28th Annual Infectious Diseases Research Day

&

15th Annual Canadian Center for Vaccinology Symposium

DALHOUSIE UNIVERSITY
FACULTY OF MEDICINE
Continuing Professional Development

Canadian Center for Vaccinology
Dalhousie University
IWK Health
NS Health

April 4, 2022
Halifax, Nova Scotia

Sponsored by:

Canadian Center for Vaccinology

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of the Departments of Pediatrics and Medicine

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In keeping with CMA Guidelines, program content and selection of speakers are the responsibility of the planning committee. Support is directed toward the costs of the course and not to individual speakers through an unrestricted educational grant.

Welcome to the 28th Annual Infectious Diseases Research Day and 15th Annual CCfV Symposium!

Glen Patriquin, MD, MSc, FRCPC
Assistant Professor, Dalhousie University Division of Medical Microbiology
Department of Pathology and Laboratory Medicine, Nova Scotia Health Authority

Welcome to the Infectious Diseases Research Day and CCfV Symposium for 2023. This annual event provides a unique learning opportunity for researchers, trainees, public health professionals, healthcare providers, and community members featuring experienced presenters, and inspired research trainees. Our goal is to highlight Canadian research by established investigators, as well as showcase emerging talent. Our program this year is filled with a variety of presentations and posters themed around various aspects of vaccinology and infectious diseases. We aim to identify research strengths and build new collaborations to extend local research connections.

Feedback and evaluation is important, and **your input is essential for our future planning**. You will receive an email inviting you to take our post-event survey shortly after the conference, and we urge you to give us your feedback to improve this learning event.

Welcome and thank you for joining us!

Scott Halperin MD, FRCPC
Director
Canadian Center for Vaccinology

The Infectious Diseases Research Day/CCfV Symposium is an important annual platform that allows local researchers to present their work and learn about the work of their colleagues. We encourage everyone to take part in this one-day event that will feature interesting topics surrounding infectious diseases. One of the great aspects of this event is that it gives researchers at different stages in their careers the opportunity to learn about the work of their colleagues, and I encourage everyone to make the most of this educational experience.

I would like to offer my sincerest thanks to our planning committee and the financial support from our corporate sponsors. This event would not be possible without the dedicated work and continued support from these individuals.

28th Annual Infectious Diseases Research Day & 15th Annual Canadian Center for Vaccinology Symposium

Schedule of Events

Tuesday, April 4, 2022
8:00am – 4:30pm

7:30 – 8:00am	**Continental Breakfast**
8:00 – 9:00am	TJ Marrie Lecture: Dr. Samira Mubareka, *Emerging zoonoses at the human-wildlife nexus*
9:00 – 9:15am	Welcome and opening remarks
9:15am – 12:00pm	Oral Presentations:
9:15am	Valerie Murphy
9:30am	Jenna MacDonald
9:45am	Cyril O'Brien
10:00am	Taylor Caddell
10:15am	Alina Butova
10:30am	**BREAK**
10:45am	Elizabeth Simms
11:00am	Katherine Wang
11:15am	Brett Duguay
11:30pm	Juliette Bougon
11:45pm	Tasha Ramsey
12:00 – 1:00pm	Lunch Break
1:00 – 2:00pm	Poster Presentations: (concurrent sessions):

POSTER PRESENTATIONS	
Faculty/Industry (Not judged)	**Industry**
Tasha Ramsey	Thomas Shin
Melissa Andrew	Mattea Thompson
Shelly McNeil	
Katharine Salter	**Research Associates**
	Madeline Stoltz
PHD/Masters/Residents	Michal Cherak
Allyson Gallant	Shawn Harmon
Tunnuo Sho	Barb Goodall
Fahima Hassan	Agnieszka Sagan
Shannen Grandy	Sharon Oldford
Yahya Shabi	
	Undergraduate Students
	Artem Kichydzhy
	Trinity Tooley
	Trinity Franklin
	Rachel Parker

2:00 – 3:00pm Presentation:
Dr. Chris Richardson
Measles Virus and SARS-CoV-2: Two Cousins With A Lot in Common

3:00 – 3:15pm Break

3:15 – 3:45pm Presentation:
Dr. Joanne Langley
Childhood immunization programs during the COVID-19 pandemic: Collateral damage and the work ahead

3:45 – 4:15pm Presentation:
Dr. Kyle Wilby
PrEP-Rx: Implementation of a community pharmacist prescribing service for PrEP in Nova Scotia

4:15 – 4:30pm Awards ceremony and closing

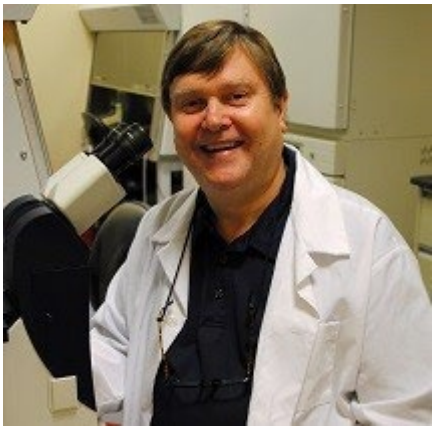
Speakers

Dr. Samira Mubareka

Samira completed her MD at Dalhousie University and Internal Medicine training at McGill University in Canada. She specialized in Infectious Diseases and Medical Microbiology at the University of Manitoba and went on to a research fellowship at the Mount Sinai School of Medicine, New York City.

Samira is currently a virologist, medical microbiologist and infectious disease physician at Sunnybrook Health Sciences Centre in Toronto, Ontario, Canada and in the Department of Laboratory Medicine and Pathobiology at the University of Toronto. Samira has been working on SARS-CoV-2 since the outset of the pandemic in North America with a focus on virus biology, bioaerosols, genomics and wildlife surveillance through close and cross-disciplinary collaborations. **She is currently focused on understanding the biology and transmission of SARS-CoV-2 variants of concern and on coronavirus and influenza virus zoonotic spillover.**

Samira served on the **Chief Science Advisor of Canada**, Dr. M. Nemer's COVID-19 Expert Panel, the Implementation Committee of the Genome Canada-led Canadian COVID-19 Genomics Network (**CanCOGeN**) VirusSeq project, ISED's Therapeutics Task Force, and the **Ontario COVID-19 Science Advisory Table. She Chaired the Royal Society of Canada's COVID-19 One Health Working Group and currently serves on the Royal Society of Canada's One Health Task Force**



Dr. Chris Richardson

Dr. Chris Richardson is a molecular virologist who has worked with a wide variety of viruses over his 40 years of research. He has a Bachelor of Science and PhD from the University of British Columbia, and did postdoctoral studies at Rockefeller University and the National Institutes of Health. Dr. Richardson's research interests involve the molecular biology of measles, canine distemper, hepatitis C, hepatitis B viruses, and SARS-CoV-2. He is particularly interested in virus-host cell receptor interactions and virus-mediated cell fusion. Upon moving his laboratory to Dalhousie University, Dr. Richardson served as the Canada Research Chair (Tier 1) in Vaccinology and Viral Therapeutics from 2006-2020. He cloned and sequenced many of the genes belonging to measles virus and identified the 3 major cellular receptors for this virus. During the recent pandemic he has participated in reviewing important COVID-19 vaccine trials and producing purified SARS-CoV-2 spike (S) protein and VSV-variant S pseudoviruses for diagnostic and vaccine purposes. Dr. Richardson is currently editing the 3rd edition of Fundamentals of Molecular Virology, which is one of the most utilized textbooks for undergraduate virology.

Dr. Joanne Langley

Dr. Joanne Langley is a Professor of Pediatrics and Community Health and Epidemiology at Dalhousie University and the Canadian Center for Vaccinology in Halifax, NS Canada, head of Pediatric Infectious Diseases at the IWK Health Centre, and lead for the Clinical Trials Network of the Canadian Immunization Research Network. She currently co-chairs the Canadian COVID-19 Vaccine Task Force. Her research is focused on the epidemiology and vaccine prevention of respiratory infections, particularly Respiratory Syncytial Virus and influenza, and immunization decision making.

Dr. Kyle Wilby

Kyle John Wilby is an Associate Professor at the College of Pharmacy, Faculty of Health at Dalhousie University in Halifax, Canada. He has a Bachelor of Science in Pharmacy from the University of Saskatchewan (2008), a post-graduate PharmD from the University of British Columbia (2012), and a PhD in Health Professions Education from Maastricht University (2019). He has spent the last ten years working abroad in Ghana, Qatar, and most recently New Zealand in academic and administrative positions. His research interests include 2SLGBTAQI+ health and education, systems-based inclusivity, and workforce development. He has published over 130 peer reviewed articles and is an Associate Editor for the American Journal of Pharmaceutical Education. He is the Founding Chair of the global think tank RxSHARE (Pharmacists for Sexual and Gender Health Advocacy, Reform, and Equity).

Oral Presentations

Time of presentation	Presenter	Title of Abstract
9:15-9:30	Valerie Murphy	PILOTING AN ALLERGY INTERVIEW TOOL AND SCORING SYSTEM TO DE-LABEL AND RISK STRATIFY PENICILLIN ALLERGIES ON A MEDICINE UNIT AT NOVA SCOTIA HEALTH
9:30-9:45	Jenna MacDonald	BURDEN OF RESPIRATORY SYNCYTIAL VIRUS (RSV) AMONG OLDER ADULTS HOSPITALIZED WITH ACUTE RESPIRATORY ILLNESS
9:45-10:00	Cyril O'Brien	SYNTHESIS AND CHARACTERIZATION OF NOVEL BENZOXABOROLE DERIVATIVES WITH POTENTIAL PHARMACEUTICAL ACTIVITY
10:00-10:15	Taylor Caddell	SARBECOVIRUS M PROTEINS BROADLY INHIBIT HOST PROTEIN TRAFFICKING AND SECRETION
10:15-10:30	Alina Butova	INVESTIGATING ROLES FOR UFMYLATION IN INFLUENZA VIRUS INFECTION
10:30-10:45	BREAK	
10:45-11:00	Elizabeth Simms	CASES OF PCR-POSITIVE BLOOD FOR ANAPLASMA PHAGOCYTOPHILIUM IN NOVA SCOTA: A REVIEW FROM MAY-SEPTEMBER 2022
11:00-11:15	Katherine Wang	INVESTIGATING THE ROLE OF ACTIVATION-INDUCED CYTIDINE DEAMINASE IN CHLAMYDIA PATHOGENESIS
11:15-11:30	Brett Dugay	THIOPURINES INHIBIT CORONAVIRUS SPIKE PROTEIN PROCESSING AND INCORPORATION INTO PROGENY VIRIONS
11:30-11:45	Juliette Bougon	INFLUENZA A VIRUS CAUSES ACCUMULATON OF NUCLEAR POLY(A) RNAs IN LATER STAGES OF VIRAL REPLICATION CYCLE INDEPENDENTLY FROM PA-X OR NS1 HOST SHUTOFF
11:45-12:00	Taha Ramsey	NOVA SCOTIA HEALTH COVID-19 NON-SEVERE THERAPY TEAM: LESSONS LEARNED FROM A HUB AND SPOKE MODEL

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(Presenter's name in **bold)**

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Oral Presentation Abstracts

(Presenter's name in **bold)**

Oral Presentation 1

Title: PILOTING AN ALLERGY INTERVIEW TOOL AND SCORING SYSTEM TO DE-LABEL AND RISK STRATIFY PENICILLIN ALLERGIES ON A MEDICINE UNIT AT NOVA SCOTIA HEALTH

Authors: V. Murphy, A. Kent, J. Toulany, P. Bonnar, L. Connors

Affiliation: Nova Scotia Health

Introduction: Penicillin allergy labels are frequently false and lead to worse patient outcomes and promote use of excessively broad antimicrobials. There is momentum Internationally to de-label and clarify penicillin allergies to align with Antimicrobial Stewardship (AMS) efforts. At Nova Scotia Health, there is no usual process to conduct detailed allergy interviews and de-label patients with erroneous penicillin allergy labels.

