VIROLOGY WORLD CONFERENCE

JUNE 2022

VIRTUAL EVENT

17-18

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BOOK OF ABSTRACTS

VIROLOGY WORLD CONFERENCE

17-18 JUNE

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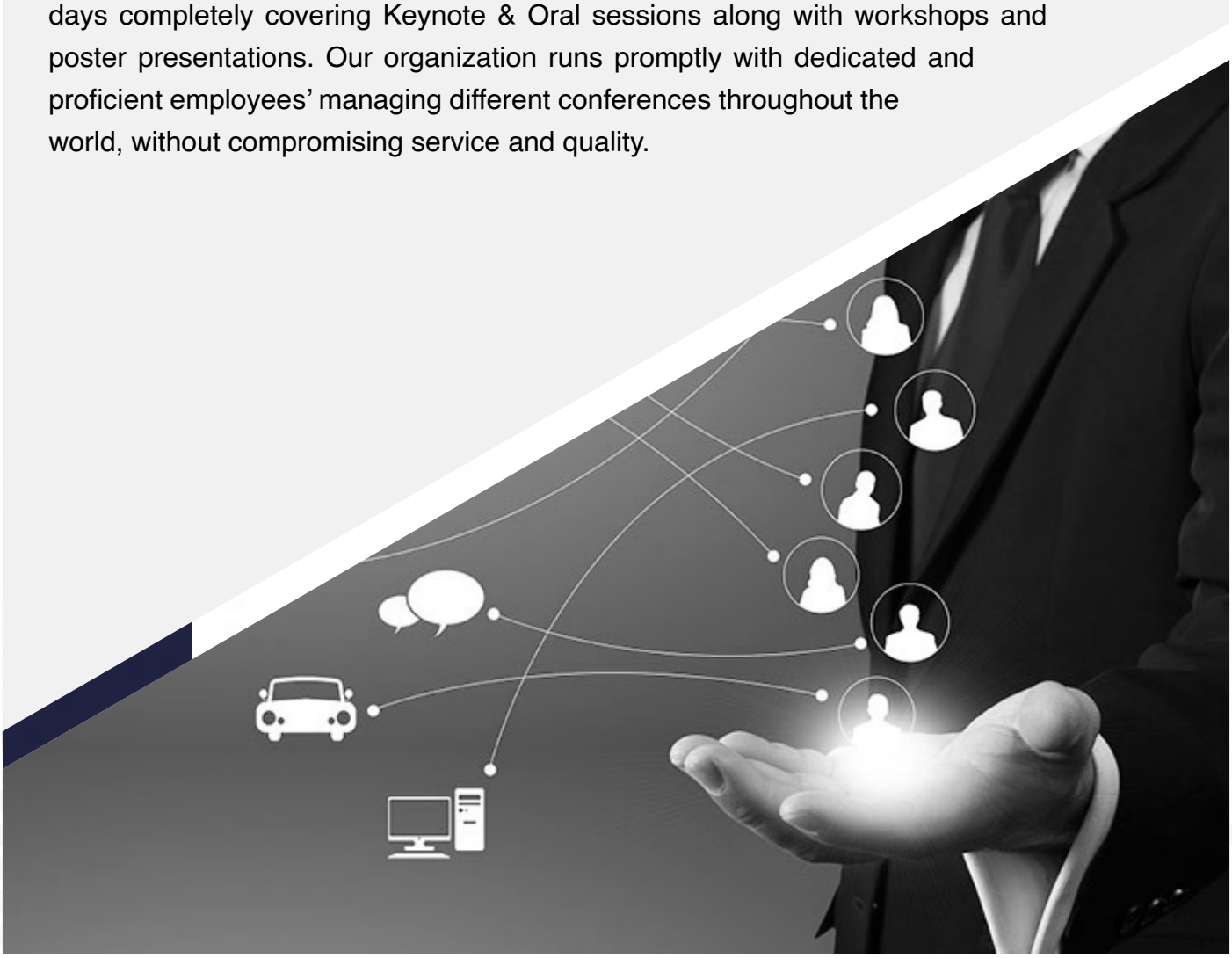
ABOUT MAGNUS GROUP

Magnus Group (MG) is initiated to meet a need and to pursue collective goals of the scientific community specifically focusing in the field of Sciences, Engineering and technology to endorse exchanging of the ideas & knowledge which facilitate the collaboration between the scientists, academicians and researchers of same field or interdisciplinary research. Magnus group is proficient in organizing conferences, meetings, seminars and workshops with the ingenious and peerless speakers throughout the world providing you and your organization with broad range of networking opportunities to globalize your research and create your own identity. Our conference and workshops can be well titled as 'ocean of knowledge' where you can sail your boat and pick the pearls, leading the way for innovative research and strategies empowering the strength by overwhelming the complications associated with in the respective fields.

Participation from 90 different countries and 1090 different Universities have contributed to the success of our conferences. Our first International Conference was organized on Oncology and Radiology (ICOR) in Dubai, UAE. Our conferences usually run for 2-3 days completely covering Keynote & Oral sessions along with workshops and poster presentations. Our organization runs promptly with dedicated and proficient employees' managing different conferences throughout the world, without compromising service and quality.



ABOUT VIROLOGY 2022

Magnus Group takes pride to announce “Virology World Conference (Virology 2022 - Virtual Event)” during June 17-18, 2022. This Conference includes numerous interactive sessions specifically designed for highly acclaimed educational activity which has been considered one of the predominant meetings on Virology. Virology 2022 creates real networking with scientists and researchers from research institutes, companies, and laboratories. A good conference forces you to grow and gives you new challenges. Meet established peers and make new connections around the world which is a great opportunity to network. Your chance of learning new skills and updates in Virology research greatly improves when you are sharing the same space as eminent experts, professors and business partners.

KEYNOTE FORUM

DAY 01

VIROLOGY WORLD CONFERENCE

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Theodoros Androutsakos

National and Kapodistrian University of Athens, Greece

Post-vaccination antibody responses against SARS-CoV-2 in patients with liver cirrhosis. What do we know so far?

Various studies have investigated the severity of coronavirus disease 2019 (COVID-19) in patients with liver diseases (PWLD) since the beginning of the pandemic and patients with cirrhosis seem to have an elevated risk for severe COVID-19 course and death, making vaccination against the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) of utmost importance for these patients. The novel vaccines against SARS-CoV-2 display encouraging safety and efficacy profiles, offering the prospect of achieving herd immunity to combat the pandemic. However, there is a paucity of data regarding safety and immunogenicity of these vaccines in PWLD, particularly in those with cirrhosis, as only few PWLD were included in the phase I–III vaccine clinical trials of the aforementioned vaccines. Moreover patients with liver cirrhosis show inadequate immune responses in seasonal flu, viral hepatitis and pneumonococcal vaccines, raising concerns about the immunogenicity of anti-SARS-CoV-2 vaccination. In my presentation I will discuss the reasons for impaired immune responses in patients with liver cirrhosis and present all available data concerning anti-SARS-CoV-2 vaccination in these patients.

Audience Take Away:

- Raise awareness concerning the higher mortality and morbidity of COVID-19 in patients with liver diseases and especially liver cirrhosis.
- Learn available data concerning antibody responses in patients with liver cirrhosis and discuss subgroups that should probably get vaccinated with a third dose after the standard 2-vaccines schedule.

Biography

Dr Androutsakos graduated from Athens Medical school in 2004 and became specialist in Internal Medicine in 2015 after residency first in Södra Älvsborg Sjukhus in Sweden and then in Laiko hospital in Greece. He also attended the Pathology department of Pittsburgh Medical School, in USA, as a visiting scholar in 2015. In January 2020 he received his PhD titled “HIV and the liver”. He is an academic fellow of Athens Medical School, working as an Internist and Hepatologist in Pathophysiology department of Laiko General Hospital since 2015. His research concerns mainly liver fibrosis and autoimmune liver disorders.

Anyou Wang

Feinstone Center for Genomic Research, University of Memphis, USA

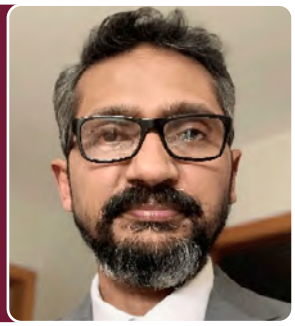
Evolutionary trajectory and origin of SARS-CoV-2

Alignment-based phylogenetics fails to uncover the evolutionary trajectory and origin of SARS-CoV-2. This study develops a novel alignment-free system based on Fréchet distance and artificial recurrent neural network to reveal the evolutionary trajectory and origin of SARS-CoV-2 from more than two millions of genome sequences. SARS-CoV-2 gradually deletes its genome during its evolution, but the mutation rate varies with genome features. Among single nucleotides, C mutates fast but T changes slowly. C-prefix dinucleotide (e.g. CG and CT) loses dramatically fast during COVID-19 outbreaks. Similarly, the virus genome also deletes several trinucleotides prefixed by C (e.g. CCT). Interestingly, trinucleotide CCT and CT centrally control the entire SARS-CoV-2 genome, and their evolutionary trajectories fit COVID-19 case spike. Therefore C-prefixed feature deletions primarily contribute to COVID-19 pandemic.

SARS-CoV-2 variants undergo both vertical and horizontal deletions during their evolutionary trajectories to infect humans. Gradual vertical mutations help variants to increase their infection, but over-mutations reduce their infection potential. Horizontal mutations make variants gain diverse mutation markers, which dramatically increase virus infection capacity, leading to COVID-19 pandemic. Mink coronavirus variants mutate 56 genome features similar to SARS-CoV-2 wild type and they are the most likely origin of SARS-CoV-2. This origin trajectory follows the order: mink, cat, tiger, mouse, hamster, dog, lion, gorilla, leopard, bat, and pangolin. Therefore, the C-feature dynamic pattern serves as the key mark of the evolutionary trajectory SARS-CoV-2 genome, and mink-origin SARS-CoV-2 gradually deletes its genome to carry diverse mutations, causing COVID-19 pandemic.

Biography

Anyou Wang received his PhD from University of California, Riverside. His research interest is in computational biology, artificial intelligence and big data. Dr. Wang develops computational algorithms to catch up the big pictures from massive data and to understand the fundamental principles of biology (combai.org). He computed petabyte level data and revealed the distinctive functional regime of endogenous lncRNAs in dark regions of human genome and unearthed that noncoding RNAs endogenously rule the cancerous regulatory realm while proteins govern the normal. Recently, Dr. Wang also developed a novel alignment-free system integrating Fréchet distance and artificial recurrent neural network to reveal the evolutionary trajectory and origin of SARS-CoV-2 from more than two millions of genome sequences.



Saurabh Chattopadhyay*[1], Sukanya Chakravarty[1], Shumin Fan[1], Karan Chawla[1], and Ritu Chakravarti[2]

[1]Department of Medical Microbiology and Immunology, University of Toledo College of Medicine and Life Sciences, USA

[2]Department of Physiology and Pharmacology, University of Toledo College of Medicine and Life Sciences, USA

Regulation of IRF3 functions to control viral infections

We have recently conducted a high throughput screen of an FDA-approved drug library to isolate small molecule regulators of IRF3 activities. IRF3 is a well-known transcription factor for inducing interferon (IFN) genes in response to viral infection. IRF3, upon virus infection, is activated by phosphorylation, leading to its translocation from the cytosol to the nucleus to transcribe the target genes, e.g., IFNs and IFN-stimulated genes (ISGs). We have uncovered that IRF3, in addition to its transcriptional activity, can trigger a direct apoptotic pathway in the virus-infected cells. In the apoptotic pathway, IRF3 is activated differentially by polyubiquitination to translocate from the cytosol to the mitochondria and activate the intrinsic apoptotic pathway. Together, both pathways are required for the optimal antiviral action of IRF3. To isolate FDA-approved compounds that can activate IRF3 functions, we performed a high throughput screen and isolated a number of compounds that activate IRF3 differentially for these two pathways. The presentation will highlight how the new regulators modulate the IRF3 activities to impact the viral replication.

Audience Take Away:

- The audience will learn how the virus-infected cells can mount antiviral programs and how we can use drugs to modulate these responses to control viral infection.
- Moreover, these mechanisms and concepts can be applied to other diseases, in addition to viral infection.

