# The Twenty-Seventh Annual Scientific Meeting

# For Health Sciences Research Trainees

# Faculty of Health Sciences

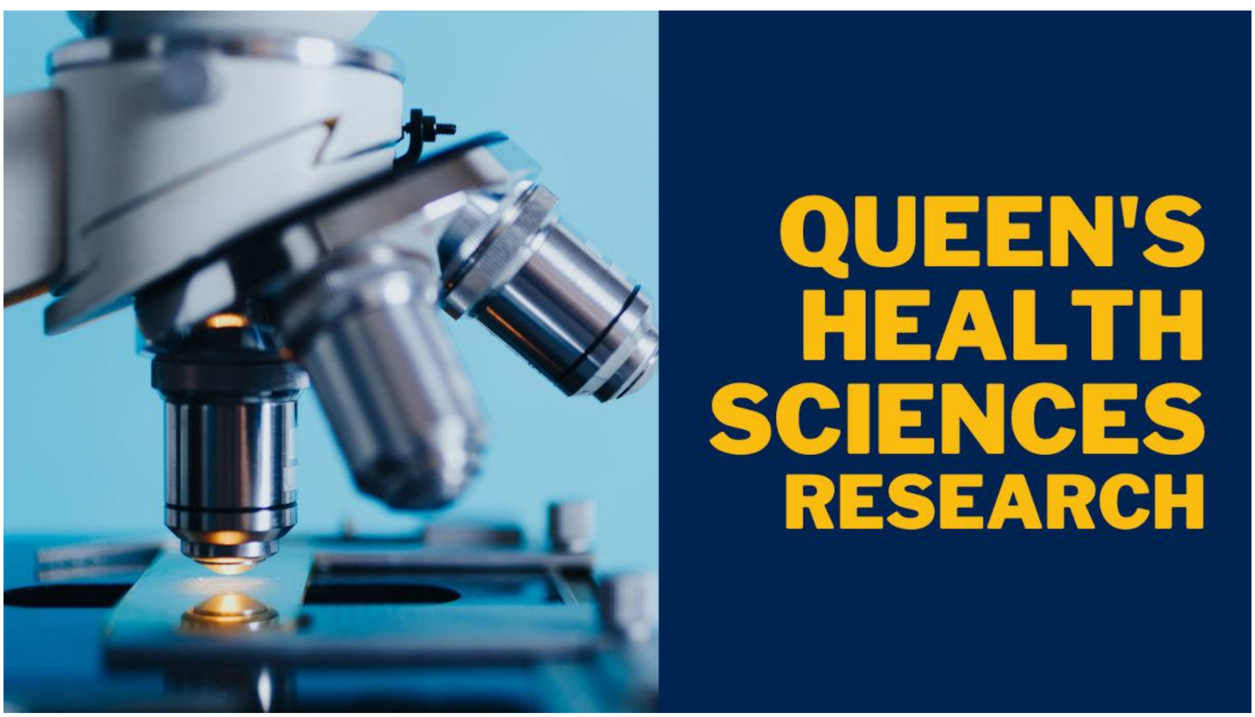
# Queen's University

Queen's
UNIVERSITY
HEALTH SCIENCES

**Wednesday, October 15th, 2025**

**Kingston Marriott**

**285 King St. East**



## Thank You.........

We would like to extend a big thank you to everyone involved in the planning and adjudication of this event! Your time and efforts are truly appreciated.

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### Event Sponsors

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### Acknowledgments

A special thank you to Mary White and Danielle Sisnett for their invaluable assistance in organizing this meeting.

# The Twenty-Seventh Annual Scientific Meeting for Health Sciences Research Trainees

## Queen's University

Wednesday, October 15th, 2025

Kingston Marriott

285 King St. East

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| 8:00 – 8:15 am | Registration – Kingston Marriott – 2nd Floor |
| | Poster set-up for morning participants – 2nd Floor, Rideau Room |
| | Oral Presentations – 2nd Floor, Banquet Hall |
| 8:15 – 8:30 am | **Welcome and Introduction**<br>Dr. Chandra Tayade, Vice Dean, Basic and Public Health Sciences |
| | **Introductory Remarks**<br>Dr. Lisa Tannock, Dean, Queen's Health Sciences |

## Oral Presentations – Session 1: Banquet Hall

Chair: Sarah Dick

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|---|---|
| 8:30 – 8:42 am | Seily Shrestha - Fibroblasts shape macrophage diversity to support muscle regeneration via CSF1 signaling |
| 8:42 – 8:54 am | Rita Nakhle - Protease-induced activation of colonic afferent neurons by a gut bacterium associated with inflammatory bowel disease |
| 8:04 – 9:06 am | Monica Aida Lopez - Investigating the Role of Mast Cell Condensates in Regulating Macrophage Phenotype and Dynamics in Tissue Repair |
| 9:06 – 9:18 am | Illia Gelman - A novel mechanism for persistent inhibition of hERG potassium channels by amiodarone after drug discontinuation |
| 9:18 – 9:30 am | Dan Vo Hoang - Evaluation of Memory T Cell Subset Repertoire in Endometriosis |
| 9:30 – 9:42 am | Ciara D. O'Connor - Microglial rhythmicity and sex differences impact neuropathic pain development |
| 9:42 – 9:54 am | Kyra Fine - Development of a machine learning model for the use of blood biomarkers to predict IBD presence and activity |

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| 9:56 – 10:30 am | Flash Talks – Kate Sitak, Danielle Harper, Natasha Iaboni, Alison Hermanutz, Brian Shkabari, Piper Holmes, Maria V. Medeleanu, Landon Montag |
| 10:30 am – 12:00 pm | Poster Session #1/Coffee Break |
| 12:00 – 1:30 pm | Lunch |

## Oral Presentations – Session 2: Banquet Hall

Chair: D.J. Cook

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| 1:30 – 2:00 pm | Jason Gallivan - Motor Learning as Autobiographical Memory: The Central Role of the Default Mode Network |
| 2:00 – 2:12 pm | Aryaman Sharma - Dexamethasone Induced Quiescence Drives Treatment Resistance in Medulloblastoma |
| 2:12 – 2:24 pm | Tasha Jawa - A Co-Designed Post-ICU Follow-Up Pathway Improves Psychosocial Recovery for Patients and Their Caregivers |
| 2:24 – 2:36 pm | Isabell Pitigoi - Blinking strategically during a cognitive task improves performance but differs across sex, age, and disease |
| 2:36 – 2:48 pm | Anthony Guglya - Transcriptional Coactivators YAP/TAZ Contribute to the Regulation of Coagulation Factor VIII Expression |
| 2:48 – 3:00 pm | Kaytlin Andrews - Identifying Molecular and Cellular Features of Glioblastoma Invasion |
| 3:00 - 3:12 pm | Madeleine Carew - Elucidating protective potential of metabolic pathways in triple negative breast cancer (TNBC) |
| 3:12 – 3:45 pm | Flash Talks – Olivia DiPaolo, Rose Binley-Ewing, Kartik Sachdeva, Erik McInnes, Danielle Shibi Rosen, Nazanin Soghrati, Chirag Chopra, Anisur Rahman |
| 3:45 – 5:15 pm | Poster Session #2/Coffee Break |
| 5:15 – 5:30 pm | Awards and Closing Remarks |
| 5:30 – 7:00 pm | Reception |

# Oral Presentations

## ***Session 1***

1. Seily Shrestha (Experimental Medicine) Fibroblasts shape macrophage diversity to support muscle regeneration via CSF1 signaling

Seily Shrestha, Danielle Shibi Rosen, Abbey L. Politeski, Clint Robbins, Sarah A. Dick

Macrophages are essential for effective skeletal muscle regeneration. Following injury, monocyte-derived macrophages (MDMs) infiltrate the tissue, first adopting a pro-inflammatory phenotype before transitioning into anti-inflammatory subsets, such as TREM2$^+$ or CD206$^+$ macrophages, that promote remodeling and resolution. Colony-stimulating factor 1 (CSF1) is a key growth factor for macrophage survival and differentiation, yet its cellular sources in injured skeletal muscle remain poorly defined. To address this, we used inducible global and stromal cell-specific CSF1 knockout mice subjected to intramuscular cardiotoxin (CTX) injury. Global loss of CSF1 caused a marked reduction in macrophage numbers and impaired monocyte-to-macrophage differentiation, establishing its essential role in the repair process. Use of stromal cell-specific knockout models revealed fibroblasts as the main CSF1 source driving macrophage proliferation and differentiation during injury. In fibroblast-CSF1 deficient mice, we observed a delayed but significant increase in monocytes, neutrophils, Ly6Chi and Ly6G$^+$ macrophages at day 5 post-CTX which returned to baseline by day 10, reflecting temporary immune imbalance. Anti-inflammatory markers, TREM2 and CD206, were reduced in macrophages, demonstrating impaired polarization. Injured muscles deficit in fibroblast-CSF1 exhibited more fibrosis and smaller regenerating fibers at day 14 post-CTX, highlighting disrupted tissue repair. These findings identify fibroblast-derived CSF1 as a critical regulator shaping macrophage dynamics during skeletal muscle injury, where its loss hinders repair and promotes fibrosis, providing a potential therapeutic target for muscle regeneration.

