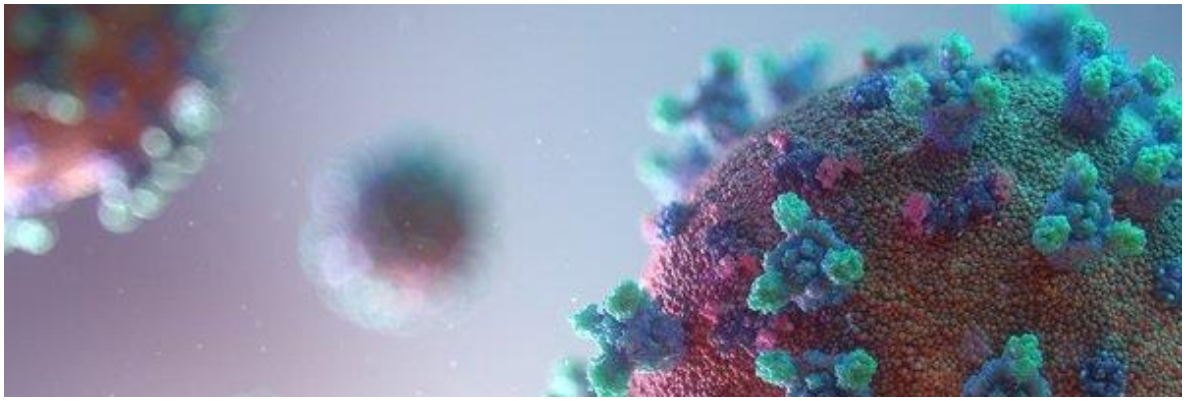


UK International Coronavirus Network Big Data: Coronaviruses at Multiple Scales Workshop (sponsored by Zoetis) and Annual General Meeting

Institute of Microbiology and Immunology
Faculty of Medicine
University of Ljubljana
Slovenia

Wednesday 13th September – Friday 15th September 2023

Department for Environment Food & Rural Affairs

UKRI Biotechnology and Biological Sciences Research Council

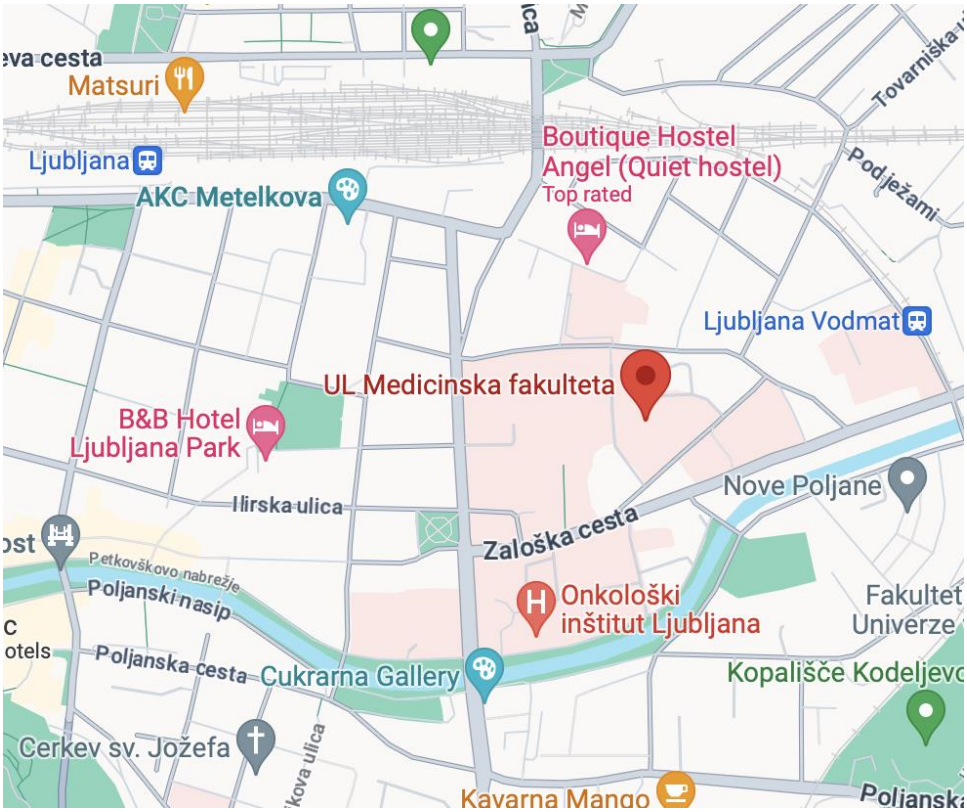
UK-ICN

University of Ljubljana | Faculty of Medicine
INSTITUTE OF MICROBIOLOGY AND IMMUNOLOGY

Contents

Venue and Location

Big Lecture Room
The Medical Faculty
University of Ljubljana
Slovenia
Korytkova ulica 2, 1000 Ljubljana, Slovenia



Bus stations near Korytova ulica 2:

- Hrvatski Trg (6 min walk)
- Klinični Center (7 min walk)
- Bolnica (7 min walk)
- Friškovec (8 min walk)
- Gornje Poljane (10 min walk)

Big Data – Wednesday 13th Sept 2023

"Big Data: Coronaviruses at Multiple Scales" Workshop

Sponsored by Zoetis

Start	End	Wednesday 13th September 2023	
10:30	10:50	ARRIVAL AND REGISTRATION	
Chair: Dr John Hardham, Zoetis, USA			
10:50	11:00	Zoetis introduction	Dr John Hardham, USA
11:00	11:30	Keynote: Genomic surveillance and functional genomics in a cohort of COVID-19 patients from Saudi Arabia	Prof Arnab Pain King Abdullah University of Science and Technology (KAUST), Saudi Arabia
11:30	11:45	Changing COVID-19 severity in patients hospitalized for community-associated Delta, BA.1 and BA.4/5 variant infection in Slovenia	Ms. Maja Mrzel, National Institute of Public Health, Slovenia
11:45	12:15	Keynote: ISARIC: Outbreak research preparedness and response	Dr Laura Merson, University of Oxford, UK
12:30	13:30	LUNCH BREAK	
Chair: Dr Tracy MacGill, US Food and Drug Administration, USA			
13:30	14:00	Keynote: Artificial Intelligence Data Science for Life Scientists: Should Everyone Learn Programming or Is There an Alternative?	Prof Blaz Zupan University of Ljubljana, Slovenia
14:00	14:30	Using TopMD to identify pathway biomarkers and stratify disease	Dr Jim Schofield, TopMD, UK
14:30	14:45	COVID-19 biomarker identification from multi-factorial analysis	Dr Rebekah Penrice-Randal, TopMD, UK
14:45	15:15	AI Virus Prediction	Prof Julian Hiscox, University of Liverpool, UK
15:15	15:45	AFTERNOON BREAK	
Chair: Prof. Julian Hiscox, University of Liverpool, UK			
15:45	16:15	The landscape of viral transmission: from fragmented data to knowledge discovery.	Dr Maya Wardeh, University of Liverpool, UK
16:15	16:45	Host in the machine: Using AI directed wet-lab work to optimise virus host range prediction	Dr Marcus Blagrove, University of Liverpool, UK
16:45	17:15	Keynote: Coronaviruses, One Health, and the Need for Integrated Biosurveillance	Dr John Hardham, Zoetis, USA
CLOSED DINNER			

Big Data Speakers

Keynote: Prof. Arnab Pain

Professor of Bioscience
King Abdullah University of Science and Technology, Saudi Arabia
Title: Genomic surveillance and functional genomics in a cohort of COVID-19 patients from Saudi Arabia

Prof. Pain received his PhD from the University of Cambridge, U.K., working on microbial pathogenesis in a bacterial pathogen of cultivated mushrooms. He had his postdoctoral training at the Weatherall Institute of Molecular Medicine (WIMM) in Oxford, U.K. where he focused on cell biology and virulence-associated phenotypes in the human malaria parasite *Plasmodium falciparum*. After spending five years in Oxford, he moved back to Cambridge and joined the Pathogen Sequencing Unit (PSU) at the Wellcome Trust Sanger Institute (WTSI) as a Senior Scientist. In WTSI, he took a leading role in coordinating several genome and transcriptome projects of several major species of malaria and other related apicomplexan parasites of humans and animals.

In 2010, he moved to Saudi Arabia to join the Biological and Environmental Sciences and Engineering (BESE) Division at King Abdullah University of Science and Technology (KAUST) as a member of the founding faculty to establish and lead a research program on Pathogen Genomics – primarily focusing on pathogens of regional and global relevance. Since 2015, he has had an appointment as a Distinguished Professor at the International Institute for Zoonosis Control, Hokkaido University in Sapporo, Japan. Currently, he also serves as an Honorary Professor at the Liverpool School of Tropical Medicine (LSTM) in the U.K. Prof. Pain is serving as the Lead PI for the 'COVID-19 Genomics- MENA' consortium funded by the UK Foreign, Commonwealth & Development Office and the Wellcome Trust.

Prof. Pain's research group uses a combination of high-throughput sequencing, comparative and functional genomics protocols and bioinformatic analysis tools to study pathogenicity determinants in selected parasitic protists, bacteria and more recently in SARS-CoV-2 and DENV.

Big Data Speakers

Keynote: Dr Laura Merson

ISARIC Head of Data
University of Oxford, UK
Title: ISARIC: Outbreak research preparedness and response

Laura's early career was spent in Vietnam, Sri Lanka and Canada, focused on the design and implementation of clinical studies in low-resource settings to treat poverty-related diseases. She has managed studies across 6 continents, including therapeutic trials in Ebola virus disease, influenza, bubonic plague, mpox, dengue, and thalassemia. Laura's research interests target changing the paradigm of public health emergency response to integrate rapid, collaborative clinical research.

Laura co-launched and served 7 years as Associate Director of the Infectious Diseases Data Observatory (IDDO), an initiative enabling sharing of data across the research, humanitarian and public health communities. She also co-led the design and launch of the Health Data Research West Africa platform.

Now, based at the University of Oxford as Head of Data for ISARIC, the International Severe and Acute Respiratory and emerging Infections Consortium, Laura works in partnership with the World Health Organization and the network of ISARIC collaborators building standards in data collection and analysis during outbreaks. She led the design and implementation of the ISARIC Data Platform, a project that is now the world's largest international collection of data on individuals hospitalized with COVID-19. Laura developed and leads on the platform's data governance, linking, security and analysis mechanism

Big Data Speakers

Keynote: Prof. Blaz Zupan

Professor of Computer and Information Science
University of Ljulbjana, Slovenia
Title: Data Science for Life Scientists: Should Everyone Learn Programming or Is There an Alternative?

