Graduate Student Research Day

Thursday June 5, 2025

Life Science Research Institute (LSRI) Atrium & McNamara Boardroom
1344 Summer St. Halifax, NS

DALHOUSIE UNIVERSITY

Faculties of Medicine, Dentistry,
Health Professions & Graduate Studies

PREP Professional & Research Education Program

Graduate Student Research Day

Welcome to the 2025 Graduate Research Day!

Graduate Student Research Day has been an annual tradition since 2005, beginning in the Faculty of Medicine and growing to include the Faculty of Health and the Faculty of Dentistry. This year, we continue the tradition of fostering collaboration and showcasing the outstanding work of graduate students.

Each year, this event features over 60 abstracts presented throughout a full day of platform and poster presentations. These presentations are thoughtfully adjudicated by experienced researchers, offering students valuable feedback to further develop their research and presentation skills. We invite all Dalhousie graduate students conducting health-related research to participate in this enriching event.

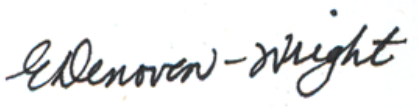
Beyond providing a platform for students to share their research, this event fosters connections and allows students to explore other areas of health research within their academic community. It serves as an opportunity for increased collaboration, enabling students to engage with researchers beyond their fields of expertise.

Graduate Student Research Day continues to highlight the excellence and significance of the research happening here.

Our Objectives:

- **Increase Awareness**: Help students and trainees gain insight into ongoing research and potential opportunities.
- **Critical Analysis**: Provide an opportunity to assess and learn from strong research projects.
- **Integrating Research and Education**: Encourage students to consider how research supports the evolving landscape of health education.

We hope you will join us in celebrating and supporting the outstanding work of these graduate students.



Eileen Denovan-Wright, PhD
Associate Dean, Research

Faculty of Medicine

Schedule of Events

8:30-8:55 Registration & Light Refreshments

9:00-9:05 Welcome - Dr. Eileen Denovan-Wright, Associate Dean, Research

9:05-9:10 Opening Remarks – Dr. David Anderson, Dean of Medicine

9:10-10:15 Presentations – Faculty of Medicine, 2025 Excellence in Research Winners

- 9:10 Introduction: Dr. Kirill Rosen, Assistant Dean, Graduate & Postdoctoral Studies, Faculty of Medicine
- 9:15 PhD – Dr. Joel Bierer
- 9:30 MSc - Jessica Latimer
- 9:45 Research Associate – Dr. Sean McWhinney
- 10:00 Postdoctoral Fellow – Dr. Gustavo Sganzerla Martinez

10:15-10:50 Presentations - Faculty of Health, 2025 Excellence in Research Winner

- 10:15 Introduction: Dr. Daniel Rainham, Faculty of Health
- 10:20 MSc - Faramarz Jalili
- 10:35 PhD - Firoozeh Bairami Hekmati

10:50-11:40 Poster Presentation – Viewing and Judging & Refreshments in the Atrium

11:40-12:20 Platform Presentations Session #1

- 11:40 Elise Bisset, Faculty of Medicine, PhD Candidate, Department of Pharmacology
- 11:50 Julia Fraiha Pegado Nobrega Mafra, Faculty of Medicine, PhD Candidate, Department of Psychiatry
- 12:00 Ebadullah Kabir, Faculty of Medicine, MSc Candidate, Department of Medical Neuroscience
- 12:10 Samuel Silva, Faculty of Medicine, PhD Candidate, Department of Community Health and Epidemiology

12:20-1:30 Poster Presentation – Viewing and Judging & Buffet Lunch in the Atrium

1:30-2:30 Keynote Presentations

- 1:30 Dr. Robin Urquhart
- 2:00 Dr. John Frampton - Spinning Life's Thread: Engineering Biomaterial Fibers for Targeted Form and Function

2:30-3:30 Platform Presentation Session #2

- 2:30 Annika Benson, Faculty of Medicine, PhD Candidate, Biomedical Engineering School
- 2:40 Laura Dauphinee, Faculty of Medicine, MSc Candidate, Department of Surgery
- 2:50 Alexa Wilson, Faculty of Medicine, PhD Candidate, Department of Microbiology & Immunology
- 3:00 Stanley Ibeh, Faculty of Medicine, PhD Candidate, Department of Biochemistry & Molecular Biology
- 3:10 Zachary Long, Faculty of Medicine, PhD Candidate, Department of Physiology and Biophysics
- 3:20 Melis Erkan, Faculty of Medicine, MSc Candidate, Department of Pathology

3:30-3:40 1st Annual People's Choice Award

3:40-4:10 Closing Remarks and Prizes – Dr. Kirill Rosen, Assistant Dean, Graduate & Postdoctoral Studies

Keynote Speakers

Dr. Robin Urquhart

Associate Professor, Canadian Cancer Society (Nova Scotia Division) Endowed Chair in Population Cancer Research

Department of Community Health and Epidemiology

From curiosity to collaboration: dispatches from the frontlines of research to practice

McNamara Boardroom, LRSI
1:30pm – 2:00pm, June 5 2025

https://medicine.dal.ca/departments/department-sites/community-health/our-people/our-faculty/robin-urqhart.html

Dr. John Frampton

Professor, Canada Research Chair (Tier II) in Cellular, Biomaterial and Matrix Interaction

School of Biomedical Engineering

Spinning Life's Thread: Engineering Biomaterial Fibers for Targeted Form and Function

McNamara Boardroom, LRSI
2:00pm – 2:30pm, June 5 2025

https://www.dal.ca/faculty/school-biomedical-engineering/our-people/our-faculty-atok/JohnFrampton.html

Campus Partners (in alphabetical order)

Advancement

We work closely with our donor community and Dalhousie alumni to better understand what matters most to them and what impact they want to have through their engagement so we can introduce them to opportunities that align with our medical research and education excellence goals. It's important to us that we help our donors stay connected to the student learners and health research projects that they care about.

We build relationships with researchers, educators, and other key players within the faculty to better understand the work happening in and out of the lab and classrooms. We help scientists talk about their work in a way that we can all understand and help them tell their stories, make connections, and continue their laudable efforts.

The more we learn about the exciting advances taking place right here at Dal, the more we can share with our donor community and find opportunities for aligned interests to make greater impact, together.

https://medicine-advancement.dal.ca/

CORES

ADVANCE YOUR RESEARCH WITH STATE-OF-THE-ART FACILITIES AND SERVICES Through its strategic CORES program (Centralized Operations of Research Equipment and Supports), the Faculty of Medicine has developed a range of multi-user research facilities providing access to sophisticated equipment and services supported by trained experts. The CORES facilities welcome users from the Dalhousie community, other academic institutions, and external commercial groups.

https://medicine.dal.ca/research-dal-med/facilities.html

Dal Innovates

Dal Innovates provides opportunities for students and faculty to explore entrepreneurship and develop the skills to translate new ideas into innovations. Since its formation in 2020, over 1,000 students and faculty from 40 universities and colleges across Canada have participated in Dal Innovates programs. Dal Innovates alumni have gone on to win international pitch competitions and raise $19 million in private and public funding. Program alumni include 3D BioFibR, Myomar Molecular, and PragmaClin Research Inc., just to name a few.

https://dalinnovates.ca/

Faculty of Graduate Studies & BIPOC

GradPD

Dal GradPD is your go-to hub to learn about professional development designed for your specific needs as a graduate student. Together with partners across the university and external providers, the Faculty of Graduate Studies (FGS) assembles an ongoing schedule of free workshops and events aimed to help you prepare for a diversity of careers.

The four pillars of the Dal GradPD program are dedicated to building skills necessary for success in any career — Communication, Career Intelligence, Health and Wellbeing, and Leadership — and are offered exclusively to graduate students and postdoctoral fellows.

https://www.dal.ca/faculty/gradstudies.html

BIPOC Graduate Student Mentoring Academy

The BIPOC (The Black, Indigenous, and People of Colour) Graduate Student Mentoring Academy provides an opportunity to connect BIPOC graduate students as mentees with mentors who share similar racial or ethnic backgrounds and are from a range of occupations. This representation allows mentees to see individuals who have successfully navigated similar challenges, providing inspiration, motivation, and a sense of possibility. The primary objective of the Mentoring Academy is to address the obstacles created by systemic racism, which often hinders these students from reaching their full potential.

The Academy offers:

- Mentoring opportunities for the students with experienced mentors
- Professional development sessions that are specifically tailored to support their aspirations
- In-person networking events
- Quarterly surveys to listen to the voices, challenges and recommendations of the students

Who Can Apply?

Graduate students who Identify as **Black, Indigenous and/or a Person of Color (BIPOC)** and are enrolled in ANY graduate program at Dalhousie University can apply to become a mentee.

University faculty and staff, public and private sector professionals, Elders, Retired professionals who identify as Black, Indigenous and/or a Person of Color (BIPOC) can enroll to become mentors.

How to get involved:

To participate in the upcoming cohort (2025-26) of the BIPOC Mentoring Academy, contact the Program Coordinator, at bipocmpd@dal.ca or visit the website at www.dal.ca/grad/bipoc

Office of Commercialization and Industry Engagement

The Office of Commercialization and Industry Engagement (OCIE) at Dalhousie University serves as a pivotal nexus between the university's cutting-edge research and the commercial sector. By facilitating partnerships, fostering collaborations, and ensuring the seamless transfer of technology, OCIE transforms academic innovations into market-ready solutions. It provides support and guidance to researchers and entrepreneurs alike, helping to navigate the complexities of intellectual property, licensing agreements, and startup creation. Through its efforts, OCIE drives economic growth, enhances industry capabilities, and positions Dalhousie as a leader in both academia and commerce.

https://www.dal.ca/research-and-innovation/about/commercialization-and-industry-engagement.html

Pulse

Pulse is a hub for students to explore innovative ideas that solve real-world healthcare problems. Our goal is to generate interest in health innovation, develop innovation as a skillset, and introduce students to interesting careers in healthcare. We accomplish this through innovation skill-building opportunities, such as health innovation challenges and workshops. Students also gain exposure to unique and exciting healthcare careers by participating in clinical tours. Pulse is sponsored by the Province of Nova Scotia and the Faculties of Health, Medicine, and Dentistry at Dalhousie University.

https://dalinnovates.ca/pulse-hands-on/

Student Presentation Schedules

Excellence in Research Awards

9:15	Dr. Joel Bierer, Faculty of Medicine, 2025 Excellence in Research Winner, PhD Award
9:30	Jessica Latimer, Faculty of Medicine, 2025 Excellence in Research Winner, MSc Award
9:45	Dr. Sean McWhinney, Faculty of Medicine, 2025 Excellence in Research Winner, Research Associate Award
10:00	Dr. Gustavo Sganzerla Martinez, Faculty of Medicine, 2025 Excellence in Research Winner, Postdoctoral Fellow Award
10:20	Faramarz Jalili, Faculty of Health, 2025 Excellence in Research Winner MSc Award
10:35	Firoozeh Bairami Hekmati, Faculty of Health, 2025 Excellence in Research Winner PhD Award

Platform Presentations

11:40	Elise Bisset, Faculty of Medicine, PhD Candidate, Department of Pharmacology
11:50	Julia Fraiha Pegado Nobrega Mafra, Faculty of Medicine, PhD Candidate, Department of Psychiatry
12:00	Ebadullah Kabir, Faculty of Medicine, MSc Candidate, Department of Medical Neuroscience
12:10	Samuel Silva, Faculty of Medicine, PhD Candidate, Department of Community Health and Epidemiology
2:30	Annika Benson, Faculty of Medicine, PhD Candidate, Biomedical Engineering School
2:40	Laura Dauphinee, Faculty of Medicine, MSc Candidate, Department of Surgery
2:50	Alexa Wilson, Faculty of Medicine, PhD Candidate, Department of Microbiology & Immunology
3:00	Stanley Ibeh, Faculty of Medicine, PhD Candidate, Department of Biochemistry & Molecular Biology
3:10	Zachary Long, Faculty of Medicine, PhD Candidate, Department of Physiology and Biophysics
3:20	Melis Erkan, Faculty of Medicine, MSc Candidate, Department of Pathology

Poster Presentations - 10:35am and 11:40am – LSRI Atrium

MSc Candidate	Supervisor	Research Title/Topic
Agustina Cohen	Dr Son Truong	Empowering diverse youth voices to enhance equitable access to nature and wellbeing in Nova Scotia: A photovoice study
Alireza Aleali	Dr. Javeria Ali Hashmi	High chronic pain severity is linked with anomalies in pain modulation and periaqueductal gray connectivity
Aran Thanamayooran	Dr. Karthik Tennankore & Leah Cahill	Effects of Pre-Transplant Hemodialysis Timing on Post Kidney Transplant Outcomes
Breanna Laffin	Dr. Emily Black	Identifying Factors of Success in Implementing an Intervention for Management of Inpatient Bacteriuria in Four Regional Hospitals in Nova Scotia.
Cameron Calder	Dr. Javeria Hashmi	Large-scale brain networks increase in integration with high prediction error during pain processing
Charlotte Maclean	Dr. John Archibald	Long-read metagenomics to explore giant viral diversity within Nova Scotian peatland
Chris Consmueller	Dr. Scott Grandy	A randomized controlled trial protocol: STudy on bluebeRries, prOteiN, and exercise for improvinG frailty and cardiovascular disease (STRONG)
Christian Rempe	Dr. Locke Davenport Huyer	Immune reaction to polymeric implantable materials.
Claerwen Sladen-Dew	Dr. Alexander Quinn	Disturbed Repolarisation-Relaxation Coupling in Atrial Mechano-Arrhythmogenesis in Ischaemic Heart Disease
Daniel Neira Agonh	Dr. Chappe and Dr. Anini	Humanized Mouse Model to Study Cystic Fibrosis-Related Diabetes
Dina Rogers	Dr. David Langelaan	Engineering of PETase-Hydrophobin Proteins for High-Turnover Plastic Degradation
Emily Thomson	Dr. James Fawcett	Characterizing NOS1AP in the rodent cerebellum
Haya Abdelwahab	Dr. Ketul Chaudhary	Role Of Stem Cell Antigen-1 Expressing Cells In Right Ventricular Remodelling In Chronic Hypoxia-induced Pulmonary Hypertension
Jeffy Fernando	Dr. Petra Kienesberger	Characterization of lipid phosphate phosphatases in skeletal muscle: regulation by nutritional stress and role in energy metabolism
Jena Barter	Dr. Barbara Karten	The Role of the Cholesterol Transporter, STARD3 in Breast Cancer
Jordan Cucksey	Dr. James Davey	Design and construction of a genetic circuit for engineering DNA methylation sensitive repressors
Kaitlyn Woodworth	Dr. Locke Davenport Huyer	Development of itaconate polymer microparticles for intracellular regulation of pro-inflammatory macrophage activation
Lauren Burton	Dr. Zhenyu Cheng	Characterization of mitogen-activated protein kinase ERK activation by Pseudomonas aeruginosa protease IV
Lauren Fong-Hollohan	Dr. Locke Davenport Huyer	Investigating the functional roles of peri-implant glycoltic macrophages
Mackenzie Searle	Dr. Kishore Pasumarthi	Therapeutic Potential of Strand-Specific microRNA Targeting in Oxidative Stress-Induced Thoracic Aortic Aneurysm
Maegan Burke	Dr. David Langelaan, Dr. James Davey	Detection of nanoplastics in water using engineered hydrophobins
Pooja Labana	Dr. James Fawcett	Characterization of the role of large tumor suppressor proteins (LATS1/2) in neuronal maturation
Radka Sevcik	Dr. Alex Quinn	Optogenetic Action Potential Modulation for Arrhythmia Prevention in Long QT Zebrafish Hearts
Robyn McGowan	Dr. Melina Agosto	Axonal trafficking and trans-synaptic complex formation of Pikachurin
Tanzima Fariha	Dr. Corey Baimel	Ventral hippocampal control of amygdala to nucleus accumbens circuits
Zachary Froom	Sr. Locke Davenport Huyer	Antifibrotic Function of Itaconate-Based Degradable Polyester Materials