Methods: The project team adapted an allergy interview tool including a detailed allergy history and the PenFast scoring system to stratify risk of penicillin allergy. A pharmacy student used the tool to interview patients with a documented penicillin allergy admitted to the medical teaching unit (MTU) at the Halifax Infirmary in the summer of 2022. Each patient was reviewed with the AMS Pharmacist and assigned to a risk category for penicillin allergy which determined intervention. Intervention options included: 1) de-labeling of allergy or 2) possible allergy (referral to an allergist for further testing).

Results: 29 patients with penicillin allergy were identified between mid June to mid August 2022 as candidates for an interview. 1 patient was discharged prior to interview and 3 were unable to give reliable interview information. 25 interviews were completed with 10 patients (40%) de-labeled based on interview alone. The other 15 patients were deemed to have a real or possible allergy, with 8 patients (32%) consenting and subsequently referred for penicillin allergy follow up by an allergist. The average time for the pharmacy student to complete the interview tool and risk stratify the patient was 9 minutes, with a range from 4 minutes-30 minutes.

Conclusions: The allergy interview tool and risk stratification system is an effective method to aid de-labeling penicillin allergies and risk stratifying patients for potential allergist follow up. Implementing this process as standard of care for patients with penicillin allergies would require a comparatively small time investment from practitioners and could significantly impact antimicrobial usage and patient outcomes at Nova Scotia Health.

Oral Presentation 2

Title: BURDEN OF RESPIRATORY SYNCYTIAL VIRUS (RSV) AMONG OLDER ADULTS HOSPITALIZED WITH ACUTE RESPIRATORY ILLNESS

Authors: MacDonald, Jenna L; Pott-Junior, Henrique; Elsherif, May; Leblanc, Jason; McNeil, Shelly A.; Andrew, Melissa K.

Affiliation: Divisions of Infectious Diseases, Geriatric Medicine and Medical Microbiology

Introduction: The burden of RSV is well understood among children, but impact on adults is less well understood. This issue is relevant given that RSV vaccines for adults are in development, and decisions makers will benefit from evidence about the burden of RSV in this population to inform recommendations for their use and jurisdictional procurement. Here we aimed to compare outcomes of RSV vs influenza vs other acute respiratory illness (ARI) in older adults admitted to Canadian hospitals.

Methods: The Serious Outcome Surveillance (SOS) Network collects annual data on patients' frailty, severity of illness and mortality during hospitalization with ARI. We used SOS data from 13 sites, between 2012-2015. Patients' admitted with respiratory symptoms were eligible for enrollment, and underwent a nasopharyngeal swab for RSV and influenza A/B. Patients were grouped as RSV positive, Influenza A/B positive and negative. Primary clinical outcomes were mechanical ventilation, ICU admission, mortality and adjusted analyses were performed using baseline frailty index.

Results: 7,635 patients were included, of which 4,027 (42.7%) had a negative respiratory virus test result, 3,277 (42.9%) had laboratory-confirmed influenza, and 331 (4.3%) laboratory-confirmed respiratory syncytial virus (RSV). Median age overall was 76 years, and 52.4% were female. Based on Frailty Index, most patients were frail (58.6%), 30.8% were pre-frail and 11.3% were non-frail. Of the 331 RSV cases, 21 (6.3%) required mechanical ventilation, 43 (13.0%) required ICU admission and 12 (3.6%) died. RSV was more likely to be associated with mechanical ventilation and ICU admission than other ARI, and less likely than influenza.

Conclusions: RSV was associated with substantial burden of illness and severe outcomes in hospitalized older adults. Prevention of RSV, including through vaccination, could be an important tool to reduce adverse outcomes in this population.

Oral Presentation 3

Title: SYNTHESIS AND CHARACTERIZATION OF NOVEL BENZOXABOROLE DERIVATIVES WITH POTENTIAL PHARMACEUTICAL ACTIVITY

Authors: C. J. O'Brien, K. Reznikov, E. Ospanow, D. L. Jakeman.

Affiliation: Dalhousie University

Introduction: With the growing issue of antimicrobial resistance worldwide, this emerging global health threat has increased the demand for novel antimicrobials. Boron-containing pharmaceuticals such as benzoxaboroles, a previously underexplored class, have gained prominence in the last two decades. They have shown great promise as β-lactamase inhibitors and therapeutic agents against bacteria, fungi, and viruses. Hence, the aims of this research was to synthesize novel benzoxaborole derivatives with the potential for antimicrobial activity.

Methods: The first class targeted for synthesis were benzoxaborole amino-acid derivatives of varying chain lengths. An efficient methodology was developed, where 2-formylphenylboronic acid (FPBA) was reacted with amino-acids to provide the benzoxaborole derivative. A second class targeted for synthesis was a benzoxaborole-penicillanic acid derivative through the tethering of 6-aminopenicillanic acid to FPBA. Compounds were screened for binding affinity against a wide range of sugars present in mammalian cells. All compounds were characterized using TLC, NMR, UV and fluorescence spectroscopy. Antimicrobial and beta-lactamase inhibitor activity was measured through out-of-house testing.

Results: Six benzoxaborole-amino acid derivatives were successfully synthesized in high yields (80-99 %), along with two further fluorinated forms (32-95 %). These compounds showed considerable binding of glucuronic acid. The compounds synthesized showed mild antimicrobial activity towards C. albicans, with an average MIC90 of 1,280 μM. Through beta-lactamase inhibitor testing, the alanine derivative at a concentration of 100 μM inhibited 50.0 % of the activity of a Serine- β-Lactamases, KPC-2. Purification of the penicillanic acid derivative has been confounded by hydrolysis of the beta-lactam ring upon compound isolation, as observed from X-ray structural data.

Conclusions: The benzoxaborole-amino acid derivatives offer insight into a previously underexplored class of boron-containing molecules. Despite their limited antimicrobial properties, our synthetic approach provided an efficient methodology for the synthesis of future benzoxaborole derivatives. Progress continues on the isolation of the penicillanic acid derivative, however, the resulting X-ray structural data has provided insight into the chemical structures of the benzoxaborole amino-acid derivatives.

Oral Presentation 4

TITLE: SARBECOVIRUS M PROTEINS BROADLY INHIBIT HOST PROTEIN TRAFFICKING AND SECRETION

Authors: T. Caddell[1]; E. Pringle[1] & C. McCormick[1]

Affiliation: [1]Dalhousie University, Faculty of Medicine, Department of Microbiology & Immunology

Not published by request

Oral Presentation 5

Title: INVESTIGATING ROLES FOR UFMYLATION IN INFLUENZA VIRUS INFECTION

Authors: Butova A., Samaraweera E., Caddell T., McCormick, C.

Affiliation: Dalhousie University

Introduction: All proteins are influenced by post-translational modifications (PTMs). The conjugation of ubiquitin-fold modifier 1 (UFM1) to proteins is known as UFMylation. UFMylation supports cellular antiviral responses. The enzymes that govern UFMylation are synthesized in response to endoplasmic reticulum (ER) stress and UFMylation regulates ER quality control mechanisms. ER stress can inhibit influenza A virus (IAV) replication, but it is not known whether UFMylation plays any role in these responses.

Methods: We used CRISPR/Cas9 genome editing to delete UFM1 or the UFM1 deconjugating enzyme , UFSP2 from human lung carcinoma A549 cells. Control cells received a non-targeting guide RNA. Cells were infected with influenza A virus (IAV) strain A/Puerto Rico/8/34(H1N1) (PR8) at low (0.5) or high (2) MOI. Supernatants were collected at 24 hours post-infection (hpi) and titered by plaque assay using standard methods. Cell lysates were collected at 2, 4, 8, 16, and 24 hpi and immunoblotted to analyze viral proteins and UFMylation pathway

Results: We confirmed that UFM1 deletion prevented protein UFMylation, whereas UFSP2 deletion caused global accumulation of UFMylated proteins. UFM1 deficiency significantly increased PR8 replication, whereas UFSP2 deficiency had no significant effect. IAV infection caused alterations in global patterns of protein UFMylation. We additionally found that the electrophoretic mobility of several viral proteins was altered in UFSP2 knockout cells compared to control cells with an intact UFSP2 gene.

Conclusions: We demonstrate that UFM1 deficiency increases IAV replication. Changes in the electrophoretic mobility of IAV proteins in cells deficient in UFSP2 suggests that viral proteins may be UFMylated. We intend to further isolate and characterize these proteins to determine if they are indeed UFMylated and the effect of this modification on protein function.

Oral Presentation 6

Title: CASES OF PCR-POSITIVE BLOOD FOR ANAPLASMA PHAGOCYTOPHILIUM IN NOVA SCOTIA: A REVIEW FROM MAY – September 2022

Authors: Elizabeth Simms, Ziyad Allehebi, Farhan Khan, Catherine R Brown, Jason J LeBlanc, Todd F Hatchette, Glenn Patriquin

Affiliation: Department of Medicine, Faculty of Medicine, Dalhousie University, Halifax, NS, Canada; Department of Pathology, Faculty of Medicine, Halifax, NS, Canada; Division of Microbiology, Department of Pathology and Laboratory Medicine, Halifax, NS, Canada; Dalhousie University, Faculty of Medicine, Department of Community Health & Epidemiology, Halifax, NS, Canada, University of Ottawa, School of Epidemiology & Public Health, Halifax, NS, Canada**Introduction:** Antimicrobial use in patients infected with COVID-19 is not well-defined. Many factors, including the use of immunomodulatory therapies, may impact co-infection and secondary infection risk and antimicrobial prescribing. This study aimed to characterize antimicrobial appropriateness for patients admitted with or for COVID-19.

Introduction: Anaplasmosis is an infectious disease caused by the bacterium Anaplasma phagocytophilum, primarily transmitted to humans through the bite of blacklegged ticks, which are endemic in Nova Scotia. Its clinical presentation can range from a mild flu-like illness to multiorgan failure and death. Since the first case of anaplasmosis in NS in 2017, there have been very few reported in subsequent years. The summer of 2022 demonstrated a significant increase in cases, suggesting emergence of this tick-borne pathogen. The purpose of this study is to identify trends in the geographic distribution, clinical presentation, and laboratory findings of patients with Anaplasma PCR-positive blood.

Methods: This study is a retrospective chart review. All patients in Nova Scotia with PCR+ blood for Anaplasma phagocytophilum from May 1st to September 30th 2022 were included. Anaplasma PCR testing had either been ordered specifically by the treating clinician or had been added reflexively by the microbiology lab to samples submitted for Lyme testing. Patient data from PCR+ samples was collected using local and provincial electronic medical records.

Results: Of the 116 cases reviewed to date, the majority (87.9%) of samples were collected from patients with postal codes in the Western Zone of the province, an area encompassing Lunenburg to Digby. Median age was 66, and 57.8% of patients were male. 64.1% had blood smears consistent with Anaplasma. Fever was the predominant presenting symptom. Laboratory abnormalities included anemia, lymphopenia, thrombocytopenia, and elevated liver enzymes.

All patients had an infectious diseases (ID) consult and 43% (119/276) of antimicrobials were prescribed by an ID physician. Ceftriaxone (55/276), piperacillin/tazobactam (48/276), and intravenous vancomycin (33/276) were prescribed the most.

Conclusions: The vast majority patients presenting to care with PCR+ blood for Anaplasma phagocytophilum in this review reside in the Western Zone of the province. Clinical presentation commonly included fever, cytopenias, and elevated liver enzymes. These findings may help clinicians

identify those patients at high risk of anaplasmosis and lead to timely testing and treatment decisions for this emerging disease in Nova Scotia.

Oral Presentation 7

Title: INVESTIGATING THE ROLE OF ACTIVATION-INDUCED CYTIDINE DEAMINASE IN CHLAMYDIA PATHOGENESIS

Authors: Katherine Wang[1,2], Dongpu Li[1,2], Jun Wang[1,2, 3], and Camille L'Espérance[2]

Affiliation: Katherine Wang[1,2], Dongpu Li[1,2], Jun Wang[1,2, 3], and Camille L'Espérance[2]

Not published by request.