Abstract: In the talk, we propose that, given the right tool, it may only take a few hours to train outsiders, including, apologies, molecular biologists, in the major data science concepts. We will showcase Orange Data Mining (http://orangedatamining.com), a tool for interactive data analytics based on workflow. Most of the presentation will consist of a hands-on demo. We will use several practical applications to demonstrate the power of integrating visual programming, machine learning, and interactive visualizations and discuss how we might tentatively organize training in these subjects.

Dr Blaž Zupan teaches artificial intelligence and machine learning at the University of Ljubljana and Baylor College of Medicine. His research has focused on explainable AI and combinations of machine learning and data visualization techniques. He runs a twenty-member bioinformatics laboratory, which also develops Orange (http://orangedatamining.com), a comprehensive open-source toolbox for machine learning.

Prof. Julian Hiscox

Chair in Infection and Global Health
University of Liverpool, UK
Title: AI Virus Prediction

Julian currently leads a $6.6M US Food and Drug Administration funded international research program on the 'Characterization of severe coronavirus infection in humans and model systems for medical countermeasure development and evaluation'. Julian has worked on coronaviruses and the closely related arteriviruses since starting his PhD on the porcine coronavirus transmissible gastroenteritis virus at the Institute for Animal Health (IAH). He has worked on severe acute respiratory syndrome coronavirus (SARS-CoV) and for the past three years, Middle East respiratory syndrome coronavirus (MERS-CoV) in Saudi Arabia.

Because of his coronavirus experience he is a co-opted member of the New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG), an expert committee of the UK Department of Health and Social Care (DHSC), which advises the Chief Medical Officer (CMO).

Big Data Speakers

Dr Maya Wardeh

Lecturer in Computer Science
University of Liverpool, UK
Title: The landscape of viral transmission: from fragmented data to knowledge discovery

Maya is a lecturer in Computer Science at UOL. Her research uses complex-network, wildlife ecology, and low-resolution features engineered from sequences to predict characteristics of emerging viruses, across the entire mammalian and avian viromes, including coronaviruses and poxviruses.

She also works on predicting mosquito virus vector-competence, reservoirs of zoonotic pathogens (including viruses), and developing state-of-the-art computational methods to enhance pandemic preparedness.

Dr Marcus Blagrove

Senior Lecturer
University of Liverpool, UK
Title: Host in the machine: Using AI directed wet-lab work to optimise virus hot range prediction

Marcus is a Senior Lecturer in the Institute of Infection, Veterinary and Ecological Sciences at the University of Liverpool.

He is interested in what governs the interactions between viruses and their hosts, with two main foci: 1) the three-way interaction between mosquito vectors, arboviruses and environmental conditions; and 2, understanding and predicting the host-range, evolution and potential for spill-over of viruses from animal populations.

Big Data Speakers

Sponsor: Dr John Hardham

Director of the Zoetis Center for Transboundary and Emerging Diseases
Zoetis, USA
Title: Coronaviruses, One Health, and the Need for Integrated Biosurveillance

Dr John Hardham is the Director of the Zoetis Center for Transboundary and Emerging Diseases and the Veterinary Medicine Research and Development Emerging Infectious Disease Program. He earned his Bachelor of Science degree from The Pennsylvania State University and his Masters' and Doctorate of Philosophy degrees from The University of North Carolina. Following his Post-doctoral Fellowship with The University of Texas Health Science Center at Houston, he joined Pfizer Animal Health in 1999 and has continued following the transition to Zoetis, Inc. in 2013.

Dr Hardham has led multiple project teams in developing vaccines and biopharmaceuticals for both livestock and companion animals. In addition to working for Zoetis, Dr Hardham is a Captain in the United States Navy where he specializes in Chemical and Biological Defense Programs and has served on various committees for the National Academies of Science. Captain Hardham is currently assigned to the United States Northern Command and is detailed to the Defense Intelligence Agency, National Center for Medical Intelligence.

Abstracts – Big Data Workshop

Big Data Abstracts

Changing COVID-19 severity in patients hospitalized for community-associated Delta, BA.1 and BA.4/5 variant infection in Slovenia.

Maja Sočan[1], Katarina Prosenc[2], Miša Korva[3], Tatjana Avšič-Županc[3], Mario Poljak[3], Maja Lunar[3] and Tina Zupanič[1]

[1]National Institute of Public Health, Zaloška cesta 29, 1000 Ljubljana, Slovenia. [2]National Institute of Health, Environment and Food, Bohoričeva ulica 15, 1000 Ljubljana, Slovenia. [3]Institute of Microbiology and Immunology, Zaloška cesta 4, 1000 Ljubljana, Slovenia.

Background: Despite decreasing COVID-19 disease severity during the Omicron waves, a proportion of patients still require hospitalization and intensive care.

Objective: To compare demographic characteristics, comorbidities, vaccination status, and previous infections in patients hospitalized for community-associated COVID-19 (CAC) in predominantly Delta, Omicron BA.1 and BA.4/5 SARS-CoV-2 waves.

Methods: Data were extracted from three national databases: The National COVID-19 Database, The National Vaccination Registry and The National Registry of Hospitalizations. Only patients admitted for CAC in Delta, BA.1, and BA.4/5 waves were included in the study.

Results: Among hospitalized CAC patients analyzed, 5512 were infected with Delta, 1120 with Omicron BA.1, and 1143 with Omicron BA.4/5 variant. From Delta to BA.4/5, the age and sex structure changed: the proportion of women, children, adolescents, and older than 80 years increased significantly. Significantly more patients had comorbidities (measured by the Charlson Comorbidity Index). Despite the increase in high-risk patients, average length of stay, need for noninvasive ventilatory support (NIVS), ICU admission, mechanical ventilation (MV), and in-hospital mortality (IHM) decreased. Multivariate analysis revealed significantly lower odds for ICU admission and IHM during the Delta period in patients who had been fully vaccinated or boosted with COVID-19 vaccine within the previous nine months. Vaccination reduced the likelihood of MV regardless of the time elapsed between the last vaccine dose and the positive COVID-19 test result. In the BA.1 variant period, patients who had less than six months elapsed between the last vaccine dose and SARS-CoV-2 positivity had lower odds for MV and IHM, but not for NIVS or ICU admission. Vaccination had no effect on NIVS, ICU admission, and MV in the BA.4/5 period but lowered the probability of IHM.

Abstracts – Big Data Workshop

Using TopMD to identify pathway biomarkers and stratify disease.

James Schofield on behalf of the TopMD team

TopMD Precision Medicine Ltd, Southampton, United Kingdom

The identification and classification of diseases is a critical step in the development of effective treatments; however, a 'one-size-fits-all' approach for disease treatment often has poor success rates. Disease rarely results from differential abundance or activity of a single gene, instead, they are a consequence of activated pathways of genes and their protein products. Discrete gene biomarkers have often proven to be insufficiently accurate and precise due to variability within a population and technical measurement variability. Genes are not expressed in isolation, but in connected pathways; it is modulation of these pathways which often determine the molecular phenotype of a patient.

TopMD is an innovative AI-enhanced technology, developed by a team of systems biologists and mathematicians at the University of Southampton, which analyses the topology of global gene expression according to a network of known gene interactions, defined as TopMD Maps. These maps characterise all the activated pathways within a patient, accurately representing their molecular phenotype. We have evaluated this approach using microarray data from 239 patients with 8 different disease states. We were able to identify their disease type with an accuracy of 97%, in addition, sub-phenotypes within each disease type were identified. The TopMD algorithm has since been applied to different disease contexts, including COVID-19, neurodegenerative diseases, inflammatory bowel diseases and more. Here we describe a recent study where we explored the relationship between enriched biological pathways in patients with Alzheimer's disease (AD) with their gut microbiomes. The blood transcriptome of AD patients and matched controls were measured using long-read sequencing (Oxford Nanopore Technologies) to identify molecular phenotypes. Our approach identified 3 sub-phenotypes of AD based on their transcriptome and further exploration of the gut microbiomes highlighted specific differences in each group. We demonstrate the utility of TopMD and multi-omics data in driving a personalised medicine approach.

Abstracts – Big Data Workshop

COVID-19 biomarker identification from multi-factorial analysis

Rebekah Penrice-Randal[1,2*], Fabio Strazzeri[1], Catherine Hartley[2], James P R Schofield[1], Paul J Skipp[1,5], Diana Baralle[3,4**], Julian A Hiscox[2,9,10], on behalf of the DRAGON consortium.

[1]TopMD Precision Medicine Ltd, Southampton, United Kingdom. [2]Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, Liverpool, UK. [3]School of Human Development and Health, Faculty of Medicine, University of Southampton, Southampton, United Kingdom. [4]National Institute for Health Research (NIHR) Southampton Biomedical Research Centre, University of Southampton, and University Hospital Southampton National Health Service (NHS) Foundation Trust, Southampton, United Kingdom. [5]Centre for Proteomic Research, School of Biological Sciences, University of Southampton, Southampton, United Kingdom. [6]NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, Liverpool, United Kingdom. [7]A*STAR Infectious Diseases Laboratories (ASTAR ID Labs), Agency for Science, Technology and Research (ASTAR) Singapore, Singapore, Singapore

The COVID-19 pandemic has placed a strain on healthcare systems worldwide. Tools that can stratify individuals according to prognosis or molecular phenotypes could allow for more efficient allocation of healthcare resources and thus improved patient outcomes. Our previous studies, using topological analysis (TopMD), have shown that gene expression data derived from whole blood at the time of admission to hospital can be used to predict admission to the intensive care unit (ICU). Rather than using a traditional binary approach such as DGE, our TopMD platform utilises every measured data point to interrogate biological pathway activation. Whole blood was collected in PAXgene tubes from patients hospitalised with COVID-19 in Liege and Florence at point of admission and 48 hours alongside clinical and CT scan data within the DRAGON consortium. RNA was extracted from blood prior to globin and rRNA depletion then RNA sequencing libraries were sequenced on the NovaSeq 6000 (Illumina). Paired-end fastq files were trimmed with fastp, and transcripts were quantified using Salmon where gene expression was inferred using the R package tximport. The host response within our cohorts was then assessed with traditional transcriptomic approaches and TopMD. TopMD molecular phenotype maps were generated for individual patients and sub-phenotypes of COVID-19 disease was explored. Finally, we conducted a multifactorial analysis including gene expression, pathway activation derived from TopMD analysis, CT scan data, and clinical measurements.

