# 2026
# University of Toronto Microbiology & Infectious Disease Research Days

## AGENDA
## Trainee Day, May 27

Room 2170, Medical Sciences Building, 1 King's College Circle

**Presented by**

UNIVERSITY OF TORONTO | EPIC Emerging & Pandemic Infections Consortium

**In collaboration with**

U of T's Division of Infectious Diseases, Department of Medicine, and postgraduate medical and clinical microbiology program, the Division of Infectious Diseases at The Hospital for Sick Children and the Institute of Health Emergencies and Pandemics.

**With support from** BIOMÉRIEUX

EPIC is a collaborative initiative between the University of Toronto and five hospital partners.

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UNIVERSITY OF TORONTO ANNUAL

# Microbiology and Infectious Diseases Research Days

## TRAINEE DAY - MAY 27, 2026
## MEDICAL SCIENCES BUILDING, ROOM 2170

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|---|---|
| 9:00 AM | **Registration**<br>David Naylor Student Commons, Medical Sciences Building |
| 9:20 AM | **Welcome and opening remarks**<br>Natasha Christie-Holmes |
| 9:35 AM | **Neisserial type XI secretion system in *Escherichia coli*: A heterologous and versatile platform for secretion of engineered antigens and biologics**<br>Dixon Ng (PI: Trevor Moraes) |
| 10:00 AM | **A sepsis-predicting diagnostic for prioritized patient care in the ICU**<br>Paul Kelly (PI: Keith Pardee) |
| 10:25 AM | ***Legionella pneumophila* anti-phage surface defences reveal links between phage resistance and ecology**<br>Elizabeth Chaney (PI: Alexander Ensminger), 2026 EPIC Doctoral Awardee |
| 10:50 AM | **Coffee break** |
| 11:15 AM | **Identifying efficacious dietary additives to improve poultry gut health**<br>Maxine Ty (PI: John Parkinson), 2026 EPIC Future Leader |
| 11:40 AM | **Characterization of canonical and non-canonical antiviral responses in white tailed deer cells infected with host-adapted SARS-CoV-2**<br>Sophie-Marie Aicher (PI: Samira Mubareka), 2024 EPIC Researcher Mobility Awardee |
| 12:05 PM | **The clearance of human cytomegalovirus using CRISPR/Cas9 RNA lipid nanoparticles**<br>Anson Lau (PI: Omar Khan), 2023 EPIC Doctoral Awardee |

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# Microbiology and Infectious Diseases Research Days

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| 12:30 PM | **Lunch** |
| 1:30 PM | **Broad neutralization of viruses with high genetic diversity by antibodies**<br>Krithika Muthuraman (PI: Jean-Philippe Julien), 2026 EPIC Future Leader |
| 1:55 PM | **Trainee Flash Talks** (8 talks, 5 mins each)<br>See next page for talk titles and presenters |
| 2:40 PM | **Coffee break** |
| 3:05 PM | **Mucosal anti-commensal immunity correlates with salivary vaccine responses and breakthrough infection timing in a pediatric cohort**<br>Salma Sheikh-Mohamed (PI: Jennifer Gommerman), 2026 EPIC Future Leader |
| 3:30 PM | **The role of NXPE3 in seasonal coronavirus infection**<br>Michelle Gontcharova (PI: Mike Tyers) |
| 3:55 PM | **From genomes to public health action: Population-level insights from the 2023/2024 influenza A season in Ontario**<br>George Long (PI: Venkata Duvvuri) |
| 4:20 PM | **Closing remarks** |

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# Microbiology and Infectious Diseases Research Days

## TRAINEE FLASH TALKS - MAY 27, 2026, 1:55 - 2:40 PM
## MEDICAL SCIENCES BUILDING, ROOM 2170

**Leprosy in a Canadian-born man with seasonal travel to Florida**

Amanda Hempel (PI: Andrea Boggild)

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**The baseline vaginal immune milieu is an important determinant of the inflammatory response induced by penile-vaginal sex**

Jinny Tsang (PI: Rupert Kaul), 2025 EPIC Doctoral Awardee

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**Role of Zbtb7b in gut mononuclear phagocytes**

Zi Yan Chen (PI: Arthur Mortha), 2026 EPIC Doctoral Awardee

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**Characterizing knowledge user participation in infectious disease transmission modeling**

Nancy Tahmo (PI: Sharmistha Mishra), 2025 EPIC Doctoral Awardee

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**Structure-guided optimization of small molecules targeting Yck2 as a strategy to combat *Candida albicans***

Bonnie Yiu (PI: Leah Cowen)

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**Identifying critical control points for zoonotic virus spillover prevention at vital interfaces: Mapping human-wildlife value chains using a One Health approach**

Will Zhang (PIs: Samira Mubareka & Cheryl Pritlove)

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**Ironing out the details: The impact of metals on key vaginal bacteria**

Daniella Serrador (PI: William Navarre), 2026 EPIC Doctoral Awardee

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**Filters for bioaerosol surveillance and infection control**

David Kormos (PI: Jeffrey Seigel), 2025 EPIC Researcher Mobility Awardee

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# 2026
# University of Toronto Microbiology & Infectious Disease Research Days

# AGENDA
# Main Programming Day, May 28

Room 3154, Medical Sciences Building, 1 King's College Circle

**Presented by**

UNIVERSITY OF TORONTO | EPIC Emerging & Pandemic Infections Consortium

**In collaboration with**

U of T's Division of Infectious Diseases, Department of Medicine, and postgraduate medical and clinical microbiology program, the Division of Infectious Diseases at The Hospital for Sick Children and the Institute of Health Emergencies and Pandemics.

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# Microbiology and Infectious Diseases Research Days

**KEYNOTE & SPOTLIGHT TALKS - MAY 28, 2026**
**MEDICAL SCIENCES BUILDING, ROOM 3154**

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| 8:00 AM | **Registration and coffee**<br>David Naylor Student Commons, MSB |
| 8:45 AM | **Welcome and opening remarks**<br>Natasha Christie-Holmes |
| 9:00 AM | **Quantifying viral dynamics following single and combination immunotherapy for HIV**<br>Alison Hill, Faculty of Arts & Science, U of T |
| 9:25 AM | **From structural snapshots to vaccine immunogens against Epstein-Barr virus and related viruses**<br>Mathew McCallum, Temerty Faculty of Medicine, U of T |
| 9:50 AM | **Data, models and equity: Generating evidence to inform pediatric RSV prevention strategies**<br>Tiffany Fitzpatrick, Dalla Lana School of Public Health & Public Health Ontario |
| 10:15 AM | **Coffee break** |
| 10:45 AM | ***Keynote***<br>**When a muskox dies in the tundra, does anybody hear?: Rethinking wildlife health surveillance in the Arctic**<br>Susan Kutz, Faculty of Veterinary Medicine, University of Calgary |

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# Microbiology and Infectious Diseases Research Days

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| 11:45 AM | **Leveraging single-cell sequencing and human clinical trials to garner insights into tuberculosis immunology and vaccine development**<br>Dylan Kain, Division of Infectious Diseases, University Health Network |
| 12:10 PM | **The microscopic world of indoor environments**<br>Sarah Haines, Faculty of Applied Science & Engineering, U of T |
| 12:35 PM | **Closing remarks**<br>Jennie Johnstone, Sinai Health |
| 12:45 PM | **Lunch**<br>David Naylor Student Commons, MSB |
| 2:00 PM | **Poster session A** (Even numbers)<br>David Naylor Student Commons, MSB |
| 3:00 PM | **Poster session B** (Odd numbers)<br>David Naylor Student Commons, MSB |

# Thank you to our volunteers!

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**WE ALSO THANK THE TALK AND POSTER JUDGES!**

2026

# Microbiology & Infectious Disease Research Days

# Abstract Booklet

## May 27th - 28th, 2026

Presented by

UNIVERSITY OF TORONTO | EPIC Emerging & Pandemic Infections Consortium

In collaboration with U of T's Division of Infectious Diseases, Department of Medicine, and postgraduate medical and clinical microbiology program, the Division of Infectious Diseases at The Hospital for Sick Children and the Institute for Health Emergencies and Pandemics at the Dalla Lana School of Public Health.

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2026

# Microbiology & Infectious Disease Research Day

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*Trainee abstract submissions and presentations at the 2026 Microbiology & Infectious Disease Research Days are coordinated by the EPIC Trainee Advisory Committee.*

*Thank you to all of our trainee volunteers and presentation judges!*

**Oral Presentation** **Poster 1**

# Neisserial Type XI Secretion System in *Escherichia coli*: a heterologous and versatile platform for secretion of engineered antigens and biologics

Dixon Ng, Quynh Huong Nguyen, Natalie YT Au, Tiana Lee, Saanvi Mazumdar, Christine Lai, Anthony Schryvers, Trevor Moraes

1. Department of Biochemistry, University of Toronto
2. Microbiology, Immunology and Infectious Diseases, University of Calgary

The Type XI secretion system (TXISS) translocates surface lipoproteins (SLPs) across the outer membrane of Gram-negative pathogens. In Neisseria meningitidis and Neisseria gonorrhoeae, conserved SLPs, including factor-H binding protein (fHbp), hapto/hemoglobin utilization protein (HpuA), and transferrin binding protein (TbpB), are critical virulence factors and prime vaccine targets. However, studying these membrane-anchored proteins is hindered by low native expression, cellular toxicity, and complex, detergent-dependent extraction protocols that impede downstream structural and immunological characterization.

To overcome these bottlenecks, we reconstituted the neisserial TXISS heterologously in Escherichia coli. By engineering the Surface Lipoprotein Assembly Modulator (SLAM) translocon into a single-vector system, we developed a highly-tunable platform that secretes normally tethered SLPs as soluble exoproteins directly into the culture supernatant. Maximizing secretion output in as little as six hours, this pipeline completely bypasses cellular lysis and membrane extraction, routinely yielding up to 50 mg/L of natively folded, highly pure neisserial antigen.

This high-throughput production enabled the rapid structural characterization of multiple virulence factors, allowing us to resolve high-resolution crystal structures for full-length meningococcal HpuA (2.1 Å), gonococcal NgoHpuA (2.0 Å), and the SLAM-dependent secreted protein sspG (2.05 Å). Expanding the platform for vaccine engineering, we utilized secreted SLPs as stable structural scaffolds to graft exogenous extracellular loops from other immunogenic targets. These engineered hybrid antigens are efficiently secreted and remain functionally accessible to targeted antibodies. Furthermore, we demonstrated the system's capacity for broad biomacromolecule delivery by using SLPs to translocate bulky reporter enzymes, including green fluorescent protein and NanoLuciferase.

Our adapted TXISS platform is a major methodological advancement. This fast, scalable, and detergent-free pipeline accelerates the structural analysis of pathogenic virulence factors and drives the rapid generation of engineered biologics and hybrid vaccine candidates.

**Oral Presentation**

# A sepsis-predicting diagnostic for prioritized patient care in the ICU

Paul Kelly[1], Riham Zayani[1], Jessica Nguyen[1], Victor Sit[2], Pouriya Bayat[1], Christina Nassif[2], Dillon Da Donte[2], Krištof Bozovicar[1], Claudia dos Santos[2,3,4], Amy Lee[5], Yufeng Zhao[1,2], Lidija Malic[2,6], Keith Pardee[1]

1. Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada
2. National Research Council Canada, Boucherville, QB, Canada
3. Keenan Research Centre for Biomedical Science, St. Michael's Hospital, Toronto, ON, Canada
4. Department of Physiology, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada
5. Department of Molecular Biology And Biochemistry, Simon Fraser University, Vancouver, BC, Canada
6. Department of Biomedical Engineering, McGill University, Montreal, QB, Canada

BACKGROUND: Sepsis, a dysregulated immune response to infection causing organ damage, is a leading cause of death worldwide. Early detection enables effective clinical intervention, but timely and accurate diagnosis remains challenging. In recent work with collaborators at St. Michael's Hospital and Simon Fraser University, we identified a panel of mRNA biomarkers capable of predicting sepsis severity based on their expression profiles.

METHODS: To translate these findings into a clinical tool, we are developing a point-of-care CRISPR-diagnostic for biomarker quantification. We designed and optimized a recombinase polymerase amplification (RPA)–Cas12a assay in both one- and two-pot formats. To enable quantification, we implemented the RPA–Cas12a assay in digital and digital droplet systems. In collaboration with the National Research Council Canada, we plan to deploy our digital RPA–Cas12a diagnostic on a lab-on-a-chip platform that automates sample preparation, purification, detection, and analysis.

RESULTS: Our two-pot RPA–Cas12a assay was ultra-sensitive and fast, detecting as low as 50 aM within 45 minutes. In contrast, the one-pot format was less sensitive and slower, detecting down to 10 fM within 90 minutes. In a digital format, our diagnostic could quantify targets across a dynamic range from 1 fM to 10 pM.

CONCLUSION: Deployment of our digital RPA–Cas12a lab-on-a-chip platform in the ICU will support real-time clinical decision-making and improve patient management.

**Oral Presentation**

# *Legionella pneumophila* anti-phage surface defenses reveal links between phage resistance and ecology

Elizabeth H. Chaney[1], Beth Nicholson[2], Alexander W. Ensminger [1,2]

1. Department of Molecular Genetics, University of Toronto, Toronto, Ontario, Canada
2. Department of Biochemistry, University of Toronto, Toronto, Ontario, Canada

Legionella pneumophila is an intracellular Gram-negative bacterium that replicates within amoebae in freshwater. It causes Legionnaires' disease in humans when aerosolized bacteria are inhaled, but person-to-person transmission does not occur. Thus, humans provide no selective pressure on the evolution of this accidental pathogen and instead its fitness is shaped by the environment. A longstanding mystery has been why a particular subset of strains found in the environment causes the vast majority (>80%) of all human disease. Our group recently characterized the first phage infectious to L. pneumophila: Legionella Mobile Element-1 (LME-1). I have shown that resistance to phage attachment coincidentally selects for surface modifications that support human disease. Specifically, a single surface-modifying gene, lag-1, acetylates the cell surface to block phage attachment, which coincidentally provides resistance to killing by human complement. Since, I have identified a lag-1 independent layer of surface anti-phage defense, whose molecular basis and impact on virulence remain unknown. This new anti-LME-1 surface defense surprisingly prevents phage attachment only during the transmissive phase, when bacteria are normally extracellular and swimming to find a new host—suggesting this defense is activated when the bacteria are otherwise most susceptible to phage. I sampled a panel of distinct L. pneumophila isolates for this phenotype and by assembling a core genome phylogeny have found a single clade with which this phage-defense belongs. In parallel, through ongoing comparative genomics and forward genetic screens, I am searching for candidate genes responsible for this switch in phage susceptibility between distinct L. pneumophila growth phases. Phages are important evolutionary partners for their host bacteria, often altering their fitness in the environment. Having already shown that lag-1 primarily serves as an anti-LME-1 defense in nature, my latest work suggests that the influence of bacteriophages extends to other aspects of Legionella ecology.

**Oral Presentation**

## Identifying efficacious dietary additives to improve poultry gut health

Maxine Ty

1. University of Toronto, The Hospital for Sick Children

Antibiotic growth promoters (AGPs) were once widely used in poultry production to improve feed efficiency, enhance bird growth and reduce disease-related mortality. However, due to their overuse and the resulting rise in antimicrobial resistance mechanisms (AMR), global bans have been enacted to address this significant threat to public health. In response, the industry has turned to alternative strategies, such as probiotics and other microbial-based interventions, to support a healthy microbiome in poultry and mitigate the risks associated with the cessation of AGP usage that impact food safety and security.

My doctoral thesis consisted of two studies that explored how microbial communities respond to microbial-based interventions in comparison to AGPs, thereby broadening our understanding of the poultry gut microbiome and its inhabitants. The first study evaluated the effectiveness of microbial interventions in reducing the burden of a foodborne pathogen in poultry and analyzed bacterial community profiles under different experimental conditions to assess changes in composition imposed by both treatment and infection. The second study expanded the scope by characterizing both bacterial and eukaryotic communities and incorporated gene expression experiments to provide a comprehensive analysis of the chicken gut microbiome under the influence of different microbial interventions. These findings led to deeper insights into the poultry gut microbiome and its relationship to host health, ultimately contributing to the industry's efforts to advance microbial-based products as viable alternatives to AGPs.

**Oral Presentation**

## Characterization of canonical and non-canonical antiviral responses in white-tailed deer cells infected with host-adapted SARS-CoV-2

Sophie-Marie Aicher[1,2], Celine Tan[1,3], Briallen Lobb[4], Max Erdmann[5], Leandro X. Neves[5], Levi Klassen[3], Shyan Mascarenhas[4], Jonathon D. Kotwa[3], Yaejin Lee[1,3], Sowmya Thanikachalam[6], Lauren Crawshaw[7], Theo J Moraes[6], Jeff Bowman[7], Edward Emmott[5], Andrew C Doxey[4], Arinjay Banerjee[1,2], Samira Mubareka[1,3]

1. Department of Laboratory Medicine and Pathobiology, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada
2. Vaccine and Infectious Disease Organization, University of Saskatchewan, Saskatoon, SK, Canada
3. Sunnybrook Research Institute, Toronto, ON, Canada
4. Department of Biology, University of Waterloo, Waterloo, ON, Canada
5. Centre for Proteome Research, Department of Biochemistry, Cell & Systems Biology, University of Liverpool, Liverpool, United Kingdom
6. The Hospital for Sick Children, Peter Gilgan Center for Research and Learning, Toronto, ON, Canada
7. Wildlife Research and Monitoring Section, Ontario Ministry of Natural Resources, Peterborough, ON, Canada

Zoonotic viruses, including SARS-CoV-2, have increasingly caused public health emergencies, yet protective mechanisms in wildlife remain poorly characterized. SARS-CoV-2 circulates subclinically in white-tailed deer (WTD) populations, where the deer-adapted B.1.641 strain emerged and subsequently spilled back to humans. Little is known about how WTD respond to SARS-CoV-2 or the factors influencing lack of clinical disease. We investigated the basis of disease tolerance in WTD through characterization of antiviral responses to host-adapted SARS-CoV-2.