Oral Presentation 8

Title: THIOPURINES INHIBIT CORONAVIRUS SPIKE PROTEIN PROCESSING AND INCORPORATION INTO PROGENY VIRIONS

Authors: Brett Duguay[1‡], Eric Pringle[1‡], Maxwell Bui-Marinos[2,3], Rory Mulloy[2,3], Shelby Landreth[4,5], Krishna Swaroop Desireddy[6], Stacia Dolliver[1], Shan Ying[1], Taylor Caddell[1], Trinity Tooley[1], Patrick Slaine[1], Stephen Bearne[6,7], Darryl Falzarano[4,5], Jennifer Corcoran[2,3], Denys Khaperskyy[1], Craig McCormick[1]

Affiliation: [1] Department of Microbiology & Immunology, Dalhousie University, Halifax, Canada, [2] Department of Microbiology, Immunology and Infectious Diseases, University of Calgary, Calgary, Canada, [3] Snyder Institute for Chronic Diseases and Charbonneau Institute of Cancer Research, University of Calgary, Calgary, Canada, [4] Department of Veterinary Microbiology, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, Canada, [5] Vaccine and Infectious Disease Organization (VIDO), Saskatoon, Canada, [6] Department of Biochemistry and Molecular Biology, Dalhousie University, Halifax, Canada, [7] Department of Chemistry, Dalhousie University, Halifax, Canada, [‡] These authors are joint senior authors on this work.

Introduction: Emerging viruses continue to highlight our need to develop broadly-acting antivirals to combat viral disease. Host-targeted antivirals interfere with host functions that are integral to viral replication across viral families. We demonstrate that thiopurines, namely 6-thioguanine (6-TG), negatively impact replication of multiple coronaviruses (CoVs) by altering host cell function.

Methods: We used ectopic overexpression and cell culture infection models to assess the effects of 6-TG on viral replication (TCID50s), RNA accumulation (RT-qPCR), and protein expression (western blotting and flow cytometry). The cell models used included: HCT-8, hTERT-BJ, 293A, and 293T cells for HCoV-OC43; Huh7.5 and hTERT-BJ cells for HCoV-229E; and Calu-3 and Huh7.5 cells for SARS-CoV-2. Defects in particle assembly were assessed using virus-like particles (VLPs) and pseudotyped lentiviruses by western blotting or infectivity assays, while TEM was used to examine OC43 virion structure. Genetic and biochemical approaches were employed to evaluate mechanism of action.

Results: 6-TG was effective at reducing viral titres of HCoV-OC43 (1.5-log10), HCoV-229E (1.5-log10), and SARS-CoV-2 (4-log10), which coincided with impaired accumulation of viral transcripts and structural proteins. The electrophoretic mobility of CoV Spike increased following 6-TG treatment, similar to Spike deglycosylated by PNGase F. Strikingly, few or no Spikes were packaged into SARS-CoV-2 VLPs, SARS-CoV-2 Spike-pseudotyped lentiviruses, or HCoV-OC43 virions following 6-TG treatment. 6-TG is converted to an active, GDP/GTP-like antiviral by a series of reactions initiated by the HPRT1 enzyme. 6-TG-mediated Spike hypoglycosylation occurred independent of Rac1 GTPase inhibition, a known target of 6-TG; however, the phenotype was reversed using a broad-acting GTPase agonist, ML-099.

Conclusions: Our work highlights the broad antiviral activities of 6-TG against multiple CoVs. Treatment with 6-TG impaired Spike glycosylation and incorporation into progeny virions. ML-099 reversed the glycosylation effects of 6-TG suggesting that GTPases are likely targets of 6-TG and are promising cellular targets for CoVs antivirals.

Oral Presentation 9

Title: INFLUENZA A VIRUS CAUSES ACCUMULATON OF NUCLEAR POLY(A) RNAs IN LATER STAGES OF VIRAL REPLICATION CYCLE INDEPENDENTLY FROM PA-X OR NS1 HOST SHUTOFF

Authors: Juliette Bougon, Eileigh C. Kadijk, Bruce Curtis, Lucie Gallot-Lavallee, John Archibald, Denys A. Khaperskyy

Affiliation: Department of Microbiology & Immunology, Dalhousie University, Department of Biochemistry & Molecular Biology, Institute for Comparative Genomics, Dalhousie University

Not published by request.

Oral Presentation 10

Title: NOVA SCOTIA HEALTH COVID-19 NON-SEVERE THERAPY TEAM: LESSONS LEARNED FROM A HUB AND SPOKE MODEL

Authors: T. D. Ramsey[1,2], L. Nodwell[1], B. Goodall[1], L. Barrett[1,2]

Affiliation: Nova Scotia Health, Dalhousie University

Introduction: In many jurisdictions, there has been difficulty providing consistent and measurable access to non-severe therapeutics in a timely manner. The Nova Scotia (NS) Health COVID-19 Non-Severe Therapy Team consists of a Pharmacist Consult Service working collaboratively with Infectious Diseases Physicians on-call to offer virtual assessment for COVID-19 treatments. The team developed a hub and spoke model to promote sustainable medication supply, equitable distribution, and measurable care.

Methods: The NS Health COVID-19 Non-Severe Therapy team was implemented March 1, 2022. Public self-referral was encouraged as the primary referral source with healthcare professional referrals used as an alternate mechanism. Data amalgamation was leveraged to achieve efficient initial prioritization for COVID-19 therapeutic assessment. Prescribing protocols were implemented to task-shift prescribing to designated pharmacists. Embedded prioritization intelligence and data analytics were implemented to enhance efficiency, monitor capacity, and optimize patient throughput.

Results: From March 1, 2022, to February 28, 2023, 82, 656 patients were initially screened, 10, 928 patients were fully assessed, and 6, 172 treatment courses were prescribed for non-severe COVID-19. The virtual hub and spoke model promoted access across NS achieving a referral distribution of 50% central zone, 21% western zone, 16% eastern zone, and 13% northern zone. Prioritization automation ensured assessment for those at high risk of progression. Upon implementation of designated pharmacist prescribing for all first-line therapies, pharmacists prescribed 95% of all COVID-19 non-severe treatments.

Conclusions: A hub and spoke model and virtual consult team provides effective access to COVID-19 non-severe therapeutics for patients across NS, supports efficient identification of people at highest risk for progression to severe disease, and enables prescribing task-shifting to pharmacists.

Poster Abstracts

(Presenter's name in **bold)**

Poster 1

Title: NOVA SCOTIA HEALTH COVID-19 VACCINE CONSULT SERVICE: VIRTUAL SUPPORT FOR HEALTHCARE PROFESSIONALS

Authors: T. D. Ramsey[1,2], J. West[1], K. Merrick[1], L. Nodwell[1]

Affiliation: Pharmacy Department, Central Zone, Nova Scotia Health; College of Pharmacy, Faculty of Health, Dalhousie University

Introduction: COVID-19 vaccine information rapidly evolves requiring healthcare professionals to navigate changing recommendations. Immunizers in Nova Scotia (NS) required support to effectively and efficiently respond to COVID-19 vaccine questions. The NS Health COVID-19 Vaccine Consult Service began June 14, 2021 to provide practitioners with access to and support interpreting current vaccine information.

Methods: The consult service provides rapid responses to vaccine efficacy, safety, dosing, storage, stability and administration questions and uses frontline feedback to generate timely and practical resources. Creating a COVID-19 vaccine information repository using REDCap® the consult service reports and evaluates quantitative metrics including number of questions, category, setting, practitioner and region, in addition to assessing qualitative measures related to caller satisfaction and suggestions for quality improvement via an electronic questionnaire.

Results: As of March 4, 2023, the consult service has responded to 2,908 vaccine questions, with 1,302 questions generated by pharmacists. Sixty-two percent of questions related to vaccine intervals, eligibility, and dosing and 21.7% related to clinical complexity or special populations. Questions came from healthcare professionals in community pharmacies, public clinics and outreach settings in all four health regions. The satisfaction survey launched March 1, 2022 with a response rate of 34%. Ninety-nine percent of respondents indicated being very satisfied with the consult service. Feedback included, "This is an extremely valuable service which gives me confidence to provide covid vaccinations."

Conclusions: Embracing a virtual model, the consult service builds system capacity, seamlessly offering real-time vaccine information to healthcare professionals in diverse settings across the province.

Poster 2

Title: VACCINE EFFECTIVENESS OF ADJUVANTED VS. NON-ADJUVANTED STANDARD DOSE INACTIVATED INFLUENZA VACCINES IN PREVENTING INFLUENZA-RELATED HOSPITALIZATION IN OLDER ADULTS: A CIRN SOS NETWORK POOLED ANALYSIS OVER THREE INFLUENZA SEASONS (2012/13;2013/14;2014/15)

Authors: Andrew, Melissa K.; Pott Henrique; Ye, Lingyun; Xidos Tessa; LeBlanc, Jason; Wilson, Kevin; McGeer, Allison; Verschoor, Chris; Hatchette, Todd F.; ElSherif, May; Ambrose, Ardith; Boivin, Guy; Valiquette, Louis; Trottier, Sylvie; Loeb, Mark; Smith, Stephanie; Katz, Kevin; McCarthy, Anne; McNeil, Shelly A.

Affiliation: Divisions of Infectious Diseases, Geriatric Medicine and Medical Microbiology

Introduction: Influenza vaccines prevent influenza-related morbidity and mortality; however, suboptimal vaccine effectiveness (VE) of trivalent and quadrivalent standard-dose inactivated influenza vaccine (TIV and QIV) in older adults has prompted the use of enhanced products such as high dose TIV/QIV (HD-TIV/QIV) and adjuvanted TIV (aTIV). Here, we present data on the overall effectiveness of aTIV compared to non-adjuvanted standard-dose TIV (NA-TIV) for preventing laboratory-confirmed influenza-associated hospitalization among older adults.

Methods: Test-negative design study using pooled data from the SOS Network-CIRN 2012-2015 influenza seasons. To deal with the numerical imbalance between groups, an inverse probability of treatment-weighted (IPT) logistic regression estimated the Odds Ratio (OR) for laboratory-confirmed influenza infection. VE was calculated as (1-OR)*100% with 95% confidence intervals. Clinical and demographic data collection included age, sex, comorbidity, smoking status, and Clinical Frailty Scale.

Results: Of 7,101 adults aged ≥65, 526 received aTIV, whereas 3,364 received NA-TIV. The overall IPT-weighted VE against hospitalization for laboratory-confirmed influenza was 45.9% (95% CI: 40.3%–51.0%) for NA-TIV compared with 53.5% (43.0%–62.1%) for aTIV. There were non-significant differences in VE estimated between aTIV and NA-TIV by age group, and influenza season, though there was a trend favoring aTIV over NA-TIV. Whereas aTIV recipients were more frail than NA-TIV recipients, an exploratory analysis revealed that frailty affected the effectiveness of the influenza vaccine: VE adjusted for frailty was 58.3% (48.6%–66.2%) for aTIV compared with 44.8% (39.1%–50.0%) for NA-TIV; the overall relative VE for NA-TIV against laboratory-confirmed influenza was 0.78 (0.64–0.96), demonstrating statistically significant benefit favouring aTIV.

Conclusions: aTIV showed better protection against influenza-associated hospitalizations in older adults than NA-TIV, with relative VE of 22% achieving statistical significance when adjusted for frailty. Frailty has a meaningful effect on vaccine effectiveness and should be considered in future clinical and surveillance studies of VE.

Poster 3

Title: VACCINE EFFECTIVENESS AGAINST OMICRON HOSPITAL ADMISSION AND SEVERE OUTCOMES: A REPORT FROM THE CIRN SERIOUS OUTCOMES SURVEILLANCE NETWORK

Authors: McNeil, Shelly A.; Pott Henrique; Ye, Lingyun; Xidos Tessa; LeBlanc, Jason; Wilson, Kevin; McGeer, Allison; Verschoor, Chris; Hatchette, Todd F.; ElSherif, May; Ambrose, Ardith; Boivin, Guy; Valiquette, Louis; Trottier, Sylvie; Loeb, Mark; Smith, Stephanie; Katz, Kevin; McCarthy, Anne; Andrew, Melissa K

Affiliation: Divisions of Geriatric Medicine, Infectious Diseases, Medical Microbiology

Introduction: The CIRN SOS Network conducts active surveillance for COVID-19 to describe disease burden and vaccine effectiveness (VE). Here we report VE against hospitalization and severe outcomes during the first Omicron wave.