2. Rita Nakhle (Microbes, Immunity and Inflammation) Protease-induced activation of colonic afferent neurons by a gut bacterium associated with inflammatory bowel disease

Rita Nakhle*, Hannah M. Wood*, Madeleine Farquhar, Prameet M. Sheth, David E. Reed, Alan E. Lomax

Background: Inflammatory bowel disease (IBD) is characterized by relapsing inflammation of the gastrointestinal tract and abdominal pain. Proteolytic activity is elevated in IBD patients and proteases can activate abdominal pain pathways. Proteases from the gut bacterium Bacteroides vulgatus are correlated with IBD severity. We hypothesize that proteases produced by B. vulgatus will activate colonic afferent nerves involved in nociception. Methods: The effects of B. vulgatus supernatant on nociceptive neurons was assessed using in vitro Ca2+ imaging of dissociated mouse dorsal root ganglia neurons, ex vivo single-unit afferent nerve recordings from mouse colons, and in vivo murine visceromotor responses to colorectal distention. Results: Exposure of neurons to B. vulgatus supernatant significantly increased Ca2+ influx in response to the pro-nociceptive mediator, capsaicin (100 nM; $p < 0.0001$, N = 7) by 49%. B. vulgatus supernatant significantly increased spontaneous activity by 50% ($p < 0.001$, N = 8) and mechanosensitivity of colonic afferent axons by 48% ($p < 0.05$, N = 8). Pre-incubation of B. vulgatus supernatant with a protease inhibitor cocktail inhibited the excitatory effect observed in both bioassays. Furthermore, enema administration of B. vulgatus supernatant significantly increased visceromotor responses to colorectal distention by 183% ($p < 0.05$, N = 10). Conclusion: Proteases secreted by B. vulgatus can sensitize nociceptive visceral afferent nerves and may be a novel target for pain management in IBD.

3. Monica Aida Lopez (Immunology, Cell Biology) Investigating the Role of Mast Cell Condensates in Regulating Macrophage Phenotype and Dynamics in Tissue Repair

Monica Aida Lopez, Paul Kubes

The peritoneal cavity contains diverse immune cells that coordinate complex processes in response to injury and disease. During tissue repair, perturbations can form within the cavity, however, the exact mechanism coordinating this function remains unclear. The first step towards the formation of perturbations is large peritoneal macrophages (LPMs) rapidly aggregate at the site of injury. I performed in-vitro assays using peritoneal fluid to induce LPM aggregation by stimulating it with calcium and ATP. This revealed that during LPM aggregation mast cells released large (1 μm) avidin-positive condensates (membraneless organelles) that were observed to be between aggregating LPMs. Confocal microscopy showed that these condensates were also positive for macrophage receptor with collagenous structure (MARCO), a scavenger receptor known to be involved with macrophage aggregation. These condensates were further defined to be membraneless using rheometry and fluorescence recovery after photobleaching (FRAP) imaging where both MARCO and avidin demonstrated recovery. Lattice light sheet microscopy demonstrated that the condensates are released by mast cells through thin, actin-positive filapodia that extend hundreds of microns in length. These motile filipodia grab the condensates from the mast cell surface and deposit them on neighboring cells throughout the fluid thereby creating a sphere of influence. These findings suggest that mast cell released condensates play a part in macrophage aggregation and may be driving the tissue-repair mechanism in the peritoneal cavity.

4. Illia Gelman (Experimental Medicine/Electrophysiology) A novel mechanism for persistent inhibition of hERG potassium channels by amiodarone after drug discontinuation

Illia Gelman, Wentao Li, Jun Guo, Reese Bogart-Cherry, Nicole Tomei, Neelakshi Sharma, Angelia Pan, Tonghua Yang, Adrian Baranchuk, Mohammad El-Diasty, Shetuan Zhang

The class III antiarrhythmic drug amiodarone (AMIO) inhibits the cardiac $K+$ current IKr that is conducted by the human ether-a-go-go related gene encoded channel, hERG. Like other class III antiarrhythmic drugs, AMIO can cause long QT syndrome (LQTS). In the present study, we investigated the effects of AMIO and its major metabolite, desethylamiodarone (DEA) on hERG channels expressed in HEK293 (hERG-HEK) as well as in cardiomyocyte-derived H9c2 cells. Our results show that after acute inhibition of hERG current (IhERG) by AMIO (IC50 of 0.2 μM) or DEA (IC50 of 0.5 μM), continuous washout of the drug for 20-25 min during whole-cell patch clamp recordings did not lead to any current recovery. Furthermore, when hERG-HEK cells were cultured with AMIO overnight and IhERG was recorded in drug-free bath solution, AMIO treatment resulted in a concentration dependent inhibition of IhERG with an IC50 of 0.3 μM. In contrast, such overnight treatments did not affect the expression of hERG channels shown by Western blot analyses. However, the mature hERG protein of AMIO-pretreated cells cultured in drug-free medium degraded much faster than that of control cells, indicating that AMIO treatment modified the property of mature hERG channels, making them non-conductive. Upon removal of amiodarone after hERG inhibition, recovery of hERG currents relies on newly made channels in a process of up to 20 hours. Thus, lingering effects after amiodarone discontinuation are anticipated, which has important clinical implications.

5. Dan Vo Hoang (Reproduction and Developmental Sciences) Evaluation of Memory T Cell Subset Repertoire in Endometriosis

Dan Vo Hoang, Kasthuri Ravishanker, Katherine B. Zutautus, Alexander Wodz, Danielle J. Sisnett, Chandrakant Tayade

Background:
Memory T cells are the key players in chronic immune responses; however, their roles in lesion formation and persistence in endometriosis remain unclear. This study investigates the presence and regulation of the three main memory T cell subsets: central (TCM), effector (TEM) and tissue-resident (TRM) memory T cells in human EM lesions and EM-induced mouse model.

Methods:
Memory T cell markers in human ectopic lesions, eutopic endometrium and controls were assessed by qRT-PCR. In a syngeneic EM mouse model, intraperitoneal injections of endometrial fragments and recombinant TGF-β1 were used to assess the effects of repeated antigen exposure and TGF-β1 on memory T cells. Flow cytometry profiled memory T cell subsets based on CD44, CD62L, CD69 and CD103 marker expression.

Results:
Human ectopic lesions showed significantly elevated expression of CD69, ITGAE, demonstrating enrichment of resident memory T cells, alongside increased expressions of TGFB1 and TGFBR2 lesions, suggesting involvement of TGF-β1 signaling. In mice, endometrial fragments expanded TCM. TGF-β1 significantly induced TEM, particularly CD103+ TEM populations. The combination of both treatments induced TCM and TEM in PF and elevated the number of CD103+ and CD69+ CD103+ resident memory γδ T cells in the lesions.

Conclusion:
Our findings suggest that repeated exposure to endometrial antigens and TGF-β1 signaling shape memory T cell reprogramming in endometriosis, potentially contributing to chronic inflammation and lesion persistence.

6. Ciara D. O'Connor (Microbes, Immunity, and Inflammation) Microglial rhythmicity and sex differences impact neuropathic pain development

Ciara D. O’Connor[1], Kaitlyn A. Tresidder[2], Nader Ghasemlou[1,2,3]
[1]Department of Biomedical and Molecular Sciences, Queen’s University, [2]Centre for Neuroscience Studies, Queen’s University, [3]Department of Anesthesiology and Perioperative Medicine, Queen’s University

Background:
Microglia drive pain development in the spared nerve injury (SNI) model of neuropathic pain in mice. Following SNI, spinal cord dorsal horn microglia proliferate and shift to a pro-inflammatory state. This cellular activation occurs contemporaneously with the development of mechanical allodynia. While both sexes have microglial activation, neuropathic pain in males develops via microglia-dependent pathways, while females utilize T-cell dependent pathways. Clinical studies show that neuropathic pain often features rhythmic fluctuations with pain peaking at night. Cellular level circadian rhythms, maintained by clock genes loops have been shown to control microglial activation. Sex differences and circadian fluctuations in pain pathways are two avenues for exploring pain development that converge through the involvement of microglia.

Methods:
Male and female mice with microglia-specific deletion of clock gene Bmal1, and littermate controls underwent SNI. Spinal cords from 7 and 28 days post-injury collected at 9 a.m. and 9 p.m. were immunostained for microglial markers to determine activation state. Mechanical allodynia was measured with the von Frey test up to 28 days post-SNI.

Results:
Male mice have diurnal fluctuations in mechanical allodynia and microglia morphology after SNI. These behavioural and cellular fluctuations were attenuated by microglia specific clock gene ablation. Female mice had no fluctuations in pain or microglia morphology. The knockout of Bmal1 did not affect behaviour or microglia morphology.