We established novel WTD cellular models by generating ciliated nasal epithelia on air-liquid interface from WTD nasal brushes. Through bulk RNA-seq transcriptomics, we characterized viral replication kinetics and host responses to SARS-CoV-2 B.1.641 (deer-adapted) and Delta variants. Transcriptomic data from naturally infected WTD nasal swabs collected through the Wildlife Emerging Pathogen Initiative provided in vivo validation of cellular findings. We observed potent upregulation of both type I and III interferons alongside robust activation of canonical antiviral genes including BST2, MX1 and RSAD2 in WTD cells. SARS-CoV-2 Delta variant induced only moderate antiviral gene expression in WTD cells, instead triggering upregulation of genes involved in extracellular matrix remodeling and cilium assembly inhibition, suggesting variant-specific adaptation mechanisms. Proteomic analysis confirmed upregulation of key antiviral effectors including MX1, MX2, and IFIT1, highlighting protein-level changes in interferon signaling pathways. Comparative analysis between naturally infected animals and experimental models showed consistent activation of antiviral immune pathways, validating our cellular systems as relevant models for reservoir host studies.

Our data demonstrate potent antiviral immune responses in WTD upon SARS-CoV-2 infection and the variant-specific differential responses suggest adaptive mechanisms. The novel WTD cellular models provide valuable tools for investigating the interplay between SARS-CoV-2 variants and potential novel wildlife reservoirs. Characterisation of viral tolerance mechanisms in reservoir species will further our understanding of zoonotic spillovers and may identify targets for therapeutic intervention against emerging viruses.

**Oral Presentation**

# The Clearance of Human Cytomegalovirus Using CRISPR/Cas9 RNA Lipid Nanoparticles

Yan Ming Anson Lau[1], Janice Pang[1], Meng Qi Jiang[1], Yikai Sun[1], Karlene L.M. Knaggs[1], Grayson Tilstra[1], Ana-Maria Oproescu[1], Julien Couture-Senécal[1], Alanna M. Manning[1], Ranim Maaieh[1], Victor H. Ferreira[2,3,4], Atul Humar[2,3,5] and Omar F. Khan[1,6]

1. Institute of Biomedical Engineering, University of Toronto, Toronto, ON, Canada
2. Toronto General Hospital Research Institute, Toronto, Ontario, Canada
3. Ajmera Transplant Centre, University Health Network, Toronto, ON, Canada
4. Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada
5. Department of Medicine, University of Toronto, Toronto, ON, Canada.
6. Department of Immunology, University of Toronto, Toronto, ON, Canada

Background: Human cytomegalovirus (HCMV) poses significant health risks to immunocompromised individuals and newborns. Current antivirals like ganciclovir inhibit viral replication but carry severe toxicities, fail against drug-resistant strains, and cannot eliminate HCMV DNA. CRISPR/Cas9 can cleave DNA, but has not been therapeutically applied to degrade HCMV DNA in infected cells. Lipid nanoparticles (LNPs) are FDA-approved, non-viral vectors capable of efficient RNA delivery. By combining LNP and CRISPR/Cas9, we propose a novel RNA antiviral that addresses the shortcomings of current treatments.

Method: Bioinformatic analyses based on viral gene essentiality and nucleotide conservation identified effective, strain-agnostic, mutation-resistant CRISPR/Cas9 targets. Single-guide RNAs (sgRNAs) and Cas9 mRNA were co-formulated into LNPs via microfluidic mixing. Anti-HCMV CRISPR LNPs were applied to HCMV-infected human fibroblasts, with infection quantified by flow cytometry and qPCR. Multiple LNP vectors were screened to examine structure-property-function relationships, and lead anti-HCMV CRISPR LNP were benchmarked against ganciclovir.

Results: All bioinformatically selected targets demonstrated significant antiviral activity in infected fibroblasts. Ablation of UL44, UL57, and UL105 produced the most potent effects. Antiviral activity depended on ionizable lipid composition and correlated with gene-editing efficiency, highlighting delivery as a key driver. The novel βN2-40 LNP showed the strongest efficacy, suppressing viral growth by up to 93.5% in a single dose. CRISPR cleavage reduced viral genomes without detectable indels, suggesting viral DNA is not repaired post-cleavage. Multiplexed βN2-40 LNPs targeting UL44/UL57/UL105 simultaneously showed onset kinetics and safety profiles comparable to ganciclovir, with 10–1000-fold reductions in DNA load across multiple HCMV strains.

Conclusion: This work demonstrates that an all-RNA CRISPR/Cas9 LNP platform can therapeutically clear established HCMV infections with efficacy and safety comparable

to current antivirals. This strategy directly degrades viral DNA, accesses undruggable viral genes, and is rapidly reprogrammable — offering a compelling alternative to address key limitations of existing HCMV treatments.

**Oral Presentation**

## Mucosal Anti-Commensal Immunity Correlates with Salivary Vaccine Responses and Breakthrough Infection Timing in a Pediatric Cohort

Salma Sheikh-Mohamed, Kevin Champagne-Jorgensen, Gary Y.C. Chao, Sabrina Pereira, Catherine Chi, Ying Liu, Karen Colwill, Geneviève Mailhot, Melanie Delgado-Brand, Tulunay R Tursun, Freda Qi, Laurie Seifried, Lesley Ward, Mousa El-Sururi, Beibei Zu, James M. Rini, Anne-Claude Gingras, Jennifer L. Gommerman

1. Department of Immunology, University of Toronto, Toronto, Canada
2. Lunenfeld-Tanenbaum Research Institute and Mount Sinai Hospital, Toronto, Canada
3. Department of Biochemistry, University of Toronto, Toronto, Canada

Intramuscular mRNA COVID-19 vaccines reduce SARS-CoV-2 infection associated morbidity and mortality. However, host-associated factors that impact vaccine-mediated protection against break-through infection, particularly in children who are highly exposed to the virus in congregant settings, remain unclear. In this study, we longitudinally profiled salivary attributes, including anti-spike and anti-commensal antibodies as well as oral microbial community structure, in a cohort of 100 SARS-CoV-2 naïve healthy children receiving two doses of intramuscular COVID-19 vaccine. Vaccination elicited a robust salivary IgG response that was boosted by a second dose, whereas variable levels of spike-specific IgA were detected post-dose 1 but waned considerably and were not boosted by a second dose. Vaccination induced a transient increase increase in anti-commensal IgA, which positively correlated with salivary spike-specific IgA. Interestingly, children who experienced an early breakthrough infection (2-13 weeks post-vaccination) exhibited lower baseline anti-commensal IgA levels and a distinct oral microbial community structure compared to children who had later breakthroughs. These data indicate that pre-existing commensal-specific IgA and oral microbiome composition are linked to salivary anti-spike IgA levels and susceptibility to SARS-CoV-2 breakthrough infection in children.

**Oral Presentation**

## Broad neutralization of viruses with high genetic diversity by antibodies

Krithika Muthuraman

PhD Thesis – The Hospital for Sick Children

Infectious agents, including viruses such as SARS-CoV-2 and HIV-1, pose significant challenges to global public health. While monoclonal antibodies (mAbs) have been deployed as antiviral therapeutics, their efficacy has been limited by viral sequence variability and the need for high therapeutic doses. A better understanding of structure-function relationships of how antibodies bind their antigenic targets, combined with protein engineering, offers the potential to unlock new avenues in combatting viral diversity. Our lab has previously described the multi-specific, multi-affinity antibody (Multabody, MB) platform, derived from the human apoferritin protomer, which enables the multimerization of antibody fragments, and can deliver highly potent and broadly acting molecules in vitro. This thesis demonstrates that the combination of avidity and multi-specificity in the MB platform confers protection and resilience against viral diversity that surpasses traditional mAb therapies. First, in a mouse challenge study, a trispecific MB targeting three distinct epitopes in the receptor binding domain of SARS-CoV-2 spike protein conferred protection at a 30-fold lower dose than the corresponding mAb cocktail, in the absence of effector functions. Monospecific Multabodies exhibited resilient neutralization against SARS-CoV-2 variants of concern compared to the corresponding mAbs conferred by augmented avidity. A trispecific Multabody was identified that demonstrated pan-sarbecovirus neutralization. Second, this thesis elucidates the molecular basis of a broad betacoronavirus antibody targeting a conserved epitope in the SARS-CoV-2 S2 subunit. Despite its low in vitro neutralization potency, this S2-directed antibody provided effector function dependent protection in vivo by targeting an epitope occluded in the S prefusion conformation. These findings highlight the potential of S2-directed antibodies for broad betacoronavirus protection. Finally, this thesis shows that incorporating broadly neutralizing antibodies with enhanced potency and breadth in a trispecific MB can achieve pan-HIV-1 neutralization at the target threshold. This is enabled by enhanced avidity, multi-epitope targeting, and synergistic interactions. Overall, this work advances our understanding of antibody-antigen interactions at the molecular level and the Multabody platform, a novel therapeutic modality, against two viruses of high genetic diversity SARS-CoV-2 and HIV-1. Findings described in this thesis open new avenues for targeting challenging pathogens where potent antibody-based therapeutics could significantly improve patient outcomes and quality of life.

**Oral Presentation**

## The Role of NXPE3 in Seasonal Coronavirus Infection

Michelle Gontcharova[1,2], María Sánchez-Osuna[2], Art Marzok[3], Hahn Li[3], Ying Liu[4], Matthew Miller[3], James Rini[4], Mike Tyers[1,2]

1. Department of Molecular Genetics, University of Toronto
2. The Hospital for Sick Children, SickKids Research Institute, Molecular Medicine
3. Department of Biochemistry and Biomedical Sciences, McMaster University
4. Department of Biochemistry, University of Toronto

Beyond the ability of the seasonally circulating human coronaviruses (HCoV) to cause a range of respiratory tract infections, from mild to severe, these pathogens are also associated with central nervous system (CNS) dysfunction and neurological complications (1). To enter the CNS, the virus hijacks several host factors in the cell, which are essential for its life cycle. These host factors are promising targets for drug development because they are less susceptible to mutations than virally-encoded ORFS, which can more readily evolve to evade treatment (2). We conducted a genome-wide CRISPR knockout (KO) screen with two seasonal coronaviruses, HCoV-OC43 and HCoV-229E, in two different human brain cancer cell lines (LN229 and U87MG). These screens revealed potential pan-coronavirus pro-viral host genes, including MDH1 (the metabolic enzyme malate dehydrogenase), IFITM3 (a known interferon-induced anti-viral factor that blocks virus fusion with endosomes) and NXPE3 (a neurexophilin that contains a lipid esterase domain). We chose to focus on NXPE3 as it is poorly characterized with no known role in viral pathogenesis. In validation experiments, we found that knockout of NXPE3 resulted in a significant reduction in cell death and decreased viral replication after HCoV-OC43 infection. Recent work shows that the Neurexophilin and PC-esterase family, of which NXPE3 is a member, has conserved sequence similarity to known sialic acid O-acetyltransferases (3,4). Given that OC43 binds 9-O-acetylated sialic acid (5), we hypothesized that NXPE3 may mediate virus binding by O-acetylation of proteins and/or lipids on the cell surface. We found that overexpression of NXPE3 dramatically increased the amount of O-acetylated sialic acid on the cell membrane, as detected by interaction of the D1 domain of the spike protein. Mutation of critical catalytic residues shared with other sialic acid O-acetyltransferases abolishes this activity of NXPE3. These results uncover a new genetic dependence for HCoV virus-host cell interactions and identify NXPE3 as a potential novel antiviral drug target.

**Oral Presentation**

## From Genomes to Public Health Action: Population-Level Insights from the 2023/2024 Influenza A Season in Ontario, Canada

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Background: Seasonal influenza is a major public health burden in Ontario, with influenza A(H1N1)pdm09 and A(H3N2) as predominant circulating strains. There is increasing interest in applying phylodynamic approaches in routine influenza surveillance because they integrate genomic and epidemiological data. This can generate population-level insights into the transmission and evolutionary dynamics shaping seasonal epidemics in Ontario and support more responsive public health action.

Methods: 286 H1N1pdm09 and 190 H3N2 hemagglutinin (HA) and neuraminidase (NA) segments from influenza-positive specimens collected in Ontario between August 2023 and May 2024 were analyzed. Bayesian phylodynamic models were used to estimate lineage diversity, effective population size, and time-varying reproductive numbers. Antigenic variation was assessed through amino acid substitution patterns and glycosylation motif comparisons. NA sequences were screened for substitutions associated with reduced susceptibility to antiviral neuraminidase inhibitors.

Results: H1N1pdm09 exhibited greater phylogenetic diversity than H3N2 with multiple co-circulating subclades. In contrast, H3N2 was dominated by the 2a.3a.1_J.2 lineage, consistent with recent global selective sweeps and a reduced lineage diversity. Both subtypes demonstrated an initial increase in transmission in October 2023; however, H1N1pdm09 showed a relatively stable epidemic trajectory, whereas H3N2 had alternating periods of expansion and contraction. Antigenic analyses indicated that the WHO recommended Northern Hemisphere 2023/2024 H3N2 vaccine strain (A/Darwin/9/2021) was substantially more distant from circulating Ontario strains than the 2024/2025 vaccine strain (A/Thailand/8/2022), supporting improved expected vaccine match in the following season. In contrast, the H1N1pdm09 vaccine strain remained broadly representative of circulating viruses. Five H1N1pdm09 viruses carried NA substitutions associated with reduced inhibitor susceptibility; no resistance-associated mutations were identified in H3N2.

Conclusions: Genomic surveillance can provide critical insights for influenza transmission monitoring, viral evolution, and vaccine strain suitability. Integrating phylodynamic and antigenic analyses into routine public health surveillance programs can strengthen seasonal preparedness, improve response strategies, and enhance population health protection against influenza.

**Flash Talk** **Poster 2**

# Leprosy in a Canadian-Born Man with Seasonal Travel to Florida

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Case Summary: A 75-year-old man presented in January 2026 with 18 months of rash. Exam revealed numerous reddish-brown papules and plaques over the torso, bilateral arms and upper legs. The lesions were not pruritic, painful or anesthetic. Neurologic exam revealed no sensory deficits, motor weakness or thickened nerves. Review of systems was otherwise unremarkable. Complete blood count and C-reactive protein were within normal limits. No contacts had a similar rash. Punch biopsy in June 2025 had shown non-specific superficial lymphocytic infiltrate. In Nov 2025 two shave biopsies showed non-necrotizing granulomatous inflammation. Fite stain was positive for acid-fast bacilli and Mycobacterium leprae PCR later returned positive. He was born in Canada. From 2008-2018 he spent winters on a horse farm in Florida. He was involved in extensive yard work in areas armadillos were known to inhabit but had no direct contact. There were no migrant workers on the farm. He had no other significant travel.

Discussion: There have been two prior reports of M. leprae infection in Canadian-born individuals without travel to areas traditionally considered endemic – both individuals had prior travel to the southeastern USA and genotyping demonstrated the M. leprae strain found in nine-banded armadillos.1,2 We report a third case of leprosy in a Canadian-born man with seasonal travel to Florida and no other traditional risk factors.

The last decade has seen a significant increase in leprosy cases in the southeastern USA.3 Approximately 1/3 of cases in Florida have no travel to endemic areas or known positive contacts, with some suggesting that Florida is now endemic for leprosy.3,4 The etiology for this rise in cases is not entirely known. A high percentage of cases involved a unique strain of M. leprae that occurs amongst wild armadillos in the region, suggesting potential zoonotic transmission.5,6 Several cases had no direct contact with armadillos but had extensive outdoor exposure in areas armadillos were known to inhabit.7 Some research has suggested M. leprae may live temporarily in soil and exposure may occur from working with infected soil.7

Clinicians need to consider leprosy on the differential for patients presenting with a compatible clinical syndrome and travel to the southeastern USA.

**Flash Talk** **Poster 3**

# The Baseline Vaginal Immune Milieu is an Important Determinant of the Inflammatory Response Induced by Penile-Vaginal Sex

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Background: Most heterosexual HIV transmission occurs during penile-vaginal sex, and we have shown that sex induces epithelial trauma and inflammation. However, most HIV immunology studies sample women after abstinence and miss the immediate post-sex mucosal window when transmission biology is most relevant. We hypothesized that inter-individual heterogeneity in post-sex inflammation is not random but is determined by the pre-existing vaginal immune milieu.

Methods: The Toronto Sex, Couples, and Science Study (SECS) prospective cohort consists of HIV-uninfected women sampled before and 1 hour after penile-vaginal sex (n=36; condomless n=29, condom-protected n=7). We quantified total cervicovaginal IgA/IgG, then performed post-hoc analyses of HIV-associated inflammatory cytokines/chemokines and epithelial disruption markers to assess predictors of post-sex inflammation using non-parametric and clustering approaches. Genital inflammation was defined dichotomously using a multi-cytokine composite score (>=5/10 immune factors above baseline upper-tertile thresholds).

Results: Sex significantly induced cervicovaginal IgA ($p=0.0017$) and IgG ($p<0.0001$). Pre-sex IgA levels were associated with inflammatory and epithelial damage markers (IL-6: Spearman's rho=0.56, $p=0.0008$; soluble E-cadherin: rho=0.55, $p=0.001$), linking antibody abundance to an activated baseline mucosal state. Higher pre-sex cytokine concentrations were strongly linked to greater concentrations after sex. Conversely, lower baseline levels predicted greater relative post-sex increases in inflammatory/epithelial markers (including IL-1α, IL-6, sE-cadherin), whereas chemokines (MIP-1β, MIP-3α, MIG) were less baseline-dependent. Overall inflammation prevalence increased after sex (30% pre-sex vs 54% post-sex; McNemar $p=0.0209$). Participants inflamed at baseline were more likely to remain inflamed post-sex (9/11, 81.8%) than baseline-immunoquiescent participants (Fisher $p=0.031$;

RR=3.3, 95% CI 0.91-12.03). Unsupervised hierarchical clustering identified a high-baseline-cytokine subgroup with persistent cervicovaginal inflammation.

Conclusions: Baseline vaginal immunology is a strong determinant of post-sex inflammation and HIV susceptibility. These findings support that HIV risk should be assessed in the context of baseline mucosal immune phenotypes (e.g., bacterial vaginosis), which may improve prevention strategies across diverse populations.

**Flash Talk** **Poster 4**

## Role of Zbtb7b in Gut Mononuclear Phagocytes

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Background: The transcriptional regulators and networks that control macrophage fates within tissue environments remain poorly understood. The transcription factor zinc finger and BTB domain-containing protein 7B (Zbtb7b) is an important regulator of monocyte commitment in bone marrow precursors. However, its expression and function(s) in differentiated macrophages are not clearly defined. We hypothesize that: Zbtb7b controls development and function of tissue macrophages.