Poster Presentations - 12:20pm and 1:30pm– LSRI Atrium

PhD Candidate	Supervisor	Research Title/Topic
Ghislain d'Entremont	Dr. Jill A Hayden	Evaluation of artificial intelligence tools for critical appraisal in evidence syntheses
Rhea Nickerson	Dr. Zhenyu Cheng	Role of the integrated stress response in modulating the host immune response to chronic Pseudomonas aeruginosa lung infection
Brianna Latremouille	Dr. Alex Quinn	Cardiomyocyte Mechanical Function is Maintained by an Optimal Range of Afterload
Mikaela Ethier-Gagnon	Dr. Sherry Stewart	The Impact of Acute Cannabidiol (CBD) on Stress and Anxiety: A Systematic Review and Meta-Analysis
Noah Doucette	Dr. Audrey Steenbeek & Dr. Jennifer Lane	Exploring the Determinants of Human Papillomavirus (HPV) Vaccine Uptake in Nova Scotia, Canada: Towards Equity and Inclusivity
Jacob van Haaften	Dr. Shannon Johnson	Health in Nature: Advancing Clinical Competencies Through Environmental Health Advocacy
Alyssa Forbes	Dr. Jeremy Brown and Dr. Thomas Landry	A Novel Surgical Procedure for Using Ultrasound and Histotripsy Transcranially
Madison Oulton	Dr. George Robertson	Metabolic basis for ibogaine-induced brain repair
Timi Idris	Dr. Barb Hamilton-Hinch	Empowering Black Women in Nonprofits: Advancing Wellbeing and Success
Emily Devereaux	Dr. Janet Curran	Factors that Influence How Pediatric Patients or Caregivers Decide to Present to an Emergency Department: Scoping Review
Emilee Fackelmann	Dr. Parisa Ghanouni & Dr. Lori Weeks	Health Equity and Belonging: Lived Experiences of University Students with Disabilities in Nova Scotia
Raymond He	Dr. David Langelaan	Discovering the role of an Î±-helix in self-assembly of a hydrophobin from Phanerochaete carnosa
Meghan Hamilton	Dr. Stephen Bearne	Transition State Stabilization: The Moderate Burden Borne by Dihydrodaidzein Racemase
Saeideh Jamali	Dr. Jun Wang	ROFILING THE HOST RESPONSES TO RESPIRATORY BORDETELLA PERTUSSIS INFECTION IN HUMAN VOLUNTEERS
Jamil Muradov	Dr. Alon Friedman	Repurposing Memantine for the Prevention of Neurological Dysfunction Following Traumatic Brain Injury: Results of a Mechanism-Driven Randomized Pre-Clinical Trial
Sayanti Dey	Dr. Andrew Makrigiannis	Delineating the role of murine Ly49C/I+ antigen specific NK cells in antitumor immunity
Shannen Grandy	Dr. Zhenyu Cheng	Characterizing the role of host stress responses during Pseudomonas aeruginosa infection
Michael Ibekaku	Dr. Caitlin McArthur	Mobility Profiles of Residents Living with Dementia in Canadian Long-Term Care Homes: A Cross-Sectional Study
Jennika Veinot	Dr. Javeria Ali Hashmi	PTSD Impairs Working Memory Systems and Disrupts Pain Regulation Pathways in Chronic Pain

Student Abstracts

Excellence in Research Award Winners

Firoozeh Bairami Hekmati Faculty of Health

Supervisors: Dr. Mohammad Hajizadeh and Dr. Jeanna Parsons Leigh, School of Health Administration, Faculty of Health

Effectiveness of non-contributory pensions in enhancing well-being among low-income older adults

The growing global aging population presents various challenges, particularly for low-income seniors who are more vulnerable to financial instability. In response, several countries have implemented retirement income support programs to provide essential financial assistance for seniors. These programs aim to improve the financial security and overall well-being of older adults, especially for those with limited resources. This scoping review aims to investigate the impact of such incomes on the physical, mental, and social well-being of low-income seniors.

A comprehensive systematic search was conducted across five key databases: PubMed, Scopus, Embase, PsycINFO, and CINAHL, covering studies published up to September 10, 2024. Following the scoping review framework by Arksey and O'Malley (2005), only studies that specifically examined the effects of income support on low-income seniors' well-being were included, excluding review articles. A total of 12,504 articles were screened, with 26 studies meeting the eligibility criteria for inclusion in the review.

The review found that income supplementation programs had a positive impact on several health indicators, including memory, lung function, and frailty. These improvements were attributed to increased access to healthcare services, nutritious food, and mental health support. Financial support alleviated the stress of economic hardship, allowing seniors to prioritize healthcare needs and potentially reducing chronic stress and its adverse physical effects. Programs that provided frequent monthly payments were found to be particularly effective in promoting healthier aging, as they helped maintain consistent consumption patterns, enabling seniors to access medical care and essential services without financial concerns.

This scoping review underscores the significant potential of retirement income support programs to improve the quality of life and health outcomes for low-income seniors. Tailored financial support plans with regular payments can mitigate the challenges faced by low-income seniors and contribute to their long-term physical and mental well-being and healthier aging.

Dr. Joel Bierer, Faculty of Medicine

Supervisors: Dr. David Horne, Division of Cardiac Surgery and Dr. Jean Marshall, Department of Microbiology & Immunology

The Role of Ultrafiltration in Mitigating Inflammation and Promoting Enhanced Recovery after Pediatric Cardiac Surgery

Cardiopulmonary bypass (CPB) is essential for corrective repair of congenital heart disease in children but provokes a systemic inflammatory response driven by complement activation and cytokine release. This inflammation contributes significantly to post-operative complications, including heart failure, multi-organ dysfunction, and prolonged intensive care requirement. Unfortunately, effective solutions remain elusive, as even steroids have shown minimal beneficial effects in this patient population. Ultrafiltration during CPB is commonly employed to remove excess fluid and inflammatory mediators, however, the optimal strategy for its application remains uncertain.

To address this, our group developed a novel dual-phase ultrafiltration strategy called subzero-balance simple modified ultrafiltration (SBUF-SMUF), used continuously throughout the surgery with the aim to maximize its anti-inflammatory effect. In a prospective observational study (PILOT), we applied this technique to 40 pediatric patients undergoing cardiac surgery with CPB. Serial sampling of patient plasma and ultrafiltration effluent facilitated inflammatory mediator profiling in a perioperative time series. A principal component analysis further identified complement activation, rather than traditional pro-inflammatory cytokines, as the primary pathway associated with post-operative morbidity. Furthermore, the ultrafiltration therapy effectively extracted the activated complement anaphylatoxins, C3a and C5a, while preserving the foundational anti-inflammatory mediator IL-10. These results informed the design of the ULTRA trial, a double-blinded randomized controlled study comparing high- versus low-exchange SBUF-SMUF assessed by the primary outcome of peak Vasoactive-Ventilation-Renal score, a validated marker of the severity of post-operative illness. ULTRA has completed patient enrollment of 104 participants, currently undergoing final analysis.

Inflammation after children's heart surgery remains an unsolved challenge. Our translational research on 144 pediatric patients has yielded important immunologic insights into the clinical systemic inflammatory syndrome observed after CPB. Informed by the results of the PILOT and ULTRA trials, future work will focus on complement-specific immunomodulatory therapies to dampen inflammation and enhance recovery after pediatric cardiac surgery.

Faramarz Jalili, Faculty of Health

Supervisor: Dr. Mohammad Hajizadeh, School of Health Administration

Socioeconomic Inequalities in Colorectal Cancer Screening Participation in Ontario, Canada

Faramarz Jalili [a,*], Nichole Austin [a], M. Ruth Lavergne[b], Mohammad Hajizadeh [a]

[a]*School of Health Administration, Faculty of Health, Dalhousie University, Halifax, NS, Canada*
[b]*Department of Family Medicine, Dalhousie University, Halifax, NS, Canada*

Objective: There is a growing acknowledgment that individuals with lower socioeconomic status face disproportionate challenges related to cancer screening. While the link between colorectal cancer (CRC) screening and socioeconomic status has been explored, it remained inadequately understood within the Canadian context. This study aimed to assess and elucidate socioeconomic inequalities in CRC screening uptake in Ontario, Canada.

Methods: The study utilized data from 2017-2018 Canadian Community Health Survey (CCHS), conducted by Statistics Canada, to assess socioeconomic inequalities in CRC uptake in Ontario, Canada. As a cross-sectional survey, CCHS contains information on healthcare service utilization, and social determinants of health among Canadians. The Wagstaff index (WI) and the Erreygers Index (EI) were employed to quantify and decompose income-related inequalities in CRC screening participation.

Results: Descriptive findings demonstrated that the overall CRC screening rate was 71.7%, with females exhibiting a higher rate of 78.4% compared to males at 69.4%. The negative values of the WI (0.193; 95% confidence interval [CI]: 0.170 to 0.215) and the EI (0.156; 95% CI: 0.138 to 0.174) indicated a pro-rich inequality in the CRC screening participation in Ontario. The decomposition analysis indicated that income (71.61%), education (8.61%), and language barriers with healthcare providers (5.76%) were the main factors explaining the observed income-related inequality in CRC screening participation in Ontario.

Conclusion: Addressing inequalities in CRC screening remains a pressing health policy issue in Ontario, Canada. Implementing targeted strategies to enhance awareness and address language barriers in accessing services has the potential to reduce income-related inequalities in screening rates.

Jessica Latimer, Faculty of Medicine

Supervisor: Dr. John Archibald, Department of Biochemistry & Molecular Biology

Mirusvirus host-virus co-evolution in microorganisms

Mirusviruses are a newly discovered group of chimeric marine viruses that connect two realms of double-stranded DNA viruses previously believed to be distinct: giant DNA viruses and animal-infecting herpes viruses. Metagenomic data suggest that mirusviruses are abundant in the world's oceans. The marine thraustochytrid protist Aurantiochytrium limacinum was recently described as the first known host for mirusviruses with two viral genomic elements: one a circular episome and another integrated into one of the nuclear chromosomes.

Publicly available genomic data from other thraustochytrid species suggest the presence of mirusvirus-like sequences as well, but these datasets are of poor quality and do not allow endogenous viral elements to be distinguished from those associated with active infection. More generally, we do not know whether endogenized mirusvirus is feature of all thraustochytrids or whether it is restricted to certain genera and species.

I have used Nanopore sequencing to produce chromosome-scale genomic assemblies for the thraustochytrid Schizochytrium aggregatum as well as several novel isolates taken from aquatic environments in Nova Scotia, Canada. In addition to light and electron microscopic investigation, these genomic data are being analyzed to (i) search for the presence of mirusvirus genetic elements and (ii) to determine whether they exist as episomal and/or endogenized forms. The production of high quality thraustochytrid genomes is important to study the distribution of mirusvirus genes and genomes across the Labyrinthulomycetes. Our research will provide a foundation for elucidating host-mirusvirus interactions and, by extension, how these enigmatic DNA viruses impact marine microbiology.

Dr. Sean McWhinney, Faculty of Medicine

Supervisor: Dr. Tomas Hajek, Department of Psychiatry

Central obesity as a predictor of altered brain structure and cognitive impairment in first episode psychosis

Obesity is disproportionately high in first episode psychosis (FEP) and is linked with many of the same changes in brain structure and cognitive impairments. This study aims to examine whether obesity and metabolic disturbances are associated with neurostructural alterations, and whether obesity-related brain changes contribute to poorer cognitive outcomes in FEP.

We obtained waist-hip ratio (WHR), BMI and metabolite concentrations in 256 control participants and 440 with FEP. Participants completed the Rey Auditory Verbal Learning Test (AVLT), Digit Span working memory test, and structural MRI. BrainAGE was computed using a machine learning model. We tested associations between FEP, indicators of obesity, BrainAGE, and cognition, using linear regression modeling. We tested whether indicators of obesity or BrainAGE mediated group differences in cognition.

Central obesity (WHR) was a stronger predictor of brain alterations than BMI or metabolite concentrations. Central obesity was also associated with verbal memory. Most importantly, higher

WHR significantly mediated the higher BrainAGE seen in FEP, which in turn mediated their poorer cognitive outcomes.

This study demonstrated that central obesity is a critical factor in brain and cognitive alterations in FEP. Monitoring and addressing central obesity early may help mitigate these changes, with implications for improving psychiatric and cognitive outcomes.

Dr. Gustavo Sganzerla Martinez, Faculty of Medicine

Supervisor: Dr. David Kelvin, Department of Microbiology & Immunology, Faculty of Medicine

Monkeypox virus pangenomics reveals determinants of subclade Ib

Mpox, formerly monkeypox, is a viral zoonotic disease caused by the monkeypox virus (MPXV). MPXV, which is phylogenetically divided into Clades I and II, was declared a Public Health Emergency of International Concern for the second time in August 2024 due to rapid geographic expansion of Clade I viruses including the newly identified subclade Ib. With a unique set of genomic mutations and sustained human-to-human transmission, subclade Ib has rapidly spread throughout the eastern Democratic Republic of the Congo as well as neighboring non-endemic regions and outside the African continent. Currently, there is a lack of comparative genomic data with which to address the potential zoonotic transmissibility and pathobiology of subclade Ib. Here, we report 105 protein-coding genes that are shared by all the queried MPXV subclade Ia, Ib, and IIb genomes. The first documented and all subsequently examined isolates of subclade Ib presented deletions on the gene pair OPG032 and OPG033, which encode the complement control protein (a vaccinia virus ortholog associated with virulence), and a Kelch-like protein associated with pathogenesis, respectively. The genomic rearrangement of MPXV suggests a functional evolution that might play an important role in the pathobiology of the new MPXV subclade Ib. Our results lay the groundwork to exploit the genomic elements of MPXV as potential targets for therapeutics development/repurposing, vaccine design, and molecular diagnostic expansion, as well as to uncover the viral diversity, and human-to-human transmission of MPXV.

Platform Presentations

Annika Benson, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Jeremy Brown, Biomedical Engineering School

A Tracked High-Resolution Ultrasound Endoscope for Minimally Invasive Brain Surgery

Background and Objectives: We have developed a novel intraoperative imaging adjunct to address limitations in neurosurgical guidance technology: a miniature, high-resolution, tracked ultrasound imaging endoscope. This report describes the fabrication and preliminary testing of the device, which aims to enhance neurosurgery by providing precise, real-time visualization of the brain within narrow surgical pathways.

Methods: The work has two components: 1) the development and clinical validation of the ultrasound endoscope, and 2) its integration with a surgical navigation system, with tracking validated in a brain phantom. A miniature (3.8 × 4 mm cross-section) 30 MHz phased array with 64 elements was developed, and probe performance and safety were tested. Investigational testing of the untracked imaging probe was performed in three adult neurosurgery cases (two glioblastoma resections and one aneurysm clipping). B-mode and Doppler imaging data were collected to explore the probe's ability to visualize anatomy intraoperatively. The probe was integrated with a commercial surgical navigation system and tested in a brain phantom containing a simulated tumor and landmark. Agreement between the landmark location based on B-mode ultrasound and navigated 3D T1-weighted MRI was characterized.

Results: The probe demonstrated axial and lateral resolutions of 33 and 116 μm, respectively. During tumor resection, it differentiated tumor from healthy tissue and identified residual tumor missed by conventional surgical guidance. Key structures were also visualized during aneurysm surgery. The ultrasound probe was successfully integrated with a surgical navigation system. When this combined system was tested in a brain phantom, there was good agreement between tumor boundaries in navigated MRI and ultrasound images, with the apparent landmark location agreeing within $\mu = 2.90$ mm over 25 trials.

Conclusion: This first-of-its-kind imaging system shows potential as a novel adjunct for neurosurgical guidance. Further clinical testing is needed to fully validate its efficacy.

Elise Bisset, Faculty of Medicine, PhD Candidate

Supervisor: Dr Susan Howlett, Department of Pharmacology

Nitrate Supplementation Increases Voluntary Exercise and Impairs Cardiac Calcium Handling in a Sex Specific Fashion in C57Bl/6 Mice

Nitrate supplements are commonly combined with aerobic exercise to potentially improve both performance and cardiac function. Whether this combination benefits cardiac function at the organ and cellular levels is unclear. C57Bl/6 mice (9-mos) were given 1mM sodium nitrate (drinking water) and/or access to a running wheel for 3 mos. Cardiac function (echocardiography) and blood pressure (tail cuff) were measured. Calcium transients (Fura-2) and contractions were measured in ventricular myocytes (2 Hz). Nitrate supplementation dramatically increased total voluntary

running in female mice (255±27 vs 349±38 km: $p<0.05$) but not in males (145±16 vs 169±42 km). Female mice also ran more than males. Blood pressure was not altered in female mice, but in males both nitrates and exercise protected against an age-related increase in blood pressure. While exercise improved cardiac function, nitrates plus exercise impaired cardiac function but only in female mice. In female controls, exercised mice had larger longitudinal strain levels than sedentary mice (-16.7±1.3% vs -20.3±1.3%: $p<0.05$). This was not seen in either exercised females supplemented with nitrates or in male mice. Female mice who exercised and took nitrates had slower ventricular myocyte contractions, smaller calcium transient peaks, slower calcium release, and slower calcium decay rates compared to exercised controls. These detrimental changes were not seen in male mice. Interestingly, after a 1-month nitrate washout period, , many of the negative changes in calcium handling in exercising females reverted to exercise control levels. This suggests that nitrate supplementation plus exercise may have detrimental effects in females when combined with exercise.