Funding: NSERC: Discovery Grant, CIHR: Project Grant

7. Kyra Fine (Gastroenterology) Development of a machine learning model for the use of blood biomarkers to predict IBD presence and activity

Kyra Fine

Background: inflammatory bowel disease (IBD) is a complex condition involving complex interaction of environmental and genetic factors. Current methods of diagnosing and tracking IBD often involve invasive or radiological imaging procedures. Given the known role that white blood cells (WBCs) and inflammation-related proteins play in IBD pathology, machine learning (ML) can chart the interactions between these biomarkers and disease activity status to allow for accurate diagnoses using a simple blood test.
Objective: To create a machine learning model to diagnose and classify IBD and its activity based

on blood samples.
Methods: 1458 bloodwork measurements from 108 IBD patients were included in this analysis. Disease activity was classified by physician global assessment score. A variety of ML and deep learning (DL) models were trained and evaluated for diagnosis and classification.
Results: The optimal model, random forest, achieved an accuracy of 73% and a specificity of 87%. The features with the highest relative importance to the model were platelets, hemoglobin, and neutrophils. Comparison with control patients without IBD showed increased platelet and neutrophil levels compared to patients with IBD in remission.
Conclusion: An ML model can be created to diagnose and track IBD efficiently and non-invasively, presenting a promising proof-of-principle for the ML-facilitated use of routine bloodwork for the diagnosis of complex immunologic conditions. These findings, once validated, could save unnecessary invasive testing and health care costs.

## ***Session 2***

Plenary Speaker: Jason Gallivan - Motor Learning as Autobiographical Memory: The Central Role of the Default Mode Network

How does the brain retrieve the memory of a learned physical skill? While traditional models have focused on motor-specific circuits, this talk will explore a new perspective: what if motor learning is a form of autobiographical memory? I will present recent neuroimaging findings from my lab suggesting that the Default Mode Network (DMN)—a system central to memory and internal thought—plays a critical role in this process. We find that faster relearning is marked by the neural 'reinstatement' of DMN activity patterns from the initial learning session. Crucially, this involves heightened functional connectivity between the DMN and motor cortex, suggesting the DMN acts to *index* and call upon the specific motor memory stored within sensorimotor systems. These results provide a new, hierarchical framework for understanding skill acquisition, bridging the gap between cognitive and motor neuroscience and holding important implications for neurorehabilitation.

1. Aryaman Sharma (Neuro-oncology) Dexamethasone Induced Quiescence Drives Treatment Resistance in Medulloblastoma

Aryaman Sharma, Kaytlin Andrews, Lauren Ellis, Alexander Brown, Yoon-Jae Cho, Margaret T. Fuller, Matthew P. Scott, Teresa Purzner *, James Purzner *

Medulloblastoma (MB), the most common malignant pediatric brain tumor, is rarely curable upon recurrence. Despite aggressive treatment, 5-year survival following relapse remains 12%. While quiescent, therapy-resistant tumor cell populations have been well described in driving recurrence, broader molecular mechanisms governing quiescence in MB, particularly with respect to supportive therapies, remain less understood. Here, we identify the cyclin-dependent kinase inhibitor p57 as a regulator of quiescence and chemotherapy resistance in Sonic Hedgehog (SHH) medulloblastoma. p57 was enriched in known stem-like MB cell populations compared to proliferative bulk. Overexpression of p57 led to increased nuclear localization, a six-fold enrichment of G0-phase cells and conferred resistance to vincristine. In human SHH MBs, elevated CDKN1C expression was correlated with significantly reduced survival. Dexamethasone, a standard supportive therapy in MB care, robustly increased nuclear p57 levels, expanded the G0 fraction and reduced vincristine-induced apoptosis by 46-48%. These findings were more pronounced in Trp53-mutant cells, exacerbating the therapeutic burden in what is already the highest-risk, most treatment-resistant MB subgroup. Together, these data establish p57 as a key regulator of quiescence and treatment resistance in SHH MB and implicate dexamethasone as a modifiable determinant of chemotherapy efficacy. Standardizing steroid timing and dosing may help restore treatment response and reduce the risk of recurrence.

The work presented here was carried out in the Departments of Medicine and Biomedical & Molecular Sciences.

2. Tasha Jawa (Critical Care Medicine) A Co-Designed Post-ICU Follow-Up Pathway Improves Psychosocial Recovery for Patients and Their Caregivers

Natasha A. Jawa, Michaela Hanley, Akasham Rajagopaul, Robin Westphal, Michelle Tryon, Rebecca Wakelin, Christine Caron, David M. Maslove, Stephanie Sibley, John Muscedere, Sunita Mathur, Afolasade Fakolade, Michelle E. Kho, J. Gordon Boyd and the Canadian Critical Care Trials Group

Introduction. Post-intensive care syndrome (PICS) and PICS-family affect most ICU survivors and their caregivers, causing long-term physical, cognitive, and psychological impairments. Despite these burdens, few follow-up programs exist to target the needs of these vulnerable groups. This study aimed to evaluate whether a co-designed, multicomponent post-ICU follow-up intervention improves emotional, psychological, cognitive, and functional outcomes in ICU survivors and their caregivers.

Methods. This was a pragmatic, mixed-methods randomized controlled trial (NCT06681649) conducted at a single medical-surgical-neurosciences ICU in Canada. Twenty patient–caregiver dyads (n=40) were randomized 1:1 to usual care or a co-designed intervention bundle: an ICU diary, informational materials, and two multidisciplinary follow-up clinic visits at 1- and 3-months post-discharge. Eligible patients were ≥18 years, high risk for PICS, and expected to survive ≥6 months; caregivers were adult relatives. At six months, outcomes were evaluated using qualitative interviews, process evaluation, and standardized clinical measures. Themes were analyzed using reflexive thematic analysis and mapped to Capacity-Opportunity-Motivation-Behavior and Theoretical Domains frameworks. Quantitative outcomes included PICS symptomatology, quality of life, caregiver burden, healthcare utilization, and functional status.

Results. At six months, 18 dyads remained (7/9 intervention; 9/9 control). The intervention was well-accepted, providing emotional reassurance, guidance, and continuity of care. ICU survivors randomized to intervention had significantly lower depression scores (p=0.034), while caregivers reported higher emotional well-being (p=0.027), higher social functioning (p=0.024), lower anxiety (p=0.007), and lower burden (p=0.014) vs. controls. Qualitative data supported these findings, revealing enhanced emotional support and preparedness.

Conclusions. A co-designed single-centre post-ICU care bundle was acceptable and improved psychological outcomes for patients and caregivers, supporting the need for larger, multi-centre trials.

3. Isabell Pitigoi (Neuroscience) Blinking strategically during a cognitive task improves performance but differs across sex, age, and disease

Isabell C. Pitigoi, Donald C. Brien, Heidi C. Riek, Blake K. Noyes, Rachel Yep, Olivia G. Calancie, Ryan H. Kirkpatrick, Brian C. Coe, Michele Morningstar, Douglas P. Munoz

Humans spend a substantial amount of waking time blinking; we blink anywhere from 16-20 times per minute, for 100-400 ms each time. Blinking must therefore be strategically timed to prioritize important visual input, tying it closely to one's psychological state (i.e., attention, interest, cognitive functioning). Here we present video-based eye-tracking data from 703 healthy participants (aged 5-91 years, 470 female) performing an interleaved pro-/anti-saccade task. We aimed to understand (1) how participants organize their blink timing; (2) whether the capacity to do so impacts task performance; and (3) how this behaviour varies with sex and age. We found that blinking quickly became minimized at times where it would compromise task performance, and that participants with high task error rates also had less organized blinking patterns. Males and females differed significantly in their blinking (only between the ages 18-45 years), yet they performed equally well on the task. Furthermore, from childhood to early adulthood, blink timing became increasingly efficient, before declining in elderly adults. This supports a link to learning capacity and inhibitory control, fundamental processes impacted by brain development. We discuss these findings alongside clinical data from neurodegenerative and psychiatric patients (n=1300) displaying blink alterations that are likely mediated by the disruption of specific critical neural pathways. This work greatly enriches our understanding of differences in blink behaviour driven by sex, age, and disease.

4. Anthony Guglya (Molecular aspects of hemostasis) Transcriptional Coactivators YAP/TAZ Contribute to the Regulation of Coagulation Factor VIII Expression

Anthony Guglya, Nathalie Tijet, Colleen Notley, Christine Brown, David Lillicrap

Background: Mechanisms for the transcriptional regulation of coagulation factor VIII (FVIII) remain poorly understood. Given endothelial production, there is rationale to explore shear stress-induced transcriptional machinery. YAP/TAZ/TEAD – one such complex – is a promising candidate after discovery of several putative TEAD binding sites in the F8 locus.

Aims: To provide mechanistic evidence of a role for YAP/TAZ in FVIII transcription.

Methods: 1.3kb of the F8 promoter was inserted into luciferase reporter constructs and nucleofected into FVIII-expressing cultured human lymphatic endothelial cells (LECs). Luciferase activity was measured before and after inactivating the lone TEAD binding site within the native promoter (n=5; n=3). Separately, YAP/TAZ gene knockdown in LECs via siRNA – alone (n=4) and in combination (n=3) – were enacted to measure the influence on FVIII mRNA and protein levels four days post-knockdown.

Results: i) F8 promoter activity decreases 42% ($p < 0.05$) after TEAD site inactivation. ii) Variable fold-changes in F8 mRNA occur after knockdown of YAP (0.88-fold decrease to 2.15-fold increase) or TAZ (1.17-fold to 1.90-fold increase). Combination knockdown induces a 1.87-fold increase in F8 transcription, but a 0.63-fold decrease in protein levels.

