent *L. monocytogenes* was originated from chicken and its serotype was 1/2a.

Biography

Naim Deniz Ayaz is Professor of the Department of Food Hygiene and Technology at Kirikkale University Faculty of Veterinary Medicine. He received his PhD in Food Hygiene and Technology from Ankara University in 2008. His main research interests are food microbiology, characterization of food-borne pathogens, bacteriophages, biocontrol of pathogens and bacterial antibiotic resistance.

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Mediterranean spotted fever in children of the Karak Province in South Jordan

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Introduction: The aim of this study was to describe the epidemiological patterns of Mediterranean spotted fever (MSF) as well as its treatment and outcomes in children in south Jordan.

Methodology: We conducted a retrospective observational study from June 2013 to December 2015. Data regarding demographics, clinical presentation, laboratory findings, treatment, and outcomes were collected.

Results: Thirty-five male and 20 female patients (mean age: 6 years \pm 3.6) were included. The incidence of MSF was 7.9 cases per 100,000 inhabitants/year; MSF affected 89% of individuals in the summer, 74.5% of those living in a rural area with tent housing, and 100% of those who had contact with animals. All cases presented with fever, and 94.5% had a skin rash. Serological tests were positive in 87.2% of cases, and *Rickettsia conorii* (the Moroccan strain) was present in all positive cases. All cases had thrombocytopenia, but none had leukocytosis. Hyponatremia was present in 71% of cases, and 49%, 61.8%, and 72.7% had increased urea, alanine transaminase, and aspartate aminotransferase levels, respectively. Doxycycline was administered to all patients, with a cure rate of 96.4% and mortality rate of 3.6%.

Conclusions: MSF caused by *R. conorii* (the Moroccan strain) is prevalent in Jordan, and contact with animals is a common route of transmission. The patients' responses to doxycycline were excellent. A high index of suspicion, an early diagnosis, and specific treatment considerably decrease mortality. MSF should be considered as a possible cause of febrile disease in those with a rash and in those living in rural areas.

Biography

Omar Nafi is a Pediatric neurologist. He is an Associated professor of Pediatrics in Mutah University- College of medicine, Pediatrics department. He has completed his MBBS in medicine 1980 from Cordoba University, Spain, Jordanian board in Pediatric 1986, training in Pediatric Neurology in Dublin, Ireland 1997. He is the Member of Royal Collage of Physician of Ireland.

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HIV care continuum outcomes: Does Ethiopia meet the UNAIDS 90-90-90 targets?

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Background: How Ethiopia's UNAIDS 90-90-90 targets is progressing was not assessed. We assessed HIV care continuum outcomes as surrogate markers for the 90-90-90 targets.

Methodology: Data were collected from a 12 years retrospective cohort from anti-retroviral therapy (ART) clinic in Southwest Ethiopia. For measuring the UNAIDS diagnosis target, prevalence rate of delayed HIV diagnosis was considered as a surrogate marker. For the treatment target, number of people on ART, number of people who discontinued from ART or transferred out, and number of people who had fair or poor adherence were used as surrogate markers. For the viral suppression target, number of CD4 counts and/or WHO clinical stages were used to assess immunological, clinical and treatment successes and further show the viral suppression. Summary statistics, trends and estimated survival time were reported.

Findings: 8172 patients were enrolled for HIV cares in 2003-2015. For the diagnosis target, 34.5% patients knew their status early (43%-children, 33%-adults). For the treatment target, 65% patients received ART, 1154 (21.9%) patients discontinued from ART, 1015 (19.3%) patients on ART transferred out to other sites, 916 (17%) of patients on ART had fair or good adherence. For the virological suppression target, 80.7, 80.3 and 65.8% of patients had immunological, clinical and treatment success displaying an estimated 66% of patients achieved the target.

Conclusions: The finding reflects that an estimated 35% of patients knew their status timely, 65% of diagnosed patients received treatment and 66% of patients on ART achieved viral suppression. This is very far from the UNAIDS 90-90-90 targets underscoring the need for concentered efforts such as use of unmanned aerial systems (or drones) for transporting laboratory specimens, immediate or same day ART initiation, community distribution of ART, runaway packs during conflict, and use of GenXpert for HIV viral load testing would help to hit the target.

Biography

Gesesew Hailay has his expertise in Epidemiology. His multi-method approach assessing in each cascades of HIV care continuum will establish a significant contribution for the AIDS Ending goal. He has been publishing a lot of peer reviewed articles in HIV care in reputable journals. His publications produced from his PhD will improve the HIV care in developing countries especially Ethiopia. He has been serving as a Clinician, Academician and Researcher.

