29th Annual Infectious Diseases Research Day

&

16th Annual Canadian Center for Vaccinology Symposium

nova scotia health
Division of Infectious Diseases

CCFV
Canadian Center for Vaccinology

Dalhousie University
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DALHOUSIE UNIVERSITY

April 23, 2024
Halifax, Nova Scotia

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Dalhousie Divisions of Infectious Diseases
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 29th Annual Infectious Diseases Research Day and 16th 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 2024. 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.

The objectives of the program are:

- to showcase local research findings in microbiology, immunology, infectious diseases, and vaccinology; and
- to foster collaboration across departments and disciplines by introducing participants to local areas of expertise

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.

29th Annual Infectious Diseases Research Day &
16th Annual Canadian Center for Vaccinology Symposium
Lord Nelson Hotel- Halifax

Tuesday April 23, 2024		
7:30-8:00am	*Continental Breakfast*	
8:00-9:00am	TJ Marrie Lecture- Dr. Isaac Bogoch *Human Mobility & Infectious Diseases* *Q&A session*	Imperial Ballroom/Zoom
9:00-9:15am	Opening remarks, Introductions- Drs. Patriquin, McNeil, Halperin	Imperial Ballroom
9:15–10:30am	Oral Presentations (5)	Imperial Ballroom
10:30-10:45am	Nutrition Break	
10:45–12:00pm	Oral Presentations (5)	Imperial Ballroom
12:00–1:00pm	Lunch	
1:00–2:00pm	Poster judging (poster's available for viewing 8:00 – 4:00)	Regency Ballroom
2:00–3:00pm	Presentation – Dr. Galit Alter *Dissecting mRNA vaccine induced immune responses* *Q&A session*	Imperial Ballroom
3:00-3:15pm	Nutrition Break	
3:15–4:00pm	Presentation- Dr. Tommy Brothers *A public health approach to injection drug use-associated bacterial infections: evidence to action* *Q&A session*	Imperial Ballroom
4:00-4:45pm	Presentation- Dr. Jason LeBlanc *A clinical lab perspective on research during a pandemic* *Q&A session*	Imperial Ballroom
4:45-5:15pm	Awards Presentations Closing Remarks – Dr. Glenn Patriquin	Imperial Ballroom

Educationally co-sponsored by Dalhousie University Continuing Professional Development and Medical Education and Continuing Pharmacy Education.

Speakers

Dr. Isaac Bogoch

Dr. Isaac Bogoch is an Associate Professor at the University of Toronto in the Department of Medicine, and an Infectious Diseases specialist at the Toronto General Hospital with a focus on tropical diseases, HIV, and general infectious diseases. Dr. Bogoch works at the intersection of clinical medicine, epidemiology, public health, and policy. He divides his clinical and research time between Toronto and several countries in Africa and Asia. He collaborates with a team that models the spread of emerging infectious diseases, and studies innovative and simple diagnostic solutions to improve the quality of medical care in low-resource settings.

Title of Presentation: Human Mobility & Infectious Diseases

1. To evaluate the impact of air travel on emerging infections with epidemic and pandemic potential
2. To describe the role of air travel in the spread of Infections including SARS-CoV-2
3. To analyze how to harness big data and molecular epidemiology to mitigate the impact of emerging infectious diseases of public health significance

Dr. Galit Alter

Galit Alter, PhD, is the Vice President of Immunology Research at Moderna. She performed her undergraduate and graduate work at McGill University, developing new tools to study the cellular immune response to HIV. Inspired by the growing world of Systems Immunology, Dr. Alter moved to Harvard University where she systematically built new tools to study innate immune responses to viral infections, and to define the unexplored role of the humoral immune response in directing the innate immune system to fight viruses, bacteria, and parasites. These efforts gave birth to a new field of Systems Serology, that coupled to Systems based antibody Fc-engineering, has begun to define the immune correlates and mechanisms of protection against a range of pathogens and diseases, providing new insights for the design of next generation vaccines and monoclonal therapeutics.

Title of Presentation: Dissecting mRNA vaccine induced immune responses

1. Review mRNA modifications that contribute to enhanced immunogenicity including nucleotide differences, improved transcription as well as engineering of secondary structure to prevent innate immune sensor activation.
2. Examine mRNA vaccine cellular delivery, duration, and mechanism of immune induction in secondary lymphoid organs resulting in targeted-but transient -vaccine antigen delivery.
3. Dissect the immunological differences in humoral immune responses occur across SARS-CoV-2 and RSV mRNA vaccines that may translate to differences in real world performance.

Dr. Tommy Brothers

Thomas (Tommy) Brothers, MD PhD FRCPC is a trainee clinician-scientist based in Halifax, currently in his final year of subspecialty residency in General Internal Medicine at Dalhousie University. He recently completed a PhD in Epidemiology & Public Health at University College London (UK), focused on infectious complications of injection drug use, where he was supported by a CIHR Fellowship. He is an internal medicine and addiction medicine specialist physician, with clinical and research interests in supporting health and improving health services for people with substance use disorders. Tommy helped to organize and implement Atlantic Canada's first supervised consumption site and first hospital-based addiction medicine consultation service, both in Halifax.

Title of Presentation: A public health approach to injection drug use-associated bacterial infections: evidence to action

1. To consider how the social determinants of health affect incidence and treatment outcomes for injection drug use-related bacterial infections
2. To review emerging evidence on harm reduction interventions, including opioid agonist treatment and needle and syringe programs
3. To explore existing programs and services in our local community that help to reduce risk and improve outcomes for people who inject drugs with bacterial infections, and imagine what we can build next

Dr. Jason LeBlanc

The foundation for Dr. Jason LeBlanc's research endeavors were forged from his BSc (Health Sciences), MSc (Biochemistry), and his interests in molecular pathogenesis during his PhD (Microbiology and Immunology). With expertise in molecular microbiology, Dr. LeBlanc helped develop rapid diagnostic tests to help meet the demands of the clinical laboratory and public health during a large mumps outbreak and a busy influenza virus season. After becoming a board-certified Clinical Microbiologist, he was employed by Nova Scotia Health (NSH). Dr. LeBlanc's now acts as Director of Virology, Immunology, and Molecular Microbiology for NSH, and currently runs a large diagnostics laboratory responsible for COVID-19 diagnostic testing in Nova Scotia. Dr. LeBlanc's research interests focus on molecular diagnostics, molecular epidemiology, and molecular pathogenesis, with application to the fields of vaccine-preventable diseases and emerging respiratory bacteria and viruses, including SARS-CoV-2, the causative agent of COVID-19.

Title of Presentation: Research during a pandemic: A clinical lab's experience

1. Describe challenges a clinical laboratory faced to provide evidence-based recommendations for laboratory testing during the COVID-19 pandemic.
2. Demonstrate local research that contributed to best practices in SARS-CoV-2 laboratory testing strategies during the COVID-19 pandemic.
3. Recommend areas of improvement for ongoing research and knowledge translation activities through active stakeholder engagement.

Oral Presentations

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Oral Presentation Abstracts

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

Oral Presentation 1

Title: PROFILING THE HOST RESPONSES TO RESPIRATORY BORDETELLA PERTUSSIS INFECTION IN HUMAN VOLUNTEERS

Authors: Saeideh Jamali[1,2], May Elsherif[1,2,3], Kara L Redden[1,3], Scott Halperin[1,2,4] and Jun Wang[1,2,4]*

Affiliation: [1]Canadian Center for Vaccinology, [2]Dalhousie University, [3]Nova Scotia Health, [4]IWK Health

Introduction: Despite high vaccine coverage, pertussis, commonly known as whooping cough, remains a significant public health concern worldwide. Our understanding about the intricate interplay between pathogen and human immune system is crucial for developing new effective vaccines. A Controlled Human Infection Model (CHIM) was established by researchers at the Canadian Center for Vaccinology. Healthy adult volunteers with equal sex and infant vaccination (wP vs aP) history were intranasally challenged with different doses of *B. pertussis* and observed as inpatients for 16-21 days. Various biological specimens (blood, nasopharyngeal aspirate, and nasal wash) were collected the day before and at multiple time points after challenge. The goal of this research project is to identify key immune components involved in host susceptibility to the *B. pertussis* infection.

Methods: Participants were classified into three clinical outcome groups: spontaneous clearance, asymptomatic infection (colonization without symptoms), and symptomatic infection (colonization with symptoms) according to defined clinical parameters. Multi-color flow cytometry was used to longitudinally monitor cellular responses to the *B. pertussis* challenge and Luminex assay was used to examine the soluble mediators in nasal washes at selected time points. The results were analyzed in all participants before and after challenge and compared between three groups.

Results: The flowcytometry panel used effectively monitored major immune cell subsets in peripheral blood samples. These include neutrophils, monocytes, natural killer (NK) cells, and mucosal associated invariant T cells (MAIT), as well as T cells and B cells. Our preliminary data showed that participants with and without clinical symptoms displayed a distinct early innate immune activation profile that involved different subsets of innate immune cells.

Conclusions: The role of early innate cellular immune responses in controlling host susceptibility to *B. pertussis* following exposure warrants further investigation.

Oral Presentation 2

Title: CLINICAL SIGNIFICANCE OF HUMAN HERPESVIRUS 6 DETECTED WITH THE FILMARRAY MENINGITIS/ENCEPHALITIS PANEL IN NOVA SCOTIA

Authors: Yahya Shabi, Elizabeth Simms, Glenn Patriquin, Jason Leblanc, Mark Robbins, Ian Davis, Todd Hatchette

Affiliation: Dalhousie University, Halifax, Nova Scotia, Canada

Introduction: Over the years, syndromic testing using highly multiplexed assays have gained popularity. The Biofire FilmArray Meningitis/Encephalitis (ME) panel allows detection of 6 bacteria, 7 viruses, and a yeast in cerebrospinal fluid (CSF), including human herpesvirus 6 (HHV-6). While HHV-6 encephalitis has been well described among hematopoietic stem cell transplant (HSCT) recipients, it is rare outside this setting and positive results could simply reflect latency rather than a true infectious cause for disease. After ME panel implementation in Nova Scotia, frequent HHV-6 positives were observed. To evaluate the clinical importance of this observation, all HHV-6 positive cases since implementation were reviewed.

Methods: A retrospective review was conducted on HHV-6 cases detected in CSF using the ME panel between January 1, 2021 and December 31, 2023. A standardized form was used to collect data on patient demographics, outcomes, and management. Cases were reviewed independently by 6 infectious disease physicians and microbiologists who assigned to possibility of disease as probable (>90% probability), possible (10%–90% probability), or unlikely (<10% probability). Final results were discussed as a group to reach consensus.

Results: Of 17 patients with HHV-6 positive CSF, the age ranged from 2 weeks to 75 years and 60% were female. None were categorized as probable CNS disease, and disease was unlikely in 16 (94%). A single case who was severely immunocompromised after receiving CAR-T cell therapy with concomitant CMV infection was categorized as possible disease. Only three patients had abnormal CNS parameters, one of whom had meningococcal disease. Three patients received antiviral therapy, but their clinical course was unchanged.

Conclusions: Given the majority of the patients had normal CNS parameters and presentations that were not compatible with HHV-6 disease, HHV-6 detection in CSF in immunocompetent patients is often reflective of latency and has limited clinical significance.

Oral Presentation 3

Title: INFLUENZA A VIRUS MUTATIONS THAT CONFER BALOXAVIR ACID RESISTANCE NEGATIVELY AFFECT THE HOST SHUTOFF ENDONUCLEASE PA-X

Authors: Jack Case, Denys Khaperskyy

Affiliation: Dalhousie University

Introduction: The polymerase acidic (PA) protein is a subunit of the trimeric influenza A virus (IAV) RNA-dependent RNA polymerase and is the target of the anti-influenza drug baloxavir acid (BXA). Since its introduction, multiple BXA resistance-associated mutations in PA nuclease domain have been identified, with I38T and I38M amino acid substitutions prevalent in clinical trials. Reports indicate that these mutations do not significantly affect viral polymerase activity, virus replication, or transmission in animal models. However, for reasons that are not well understood, viruses with BXA resistance substitutions have not been able to compete with the parental circulating strains. The IAV genome segment encoding PA also encodes the host shutoff nuclease PA-X, which shares the endonuclease domain with PA but has a unique C-terminal domain accessed through ribosomal frameshifting. Because PA-X shares the nuclease domain with PA, it contains the BXA binding site and any BXA resistance-associated substitutions. Unlike their effects on PA activity, effects of BXA or the I38T/M substitution on PA-X function remain uncharacterized.

Methods: PA-X and a fluorescent reporter were co-transfected in HEK293A cells. A decrease in reporter fluorescence was used to measure PA-X host shut off activity. Mutagenized PA-X plasmids, containing the I38T/M mutation, or treatment with BXA was used to investigate the effects of BXA and BXA resistance-associated substitutions on PA-X activity.

Results: We show, for the first time, that BXA inhibits PA-X activity in a dose dependent manner. Further, we also show that PA I38T and PA I38M mutations have negative effects on PA-X activity.

Conclusions: The high genetic conservation of IAV PA-X points to its important role in viral fitness. Our work suggests that the deleterious effects of the BXA resistance mutations on PA-X function may represent an important barrier to the spread of viruses that acquire this substitution.