Conclusion: The role of YAP/TAZ/TEAD on FVIII transcription appears when modulating both YAP/TAZ activity and F8-specific TEAD activity. The discrepancy between FVIII mRNA and protein-level effects in our combination knockdown suggests a role for YAP/TAZ beyond the transcriptional level or secondary effects on FVIII translation.

5. Kaytlin Andrews (Neurooncology) Identifying Molecular and Cellular Features of Glioblastoma Invasion

Kaytlin Andrews, Leila White, James Purzner, Teresa Purzner

Background:
Glioblastoma (GB) is a highly invasive brain tumor that almost universally recurs despite treatment. About 80% of recurrences arise within the surgical cavity, suggesting residual tumor cells drive relapse. Identifying high-risk regions remains challenging due to the lack of spatially resolved sampling tools.
Methods:
We developed a neuronavigation-compatible biopsy tool that enables precise, repeatable sampling from the resection cavity. Following resection, MRI-guided biopsies are mapped to pre-operative imaging and used to generate patient-specific tissue microarrays for immunofluorescence (IF) and spatial analysis. We also collect ex-vivo lobectomy specimens and sampled at defined intervals from tumor core to cortex for IF to map invasive gradients.
Results:
The biopsy tool reduces sampling variability and improves spatial traceability. Early clinical use has yielded spatially registered samples from GB cavities. Preliminary IF analyses demonstrate regional heterogeneity in cancer stem cells and vascular density, indicating spatially distinct microenvironments that may influence recurrence.
Conclusion:
This approach integrates engineering design with molecular pathology to interrogate GB invasion and recurrence. By linking spatially mapped samples to outcomes, this work seeks to define high-risk features that inform patient-specific surgical and radiation strategies, advancing precision treatment in GB.

The work presented here was completed in the Departments of Medicine and Biomedical and

Molecular Sciences. This research is funded by the CIHR CGS-M and the Marathon of Hope Health Informatics and Data Sciences awards.

6. Madeleine Carew (Breast Cancer) Elucidating protective potential of metabolic pathways in triple negative breast cancer (TNBC)

Madeleine Carew1, Natasha Iaboni1, Elizabeth Lightbody2, Martin Kaufmann3,4, Rachel E. Rubino5, John Rudan3,4, and Christopher JB Nicol1,5

Triple negative breast cancer (TNBC) is an aggressive form of breast cancer (BC) associated with a poor prognosis, high risk of recurrence and few treatment options. Genomic/proteomic studies have advanced TNBC understanding, but more work is needed. An emerging approach is to define metabolomic signals of TNBC tumours to shed light on novel prognostic/predictive biomarkers. We previously used a non-destructive mass spectrometry (MS) technique, desorption electrospray ionization-MS imaging (DESI), to metabolically profile human breast and colorectal tumours, revealing metabolic signals that significantly correlate to gold standard pathological and prognostic features, which may help improve clinical decisions. We and others also showed the expression and activation of peroxisome proliferator-activated receptor γ (PPARγ), critical to normal sugar and lipid metabolism, suppresses BC progression, but its role in TNBC is unknown. Thus, I hypothesized metabolomic profiles would reveal protective PPARγ signaling pathways that reduce TNBC growth and spread in vivo. I generated in vivo murine xenografts using human TNBC metastatic MDA-MB-231cells and found the expression and activation of PPARγ significantly decreased primary mammary tumour volumes and lung metastases vs. controls. I then DESI profiled the xenografts and showed PPARγ expression and activation significantly downregulated a group of long- and very long-chain fatty acids (FAs), intermediates of FA elongation and synthesis that promote cancer proliferation. Together, these data provide the first evidence that activating PPARγ protects against TNBC growth and spread in vivo, is detectable by DESI, and elucidates mechanistic targets to explore as novel anti-TNBC biomarkers.

# Flash Talk Presentations

## ***Session 1***

1. Kate Sitak (Reproduction and Cancer) Inflammation-associated pregnancy complications are linked with reduced postpartum breast cancer growth in a mouse model

Kate Sitak, Christina Ferazzutti, Charles H. Graham, Tiziana Cotechini

Background: Postpartum breast cancer (PPBC) is defined as breast cancer diagnosed within ten years of giving birth and is associated with poor prognosis relative to age-matched nulliparous women with breast cancer. Contrastingly, pre-eclampsia (PE), an inflammatory pregnancy complication associated with placental damage and dysfunction, confers protection against the development of PPBC. The biological mechanisms associated with pregnancy complication-mediated protection against PPBC are not understood. Moreover, whether inflammation-associated pregnancy complications are also linked with improved tumour outcomes is unknown. Using a well-described mouse model of PPBC, we test the hypothesis that inflammation-associated pregnancy complications protect against PPBC growth.
Methods: Female BALB/c mice were mated with C57BL/6 male mice to establish allogeneic pregnancies. To induce an inflammatory pregnancy complication, dams were injected with lipopolysaccharide (LPS; 20 µg/kg) or saline (controls) on gestational day (GD) 10.5. A separate cohort of dams underwent a reduced uterine perfusion pressure (RUPP) surgery or sham surgery (controls) on GD 14.5 to induce fetal growth restriction. To investigate PPBC growth, 66cl-4 mammary carcinoma cells were injected into the fourth mammary gland two days following forced weaning and tumour kinetics were evaluated for 28 days.
Results: Mammary tumour growth in LPS-exposed mice was significantly reduced compared with saline controls. Tumour growth was also significantly reduced in dams that underwent the RUPP procedure compared with surgical sham controls.
Conclusion: Inflammation-associated pregnancy complications are associated with reduced PPBC growth.

2. Danielle Harper (Breast Cancer) Genetic Disruption of Calpain-1 and Calpain-2 Impedes Triple Negative Breast Cancer Metastasis

Danielle Harper, Ivan Shapovalov, Jenny Min, Samantha Cockburn, Anya Aaron, Yan Gao, Peter Greer

Calpains are calcium-activated cysteine proteases that have emerged as potential therapeutic targets in triple negative breast cancer (TNBC). They regulate the function of their substrates via limited proteolytic processing and are involved in membrane-cytoskeletal remodeling events associated with cell migration and invasion. At present, no clinically relevant calpain inhibitors are available. Using genetic approaches, we demonstrate that calpain deficient TNBC cells are less migratory and invasive in vitro and less metastatic in orthotopic engraftment mouse models. To explore potential off-target effects associated with systemic calpain inhibition, we have established a novel transgenic mouse with conditional deletion of calpain-1 and calpain-2 in its hematopoietic stem cell lineage.

3. Natasha Iaboni (Breast Cancer) Differentiating in situ vs invasive ductal carcinoma using spatial metabolomics

Natasha Iaboni, Teaghan Kooster, Martin Kaufmann, Madeleine Carew, Amoon Jamzad, Abdulhameed Abdulhameed, Rachel Rubino, Kevin Ren, John F. Rudan, Parvin Mousavi, Sonal Varma, Christopher J.B. Nicol.

Ductal carcinoma in situ (DCIS) is a breast cancer subtype contained within the ductal system, which may or may not progress to invasive ductal carcinoma (IDC). Women diagnosed with DCIS are often over-treated because of the prognostic challenges of knowing if DCIS will progress to IDC or not. To distinguish aggressive from non-aggressive DCIS tumours, we employ desorption electrospray ionization (DESI), a non-destructive mass spectrometry imaging technique that detects lipids using spectrums of mass to charge (m/z) ratios. We hypothesize DESI profiles of DCIS and IDC will reveal unique prognostic signatures. To test this, we performed a feasibility study using locally accrued human (DCIS/IDC, n=34) breast tumour samples. Sections of FFPE samples were analyzed by DESI using negative ionization, then H&E stained and annotated for tumour and non-tumour zones by pathologists. Multivariate analyses (m/z 50-1200) were performed on randomized regions of interest per pathological zone. My data suggest a series of pro-tumourigenic, inflammatory omega-6 fatty acids are significantly upregulated in IDC, while anti-inflammatory prostaglandins, including 15d-PGJ2, are significantly upregulated in DCIS. As 15d-PGJ2 is an activator of PPARγ, a regulator of lipid metabolism and involved in breast tumour suppression, using immunohistochemistry, we observed a significant increase in PPARγ expression in DCIS samples compared to IDC. This suggests 15d-PGJ2 and PPARγ expression may help inform the aggressive potential of DCIS patients.

4. Alison Hermanutz (Experimental Medicine) Investigating Aging-Associated Loss of Sex Chromosomes and Response to Bacillus Calmette-Guérin Immunotherapy in Bladder Cancer

Alison Hermanutz, Kartik Sachdeva, Priyanka Yolmo, Gwenaëlle Conseil, David M. Berman, D. Robert Siemens, Madhuri Koti

The average age of diagnosis for bladder cancer is 73 years. The majority of bladder cancer cases are diagnosed as non-muscle invasive bladder cancer (NMIBC). Patients at a high risk of recurrence or progression are treated with intravesical Bacillus Calmette-Guérin (BCG) immunotherapy. Our previous findings from aging murine models and patient tumours have demonstrated that aging-associated immune dysfunction and exhaustion is a major factor underlying poor outcomes following treatment with BCG. Concurrent to aging-associated immune function decline, somatic loss of Y (LOY) or loss of X (LOX) chromosome occurs in peripheral blood cells of aging males and females. LOY is known to increase the risk for bladder cancer and influence response to immune checkpoint inhibitors. In this study, we explore the association between immune cell intrinsic LOY and LOX, and response to BCG.