AGM Programme

AGM: Thursday 14th Sept 2023

Start	End	Thursday 14th September 2023	
08:15	08:50	ARRIVAL AND REGISTRATION	
08:50	09:00	Welcome address and introduction	Prof Julian Hiscox and Prof. Tatjana Avšič - Županc
Session 1: One Health and Zoonoses *Chair: Prof. Wim Van Der Poel, Wageningen University, The Netherlands* *Dr Giulia Gallo, The Pirbright Institute, UK*			
09:00	09:30	Keynote: Beyond SARS-CoV-2	Prof. Diana Bell University of East Anglia, UK
09:30	09:45	Immune consequences of bat-coronavirus interactions	Dr Arinjay Banerjee University of Saskatchewan, Canada
09:45	10:00	Zoonotic and spillover potential of APN-using alphacoronaviruses: a genus-wide investigation of viral entry	Dr Giulia Gallo The Pirbright Institute, UK
10:00	10:15	Investigating the role of SARS-CoV-2 NTD Spike mutations in viral entry, transmission, and evading host immunity.	Miss Nazia Thakur The Pirbright Institute, UK
10:15	10:45	MORNING BREAK	
Session 1: One Health and Zoonoses Continued *Chairs: Dr James Stewart, University of Liverpool, UK* *Dr Arinjay Banerjee, University of Saskatchewan, Canada*			
10:45	11:15	Invited speaker: Coronavirus One Health Research Integration, Outcomes of the COVRIN-project	Prof. Wim Van Der Poel Wageningen University, The Netherlands
11:15	11:30	Animal Coronaviruses Workshop GAP analysis summary	Prof. Louise Cosby Queen's University Belfast, UK
11:30	12:00	Keynote: Zoonotic spillover of emerging viruses in west Africa	Prof. Miles Carroll University of Oxford, UK
12:00	13:00	LUNCH BREAK AND POSTER VIEWING	

AGM Programme

Start	End	Thursday 14th September 2023	
Session 2: Surveillance; Characterisation and Detection *Chair: Prof. Tatjana Avšič, University of Ljubljana, Slovenia* *Dr Misa Korva, University of Ljubljana, Slovenia*			
13:00	13:15	Co-detections of herpesviruses in lower respiratory tract samples of severely ill SARS-CoV-2 positive patients	Dr Gašper Grubelnik University of Ljubljana, Slovenia
13:15	13:30	Application of a HRM variant calling assay for monitoring SARS-CoV-2 variants in Burkina Faso & Kenya	Miss Caitlin Greenland-Bews Liverpool School of Tropical Medicine, UK
13:30	13:45	Review of diagnostics of non-SARS human coronaviruses in Slovenia- what have we learned?	Dr Monika Jevšnik University of Ljubljana, Slovenia
13:45	14:15	Invited speaker: Diagnostics of SARS-CoV-2 in the Post-Covid Era	Dr Miša Korva University of Ljubljana, Slovenia
14:15	14:45	AFTERNOON BREAK	
Session 3: Social Behaviour and Policy *Chair: Dr Katie Adam, University of Edinburgh, UK*			
14:45	15:15	Keynote: Social Behaviour and Policy Preparedness for the SARS-CoV-2 pandemic	Prof. Alemka Markotic University Hospital for Infectious Diseases Zagrab, Croatia
15:15	15:30	Pandemics and the politics of knowledge: Examples from participatory research with young people in London, UK, and Cleveland, OH, USA	Ms. Tabitha Hrynick University of Sussex, UK
15:30	16:00	The ISARIC WHO Clinical Characterisation Protocol: A case study of how being prepared to create a timely understanding of a pandemic pathogen saved lives #DataSavesLives	Prof. Calum Semple (OBE) University of Liverpool, UK
16:00	16:15	COVID-19 and pandemic preparedness: local and global concepts and practices in tackling disease threats in Africa	Prof. Hayley MacGregor University of Sussex, UK
16:15	17:00	Panel discussion: Integrating social science perspectives on pandemic preparedness.	
CLOSED DINNER			

AGM Programme

AGM: Friday 15th Sept 2023

Start	End	Friday 15th September 2023	
08:45	9:00	ARRIVAL	
Session 4: Countermeasures and interventions *Chairs: Prof Louise Cosby, Queen's University Belfast, UK* *Dr Isobel Webb, University of Bristol, UK*			
09:00	09:30	Keynote: COVID-19 Lessons Learnt	Prof Tess Lambe University of Oxford, UK
09:30	09:45	Discovery of broadly neutralising bovine monoclonal antibodies against SARS-CoV-2	Miss Emily Park University of Nottingham, UK
09:45	10:00	Omicron (BA.1)-induced antiviral response attenuates RSV infection in WD-PBECs	Miss Erin Getty Queens University Belfast, UK
10:00	10:15	Access to transnational facilities through ERINHA & ISIDORe	Mr. Dylan Bonfils and Ms. Claire Connellan, ISIDORe, Europe
10:15	10:30	BBSRC/UKRI Funding	Dr Nikki Mackie BBSRC, UK
10:30	11:00	MORNING BREAK	
Session 5: SARS-CoV-3 and the Future *Chairs: Prof. Paul Digard, The Roslin Institute, UK* *Miss Caitlin Greenland-Bews, Liverpool School of Tropical Medicine, UK*			
11:00	11:30	Keynote: SARS-CoV-3 and the Future	Ms. Felicity Bennee Public Health Wales, UK
11:30	11:45	Sarbecovirus usage of mammalian ACE2: Investigating the receptor binding and genetic determinants of host range	Miss Yeonjae Lee, The Pirbright Institute, UK
11:45	12:00	A comparison of different variants of SARS-CoV-2; Severity of Omicron and Delta-associated pathogenesis differs in a mouse model	Dr Parul Sharma/Mr. Adam Kirby University of Liverpool, UK
12:00	12:30	Strengthening Regulatory Science for Pandemic Preparedness	Dr Tracey MacGill, FDA, USA
12:30	13:00	FINAL DISCUSSION AND MEETING CLOSE	

Annual General Meeting Speakers

Keynote: Prof. Diana Bell

Professor of Conservation Biology
University of East Anglia, UK
Title: Beyond SARS-CoV2

Diana is Professor of Conservation Biology at UEA whose research includes a One Health approach to emerging wildlife and zoonotic diseases. She investigated the origins of SARS and SARS-CoV2 as a specialist in illegal wildlife trade and has published on other Sarbecovirus in UK bats.

She also currently works on HPAI H5N1, pox viruses, *Trichomonas gallinae,* neglected vectors and Lagomorph caliciviruses in addition to ecosystem and endangered species restoration globally and the conservation of mega biodiverse water catchment habitats.

Prof. Wim van der Poel

Professor and Research Leader on "Emerging and Zoonotic Viruses"
Wageningen University, The Netherlands
Title: Coronavirus One Health Research Integration, Outcomes of the COVRIN-project

Wim H. M. van der Poel, DVM, PhD, dipl. ECMV, is a senior scientist at Wageningen Bioveterinary Research and special Professor of 'Emerging and Zoonotic viruses' at Wageningen University. He is a member of the Executive Board of the Netherlands Centre for One Health (NCOH) and the project management board of the European Joint Programme for One Health (EJPOH). He is coordinator of the EPIZONE European Research Group and chairs the Scientific Committee of International Research Consortium for Animal Health.

The research work of Prof. Van der Poel involves three main areas: New and emerging viruses, Foodborne and Zoonotic viruses and 'Global One Health'.

Annual General Meeting Speakers

Keynote: Prof. Miles Carroll

Professor, High Consequence Emerging Viruses
University of Oxford, UK
Title: Zoonotic spillover of emerging viruses in West Africa

Prior to establishing the High Consequence Emerging Viruses Group within University of Oxford's Pandemic Sciences Institute, Miles was head of Research at the National Infections Service at Public Health England, Porton Down from 2008-2022. His current research portfolio includes naturally acquired immunity to EBOV & other high consequence pathogens, understanding the host response to infection, high consequence emerging disease vaccines, and the application of molecular epidemiology to outbreaks. He is also involved in ongoing infectious disease research in west Africa which supports capacity building for the region.

Miles gained his PhD on HIV vaccine research from the Medical Faculty at the University of Manchester which enabled him to obtain a fellowship to continue his studies on recombinant poxviruses at the National Institutes of Health, USA. On his return to the UK, Miles joined Oxford Biomedica (OBM) as Vice President of Immunotherapy.

Miles has authored >250 publications primarily in the fields of recombinant vaccines, host pathogen interactions and molecular epidemiology, and is the recipient of >15 granted patents. Miles serves on a variety of Scientific Advisory Boards including the UK Animal and Plant Health Agency, Defence Science & Technology Laboratories, UK Vaccines Network and the WHO R&D Road Map for Priority Pathogens. He has been awarded various honorary awards in recognition of his research contributions to the field of infectious diseases.

Annual General Meeting Speakers

Dr Misa Korva

Head of COVID-19 Diagnostics Lab
University of Ljubljana, Slovenia
Title: Diagnostics of SARS-CoV-2 in the Post-Covid Era

Dr Misa Korva joined the Laboratory for diagnostics of zoonoses at the Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Slovenia in 2007 and defended her PhD thesis on the pathogenesis of hemorrhagic fever with renal syndrome in 2011.

Currently, she is an operational team leader of intervention teams for counter bioterrorism treat and the Head of the COVID-19 diagnostic laboratory at the IMI, Slovenia. As a researcher, she has been involved in clinical diagnostics and research of zoonotic vector-borne diseases, viral hemorrhagic fevers and highly pathogenic bacteria. She is a principal investigator in a national project "Clinical Metagenomics Sequencing for Pathogen Detection in Patients with Central Nervous System Infections" and has been deeply involved in development of continuous surveillance of SARS-CoV-2 variants in Slovenia.

She is also involved in several international and national collaborative projects and has worked in the BSL-3 laboratory at USAMRIID, Fort Detrick, Maryland, USA and at BLS -4 BNI in Hamburg, Germany. As a member of the European Mobile Lab, she participated in the WHO /GOARN Ebola Emergency Response Mission in Guéckédou, Guinea in 2014. As an Assistant Professor at Faculty of Medicine, she lectures on emerging pathogens, biological warfare, biosafety and biosecurity, and virology.