Methodology/Results: Using Zbtb7b-GFP reporter mice, we revealed heterogenous Zbtb7b expression in macrophages across multiple organs in adult and fetal mice. To determine whether Zbtb7b functions in regulating macrophages at the steady-state, adult Zbtb7b-/- animals were analyzed, uncovering significant changes in macrophage frequencies and numbers in colon and liver. As Zbtb7b regulates other immune cells, too, mixed control and Zbtb7b-/- bone marrow chimeras were analyzed to determine macrophage-intrinsic effects of Zbtb7b. Compared to wild-type, Zbtb7b-/- macrophages had significantly reduced frequencies in the colon 8 weeks post reconstitution. A macrophage-specific, tamoxifen-inducible, deletion of Zbtb7b revealed a significantly increased frequency in apoptotic, Annexin V+ macrophages in colon. Current fate-tracking approaches are addressing the turnover rate of macrophages in the presence and absence of Zbtb7b. Moreover, preclinical models of enteric infections will aid in determining whether Zbtb7b contributes to anti-microbial immunity at mucosal surfaces through regulation of macrophages in the gut.

Conclusion: Our results suggest that Zbtb7b acts as a core transcription factor that governs the survival and potentially functional program of intestinal macrophages. These data further, strongly imply a role for Zbtb7b in supporting the macrophage-dependent maintenance of intestinal barrier defense.

**Flash Talk** **Poster 5**

## Characterizing knowledge user participation in infectious disease transmission modeling

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Background: Infectious disease transmission modeling is increasingly used to inform policy decisions, yet concerns persist that those affected by model outputs are hardly involved in model development. Knowledge user participation has been proposed to improve model relevance. However, how participation occurs across the modeling process remains poorly characterized. We aimed to characterize who participates, when participation occurs, and how engagement is distributed across the modeling process.

Methods: We conducted a scoping review of participatory approaches in infectious disease transmission modeling studies published between 2000-2024, in any language.

Studies were included if they reported participation in at least one modeling step and modeled a specific infectious disease. To support the review, we developed a machine-assisted screening workflow. We assessed equitable participation using predefined indicators, including capacity building.

Results: After deduplication, 9,846 studies were screened and 156 included. The machine-assisted workflow reduced screening workload by 88.8% for title and abstract screening and 74.8% for full-text screening.

Included studies represented 98 countries; 55% modeled COVID-19 and 50% were published between 2020-2022. Participation was concentrated among policymakers and technical support partners (94% of studies), with lower representation of community-based organizations (13%) and people with lived experience (9%).

Participation was more common in downstream modeling steps (sourcing model inputs (78%), interpreting results (64%), selecting model scenarios (53%)) than upstream steps (interrogating model structure and assumptions (39%) and developing the research question (46.8%)).

Five participatory approaches emerged across a spectrum, from no direct (crowd-sourcing), indirect (third-party mediation, plug-and-play), to more direct (commissioning, active co-production) interaction with modelers. Most studies did not report equitable engagement; 28% reported efforts to build capacity for future engagement.

Conclusions: As infectious disease modeling continues to inform public health decision-making, strengthening how knowledge users are engaged across the modeling process has the potential to improve the relevance and application of modeling outputs.

**Flash Talk** **Poster 6**

## Structure-guided optimization of small molecules targeting Yck2 as a strategy to combat *Candida albicans*

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Candida albicans is the most common cause of life-threatening fungal infections in the developed world, but remains a therapeutic challenge. Treatment of systemic fungal disease is limited to only four front-line antifungal classes, including the echinocandins, which function by inhibiting cell wall synthesis. Protein kinases have been rewarding drug targets across diverse indications but remain untapped for antifungal development. Previously, screening kinase inhibitors against an echinocandin-resistant strain of C. albicans revealed a 2,3-aryl-pyrazolopyridine, GW461484A (GW), as an inhibitor of the casein kinase 1 (CK1) family member, Yck2, which possessed both single-agent and echinocandin-potentiating activity. Yck2 is required for growth under physiological conditions, is important for echinocandin resistance, and plays a role in virulence in a mouse model of infection. However, GW displays poor metabolic stability, limiting its in vivo utility. To overcome these limitations, we are collaborating with an interdisciplinary team to optimize novel Yck2 inhibitors with improved fungal selectivity, whole cell antifungal activity, and pharmacological properties. Characterization of dozens of compounds revealed YK-I-55 as a GW analog with improved pharmacological properties that retains whole-cell bioactivity and selectivity for fungal Yck2 compared to human CK1α or p38α. YK-I-55 also demonstrated broad-spectrum activity against all species listed as a “critical group” on the World Health Organization’s Fungal Priority Pathogen’s list, including Candida auris, Aspergillus fumigatus, and Cryptococcus neoformans. In co-culture assays, YK-I-55 effectively cleared C. albicans and preserved HepG2 cell viability at concentrations as low as 6.25 μM, highlighting its therapeutic potential. Furthermore, pharmacokinetic profiling of YK-I-55 in mice revealed favorable bioavailability and low toxicity. Ongoing studies are assessing its efficacy in a mouse model of invasive candidiasis. These results validate Yck2 as a promising antifungal target and support further development of casein kinase inhibitors as a new class of antifungal agents.

**Flash Talk** **Poster 7**

## Identifying critical control points for zoonotic virus spillover prevention at vital interfaces: Mapping human-wildlife value chains using a One Health approach

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BACKGROUND: Highly pathogenic avian influenza (HPAI) A(H5N1) virus is a zoonotic pathogen that infects diverse avian species with the potential for spillover to humans. Animal health interest-holders, including wildlife rehabilitators, veterinarians, and hunters, provide valuable insights regarding HPAI transmission risks through their close involvement with animals. An integrative One Health approach is critical to understanding these human-animal interactions. Value-chain analysis (VCA) is an economics framework that can be applied to animal disease management by mapping human-animal contact points in animal health sectors. VCAs have been conducted in other regions with different interest-holders, but no previous VCAs have been published in Ontario for HPAI A(H5N1).

METHODS: We recruited participants via snowball sampling and conducted semi-structured interviews with eleven interest-holders to investigate workflows, challenges, and interprofessional collaboration surrounding HPAI A(H5N1). We analyzed interview data using a reflexive thematic approach, guided by a constructivist framework, to construct a value-chain for HPAI A(H5N1) management in Ontario.

RESULTS: Key human-animal contact points were identified across the value-chain. During the provision stage, where citizens and agencies transport animals to rehabilitation centres, there is limited guidance on how to maintain biosafety. In the processing stage, formal and informal protocols are used to minimize transmission risk between animals and humans. Animals may be transported between multiple professionals and facilities to support resource-intensive veterinary care. Safe release practices are under-documented, and there is inconsistent long-term monitoring of human and animal health following release.

CONCLUSION: We conducted the first VCA for HPAI A(H5N1) management in Ontario and mapped key transmission risks in animal health sectors. Future work will include more participants across diverse interest-holder groups and leverage findings to inform government policy and public education.

**Flash Talk** **Poster 8**

## Ironing out the details: The impact of metals on key vaginal bacteria

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Lactobacillus iners is estimated to be the most common vaginal bacterium globally, but its role in health is unclear. A significant proportion of women are stably colonized by L. iners, but it is also present during bacterial vaginosis (BV), a dysbiosis of the vaginal microbiome. As such, it is currently considered a “transition” species between protective Lactobacillus crispatus and BV-associated bacteria, such as Gardnerella species. Understanding factors that impact L. iners growth could explain why many women are colonized by L. iners and suggest treatments to inhibit L. iners growth in the vaginal microbiome. One such factor may be metals. L. iners relative abundance can increase during menstruation, which could be due to metals in menstrual fluid. I have found that L. iners strains lack a putative manganese importer (mntH) that is conserved among Lactobacillus species, but L. iners encodes a highly conserved zinc importer (znuABC). I have also found that L. iners growth is inhibited by iron and manganese at levels tolerated by L. crispatus and Gardnerella vaginalis, but the three species have similar zinc tolerance. Cysteine, a known antioxidant, increases L. iners metal tolerance, which suggests that toxicity may be due to iron and oxygen producing free radicals through the Fenton reaction; in this case, vaginal oxygen may significantly impact bacterial colonization. This work will characterize the physiology of L. iners, a prevalent bacterium, suggest whether metals in the vaginal tract predispose women to colonization by specific species, and may identify metals that could eventually be used for BV prevention.

**Flash Talk** **Poster 9**

## Filters for Bioaerosol Surveillance and Infection Control

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Airborne infectious diseases are transmitted through bioaerosols generated primarily by human activity in occupied indoor environments. Filtration systems provide a unique opportunity to both reduce exposure and collect time-integrated biological material for surveillance of bacterial and viral aerosols. This work explores the use of filtration devices and aerosol samplers as bioaerosol sampling media across different built environments and disease contexts. Two complementary bioaerosol sampling approaches were employed. In occupied classroom environments, long-duration air sampling was conducted during typical operating hours using high volume samplers (InnovaPrep). Sampling was performed under multiple HVAC filtration conditions, including five filter configurations spanning a range of efficiencies, including a high efficiency portable air cleaner (PAC), and a zero-filter screen baseline. Samples were processed using standardized workflows for DNA extraction. Total airborne bacterial material was quantified using quantitative polymerase chain reaction (qPCR) targeting the 16S rRNA gene. Results indicate that filter efficiency meaningfully influences airborne biological reduction, with higher-efficiency filtration associated with lower bacterial concentrations. In parallel, a preliminary hospital-based study was conducted in Nigeria to evaluate filter-based bioaerosol sampling for tuberculosis (TB) surveillance. Swab samples were collected from a low-cost PAC filter deployed in a TB ward at a healthcare facility and submitted for molecular analysis. Samples were processed using similar DNA extraction and qPCR workflows. All PAC filter swabs were positive for bacterial 16S rRNA, supporting the feasibility of filter-based sampling for airborne microbial surveillance. Broad bacterial measurements form the initial phase of this work, with planned extensions to organism-specific bacterial targets and viral markers, including influenza and SARS-CoV-2, using digital PCR (dPCR) for enhanced sensitivity. Together, these studies demonstrate the potential for filters to serve dual roles as exposure control technologies and scalable tools for bioaerosol surveillance in real-world indoor environments.

**Poster 10**

# Impact of Sexual Debut on the Immune Milieu and Microbiome of the Penile Urethra in Adolescent Males from Rakai, Uganda

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Background: The penile urethra is a primary site of HIV acquisition in males, but little is known about urethral determinants of HIV acquisition. Inflammation at other genital sites enhances risk, and studies in adults suggest that some inflammatory bacteria may be acquired from the vagina of female sexual partners. Here, we characterize the impact of sexual debut on the microbiome and immune milieu of the penile urethra in adolescent males from Rakai, Uganda.

Methods: A cohort of 185 sexually naïve adolescent males were enrolled in a 3-year longitudinal study in Rakai, Uganda with follow-up every 3 months, and urethral swabs collected annually. Urethral levels of 9 soluble immune factors (IL-1α, IL-1β, IL-8, MIP-1β, sEcad, resistin, TIMP-1, VEGF, and MMP-9) were quantified by chemiluminescent multiplex immunoassay, and 16S rRNA sequencing was performed to characterize the urethral microbiome. Unsupervised clustering and mixed-effects models were used to evaluate the impact of sexual debut on the urethral microbiome and immune milieu.

Results: Median participant age at enrollment was 16 years, and during the follow-up period 80/185 (43%) reported penile-vaginal sexual debut. Although the urethral microbiome was highly diverse, at 36 months unsupervised clustering identified two distinct Community State Types (CSTs): CST-1 was dominated by Streptococcus mitis/oralis and CST-2 by BV-associated bacteria (Gardnerella vaginalis, Sneathia spp. and Fannyhessea vaginae). CST-2 was greatly enriched at 36 months compared to baseline and was strongly associated with prior sexual debut (LR= 6, p=0.01). Specific taxa enriched in CST-2 were significantly associated with sexual debut and urethral inflammation, independent of serum testosterone and circumcision status.

Conclusion: Sexual debut resulted in colonization of the penile urethra by BV-associated bacteria. This may have adverse effects on male reproductive health by inducing urethral inflammation and may serve as a reservoir for reintroduction of BV-associated bacteria into the vagina of female sexual partners.

**Poster 11**

# A Colorectal Cancer-Associated Fecal Mirnome and its Potential to Alter *Fusobacterium nucleatum* and *Escherichia coli* Gene Expression

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Background: Intestinal cells release microRNAs (miRNAs) in gut lumen. We found that a core set of miRNAs (miRNome) are shared across healthy individuals. Select fecal miRNAs have been proposed as biomarkers of colorectal cancer (CRC). However, the existence of a fecal miRNome in CRC is unknown. In addition, fecal miRNAs were suggested as modulators of bacterial growth in the gut. A subset of Fusobacterium nucleatum and Escherichia coli strains has been linked to CRC carcinogenesis. However, the interaction between CRC fecal miRNAs and these bacteria remains under-investigated.

Aims: To determine the shared fecal miRNome in patients with CRC and to identify the potential gene targets of shared miRNAs in F. nucleatum and E. coli strains.

Methods: PubMed and the Cochrane library were systematically searched for fecal miRNA profiling studies on patients with CRC. Shared miRNA species were identified (ComplexHeatmap R package). The genomes of select F. nucleatum and E. coli strains were extracted from NCBI and used to identify potential gene targets of the shared miRNAs via BLAST, followed by in silico validation (RNAup, ViennaRNA software).

Results: Of the 157 papers identified, 154 were excluded and 3 datasets were extracted from the 3 remaining papers (n=298). 31 miRNAs were present in all 3 datasets. Both shared and unique genes targets were found across F. nucleatum strains (6-11 targets/strain), which differed from those found in E. coli (13 targets). Many of these genes are known to be involved in key cellular activities such as translation and metabolism.

Conclusion: CRC fecal miRNomes exhibit some degrees of similarity, which may potentially signify a marker of disease progression and gut microbiota dysbiosis. F. nucleatum and E. coli gene expression can potentially be modulated by miRNAs found in CRC stools, which may serve as a novel approach to understand host-microbe interaction in CRC.

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**Poster 12**

# Macrophages control *Aspergillus fumigatus* hyphae through an adapted phagocytic program

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Macrophages are tissue-resident immune cells that play fundamental roles in homeostasis and host defense. Central to these functions is phagocytosis, a process by which macrophages recognize, internalize, and degrade apoptotic cells and invading microorganisms within phagosomes that mature through fusion with endo-lysosomal compartments. While phagocytosis is well described for small targets, macrophages frequently encounter microbes that exceed their internalization capacity yet remain critical for their control through poorly understood mechanisms. This is the case for Aspergillus fumigatus, an opportunistic fungal pathogen that rapidly germinates into long hyphae upon inhalation into the respiratory tract. If not controlled by resident macrophages, infection can become life-threatening. Our work investigates how macrophages adapt phagocytosis to contain non-phagocytosable A. fumigatus hyphae. Using multiple microscopy approaches, we challenged macrophages with hyphae (>50 µm) and followed their interactions over time. We found that macrophages tightly encapsulate hyphal tips in long-lasting structures termed hypha-holding phagocytic cups (H-PCs), which can remain engaged for over 24 hours. Although these open cups never fully seal around the hyphae, they undergo phagosome-like maturation, sequentially acquiring early markers (PI(3)P, Rab5) and late markers (Lamp-1, Rab7). Despite lacking acidification and hydrolytic activity, H-PCs restricted hyphal growth and damaged the fungal cell wall and membrane. This antifungal activity depended on sustained macrophage reactive oxygen species (ROS) production within H-PCs. Mechanistically, unlike canonical phagosomes, sustained ROS enrichment at H-PCs is not governed by PI(3)P. Instead, the phosphoinositide PI(3,4)P2 accumulates at hyphal tip engagements for hours and drives prolonged ROS production. This work demonstrates that macrophages can adapt phagocytosis when confronting non-phagocytosable hyphae.

Poster 13

# Binding of the Early Endosomal Antigen 1 (EEA1) to the Viral Protein 3 (VP3) Drives Organellar Remodeling and Trafficking of Virus-hijacked Endosomes

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Infectious bursal disease virus (IBDV) and infectious pancreatic necrosis virus (IPNV) are significant pathogens within the family Birnaviridae. These viruses place a heavy burden on the poultry and aquaculture industries and threaten food security; however, effective vaccines and antiviral therapies have yet to be developed for either. Birnaviruses display a unique architectural organization among dsRNA viruses. The genome is packaged into ribonucleoprotein complexes (RNPs) composed of the dsRNA, the polymerase VP1, and the multifunctional protein VP3. These RNPs function as the minimal units for both replication and transcription. In an interesting evolutionary departure, IBDV replicates in association with host endosomes. These endosomes harbor RNPs on their cytosolic leaflet and are localized to the perinuclear region of the cell, near the Golgi complex. Indeed, the moonlighting protein VP3 is the driver of RNPs localization, which depends on the early endosomal lipid PtdIns(3)P. In this work, we addressed the molecular mechanism behind VP3 association to endosomes, the role of VP3 in shaping organellar remodeling and trafficking, and whether there is conservation for this replication strategy across birnaviruses. Our results show VP3 binds to the PtdIns(3)P effector EEA1 and captures endosomes away from lysosomal degradation (VP3-Es), while favoring the docking of VP3-Es at the Golgi complex via ESCPE-1-mediated retrograde transport. Interestingly, IPNV too exploits endosomes for replication via PtdIns(3)P-VP3 interactions, although independently of EEA1. Overall, our work shed light on the pivotal role of VP3 in orchestrating the remodeling of intracellular compartments and trafficking to suit birnaviruses' need for establishing a replication hub.

**Poster 14**

# Expansion of the functional genomics GRACE library reveals genes relevant for temperature-dependent fitness in *Candida albicans*

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A small percentage of species in the fungal kingdom can cause devastating infections in humans, with Candida albicans reigning as a leading cause of systemic disease. One of the key virulence phenotypes for pathogenic fungi is the ability to survive at host body temperature; however, a comprehensive understanding of the mechanisms that orchestrate thermal adaptation in fungi remains incomplete. In this study, we expand the largest functional genomics resource in C. albicans, reaching 71.3% coverage of the entire genome, and perform screens under six different temperatures to identify genes important for temperature-dependent fitness. We describe the function of genes involved in translation (GAR1), splicing (C1_11680C or YSF3), and cell cycle progression (C6_00110C or RHT1) in enabling fungal survival at both low and high temperatures. Through experimental evolution, we also show that C. albicans can rapidly overcome deleterious mutations and adapt to extreme temperature environments. Overall, our study highlights the transformative potential of genome-wide functional genomics to uncover critical vulnerabilities in pathogenic fungi.