Oral Presentation 4

Title: PATHOGENIC *VIBRIO* SPECIES USE A NOVEL MECHANISM OF TRANSCRIPTIONAL ACTIVATION AT CRUCIFORM DNA STRUCTURES TO COORDINATE VIRULENCE GENE EXPRESSION

Authors: Oriana Robinson, Nikhil Thomas

Affiliation: Department of Microbiology and Immunology; Department of Medicine, Division of Infectious Diseases

Introduction: Virulence gene expression supports infection, leading to disease progression. In the cases of clinically relevant pathogenic *Vibrio* species (including *V. parahaemolyticus, V. cholerae, and V. vulnificus*), the HlyU transcription regulator serves to activate multiple virulence genes. We recently demonstrated that HlyU binds near chromosomal DNA cruciform structures (unusual 4-way DNA junctions). This mechanism suggested that *Vibrio* species use HlyU to resolve DNA cruciforms and activate virulence gene expression. We therefore set out to identify additional HlyU regulated DNA cruciform structures in pathogenic *Vibrios*.

Methods: Using chromatin-immunoprecipitation coupled with next generation sequencing (ChIP-Seq), we assessed the global binding of HlyU during infection conditions in *V. parahaemolyticus*. Sequenced reads were aligned to *V. parahaemolyticus* RIMD 2210633 reference genome and peaks of enrichment were identified. The intergenic region upstream of one of the targets ExeM was PCR amplified and cloned into vector backbones pBS, for mapping of cruciform-forming DNA structures, and pVSVlux to perform real-time *in vivo* quantitative analysis of transcriptional activity.

Results: ChIP-Seq identified three targets of interest after 4 hours of infection conditions in *V. parahaemolyticus*. Of interest was *exeM,* an extracellular endonuclease which has been implicated in the degradation of Neutrophil Extracellular Traps (NETs) in the human intestine during infection. *In silico* cruciform mapping coupled with T7 endonuclease and restriction enzyme mapping of cruciform structures identified two possible cruciforms in the intergenic region of *exeM.* To begin characterizing HlyU-specific regulation of *exeM* expression, we performed lux reporter assays and found that in an *hlyU* mutant, *exeM* had a statistically significant reduction in expression compared to parental (WT) *V. parahaemolyticus.*

Conclusions: Taken together, we have identified three putative targets of HlyU in *V. parahaemolyticus*. Further characterization of the *exeM* intergenic region supported our initial ChIP-seq results and previous findings of the Thomas Lab. Firstly, DNA superstructures like cruciform are an alternative mechanism for regulation of gene expression in *Vibrio* spp. and HlyU appears to be implicated in the de-repression of gene expression by relieving the DNA supercoiling. And secondly, that like in other pathogenic species (*V. cholera* and *V. vulnificus*), HlyU acts as a global virulence regulator during *V. parahaemolyticus* infection.

Oral Presentation 5

Title: MEASURING THE EFFECTS OF RESTRICTED PALIVIZUMAB ELIGIBILITY ON SEVERE RSV ILLNESS IN OTHERWISE HEALTHY PRETERM INFANTS BORN IN NOVA SCOTIA

Authors: [1]**Yolanda Evong**, MD (1st author and presenter), [2]Joanne Langley, MD FRCPC

Affiliation: [1]Dalhousie University Faculty of Medicine, IWK Health Centre; [2]Department of Pediatrics, Department of Community Health and Epidemiology, Dalhousie University Faculty of Medicine, IWK Health Centre.

Introduction: Respiratory Syncytial Virus (RSV) is the leading cause of hospitalization in the first year of life, and Palivizumab is the only licensed prophylactic agent to reduce RSV-associated hospitalizations (RSVH) among high-risk infants. Historically, all Canadian infants born before 32 weeks gestation were eligible for prophylaxis but Palivizumab is expensive and optimal eligibility criteria are unclear. In 2016, following updated Canadian Pediatric Society guidelines, Nova Scotia became one of the first provinces to exclude otherwise healthy infants born between 30 and 32 weeks gestation from their Palivizumab eligibility criteria. We examined whether this provincial policy change was associated with a change in RSVH rates.

Methods: We identified a retrospective cohort of Nova Scotian infants born between 30 and 32 week gestation from April 2012 to September 2019 by linking 6 provincial databases. We excluded infants who were eligible for Palivizumab irrespective of their gestational age. Diagnostic codes were used to identify RSVH during the first year of life.

Results: Our cohort contained 327 infants from 9 RSV seasons; 195 pre-policy change and 132 post. The proportion of these infants who received Palivizumab decreased from 35.3% to 8.9% while the number of RSVH increased (rate ratio 10.3) following the policy change. Similar trends were observed with RSV related ambulatory visits (RSVA).

Conclusions: Periodic evaluation of healthcare policy is essential to assess impact on patient outcomes. This policy change has been associated with increased RSVH rates; therefore, we urge decisionmakers to reconsider Palivizumab eligibility criteria in this patient population.

Oral Presentation 6

Title: CHARACTERIZATION OF IMMUNE MODULATION BY PROTEASE IV IN PSEUDOMONAS AERUGINOSA ACUTE MURINE LUNG INFECTION

Authors: L. Burton, R. Nickerson, X. Zhang, A. Stueck, Z. Cheng

Affiliation: Dalhousie University

Introduction: *Pseudomonas aeruginosa* is an opportunistic pathogen capable of causing a variety of infections. A key *P. aeruginosa* virulence factor, protease IV (PrpL), has been shown to exacerbate the inflammatory response to lipopolysaccharide in murine macrophage cells *in vitro*, but this immune modulation has yet to be investigated *in vivo*. In this study, we further investigated the role of PrpL in *P. aeruginosa* acute lung infection.

Methods: Mice were intratracheally infected with either *P. aeruginosa* PA14 or a mutant strain with a deletion of the *prpL* gene, PA14/Δ*prpL* (Δ*prpL*). Mice were assessed for morbidity and weight loss over the 24-hour course of infection, and lung bacterial burden post-infection was quantified. Modulation of the inflammatory response was assessed by comparing the expression of key inflammatory cytokines and mitogen-activated protein kinase (MAPK) activation, as well as immune profiling by flow cytometry and histological analysis.

Results: There were no significant differences in weight loss, morbidity, or lung bacterial burden between the two *P. aeruginosa* strains, suggesting PA14 and Δ*prpL* are similarly virulent. There were also no differences in lung inflammation, immune cell recruitment, or MAPK activation between strains. Cytokine expression was similar between strains, except that the relative expression of IL-6 was found to be significantly higher in female mice infected with PA14 compared to Δ*prpL*.

Conclusions: Overall, the virulence and immune response to both *P. aeruginosa* strains were highly similar. This similarity may be due to the many other proteases secreted by *P. aeruginosa* compensating for the lack of PrpL activity in the Δ*prpL* strain. It is possible that using a higher infectious dose of bacteria or earlier infection endpoint could help to reveal subtle differences between the strains. Alternatively, the intratracheal instillation of purified PrpL and lipopolysaccharide may help to reveal the effect of PrpL without interference from other *P. aeruginosa* virulence factors.

Oral Presentation 7

Title: STAKEHOLDERS' EXPERIENCES WITH SCHOOL-BASED IMMUNIZATION PROGRAMS DURING THE COVID-19 PANDEMIC IN THE MARITIMES: A QUALITATIVE STUDY

Authors: Allyson Gallant, Catie Johnson, Audrey Steenbeek, Scott Halperin, Jeanna Parsons Leigh, Janet Curran

Affiliation: PhD in Health Program, Faculty of Health, Dalhousie University

Introduction: School-based immunization programs (SBIP) support access to routine vaccines for adolescent students. Across Canada, the COVID-19 pandemic and subsequent public health measures affected SBIP service delivery. The objectives of this study were to explore 1.) stakeholders' experiences with SBIP and changes to programs during COVID-19, and 2.) how the pandemic affected parents' and adolescents' vaccine views.

Methods: Semi-structured interviews were conducted with parent-student dyads, healthcare providers, health officials and teachers across three Canadian provinces between February-August 2023. Interview guides were informed by literature reviews, the COM-B model and Theoretical Domains Framework. Deductive and inductive analyses saw participant quotes mapped to relevant domains by two trained coders, then reviewed to identify key themes and subthemes.

Results: Participants (n=39) identified five themes: 1) enablers to SBIP delivery, 2) barriers to SBIP delivery, 3) desired changes to SBIP delivery, 4) student anxiety, and 5) vaccination views and changes since the COVID-19 pandemic. Public health measures facilitated more space for clinics, as did taking smaller cohorts of students. School staff-healthcare provider relationships could help or hinder programs, particularly with high turnover in both professions during the pandemic. Teachers often described a lack of confidence addressing SBIP and vaccine questions. Adolescents played a passive role in vaccine decision making, with mothers often being the sole decision maker.

Conclusions: Continued efforts are needed to ensure SBIP and catch-up programming remains accessible for all adolescents to catch-up on missed vaccines before graduation. Parents and adolescents' vaccination views suggest changes in vaccine coverage since the pandemic may be due to accessibility of services rather than vaccine hesitancy. Interventions are needed to engage school staff in SBIP. Future research is needed to engage adolescents in their vaccine decision making.

Oral Presentation 8

Title: DISSECTING ESSENTIAL NKR-P1B RECEPTOR INTERACTIONS AND SIGNALLING IN ALVEOLAR MACROPHAGES

Authors: S. Dey, M. Scur, B.D. Parsons, A.P. Makrigiannis

Affiliation: Dalhousie University

Introduction: Alveolar macrophages (AMs) are the most essential immune population for defence against inhaled pathogens and protection from damaging lung inflammation but are also uniquely adapted for debris clearance and surfactant metabolism. We previously observed that the NK cell-associated inhibitory receptor, NKR-P1B, is expressed by AMs and is crucial for lung homeostasis. Mice that lack the Nkrp1b gene, exhibit dysfunctional lipid metabolism in AMs and are more susceptible to infections. This research project aims to better define the role of NKR-P1B signalling in AM immune and metabolic processes in the lung by identifying both the signalling relays that emanate from the NKR-P1B receptor and the ligand binding requirements for NKR-P1B.

Methods: The metabolic dysregulation due to loss of NKR-P1B was captured by profiling several metabolic targets by flow cytometry. AM transcriptome and phospho-kinome data from the Nkrp1b$^{-/-}$ mice were used for respective pathway enrichment analyses to identify the potential signalling pathways related to NKR-P1B receptor. Immunoblot analyses of several cell signalling adapter molecules were also performed to assess their roles downstream of NKR-P1B signalling.

Results: Our metabolic profiling data clearly indicates that NKR-P1B loss renders AMs with a pro-inflammatory phenotype with dysregulated glycolysis and lipid metabolism. AMs from Nkrp1b$^{-/-}$ mice have upregulated pathways related to apoptosis as well as growth factor signalling. It is also observed that transcription factors, PPAR gamma and STAT5 are highly upregulated and activated in AMs from Nkrp1b$^{-/-}$ mice.

Conclusions: This study shows that NKR-P1B is a crucial mediator for AM lipid metabolism and overall lung homeostasis. Further investigation of this receptor signalling would enhance our current understanding of mucosal immunity and can be exploited for respiratory diseases.

Oral Presentation 9

Title: IMPLEMENTATION OF *STAPHYLOCOCCUS AUREUS* DECOLONIZATION IN CARDIAC SURGERY

Authors: Dominique de Waard, Ryan Gainer, Meaghan Sim, Claudia Cote, Paul Bonnar, Gregory Hirsch

Affiliation: Dalhousie University, Nova Scotia Health

Introduction: *Staphylococcus aureus* screening and decolonization is a guideline recommended treatment for the prevention of surgical site infections in cardiac surgery. Our objective was to assess the implementation of *S. aureus* screening and decolonization at our institution.

Methods: Targeted *S. aureus* screening and decolonization started in November 2022. Non-urgent in- and outpatients considered for cardiac surgery underwent screening, which involved performing a nasal swab to detect *S. aureus.* For positive patients accepted for open-heart surgery, decolonization included Mupirocin 2% nasal ointment twice daily and Chlorhexidine 2% wipes once daily for five days. Informed by the Consolidated Framework for Implementation Research, we conducted focus group interviews midway through the study to explore factors influencing implementation. At the end of the one-year study period, the uptake of screening and decolonization was analyzed using descriptive statistics. A times series analysis was done to assess trends in uptake pre- and post-focus group interviews.

Results: At one-year, 563 inpatients and 232 outpatients were consulted to cardiac surgery. 95% of inpatients and 91% of outpatients considered for cardiac surgery were screened. *S. aureus* was detected in 113 inpatients (8 methicillin-resistant *Staphylococcus aureus* [MRSA], 105 methicillin-sensitive *Staphylococcus aureus* [MSSA]) and 44 outpatients (3 MRSA, 41 MSSA). Of the patients accepted for surgery, 50% of positive inpatients underwent decolonization in the first six months compared to 67% in the following six months. For outpatients, 77% were decolonized in the first six months compared to 78% in the following six months.

Conclusions: *S. aureus* screening and decolonization was implemented as a standard of care at our institution with the help of an Implementation Science framework. By engaging stakeholders and healthcare staff throughout the implementation process and by regularly addressing barriers, we developed a sustainable *S. aureus* screening and decolonization program. Ongoing adjustments continue to be made to increase decolonization uptake.