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Seroprevalence of HIV, Hepatitis B and C viruses among antenatal clinic attendees of secondary healthcare facilities in Akoko area of Ondo State, Nigeria

Festus A Olajubu, Peace I Edeani and Victoria T Folorunso
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Background & objectives: Vertical transmission of HIV, HBV and HCV is associated with high risk of maternal complications, fetal death or impaired mental and physical health. A standing regulation from Government on screening of all pregnant women is often avoided by the patients and hospitals alike. This study was therefore designed to assess the incidence of these infections among antenatal patients with the view of re-emphasizing (with data) the need for screening by all health facilities of antenatal patients.

Methods: The study was carried out among four hundred and thirty-two (432) pregnant women attending ante-natal clinics of State General Hospital and Inland Maternity Center, Ikare-Akoko, Ondo State, Nigeria. Two milliliters (2 ml) of blood samples were collected from volunteers between April and September 2015 and screened for, HIV, HBV and HCV using rapid chromatographic immunoassay methods in accordance with the national algorithm.

Results: The age of the patients ranged between 15 and 40 years (mean age = 25.4 years). A total of 11(2.6%); 8(1.9%) and 3(0.7%) patients were seropositive for HIV, HBV and HCV infections respectively. Co-infections of HIV and HBV were diagnosed among 3(0.7%) of the volunteers. There was no case of co-infection of HIV with HCV or HBV with HCV. Contacts were made with the husbands of all seropositive patients.

Conclusion: The prevalence rates recorded for these three infectious diseases though, lower than the national averages, call for an aggressive advocacy for compulsory screening of all antenatal patients by all health facilities. The multiplication effect of infected pregnant women in the studied community can be reduced or eliminated with early detection of infection through screenings like this. Reduction in cost of laboratory investigations to serve as incentive to the patients is highly advocated.

Biography

Festus A Olajubu has trained as a Medical Laboratory Scientist at Federal School of Medical Laboratory Technology, NVRI, Vom, Nigeria, Infection Control Practitioner at University College Hospital, Ibadan, Nigeria and Medical Microbiologist at Olabisi Onabanjo University, Ago-Iwoye, Nigeria. He has completed his Doctoral degree in Medical Microbiology and Public Health from Federal University of Agriculture, Abeokuta, Nigeria. He is a Senior Lecturer in Microbiology Department of Adekunle Ajasin University, Akungba-Akoko, Nigeria. He has twenty-eight (28) papers published in local and international journals. He has taken part in researches organized by Institute of Human Virology, Nigeria (IHVN) and Department for International Development (DFID) on HIV, Tuberculosis and Sexually Transmitted Infections (STIs). He is a Member of American Society for Microbiology, Nigerian Society for Microbiology, Infection Control Society of Nigeria and Association of Medical Laboratory Scientists of Nigeria. Infectious diseases diagnosis is his current area of interest.

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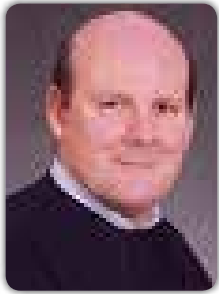
Workshop Day 2

Euro Infectious Diseases 2017

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Philip Norrie

Sydney, Australia

A history of infectious disease in ancient times – More lethal than war - An alternative medical history perspective of ancient history

When one thinks of ancient history one thinks of ancient historians and archaeologists; one does not think of medical historians. But one should, because most major changes in the ancient world were precipitated by an infectious disease epidemic of some kind. It is very naïve of ancient historians not to factor in the possibility that an infectious disease epidemic ended the civilization they are studying because it would have been a daily struggle not to die from an infectious disease in the ancient world. Hence the possibility of an infectious disease epidemic is the first thing ancient historians should eliminate during their research. This lecture will discuss the possibility of such an occurrence happening firstly in Sumer c.2000 BCE, the site of the world's first cities, followed by the Indus Valley Civilization c.1900 - 1350 BCE, Pharaonic Egypt during the 18th Dynasty c.1350 BCE, Haft Tappeh in Elam c.1350 BCE, then the end of the Hittite Empire c.1200 BCE, and finally the end of the Bronze Age in the Near East c.1200 BCE. This hypothesis challenges the current ancient history theories for the end of these civilizations and will upset ancient historians trained in the arts and not trained in using the medical model; which unfortunately is the vast majority. Infectious diseases such as influenza, measles, polio, tuberculosis, dysentery, malaria, typhoid, leprosy and finally the “big two” infectious disease epidemics namely smallpox and plague; decimated the ancient world.