Annual General Meeting Speakers

Keynote: Dr Alemka Markotić

Director
University Hospital for Infectious Diseases, Croatia
Title: Social Behaviour and Policy Preparedness for the SARS-CoV-2 pandemic

Alemka Markotić**,** MD, PhD is the director of the University Hospital for Infectious Diseases, Zagreb Croatia, a full professor at the Faculty of Medicine of the University of Rijeka and the Faculty of Medicine of the Catholic University of Zagreb, Croatia, and a member of the Academy of Sciences and Arts of Bosnia and Herzegovina. She is also the president of the Croatian Academy of Medical Sciences. Her research focuses on zoonoses.

During the COVID-19 pandemic she was a member of the Croatian National Crisis Headquarters for COVID-19, a member of the Scientific Council of the Prime Minister of the Republic of Croatia, the EU Scientific Advice Platform COVID-19, the European expert group on SARS-CoV-2 variants and the EU Expert Sub-group on COVID-19 therapeutics and the European Commission's advisory panel on COVID-19.

Annual General Meeting Speakers

Keynote: Prof. Calum Semple

Professor of Child Health and Outbreak Medicine, Consultant Respiratory Paediatrician
University of Liverpool, UK
Title: The ISARIC Who Clinical Characterisation Protocol: A case study of how being prepared to create a timely understanding of a pandemic pathogen saved lives #DataSavesLives

Professor Calum Semple has studied severe virus disease outbreaks since 1989 in the fields of diagnostics, clinical characterization, and clinical trials. He was one of the founders of the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC). He has led research on HIV, RSV Bronchiolitis, human metapneumovirus, Pandemic Influenza, Ebola (EVD and Survivors), Monkeypox, COVID-19, and Acute Severe Hepatitis in Children, at times field-deployed in austere circumstances.

Calum was a regular participant on the Scientific Advisory Group for Emergencies (SAGE) for the UK COVID-19 response and their New Emerging Respiratory Viral Treats Advisory Group (NERVTAG), and a former member of the WHO Scientific Technical Advisory Committee for Ebola Emergencies (STAC-EE). He was appointed Officer of the Most Excellent Order of the British Empire in the Queen's Birthday Honours 2020 for his role in the COVID-19 response and made a Distinguished Fellow of the Faculty of Public Health in 2022.

Annual General Meeting Speakers

Keynote: Prof. Teresa Lambe

Professor of Vaccinology and Immunology
University of Oxford, UK
Title: COVID-19 Lessons Learnt

Teresa Lambe is the Calleva Head of Vaccine Immunology and a Professor of Vaccinology & Immunology at the University of Oxford. She is leading a research group which improves human health by controlling disease through vaccination – stopping epidemics before they become pandemics. Prof Lambe is one of the Principal Investigators overseeing the Oxford/AstraZeneca vaccine programme; she co-designed the vaccine in January 2020, led the preclinical studies, and then oversaw the delivery of the immune results needed to support regulatory approval in late 2020. The vaccine has played a pivotal role in the fight against COVID-19 – estimated to have saved >6 million lives globally. Prof. Lambe was appointed as an honorary OBE for her services to Sciences and Public Health in the 2021 Queen's Birthday Honours and received the Presidential Distinguished Service Award for the Irish Abroad in 2022.

Prof Lambe's group are particularly interested in delineating the protective immune response post infection and using these findings to rationally design vaccination strategies to prevent disease. The establishment of long-lived immunity, post vaccination, is also critically important in protecting against infectious disease and is a key focus of the research. The Lambe group is currently developing and testing vaccines against a number of outbreak pathogens including Crimean-Congo haemorrhagic fever virus, Ebola virus, Marburg virus Disease and Coronaviruses. A number of these vaccines have progressed to clinical trial assessment, including a vaccine against Ebola virus diseases (ChAdOx1 biEBOV); in late 2022, this vaccine was one of three chosen by the WHO to be included in a ring vaccination protocol against the Sudan ebolavirus outbreak in Uganda. In 2023, the team's candidate vaccine against Marburg virus disease was selected by WHO for inclusion in trials to combat Marburg virus disease.

Annual General Meeting Speakers

Keynote: Ms Felicity Bennee

Head of Data
Public Health Wales, UK
Title: SARS-CoV-3 and the Future

Fliss Bennee is the Head of Data in Public Health Wales and spends most of her life translating between different groups of experts to deliver shared understanding through a common language.
Having spent most of her career in the civil service, her passion is for clear communication and understanding of science, technology, and data as enablers of public policy, health and wellbeing.

Before joining Public Health Wales, Fliss has held roles at the Welsh Government and the UK Government, including Department for Digital, Culture, Media and Sport, Cabinet Office, Government Digital Service, Home Office and Charity Commission. Whether investigating social capital, supporting charity legislation, delivering IT portfolio outcomes, or forming data policy, she finds it usually helps to accept that what people need is not the same as what you want to make/do.

In her previous role, Fliss was responsible for providing high quality, impartial scientific and technical advice to Welsh Government Ministers and Officials and contributing as a member of SAGE to the wider UK effort to minimise harms arising from COVID-19 and the pandemic response.

Annual General Meeting Speakers

Invited: Dr Tracy MacGill

Director
MCM Regulatory Science, US Food and Drug Administration
Title: Strengthening Regulatory Science for Pandemic Preparedness

Dr. Tracy MacGill is Director, Medical Countermeasure Regulatory Science for FDA's Office of Counterterrorism and Emerging Threats (OCET) and the Medical Countermeasures Initiative (MCMi). She leads the MCMi Regulatory Science Program, oversees intra- and extramural research programs, and works with FDA Centers, PHEMCE stakeholders, and other U.S. and international partners on medical countermeasure-related regulatory science issues. OCET is part of FDA's Office of the Chief Scientist, in the Office of the Commissioner.

Prior to joining OCET, Dr. MacGill served as a Program Officer in the Office of Biodefense Research Affairs (OBRA), at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), where she managed a portfolio focused on the development of biodefense animal models to support product development. Previously, Dr. MacGill was a Microbiologist in the Office of Counter-Terrorism and Emergency Coordination (OCTEC), in FDA's Center for Drug Evaluation and Research (CDER).

Dr. MacGill also served on active duty with the United States Army as a research microbiologist in the Department of Immunology at the Walter Reed Army Institute of Research (WRAIR), working with non-human primate malaria models. Following the anthrax mail attacks in 2001, she was assigned to a counterterrorism augmentation team at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) at Fort Detrick, Maryland.

Dr. MacGill is now an officer in the Commissioned Corps of the United States Public Health Service and holds the rank of Captain. CAPT MacGill earned a doctorate in Cellular and Molecular Biology from the University of Nevada, Reno.

Annual General Meeting Speakers

Mr Dylan Bonfils

Communication and External Affairs Manager
European Research Infrastructure on Highly Pathogenic Agents
Title: Access to transnational facilities through ERINHA & ISIDORe

Dylan Bonfils joined ERINHA-AISBL in January 2021 as Communication and External Affairs Manager. He graduated from the University of Tartu, Estonia in Political Sciences, and International Relations, specializing in the post-Soviet era.

He previously worked four years with several French officials in the parliament on European and International co-operations topics.

Ms Claire Connellan

European Project Manager
European Research Infrastructure on Highly Pathogenic Agents
Title: Access to transnational facilities through ERINHA & ISIDORe

Claire Connellan is the European Project Manager at the European Research Infrastructure on Highly Pathogenic Agents (ERINHA). Claire is the project manager of the Integrated Services of Infectious Disease Outbreak Research (ISIDORe) project, an EU funded project which launched in February 2022 and aims to improve our preparedness and responsiveness to pandemic prone pathogens.

Claire has a background in project management and policy development, and holds an MA International Peace and Security from King's College London. Prior to joining ERINHA in January 2022, Claire worked for an international child rights organisation in London.

Annual General Meeting Speakers

Dr Nikki Mackie

Senior Portfolio Manager
UKRI BBSRC
Title: Funding Opportunities

Nikki Mackie is a Senior Portfolio Manager within Research Strategy and Programmes at BBSRC. Her portfolio focuses on animal health and one health within the Bioscience for an Integrated Understanding of Health team.

Previously, I was a Portfolio Manager at BBSRC working on Animal Health programmes in Europe, focussing on the ICRAD ERA-NET. Before joining BBSRC I completed a PhD at Bristol University focussing on the health, welfare, and behaviour of laying hens.

Abstracts – AGM Oral Presentations

AGM Oral Presentation Abstracts

Immune consequences of bat-coronavirus interactions

Kaushal Baid[1], Victoria Gonzalez[1,2], Rita Quintela Tizon[1,2], and **Arinjay Banerjee[1,2,3,4,5]**

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Bat species can harbour viruses from multiple families, including sarbecoviruses and merbecoviruses from the genus *Betacoronavirus* that are closely related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and Middle East respiratory syndrome coronavirus (MERS-CoV). Vesper bats harbor sarbecoviruses and merbecoviruses and are thought to be the ancestral reservoirs of MERS-CoV. Despite studies demonstrating the existence of MERS-CoV-like and SARS-CoV-2-like viruses in vesper bats, the dynamics of virus infection in these bats remain unknown.

In this study, we characterized the host responses in *betacoronavirus* infected vesper bats and bat-derived cells. Upon infection, host cells mounted an antiviral response faster than human cells. Furthermore, we characterized the antiviral interferon-mediated response in multiple bat cells and discovered canonical and non-canonical activation of transcription factors and the upregulation of both known and previously unknown antiviral genes.

In conclusion, data from our study demonstrate that bat cells have evolved both conserved and non-canonical processes to better tolerate virus infection.

Abstracts – AGM Oral Presentations

Zoonotic and spillover potential of APN-using alphacoronaviruses: a genus-wide investigation of viral entry

Giulia Gallo[1], Aghnianditya Kresno Dewantari[1,2], Antonello Di Nardo[1], Stephen C Graham[3], Dalan Bailey[1]

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Alphacoronaviruses (alphaCoVs) are emerging viruses with zoonotic potential. While the majority of alphaCoVs have been found associated to bats, they can also infect other mammals, such as humans, cats, dogs, and pigs. In these hosts, viruses can cause different degrees of pathology, occasionally resulting in lethal outcomes. It has been showed that some alphaCoVs infect their hosts through binding of their Spike attachment protein to the receptor aminopeptidase N (APN). However, the broad zoonotic potential of these viruses has not been exhaustively evaluated.