Laura Dauphinee, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Sean Christie, Department of Surgery

Establishing a Spatio-Temporal Atlas of Gene Expression after Traumatic Spinal Cord Injury

Traumatic spinal cord injury (tSCI) occurs due to an abrupt mechanical force that disrupts the spinal cord's cellular architecture. This triggers a biochemical and molecular cascade known as secondary spinal cord injury (sSCI). Despite decades of research, there is no current treatment for tSCI. Promising approaches will likely involve targeting sSCI mechanisms to prevent further functional loss and promote recovery. Past studies have focused on tissue-level analyses of gene expression and cellular reactions following injury. However, standard tissue transcriptomic methods utilize homogenized tissue samples, resulting in the loss of spatial context. This information is critical because pathologies such as tSCI are often characterized by abnormal spatial organization within tissues. The varying resilience within heterogenous cell populations calls for a more granular understanding of gene expression throughout sSCI. Therefore, the goal of this research is to construct a spatio-temporal atlas of gene expression following tSCI using spatial transcriptomics.

Transgenic female mice underwent standard laminectomy at the T9 and T10 vertebrae. A graded contusion injury of moderate force was delivered at the T12 spinal segment. Spinal cords were extracted at 4 hours, 48 hours, and 7 days after tSCI, along with a healthy mouse as control. Longitudinal sections ~420µm deep from the dorsal surface and coronal sections ~1.25mm distal to lesion epicenter were selected to undergo 10x Genomics Visium HD spatial transcriptomic analysis.

Standard analyses, such as graph-based clustering, cell-type deconvolution, spatially-variable gene detection, gene expression mapping, GO enrichment, and ligand-receptor analysis have been completed. Several genes demonstrated clear variability in expression at different timepoints and locations within the injured spinal cord. Follow-up analyses investigating specific genes of interest are ongoing.

Results focusing on the established gene expression patterns present in varying tissue regions at different time points will be discussed in the context of current knowledge.

Melis Erkan, Faculty of Science, MSc Candidate

Supervisor: Dr. Victor Martinez, Department of Pathology, Faculty of Medicine

Unveiling Molecular Signatures of Arsenic-Induced Lung Cancer: A Multi-Omics Analysis

Introduction: Arsenic, a carcinogen that contaminates underground water sources, contributes to lung cancer through chronic low-dose exposure. In Nova Scotia, elevated arsenic levels in drinking water, particularly well water in rural areas, are believed to play a role in the rapidly rising lung cancer rates, even among non-smoking populations. We aim to identify biomarkers of arsenic-induced damage using lung models exposed to physiologically relevant arsenic concentrations.

Methods: We created lung organoids using human bronchial epithelial cells (HBECs) and exposed them to varying concentrations of sodium arsenite (0.08μM and 2μM) at multiple time points. Cells underwent treatment following a controlled exposure protocol with treatment cycles of 48-96 hours between passages over a period of up to 12 days, with one group having arsenic removed after the final passage. DNA and RNA were isolated from treated cells for multi-omics analysis. RNA-Seq was conducted on a NextSeq2000 instrument (Illumina) with 2x150 paired-end sequencing, aiming for over 100 million reads per sample.

Results: The first 18 samples have been sequenced and processed. Currently, data quality assessment and normalization of gene expression are being conducted in preparation for differential expression analysis via DESeq2. Initial analysis will focus on identifying arsenic-induced changes in gene expression that are maintained over time. In subsequent phases we will investigate irreversible changes through a dual approach: removing arsenic after exposure and co-treating cells with arsenic chelating agents to block its effects. These complementary strategies will help confirm arsenic damage specificity and persistency. We will validate the identified biomarkers in lung tumours of individuals from high-arsenic areas using the Nova Scotia Lung Tumour Biobank.

Conclusion: Identifying biomarkers of arsenic-induced lung damage will contribute to the development of prevention strategies and early detection methods for arsenic-related lung cancer, addressing a significant public health concern both in Nova Scotia and globally.

Julia Fraiha Pegado Nobrega Mafra, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Tomas Hajek, Department of Psychiatry

Trace lithium levels in drinking water and risk of dementia: A systematic review.

Background: Lithium (Li) since its debut in 1949, has been regarded as a golden standard therapy for mood stabilization. Its neuroprotective attributes have been validated across the field ranging from tissue cultures to human studies. This has generated interest in potentially repurposing this drug. However, the optimal dosage for eliciting neuroprotective effects remains unclear. The doses needed for treatment of bipolar disorders may differ from the doses needed to elicit neuroprotective effects. Recent studies on trace-Li levels in the water suggest that Li, could slow cognitive decline and prevent dementia with long-term use even at very low doses. The current review aims to synthesize the data on the topic and challenge the conventional high-dose paradigm.

Results: We systematically reviewed five available studies, which reported associations between trace-Li in water ranging between 0.012 mg/L to 0.056 mg/L and incidence or mortality from dementia. Association between trace-Li levels and a lower risk of dementia were observed between 0.012 mg/L to 0.027 mg/L of Li in drinking water. Meanwhile, levels below 0.002 mg/L did not elicit this effect. Although three of the five studies found dementia protective properties of Li in both sexes, women generally require lower doses to demonstrate such effects.

Conclusion:The reviewed evidence shows that trace-Li levels in the water are sufficient to lower the incidence or mortality from dementia. Considering the lack of treatments for the prevention and improvement of dementia, we should not ignore these findings. Future trials of Li should focus on low or even micro doses of Li in the prevention or treatment of dementia.

Stanley Ibeh, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Barbara Karten, Department of Biochemistry & Molecular Biology

Neuronal Cholesterol Turnover Influences Synapse Maturation and Function

Cholesterol turnover by CYP46A1 is the primary mechanism through which the brain removes cholesterol. CYP46A1 converts cholesterol into 24-hydroxycholesterol, which can diffuse through the blood-brain barrier. Excitatory neurotransmission leads to CYP46A1-mediated cholesterol loss in synaptic membranes. However, it is yet to be fully understood how CYP46A1 regulates synaptic plasticity. We propose that transient changes in synaptic cholesterol can lead to structural remodeling of dendritic spines in response to neuronal activity. To investigate the role of cholesterol turnover, we depleted CYP46A1 in primary hippocampal neurons using RNA interference and investigated the effects on spine density and plasticity. Our results show that CYP46A1 depletion significantly reduced spine density, particularly the more mature mushroom spines. Neurons depleted of CYP46A1 also showed reduced calcium signals in the cell body following chemical LTP, indicating decreased excitability or changes in signaling. Additionally, dendritic spine calcium influx, AMPA receptor exocytosis, and the activity-induced enlargement of the spines were reduced in CYP46A1 knockdown neurons. Overexpression of CYP46A1 also reduced spine density, suggesting that a precise regulation of CYP46A1 is required for dendritic spine maturation. Together, these findings suggest that CYP46A1 could influence synaptic activity. Further studies are necessary to relate these functional effects to CYP46A1-induced changes in membrane cholesterol.

Ebadullah Kabir, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Sultan Darvesh, Department of Medical Neuroscience

Butyrylcholinesterase Activity and Cellular Senescence Within the Temporopolar Region in Alzheimer's Disease.

Butyrylcholinesterase (BChE) associates with amyloid-β (Aβ) plaques in Alzheimer's Disease (AD). BChE is thought to be involved in transforming benign (diffuse) Aβ plaques into toxic malignant (fibrillar) Aβ plaques, suggesting that BChE may be implicated in AD pathology progression. Importantly, fibrillar Aβ plaques seem to induce detrimental molecular events like cellular senescence (CS), where cells permanently terminate cell division and subsequently release harmful pro-inflammatory cytokines. For instance, more microglia express senescent markers,

such as p16, when colocalized with fibrillar Aβ plaques. Assessing the spatial distribution of senescent microglia around plaques may be another way to corroborate the notion that BChE may play a role in AD pathology progression. Given that plaques induce a spectrum of extracellular damage from most to least for fibrillar and diffuse Aβ plaques, respectively, it is anticipated that the number of senescent microglia colocalizing with plaques will range from greatest to least for fibrillar Aβ plaques, Aβ plaques positive for BChE, and diffuse Aβ plaques, respectively. We also hypothesize that AD brains will have more senescent microglia than cognitively normal (CN) brains. We will examine these hypotheses by quantifying the overall number of senescent microglia and the number that colocalizes with different plaque types within the temporopolar region (TPR) in AD and CN brains. Sex- and age-matched tissue blocks of the TPR from AD and CN brains will be stained using histochemical, immunohistochemical, and histofluorescence techniques to reveal microglia, Aβ, fibrillar Aβ, and BChE-positive plaques, and p16. This work may help facilitate further research in understanding the role of senescent microglia and BChE in AD and the development of novel disease-modifying drugs, with BChE and microglia as key therapeutic targets.

Zachary Long, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Alex Quinn, Department of Physiology & Biophysics

Computational Models of the Zebrafish Atrial and Ventricular Action Potential and Calcium Transient

Introduction: The zebrafish is an increasingly popular experimental model for studying cardiac electrical activity due to its electrophysiological similarity to humans. While computational modeling of cardiac action potential (AP) and calcium (Ca2+) transients has provided important (patho)-physiological insights using many experimental species, no zebrafish-specific model exists. To address this, we present the development of novel computational models of the zebrafish atrial and ventricular AP and Ca2+ transient through an experimental-computational approach.

Methods: Ion current formulations in the 2004 TenTusscher and Panfilov computational AP and Ca2+ transient model were re-parameterised using existing patch-clamp data from zebrafish. The AP model was further modified by removing the transient outward potassium current and including the T-type Ca2+ current. Atrial and ventricular AP and Ca2+ transients were acquired from adult zebrafish isolated hearts through microelectrode and optical mapping experiments, which were used to further re-parameterise the model by adjusting ion channel conductances using a Monte-Carlo and sensitivity analysis approach. Computational simulations were then performed, to validate the model against additional experimental data, generated using restitution pacing protocols.

Results: The models replicated the morphology of the experimental AP and Ca2+ transients, and the restitution simulations produced similar effects on AP and Ca2+ transient duration, demonstrating the model's ability to replicate rate-dependent changes.

Conclusion: We have developed the first zebrafish-specific computational models of the atrial and ventricular AP and Ca2+ transient, which are valuable tools for future experimental-computational investigations of cardiac (patho)-physiology and pharmacological interventions using zebrafish.

Samuel Silva, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Jill Hayden, Department of Community Health and Epidemiology

Improving exercise treatment prescription and program adherence for the management of chronic low back pain: A research proposal

Chronic low back pain (CLBP) is the leading cause of disability globally, and exercise is a first-line treatment for this condition. However, exercise treatments are complex and can be challenging to implement in real-world settings.

This will be a three-phase project. In Phase 1, I will identify 1) barriers and facilitators to prescribing exercise to patients with CLBP from the perspective of physiotherapists, and 2) barriers and facilitators to adhering to exercise from the perspective of individuals living with CLBP. In Phase 2, I will develop a toolkit that supports physiotherapists in designing individualized exercise programs and supports patients in overcoming barriers identified in Phase 1. In Phase 3, I will test the implementation of the toolkit in Nova Scotian physiotherapy settings.

In Phase 1, I will conduct a qualitative study following the interpretive description methodology. I will conduct semi-structured interviews with physiotherapists and individuals living with CLBP. Inductive and deductive approaches will be used to identify themes. In Phase 2, I will use iterative co-creation cycles with provider and patient partners, participants from Phase 1, and computer scientist partners to develop a multi-component toolkit that recommends individualized exercise programs based on patients' and providers'/settings' characteristics. Patients will also be able to provide input into the toolkit and receive support to remain engaged. The toolkit will include a knowledge base with data from a large systematic review on exercise for CLBP. In Phase 3, I will conduct a mixed-methods study with a six-month implementation period to assess the feasibility of implementing the tool in Nova Scotian physiotherapy settings and the toolkit's effectiveness in improving CLBP-related outcomes and exercise program adherence.

This project will provide a useful tool for supporting physiotherapist in delivering greater patient-centered care and supporting patients in engaging in their treatment program.

Alexa Wilson, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Craig McCormick, Department of Microbiology & Immunology

Kaposi's sarcoma-associated herpesvirus primary envelopment at the nucleoplasmic reticulum.

Herpesvirus egress begins with primary envelopment of newly assembled capsids at the inner nuclear membrane (INM) facilitated by a highly conserved viral nuclear egress complex (NEC). Primary envelopment has been observed at the peripheral INM as well as at membranous structures known as nuclear infoldings. Nuclear infoldings resulting from invaginations of the INM are known as Type-I nucleoplasmic reticulum (NR), whereas infoldings of both INM and outer nuclear membrane (ONM) are known as Type-II NR. Here we report that Kaposi's sarcoma-associated herpesvirus (KSHV) utilizes both the peripheral INM and the Type-I NR for primary envelopment during viral egress. Transmission electron microscopy on samples collected over a time-course of infection revealed the predominance of DNA-containing KSHV C-capsids budding

into nuclear infoldings contiguous with the INM and sparsely decorated with nuclear lamina, characteristic of Type-I NR. These Type-I NR structures co-localized with puncta containing CTP:phosphocholine cytidylyltransferase (CCTα), which catalyzes the rate-limiting step in phosphatidylcholine (PtdCho) synthesis. CCTα is responsible for de novo membrane biogenesis and the induction of membrane curvature required for NR expansion. This is consistent with our observations of NR expansion over the course of the KSHV lytic replication cycle, providing sufficient Type-I NR to match requirements for KSHV nuclear egress. We also observed accumulation of de-enveloped KSHV C-capsids in second order nuclear infoldings, suggesting a model whereby primary envelopment and de-envelopment can occur not only at the nuclear periphery, but also in nuclear infoldings.

Poster Presentations

Haya Abdelwahab, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Ketul Chaudhary, Department of Physiology & Biophysics, Faculty of Medicine

Role Of Stem Cell Antigen-1 Expressing Cells In Right Ventricular Remodelling In Chronic Hypoxia-induced Pulmonary Hypertension

Most cardiac stem cell antigen-1 expressing cells (Sca-1+ cells) are tissue-resident endothelial stem/progenitor cells and may contribute to cardiac angiogenesis. Adequate angiogenic response has been shown to be critical for right ventricular (RV) adaptation and survival in pulmonary hypertension (PH). We examined the relevance of Sca-1+ cells in RV remodelling using the rat chronic hypoxia model.

Methods: To assess the effect of RV pressure overload, male and female Fischer CDF rats were subjected to 3 weeks of hypoxia (10% O2) and cardiac structure and function were assessed using echocardiography and pressure was measured by catheterization. Fulton index was measured to assess RV hypertrophy. Flow cytometry and immunofluorescence straining was performed to assess abundance and localization of Sca-1+ cells.

Results: In response to hypoxia, RV systolic pressure was increased significantly in male and female rats compared to controls. Significant elevation in the RV hypertrophy was observed in male and female rats compered to controls. These rats demonstrated adaptive RV remodelling and preserved RV function in response to chronic hypoxia as indicated by similar RV fractional shortening and cardiac index in hypoxia treated rats compared to controls. Adaptive RV remodelling in hypoxia treated rats was associated with an increase in the abundance Sca-1+ cells in the RV of male and female rats compared to controls. Immunofluorescence staining demonstrated localization of Sca-1+ cells to vascular endothelium in the RV.

Conclusion: Adaptive RV remodeling in chronic hypoxia-induced PH is associated with increased abundance of Sca-1+ cells that may contribute to RV angiogenesis and preservation of RV vascular density.

Alireza Aleali, Faculty of Medicine, MSc Candidate

Supervisor: Javeria Ali Hashmi, Department of Medical Neuroscience, Faculty of Medicine

High chronic pain severity is linked with anomalies in pain modulation and periaqueductal gray connectivity

Chronic pain (CP) remains poorly understood, with complex mechanisms contributing to its severity and impact. Its frequent co-occurrence with mood disorders suggests a distinct clinical phenotype requiring precision-based interventions. Many CP patients experience significant treatment refractoriness and heightened fear of pain, which may further contribute to the persistence and severity of their condition. Disruptions in pain modulation pathways, particularly abnormalities in the periaqueductal gray (PAG), have been implicated in CP pathophysiology. This study employs Expectation-Induced Pain Modulation (EIPM), a framework for investigating how mismatches between expected and actual pain (prediction error) shape pain modulation.

We examined whether CP patients exhibit variations in treatment refractoriness, fear of pain, impairments in EIPM, and aberrant PAG connectivity, stratifying them into high- and low-severity groups, with healthy controls (HC) serving as a benchmark.