Biography

Philip Norrie is a Family Physician from Sydney, Australia whose main interest is Medical History. This medical history interest is in two parts. Firstly in the history of wine as a medicine for the past 5,000 years which was the topic of his PhD. After this he developed the world's first fully resveratrol enhanced wine [REW]. The second interest is the role of infectious disease in the demise of ancient civilizations, which was the basis of his MD thesis and his current MPhil thesis. He is a Conjoint Senior Lecturer at the Faculty of Medicine at the Universities of New South Wales and Newcastle in Australia; as well as being an Affiliate in Medical History at the University of Montana, USA as an Adjunct in the National Institute of Complementary Medicine at the Western Sydney University [relating to REW] and the Vice Chairman of the Medical Advisory Committee at the Northern Cancer Institute in Sydney.

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Scientific Tracks & Abstracts Day 2

Euro Infectious Diseases 2017

Major Sessions:

Day 2 September 08, 2017

Infectious Agents and the Human Immune Response | Molecular Diagnostics of Infectious Diseases | Bacterial Infectious Diseases | Infectious Disease Epidemiology | Nocosomal Infections

Session Chair

Philip Norrie

Universities of New South Wales, Australia

Session Chair

Janak Kishore

Sanjay Gandhi Postgraduate Institute of Medical Sciences, India

Session Introduction

Title: The anti-hiv candidate abx464 dampens intestinal inflammation by triggering il22 production in activated macrophages

Jamal Tazi, University of Montpellier, France

YRF: Role of *in vivo* expressed gene candidates for development of molecular and immunological assays to diagnose pulmonary tuberculosis

Sumedha Sharma, PGIMER, India

YRF: Transcriptional signatures of *Mycobacterium tuberculosis* in mouse model of experimental intraocular tuberculosis

Sudhanshu Abhishek, PGIMER, India

YRF: Global gene expression in *Escherichia coli*, isolated from the diseased ocular surface of the human eye with a potential to form biofilm

Ranjith Konduri, LV Prasad Eye Institute, India

Title: Genetic analysis of Crimean Congo haemorrhagic fever virus in Iran

Nariman SHAHHOSSEINI, Bernhard Nocht Institute for Tropical Medicine, WHO, Germany

Title: Prevalence of pathogenic bacteria in open and surgical wounds of patients attending hospitals in Buea Municipality

Nde Godlove Tsi, University of Buea, Cameroon

Title: Targeting RNA binding proteins: A versatile platform for the discovery and development of new antivirals

Jamal Tazi, University of Montpellier, France

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The anti-HIV candidate abx464 dampens intestinal inflammation by triggering il22 production in activated Macrophages

Jamal Tazi

University of Montpellier, France

The progression of human immunodeficiency virus (HIV) is associated with mucosal damage in the gastrointestinal (GI) tract. This damage enables bacterial translocation from the gut and leads to subsequent inflammation. Dextran sulphate sodium (DSS-treatment) is an established animal model for experimental colitis that was recently shown to recapitulate the link between GI-tract damage and pathogenic features of SIV infection. The current study tested the protective properties of ABX464, a first-in-class anti-HIV drug candidate that has demonstrated anti-viral activity in HIV treatment of naïve patients. ABX464 also induced a long-lasting control of the viral load in HIV infected humanized mice after treatment arrest. ABX464 treatment strongly attenuated DSS-induced colitis in mice and produced a long-term protection against prolonged DSS-exposure after drug cessation. Consistently, ABX464 reduced the colonic production of the inflammatory cytokines IL-6 and TNF as well as that of the chemoattractant MCP-1. However, RNA profiling analysis revealed the capacity of ABX464 to induce the expression of IL-22, a cytokine involved in colitis tissue repair both in DSS-treated mice. A comprehensive analysis of the gene expression profiles by RNAseq demonstrated that the expression of IL22 was preferentially induced by ABX464 in mouse bone marrow derived macrophages only upon stimulation with LPS. Importantly, anti-IL22 antibodies abrogated the protective effect of ABX464 on colitis in DSS-treated mice. Because reduced IL-22 production in the gut mucosa is an established factor of HIV and DSS-induced immunopathogenesis, our data suggest that the anti-inflammatory properties of ABX464 warrant exploration in both HIV and inflammatory ulcerative colitis (UC) disease. In the DSS induced colitis model, ABX464 protects mice from inflammatory response by prevention of weight loss and colon size, reduced macrophage recruitment into the intestine, decreased levels of pro-inflammatory cytokines and long-lasting effect (like in the HIV humanized mouse model)

Biography

Jamal Tazi is Professor of Functional Genomics at the University of Montpellier and Deputy Director of the Health Centre Biology "Rabelais" responsible for education and training. For 20 years, he led the team "messenger RNA metabolism in metazoans" within the Institute for Molecular Genetics in Montpellier (IGMM) where he made important contributions to understand the fundamental mechanisms of the expression of our genes and editing of their products. These discoveries are used today in the medical field through the development of a new therapy based on the use of small molecules to fight against viral infections. To ensure the transition between basic and applied research, and also to support these innovative projects to clinical stage, Hel founded in 2008 the company Splicos and established its partnership with public institutions as a cooperative laboratory where, he became the Scientific Director