The four-core genotype murine model was used to determine chromosomal complement associated profiles of immune cells using multiparametric flow cytometry, following repeated exposure to BCG. Fluorescence in situ hybridization using probes for X and Y chromosomes was performed on treatment-naïve tumours from patients categorized as BCG responders and non-responders.

Findings suggest a potential influence of sex chromosomal loss in response to BCG. Ongoing characterization of LOY and LOX in peripheral blood cells from patients undergoing BCG treatment will inform the development of predictive biomarkers.

5. Brian Shkabari (Health Services, Cancer Policy) The Landscape of U.S. FDA Approvals of Adult Solid Cancer Medicines (2009-2024)

Brian Shkabari1, Nicole Vorko1,2, Wesley Geerlinks3,4, Svasti Sutaria1, Claire Diana-Gonsalves1, Bishal Gyawali1,2,5

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The U.S. Food and Drug Administration (FDA) is the main regulatory body responsible for cancer medicine approvals in the U.S. and must manage a delicate balance between approving cancer medicines with speed, whilst ensuring supporting clinical trial data reflect outcomes that matter to patients. The FDA is considered the gold-standard for drug approvals and is a noted influence for regulatory systems worldwide. In this study, we assessed the approval trends of adult, solid cancer medicines by the FDA over the last 16 years (2009-2024) to better understand the landscape of the approval system, and whether approved medicines improve outcomes for patients. Three hundred thirty-six unique approvals were extracted with 272 regular approvals and 64 regular approvals, with 39.5% of coming between 2021-2024. The most targeted sites were lung (n=83), breast (n=37), melanoma (n=22), and prostate (n=21). Median improvement in overall survival was 2.90 months (0.70 HR), and progression free survival was 3.90 months (0.56 HR). 68.8% of regular approvals from 2021-2024 were approved on the basis of surrogate endpoints, an increase from 56.4% from 2009-2020. While the number of FDA approvals for adult cancer medicines are increasing over time, there is a growing reliance on surrogate endpoints, especially for regular approvals. While we strive for innovation, we need an equal push for quality, not just quantity in new treatment options for people living with cancer.

6. Piper Holmes (Reproduction and Developmental Biology) Characterization and surface markers analysis of endometriosis patient-derived extracellular vesicles and their unique signatures associated with disease

Jaelis P. Holmes, Katherine B. Zutautas, Danielle J. Sisnett, Chandra Tayade

Endometriosis (EM) is a chronic inflammatory disease with high heterogeneity in phenotype and symptom severity, resulting in diagnostic delays of 4-11 years. Small extracellular vesicles (sEVs) contain bioactive molecules and show distinct expression profiles between EM patients and controls, making them potential candidates for disease biomarkers. This study aims to profile sEVs in mild and severe EM cases using multi-omics data, to unravel biomarkers associated with EM.

sEVs isolated from matched ectopic lesions, eutopic endometrium, plasma, and peritoneal fluid from EM patients and healthy controls, were characterized using nanoparticle tracking analysis, transmission electron microscopy and MACSPlex flow cytometric analysis of 39 surface markers. Plasma-derived sEVs from severe EM patients showed elevated adhesion and platelet/endothelial markers, while peritoneal fluid sEVs from mild EM patients showed higher stemness and cell adhesion markers. Ectopic lesions had reduced epithelial adhesion markers, and HLA-II was increased in severe EM, suggesting enhanced immune activation and/or tolerance in advanced disease.

sEV molecular content (RNAs, proteins, lipids) profiling is in progress using transcriptomic, proteomic, and lipidomic approaches. Preliminary proteomics screening identified proteins involved in extracellular matrix remodeling, angiogenesis, and immune signaling, while lipidomic and transcriptomic analyses are ongoing. So far, these findings have captured unique differences in surface marker profiles in sEVs between EM patients and controls. Integrated molecular profiling of sEVs, will reveal stage-specific signatures, associated with EM and offer potential biomarkers for improved diagnostics in the near future.

7. Maria V. Medeleanu (Respiratory Medicine/Allergy Immunology/Pediatrics) Antibiotics in early life partially mediate the association lower respiratory tract infections and development of asthma

Maria V. Medeleanu, Myrtha E. Reyna, Darlene L.Y. Dai, Geoffrey L. Winsor, Fiona S.L. Brinkman, Rahul Verma, Ella Nugent, Nashita Riaz, Elinor Simons, Piushkumar J. Mandhane, Meghan B. Azad, Stuart E. Turvey, Theo J. Moraes, and Padmaja Subbarao

Objective: Lower respiratory tract infections (LRTIs) in early life are one of the strongest risk factors for childhood asthma and are often treated with systemic antibiotics (IV or oral). We aimed to explore the association between early-life LRTIs and systemic antibiotics on asthma development and the potential mediating role of antibiotics in this relationship.

Methods: Data were collected as part of the longitudinal, general Canadian population CHILD Study. LRTIs during the first 18 months of life were identified through parental symptom report at regular study visits. Systemic antibiotic use was defined as at least one dose of oral/intravenous antibiotics between birth and the 18-month visit and were further categorized by indication as either given for a respiratory indication (upper or lower respiratory symptoms) or non-respiratory indication. Asthma was diagnosed by in-study pediatricians at the 5-year study visit. Adjusted logistic regression models and mediation analyses via systemic antibiotics use were performed.

Results: Among 2,073 participants included in our analysis, 72 (4.9%) had asthma at age 5, and 609 (29.3%) used systemic antibiotics before the 18-month visit. Among children who had taken antibiotics, 61.6% also had an LRTI in that period compared to 49.7% among children without exposure to systemic antibiotics ($p < .001$). Moderate-severe LRTIs before age 18 months were associated with higher odds of 5-year asthma [aOR 4.12 (95%CI 2.04–7.95) $p < .001$]. Antibiotics taken for respiratory indications were associated with higher odds of asthma at age 5 [aOR 2.36 (95%CI 1.59–3.48) $p < .001$]. Children who received systemic antibiotics for only non-respiratory indications during the first 18 months of life were not associated with increased odds of asthma [aOR 1.08 (95%CI 0.44–2.30) $p = .851$]. Using mediation analysis, 21.7% of the association between LRTI and asthma is estimated to be mediated through use of early-life systemic antibiotics. However, a significant direct effect of moderate-to-severe LRTIs on asthma risk remained in adjusted mediation models ($p = .014$).

Conclusion: Using mediation modeling we estimate that the increased risk of asthma at age 5 associated with moderate-severe LRTIs may be partially mediated by systemic antibiotics taken during the first 18 months of life. This underscores the importance of public health strategies focused on antibiotic stewardship and reducing early life LRTIs to mitigate asthma risk.

8. Landon Montag (Pain Research) Who's Checking the Blindfold? A Review of Blinding Assessment Practices in Pharmacotherapy & Neuromodulation RCTs for Neuropathic Pain in Adults

Montag LT; Soliman N; Haroutounian S; Finnerup N; Attal N; Moisset X; Ferraro MC; Ciampi de Andrade D; Baron R; Belton J; Bennett DLH; Calvo M; Dougherty P; Hietaharju AJ; Hosomi K; Kamerman PR; Kemp H; Enax-Krumova EK; McNicol E; Price TJ; Raja SN; Rice ASC; Smith BH; Talkington F; Truini A; Vollert J; Vase L; Colloca L; Salomons TV; Abuukar Abdullahi R; Evans M; Gwyther B; Phillips H; Ramirez Piriz C; Rottenberg A; Hohenschurz-Schmidt D; Wang C; Zachariadis A; Wandrey JD; Freigang S; Kubota GT; Phalip J; Pramitasuri TI; Taule-Lim N; Than QV; Zunaid MD; Gilron I

In randomized controlled trials (RCTs), a double-blind design is recommended to minimize bias. To determine blinding effectiveness, participants and/or research personnel may be asked which treatment they believe the participant received. But despite the importance of blinding in RCTs, no standardized methodology exists for blinding assessment (BA), analysis, nor result reporting. As such, we characterized BA reporting in pharmacotherapy and neuromodulation neuropathic pain RCTs. Of 290 studies included in a recent neuropathic pain meta-analysis, only 37 (13%) reported BAs. All studies reported participant BAs, and 10 also reported BAs completed by a blinded research team member. 38% included an 'unsure' option when asking which treatment the participant believed they received, and 27% asked the reason for their response. 13 parallel studies

(15 BAs) provided sufficient data to calculate Bang's Blinding Index (BI). Blinding was effective (BI=0±0.2) in 9/15 placebo and 10/15 treatment arms. 5 placebo and 3 treatment arms trended towards unblinding (BI>0.2), whereas 1 placebo and 2 treatment arms trended towards misinformed guessing (B<-0.2). This variability is likely due to treatment characteristics and study design. Our findings suggest that BA is done in a minority of neuropathic pain trials, and with variable methodology. Given the importance of minimizing risk of bias due to treatment unblinding, further research is necessary to determine if/how BA should be conducted and interpreted in analgesic clinical trials.