Biography

Dr. Saurabh Chattopadhyay is an Assistant Professor at the Department of Medical Microbiology and Immunology, University of Toledo College of Medicine and Life Sciences, Toledo, Ohio, USA. He did his PhD from the Indian Institute of Technology Delhi and then a postdoctoral fellowship at Cleveland Clinic. Dr. Chattopadhyay and his team are studying how the host innate immune responses can control virus infection and inflammatory diseases. He has published numerous research articles in the area of viral immunology.

SPEAKERS

DAY 01

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Naveen Khatri*, Harkesh

College of Pharmacy, Pt. BD Sharma, University of Health Sciences, India

Robotics in the field of virology

The stories of robots started surfacing from the start of 20th century and first autonomous robot capable of playing chess was introduced in 1912. Since then, many advancements in the field of robotics have been made and now wide range of robots are available to replace variety of human tasks. The first humanoid robot named “Sophia” was created by Hanson Robotics in 2016. Working conditions in many sectors like space, virology etc. are critical for human lives. Replacement of human beings with robots in areas that are critical to human lives can substantially reduce the risk of human life like handling virus samples in virology labs. Use of robots in different types of viral diseases including SARS provide more safety to human lives. Various medical institutes used robots for testing during coronavirus. Asimov Robotics created a robot to spread awareness about the coronavirus. Robots have also been used for monitoring patients, makings vaccines and medicine, sanitizing hospitals, making deliveries, sample analysis, and cleaning tasks. All these applications of robots are aimed to avoid exposure to virus, save the time and human labor. Till now most of the robotic works are directly controlled by human beings while few are automated. Future of robotics is fascinating where robots would be freestanding, independent and self-growing. With the advancements in artificial intelligence robots would be independently capable of research & development arena and dealing with patient related activities.

Audience Take Away:

- From this presentation, audience would be able to know the history of robotics, how it started & predict the future of robotics.
- Audience will come to know the benefits of the robot in the hospitals, pandemics, and production of medicines.
- Audience can implement this knowledge to their research, they can use robotics in their field to get several benefits.
- This is a review that other faculty could use to expand their research or teaching.

Biography

Dr. Naveen Khatri is working as Assistant Professor in College of Pharmacy, Pt. B. D. Sharma, University of Health Sciences, Rohtak, Haryana since 2006. He has more than 17 years of teaching and research experience. He did his B. Pharm. degree from MDU, Rohtak and M. Pharm. degree from GJU, Hisar. He did his Ph.D. under the guidance of Prof. A. K. Madan. All his research papers are published in high impact factor international journals. His research interest is QSAR, Molecular Modeling, design and development of novel molecular descriptors. He has conceptualized novel molecular descriptors which have immense utility in drug development. He is an expert in the field of pharmaceutical analytical techniques.

J.A.A.S. Jayaweera*, W.W. Kumbukgolla and N.P. Sunilchandra

Department of Microbiology, Rajarata University of Sri Lanka, Sri Lanka

Hantavirus infections and the occurrence of chronic kidney disease of uncertain etiology in the north central province of Sri Lanka

Chronic Kidney disease of uncertain etiology (CKDu) has become a significant disease burden, affecting farming community of Sri Lanka and the exact etiology, which could be multifactorial, is not hitherto established. This study is aimed to determine the association of past Hantavirus infection and leptospirosis with the occurrence of CKDu. A cohort (n = 179) of known CKDu patients living in high-CKDu prevalent areas of Anuradhapura district of Sri Lanka was compared with a group of 49 healthy, sex-matched younger blood relatives of CKDu patients (control-1) and another 48 healthy, age, and sex-matched individuals living in low-CKDu prevalent area (control-2) of the same district where same life style and climate conditions prevail.

Fifty out of 179 (27.9%) CKDu patients, 16/49 (32.7%) of control-1 and 7/48 (14.6%) of control-2 were found positive for IgG antibodies to Puumala, Hantaan or both strains of Hantaviruses. Hantaan strain specificity was found to be predominant in all study groups. Hantavirus IgG sero-prevalence of healthy individuals living in low-CKDu prevalent area was significantly lower compared to CKDu patients and healthy younger blood relatives living in high-CKDu prevalent areas ($p = 0.03$). Past Hantavirus infection possesses a significant risk for the occurrence of CKDu (OR = 4.5; 95% CI-3.1-5.4, $p = 0.02$). In contrast, IgG seroprevalence to Hantaviruses was not significantly different in CKDu patients and healthy younger blood relatives living in high-CKDu prevalent areas indicating past Hantavirus infection has no association with the occurrence of CKDu or possibly, younger relatives may develop CKDu in subsequent years. Seroprevalence to leptospirosis showed no significant difference between CKDu patients and healthy controls.

Audience Take Away:

- CKDu is burden in tropical countries and knowledge on disease aetiology is still evolving. Herein, we have postulated the previous exposure to Hantavirus and development of CKDu.
- This association would open up an infectious aetiology and implementing infection control strategies will be helpful to reduce the development of CKDu.

Biography

Dr. J.A.A.S. Jayaweera acquired his MD in medical microbiology and MPhil in medical virology. Dr. Jayaweera has over ten years of research experience in microbiology, biochemistry, nano-biotechnology, complementary and alternative medicine, and biostatistics. He has so far published more than 30 research articles in international peer-reviewed journals. He has won several international awards, and he is serving as a reviewer for many reputed groups of journals in the Global Journal of Medical Research and BMC antimicrobials and infection control. Further, he is an honorary editor in the Annals of clinical immunology and microbiology journal and the chief editor in Asian journal of dermatological sciences.

Rosamaria Pennisi*, Maria Pia Tamburello, M. T. Sciortino
Department of Chemical, University of Messina, Italy

The HSV-1-tegument protein Us11 is enrolled in the Caspase-8 cleavage

The ability of Herpes simplex virus-1 (HSV-1) to replicate and spread is due to several virulence factors which hamper the antiviral response. HSV-1 is known to modulate several intracellular signaling pathways including the FADD/caspase-8 death-signalling. Caspase-8 is an initiator caspase which normally triggers the apoptotic event following its activation mediated by proteolytic processing. Besides its role in apoptosis, pro-survival functions of caspase-8 were described. HSV-1 it is known to efficiently modulate apoptosis to promote its replication through the expression of several virulence factors. One of them is the tegument protein Us11, which is known to counteract the heat and staurosporine-induced apoptosis as well as the autophagy response. Based on this, the aim of this study was to: i) investigate the role of US11 on canonical caspase-8 functions related to apoptosis response; ii) verify the physical interaction of Us11 and caspase-8 in the contest of viral infection as well as in a cell-free in vitro system (iii) investigate the role of caspase-8 on HSV replication. The human monocytic leukemia cells (THP-1), embryonic kidney cells (293T), and wild type and caspase-8 deficient ($CASP8^{-/-}$) epithelial cells derived from a larynx carcinoma (HEp-2) were employed as models with different permissivity to viral infection in order to study the role of caspase-8 during HSV-1 replication. A combinatory approach of HSV-1 mutant (R3630-ΔUs11/ΔUs12) infection and Us11- and Us12-encoding plasmid transfection was employed to investigate the ability of Us11 to interact with caspase-8. Moreover, GST-Us11 and GST-caspase-8 recombinant proteins were produced by using the Baculovirus Expression Vector System (BEVS) technology proteins and used to verify the interaction of these proteins in a cell-free system.

Our results can be summarized as follows: i) HSV-1 accumulates caspase-8-p18 active fragment in US11-dependent manner in both monocytes and epithelial cells; ii) Us11-recombinant protein induces caspase-8-p18 cleavage by physically interacting with the caspase-8 recombinant protein as reported by immunoprecipitation assay in infected cells and by Caspase-8 cleavage assay in cell-free system; iii) the canonical cleavage of procaspase-8, induced during HSV-1 and R3630 infection, results in apoptosis induction as confirmed by p43/41-dependent PARP and caspase-3 cleavage otherwise, Us11-dependent p18 accumulation does not trigger apoptosis. Therefore, to understand the biological role of Us11-dependent p18 accumulation we analyzed Atg3 protein as a representative substrate of activated caspase-8 protein during HSV-1 replication. We found that HSV-1 specifically cleaves Atg3 protein as shown by the reduction in the full-length protein compared to the basal levels and by detecting cleavage fragment. Otherwise, the addition of the caspase-8 inhibitor z-IETD-fmk as well as the transfection with a pool of chemically synthesized caspase-8 siRNAs resulted in the block of Atg3 cleavage suggesting a direct connection between the activation of caspase-8 mediated by HSV-1 and Atg3 degradation. This ubiquitously expressed mechanism in THP-1 and HEp-2 cells, allow us to investigate the role of caspase-8 during viral replication by comparing the cytopathic effect, viral title, viral DNA accumulation and the HSV-1 proteins cascade expression in wild type HEp-2 ($CASP8^{+/+}$) and $CASP8^{-/-}$. Our finding report that the accumulation of viral proteins and DNA, as well as virus yield, were affected in $CASP8^{-/-}$ suggesting that caspase-8 might have a pro-viral role during HSV-1 replication. Therefore, we speculate that the "non-canonical" activation of caspase-8 by HSV-1 can be a new viral immune escape mechanism to, through the fragmentation of ATG3, block autophagy and support better replication.

Audience Take Away:

- The pandemic period that we are living has demonstrated that the best way to respond to viral infection is the knowledge of host-virus interaction to predict human susceptibility to viral infections. Thus, knowledge of immune evasion will help us better understand the pathogenesis of viral infection, and provide insights into developing antiviral strategies and improvement of vaccines.

- Our findings report a new evasion strategy employed by HSV-1 which support viral replication. Thus, these findings can be useful to formulate new therapeutics and vaccines which interfere with a specific pathway and prevent and treat herpetic infections.
- The virus can subvert the host intracellular pathways to support better replication. This work highlights how a cellular pathway, previously related to death event, can be subverted by virus to promote better replication.

Biography

Dr. Pennisi studied Biology at the University of Messina, Italy and graduated as MS in 2014. She joined the research group of Prof. Sciortino at the University of Messina working in the field of Virology, analyzing the molecular pathways linked to immune evasion during HSV-1 infection. She received her PhD degree in 2018 at the same institution. She collaborated with foreign research groups such as IARC in Lyon, SIIBR in Shenzhen and University of Turku in Finland, as documented by the related scientific production which were carried out in collaboration with. After two- year postdoctoral fellowship supervised by Prof. Zhou Grace at the International Institute for Biomedical Research (SIIBR) in Shenzhen, she obtained the academic position as a researcher in Microbiology at the University of Messina and the host-virus interaction and the molecular pathways involved in the regulation of the innate immune response mediated by HSV-1.

Maira Zorzan*, P. Drzewniokova, B. Zecchin, B. Tramontan, S. Leopardi, P. De Benedictis

Istituto Zooprofilattico Sperimentale delle Venezie, Italy

An innovative in vitro system to replace in vivo experiments for rabies diagnostic interlaboratory trials: A sustainable application of the 3Rs principle

Post-mortem laboratory diagnosis of rabies is based on methods for detecting viral antigens, viable virus or viral nucleic acids with the current reference and gold standard technique, the Direct Fluorescent Antibody Test (DFA). Interlaboratory trials (ILTs) for rabies diagnosis are organized to assess the diagnostic capacity of participating laboratories, the interlaboratory variability of results and the diagnostic methods in use. The samples included in the ILT panel are usually produced by the intracerebral inoculation of mice, meaning that thousands of animals are sacrificed every year. Distress, pain and severe suffering are a natural consequence of the virus inoculation procedure and, particularly, of the experimental endpoint represented by overt nervous symptoms of rabies infection. The aim of the present work is to validate a sustainable in vitro system to replace *in vivo* experiments for preparing rabies positive samples for proficiency test (PT) exercise. The innovative in vitro technique is based on the *in vitro* replication of rabies virus, the collection and quantification of infected cells and the dilution of this material in field brain tissue previously tested negative for rabies. As currently done for samples prepared with mouse brain, cell-based samples are then lyophilized to better preserve proteins and nucleic acids. This *in vitro* method was first developed using the fixed rabies virus strain CVS-11 and then adapted to several African strains belonging to different lineages (Africa 2, Africa 3, Cosmopolitan). To this purpose, rabies viral strains previously isolated from field samples were adapted to cell culture through serial cell passages.