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Role of *in vivo* expressed gene candidates for development of molecular and immunological assays to diagnose pulmonary tuberculosis

Sumedha Sharma¹, Rakesh Yadav¹, Ashutosh N Aggarwal¹, Suman Laal² and Indu Verma¹¹PGIMER, India²School of Medicine, USA

Statement of the Problem: Tuberculosis (TB) diagnosis is a one of the major areas of interest to control the spread of TB disease in community. Therefore, there is a need to develop rapid and specific diagnostics easily usable at different health care levels. Our previous work on mycobacterial gene expression pattern in sputum from pulmonary tuberculosis patients lead to identification of newer targets, as potential biomarkers. In view of this, the current study was planned to evaluate the role of these candidate biomarkers in molecular and serodiagnostic tests.

Methodology: Three of the genes, Rv0986 & Rv0971 along with one Region of Difference (RD) gene Rv3121, were evaluated for their diagnostic potential in RNA based real time (RT) polymerase chain reaction (PCR). Simultaneously, the peptides from proteins corresponding to these genes along with five other RD genes were evaluated for their serodiagnostic potential using a peptide based enzyme linked immunosorbent assay (ELISA) technique.

Findings: The use of the target genes Rv0986, Rv0971 and Rv3121 in a molecular RNA based assay lead to the detection of smear positive patients with 100%, 87% and 94% sensitivity and of smear negative TB patients with 50%, 58% and 67% respectively. However, of all the peptides corresponding to different proteins which were tested in the serodiagnostic ELISA the maximum sensitivity that could be attained was 37% for smear positive PTB patients and 32% for smear negative PTB patients.

Conclusion & Significance: A subset of the proteins encoded by the genes expressed by mycobacteria in the sputum have shown less sensitivity for the development of a serodiagnostic assay, but these genes have shown promising results for the development of a RNA based molecular assay that can be optimized further after evaluation in a larger cohort of patients.

Biography

Sumedha Sharma started her research career with her dissertation in the Postgraduate degree where she worked on the effect of *Ocimum gratissimum* on the colon cancer. She qualified various national eligibility test (Indian Council of Medical Research & Council of Scientific & Industrial Research, India) to pursue her goal in research and academics. Her inclination towards research led her to join the Doctorate Program where her research was focused on tuberculosis (TB). During her Doctorate Degree, she was selected as a Training Participant in AIDS and TB international training and research program (AITRP) sponsored by Fogarty International Centre, NIH, USA where she was trained on Microarray Technology. Her microarray work on sputum of PTB patients gave an insight to the mycobacterial genome specifically expressed in active TB patients, leading to identification of mycobacterial targets, which can be exploit as potential vaccine and diagnostic candidates.

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Transcriptional signatures of *Mycobacterium tuberculosis* in mouse model of experimental intraocular tuberculosis

Sudhanshu Abhishek, Michelle B Ryndak, Amod Gupta, Tulika Gupta, Shobha Sehgal, Suman Laal and Indu Verma

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Statement of the Problem: Intraocular tuberculosis (IOTB), one of the extrapulmonary form of tuberculosis (TB), is a significant cause of inflammation and visual morbidity in TB endemic countries. Studies on IOTB are extremely challenging due to lack of appropriate human IOTB specimens, hence animal models of IOTB are required.

Methodology & Theoretical Orientation: In the present study, a mouse model of IOTB was established by infecting the animals with *Mycobacterium tuberculosis* (M. tb; H37Rv) via intravenous (i.v.) route. Bacteriological evidence, histopathological changes and whole genome microarray study was done to identify the M. tb transcriptional signatures in mouse eye.

Findings: At 45 days, post-infection (dpi), M. tb bacilli were observed in the eyes of 5 out of 12 (45%) M. tb challenged mice, whereas all the 12 animals showed positivity for M. tb RNA. Apart, histopathology of one CFU positive eye demonstrated intraretinal granuloma and moderate tissue damage in comparison to CFU negative eye that showed mild disease condition with no granuloma. *Mycobacterium tuberculosis* transcriptome analysis through microarray platform in the infected eyes, showed upregulation (≥ 1.5 -fold) of 12 M. tb genes, where top three upregulated transcripts included Rv0962c, Rv2612, and Rv0984. Real-time validation of these top three genes showed an average of 7.40, 4.13 and 3.47 Log₂ fold upregulation ($p < 0.05$), respectively.

