



Univerza v Ljubljani | Medicinska fakulteta
INŠTITUT ZA MIKROBIOLOGIJO IN IMUNOLOGIJO

vabita na

2. MED-AKADEMIJSKI ZNANSTVENI SIMPOZIJ

ZOONOZE

Ljubljana, 27. oktober 2016

Slovenian Academy of Sciences and Arts
Academy of Sciences and Arts of Bosnia and Herzegovina
Croatian Academy of Sciences and Arts

welcome you to the

2nd INTER-ACADEMY SCIENTIFIC SYMPOSIUM

EMERGING ZOOZOSES

Ljubljana, 27th of October 2016

SCIENTIFIC COMITEE

Acad. prof. dr. Tatjana Avšič-Županc, PhD (SAZU)

Acad. prof. dr. Mirsada Hukić, MD, PhD (ANUBIH)

Acad. prof. dr. Alemka Markotić, MD, PhD (HAZU)

ORGANIZING COMITEE

President: Acad. prof. dr. Tatjana Avšič-Županc, PhD

Members: Miša Korva, Nataša Knap Gašper, Lea Korva

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2nd Inter-Academy Scientific Symposium

EMERGING ZONNOSES

27th of October, Velika dvorana SAZU, Novi trg 3, Ljubljana

Programme:

- 12:00– 12:45 **Registration and welcome lunch– Prešernova dvorana, Novi trg 4, SAZU**
- 12:45– 13:00 **Acad. prof. dr. Robert Zorec, PhD** - Opening of the Symposium by the Secretary of Section of Natural Sciences
- Acad. prof. dr. Tadej Bajd, PhD** - Welcome address by the President of SAZU
- Prof. dr. Miroslav Petrovec, MD, PhD** – Welcome address by the Director of Institute of Microbiology and Immunology
- Acad. prof. dr. Tatjana Avšič-Županc, PhD** – Introduction to the Symposium
- Chair: T. Avšič-Županc, M. Petrovec**
- 13:00– 13:30 **Prof. dr. Giorgio Palù, MD, PhD:** Evolution and emergence of vector borne diseases
- 13:30 – 14:00 **Prof. dr. Stephan Günther, PhD:** Ebola virus disease in West Africa - outbreak response and operational research
- 14:00– 14:30 **Acad. prof. dr. Mirsada Hukić, MD, PhD:** Recognizing Bioterrorism in the face of emerging and reemerging zoonotic pathogens in Bosnia and Herzegovina: The result of a Biological Attack during the war (1992 - 1995)
- 14:30– 15:00 **Acad. prof. dr. Alemka Markotić, MD, PhD:** Multiple zoonotic infections – clinical, diagnostic and epidemiological impact
- 15:00– 15:30 **Acad. prof. dr. Franc Strle, MD, PhD:** Lyme borreliosis – global emerging zoonosis
- 15:30 – 16:15 **Break – Prešernova dvorana**
- Chair: A. Markotić, M. Hukić**
- 16:15 – 16:35 **Acad. prof. dr. Tatjana Avšič-Županc, PhD:** Zika virus: an old virus with a new face
- 16:35 – 16:55 **Dr. Lidija Cvetko Krajnovič, PhD:** Parameters of innate immune response in peripheral circulation of patients infected with Puumala virus
- 16:55 – 17:15 **Dr. Ivan-Christian Kurolt, PhD:** Micro RNAs in urine – biomarkers for disease severity in patients infected with Puumala virus
- 17:15 – 17:35 **Dr. Miša Korva, PhD:** Tularemia in Slovenia: a rare zoonotic disease occurring in clusters

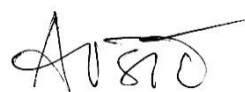
PREFACE

After the first successful Inter-Academy Symposium organized in October 2015 by the Croatian Academy of Sciences and Arts in Zagreb it was accepted that an annual symposium of three academies: Slovenian Academy of Sciences and Arts, Croatian Academy of Sciences and Arts and Academy of Sciences and Arts of Bosnia and Hercegovina, will become a tradition. The main topic of these Scientific symposia will be Emerging Zoonoses.