A total of 159 CP patients were classified using PCA and K-means clustering, alongside 72 healthy controls. Treatment refractoriness and fear of pain were assessed using validated clinical scales. EIPM was evaluated through tasks measuring prediction error and pain perception using visual threat cues and thermal stimuli. Resting-state seed-to-seed connectivity analyses focused on dorsolateral/lateral (dl/lPAG) and ventrolateral (vlPAG) PAG columns.

High-severity CP patients exhibited significantly greater treatment refractoriness and fear of pain, as well as impaired pain modulation ($P < 0.05$). Resting-state analyses revealed more negative dlPAG connectivity with cognitive appraisal networks in the high-severity group. Reduced connectivity contrast between dlPAG and vlPAG with sensory and ventral attention networks correlated with poor pain modulation.

These findings suggest that severe CP constitutes a distinct phenotype characterized by neurobehavioral disruptions, reinforcing the need for targeted interventions.

Jena Barter, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Barbara Karten, Department of Biochemistry & Molecular Biology, Faculty of Medicine

The Role of the Cholesterol Transporter, STARD3 in Breast Cancer

Cholesterol is an essential component of all animal cell membranes. Endocytosed cholesterol is distributed throughout the cell via a dynamic network of interconnected membranes known as endosomes. Cancer cells rely on endosomal trafficking to meet their increased cholesterol demand for growth, survival, and metastasis. In addition, cholesterol influences mobility and positioning of endosomes, thus influencing endosomal trafficking of receptors and cell surface proteins. This study investigates the role of endosomal cholesterol and its transporter StAR-related lipid transfer domain-3 (STARD3) in breast cancer cells. STARD3 has a cholesterol-binding transmembrane domain that spans the late endosomal perimeter membrane and a cytosolic cholesterol transfer domain, which mediates cholesterol transfer between late endosomes and the endoplasmic reticulum (ER) or mitochondria, depending on cholesterol availability. STARD3 can also form a tether at endosome-ER membrane contact sites. Given that STARD3 is often co-amplified and co-expressed with HER2 in breast cancers, and that its inhibition or depletion reduces proliferation under some conditions, STARD3 has been proposed as a potential therapeutic target. However, the mechanism of STARD3's role in cancer remains unclear. To investigate the role of STARD3 in breast cancer cells with and without HER2 amplification, we used microRNA-mediated RNA interference to deplete STARD3 in MCF-7 (ER+/PR-/HER2-) and SK-BR-3 (ER-/PR-/HER2+) cells and assessed proliferation and migration. Preliminary results indicate that STARD3 depletion increased proliferation in both cell lines, while reducing migration in MCF-7. Gene expression analysis revealed an upregulation of cell cycle genes CDK1 and GINS2, alongside changes in the cell cycle. Future experiments will aim to elucidate the signaling events leading to the changed growth and further investigate which aspects of STARD3 function are responsible for its effects in breast cancer by conducting domain specific mutation analyses. These studies will

help determine how STARD3-mediated cholesterol trafficking and/or endosomal-ER contact sites influence breast cancer progression.

Maegan Burke, Faculty of Medicine, MSc Candidate

Supervisor: David Langelaan, James Davey, Department of Biochemistry & Molecular Biology, Faculty of Medicine

Detection of nanoplastics in water using engineered hydrophobins

Plastics are one of the most widely produced materials. Despite widespread recycling programs more than 50% of plastic material accumulates in landfills and the ocean. Plastics do not naturally decompose. Instead, plastics mechanically disintegrate to produce micro- and nanoplastic waste. Due to their suspected impacts on human health and documented adverse effects on the environment, it would be useful to develop biochemical probes that can both sequester and monitor the presence of plastics. Current methods for quantifying microplastics have limitations that restrict their utility. For example, conventional detection methods such as Raman spectroscopy and mass spectroscopy require highly specialized equipment, involve sample destruction, or lack the ability to simultaneously detect and sequester nanoplastics.

In this work, we developed a novel fluorescence anisotropy-based assay to quantify the binding of fluorescently labelled hydrophobins to polystyrene (PS) nanoplastics in aqueous samples. A genetically encoded fluorophore (mScarlet3) was fused to either the hydrophobins SC16 or NC2. The change in fluorescence anisotropy was monitored as a function of PS concentration to quantify binding between the fluorescent hydrophobin to PS. Our results showed a change in anisotropy of the mScarlet3-SC16 and mScarlet3-NC2 fusion proteins, indicating plastic binding activities. Appropriate background measurements were collected to account for light scattering effects of the PS. Binding of the fusion proteins to PS was corroborated with fluorescence images of bound protein to PS discs. In an alternative approach, the purified hydrophobins will be covalently conjugated to NHS-fluorescein to explore changes in PS binding with variations in molecular size. Currently, we are constructing a recombinant protein secretion system for the development of a high-throughput plastic binding assay of protein variants. Further research will investigate rational computational design methodologies to engineer the hydrophobin affinity and selectivity for PS and other plastics.

Lauren Burton, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Zhenyu Cheng, Department of Microbiology & Immunology, Faculty of Medicine

Characterization of mitogen-activated protein kinase ERK activation by Pseudomonas aeruginosa protease IV

Pseudomonas aeruginosa is an opportunistic bacterial pathogen capable of causing a variety of infections. One of P. aeruginosa's secreted virulence factors, protease IV (PrpL), was found to exacerbate inflammation in lung infection models and degrade proteins important for host immunity. Previously, our lab found that PrpL activates a conserved inflammatory signaling pathway, the extracellular signal-regulated kinase (ERK) mitogen-activated protein kinase pathway. In this study, we are investigating how PrpL activates this pathway and characterizing the resulting inflammatory effects. Purified PrpL was intratracheally instilled into the lungs of mice at a dose of

0.5 µg per g body weight. Inactive mutant PrpL was used as a negative control, and P. aeruginosa lipopolysaccharide (LPS) served as an inflammatory positive control. Lungs and bronchoalveolar lavage fluid (BALF) were collected at 24 hours post-instillation. Mice that received wild-type PrpL, LPS, or both PrpL and LPS all experienced significant but similar weight loss and clinical symptoms. PrpL and/or LPS also resulted in increased levels of inflammatory cytokines IL-1β, IL-6, and TNF in both the lung and BALF. Phosphorylation (activation) of ERK in the lung was more strongly induced following PrpL instillation compared to LPS. The lungs also showed phosphorylation of c-Jun and c-Fos, subunits of the AP-1 transcription factor that is known to assemble downstream of activated ERK. Our results suggest that following activation by PrpL, ERK is triggering the assembly of AP-1, which likely leads to inflammasome formation and results in the elevated inflammatory cytokine levels seen in response to PrpL. This project is ongoing, and future directions include mapping the upstream signaling cascade leading to ERK activation and determining the substrates cleaved by PrpL to trigger this signaling.

Cameron Calder, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Javeria Hashmi, Department of Medical Neuroscience, Faculty of Medicine

Large-scale brain networks increase in integration with high prediction error during pain processing

System segregation (SS) is a network characteristic that reflects the functional independence of brain modules, facilitating specialized and efficient processing. Reduced SS, or increased integration, may support large-scale network coordination, although at higher metabolic cost. In accordance with this, both individual differences in SS and its flexible modulation in response to task demands have been linked to cognitive performance. A likely mechanism linking SS and cognition is the brain's ability to utilize prediction errors, mismatches between predicted and actual outcomes, in updating internal expectations. We suggest that integration of large-scale networks facilitates the propagation of prediction error signals and coordinated expectation updating. Thus, we hypothesized that as prediction errors increase, system segregation will decrease.

To test this, fifty-one healthy adults completed a pain expectancy task during fMRI, where visual cues (0–100%) predicted upcoming heat pain (43.8°C–47°C). On some trials, cues predicting low pain intensity were paired with high-intensity stimuli (47°C), generating varying levels of prediction error (0–3.2°C). Functional connectivity was computed from short time windows of BOLD activity across independent task blocks, which was used to quantify SS using previously established methods. A secondary analysis used the Integration Segregation Difference (ISD) metric, which, unlike SS, does not rely on predefined network labels.

We found that SS significantly decreased (indicating increased integration) in task blocks with high prediction error (>1.3°C). This result remained significant after false discovery rate correction. These results were replicated when using the ISD index, demonstrating that the effect is robust to parcellation method.

These findings show that prediction error dynamically drives increased network integration, possibly to support the high-cost communication needed to optimally update internal models. This is the first study to demonstrate that prediction errors are tracked by SS, providing new links between graph theory, large-scale network dynamics and computational theories of learning.

Ernest Chan, Faculty of Medicine, MD Candidate

Supervisor: Dr. Justin Paletz, Dr. Michael Bezuhly, Department of Surgery, Faculty of Medicine

Assessment of the Z-Plasty as a Method for Scar Camouflage: An Eye-Tracking Study

Background: Facial scars can profoundly affect self-image and contribute to psychosocial distress, often influencing both how individuals perceive themselves and how they are perceived by others (Brown et al., 2010; Rankin & Borah, 2003). Thus, scar revision techniques have been developed to reduce a scar's visibility. This is particularly true when assessing scars on the face, where even subtle imperfections can feel magnified. Among these, the Z-plasty remains a cornerstone approach, designed to redistribute tension and break up linear contours that tend to attract attention (Shockley, 2011; Hudson, 2000; Hove et al., 2001). While its benefits are widely accepted in surgical practice, there is a surprising lack of empirical evidence assessing whether Z-plasty scars attract less visual attention than their unrevised linear counterparts.

Objective: This ongoing study aims to determine whether Z-plasty revision reduces the visual attention drawn to facial scars compared to unrevised linear scars.

Methods: Thirty participants with normal or corrected-to-normal vision will be recruited from Dalhousie University. Using ten headshots from a public photobank, we will digitally generate three versions of each face: unscarred, with a linear scar, and with a Z-plasty scar. Eye movements will be recorded using the EyeLink 1000 eye-tracking system as participants view the images. Fixation time and saccades will be analyzed using repeated measures ANOVA to assess attentional bias and dwell times across distinct interest areas of the face (e.g eyes, nose, mouth, brow, ears). Participants will be asked to guess the age of the face to maintain a standardized task across images and minimize attentional biases.

Expected Outcomes: We hypothesize that Z-plasty scars will draw significantly less visual attention than linear scars, as indicated by shorter fixation times and reduced gaze clustering. Findings may provide quantitative support for Z-plasty's effectiveness in scar camouflage and inform surgical decision-making.

Agustina Cohen, Faculty of Health, MA Candidate

Supervisor: Dr Son Truong, Department of Therapeutic Recreation, Faculty of Health

Empowering diverse youth voices to enhance equitable access to nature and wellbeing in Nova Scotia: A photovoice study

Introduction: Research shows that participating in nature-based activities supports positive youth development and wellbeing; however, many youth face barriers to accessing nature, particularly those from equity-owed communities. As such, there is a need for more inclusive and accessible nature-based opportunities in Nova Scotia (NS). This study aimed to engage youth as coresearchers to explore their experiences in nature, identify barriers youth face when accessing nature, and provide recommendations to enhance access to nature-based services within the province.

Methods: This project used photovoice methods, which empowers participants to document community issues and advocate for change through photography. For this project, we partnered with Leave Out Violence NS, a Black-led community organization dedicated to supporting diverse and underserved youth in NS. Twelve youth participated in a series of five sessions, including photography workshops, focus groups, and collaborative analysis. The resulting photographs underwent a three-phase participatory analysis with our youth coresearchers, which consisted of selecting photos, contextualizing, and codifying issues to identify themes that resonate with their lived experiences. The photographic results and themes were combined to create an action plan for a final youth-led knowledge translation project.

Conclusions and Anticipated Impact: Preliminary findings from collaborative thematic analysis will be discussed, including youth photographs and primary themes identified that represent the experiences of youth accessing nature for wellbeing in NS. This research offers potential for youth capacity building and community enrichment by engaging participants as co-researchers and advocates for local community issues. In the future, we plan to hold a knowledge mobilization event that will serve as a platform for youth to present their final project, facilitating dialogue with policymakers, stakeholders, educators, and youth workers across the province. The results of this research will provide valuable youth perspectives to inform ways of enhancing access to nature-based services in NS for diverse youth populations.

Chris Consmueller, Faculty of Health, MSc Candidate

Supervisor: Dr. Scott Grandy, School of Heath & Performance, Faculty of Health

A randomized controlled trial protocol: STudy on bluebeRries, prOteiN, and exercise for improvinG frailty and cardiovascular disease (STRONG)

Introduction: Cardiovascular diseases (CVD) are a leading cause of death worldwide. Accelerated aging presents a greater risk of adverse health outcomes, CVD, co-existing diseases, and death. Frailty is a state of health decline that increases the likelihood for adverse health outcomes. Exercise and dietary modifications (protein and blueberry intake) can reduce frailty and CVD; however, the combined long-term effects of these three lifestyle behaviors have yet to be studied.

Objective: The purpose of this study is to determine if a 12-month protocol of exercise, protein, and blueberries (STRONG) reduces frailty and CVD risk in older Nova Scotians.

Methods: This randomized controlled trial will recruit 240 Nova Scotians (≥65 years, ~120 females and ~120 males). Participants will be randomly assigned to control or intervention (STRONG) groups. Control participants will receive standard medical care. The STRONG group will consume 30 grams of a protein supplement and 150 grams of wild blueberries daily, in addition to participating in three 60-minute exercise sessions per week, focusing on aerobic exercise, resistance training, and mobility. Measured outcomes will include changes in CVD risk factors, cardiovascular health, inflammatory markers, frailty, physical fitness, and health-related quality of life.

Implications: In Nova Scotia, CVD and frailty each present a significant burden on the health care system and negatively affect the health of its residents. STRONG study findings may offer needed

evidence-based lifestyle intervention treatment plans aimed at lowering rates of frailty, CVD, and easing the burden on healthcare system.

Jordan Cucksey, Faculty of Medicine, MSc Candidate

Supervisor: Dr. James Davey, Department of Biochemistry & Molecular Biology, Faculty of Medicine

Design and construction of a genetic circuit for engineering DNA methylation sensitive repressors

Protein engineers strive to create and improve protein functions and properties. For example, enzymes have been engineered to reduce environmental impact with the production of chemical commodities and engineered proteins comprise the functional components for many therapeutics and medical diagnostics. This endeavour is accomplished using the protein engineering workflow. And, although this experimental workflow has shown success, it has limitations. One limitation is the application of candidate screening procedures that require the evaluation of both functional and non-functional variants. This limitation is exacerbated when engineering protein sequences to perform multiple objectives. For example, the identification of a protein variant that can discriminate the methylation status of DNA. Using the conventional workflow, the repressor library must first be screened for binding to methylated DNA. This initial screening process would create an intermediate library of repressors that are then subjected to a second screening process to eliminate variants recognizing unmethylated DNA. This two-step strategy decreases the throughput of the protein engineering workflow by doubling the labour. In addition, the protein sequences identified by the initial round of screening does not guarantee that remaining variants satisfy the engineering objective in the second round. In living organisms, complex systems of interacting proteins catalyze reactions and organize processes critical to life. Drawing inspiration from these evolved biological systems, we propose that genetic circuits can serve as a platform to expand the scope and utility of the protein engineering workflow. Through the organization of multiple repression events our circuit condenses the fulfillment of multiple desired and undesired binding events into a single gene expression event, allowing for the identification of successful repressor variants through a single round of selection. Successful application of our selection process will establish a system of repressors, methyltransferases, and genetic elements that can be used in the development of epigenetic editing biotechnologies.

Ghislain d'Entremont, Faculty of Medicine, PhD Candidate

Supervisor: Jill A Hayden, Department of Community Health and Epidemiology, Faculty of Medicine

Evaluation of artificial intelligence tools for critical appraisal in evidence syntheses

The gold-standard of evidence synthesis is the systematic review. Artificial intelligence (AI) tools have shown promise in automating the essential, but time-consuming, systemic review step of critical appraisal. However, the available evidence on the accuracy of these AI tools has not been synthesized, and there is a lack of evidence regarding their reliability and applicability.

Phase 1: We will conduct a systematic review of peer-reviewed evaluation studies of all AI tools used to automate at least one critical appraisal item/domain. We will perform study screening, data extraction, and quality assessments (using QUADAS-2) in duplicate, with a third reviewer available

to resolve disagreements. We will summarize accuracy, efficiency (time savings) and usability outcomes.

Phase 2: We will evaluate the accuracy and efficiency of the most promising artificial intelligence tools identified during Phase 1 using datasets from existing systematic reviews, including one of Cochrane's largest published reviews. We will compare a) fully automated and b) semi-automated responses to c) human-only responses. In the semi-automation condition, our critical appraisers will receive forms pre-populated with AI suggestions.