Conclusion & Significance: Although, ocular bacterial load was low, but detection of M. tb RNA with undetectable tubercle bacilli in the animals confirmed the paucibacillary nature of IOTB developed under experimental conditions, similar to that observed in human IOTB patients. Upregulation of mycobacterial genes, suggest that the adaptation of M. tb in ocular environment, an immune-privileged site, may be associated with enhanced transcription of genes whose products are required for virulence and survival in intraocular environment. These genes/gene products could be important candidates for understanding the pathogenesis as well as development of new diagnostics/therapeutics for IOTB.

Biography

Sudhanshu Abhishek has evolved from his Biotechnological skills and with Post-graduation in Human Genetics, to understand the infectious disease-like, Tuberculosis (TB). During his mid-tenure of PhD thesis, he was selected for NIH-FOGARTY Fellowships (USA), to be trained on Microarray Technology at NYU School Medicine, NY, USA. His keen evaluation and interest to understand the host-pathogen interaction has opened new avenues of research in intraocular TB through the models (animal and cell line), with a goal to understand the pathogenesis and early diagnosis of intraocular TB, which may lead to better therapeutics. He has grown well from his 6 years of Pre-doctoral training in this field through his continuous research, actively participating in teaching program of the department.

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Global gene expression in *Escherichia coli*, isolated from the diseased ocular surface of the human eye with a potential to form biofilm

Ranjith Konduri

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The surface of the eye is colonized by several bacteria, which survive as resident or transient commensals. But following trauma or under immuno-compromised conditions these commensals cause infection of the eye (such as keratitis, endophthalmitis, orbital cellulitis etc.) often leading to loss of vision. Normally the infection is resolved following treatment with antibacterial agents. However, over the years many of these organisms have become resistant to drugs due to excessive and indiscriminate use of drugs. Resistance to drugs may be due to biofilm formation which makes the bacteria impervious to antibiotics. In the present study ocular *E. coli* from patients with ocular infectious disease is used as a model system and was screened for their ability to form biofilm, antibiotic susceptibility. In addition, to understand the molecular mechanisms underlying the biofilm formation and resistance to antibiotics in biofilm phase we used DNA microarray. Ten of twelve ocular *E. coli* isolates were resistant to at least one or more of nine antibiotics tested and majority of isolates were positive for biofilm formation. *E. coli* L-1216/2010 is best biofilm forming isolate confirmed by confocal and scanning microscopy. Further *E. coli* in the biofilm phase was 100 times more resistant to antibiotics tested compared to planktonic phase. DNA microarray analysis could differentiate *E. coli* biofilm forming cells from non-biofilm forming planktonic cells. It was noted that 30% (10.5% up and 19.5% down-regulated) genes were differentially regulated in the sessile biofilm forming cells compared to the non-biofilm cells. Genes encoding cell adhesion genes, extracellular matrix are upregulated in biofilm phase. In addition, some of the up-regulated genes encoding antimicrobial efflux virulence, toxin production, and other metabolites are known to affect the antibiotic susceptibility of planktonic. These genes serve as potential targets for hacking biofilms. This is the first study on whole genome expression of ocular *E. coli* isolates with a potential to form biofilm. Study on native pathogenic ocular isolates for biofilm and antibiotic susceptibility is more relevant than type strains which do not necessarily mimic native isolates.

Biography

Ranjith Konduri has done his MSc from the Department of Biotechnology, School of Life Sciences, Pondicherry University, Pondicherry. He has qualified GATE with percentile of 99.7%. Currently he has registered for PhD with infectious diseases as area of interest. The work involves the identification and functional characterization of genes involved in antibiotic resistance and biofilm formation. It aims to identify and understand various molecular mechanisms involved in cell adhesion for the dispersal of the biofilm. Very recently he has published a research article on Biofilm in Journal Gut Pathogens.

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Prevalence of pathogenic bacteria in open and surgical wounds of patients attending hospitals in Buea municipality

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University Of Buea, Cameroon

Wound infections often cause harmful and costly clinical complications to our health care systems. Infected wounds impose a significantly negative effect on patient care and recovery as infection hinders wound healing, resulting in increased patient morbidity and mortality. We screened 212 wound specimens from patients in some health institution in Buea municipality and analyzed for common bacteria pathogens using standard microbiological and biochemical methods. Antimicrobial susceptibility of isolates was determined using the disc diffusion assay. A total of 169 (79.9%) samples were infected. The frequencies of isolation from various sources were as follows; burns 100%, ulcers 86.7%, post-operative wounds 79.3% and open wounds 78.8%. 12 bacterial species were identified; *Staphylococcus aureus*, *Escherichia coli*, *Enterobacter cloacae*, *Enterobacter aerogenes*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Hafnia alvei*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Serratia rubideae*, *Serratia sakazakii* and *Streptococcus sp.* Results of antibiotic sensitivity tests revealed the most active drugs against these infectious agents to be ofloxacin (100%) and perfloxacin (100%), followed by ceftriaxone (94.2%) and gentamicin (92%). Isolate exhibited complete resistance to oxacillin (100%). Multi-drug resistance (resistance to five or more drugs) was exhibited by over 71.7% of isolates. Multi-drug resistance was commonly encountered in *Staphylococcus aureus* with 31.5% of this organism being resistant to seven drugs.