**Poster 15**

## Investigation of Heme Acquisition via a Bipartite TonB-Dependent Receptor System in *Acinetobacter baumannii*

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Acinetobacter baumannii is a gram-negative pathogen highly resistant to broad-spectrum antibiotics. This enables A. baumannii to persist in hospital environments—particularly intensive care units—where it accounts for up to 20% of all nosocomial infections and exceeds mortality rates of 20%. We aim to identify therapeutic targets within clinical A. baumannii strains by elucidating pathogenic mechanisms required for survival. Iron is critical for several biological processes, and bacteria must acquire essential nutrients from sources like heme, which constitutes the largest iron reservoir in humans. Previous research identified a high-affinity heme acquisition cluster in A. baumannii essential for virulence and mortality, which is composed primarily by two proteins termed HphA and HphR. HphA is a heme-binding protein, secreted into the extracellular matrix, which passively scavenges heme. HphR is an outer membrane protein that functions as a receptor for HphA and together work to transport heme across the outer membrane in a TonB-dependant manner. We hypothesize that heme acquisition presents an attractive therapeutic target in Acinetobacter baumannii, and elucidation of these pathogenic mechanisms will identify potential intervention targets due to the gaps in our understanding of A. baumannii iron uptake. Here in, I present a high-resolution structure of the holo HphA:HphR complex, which has been resolved by cryo-EM globally to 2.70Å. Structural insight of these proteins has accelerated research investigating the heme handoff mechanism from the hemophilin (HphA) to the transmembrane receptor (HphR). Further elucidation of heme acquisition built on this preliminary data can close gaps in our understanding of how these pathogens thrive, and support therapeutic research to combat multidrug resistant Acinetobacter baumannii.

**Poster 16**

# Characterizing the accessory proteins in novel rodent Embecoviruses

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Embecoviruses are a subgenus of betacoronaviruses that can infect a variety of mammalian species, including rodents, livestock, and humans. Well-studied viruses include mouse hepatitis virus, bovine coronavirus, and human coronavirus OC43, which causes seasonal respiratory disease in humans. We recently identified three novel Embecoviruses circulating in Peromyscus spp. in Ontario, Canada. These viruses are phylogenetically related to known pathogenic Embecoviruses.

Genome annotation of these novel coronaviruses suggests the presence of putative transcription-regulating sequences followed by multiple open reading frames, homologs of accessory proteins identified in other Embecoviruses. Understanding these accessory proteins is essential, as they have been shown to regulate virus-host interactions; for example, the NS2 protein in mouse hepatitis virus is type I interferon-induced and an antagonist that promotes viral replication.

In this project, we aim to characterize the functional roles of putative accessory proteins. Mammalian expression constructs were designed to emulate the architecture of the viral subgenomic RNA transcript. These constructs will be transfected, and protein expression will be evaluated by Western blotting. To determine subcellular localization, immunofluorescence confocal microscopy will be used in colocalization studies with known cellular markers. This work establishes a system to experimentally validate the expression of accessory proteins in novel Peromyscus coronaviruses. Ultimately, we aim to evaluate the role of these proteins during infection. Thus far, we have successfully isolated one of the three viruses, Highland Creek Peromyscus coronavirus, and will perform infection studies using host and other mammalian cell lines.

Poster 17

# A Systematic Review of Targeted Therapies for Helminthic Eosinophilic Meningitis: Implications for Refugee, Migrant, and Returning Traveller Populations

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Background: Helminthic eosinophilic meningitis (HEM) is a parasitic infection of the central nervous system, mainly caused by Angiostrongylus cantonensis, Gnathostoma spinigerum, and Baylisascaris procyonis. Refugees, migrants, and travellers from endemic areas are at increased risk due to contaminated food and water and may experience delays in diagnosis and treatment, leading to severe complications. There is currently no standardized treatment for HEM, resulting in varying outcomes. This systematic review assesses the effectiveness of targeted therapies for HEM.

Methodology: Following PRISMA guidelines, we conducted a systematic search of relevant databases for studies on HEM treatment outcomes. We assessed the risk of bias and evidence quality and then performed narrative and subgroup data analyses to evaluate treatment effectiveness.

Results: Preliminary findings indicate that the best outcomes result from a multimodal treatment combining supportive care, corticosteroids, and anthelmintics. Essential supportive interventions include lumbar punctures, pain management, and intravenous fluids. Corticosteroids like dexamethasone reduce immune damage, while albendazole treats A. cantonensis infections. However, B. procyonis cases can cause neurological deficits. Delayed diagnoses and limited healthcare access among refugees, migrants, and travellers increase morbidity and mortality.

Conclusions: HEM is an emerging health concern in Canada and other developed nations, primarily due to migration and travellers returning from endemic areas. Local cases also suggest HEM might be present in non-endemic regions. Effective management relies on early detection and targeted treatment, making it essential for physicians to be knowledgeable about HEM. Future research should focus on improving refugee health policies, enhancing clinician education, and establishing standardized treatment protocols.

**Poster 18**

## Unlocking the Biosynthetic Potential of *Streptomyces* Through Global Metabolic Regulation

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Streptomyces, a genus of filamentous bacteria, is a major source of bioactive compounds, producing over 50% of clinically relevant antibiotics. However, many biosynthetic gene clusters (BGCs) remain silent under standard conditions, limiting their potential for novel drug discovery. My research aims to unlock this latent potential by targeting global metabolic regulators. Our lab has identified two previously uncharacterized proteins in Streptomyces coelicolor: Srb, an RNA-binding protein, and FadR, a transcriptional regulator. Deleting srb and fadR activates multiple BGCs, including silent ones, and enhances secondary metabolite production. Srb appears to regulate gene expression through RNA binding, while FadR resembles a repressor of fatty acid degradation. We hypothesize that disrupting lipid metabolism increases short-chain acyl-CoAs—key precursors for secondary metabolites—thereby promoting their synthesis. Applying this approach to other antibiotic-producing strains could improve yields of important compounds and activate cryptic pathways for novel bioactive molecules. Furthermore, characterizing Srb may uncover new small RNAs and deepen our understanding of post-transcriptional regulation in Streptomyces. This work provides a strategy to both enhance antibiotic production and address the urgent need for new drugs in the face of rising antimicrobial resistance.

**Poster 19**

## Phagocytic oxidative burst and intracellular *Leishmania braziliensis* differentiation: A paradoxical ally?

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Leishmania spp. protozoa are the etiological agent of Leishmaniasis, a vector borne tropical neglected diseases that affects 12 million people annually worldwide. The disease presents a broad spectrum of clinical manifestations, ranging from self-healing cutaneous lesions to fatal visceral forms. In infected mammalian host, Leishmania resides primarily inside macrophages, where they establish a niche known as parasitophorous vacuole. Within this compartment, parasites undergo structural and molecular changes, differentiating from the flagellated promastigote form into the rounded and non-flagellated amastigote, adapting itself for intracellular survival and subsequent infections. However, the early signaling events that orchestrate parasite entry and amastigogenesis remain unclear. In this study, we followed the internalization of Leishmania braziliensis into macrophages and observed that uptake is predominantly driven by the parasite's flagellum. This entry mechanism is associated with actin-rich long-lasting phagocytic cups that tightly engulf the flagella. Using high resolution imaging, we showed that these structures acquired both early and late endosomal markers, and their remodeling at the entry site may contribute to the establishment of a permissive niche for intracellular development. We further detect a durable, localized and robust production of reactive oxygen species (ROS) consistent with the host's oxidative burst triggered by parasite recognition at the phagocytic cups. However, the oxidative burst seems not to compromise the parasite internalization and further differentiation in these vacuoles. Notably, impairing the macrophage ability to generate ROS either through pharmacological inhibition or genetically deficiency in NAPDH oxidase complex components using p22phox knockouts macrophages, L.braziliensis failed to differentiate into amastigotes. Altogether, our findings indicate that the exposure of L. braziliensis to reactive oxygen species may play a role in their intracellular proliferation, attesting the complexity of this early hostparasite interaction in the establishment of the infection.

**Poster 20**

# A Systematic Review of Lifestyle Interventions for Neuropathy and Neuropathic Pain: Alcohol Consumption and Avoidance

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Background: Neuropathy and neuropathic pain (NP) are globally prevalent, remain difficult to manage, and are often exacerbated by underlying lifestyle factors. Alcohol use, particularly in the context of chronic consumption or dependence, is a recognized contributor to peripheral nerve damage, yet its association with neuropathy/NP has not been systematically evaluated. This systematic review synthesizes the current evidence on alcohol exposure, including quantity, frequency, and dependency, and its effect on the incidence, prevalence, and severity of neuropathy/NP. Methods: This systematic review included observational studies assessing alcohol consumption patterns or dependence in relation to neuropathy/NP outcomes and was conducted in accordance with PRISMA guidelines. Exposure types were analyzed independently, and pooled odds ratios and relative risks were generated when sufficient data were available. The review was registered with PROSPERO number 484158. Results: Following de-duplication and exclusions, 76 studies were included, comprising cohort (n=15), case-control (n=12), and cross-sectional (n=49) designs. While associations varied by study design and exposure category, alcohol dependence and consumption were more consistently linked with in-creased neuropathy incidence and severity, including electrophysiological evidence of compromised function. Notably, in studies examining alcohol cessation, abstinence was linked to clinical improvements in neuropathy/NP symptoms such as {burning paresthesia, weakness….}. While heterogeneity and risk of bias were present, largely due to the subjective classification of alcohol exposure and a lack of universally applied objective neuropathy measurement tools, multiple pooled estimates reached statistical significance. Conclusion: Evidence supports a potential role of alcohol use, especially dependence, in the development and progression of neuropathy/NP. Abstinence may offer therapeutic benefit, though further abstinence- and/or harm reduction related interventional studies are required to clarify causality and guide low-cost, adjunctive strategies for alcohol-related neuropathy/NP.

**Poster 21**

# Targeted Pharmacological Interventions for the Prevention and Treatment of Viral Hemorrhagic Fever: A Systematic Review of Updated Intelligence from the 74th Annual Meeting of the American Society of Tropical Medicine and Hygiene

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Background: Viral hemorrhagic fevers (VHF) are high-consequence, life-threatening illnesses characterized by systemic disease, hemorrhage, and high mortality. The American Society of Tropical Medicine and Hygiene (ASTMH) Annual Meeting functions as a major international forum for the presentation of emerging data on infectious diseases, including novel pharmacologic and biologic interventions for VHF. However, while ASTMH presentations provide timely and high-impact insights, there is no consolidated synthesis of this rapidly evolving evidence base. Given the acute, outbreak-prone nature of VHF and the need for rapid translation of emerging data into clinical and public health practice, a structured synthesis of these data is warranted.
Methods: This systematic review follows PRISMA guidelines and is limited to presentations delivered at the ASTMH Annual Meeting in Toronto (November 9-13, 2025) in order to capture evolving evidence as it emerges. Titles and abstracts were screened for inclusion and eligible symposia, oral presentations, and poster abstracts, attended in person, will undergo data extraction. Studies of all designs evaluating vaccines, chemoprophylactic agents, or targeted biological therapies for the prevention or treatment of VHF in adults and children will be included. Methodological quality will be assessed using the GRADE framework, with risk of bias evaluated using JBI tools.
Results: Data will be extracted on incidence of VHF among exposed populations, safety, toxicity, and tolerability of preventive and therapeutic interventions, and morbidity and mortality outcomes among treated individuals. Secondary outcomes will include hospitalization length-of-stay, economic outcomes, and measures of feasibility, acceptability, accessibility, and health equity. Currently, 11 abstracts have been identified for final inclusion and data synthesis.
Discussion/Conclusion: This systematic review will provide a rapid, structured synthesis of targeted pharmacological interventions presented as emerging evidence at an expert scientific venue, while addressing the current lack of a consolidated accessible summary of emerging VHF evidence. By rapidly organizing and evaluating these data, this work facilitates timely interpretation and application in clinical and public health settings where rapid decision-making is critical.

**Poster 22**

# A case of concurrent dengue and *Plasmodium vivax* malaria in a returned traveler to India: Case report

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Background: Dengue and malaria are common vector-borne diseases and are associated with high morbidity and mortality. Co-infection of malaria and dengue is underestimated due to the parsimonious approach to testing once the diagnosis of either is made.

Objective: We present a case of dengue and Plasmodium vivax co-infection in a returned traveller from an endemic region.

Case Summary/Methods: A 27-year-old man of Indian origin from Southern Ontario took a 2-week trip India to visit his friends and relatives (VFR) and developed fatigue, myalgia, headache and generalized weakness 10 days following his return. He presented to the emergency department (ED), when his symptoms worsened with fever and chills and his complete blood count was notable for mild anemia with moderate lymphopenia of 0.3109/L and profound thrombocytopenia of 66 109/L.

Results: The initial work up by rapid diagnostic test for malaria demonstrated non-falciparum malaria and thin smear showed a parasitemia level of 0.7%. Along with infectious investigations including blood cultures and serologic testing for dengue virus, he was started on Atovaquone/proguanil 1000/400mg daily for 3 days. While seen in follow-up 5 days after discharge for ED, his malaria was identified as P. vivax. As such, he was started on primaquine phosphate 30-mg PO daily for 14 days as radical cure. His dengue serologic test reported reactive for IgM and IgG ELISA, confirming the diagnosis of malaria and dengue co-infection. He was clinically stable without bleeding manifestations and repeat parasitemia was 0% with resolution of deep thrombocytopenia.

Conclusion: Dengue and malaria concurrent infection might be commoner than previously estimated. Patient presenting with either infection acquired from an endemic area for both along with low parasitemia level, moderate to severe thrombocytopenia and leukopenia and bleeding manifestations might clues for concurrent infection.

**Poster 23**

# Characterization of Epstein-Barr Virus LF1 protein and its Contribution to Oncogenesis

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Epstein-Barr Virus (EBV) infects >95% of adults and is a causative agent for several diseases including infectious mononucleosis, multiple sclerosis and several cancers. While EBV-induced tumour cells are latently infected, they also express select lytic EBV transcripts, suggesting that the encoded proteins contribute to oncogenesis. These include a transcript encoding the uncharacterized lytic protein, LF1. We have found that LF1 is expressed late in lytic infection, and that knocking out LF1 impairs late protein expression and virion production. To gain insight into cellular interactions of LF1, we performed affinity purification-mass-spectrometry (AP-MS) and discovered that LF1 interacts with Rae1 and Nup98, components of the nuclear pore complex with roles in mRNA nuclear export. Interestingly, LF1 homologues in Kaposi's Sarcoma-Associated Herpesvirus (KSHV; ORF10) and Murine Gammaherpesvirus 68 (MHV-68) have also been found to interact with Rae1/Nup98 and to inhibit nuclear export of a subset of host mRNAs, including transcripts encoding tumor suppressors, suggesting an oncogenic mechanism. To determine if this is also true for LF1, we performed Poly(A) fluorescence in situ hybridization (FISH) and confirmed that LF1 causes mRNA nuclear retention. Based on homology with ORF10, we designed an LF1 mutant that is defective in Rae1/Nup98 binding, and found that this mutant was defective in mRNA nuclear retention and nuclear membrane localization. To ascertain which cellular mRNAs are affected by LF1, we performed mRNA-Seq on nuclear and cytoplasmic fractions. We are currently analyzing this data to determine how LF1 may be contributing to viral infection and oncogenesis by affecting mRNA nuclear export.

# Perceptions of Canadian vaccination-involved health professionals regarding adult vaccination

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Understanding the perceptions and barriers faced by vaccination-involved health professionals (VHPs) may help identify strategies/programs to improve adult vaccine coverage. We conducted a 22-question online survey asking VHPs questions regarding their perceptions on current adult immunization coverage, barriers to improving coverage, and the creation of a simplified life-course vaccination schedule. The survey was disseminated by 16 Canadian professional organizations with VHP members between 9/6/2025 and 14/1/2026.

We received responses from 541 individuals to the initial question regarding vaccine coverage, with 331 completing the survey. Respondents comprised 40% nurses/nurse practitioners, 15% pharmacists, 19% physicians, 9% public health staff and 17% others; 84% were vaccine providers/prescribers. 86% (463/541) of respondents stated it was “very important” or “important” to increase adult vaccination coverage, commonly citing improvement to health (58%), herd immunity (18%), and reduced healthcare burden (16%). Barriers specified included funding for public health (82%), access to primary care (92%), education of public (95%) and providers (87%), surveillance (89%), and vaccine registry availability (88%). Overall, 68% (224/331) of respondents (80% were vaccine providers/prescribers) perceived that vaccinators have difficulty navigating the definitions of eligibility for respiratory vaccines, and 72% of them (162/224) believed that this difficulty reduces the likelihood of vaccine recommendation. Additionally, 65% (146/224) believed that this problem could be solved by a single comorbidity list defining eligibility for respiratory vaccines. Overall, 72% (252/331) respondents agreed that a simplified life-course vaccination schedule would be possible for some or all adult vaccines, 89% (296/331) believed it would increase vaccine coverage, and 82% (243/296) believed that the benefits would outweigh the potential harms and costs. VHPs in Canada agree that improving adult vaccine coverage is important. There was substantial but incomplete consensus that a consolidated list of co-morbidities defining

eligibility for respiratory vaccines and a simplified life course vaccine schedule would improve vaccine coverage.

Poster 25

# Estimating the Health System Burden of a Potential H5NX Influenza Pandemic in Ontario, Canada: A Microsimulation Model

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Avian influenza viruses of the H5NX subtype pose a growing risk of zoonotic spillover and human pandemic due to increasing mammalian adaptation, highlighting urgency for preparedness. We estimated the impact of a potential H5NX pandemic on health system resources in Ontario to inform resource allocation planning.

We developed an integrated transmission–discrete event simulation (DES) model of influenza spread and associated healthcare utilization in Ontario's adult population (n=16,258,260). A compartmental Susceptible–Infected–Recovered model was used to estimate daily infections over one year under seven hypothetical epidemiologic scenarios defined by combinations of transmissibility and clinical severity, assuming no public health interventions. The base case reflected a high-transmission, low-severity scenario based on the 2009 H1N1 pandemic. The outputs informed a patient-level DES simulating healthcare use, including emergency department (ED) visits, ward and intensive care unit (ICU) admissions, mechanical ventilation (MV), and antiviral use. Patients waited for unavailable resources, while those requiring MV without access were assumed to die. Analyses were conducted in R version 4.4.3; simmer package.

Our base case estimated 466,859 H5NX infections over one year, resulting in 1,885 deaths (case fatality rate [CFR]=0.4%), with estimated 10,052 individuals presenting to EDs and requiring antiviral medications. Resource demand did not exceed Ontario's health system resource capacity. Across scenarios, capacity exceedance was driven by clinical severity: ward capacity was exceeded only in a high-transmission, moderate-severity scenario, whereas ICU and MV capacity were exceeded in all moderate- to high-severity scenarios. Peak demand reached 3,652 ICU beds and 2,202 ventilators (vs. 600 and 175 available, respectively), resulting in up to 5,032 additional deaths due to MV unavailability.