Oral Presentation 10

Title: LYME DISEASE CHEMOPROPHYLAXIS PRESCRIBING BEFORE AND AFTER PHARMACIST PRESCRIPTIVE AUTHORITY IN NOVA SCOTIA

Authors: Madison Bell, Tasha Ramsey, Shanna Trenaman, Todd Hatchette, Samuel Campbell, Andrea Bishop, Katrina Hurley, Melanie MacInnis, Emily Black*

Affiliation: Dalhousie University, Nova Scotia Health

Introduction: Lyme disease is a bacterial infection transmitted to humans through bites from infected *Ixodes* species of ticks. Prophylaxis with a single dose of oral doxycycline following a bite from an infected tick reduces the risk of developing Lyme disease. Pharmacists in Nova Scotia (NS) were among the first in Canada to prescribe for this indication. The primary objective of this study is to describe experiences with pharmacist prescribing prophylaxis after tick bites in NS.

Methods: A retrospective cohort study using health administrative data 16 months before and after pharmacists were authorized to prescribe Lyme disease chemoprophylaxis (August 1, 2021) was performed. All dispensations of a single dose of oral doxycycline from a community pharmacy in NS were included. Data included date of single dose doxycycline dispensation, county where doxycycline was dispensed, and prescriber type (pharmacist, physician, nurse practitioner, other). Comparisons of dispensations were completed before and after pharmacists gained prescriptive authority and relative to other prescribers. Dispensations were described descriptively.

Results: Over the study period, 12549 single dose doxycycline prescriptions were dispensed in NS. Before pharmacist prescribing was implemented (April 1, 2020 to July 31, 2021), 3900 single doses of doxycycline were dispensed. After pharmacists' scope was expanded to include prescribing for Lyme chemoprophylaxis (August 1, 2021 to November 30, 2022), 8649 single doses of doxycycline were dispensed. The percentage of pharmacist prescribers increased from 1.3% to 63.3% following implementation of expanded scope.

Conclusions: Pharmacists have become the primary prescribers for Lyme disease chemoprophylaxis in the province. This suggests that pharmacist prescribing for this indication provides patients with increased access to post-tick exposure care and may decrease burden on other areas of the healthcare system.

Poster Abstracts

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

Poster 1

Title: PRELIMINARY ASSESSMENT OF THE IMPACT OF MASK MANDATES ON RATES OF NOSOCOMIAL COVID IN NOVA SCOTIA HEALTH HOSPITALS

Authors: Kevin Wilson, Angela Keenan, **Shelly McNeil** on behalf of the NS Health Emerging and Re-emerging Infections Network

Affiliation: Division of Infectious Diseases, Department of Medicine and NS Health Emerging and Re-emerging infections Network

Introduction: Mandates requiring mask use by HCW and visitors have been a mainstay of preventive strategies to mitigate introduction and transmission of COVID in acute care facilities. Understanding impact of this measure on risk of nosocomial infection is critical to inform future masking policies.

Methods: All patients with nosocomial COVID at NSH acute care facilities from 1JUL2023-31-Dec2023 were included. Charts were reviewed and data collected on demographics, treatment and outcomes. Impact of masking was examined by comparing the odds that a hospitalized case was nosocomially acquired (vs community-acquired) before and after implementation of the mask mandate on 16OCT2023.

Results: There were 874 cases of nosocomial COVID during the study period. Amongst those in whom data collection is complete, 50.3% were female, median age was 78y (range 70-86y); median onset of nosocomial COVID was 25d (10-62d) post admision. 24.1% of cases had received <3 doses of COVID vaccine. Overall, 47.7% of cases received COVID treatment (44.5% for mild disease and 3.2% for moderate-severe); 8.7% were admitted to ICU and 16.5% died. Overall, pre-mask mandate, 54.9% of hospitalized cases were nosocomial; post mask mandate, 40.1% were nosocomial (OR 0.6; 95%CI 0.5-0.7; p<.001); the magnitude of the difference was similar across zones with post-mandate reductions in the proportion of hospitalized cases being nosocomial in CZ (56.7% pre to 37.1% post; OR 0.6; 0.3-0.6, p<.001), EZ (61.9% vs 43.9%; OR 0.5; 0.4-0.8, p<.001), NZ (57.5% vs 34.3%; OR 0.4; 0.2-0.7; p<.001) and WZ (48% vs 43%; OR 0.8; 0.6-1.2; p NS.

Conclusions: Nosocomial COVID largely impacts frail older adults and is associated with significant morbidity and mortality. Introduction of a mask mandate was associated with a 40-60% reduction in the odds that a hospitalized case of COVID was acquired in hospital. These data suggest that masking of HCW and visitors during periods of high community transmission is an effective strategy to reduce the risk of nosocomial COVID and protect vulnerable patients.

Poster 2

Title: TREATMENT OF HOSPITALIZED OLDER ADULTS WITH INFLUENZA WITH OSELTAMIVIR REDUCES MORTALITY

Authors: Henrique Pott, Jason LeBlanc, Todd Hatchette, Melissa K. Andrew, **Shelly McNeil** on behalf of the Serious Outcomes Surveillance Network of the Canadian Immunization Research Network

Affiliation: Divisions of Geriatric Medicine and Infectious Diseases, Department of Medicine and Division of Medical Microbiology, Department of Pathology and Laboratory Medicine, Dalhousie University

Introduction: Oseltamivir is recommended for treatment of all adults hospitalized with influenza. Compliance with this recommendation is poor, perhaps owing to ambivalence of providers about the quality of the evidence of benefit.

Methods: We enrolled patients aged ≥65y admitted with lab-confirmed influenza to participating hospitals of the CIRN SOS Network over 8 influenza seasons and compared clinical characteristics and outcomes between patients treated or not treated with oseltamivir.

Results: 8,135 patients ≥65y hospitalized with influenza were included; 6,009 (35.4%) received oseltamivir. 37.3% were ≥ 85y, 35.7% 75-85y and 27.0% 65-75y. Most were admitted from home (65.5%) and required regular support for daily activities (57.1%). The majority had a median Charlson Comorbidity Index of 1 with an estimated 10y mortality risk ≥ 5% for 9.2% of patients. 52.0% had not had influenza vaccine. 73.8% had Influenza A and 26.0% influenza B. 395 patients were excluded due to hospitalization >30d. Mortality within 30d of hospitalization was 8.4% (653/7740); 53.9% of deaths occurred during the 1st week of hospitalization. There was a significant difference in the 30d survival probability between patients who did or did not receive oseltamivir. The 30d mortality was 9.77% (199/2036) for those who did not receive oseltamivir and 7.96% (454/5704) for those who did (p=0.013). The mortality incidence risk among those who received oseltamivir was 0.81 (95% CI, 0.69 to 0.95) times less than those who did not receive it. An IPT-weighted HR indicated that individuals who received oseltamivir had a 0.69 (95% CI, 0.58-0.83; p < 0.001) lower risk of 30d mortality vs those who didn't. The HR was lower for influenza A (HR=0.66 [95% CI, 0.53-0.82]; p < 0.001) than influenza B (HR=0.80 [95% CI, 0.57-1.12]; p = 0.189).

Conclusions: Oseltamivir treatment in older adults hospitalized with influenza is associated with a clinically important reduction in 30d mortality and quality initiatives to improve prescribing should be a priority.

Poster 3

Title: NOVA SCOTIA HEALTH INFLUENZA TREATMENT TEAM: PILOT INITIATIVE REVIEW

Authors: E.K. Reid[1], S. Opie[1], L. Nodwell[1], S.A. McNeil[1,2], T.D. Ramsey[1,2]

Affiliation: [1]Nova Scotia Health, [2]Dalhousie University, Halifax, NS

Introduction: Canadian guidelines recommend oseltamivir as soon as possible for influenza treatment in outpatients with risk factors for complications. The Nova Scotia (NS) Health Influenza Treatment Team, staffed by pharmacists and an on-call physician, piloted a phone consult initiative to connect eligible Nova Scotians with timely access to oseltamivir.

Methods: Positive influenza PCR results were referred from NS Health microbiology laboratories to the Influenza Treatment Team. Outpatients aged ≥1 year, not already prescribed oseltamivir, who were tested 1) in a NS Health emergency department or 2) in an outpatient clinic with no documented primary care provider, were phoned to assess symptoms and risk factors, and provide education. Those with risk factors and within 7 days of symptom onset were offered oseltamivir, prescribed by the assessing pharmacist. Long-term care residents were excluded. If requested, symptomatic household contacts of influenza-confirmed patients were also assessed for treatment.

Results: Between January 23 and March 18, 2024, the team completed initial assessments for 1095 referrals (1086 PCR positive referrals and 9 household contacts) and identified 663 patients for phone assessment. Full assessments after connecting with the patient or caregiver by phone were completed for 80% (530/663). Those fully assessed had a mean age of 38 years, and 16% (85/530) were ≥65 years. Oseltamivir was initiated for 19% (101/530) of patients. The mean time from referral to full assessment completion was 16 hours. For those prescribed oseltamivir, the time from referral to prescription was a mean of 11 hours.

Conclusions: This pilot initiative successfully reached a high proportion of outpatients soon after positive influenza PCR reporting, with timely oseltamivir initiation when appropriate. Implementing targeted phone assessments for high-risk outpatients in NS has potential to increase access to oseltamivir and improve influenza-related outcomes.

Poster 4

Title: A SYMPTOMATIC PERTUSSIS CONTROLLED HUMAN INFECTION MODEL: THE FIRST IN NORTH AMERICA

Authors: May ElSherif [1,2,3], Kara Redden[1,4], Lingyun Ye[1,2], Wade Blanchard[1,2], Jillian Filliter[1,2,4], Todd Hatchette[1,2,3], Jason LeBlanc[1,2,3], Shelly McNeil[1,2,3], Joanne Langley[1,2,4], Scott Halperin[1,2,4]

Affiliation: [1] Canadian Center for Vaccinology, [2] Dalhousie University, [3] Nova Scotia Health, [4] IWK Health

Poster 5

Title: INHIBITION OF GLYCOPROTEIN BIOSYNTHESIS IN HELICOBACTER PYLORI

Authors: David L. Jakeman

Affiliation: College of Pharmacy and Department of Chemistry, Dalhousie University, Halifax, Nova Scotia

Introduction: *Helicobacter pylori* is an aetiological factor for gastric cancer. The *H. pylori* lipopolysaccharide is a cell surface component that plays essential roles in host-pathogen interactions. Controlling lipopolysaccharide biosynthesis may offer mechanisms to mediate these interactions. Herein we describe novel inhibitors of glycoprotein biosynthesis and demonstrate their activity upon wild-type *H. pylori* glycoprotein biosynthesis.

Methods: Chemical synthesis provided access to the novel glycoprotein biosynthesis inhibitors. *H. pylori* was cultured in the presence and absence of potential glycoprotein biosynthesis inhibitors. Glycoprotein production was visualized on SDS-page gel through the use of metabolic oligosaccharide engineering.

Results: Inhibition of *H. pylori* glycoprotein biosynthesis was observed in a dose-dependent manner using western-blot analysis with an anti-FLAG antibody.

Conclusions: Future studies will investigate wild-type and mutant *H. pylori* motility, biofilm, growth and antibiotic synergy and compound metabolism.

Poster 6

Title: EVALUATION OF THE IMPLEMENTATION AND IMPACT OF PIPERACILLIN-TAZOBACTAM PROLONGED INFUSIONS IN CRITICALLY ILL PATIENTS: A SINGLE-CENTER RETROSPECTIVE CHART REVIEW

Authors: K. Landry[1,2], M. MacKenzie[1,2], S. Burgess[2], P. Bonnar[2], Y. Shabi[2], G. Patriquin[2], V. Eichhorn[2], K. Holland[2]

Affiliation: 1 Nova Scotia Health, 2 Dalhousie University

Introduction: In critically ill patients, pharmacokinetic variability can cause inadequate antimicrobial concentrations. The minimum inhibitory concentration (MIC) of beta-lactams is increasing for non-fermenting gram-negative bacilli (NF GNB). Guidelines recommend targeting 4-8 times the MIC for the dosing interval with prolonged beta-lactam infusions. In 2019, a prolonged piperacillin-tazobactam protocol was implemented in two Intensive Care Units (ICUs) as a quality improvement initiative. The primary objective was to describe and determine if implementation of a prolonged piperacillin-tazobactam infusion protocol was successful. Secondary objectives aimed to describe ICU mortality and length of stay (LOS), describe safety incidents related to the protocol, and prevalence of NF GNB and associated piperacillin-tazobactam MICs.

Methods: This single-center, retrospective study included a convenience sample of 200 patients who received ≥ 2 doses of piperacillin-tazobactam while admitted to an ICU between October 2020 and October 2022. Data on drug administration, hospital stay characteristics and patient outcomes were collected from digital patient records and the Critical Care Database. Eight criteria for successful implementation of the protocol were established, with success defined as meeting 6 of 8.

Results: Implementation of the prolonged infusion protocol was successful in 78% of ICU patients, 41 patients died in ICU (20.5%) and median ICU LOS was 4.9 days (IQR 2.4-10.7). No safety incidents were identified. The prevalence of NF GNB was 3.1% for all ICU patients over 2-years.

Conclusions: There are areas for improvement with 78% successful implementation of the prolonged infusion protocol by editing order sets and interprofessional education and collaboration.

Poster 7

Title: INVASIVE MENINGOCOCCAL DISEASE (IMD), MENINGITIS B (MENB) AND VACCINATION: INITIATING DISCUSSIONS AROUND VACCINATION IN PRACTICE

Authors: K. Salter[1], S. Yasar[1], B. Selig[1], M. Kervin[1], J. Langley[1]

Affiliation: [1]Canadian Center for Vaccinology, Dalhousie University

Introduction: To support vaccine decision-making around MenB immunization, it is important to understand knowledge mobilization in practice, and to identify challenges that need to be addressed to support vaccine discussion and recommendations. We surveyed HCPs across Canada to examine what they understand, need, or want to know about MenB vaccines.