Methods: Patients with laboratory-confirmed COVID-19 and test-negative controls admitted to eleven sites in Ontario, Quebec, Alberta, and Nova Scotia between December 1/2021 - March 31/2022, were enrolled. Individuals reporting two or more COVID vaccine doses were considered vaccinated. Measures included age, frailty, demographics, vaccination status, ICU admission, and death. VE against hospital admission was calculated using a test-negative design as 1-Odds of vaccination in cases vs. controls; VE against the most severe outcomes among individuals admitted with COVID-19 was estimated by comparing the rate ratio of events in vaccinated vs. unvaccinated cases. Estimates were age-stratified and adjusted for age, sex, frailty, and comorbidity.

Results: Of 2,991 cases and 1,313 test-negative controls, mean age was 68.8 ±18.5 years (cases) and 72.8 ±24.9 (controls); 46.8% were women, and 64.1% of cases and 89.3% of controls had received ≥2 COVID-19 vaccine. Among those with known frailty status, 46.4% of cases and 54.6% of controls were frail. ICU admission was experienced by 20.3% of those aged <65 years vs. 10.5% aged 65+ and 5.3% vs. 16.4% died. Adjusted VE against Omicron hospitalization was 79.6% (95%CI 75.1-83.3%) overall and differed slightly according to age: 82.8% (77.6-86.8%) for those with 65+ vs. 74.6% (65.4-81.3%) for age <65 years. Comparing rate ratios among admitted cases, VE against ICU admission was 48% (35-57%) and against death was 24% (3-41%).

Conclusions: Age and frailty are essential factors when interpreting clinical outcomes and VE. VE against Omicron variant-related hospitalization was high and was similar to higher for older vs. younger adults. Notably, VE against severe outcomes was also substantial and was not only due to the prevention of hospitalization in the first instance.

Poster 4

Title: THE PANDEMIC OF VIOLENCE IN THE SHADOW OF COVID-19: DISTANCING RESTRICTIONS AND THE RISE OF GENDER-BASED VIOLENCE

Authors: K. Salter[1], M. Kervin[1], B. Selig[1], C. Salyzyn[1], D. Halperin[1,2], S. Halperin[1]

Affiliation: [1]Canadian Center for Vaccinology, Dalhousie University; [2]St. Francis Xavier University

Introduction: In April 2020, a statement released under the auspices of the UN suggested that some measures implemented to contain COVID-19 (e.g. restrictions in movement & staying at home) increased the risk for experiencing gender-based violence (GBV), particularly for individuals already in abusive relationships. To explore the current state of knowledge regarding the link between distancing strategies & GBV, we conducted a scoping review of literature published from Mar 2020-Nov 2021.

Methods: Arksey & O'Malley's (2005) 5-stage framework guided the review process. To address our objective, we worked with a librarian to develop a comprehensive search strategy across multiple databases focusing on studies that examined COVID-19 distancing strategies and GBV. Search results were uploaded to Covidence for team-based review. With duplicates removed, 2 reviewers assessed each article by: 1) title and abstract & 2) full text review. Data extraction was charted in Covidence. Conflicts were resolved via consensus.

Results: Of 1,715 studies, 287 met the inclusion criteria. Though international in scope, studies originating in the Global North accounted for 53.7% of those included. Most research (n=230) focused on GBV arising early in the pandemic (between Mar-Jul 2020). 168 studies reported the collection/analysis of data using quantitative (n=120), qualitative (n=45) or mixed methods (n=3). Reported data sources included surveys (n=60), existing police/hospital databases (n=50), interviews/focus groups (n=29), news media (n=10), social media (n=5), or a combination (n=14). 119 studies did not report data collection or analysis.

Conclusions: It is important, in any jurisdiction, to gain an understanding of the impact of unintended consequences, like GBV, that may be associated with strategies used to contain COVID-19. Based on data extracted, we will examine patterns of reported GBV incidence and prevalence over time, associated risk factors, and recommendations for strategies, policies or programs to address GBV.

Poster 5

Title: CHANGES TO SCHOOL-BASED IMMUNIZATION PROGRAMS (SBIP) THROUGHOUT THE COVID-19 PANDEMIC: AN ENVIRONMENTAL SCAN OF THE CANADIAN MARITIMES

Authors: A Gallant, A Steenbeek, S Halperin, J Parsons Leigh & J Curran

Affiliation: Faculty of Health, Dalhousie University

Introduction: Schools are ideal settings for public health initiatives, including SBIP, to support equitable health outcomes in students. SBIP were affected by the COVID-19 pandemic as schools switched between in-person and virtual attendance. We aimed to identify how SBIP in the Maritimes were affected by the pandemic, including catch-up programming used and changes in vaccine coverage.

Methods: Data related to SBIP programs and procedures since 2018 were collected through grey literature searches and provincial public health stakeholders. Data from the 2018/2019 school year was used to provide baseline details of SBIP programs and vaccine coverage. Data from 2019/2020-2021/2022 identified changes to SBIP, catch-up programming offered during school closures, and changes to vaccine coverage. Data from 2022/2023 was used to identify any remaining catch-up programs and any changes to SBIP delivery as a result of the pandemic.

Results: Baseline data revealed provincial differences in SBIP procedures, with variations in vaccines administered and the grades offered. Provinces were meeting meningococcal coverage targets but fell short for HPV and TDaP coverage goals. Each province's SBIP clinics were cancelled in spring 2020, with catch-up programs used when in-class learning resumed throughout 2020-2022. NS also utilized summer catch-up programming. Preliminary findings indicate vaccine coverage dropped between 2-10% since the 2018/2019 school year for most vaccines offered.

Conclusions: SBIP had difficulties reaching vaccine targets prior to 2020, which the COVID-19 pandemic exacerbated with school closures and increases in vaccine hesitancy. Spring 2020 SBIP clinics were cancelled in each province as a result of COVID-19 school closures. Despite ongoing COVID-19 school closures and public health measures, there have been minimal disruptions to SBIP since fall 2020. SBIP may benefit from updates to service delivery to address pre-existing barriers and new challenges as a result of the pandemic.

Poster 6

Title: RECEPTOR OF ACTIVATED PROTEIN C KINASE (RACK 1) REGULATES PROTEASOME ACTIVITY

Authors: Yunnuo Shi, Zhenyu Cheng

Affiliation: Dalhousie University

Introduction: RACK1 is a multifunction scaffolding protein that regulates various cellular machinery involved in proteome homeostasis. However, whether RACK1 regulates the function of protein degradation machinery remain to be investigated. Our lab identified a novel interaction between RACK1 and proteasome. Proteasome is a multi-subunit protease complex degrades ~80% of cellular proteins. Inhibiting proteasome function has shown promising therapeutic value in treating cancers, neurodegenerative disease, infectious disease, and autoimmune diseases, while the mechanisms of proteasome regulation are still not fully understood. We hypothesize that RACK1 regulates proteasome function through their direct interaction.

Methods: The goal of this study is to investigate the structural and functional relation between RACK1 and proteasome. Direct binding assay was used to test whether the purified RACK1 could interact with purified core particle (20S) or regulatory particle (19S) of the proteasome. Mutagenesis approach was used to map which of WD40 domain of RACK1 is responsible for its interaction with proteasome. Various truncated mutants of RACK1 were constructed and expressed in HEK293 cells as Flag-Strap tag fusion protein. The interaction of RACK1 mutants with proteasome was tested using Flag co-immunoprecipitation (co-IP). The effects of RACK1 on proteasome function were characterized using purified proteins. The protease activities of the proteasome with or without interacting with RACK1 were measured using fluorescent peptidase assay.

Results: RACK1 could directly interact with both 19S and 20S proteasome. The co-IP of the RACK1 mutants showed that deleting the first 136 amino acids of RACK1 dramatically reduced its binding to proteasome in HEK293 cells. In addition, the fluorescent peptidase assay showed that the direct binding of RACK1 to proteasome significantly enhanced the trypsin-like protease activity of the purified proteasome.

Conclusions: The current study demonstrated that RACK1 directly interacts with multiple proteasome subunit proteins, which are belongs to the regulatory and core particle of the proteasome. The N-terminus three WD40 domains of RACK1 are critical for RACK1-proteaosme interaction. RACK1 showed regulatory effects on the trypsin-like protease activity of the proteasome vis direct binding.

Poster 7

Title: ESTIMATING THE ASSOCIATION BETWEEN ACUTE SARS-COV-2 INFECTION AND FEBRILE SEIZURE IN CHILDREN USING THE CANADIAN IMMUNIZATION MONITORING PROGRAM-ACTIVE (IMPACT)

Authors: Fahima Hassan,[1,2] Julie A Bettinger[3], Laura Sauve[3], Manish Sadarangani[3], Taj Jadavji[4], Cora Constantinescu[4], Scott A Halperin[1,5], Shaun K Morris[6], Karina A. Top[1,2,5] for the Canadian Immunization Monitoring Program Active Investigators

Affiliation: [1]Canadian Center for Vaccinology, IWK Health, [2]Department of Community Health & Epidemiology, Dalhousie University, [3]Vaccine Evaluation Center, BC Children's Research Institute and Dept of Pediatrics, University of British Columbia, [4]Alberta Children's Hospital, [5]Department of Pediatrics, Dalhousie University, [6]Hospital for Sick Children and University of Toronto

Introduction: Most children with acute SARS-CoV-2 infection exhibit only mild or no symptoms, but neurological complications are reported. Febrile seizures (FS) are a common occurrence in children with viral infections, and it is important to investigate the relationship between SARS-CoV-2 infection and FS.

Methods: *Objective:* To estimate the association between acute SARS-CoV-2 infection and hospitalization for FS in children aged <7 years presenting to a Canadian Immunization Monitoring Program-Active (IMPACT) emergency department (ED) or hospitalized with FS from 1 Aug 2021 to 31 Jul 2022.
Design and Method: We are conducting prospective active surveillance for FS for children aged <7 years who visited the ED and/or were admitted to 1 of 12 pediatric tertiary care centers within IMPACT. At each center, trained nurses screen ED visit and hospitalization records for cases of fever (temperature ≥38.0°C) and FS diagnosed by a physician. Subjects with history of afebrile seizure, recurrent ED visit for FS within 30 days and preexisting neurological conditions will be excluded from the analysis. The exposure variable is microbiologically confirmed acute SARS-CoV-2 infection within 10 days prior or 1 day after ED or hospital admission. The primary outcome is hospitalization for FS. Descriptive analysis will summarize demographic and clinical characteristics of hospitalized (cases) versus non-hospitalized patients with FS who were discharged from ED (control). Using a case-control study design and multivariate logistic regression, the association between SARS-CoV-2 infection and hospitalization for FS will be estimated as an adjusted odds ratio with a 95% confidence interval adjusting for potential confounders such as age, sex, month of ED/hospital visit, non-SARS-COV-2 infections, FS history.

Conclusions: *Expected impact:* We will assess the relationship between SARS-COV-2 and severe FS, contributing to the understanding of SARS-CoV-2 disease burden in young children and informing strategies for prevention in this age group.

Poster 8

Title: CHARACTERIZING THE ROLE OF HOST STRESS RESPONSES DURING CHRONIC PSEUDOMONAS AERUGINOSA INFECTION

Authors: Shannen Grandy, Zhenyu Cheng

Affiliation: Dalhousie University, Faculty of Medicine, Department of Microbiology and Immunology

Introduction: Pseudomonas aeruginosa is a Gram-negative bacterium and opportunistic pathogen. P. aeruginosa is the most common pathogen to cause lung infection in cystic fibrosis patients, resulting in exacerbated and chronic lung inflammation. P. aeruginosa secretes an abundance of virulence factors including proteases and elastases that, in combination with the innate inflammatory response, cause significant damage to the host lungs. With the lack of effective antibiotics against P. aeurignosa, there is a high demand for alternative strategies to alleviate inflammation. Our lab has found that inhibiting the integrated stress response (ISR) reduces the host inflammatory response, presenting a promising therapeutic target to alleviate inflammation.