Phase 3: We will conduct a prospective, randomized trial, with three study arms: a) full automation, b) semi-automation, and c) human-only. We will evaluate AI tool accuracy and efficiency in a 'real-world' research setting. We will randomly assign each critical appraiser within a pair to either the human-only or semi-automation condition for each included trial. The consensus of this pair will serve as the reference standard.

We aim to provide the robust testing required to responsibly implement AI tools into the systematic review process, allowing health researchers to create and maintain more up-to-date clinical evidence.

Emily Devereaux, Faculty of Health, PhD Candidate

Supervisor: Dr. Janet Curran, School of Nursing, Faculty of Health

Factors that Influence How Pediatric Patients or Caregivers Decide to Present to an Emergency Department: Scoping Review

Introduction: Studies in countries with universal health care systems have suggested that patients consider using services outside of the hospital for care, however, often end up presenting to an emergency department (ED). Understanding how pediatric patients and caregivers decide to present to an ED can inform health care design to mediate decisions before an ED presentation.

Objective: To map and describe the extent and type of evidence in relation to factors that influence how pediatric patients, or their caregivers decide to present to an ED.

Methods: A scoping review using JBI methodology is being conducted and includes published studies and a targeted grey literature search. Published studies include those assessing patients between 0-17 years who present to an ED in a country that has membership in the Organization for Economic Co-Operation and Development and has universal health care. Studies included report reasons for ED attendance from perspectives ofpatients or caregivers. CINHAL, MEDLINE, PsychInfo and Embase were searched with no date limits or language restrictions. Screening and data extraction are being conducted by two independent reviewers, conflicts being resolved by a third reviewer or discussion. Data will be analyzed through tables with an accompanying narrative summary. Grey literature will assess websites of pediatric hospitals in Canada, Australia, and United Kingdom (UK) that provide guidance on attending the ED.

Results: Data extraction is ongoing, the study expected to be completed by April 2025. A search of published literature in specified databases and select references of relevant reviews found 4394 studies for title/abstract screening, 171 for full-text screening, and 69 for data extraction. Grey

literature search has found ED guidance from 13 pediatric hospitals in Canada, 8 in Australia and 20 in the UK.

Conclusion: This scoping review may contribute to interprofessional collaborative practice and help strengthen health systems.

Sayanti Dey, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Andrew Makrigiannis, Department of Microbiology & Immunology, Faculty of Medicine

Delineating the role of murine Ly49C/I+ antigen specific NK cells in antitumor immunity

Background: Natural killer (NK) cells, a subset of innate immune cells, are well recognized for their effector cytolytic functions against tumors and virally infected cells. Interestingly, we have recently identified that NK cells can mediate antigen-specific memory responses depending on the interaction between Ly49C and/or Ly49I (Ly49C/I) surface receptors and their cognate ligand MHC I. We have observed that the memory NK cells can provide antigen specific, long-lasting antitumor protection in Rag1-/- mice. However, in the absence of Ly49C/I receptors, the protection is lost. Hence, to characterize the tumor infiltrating Ly49C/I+ NK cells, we have isolated immune cells from tumor microenvironment (TME) and performed high through-put single cell RNA sequencing (scRNA seq). By analyzing the data, we are able to distinguish 5 different states/ subsets of NK cells in the tumor micro-environment and indicate a potential memory NK cell population that might be rendering antitumor protection.

Hypothesis: Antigen specific memory NK cell population from TME has a different transcriptomic, and metabolic signature compared to circulating bona-fide conventional NK cells.

Results: ScRNA-seq data analysis revealed 17 major immune cell clusters exhibiting high heterogeneity within the TME, with NK cells being the largest population. Re-clustering using NK1.1 and NKp46 markers identified five NK cell subsets and one ILC1 subset. NK1 displays high expression of cytotoxicity-related molecules, indicating a mature cytotoxic phenotype, and are the bona-fide conventional NK cells. NK2 shows up regulated transcripts linked to a stem-cell-like state, suggesting immaturity and migratory potential. NK3 and NK4 are distinct and only found in the vaccinated, but not in the control group. They exhibit high pro-inflammatory cytokine expression and mitochondrial metabolic dependency like memory T cells, indicative of an effector memory phenotype. These findings highlight the heterogeneity and functional diversity of NK cells and allow us to capture markers that might be associated with memory cells.

Conclusion: This study identifies existing heterogeneity within the tumor infiltrated NK cells and allow us to understand how NK cells might be transitioning within the TME. It is also indicative of a potential NK memory population with high Ly49I expression, exhibiting antigen-specificity.

Noah Doucette, Faculty of Health, PhD Candidate

Supervisor: Drs. Audrey Steenbeek & Jennifer Lane, School of Nursing, Faculty of Health

Exploring the Determinants of Human Papillomavirus (HPV) Vaccine Uptake in Nova Scotia, Canada: Towards Equity and Inclusivity

Introduction: Human Papillomavirus (HPV) is the most common sexually transmitted infection, responsible for more than 630,000 new cancer diagnoses worldwide each year. Vaccination remains the most effective way of preventing HPV-related morbidity and mortality, yet uptake remains low, particularly amongst various Canadian sub-populations (e.g., transgender individuals, men who have sex with men, young adults). Existing evidence about HPV vaccine hesitancy- an attitude/sentiment of indecision/uncertainty that precedes one's decision to become vaccinated (or not)- focuses predominantly on parents of adolescents, with scant attention to other eligible populations. Social categories of identity- including sex, gender, sexual orientation, race/ethnicity, amongst others- have been found to influence one's decision to vaccinate. These determinants do not exist in isolation; an unvaccinated individual may encounter various identity positions that further implicate their decision about vaccination. Understanding the intersectional determinants of HPV vaccine uptake are imperative to devising inclusive public health strategies aimed at equitably increasing HPV vaccination coverage in Canada.

Methods: Informed by intersectionality theory, we propose a multi-phased project to explore the determinants of HPV vaccine uptake in Nova Scotia. Phase 1 will include a scoping review to map out existing evidence about the determinants (across social categories of identity) of HPV vaccine uptake. Phase 2 will involve purposeful selection of 20 diverse young adult service users (10 vaccinated & 10 unvaccinated) and 10 service providers to complete semi-structured interviews about their perspectives and/or experiences of HPV vaccine hesitancy. Using a community-centered approach (e.g., focus groups), phase 3 will synthesize the findings from phase 1 and 2 to develop inclusive vaccine promotional materials aimed at normalizing equitable HPV vaccine uptake.

Conclusion: Normalizing inclusive HPV vaccination is a critical step towards optimizing vaccine uptake in Canada. Understanding the intersectional determinants of HPV vaccine acceptance has implications to mitigate the persistence of HPV-related morbidity and mortality, and make equitable vaccine uptake a tangible public health objective.

Mikaela Ethier-Gagnon, Faculty of Science, PhD Candidate

Supervisor: Dr. Sherry Stewart, Department of Psychiatry, Faculty of Medicine

The Impact of Acute Cannabidiol (CBD) on Stress and Anxiety: A Systematic Review and Meta-Analysis

Background: Cannabidiol (CBD), a non-intoxicating cannabinoid, has generated considerable interest for its purported stress- and anxiety-relieving properties. Some preclinical studies have supported the efficacy of acute CBD treatment in anxiety disorders and trauma- and stressor-related disorders. However, others have reported equivocal results. The impact of acute CBD vs. placebo administration on both psychological and biological stress- and anxiety-related outcomes remains unknown. A systematic review and meta-analysis is indicated.

Methods: MEDLINE ALL, PsychINFO, EMBASE, and CINAHL databases were searched from inception to July 2024. Study selection, data extraction and Cochrane Risk of Bias assessments were conducted according to PRISMA guidelines and registered on the PROSPERO database (CRD42024574751). A total of k=32 full-text randomized trials investigating the impact of acute CBD administration on stress- and anxiety-related outcomes (i.e., subjective, physiological, and endocrine) in adults were systematically reviewed. Results were narratively reviewed among healthy, obsessive-compulsive disorder, trauma-exposed, generalized anxiety disorder, social anxiety disorder, panic disorder, and elevated trait worry and paranoia populations. A meta-analysis was conducted with the subset of k=6 studies that included the data needed for a meta-analysis (all on subjective stress/anxiety outcomes).

Results: In the narrative review, findings across population categories and outcome measures were mixed. Results of the meta-analysis suggested that acute CBD administration did not significantly decrease subjective stress- and anxiety-related outcomes following a stress task relative to placebo (d= -0.12, p=0.46, 95% CI: -0.43 to 0.19, I2= 31.49%). As there was not sufficient heterogeneity, we could not test for any significant moderators of this effect.

Conclusions: Based on the current review, there is not sufficient evidence to suggest CBD as an effective treatment for stress and/or anxiety among both clinical and healthy populations. Future studies may consider investigating the impact of diverse routes of administration, sex differences, and expectancy effects on CBD's purported anxiolytic properties.

Emilee Fackelmann, Faculty of Health, PhD Candidate

Supervisor: Dr. Parisa Ghanouni & Dr. Lori Weeks, School of Occupational Therapy, School of Health Administration

Health Equity and Belonging: Lived Experiences of University Students with Disabilities in Nova Scotia

This doctoral research investigates the intricate relationship between disability, health, and belonging among young adult students in Nova Scotian universities, focusing on equitable access, accommodation, and health outcomes. Employing a mixed-methods approach, this study critically analyzes provincial and university policies governing disability and accessibility, examining their impact on student health. A key component is the analysis of the social versus medical models of disability within these policies, addressing variations in implementation and their effects on health equity.

Through qualitative interviews and quantitative surveys, the research explores the determinants of health, including academic accommodations, physical accessibility, health service utilization, and assistive technology. It examines the intersectionality of disability with other social identities and its influence on health disparities. The study investigates the effectiveness of inclusive education practices and the accessibility of assistive technologies, assessing faculty and staff training and its contribution to student health and wellbeing.

Furthermore, this study investigates social inclusion, belonging, and the prevalence of ableism, analyzing their impact on mental and physical health. It assesses the role of universities in promoting disability as a form of diversity and its contribution to health equity. Access to and

quality of healthcare, including mental health services, is critically evaluated, examining barriers to timely and appropriate care, and its impact on health outcomes.

Finally, the research synthesizes findings to identify systemic barriers to equitable access and inclusion, developing evidence-based recommendations for policy and practice improvements that prioritize health promotion. This study aims to enhance understanding of the health challenges faced by students with disabilities, promoting a more inclusive and equitable post-secondary environment that fosters positive health outcomes.

Tanzima Fariha, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Corey Baimel, Department of Pharmacology, Faculty of Medicine

Ventral hippocampal control of amygdala to nucleus accumbens circuits

While humans possess cognitive abilities that set us apart from other species, we share fundamental emotional behaviours with other species. These responses to emotionally significant stimuli help sustain life and enable both humans and animals to navigate the world, seeking resources and avoiding threats. The basolateral amygdala (BLA) is an evolutionarily well-conserved brain region that responds to emotionally significant stimuli and acts as an interface between perception and action. It does this through a wide array of connections with other brain regions, including to the nucleus accumbens (NAc), but many of these connections are not well defined. Preliminary data from our lab has shown that distinct populations of BLA neurons target different subregions of the NAc, the medial and lateral shell, and that these individual cell populations are differentially engaged in reward learning. This project will build on this preliminary data and examine the functional connectivity of long-range presynaptic inputs onto BLA neurons that project to the nucleus accumbens. I hypothesize that BLA to nucleus accumbens medial and lateral shell neurons may be regulated by cell-type synaptic connections from other regions of the brain, specifically inputs from the ventral hippocampus. To examine this, I will use a combination of anatomical and electrophysiological experiments to characterize functional connectivity between ventral hippocampal inputs and amygdala outputs to the nucleus accumbens. Understanding the intricacies of this circuitry is important given that both the BLA and the nucleus accumbens are implicated in a wide range of disease states, including addiction, autism and anxiety disorders.

Jeffy Fernando, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Petra Kienesberger, Department of Biochemistry & Molecular Biology, Faculty of Medicine

Characterization of lipid phosphate phosphatases in skeletal muscle: regulation by nutritional stress and role in energy metabolism

Background:
Obesity is a multifactorial metabolic disorder linked to insulin resistance, type 2 diabetes, and cardiovascular disease. In skeletal muscle, dysregulated lipid metabolism and mitochondrial dysfunction contribute to these complications. Increased signalling induced by lysophosphatidic acid (LPA) has been linked to obesity and insulin resistance in skeletal muscle and heart. LPA is degraded by lipid phosphate phosphatases (LPP1–3), but their roles in skeletal muscle metabolism and LPA signalling remain poorly understood.

Hypothesis:
We hypothesize that LPPs are differentially expressed in glycolytic and oxidative skeletal muscle depots at baseline and under obese conditions and modulate insulin signalling, lipid/glucose metabolism, and mitochondrial function.
Methods and Results:
To explore the regulation of LPP3 by diet, male and female C57BL6/J mice were fed a low-fat diet (LFD) or high-fat diet (HFD) for 21 weeks. Western blot analysis revealed increased LPP3 protein levels in the gastrocnemius compared to the soleus muscle in female mice. In both skeletal muscle and heart, diet had no effect on LPP3 protein levels. To investigate the regulation of LPPs during muscle development, we analyzed protein levels of LPPs during the myogenic differentiation of C2C12 cells. LPP3 protein content was highest in undifferentiated myoblasts, declining as cells differentiated, while LPP1 protein content increased early during differentiation. LPA treatment (10 μM, 18 h) of differentiated C2C12 myotubes upregulated LPP3 protein levels, which was associated with impaired ADP-stimulated mitochondrial respiration.

Conclusions:
LPP3 protein levels are higher in glycolytic compared to oxidative muscle depots in female mice but are not influenced by HFD feeding in skeletal muscle or heart in male and female mice. LPP1 and LPP3 are differentially expressed at the protein level early during differentiation of C2C12 myoblasts. Additionally, LPA-induced metabolic stress and mitochondrial dysfunction are associated with increased LPP3 protein levels, perhaps in an attempt to counter excessive LPA signalling

Lauren Fong-Hollohan, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Locke Davenport Huyer, Department of Microbiology & Immunology, Faculty of Medicine

INVESTIGATING THE FUNCTIONAL ROLES OF PERI-IMPLANT GLYCOLYTIC MACROPHAGES

Introduction: To combat depression and body dysmorphia, silicone implants used in breast reconstruction provide structural support and breast restoration following mastectomy (~14,000 cases/yr in Canada)1. Fibrosis driven capsular contracture (CC) remains a significant complication to these procedures, with incidence rates up to 45%, the majority occurring within one year post-surgery2. The foreign body response (FBR), a persistent, macrophage-driven inflammatory reaction induced by foreign material, underlies CC wherein dysregulated inflammation results in contractile fibrous capsule formation3,4. Recent findings from our group suggest that glycolysis defines peri-implant macrophages that drive pathological fibrosis. In this study, we used single-cell RNA-sequencing (scRNA-seq) analysis to correlate metabolic adaptations in the FBR macrophages to pathological fibrotic function.

Methods: To uncover the functional involvement of FBR-associated glycolytic macrophages, we analyzed a scRNA-seq dataset in a silicone implant murine model explanted at 1- and 6-weeks post-implantation5. The Seurat package for R studio was used for the downstream scRNA-seq analysis. A subset consisting of only macrophage clusters was generated and differential gene

expression (DGE) analysis was performed. Glycolytic macrophages were identified by significant differential expression of Slc2a1. Gene ontology (GO) enrichment analysis was conducted using the top 100 differentially expressed genes (DEG) to identify the top 10 biological processes for each macrophage cluster.

Results: DGE analysis revealed an upregulation of genes involved in pro-inflammatory and pro-fibrotic functions in the glycolytic macrophage population. For example, inflammation-associated Itgb2 and pro-fibrotic Fn1 were among the top 10 DEGs within the glycolytic macrophage cluster in both datasets6,7. Following GO analysis, biological processes such as wound healing were enriched in the glycolytic macrophage population during chronic inflammation, thus supporting their role in driving dysregulated wound healing.

Conclusion: Our findings highlight a potential direct contribution of peri-implant glycolytic macrophages to chronic inflammation and fibrosis, thus informing the development of novel implant designs and therapeutic approaches.