Biography

Nde Godlove Tsi is currently a Second Year Student at the Faculty of Health Sciences with a Major in Medicine at the University of Buea – Cameroon.

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Targeting RNA binding proteins: A versatile platform for the discovery and development of new antivirals

Jamal Tazi

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ABX464 is a first-in-class, novel, small molecule inhibiting HIV replication through an entirely new mechanism of action. For the first time in the treatment of HIV, this molecule could reduce or eliminate the viral reservoirs, and thus potentially deliver a long lasting reduction in the viral load of HIV-patients., ABIVAX designed ABX464 with the goal of targeting the viral reservoirs of immune cells with integrated genetic material from the HIV-virus. These reservoirs are not affected by current antiretroviral therapies, and lead to viral load rebound once treatment is stopped. ABX464 inhibits the biogenesis of viral RNA required for the replication of the HIV virus by targeting the Cap Binding Complex (CBC). During replication HIV RNA is first spliced to give rise to spliced RNA from which essential auxiliary proteins, like Rev and Tat proteins, are synthesized but later during infection unspliced viral RNA are produced to generate structural protein and viral genome. ABX464 by stabilizing CBC complex on HIV RNA prevent the synthesis of unspliced RNA.

This unique mode of action and the preclinical data to-date suggest that ABX464 has the potential to:

Reduce or eliminate the viral reservoirs in patients with HIV

Induce long term control of the viral load

Prevent the emergence of HIV mutants that are resistant to treatment

Be less frequently administered over a shorter period than standard treatments

Reduce healthcare costs and offer broader access to treatment.

ABX464 is the first candidate molecule coming from ABIVAX's proprietary antiviral platform and chemical library. This library of more than one thousand small molecules targets the formation of RNP's in the nucleus or the cytoplasm of the infected cell during viral infection. Indeed, to replicate, viruses need to generate RNA-Protein complexes (RNP) from the host cell material. RNP complexes are composed of viral RNA and cellular and viral proteins. Those complexes can "hijack" the cellular machinery of the host cells to express viral RNA and generate new viruses. This approach can be applied to any type of viruses.

ABX311 is the second molecule coming from the ABIVAX antiviral platform. ABX311 is a small molecule able to inhibit Chikungunya viral replication in vitro with an IC50 in the nanomolar range. ABX311 will enter preclinical development Q4 2017.

Biography

Jamal Tazi is Professor of Functional Genomics at the University of Montpellier and Deputy Director of the Health Centre Biology "Rabelais" responsible for education and training. For 20 years, he led the team "messenger RNA metabolism in metazoans" within the Institute for Molecular Genetics in Montpellier (IGMM) where he made important contributions to understand the fundamental mechanisms of the expression of our genes and editing of their products. These discoveries are used today in the medical field through the development of a new therapy based on the use of small molecules to fight against viral infections. To ensure the transition between basic and applied research, and also to support these innovative projects to clinical stage, He founded in 2008 the company Splicos and established its partnership with public institutions as a cooperative laboratory where, he became the Scientific Director

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Scientific Tracks & Abstracts Day 3

Euro Infectious Diseases 2017

Parasitic Diseases, Vaccines

Session Chair

Huseyin Kayadibi

Hitit University School of Medicine, Turkey

Session Introduction

YRF: Comparison of screening method and cohort design to estimate pertussis vaccine effectiveness in Denmark, 2000-2014.

Lara Ricotta, Statens Serum Institut, Copenhagen, Denmark

Title: Benchmarking of healthcare-associated infections in Gulf Cooperation Council (GCC) states

Aiman El-Saed, Gulf Cooperation Council (GCC), Saudi Arabia

Title: Sero characterization of Plasmodium species in Limu Kossa District of Jimma Zone, Western Ethiopia

Sindew Mekasha Feleke, Ethiopian Public Health Institute (EPHI), Ethiopia

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Comparison of screening method and cohort design to estimate pertussis vaccine effectiveness in Denmark, 2000-2014

Lara Ricotta^{1,2}, J Nielsen¹, P Valentiner-Branth¹ and K Mølbak¹¹Department of Infectious diseases Epidemiology, Statens Serum Institut, Copenhagen, Denmark²European Programme for Intervention Epidemiology Training (EPIET), European Centre for Disease Prevention and Control, (ECDC), Stockholm, Sweden

Background: In Denmark, laboratory-confirmed pertussis is notifiable, and national laboratory, vaccination and population registries permit individual data linkage for analysis. Since 1997, acellular pertussis vaccine has been delivered as a primary series (PS) of three doses at 3, 5 and 12 months, with a pre-school booster at age 5. We estimated VE for children receiving PS versus unvaccinated children, and for those receiving booster dose versus not having received the booster, comparing estimates from a screening method and a cohort design (CD).