Many emerging infectious diseases are zoonotic, where an animal reservoir incubates pathogenic microorganism, with only occasional transmission into human populations. Several factors contribute to disease emergence, like microbial adaptation and genetic variation, climate and weather, change in human demographic and trade, change in human susceptibility, economic development, breakdown of public health systems, poverty, war and bioterrorism. In recent years, several factors have considerably changed the interactions among humans, animals and the environment. These changes have triggered the emergence and re-emergence of numerous zoonotic microorganisms, including several vector-borne pathogens such as West Nile virus, Zika virus, borreliae, francisellae, leptospirae, or have contributed to the (re)emergence of outbreaks or even epidemics like Ebola virus disease, hantavirus disease, Yellow fever, Lassa fever and brucellosis.

During the Symposium some of the afore mentioned emerging zoonotic diseases will be presented and discussed by internationally recognized scientists and experts who will exchange their knowledge and experiences working with emerging pathogens of national or global importance.

With the 2nd Inter-Academy Scientific Symposium, we would like to keep and strengthen the research collaboration between the three national academies on this important public health topic and thus provide scientific meetings where annually updates and achievements on research in the respective countries will be presented and discussed.



Acad. prof. dr. Tatjana Avšič Županc

EVOLUTION AND EMERGENCE OF VECTOR BORNE DISEASES

Prof. dr. Giorgio Palù, MD, PhD

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Short biography:

Giorgio Palù is a professor of Microbiology and Virology, University of Padova, School of Medicine and Director of the Clinical Microbiology and Virology Division of Padova University Hospital. Former Pro-Rector International Scientific affairs and former Dean of the School of Medicine, University of Padova. Founder and Director of the Department of Molecular Medicine, University of Padova. Visiting Professor at Yale, UCSD, ICL, Ulm and Harvard Universities; Adjunct Professor at Temple University, School of Medicine and School of Biology. Member of the Scientific Advisory Board of many National and International Institutions. Member of the Editorial Board and Associate Editor of a number of scientific Journals of Virology and Gene Therapy. Author of over 500 publications, appeared in International Journals of Biomedicine and of 35 among reviews, volumes and book chapters. His research interests cover the fields of Molecular and Medical Microbiology, Molecular therapies and Gene and cell therapy for neoplastic, infectious and genetic diseases.

Abstract:

Vector borne diseases include an endless list of pathological syndromes affecting animals and humans with enzootic, zoonotic and human to human transmission that are caused by a variety of infectious agents (viruses, protozoa, bacteria). Vectors involved are mainly haematophagous insects and Malaria and Dengue are the most common vector (mosquito) borne human to human transmitted diseases. A complex network of interactions involving the pathogen, the vector, the animal reservoir and the human host are essential in allowing the agent to maintain infectivity and to be successfully propagated throughout its life cycle. The comprehension of these interactions will certainly provide a clue to interrupt the genetic determinants affecting vector borne infectious agent transmission. The focus of this presentation will deal with an attempt to dissect some of the host-microbe interactions that might be relevant to the pathogenesis of some recently emerged arboviral diseases, circulating in our Mediterranean-European area.

EBOLA VIRUS DISEASE IN WEST AFRICA - OUTBREAK RESPONSE AND OPERATIONAL RESEARCH

Prof. dr. Stephan Günther, PhD

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Short biography:

Stephan Günther has had a 23-year career in virology. After training in medicine, he began research on hepatitis B virus at the Heinrich Pette Institute for Experimental Virology and Immunology in Hamburg, Germany, in 1993. In 1998, he transferred to the Bernhard Nocht Institute for Tropical Medicine in Hamburg, where he studied hemorrhagic fever viruses (VHF) of risk group 4 in the laboratory and in Africa, focusing specifically on Lassa fever virus. In 2005, he became the head of the Department of Virology and the WHO Collaborating Centre for Arboviruses and Hemorrhagic Fever Reference and Research. His group established replicon and reverse genetics systems for Lassa virus as well as small animal models to study pathogenesis and immunology of VHF. Major focus of clinical research programs is identification and characterization of emerging viruses in Africa and the development of novel diagnostic tools. He is head of several collaborative projects with West African countries, including Nigeria, Guinea, Sierra Leone, and Ghana on VHF in humans and the animal reservoirs. He is coordinator of the European Mobile Laboratory, which performed diagnostics and operational research during the West African epidemic of Ebola virus disease.