Alyssa Forbes, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Jeremy Brown and Dr. Thomas Landry, School of Biomedical Engineering

A Novel Surgical Procedure for Using Ultrasound and Histotripsy Transcranially

Glioblastoma multiforme (GBM) is a terminal brain cancer with an average survival time post-diagnosis of 12 months. With approximately 1000 new diagnoses of GBM in Canada every year, improving the gold standard treatment is critical to increasing patient survival time. Current gold standard treatment involves a preoperative MRI, followed by endoscopic resection and subsequent chemotherapy and radiation. Complete resection of GBM tumor is improbable with current limitations of resection surgeries; Inaccurate preoperative MRIs from tissue movement and lack of intraoperative image guidance lead to conservative surgical approaches that limit survival outcomes. In attempts to improve treatment outcomes, the Microsonic Lab has developed an endoscopic ultrasound probe for intraoperative guidance. To improve treatment outcomes further, histotripsy, a mechanical ultrasound ablation technique, can be used to simultaneously ablate tumor tissue under ultrasound image guidance. During preclinical rodent testing, where a small craniectomy was performed, initial use of this combination ultrasound imaging-histotripsy device encountered challenges due to the relative size of skull opening during recovery experiments. In response, a novel surgical technique involving thinning the skull to ~50μm, and decalcifying it for 15 minutes with 20% ethylenediaminetetraacetic acid (EDTA) with simultaneous sonication has been developed and tested in-vivo. Ultrasound imaging significantly improved from sham treatment and was not significantly different from a craniectomy control. Histotripsy cavitation threshold agreed with previous experiments (avg. 29.9MPa): was significantly higher in sham treatments, and was not significantly different from a craniectomy control. There was visual evidence of subcranial tissue damage with H&E staining; Preliminary fluorescent immunohistochemistry staining for GFAP found astrocyte damage in cortical layer I was greater with longer exposure times to EDTA. This novel surgical technique will not only progress preclinical experiments in our lab, but could be translated to other ultrasound applications through the skull, as well as to clinics in lieu of MRIs.

Zachary Froom, Faculty of Medicine, MSc Candidate

Supervisor: Sr. Locke Davenport Huyer, School of Biomedical Engineering

Antifibrotic Function of Itaconate-Based Degradable Polyester

Materials

Pathological fibrosis is a chronic disease, characterized by excessive extracellular matrix deposition, that remains a significant global health challenge. Despite its prevalence, current anti-fibrotic therapies are limited due to the complex interplay and signaling of pro-fibrotic macrophages and fibroblast cells that underlies fibrotic tissue microenvironments. This study investigates a novel approach to combat fibrosis, harnessing the anti-fibrotic properties of the endogenous metabolite itaconate (IA) to target the pathological activation of the macrophage-fibroblast axis in fibrotic disease. To achieve therapeutic delivery relevant to the chronic nature of fibrotic conditions, we incorporated IA into the backbone of biodegradable polyester polymers, poly(dodecyl itaconate) (poly[IA-DoD]), capable of long-term localized release of IA. Degradation characterization of poly(IA-DoD) revealed that IA, as well as water soluble IA-containing oligomeric groups, are released in a sustained manner. Treatment of murine bone marrow-derived macrophages and human dermal fibroblasts demonstrated that the degradation products of poly(IA-DoD) effectively modulated pro-fibrotic behavior. Macrophages exposed to the degradation products exhibited reduced pro-fibrotic responses, while fibroblasts showed decreased proliferation and myofibroblast α-smooth muscle actin expression. These findings suggest that poly(IA-DoD) has the potential to disrupt the fibrotic cycle by targeting key cellular players. This polymer-based delivery system offers a promising strategy for the treatment of fibrotic diseases.

Shannen Grandy, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Zhenyu Cheng, Department of Microbiology & Immunology, Faculty of Medicine

Characterizing the role of host stress responses during Pseudomonas aeruginosa infection

Pseudomonas aeruginosa is a Gram-negative bacterium and opportunistic pathogen. P. aeruginosa lung infection is the leading cause of morbidity and mortality in people with cystic fibrosis. Due to P. aeruginosa's intrinsic and acquired antibiotic resistance, and lack of recent antibiotic development, alternative therapies to alleviate the consequences of P. aeruginosa infection are urgently needed. Our lab has found that inhibiting the integrated stress response (ISR) reduces inflammation during P. aeruginosa infection. Therefore, the ISR is a promising therapeutic host target to alleviate some of the damaging inflammation during infection. The ISR is a highly conserved eukaryotic signalling pathway that responds to different types of cellular stress. Stress is detected by four kinases HRI, PKR, PERK, and GCN2. Once activated, all kinases act to phosphorylate the eukaryotic translation initiation factor 2 alpha (eIF2α) which inhibits general protein synthesis but allows for the select translation of ISR effectors.

We treated the human cell lines A549, 16HBE, or THP-1 with purified secreted proteases from P. aeruginosa and assessed the levels of ISR markers via western blotting. In this study, we show that the following three secreted proteases also activate the ISR: alkaline protease, elastase A, elastase B (LasB), and protease IV. Additionally, by using cell lines which lack one of the ISR kinases, we determined that GCN2 was required for LasB to activate the ISR. Activation of the GCN2-ATF4

signalling axis has been linked to autophagy which led us to assess the accumulation of the classic autophagy marker LC3-II. LasB in combination with chloroquine (Cq), an inhibitor of autophagic flux, increased the accumulation of LC3-II compared to Cq alone at different timepoints in WT cells and GCN2-/- cells. Additionally, we found that LasB induced LC3-II accumulation in the macrophage cell line THP-1, indicating that autophagy induction is not cell type specific.

Meghan Hamilton, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Stephen Bearne, Department of Biochemistry & Molecular Biology, Faculty of Medicine

Transition State Stabilization: The Moderate Burden Borne by Dihydrodaidzein Racemase

Plant-based foods are known to reduce morbidity and mortality from various chronic diseases. Diets rich in plant isoflavones afford potential health benefits, including decreased risk of cancers, osteoporosis, cardiovascular and neurodegenerative diseases, and postmenopausal symptoms. Among the most chemoprotective phytoestrogens is (S)-equol, a metabolite of the soybean isoflavone daidzein, produced by gut bacteria in only 30-50% of individuals and acting through endocrine pathways. (S)-Equol exhibits the highest antioxidant activity, bioavailability, and slowest clearance rate among soy-derived isoflavones. Its affinity for estrogen receptor β is much greater than that of daidzein. Accordingly, there is interest in supplying (S)-equol as a health supplement via in vitro production or microbiome modulation. Over the past decade, the pathway for biotransformation of daidzein to (S)-equol has been elucidated and a novel dihydrodaidzein racemase (DDRC) was discovered that catalyzes the interconversion of (R)-dihydrodaidzein and (S)-dihydrodaidzein, with the latter compound being reduced to yield (S)-equol by the action of (S)-dihydrodaidzein reductase (DHR) and tetrahydrodaidzein reductase (THR). Recombinant DDRC has been expressed, purified, and shown to catalyze the racemization reaction. However, very little is known about the enzyme except that it has a molecular mass of 20 kDa and an amino acid sequence similarity to methylmalonyl-coenzyme A epimerases from Chlorobium species. We successfully established a circular dichroism (CD)-based assay for DDRC activity to determine the catalytic efficiency of the enzyme. Additionally, the non-enzymatic racemization rate of (S)-DHD was determined, allowing for the estimation of the enzyme's transition state stabilization. Site-directed mutagenesis was used to identify key Brønsted acid-base residues involved in catalysis. These studies afford the first characterization of the mechanism of a racemase that utilizes an isoflavanone as a substrate. Knowledge of this mechanism and the kinetic properties of the enzyme will facilitate the design of inhibitors that could reduce the estrogen-like effects of (S)-equol.

Raymond He, Faculty of Medicine, PhD Candidate

Supervisor: David Langelaan, Department of Biochemistry & Molecular Biology, Faculty of Medicine

Discovering the role of an α-helix in self-assembly of a hydrophobin from Phanerochaete carnosa

Hydrophobins are small secreted proteins that play vital roles in the growth and development of filamentous fungi. Hydrophobins can self-assemble into larger structures called rodlets. These rodlets coat surfaces such as fungal spores, making them extremely water-repellent. Hydrophobins are functionally separated into two different classes. Class I hydrophobins form durable amyloid-like rodlets, that are heat and acid resistant as well as insoluble in detergent. In contrast, class II hydrophobin assemblies are less stable and can be dissociated by detergent solutions. Hydrophobins have been used to modify surfaces to prevent fouling or biofilm formation, as new drug delivery agents, as biosensors, and to make hydrophobic surfaces more biocompatible, which is important for the success of medical implants. It is necessary to understand the structure and self-assembly mechanisms of hydrophobins so that their properties can be controlled and applied. This project focuses on PC1, a model hydrophobin from Phanerochaete carnosa. From previous research, we determined that an α-helix structure is lost during hydrophobin self-assembly. Based on these results, In this work, we created a hydrophobin variant (PC1 NA) with predicted amyloidogenic residues in the α-helix mutated. We compared the self-assembly efficiency of these hydrophobins through thioflavin T (ThT) fluorescence assays. We also used atomic force microscopy to compare differences in rodlet morphology between variants. Lastly, structural differences were compared by circular dichroism and Fourier-transform infrared spectroscopy. These results shed light on the importance that the α-helix of hydrophobins might have for controlling self-assembly.

Michael Ibekaku, Faculty of Health, PhD Candidate

Supervisor: Dr. Caitlin McArthur, School of Physiotherapy, Faculty of Health

Mobility Profiles of Residents Living with Dementia in Canadian Long-Term Care Homes: A Cross-Sectional Study

Background:

People living with dementia experience a decline in mobility resulting in adverse health outcomes. This study aimed to describe the mobility profiles of residents living with dementia in long-term care (LTC) homes in Canada.

Method: Using data from interRAI MDS 2.0 and interRAI LTCF assessments, we conducted a cross-sectional study of LTC residents living in four Canadian Provinces. Mobility was evaluated using four measures: bed mobility, transfers, locomotion, and walking. Ordinal logistic regression using the Generalized Logit Model (GLM) was used to analyze the association between mobility and selected determinants.

Results: The records of 79773 LTC residents with a mean age of 86.17 (7.96 standard deviation) were included in the study. The female residents accounted for about two-thirds of the sample; the majority were Ontario residents. There was a significant association between physiological,

subjective, and contextual factors with mobility measures. Different levels of cognitive impairment reduced independence, with ORs ranging between 0.01 and 0.75 (CI: 0.01-0.91, $p < 0.05$). Residents with depression had the highest odds of requiring limited assistance in mobility measures with OR ranging from 1.50 to 1.72 compared to being independent (1.38-1.57) or requiring extensive assistance (1.37-1.61). Contextual factors, including the province of residence, showed that residents in Manitoba had the highest odds of independence compared to provinces, with ORs ranging from 1.71 to 9.09 (CI: 1.17-10.19$p < 0.05$). Receiving physiotherapy or occupational therapy was associated with lower odds of independence (ORs between 0.32 and 0.77, $p < 0.05$), likely due to prioritization of residents with severe impairments.

Conclusion: The mobility of residents with dementia in LTC is associated with physiological, subjective, and contextual factors. These should be considered in the development interventions to improve mobility across different provinces. Future studies should use a longitudinal approach to explore these associations.

Timi Idris, Faculty of Health, PhD Candidate

Supervisor: Dr. Barb Hamilton-Hinch, School of Health and Human Performance, Faculty of Health

Empowering Black Women in Nonprofits: Advancing Wellbeing and Success

Nonprofit organizations provide essential services that support societal well-being, but their workers, particularly racialized women, face significant challenges. Black women in nonprofits often experience systemic inequities, precarious employment, and burnout exacerbated by racial and gender-based discrimination. The concept of "Black Fatigue" describes the cumulative mental and physical toll of enduring systemic racism. This research explores how collaborative approaches in organizational practices and health policies can enhance access, inclusion, and well-being for Black women in the nonprofit sector. This qualitative study will use snowball sampling to conduct in-depth, semi-structured interviews with 20 Black women employed in nonprofit organizations across Nova Scotia. The interviews will investigate workplace barriers, the impact of wellness policies, and the role of intersectional identities in shaping experiences. Data will be analyzed using thematic analysis to identify key themes. Additionally, focus group discussions with nonprofit leaders will further explore actionable solutions. The study is grounded in critical race theory and intersectionality, emphasizing storytelling as a method to amplify marginalized voices. The research anticipates uncovering systemic barriers affecting the well-being of Black women, including inequitable workplace practices, unpaid emotional labor, and limited access to benefits. Collaborative approaches, such as inclusive health programs and leadership development initiatives, are expected to improve equity and workplace wellness. This research emphasizes the need for systemic changes in nonprofit organizations to address intersectional inequities. Findings will offer actionable recommendations to improve access and inclusion, benefiting not only Black women but also the broader nonprofit sector. Insights may also inform equity-focused practices in healthcare fields.

Saeideh Jamali, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Jun Wang, Department of Microbiology & Immunology, Faculty of Medicine

ROFILING THE HOST RESPONSES TO RESPIRATORY BORDETELLA PERTUSSIS INFECTION IN HUMAN VOLUNTEERS

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

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

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

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

Pooja Labana, Faculty of Medicine, MSc Candidate

Supervisor: Dr. James Fawcett, Department of Pharmacology, Faculty of Medicine

Characterization of the role of large tumor suppressor proteins (LATS1/2) in neuronal maturation

Background: LATS1/2, core kinases of the Hippo pathway, have been linked with the polarity protein Scribble to regulate cell proliferation and differentiation. In post mitotic neurons, Scribble has been linked to the synapses and the axon initial segment (AIS). This suggests that proteins important for regulating cell polarity in proliferating cells play important roles in post-mitotic neurons. Given the link between Scribble and LATS1/2, we hypothesize that LATS1/2 may function in the AIS and/or synapses in neurons.

Objective: This study investigates the role of LATS1/2 by examining their expression and localization in dissociated hippocampal neurons and in brain tissue, and its potential association with Scribble.

Methods: We investigated LATS1/2 in neurons using: (1) fluorescent and simulated-depletion emission (STED) microscopy of dissociated hippocampal neuron (in-vitro) and mouse brain (in-vivo) for subcellular localization of LATS1/2, (2) protein interactions of LATS1/2 with Scribble using immunoprecipitation and Western blotting, and (3) phenotypic analysis of CamK2αCre; LATS1f/f; LATS2f/f, TDtomato LATS1/2 knockout mouse.

Key findings: We confirmed endogenous localization of Scribble to the AIS. Next, we showed that Scribble can precipitate LATS protein from rodent brain lysate and that LATS protein localizes to the AIS of hippocampal neurons both in vitro and in vivo. Using STED microscopy, we find that both Scribble and LATS form distinct puncta interspaced between Ankyrin G. Quantification reveals the Scribble puncta are 190nm apart from one another. Next, we utilized a conditional knockout approach to reduce LATS proteins in post mitotic neurons. Our conditional approach was unsuccessful as the Cre driver we used was highly expressed hippocampal neurons of the CA1 region, while LATS expression was high in the CA3/CA4 region of the hippocampus.

Significance of the study: Our work identifies that Scribble forms a complex with LATS in brain tissue and that LATS as a novel AIS protein. Given the AIS's important role in neurological disorders like epilepsy, these foundational findings open new research directions for LATS proteins in the nervous system.

Breanna Laffin, Faculty of Health, MSc Candidate

Supervisor: Dr. Emily Black, College of Pharmacy

Identifying Factors of Success in Implementing an Intervention for Management of Inpatient Bacteriuria in Four Regional Hospitals in Nova Scotia

Antimicrobial resistance (AMR) is a global health threat largely driven by inappropriate antimicrobial use. A multifaceted intervention incorporating education, audit, and feedback was implemented at four regional hospitals in Nova Scotia to improve prescribing for inpatients with bacteriuria. The intervention had variable success, highlighting the need to understand barriers and facilitators influencing implementation at each site. This study aimed to identify factors that impacted success at individual, unit, and organizational levels.

This qualitative descriptive study used semi-structured virtual interviews. Pharmacists involved in developing, implementing, or delivering audit and feedback, as well as healthcare providers who received feedback, were invited to participate. Interviews were transcribed verbatim and deductively coded to the Consolidated Framework for Implementation Research (CFIR), followed by inductive thematic analysis within each CFIR domain to identify local implementation factors.

All eight pharmacists who implemented education or delivered feedback participated, but no healthcare providers who received feedback were recruited. Analysis identified barriers and facilitators across study sites, with most themes falling within the inner and outer setting domains. Barriers in both settings included "staffing challenges" and "overuse of microbiology testing," which affected sustainability. Facilitators such as "interprofessional relationships" and "tailoring the intervention to professional roles" positively influenced implementation. These findings highlight interconnected factors shaping the intervention's success.

Barriers and facilitators influencing this intervention were identified at individual, unit, and organizational levels. Findings will inform recommendations to optimize province-wide inpatient antimicrobial stewardship initiatives, with implications for improving practice, policy, and health outcomes in regional hospitals across Nova Scotia.