The *in vitro* growth conditions were optimized to maximize the yield of the virus produced and the percentage of infected cells obtained. The infected cells/brain tissue ratios necessary to simulate samples with different degrees of positivity were also experimentally defined. All samples prepared by cell-based methods were successfully analysed by major rabies diagnostic techniques, including DFA, virus isolation in cell culture, real time RT-PCR and end point RT-PCR. To validate the in vitro method of preparation of PT panels, homogeneity and stability tests were also performed up to two months after samples preparation, in accordance with international guidelines (ISO/IEC 17043 e ISO 13528). A pilot interlaboratory trial is currently being organized; a panel prepared through the innovative in vitro system will be sent together with a panel prepared by the standard *in vivo* method. Both panels will be analysed by 26 laboratories participating on a voluntary basis to the proficiency test 2022 for the diagnosis of animal rabies, organized by the FAO and National Reference Centre for rabies at the Istituto Zooprofilattico Sperimentale delle Venezie (Italy). The *in vitro* and *in vivo* samples will be blind-coded and analysed by DFA and/or RT-PCR, at the discretion of the participating laboratory. Statistical analysis of results from testing both sample panels will be performed in May 2022 and will highlight any significant differences between the two production methods. This interlaboratory exercise will be used to definitively validate the *in vitro* system for producing rabies positive samples.

Audience Take Away:

- The introduction of an *in vitro* system to prepare samples for interlaboratory proficiency exercises for rabies diagnosis represents a significant improvement of animal welfare and a novel implementation of the Three Rs principle (Replacement, Reduction and Refinement), the ethical oversight of scientific animal care and use worldwide.
- The present work provides the proof of principle that a complete replacement of animals currently used for preparation of rabies positive samples is actually possible thanks to the newly developed method based on dilution of rabies-infected cells in field brain material.
- The innovative *in vitro* method is absolutely sustainable as no laboratory animals are required for the production of rabies positive material, while uninfected samples are usually available in large amounts in regions where effective surveillance plans for rabies are applied in the field.

- Thus, this method can be adopted by all reference centers that regularly organize proficiency tests for rabies diagnosis, avoiding the experimental infection and sacrifice of thousands of mice every year and reducing the risks for operators.

Biography

Maira Zorzan graduated in Medical Biotechnologies at Padua University, Italy in 2014. She worked for 4 years in the field of Neurosciences at the Department of Molecular Medicine, University of Padua and in 2018 she earned her PhD degree. In 2018, she joined the Laboratory for zoonosis, emerging and remerging pathogens, National and FAO Reference Centre for rabies at the Istituto Zooprofilattico Sperimentale delle Venezie in Padua as a postdoctoral research fellow. In 2020, the Italian Ministry of Health awarded her as principal investigator of a Starting Grant focused on the development of novel in vitro systems to replace animal use in rabies diagnostic inter laboratory trials.

Giulia Franzoni*[1], Susanna Zinellu[1], Elisabetta Razzuoli[2], Lorena Mura[1], Chiara Grazia De Ciucis[2], Livia De Paolis[2], Antonio Anfossi[3], Simon Paul Graham[4], Bernardo Chessa[3], Silvia Dei Giudici[1], Annalisa Oggiano[1]

[1]Istituto Zooprofilattico Sperimentale della Sardegna, Italy
[2]National Reference Center of Veterinary and Comparative Oncology (CEROVEC), Italy
[3]Department of Veterinary Medicine, University of Sassari, Italy

Targeting toll like receptor 2: Porcine macrophages primed for enhanced cytokine responses and increased susceptibility to african swine fever infection

Toll-like receptor 2 (TLR2) ligands are attracting significant attention as prophylactic and immunopotentiator agents against several viruses. We investigated the impact of a synthetic diacylated lipopeptide (Mag-Pam2Cys_P48) on porcine monocyte-derived macrophages (moMΦ) and we observed that it induced up-regulation of activation markers and release of pro-inflammatory cytokines. Then, we investigated its role in modulating macrophages responses against African swine fever virus (ASFV), the aetiological agent of a great threat to the global pig industry. The impact of Mag-Pam2Cys_P48 on moMΦ responses to two ASFV isolates of diverse virulence (the attenuated NH/P68 and the virulent 26544/OG10) was analyzed. Untreated and Mag-Pam2Cys_P48-treated moMΦ were infected using a multiplicity of infection (MOI) of 1, and we observed that Mag-Pam2Cys_P48 did not influence virus infection nor its modulation of surface markers expression 21 h post-infection. However, Mag-Pam2Cys_P48 treated moMΦ released higher levels of IL-1α, IL-1β, IL-1Ra, IL-18 in response to infection with the attenuated NH/P68 ASFV compared to mock-infected controls. The effect of this diacylated lipopeptide to influence ASFV ability to grow in moMΦ was also investigated. When infected using a MOI of 0.01, Mag-Pam2Cys_P48 enhanced the ability of both NH/P68 and 26544/OG10 strains to replicate in moMΦ. These results suggest that ASFV developed mechanisms to enhance replication in macrophages in a pro-inflammatory state. Although our data suggest caution in the use of TLR2 agonists as prophylactic or immunopotentiator agents against ASFV, we provided a better understating of how the virus eludes host defences, hopefully aiding the rational design of therapeutic strategies against ASFV.

Audience Take Away:

- Immunomodulatory impact of a TLR2 agonist on porcine macrophages.
- Impact of a TLR2 agonist on porcine macrophages infection and responses to ASFV, one of the greatest threats to the swine industry.
- Better understanding on how ASFV evades host defenses.
- Differences in macrophage responses to ASFV strains of diverse virulence.

Biography

Dr. Giulia Franzoni studied Veterinary Medicine at the University of Parma, Italy and graduated with honors in 2008. Soon after she joined the research group of Prof. Simon Paul Graham at Animal Health Plant Agency(formerly known as HAHVLA), United Kingdom. She received her PhD degree in 2013 at the University of Surrey (UK). In 2014, she joined the Virology Laboratory of the Istituto Zooprofilattico Sperimentale della Sardegna, Italy, where she is currently employed as an Expert Veterinarian in several project on ASFV, including the EU Project 'VACDIVA'. Her main research activities focused on ASFV immunology and porcine macrophage polarization.

Anna Pikuła
Department of Poultry Disease, Poland

Evolutionary and phenotypic characterization of reassortants of infectious bursal disease virus (IBDV) circulating in Europe

Infectious bursal disease virus (IBDV) is a bi-segmented dsRNA virus that causes worldwide serious economic losses in poultry production. Recently, the emergence and circulation of novel reassortants of IBDV (assigned to A3B4 genotype) containing the segment A from very virulent strains and segment B from an unidentified source, was reported in Europe. Interestingly, these strains competed with the well-established very virulent IBDV, becoming prevalent in Poland and disseminating to other countries in Europe. In the present study, we analysed the evolution and dynamics of infection under *in vivo* conditions compared to a very virulent strain. As shown by the temporal analysis, tMRCA for segment A and B of the A3B4 IBDV genotype, were determined around 1988 (95% HDP: from 1984 to 1992) and 1981 (95% HDP from 1978 to 1992), respectively, indicating a likely reassortment time in the late 1980s that coincides with the first detected field strain in 1992. Moreover, the estimated evolutionary rates for this lineage is considerably high for both segments, suggesting that these strains are in a fast-rate evolutionary process. In turn, from the population dynamics reconstruction, it was inferred that the reassortants has increased its genetic diversity that could be indicative that the new genetic constellation enhance their genetic fitness.

The infection of five-week old SPF chickens with the novel reassortant strain (genotype A3B4) and very virulent isolate (genotype A3B2) caused clinical symptoms (depression, ruffled feathers and diarrhoea), gross lesions (enlarged and mottled spleens with necrotic foci, swollen kidneys or congested duodenum) and mortality (rA3B4: 20% and A3B2: 50%). Moreover, both strains replicated in examined lymphoid and non-lymphoid tissues with comparable efficiency, while a significant higher RNA load of vvIBDV was observed at 2 and 7 dpi in bursa, and at 7 dpi in spleen, cecal tonsils and proventriculus. In turn, birds infected with the reassortant strain showed severe and precocious bursa atrophy at 4 dpi, while in birds infected with vvIBDV from 7 dpi onwards. Moreover, reduced weight gains of infected birds from 4 and 7 dpi was observed in the reassortant and very virulent group, respectively. The results obtained confirm that the acquired viral polymerase (encoded by segment B) of A3B4 IBDV firstly provides greater diversity of this genetic lineage, and secondly does not adversely affect the ability to multiply in the host. These strains are fuelled by efficient replication in lymphoid and non-lymphoid organs, but due to lower mortality rate, the presence of virus may be less pronounced and consequently facilitate their spread. Moreover, the resulting immunosuppression and poor performance indicates that these strains pose a threat for poultry production.

Audience Take Away:

- The results presented here provide an interesting example of the evolution of pathogenic viruses. Reassortment is an important mechanism that triggers viral evolution among RNA viruses with segmented genome and can lead to host switching, altered virulence properties and enhanced transmissibility, thus consequently changes the epidemiological situation.
- As demonstrated by computational and in vivo studies, the population of A3B4 genetic lineage of infectious bursal disease virus has acquired a number of adaptive features, such as an increased fitness landscape in the viral quasispecies composition and better adaptability to dissimilar environmental conditions, and consequently becoming the dominant population.
- The reassortant strains also exhibited a decreased virulence, which also can facilitate their spreading.

Biography

Dr. Pikuła studied Biology at the University of Maria Curie-Skłodowska, Poland and graduated as MS in 2003. She then joined the research group of Prof. Minta at the National Veterinary Research Institute, Poland, Pulawy (PIWet). She received her PhD degree in 2016 at the same institution. She has published dozens of scientific articles including 17 from JCR-listed journals.

Nashwa Elsayed Mohammed Ibrahim Elkasaby*[1], Maysaa El Sayed Zaki[2]

[1]Department of Medical Microbiology and Immunology, Mansoura University, Egypt

[2]Department of Clinical Pathology, Mansoura University, Egypt

Study of Hepatitis E virus in blood donors

Hepatitis E (HEV) is a major health problem affecting around one third of the world population. The prevalence of antibodies to HEV among blood donors have been documented in several countries in Europe and Asia. The aims of the study were to estimate the seroprevalence of hepatitis E antibodies among healthy blood donors and to explore the factors associated with positive HEV antibodies among healthy blood donors. Moreover, to detect HEV viremia by real time polymerase chain reaction among seropositive blood donors for HEV. The study included 200 apparent healthy blood donors from Dakahlia Governorate, Egypt. Blood samples were collected from the blood donors for serological determination for specific hepatitis E virus immunoglobulin G (anti-HEV IgG) and specific hepatitis E virus immunoglobulin M (anti- HEV IgM). Positive samples for anti-HEV IgM were further subjected for determination of HEV-RNA by real time Polymerase Chain Reaction (PCR). Anti-HEV-IgG was positive in 50 donor (25%) anti-HEV-IgM was positive in 10 donors (5%) and HEV-RNA was positive in 6 donors (3%).

The comparison between blood donors positive for anti-HEV-IgG and negative blood donors negative reveals significant association between anti-HEV-IgG and donors with older age (42.0 ± 9.7,P = 0.001),rural residence (76%, P = 0.001), workers in agricultural works (92%, P = 0.035) and elevated AST (31.28±14.28, P = 0.04). Regarding viral markers, there was significant prevalence between positive anti-HCV-IgG and positive anti-HEV-IgG (P = 0.003). Univariate analysis for risk factors associated with positive anti-HEV IgG reveals significant prevalence with older age (P = 0.001), rural residence (P < 0.001), positive anti-HCV- IgG (P = 0.004) and increase in AST (P = 0.045). However, on Multivariate analysis HEV infection was independently prevalent with older age (P < 0.001) and rural residence (P = 0.002).

Audience Take Away:

- The present study highlights that HEV seroprevalence in blood donors is common finding. Further finding is the statistically significant correlation between antibodies to HCV and serological markers for HEV and even HEV viremia.
- Longitudinal studies may be needed to explore the clinical significance and cost effectiveness of screening of the blood donors for hepatitis E virus by serological tests and/or detection of viremia by Molecular testing.

Biography

Dr. Nashwa Elkasaby, MSc, PhD is an associate professor of Medical Microbiology and immunology at the University of Mansoura. She received her, Ph.D. degree in Medical Microbiology with a specialization in Virology 2011 from Faculty of Medicine, Mansoura University, Egypt. Dr. Nashwa has an experience of more than 15 years in research and teaching and has collaborated with researchers from different countries. Alongside her academic work, Dr. Nashwa was an active member in Infection prevention and control Committee and Antibiotic Stewardship Programs in Mansoura university hospitals (Egypt) and Sohar hospital (Oman).