Methods: This project has two objectives first, identifying how P. aeruginosa activate the ISR and its consequential impact on inflammation and second, determining the impact ISR activation has on infection outcome. To determine how P. aeruginosa activates the ISR, lung epithelial A549 cells were treated with lipopolysaccharide (LPS) or proteases secreted by P. aeruginosa. The 4 secreted proteases used were elastase A (LasA), elastase B (LasB), protease IV (PrpL), and alkaline protease (AprA). Cells were harvested and prepared for western blots which were probed for ISR pathway proteins.

Results: LPS treatment did not cause early activation of the ISR. All 4 secreted proteases were able to activate the ISR at 15 minutes and 1 hour of treatment. AprA activation of the ISR has been published, the other three proteases are therefore novel elicitors of the ISR. Notably, LasB caused consistent and strong activation of the ISR and seemed to be acting through a kinase PKR.

Conclusions: *P. aeruginosa* secreted proteases contribute to virulence and enable the establishment of acute and chronic infections. Here, we have shown that LasA, LasB, PrpL and AprA can activate the ISR, a host stress response system which is activated by a diverse range of conditions. How the proteases can elicit these responses and the role ISR activation plays in inflammation remain to be elucidated. Understanding how the ISR gets activated by *P. aeruginosa* virulence factors and the impact this has on infection outcomes will allow for the identification of potential therapeutic targets..

Poster 9

Title: TURN-AROUND TIME OF POSITIVE BLOOD CULTURE IN COMMUNITY HOSPITALS IN CENTRAL ZONE HALIFAZ – A QUALITY ASSURANCE PROJECT

Authors: Yahya Shabi, Ross Davidson, David Haldane, Ian Davis, Joline Head, Paul Bonnar, Glenn Patriquin

Affiliation: Department of Pathology and Laboratory Medicine, Nova Scotia Health and Dalhousie University, Halifax, Nova Scotia, Canada

Introduction: Blood cultures are essential in diagnosing bloodstream infections and integral for patient management. Smaller facilities may lack the capability to perform blood cultures, therefore blood cultures are often sent to central laboratories. Bottles requiring transport may face delays in reporting given the time encountered in transportation, which could impact appropriate antimicrobial management, compromising the quality of care. Focusing on common bacterial organisms, *Staphylococcus aureus, S. lugdunensis*, Enterobacteriales, and afermenters (*Pseudomonas spp., Acinetobacter spp.,* and *Burkholderia spp*.), we examined the effect of

Methods: Dates and times of sample collection, arrival at the laboratory, Gram stain and final reports from both the community and central laboratory were examined. Retrospective data were collected from the laboratory information system for 19 months. Time from collection to results was recorded and stratified by organism and location of blood collection. The time of arrival to the central laboratory served as a surrogate for the start of incubation, and the time of Gram stain served as a surrogate for the detection of a positive culture. We also simulated potential delays of 0, 3, 12, and 24 hours at room temperature using spiked blood culture bottles before placement on the automated blood culture instrument.

Results: A total of 3221 of isolate, 1684 from central and 637 community hospital. Table below shows median times from central and community sites. Average turnaround times for staphylococci are 60:24 and 62:12 for central and community sites respectively. Averages turnaround times for Enterobacterales are 59:30 and 60:52 for central and community sites respectively. Average turnaround times for Afermenters are 69:35 and 78:24.

Conclusions: Despite prolonged transport to the central laboratory, the time required for preliminary and final reports between sites is insignificant. Our study supports the centralization of blood cultures.

Poster 10

Title: USING *IN SILICO* MODELLING TO IDENTIFY GTPASE TARGETS OF 6-THIOGUANINE

Authors: M. Stolz[*], K. Forrestall[‡], E. Pringle[*], B. Duguay[*], I. Pottie[‡], S. Darvesh[*], C. McCormick[*]

Affiliation: [*]Dalhousie University, [‡]Mount Saint Vincent University

Introduction: Coronaviruses use extensively glycosylated spike (S) proteins for entry into host cells. We showed that cells convert the FDA-approved drug 6-thioguanine (6-TG) to a nucleotide form that inhibits coronavirus replication by preventing S glycosylation and maturation. The pan-GTPase agonist ML-099 rescued proper S glycosylation in the presence of 6-TG, thereby implicating an unknown GTPase in this antiviral mechanism. GTPases are signal transduction enzymes that cycle between an active, GTP-bound state and an inactive, GDP-bound state and control various cellular functions. Cell-metabolized 6-TG-triphosphate is structurally similar to cellular GTP and could thus disrupt GTPase function and cycling. To identify potential GTPase targets of 6-TG, we deploy a computational approach using in silico modelling to evaluate binding of 6-TG metabolites to cellular GTPases.

Methods: We used Molecular Operating Environment (MOE) software produced by Chemical Computing Group to simulate 6-TG binding to 146 GTPases with known molecular structures, obtained from the Protein Data Bank or the AlphaFold Protein Structure Database. GTPases were prepared for modelling at pH 7.0 and a salt concentration of 0.1 mol/L. Each modelling experiment was done in triplicate, and each replicate produced 10,000 possible poses, which were scored based on free binding energy. Binding affinities for the five best-scoring poses were calculated and each were visually examined.

Results: Preliminary modelling shows the predicted binding sites for 6-TG coincide with the known nucleotide binding site for most GTPases. Predicted interactions between GDP or GTP and amino acid side chains in the enzyme binding pocket also reflect those in known crystal structures. Rab5A, Rab28, and N-Ras were identified as GTPases with binding affinities of ~-40 kJ/mol for 6-TG metabolites, which exceed their respective predicted affinities for GTP or GDP by 1.2-1.6-fold.

Conclusions: We conclude MOE is effective at modelling drug-enzyme interactions and identifies several candidate GTPases that may be direct targets of 6-TG. We suggest this in silico approach will inform experimental approaches to identify molecular targets of 6-TG and may highlight the importance of GTPases in coronavirus and glycoprotein biology and facilitate development of more potent drugs to combat coronaviruses.

Poster 11

Title: FACTORS AFFECTING KNOWLEDGE, BELIEFS, AND BEHAVIOUR TOWARD COVID-19 VACCINE BOOSTER DOSES: A CROSS-NATIONAL SURVEY.

Authors: Michal S. Cherak,[1] Emily A. FitzGerald[1], Stephana J. Moss[1,2,3], Rebecca Brundin-Mather[4], Alexandra Dodds[1], Henry T. Stelfox[4,5], Ève Dubé[6,7], Kirsten M. Fiest[4,5,8], Donna Halperin[9,10], Sofia Ahmed[11,12], Shannon E. MacDonald[13,14], Sharon E. Staus[15,16,17], Terra Manca[9,18], Josh Ng Kamstra[4], Andrea Soo[4,19], Shelly Longmore[4], Shelly Kupsch[4], Bonnie Sept[4], Scott Halperin,[9,18,20] Jeanna Parsons Leigh[1,2]

Affiliation: [1]Faculty of Health, School of Health Administration, Dalhousie University, Halifax, Nova Scotia, Canada
[2]Department of Critical Care Medicine, Dalhousie University, Halifax, Nova Scotia, Canada
[3]CRISMA Center, Department of Critical Care, University of Pittsburgh, Pittsburgh, United States
[4]Department of Critical Care Medicine, University of Calgary, Calgary, Alberta, Canada
[5]Department of Community Health Sciences and O'Brien Institute for Public Health, University of Calgary, Calgary, Alberta, Canada
[6]Centre de Recherche du CHU de Québec, Université Laval, Québec, Canada
[7]Institut National de Santé Publique du Québec, Québec, Canada
[8]Department of Psychiatry & Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada
[9]Canadian Center for Vaccinology & Scientific Staff, IWK Health Center, Halifax, Nova Scotia, Canada
[10]Rankin School of Nursing, St. Francis Xavier University, IWK Health Center, Halifax, Nova Scotia, Canada
[11]Department of Medicine, University of Calgary, Calgary, Alberta, Canada
[12]Libin Cardiovascular Institute, University of Calgary, Calgary, Alberta, Canada
[13]School of Public Health, University of Alberta, Edmonton, Alberta, Canada
[14]Faculty of Nursing, University of Alberta, Edmonton, Alberta, Canada
[15]Li Ka Shing Knowledge Institute of St. Michael's Hospital, Unity Health Toronto, Toronto, Ontario, Canada
[16]Department of Medicine, University of Toronto, Toronto, Ontario, Canada
[17]Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, Ontario, Canada
[18]Department of Pediatrics, Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada
[19]Alberta Health Services, Calgary, Alberta, Canada
[20]Department of Microbiology and Immunology, Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada

Not published by request.

Poster 12

Title: A FRAMEWORK FOR LEGISLATED GOVERNANCE OF IMMUNIZATION ACROSS CANADA

Authors: Shawn Harmon, Ksenia Kholina, Janice Graham

Affiliation: Technoscience and Regulation Research Unit, Department of Pediatrics (Infectious Diseases), Dalhousie University

Introduction: The COVID-19 pandemic has demonstrated—once again—that sustained attention to, development of, and funding for public health (PH) is critical to individual and population health, but that current programs, practices, policies and infrastructure make it difficult/impossible to achieve maximum social benefit. For Canada to realize the promise of immunization as an essential component of PH, more attention needs to be paid to its governance.

Methods: This study employed mixed-methods constant comparative approach that triangulated multiple sources of data to interrogate a range of governance-related questions against the backdrop of the COVID-19 epidemiological data. The data were collected via following methods:

1. Legal Landscaping: Examined the content of 568 documents, 242 of which were statutes and regulations (Federal, NS, NB, ON, MB, AB, BC, NU, YK).
2. Qualitative Fieldwork: 34 semi-structured interviews (Sept to Dec 2021) with key-informants (selected via purposive and snowball sampling) from across Canada (Federal, PEI, NS, NB, QC, ON, SK, AB, BC, NWT) encompassing 4 groups: public health officials (n=18); frontline healthcare workers (n=8); healthcare union leaders (n=3); and health scholars (n=5). Interview data were analyzed using a thematic analysis approach.

Results: Immunization is shaped by laws, policy documents, and unscrutinized practice, leading to a disjointed landscape that fails to support coherency of governance or integration of practice. Two related and mutually enhancing law-based phenomena were particular confounders of effective immunization: importation of standards (applying standards that were designed for other activities) and system fragmentation (evident in decision-making, service delivery, and program design). Immunization governance is suboptimal and demands a legislative foundation.

Conclusions: Drawing on the study findings and the literature around 'good governance', which is one of three key pillars for the legitimacy of the exercise of power by modern states, we developed a **framework** for a model *Canadian Immunization Act*. A model Act that reflects the governance values and associated operational practices identified in this framework could facilitate better outcomes, including greater setting integration, clearer evidence-based decision-making, greater reflexivity and public engagement, all of which impacts on public trust, and, ultimately, vaccine uptake.

Poster 13

Title: PRE- AND POST OMICRON: MODERATE – SEVERE COVID HOSPITALIZATION DEMOGRAPHICS, CLINICAL FACTORS, AND OUTCOMES

Authors: Goodall, Barbara; Curl, Tiffany; Bai, Isaac; Bonnar, Paul; Burgess, Sarah; Davis, Ian; Di Quinzio, Melanie; Fraser, Sophie; Ghaly, Ahmed; Hatchette, Todd; Johnston, Lynne; Lata, Chris; MacAdam Emily; McNeil, Shelly; Moses, Brian; Neale, Siony; Oldford, Sharon; Ramsey, Tasha; Reid, Emma; Simms, Elizabeth; Srivatsa, Kris; Yee, Carmen; Barrett, Lisa; and COVIC Team.