Abstract:

The European Mobile Laboratory (EMLab) consortium has set up 3 mobile laboratory units for diagnostics of pathogens up to risk group 4. All units were deployed to assist with diagnostics and differential diagnostics during the outbreak of Ebola virus disease (EVD) in West Africa. The first unit was deployed to Guéckédou, Guinea, in March 2014. It remained in operation until autumn 2016. The second unit was stationed in Nigeria and has been later on deployed within Nigeria and then to Sierra Leone. The third unit has been deployed to Liberia and Sierra Leone. Until end of mission, EMLab has tested more than 22,000 samples from EVD suspected cases with about 3,500 samples being positive for Ebola virus. Based on its diagnostic activities in the field, EMLab implemented a research program on virus evolution, immunology and pathophysiology of EVD, virus diagnostics, persistence, co-infections, and outcome determinants and supported vaccine and drug trials of WHO and other partners in the field. EMLab was a technical partner of the WHO Emerging and Dangerous Pathogens Laboratory Network, and the Global Outbreak Alert and Response Network.

RECOGNIZING BIOTERRORISM IN THE FACE OF EMERGING AND REEMERGING ZONOTIC PATHOGENS IN BOSNIA AND HERZEGOVINA: THE RESULT OF A BIOLOGICAL ATTACK DURING THE WAR (1992 - 1995)

Acad. Prof. dr. Mirsada Hukić, MD, PhD

Member of Academy of Sciences and Arts of Bosnia and Herzegovina (ANUBIH)
Member of European Academy of Sciences (EURASC)
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Short biography:

Mirsada Hukić has more than 35 years of extensive research experience ecology, physiology and genetics of microorganisms. Since 1992 her focus has been on viral hemorrhagic fevers and she has also worked in clinical diagnostics and research of zoonotic diseases. She obtained her MD in 1974 and subsequently completed her residency in the microbiology and parasitology laboratories at the University of Sarajevo, where she obtained a MSc degree in 1981 and a PhD degree in 1992. She is a founder and scientific director of the Institute for diagnostic and biomedical research Nalaz as well as a professor of microbiology and immunology at International Burch University. She is a representative of Bosnia and Hercegovina within the H2020 Programme Committee for the Health, demographic change and well-being configuration. With an extensive publication repertoire, her scientific and professional involvements include participations in national as well as international projects. While Prof. Dr. Hukic holds the title of President of the Association of Microbiologist of Bosnia and Hercegovina, she is also a member of various worldwide scientific associations and societies.

Abstract:

Bosnia and Herzegovina was faced with outbreaks of emerging and reemerging diseases, with a severe clinical presentation and high mortality during the war (1992-1995). The largest and most prominent outbreaks were hemorrhagic fever with renal syndrome (HFRS) (with thousands of reported cases) and tularemia (with hundreds of reported cases). During that period, the tularemia epidemic was in the shadow of the HFRS epidemic and yet suspected use of agents of biological warfare remains unexplored. Twenty years later, we conducted a retrospective analysis of the 1995 tularemia outbreak with an aim to discern whether its occurrence was due to intentional use of biological warfare agents or due to natural outbreaks of infectious diseases. We researched epidemiological, clinical and microbiological aspects of the epidemic. We analysed meetings minutes of the Institute of Public Health, reports of the WHO team, patient questionnaires, medical records, microbiological findings and geographical maps of the different areas affected by the epidemic. Some aspects of our findings imply that *Francisella tularensis* was likely used as a bioterrorism agent in the tularaemia epidemic in Bosnia and Herzegovina in 1995.