## ***Session 2***

1. Olivia DiPaolo (Obesity) Investigating the role of orexin signaling in impaired satiety sensing in obesity.

Olivia I. DiPaolo, Ananya Chakraborty, Sahil Sachdev, Ayssar Tashtush, David E. Reed, Alan E. Lomax

Background: Obesity is linked to overeating, driven by impaired satiety sensing. Satiety is conveyed from the gut to the brain by vagal afferent neurons (VANs) with cell bodies in the nodose ganglia (NG). We have previously shown that fecal supernatants from both obese mice and humans decreased the excitability of VANs, an effect that was prevented by pre-incubation with the orexin-1 receptor antagonist SB-334867 (OX1R-ant). We aimed to determine whether in-vivo administration of OX1R-ant improves satiety sensing during obesity. Methods: Mice were fed a high-fat diet (HFD) or low-fat diet (LFD) and received daily injections of OX1R-ant (10 mg/kg) to assess its effect on food intake and body weight. Results: HFD mice were heavier than LFD mice (HFD = 31.77 g ± 1.03 g vs. LFD = 22.92 g ± 0.97 g) and had greater food intake (HFD = 12.04 ± 0.48 vs. LFD = 3.18 ± 0.53 kcal/g body weight) than LFD controls. After a week of daily OX1R-ant injections, HFD mice, but not LFD mice, had a 55% decrease in daily food intake and an 8% decrease in body weight (one-way ANOVA, $p<0.05$ in all comparisons). These effects were reversed after a week-long washout period. Conclusions: In-vivo administration of OX1R-ant significantly reduces food intake and weight only in HFD mice, implicating orexin receptor signaling in obesity-related satiety impairment.

2. Rose Binley-Ewing (Immunology and cancer research) Investigating The Role of Neutrophils in the Lung Pre-Metastatic Niche

Rose Binley-Ewing, Paul Kubes

The fatality rate for metastatic cancers remains high with the lungs being a common and deadly site of metastasis. The early events of metastasis involve tissue remodeling that favours tumour cell colonization creating the pre-metastatic niche. Neutrophils populate the pre-metastatic niche, but their phenotype and whether they support metastasis remains unclear. This project proposes to characterize the behaviour and impact of neutrophils in the pre-metastatic niche. A model of E0771-GFP breast cancer cells that metastasize to the lungs was established where the pre-metastatic niche and arrival of cancer cells can be captured using intravital microscopy. The Kubes Lab has previously demonstrated that under healthy conditions, the majority of resident lung neutrophils crawl along the alveolar capillary wall seeking perturbations. Behavioural analysis of neutrophils imaged in pre-metastatic lungs showed reduced crawling and adhesion to the endothelium. Further, pre-metastatic neutrophils were imaged in the presence of both intravenously injected and spontaneously escaped cancer cells. In both cases, neutrophils exhibited limited interactions with cancer cells. In contrast, in healthy lungs, numerous neutrophils maintained prolonged contact with injected cancer cells. Super-resolution microscopy of healthy resident lung neutrophils showed acquisition of GFP+ particles following interaction with cancer cells. The results of this study indicate that the pre-metastatic niche influences neutrophil behaviour and responsiveness to cancer cells. These findings lay the foundation for therapeutic targeting of neutrophils to prevent metastatic seeding.

3. Kartik Sachdeva (Immunology/Cancer) Integrated transcriptomic and spatial immunophenotyping reveals T cell exhaustion associated immunosuppression in BCG-Unresponsive non-muscle invasive bladder cancer

Kartik Sachdeva1, Priyanka Yolmo1, Gwenaelle Conseil1, Abdulhameed Abdulhamed2, Alanna Brewer3, David M. Berman1, Sia Viborg Lindskrog4, Trine Strandgaard4, Lars Dyrskjøt4, D. Robert Siemens1,3 and Madhuri Koti1,2 1Sinclair Cancer Research Institute, 2Department of Pathology and Molecular Medicine, 3Department of Urology, Queen's University, Kingston, Ontario, Canada; 4Department of Molecular medicine, University of Aarhus, Denmark

Introduction: More than 50% of patients with non-muscle invasive bladder cancer (NMIBC) experience early recurrence or progression following treatment with Bacillus Calmette Guerin (BCG) immunotherapy. Our previous findings from aging murine models and patient tumors demonstrated that treatment naïve tumors from BCG non-responders exhibit an overall increased T, B and myeloid cell exhaustion with increased density of peri-tumoral tertiary lymphoid structures. Factors underlying such tumor phenotypes span from older age to persistent chronic mucosal inflammation within the bladder. This study was conducted to delineate the T cell effector responses triggered by repeated administration of intravesical BCG and their association with immune exhaustion in patients with high-risk NMIBC.
Methods: Bulk-RNA sequencing based whole transcriptome profiles of pre-BCG tumors were analyzed. Circulating T cell functional and transcriptomic states, at pre- and post-BCG time points from patients undergoing treatment at the Kingston Health Sciences, were characterized using multiparametric flow cytometry and single cell RNA-sequencing. Single cell spatial transcriptomic profiling and multiplex immunofluorescence of corresponding tumors was performed.
Results and Conclusion: Terminal effector T cells were increased in BCG-non-responders. Cellular neighbourhood analysis revealed an association of exhausted B cells with regulatory T cell subsets within the tumor immune microenvironment of BCG non-responders. Findings from this study advance the current knowledge on BCG induced anti-tumor T cell response and will inform future biomarker development or therapeutic interventions.

4. Erik McInnes (Macrophage Immunology) Effects of CSF1R Deletion on Resident Macrophage Proliferation During Injury

Erik C. McInnes1, Abbey L. Politeski2, Seily Shrestha1, Sarah A. Dick1

Affiliations:

1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, CA.
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Skeletal muscle regeneration is a highly regulated process directed by a heterogeneous immune response, with macrophages serving as key mediators. In aging and muscle wasting diseases, this regenerative ability is impaired, highlighting the need to understand mechanisms that regulate macrophages toward a pro-regenerative state.

During embryogenesis, macrophages migrate to tissues and form pro-reparative tissue resident macrophages (TRM). TRMs undergo self-proliferation within their tissue niche through locally produced colony stimulating factor 1 (CSF1). In contrast, monocyte-derived macrophages (MDMs) arise from bone marrow progenitors via bone marrow hematopoiesis and form recruited inflammatory populations. After recruitment, monocytes differentiate into MDMs through CSF1 binding to its receptor CSF1R. Given CSF1's role in promoting both proliferation and differentiation in both these populations, we hypothesized that loss of CSF1R in monocytes would reduce MDMs while increasing TRM proliferation.

To test this, we used a monocyte-specific inducible CSF1R knockout mouse model (Ccr2CreER/+: Csf1rflx/flx). Injury was induced in the left gastrocnemius muscle with cardiotoxin (CTx), and macrophage populations were analyzed by flow cytometry at days 3, 5, and 7 post-injury.

We found that monocytes could not complete their transition into MDMs, leading to an overall reduction in macrophage count. However, TRM self-proliferation compensated, maintaining stable macrophage levels. These findings highlight the synergistic interactions between macrophage subsets and the essential role of CSF1 in orchestrating their injury response, with therapeutic implications for muscle regeneration.

Supporting Agency:
CIHR and NSERC Grants

5. Danielle Shibi Rosen (Immunology) Exploring the function and origin of kidney capsule macrophages

Danielle Shibi Rosen1, Seily Shrestha2, Abbey Politeski1, Sarah A. Dick2

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Macrophages are innate immune cells involved in pathogen detection, homeostasis, tissue development, and inflammation. They can be tissue resident and self-renewing, or recruited from the bone marrow via a monocyte intermediate. Three main subsets of tissue resident macrophages, with conserved ontogeny and self-renewal capacity across tissues, have been identified: TLF+ (expressing TIMD4, LYVE1, and FOLR2), MHCIIhi, and CCR2+. The kidney parenchyma notably lacks TLF+ macrophages, a yolk sac–derived subset capable of self-renewal and wound repair. The kidney capsule, a fibrous tissue surrounding the parenchyma, remains understudied. It was recently shown to contain TLF+ macrophages, though the function and origin of this population are unclear. Here we demonstrate a specific role for fibroblast-derived macrophage colony stimulating factor (mCSF) in maintaining this population, which is dispensable for macrophage maintenance in the parenchyma. We show that self-renewing TRMs appear to cluster on the capsule surface, while others are replaced by infiltrating monocytes at a higher rate than kidney parenchymal macrophages. This supports their dependence on fibroblast-mCSF, which we show is required for monocyte differentiation in injury. Future work will explore the functional role of these cells, as preliminary data shows their infiltration into the renal parenchyma post-injury.
Funding: NSERC & Kidney Foundation of Canada