Brianna Latremouille, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Alex Quinn, Department of Physiology & Biophysics, Faculty of Medicine

Cardiomyocyte Mechanical Function is Maintained by an Optimal Range of Afterload

Background: Adaptation to acute changes in mechanical load is essential for proper heart function. The response of cardiomyocytes (CM) to stretch ('preload') is well-defined, however due to difficulties in the experimental control of the load against which CM contract ('afterload'), its direct effects are poorly understood. Recently, a novel 'cell-in-gel' technique has overcome this limitation, demonstrating that during short periods of increased afterload, CM maintain their contractile function through increases in Ca2+ release. Yet, how CM respond to (patho)physiological increases in afterload over longer time periods is unknown.

Objective: Determine the response of CM to sustained (patho)physiological increases in afterload.

Methodology: Adult rabbit isolated left ventricular CM were studied under load free (LF) conditions or varying levels of afterload by embedding in a poly-vinyl alcohol (PVA)/4-boronate-poly-ethelene glycerol (PEG) hydrogel, whose stiffness is determined by PEG crosslinker (CL) concentration (5.0-17.5%). Contractile function was measured by sarcomere length (SL) tracking at 15min intervals across 90min.

Results: Initially, parameters were similar across all afterload conditions ($p>0.05$). Over 90min, EDL continuously decreased in all groups ($p<0.0001$). % SL shortening, dSL/dtmin, and dSL/dtmax decreased over the first 30min with low afterload (LF and 5-10% CL), followed by stabilisation to 90min ($p<0.05$). Conversely, mechanical function was maintained across 90min with moderate and high afterload (11.25-12.5% and 15-17.5% CL, respectively), but was greatest for moderate levels ($p>0.05$).

Significance: Determining the effects of increased afterload on CM function will provide pathophysiological insight that may help identify novel therapeutic targets for treatment of left ventricular pressure overload.

Charlotte Maclean, Faculty of Medicine, MSc Candidate

Supervisor: Dr. John Archibald, Department of Biochemistry & Molecular Biology, Faculty of Medicine

Long-read metagenomics to explore giant viral diversity within Nova Scotian peatland

Metagenomic sequencing is a cultivation-independent approach used to survey the microbial diversity of an environment. Among bacterial, archaeal, and eukaryotic sequences, metagenomic reads may also be derived from viral genomes circulating in the environment. Probing metagenomic data for viruses has since revealed the global distribution and expansive diversity of viral metagenomically assembled genomes (MAGs). One such lineage of viruses that has been

revolutionized by metagenomic sequencing are viruses in the Kingdom Bamfordvirae. These double-stranded DNA viruses infect a wide range of eukaryote hosts including protists. Within Bamfordvirae are members of Nucleocytoviricota, or Nucelocytoplasmic large DNA viruses (NCLDVs). NCLDVs have redefined the expected bounds of viral genome and particle size, presenting a challenge for the assembly of resolved giant viral MAGs using typical short-read technology. In this pilot study a long-read metagenomic approach was leveraged to assess the evolutionary and functional diversity of Bamfordvirae in a Nova Scotian peatland. Peatlands are carbon-rich, semi-aquatic environments that harbour a diversity of microeukaryotes and their associated viruses. Bioinformatic methods were employed to recover high-quality viral MAGs from viruses within Bamfordvirae. Giant viral MAGs and contigs derived from Nucleocytoviricota's agonistic sister clade (Preplasmivicota) were subjected to functional and phylogenetic investigation to infer ecological and evolutionary relationships within the metagenome. Preliminary data suggests that this environment contains divergent viral lineages within previously identified NCLDV orders, including Asfuvirales, Pimascovirales, and Imitervirales. Prior investigations have also identified NCLDVs as key regulators of biogeochemical cycling and lateral gene transfer (LGT). Genes commonly acquired from NCLDVs have the functional potential to modulate processes such as nutrient uptake, light-harvesting, and carbon and nitrogen metabolism. A key aim of this project will be to generate a network of gene-sharing between viruses and their hosts, potentially mapping how viral-mediated LGT has influenced host metabolism and carbon-cycling within this peatland environment.

Robyn McGowan, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Melina Agosto, Department of Physiology & Biophysics, Faculty of Medicine

Axonal trafficking and trans-synaptic complex formation of Pikachurin

Rod and cone photoreceptors (PRs) are specialized neurons that are responsible for the sensory transduction of visual stimuli. In the retina's outer plexiform layer (OPL), PRs transmit information to bipolar cells (BCs); this process is critical for normal vision. Pikachurin (PIKA) is a multi-domain heparan sulphate (HS) proteoglycan expressed in PRs and secreted into the synaptic cleft. PIKA knockout mice have structural defects in rod synapses and abnormalities in electroretinogram recordings, demonstrating its importance for normal vision. PIKA forms a trans-synaptic complex (TSC) with pre-synaptic dystroglycan (DG) and post-synaptic GPR179, as well as the post-synaptic cell adhesion molecule LRRTM4. Using a combination of in vitro and in vivo experiments, we aim to identify sequence determinants of PIKA-LRRTM4 binding and synaptic localization at PR terminals. Wild-type and mutant PIKA expression constructs with domains individually deleted were constructed. In vitro binding experiments were performed using a co-immunoprecipitation assay followed by western blotting. Synaptic localization was tested by subretinal injection and electroporation of plasmids expressing wild-type or mutant PIKA under the control of a murine opsin promoter for specific expression in PRs. Our preliminary data suggest that a region of unknown function between a.a. 240-342 is necessary and sufficient for LRRTM4 binding. Treatment with heparinase suggests that heparin sulfates are located within a.a. 244-564, consistent with the known requirement of heparan sulfate for LRRTM4 binding. However, the LRRTM4-binding region was not required for correct PIKA localization at PR-BC synapses. We demonstrated that none of the known functional domains of PIKA are required for LRRTM4 binding, but rather a novel region,

between the second fibronectin and first EGF-like domain, is required. This is in contrast to binding with GPR179, which is mediated by the C-terminal laminin G domain of PIKA. Our results additionally suggest that PIKA binding to LRRTM4 is not required for correct localization at PR-BC synapses.

Jamil Muradov, Faculty of Medicine, PhD Candidate

Supervisor: Alon Friedman, Department of Medical Neuroscience, Faculty of Medicine

Repurposing Memantine for the Prevention of Neurological Dysfunction Following Traumatic Brain Injury: Results of a Mechanism-Driven Randomized Pre-Clinical Trial

Background: Cortical spreading depolarizations (CSD) represent one of the earliest pathological mechanisms underlying poor outcomes of a traumatic brain injury (TBI). Here we: (1) demonstrated a mechanistic link between post-traumatic hypoxia, CSD occurrence, neurovascular dysfunction and poor neurological outcomes; (2) blocked CSDs and improved outcomes of TBI using a safe FDA-approved drug, memantine, in a randomized blinded trial.

Methods: 9-week-old Sprague-Dawley rats received a single moderate TBI, using an established weight-drop model. Acutely, animals underwent epidural electrocorticography and cardiorespiratory monitoring. The animals' neurological severity scores (NSS) were assessed at 20 min, 24 h and 48 h following impact. A group of animals underwent cranial window surgery to assess the neurovascular correlates of poor NSS. Memantine (10 mg/kg IP) was tested in vivo to block triggered CSDs in brain impacted and non-impacted animals. Neurological outcomes of treatment were assessed.

Results: Reduction in serum oxygen saturation post-impact was correlated with the latency to righting ($R2=0.71$, $p<0.0001$) and CSD occurrence ($p<0.05$). Animals displaying post impact CSDs had significantly lower NSS at 20 min, 24 h and 48 h ($p<0.001$, 0.001, 0.0001, respectively). At 48 h, these animals displayed impaired neurovascular response to repeated electrically triggered CSDs. In TBI animals, memantine reduced the occurrence of electrically triggered CSDs by 42-73%. It significantly reduced spreading depression and cortical hypoperfusion following CSD. Animals treated with memantine in the controlled trial had higher mean NSS (9.27 (SD 3.08) vs 5.56 (SD 3.05), $p<0.001$) compared to saline treatment.

Conclusion: Post impact hypoxia underlies the occurrence of CSDs contributing to neurological decline and neurovascular function impairment. Memantine can be used to block CSDs and improve neurological outcomes of TBI.

Daniel Neira Agonh, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Chappe and Dr. Anini, Department of Physiology & Biophysics, Faculty of Medicine

Humanized Mouse Model to Study Cystic Fibrosis-Related Diabetes

Introduction: Up to 50% of people with cystic fibrosis (pwCF) develop CF-related diabetes (CFRD), accelerating lung function decline and mortality, particularly among women. Our study aims to validate a novel CF mouse, B6-Tg(CFTR508del)Cwr (hCF) which expresses the human ΔF508del cftr gene to study CFRD.

Methods: Male and female hCF were obtained from Case Western Reserve University. hCF and C57BL/6 (WT) mice underwent intraperitoneal (IP) or oral glucose tolerance tests (OGTT). Structural analyses were performed on pancreatic islets (α- and β-cells), and ileal L-cells (GLP-1-positive). ELISAs or multiplex assays were performed to measure hormone and cytokine levels in the pancreas, ileum, or plasma.

Results: Following IPGTT, hCF mice showed glucose intolerance with higher glucose area under the curve (AUC) compared to WT regardless of sex and age. In hCF tissues, we found a reduction in islet size and density, but similar β- and α-cell distribution than in WT. Density of ileal L-cells and circulating GLP-1 levels were elevated in hCF mice. Basal plasma and pancreatic insulin levels showed no differences across experimental groups; however, glucagon was elevated in hCF compared to WT mice. Proinflammatory cytokines, Interferon-γ and Interleukin-1β, were elevated in hCF pancreatic and plasma samples.

Conclusions: hCF mice exhibited glucose intolerance at all ages tested, in both sexes. Decreased islet size and density; elevated glucagon; and increased pro-inflammatory cytokines may contribute to CFRD development. Increased GLP-1 expression in hCF mice suggest a compensatory incretin response to oral glucose. Ongoing studies aim to further characterize CFRD in these mice.

Rhea Nickerson, Faculty of Medicine, PhD Candidate

Supervisor: Dr. Zhenyu Cheng, Department of Microbiology & Immunology, Faculty of Medicine

Role of the integrated stress response in modulating the host immune response to chronic Pseudomonas aeruginosa lung infection

Pseudomonas aeruginosa is a highly adaptable environmental Gram-negative bacterium which causes diverse opportunistic infections in humans, particularly chronic lung infections in people with cystic fibrosis (pwCF), where it causes persistent inflammation leading to lung damage and respiratory failure. P. aeruginosa is highly antibiotic-resistant, and during its transition to chronicity adapts to exploit the lung niche and evade immune clearance, making it very difficult to treat. My project aims to deepen our understanding of this host-pathogen interaction and develop novel treatments by exploring the relationship between chronic P. aeruginosa infection and the host integrated stress response (ISR). The ISR is a highly conserved eukaryotic stress response mediated by phosphorylation of eIF2α and activation of transcription factor ATF4 to promote cellular stress adaptation and recovery, or cell death depending on stress intensity and duration.

Our lab is developing a model of chronic lung infection utilizing P. aeruginosa-embedded agar beads in C57BL/6 mice. Using this model, we have been able to establish infection for up to one week, with sustained production of inflammatory cytokines and neutrophil recruitment, recapitulating hallmark features of human chronic infection. In this model, chronic infection led to ISR activation in the lungs at 1-week post-infection, indicated by increased eIF2α phosphorylation and upregulation of ATF4. Daily intraperitoneal treatment with the drug integrated stress response inhibitor (ISRIB) attenuated this ISR activation in vivo, improved weight recovery, and reduced clinical symptoms. To our knowledge, this is the first demonstration of ISR activation by P. aeruginosa in vivo in a chronic infection model, and the first indication that inhibiting this ISR activation may have clinical benefits in this setting. These observations position ISR inhibition as a potential novel strategy to modulate the host response to chronic P. aeruginosa lung infection and reduce infection-associated morbidity and mortality in pwCF and other chronic lung diseases.

Madison Oulton, Faculty of Medicine, PhD Candidate

Supervisor: Dr. George Robertson, Department of Pharmacology, Faculty of Medicine

Metabolic basis for ibogaine-induced brain repair

Ibogaine has been used for millennia by African tribal communities to induce a deep introspective state that promotes self-healing. In combat veterans with traumatic brain injuries, ibogaine has recently been shown to dramatically reduce PTSD, anxiety and depression scores. These remarkable therapeutic benefits have been attributed to enhanced synaptic plasticity and brain repair. However, the mechanisms remain unclear. Ibogaine is rapidly converted into the active metabolite noribogaine. Unlike ibogaine, noribogaine has been shown to increase morphological signs of synaptic plasticity in primary cultures of mouse cortical neurons. Studies performed in yeast suggest that ibogaine initially supresses energy production that is followed by a metabolic rebound when it has been converted to noribogaine. By transiently suppressing glycolysis and mitochondrial respiration, ibogaine is hypothesized to produce metabolic adaptations that fuel enhanced noribogaine-induced synaptic plasticity and brain repair. To test this hypothesis, we compared the effects of vehicle, ibogaine, noribogaine, and ibogaine followed by noribogaine on glycolysis and mitochondrial function in mouse cortical neuron cultures using the XFe96 Extracellular Flux Analyzer. In the presence of ibogaine, glycolysis and respiration were reduced. Sixteen hours after the removal of ibogaine, there was a modest increase in glycolysis and mitochondrial respiration. The addition of noribogaine after the removal of ibogaine markedly increased glycolysis and mitochondrial respiration. This synergistic increase in energy production is proposed to play an important role in the ability of ibogaine to enhance synaptic plasticity and brain repair.

Christian Rempe, Faculty of Medicine, MSc Candidate

Supervisor: Locke Davenport Huyer, Department of Microbiology & Immunology, Faculty of Medicine

Immune reaction to polymeric implantable materials.

Purpose: The foreign body response (FBR) is a chronic, macrophage-driven reaction. The associated inflammation and fibrosis underly implant failures. Therapeutically targeting the FBR is challenged by the failure of canonical classification systems to comprehensively identify pathological cells. This limitation is particularly true for multinucleated giant cells (MNCs), frustrated macrophages believed to have a primary role in driving fibrosis in the FBR. Recent evidence indicates strong links between glycolytic energy production and chronic inflammation. In this study, we investigated persistent glycolysis in the context of the FBR to polymeric implants.

Methodology: Three clinically relevant polymers (polyethylene, polypropylene, polydimethylsiloxane) were subcutaneously implanted in mice. Fibrotic capsules were analysed one-, three- and six-weeks post-implantation (WPI). Masson's Trichrome (MT) staining was used to quantify implant-fibrosis. A flow cytometrybased method of metabolic profiling (SCENITH) was used to determine peri-implant metabolic and functional cell dynamics. ImageStream flow cytometry was used to assess metabolic behaviour in MNCs. Immunofluorescent (IF) staining was used to determine spatial dynamics of cellular metabolism and fibroblast activation.

Results: Histological quantification of implant-associated fibrosis revealed similar responses to each material. SCENITH assessment indicated that glycolytic cells occupied an increasing percentage of the total macrophage population in each material over time, despite total macrophage numbers being reduced six-WPI. ImageStream analysis of MNCs indicated a reliance on glycolytic energy production, and increased rates of fusion at six-WPI compared to three-WPI. IF histology confirmed upregulation of glucose transport in the implant-proximal fibrotic capsule and confirmed the localization of MNCs at the implant interface. This, correlated with upregulation of α-SMA (fibroblast activation) in the proximal regions of the capsule indicates co-localization of glycolytic cells and fibroblast activation.

Conclusion/Significance: Glycolysis is identified as the primary metabolic pathway of pathological macrophages and MNCs in the FBR. Therapeutically targeting glycolysis could therefore be used to treat inflammation in the FBR.