Athanasios-Dimitrios Bakasis

National and Kapodistrian University of Athens, Greece

Immunogenicity, safety, and efficacy of the novel SARS-CoV-2 vaccines in patients with systemic rheumatic diseases

Systemic rheumatic disease (SRD) patients under immunosuppressive/immunomodulatory therapy are at a higher risk for COVID-19 hospitalization and worse outcomes compared to the general population and as such, were prioritized for immunization against SARS-CoV-2 before the general population. SRD patients, demonstrating hyporesponsiveness to non-COVID-19 vaccines, either were excluded or included in a relatively small number in phase II/III clinical trials evaluating the efficacy and safety of the SARS-CoV-2 vaccines. This presentation aims to review data from the published literature, including our department's findings, regarding humoral immune responses in patients with SRD after SARS-CoV-2 vaccination. SRD patients show decreased seroconversion rates and cellular immune responses compared to individuals of similar age and sex not on immunosuppressive treatments.

High risk factors negatively associated with antibody responses are increased age and use of rituximab, mycophenolate, and glucocorticoids. Results regarding methotrexate and anti-cytokine treatment remain controversial. Therefore, treatment modifications during SARS-CoV-2 vaccination were rapidly recommended by experts and rheumatology societies; (a) temporal withhold (1-2 week and/or after dose administration) of conventional synthetic disease modifying drugs, (b) decrease in corticosteroids dose and (c) longer time intervals between immunization and rituximab administration until B-cell repopulation. As far as safety is concerned, adverse events (such as pain at the injection site, fatigue, fever), though common, were mild, self-limiting, and comparable to those reported among healthy individuals. Among disease flares of the underlying SRD reported (up to 10% of vaccinated patients), the majority were mild not necessitating treatment adjustments. Data on efficacy of SARS-CoV-2 vaccination in SRD patients are now emerging and fully vaccinated SRD patients with breakthrough COVID-19 demonstrate better outcomes compared with unvaccinated counterparts with similar disease/treatment characteristics. Importantly, most breakthrough infections occur in cases where social preventive measures were omitted. Finally, recent reports have additionally shown the ability of a third dose to induce immune responses in non-responders and boost responders and only those SRD patients treated with rituximab exhibit a significant high risk of not responding.

Audience Take Away:

- Identify patients with systemic rheumatic diseases who are less likely to develop insufficient humoral immune responses after SARS-CoV-2 vaccination.
- Adopt specific vaccination strategies for patients with systemic rheumatic diseases in order to dampen the effect of immunosuppressive therapy and achieve the best possible immune responses following SARS-CoV-2 vaccination.
- Vaccine-induced immunization against SARS-CoV-2 is safe and efficacious for preventing severe COVID-19 and adverse outcomes in patients with systemic rheumatic diseases; however, social protection measures remain the core stone during COVID-19 pandemic.

Biography

Dr. Bakasis studied Medicine at the School of Medicine, University of Ioannina, Greece and graduated in 2018. He then completed his general training in Internal Medicine at the Department of Pathophysiology at "Laiko" University Hospital, Athens, Greece. At the same institution, he joined the research group of Prof. Haralampos M. Moutsopoulos and Athanasios G. Tzioufas and attended a PhD program on COVID-19. More specifically, he examines the clinical presentation and outcomes of COVID-19 in patients with systemic rheumatic diseases, as well as the immunogenicity, safety, and efficacy of the novel SARS-CoV-2 vaccines in such patients.

Olivia Munoz*[1], Riddhima Banga[1], Rachel Schelling[1], Francesco Andrea Procopio[1], Andrea Mastrangelo[1], Pauline Nortier[1], Khalid Ohmiti[1], Jean Daraspe[2], Matthias Cavassini[3], Craig Fenwick[1], Laurent Perez[1], Matthieu Perreau[1]

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Active PD-L1 incorporation within HIV virions functionally impairs T follicular helper cells

The limited development of broadly neutralizing antibodies during the course of HIV infection is classically attributed to an inadequate B-cell help brought by functionally impaired T follicular helper (Tfh) cells. However, the determinants of Tfh functional impairment and the signals contributing to this condition remain elusive Interestingly, Tfh cells express high level of functionally active PD-1, however, in LNs, PD-1 ligands *i.e*. PD-L1 and PD-L2 are predominantly expressed on cells locating in extrafollicular area. These data suggest that the source of immune checkpoint ligands (IC-Ls) interfering with Tfh cell functionality might not be dependent on the tissue expression of IC-Ls.We therefore hypothesized that membrane-bound extracellular vesicles such as exosomes and/or HIV virions may incorporate functionally active IC-Ls that may subsequently interfere with Tfh cell functionality. In the present study, we showed that HIV virions represent the major source (>70%) of PD-L1+ extracellular vesicles as compared to exosomes in plasma of viremic HIV-infected individuals, which translated into a significant increase of soluble plasmatic PD-L1 levels. Furthermore, PD-L1 incorporation within plasmatic HIV virions was more frequently detected than HLA-DR (PD-L1=37.5%; HLA-DR=23.3%), demonstrating the preponderance of this phenomenon *in vivo*.

In addition, we showed that PD-L1 is incorporated within HIV virions during budding processes, through an active mechanism involving p17 HIV matrix protein interactions with the cytoplasmic tail of PD-L1. Using a reconstructive approach, we subsequently showed that *in vitro* produced PD-L1^{high} but not PD-L1low HIV virions, significantly reduced Tfh cell proliferation and IL-21 production, which ultimately translated into reduced IgG1 production from LN germinal center B cells. Interestingly, Tfh cell functions were fully restored in presence of anti- PD-L1/2 blocking mAbs treatment, demonstrating that the incorporated PD-L1 proteins were functionally active. Taken together, the present study unveils an immunovirological mechanism by which HIV specifically exploits the regulatory potential of PD-L1 to suppress the immune system during the course of HIV infection.

Audience Take Away:

- First, this study proposes to re-evaluate the role of soluble IC-L in the functional alteration of T cells during HIV infection.
- Second, this study highlights a novel active mechanism by which HIV exploits a physiological mechanism developed to protect tissues from collateral damages associated with unregulated immune responses.
- These new observations were made possible by the development of a novel methodology combining the immunocapture of HIV virions and a comprehensive characterization by mass cytometry of host molecules incorporated into HIV virions.

Biography

Olivia Munoz studied medical biology with a focus on immunology and cancer at the University of Lausanne (Switzerland) and graduated as MS in 2018. She then joined the research group of Prof. Matthieu Perreau at the Services of Immunology and Allergy (IAL) of the Lausanne University Hospital (CHUV) in 2018 to start her PhD working on HIV pathogenesis.

Zainab Alsharef*[1], Desiree Van Oorschot[2], Abdullah Alkhenizan[3], Ahmed Mohy[4], Thatiana Pinto[5]

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Public health impact of introducing an adjuvanted recombinant zoster vaccine in the kingdom of Saudi Arabia

Immunosenescence due to ageing or an immunosuppressed condition may lead to the reactivation of latent varicella-zoster virus, resulting in Herpes Zoster (HZ), also called Shingles. Without vaccination, 30% of people will develop HZ during their lifetime.1,2 Recently, the adjuvanted recombinant zoster vaccine (RZV) was approved for public market use in Saudi Arabia. This study evaluated the public health impact (PHI) of introducing an adjuvanted RZV to the Saudi population ≥50 years of age (YOA) compared with no vaccination scenario. The ZOster ecoNomic Analyses (ZONA) model was used to estimate the PHI of introducing RZV versus no vaccination. The base-case population considered a 2016 Saudi Arabia cohort of 4,424,203 individuals aged ≥50 YOA eligible for vaccination. In addition to this demographic survey, the United Nations population prospects for Saudi Arabia (≥85 YOA) in 2020 were used to calculate all-cause mortality probability. Calculations were based on HZ incidence data from a worldwide meta-regression[3]. The proportion of post-herpetic neuralgia (PHN) cases, general practitioner (GP) consultations and complications were obtained from a Saudi study.4 It was assumed a first-dose coverage of 80% and 70% compliance for the second dose of RZV. Vaccination with RZV versus no intervention would avoid 502,506 HZ cases, 77,386 PHN cases, 19,899 complications and 659,144 GP consultations. Amongst the whole eligible population aged ≥50 YOA, the greatest PHI with RZV could be achieved in the 50–59 YOA age group. The estimated number needed to vaccinate to prevent 1 HZ case was 8 with RZV. The present study shows that vaccinating with RZV can alleviate some of the disease burden due to HZ in KSA.

Audience Take Away:

- Raising awareness of adult vaccination including Recombinant Zoster Vaccine (RZV).
- To always consider prevention “with vaccination” as a first option with older adults which is part of healthy aging concept.
- Practicing vaccination against HZ and its complication in population ≥50 years.
- The vaccinators (family medicine specialists and GPs) will be able to identify the importance of RZV in their practice based on the public health impact that have been demonstrated in our model.

Biography

Dr. Zainab studied medicine & surgery at King Abdulaziz University, Jeddah, KSA and graduated as physician in 2012. Joined the Saudi board of internal medicine at King Fahd General Hospital, Jeddah, KSA in 2013. She received her MSc in international health from Vrije University, The Netherlands in 2019. She joined GSK as Vaccines Medical Advisor in 2020.

Pallavi Rai*, Emily M. Webb, Chelsea Cereghino, Jeffrey M. Marano, James Weger-Lucarelli

VA-MD Regional College of Veterinary Medicine, United States

Determining the role of obesity on the transmission of chikungunya virus by mosquitoes

Mosquito-borne alphaviruses like chikungunya (CHIKV), Mayaro (MAYV) and Ross River (RRV) virus are distributed globally and cause sporadic disease outbreaks characterized by chronic debilitating polyarthralgia. Of these, CHIKV is the most medically relevant due to its re-emergence over the last two decades, leading to major outbreaks across Africa, Asia, Europe, and the Americas. Emergence and re-emergence of RNA viruses like CHIKV is due to their rapid and error-prone replication that enables them to adapt to varying environmental conditions. One such mutation (A226V) in the E1 protein of CHIKV expanded its vector range and improved its transmissibility to the vertebrate host. However, a critical gap exists in identifying the host factors affecting the transmission of arboviruses by the vector and leading to its emergence/re-emergence. Recently it was shown that the obesity-related microenvironment promoted the emergence of virulent strains of influenza virus and has been identified as a risk factor for severe disease outcome for other viruses like SARS-CoV-2, WNV and several alphaviruses. This is concerning because obesity affects ~13% adults globally and 43% adults in the United States. Here we show that obesity reduces the infection and transmission of CHIKV by mosquitoes.

To understand the influence of obesity on alphavirus transmission, we utilized a natural transmission cycle between CHIKV-infected lean or diet-induced obese (DIO) mice and Aedes aegypti mosquitoes. We showed that mosquitoes fed on CHIKV-infected DIO mice had significantly lower infection and transmission rates than those fed on CHIKV-infected lean mice, despite ingesting similar amounts of virus. Towards understanding the host molecular drivers influencing this shift, we found significantly elevated insulin levels in DIO mice at peak viremia, as compared to lean mice. Mammalian insulin has been shown to reduce the replication of various arboviruses in mosquito cells and live mosquitoes through the involvement of mosquito antiviral immune pathways. RT-qPCR analysis on the midguts of mosquitoes fed on CHIKV-infected DIO mice showed significant upregulation of genes associated with various mosquito antiviral immune pathways, in alignment with insulin's impact on mosquito antiviral responses. Based on our preliminary studies and literature support, we hypothesize that insulin present in the blood of alphavirus infected DIO mice activates mosquito antiviral immune pathways, thereby limiting infection and transmission of the virus as compared to those fed on infected lean mice. Although studies demonstrating the role of insulin in reducing viral infection have previously been published, they suffer from drawbacks: a) none of them have used a natural transmission cycle between mammalian host and mosquitoes; b) none of them have shown the effect of insulin on transmission of the virus, which is the most relevant component of vector competence and c) with the exception of one study, other studies used insulin at concentrations much higher than the physiologically plausible levels in a mammalian host. With this study, we are pursuing the novel concept that obesity alters the transmission of arboviruses which would lay the foundation for future mechanistic studies to isolate the component(s) in an obese host responsible for this effect.