Affiliation: Nova Scotia Health

Introduction: COVIC is a province-wide, adaptive, pragmatic study to assess investigational COVID-19 therapies in those with moderate to severe disease requiring hospitalization. Understanding the impact of emerging variants is important and can inform public health strategy and planning for resource allocation. The objective of the study is to describe demographics, clinical characteristics, and outcomes in COVID enrolled moderate to severe COVID-19 hospitalized Nova Scotians in early waves (waves 1-3, Apr 2020 to Jul 31, 2021) and later waves (waves 4-7, Aug 1, 2021 to present).

Methods: Hospitalized Nova Scotians identified by the study and primary team to have moderate to severe COVID-19 disease were offered participation in study. Drug assignment was based on severity, drug availability, and assessment of inclusion/exclusion criteria. Study drugs included baricitinib, remdesivir, and tocilizumab. Clinical characteristics including comorbidities, age, sex, length of hospitalization, COVID vaccination status, presenting symptoms, and 30-day mortality were compared for patients between early (waves 1-3, Apr 2020 to Jul 31, 2021) and later waves (waves 4-7, Aug 1, 2021 to present).

Results: 362 participants were enrolled in study between Apr 14, 2020 and Jan 5, 2023. There was a significant shift in median age from 52 in early waves (N=143) to 69 in later waves (N=220) ($p<0.0001$). Comorbidities were increased in later waves, with 70% of participants having more than three comorbidities compared to 53% in early waves. The 30-day mortality rate in the later waves was 14% compared to 7% in earlier waves. The median length of hospitalization was 11 days during both time periods. Assessment of time from symptom onset to hospitalization, and presenting symptoms is pending. Stratification by medication and vaccination status are ongoing, and will also be presented.

Conclusions: During later COVID-19 waves, age, comorbidity, and 30 day mortality was higher among COVIC participants with moderate to severe COVID disease. This highlights the importance of continued data collection and analysis to assess expected versus actual impact of COVID in a highly vaccinated population. Vulnerable and comorbid individuals are proportionally more represented, and ongoing mitigation strategies in high risk populations remain relevant.

Poster 14

Title: PRAGMATIC RESEARCH: A COVID CASE STUDY WITH STBBI IMPLICATIONS

Authors: Goodall B[1,2], Bonnar P[1,2], Burgess S[1,2], Curl T[1], Davis I[1,2], Di Quinzio M[1,2], Ghaly A[1,2], Hatchette T[1,2], Johnston L[1,2], Lata C[1,2], MacAdam E[1,2], McNeil S[1,2], Moses B[1,2], Oldford S[1,2], Ramsey T[1,2], Reid E[2], Simms E[1,2], Srivatsa K[1,2], Barrett L[1,2], and COVIC Team[1,2]

Affiliation: Dalhousie University, Nova Scotia Health

Introduction: Epidemic and pandemic infectious diseases, including STBBIs, are a distinct challenge for clinical research. Timely data generation are important to optimize consistently applied individual and population access, particularly when a clear standard of care does not exist or rapidly evolves. Traditional clinical trial design is slow and does not usually focus on programmatic treatment delivery, especially outside established trial centers. We describe design and implementation of the NS pragmatic, moderate-to-severe COVID treatment study (COVIC) to facilitate timely access and outcome delineation across all NS COVID care centers.

Methods: In March 2020, a provincial health systems' decision was made to provide all inpatient COVID therapeutics for patients with moderate-to-severe infection hospitalized at 6 defined academic and non-academic COVID treatment sites through a NSHA ethics approved pragmatic study using a hub-and-spoke model. Baseline clinical phenotype, laboratory data, and outcomes were collected as standard of care. A pragmatic implementation framework was used to retrospectively identify successes, challenges, facilitators, implemented solutions, and unmet needs.

Results: 362 people have been enrolled in the study to date. Successes include: structured data collection supported by strong health authority and frontline provider buy in; timely ethics review (3 weeks); access equity and treatment consistency for rural and urban patients; and drug supply durability. Challenges include: large volume research documentation despite pragmatic approach using already approved medications and lack of hospital and community research embedded EMR to facilitate rapid data collection.

Conclusions: Centralized, task-shifted, registry based, locally adapted clinical care and pragmatic research facilitates equitable and consistent geographic access to care, including new therapeutics, while clinical expertise developed. For reportable and communicable infections, such as COVID and STBBI, that are characterized by rapidly evolving information, this approach may provide better access to scarce resources and improve real world and health system information.

Poster 15

Title: IMPACT OF CMV ON IMMUNITY TO SARS-COV-2 IN LONG TERM CARE RESIDENTS

Authors: A. Sagan[1], S. Oldford[1,2], G. Marivel[1], J. Heath[1], D. Medina-Luna[1], M. Qurashi[1], C. O'Reilly[1], C. Arnold[3], K. Nakka[3], M. Pelchat[3], M-A. Langlois[3], L. MacDonald[2], S. Fraser[2], B. Goodall[2], S. Meeker[2], A. Falkenham[2], B. Clarke[2], S. Searle[1,2], M. Andrew[1,2], T. Hatchette[1,2], O. Theou[1,2], K. Rockwood[1,2], U. Perez-Zepeda[1,2], J. Leblanc[1,2], G. Patriquin[1,2], E. MacAdam[1,2], S. McNeil[1,2], L. Barrett[1,2]

Affiliation: [1]Dalhousie University, [2]Nova Scotia Health Authority, Halifax, NS, Canada, [3]University of Ottawa, ON

Introduction: Older individuals are at increased risk of death from infections, possibly related to chronic CMV associated senescence. However, detailed immunologic assessment in highest risk settings such as longterm care facilities (LTCF) to support this hypothesis is limited. In particular, response to a novel pathogen would provide valuable information on primary immune response in the older adult in congregate settings. The objective of this study was to describe CMV associated T and B cell phenotype and function in long term care residents, including primary response to the novel viral pathogen, SARS-CoV-2.

Methods: During Wave 1 (March – Jun 2020), 108 LTCR consented to clinical data and blood collection in the ethics approved LIFE-CO study. CMV stratified T and B cell phenotype (flow cytometry), as well as T cell function (ELISPOT) and B cell function (IgG serology) were assessed in peripheral blood mononuclear cells and plasma from a cross-sectional cohort of 48 COVID naïve and 60 COVID infected individuals (median 84 yo, range 50-103 yo).

Results: CD8+ and CD4+ T cells from CMV+ LTCR have lower costimulatory CD27 expression ($p<0.001$) and increased CD57 expression ($p=0.002$) compared to CMV- LTCR. Functionally, CMV+ LTCR have strong memory responses to CMV and H1N1 influenza T cell responses, however recall responses to human coronaviruses OC43, 229E, NL63 and HKU1 are limited regardless of CMV infection. With respect to B cells, CMV+ LTCR have fewer plasmablasts ($p=0.014$) and plasma cells ($p=0.062$) and increased resting atypical memory B cells (p=ns). In response to SARS-CoV-2 infection, CMV+ and CMV- LTCR had similar magnitude primary T cell responses to SARS-CoV-2 spike, membrane and nucleoprotein, though there was a biologic trend toward higher magnitude responses in CMV+ individuals. Despite fewer circulating B cells ($p=0.037$) and increased resting atypical memory B cells (p=ns) in CMV+ SARS-CoV-2+ PBMC compared to CMV- SARS-CoV-2+ individuals, the magnitude of anti-SARS-CoV-2 serologic responses after natural primary infection was similar.

Conclusions: In this cohort of older LTCR, immunologic profile and senescence are associated with CMV infection, including marked CMV specific T cell expansion, and limited seasonal coronavirus recall responses. CMV coinfection does not significantly quantitatively alter primary SARS-CoV-2 responses, but the observed biologic trend suggests T cell responses to novel pathogens may be altered in CMV+ individuals.

T cells play an important role in protecting against severe disease and following SARS-CoV-2 vaccination.[1-3] It may be very important to understand CMV infection in the context of vaccine associated protection from severe COVID disease.

Poster 16

Title: SARS-COV-2 VACCINE RESPONSE IS INCREASED IN COVID RECOVERED LONG TERM CARE RESIDENTS AND MODIFIED BY CMV COINFECTION

Authors: S. Oldford[1,2], A. Sagan[1], G. Marivel[1], J. Heath[1], D. Medina-Luna[1], M. Qurashi[1], C. O'Reilly[1], C. Arnold[3], K. Nakka[3], M. Pelchat[3], M-A. Langlois[3], L. MacDonald[2], S. Fraser[2], B. Goodall[2], S. Meeker[2], A. Falkenham[2], B. Clarke[2], S. Searle[1,2], M. Andrew[1,2], T. Hatchette[1,2], O. Theou[1,2], K. Rockwood[1,2], U. Perez-Zepeda[1,2], J. Leblanc[1,2], G. Patriquin[1,2], E. MacAdam[1,2], S. McNeil[1,2], L. Barrett[1,2]

Affiliation: [1]Dalhousie University, [2]Nova Scotia Health Authority, Halifax, NS, Canada, [3]University of Ottawa, ON

Introduction: Elderly populations, particularly long-term care facility (LTCF) residents have been disproportionately affected by COVID-19 and have suffered significant mortality and morbidity. Vaccination protects against severe disease but responses wane over time. Elderly individuals are also often co-infected with cytomegalovirus (CMV), which may impact vaccine induced SARS-CoV-2 immunity. The objectives of this study were to assess post-natural SARS-CoV-2 infection hybrid SARS-CoV-2 vaccine responsiveness and COVID naïve SARS-CoV-2 vaccine responsiveness in long term care residents (LTCR) and evaluate the impact of CMV coinfection on vaccine induced immunity.

Methods: 356 LTCR consented to clinical data and blood collection in the ethics approved LIFE-CO COVID-19 vaccine study. T and B cell phenotype (flow cytometry), as well as T cell function (ELISPOT) and B cell function (IgG serology) were assessed in peripheral blood mononuclear cells (PBMC) and plasma.

Results: The vaccine cohort is a low COVID penetrance LTC population with 77% COVID naïve participants at baseline. 82 individuals had previous COVID infection (average of 8.5 months pre vaccine). COVID recovered individuals had significantly higher anti-RBD ($p<0.0001$) and anti-Spike IgG ($p=0.006$) post vaccination than COVID naïve LTC participants. Hybrid immunity also resulted in increased frequency of SARS-CoV-2 spike T cell responses. CMV co-infection did not impact vaccine only or hybrid antibody responses, but vaccine induced T cell responses in COVID naïve LTC were greatest in CMV- individuals ($p=0.0149$).

Conclusions: LTCR with hybrid immunity have quantitatively more robust T and B cell responses. CMV coinfection may limit vaccine induced T cell responses. This may be important for LTCR COVID protection durability, given that T cell responses are associated with prevention of severe disease and death. Further study will determine the impact of post-vaccine infection and the longer term impact of CMV on post-COVID T cell immunity. Chronic coinfections may impact response to vaccines in some vulnerable populations, and population level study is needed to identify and quantify clinical correlations.

Poster 17

Title: PLASMA ADIPOKINES IN MODERATE TO SEVERE COVID-19 PATIENTS MAY BE DYSREGULATED BY CMV CO-INFECTION AND DISEASE SEVERITY

Authors: S. Oldford[1,2], M. Qurashi[1], K. Levesque[1], B. Goodall[2], T. Curl[2], C. Myers[1], G. Marivel[1], A. Sagan[1], D. Medina-Luna[1], T. Ramsey[1,2], L. Johnston[1,2], S. McNeil[1,2], M. Robbins[1,2], W. Schlech[1,2], I. Davis[1,2], P. Bonnar[1,2], M. Andrew[1,2], E. MacAdam[2], T. Hatchette[1,2], D. Haldane[1,2], G. Patriquin[1,2], J. LeBlanc[1,2]; T. O'Leary[1,2], O. Loubani[1,2], R. Green[1,2], S. Burgess[1]; M. Di Quinzio[1,2], C. Lata[1,2], A. Ghaly[2]; B. Moses[2], K. Srivatsa[2], V. Bakowsky[1,2], D. Kelvin[2], J. Sapp[1,2], P. Andreou[1,2], K. Tennankore[1,2], G. Wells[3]; B. Goodall[1,2]; L. Barrett[1,2]

Affiliation: [1]Dalhousie University, Halifax, NS; [2]Nova Scotia Health Authority; [3]University of Ottawa

Introduction: Highly elevated BMI is associated with increased risk of severe disease and higher mortality in COVID-19 patients. A hallmark of markedly elevated BMI is dysregulated adipokine and cytokine production. The role of these biologic mediators, and the additional role of chronic CMV infection, in ongoing immune activation and response to novel pathogens is not well described. The objective of this study was to determine the relationship between BMI and plasma adipokines, CMV, T cell function and COVID-19 severity in a subset of moderate to severe COVID-19 patients.