An unmitigated H5NX pandemic would substantially exceed Ontario's acute care capacity under plausible high-severity or high-transmission epidemiologic scenarios,

emphasizing the need for early intervention planning. This analysis provides a foundation for assessing potential mitigation strategies.

Poster 26

# Attenuating Influenza A Virus Infection with Alveolar-like Macrophages

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Background: Influenza A virus (IAV) infects 1 billion people annually, resulting in 300 000 to 650 000 deaths. One of our body's first lines of defence to combat respiratory pathogens are alveolar macrophages (AMs), which clear our airways of foreign particles. Stem cell-derived alveolar-like macrophages (ALMs) have been generated to phenotypically represent endogenous AMs in vitro. ALMs attenuated respiratory syncytial virus infection in vitro and in vivo, but the full breadth of ALM therapeutic capacity towards IAV has yet to be determined.

Methods: MLE-15 and ALM cells were infected with PR8 IAV at 1 MOI for 6, 16, and 24 hours. IAV infection was measured using a 50% tissue culture infectious dose (TCID50) assay on infected cell supernatants. PCR and Western blot were conducted to verify the expression and production of IAV genes and proteins. Immunocytochemistry (ICC) was performed to allow for visualization of the presence of virions within the cell. Male 6–8-week-old C57/Bl6 mice were then instilled with 0, 2 million, or 4 million ALMs one day prior to a 100 pfu challenge of IAV.

Results: Log TCID50/mL values show that ALMs reduce IAV titers at 16 hours to 0 from ~106 in MLE-15 cells. Upon PCR and Western blot analysis, we observe similar transcript and protein abundance across all cell types. These findings were confirmed by ICC, which showed that IAV is found in every infected cell type. In vivo, IAV titers in mice lungs were reduced to 0 from ~105 TCID50/g of lung when prophylactically instilled with either 2 million or 4 million ALMs.

Conclusions: ALMs internalize IAV in a manner that allows viral reproduction but prevents the release of new virions to infect other cells in vitro and in vivo. The mechanism by which ALMs halt the IAV life cycle remains to be determined.

**Poster 27**

## Vaginolysin-mediated pathogenic differences among *Gardnerella* in bacterial vaginosis

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The vaginal microbiome is optimally dominated by Lactobacillus bacteria. In contrast, diversity increases in bacterial vaginosis (BV) as anaerobic bacteria, primarily Gardnerella species, overgrow. BV affects 1/3 of reproductive-age women globally, it presents with symptoms such as abnormal vaginal discharge, and it also increases the risk of contracting sexually transmitted infections. Gardnerella secrete vaginolysin (VLY), a cytolysin that lyses host epithelial and red blood cells. VLY levels are increased during BV causing damage to the vaginal epithelium. Interestingly, over 50% of BV cases are asymptomatic; this anomaly suggests that all Gardnerella are not equally pathogenic. Gardnerella are a genetically diverse multi-species bacterial group. My project explores vaginolysin-mediated cytotoxicity differences among Gardnerella species to improve our understanding of their diversity and role in BV clinical outcomes. To investigate Gardnerella's cytotoxic diversity, I am using a collection of over 200 Gardnerella isolates from the vaginal samples of a cohort of Kenyan women that I have cultured and genetically categorized. Vaginal epithelial cells treated with cell-free supernatants (CFS) from diverse Gardnerella isolates demonstrate variability in cytotoxicity, which is not conserved to a single species. All cytotoxic Gardnerella encode vaginolysin (vly). However, there are vly-encoding non-cytotoxic isolates that exhibit a lower expression of VLY in their CFS compared to cytotoxic isolates. Gardnerella rely on glycogen for vaginal colonization; this carbon source and others increase VLY secretion from a subset of Gardnerella isolates. In contrast, there are some highly cytotoxic isolates that do not require increased carbon availability to produce high VLY levels. These results highlight pathogenic diversity among Gardnerella species; from encoding vly, to diversity in cytotoxicity among vly-encoding isolates and their cytotoxic regulation. Therefore, which Garderella are present during BV, and their abundance may play a role in the variable manifestation of symptoms mediated by Gardnerella.

**Poster 28**

# Exploring the use of saliva for the detection of Group A *Streptococcus*

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Background: Streptococcus pyogenes (Group A Streptococcus, GAS) is a gram-positive bacterium that causes infections ranging in severity from pharyngitis to necrotizing fasciitis. The gold standard for detecting GAS pharyngitis is a throat bacterial culture, but those tests can take 24-48 hours to produce results, delaying treatment.

Objective: Compared to throat swabs, saliva specimens are less invasive, can be easier to collect, and are often more tolerable for pediatric patients. The goal of this study was to assess the effectiveness and use of saliva samples for the detection of GAS using molecular methods for the diagnosis of pharyngitis.

Methods: This prospective cohort study recruited patients under the age of 19 from the SickKids Emergency Department (ED) who presented with pharyngitis and had a GAS bacterial throat culture collected based on clinician judgment. Participants provided a bacterial throat swab and/or saliva sample following routine clinical recommendations. 200 saliva samples underwent molecular testing for the detection of GAS and cycle threshold (CT) values were recorded. Specificity and sensitivity were calculated, and statistical tests were run to evaluate correlation coefficients.

Results: Using throat culture results as a reference, testing of saliva samples yielded a sensitivity of 94.4% and a specificity of 92.2%. A Pearson correlation test result of -0.44 reflected a moderate relationship between high CT values and negative throat cultures, and low CTs and positive results.

Conclusions: We found that saliva was a reliable method to diagnose GAS pharyngitis using molecular methods in place of throat swabs. Saliva specimens were a non-invasive alternative, providing accurate and timely results for Group A Streptococcus pharyngitis detection in ED patients.

**Poster 29**

# Predicting Fluoroquinolone Resistance in *Shigella* Using Interpretable Machine Learning and Whole Genome Sequencing

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Background: Antimicrobial resistance (AMR) is increasingly compromising the effectiveness of first-line therapies for Shigella, including ciprofloxacin (CIP), levofloxacin (LEV), and trimethoprim–sulfamethoxazole (TMP SMX). Although conventional antimicrobial susceptibility testing remains the reference standard, it is labor-intensive and can delay timely clinical decision-making. Whole-genome sequencing (WGS), combined with machine learning (ML), offers a promising alternative for rapid prediction of AMR directly from genomic data. In this study, we employed an integrated WGS–ML framework targeting resistance to fluoroquinolones (ciprofloxacin and levofloxacin).

Methods: We analyzed 1,719 Shigella isolates (2018–2025) tested by Public Health Ontario (PHO), combining phenotypic susceptibility results with WGS data. A custom pipeline identified resistance-associated genes, from which 11-nucleotide k-mers were extracted and linked to corresponding susceptibility phenotypes (resistant or susceptible). K-mers were generated from established genetic targets implicated in fluoroquinolone resistance, including chromosomal quinolone resistance–determining regions (QRDRs) within gyrA and parC, as well as plasmid-mediated resistance genes (qnr). Unique genomic features were compiled into a feature matrix to train ML classifiers, including Random Forest (RF), logistic regression, XGBoost, and SVM, evaluated using standard performance metrics. Comparisons were made between models incorporating only chromosomal markers and those integrating both chromosomal and plasmid-associated determinants.

Results: CIP and LEV resistance was observed in 40% (CIP) and 51% (LEV) of isolates. Inclusion of plasmid-mediated resistance features led to improved predictive accuracy compared with chromosomal-only models. The RF model for CIP achieved high predictive performance: sensitivity 0.924, F-1 score 0.956, and AUC of 0.976, indicating robust discrimination between resistant and susceptible isolates. LEV model evaluation is ongoing. SHAP-based interpretation highlighted influential k-mers mapping to known QRDR regions in gyrA and parC, reinforcing biological plausibility.

Conclusion: An integrated WGS-ML framework shows promise for rapid AMR prediction in Shigella. Applying this strategy within genomic surveillance systems could support early detection of fluoroquinolone resistance and guide evidence-based treatment decisions.

Poster 30

# Rifampin-Ofloxacin-Minocycline (ROM) for the Treatment of Paucibacillary Leprosy: A Systematic Review

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Leprosy is a complex tropical infection from a diagnostic and management perspective, as patients with leprosy are at risk of numerous related complications from the disease itself and its treatment. Standard WHO multi-drug treatment (MDT) consists of medications that are potentially harmful and cause a range of adverse systemic effects.

Monthly- or single dosing of combined rifampicin, ofloxacin, and minocycline (ROM) has emerged as a potential treatment option for leprosy, however, a recent synthesis of the evidence supporting ROM does not exist. Paucibacillary leprosy, characterized by limited skin lesions and a low bacillary load, may be most amenable to a fluoroquinolone-based treatment protocol.

We performed a systematic review of relevant literature to evaluate the safety and efficacy of ROM-based treatment for paucibacillary leprosy. The systematic review will focus on assessing and reporting on the efficacy, and safety of monthly ROM in the treatment of paucibacillary leprosy within a human population. 1,201 records were retrieved for title and abstract screening, however, after a multi-step de-duplication pipeline, 625 articles remained. Thus far, 28 articles have been identified for final inclusion, however screening remains ongoing.

Results: Interim findings suggest that patient lesion clearance and treatment failure is greater in the comparator group (+4.69% and +2% respectively), and that relapse, side effects, and reversal reactions are more frequent in the ROM group (+0.39%, +0.42%, and +8.15% respectively). This suggests that ROM may be slightly less efficacious than its comparator, however, a more robust analysis is necessary. Determinants of health identified in the treatment of leprosy include social environments, patient education, health services, gender, and income.

Synthesizing the current evidence discussing the efficacy of monthly ROM, will strengthen the current body of knowledge surrounding the treatment of paucibacillary leprosy, and may allow for the development of standardized fluoroquinolone-based treatment protocols.

Poster 31

# Leptospirosis Acquired by Recreational Freshwater Exposure: A Systematic Review

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Leptospirosis is a globally distributed zoonosis with potentially severe outcomes, increasingly associated with recreational freshwater exposures. Despite mounting recognition of transmission via activities such as swimming, rafting, and kayaking, a systematic evaluation of its epidemiological profile and global burden of has yet to be conducted.

A systematic review was conducted in accordance with PRISMA guidelines to identify and appraise studies describing leptospirosis acquired through recreational freshwater exposure. Comprehensive database searches were performed in PubMed, MEDLINE, Embase, and Scopus using controlled vocabulary and keyword strategies related to leptospirosis and leisure water activities. Additional grey literature was sourced via targeted searches in Google and Google Scholar. Eligible studies included those involving human participants with a confirmed diagnosis of leptospirosis and a clearly documented recreational freshwater exposure. Studies focused exclusively on occupational, flood-related, or animal-associated exposures were excluded. Title and abstract screening, followed by full-text review, was completed independently by a team of reviewers, with discrepancies resolved through consensus or third-party review.

A total of 1,535 records were identified after deduplication. After screening 805 titles and abstracts, 316 full texts were assessed for eligibility. 116 studies met inclusion criteria. Exclusions were primarily due to non-recreational exposure (n = 23), review-only format (n = 63), insufficient exposure detail (n = 58), non-human subjects (n = 43), or ineligible study design (n = 7). Data extraction is ongoing and will include study design, types of recreational activity, diagnostic methods, clinical manifestations, preventive or therapeutic intervention and outcomes.

This is the first systematic review to comprehensively examine leptospirosis linked to recreational freshwater exposure. By consolidating evidence across diverse activity types and regions, this review will support improved clinical recognition, pre-travel counseling, and public health prevention strategies.

**Poster 32**

## Developing Novel Pro-Insecticides to Kill Mosquito Vectors of Disease

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Mosquitoes kill over 700,000 people annually and sicken 100s of millions more via the transmission of disease. Alarmingly, disease-transmitting mosquitoes like A. gambiae and A. aegypti have evolved resistance to commonly used insecticides, which we rely heavily upon to control mosquito populations and limit the spread of vector-borne diseases. A key mechanism of insecticide resistance is through the upregulation of detoxifying enzymes called cytochrome P450s. The Roy lab has previously identified a novel class of nematicides that are selectively bioactivated by nematode P450s into lethal metabolites. We have shown that heterologous expression of the nematode P450 responsible for bioactivation in yeast S. cerevisiae can recapitulate P450-dependent metabolism and lethality in yeast. Using yeast to express individual P450s from A. gambiae and A. aegypti, we have developed a pipeline to identify similarly P450-bioactivated candidate insecticides that selectively kill mosquitoes, weaponizing their P450 upregulation against them. A screen of 6,274 small molecules identified 8 structurally distinct molecules that selectively kill yeast expressing a P450 from both A. gambiae or A. aegypti. We have generated and tested over 50 analogs of our hits in our yeast assay and have moved a total of 20 structures to tests against adult mosquitoes and larvae. Our technology holds the potential to identify new molecules to selectively control insecticide-sensitive and resistant mosquitoes.

Poster 33

# The Epstein-Barr virus protein BMRF1 recruits the host NuRD complex to promote viral lytic genome replication

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Epstein-Barr virus (EBV) is a ubiquitous herpesvirus that infects ~90% of humans, and is causatively associated with infectious mononucleosis, multiple malignancies, and multiple sclerosis. EBV alternates between latent and lytic infectious cycles, the latter of which involves expression of ~70 proteins leading to viral genome amplification at nuclear replication centers and virion production. The BMRF1 lytic protein localizes to replication centers and serves an essential role as the processivity factor for the viral DNA polymerase. BMRF1 also has an additional role in activating the transcription of some EBV late genes. Through affinity-purification coupled to mass spectrometry, we determined that BMRF1 interacts with the cellular NuRD (nucleosome remodelling and deacetylation) complex, which affects cellular gene expression and DNA repair through chromatin modifications. We showed that BMRF1 binds the MTA2 and RBBP4 NuRD subunits through a consensus motif, and that point mutation of this motif in BMRF1 (RK mutant) abrogates NuRD binding and transcriptional activation by BMRF1 (2019 J Virol.93:e01070). In addition, NuRD subunits co-localize with BMRF1 at viral replication centers, prompting us to investigate the importance of NuRD in EBV DNA amplification. Silencing of NuRD subunits decreased EBV genome amplification and impaired late gene expression. Additionally, studies comparing EBV virus containing the BMRF1 RK mutation to WT virus showed that NuRD localization to replication centers and lytic genome amplification are both significantly reduced. The results indicate that BMRF1 recruits NuRD to EBV replication centres, where it contributes to viral genome amplification and transcriptional activation, likely through its chromatin remodelling effects.

**Poster 34**

# Optimizing the Vaginal Microbiome in Black Women from Toronto, Canada: Defining Clinical Endpoints and Community Priorities

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Background: Bacterial vaginosis (BV) involves a microbial shift from an optimal, Lactobacillus-dominant state (e.g., L. crispatus) to a diverse, high bacterial load state (e.g., Gardnerella, Prevotella) associated with inflammation, increased HIV risk and preterm birth 1,2. Diagnosis varies across clinical (Amsel), microbiological (Nugent), and sequencing-based (molecular) methods 3,4,2. Notably, molecular BV is 2–3 times more prevalent among Black women in North America 5,6. Despite the absence of symptoms such as abnormal discharge and/or odour, many women in this demographic frequently exhibit varied levels of inflammation. Research specifically detailing symptoms of vaginal health in Black women is limited. It also remains unclear if BV-related symptoms are driven by the bacteria themselves or the host's variable inflammatory response.

Objective: This study aims to characterize Black women's perspectives on vaginal health and the acceptability of future interventions. Additionally, it investigates the interplay between vaginal symptoms, genital inflammation and microbiome composition among Black women with molecular BV to better understand pathogenesis and inform future clinical trials that will optimize vaginal health in Black women.

Method: A mixed-methods approach will be used. Qualitative data will be collected through 9 focus groups (5–8 per group) with Black cisgender women, women who primarily have sex with women, and Black men who are sexual partners of Black women. Discussions will explore perceptions of vaginal health and intervention preferences. Data are analyzed via thematic analysis. 200 HIV-uninfected Black women will be enrolled through a community health centre in Toronto, providing cervicovaginal secretions via SoftCup and completing a questionnaire. The microbiome will be characterized using 16S rRNA sequencing and qPCR, while inflammation is quantified by measuring pro-inflammatory cytokines (e.g., IL-1α, IL-1β, IP-10) using Meso Scale Discovery

Progress and Expected Results: Qualitative data collection is nearing completion, and sample collection is ongoing. We anticipate a molecular BV prevalence of 40% and genital inflammation in 50% of participants. Through mediation analysis, we hypothesize that both traditional and newly defined vaginal symptoms will correlate more strongly

with inflammation than with molecular BV status alone, suggesting that the host immune response is the primary driver of symptom experience.

Poster 35

# Evolutionary insights and genomic analysis of betacoronaviruses in wild Peromyscus mice and other terrestrial small mammals

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Coronaviruses (CoVs) are diverse RNA viruses infecting a wide range of hosts; many are important pathogens of humans and domestic animals. Certain human and livestock CoVs are thought to have rodent origins. Surveillance for rodent CoVs in North America remains limited, particularly in Canada. Through the Wildlife Emerging Pathogens Initiative (WILD-EPI), we surveyed wild rodents and eulipotyphlans in Ontario, Canada. We detected four species of beta-CoVs across host species and geographic location suggesting potentially low barriers to cross-species transmission among myomorphan rodents. Whole Peromyscus CoV (PCoV) genomes were recovered from Peromyscus mice, which were highly related to important human and animal Betacoronavirus gravedinis viruses (e.g., human coronavirus OC43, bovine coronavirus [BCoV]). We identified at least three PCoV genotypes resulting from recombination with other B. gravedinis viruses, suggesting cross-species transmission events have occurred. We found high similarity of predicted sialoglycan-binding sites on the spike glycoprotein structure for PCoV, OC43, and BCoV. This study highlights the need for continued viral discovery to further support investigation of CoV evolution and ecology in North American terrestrial small mammals.