6. Nazanin Soghrati (Rheumatology) Clinically Available Biomarkers Associated with Systemic Autoimmune Rheumatic Disease (SARD) Progression in Anti-nuclear Antibody (ANA) Positive Individuals

Nazanin Soghrati, Sindhu R. Johnson, Zahi Touma, Zareen Ahmad, Dennisse Bonilla, Linda T. Hiraki, Arthur Bookman, and Joan E. Wither

Objective: The presence of ANAs is a hallmark of SARD. ANAs are also found in up to 25% of women, only a small fraction of whom will develop a SARD. As the onset of symptomatic disease is not infrequently associated with organ damage, there is tremendous interest in the identification of biomarkers associated with a high risk of progression. Here, we sought to determine whether any of the tests typically available to Rheumatologists can be used to identify ANA-positive individuals at high risk of imminent progression.
Methods: Study participants were recruited from the Early Autoimmune Rheumatic Disease Clinic at Toronto Western Hospital where ANA-positive individuals without a SARD diagnosis were followed yearly for development of symptoms.
Results: 124 ANA-positive individuals were followed a minimum of 2 years, 15 of which clinically progressed within 2 years. The mean age and proportion of female progressors did not differ significantly from non-progressors, however progressors were more likely to be non-Caucasian. While ANA titer and serum complement levels were similar, progressors had significantly more specific ANAs. Except for anti-dsDNA antibodies, all specific ANAs were more prevalent in progressors, but this difference was only significant for anti-La antibodies. The most prevalent antibody in both cohorts was anti-Ro. Within anti-Ro positive individuals, discrimination between

anti-Ro52 and –Ro60 showed that anti-Ro52, but not anti-Ro60 antibodies, were significantly associated with progression.

7. Chirag Chopra (Medical Education) Evaluating a Specialized Extended Reality (XR) Modality as a Teaching Tool for Undergraduate Medical Education

Chirag Chopra, Souzan Yacob, Bonnie Yang, Nicholas Laflamme, Eleftheria Laios, Wiley Chung

Background: Extended reality (XR) is an emerging educational modality with potential to enhance both procedural and communication training in health professions education. While XR has shown promise in nursing and surgical training, its role in integrated undergraduate medical education (UME) remains underexplored.

Objective: This study aims to evaluate the effectiveness of our specialized XR training module compared to traditional small group learning (SGL) and video-based instruction in teaching procedural and communication skills to undergraduate medical students at Queen's University.

Methods: First-year medical students will be randomized into one of three learning interventions: (1) video instruction, (2) SGL using the Echelon 3000 surgical stapler, or (3) an XR-based mixed reality simulation. XR will use a 3D-printed stapler integrated with digital overlays and AI-powered chatbot guidance, spanning three modules: device familiarization, guided procedural training, and troubleshooting with team communication. Pre- and post-intervention assessments will measure communication (CC-SET), anxiety (STAI), and cognitive load (NASA-TLX, physiologic indices, EEG). Participants will subsequently complete a standardized patient encounter to assess skill transfer. Data will be analyzed using ANOVA/MANOVA, with effect sizes calculated.

Hypothesized Results: This study will identify strengths and limitations of XR as a pedagogical tool relative to established methods in UME. We hypothesize that XR will improve communication, procedural competency, and learner confidence while maintaining acceptable cognitive load.

Conclusion: Findings may guide scalable integration of XR into competency-based UME curricula, offering insights into its utility as an immersive training platform for interprofessional and procedural education.

8. Anisur Rahman (Computational Biology) A Fragment Size Correction Algorithm for Improved Nucleosome Positioning from MNase-Seq Data

Anisur Rahman , Shuxiang Li , Anna R. Panchenko

In eukaryotic genomes, nucleosomes are arranged like "beads on a string," with approximately 147 base pairs (bp) of DNA wrapped around histone proteins. The genomic distribution of these nucleosomes, known as nucleosome positioning, is not random and is governed by diverse regulatory factors. However, these positions are dynamic and can vary between cells, which makes accurate identification of their positions particularly challenging. Nucleosome positioning provides insight into chromatin architecture, gene regulation, and the epigenetic landscape of a cell population. Such knowledge is crucial for understanding diseases like cancer and developing diagnostic and therapeutic solutions.

Micrococcal nuclease (MNase) digestion is commonly used to isolate DNA fragments bound to nucleosomes, and various computational tools are then employed to infer nucleosome positions from the resulting sequencing data. However, MNase exhibits sequence bias, and the inherent variability of nucleosome positions, combined with methodological constraints, leads to a significant amount of noise in the sequencing data. Although current nucleosome identification methods apply different smoothing and filtering strategies to mitigate these issues, their accuracy remains limited.

In this work, we propose NuFix, an algorithm that computationally adjusts fragment lengths by incorporating the distribution of surrounding fragments. This approach significantly enhances the accuracy of nucleosome positioning identification. After applying the algorithm to MNase-seq data, we were able to identify more nucleosomes in the human genome with better accuracy and confidence.

# Poster Presentations

## ***Morning Session***

1. Doriana Taccardi (Microbes, Immunity, and Inflammation) It's Time for a better way to treat chronic diseases

Doriana Taccardi*, Hailey G.M. Gowdy, Amanda M. Zacharias, Mitra Knezic, Zihang Lu, M. Gabrielle Pagé, Marcia Finlayson, Qingling Duan, and Nader Ghasemlou.

Chronic diseases such as chronic pain and multiple sclerosis (MS) are increasingly prevalent in Canada, presenting new challenges for our health system. They are influenced by a combination of genetics, lifestyle, and environmental determinants of health. A better understanding of these factors may facilitate the implementation of effective strategies to improve prevention and management in diverse global settings.
My work is focused on identifying inter- and intra-individual fluctuations in symptomatology, like pain intensity, which pose a major challenge to treatment efficacy, with most people perceiving their pain relief as inadequate. People with chronic pain and MS rated their pain three times a day (8 am, 2 pm, 8 pm) for several days and completed two blood samples within 12 hours (8 am, 8 pm). While most individuals displayed constant or unpredictable/mixed pain phenotypes, a subset had daily fluctuations of increasing pain scores (>30% change in intensity over 12 hours in ≥4/7 days). This population had no opioid users, better biopsychosocial profiles, and differentially expressed transcripts relative to other pain phenotypes. The circadian-governed neutrophil degranulation pathway was particularly enriched among arhythmic individuals.
Our findings identify pain rhythmicity and the circadian expression of neutrophil degranulation pathways as indicators of health outcomes. Characterizing the experience of pain more comprehensively and matching it with biological and immune profiles may be key to advancing towards better and more personalized care.

Funding: Canadian Institutes of Health Research (#497592) and the CIHR-Strategy for Patient-Oriented Research Chronic Pain Network (#SCA-145102).
DT is funded by MS Canada with an endMS Doctoral award (#1369236).

2. Hailey Gowdy (Neuroimmunology) CircaPain: Examining inter-individual differences in chronic pain via time-dependent variability

Hailey G.M. Gowdy, Doriana Taccardi, Amanda M. Zacharias, Élisabeth Lamoureux, Lesley Norris Singer, Jennifer Daly-Cyr, Manon Choinière, M. Gabrielle Pagé, Qingling Duan, Zihang Lu, and Nader Ghasemlou

Introduction: In the pursuit of individualised chronic pain management strategies, it is crucial to know why and when someone has pain. Our study explores how variability across time – as a proxy for circadian rhythmicity – could be an important factor in understanding inter-individual differences in pain experiences, and if distinct temporal patterns exist.

Methods: Following an initial questionnaire, recruited participants (n=907) completed electronic symptom-tracking diaries, in which they rated their pain intensity, affect, and fatigue on a 0-10 scale daily at 3 timepoints (08:00, 14:00, 20:00) over 7 days. Preliminary groups based on time-dependent changes in pain scores were identified using means and standard deviation.
Results: Compliant diaries (diary entry submitted within 2 hours of being sent) of 1 or more full days were completed by n=585 participants. Five preliminary pain rhythmicity groups were identified: constant low (23.0% of total), constant high (27.0%), increasing (rhythmic↑; 16.0%), decreasing (rhythmic↓; 4.1%), and arrhythmic (mixed; 29.9%). A latent class mixed effects model enabled the identification of alternative groups with a more data-driven approach. The effect of pain rhythmicity on baseline biopsychosocial outcomes was also assessed.
Discussion/Conclusions: The inter-individual differences in pain variability observed in our sample present a tool to characterise chronic pain, with potential ramifications for our clinical understanding of pain and circadian rhythmicity.

This work is supported by CIHR and the CIHR-SPOR Chronic Pain Network.

3. Sarah Nash (Reproduction and Development) Investigating Autoimmunity as a Driver for Interstitial Cystitis / Bladder Pain Syndrome with Hunner Lesions

Sarah Nash[1], Vina W. Li[1], Madhuri Koti[1], R. Christopher Doiron[2], Tiziana Cotechini[1]

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Supporting Agency: CIHR

Introduction: Hunner lesions (HL) are inflammatory lesions that occur in 5-10% of patients with interstitial cystitis/bladder pain syndrome (IC/BPS) and are more prominent in women. Patients with HL-IC/BPS experience severe symptoms including debilitating pain, more frequent urination, and poor quality of life. The underlying pathophysiology of HL-IC/BPS is unknown, however the presence of tertiary lymphoid structures (TLS) in HLs and the more frequent occurrence of IC/BPS in patients with systemic lupus erythematosus, autoimmune thyroiditis, Sjögren syndrome, and Rheumatoid Arthritis support the concept that this disease may have an underlying autoimmune etiology. We hypothesize that HL-IC/BPS is an autoimmune disease, and our goal is to develop a pre-clinical model of HL-IC/PBS through induction of Experimental Autoimmune Cystitis (EAC) using autoimmune-prone mice.