Methods: 214 individuals hospitalized with moderate to severe COVID-19 consented to the COVIC pragmatic treatment immune substudy. Age, sex, BMI and disease severity data were collected by electronic chart review. Adipokines were measured in plasma in a subset of participants (N=38) at enrollment and Day 15, via multiplex bead assay. CMV serostatus and levels of high molecular weight adiponectin were determined by ELISA. T cell function was assessed by IFN-g ELISPOT of PBMC collected from 10 COVID vaccine naïve and 2 partially vaccinated individuals at Day 29.

Results: In the COVIC immune sub study cohort, 39% had BMI >= 35 and BMI was higher in early COVID waves 1-3 versus later waves 4-7 (34.4 vs 28.2, $p<0.0001$). Participants admitted to ICU due to COVID had significantly higher BMI (Median (IQR) = 36.7 (13.4) vs 32.5 (9.5), $p=0.0371$). CMV seropositive individuals had a distinct adipokine and pro-inflammatory cytokine signature compared to CMV negative individuals. BMI negatively correlated circulating adiponectin levels (ρ=-0.375, $p=0.049$). Adiponectin was lowest in CMV positive individuals with BMI>=35 ($p=0.018$). Adipsin and leptin levels were increased by day 15 in individuals admitted to ICU ($p=0.026$ and $p=0.013$) compared to baseline. T cell responses were detected in 11/12 individuals at day 29 (10 individuals unvaccinated, 2 had received 1 dose of vaccine). T cell responses were similar across BMI and disease severity (characterized by COVID related ICU admission). 45% of individuals demonstrated broad T cell responses against SARS-CoV-2 Spike, Membrane and nucleoprotein.

Conclusions: Dysregulated adipokine secretion in high BMI COVID positive participants may be affected by CMV co-infection and disease severity. Ongoing studies explore the relationship between circulating adipokine levels, CMV co-infection, and polyfunctional T cell responses in moderate to severe COVID disease.

Poster 18

Title: INFLUENCE OF INFLUENZE A INFECTION ON UFMYLATION OF RIG-I SIGNALLING PATHWAY

Authors: Kichydzhy K., Butova A., Samaraweera E., McCormick C**.**

Affiliation: Department of Microbiology & Immunology, Dalhousie University

Introduction: Post-translational modifications (PTMs) impact all proteins. One type of PTM involves the attachment of ubiquitin-fold modifier 1 (UFM1) to proteins, a process referred to as UFMylation. This modification is crucial for cellular antiviral responses. Also, it was found that Retinoic Acid-Inducible Gene I (RIG-I), a protein that is responsible for antiviral response, undergoes UFMylation during its complex interdependent signaling pathway. While influenza A virus (IAV) non-structural protein 1 (NS1) inhibits RIG-I signaling pathway, it remains uncertain whether it influences UFMylation of said protein.

Methods: Using CRISPR/Cas9 genome editing, we deleted UFM1 from A549 human lung carcinoma cells. The control group was treated with a non-targeting guide RNA. Next, we modeled the pHW2000 NS1 protein plasmid and introduced a mutation at the RIG-I interaction site R21Q. Subsequently, we used site-directed mutagenesis to perform the cloning process. We constructed both the wild-type influenza A virus (IAV) strain A/Puerto Rico/8/34(H1N1) (PR8) and the NS1 RIG-I mutant using the reverse-genetics technique. After 57 hours post-infection (hpi), we collected supernatants and measured their titer through a plaque assay using standard methods.

Results: The cloning product pHW2000 plasmid containing NS1 gene with R21Q mutation was sequenced to confirm that the site-directed mutagenesis went successfully. Following with the reverse-genetics method to build IAV PR8 wild type and RIG-I mutants. Viruses were collected and titered by plaque assay. As expected, mutant IAVs titer was low so subsequent propagation was performed.

Conclusions: We have successfully constructed and established the viability of IAV with a mutation in the RIG-I interaction site of the NS1 protein. This will be valuable for future investigations into the effects of IAV infection on the innate immune response within the cell.

Poster 19

Title: INVESTIGATING THE ROLE OF UFMYLATION DURING CORONAVIRUS INFECTION

Authors: Trinity H. Tooley, Brett A. Duguay, and Craig McCormick.

Affiliation: Department of Microbiology & Immunology, Dalhousie University

Introduction: Coronaviruses (CoVs) encode viral proteins that are synthesized in the endoplasmic reticulum (ER) and use ER membranes to build viral replication compartments. Therefore, control of host machinery and antiviral responses at this organelle are critical for productive CoV replication. UFMylation is a cellular post-translational modification where the ubiquitin fold modifier 1 (UFM1) protein is conjugated onto target proteins on the ER surface. ER stress causes synthesis of the XBP1s transcription factor that transactivates genes involved in ER stress mitigation, including UFMylation pathway genes. As viruses are known to regulate ER stress, we hypothesize that CoVs will alter UFMylation through modulating ER stress responses.

Methods: We infected human embryonic kidney 293T cells with human coronavirus OC43 (OC43) and harvested protein and RNA at 6, 12, 18, 24 and 36 hours post infection. We characterized the effects of OC43 infection on UFM pathway gene expression via immunoblotting and reverse transcriptase quantitative polymerase chain reaction (RT-qPCR).

Results: We demonstrate that OC43 infection increased steady-state levels of Xbp1 mRNA, as well as the splicing of this mRNA, which is required for synthesis of the XBP1s protein. We observed increases in transcription of XBP1s-responsive genes, including UFM1, indicating that XBP1s function remains intact during infection. However, we did not observe corresponding increases in the protein products of the XBP1s-responsive genes. Accordingly, levels of UFMylation pathway proteins and global rates of UFMylation did not change during infection. Interestingly, a faster-migrating species of XBP1 protein that accumulates to high levels during infection is observed.

Conclusions: We conclude that OC43 infection results in a strong accumulation of XBP1s protein and transactivation of XBP1s-responsive genes; however, this did not cause an accumulation of stress response proteins or an alteration in global patterns of protein UFMylation. By establishing a relationship between CoV infection and UFMylation, we can develop a better understanding of virus-host interactions that could be exploited for the development of new antivirals.

Poster 20

Title: INVESTIGATING THE EFFECTS OF KSHV HOST SHUTOFF ON THE UNFOLDED PROTEIN RESPONSE

Authors: Trinity C. Franklin, Brett A. Duguay, Alexa N. Wilson, and Craig McCormick

Affiliation: Department of Microbiology & Immunology, Dalhousie University

Introduction: Kaposi's sarcoma-associated herpesvirus (KSHV), or human herpesvirus 8, is the etiologic agent of Kaposi's sarcoma, Multicentric Castleman's disease, and Primary Effusion Lymphoma. During KSHV infection, the synthesis of many host proteins is inhibited through a process known as host shutoff. This benefits the virus by inhibiting antiviral gene expression and providing viral mRNAs with priority access to host translation machinery. KSHV encodes two proteins that coordinate host shutoff: ORF10 inhibits mRNA export from the nucleus to the cytoplasm, and SOX cleaves mRNAs to remove them from the actively translating pool and accelerate their degradation. There is also evidence for additional KSHV host shutoff mechanisms that remain poorly described. We observed for the first time that KSHV reactivation from latency and progression through the lytic cycle coincided with sharp decreases in the steady-state levels of the mRNA that encodes the unfolded protein response (UPR) sensor PERK. This correlated with decreased steady state mRNA levels for ATF4 target genes that are normally stimulated by PERK activation..

Methods: Using Site Directed Mutagenesis, methionine 413 of PLJM1-ORF10 was substituted to an alanine and the resulting mutant was named PLJM1-ORF10-M413A. PLJM1-ORF10-WT and PLJM1-ORF10-M413A were then tagged with FLAG using PCR. Using cut and paste cloning techniques, ORF10-WT-FLAG and ORF10-M413A-FLAG genes were cut out of their PLJM1 backbone and inserted into a PTRE backbone that contains a DOX-inducible TET-ON promoter. To ensure these plasmids were functioning properly, GFP expression was analyzed in 239A cells expressing ORF10-WT and ORF10-M413A.

Results: Methionine 413 of ORF10 is essential in its host shutoff function. Therefore, PLJM1-ORF10-M413A contains an inactive binding site that renders it non-functional. To test this, GFP expression in 293A cells was analyzed in the presence of wild type and mutant ORF10 in a PLJM1 backbone. As GFP is a confirmed target of ORF10, it was speculated that GFP expression would be downregulated in the presence of ORF10, whereas in the presence of the ORF10 mutant, GFP expression would be restored. In the presence of PLJM1-ORF10-WT-FLAG, GFP expression was seemingly downregulated. In the presence of PLJM1-ORF10-M413A-FLAG, GFP expression was seemingly restored to steady state levels when compared to samples that contained an empty vector.

Conclusions: Results obtained from these experiments confirm that the PLJM1-ORF10-WT-FLAG and PLJM1-ORF10-M413A-FLAG vectors are functioning as expected. Sophisticated microscopy techniques are required to obtain conclusive data regarding the downregulated GFP expression observed in cells expressing mutant ORF10. Additionally, further research needs to be done to determine if PTRE-ORF10-WT-FLAG and PTRE-ORF10-M413A-FLAG vectors also function properly. Upon verification of the function of these lentiviral vectors, qPCR can be done to probe for PERK mRNA levels in cells expressing these different host shutoff protein variations. Upon investigation of PERK mRNA levels in cells expressing these host shutoff proteins, conclusions can be speculated regarding the involvement of

ORF10 and SOX, individually, or in combination in the observed downregulation of PERK mRNA during lytic KSHV infection.

Poster 21

Title: RSV-RELATED HEALTH AND ECONOMIC OUTCOMES ASSOCIATED WITH IMPLEMENTING AN EXTENDED HALF-LIFE MONOCLONAL ANTIBODY FOR AN ALL-INFANT POPULATION IN CANADA: A STATIC MODEL

Authors: Thomas Shin[1,2], Jason KH Lee[1,3], Gary Lam[1,3], Alexia Kieffer[1]

Affiliation: [1] Sanofi, [2] York University Department of Mathematics and Statistics, [3] Leslie Dan School of Pharmacy, University of Toronto

Introduction: Respiratory syncytial virus (RSV) is a highly infectious respiratory virus and the leading cause of hospitalizations among infants <4 years in Canada. Nearly all children will be infected with RSV by 24 months, with a significant amount of burden experienced by healthy full-term infants. In order to protect all infants from severe RSV disease, an extended half-life monoclonal antibody (i.e. nirsevimab) was developed as the basis for a universal immunoprophylaxis strategy. Modelling was utilized to assess the health and economic burden of RSV disease, comparing nirsevimab to the standard of care (i.e. palivizumab) in Canada.

Methods: Utilizing a static decision tree model, various health outcomes (inpatient hospitalization, ICU, mechanical ventilation, ER, primary care, mortality) and associated direct healthcare costs were calculated over one RSV season for three infant categories (palivizumab-eligible, preterm, term). Scenario analysis explored four costing matrices ranging from conservative to liberal. All health-related parameters and costs were tailored to the Canadian environment with appropriate CPI adjustments.

Results: Implementing both an in-season and out-season immunization strategy with nirsevimab across all three infant categories (i.e. all-infant) during an infant's first RSV season may reduce healthcare-related outcomes in Canada by approximately 24,600 hospital-related admissions. Among the various scenarios, direct healthcare savings reached a maximum net amount of $95.7 million CAD.