In our study, we used a greedy algorithm to select representatives of the alphaCoV genus from publicly available sequence databases. The selected S proteins of these viruses were pseudotyped using a lentiviral system, and their tropism for APN of different mammalian species was analysed. We found that most of our S could pseudotype, but only few of them would interact with our bank of APNs. Interestingly, we observed that two alphaCoVs found in bats could use APN obtained from different chiropter species, broadening our understanding of S/APN interaction within the viral genus. We also observed host range differences among human, pig and canine alphaCoVs.

Our data shed light on APN usage among alphaCoVs and identified viruses with broad receptor usage ability – generalists – versus viruses restricted to a small number of mammalian species – specialists. From a One-health perspective, our results support the importance of studying zoonotic potential at a broad scale, both in terms of viral sequences and receptors' origin, providing information about likelihood of spill-over and potential intermediate reservoirs.

Abstracts – AGM Oral Presentations

Investigating the role of SARS-CoV-2 NTD Spike mutations in viral entry, transmission and evading host immunity.

Joseph Newman[1], Cameron Bissett[2], Ahmed ME Elrefaey[1], Jeffrey Seow[3], Katie Doores[3], Teresa Lambe[2,4], Dalan Bailey[1]
Presented by **Nazia Thakur**[1,2]

[1] Viral Glycoproteins Group, The Pirbright Institute,UK
[2] Nuffield Department of Medicine, The University of Oxford, UK
[3] Department of Infectious Diseases, School of Immunology & Microbial Sciences, King's College London, UK
[4] Chinese Academy of Medical Science (CAMS) Oxford Institute, University of Oxford, UK.

Repeated epidemic waves of infection during the COVID-19 pandemic gave rise to variants including Alpha, Delta and Omicron, following mutations within the SARS-CoV-2 genome. Mutations within the Spike protein are of particular significance as Spike is the main target for neutralising antibodies (nAbs), with the majority of nAbs targeted against the S1 domain of Spike, especially the receptor binding domain (RBD). Antibodies are also able to potently bind a "supersite" on the N-terminal domain (NTD) within S1, but this mode of action is less well understood.

To investigate this, we synthesised a database of individual or combinatorial extant Spike NTD mutations or deletions, which were subsequently used to generate lentiviral-based pseudotypes and to assess neutralisation. We observed productive viral infections for all the mutations and deletions, suggesting none were imperative for entry. We screened pseudotypes against sera and monoclonals antibodies from vaccinated and/or infected individuals/mice exposed to different SARS-CoV-2 variants. This revealed deletions at key sites within the NTD impacted nAb responses and were important for immune escape.

Elucidating the effect of RBD and NTD-specific mutations on nAb responses, either alone or in combination, is an important element of continued SARS-CoV-2 surveillance.

Abstracts – AGM Oral Presentations

Co-detections of herpesviruses in lower respiratory tract samples of severely ill sars-cov-2 positive patients

Gašper Grubelnik[1], Miša Korva[1], Rok Kogoj[1], Tina Polanc[1], Darja Keše[1], Katja Seme[1], Matjaž Jereb[2,3], Matej Mavrič[2], Tatjana Avšič-Županc[1].

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Background: Viral, bacterial and fungal co-detections in hospitalized patients became evident shortly after the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, limited studies of herpesvirus co-detections in lower respiratory tract (LRT) samples are available.

Methods: In our retrospective study, 229 SARS-CoV-2 positive patients admitted to the largest intensive care unit (ICU) in Slovenia of the Department for Infectious Diseases and Febrile Conditions at the University Medical Centre Ljubljana were investigated for the prevalence of herpesvirus co-detections. Collectively, 1472 LRT samples were investigated. Detection of SARS-CoV-2, cytomegalovirus (CMV), Epstein - Barr virus (EBV), herpes simplex virus 1 (HSV-1), herpes simplex virus 2 (HSV-2) and varicella-zoster virus (VZV) was performed using (rt)RT-PCR tests.

Results: In our study at least one co-detection was observed in 89.1% (204/229) of patients. Most common co-detections were EBV, HSV-1, and CMV with 74.7% (171/229), 58.1% (133/229) and 38.0% (87/229) of positive patients, respectively. Conversely, VZV and HSV-2 were detected in less than 1% (2/229) of patients. Co-detections with more than one pathogen were observed in 61.1% (140/229) of patients. Most often, along SARS-CoV-2, two additional pathogens were detected with 38.4% (88/229) of such patients. EBV, HSV-1 and CMV were on average detected 11 to 20 days after first SARS-CoV-2 confirmation in LRT samples.

Conclusions: Taken together, our results indicate that in addition to SARS-CoV-2 herpesviruses are frequently detected in LRT samples of ICU patients, particularly EBV, CMV, and HSV-1, suggesting that SARS-CoV-2 infection could be one of the risk factors for possible reactivation of herpesviruses in LRT of severely ill SARS-CoV-2 positive patients. However, whether molecular co-detection alone does not distinguish reactivation, superinfection, or involvement in comorbidity requires further clinical investigation to better understand the true impact of such cases on the treatment and recovery of SARS-CoV-2 patients.

Abstracts – AGM Oral Presentations

Application of a HRM variant calling assay for monitoring SARS-CoV-2 variants in Burkina Faso & Kenya

Caitlin Greenland-Bews[1], Sonal Shah[2], Alice J Fraser[2], Samuel S. Serme[0], Kephas Otieno[4], Issiaka Soulama[0], Tegwen Marlais[2, 0], Emily Adams[1] , Simon Kariuki[4], Prof Chris Drakeley*[2], Prof Feiko O ter Kuile*[4,6] David J Allen[2] , Thomas Edwards[1]

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The rapid emergence and global dissemination of SARS-CoV-2 highlighted a need for robust, adaptable surveillance systems. However, financial and infrastructure requirements for whole genome sequencing (WGS) mean most surveillance data has come from higher-resource geographies. Consequently, the molecular epidemiology of SARS-CoV-2 in low- and middle-income countries (LMICs) is limited, and there is a need for more cost-accessible technologies in LMICs to help close data gaps in variant surveillance. To address this, we have developed two high-resolution melt curve (HRM) assays that target key variant-defining mutations in the SARS-CoV-2 genome, which give unique signature profiles that define different SARS-CoV-2 variants of concern (VOCs).

Extracted RNA from SARS-CoV-2 positive samples collected from 208 participants (112 Burkina Faso, 96 Kenya) on the day of enrolment in the MALCOV study (Malaria as a Risk Factor for COVID-19) between January 2021 and January 2022 were analysed using our optimised HRM assays and compared to WGS. Both assays demonstrated high sensitivity when compared to nanopore sequencing and offer a lower-cost approach to enable molecular epidemiology as part of wider surveillance strategies. The assays are readily adaptable and can focus on local epidemiological surveillance questions or be updated quickly to accommodate the emergence of a novel variant.

Abstracts – AGM Oral Presentations

Review of diagnostics of non-SARS human coronaviruses in Slovenia- what have we learned?

Monika Jevšnik Virant[1], Tina Uršič[1], Miroslav Petrovec[1]

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Human coronaviruses (HCoVs) are associated with a variety of clinical presentations in children and adults, but their role in disease remains uncertain. Because of their animal origin, they are very interesting for study. Before 2007, HCoVs were not included in routine respiratory virus diagnostics in Slovenia. After a retrospective study in which we detected HCoVs for the first time in young children with acute respiratory tract infection, we included HCoVs in routine diagnostics by using in house real-time RT-PCR. All four HCoVs species were present and seasonally distributed in Slovenia, but most of them (70%) were co-detected with other respiratory viruses.

Association between the estimated quantity of HCoV viral nucleic acids present and the age of the children was observed. The association was nonlinear ($P < 0.001$), and the highest estimated viral load was detected in children around 10 months old. Because SARS-CoV was associated with gastrointestinal symptoms and probably the correlation could also be for other HCoVs, a prospective 2-year study was conducted to investigate HCoVs associations with various clinical presentations in hospitalized children up to 6 years of age.

The study included children hospitalized with acute bronchiolitis (AB), acute gastroenteritis (AGE), or febrile seizures (FS), and children admitted for elective surgery (healthy controls). Patients with AB, AGE, and FS, had a nasopharyngeal (NP) swab, a stool and a blood sample taken at admission and at follow-up 14 days later, whereas healthy controls had a NP swab and a stool sample taken at admission. The pathogenic potential of HCoVs is most probably minor in children with AB and AGE, but is more likely in children with FS, considering that they had a higher proportion of positive HCoVs results than patients with AB and those with AGE, and also had the highest viral load.

Abstracts – AGM Oral Presentations

Pandemics and the politics of knowledge: Examples from participatory research with young people in London, UK and Cleveland, OH, USA

Megan Schmidt-Sane[1], Santiago Ripoll[1], **Tabitha Hrynick[1]** and Elizabeth Benninger[2]

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Research on the context of COVID-19 vaccine 'hesitancy' can highlight a wide range of long-standing historical, political-economic, and social issues faced by marginalised communities. Young people, for example, were often labelled 'vaccine hesitant' when COVID-19 vaccines first became available, as uptake was lower amongst youth in the United Kingdom and United States. Such labelling can portray young people as 'ignorant' without addressing the deeply rooted causes of vaccine hesitancy. We know from social science research on vaccination that uptake of vaccines is rooted in context. Community experiences with authorities and the medical establishment can influence who they trust.

Our research, funded by the British Academy, used collaborative and participatory methods with young people (ages 12-18) in the Ealing borough of London and Cleveland, Ohio to understand how social context, including experiences of systemic racism and structural inequalities, shape responses to COVID-19 vaccines. We will report on findings from this study in this presentation. Using a comparative case study approach and a 'political economy of health' lens, we found that vaccine uptake was patterned by age (younger youth were more likely to get a vaccine), experiences of marginalisation and deprivation, and family and peer influence. Rather than encountering misinformation on social media, young people were inundated with information (both good and bad) in the news, on social media, and from friends and family. Young people who were vaccinated were more likely to have friends and family who were vaccinated, and vice versa. Most importantly, young people's engagement with COVID-19 vaccines reflected their experiences as youth in the UK and US. This showed up in mistrust between racially minoritised youth and local authorities.

Abstracts – AGM Oral Presentations

COVID-19 and pandemic preparedness: local and global concepts and practices in tackling disease threats in Africa

Hayley Macgregor[1]

The Pandemic Preparedness Project Team (PI Melissa Leach) from the Institute of Development Studies (Leach, MacGregor, Wilkinson), Gulu University, Uganda (Grace

Akello, Bob Okello, Moses Baluku, Bono Osungu, Peter Kermundu), Njala University, Sierra Leone (Paul Richards, Esther Mokuwa, Foday Komara, Marion Nyakoi, Lawrence Babawo), CRCF, Senegal and IRD, France (Khoudia Sow, Alice Desclaux, Kelley Sams), LSHTM (Melissa Parker, Fred Martineau).