Methods: From April 20-May 11, 2023, we administered a national-level online survey of HCPs in Canada. The data were analyzed using descriptive statistics. Non-parametric statistical tests were used to examine differences between HCP groups.

Results: Of 250 respondents, 40.2% were General Practitioners (GPs), 21.7% Nurses, 19.3% Paediatricians, and 18.9% Nurse Practitioners (NPs). 78% indicated they often/always initiate discussions about vaccination, most frequently with parents of young children. 59% (most often Nurses or NPs) indicated they were likely to initiate a discussion about vaccines with young adults (aged 18-25). Information about unfunded vaccines, like MenB, was often/always included by 44% of HCPs. Although 87% indicated they had information adequate to inform important topics that might arise during conversations, they also identified gaps addressing affordability, vaccine hesitancy/myths & misinformation, real world & up-to-date data. 64% reported that perceived affordability impacted their decision to recommend an unfunded vaccine; most (81%) reported no knowledge of programs to support access. Many HCPs indicated the current climate of myths and misinformation presents a challenge to discussions about vaccinations. 65% identified feeling affected, citing: parental beliefs, cultural shifts and loss of trust, conspiracy theories, proliferation of misinformation through social media, and overall increase in vaccine hesitancy.

Conclusions: Although discussions about IMD and vaccination are frequently initiated, HCPs report initiating discussions less frequently with young adults. This may reflect gaps identified in the current information available (e.g. not specific to risk group, location or disease serotype, recommendations for practice are unclear, lacking real world & up-to-date data). In addition, HCPs identified challenges around time spent debunking vaccine myths, addressing vaccine hesitancy, and attempting to support vaccine accessibility.

Poster 8

Title: INVASIVE MENINGOCOCCAL DISEASE (IMD), MENINGOCOCCAL B (MENB) DISEASE AND VACCINATION: UNDERSTANDING WHAT PATIENTS/FAMILIES/CARERS VALUE IN VACCINE DECISION-MAKING

Authors: K. Salter[1], S. Yasar[1], B. Selig[1], M. Kervin[1], J. Langley[1]

Affiliation: [1]Canadian Center for Vaccinology, Dalhousie University

Introduction: To support vaccine decision-making around immunization against MenB, it is important to understand knowledge mobilization in clinical practice, and to understand what HCPs believe to be valued by patients/families/carers in making decisions about vaccines. We surveyed Canadian healthcare professionals (HCPs) to examine what they understand, need, or want to know about MenB vaccines.

Methods: From April 20-May 11, 2023, we administered a national-level online survey of HCPs. Data were analyzed using descriptive statistics. Non-parametric statistical tests were used to examine differences between HCP groups.

Results: Of 250 respondents, 40.2% were General Practitioners (GPs), 21.7% Nurses, 19.3% Paediatricians, and 18.9% Nurse Practitioners (NPs). When asked about what aspects of the decision-making process were most valued by patients/families/carers, all professional groups ranked having dedicated time to discuss information, concerns and options associated with IMD and MenB vaccines with their HCP as most valued. Having a variety of knowledge resources, clear recommendations and support for payment were all ranked as likely to be highly valued. However, these values overlap with challenges in information provision identified by HCPs. For example, 56.2% identified finding time for discussions to be a significant challenge. Many expressed a need for improved clarity around practice recommendations and support for vaccine accessibility. In addition to discussion, HCPs reported using flyers/leaflets, information sheets, posters, or directing patients to websites. Although flyers/information sheets are used frequently, this type of information provision was perceived as less valued. Nurses and NPs reported greater awareness than other HCPs of community-based supports for vaccine decision-making.

Conclusions: Important tensions exist between what HCPs perceive as important to patients/families/carers and what they may be able to provide in practice, based on identified challenges in information provision. More work needs to be done to develop knowledge mobilization tools and supports for decision-making that complement practice contexts. In phase 2 of this research, we are exploring knowledge needs and values from the perspective of patients/families/carers to support improved decision-making.

Poster 9

Title: THE HERPESVIRUS PROTEIN K3 REGULATES THE CELLULAR STRESS RESPONSE

Authors: Alexa Wilson, Craig McCormick

Affiliation: Dalhousie University

Introduction: The unfolded protein response (UPR) senses the accumulation of misfolded proteins in the endoplasmic reticulum (ER) and initiates transcriptional responses to support ER proteostasis. It is supported by three stress-sensing proteins, PERK, IRE1 and ATF6. Kaposi's sarcoma-associated herpesvirus (KSHV) usurps the UPR to reactivate from latency. Progression through lytic replication features UPR sensor activation coupled with inhibition of downstream transcriptional responses; this UPR inhibition is required for generation of viral progeny. However, the viral gene products that regulate the UPR remained unknown.

Methods: Through the ectopic expression of viral proteins in mammalian cells I studied how KSHV regulates the PERK arm of the UPR. I used flow cytometry, western blotting, and immunofluorescence methods to elucidate the detailed molecular mechanisms employed by KSHV to attack PERK. Site directed mutagenesis enabled the identification of domains in each protein required for this interaction. Mutant herpesviruses that contain a knockout of our viral protein of interest are currently being used to understand how this interaction impacts viral fitness.

Results: I discovered that steady-state levels of PERK protein decrease during KSHV lytic replication. KSHV encodes an E3 ubiquitin ligase, K3, that interferes with immune responses by directing the ubiquitination and lysosomal degradation of immune synapse proteins. I determined K3 is sufficient to target PERK for lysosomal degradation, but rather than being constitutively degraded, PERK turnover is accelerated by ER stress. There are many potential triggers of ER stress during infection, including the viral G-protein coupled receptor (vGPCR) which triggers ER stress. I determined that vGPCR activates the UPR and accelerates K3-dependent PERK degradation when these viral proteins are ectopically expressed. However, K3 also binds vGPCR and targets the protein for lysosomal degradation. This marks the first documentation of a KSHV E3 ligase targeting a viral protein.

Conclusions: I now seek to understand the impact of K3-dependent vGPCR degradation on viral fitness. *vGPCR* is a KSHV early gene that is part of feedback loop that amplifies early lytic gene transcription. I hypothesize that K3 mediated degradation of vGPCR terminates this positive feedback loop to allow progression through the lytic cycle. This work highlights how K3 controls the UPR to benefit KSHV by targeting both host and viral proteins.

Poster 10

Title: EVALUATION OF A VSVΔG S (SARS-COV-2 ORIGINAL VARIANT) HYBRID REPLICATING VIRUS AS A MODEL OF MILD COVID-19 DISEASE

Authors: Brianna Kelly, Nicole Grass, Christa Davis, Jillian Matlock, Jessica Trevors, Saki Sultana, Christopher Richardson, Kimberly Brewer

Affiliation: Dalhousie University

Introduction: SARS-CoV-2 can lead to highly variable illness, ranging from mild and self-limiting to fatal. Several unknowns remain about the pathology of SARS-CoV-2, particularly about the dynamics of long COVID (PASC). A limitation in the study of SARS-CoV-2 is the availability of facilities that support CL-3 research. By using a VSVΔG S hybrid replicating virus, the study of spike-mediated viral migration and pathology can be done in a level 2 lab. Our study uses molecular imaging and metabolic radiotracers to track viral-associated inflammation throughout the body longitudinally. FDG-PET scans detects regions with increased glucose metabolism. This work also uses flow cytometry (FC) to investigate changes in immune cell populations.

Methods: This study tested two titres of VSVΔG S (SARS-CoV-2 original variant): 5x104 PFU/mL (low) and 1x105PFU/mL (high). Naïve and mock-infected controls (VSVΔG empty) were also used. The K-18 hACE2 mouse model was used as it expresses human ACE2 on tissues similar to humans. Infection was done intranasally at a volume of 30µL per mouse. Blood samples were collected weekly, and organ harvest was performed at termination.

Results: Early imaging results show a moderate increase in FDG concentration in the lungs of infected mice compared to naïve and mock infection controls. Temporal increases in FDG uptake were observed in the heart, lungs, brain, spleen, and kidneys for both infected groups, suggesting that inflammation from infection persisted up to 4 weeks. FC data revealed that the percentage of cells identified as neutrophils, monocytes, eosinophils, and basophils was increased in infected mice. Other myeloid lineage cells, including eosinophils and basophils, were also increased for infected groups, with NK cells showing a highly significant increase. T cells showed the opposite trend, with CD4+ T cells having a significant decrease in infected groups compared to controls.

Conclusions: Immune cell data suggests a milder disease phenotype compared to that produced by full SARS-CoV-2 infection in the same mouse model, similar to what is reported in the literature. Observed levels of myeloid cells, NK cells and T cells in infected groups match reports of mild to moderate disease and have been associated with PASC. Currently, there is no animal model for PASC, making findings highly promising as a possible way to study this phenomenon *in vivo*.

Poster 11

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

Introduction: Human coronaviruses (hCoVs) circumvent host antiviral responses and take control of host cell processes to provide an optimal environment for viral replication through mechanisms that remain poorly understood. We have new evidence that the hCoV structural protein Membrane (M) inhibits several host signaling pathways that require activation in the endoplasmic reticulum (ER) and translocation via the cellular secretory pathway to execute their function. Our goal is to elucidate the mechanism of action of M.

Methods: Structural proteins from SARS-CoV-2 and related hCoVs were ectopically expressed in human cells to study effects on host ER-localized sensor proteins that operate in the secretory pathway including ATF6 (unfolded protein response), SREBP2 (cholesterol biosynthesis) and STING (interferon response) using luciferase reporter assays, immunoblotting and immunofluorescence microscopy. Broader effects on secretory pathway function were monitored using a secreted Gaussia luciferase (Gluc) assay. Ectopic expression experiments were complemented by infection assays using hCoV-OC43 or hCoV-229E.

Results: We discovered that all hCoV M proteins inhibits signaling pathways that operate in the early secretory pathway, including ATF6, SREBP2 and STING. This is supported by our observation that M also inhibits the secretion of the Gluc reporter. These pathways were also inhibited when SARS-CoV-2 M was co-expressed with the other SARS-CoV-2 structural proteins Spike, Envelope and Nucleoprotein. Preliminary results suggest selective activation of the ATF6 pathway reduces hCoV-OC43 and hCoV-22E replication, suggesting potential antiviral activity for ATF6; however, further investigation is required.

Conclusions: Our study suggests hCoV membrane proteins have a conserved function making them important players in subverting host cell processes during replication and play a role beyond structural function and virus assembly. These newly identified roles will be important to take into consideration when developing antivirals and vaccine treatments for future potential hCoV outbreaks.

Poster 12

Title: EVALUATION OF EQUITY AND DIVERSITY IN RECRUITMENT STRATEGIES EMPLOYED IN THE PREP-RX STUDY

Authors: Pilar Robinson Gonzalez, Shanna Trenaman, Emily Black, Kyle John Wilby

Affiliation: Dalhousie University

Introduction: Community pharmacists have the potential to increase healthcare accessibility and therefore improve health equity. The reach of community pharmacy services to underserved populations is not known. The PrEP-Rx (Implementation of Pre-Exposure Prophylaxis [PrEP] by Pharmacists in Nova Scotia) study was conducted in 2023 to improve access to PrEP therapy. The study enrolled 50 participants with over 80% identifying as white, and almost 100% identifying as gay or bisexual men who have sex with men (gbMSM). Eligible gender diverse populations and those individuals that inject drugs were not represented. This relatively homogeneous participant pool is indicative of the difficulty faced in encouraging uptake of services by underserved populations in pharmacy settings. The objective of this study was to identify facilitators and barriers faced by underserved populations related to accessing pharmacy-based services for PrEP and sexually transmitted infections (STI).

Methods: This was a qualitative case study using interviews. Eligible participants (pharmacists who participated in the PrEP-Rx study and community partners from underrepresented groups) were invited to complete a 30 minute to 1 hour interview to elicit their perceptions of facilitators and barriers for accessing pharmacy-based PrEP and STI services, as well as to specifically evaluate the social media-based PrEP-Rx recruitment initiatives. Thematic analysis procedures were used to analyze data and interpret results.

Results: A total of nine participants completed the study interview. Privacy, education, and representation were three main themes identified in this study. Privacy was mentioned by both pharmacists and community partners and was of particular importance when addressing stigmatized issues like STIs in pharmacies. Pharmacists' education played considerably into whether an individual felt safe going into a pharmacy to obtain care. In particular, education to improve understanding of sex and gender, and trauma informed care, were identified as areas for future improvement. Representation in the form of visible diversity of pharmacy staff and people in recruitment advertisements could be used to facilitate uptake of services.

Conclusions: This study supports the notion that structural (privacy), interpersonal (representation), and individual (education) considerations should be addressed to improve the reach of pharmacy-based PrEP and STI services for both research and practice initiatives. Further research should be conducted to determine the effectiveness of strategies implemented to address these findings.