Conclusions: All possible scenarios for an all-infant immunization strategy with nirsevimab (relative to the standard of care) resulted in reductions in RSV-related health and economic burden across Canada. Additional considerations pertaining to societal impact and downstream sequelae may optimize this model's final results.

Poster 22

Title: A PHASE 1, RANDOMIZED, DOUBLE-BLIND STUDY TO EVALUATE THE SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF A 21-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV) (V116) IN ADULTS

Authors: Heather Platt[1], Doreen Fernsler[1], Nancy Gallagher[1], Aditi Sapre[1], Adam Polis[1], Lori Hall[1], Gretchen Tamms[1], Howard Schwartz[2], Julie Skinner[1], Joseph Joyce[1], Rocio Murphy[1], Luwy Musey[1]
Presented by **Steven Findlay** on behalf of the authors**.**

Affiliation: [1]Merck & Co., Inc., Kenilworth, NJ, [2]Research Centers of America, LLC, Hollywood, FL, USA

Introduction: V116, an investigational 21-valent PCV, contains the following pneumococcal polysaccharides (PnPs): 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 16F, 17F, 19A, 20, 22F, 23A, 23B, 24F, 31, 33F, 35B, and a de-O-acetylated 15B (deOAc15B). This phase 1 study evaluated the safety, tolerability, and immunogenicity of V116 in pneumococcal vaccine-naïve adults compared with the 23-valent polysaccharide pneumococcal vaccine (PPSV23).

Methods: Adults (n=90) 18-49 years were randomized 1:1:1 to receive a single dose of V116-1 (2 µg dose/each PnPS, V116-2 (4 µg dose/PnPS) or PPSV23. Adverse events (AEs) were collected following vaccination. Pneumococcal serotype-specific opsonophagocytic activity (OPA) was measured prior to and 30 days postvaccination (Day 30).

Results: There were no serious AEs, deaths, or discontinuations due to AEs. Immune responses at Day 30 in the V116-1 and V116-2 groups were generally comparable to PPSV23 for the common serotypes and higher than PPSV23 for the unique serotypes. At Day 30, the OPA GMTs were higher in the V116-2 group compared to the V116-1 group for all serotypes except 9N. The OPA geometric mean titer ratio (95% CI) (V116-2/PPSV23) ranged from 0.89 (0.58, 3.51) to 2.40 (1.24, 4.62) for all common serotypes and 2.80 (1.64, 4.79) to 58.07 (25.10, 134.33) for all unique serotypes; the lower bound of the 95% CI for the OPA GMT ratio (V116-2/PPSV23) was > 0.5 for all common serotypes and >1.0 for all unique serotypes.

Conclusions: These safety and immunogenicity data support the continued development of V116 for the prevention of pneumococcal disease in adults.

Poster 23

Title: INTERIM ANALYSIS OF A PHASE 1/2 RANDOMIZED CLINICAL TRIAL ON THE SAFETY, REACTOGENICITY, AND IMMUNOGENICITY OF A QUADRIVALENT, MRNA-BASED SEASONAL INFLUENZA VACCINE (MRNA-1010) IN HEALTHY ADULTS

Authors: Raffael Nachbagauer, Ivan Lee, Lizbeth Carmona, Kristi Schaefers, Andrei Avanesov, Daniel Stadlbauer, Carole Henry, Ren Chen, Wenmei Huang, Jintanat Ananworanich, Robert Paris

Affiliation: Moderna, Inc., Cambridge, MA, USA

Introduction: Influenza is associated with substantial disease burden worldwide, causing seasonal epidemics of variable severity. Vaccines are available but often provide limited efficacy; mRNA technology has the potential to address the limitations of traditional platforms, including avoidance of mutations acquired by egg- or cell-culture, improved efficacy in older adults through the induction of strong cellular immune responses, and by potentially enabling future strain selection closer to the influenza season to decrease the chance of a vaccine mismatch. mRNA-1010 is a quadrivalent, mRNA-based seasonal influenza vaccine encoding the hemagglutinin surface glycoproteins of strains recommended by WHO: A/H1N1, A/H3N2, B/Victoria, and B/Yamagata. We present interim safety and immunogenicity findings of mRNA-1010 in healthy adults from a phase 1/2 clinical trial.

Methods: This first-in-human, observer-blind study (NCT04956575) enrolled healthy adults (aged ≥18 years), stratified by age, who were randomized to receive different dose levels of mRNA-1010. This interim analysis presents safety and humoral immunogenicity data in younger and older adults against vaccine-matched influenza A and B strains measured 28 days after vaccination.

Results: No study pause rules were met, and there were no reported serious adverse events (AEs), discontinuations due to AEs, or deaths among mRNA-1010 recipients related to the study vaccine. Solicited local and systemic adverse reactions were more frequent among younger than older adults and were dose-dependent. All mRNA-1010 dose levels elicited increases in hemagglutination inhibition antibodies from baseline across all age groups.

Conclusions: The quadrivalent mRNA-1010 candidate was immunogenic against all tested influenza strains in younger and older adults and had an acceptable safety profile. These interim safety and immunogenicity data support continued development of mRNA-1010.

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Title: SAFETY AND EFFICACY OF MRNA-1345, AN MRNA-BASED VACCINE AGAINST RESPIRATORY SYNCYTIAL VIRUS, IN ADULTS 60 YEARS AND OLDER

Authors: E. Wilson, J. Goswami, S. K. Stoszek, R. Mithani, S. Mehta, A. Kapoor, W. Huang, L. Lan, L. El Asmar, C. A. Panozzo, P. Ghaswalla, A. August,* C. A. Shaw, J. Miller, G. L. Chen

Affiliation: Moderna, Inc., Cambridge, MA, USA

*A. August was a Moderna, Inc., employee at the time of the study.

Introduction: There is a substantial unmet need for a respiratory syncytial virus (RSV) vaccine in older adults. Here, we present an interim analysis (IA) from a pivotal phase 3 clinical trial in adults aged ≥60 years assessing mRNA-1345, an investigational mRNA vaccine encoding the membrane-anchored RSV F glycoprotein stabilized in the prefusion conformation.

Methods: The ongoing phase 3, randomized, double-blind, placebo-controlled, case-driven study in adults aged ≥60 years (NCT05127434) enrolled participants from 22 countries; participants were randomized 1:1 to receive 1 dose of mRNA-1345 50 μg or placebo. The primary efficacy endpoints were the prevention of a first episode of RSV-associated lower respiratory tract disease (RSV-LRTD) with ≥2 or ≥3 symptoms between 14 days and 12 months post-injection.

Results: The IA included 35,538 participants (mRNA-1345, n=17,792; placebo, n=17,746). The mean age was 68.1 years, 50.9% were male, 36.1% were non-White, and 34.5% were Hispanic or Latino. A single dose of mRNA-1345 was well-tolerated and no safety concerns were identified. The primary efficacy endpoints for the study were met: mRNA-1345 was efficacious in preventing the first episode of RSV-LRTD in participants with ≥2 and ≥3 symptoms.

Conclusions: A single dose of mRNA-1345 had a favorable safety and tolerability profile and was efficacious in preventing RSV-LRTD with ≥2 and ≥3 symptoms in adults aged ≥60 years.

Poster 25

Title: CHARACTERISTICS AND HEALTHCARE RESOURCE USE PRIOR TO CYTOMEGALOVIRUS DIAGNOSIS IN THREE DISTINCT US PAYER POPULATIONS

Authors P. Buck[1], G. J. Demmler-Harrison[2], J. R. Marden[3], A. Anderson[3], S. Basnet[1], K. Gaburo[3], D. Peterson[3], K. Kawai[1*], N. Kirson[3], U. Desai[3], J. Diaz-Decaro[1]

Affiliation: [1]Moderna, Inc.; [2]Baylor College of Medicine, Texas Children's Hospital; [3]Analysis Group, Inc.

Introduction: Cytomegalovirus (CMV) infects ~50% of the US population by age 40; infection rates increase with age. While mostly self-limiting in healthy individuals, CMV can adversely impact those with compromised immune systems. As patient characteristics preceding a CMV diagnosis are generally unknown, we describe the comorbidity profile and healthcare resource utilization (HRU) before initial diagnosis of CMV in the US

Methods: This retrospective study utilized Merative MarketScan® Commercial Claims and Encounters, Medicare Supplemental, and Multi-State Medicaid data from 2010 to 2019. Patients with ≥1 diagnosis code for CMV or congenital CMV >12 months (mo) after birth (cases) were matched to those with no CMV diagnosis (controls). Index date was defined as date of first diagnosis for cases and a random HRU visit >12 mo after birth for controls. Continuous health plan enrollment pre-index (baseline) of ≥6 mo was required. Cases were matched 1:1 to controls on demographics, insurance type, birth year, and index year for each payer population. 6-mo baseline comorbidities and all-cause HRU were compared between cohorts.

Results: 10,342 Commercial, 2009 Medicaid, and 784 Medicare matched pairs were included. Cases had higher rates of select comorbidities in the 6 mo before diagnosis vs controls. Proportions of transplants among cases vs controls were 30.6% vs 0.3%, 22.3% vs 0.4%, and 40.9% vs 0.4% in the Commercial, Medicaid, and Medicare populations, respectively. Cases had more all-cause medical visits than controls. The proportion of cases vs controls with all-cause inpatient visits were 33.7% vs 4.1%, 41.0% vs 9.3%, and 49.5% vs 11.2%, respectively.

Conclusions: Patients diagnosed with CMV have substantially higher baseline rates of comorbidities, particularly transplants, and more all-cause HRU than those without a CMV diagnosis. Future studies should explore the reasons underlying initial CMV diagnosis and evaluate subsequent HRU and costs.

Poster 26

Title: COVID-19 MASKING IN THREE CANADIAN PROVINCES: UNCERTAIN EVIDENCE & POLITICAL DECISION-MAKING

Authors: Parker R, Kholina K, Harmon S.H.E., Graham J. E.

Affiliation: Dalhousie University, IWK Health Centre, Canadian Center for Vaccinology

Introduction: Masks emerged as a critical preventive measure against COVID-19 transmission amid a lacuna of robust evidence on their effectiveness, uneven access to high-quality masks, and wide inconsistencies in adoption. We examine the epidemiology and polices surrounding masking recommendations and mandates in three Canadian jurisdictions: Alberta, Nova Scotia and Ontario.

Methods: We applied a mixed-methods approach that triangulated epidemiological data, key jurisdictional legal and policy instruments and updates, and interviews with healthcare experts. Epidemiological data on COVID-19 cases, deaths, and vaccine delivery were extracted from the federal Public Health Infobase. Policy updates and related press conferences were collected from provincial government websites. Purposive and snowball sampling strategies were used to recruit public health officials, researchers, frontline healthcare workers and union leaders for semi-structured, qualitative interviews. Transcripts were analyzed using a three-round team-based approach.

Results: Provinces showed inconsistencies in the timing of masking policies, both initial masking recommendations and transition to mandates, that were not commensurate with epidemiological landscapes. Health officials expressed concern about political interference, recommendations versus mandates in light of the lack of robust evidence, and the downloading of responsibility for masking decisions onto local jurisdictions, care providers and ordinary citizens.

Conclusions: Our findings demonstrate that masking policies were not grounded in evidence linked to scientific and epidemiologic data, and evidence was neither clearly communicated nor referenced in conjunction with jurisdictional policy changes. Provincial ideological and political sensibilities influenced PHMs. Incoherent policies without evidence undermined public trust. Responsibility for masking was downloaded onto individuals and micro-actors. We suggest that communication corresponding to transparent epidemiological evidence, standardizing response commensurate with the scientific evidence, and recognizing the triggers of public health response could garner greater public trust and uptake of public health measures, including masking where and when appropriate.

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Planning Committee Members

Glenn Patriquin, Chair
Asra'a Abidali
Jeannette Comeau
Jennifer Isenor
Elizabeth Simms
Michael Fleming
Susan Brushett
Zhenyu Cheng
Nik Thomas
Stephanie Duncan