Dina Rogers, Faculty of Medicine, MSc Candidate

Supervisor: Dr. David Langelaan, Department of Biochemistry & Molecular Biology, Faculty of Medicine

Engineering of PETase-Hydrophobin Proteins for High-Turnover Plastic Degradation

With 400 million metric tonnes of global production per year, the majority of plastic accumulates harmfully in the environment due to lack of effective recycling processes. The bacterial enzyme PETase has potential to provide an effective and environmentally friendly solution to plastic pollution due to its native PET degradation activity. However, PETase is maladapted for degradation of commercial PET-based plastics at ambient temperatures. To overcome this challenge, we have produced PETase-hydrophobin fusion proteins. Hydrophobins are robust proteins produced by filamentous fungi that self-assemble into rodlets to form a durable biolayer that is resistant to degradation by heat and chemicals. Here, we fused PETase to hydrophobins NC2, SC16, and HYD5 to identify the best candidate for this biological recycling process. Fusion proteins were recombinantly expressed in E. coli and purified by immobilized Nickel affinity chromatography. PET degradation activity was monitored by bulk absorbance at 240 nm and products of the reaction were identified by NMR as well as reverse-phase HPLC. Structural and functional studies show that the enhanced PET degradation ability of these fusion proteins depends on intrinsic properties of the hydrophobin, suggesting that the diversity of hydrophobin protein sequences and tertiary structures plays a key role in their surface modification capabilities. Here, hydrophobins with high surface activity enhance the hydrophilicity of PET, thereby facilitating PETase surface interaction and enhancing PET degradation. Overall, this work highlights the potential of direct fusion of PETase to hydrophobins for high-turnover PET degradation, establishing a unique protein engineering approach to biological recycling.

Mackenzie Searle, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Kishore Pasumarthi, Department of Pharmacology, Faculty of Medicine

Therapeutic Potential of Strand-Specific microRNA Targeting in Oxidative Stress-Induced Thoracic Aortic Aneurysm

Thoracic aortic aneurysms (TAAs) are characterized by the weakening and bulging of the thoracic segments of the aorta, which can cause wall rupture and sudden death. Currently, there are no effective pharmacological interventions to stop or reverse TAA progression. Vascular injury exacerbated by oxidative stress plays a critical role in TAA development, but the underlying mechanisms are not well understood. The guide strand of microRNA-21 (miR-21-5p) is upregulated in aortic aneurysms of both human patients and experimental models, however, whether it plays a protective or causal role remains disputed. In contrast, the role of miR-21 passenger strand (miR-21-3p) in TAA has never been explored. We hypothesize that oxidative stress in vascular smooth muscle cells (VSMC) can cause dysregulation of both miR-21 strands and strand-specific modulation of miR-21 is necessary for prevention of TAA pathology. We treated the mouse aortic VSMC cell line (MOVAS) with varying concentrations (100-500μM) of hydrogen peroxide (H_2O_2) for 15 hours to induce oxidative stress and mimic TAA pathology *in vitro*. An AlamarBlue assay was used to confirm concentration-dependent cytotoxic effects of H_2O_2 in MOVAS cells. Using miR-27b as a normalization control, the relative gene expression analysis indicated differential expression

profiles for both miR-21-5p and miR-21-3p in VSMCs subjected to oxidative stress. Future experiments will examine the effects of miR-21-5p and miR-21-3p mimics and inhibitors on VSMC cell viability in cultures subjected to oxidative stress. In addition, we will examine the expression profiles of both miR-21 strands in experimental animal models of TAA. We will characterize the mechanisms underlying aortic pathology natriuretic peptide receptor A (NPRA) knockout mice and test the effects of a high-fat diet on accelerating TAA abnormalities and changes in the aortic vascular wall. Collectively, these findings will validate benefits of strand-specific miR-21 targeting in TAA patients.

Radka Sevcik, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Alex Quinn, Department of Physiology & Biophysics, Faculty of Medicine

Optogenetic Action Potential Modulation for Arrhythmia Prevention in Long QT Zebrafish Hearts

Background: Long QT syndrome (LQTS) is a potentially lethal condition in which repolarisation of the cardiac action potential (AP) is impaired due to decreased outward repolarising current (e.g., rapidly-activating delayed rectifier K+, IKr) and/or an increase in inward depolarising current (e.g., L-type Ca2+, ICa,L). These changes in ionic currents and the resulting AP prolongation can lead to early after depolarisations (EAD) and ectopic excitation, which may result in deadly re-entrant arrhythmias. Current therapeutic options for LQTS are limited, warranting the exploration of novel treatment options.

Goal: The goal of my work is to develop a drug-induced experimental model of EAD-induced ectopic excitation in the zebrafish isolated heart and use optogenetics to normalise AP morphology as an anti-arrhythmic therapy.

Methods: Zebrafish represent a powerful experimental model based on the ease of their genetic alteration and the similarity of their cardiac electrophysiology and AP morphology to human. Hearts isolated from zebrafish expressing the light-activated repolarising K+ channel HcKCR1 will be exposed to dofetilide (IKr blocker) and Bay K8644 (ICa,L activator) to induce AP prolongation and EAD-induced ectopy. Effects on the AP will be measured with sharp electrode recordings of membrane potential. Green light will be applied with a fibre optic cannula to the measurement region and its intensity modulated with a custom light-control device for local AP modulation.

Significance: By demonstrating the utility of optogenetics for local AP modulation and the prevention of ectopic excitation, we will support the potential future use of optogenetics for the treatment of LQTS.

Claerwen Sladen-Dew, Faculty of Medicine, MSc Candidate

Supervisor: Dr. Alexander Quinn, Department of Physiology & Biophysics, Faculty of Medicine

Disturbed Repolarisation-Relaxation Coupling in Atrial Mechano-Arrhythmogenesis in Ischaemic Heart Disease

Background: Ischemic heart disease is associated with comorbidities, including risk for atrial fibrillation. Atrial fibrillation can be triggered by acute electrophysiological fluctuations, including altered excitability, repolarisation, conduction, and calcium dynamics, caused by acute pathophysiological variations in the heart's mechanical load ('mechano-arrhythmogenesis'). If acute mechanically-induced electrophysiological responses interact with persistent structure-function alterations often found in ischaemic tissue, it may result in sustained atrial fibrillation. In the ischaemic ventricle, it has been shown that mechano-arrhythmogenesis is enhanced by a disturbance of repolarisation-relaxation coupling, however whether this is also true for the atrium is unknown.

Objectives: Determine the impact of disturbed repolarisation-relaxation coupling on the incidence of stretch-induced arrhythmias in rabbit and human atrial tissue.

Methods: Atrial tissue excised from rabbit hearts and from the hearts of human patients with ischemic heart disease during cardiac surgery will undergo functional fluorescence imaging for simultaneous measurement of voltage and calcium to assess the duration of repolarisation-relaxation coupling. Tissue will be subjected to controlled, transient stretch with a specialised tissue work-loop system, before and after ATP-sensitive potassium channel (KATP) activation with pinacidil (to simulate an ischaemia-induced disturbance of repolarisation-relaxation coupling) or KATP block with glibenclamide.

Significance: Arrhythmias are a leading cause of morbidity and mortality in ischaemic heart disease, exacerbated by limited efficacy of current anti-arrhythmic therapies. Causes of arrhythmias are complex, with mechano-sensitive mechanisms hypothesised to be a key contributor. This study will determine the role of disturbed repolarisation-relaxation coupling in atrial mechano-arrhythmogenesis in ischaemic heart disease to identify molecular targets for novel therapies.

Alia Syeda, Faculty of Medicine, PDF

Supervisor: Dr Yassine El-Hiani, Department of Physiology & Biophysics, Faculty of Medicine

TRPML1 signalling at lysosomes-mitochondria nexus drives triple-negative breast cancer mitophagy, metabolic reprogramming and chemoresistance

Inter-organelle signalling mechanisms, particularly those at the lysosomes-mitochondria interface, are critical for cancer cell metabolism, mitophagy and survival. However, the incomplete understanding of these mechanisms has limited the development of effective therapies, especially for the triple-negative breast cancer (TNBC). Here, we demonstrate the lysosomal Ca^{2+}-release channel TRPML1 as a master regulator of mitochondrial bioenergetics in TNBC cells. TRPML1 knockdown (ML1-KD) in TNBC cells selectively compromises mitochondrial respiration, reprograms cell metabolism, and induces mitochondrial fragmentation without impacting non-cancerous cells.

Mitochondria of ML1-KD TNBC cells sequester around the endoplasmic reticulum (ER), increasing mitochondria-ER contact sites at the expense of mitochondria-lysosomes contacts. Mechanistically, ML1-KD reduces lysosomal acidification, thus hindering autophagic flux and completion of autophagy. ML1-KD inhibits TFEB-mediated mitophagy and oxidative defence mechanisms while causing mitochondrial Ca2+ overload, further impairing mitochondrial function. These alterations render ML1-KD TNBC cells highly sensitive to doxorubicin and paclitaxel even at reduced doses. Together, our findings establish TRPML1 as a critical inter-organelle regulator and highlight its potential as a therapeutic target to exploit metabolic vulnerabilities in TNBC cells.

Aran Thanamayooran, Faculty of Medicine, MSc Candidate

Supervisor: Karthik Tennankore & Leah Cahill, Department of Community Health and Epidemiology, Faculty of Medicine

Effects of Pre-Transplant Hemodialysis Timing on Post Kidney Transplant Outcomes

For hemodialysis patients, a longer number of days from the last dialysis session is associated with poor health outcomes including mortality and hospitalization. However, there is very little evidence examining how the timing of individual hemodialysis sessions prior to kidney transplant may affect short and long-term post-transplant outcomes.

We hypothesize that longer intervals between hemodialysis timing and kidney transplantation are associated with worse transplant outcomes.

1. To determine the association between the timing of the last session of hemodialysis prior to kidney transplantation and delayed graft function.

2. To determine the association between the timing of the last session of hemodialysis prior to kidney transplantation and A) kidney transplant graft failure, B) hospital length of stay, C) perioperative hypotension, and D) postoperative hypotension.

A retrospective cohort study of hemodialysis patients (n=661) who received a kidney transplantation from 2006-2020 was conducted using the Nova Scotia Health Multi-Organ Transplant Program's Transplant Data Repository, which includes all transplant recipients from the Atlantic Canada provinces. The association between hemodialysis timing and kidney transplant graft failure was analyzed using a multivariable-adjusted Fine and Gray regression model. The associations between hemodialysis timing and remaining study outcomes were analyzed using a multivariable-adjusted logistic regression model.

There was no significant association between hemodialysis timing and the primary outcome of delayed graft function (odds ratio. 0.78 (95% confidence intervals. 0.47-1.28)) when comparing hemodialysis ≥1 day before transplant to hemodialysis the same day as transplant. Similarly, no significant relationships were observed between hemodialysis timing and other study outcomes: graft failure (sub-hazard ratio. 0.83 (0.32-2.16)), length of stay (odds ratio. 1.14 (0.73-1.80)), perioperative hypotension (odds ratio. 0.92 (0.58-1.47)), and postoperative hypotension (odds ratio. 0.76 (0.41-1.42)).

Our findings suggest that hemodialysis timing may not be a useful target for improvement of transplant outcomes.

Emily Thomson, Faculty of Medicine, MSc Candidate

Supervisor: Dr. James Fawcett, Department of Pharmacology, Faculty of Medicine

Characterizing NOS1AP in the rodent cerebellum

Nitric Oxide Synthase 1 adaptor protein (NOS1AP) has been implicated in several diseases including mood disorders, schizophrenia, and PTSD. NOS1AP functions as an adaptor protein that can bind to a number of different proteins, including neuronal nitric oxide synthase (nNOS). Mutant mice of NOS1AP isoforms were generated by the Fawcett lab and behavioural testing revealed they have a significant defect in their balance and gait, consistent with defects in the cerebellum. This project will characterize NOS1AP isoforms in the cerebellum using immunoprecipitation and immunofluorescent tissue staining. It is hypothesized that NOS1AP isoforms play an important role in cerebellar development and that loss of NOS1AP will affect the development of cerebellar circuits and motor behaviours. To address this, I have 2 aims; first to define the cells in the developing and mature cerebellum that express NOS1AP isoforms. Secondly, to determine whether loss of NOS1AP isoforms affects the morphology of cells in the cerebellum. Preliminary results have shown that NOS1AP isoforms are expressed in inhibitory interneurons and Bergmann glia within the cerebellum. In mutant mice compared to controls, there was differential localization of nNOS, and vesicular glutamate transporter 2 (VGLUT2). While there are no significant differences in cell morphology, these differences are still undergoing investigation. These results suggest that NOS1AP plays a role in signaling cascades responsible for regulating inhibition and excitation of cerebellar neurons, but it has yet to be shown that NOS1AP has large scale impact on cerebellar morphology.

Jacob van Haaften, Faculty of Science, PhD Candidate

Supervisor: Shannon Johnson, Department of Psychology and Neuroscience, Faculty of Medicine

Health in Nature: Advancing Clinical Competencies Through Environmental Health Advocacy

Considerable research evidence indicates that spending time in nature benefits human health and well-being. Health practitioners around the world are increasingly communicating these benefits and prescribing nature to patients, through programs such as Canada's Park Prescriptions (PaRx). Beyond clinical roles, various professional standards and ethical codes call on health practitioners to serve as health advocates. Advocating for nature and the environment to ensure that patients can continue to experience the benefits of nature for generations to come uniquely embodies this role. The current study, a collaborative project between Dalhousie University, the Canadian Association of Physicians for the Environment (CAPE), and the Ecology Action Centre (EAC), explored this role by contributing to a local environmental action campaign to protect Sandy Lake Regional Park from development. The park offers free, accessible natural spaces and is among a declining number of protected urban nature areas. To evaluate health benefits of spending time in this park, 18 adult community member participants engaged in a guided walk in the park. Participants provided salivary cortisol samples and completed self-report measures of affect and feelings of vitality before and after the walk. Paired-samples t-tests revealed significant changes between time points with large effect sizes for all outcome measures. Consistent with previous research, salivary cortisol and negative affect were lower after the walk, whereas positive affect and vitality were higher. These findings are now informing the ongoing campaign to protect Sandy

Lake. This study demonstrates how health practitioners can leverage research and collaborate with environmental organizations to promote the preservation of natural spaces for health and well-being. In addition to providing further evidence for nature's health benefits, this project offers a model for health practitioners to enact their roles as health advocates to promote both environmental and human health.

Jennika Veinot, Faculty of Medicine, PhD Candidate

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PTSD Impairs Working Memory Systems and Disrupts Pain Regulation Pathways in Chronic Pain

Post-traumatic stress disorder (PTSD) symptoms are common among people with chronic pain, but its role in pain etiology is unclear. Both involve working memory deficits. Successful working memory depends on dorsolateral prefrontal cortex (dlPFC) function, which provides top-down signals to brainstem regions like the periaqueductal gray (PAG) to regulate pain. We have recently shown that low working memory predicts abnormalities in how these two regions respond during pain modulation and also predicts chronic back pain severity (Veinot et al., 2025, JPAIN). Here we test whether high PTSD symptoms disrupt working memory processes in the dlPFC and dlPFC connectivity with PAG in people with chronic back pain.

60 participants with chronic back pain underwent functional MRI while performing a working memory task, and completed questionnaires assessing trauma, PTSD, and chronic pain.

Higher number of traumatic events endured were associated with a greater experience of affective pain and low working memory performance. High PTSD symptoms resulted in decreased dlPFC activity during demanding events of the working memory tasks and increased dlPFC – PAG functional connectivity. These metrics predicted higher affective load and abnormal pain modulation.

These findings show that PTSD may deplete neural resources for working memory, impairing the ability to contextualize pain cues. This can weaken top-down inhibition from the dlPFC to the brainstem, altering threat vigilance and pain perception. Taken together with previous findings, high affective load of PTSD alters working memory circuitry, and results in abnormalities in pain regulation and in turn, more resistant forms of chronic pain.

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Development of itaconate polymer microparticles for intracellular regulation of pro-inflammatory macrophage activation

Itaconate (IA) is an endogenous metabolite and a potent regulator of the innate immune system. Its use in immunomodulatory therapies has faced limitations due to challenges in controlled delivery and requirements of high extracellular concentrations for internalization of the highly polar small molecule to achieve its intracellular therapeutic activity. Microparticle (MP)-based delivery strategies are a promising approach for intracellular delivery of small molecule metabolites through macrophage phagocytosis and subsequent intracellular polymer degradation-based delivery.

Toward the goal of intracellular delivery of IA, degradable polyester polymer- (poly(dodecyl itaconate)) based IA polymer microparticles (IA-MPs) were generated using an emulsion method, forming micron-scale (~ 1.5 μm) degradable microspheres. IA-MPs were characterized with respect to their material properties and IA release kinetics to inform particle fabrication. Treatment of murine bone marrow-derived macrophages with an optimized particle concentration of 0.1 mg/million cells enabled phagocytosis-mediated internalization and low levels of cytotoxicity. Flow cytometry demonstrated IA-MP-specific regulation of IA-sensitive inflammatory targets. Metabolic analyses demonstrated that IA-MP internalization inhibited oxidative metabolism and induced glycolytic reliance, consistent with the established mechanism of IA-associated inhibition of succinate dehydrogenase. This development of IA-based polymer microparticles provides a basis for additional innovative metabolite-based microparticle drug delivery systems for the treatment of inflammatory disease.