Poster 13

Title: INVESTIGATING THE ROLE OF AID ENZYME IN IMMUNE RESPONSE AGAINST *CHLAMYDIA* INFECTION

Authors: Parnian Jahanbani[1,2], Jun Wang[1,2]

Affiliation: [1]Dalhousie University, [2]Canadian Center for Vaccinology

Introduction: *Chlamydia trachomatis* is the leading cause of bacterial STI worldwide. This pathogen preferentially targets epithelial cells of the reproductive tract. If left untreated, it can lead to pelvic inflammatory diseases and infertility. While the cellular immunity, especially Th1 response, has the primary role in host defense against *Chlamydia,* humoral immunity is also of a great importance in response to this infection. B cell-mediated humoral response relies on the formation of structures in lymphoid organs named germinal centers, in which B cells interact with cognate follicular T helper (Tfh) cells and acquire the ability to transform into memory B cells and high affinity IgG producing plasma cells. Germinal center reaction is governed by a key enzyme named Activation Induced cytidine Deaminase (AID). It is proven that impairment in AID results in compromised IgG production and hyper IgM syndrome. But how AID deficiency impacts B cell phenotype and its interaction with cellular immunity is not fully understood.

Methods: AID knockout and wild type mice are intravaginally infected with five doses of *Chlamydia muridarum*. At different timepoints after infection (D17, D30, D53) mice are euthanized and various organs (spleen, iliac lymph nodes, genital tract) are collected. Several assays including flowcytometry, qPCR, cytokine ELISA and RNA sequencing are done to characterize immune response.

Results: Our preliminary data show that AID deficiency leads to B cell hyper-activation and -proliferation. In addition, in the absence of AID, the balance between Th1/Tfh cell differentiation is impaired which results in deficient cellular response against *Chlamydia*.

Conclusions: AID deficiency not only impairs IgG production by B cells, but also impacts other aspects of B cell function including its interaction with T cells and cellular immunity.

Poster 14

Title: NK CELL MEMORY IN THE ABSENCE OF TCR GENES

Authors: Safyha Bryan, Gayani Gamage, Dr. Brendon Parsons, Daniel Medina-Luna, Dr. Andrew Makrigiannis

Affiliation: Dalhousie University

Introduction: The immune response, mediated by the cells of the innate immune systems, is generally considered broad and non-specific. Conversely, cells of the adaptive immune system mediate their responses in an antigen-specific manner, forming immunological memory, which allows them to mediate robust, long-lasting antigen-specific responses upon re-exposure to the same pathogen. Natural killer (NK) cells are among the founding members of innate lymphoid cells, specialized in the recognition and elimination of virally infected cells, tumor cells, and abnormal cells. Recent research studies have uncovered that NK cells also exhibit adaptive immune features similar to T and B cells, which holds promise for using the NK cell memory for the development of new cancer and viral immunotherapies. Research in our lab demonstrated that NK cells can elicit immunological memory in Rag $1^{-/-}$ mice, which are devoid of the adaptive T cells and B cells. However, there remains a need to explore whether this phenomenon persists in the complete absence of TCR genes.

Methods: The ability of NK cells to mediate adaptive responses was evaluated by studying the contact hypersensitivity ear swelling response to chemical haptens and peptides in TCR $\beta^{-/-}\delta^{-/-}$ mice, in conjunction with NK cell depletion via anti-NK1.1.

Results: Preliminary results show memory responses can be attributed to NK cells in the absence of TCR genes and is antigen specific.

Conclusions: This study shows that NK cells are a physiologically relevant contributor to the adaptive immune response as immunological memory can be observed in the absence of TCR genes. A better understanding of the adaptive NK cell responses elicited in these studies can be exploited in therapeutic and prophylactic treatments of cancer and viral infections.

Poster 15

Title: INVASIVE PULMONARY *IRPEX LACTEUS* INFECTION IN AN IMMUNOCOMPROMISED PATIENT WITH MYELODYSPLASTIC SYNDROME

Authors: Elizabeth Simms[1,2], Tanis C. Dingle[3], Alexander Pupek[1], Shelly McNeil[1], David Haldane[2]

Affiliation: [1]Department of Medicine, Faculty of Medicine, Dalhousie University, Halifax, NS, Canada. [2]Department of Pathology, Faculty of Medicine, Dalhousie University, Halifax, NS, Canada. [3]Alberta Precision Laboratories – Public Health Laboratory, Calgary, AB, Canada

Objectives: To discuss a case of *Irpex lacteus* invasive pulmonary infection in an immunocompromised patient and review the limited literature regarding this fungus as an uncommon agent of human disease.

Case: A female in her 60s with high risk MDS on azacytidine treatment presented to hospital with febrile neutropenia in June 2023. Initially she was hemodynamically stable with no supplemental oxygen requirements and no localizing foci of infection. Neutrophil count was 0. Piperacillin-tazobactam was empirically started. Chest x-ray was unremarkable, PCR testing for respiratory viruses was negative, and multiple blood cultures and urine cultures were negative. She had persistent daily fevers and developed respiratory symptoms. CT scan of the chest demonstrated multiple pulmonary nodules and bronchial wash galactomannan was 6.488 (reference range < 1). Voriconazole was initiated. Bronchoscopy fungal culture grew a filamentous fungus identified as *Irpex lacteus* by local MALDI-TOF MS with confirmatory testing done by ITS and D1/D2 sequencing at the Provincial Public Health Laboratory in Edmonton, Alberta. Voriconazole was switched to amphotericin B because of side effects, with posaconazole added due to progressive clinical deterioration. She had persistent cytopenias, ongoing fevers, escalating supplemental oxygen requirements, and worsening CT findings despite antifungal therapy. She passed away in September 2023.

Discussion: We describe a case of fatal pulmonary *Irpex lacteus* infection in the context of MDS with prolonged neutropenia. Invasive molds are a significant cause of fungal disease in immunocompromised patients, with the bulk of infections caused by *Aspergillus, Fusarium, Mucorales,* and *Scedosporium* species. *Irpex lacteus* is a common environmental wood rot fungus, but an unusual human pathogen, with only a few cases of disease reported in the literature. There are no published antimicrobial breakpoints for this organism and no defined therapeutic regimens, making treatment decisions challenging. Along with other basidiomycetes, *Irpex lacteus* may represent an emerging cause of invasive mold infection in immunosuppressed individuals.

Poster 16

Title: ASSESSING THE POTENTIAL FOR SPECIMEN POOLING TO STREAMLINE NOSOCOMIAL SURVEILLANCE OF METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA)

Authors: Mohammed Alqahtani[a], Isabella Pagotto[b], , Greg R. McCracken[a], Glenn Patriquin[a,], Ian R. Davis[a,], Jason J. LeBlanc[a,b,*]

Affiliation: [a]Division of Microbiology, Department of Pathology and Laboratory Medicine, Nova Scotia Health, Halifax, Nova Scotia, Canada; [b]Department of Microbiology and Immunology, Dalhousie University, Halifax, Nova Scotia, Canada.

Introduction: In hospitals, identification of methicillin resistant *Staphylococcus aureus* (MRSA) is important to reduce possible transmissions and serious outcomes. Traditional culture and susceptibility testing require 48-72h, whereas Xpert polymerase chain reaction (PCR) can provide accurate MRSA detection in <1h. Unfortunately, the high cost of such commercial PCRs precludes their use in many laboratories. Using MRSA as a model, this study hypothesized that specimen pooling in a setting of low prevalence could reduce PCR costs and provide rapid results.

Methods: 424 sequential nasal/groin specimens submitted for MRSA detection were subjected to routine culture-based detection using chromogenic media, and suspect colonies were confirmed using mass spectrometry and cefoxitin disk diffusion testing. These specimens were also pooled 1:8 or processed individually by Xpert MRSA PCR. Analytical sensitivity of PCR with and without pooling was compared to culture using triplicate 10-fold serial dilutions of a MRSA reference strain.

Results: The analytical sensitivity and clinical performance of specimen pooling paired with Xpert MRSA PCR was equivalent to traditional culture-based detection. Of specimen pools, 66.0% (35/53) were MRSA-negative and 34.0% (18/53) were MRSA-positive. Pool resolution by PCR showed similar results as culture, identifying 116 MRSA-negative and 28 MRSA specimens.

Conclusions: At a prevalence of 6.6% (28/424), 1:8 specimen pooling with Xpert PCR provided equivalent results to culture-based methods and reduced the overall number of PCR reactions by 53.5%. Compared to individual PCR testing, specimen pooling would lower overall PCR costs, but the feasibility of this approach and extent of benefits afforded would depend on MRSA prevalence.

Poster 17

Title: A PHASE 3 STUDY TO EVALUATE THE SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF V116, A PNEUMOCOCCAL CONJUGATE VACCINE DESIGNED FOR ADULTS (STRIDE-3)

Authors: Heather L. Platt[1], Christopher Bruno[1], Erik Buntinx[2], Enrique Pelayo[3], Jackie M. Kamerbeek[4], Diego Garcia-Huidobro[5], Elizabeth A. Barranco-Santana[6], Folke Sjoberg[7], Joon Young Song[8], David Greenberg[9], Carlos G. Grijalva[10], Walter A. Orenstein [11], Leslie Morgan[1], Doreen Fernsler[1], Weifeng Xu[1], Muhammad Waleed[1], Jianing Li[1] and Ulrike K. Buchwald[1]. Presented by **Sakna Bazzi** on behalf of the authors.

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Introduction: Pneumococcal disease (PD) prevention remains an unmet medical need in adults. V116 is an investigational pneumococcal conjugate vaccine (PCV) containing the most prevalent serotypes associated with PD in adults in regions with established pediatric vaccination programs. This phase 3 study evaluated safety, tolerability, and immunogenicity of V116 compared with PCV20 in adults.

Methods: Pneumococcal vaccine-naïve adults ≥18 years were eligible. Cohort 1 (≥50 years, n=2362) was stratified by age (50-64, 65-74, 75-84, and ≥85) and randomized 1:1 to receive 1 dose of V116 or PCV20, and cohort 2 (18-49 years, n=301) was randomized 2:1 to receive 1 dose of V116 or PCV20. Pneumococcal serotype-specific opsonophagocytic activity (OPA) and immunoglobulin G (IgG) responses were measured at baseline (Day 1) and 30 days post vaccination (Day 30). Primary objectives included assessment of 1) noninferiority of immune responses for the serotypes common to V116 and PCV20 in cohort 1, 2) superiority of serotypes unique to V116 compared to PCV20 in cohort 1, and 3) immunobridging from adults 18-49 to adults 50-64 for all 21 serotypes in V116. Safety was evaluated by the proportion of participants with adverse events (AEs).

Results: Overall, a total of 2,656 participants received study intervention and the majority (>97%) completed the study. V116 met non-inferiority criteria compared to PCV20 for the 10 serotypes common to both vaccines (the lower bound of the 95% CI of the OPA GMT ratio [V116/PCV20] was >0.5 for all common serotypes). V116 met superiority criteria compared to PCV20 for 10 of 11 unique serotypes as measured by OPA GMTs at Day 30 (the lower bound of the 95% CI of the OPA GMT [V116/PCV20] ratio was >2.0 for all serotypes except 15C, which was 1.77) and based on the proportions of participants with a ≥4-fold rise in OPA from Day 1 to Day 30 (the lower bound of the 95% CI of the differences [V116-PCV20] was >10 percentage points for all serotypes except 15C, which was 5.6). The predefined criteria for immunobridging were met for V116 participants 18-49 years of age compared to 50-64 years of age for all 21 serotypes in V116 as assessed by serotype-specific OPA GMTs 30 days postvaccination (lower bound of the 95% CI of the OPA GMT ratio [V116 18-49 years/V116 50-64 years] was >0.5 for all 21 serotypes).

Overall, 61.7% and 67.2% of participants vaccinated with V116 and PCV20, respectively, had ≥ 1 AE. There were no vaccine-related serious AEs or vaccine-related deaths.

Conclusions: V116 elicits immune responses that are noninferior to PCV20 for the common serotypes, superior to PCV20 for 10 of 11 unique serotypes in V116 and has a safety profile comparable to PCV20. This pivotal study supports V116 as a novel population-specific PCV for the prevention of PD in adults.

Poster 18

Title: A PHASE 3 CLINICAL STUDY TO EVALUATE THE SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF V116 IN PNEUMOCOCCAL VACCINE-EXPERIENCED ADULTS 50 YEARS OF AGE OR OLDER (STRIDE-6)

Authors: Paul Scott[1], Miwa Haranaka[2], Yi-Ching Yang[3], JungHyun Choi[4], Helen Stacey[5], Marc Dionne[6], David Greenberg [7], Carlos G. Grijalva[8], Walter A. Orenstein[9], Doreen Fernsler[1], Nancy Gallagher[1], Tiantian Zeng[1], Jianing Li[1], Heather Platt[1]. Presented by **Steven Findlay** on behalf of the authors.

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Introduction: Pneumococcal diseases (PD), including non-invasive disease such as pneumonia and invasive disease such as meningitis, cause considerable morbidity and mortality in adults. V116 is an investigational 21-valent pneumococcal conjugate vaccine (PCV) specifically designed to protect adults from pneumococcal serotypes responsible for the majority of residual PD. This phase 3 study evaluated safety, tolerability, and immunogenicity of V116 in pneumococcal vaccine-experienced adults ≥50 years.

Methods: A total of 712 generally healthy adults were vaccinated with a single dose of pneumococcal vaccine as follows: Cohort 1 previously received PPSV23 and were randomized 2:1 to receive V116 or PCV15, respectively; Cohort 2 previously received PCV13 and were randomized 2:1 to receive V116 or PPSV23, respectively; Cohort 3 previously received PPSV23+PCV13, PCV13+PPSV23, PCV15+PPSV23, or PCV15 and all received open-label V116. Immunogenicity was evaluated 30 days postvaccination using opsonophagocytic activity (OPA) geometric mean titers (GMTs) for all V116 serotypes. Safety was evaluated as the proportion of participants with adverse events (AEs).