MULTIPLE ZONOTIC INFECTIONS – CLINICAL, DIAGNOSTIC AND EPIDEMIOLOGICAL IMPACT

Acad. Prof. dr. Alemka Markotić, MD, PhD

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Short biography:

Alemka Markotić received her M.D. at the Medical School, University of Sarajevo, Bosnia and Herzegovina (1989), a MSc. in Medical Microbiology and Parasitology (1996), and a Ph.D. in Infectious Diseases (1999) from the University of Zagreb Medical School. She is specialist in Clinical Immunology and Infectious Diseases. She received a National Academy of Sciences, National Research Council Postdoctoral Fellowship at USAMRIID, Maryland, USA. Dr. Markotić's research on the epidemiology, diagnostics and immunopathogenesis of hantaviruses has earned her seven national and nine international awards. She has published over 100 peer-reviewed papers and delivered numerous presentations at national and international conferences. She has been principal investigator on several research projects studying immune responses, clinical characteristics and molecular epidemiology of zoonotic diseases. Dr. Markotić founded Croatian Society for Biosafety and Biosecurity and currently is president of the Society.

Abstract:

Croatia is a natural focus for many zoonosis. Simultaneous infection by multiple microorganisms is commonplace, although we usually do not consider it regularly in daily clinical practice. Robust, powerful multiplex molecular diagnostic tools are prerequisite for detection of multiple infections in animals and humans. We are continuously focused on multiple zoonotic infections in humans and rodents. Our recent survey of 242 rodents and small mammals, collected at eight sites in Croatia over an 8-year period showed multiple infections in 32 rodents (13.2%). Dual infections were found in 10.7% rodents, triple infections in 2.9%, and quadruple infections in 0.8% rodents. Our findings indicate that rodents in Croatia harbour a wide range of bacteria and viruses that are pathogenic to humans. Our experience in management of the patients with multiple zoonotic infections or co-infections with other pathogens shows that co-infected humans have worse clinical picture and outcome than those with single infections.

LYME BORRELIOSIS – GLOBAL EMERGING ZONOSIS

Acad. Prof. dr. Franc Strle, MD, PhD

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University Medical Centre Clinic for Infectious Diseases and Febrile Illnesses

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Short biography:

Franc Strle is a specialist in internal medicine and infectious diseases at the University Medical Centre Ljubljana. From 2002 to 2016 he was the director of the Clinic for Infectious Diseases and Febrile Illnesses. Since 1999, he is the Head of the research activities at the clinic, as well as the Head of the Research Council and a member of the expert council of the UMC Ljubljana. His main clinical and research interest are tick-transmitted infections, especially Lyme borreliosis, tick-borne encephalitis and human granulocyte ehrlichiosis. For the last 30 years he is a regular honorary speaker at international conferences on Lyme borreliosis and other tick transmitted diseases. He has published over 200 articles in prestigious international scientific journals and he is co-author of 7 book chapters. Due to his outstanding research achievements and devoted pedagogic and clinical work he has been elected as a full member of the Slovenian Academy of Sciences and Arts in 2009.

Abstract:

Lyme borreliosis (LB) is the most common tick-borne disease in the Northern Hemisphere. In Europe it is caused predominantly by *Borrelia afzelii*, which usually remains localized to the skin, and *Borrelia garinii* which is associated particularly with nervous system involvement. In North America *Borrelia burgdorferi* is almost the sole agent of LB and is especially arthritogenic. LB usually begins with an expanding skin lesion, erythema migrans. If untreated, borreliae can disseminate from skin to the nervous system, heart, or joints. Clinical manifestations are thought to result from the host immune response to the spirochete. The diagnosis of erythema migrans is clinical while other clinical manifestations are diagnosed based on a characteristic clinical picture and demonstration of borrelia infection. LB can usually be treated successfully with appropriate antibiotic regimens (principally with doxycycline), but the disease may be followed by post-infectious sequelae. Prevention primarily involves avoidance of tick bites by personal protection measures; vaccination is not currently available.