Methods: The Danish civil registration number was used to link individual case laboratory data to vaccination and population registries. We estimated PS VE by birth cohort from 2000 to 2014, and for the booster from 2000 to 2010, using both methods. For the SM, VE was calculated for PS using the proportion of PS-vaccinated versus totally unvaccinated among cases, and in the population to January 2015. For the CD, linked data was used to estimate time at risk among individuals in each birth cohort from birth or arrival in Denmark, until tested positive for pertussis, moved out of country, death or end of study period. VE was estimated as 1 minus the incidence rate ratio (IRR) between incidence rate (IR = cases/time at risk) among PS-vaccinated and IR for totally unvaccinated using Poisson regression. For the booster, VE was estimated for the booster-vaccinated versus no-booster, independent of other vaccines received.

Results: From 2000 to 2015, 3621 confirmed cases were reported among 1,024,906 children in all birth cohorts. Using SM, the median VE for PS was 89.1% (range 63.9% to 99.7%). For the CD, median VE was, 77.2% (range 38.2% to 96.2%). For the booster, SM produced a VE median estimate of 94.0% (range 88.7% to 98.2%), compared to 57.2% (range 50.2% to 69.7%) using CD.

Conclusions: This study shows that acellular pertussis vaccine is highly effective. However, VE estimates for children who received PS, and for those who received booster, are substantially higher using SM than CD. CD incorporates the dynamics of time-at-risk and produces a more robust VE estimates. Therefore, SM is likely to overestimate VE, and countries using this approach need to be aware of this limitation. When individual data can be collected or linked, we recommend using the cohort design to obtain a more valid VE estimate.

Biography

Lara Ricotta, she had completed her medicine in preventive medicine, Epidemiology, Public Health and Neurology from 2000-2008 and Preventive Medicine Residency Program (PMRP) from 2010-2015 University of Bologna. She had worked with Istituto Superiore di Sanità, Rome, Italy from 2012 to 2014. And from 2015 to present she is working European Centre for Disease Prevention and Control (ECDC) Università di Bologna

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Sero characterization of Plasmodium species in Limu Kossa District of Jimma Zone, Western Ethiopia

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Ethiopia is among the sub-Saharan African countries successful in reducing malaria burden in the last decade. The Government of Ethiopia launched elimination strategy taking advantage of this reduction in line with the commitment of African leaders to attain malaria elimination in 2030. However, unlike other settings Ethiopia requires additional efforts to achieve this ambitious elimination plan in due to the co-existence of both *P. falciparum* and *P. vivax*. The current case management mainly target both species. Despite the previous reports of the existence of the other two human malaria parasites including *P. ovale* and *P. malariae* in the past, there is no adequate and current information in this regard. This is, therefore, to describe the existence of *P. ovale* and *P. malariae* using an advanced molecular technique that helps to investigate Plasmodium spp. in Limu Kossa District, Jimma Zone, and Southwestern Ethiopia. A total of 180 serum samples were collected from three villages located in Limu Kossa District, 400 Km southwestern Ethiopia during October 2016. Longitudinal follow up and monitoring performance Onchocerciasis elimination program was underway for the last years in Arengama 1, Arengama 2 and Konche villages. Serum was prepared from whole blood collected from the residents to investigate the presence of human malaria parasite marker antibodies. The investigation was conducted using LUMINEX, which is an advanced technique as briefly described below. Serum samples (1µl) diluted with 399 µl of 30ml buffer B and 20µl of 6mg/ml E.coli extracts and incubated for 1 hrs at 37 oC and stored at 4oC overnight. Next morning the Luminex plate pre wetted with 200ul PBST buffer and empty with vacuum. The tubes with coupled beads solution with each of the 7 different malaria antigens (CSP (5), AMA1 (33), PfMSP1 (36), PvMSP1 (91), PmMSP1 (16), PoMSP1 (45), LSA1 (23)) were mixed with vortex and from each antigen coupled beads solution 15ul transferred to conical tube and mixed with 5ml buffer. The antigen coupled beads and buffer-A solution poured to the tray and 50µl transferred to all wells of the Luminex plate using multichannel pipette and washed twice with 100ul of PBST, vacuumed and 50µl of sera dilution added in duplicate plate well followed by incubation for 1 hour and 30 minutes at room temperature on a shaker. After incubation the plate washed with PBST buffer, vacuumed and 50 µl of secondary antibody buffer A solution added to each well using multichannel pipette and incubated for 45 minutes at room temperature on a shaker. The procedure followed by plate wash, vacuum and 50µl streptavidin-phycoerythrin and buffer A solution added to each well and incubated at room temperature for 1 hour on a shaker. The plate washed with 100µl of PBST, vacuumed and 50ul of buffer A added to each well and incubated for 30 min at room temperature on a shaker. The last step was the plate washed and 125µl of PBS-PH 7.2 added to each well, incubated for 2 minutes and followed by immediate load on the calibrated and programmed Luminex machine and run the experiments. Among 180 samples processed four human malaria parasites were detected using the state-of-the-art technique. Plasmodium falciparum accounted most of the antibodies detected. More interestingly, antibodies of both *P. ovale* and *P. malariae* were identified in the present analysis. Details of the findings of laboratory analysis are presented in Table 1 below. The Cumulative exposure history over the last five years for Pf MSP1 and AMA was 39.4%(n=71) and the recent exposure history over the last 12 months for Pf CSP and Pf LSA antigens was 11.1% (n=20). Our preliminary finding from the field demonstrated the significant exposure history of study participants to all plasmodium species using LUMINEX. The present result showing the existence of recent exposure to *P. malariae* and *P. ovale* remains a challenge for malaria control and elimination strategy. This local findings call for performing large scale survey and redefining the Plasmodium species composition to well inform the National Malaria Control Program in improving malaria microscopy in the country.