Results: V116 was immunogenic across all 3 cohorts as assessed by serotype-specific OPA GMTs postvaccination for all 21 serotypes. V116 elicited comparable immune responses to serotypes shared with PCV15 (Cohort 1) or PPSV23 (Cohort 2), and higher immune responses to serotypes unique to V116. The proportions of participants with solicited AEs were generally comparable across cohorts.

Conclusions: V116 is well tolerated with a safety profile comparable to currently licensed pneumococcal vaccines, and generates functional immune responses to all V116 serotypes, regardless of prior pneumococcal vaccine received.

Poster 19

Title: IMMUNOGENICITY OF MRNA-1345: RESULTS FROM THE RSV PHASE 3 PIVOTAL TRIAL IN ADULTS AGED ≥60 YEARS

Authors: Jaya Goswami,[1] Lan Lan,[1] Jiejun Du,[1] Archana Kapoor,[1] Abdullah H. Baqui,[2] Wenmei Huang,[1] Honghong Zhou,[1] Frances Priddy,[1] Nina Lin,[1] Nancy Le Cam,[1] Sonia K. Stoszek,[1] Christine A. Shaw,[1] Karen Slobod,[1] Eleanor Wilson,[1] Jacqueline M. Miller,[1] Rituparna Das[1]. Presented by **Kyle Brown** on behalf of the authors.

Affiliation: [1]Moderna, Inc., Cambridge, MA, USA; [2]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Introduction: mRNA-1345 demonstrated efficacy against RSV-associated disease in adults in a phase 3 trial, with no evident safety concerns. We present humoral immunogenicity of mRNA-1345 in a subset of study participants.

Methods: In this ongoing phase 2/3, multi-country, double-blind, placebo-controlled study (NCT05127434), adults ≥60 years were randomized (1:1) to receive 1 dose of mRNA-1345 (50 µg) or placebo. RSV-A and RSV-B neutralizing antibody (nAb) geometric mean titers (GMTs) and binding antibody (bAb) geometric mean concentrations (GMCs) were assessed at baseline and Day 29 (D29) and seroresponse rates calculated in the randomly selected per-protocol immunogenicity set (mRNA-1345, n=1515; placebo, n=333).

Results: mRNA-1345 increased nAb GMTs (95% CI) from 2552.8 (2414.3-2699.4) and 1425.4 (1352.7-1501.9) IU/mL at baseline to 21,475.4 (20,273.9-22,748.1) and 7246.0 (6864.8-7648.4) IU/mL at D29 against RSV-A and RSV-B, respectively (geometric mean fold-rise: RSV-A=8.4; RSV-B=5.1). Seroresponse rates for mRNA-1345 (4-fold rise from baseline) were 74.2% and 56.5% against RSV-A and RSV-B, respectively; participants meeting seroresponse criteria had lower baseline GMTs than those who did not. A similar pattern was observed for preF bAb GMC. D29 responses across demographic and risk subgroups were generally consistent with the general study population.

Conclusions: mRNA-1345 boosted nAb and bAb levels in adults ≥60 years, including those at higher risk for severe disease, consistent with previously demonstrated efficacy against RSV disease.

Poster 20

Title: MAPPING THE PARTICIPANT EXPERIENCE IN CONTROLLED HUMAN INFECTION MODEL (CHIM) TRIALS: A MODIFIED GROUNDED THEORY STUDY

Authors: A. Mack[1], D. Halperin[1,2], B. Condran[1], B. Selig[1], S. Halperin[1]

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

Introduction: In CHIM trials, healthy participants are intentionally infected with a disease-causing pathogen to study the pathogenesis and clinical course of disease in humans within a tightly controlled environment. These trials are powerful tools for vaccine development; however, their success is dependent on the availability of willing and eligible volunteers. We conducted interviews with CHIM trial participants to explore their decision-making processes and experiences over time.

Methods: This study used a modified grounded theory approach, guided by a pragmatic interpretive paradigm and patient-centred lens. Participants were recruited from an ongoing *B. pertussis* CHIM trial conducted at CCfV. Semi-structured interviews were conducted at four time points throughout participants' year-long involvement in the trial and analyzed using the constant comparative method, with a journey mapping activity being conducted simultaneously to visualize the participant experience.

Results: To date, 23 participants have been interviewed at various time points throughout their involvement in the CHIM trial. Four preliminary themes describing the CHIM trial participant experience over time were identified: learning about the trial and making the decision, getting ready for the trial and setting expectations, living in the challenge unit, and transitioning from in-patient participation to out-patient. The multitude of factors influencing the decision-making process are subject to evolve over time. The in-patient period is associated with several challenges; however, participants identify positive aspects of the isolation as well. Common challenges experienced by participants were shared with the challenge unit staff throughout the research process.

Conclusions: This study highlights the complex nature of the CHIM trial participant decision-making process, as well as the intricacies of the in-patient isolation stay. Understanding these experiences is vital to devise strategies to ameliorate challenges faced by participants and improve recruitment and retention to encourage the success of future CHIM trials.

Poster 21

Title: INVASIVE MENINGOCOCCAL DISEASE (IMD), MENINGITIS B (MENB) AND VACCINATION: EXPLORING INFORMATION SEEKING AMONG HEALTHCARE PROFESSIONALS (HCPs)

Authors: M. Kervin[1], K. Salter[1], S. Yasar[1], B. Selig[1], J. Langley[1]. Presented by **Jade MacDonald** on behalf of the authors.

Affiliation: [1]Canadian Center for Vaccinology, Dalhousie University

Introduction: To support vaccine decision-making around immunization against MenB, it is important to understand what types and sources of knowledge are most valued, and which challenges need to be addressed to support discussion and recommendations around vaccines and vaccination. We surveyed HCPs across Canada to examine what they understand, need, or want to know about MenB vaccines.

Methods: From April 20-May 11, 2023, we administered a national-level online survey of HCPs in Canada. The data were analyzed using descriptive statistics. Non-parametric statistical tests were used to examine differences between HCP groups.

Results: Of 250 respondents, 40.2% were General Practitioners (GPs), 21.7% Nurses, 19.3% Paediatricians, and 18.9% Nurse Practitioners (NPs). Most indicated they have access to/are aware of current clinical practice guidelines/recommendations for the administration of the MenB vaccine in Canada (83.9%), and receive updates about both IMD and immunization and/or vaccines for IMD on a regular basis. While 33.5% indicated they did not seek out additional information, 59.8% indicated they did seek out information on their own. Among HCPs seeking out information, varied sources were preferred by each group. Nurses preferred product monographs (83.3%), while GPs, NPs and Paediatricians preferred NACI or PHAC announcements (76%, 65.7%, 80.6%). HCPs expressed high levels of confidence in the reliability and completeness of information obtained from their sources, especially those considered more traditional and authoritative. 87.4% of HCPs felt that the information they had was adequate to support conversations with families/carers or patients about IMD and MenB vaccines. However, HCPs identified lack of time to update knowledge & review current information, lack of clear clinical practice guidelines, and lack of clear evidence as the most significant challenges to information sharing and knowledge provision.

Conclusions: Almost 2/3 of HCPs surveyed reported actively seeking out information about IMD, vaccination and MenB vaccines, mostly from sources considered reliable and authoritative. However, challenges remain in mobilizing knowledge and information in ways that will support time sensitive opportunities to update personal knowledge for practitioners and foster clarity around recommendations for practice in this area.

Poster 22

Title: GENERATION OF INFECTIOUS HCOV-OC43 RECOMBINANT VIRUSES USING A YEAST REVERSE GENETICS PLATFORM

Authors: Brett Duguay, Trinity Tooley, John Rohde, and Craig McCormick

Affiliation: Department of Microbiology & Immunology, Faculty of Medicine, Dalhousie University, Halifax, NS

Poster 23

Title: CASE STUDY: *BORDETELLA BRONCHISEPTICA* INFECTION COINCIDING WITH ELEVATED ANTI-PT TITER, A POTENTIAL DEPICTION OF HOST ADAPTATION

Authors: Leah MacIsaac, May ElSherif, Michelle Warhuus, Ann MacMillan, Kristen Bouma, Peter Robertson, Shakiba Faghani, Bahaa Abu-Raya, Scott Halperin

Affiliation: Canadian Center for Vaccinology, Dalhousie University, IWK, Nova Scotia Health

Introduction: An ongoing novel *Bordetella pertussis* (Bp) clinical trial aims to develop a Controlled Human Infection Model (CHIM) via a dose escalation study design. A Bp CHIM trial participant was found to be infected with *Bordetella bronchiseptica* (Bb) post study admittance. Bb rarely infects humans, and although has the Pertussis Toxin (PT) gene, is not thought to express PT antigen in a mono-species infection. This case study presents the possibility of circulating Bb strains with the ability to produce PT as a potential adaptation to the human host.

Methods: As per the CHIM protocol, nasal samples and sera were collected before and after challenge throughout the course of the study. Nasal samples were tested using PCR and plating onto charcoal agar to detect and quantify Bp shedding post-challenge. An ELISA assay is run on participant's sera before and after challenge to determine anti-PT antibody levels. PCR, culture, and ELISA signals led to a suspected case of Bb, and in turn further confirmatory testing.

Results: Using a BD MAX multiplex PCR kit designed to differentiate species of Bordetella, the suspected Bb strain gave *ptxS1* but not *IS481* signals, the first indication of a non-pertussis species present. ELISA testing showed elevated anti-PT antibodies prior to being challenged with Bp. A dramatic increase in anti-PT titer was seen between the screening serum sample, and the baseline plasma sample, drawn 6 weeks apart. The anti-PT titer continued to elevate prior to the check-in visit, one day prior to dosing with Bp. The titer stabilized for the remainder of the inpatient samples. Bb colonies were expanded via culture and sent for biochemical identification using an API kit from APIWEB. The confirmed B. *bronchiseptica* isolate is being prepared for growth in Stainer-Scholte media for purification and Illumina sequencing.

Conclusions: Sequencing results are needed to confirm the presence of mutations in the Bb isolate. However, the biochemical identification of an active Bb infection together with the elevated PT antibody titers prior to introduction to Bp, allow for a plausible hypothesis that Bb has mutated. If confirmed this would be a novel discovery for *Bordetella* research as it is currently thought only Bp can produce PT toxin in a mono-species infection. A Bb strain capable of producing PT toxin could depict a mutation conferring fitness in the evolution of becoming a more common human pathogen.

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Title: INVESTIGATING ANTIBODY RESPONSE TO *BORDETELLA PERTUSSIS* ANTIGENS IN A CONTROLLED HUMAN INFECTION MODEL (CHIM) OF *BORDETELLA PERTUSSIS (Bp)*

Authors: Shakiba Faghani [1,4], May ElSherif [1,2,3], Ann MacMillan[1,2], Danielle Lemieux[1,2], Kelly Sit[1,2], Jinwon Jang[1,2], Scott Halperin[1,2,4]

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Introduction: Despite extensive vaccination initiatives worldwide, pertussis, also known as whooping cough, remains a persistent threat to infants and children. A Controlled Human Infection Model of *B. Pertussis (Bp)* was developed at the Canadian Center for Vaccinology to facilitate in-depth understanding of its pathology and immune response in humans. This study aims to investigate the antibody response pattern elicited by *Bp*.

Methods: Healthy adult participants received varying experimental doses of *Bp* ranging from 10^4 CFU to 5x10^7 CFU, tailored to their respective cohorts. Blood samples for serum were collected at different time points relative to the challenge day 0, including days -1, 28, 42, and 56. Participants were grouped based on post-challenge clinical outcomes: spontaneous clearance, colonization, and symptomatic infection. Serum antibody titers against four antigens including Pertussis Toxoid (PT), Pertactin (PRN), Fimbriae (FIM), and Filamentous Hemagglutinin Adhesion (FHA) were evaluated using an in-house Enzyme Linked Immunosorbent Assay (ELISA).

Results: Among symptomatic participants, 68% (19/28) displayed seroconversion for PT antigen with a 2-4 fold increase, while 53.5% (15/28) exhibited a similar rise in FHA titer. Only 28% (8/28) experienced a 2-4 fold increase in PRN and/or FIM titers. The majority of these participants (64%) had no or low baseline PRN titers. While none of those who spontaneously cleared or became colonized post-exposure showed seroconversion for any antigen, 56% of them demonstrated elevated PRN titers at the baseline. With increasing experimental doses, a general upward trend in PT IgG seroconversion was noted. However, a relatively rapid decline in PT IgG titer was observed beginning 84 days post-exposure.

Conclusions: Our findings suggest a higher immune sensitivity and response to PT toxin and FHA compared to PRN and FIM, likely due to the secretion and diffusion of PT and FHA into the host system, unlike PRN and FIM, which are surface proteins. Our model effectively stimulated antibody production against all antigens in majority of participants who experienced symptoms. The impact of baseline anti-PRN antibodies on the rate of clearance and the severity of symptomatic illness will be further investigated.