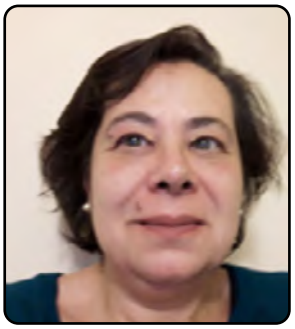
Audience Take Away:

- Obesity is a globally prevalent condition and has been widely studied for influenza in terms of disease severity and viral evolution. But its role in the transmission of arthropod-borne (arbovirus) diseases has never been studied using a natural transmission cycle. This research aims at studying a novel concept that obesity alters the transmission of alphaviruses by the mosquitoes.
- From this study, we can further dissect the components in an obese host that could be directly responsible for reducing the transmission of alphaviruses by the mosquitoes. This could aid research on other arboviruses to develop strategies to block their transmission and prevent disease outbreaks.

- We can further use this study to identify the role of host factors in the emergence of novel strains of virus e.g. is there a difference in the viral diversity obtained from mosquitoes fed on infected obese mice compared to the lean ones? Or are the viruses obtained from mosquitoes fed on infected obese mice more pathogenic and/ or more transmissible than those obtained from infected lean mice?

Biography

Pallavi Rai completed her Bachelors in Veterinary Science and Animal Husbandry from G. B. Pant University, India in 2008 and her Post-graduate Diploma in Agri-warehousing and Supply Chain Management from MANAGE, Hyderabad, India in 2009. She is currently a third tear PhD student in the Weger-Lucarelli lab at Virginia Tech. The focus of her research is to study the effect of obesity on the transmission of alphaviruses like CHIKV and the disease severity of coronaviruses using the mouse hepatitis virus (MHV) as a model coronavirus. She has published 1 article and co-authored 3 articles till date.



Maria D. I. Manunta*[1], Giuseppe Lamorte[1], Francesca Ferrari[1], Elena Trombetta[2], Mario Tirone[2], Cristiana Bianco[1], Alessandra Cattaneo[2], Luigi Santoro[1], Guido Baselli[1], Manuela Brasca[1,3], Mahnoosh Ostadreza[1], Elisa Erba[1,3], Andrea Gori[4,5], Alessandra Bandera[4,5], Laura Porretti[2], Luca V. C. Valenti[1,6], Daniele Prati[1]

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[6]Department of Pathophysiology and Transplantation, Italy

Impact of SARS-CoV-2 virus on peripheral blood mononuclear cells isolation procedure

SARS-CoV-2 virus infection is responsible for coronavirus disease (COVID-19), which is characterised by a hyperinflammatory response that plays a major role in determining the respiratory and immune-mediated complications of this condition. At the beginning of the pandemic, while isolating peripheral blood mononuclear cells (PBMCs) from whole blood of COVID-19 patients by density gradient centrifugation, we noticed some changes in the floating properties and in the sedimentation of the cells on density medium. Investigating this further, we found that in early phase COVID-19 patients, characterised by reduced circulating lymphocytes and monocytes, the PBMC fraction contained surprisingly high levels of neutrophils. Furthermore, the neutrophil population, analysed by flow cytometry, exhibited alterations in the cell size and in the internal complexity. This finding is consistent with the presence of low density neutrophils (LDNs) and immature forms which may explain the shift seen in the floating abilities and that may be predictive of the severity of the disease. The percentage of this subset of neutrophils found in the PBMC band was rather spread (35.4±27.2%, with a median 28.8% and IQR 11.6-56.1, Welch's t-test early phase COVID-19 versus blood donor healthy controls $P<0.0001$). Results confirm the presence of an increased number of LDNs in patients with early stage COVID-19, which correlates with disease severity and may be recovered by centrifugation on a density gradient together with PBMCs.

Audience Take Away:

- The infection of SARS-CoV-2 can affect the floating properties and in the sedimentation of the blood cells on density medium.
- The sedimentation on density gradients of blood cells is an easy method to assess an alteration in the cell composition of the circulating blood.
- The cell populations collected post-ficoll were assessed using an automated hematology cell analyser, which is inexpensive and available also in small peripheral hospitals and in low income countries.

Biography

Maria D.I. Manunta is currently working as biologist at the Fondazione IRCCS Ca' Granda Ospedale Maggiore Milan. She holds a Biological Sciences degree from the University of Sassari. She obtained the post-graduate specialisation in Microbiology and Virology from the University of Pisa. She received her Dr. rer. nat. (PhD) degree from the Johannes Kepler Universität Linz. She previously worked for the Italian National Health Service and as a researcher in the U.K., at the University of Edinburgh, University College London, University of Glasgow, Cardiff University and Imperial College London. She has published several research articles in mid/high impact journals (https://orcid.org/0000-0002-1875-5335).

POSTER

DAY 01

VIROLOGY WORLD CONFERENCE

17-18 JUNE

Lucija Nuskern*[1], Mirta Tkalec[2], Bruno Srezović[1], Marin Ježić[1], Martina Gačar[1] and Mirna Ćurković-Perica[1]

[1]Division of Microbiology, Department of Biology, University of Zagreb, Croatia

[2]Division of Botany, Department of Biology, University of Zagreb, Croatia

Inconsistent changes in laccase activity of chestnut blight fungus upon cryphonectria hypovirus 1 infection

Blight disease pandemic of chestnuts, caused by infection of the tree bark with fungus *Cryphonectria parasitica*, severely damaged forest ecosystems worldwide, making this ascomycete one of the top 100 most dangerous invasive species according to the Global Invasive Species Database. Apart from its devastating effects on the stands of American (*Castanea dentata*) and European chestnut (*C. sativa*), C. parasitica is scientifically interesting due to a phenomenon called hypovirulence, caused by an infection of the fungus with the mycovirus *Cryphonectria hypovirus 1* (CHV1). Infection with CHV1 reduces growth, sexual and asexual reproductive ability, and virulence of the infected fungus, leading to its debilitation, which in turn facilitates the recovery of the diseased chestnuts. That is why CHV1 treatment of infected cankers (lesions on the chestnut bark) has long been used in biological control of chestnut blight. Reduced activity of fungal laccases (enzymes involved in fungal pathogenic process) has been considered as one of the hallmarks of hypovirulence, based on the observations on the prototypic laboratory experimental system (fungal isolate EP155 and its isogenic virus-infected strain EP155/EP713) supported by limited experiments with field isolates of the fungus and its associated virus.

Having in mind the vast diversity of fungal isolates and virus strains and their effects on the phytopathogenic processes observed in nature, we investigated the effect of different virus strains on intracellular and extracellular laccase activities in several *C. parasitica* isolates. Furthermore, to reinforce our observations, we assessed the role of different culturing conditions on laccase activities and evaluated the suitability of two substrates commonly used for laccases' activities measurement - 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) and 2,4-dimethoxyphenol (DMOP). We have demonstrated that the majority, but not all of viral isolates indeed decrease the activity of laccases. However, several CHV1 strains, contrary to previous assumptions, caused an increase of the activity of *C. parasitica* laccases upon infection. The particular fungal isolates used in the experiments and culture conditions affected the results as well. Furthermore, we have demonstrated that ABTS and DMOP cannot be used interchangeably in *C. parasitica* laccase activity measurements. Our experiments demonstrate the importance of conducting this type of study in systems which represent the diversity of hosts and pathogens present in nature, as well as utilising the appropriate procedures to mimic the natural conditions as much as possible to be able to infer the most relevant conclusions applicable to natural populations, which is of the utmost importance in the research of pathogens.

Audience Take Away:

- Viruses can be used in biocontrol of plant pathogenic fungi: *Cryphonectria hypovirus 1* (CHV1) is an example of successful biocontrol agent of chestnut blight fungus *Cryphonectria parasitica*.
- The importance of wide range of genetically diverse host isolates and virus strains utilized in experiments to infer the correct conclusions about the impact of a virus species on natural host populations: contrary to previous assumptions, some CHV1 strains can increase the activity of *C. parasitica* laccases.
- Experimental design, growing conditions and analytical procedures can drastically affect the outcome of enzymes' activities measurements, making correct choices in such experiments of the utmost importance.

Biography

Dr. Nuskern studied Environmental Science at the University of Zagreb, Croatia and graduated as MS in 2012. She then joined the research group of prof. Ćurković-Perica at Faculty of Science, University of Zagreb. She received her PhD degree in 2017 at the same institution working on *Cryphonectria parasitica-Cryphonectria hypovirus 1* interactions. She is currently postdoctoral researcher and teaching assistant at the Division of Microbiology at the same faculty. She has published 8 research articles in SCI (E) journals.

KEYNOTE FORUM

DAY 02

VIROLOGY WORLD CONFERENCE

17-18 JUNE

Maria Grazia Amoroso*[1], Maria Dimatteo[2], Ilaria Di Bartolo[3], Michele Iafusco[4], Alessia Pucciarelli[2], Francesco Serra[1], Giovanni Ianiro[3], Luigi Martemucci[4], Federica Boccia[5], Carmine Carbone[5], Lucio De Maio[6], Valeria Russo[2], Daniela Ferrara[4], Esterina De Carlo[1], Giovanna Fusco

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[2]University of Naples Federico II, Via Delfino 2, Italy

[3]Istituto Superiore di Sanità Department of Food Safety, Italy

[4]Pediatrics Department, Italy

[5]Department of prevention, Italy

[6]Sea Unit, ARPA Campania, Italy

Enteric viruses circulation in the environment and their occurrence in cases of infantile gastroenteritis

Infective gastroenteritis (GA) represent a world public health relevant problem. Enteric viruses are the pathogens mainly involved in the episodes of GE, causing about 70% of the cases. In Italy most of the GA are not notified because of a mild symptomatology which does not require medical support. In the present study we investigated the presence of 10 different viruses in the faeces of children hospitalized with GE in the Campania Region (Southern Italy). The same viruses were also investigated in samples of marine water and shellfish from the coastal area surrounding the Region with the aim to trace a picture of their circulation in the environment. Results showed that 58.6% of the feces were positive to at least one virus, and the most frequently identified was adenovirus (AdV). Some samples showed the co-presence of more than one pathogen, with norovirus (NoV) GII and AdV almost always found together. Environmental samples showed an intense circulation of the enteric viruses, with the presence of all the investigated ones. Mussels were 38.23% positive to at least one virus. Results revealed the predominant presence of NoV. Looking at seawaters, 29% were positive to minimum one virus with RV the prevalent one. RV showed a definitely low prevalence in the faeces even if it was the main circulating virus in the environment. Considering that it is the most common cause of GE in children < 5 years in the world, we could conclude that its lower involvement in GE could be attributed to implementation of the vaccination plan in our Region.

Audience Take Away:

- Infective gastroenteritis (GA) represent a world public health relevant problem. Most of the GA are not notified because of a mild symptomatology.
- Only in cases of hospitalization (prevalently children) the cause of the disease is further investigated. However the viruses usually searched are the pathogens more commonly associated to GE (rotavirus, norovirus, and adenovirus) and very often (in 1/3 of the cases) the patient is discharged without knowing the infective agent.
- The diagnostic gap lead us to hypothesize that there are other viruses involved, as demonstrated by recent surveillance studies which show interesting prevalences of emerging viruses.
- The results of our research highlight the probable involvement of other viral pathogens in the episodes of GE, most of them neglected up to know.
- Other research groups could carry out the same researches to look at viruses circulation in their environment and compare it with presence of viruses in cases of gastroenteritis.
- Emerging viruses (not considered so far) could be better investigated as causes of GE.

Biography

Dr. Maria Grazia Amoroso studied Food Technology at the University of Naples and graduated in 2000. She then joined, as a PhD student, the research group of Immunology at the same University. During her PhD she won a Marie Curie Fellowship at the University of Utrecht. She received her PhD degree in 2004. She worked as researcher in the Laboratory of Virology, Zooprofilactic Experimental Institute of Southern Italy (IZSM). In 2013 she graduated in Biology at the University of Naples. From 2017 she is responsible of the Unit of Viral Genetics at the IZSM. She has published more around 40 research articles in peer reviewed journals.

Oscar Fornas

Pompeu Fabra University and Centre for Genomic Regulation, Spain

Single-virus sorting by flow cytometry : A methodology to elucidate the virosphere

Viruses is the biological entity with highest biodiversity. However, we estimate that only 1% are known. Virosphere elucidation is key to the understand global microbiome. Most studies use metagenomics to find new viruses in different ecosystems, including human body, but unfortunately only allow to identify the most abundant ones. To discover nonabundant viruses, we must go for other approaches, such as single-virus genomics. Flow cytometry is a technology that allow us to isolate particles at single-particle level and, high-resolution flow cytometry can isolate nanoparticles at single-particle level.