Biography

Sindew Mekasha Feleke, born on Feb-04-1985 and Employed in Ethiopian Public Health Institute in 2007 GC. He had did his Biology (BSc) from Dilla University ,Tropical and Infectious Disease (MSc) from Addis Ababa University, Guest Researcher Fellowship at CDC lab Atlanta, USA for one and half months, Guest Researcher Fellowship at University of South Florida (USF) lab, USA for two months And he had more than Nine (9) years work experience at the Ethiopian Public Health Institute (EPHI) since 2007 GC until know. Currently he is working as an Malaria and Neglected tropical Diseases Team Leader, Head for Malaria RDT QA and Onchocerciasis Molecular Laboratory and Researcher 1

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Benchmarking of healthcare-Associated infections in Gulf Cooperation Council (GCC) states

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Statement of the problem: Although there are few international benchmarks for the healthcare-associated infections (HAI), several methodological and logistic issues make the use of such benchmarks unfair. It has been long suggested to establish a local benchmark for Gulf Cooperation Council (GCC) states that consider the challenges of the newly established regional surveillance programs. The purpose of this project was to set a GCC benchmark to promote standardized surveillance in the hospitals of the GCC countries.

Methodology: The GCC Center for Infection Control located in Riyadh (Saudi Arabia) did several activities to promote standard surveillance methodology for the GCC countries. This included publishing a surveillance manual, creating unique data collection forms, organizing multiple educational and training activities, and data auditing and validation on-site visits. Aggregate HAI surveillance data were pooled from 6 hospitals in three GCC countries; Saudi Arabia, Oman, and Bahrain. Standardized infection ratio (SIR) of HAIs in GCC hospitals were calculated using published reports of the US National Healthcare Safety Network (NHSN) and International Nosocomial Infection Control Consortium (INICC).

Findings: We have published major benchmarking reports on ventilator associated pneumonia (VAP) and catheter-associated urinary tract infections (CAUTIs) in the American Journal of Infection Control. A third report about central line-associated bloodstream infections (CLABSI) is in the process of publication. A common finding from the three reports confirm that the risk of HAIs including VAP, CAUTI, and CALBSI in GCC countries is higher than pooled U.S. VAP rates but lower than pooled rates from developing countries participating in the INICC.

Conclusion & significance: Although we have accomplished a distinguished step towards setting a regional benchmark, more efforts are still needed to improve regional collaboration in HAI surveillance activities. We are currently working on recruiting more facilities to submit data for future larger-scale benchmarking reports on HAIs and antimicrobial resistance.

Biography

Aiman El-Saed is MD physician from Egypt who had PhD and MPH in epidemiology from the University of Pittsburgh, Pennsylvania, USA in 2004. Worked as a researcher at the University of Pittsburgh for 3 years between 2004 and 2007. Currently working as Assistant Professor of Epidemiology & Biostatistics at the College of Public Health and Health Informatics of King Saud bin Abdulaziz University for Health Sciences (Riyadh, Saudi Arabia). He is also working as advisor of health surveillance at the infection Prevention & Control Department, National Guard hospital, Riyadh, Saudi Arabia. He is serving as primary or co-investigator of several research grants. He had a strong epidemiologic and statistical research experience.

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