Poster 25

Title: UNVEILING THE IMPACT: UNDERSTANDING LONG-TERM CARE WORKERS' EXPERIENCES AND PERCEPTIONS OF RESIDENT CHALLENGES AMIDST THE COVID-19 PANDEMIC

Authors: B.M. Selig[1], A. Mack[1], D. Halperin[1,2], K. Salter[1], M. Orhierhor[3], J. Bettinger[3], J. Parsons[4], S. Halperin[1]

Affiliation: [1]Canadian Center for Vaccinology, Dalhousie University; [2]St. Francis Xavier University; [3]University of British Columbia; [4]Unity Health Toronto

Introduction: Policies enacted by provincial government authorities to reduce the spread of COVID-19 had a profound, disproportionately negative impact on long-term care (LTC) workers, residents, and their loved ones. Interviews were conducted to explore how public health policy measures affected those working and living within LTC in BC and NS during the COVID-19 pandemic, and to provide insights for improved policy implementation during future public health emergencies.

Methods: This study primarily used Stake's (1995) constructivist case study design. Semi-structured interviews were conducted with LTC workers, including leadership, front-line healthcare providers, and support services from multiple LTC facilities in both urban and rural settings in BC and NS from Apr-Oct 2021. Using thematic analysis, we identified, analyzed, and reported patterns within the data. Between-site analysis was used to identify shared themes and highlight commonalities and differences among the two sites.

Results: A total of 14 interviews were completed. Four themes around shared challenges experienced by participants were identified: 1) The integration of one-size-fits-all policies proved unrealistic at the implementation level and increased existing workloads for staff; 2) Tensions between safeguarding residents from COVID-19 and retaining their sense of home were experienced, significantly impacting participants' mental health; 3) The sense of helplessness experienced by those working in LTC during the pandemic; and 4) The personal impacts of COVID-19 policies on LTC workers. To combat these challenges, participants highlighted strategies adopted to maintain meaningful connections with residents and reduce social isolation, while adhering to pandemic policies.

Conclusions: This study highlighted the lack of involvement of LTC staff in the development of pandemic policies and the resulting impacts on front-line workers and residents. There is a need for more consideration of mental health when devising infection control policies, as they were found to have an impact on LTC residents' experience of home and the mental health of LTC workers. Minimizing psychological distress among front-line workers should be a top priority to mitigate long term mental health impacts, increase retention rates, and enhance the resilience of the healthcare system.

Poster 26

Title: RAPID PUBLIC HEALTH POLICY CHANGES DURING COVID-19: EXPLORING POLICY COMMUNICATION WITH LOCAL STAKEHOLDERS

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Introduction: Public health policy decisions during the COVID-19 pandemic were made rapidly amid evolving evidence within complex social contexts. Policy was revised frequently, sometimes daily, and individuals working at the interface between policy, program and the public relied on communication of information about public health policy/strategies, how, when, and if they would be implemented. We conducted interviews to explore the challenges experienced around policy communications during the COVID-19 pandemic and strategies created to address these challenges.

Methods: Semi-structured interviews were conducted from September 2020-October 2021 with a variety of key stakeholders from across NS, including policymakers (PM), healthcare providers (HCPs), and staff/leadership from non-governmental organizations (NGO) who serve populations experiencing poverty, homelessness, and food insecurity. Using interpretative thematic analysis, we identified patterns within and across the interview transcripts.

Results: A total of 31 interviews were completed across NS (3 PMs; 11 HCPs; 17 NGOs). Four themes around the challenges experienced related to the communications of Public Health policies were identified, which included: 1) confusion and uncertainty; 2) information overload; 3) rapid and ongoing change in the information released; and 4) contradictions or lack of clarity in the messaging. Corresponding strategies to address challenges included connecting with Public Health (e.g., Public Health inspectors, helpline, COVID-19 specific website), collaboration, networking and cross-sectoral engagement.

Conclusions: Analysis revealed the confusion experienced by individuals working within contexts of information and policy uncertainty. While this experience was mitigated via the eventual availability of sector-specific guidelines to assist in implementation as well as dedicated phone lines and on-site representatives from Public Health, there was also a noted lack of two-way communication or opportunities for feedback from local organizations to impact policy decision-making. Additionally, local decision-making and cross-sector collaboration highlighted both the existing local social complexity in policy implementation and potential benefits for ongoing community engagement in public health decision-making.

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Title: A FRAILTY INDEX FROM COMMON CLINICAL AND LABORATORY TESTS NEGATIVELY CORRELATES WITH T CELL IMMUNITY TO SARS-COV-2 IN VACCINE-NAÏVE, ELDERLY LONG-TERM CARE RESIDENTS.

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Objective: Assess post-natural SARS-CoV-2 infection antibody and T cell responses in long term care residents (LTCR) and evaluate the impact of frailty on immunity to a novel pathogen.

Methods: In a prospective cohort study of LTCR, 108 individuals were enrolled and consented to clinical data and blood collection amid a facility COVID outbreak between April and May 2020 in Halifax, Nova Scotia. COVID-19 infection was assessed via nasopharyngeal swab and PCR. 60 individuals were positive for COVID-19 at the time of enrollment, and 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 from these individuals. Clinical data, including clinical frailty score (CFS), was collected by electronic chart review. A laboratory frailty index (FI-Lab) was created using standard criteria and routinely collected clinical care laboratory tests. The resulting FI-Lab, calculated as the ratio of abnormal labs to total labs collected, provided a measure for frailty assessment.

Results: CFS (median [IQR], 6 [6-7]) did not associate with either IgG antibody to multiple antigens of SARS-CoV-2 (Spike, RBD and nucleoprotein) or T cell IFN-g responses to peptide pools from SARS-CoV-2 antigens (Spike, membrane, nucleoprotein). FI-Lab (median [IQR], 0.275 [0.170-0.365] did not associate with IgG levels but negatively correlated with naïve T cell IFN-g responses to SARS-CoV-2 (Spike r=-0.31, p=0.0349; nucleoprotein r=0.29, p=0.048) and memory T cell responses to common coronaviruses (229E, NL63, OC43, HKU1 Spike pool, r=0-0.46, p=0.011).

Conclusions: This study highlights the potential of using FI-Lab to assess frailty-related impacts on immune function in LTCR. This exploratory study is limited in terms of a relatively small sample size. Therefore, these findings should be interpreted cautiously and confirmed in a larger cohort. Ongoing studies are investigating post vaccine immune responses to discern the impacts of frailty on vaccine induced immunity to SARS-CoV-2 in LTCR.

Poster 28

Title: ADAPTING AN IMMUNIZATION ASSESSMENT TOOL TO INCREASE ADULT IMMUNIZATION COVERAGE: AN ENVIRONMENTAL SCAN TO MAP THE IMMUNIZATION ADMINISTRATION CONTEXTS OF PEI, NS, AND ON

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Introduction: Immunization assessment tools (IAT) enable individuals and healthcare providers to generate a personalized list of recommended vaccines based on demographic and behavioural characteristics and immunization schedules. IATs can also be used to provide information on how to obtain vaccines. IATs have been shown to improve adult vaccination depending on implementation setting, skills of those utilizing the IAT, and the features of the IAT itself. This environmental scan provides an analysis of the immunization administration contexts as shaped by the guiding documents, organizational systems, and health strategies of PEI, NS and ON.

Methods: Adult vaccine regulations were identified through review of institutional websites, peer-reviewed and grey literature, and meetings with Public Health partners. Data extraction and thematic analysis were guided by the integrated Promoting Action on Research Implementation in Health Services (i-PARIHS) framework, which supports putting evidence-based health research into action.

Results: Six themes were identified as defining the immunization administration contexts in PEI, NS, and ON: 1) supply, distribution, and administration of vaccines; 2) use of personal health information; 3) funding; 4) eligibility; 5) priority groups; and 6) barriers to uptake. Contexts such as the primary healthcare systems in each province, mitigation strategies for issues such as physician shortages, and the presence of high-risk groups all influence immunization administration across provinces. The approaches did vary between provinces, however, as health systems are influenced at the local level. For example, while Registered Nurses often lead delivery of vaccines in ON and NS, they face the barrier of being unable to do so without prescription by a pharmacist, physician, or nurse practitioner in PEI.

Conclusions: The design of IATs must allow for adaptability in response to the presence of health strategies and systems unique to a given region for optimal uptake. Future phases of the study include drafting and piloting an IAT for Nova Scotia informed by the immunization administration context of the province.

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Title: FUNCTIONAL INTERPLAY BETWEEN PA-X AND NS1 IN MEDIATING HOST SHUTOFF AND NUCLEAR PABPC1 ACCUMULATION DURING INFLUENZA A VIRUS INFECTION

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

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Introduction: Influenza A virus (IAV) host shutoff is executed by the viral polymerase acidic X protein (PA-X) and the non-structural protein 1 (NS1). Previous studies suggest that these two proteins co-evolve to ensure an optimal balance between the magnitude of host shutoff and the viral replication that requires some host gene expression. Our previous functional analyses identified two characteristic features of PA-X activity: the increase in nuclear poly(A) RNAs, and the nuclear relocalization of the cytoplasmic poly(A) binding protein (PABPC1). However, the functional interplay between PA-X and NS1 remains unexplored.

Methods: In this study, we aimed to determine if NS1 function has a direct effect on PA-X activity by analyzing nuclear PABPC1 relocalization and the levels of host transcripts in A549 cells infected with the wild-type IAV, the PA-X deficient mutant, or a panel of NS1 mutants. To determine which RNAs are present in the nuclei of IAV-infected cells and whether their hyperadenylation is responsible for increased nuclear poly(A) signal, we isolated nuclear poly(A) RNAs and analyzed them using direct RNA sequencing via Oxford Nanopore.

Results: Our results show that the nuclear accumulation of PABPC1 is dependent on both PA-X and the NS1 effector domain, but neither are required for the nuclear accumulation of poly(A) RNAs in infected cells. Compared to uninfected cells, we observed a general decrease of host nuclear poly(A) RNA abundance and their poly(A) tail shortening in IAV-infected cells. Furthermore, our analysis revealed that in infected cells, the increase in nuclear poly(A) RNA signal is largely due to the accumulation of viral poly(A) transcripts.

Conclusions: Our work demonstrates that the host shutoff by IAV is the result of a concerted action of PA-X and NS1 proteins. Specifically, NS1 is required for PA-X function in virus-infected cells. NS1 plays major role in ensuring efficient viral protein synthesis, and the effect of NS1 on PA-X may, at least in part, be due to increased PA-X accumulation. However, our research reveals that the effects of PA-X and NS1 on host gene expression are not simply additive, and that the two host shutoff proteins of IAV functionally interact.

Poster 30

Title: TAQMAN PACMAN: A SIMPLE MOLECULAR APPROACH FOR POSITIVE RAPID ANTIGEN TEST CONFIRMATION DURING PERIODS OF LOW PREVALENCE

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Introduction: Antigen-based rapid diagnostic tests (Ag-RDTs) were widely deployed to enhance SARS-CoV-2 testing capacity during the COVID-19 pandemic. Consistent with national guidance for low prevalence settings, positive Ag-RDTs were confirmed using nucleic acid amplification tests (NAATs) to avoid false positive results. However, increasing demands for positive Ag-RDT confirmation competed with other testing priorities in clinical laboratories. This work hypothesized that real-time RT-PCR without nucleic acid extraction (NAE) would be sufficiently sensitive to support positive Ag-RDT confirmation.

Methods: Ag-RDT and NAAT results from community-based asymptomatic testing sites prior to the omicron variant wave were compared to calculate the weekly false positive rate (FPR) and false detection rate (FDR). Real-time RT-PCR was compared with and without NAE using 752 specimens previously tested positive for SARS-CoV-2 using commercial NAATs and 344 specimens from Ag-RDT-positive individuals. The impact of SARS-CoV-2 prevalence on laboratory resources required to sustain Ag-RDT confirmation was modelled for the RT-PCR with and without NAE.

Results: Overall, FPR was low [0.07% (222/330,763)] in asymptomatic testing sites, but FDR was high [30.7% (222/724)]. When RT-PCR was compared with and without NAE, 100% concordance was obtained with NAAT-positive specimens, including those from Ag-RDT-positive individuals. NAE-free RT-PCR significantly reduced time to results, human resources, and overall costs.

Conclusions: A 30.7% FDR reaffirms the need for NAAT-based confirmation of positive Ag-RDT results during low SARS-CoV-2 prevalence. NAE-free RT-PCR was shown to be a simple and cost-sparing NAAT-based solution for positive Ag-RDT confirmation, and its implementation supported data-driven broader Ag-RDT deployment into communities, workplaces, and households.

Poster 31

Title: DOES INCREASED VANCOMYCIN MIC INCREASE THE RISK OF COMPLICATIONS IN PATIENTS WITH METHICILLIN-SENSITIVE *STAPHYLOCOCCUS AUREUS* BLOODSTREAM INFECTIONS? A RETROSPECTIVE REVIEW.

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Introduction: *Staphylococcus aureus* (SA) is a common cause of community and hospital-associated infections, including bloodstream infection (BSI). Studies have documented worse outcomes of methicillin-resistant (MRSA) bacteremia if the vancomycin MIC is ≥ 1.5 mg/L. Limited studies in patients with methicillin-sensitive SA (MSSA) BSI, indicate that a higher vancomycin MIC have poorer outcomes suggesting that reduced vancomycin susceptibility is a marker for poorer prognosis. This study aims to explore the outcome of patients with MSSA-BSI in relation to the vancomycin MIC.

Methods: A retrospective chart review of 305 patients with MSSA-BSI admitted to the hospital between October 2015 and June 2018 was conducted. Patients were classified based on vancomycin MIC; low (<1.5 mg/L) and high (≥1.5 mg/L). The primary outcome assessed was all-cause mortality up to 90 days after onset of the MSSA-BSI. The secondary outcomes assessed were cure with or without complications. Additional information gathered included demographics, comorbidities, investigations, management, and antibiotic treatment.