**Poster 36**

## Characterization of the divergent white-tailed deer-derived SARS-CoV-2 lineage B.1.641 virus, from field to phenotype

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We previously identified a highly divergent SARS-CoV-2 lineage (B.1.641) in white-tailed deer in Ontario reflecting protracted and sustained viral transmission among deer. In addition, this lineage clustered with a geotemporally-related human case, suggestive of deer-to-human transmission. We sought to determine the biological implications of this variant for across host species, including humans. Entry assays revealed that virus-like particles (VLPs) harboring spike proteins from both deer and human-derived B.1.641 variants were able to enter cells expressing either human angiotensin-converting enzyme-2 (hACE2) or deer ACE2 (dACE2). We also demonstrate that B.1.641 replicates efficiently in continuous cell lines, human-derived ex vivo models, and golden Syrian hamsters to comparable titres of D614G (wild-type SARS-CoV-2). However, transmission of B.1.641 by the respiratory route was reduced following 4 hour exposure in the hamster model. These findings suggest that while B.1.641 is capable of infecting and replicating in non-deer hosts, implications for human health may be limited in the absence of enhanced viral replication, pathogenesis or transmission.

Poster 37

# Association of SARS-CoV-2 Omicron Variant Ct values at admission with hospitalization outcomes

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Introduction: Cycle threshold (Ct) values generated during diagnostic testing for SARS-CoV-2 infection have been evaluated as proxies for viral load and predictors of hospitalization outcomes. Most studies were conducted early in the pandemic. It remains uncertain whether these associations apply to Omicron–infected patients. We examined the association between Ct values at hospital admission and outcomes during Omicron.

Methods: Adults hospitalized with respiratory illness at three hospitals during the 2022/2023 winter season were enrolled. Ct values from the first nasopharyngeal swab (NPS) obtained were analyzed. Clinical data were extracted from chart review and patient interview. Outcomes included the composite of death or ICU admission and hospital length of stay (LOS). Associations were assessed using multivariable regression models. For patients with more than one NPS, change in Ct was also assessed.

Results: Among 201 patients, the median age was 81 years (IQR 73–87): 7.4% required ICU admission and 4.0% died; 10.4% met the composite outcome. Median LOS was 6 days (IQR 3-11). Median Ct value of first NPS was 22.6 (IQR 18.4–25.7). In univariate analyses, Ct values increased with days since symptom onset (β=0.27 Ct/day; 95% CI 0.08–0.47; p=0.007) and decreased with age (β=−0.08 Ct/year; 95%CI −0.14- −0.01; p=0.02). Ct value was not associated with mortality/ICU admission ( OR 1.06; 95%CI 0.96–1.20; p=0.24), or LOS (−0.97%; 95%CI −3.40%-1.50%; p=0.43). In 180 patients with 2 NPS, median Ct change was 4.53 per day (IQR 1-8.46). Decline in Ct from 1st to 2nd NPS was not associated with mortality or ICU admission (OR 0.97; 95% CI 0.93–1.00; p=0.15) but was associated with a small decrease in hospital length of stay (−1.1%; 95% CI −2.11% to −0.11%; p=0.03).

Conclusion: In this Omicron-variant infected hospitalized cohort, admission Ct values were not associated with mortality, ICU admission, or hospital length of stay.

**Poster 38**

## Identifying EBV-Conditional Host Fitness Genes to be used as targets for drug development to treat EBV-associated diseases

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Epstein-Barr Virus (EBV) is a widespread virus which infects more than 90% of the human population. It persists as an episome, where it establishes a lifelong latent infection in memory B-cells. There are different EBV latency states that are implicated in various diseases, including multiple sclerosis and different types of cancers. Despite its prevalence and association with several diseases, there are currently no approved vaccines or drugs specifically targeting EBV. Therefore, we propose a novel approach by leveraging the concept of synthetic genetic interactions, which aims to target EBV infected cells via targeting host genes that become essential or important for cell fitness due to EBV infection. Using a synthetic drop-out genome-wide CRISPR screen, I have identified EBV-conditional host fitness genes that could be used as a potential druggable targets for the elimination of the EBV-infected cells that cause EBV-associated diseases. In my screen, three main pathways were identified: RNA processing, actin nucleation and cell cycle. Finally, 13 hits were prioritized for validations including METTL3 and METTL14 that were found to have a role in EBV tumorigenesis in both epithelial and B-cells. In addition, I aim to uncover the mechanism of how EBV hijacks the METTL3/14 complex and other complexes to promote cell survival.

Poster 39

# Toward Hospital-Ready Solutions: Applying Dry-Surface Biofilm Models to Evaluate Micro-topographical Glove Modifications

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Hospital-acquired infections (HAIs) remain a serious problem within our healthcare systems, stretching healthcare resources and drastically affecting patient health. These infections are caused by a wide variety of microorganisms, including the continuing rise of antimicrobial-resistant species. Pathogenic transmission within hospitals occurs primarily through contact between infected and uninfected persons and the surfaces within their environments, with fomite surfaces playing a central role in the persistence and spread of pathogens.

Traditional laboratory models of surface contamination use droplet suspensions or wet biofilm inoculations, which may not accurately reflect the dry conditions of real fomite surfaces. Dry-surface biofilms (DSBs) represent a clinically relevant model, which replicates the desiccated, surface-associated microbial communities commonly found on fomites. In this study, DSBs of Staphylococcus aureus and Klebsiella pneumoniae were established on acrylonitrile butadiene styrene (ABS) and stainless steel to evaluate the capacity for micro-topographically modified medical gloves to reduce the force-dependent transmission of microbial cells under these realistic conditions.

Results demonstrated that micropost microtopographies (10 μm diameter) exhibited log reductions of 1.32 to 2.02 for S. aureus and 1.48 to 1.72 for K. pneumoniae. For straight-walled grooves (15 μm groove width), slightly lower but comparable reductions between 0.96 to 1.55 log were achieved. The degree of pathogen transfer observed from these DSBs was strongly dependent on the force of contact, with higher applied forces consistently associated with greater microbial transmission across all modifications tested. Notably, these findings are consistent with previously reported wet transmission results at equivalent contact forces. These results highlight the translational potential for micro-topographical surface modification of medical gloves in real healthcare settings, where dry-surface persistence represents one of the most significant drivers of pathogen transmission.

**Poster 40**

## Who Sustains the System? Disability, Care, and Inequities in Pandemic Response

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The COVID-19 pandemic exposed critical gaps in health systems, particularly in how care is organized, delivered, and sustained during public health emergencies. While significant attention has been given to biomedical and clinical responses, less focus has been placed on the invisible care work that underpins these systems - especially among those most structurally marginalized.

Disabled women who simultaneously provide and receive care occupy a particularly overlooked position within pandemic and infectious disease contexts. Despite engaging in complex forms of unpaid care work - such as coordinating care, navigating health services, supporting psychosocial needs, and adapting to rapidly shifting public health guidelines - their contributions remain largely absent from infectious disease and health systems research. Dominant frameworks continue to position disabled individuals primarily as care recipients, obscuring the realities of those who exist at the intersection of both roles.

This study explores the experiences of disabled women in the Greater Toronto and Hamilton Area who identify as both caregivers and care receivers while navigating health and rehabilitation systems during and beyond the COVID-19 pandemic. Guided by Critical Disability Studies and intersectionality, the research examines how disability, race, gender, and care labour shape access to care, risk exposure, and health outcomes in the context of public health crises. Using qualitative narrative inquiry, semi-structured interviews center participants' experiences of navigating services, disruptions in care, and the impacts on their health and well-being.

By foregrounding these narratives, this work expands how we understand pandemic response beyond clinical and epidemiological frameworks, highlighting the essential role of the care economy. Findings aim to inform more equitable, responsive approaches to infectious disease preparedness, health system design, and public health policy.

**Poster 41**

# Development of *in vitro* models of wildlife and livestock species to study host responses to highly pathogenic avian influenza viruses

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Highly Pathogenic Avian Influenza A (HPAI) viruses of clade 2.3.4.4b (H5N1 and H5N5) have caused outbreaks in livestock and wildlife species worldwide. While species such as red foxes and raccoons exhibit severe clinical signs of infection, other species such as pigs and coyotes display fewer clinical signs. Little is known about the innate immune mechanisms that contribute to differences in tolerating infections in these four hosts. More importantly, advancements in studying host-virus interactions are hampered by the lack of molecular tools for non-model species.

Here, we generated upper respiratory tract models on air-liquid interface (ALI) from red fox, raccoon, pig, and coyote nasal brushings. We demonstrated full differentiation of our models with beating cilia and mucus formation after 21 days. We showed immunocompetence in fox cells via dsRNA ligand stimulation and probed for innate immune gene expression with custom oligonucleotides. Preliminary infections using A/British_Columbia/PHL-2032/2024 (H5N1) at MOIs 0.1 and 1 show higher replication in fox than raccoon cells with slightly more cytopathic effect in fox cells. We immortalized each cell line using SV_40 and intend to compare host responses to HPAI infections across the four species in overexpression and gene knockdown studies. As another validation step for the models, immunofluorescent staining will be performed to visualize sialic acid receptor expression and cell morphology.

These novel models enable us to analyse antiviral responses to HPAI infection across clinically susceptible and tolerant mammalian hosts. This will provide critical insight into host determinants of HPAI pathogenesis and establish molecular resources for non-model species.

**Poster 42**

## Structural insights into bimodal fatty acid production by *Mycobacterium tuberculosis* fatty acid synthase-I

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De novo fatty acid synthesis is a conserved and essential process for nearly all organisms. Uniquely in mycobacteria, fatty acid synthase-I (FAS-I) can produce fatty acid chains of two different lengths, C18 and C26. These products are precursors of mycolic acid, the main component of waxy mycobacteria outer membrane which confers virulence and resistance to antimicrobials. Recently, we discovered an extra cavity in the malonyl-palmitoyl transferase (MPT) domain of Mycobacterium tuberculosis FAS-I (Mtb FAS-I) that is suspected to allow the production of longer fatty acid chains. In this study, our preliminary analyses show that the MPT domain extra cavity is not engaged even after incubation with the C26 product, suggesting a potential explanation where the long product may be folded within the same cavity without occupying the extra cavity. However, further model refinements are required to obtain a high-confidence model. Ultimately, structural insights into this uniquely bimodal fatty acid production by Mtb-FAS-I can potentially help develop new antimicrobial drugs to tackle tuberculosis.

Poster 43

# Recurrent Pyogenic Cholangitis with Intercurrent Latent Clonorchiasis in a Filipino Migrant to Canada: Implications for Diagnosis and Management

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Background: Clonorchiasis is a parasitic infection caused by the trematode Clonorchis sinensis, which is endemic to East Asia but increasingly observed in non-endemic regions due to global migration. Chronic infection can lead to recurrent pyogenic cholangitis (RPC) and other hepatobiliary complications including cholangiocarcinoma.

Case: A 39-year-old Filipino woman residing in Canada presented with a two-year history of intermittent right upper quadrant pain, liver enzyme derangement, and imaging features consistent with RPC. Despite negative stool ova and parasite (O&P) testing, empirical treatment with praziquantel (1800 mg three times daily for two days) led to clinical and biochemical improvement.

Discussion: Clonorchiasis can be challenging to diagnose in non-endemic areas due to low parasitologic test sensitivity and non-specific clinical features. Imaging findings and epidemiologic context are critical for raising clinical suspicion and guiding management.

Conclusion: Healthcare providers in non-endemic regions should include clonorchiasis in the differential diagnosis of unexplained cholestasis, particularly in migrants from areas endemic for clonorchiasis and opisthorchiasis. Negative stool tests do not exclude infection, and early empirical treatment may prevent irreversible hepatobiliary damage and reduce long-term malignancy risk.

**Poster 44**

## Utilizing natural competence to genetically manipulate *Lactobacillus iners*

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The healthy vaginal microbiome is generally dominated by a single Lactobacillus species (L. crispatus, L. jensenii, L. gasseri, or L. iners) which inhibit growth of opportunistic pathogens and are thought to be protective against bacterial vaginosis (BV). BV is characterized by bacterial overgrowth of diverse anaerobes and depletion of lactobacilli. The disease affects roughly a quarter of reproductive-age women globally and is a significant risk factor for STIs such as gonorrhea, chlamydia, and HIV. The role of Lactobacillus iners in the vaginal microbiome is controversial as a large proportion of women are stably colonized by L. iners, yet individuals with an L. iners-dominated microbiome are more susceptible to transitioning to BV. Currently, L. iners' biology is poorly characterized despite it being the most common vaginal bacteria globally. One of the major obstacles to better understanding L. iners' role in the microbiome is a lack of genetic editing tools. I've discovered that L. iners can uptake DNA and undergo transformation; this phenomenon is called natural competence and enables L. iners to uptake DNA in its environment which can lead to genomic reincorporation of homologous DNA. I have successfully demonstrated that L. iners is competent by transforming erythromycin susceptible strains with the genomic DNA of erythromycin resistant strains. To demonstrate that we can perform targeted genetic manipulation of L. iners, we have used Gibson assembly PCR products to knockout L. iners' pore-forming toxin, inerolysin, as well as its competence gene, comGA. comGA knockout strains lose their competence confirming this gene's role in L. iners' exogenous DNA uptake. This presents a newfound toolkit to easily genetically manipulate L. iners' which will lead to future studies that will uncover the biology of this understudied organism in the context of the vaginal microbiome.

**Poster 45**

## SLAM! Because Surface Lipoproteins Can’t Just Walk Through Membranes

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Gram-negative pathogens deploy a diverse array of virulence factors to persist within the host environment. Surface lipoproteins and secreted exoproteins must traverse the bacterial envelope to facilitate critical functions, including nutrient acquisition, immune evasion, and host cell adhesion. A key mechanism for the surface display of these virulence factors is the two-partner Type XI Secretion System (T11SS), comprising the integral outer membrane translocon SLAM (Surface Lipoprotein Assembly Modulator) and its cognate substrates. While the general periplasmic targeting of these substrates is understood, the precise molecular mechanisms dictating substrate recognition and translocation by SLAM remain elusive. Here, I employ an integrated structure-function and protein engineering approach to elucidate the domain-specific coordination of SLAM-mediated substrate specificity and translocation.

To determine the structural basis of SLAM-substrate engagement, we utilized antibody-based fiducials and engineered substrates to stabilize transient translocation complexes. High-resolution structural characterization, using a combination of cryo-electron microscopy and protein X-ray crystallography, enabled the generation of a pseudo-atomic resolution model defining the SLAM translocation mechanism.

Furthermore, to delineate the determinants of substrate specificity, I engineered a library of chimeric SLAM constructs derived from three distinct Neisseria gonorrhoeae homologs. By systematically exchanging putative recognition domains, we evaluated the capacity of these chimeras to translocate cognate substrates within an in-house optimized heterologous Escherichia coli secretion system.

Collectively, these structural and functional insights provide a comprehensive mechanistic understanding of SLAM-mediated translocation, establishing a foundation for the rational design of novel targeted therapeutics against T11SS-dependent virulence in Gram-negative pathogens.

Poster 46

# Establishing a Quality Assurance Framework for Tiled Amplicon-Based Whole Genome Sequencing Schemes in Clinical Microbiology Laboratories

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Background: The integration of whole genome sequencing (WGS) into clinical microbiology laboratories requires robust quality assurance (QA) to support complex workflows. Tiled amplicon-based WGS strategies (TAB-WGS) are widely used for respiratory virus genomic surveillance due to their streamlined workflow and cost-effectiveness. However, ongoing review of TAB-WGS schemes is essential to ensure their compatibility with emerging variants, as primer-target mismatches can cause amplicon dropout, reduced genome coverage, and incomplete genomes that may affect downstream interpretation.

Methods: We developed and implemented a structured QA framework for TAB-WGS as part of a new microbial genomics program at our institution. Our framework integrates five core components: routine monitoring of data quality, bioinformatic assessment of primer-target agreement and specificity, expert review, structured documentation, and controlled introduction of updates to support sustained assay performance and compliance with accreditation requirements. We applied this QA framework to investigate and resolve primer quality issues noted in the SARS-CoV-2 ARTIC V5.3.2 TAB-WGS scheme.

Results: Our QA process identified reduced performance of some primer pairs following the emergence of the SARS-CoV-2 JN.1 variant in late 2024. This was limited to primers targeting a 353bp region of the spike region. Re-validation of the ARTIC v5.3.2 scheme with redesigned spike-in primers improved genome completeness and coverage at this genomic region. All changes were reviewed, validated, and documented in accordance with clinical microbiology laboratory accreditation requirements.

Conclusions/Significance: Our TAB-WGS QA framework supports sustained assay performance and data integrity. Its design is adaptable and could be used by other laboratories to support high-quality genomic surveillance.

**Poster 47**

# Identification and Characterization of Genes Important for Virulence in the Fungal Pathogen Candida albicans

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Fungal pathogens are responsible for ~2.5 million deaths worldwide resulting in a significant public health burden. Candida albicans is an opportunistic fungal pathogen that is the leading cause of serious mycotic infection with high mortality rates. With only three major classes of antifungal drugs available to treat systemic infections and resistance increasing worldwide, the need to identify new therapeutic targets is urgent. Establishing infection requires C. albicans to survive the diverse physiological environments encountered within the host, yet the genetic determinants that enable survival in vivo remain poorly defined. We have aimed to systematically identify and characterize genes essential for C. albicans virulence in a mouse model of infection. To do so, we leveraged the Gene Replacement and Conditional Expression (GRACE) library, which consists of 4,452 C. albicans barcoded mutant strains in which gene expression is controlled by a doxycycline-repressible promoter system. Pooled competitive screens have been performed in a mouse model of systemic infection, allowing for the identification of genes important for survival during bloodstream infection. In total, 86 genes were identified as specifically important for systemic infection, but not growth in vitro, including 49 genes that are poorly characterized, representing a substantial reservoir of unexplored biology. To define the environmental pressures that shape in vivo fitness, we systematically profiled these mutants across a panel of optimized host mimicking stress conditions. Conditions included elevated temperature, oxidative stress, osmotic stress, cell wall stress, cell membrane stress, oxygen depletion, and nutrient limitation. These phenotypic screens revealed distinct stress response signatures for individual genes and identified subsets of genes required for specific host relevant pressures. Together, these findings define a core network of C. albicans genes important for systemic infection. Future work will further characterize the mechanisms by which these genes govern pathogenicity.