ZIKA VIRUS: AN OLD VIRUS WITH A NEW FACE

Acad. Prof. dr. Tatjana Avšič-Županc, PhD

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Short biography:

Tatjana Avšič is a full Professor of Medical Microbiology at Faculty of Medicine, University of Ljubljana and Head of the Laboratory for diagnostics of zoonoses at the Institute of Microbiology and Immunology, Ljubljana, Slovenia. She has over 30 years of experiences in the clinical diagnostics and research of zoonotic vector-borne diseases, mainly arboviruses and viral hemorrhagic fevers represented in more than 180 SCI publications. She is head of the laboratory that has the role of reference center at the national and international level, for Hantaviruses, TBE and CCHF viruses. Her laboratory conducts research on genetic variability of the above mentioned pathogens with the relation to their host-vector-man relationship. Based on many years of experiences in the research of VHF her Laboratory is partner of GOARN/WHO. Over the past 25 years she was the principal investigator on numerous national and international research projects. Due to her scientific achievements she has been elected as a full member of the Slovenian Academy of Sciences and Arts in June 2015.

Abstract:

Zika virus is a mosquito-borne flavivirus that represents a public health emergency at the ongoing epidemic. This obscure virus was limited to sporadic cases in Africa and Asia, until the emergence of Zika virus in Brazil in 2015, when it rapidly spread throughout the Americas. Most Zika virus infections are subclinical or characterized by mild febrile illness. However, neurological complications, including Guillain-Barré syndrome in adults, and congenital anomalies, including microcephaly in babies born to infected mothers, raised a grave concern. Currently, there is no specific antiviral treatment or vaccine available for Zika virus infection. Thus, international public health response is primarily focused on preventing infection, particularly in pregnant women, and on providing up-to-date recommendations to reduce the risk of non-vector transmission of Zika virus. The presentation will focus on the results of Slovenian researchers who were the first to prove a strong association between Zika virus and microcephaly.

PARAMETERS OF INNATE IMMUNE RESPONSE IN PERIPHERAL CIRCULATION OF PATIENTS INFECTED WITH PUUMALA VIRUS

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Short biography:

Lidija Cvetko Krajinović has graduated in molecular biology in 2001 at the Faculty of Science, University of Zagreb, where she also obtained her PhD degree in natural sciences in 2014. She started her career at the Institute of Immunology and since 2006 she has been working in the Research Department of University Hospital for Infectious Diseases, Zagreb. She is a research associate at the School of Medicine University of Zagreb. She performed several professional educations at Haartman Institute in Helsinki, Istituto Clinico Humanitas in Milan, and Lautenberg Center for General and Tumor Immunology in Jerusalem. She participates in teaching on specialist postgraduate studies in infectious diseases and epidemiology and undergraduate study in forensics. She is involved in several scientific projects. As a researcher she has been involved in molecular epidemiology and diagnostics of zoonotic diseases. Her main scientific and professional interests are immunobiology and pathogenesis of viral infectious diseases, with particular emphasis on infections caused by hantaviruses.

Abstract:

Pathogenic hantaviruses significantly differ by their pathogenicity resulting in broad spectra of clinical presentations in human infections. It is considered that pathogenesis of HFRS is mainly mediated by immune response. The aim was to explore the components of innate and adaptive immunity important in the peripheral immune response as well as the possible regulatory effect of miRNA on early immunoreactions during the hantaviral infection. The results showed down regulation of genes coding the synthesis of PRRs, chemokines and their receptors, cytokines, TF, as well as some signalling molecules. Differential expression resulted in modulation of inflammatory response by interfering with various cell-signalling pathways. Biological importance of miRNA in the regulation of immune response during HFRS was shown. Changes detected at the immune response level have also been associated with disease severity. The results showed initial suppression of the early immune response to PUUV which was more pronounced in more severe form of the disease.