Results: Seven patients were excluded due to insufficient chart information. Of the 298 patients, 116 (38.9%) were female and the mean age was 61.8 years. The proportion of patients with a vancomycin MIC of <1.5mg/L and ≥1.5mg/L was 79.9% (238/298) and 20.1% (60/298) respectively. All-cause mortality at 90 days was 20.5% (47/238) and 19.0% (11/60) respectively. More patients in the low vs high MIC group, 53.4% (126/238) versus 45.8% (27/60) respectively, were cured without complications but this was not statistically significant.

Conclusions: MSSA bacteremia is a common cause of mortality and complications in patients. In our study elevated vancomycin MIC did not show increased mortality and although it demonstrated a trend towards increased complications and longer length of stay this was not statistically significant.

Poster 32

Title: ELUCIDATING THE PROTECTIVE FEATURES OF THE TIAR 5’ UTR DURING SARS-CoV-2 NSP1 HOST SHUTOFF

Authors: Caleb I. Galbraith, Denys A. Khaperskyy

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains a significant pathogen worldwide. Non-structural protein 1 (Nsp1) is a viral host shutoff factor that blocks host translation by directly blocking the mRNA entry channel in the ribosome and by promoting cytosolic mRNA degradation. Importantly, the 5’ untranslated region (UTR) of the viral RNA renders it resistant to Nsp1-mediated translation arrest. Furthermore, it has been reported that mRNAs containing a 5’ terminal oligopyrimidine (TOP) tract are resistant to Nsp1-mediated shutoff. Previously, we have identified TIA1 cytotoxic granule-associated RNA binding protein (TIAR) as being upregulated in Nsp1-expressing cells. The TIAR transcript lacks a 5’ TOP tract or homology to the viral RNA and the specific features that confer its escape from Nsp1 shutoff are unknown.

Methods: The TIAR 5’ UTR was inserted upstream of a fluorescent reporter protein. HEK293A cells were transfected with the reporter construct and an Nsp1 plasmid. Nsp1-mediated downregulation of reporter expression was compared to vector controls. The TIAR 5’ UTR was systematically mutagenized towards identifying the elements required for Nsp1 resistance.

Results: The first 51 nucleotides of the TIAR 5’ UTR are necessary and sufficient to not only protect against Nsp1-mediated shutoff but also to upregulate expression to a degree comparable to the SARS-CoV-2 5’ UTR. Starting 10 nucleotides downstream from the 5’ cap there is an 8 nucleotide stretch devoid of guanosine residues, substituting two guanosine residues in this window render the full length TIAR 5’ UTR susceptible to Nsp1-mediated shutoff.

Conclusions: The full landscape of resistant host transcripts to Nsp1-mediated shutoff remains incomplete. Here we propose a new category of Nsp1-resistant host transcripts that harbour at least an 8 nucleotide stretch devoid of guanosine located 10 nucleotides downstream of the 5’ cap. Future work will use bioinformatic tools to identify and validate putative resistant transcripts. We will also characterize the functional relevance of TIAR, and other resistant transcripts during SARS-CoV-2 infection.

Poster 33

Title: PRESCRIBING AND DISPENSING DELAYED ANTIBIOTICS TO PEDIATRIC PATIENTS WITH ACUTE OTITIS MEDIA AND PHARYNGITIS

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Affiliation: Dalhousie University, IWK Health

Introduction: A delayed antibiotic prescription is often provided to patients with suspected or confirmed infections to decrease unnecessary overuse of antibiotics. Although "watchful waiting" is recommended in specific cases for pediatric conditions, little is known about delayed prescribing at IWK Health. The primary objectives were 1) to characterize delayed prescriptions for pediatric patients with acute otitis media (AOM) or pharyngitis, and 2) to determine the proportion of delayed antibiotic prescriptions dispensed prematurely by a community pharmacy.

Methods: This study was a retrospective chart review. Pediatric patients discharged with a diagnosis of AOM and pharyngitis from the IWK Health Emergency Department between March 1, 2019 to February 28, 2021 were included. Data on antibiotic dispensations for each patient included in the chart review was obtained from the Drug Information System by Health Data Nova Scotia. The main outcome measures were frequency of delayed antibiotic prescribing; number of patients who filled delayed prescriptions; and adherence to clinician's delayed instructions. Data was analyzed descriptively.

Results: Delayed antibiotics were prescribed to 26.8% (332/1241) of patient encounters during the study period. The majority of these prescriptions were prescribed for AOM (77.7%, 258/332). Less than half of the patients who received a delayed prescription filled the prescription (40.4%, 134/332). Most patients filled prescriptions the same day they were discharged (41%, 55/134) or the next day (33.6%, 45/134). Of the patients who filled prescriptions, 36.6% (49/134) adhered to clinician's delayed instructions and 41% (55/134) were non-adherent (the remaining 22.4% of patients were unable to be assessed). Most commonly, patients who were non-adherent prematurely filled their prescription (65.5%, 36/55).

Conclusions: Delayed prescribing may have led to reduced antibiotic use for AOM and pharyngitis at IWK Health; however, a proportion of these patients continue to fill antibiotics prematurely when they may not be necessary. Additional strategies to reduce premature dispensing of antibiotics through community pharmacies should be considered.

Poster 34

Title: AN ENVIRONMENTAL SCAN OF THE IMMUNIZATION LANDSCAPE IN COMMUNITY PHARMACIES ACROSS CANADA

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Introduction: NACI provides recommendations on vaccinations for children and adults, while provinces/territories (P/Ts) decide which vaccines to publicly fund and include in program implementation. Lack of public funding can result in low vaccine uptake due to potential out-of-pocket costs. In most Canadian jurisdictions, pharmacists and pharmacy technicians have the authority to administer vaccines. An environmental scan on the immunization landscape across Canada was conducted to gain a comprehensive overview of NACI recommended immunizations that are publicly funded and available for administration in pharmacies in each Canadian P/T.

Methods: This environmental scan used openly accessible information to determine which NACI recommended vaccine schedules for children and adults are publicly funded in each P/T. To determine NACI recommendations, the Canadian Immunization Guide (CIG) and NACI statements were reviewed. Public Health and Pharmacy Association websites in each P/T were cross referenced with the CIG to determine which publicly funded vaccines are available in pharmacies. Additionally, Standards of Practice and Pharmacy Acts were analyzed to determine pharmacy professionals' authority to prescribe/administer vaccines in each P/T.

Results: Pharmacists are authorized to prescribe vaccines in 8 P/Ts and administer vaccines in 11 P/Ts. Pharmacy technicians are also authorized to administer vaccines in 7 P/Ts. To date, pharmacy professionals in the Northwest Territories and Nunavut do not have authority to immunize. Some public funding for pharmacy professionals to prescribe and/or administer immunizations for specific vaccines is provided in 11 P/Ts. Of the 30 NACI recommended vaccines analyzed, British Columbia and Yukon provide the most funding for administration of immunizations in pharmacies with 21 of 30 vaccines being publicly funded. Whereas Newfoundland, Nova Scotia, Ontario, and Saskatchewan provide funding for only influenza and COVID vaccines in pharmacies.

Conclusions: Discrepancies across P/Ts in public funding that may improve access to NACI recommended vaccines through pharmacy professionals in Canada has been identified through this environmental scan. Additional public funding in pharmacies across Canada may decrease cost-related barriers to immunization and increase vaccine accessibility and uptake.

Poster 35

Title: MEASURING SARS-COV-MPRO-MEDIATED CLEAVAGE OF GALECTIN-8 IN VITRO AS A METHOD TO SCREEN FOR MPRO INHIBITORS

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Introduction: Coronavirus (CoV) proteases cleave viral polyproteins into non-structural proteins (nsps) that perform essential functions including replication organelle formation, viral RNA synthesis, and inhibition of host antiviral responses. This makes CoV proteases attractive targets for antiviral drug discovery. The host protein galectin-8 (gal-8) regulates innate and adaptive immune responses and has been previously identified as a SARS-CoV-2 main protease (Mpro) substrate. We established an in vitro assay of SARS-CoVMpro activity using gal-8 as the substrate to facilitate screening of candidate Mpro inhibitors.

Methods: We produced hexahistidine-tagged gal-8 in E. coli BL21 cells and harvested protein for purification on a Ni- NTA affinity resin (Thermo Fisher). Purified gal-8 was incubated with purified Mpro (Sigma-Aldrich) in different ratios and in a variety of buffer formulations to establish optimal parameters for gal-8 cleavage, which was assessed by SDS-PAGE and Coomassie brilliant blue staining. The Mpro inhibitor nirmatrelvir was used as a control.

Results: We determined that all buffer formulations tested supported efficient Mpro-mediated gal-8 cleavage in 24 hours at 37 °C. Gal-8 cleavage was observed by 4.5 hours, with nearly complete cleavage occurring by 24 hours. The sizes of the cleavage products were consistent with the sizes mentioned in literature. We selected the 20 mM Bis-Tris buffer for further experiments. Nirmatrelvir prevented gal-8 cleavage by Mpro under these reaction conditions.

Conclusions: Mpro efficiently cleaves gal-8 in vitro in several buffer formulations. The cleavage of gal-8 is prevented by co-incubation with nirmatrelvir. We conclude that this assay will be useful for investigating the function of novel CoV Mpro inhibitors in vitro. We will pair this assay with an additional in-cell, fluorescence-based assay to monitor Mpro activity in the presence of absence of inhibitors using a more physiologically relevant system.

Poster 36

Title: CHARACTERIZATION OF ANTIBIOTIC TOLERANCE AND PROTEIN SYNTHESIS OF *PSEUDOMONAS AERUGINOSA* RIBOSOMAL TRANSPOSON MUTANTS

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Introduction: *Pseudomonas aeruginosa* is a ubiquitous, Gram-negative, opportunistic pathogen. As it has high levels of intrinsic and acquired resistance mechanisms, *P. aeruginosa* has developed resistance to many classes of antibiotics and is a critical priority for research. A previous study suggested that ribosomal mutations conferred antibiotic resistance in *Mycobacterium smegmatis*. For this study, we set out to characterize ribosomal transposon mutants of *P. aeruginosa* by testing their survivability against several classes of antibiotics as well as their protein synthesis capabilities.

Methods: We tested 8 transposon mutants against the wild type strain PA14, five were ribosomal mutants, two contained mutated genes associated with ribosome function, and one was a transposon mutant control. Growth curves and MIC assays were performed as preliminary work. Then, survivability assays and protein synthesis assays were conducted and measured using flow cytometry.

Results: Mutant growth was similar to wild type with the exception of two slower growing ribosomal transposon mutants. Survivability compared to wild type was highly variable depending on the mutant, the antibiotic, and the antibiotic concentration. Notably, all mutants were observed to be highly resistant to tobramycin when tested at 1 MIC compared to wild type. The protein synthesis of the mutants did not differ significantly compared to wild type, with one exception. The protein synthesis capabilities of the mutants were also more variable than wild type.

Conclusions: Overall, there were no clear trends in transposon mutant survivability compared to wild type when tested against multiple classes of antibiotics, suggesting that mutations of the small and large ribosomal subunits do not confer multidrug resistance in *P. aeruginosa*. While the protein synthesis of the control was consistent whereas that of the mutants was highly variable, that may suggest that the protein synthesis of the mutants is more sensitive and easily influenced by other factors.

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Title: 6-THIOGUANINE INHIBITS THE REPLICATION OF DNA VIRUSES

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Introduction: 6-thioguanine (6-TG) is a pro-drug that can be metabolized into an active nucleotide form that inhibits GTPase enzymes. We have previously shown that 6-TG metabolites inhibit RNA viruses, including influenza A viruses (IAV) and coronaviruses (CoVs), and that antiviral activity is mechanistically linked inhibition of host GTPases. This host-directed antiviral activity has the potential for broad inhibition of diverse viruses. Here we report the effects of 6-TG metabolites on several viruses with DNA genomes.

Methods: Human 293A, HeLa, and MRC5 cells were treated with a range of concentrations of 6-TG for 20 h or 44 h and viability was evaluated using an alamarBlue assay. Percent viability was determined relative to DMSO vehicle control. Adenovirus (Ad5-GFP) and HSV-1 (syn17+) infections were performed in 293A and HeLa cells, respectively, at an MOI of 0.1 and treated with DMSO or varying concentrations of 6-TG for 24 h. Harvested viruses were serially diluted and titered in 293A (AdV) or Vero cells (HSV-1). HCMV (AD169) susceptibility to 6-TG (relative to DMSO) was determined via plaque reduction assays in MRC5 cells.

Results: 6-TG had minimal effect on cell viability in all infection models. In each infection model, production of viral progeny (HSV-1, AdV), or plaque formation (HCMV), was reduced >20-fold in the presence of higher 10μM 6-TG treatment. Lower doses also yielded modest yet significant reductions for all three infection models.

Conclusions: We determined that 6-TG metabolites can inhibit DNA viruses as well as RNA viruses. Previously, we noted deficiencies in IAV and CoV envelope glycoprotein processing in our model of 6-TG antiviral activity. However, our new data demonstrates that non-enveloped AdVs are equally susceptible as enveloped viruses. Thus, 6-TG has antiviral activity against diverse viruses. We speculate that 6-TG metabolites create an inhospitable cellular environment by disabling key host GTPases that normally support viral replication.

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