Poster 48

## Bacterial antiviral immunity is a coordinated population-level response

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Anti-phage defence systems are widespread in bacteria, yet the signals and pathways that control their expression remain poorly understood. In Pseudomonas aeruginosa, quorum sensing has been implicated in CRISPR-Cas activation, but whether it also regulates other defence systems is largely unknown. Here, we examine regulatory control of anti-phage defences across diverse P. aeruginosa strains. We observed density-dependent differences in phage defence under native conditions, suggesting quorum-dependent regulation. In P. aeruginosa PA14, we found that the Gabija, Shango, and CRISPR-Cas systems are driven by the Rhl quorum-sensing pathway. RNA-seq revealed upregulation of these and additional defence systems, pointing to broader population-level control. To monitor defence expression in situ, we developed a modular GFP reporter platform using predicted defence system promoters. This approach provided evidence that the Olokun system in P. aeruginosa ATCC 33348 is regulated by PQS, while expression of the DS-1 system in P. aeruginosa EnvYK2 is modulated by the cAMP-Vfr regulon. Together, our results show that anti-phage defence systems are integrated into major regulatory networks in P. aeruginosa, adding an important new layer to bacterial immune control.

**Poster 49**

## Antiviral defence is a conserved function of diverse DNA glycosylases

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Vibrio pathogens represent a critical global health threat, causing millions of seafood borne infections and severe diseases like cholera annually. Rising ocean temperatures are currently expanding their geographic range, while emerging antimicrobial resistance (AMR) renders traditional treatments ineffective. Phage therapy is a leading alternative to antibiotics, using bacterial viruses (known as phages) to clear pathogenic bacteria. However, its efficacy is limited by the “bacterial immune system,” a complex arsenal of anti-phage defence proteins. To engineer “escaper” phages capable of broad-spectrum biocontrol, we must first decipher the molecular mechanisms underlying the bacterial anti-phage systems.

Although systems like CRISPR-Cas and restriction-modification (R-M) have been well-studied, recent discoveries have revealed a vast landscape of "hidden" anti-phage effectors, many of which serve as evolutionary precursors to eukaryotic immunity. Our work highlights two novel defence-associated DNA glycosylase enzymes in the pandemic strain of Vibrio parahaemolyticus, and further characterization demonstrates that they defend against phages through removal of covalently modified nucleobases across phage DNA and introducing single-stranded breaks to degrade phage DNA. Using a structure-guided discovery approach, we identify 17 families of DNA glycosylases that function as versatile antiviral effectors across diverse diverse bacterial lineages. Our findings underscore DNA glycosylases as a fundamental, conserved strategy in the perpetual molecular arms race between bacteria and their viruses and provides insights into designing phage counter-defence strategies to evade bacterial defence enzymes.

**Poster 50**

# Characterizing EV1-026 and EV1-027: A Novel Two-Gene Anti-phage Defence in the Vibrio parahaemolyticus Integron

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Vibrio parahaemolyticus are marine pathogenic bacteria that infect shellfish and humans, severely impacting aquaculture and public health. Due to rising antibiotic resistance among these pathogens, bacteriophage (phage) therapy has been employed as an alternative treatment, shown to be effective against multi-drug resistant infections. Phage therapy utilizes bacteriophages, the natural viral predators of bacteria. However, to protect themselves from phage predation, bacteria have evolved many diverse anti-phage defence systems that raise significant barriers to effective phage therapy, many of which remain uncharacterized. Therefore, these defence systems must be better understood to inform future implementations of phage therapy. Previously, our lab has shown that Vibrio spp. integrons, genomic regions that contain horizontally acquired gene cassettes, act as reservoirs of many different anti-phage defence systems. By screening libraries of integron gene cassettes generated by our collaborator, Dr. José Escudero, I identified EV1-026 and EV1-027, two distinct gene cassettes that provide 10,000-fold defence against E. coli phage T4 when expressed together. Despite structural similarity to DNA and RNA-binding domains that recognize methylated cytidine derivatives, EV1-027 does not recognize the glucosylated 5-hydroxymethyl-cytidine (5ghmC) modifications present in the T4 genome, suggesting another mechanism. By performing cell survival assays, I have shown that EV1-026 and EV1-027 act abortively to prevent successful phage infection, halting cellular processes before phage replication can be completed. Moving forward, I plan to perform Electrophoretic Mobility Shift Assays (EMSAs) to assess the ability of EV1-027 to bind nucleic acids, as well as visualize how EV1-026 and EV1-027 localize in the cell before and during phage infection using fluorescent microscopy. These experiments will aid in determining how EV1-026 and EV1-027 confer defence, expanding the collection of characterized anti-phage defence systems and informing future implementations of phage therapy.

**Poster 51**

## Characterization of compounds that inhibit filamentation in the human fungal pathogen *Candida albicans*

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Candida albicans, both a commensal of the healthy human microbiota and a leading opportunistic fungal pathogen, represents the most prevalent etiological cause of candidiasis, with a mortality rate approaching 40% despite therapeutic intervention. The high disease burden is due in part to the limited arsenal of antifungal agents for systemic infections—a challenge further compounded by the growing prevalence of drug resistance. In light of this, an alternative strategy to combat fungal infections is to target virulence traits implicated in pathogenicity without impairing growth. Such an approach can potentially expand the therapeutic target space while minimizing disruption to the host microbiota and reducing selective pressure on the pathogen to develop resistance. In C. albicans, the ability to transition between yeast and filamentous forms represents a particularly promising target for anti-virulence therapy, as most mutants locked in either state show virulence defects in mouse models of systemic candidiasis. This work explores this approach by performing a high-throughput screen of ~50,000 compounds to identify those that inhibit C. albicans filamentation without impacting growth. Out of 14 prioritized compounds, we followed up on two that inhibit the yeast-to-filament transition through distinct mechanisms. UT1 inhibits filamentation in response to multiple inducing cues by targeting sterol C4-methyl oxidases in the ergosterol biosynthesis pathway and also engages additional cellular targets at higher concentrations that remain to be identified. In contrast, N1 inhibits filamentation by acting as a cationic amphiphilic drug, disrupting vacuolar integrity and lipid homeostasis in a pH-dependent manner. Future work will focus on further elucidating the compounds' mechanism of action and assessing their therapeutic potential as an anti-virulence strategy.

**Poster 52**

# Discovery of antiphage defence systems targeting a novel bacteriophage of Legionella pneumophila

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As part of the evolutionary arms race between bacteria and the viruses that infect them, called bacteriophages, bacteria have evolved diverse mechanisms to defend themselves. In recent years, the rate at which novel mechanisms of antiphage defence have been discovered has rapidly increased, providing fascinating insights into the immune systems of bacteria. However, the majority of these studies have focused on well-described model species of bacteria, leaving questions regarding the defence systems of other bacteria. Recent work in the Ensminger lab has identified and characterized the first bacteriophage infecting Legionella pneumophila, a gram-negative bacterial pathogen and the causative agent of Legionnaires' disease. Investigation of the interaction between this phage, called LME-1, and Legionella has already revealed multiple mechanisms by which Legionella defends itself. Further, we have observed a subset of L. pneumophila strains which defend themselves through a distinct additional mechanism. My investigation has shown that the genes responsible for this defence are likely encoded on a mobile genetic element and that these elements are a potentially rich source of antiphage defence systems in the Legionella genus. Overall, this work will reveal additional mechanisms Legionella uses to defend itself against phages, and expand the general understanding of prokaryotic immune systems in more diverse species.

Poster 53

# Beyond viability: comparative functional evaluation of live and inactivated industrial biomasses of probiotic lactobacilli

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Non-viable microbial cells are increasingly used as postbiotic or paraprobiotic ingredients, yet the functional impact of industrial inactivation remains poorly characterized. This study provides an integrated functional analysis of industrially fermented, inactivated, and lyophilized probiotic biomasses. Four probiotic strains (Lacticaseibacillus rhamnosus LRH020, Lactobacillus acidophilus PBS066, Lactiplantibacillus plantarum PBS067, and Lacticaseibacillus paracasei LPC1114) and their corresponding industrial biomasses were examined. Multiple thermal and mechanical inactivation protocols were compared. Flow cytometry showed complete loss of culturability and viability-associated markers in all non-viable biomasses. Functional assays revealed strain- and protocol-dependent effects on epithelial adhesion and Toll-like receptor 2 (TLR2) engagement. For LRH020, one thermal protocol consistently preserved adhesion and TLR2 activation across three industrial batches, whereas high-pressure processing abolished adhesion. Anti-inflammatory activity, assessed as inhibition of IL-1β-induced nuclear factor kappa B (NF-κB) activation in Caco-2 cells, was retained in all LRH020 and PBS066 biomasses, but absent in PBS067 and LPC1114. Industrial inactivation shapes the functional properties of non-viable probiotic biomasses. The biological potency of postbiotic/paraprobiotic ingredients depends on the specific strain-process combination, underscoring the need to use industrially produced materials, rather than laboratory cultures, for preclinical characterization and nutritionally relevant postbiotic development.

**Poster 54**

# Do strain diversity and/or dietary context determine the pathogenic potential of *Collinsella aerofaciens* in metabolic inflammation?

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In recent years, interest in the role of gut microbiota alterations in the pathogenesis of non-communicable diseases (NCDs) has grown significantly. An overgrowth of Collinsella aerofaciens - a bacterium widely present in the gut ecosystem but suggested to act as a pathobiont - appears to be a common feature in individuals with NCDs and may contribute to key mechanisms such as increased intestinal permeability, low-grade inflammation and gut-liver axis dysregulation. Two non-mutually exclusive hypotheses may explain this association: 1) C. aerofaciens, which shows signatures of long-term association with the human host, can shift from a health-associated commensal to a context-activated pathobiont under industrialized-lifestyle exposures; and 2) given its high intraspecies diversity, discrete biotypes may harbor accessory genetic determinants that drive disease-associated host phenotypes. Here, we combined cell-based and ex vivo approaches to assess whether C. aerofaciens pro-inflammatory potential is primarily driven by dietary background, strain-level diversity, or both. We first characterized the C. aerofaciens type strain DSM 3979$^T$ using a Caco-2 pNiFty2-SEAP reporter model to quantify NF-κB activation, where DSM 3979$^T$ elicited a moderate but significant NF-κB activation. We then tested whether fecal substrates derived from short-term dietary interventions modulate C. aerofaciens fitness. Fecal samples collected from healthy volunteers after dietary phases (balanced, high-fat/low-fiber, and Western diet) were processed under anaerobic conditions and used as growth matrices for standardized inocula of DSM 3979$^T$ in batch cultures. The dietary background of the fecal substrate influenced C. aerofaciens growth, supporting the hypothesis that diet-driven changes in fecal composition can differentially support C. aerofaciens expansion. Ongoing work extends NF-κB screening to a strain panel to identify divergent host-interaction profiles. Selected high- and low-risk biotypes will then be evaluated in a murine colonization model under chow or Western-style diet to determine whether dietary context modulates C. aerofaciens-driven effects on intestinal inflammation, barrier function, and gut-liver axis-related outcomes.

**Poster 55**

# Identification and characterization of antifungals with novel activities against diverse fungal pathogens

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Fungal pathogens are an escalating global health threat, responsible for over 2.5 million deaths annually. The opportunistic fungi Candida albicans, Candida auris, Cryptococcus neoformans, and Aspergillus fumigatus are leading causes of invasive infections with high mortality rates despite treatment, prompting the World Health Organization to classify them as “critical priority pathogens.” Treatment options remain severely limited; only three major antifungal drug classes – azoles, polyenes, and echinocandins – are currently available to treat invasive infections, but their use is constrained by host toxicity, narrow spectrum of activity, and/or emerging resistance. Thus, there is an urgent need for antifungal compounds that act through novel mechanisms of action and possess broad-spectrum activity. To address this, I leveraged a high-throughput screen of ~50,000 compounds from the University of Tokyo’s Advanced Core Library and the RIKEN Natural Products Depository to identify growth inhibitors of C. albicans. From this dataset, 25 compounds were prioritized based on potency (≥80% growth inhibition) and availability. Characterization of activity against a panel of clinically-relevant fungal pathogens revealed diverse activity profiles, with most compounds exhibiting activity against multiple species. To identify potential drug targets, I will employ chemogenomic profiling using double-barcoded mutant libraries in C. albicans and the model yeast Saccharomyces cerevisiae. Such approaches are based on the principle that strains with reduced gene dosage of a drug target, or processes required to buffer drug-induced toxicity, exhibit hypersensitivity to the compound. Applying this strategy has led us to predict that a C. neoformans-active prioritized compound targets a cytoskeletal-related process. Ongoing work will further explore compound mode of action through such genetic strategies, as well as assess the therapeutic potential of hit compounds through mammalian cell cytotoxicity assays. Collectively, this work aims to address a critical gap in antifungal drug discovery and support the identification of new therapeutic strategies to combat fungal disease.

**Poster 56**

## Targeting the *Klebsiella pneumoniae* surfaceome via *de novo* mini-protein binders

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Antimicrobial resistance (AMR) remains a formidable threat to global health, with the clinical antibiotic pipeline being insufficient to keep up with the rapid evolution of bacterial resistance. The O'Neill report estimates the AMR total death count to surpass 10 million people per year by 2050, costing a cumulative economic loss of USD$100 trillion. Being one of the leading pathogens in AMR-related deaths, the emergence of antibiotic-resistant Klebsiella pneumoniae (K. pneumoniae) has highlighted the need for alternative therapies beyond traditional antibiotics. As bacterial virulence is mediated by surface proteins that recognise host cells, blocking these proteins can disarm the pathogen while minimising selective pressure for resistance. While monoclonal antibodies have traditionally been used to target extracellular antigens, recent breakthroughs in machine learning algorithms have enabled the de novo design of mini-proteins that bind any given target of interest. Mini-protein binders offer many advantages over traditional antibodies, including ease of design and screening, extreme thermostability and protease resistance, high target affinity, high-level production, and small size (typically 40-70 amino acids, which allows access to most compartments). As such, we aim to develop mini-protein binders against known and predicted proteins of the K. pneumoniae surfaceome. To deploy the binders in a biological context, we will engineer the probiotic yeast strain Saccharomyces boulardii (S. boulardii) to either secrete or surface-display successful binders. The binders will then be tested in in vitro assays and in vivo infection models of K. pneumoniae, to determine whether they can neutralize or sequester pathogenic bacteria from the nasopharyngeal or gastrointestinal tract. Ultimately, this project will serve as a proof-of-concept to instantiate a generalizable pipeline for designing binders against any bacterial pathogen.

**Poster 57**

## Phenotypic Screening and Characterization of Phosphatases in the Human Fungal Pathogen *Candida albicans*

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Candida albicans is a commensal fungus that can cause both superficial and deadly systemic infections, particularly in immunocompromised patients. Phosphatases are enzymes that catalyze the removal of phosphate groups and play key roles in cellular homeostasis. While phosphatase function has been comprehensively explored in other fungal species, a systematic functional analysis of phosphatases in C. albicans has yet to be conducted. The Gene Replacement and Conditional Expression (GRACE) collection encompasses 4,450 heterozygous deletion mutants in which the second allele is placed under the control of a doxycycline-repressible promoter. The recent addition of 1,240 GRACE strains expands the coverage of this library to ~71% and includes all phosphatases and phosphatase regulators. Leveraging this library, screens were conducted to identify phosphatases important for fitness, antifungal susceptibility, and morphogenesis, revealing several genes as important regulators of these diverse traits. For example, Sds22, a putative regulator of the phosphatase Glc7, was identified as being important for caspofungin susceptibility in C. albicans. Follow-up experiments revealed that although both Sds22 and Glc7 positively regulate caspofungin susceptibility, Sds22 negatively regulates Glc7, as its overexpression blocked the Glc7-medited upregulation of the caspofungin-responsive gene, PGA13. This suggests a complex regulatory network by which Sds22 regulates the cell wall stress response, which is being further investigated. In addition, the RNA triphosphatase Cet1 was shown to be important for growth, antifungal susceptibility, and filamentation. While this large subunit of the Cet1-Cgt1-Abd1 mRNA capping complex played important roles in regulating these phenotypes, genetic depletion of ABD1 and CGT1 had no impact on C. albicans filamentation, suggesting that Cet1 could possess previously undescribed functions that are important for governing the yeast-to-filament transition. Overall, this study implicates diverse C. albicans phosphatases as regulators of growth, antifungal susceptibility, and morphogenesis and highlights undescribed functions of these enzymes and their regulators that remain to be explored.

**Poster 58**

# Carbapenemase-Producing *Enterobacterales* (CPE) in Long-Term Care in Ontario, Canada

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Background: CPE threaten healthcare systems worldwide. In Canada, CPE were first identified in 2007, and incidence continues to rise. Acute care hospitals (ACH) have been the primary surveillance focus, and the role of our residential long-term-care homes (LTCHs) in transmission remains unclear. We used existing surveillance data to assess the epidemiology of CPE in LTCHs in our population base.

Methods: Population-based surveillance data were used to identify CPE-colonized/patients linked to LTCHs from 2007–2023. Epidemiological review and whole genome sequencing (WGS) were used to trace sources of CPE acquisition.

Results: Using population-level data, 57 CPE patients associated with LTCH, representing 2.9% of 1938 regional CPE cases (and among ~19,000 LTC beds), were identified. Estimated CPE incidence was 7.1/100,000 bed-years in LTCHs (95% CI 4.6-10.6) versus 2.6/100,000 person-years in the general population (95% CI 2.5-2.7). Carbapenemase enzymes and CPE species differed between LTCH-associated cases and other patients with CPE, with LTCH cases more likely to involve KPC (23/57 (40%) vs 269/1881 (14%), p<0.001) and Klebsiella pneumoniae (26/57 (46%) vs 500/1881 (27%), p=0.003). Acquisition sources could be determined for 33/57 (58%) LTCH cases: 7 (21%) outside Canada, 5 (15%) from LTCHs, and 21 (64%) during Canadian hospital admissions (Figure 1). Approximately half (28/57) of LTCH-associated cases definitely exposed LTCH residents to CPE; most others possibly exposed LTCHs (Figure 2). Of 12 LTCH patients epidemiologically linked to another LTCH or hospital patient with the same species and gene with WGS available, transmission was confirmed by WGS (i.e., ≤20SNVs different) in 6 (50%), undetermined (21-100SNVs) in 3 (25%), and ruled out (>100SNVs) in 3 (25%).

Conclusions: LTCHs are emerging CPE reservoirs. Most LTCH residents acquired CPE in hospitals, but most likely exposed LTCH residents to CPE, and transmission occurred in both hospitals and LTCHs. LTCH residents face greater CPE risk than the general population. Residential LTCHs should be incorporated into regional CPE control programs. Coordinated surveillance, regional protocols, shared educational resources, and improved communication are essential between ACH and LTCH.

Poster 59

# Characteristics of invasive pneumococcal disease (IPD) among children and adults in 2022-2025, in southern Ontario, Canada

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Toronto Invasive Bacterial Diseases Network

Background: In July 2024, Ontario's publicly-funded PCV program changed from PCV13 to PCV15 for children (PCV20 if high risk), and from PPV23 to PCV20 in eligible adults.