MICRO RNAS IN URINE – BIOMARKERS FOR DISEASE SEVERITY IN PATIENTS INFECTED WITH PUUMALA VIRUS

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Short biography:

Ivan-Christian Kurolt graduated in 2006 at the Institute of Virology, Marburg University, Germany. Since 2007 he is employed at the University Hospital for Infectious Diseases „Dr. Fran Mihaljević“ in Zagreb, Croatia, first as a technological assistant and then as a PhD student. He defended his dissertation in 2014 on the influence of Puumala virus on microRNA expression. As a PhD student he was awarded a Doctoral Student Fellowship by the Croatian Science Foundation for a one-year stay at the University of Texas Medical Branch, Galveston, USA. His main research focus is molecular epidemiology of viral zoonotic diseases and immunopathogenesis of hantaviruses. Besides research he is involved in the molecular diagnostics of emerging and re-emerging zoonotic diseases and is a lecturer within the bioterrorism module of the Forensic science studies at the University Split, Croatia. In addition he acquired good knowledge in the fields of Biosafety and Biosecurity.

Abstract:

MicroRNAs (miRNAs) are a class of small RNAs that represent a way of posttranscriptional regulation of gene expression. They have been detected in several bodily fluids, implicating a possible regulation of selected tissues or organs. Certain urinary miRNAs can be predictors of disease outcome in various renal pathologies, e.g. glomerulonephritis or diabetic nephropathy. We measured, for the first time, levels of selected miRNAs in midstream urinary samples of 30 patients with hemorrhagic fever with renal syndrome (HFRS) after Puumala virus infection and compared them to 15 patients with pyelonephritis and healthy controls. A custom real-time PCR Array was designed for the detection of seven selected miRNAs which were correlated with laboratory and clinical parameters. Here we show a distinct profile of miRNA abundance in urine of HFRS patients and patients with acute pyelonephritis, which could serve as HFRS biomarkers as they correlate significantly with hallmarks of HFRS progression and severity.

TULAREMIA IN SLOVENIA: A RARE ZONOTIC DISEASE OCCURRING IN CLUSTERS

Dr. Miša Korva, PhD

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Short biography:

Miša Korva, has graduated from Faculty of Biotechnology in 2007 and continued her studies in field of medical microbiology. As a young researcher she joined the Laboratory for diagnostics of zoonoses at the Institute of Microbiology and Immunology, Faculty of Medicine. She has defended her doctoral thesis, on the pathogenesis of hemorrhagic fever with renal syndrome, in 2011. During her PhD studies she visited training programs at University of Texas Medical Branch in Galveston and Johns Hopkins University in Baltimore. As a researcher she has been involved in the clinical diagnostics and research of zoonotic diseases, viral hemorrhagic fevers, arboviruses and intracellular bacteria. Her current research is focused on pathogen genetic variability with the relation to the host-vector relationship. She is involved in several international research projects. She is a member of the European Mobile Laboratory and was involved in diagnostics of the Ebola outbreak in Guinea. As an assistant, she participates in lectures on Virology, Emerging pathogens and Biological warfare.

Abstract:

Slovenia is a small Central European country with rare and sporadic cases of tularemia. In the last twenty years up to two cases per year were reported. However, between 2012 and 2013 six patients with the ulceroglandular form of tularemia were recognised in the same town. The clinical manifestation varies depending on the route of infection, but the virulence, the dose of the pathogen and the immune status of the host. In our case, epidemiological data indicated transmission by a tick bite in at least 50% of patients. The aim of the study was an investigation of genetic diversity of tularemia in Slovenian patients. From 2007 to 2016, we have amplified tularemia DNA from 10 clinical samples and they all corresponded to *F.tularensis* subspecies *holarctica*. Additionally, we have analyzed genetic diversity of tularemia strains by amplifying 5 VNTR markers. Out of 10 samples 4 different VNTR genotypes were recognized. In comparison to neighboring countries, Slovenian tularemia strains show low genetic diversity which most probably corresponds to localized disease clusters.

Notes:

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