Nanoparticle sorting is one of the most complex applications of flow cytometry. Basically, because we are very close to or below the resolution limit of the technique. Precisely for this reason, unlike large-particle applications, we must use other technologies to validate methodology using nano-cytometry approaches. Without such validations, we cannot fully believe the data we obtain by cytometry. Huge amount of published data of nanoparticles analysis by flow cytometry generate interesting discussions but unfortunately a methodological consensus has not yet been reached. We developed a robust and reliable methodology, using high-resolution flow cytometry, to isolate viruses at single-virus level, for subsequent single-virus genomics to reveal nonabundant viruses as a tool to elucidate global virosphere. This approach is useful study viruses at any ecosystem, from human body, oceans, to any other environment.

Audience Take Away:

- The aim of this presentation is showing a new approach to isolate nanoparticles by flow cytometry. How to validate a new flow cytometry methodology of nanoparticles.
- Finally, the idea is sending a message how nanoparticles must we manage by flow cytometry. This presentation will introduce the tips and tricks to deal with nanoparticles in general. Further than viruses, this can be used as an approach for all nanoparticles, such as extracellular vesicles or inorganic particles.

Biography

Dr. Oscar Fornas studied Biology at the Autonomous University of Barcelona (UAB). In 1997 he received his PhD in Biochemistry at the same University. He started his first Postdoc in 1997 at the Cancer Research Institute in Barcelona, Spain until 2000, when started as PI at the IDIBAPS, a Research Institute of Hospital Clinic, Barcelona, Spain. Since 2001 is the of Head of Flow Cytometry Unit at University Pompeu Fabra and Centre for Genomic Regulation in Barcelona, Spain. He has published relevant research articles developing strategies and new flow cytometry applications.

SPEAKERS

DAY 02

VIROLOGY WORLD CONFERENCE

17-18 JUNE

Ndifontiayong Adamu Ndongho
Dschang University, Cameroon

Immune response after 24 months of antiretroviral therapy in patients with HIV and hepatitis B or C virus co-infections in Kumba health district, South west region of Cameroon

Hepatitis B (HBV) and C (HCV) are two among the numerous forms of infections whose clinical degeneration, morbidity-mortality and low immune responsiveness in people living with human immuodeficiency virus (HIV) are highly evident. Co-infection between HIV, HBV and HCV has been associated with reduced survival, increased risk of progression to liver diseases and increased risk of hepatotoxicity associated to antiretroviral therapy. The aim of this study was to establish the prevalence of hepatitis B surface antigen (HBsAg) and hepatitis C antibody (HCVAb) among HIV-infected individuals, treatment outcomes and identified tha associated risk factors in Kumba Health, in the South West Region of Cameroon.

We performed a systematic screening using RDT (Rapid Diagnostic Test), for HBsAg (hepatitis B surface antigen) and HCVAb (hepatitis C virus antibody) among 299 HIV-positive patients enrolled at Kumba District hospital, CMA Kumba Town hospital and Banga-Bakundu Apostolic Hospital in Kumba Health District with all positives for HBV or HCV confirmed by the ELISA test. The results were analyzed using SPSS version 20 to determine the prevalence, the effect of hepatitis B and C in response to HAART in HIV patients and the possible risk factors.

For the follow up cohort (patients free of tuberculosis, participants not on option B+, participants with healthy life styles (nonaddiction to alcohol), and participants at most at stage III of HIV infection and not on treatment for more than one year) were involved. From the above 299 participants, a total of 52 HIV patients, 36 HIV/HBV and 12 HIV/HCV patients were involved in the prospective cohort study for 24 months follow up. We performed CD4 counts, viral load test, analyzed ALAT/ASAT, albumin, bilirubine, creatinine and measured the weights of HIV patients, HIV/HBV and HIV/HCV, enrolled in Kumba Health District. Out of the 299 HIV positive patients screened for HBV and HCV, 36 (12.0%) were positive for HBV and 12 (4%) for HCV by both RDT and ELISA. In addition, majority of the study participants were Single/Cohabiting/ Separated 160 (53.5%), Christians 282 (94.3%), Famers 100 (33.4%), and from rural areas 202 (67.6%).

Concerning the follow up of patients on HAART, here was a significant decrease in mean ALAT (p< 0001) and ASAT (p< 0001) values from baseline to 24 month follow up. The co-infection whether for HBV or HCV leads to significant increase (P<0.05) of transaminases all over the follow up period compared to mono-infected patients. Whether mono-infected or co-infected, there was a significant decrease of ALAT and ASAT over the time from baseline to 24 month in similar manner like total bilirubin level. Also, there was a general decrease in creatinine level in both mono and co-infected patients from month 6 to month 24 (HIV/HBV and HIV/HCV) and a total decrease of creatinine level for HIV/HCV from month 1 to month 24. We equally noted that irrespective of infection status, there were positive variations among these variables (CD4 and viral load) after 24 months though significant. The result of this study could be used for health decision making and proper follow up of HIV/HBV and HIV/HCV co-infected patients.

Keywords: HIV, hepatitis B and C, co-infection, prevalence, risk factors, immune response, Kumba Health District.

Biography

DR. NDIFONTIAYONG ADAMU NDONGHO has completed his PhD at the age of 33 years from Dschang University and he is a Senior Public Health Administrator from the National School of Administration and Magistracy Yaounde. He is a Chief of Bureau Health, District and Regional Data Managers and Focal Point Disease Surveillance in the South West Region of Cameroon and also a reserved Officer. He is a Frontline field Epidemiologist and an expert in Incidence and Risk management. He has published articles in International Journals and has been a speaker in International Conferences and serving as main facilitator and supervisor of health activities in Kumba.

Ioanna E. Stergiou
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Post-vaccination humoral immune responses against SARS-CoV-2 in patients with haematologic malignancies

Patients with haematologic malignancies are at high risk for coronavirus disease 2019 (COVID-19) related complications, with reported high mortality rates compared to the general population. While vaccination constitutes the cornerstone of protection against COVID-19 for healthy individuals, patients with haematologic malignancies display disease related immune dysregulation and/or therapy related immunosuppression, with both factors being implicated in low humoral responses after SARS-CoV-2 vaccination. Decreased antibody responses have been reported both in patients with lymphoid and myeloid malignancies, though research mainly focuses on patients with malignancies of lymphoid origin. The striking variability in antibody responses amongst these patients is attributed to different disease biology and treatment modalities. This presentation aims to review data from the published literature regarding humoral immune responses in patients with hematologic malignancies after SARS-CoV-2 vaccination. Amongst patients with haematologic malignancies, those receiving anti-CD19 targeted CAR-T cell therapy or hematopoietic stem cell transplantation are reported to have to the lowest seroconversion rates.

Chronic lymphocytic leukemia patients demonstrate low seroconversion rates after SARS-CoV-2 vaccination, ranging though from 39% to 71% in different published cohorts. These discrepancies may be attributed to different approaches, from active therapy to monitoring. Immunoparesis and treatment with Bruton's tyrosine kinase (BTK) inhibitors have been correlated with lower antibody responses, while correlations regarding B-cell lymphoma 2 (BCL-2) inhibitors or anti-CD20 therapy are not consistent between different studies. The seroconversion rates in patients with non-Hodgkin lymphoma (NHL) are reported to range from 42% to 75%. It seems that the timing between therapy and vaccination is the main factor attributing to this wide range. It is striking that serologic responses could be as low as 3% for patients are vaccinated within the first 2 months from anti-CD20 therapy and reach levels as high as 80% if therapy preceded at least 12 months.

For multiple myeloma patients the seroconversion rate ranges between 65% and 95%. Factors attributing to the reported variability include age, hypogammaglobulinemia level, number of lines of therapies and active treatment with an anti-CD38 antibody, anti-BCMA therapy, or corticosteroids, all of which are significant factors resulting in lower antibody response rates. It has been demonstrated that patients with acute myeloid leukemia, chronic myeloid leukemia and myelodysplastic syndromes show antibody responses that are close to those of healthy individuals, while other published data indicate that among myeloid malignancies patients with myeloproliferative neoplasms and myelodysplastic syndromes demonstrate the lowest antibody response rates.

Overall, for patients with haematologic malignancies, the lower antibody response rates after SARS-CoV-2 vaccination are predominantly reported for those under active therapy, with anti-CD20 therapy, BTK inhibitors, Janus kinase inhibitors and BCL-2 inhibitors having a negative impact on seroconversion, especially if the vaccination takes place in less than 12 months after the last treatment. Although, solely estimating the rates of seroconversion may underscore the level of protection against COVID-19, since the immunological responses are far more complex and implicate mechanisms other than antibody production, we should tailor the sequence and timing of vaccination and vaccine boosters to achieve the best possible antibody responses in patients with haematologic malignancies.

Audience Take Away:

- Identify patients with haematologic malignancies who are more likely to develop insufficient humoral immune responses after SARS-CoV-2 vaccination.

- Adopt specific vaccination strategies for patients with haematologic malignancies to achieve the best possible antibody response after SARS-CoV-2 vaccination.
- Consider treatment modifications, when possible, to dampen the effect of immunosuppressive therapy on SARS-CoV-2 vaccination efficacy.

Biography

Dr. Stergiou received her Medicine degree at School of Medicine, National and Kapodistrian University of Athens in 2011 and completed her Hematology Residency at the Department of Pathophysiology in2019. She received her Master of Science on "Hemorrhage, Thrombosis and Transfusion Medicine" in 2017 and her PhD degree in 2021 under the supervision of Prof. M. Voulgarelis. She is currently an attending Hematologist in the Pathophysiology Clinic of Laikon General Hospital of Athens. Her research interest focuses on myelodysplastic syndromes' pathophysiology and lymphomagenesis in the setting of autoimmunity. She has published 12 articles in SCI(E) Journals.

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Lymph node dendritic cells are HIV reservoirs containing replication competent virus in patients under suppressive therapy

Background: The comprehensive characterization and quantification of where HIV persists as "reservoirs" during anti-retroviral therapy is required to design appropriate therapeutic intervention(s) to achieve a cure for HIV infection. While plethora of studies are being designed to target HIV-infected CD4 T cells – the major cell compartment documented in which HIV persists, recent studies performed in animal models or using in vitro models have indicated that myeloid cells may also serve as relevant HIV reservoirs during therapy. Indeed myeloid cells are relatively resistant to viral cytopathic effects, to the destruction by cytotoxic T-cells, and can store HIV in 'virus-containing compartments'. Together with their long half, potentially due to their self-renewing nature in tissues, HIV-infected myeloid cells could therefore represent a potential and yet unexploited tissue reservoir.

Methods: To address this issue, we performed 1) an in-depth transcriptomic, phenotypic and functional characterization of Lymph Node (LN) myeloid dendritic cells (DC) subsets; 2) assessment of the susceptibility of LN DC subsets to HIV infection in vitro; 3) assessment of major virological parameters associated with HIV persistence in ex vivo isolated LN DCs in viremic and aviremic ART treated HIV-infected subjects and 4) near-full length single genome HIV DNA sequencing.

Results: We showed that the two myeloid LN DC subsets i.e. migratory (Lin-HLA-DR+CD45+CD11c+CCR7+) and resident (Lin-HLA-DR+CD45+CD11c+CCR7-) DCs could be identified directly ex vivo in LNs of healthy, HIV viremic and ART treated individuals. The two DC subsets transcriptomically clustered away from each other on the basis of

≈500 differentially expressed genes ($P<0.05$). Interestingly, viral restriction factors – SAMHD1 and APOBEC3A were significantly upregulated within resident DCs as compared to migratory DCs. We therefore assessed the capacity of LN DC subsets isolated from healthy individuals to get infected with HIV in vitro and showed that while both DC subsets were susceptible to HIV infection, LN migratory DCs harbored a much higher propensity to become infected ($P<0.05$). In addition, VPX (SAMHD1 counteracting protein), modulated significantly the infection levels in resident DCs ($P<0.05$). Interestingly, LN migratory isolated from viremic HIV-infected individuals (N=5) harbored on an average about 1875 cells/million containing integrated HIV DNA, whereas LN resident DCs harbored about 620 cells/million (N=5).