Methods: We conduct population-based surveillance for IPD in an urban/suburban population of 4.5M. Clinical/vaccination data are from chart review/interview; serotyping (ST) is from Canada's National Microbiology Laboratory. We report post-pandemic incidence and clinical characteristics of IPD.

Results: From 1/2022-12/2025, 1584 episodes of IPD occurred, 13.4% (213) among children. Median age was 61y (IQR, 41-73); 41% (647/1584) were female. Of 1367 with clinical information, 63% (864) had co-morbidities (30% (407) were immunocompromised), 11% (156) were homeless. In 2024/2025, IPD incidence was 13.5, 2.3, 4.9 and 19.2 cases/100000/yr among children<5yrs, children 5-17yrs, adults 18-64yrs, and adults ≥65yrs, respectively. IPD incidence, clinical characteristics and outcomes in 2024/2025 did not differ from those in 2018/2019 (Figure 1). Among children, PCV13, PCV15 and PCV20 STs caused 27%, 44% and 71% of IPD; the most common STs were 15B/C (18%), 22F (14%), 19A (9%). Among 18-64yr-olds (N=667) and ≥65yr-olds (N=564) PCV20 STs caused 72% and 59%, and PCV21 STs 69% and 80% of IPD, respectively. Among adults the most common STs were ST3 (15%), ST22F (8%), ST12F (6%), ST9V (6%). Of 42 pediatric cases due to PCV13 STs there were 2 unvaccinated, 6 incompletely vaccinated, 34 vaccine failures (13 ST3, 15 ST19A, 14 ST19F). Of 14 children fully vaccinated/up-to-date with PCV15, none had IPD from PCV15 STs. Overall, 49/332 (15%) of at risk 18-64year-olds and 163/371 (44%) ≥65year-olds had received a pneumococcal vaccine in the 10 years before their IPD.

Conclusion: IPD has returned to pre-pandemic epidemiology in our population. It is too early to assess impact of changes to the pediatric program; lack of change in adult disease in 2025 may be a result of limited vaccine uptake.

# Incidence and characteristics of invasive Group A streptococcal infection post-pandemic (2022 to 2025)

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Toronto Invasive Bacterial Diseases Network (TIBDN)

Background: Invasive group A streptococcal infections (iGAS) increased significantly in 2022/2023, especially among children. We assessed the continuing epidemiology of iGAS in our population.

Methods: Population-based surveillance for iGAS was conducted in an urban/suburban population of 4.9 million. Laboratories serving residents report iGAS isolates from sterile sites to the study office. Clinical information is collected by medical record review. Canada's National Microbiology Laboratory provides emm-typing, and Statistics Canada provides population data.

Results: From 2022–2025, 1250 iGAS episodes occurred, including 113 (9%) among children. Median age was 55.0 years (IQR 38.0–69.0), and 493 (39%) were female. Among adults, persons experiencing homelessness accounted for 18% (90/503) of iGAS in 2022/2023 and 16% (48/299) in 2025 (P=.57). To contextualize 2022–2025 findings, incidence since 2011 was compared. In both children and adults, iGAS has increased since surveillance began in 1992. Incidence declined during the pandemic, resurged in 2023, and has now returned to pre-pandemic levels. In 2025, iGAS incidence was 2.7/100,000/year in children (IRR=0.82, 95%CI 0.46–1.46 vs 2019) and 7.2/100,000/year in adults (IRR=0.96, 95%CI 0.82–1.14 vs 2019). Among cases with clinical information, diagnosis, severity, and outcomes were similar in 2025 and 2022/2023. In both children and adults, STSS occurred in 13% of cases in both periods, necrotizing fasciitis in 7.1% in 2022/2023 and 5.7% in 2025, and case fatality was 12% in both periods. The most common emm type in both children and adults was emm1, and it was consistently more common among children (in 2022-2025, 46% and 17% of cases respectively). emm12 also contributed to the post-pandemic resurgence, while other emm types varied irregularly. This is in contrast to the pandemic years (2020 and 2021), where disease due to emm82 was increased.

Conclusion: In 2025, iGAS incidence returned to pre-pandemic levels in both children and adults.

**Poster 61**

# Incidence of colonization and infection with Carbapenemase-producing *Enterobacterales* in Toronto and Peel Region, 2007-2025

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Background: Carbapenemase-producing Enterobacterales (CPE) are an urgent public health threat. Monitoring epidemiological changes is critical to the development of action plans against antimicrobial resistance.

Methods: Our network conducts population-based surveillance for CPE in Toronto and Peel Region, Ontario, with a population of 4.5M persons. Laboratories report all isolates of CPE to the study; confirmation of CPE is by PCR. Population data are obtained from Statistics Canada. This analysis includes data from 2007-2025.

Results: The incidence of CPE colonization/infection increased from 0.03/100,000/year in 2007 to 4.44/100,000/year in 2025. The incidence of bacteremia in 2025 is 0.86/100,000/year. Escherichia coli was the most common organism identified in clinical CPE isolates (582/1268, 46%), followed by Klebsiella pneumoniae (406/1268, 32%). blaNDM and blaOXA-48-like were the most common genes carried by E. coli (blaNDM (347/582, 60%), blaOXA-48 like (189/582, 32%), blaNDM+blaOXA-48-like (30/582, 5%)) and K. pneumoniae (blaNDM (130/406, 32%), blaOXA-48-like (131/406, 32%), blaNDM+blaOXA-48-like (71/406, 17%)). The proportion of persons first identified in hospital laboratories as positive from a screening swab (vs a clinical isolate) increased from 45.2% (66/146) in 2010-2014 to 76.7% (1127/1469) in 2022-2025. Of 361 patients rectally colonized with CP-K. pneumoniae, 62 (17%) had a subsequent clinical isolate (a

median of 28 days later) and 25 (7%) subsequently became bacteremic (a median of 51 days later).

Conclusion: The incidence of CPE bacteremias in our population continues to increase. Expansion of screening programs has resulted in a greater proportion of patients identified while colonized, but has been insufficient to control transmission and reduce incidence. Patients colonized with CPE are at substantial risk of later CPE infection. Improved transmission control programs are needed to mitigate the impact of CPE in hospitals in our population area.

Poster 62

# ENPP1 dampens inflammatory response to microbial PAMP ADP-heptose

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Host detection of pathogenic bacteria is essential for microbial clearance and the resolution of inflammation. Innate and adaptive immune cells recognize foreign microbes through microbe-associated molecular patterns (MAMPs), which are detected by host pattern recognition receptors. Heptose phosphates (HPs), highly conserved intermediates in lipopolysaccharide biosynthesis, represent a recently described class of MAMPs. Once in the host cytosol, HPs are sensed by alpha kinase 1 (ALPK1), which phosphorylates TIFA and triggers the assembly of TIFAsome complexes. These complexes act as signaling platforms that drive sustained NF-κB-dependent inflammatory responses, enabling direct detection of replicating intracellular Gram-negative bacteria.

Although the ALPK1-TIFA pathway is well positioned to detect intracellular infection, its role in responding to extracellular pathogens has been less clear, largely because exogenously applied HPs are poorly sensed by host cells. While this was previously attributed to inefficient import, my work reveals an additional regulatory mechanism: ENPP1, an extracellular enzyme known to degrade ATP and the STING agonist 2’3’-cGAMP, also cleaves HPs and markedly reduces their immunostimulatory activity. However, in the presence of extracellular ATP, such as that released during cell damage in the context of live bacterial infection, ENPP1 preferentially cleaves ATP, preserving HP activity and enabling HP-dependent activation of the ALPK1-TIFA pathway. Together, these findings redefine how host cells interpret HPs during bacterial infection and identify ENPP1 as a key extracellular regulator of ALPK1-TIFA signaling. This work provides new insight into how HP sensing contributes to innate immune detection of bacteria and suggests that regulation of this pathway may influence whether inflammation is protective or pathogenic during infection.

Poster 63

# Generating an Inducible Oligodendrocyte Line to Investigate the Acute Effects of Human Herpesvirus 6 on Central Nervous System Myelination

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Human herpesviruses have long been associated with neurodegenerative diseases, including demyelinating disorders such as multiple sclerosis. Specifically, Human Herpesvirus 6A (HHV-6A) has been implicated in central nervous system (CNS) pathology and is suggested to exhibit tropism for multiple CNS cell types. However, the direct and indirect effects of HHV-6A infection on oligodendrocytes, and its role in demyelinating disorders remain poorly understood. Several experimental limitations make it difficult to study HHV-6A, including limited access to primary human tissue, post-mortem samples unable to capture the acute events following infection, and the lack of human models. To address these limitations, our lab uses stem cell engineering to generate glial cell lines through expression of key developmental regulators. OLIG2 and SOX10 are transcription factors essential for driving oligodendrocyte lineage specification. In our previous inducible iPSC line, the OLIG2/SOX10 and Tet-On regulatory components were inserted into separate safe-harbor loci AAVS-1 and ROSA26. While this dual knock-in system enabled controlled induction of differentiation, it required two successful integration events, reducing efficiency and introducing cell-to-cell variability in transgene expression. Thus, the aim of this project was to generate an inducible Tet-on iPSC line with a single OLIG2 and SOX10 cassette, and an rtTA system integrated at a single locus. This system allows for efficient differentiation into mature oligodendrocytes. Successful cloning into the rtTA construct was confirmed through restriction digestion, PCR amplification, and whole plasmid sequencing. Functional validation showed doxycycline-inducible expression in both HEK293T cells and the OLIG2/SOX10 iPSC line. Differentiation of the iPSC line was initiated, and neural progenitor-like cells were observed. Further maturation into oligodendrocytes was performed through doxycycline induction, and genomic validation analyses have begun. Overall, the inducible OLIG2/SOX10 iPSC line provides a physiologically relevant and accessible platform to study HHV-6A, its effects on oligodendrocytes, and creates valuable insights for therapeutic development targeting viral-induced demyelinating disorders.

Poster 64

# A Surface-Exposed Bacterial Lipoprotein Mediates Complement Immune Evasion

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Many Gram-negative pathogens display surface-exposed lipoproteins that function as virulence factors, enabling them to overcome host immune defenses and cause disease. The zoonotic pathogen Mannheimia haemolytica is the primary causative agent of bovine respiratory disease (BRD), which results in more than $1 billion in annual losses in North America. Management of BRD relies heavily on antimicrobial use; however, the rise of antibiotic resistance highlights the need for more effective vaccine formulations and protective antigens.

M. haemolytica expresses a surface lipoprotein, MhSLP1, that is highly immunogenic in cattle, although its function has not been well characterized. We previously demonstrated that a protein termed surface lipoprotein assembly modulator (Slam) mediates the translocation of several virulence-associated lipoproteins in Gram-negative bacteria. MhSLP1 is a Slam-dependent surface lipoprotein and can be displayed on the surface of E. coli co-expressing MhSLP1 and Slam1. Surface expression of MhSLP1 confers resistance to complement-mediated killing in bovine serum.

Co-immunoprecipitation coupled with mass-spectrometry shows that MhSLP1 binds directly to the complement regulatory protein factor I. Formation of this complex has been confirmed with size exclusion chromatography. Additionally, we demonstrated that MhSLP1 protects cells by activating factor I, allowing it to proteolytically inactivate C3b, a potent opsonin that is required for the terminal stages of the complement immune response. As such, MhSLP1 likely protects the cell by eliminating active C3b in the extracellular milieu, thereby preventing opsonization and complement-mediated bacterial lysis.

Together, these findings identify MhSLP1 as a virulence factor that facilitates complement evasion and highlight its potential as a vaccine antigen. Our future structure–function analysis of MhSLP1 aims to guide the development of broadly protective vaccines against BRD and improve our understanding of immune evasion mechanisms employed by bacterial pathogens.

**Poster 65**

# Uncovering the viral tropism and pathological effects of HHV-6 infection in the cells of the central nervous system using human iPSC-derived 2D and 3D models

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Research question and hypothesis: Human herpesvirus 6 (HHV-6), infecting over 90% of individuals by age two, is becoming increasingly linked to epilepsy, encephalitis, and multiple sclerosis. However, understanding its effects on the central nervous system (CNS) is challenging due to the limited availability of primary human samples. We hypothesize that HHV-6A infects glia and neurons, contributing to neurological disease through chronic brain inflammation.

Materials and methods: To better understand the effects of infection in the CNS, we leverage stem cell engineering to describe HHV-6A infection in vitro. We differentiated human induced pluripotent stem cells into neurons, microglia, and astrocytes, forming both 2D monocultures and 3D immune-competent cortical spheroids, followed by exposure to HHV-6A. We used RNA sequencing to uncover activated pathways in each cell type, live imaging to characterize microglial death, LDH assays to measure lytic cell death, and qPCRs to track lytic phases of viral replication. We performed immunofluorescent staining to determine viral neurotropism, and multi-electrode array recordings to assess neuronal firing patterns.

Results and conclusion: Our results showed that HHV-6 efficiently infects all three CNS cell types. In microglia, we observed a significant 95% drop in viability, along with reduced movement speed and displacement. Astrocytes showed decreased viability throughout infection, but continued to harbour the virus 30 days later and formed syncytia, suggesting they may serve as viral reservoirs. Neurons displayed disrupted network synchronicity, but individual neurons became more rhythmic and burst-prone after infection. Importantly, HHV-6 activated interferon response genes such as IFI6 and IFITM3 across both 2D and 3D models, pointing to strong inflammatory signatures. Microglia and neurons are highly vulnerable to HHV-6 induced dysfunction, while astrocytes sustain chronic infection and may enable viral integration and potential

reactivation. These insights help us better understand HHV-6's effects on the brain and may inform therapeutic strategies to protect against infection or suppress viral reactivation.

Poster 66

# Reactivation of Old World Tegumentary Leishmaniasis Following Iatrogenic Immunosuppression: Occurrence and Role for Secondary Prophylaxis

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Background/Objective: Old world cutaneous leishmaniasis (OWCL) is a neglected tropical disease caused mainly by the species L. donovani, L. aethiopica, L. tropica, L. major and L. infantum. Increases in global migration, travel, and climate change have contributed to the growing burden of OWCL. Moreover, the widespread availability of iatrogenic immunosuppression (IS) can increase the risk of reactivation and severe disease manifestations due to weakened immunological control. Currently, the role for secondary prophylaxis in preventing such outcomes is unknown. Therefore, we synthesized data surrounding secondary prophylaxis in preventing OWCL reactivation in the context of IS regimens to reduce this knowledge gap in disease management. Methods: PubMed, Medline, Embase, Web of Science, and LILACS were searched from inception to December 2022. Quality assessment of studies reporting therapeutic interventions will be conducted using the GRADE approach. Results: 1297 full texts were assessed, 55 of which progressed to data extraction. Visceral and cutaneous leishmaniasis were the most common forms of reactivation in transplant recipients and inflammatory disease patients receiving IS regimens, respectively. Three case studies report secondary prophylaxis to use for OWCL reactivation prevention. Two of which demonstrated successful prevention, while one resulted in failure with three subsequent recurrences. Conclusions: The role of secondary prophylaxis in the context of OWCL remains inconclusive due to the dearth of data around this topic. Thus, this systematic review aims to further investigate the role of secondary prophylaxis to provide the necessary information required by healthcare providers in guiding the clinical management of this patient population.

Poster 67

# Fruit-Bearing Plant Ethnopharmaceuticals for the Treatment of Old World Cutaneous Leishmaniasis

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Background: Old World Cutaneous Leishmaniasis (OWCL), caused by Leishmania species, is endemic in regions like the Middle East, Mediterranean, and Africa. Current treatments are toxic, expensive, and inaccessible in low-income countries. Despite the high disease burden, no new drugs have been developed in over 50 years. Plant-based compounds, particularly from fruit-bearing plants, show promise as alternative treatments. This research aims to evaluate the efficacy, safety, and mechanisms of action of fruit-bearing plant ethnopharmaceuticals in treating OWCL, with a focus on their anti-leishmanial activity and potential adverse effects. Methods: This systematic review searched four electronic databases (PubMed, Medline, Embase, and Web of Science) for studies on the efficacy, safety, lesion resolution, or tolerability of ethnopharmaceuticals for OWCL. Data extraction was done using Covidence, assessing risk of bias with Joanna Briggs Critical Appraisal Tools. Two reviewers extracted data and verified data based on the GRADE system, and resolved discrepancies through discussion. Results/Discussion: This research will assess the efficacy and safety of fruit-bearing plant ethnopharmaceuticals for OWCL, aiming to develop novel, cost-effective treatments. By evaluating plant-based therapies in clinical trials, it seeks to provide safe, accessible, and sustainable alternatives to current treatments in endemic regions, addressing this neglected disease. Conclusion: Evidence supporting specific ethnopharmaceutical strategies for OWCL is limited. This review synthesizes literature on fruit-bearing plant ethnopharmaceuticals, showing promising efficacy, with some compounds like Physalis minima and Morinda citrifolia achieving cure rates comparable to current treatments. Despite biases and small sample sizes, further well-conducted RCTs are needed to explore these potential therapies.

**Poster 68**

# The Influence of Host Nutriome on Immunological Control of Leishmania Infection

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Background: Immunologic control of parasitic infections arises from a combination of humoral and cellular mechanisms, both of which may be influenced by host nutritional status. Leishmaniasis is tissue-dwelling parasitic infection in which disease severity is determined by the host's immune system. Research suggests that acquired factors such as nutritional inadequacies play a significant role in immunosuppression and enhanced pathogenicity. Objectives: We aim to synthesize the knowledge surrounding the interplay between host micronutrient status and Leishmania infections. Methods: Five electronic databases were searched with combinations of search terms from database inception to March 2022. A total of 9,814 articles were retrieved with 7,828 remaining after deduplication. Screening was performed independently by two reviewers with discrepancies arbitrated by a tertiary reviewer. Currently, 206 articles have been full text screened leaving 12 eligible for final inclusion. Following screening, a comprehensive bias assessment will be carried out using the GRADE approach. Results: Interim findings suggest that malnourished individuals are at greater risk of acquiring a significant leishmanial infection. Deficiencies reported to impact the disease severity and parasitologic parameters include malnourishment in general, as well as deficiencies in vitamin A, zinc (n=3 each), iron (n=2), fiber, vitamin E, potassium, selenium, and copper (n=1 each). Disruptions to white blood cell count (n=3), and antibody levels (n=1) were also noted. Conclusions: The data will be summarized to systematically map published literature that will illuminate several ways in which nutrient deficiencies or abnormal micronutrient status alter and impair immune function in persons with leishmaniasis.