In the years prior to the recent pandemic, the concept of epidemic 'preparedness' had gained prominence in global health discourse as concern about (re)emerging diseases with pandemic potential had grown. The COVID-19 pandemic thrust a political spotlight on 'preparedness' and called into question received assumptions, highlighting also the contextual nature of practices aimed at controlling disease outbreaks.

I will present findings from a Wellcome-funded project (2019-2023, PI Leach) on meanings and practice of preparedness. It involved social science research to explore the connections and/or disconnections between discourses of preparedness in global fora and local concepts of, and responses to, outbreaks and misfortune. Fieldwork was conducted in rural villages that had encountered Ebola in Sierra Leone and Uganda respectively, and focused on people's responses to uncertainty in the form of ongoing threats to health and life. Fieldwork revealed the evolution of understandings of COVID-19, tracking how public health measures and messaging were received and experienced and the social responses and relations that were mobilised to protect both health and livelihoods, in contexts where people were navigating intersecting precarities.

We argue that ethnographic insights are critical for a more nuanced understanding of the immediate effects and broader repercussions of epidemics. Debates about preparedness and response should consider such perspectives on preparedness 'from below' in order to interrogate who is being prepared for what, how and by whom. As the pandemic accord process proceeds, our research points to the need to incorporate longer term systems strengthening as a key aspect of preparedness. Standard technical approaches to preparedness have an important place but preparedness and response also involve social and political processes.

Abstracts – AGM Oral Presentations

Discovery of broadly neutralising bovine monoclonal antibodies against SARS-CoV-2

Emily Park[1], Theocharis Tsoleridis[1], Joshua Duncan[1], Joseph Chappell[1], C. Patrick McClure[1], Alexander W. Tarr[1], Richard A. Urbanowicz[2], Jonathan K. Ball[1].

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The urgency for therapeutics in the arms race against SARS-CoV-2 increases with the emergence of each novel variant. Although current vaccines provide protection against severe disease in the majority of the population, there is still a great need for therapeutics for immunocompromised and severely ill patients. Broadly neutralising antibodies are highly adept at binding conserved epitopes, and, with a short developmental timescale, they are ideal candidates for antibody therapies.

In this study, we present broadly neutralising bovine antibodies which can neutralise, in vitro, all the SARS-CoV-2 variants to date. We performed consecutive immunisations on two cows with Lineage A SARS-CoV-2 spike and peripheral blood mononuclear cells were isolated from the last bleed. Using two methods, single B cell sorting and phage display, antibody heavy and light chains were cloned into a human antibody cassette and expressed in mammalian cells. Full characterisation was performed with binding and neutralisation assays using spikes from different variants to assess breadth and potency. Two mAbs, 99, isolated from the sorting technique, and p7, isolated through phage display, were selected based on the consistent EC50 and IC50 values across all variants. 99, with a CDRH3 of 28 amino acids, protected in vivo, however, exhibited less breadth than p7, with a CDRH3 of 61 amino acids. Further tests will be performed against new variants to determine the clinical potential of both mAbs. These approaches identify pipelines for tapping into the bovine immune repertoire, which may be a powerful tool for combating rapidly emerging pathogens.

Abstracts – AGM Oral Presentations

Omicron (BA.1)-induced antiviral response attenuates RSV infection in WD-PBECs

Erin Getty[1], Lindsay Broadbent [1&2], Sheerien Manzoor[1], Judit Barabas[1], Connor G. G. Bamford[1&3], Olivier Touzelet[1], Rebecca C. Coll[1], Ultan F. Power[1]

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Aside from SARS-CoV-2, several respiratory viruses are considered a major threat to public health. This includes respiratory syncytial virus (RSV). Typically, RSV circulates in temperate climates in the winter months causing >33 million cases and >100,000 deaths in infants worldwide each year. However, mitigations and lockdown(s) to control SARS-CoV-2 spread resulted in a virtual elimination worldwide of RSV circulation in 2020. Thereafter, RSV has surged in out of season epidemics resulting in co-circulation of RSV and SARS-CoV-2.

To explore the consequence of RSV and SARS-CoV-2 co-infections, well-differentiated primary bronchial airway epithelial cell cultures (WD-PBECs) from adult donors were infected with RSV (BT2a), SARS-CoV-2 (Omicron BA.1) or were co-infected (sequentially or concurrently). Apical and basolateral washes were collected every 24 h post-infection. Viral growth kinetics were determined for both viruses. Expression of *IFNλ1*, *IFNβ*, *ISG15,* and *Mx1* genes and secretion of their encoded proteins were quantified.

Infection of WD-PBECs with SARS-CoV-2 or RSV resulted in infectious titres peaking at 48 and 72 hpi, respectively. SARS-CoV-2 infection 48 h before secondary RSV infection resulted in significantly reduced RSV titres, compared to RSV alone. Simultaneous co-infection of SARS-CoV-2 and RSV also slightly reduced both SARS-CoV-2 and RSV growth kinetics. Irrespective of whether WD-PBECs were infected with RSV or SARS-CoV-2, infection induced an antiviral state, as shown by the upregulation of *IFNλ1*, a type III IFN, and interferon stimulated genes. Induction of an antiviral state was also evident at the protein level with both RSV and SARS-CoV-2 infection resulting in the secretion of IFNλ1. While type III IFNs are considered to produce a more localised response to infection compared to type I IFNs due to the expression pattern of the type III IFN receptor, SARS-CoV-2 infection upregulated *IFNβ* expression. Previous work demonstrated that Omicron induced biologically active IFNβ that peaked at 24 hpi, which caused a protective antiviral response that prevented influenza infection (Bojkova et al., 2023). Therefore, upregulation of *IFNβ* expression might explain the attenuation in RSV growth kinetics. Indeed, WD-PBECs treated with SARS-CoV-2 conditioned medium in the presence of ruxolitinib (a JAK-STAT inhibitor) restored RSV growth kinetics, suggesting that IFNs are in part responsible for attenuating RSV growth kinetics via the JAK-STAT signalling pathway. Differential sensitivity to IFNs, as well as the timing of the superinfection, is also important in determining the infection outcome. Importantly, SARS-CoV-2 infection before RSV or co-infection with both viruses is unlikely to result in exacerbated RSV disease.

Abstracts – AGM Oral Presentations

Sarbecovirus usage of mammalian ACE2: Investigating the receptor binding and genetic determinants of host range

Yeonjae Lee[1,2], Joseph Newman[1], Nazia Thakur[1,3], Ahmed ME Elrefaey[1], Dalan Bailey[1]

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Sarbecoviruses (including SARS-CoV-2) can bind to range of mammalian angiotensin-converting enzyme 2 (ACE2) receptors, allowing them to infect a broad range of hosts. Many bats, particularly those from the *Rhinolophus* family, have been found to contain *Sarbecovirus* isolates and sequences. Several animal species have also been affected by spill-back of SARS-CoV-2 from humans, however, the ability of SARS-CoV, SARS-CoV-2 and different bat sarbecoviruses to use different mammalian ACE2 proteins for cell entry *in vitro* appears highly variable.

To investigate whether these differences were due to the initial binding event of the viral spike to ACE2, we produced recombinant spike receptor binding domain (RBD) and ACE2 proteins. The RBDs represented a cross-section of SARS-CoV-2 variants of concern (VOCs) as well as bat sarbecoviruses; with the ACE2 orthologues chosen from a range of known susceptible animal species (including bats). We quantified the interactions of these RBD and ACE2 proteins by both ELISA and flow cytometry assays, allowing us to identify key residues in mammalian ACE2 receptors that likely determine efficient viral binding. Our overall aim is to better understand the host tropism of sarbecoviruses and inform surveillance of future outbreaks by monitoring hosts with spillover potential.

Abstracts – AGM Oral Presentations

A comparison of different variants of SARS-COV2; Severity of Omicron and Delta-associated pathogenesis differs in a mouse model.

Parul Sharma[†1], Adam Kirby[†1], Ellie Bentley[†1], Ximeng Han[1], Anja Kipar[1,2], Daniele F. Mega[1], Rhiannon Johnson[1] & James P. Stewart[1].

[1]Department of Infection Biology & Microbiome, University of Liverpool, UK. [2]Institute of Veterinary Pathology, University of Zurich, Switzerland

COVID-19, caused by SARS-COV2 has affected worldwide human population and since emergence of new variants of concern, challenged the treatment regimen as well as the vaccine development program. In this study, we aimed to compare the pathogenesis of different variants of SARS-COV-2, in context to omicron (B1.1.529) and other sub-lineages such as BA.2, BA.5, and Delta (B.1.672) which is highly pathogenic.

We utilized K-18 hACE2 mice as they serve as a good model to mirror human infection. 6-8 weeks old mice were infected with 10^3 pfu of a different strain of SARS-COV-2 intranasal and monitored daily for weight loss or any possible respiratory symptoms. The oropharyngeal swabs were taken on 1, 3, and 5 days post-infection to identify the viral load by qPCR. On day 7 post-infection all mice were culled and lung, brain and nasal turbinates' were harvested to quantify viral load by qPCR. Formalin fixed Lung and Brain tissue were analysed after H and E staining to see the virus antigen.

The data reveal that delta is the most pathogenic among them and infected mice lost more weight with a high viral load in swabs, lung, and nasal turbinates'. In terms of omicron, BA.1, BA.2, and BA.5 show similar levels of viral load in different tissue. Although there was more viral load in the early days of infection in omicron compared to the delta. In conclusion, omicron lineage associated infection is less severe than delta and associated with recovery, unlike delta variant.

Abstracts – AGM Poster Presentations

AGM Poster Presentation Abstracts

#1: Proteomic Analysis of Coronavirus Envelope and Membrane Proteins interactor in Humans, Bats, and Camels cells

Alaa S. Abed[1], Andrew D. Davidson[1] and David A. Matthews[1].

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The Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) and Middle East respiratory syndrome coronavirus (MERS-CoV) are Betacoronaviruses capable of causing fatal human infections. Both viruses are believed to have entered the human population via an intermediate host (camels for MERS-CoV, unknown for SARS-CoV-2).