In addition, both LN DC subpopulations harbored cells containing HIV unspliced gag RNA and ms tat-rev HIV RNA at levels and frequencies comparable to those detected in LN T follicular helper (Tfh) cells, previously shown to be a major cell compartment for HIV transcription and production. In addition, LN migratory DCs supported higher reactivation of HIV production (in the absence of CD4) and replication (in the presence of CD4) in vitro ($P<0.05$). We subsequently showed that the presence of cells harboring integrated HIV DNA in ART treated HIV-infected individuals was more frequently detected within LN migratory DCs than in LN resident DCs. Interestingly, LN migratory DCs of ART treated individuals

also supported much higher levels of HIV reactivation, production and replication when co- cultured with target CD4 T cells in vitro ($P<0.05$). Notably, the presence of inducible replication competent virus was more frequently detected within LN migratory DCs (85% of the individuals) as compared to LN resident DCs (28% of the individuals) ($P<0.05$). Analysis of individual proviral DNA sequences from lymph nodes of viremic HIV-infected individuals (N = 3) showed that the proviral landscape in LN migratory DCs was indeed dominated by genome-intac proviral species (55%) as compared to LN resident DCs (40%).

Conclusions: LN migratory DCs isolated from ART treated HIV-infected individuals represents a major source of replication competent HIV despite more than two years of suppressive therapy. These cells could therefore act as a source of de novo virion production that could infect surrounding LN CD4 T cells upon ART cessation, and may contribute to viral rebound.

Audience Take Away:

- First study based on dendritic cells directzly isolated from lymph node tissues of ART-treated HIV infected individuals.
- This study demonstrates that HIV may not only hijack the inherent migratory properties of DCs to gain access to LNs but in the process, may also infect LN DCs.
- Contrasting to the original paradigm, HIV infected LN DCs are detectable after prolonged ART and can be induced to produce replication competent virus.
- Therefore, strategies attempting to eradicate viral reservoirs in ART treated HIV-infected individuals by reactivating HIV, may also consider and evaluate the occurrence of replication competent viruses within LN DCs in addition to LN CD4 T cells.

Biography

Ms. Riddhima Banga performed a Master's Degree in 2012 in Integrated Immunology at University of Oxford (UK) under the supervision of Dr. Nilu Goonetilleke in the laboratory of Prof. Andrew McMichael. Soon after her graduation, she joined in his laboratory at the Division of Immunology and Allergy, Lausanne University Hospital, Lausanne, Switzerland in March 2013 to start her PhD. She obtained her PhD in 2017 working on the characterization of HIV reservoirs. Since then has been working as a Post-doctoral fellow in the same lab. She has already published twelve articles among which six main articles in Journal of Virology, 2015, in Current Opinion in HIV and AIDS, 2016 and 2021, in Nature Medicine, 2016, Frontiers of Immunology, 2018 and in PLOS Pathogens, 2019 in first author position. She has also received two major Swiss prizes in 2018 i.e. the Pfizer prize in Infectiology, Rheumatology and Immunology and the Lausanne University prize of excellence.

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Footprints of SARS-CoV-2 genomic diversity in Pakistan during two years of pandemic

The rapid spread of SARS-CoV-2 since the start of pandemic has posed a major effect on public health system worldwide. After almost one year of pandemic new variants of SARS-CoV-2 has emerged with larger number of mutations in the genome. These variants lead to the emergence of new pandemic waves in the country. Like all other parts of the world, Pakistan has also experienced five waves of case resurgence within two year of pandemic. In the present study, the genomic diversity of SARS-CoV-2 has been explained during different waves of pandemic in the country. The distribution of lineages have shown that during first wave of pandemic (April-June, 2020) about 58% of isolates were classified as B.1. Other than B.1 other circulating lineages were B.1.1.1, B.1.36 and A. During the second wave (October 2020-January, 2021). Different lineages (B1.36.31, B1.471, and B1.562) were observed with a large number of isolates belonging to B.1.36.31.

The first case of B.1.1.7 (Alpha) was detected in January, 2021. The detection of Alpha variant in the country lead to the emergence of third wave of pandemic (February-June, 2021) that peaked in March, 2021. During the third wave the first cases of B.1.351 (Beta) and B.1.617.2 (Delta) were also detected in March and April, 2021, respectively. The major circulating variants during third wave of pandemic were alpha, beta, and delta. The presence of delta variant and its sub-lineages lead to the emergence of fourth wave of pandemic (August-October, 2021). During November and December, 2021 the decline in number of cases were observed but the detection of Omicron variant on December 13, 2021 lead to the emergence of fifth wave of pandemic (January-March, 2022) in Pakistan. The omicron has replaced the delta variant during the fifth wave of pandemic. Currently, the fifth wave of pandemic has been ended in Pakistan with <0.5% positivity rate. However, the past trends on SARS-CoV-2 variants emergence advocate for stringent genomic surveillance. Since the XE variant of SARS-CoV-2 has been reported in few countries which holds a sizable population of Pakistani expatriates, they can be source of new variant importation as had been the case in the past. This further warrants genomic surveillance particularly on border control points. These initiatives can ensure timely check on emerging COVID-19 numbers.

Audience Take Away:

- The current study explains the genomic diversity of SARS-CoV-2 during 2 years of pandemic. This is the first comprehsive study explaining the diversity of SARS-CoV-2 in Pakistan. So it will give an overview about COVID-19 condition in Pakistan.
- The audience can also perform the similar analysis on the sequences generated by their own country. This will help researcher to design specific drugs or vaccines targeting the circulating strains in the population.

Biography

Dr. Rehman is a Bachelors in Bioinformatics and later done her MPhil in Virology & Immunology from National University of Sciences & Technology (NUST) Islamabad, Pakistan. Her major work during the period was on Hepatitis and Influenza viruses. She then completed her PhD studies in Applied Biosciences in 2019 from NUST where her primary work was chemotherapy resistance biomarkers and lead identification for chemotherapy resistance inhibition. She later joined National Institute of Health (NIH), Pakistan in 2020 where she has been the one of the focal person for Bioinformatics analysis reporting on viral sequencing for SARS CoV2 till date.

Joanna Sajewicz-Krukowska*[1], Paweł Mirosław[2], Jan Paweł Jastrzębski[3], Katarzyna Domańska-Blicharz[1], Karolina Tarasiuk[1], Barbara Marzec-Kotarska[4]

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MiRNA expression signatures induced by chicken astrovirus infection in chickens

Non-coding RNAs have superior regulatory functions involved in the recognition of specific sequences within the genome. A special role in the large family of non-coding RNAs has been attributed to the short 19-25 nucleotide microRNA (miRNA) found in animals including human and poultry. miRNAs have emerged as a class of crucial regulators for gene expression and are involved in the regulation of virus defence and immunological processes. Astrovirus infections pose a significant problem in the poultry industry, leading to multiple adverse effects such as a decreased egg production, breeding disorders, poor weight gain, and even increased mortality. The commonly observed chicken astrovirus (CAstV) was recently reported to be responsible for the "white chicks syndrome" associated with an increased embryo/chick mortality. CAstV-mediated pathogenesis in chickens occurs due to complex interactions between the infectious pathogen and the immune system. Many aspects of CAstV–chicken interactions remain unclear, and there is no information available regarding possible changes in microRNAs (miRNAs) expression in the chicken spleen in response to CAstV infection in chickens.

The objective of this study was to identify miRNAs associated with CAstV infection in chicken spleens. By comparing these data to healthy chickens, a total of 58 differentially expressed (DE) miRNAs were identified (19 downregulated and 39 upregulated). The bioinformatics prediction of target genes of differentially expressed miRNAs using miRDB identified 403 targets for miRNAs. The predicted target genes were used for Gene Ontology (GO) analysis using DAVID 8.6. and showed many significant terms to be enriched. These terms included binding activities, apoptosis and transcription regulation, and cell proliferation. Functional pathway analysis of KEGG database showed that the predicted targets of these miRNAs were significantly enriched in several pathways including MAPK signaling pathway, Gap junction, Regulation of actin cytoskeleton, Adrenergic signaling in cardiomyocytes, Phosphatidylinositol signaling system, mTOR signaling pathway and ErbB signaling pathway.

To our knowledge, this is the first study on miRNA gene expression in CAstV infected chickens using a deep sequencing approach. During CAstV infection, many host miRNAs were differentially regulated, supporting the hypothesis that certain miRNAs might be essential in the host-pathogen interactions. These results are significant for the study of immune responses to infection with CAstV mediated by miRNAs as well as the interaction between the chicken host and the virus.

Audience Take Away:

- Our study provided broad insight into the CAstV-induced host response and a basis for further studies that may clarify the interactions between virus and host. It provided a global analysis of host miRNA changes that occur during CAstV infection in vivo and a strong basis for further studies.
- We demonstrated that during CAstV infection, many host miRNAs were differentially regulated, supporting the hypothesis that certain miRNAs might be essential in the host-pathogen interactions.
- These results are significant for the study of immune responses to infection with CAstV mediated by miRNAs as well as the interaction between the chicken host and the virus. These findings have important implications for the study of the miRNA-mediated immune response to CAstV infection, but also more generally for host-virus interactions.

Biography

Dr. Sajewicz-Krukowska studied Biotechnology at the University of Maria Curie-Skłodowska, Lublin and graduated as MS in 2007. She received her PhD degree in 2012 at the Medical University of Lublin. Since 2014 she has been employed at the Department of Poultry Diseases of the National Veterinary Research Institute in Pulawy, Poland. Her scientific interests focus mainly on viral diseases in poultry, especially on the development and implementation of the molecular biology methods for their diagnosis and characterization. She has published dozens of research articles in international peer-reviewed journals.

Larise Oberholster*[1], Sylvain Perriot[1], Mathieu Canales[1], Samuel Jones[1], Amandine Mathias[1] and Renaud Du Pasquier[1,2]

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In vitro human induced pluripotent stem cells(hiPSC) -derived astrocytes to study JCV biology: From mechanistical insights to new biomarker identification

JC virus (JCV) is the causative agent of progressive multifocal leukoencephalopathy (PML), a devastating disease of the central nervous system (CNS) that results in the widespread formation of lesions across the brain parenchyma. JCV is an opportunistic virus that resides in a latent state in the kidneys of more than half of the adult population. However, in rare cases of severe immune suppression, such as patients receiving immunomodulatory treatment, the virus is able to establish infection of astrocytes and oligodendrocytes in the brain, resulting in rapid demyelination. There exists no treatment strategies against JCV and the only means to halt the disease progression is to reconstitute an adequate immune response. Unfortunately, initial symptoms of PML often go unnoticed and only receive medical attention once the disease is already widespread in the brain. The potential of extracellular vesicles (EVs) to cross the blood-brain-barrier has paved the way in which brain-derived EVs can serve as non-invasive markers of neurological disease.

Such a biomarker, that has the benefit of being monitored at regular intervals, could aid clinicians to determine early disease onset in patients at-risk for developing PML. In our group, we use human induced pluripotent stem cells (hiPSCs) that we differentiate into glial cells to model JCV infection in the brain. We first validate our hiPSC-*in vitro* model using a combination of techniques including qPCR, fluorescence microscopy and transmission electron microscopy. We for the first time perform an in-depth characterization of the effect of JCV on the cell proteome and show an upregulation in proteins involved in the cell cycle and DNA damage response. These data correspond to what is known for other polyomaviruses and further strengthen the validity of our unique model. Next, we perform proteomic analysis on EVs isolated from JCV-infected astrocytes and show that EVs from infected cells have a different proteomic signature as compared to the uninfected control. Ultimately, comparing this profile to that of EVs isolated from the cerebrospinal fluid (CSF) of PML patients may help in determining an early biomarker that could aid clinicians in identifying patients at-risk for developing PML before the onset of severe neurological sequelae and improve patient care.

Audience Take Away:

- In-depth characterization of how JCV influences the host proteome, which will aid towards the development of future antiviral targets and early biomarkers of disease onset.
- Strategies on how to analyze proteomic data for determining putative targets towards the aim of biomarker development.

Biography

Larise Oberholster is a PhD candidate in the group of Prof. Renaud Du Pasquier at the University of Lausanne, Switzerland. Her research project focuses on the utilization of human induced pluripotent stem cells that are differentiated into brain cells to model JCV infection in the central nervous system.

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Anticoronavirus formulations based on chitosan

Our interdisciplinary working group was motivated by the challenge of proposing tools for the fight against the sudden pandemic caused by SARS-CoV-2 in 2020 and the present. We have obtained several formulations based on chitosan, a biodegradable, non-antigenic, non-toxic, and biocompatible natural polymer. These formulations have different characteristics and applications. We developed novel antiviral cotton fabrics impregnated with different formulations based on Chitosan, citric acid, and Cupper nanoparticles. The resulting impregnated textiles exhibited integrated properties of good adhesion without substantially modifying their appearance and anti-herpes virus and betacoronavirus efficacy (~ 100%), which enabling to serve as a scalable biocidal layer in protective types of equipment by providing contact killing against pathogens. The antiviral activity of formulations based on chitosan with copper nanoparticles was described for the first time in our work. This proposal may be considered a potential tool to inhibit the propagation and dissemination of enveloped viruses, including SARS-CoV-2.

Another of the main current challenges is to optimize the use of personal protection elements without the detriment of biosecurity. For this proposal, we obtained sprayable formulations based on chitosan. It is known that the combination of both metals (copper and silver) enhances the antibacterial activity of each one individually. We obtained the first antiviral spray based on chitosan and both (silver and copper) nanoparticles. The spray has simplified production, with potential use in industry, it´s easy to use and apply, for domestic use, is biodegradable, has immediate antiviral action, has antibacterial, and it is non-toxic, and does not produce skin irritation. The spray is applicable to any type of woven or non-woven fabric, and plastic surfaces. Implementing this kind of sprayable product would allow the face masks to be reused without the need sterilization or their elimination after use. Therefore, the two major advantages attributable to Chitosan formulations are the prevention of the spread of viruses, including SARS-CoV-2. Secondly, these technologies will contribute significantly to the reduction of waste production.

Audience Take Away:

- The present work contributes to expanding knowledge in the development of antivirals applicable in materials.
- The audience will learn how certain antivirals can be applied on materials converting them into functionalized materials.
- This work will provide tools to develop antivirals applicable to surfaces for different types of viruses, the constant emerging and re-emerging viruses worldwide needs to be stopped with products that not only act on the patient but also prevent viral spread.

Biography

Dr. Victoria Ayala studied Biochemistry at the Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina, and graduated in 2008. She then joined the research group of Dr. Scolaro Luis at the Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Argentina and in the Dr. Graciela Santillán group at UNS. She received her PhD degree in 2014 at the same institution. She is Assistant Professor at the UNS. She founded two laboratories of virology and is chief of one of them. She was twice awarded for her achievements in virology. Together with his work group obtained the patenting of an antiviral product. She has published more than 10 research articles in SCI(E) journals.

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Modulation of MIR-663a expression by EBV-encoded G protein–coupled receptor (GPCR), BILF1, in burkitt lymphoma

The Epstein–Barr virus (EBV) is a γ-herpesvirus infecting over 90% of adults worldwide1. Similar to other herpesviruses, EBV encodes for a G protein–coupled receptor (GPCR), BILF1, affecting a multitude of cellular signaling pathways. BILF1 has been identified to promote immune evasion and tumorigenesis, ensuring a life-long persistence of EBV2. The structure and infection mechanism of EBV have been well studied, but the role of BILF1, is not fully understood. Given the important role of miRNAs in regulating nearly every aspect of biology, here, we have studied the impact of BILF1 on genes encoding miRNAs in B-cells and BL primary tumours3.

Material & Methods: We transfected isolated primary human germinal centre (GC) B cells, the presumed progenitors of BL, with BILF1 plasmid and performed RNAseq assay. We also re-analyzed BL cases expressing BILF1 by Abate et al4.

Results: We found that when expressed in B cells, BILF1 was able to regulate the expression of several genes encoding miRNAs. In particular, BILF1 was significantly associated with an upregulation of miR-663a host gene (HG). This gene encodes for miR663a which has been described as oncomiR in other diseases; however, its role in BL has never been studied. The dynamic changes in miR663aHG expression observed in B cells were validated in BL primary tumorus where this gene was similarly up-regulated in primary eBL expressing BILF1. Moreover, we observed that the expression levels of miR-663aHG significantly correlated with miR-663a, suggesting that miR-663a was co-expressed with its host gene miR663aHG under the regulation of the host gene promoter. We also found a positive correlation between BILF1 and miR663a in both B-cells and primary tumours. Thus, we defined the role of miR663a. After defining the validated and predicted target genes of miR-663a, a gene ontology analysis revealed that miR663a-targets were enriched for genes involved in B-cell differentiation, immune response to viruses and fatty acid metabolism.

Conclusions: This study defined a new role of BILF1, highlighting a positive correlation with miR663a which may play a substantial role in the aetiology of BL by regulating networks involved in B-cell proliferation and differentiation.

Audience Take Away:

- This topic contributes to better understand the pathological mechanisms induced by EBV in Burkitt lymphomas.
- It will also focus the attention to a new target (BILF1) that escaped the attention of the scientific community.

Biography

Mundo is a Marie Curie Fellow at the University of Limerick and Professor Adjunct in Molecular Pathology at the University of Nairobi. His research is focussed on novel insights into the pathogenesis of virus-associated malignancies for the development of new therapies. His work received grant support totalling ~€1m. Mundo has contributed several important discoveries in the field: the first description of a non-canonical EBV-latency program in non-Hodgkin lymphoma (Abate et al. PLoS Pathogens, 2015); the first documented evidence of EBV in-situ in primary tumours classified as virus-negative (Mundo et al., Frontiers in Microbiology, 2017; Mundo et al, Modern Pathology, 2020).

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Evolutionary pressure from cross-reactive flavivirus serums generates mutations with altered serum sensitivity and fitness in mammalian cells

Flaviviruses, such as dengue virus (DENV) and Zika virus (ZIKV), cause recurrent febrile and hemorrhagic disease resulting in 400 million infections annually. These viruses are in a constant arms race with their host's immune system, which drives continuous evolution. Due to co-circulation, these viruses must respond to the specific immune pressures and pre-existing immunity to closely related co-circulating pathogens. However, the impact of pre-existing cross-reactive immunity as a driver of evolution is not well understood, leaving us underprepared to handle the emergence of cross-reactive immune escape variants. Therefore, in this study, we investigated cross-reactive anti-DENV antibodies' role as drivers of evolution in ZIKV infection. We used an in vitro evolution system to passage ZIKV in mammalian cells with antibodies from patients previously infected with DENV (anti-DENV serum) or antibodies from DENV-naïve patients (control serum). Following five passages, next-generation sequencing was performed to identify any mutations that arose within the viral populations. Twenty-one mutations were detected with an allelic frequency greater than 5%. A subset of the non-synonymous mutations found in common antibody targets (M, E, and NS1)were inserted individually into a ZIKV infectious clone to assess their effects.

The mutation found in NS1 (NS1-T139A) showed an escape phenotype, while the mutation in E (E-V355I) had sensitized to anti-DENV serum. When assessed in Vero cells both with and without supplementation of anti-DENV serum, both viruses showed enhanced fitness. This fitness increase held in human lung epithelial cells (A549). When assessed in human monocytes (THP-1), E-V355I demonstrated a reduction in fitness, while there was no change in fitness for NS1-T139A. To fully characterize the impact of these mutations, the mutant virus will be assessed in *Aedes aegypti* mosquitos to understand how cross-reactive serum drives evolution more fully and its impact on sustained transmission.

Audience Take Away:

- This work demonstrates the need to study pre-existing cross-reactive immunity on evolution, not only pathology.
- The techniques used, such as competition assays, demonstrate a direct way to assess replicative fitness.
- This work highlights bacterial-free approaches to generating mutant viruses.

Biography

Jeffrey Marano studied Biomedical Engineering at Boston University, where he received his bachelor's degree. While there, he worked in the labs of Drs. Wilson Wong and Douglass Densmore where he engineered biocomputers using CRISPR technologies. During this time, he led a team of undergraduate students from Boston University at the International Genetically Engineered Machines competition, where the team received a gold medal. After graduating, he enrolled in the Translation Biology, Medicine, and Health doctoral program at Virginia Tech. There, he joined the lab of Dr. James Weger-Lucarelli, where he studies viral evolution and reverse genetics.

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Reduced dengue incidence and aedes vector densities during the COVID-19 movement restrictions

The impact of public health measures, notably restrictions on movement of people to curb COVID-19 transmission, on the incidence of dengue during the period March 2020 to April 2021 was investigated in the Jaffna district and elsewhere in the island of Sri Lanka. A Seasonal Autoregressive Integrated Moving Average (SARIMA) model was used to predict the monthly dengue incidence for each of the country's 25 districts based on five years of pre-pandemic data, and compared with the actual recorded incidence of dengue during this period. Ovitrap collections of *Aedes* larvae were performed in Jaffna city in the Jaffna district in the pandemic period and compared with similar collections made in the pre-pandemic period from March 2019 to December 2019.The recorded numbers of dengue cases for every month from March 2020 to April 2021 in the whole country and for all 25 districts over the same period were lower than the numbers of dengue cases predicted from data for the five years (2015–2019) immediately preceding the COVID-19 pandemic. The number of dengue cases recorded nationwide represented a 74% reduction from the predicted number of dengue cases. The numbers of *Aedes* larvae collected from ovitraps per month were reduced by 88.6% with a lower proportion of *Ae. aegypti* than *Ae. albopictus* in Jaffna city from August 2020 until April 2021 compared with March 2019 to December 2019. Reduced access to blood meals and lower vector densities, particularly of *Ae. aegypti*, resulting from the restrictions on movement of people, are suggested to have contributed to the lower dengue incidence in Sri Lanka.

Audience Take Away:

- Appreciation of dengue virus transmission and Aedes mosquito vector densities.
- Assist teaching of public health and virology.
- Help further research to advance knowledge on dengue virus transmission.
- Understand neglected aspects of population exposure to mosquito disease vectors.
- Appreciate public health aspects of dengue and other mosquito-borne diseases.

Biography

Ranjan Ramasamy graduated from the University of Cambridge, UK and then obtained a PhD also from the University of Cambridge. He has since held academic appointments in the UK and abroad including Australia, Sri Lanka and the USA. He was the Chairman of the National Science Foundation of Sri Lanka, Professor of Life Sciences at the Institute of Fundamental Studies in Kandy in Sri Lanka, Professor of Biochemistry in the University of Jaffna in Jaffna Sri Lanka, Professor of Immunology in the University Brunei Darussalam Medical School and held institute appointments at the Babraham Institute in Cambridge in the UK & Scripps Clinic and Research Foundation in La Jolla in the USA. He has more 250 publications in fields pertaining to Medical Sciences.

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Genetic factors in early innate immunity to SARS-CoV-2 in the upper respiratory tract

The nasal epithelium is the initial site of SARS-CoV-2 infection. Early and effective immune responses in the upper respiratory tract (URT) can limit and eliminate the infection in the URT, thereby preventing infection of the lower respiratory tract and the development of severe COVID-19. SARS-CoV-2 interferes with innate immunity signalling and evolves mutants that can reduce antibody-mediated immunity in the URT. Recent genetic and immunological advances in understanding innate immunity to SARS-CoV-2 in the URT, and the ability of prior infections as well as currently available injectable and potential intranasal COVID-19 vaccines to generate anamnestic adaptive immunity in the URT, are reviewed. It is suggested that the more detailed investigation of URT immune responses to all types of COVID-19 vaccines, and the development of safe and effective COVID-19 vaccines for intranasal administration, are important needs.

Audience Take Away:

- Cutting edge appreciation of protective immunity to SARS-CoV-2.
- Assist teaching.
- Help design additional research to advance knowledge of immunity to SARS-CoV-2.
- Advance appreciation of the need to develop more effective vaccines.
- Help design better vaccines for COVID-19.

Biography

Ranjan Ramasamy graduated from the University of Cambridge, UK and then obtained a PhD also from the University of Cambridge. He has since held academic appointments in the UK and abroad including Australia, Sri Lanka and the USA. He was the Chairman of the National Science Foundation of Sri Lanka, Professor of Life Sciences at the Institute of Fundamental Studies in Kandy in Sri Lanka, Professor of Biochemistry in the University of Jaffna in Jaffna Sri Lanka, Professor of Immunology in the University Brunei Darussalam Medical School and held institute appointments at the Babraham Institute in Cambridge in the UK & Scripps Clinic and Research Foundation in La Jolla in the USA. He has more 250 publications in fields pertaining to Medical Sciences.

Participants List

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