MERS-CoV and SARS-CoV-2 are enveloped positive-sense RNA viruses which encode four structural proteins (envelope (E), nucleocapsid, spike, and membrane (M)). The E and M proteins are involved in the assembly, budding, formation of the virus's envelope, and pathogenesis of the virus. Finding conserved cellular protein interactors for these viral proteins will help us better understand the coronavirus lifecycle and identify potential antiviral targets.

Three cell lines (human HEK293, bat *Pteropus alecto* Pakit and *Camelus dromedarius* Dubca) were used for transient expression of the MERS-CoV and SARS-CoV-2 E and M proteins (FLAG epitope-tagged) followed by co-immunoprecipitation (co-IP) and high-throughput mass spectrometry-based interactomic analysis. There were 32 high-confidence cellular interaction proteins conserved amongst the different cell lines and viruses ($p < 0.05$, 1.5-fold change compared to the controls).

To determine the importance of these 32 cellular proteins conserved across species in the virus lifecycle, functional validation was done by siRNA depletion in human cells, followed by infection with SARS-CoV-2. UBA52 protein depletion was significantly reduces the SARS-CoV-2 replication.

Abstracts – AGM Poster Presentations

#2: Broad analysis of human and domestic alphacoronavirus usage of mammalian APN receptors: Identifying generalists and specialists within this genus

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Intensified human-animal interactions can promote spillover and emergence events leading to zoonosis. At the molecular level, functional interactions between the host receptor and viral binding protein determine host range. The spike (S) protein of alphacoronaviruses human-CoV 229E (hCoV-229E), canine CoV (CCoV) and a porcine CoV (PCoV) employ human, canine and porcine Aminopeptidase N (APN) respectively for entry, although natural transmission has been reported in other animals. This interspecies transmission could potentially promote spillover to new hosts and it is therefore necessary to elucidate the spectrum, limitations and drivers of such events. This project aims to define the host range of alphacoronaviruses at the point of cellular entry, to uncover the relationship between viral entry and interspecies transmission.

We investigated receptor usage using lentiviral-based pseudoviruses bearing the S of hCoV-229E, 4 canine alphacoronaviruses and PCoV, and examined entry with HEK-293T harbouring 25 different mammalian APNs. Our preliminary results found that hCoV-229E, in addition to naturally reported human and camel cases, could also use cat and velvety bat APN. Interestingly, we found that two CCoV, CCoV/HuPn19 and Z19, were able to utilize APN from a variety of mammalian species while two others, CCoV/A76 and CCoV/SD-F3, were restricted to the canid family. In addition, PCoV (PRCV/ISU-1) showed broad APN usage, including APNs from the carnivore and chiropter orders.

Our findings highlight the suitability of receptor usage assays to investigate the first molecular steps implicated in spillover events and emphasise the important role they could play in pandemic preparedness.

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#3: Investigating the Interactome of Seasonal and Highly Pathogenic Human Coronaviruses.

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Human coronaviruses can be divided into seasonal coronaviruses (that cause mainly mild disease in most age ranges) and those that cause severe disease (such as severe acute respiratory syndrome coronavirus (SARS-CoV). Since the discovery of SARS-CoV in 2002, two highly pathogenetic novel coronaviruses have emerged within the population (MERS-CoV in 2012, and SARS-CoV-2 in 2019). The coronavirus nucleocapsid (N) protein has a vital role in viral biology, including replication and transcription regulation, genome packing and aiding in viral assembly, among others. Additionally, N can interact with host proteins some of which may be common across coronavirus species. However, some may be unique, contribute to novel aspects of pathogenesis. The interactome of SARS-CoV-2 verses other human coronaviruses is not well understood therefore the aim of this study is to compare the interactomes of seasonal and highly pathogenic coronaviruses. Furthermore, this research into this may help identify new therapeutics targets for existing and possible future coronaviruses.

N proteins from both seasonal (HCoV-229E, HCoV-OC43 and HCoV-NL63) and SARS-CoV-2 were cloned, tagged to EGFP and expressed in 293T cells. Expression was assessed by fluorescent microscopy and western blot. Interactome studies were performed by pull-down purification using a GFP-Trap, followed by shotgun DDA MS/MS. Identified protein-protein interactomes were validated using western blot and reverse pulldowns. Due to the role of N protein in RNA binding, RNAse treatment was used to eliminate protein interactions mediated by RNA binding.

Pilot data identified cytoplasmic and nucleolar SARS-CoV-2 N localisation, which is not observed in human seasonal CoV N which appears to localise in the cell cytoplasm. Mass spectrometry data indicated that interactome partners included ribosomal proteins, splicing factors and RNA helicase proteins. These are being investigated using functional assays to assess the role of these proteins in the viral cycle.

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#4: SARS-CoV-2 population dynamics in immunocompetent individuals in a closed transmission chain shows genome diversity over the course of infection

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SARS-CoV-2 is rapidly evolving, and many biologically important genomic mutations have characterised novel SARS-CoV-2 lineages, which have emerged during successive global waves of the pandemic. Worldwide genomic sequencing has been able to monitor these outbreaks, track transmission clusters, and examine viral evolution in real-time to help inform policy. One school of thought is that an apparent greater than average divergence in an emerging lineage from contemporary variants may require persistent infection, for example in an immunocompromised host. However, genomic diversity that has been identified in other coronaviruses has not or may not rely on this type of mechanism. We investigated evolutionary trends within a cluster of SARS-CoV-2 infected, immunocompetent individuals in a closed transmission chain to understand the dominant and minor genomic variation over time without obvious host selection pressure.

A closed transmission chain of 16 SARS-CoV-2 infected immunocompetent patients aged 20 to 40 years old was identified. Longitudinal nasopharyngeal swab sampling was completed throughout infection and virus populations characterised through high resolution sequencing. The resulting data allowed characterisation of intra-host variation over time at both the dominant and minor genomic variant levels. Viral evolution was observed over the course of acute infection and dynamic changes in viral lineages were classified at different timepoints. Both dominant and minor genomic variation occurred individually across time within patients under no obvious selection pressure (apart from the immune response). In several cases minor genomic variation was observed at early timepoints which increased to dominant changes at later timepoints.

This reported data suggests that minor genomic variation has a role in determining the direction of evolution and occurs at varying rates in immunocompetent populations. The work also highlights the possibility for monitoring the minor genomic variant population to reveal future evolutionary trajectories to prepare for novel and emerging SARS-CoV-2 lineages.

Abstracts – AGM Poster Presentations

#5: Understanding the risk of bat sarbecovirus spillover into humans – correlating host range, affinity and antigenicity.

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Sarbecoviruses including severe acute respiratory syndrome virus coronavirus (SARS-CoV) and SARS-CoV-2 have been shown to have broad mammalian angiotensin converting enzyme 2 (ACE2) tropism. It has also been shown that there is limited cross-neutralisation of SARS-CoV-2 using SARS-CoV convalescent sera and vice versa. However, it is less well characterised whether there is an interplay between host range and antigenicity. Given that SARS-CoV-2 likely originated from a bat reservoir, we wanted to understand the potential of future spillover from bat sarbecoviruses into humans by investigating determinants of ACE2 usage.

We performed RBD-based binding assays and pseudotype-entry assays using full-length Spike to assess the affinity and host range of SARS-CoV-2 variants and bat coronaviruses to different species of bat and human ACE2 receptors. We detected broad but varied bat ACE2 usage with SARS-CoV-2 variants and the BANAL viruses, but more restricted usage with the distantly related clade 2 and 3 sarbecoviruses. We also observed differential antigenicity of the sarbecoviruses using sera and mAbs derived from SARS-CoV-2 infections, which correlated with ACE2 binding and entry. Viruses with broad ACE2 tropism exhibited the highest levels of neutralisation with the converse being seen with specialised ACE2 users. Using mutational analysis and chimeras, we were able to attribute this diversity in host range, affinity and antigenicity to specific residues in the ACE2-RBD binding interface. Monitoring key mutations in circulating bat sarbecovirus Spikes and the ongoing surveillance of associated bat reservoirs will be imperative to forewarn future outbreaks in humans.

Abstracts – AGM Poster Presentations

#6: Detection of Alpha and Beta Coronaviruses in Bats in England during 2021-2022

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Bat carcasses are submitted to APHA as part of the UK passive surveillance scheme for bat lyssaviruses. In addition, oral and faecal swabs were collected from bat roosts via active surveillance programmes. Throughout 2021-2022, oral and faecal swabs from 361 bats were screened for coronaviruses. Extracted RNA was tested by pan-coronavirus RT-PCR targeting a conserved region of the RdRp gene.

In total, six faecal swab samples were positive for coronavirus RNA (1.6%) collected from natterer's bats (*Myotis nattereri,* 2/11, 18%), brown long-eared bats (*Plecotus auritus*, 2/60, 3.3%), a Daubenton's bat (*Myotis daubentonii,* 1/29, 3.4%) and a common pipistrelle (*Pipistrellus pipistrellus*, 1/173, 0.56%). Sanger sequencing identified alphacoronaviruses from the *M. nattereri, M. daubentonii,* and *P. pipistrellus*, and betacoronaviruses from the *P. auritus*. The sequence obtained from the *M. nattereri* had 99.24% nucleotide similarity with alphacoronavirus detected in the same species in the UK collected in 2009. The sequence obtained from the *M. daubentonii,* and *P. pipistrellus* had 98.98-99.49% nucleotide similarity with novel alphacoronaviruses from the *Pedacovirus* subgenus detected in the same species in the UK collected during 2020-2021. The coronavirus sequence from *M. daubentonii* is also closely related (99.49-99.75%) to other bat coronaviruses from the same species in Denmark collected during 2014-2015. Two betacoronaviruses collected from *P. auritus* had 98.48% nucleotide sequence similarity to a novel betacoronavirus from the *Merbecovirus* subgenus detected in the same species in the UK collected during 2020.

Coronavirus surveillance in UK bats is ongoing during 2023 and the results will be presented. The study provides insight into the diversity of coronaviruses among UK bat populations, contributing to our understanding of the potential for zoonotic risk.

Abstracts – AGM Poster Presentations

#7: Exploring Microbiome Differences in Upper and Lower Respiratory Tract of COVID-19 Patients

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The COVID-19 pandemic has highlighted the importance of understanding the microbiome dynamics and host response in respiratory tract infections. Understanding the microbial communities residing in different regions of the respiratory tract and their potential interactions with the host immune system during COVID-19 infection will allow for the development of targeted therapeutic interventions and personalized treatment strategies for respiratory infections. The primary aim of this study was to compare the microbiome composition and diversity between the upper and lower respiratory tracts.

mNGS approaches can detect sequence information of SARS-CoV-2, as well as identify mRNAs associated with active transcription in the microbiome and host RNA. Here, we employ a Single-independent, single primer amplification (SISPA) approach coupled with Nanopore sequencing to investigate the microbiome composition in the upper respiratory and lower respiratory samples of COVID-19 patients. Longitudinal clinical samples were collected from patients over the course of their illness, allowing us to assess temporal changes in the respiratory microbiome

By analysing the metatranscriptomic change to infection over time, we aim to gain insights into microbiome differences of anatomic site and associated with viral load and different variants with disease progression and severity on hospitalised COVID-19 patients. By elucidating the microbiome differences and host response dynamics, this study contributes to our understanding of respiratory tract infections, particularly in the context of COVID-19.

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#8: Inconclusive SARS-COV-2 PCR test: the follow up results

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Background:
Regular population screening is the most important preventive measure to contain the spread of SARS-CoV-2 and enable detection and quarantine of positive individuals. Effective, accurate, time- and cost-saving tests for the detection of SARS-CoV-2 are critical to maintaining routine epidemiological car. Inconclusive results are present in the proportion of tests, regardless to SARS-CoV-2 detection method used, delaying results and impeding effective prevention of spread.

Objectives:
In this retrospective study, we followed up borderline SARS-CoV-2 patients and aimed to determine the proportion of positive conversions up to 10 days after or before SARS-CoV-2 inconclusive RT PCR result.

Methods:
Borderline SARS-CoV-2 patients were retested (from the second sample with the same method) at the Molecular diagnosis laboratory of National laboratory of health, environment and food (Koper, Slovenia). The study group included different asymptomatic and symptomatic populations.

Results:
Of a total of 58039 SARS-CoV-2 RT PCR analyses performed during 18-months period, 45278 were negative, 12452 were positive, and 309 were inconclusive (borderline patients). Negative follow-up results were obtained for 175 and positive for 131 borderline patients. For the positive follow-up results, 87 of these patients converted to positive within 10 days of an inconclusive result, whereas 44 patients had previously a positive RT-PCR result. The majority of borderline patients became positive within the first 5 days of the inconclusive result.

Conclusion:
Reporting inconclusive results, resampling, and retesting borderline patients saves valuable response time for effective prevention logistics. Follow-up testing for inconclusive PCR results within 5-10 days identifies additional positive patients, reducing the potential risk of SARS-CoV-2 transmission.

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#9: Enhancing genomic surveillance: Croatia's journey towards effective SARS-CoV-2 variant monitoring

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Recognizing the significance of genomic surveillance, the Croatian Institute of Public Health (CIPH) launched initiatives to increase Croatian capability for SARS-CoV-2 sequencing, utilizing funding from the HERA incubator. WGS equipment with high-throughput sequencing capabilities was procured. This acquisition aimed to provide a solid foundation for widespread genomic surveillance of SARS-CoV-2 across the country.

Laboratory personnel, microbiologists, epidemiologists, and bioinformaticians were trained on the WGS and how to apply acquired data to SARS-CoV-2 surveillance, using the high-quality ECDC's training packages. These capacity-building efforts aimed to make sure that the WGS equipment purchased was used efficiently and that the data produced would be accurately interpreted.

From February 2021 Croatia used ECDC's sequencing support for SARS-CoV-2 variant monitoring. Acquired infrastructure and subsequent capacity-building efforts enabled us to start a nationwide SARS-CoV-2 sequencing program on our own.

Viral samples that have been gathered from various regions of the country are collected and sequenced. The generated genomic data are integrated into national and international databases to enable comparative analyses and timely identification of emerging variants. From November 2022 to June 2023 CIPH uploaded 3852 SARS-CoV-2 sequences to the GISAID database, sampled according to ECDC's guidance. The SARS-CoV-2 variant pattern in Croatia follows the variant trends in Europe.

SARS-CoV-2 sequencing has provided important information about the spread and development of the virus within Croatia. It has enabled tracking variants of concern and direct public health initiatives. The necessity for cross-border preparedness for disease outbreaks led to a new international collaboration for establishing alert systems and WGS and RT-PCR protocols and pipelines for the detection of possible pathogens. In this collaboration under the HERA2 project, public health institutes from Austria, Croatia, Greece, and Hungary joint their efforts in protecting the health of EU citizens.

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#10: A comparison of different variants of SARS-COV2; Severity of Omicron and Delta-associated pathogenesis differs in a mouse model.

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COVID-19, caused by SARS-COV2 has affected worldwide human population and since emergence of new variants of concern, challenged the treatment regimen as well as the vaccine development program. In this study, we aimed to compare the pathogenesis of different variants of SARS-COV-2, in context to omicron (B1.1.529) and other sub-lineages such as BA.2, BA.5, and Delta (B.1.672) which is highly pathogenic. We utilized K-18 hACE2 mice as they serve as a good model to mirror human infection. 6-8 weeks old mice were infected with 103 pfu of a different strain of SARS-COV-2 intranasal and monitored daily for weight loss or any possible respiratory symptoms. The oropharyngeal swabs were taken on 1, 3, and 5 days post-infection to identify the viral load by qPCR. On day 7 post-infection all mice were culled and lung and nasal turbinates' were harvested to quantify viral load by qPCR. Formalin fixed Lung and Brain tissue were analysed after H and E staining to see the virus antigen.

The data reveal that delta is the most pathogenic among them and infected mice lost more weight with a high viral load in swabs, lung, and nasal turbinates'. In terms of omicron, BA.1, BA.2, and BA.5 show similar levels of viral load in different tissue. Although there was more viral load in the early days of infection in omicron compared to the delta. In conclusion, omicron lineage associated infection is less severe than delta and associated with recovery, unlike delta variant.

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#11: Development and adaptation of a SARS-CoV-2 infection model in human microphysiological systems at high containment with applicability to Disease X

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The WHO has published an R&D emergency context priority disease list, with all but one of these pathogens being viruses that require work to be conducted within a containment level 3 or 4 facility (BSL3 or BSL4). Disease X, featured on this list, may not infect current cell lines or animal models commonly used in virus research. There is therefore a need for more relevant human data in our research which also aligns with our ambition to reduce, refine and replace the use of animals in scientific research. This highlights the need for physiologically relevant in vitro systems to assist pre-clinical research and development of novel therapeutics.

Microphysiological systems (MPS) provide an ideal platform for this type of infectious disease model development. Not only would they reduce our dependence on animal experimentation, but also leave us better prepared for a Disease X pandemic. Our focus is therefore to develop models with primary human tissues and infect these with representative virus isolates. We are using the Emulate organ chip system as well as a bespoke 3D-printed interconnected chip system as a platform to model viral infection. Containing the instrument within a custom-built flexible film isolator (FFI) provides a convenient way to work safely with MPS systems at high containment. As FFIs are routinely used at both BSL3 and BSL4 in the UK, this approach is amenable to the study of HG4 pathogens.

Here we describe the engineering controls we have developed to perform these experiments and will present the characterisation of SARS-CoV-2 infection in a human lung MPS using low passage community isolates of virus. These proof of principle experiments will demonstrate the feasibility of using MPS at high containment, validate the approach and provide the evidence for future preclinical research and development studies.

Abstracts – AGM Poster Presentations

#12: Metagenomics of severe coronavirus infection SARS-CoV-2 in humans

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Throughout the COVID-19 pandemic, extensive research has been conducted in SARS-COV-2 to elucidate its genome, prognosis, and possible treatments. In the Kingdom of Saudi Arabia, several studies have been conducted in order to determine the prevalence of the SARS-COV-2 in the country, its whole genome analysis and prognosis. However, none looked at the microbial biomarkers that could be explored in infected patients and that could predict the possible disease severity. The aim of this study is to compare the nasopharyngeal microbiota of healthy subjects HS), moderate (M), under medication (UM) and recovered SARS-COV-2 patients, 2020.

Forty-two samples (38 nasopharyngeal and 4 anal) were collected from 7 healthy patients, 14 moderates, 10 under medication and 7 recovered SARS-COV-2 patients at King Fahad Medical city. In addition, 4 anal samples (2 M, 1 UM, 1 R) were collected. Demographic as well as clinical characteristics of included patients were also retrieved. Metagenomic sequencing was performed using Minion Oxford nanopore sequencing.

Metagenomic analysis revealed that the most common species detected in all samples were Leptospira, Haemophilus parainfluenzae, Capnocytophaga gingivalis and Neisseria gonorrhoeae. In anal samples, the most common species detected were Klebsiella spp, Salmonella enterica, Escherchia coli and Murdochiella vaginalis. Interestingly, in one sample from a moderate patient, SARS-COV-2 was detected. We currently in the process of elucidating alpha diversity, beta diversity and principal component analysis. This is for an in-depth comparison of the microbiome in SARS-COV-2 patients with different prognosis.

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#13: Molecular Analysis of SARS-CoV-2 Introductions in Slovenian Long-Term Care Facilities

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Since the emergence of SARS-CoV-2, nursing homes and long-term care facilities (LTCF) have experienced most of the COVID -19 burden. In our study, a total of 1202 residents and 564 LTCF workers who tested positive for SARS-CoV-2 were selected to analyse the outbreaks of SARS-CoV-2 in LTCFs. We determined the genetic variants circulating among residents and staff using next-generation sequencing over two time periods and assessed whether multiple introductions occurred within one outbreak and analysed the rate of introduction of variant of concern Alpha into LTCFs.

Of total samples collected from residents and staff at LTCFs, 77.5% and 82.4% were successfully sequenced, respectively. In October 2020, 9 lineages were observed in residents and 10 lineages in workers. The most common lineage was B.1.1.70 with 36% and 36%, followed by B.1.160 with 33% and 25%, and B.1.258.17 with 18% and 17% in residents and workers, respectively. In the second period (January to April 2021), 10 lineages were detected in residents and 17 in workers. Lineage B.1.258.17 was the most abundant in both subpopulations, with 65% and 64% among residents and workers, respectively. The composition of the remaining lineages was much more diverse during this period, especially among workers.

The results showed that in some LTCFs there were multiple introductions of COVID-19 within a single outbreak, which has important implications for public health measures. Genome sequencing is a powerful additional tool to study the transmission dynamics of SARS-CoV-2 and can in conjunction with epidemiologic data facilitate in determining the need for future improvement of additional control measures aimed at limiting introductions of COVID-19 into LTCF.