Methods: To induce EAC, Non-Obese Diabetic mice (6-8 weeks) were vaccinated with a 1:1 emulsion of bladder homogenate with Complete or Incomplete Freund’s Adjuvant via subcutaneous injection. Control mice received PBS in place of bladder homogenate. All mice were boost immunized two weeks later. Micturition habits were assessed weekly for four weeks following boost immunization.

Results: Urine output was significantly reduced in mice receiving Complete Freund’s Adjuvant while urination frequency was significantly reduced in mice receiving blader homogenate. Histological examination of bladders revealed marked mucosal abnormalities in experimental mice.

Conclusion: Induction of EAC in autoimmune prone mice does not entirely recapitulate features of HL-IC/BPS. Additional studies are ongoing.

4. Mara Majer (Pain chronobiology) Using dried blood spots to investigate rhythmicity in chronic low back pain: a feasibility study

Mara Majer, Doriana Taccardi, Hailey Gowdy, Amanda Zacharias, Élisabeth Lamoureux, Gabrielle Pagé, Nader Ghasemlou

Effective treatments for chronic pain are lacking, and existing medications (e.g., opioids) can lead to burdensome and often devastating side effects. The nature and experience of pain are extremely variable between different individuals and even within the same person at different times, indicating there is likely no "one size fits all" treatment. One way to examine variability is by addressing the chronobiology of pain. Circadian (24-hour) rhythms align physiological functions with the environment and are controlled by an internal clock system.

To better understand how biomarkers and psychosocial factors interact with pain variability, we need efficient, minimally invasive ways to collect protein to detect circadian rhythm-associated changes in gene expression on a large scale. We hypothesize that people with chronic low back pain will exhibit variability in pain rhythmicity that will be associated with changes in biomarkers (e.g., protein expression) and self-reported symptoms at multiple times of day (e.g., pain, mood, and fatigue).

Our objectives are to capture rhythmicity using ecological momentary assessments and dried blood spots; to determine if protein expression is associated with self-reported symptoms; and to test the feasibility of this study design in people with chronic low back pain. By identifying how circadian rhythms drive changes in immune cells, we can gain a better understanding of how to manage chronic pain.

This project is funded by the Quebec Pain Research Network.

5. Wesley Geerlinks (Experimental Medicine) BCG strain associated transcriptomic alterations in the bladder microenvironment of a murine model of non-muscle invasive bladder cancer

Wesley Geerlinks, Victoria Velazquez Becerra, Alison Hermanutz, Priyanka Yolmo, Kartik Sachdeva, Gwenaëlle Conseil, D. Robert Siemens, Madhuri Koti

Introduction: High-risk non-muscle invasive bladder cancer (NMIBC) is treated using intravesical Bacillus Calmette-Guérin (BCG) immunotherapy. The ongoing shortage of BCG TICE® in North America has led to a renewed interest in understanding strain-associated differences in clinical outcomes. Phylogenetic differences among the early (Moscow) and late (TICE) strains of BCG bacteria are well established with regard to their T cell epitopes and immunogenicity. We examined whether the two clinically used strains of BCG trigger differential immune responses and ultimately alter recruitment of immune cells to the bladder microenvironment upon intravesical administration.

Methods: Aging female mice exposed to bladder specific carcinogen were treated with the two strains of BCG via three weekly intravesical instillations. Bulk-RNA sequencing was performed on whole bladders collected at 24-hours and 1 week post 1st instillation. Spatial immune profiling using multiplex immunofluorescence was performed on whole bladder sections. Systemic immune profiling was performed using multiplex cytokine profiling and multiparametric flow cytometry on immune cells isolated from bone marrow, blood and spleen.

Results and conclusion: Bulk RNA-sequencing based whole transcriptomic profiling of the bladders post treatment revealed differential activation of immune-related pathways between the two strains. Bladder microenvironment of mice treated with the Moscow strain showed higher T cell infiltration. Further studies are required to evaluate BCG strain-associated differences in the bladder immune microenvironment and clinical outcomes of patients with high-risk NMIBC.

6. Christina Meier (Neuroimmunology) Time-of-day differences in cell composition in a model of chronic pain

Christina M. Meier, Amanda M. Zaccharias, Courtney A. Bannerman, Jaqueline Raymond Silva, Robert Colautti, Qingling Duan, Nader Ghasemlou

Chronic pain is caused by damage to the nervous system. Although highly prevalent, it lacks effective treatment options. Circadian rhythms are roughly 24-hour cycles in biological processes that have been observed in the pain sensitivity of both mice and humans. Understanding why pain follows these rhythms could provide new insights into the development and persistence of chronic pain. The dorsal root ganglia (DRG) and spinal cord (SC) are key structures in the nervous system that contribute to the initiation and maintenance of this pain. Throughout the pain signaling pathway, neurons constantly communicate with immune cells, including microglia, macrophages, and astrocytes, to mediate pain sensitivity. A computational approach called cell deconvolution was used to estimate the proportions of different cell types in heterogeneous samples of DRG and SC tissue in a model of chronic pain (spared nerve injury (SNI)). This study aims to 1) compare cell type compositions in naive and SNI conditions in the DRG and SC, and 2) explore how cell type compositions in the DRG and SC vary across the day-night cycle. Cell type compositions in the DRG and SC differed significantly between naive and SNI conditions ($p < 0.05$). Notable differences were also observed in LDA axes between day and night sample groups. These findings show that further characterization of rhythmicity in the DRG and SC is needed, which may lead to novel therapeutic options for treating chronic pain.

7. Emily Robichaud (Experimental Medicine) Inhibiting Tyrosine Phosphorylation Opens A Non-Selective Cation Channel in Aplysia Neuroendocrine Cells

Ms. Emily M Robichaud (presenting), Dr. Neil S Magoski
Department of Biomedical and Molecular Sciences, Experimental Medicine Field

Alongside the more common serine and threonine phosphorylation, ion channels are also regulated by the state of phosphotyrosine. In the hermaphroditic sea snail, Aplysia californica, the neuroendocrine bag cell neurons trigger egg-laying behaviour through a period of persistent firing, termed the afterdischarge. This persistent firing is driven by the 2nd messenger-dependent gating of nonselective cation channels. Prior immunostaining established that phosphotyrosine is reduced following an afterdischarge, while single-channel recordings confirmed tyrosine dephosphorylation promotes cation channel gating. Thus, we employed whole-cell recording from cultured bag cell neurons to test the effects of tyrosine dephosphorylation on macroscopic current and membrane potential. In standard $Na^+$-based external, with a $Cs^+$-based internal, the tyrosine kinase inhibitors, PP1 (25 μM) and SU6656 (10 μM), evoked inward currents of ~980 pA and ~526 pA, respectively. Both currents were associated with an increase in membrane conductance, linear current between -60 and +40 mV, and presented reversal potentials of ~-30 mV, consistent with the opening of a voltage-independent nonselective cation channel. Moreover, under current-clamp, PP1 triggered an ~40 mV depolarization. Lastly, the PP1-induced current was potentiated by prior exposure to $H_2O_2$, a reactive oxygen species that is increased during the afterdischarge. Therefore, tyrosine dephosphorylation-induced cation channel gating may contribute to the depolarization that maintains the afterdischarge, suggesting a role for phosphotyrosine in persistent firing.

8. Kasthuri Ravishanker (Reproductive and Developmental Sciences) Determining the Role of Cannabinoids in Modulating Neuroinflammatory Pathways in Endometriosis

Kasthuri Ravishanker, Alison McCallion, Dan Vo Hoang, Harshavardhan Lingegowda, Chandrakant Tayade

Department of Biomedical and Molecular Sciences

Objective: Characterize immune cell composition of dorsal root ganglia (DRGs) in endometriosis (EM) and assess cannabinoid treatment effects on the DRG immune microenvironment.

Study Methods: EM was induced in C57BL/6 mice (n=6) and treated with CBD (20 mg/kg) or vehicle, either by intraperitoneal (IP) injection or oral gavage (OG) every 48 hours for 8 doses. Flow cytometry was performed on peritoneal fluid (PF) and spleen cells. Cytokine analysis was conducted on peritoneal fluid. In a separate experiment, total RNA was extracted from thoracic and lumbar DRGs from EM vs. sham-operated mice (n=1), and Nanostring transcriptomic analysis was performed to identify inflammation-related genes. To determine the immune composition of baseline DRGs, flow cytometry was conducted on DRGs isolated from baseline mice.

Results: In mice receiving OG, flow cytometry of PF cells revealed a significant decrease in dendritic cells in the CBD group compared to the vehicle group. Flow cytometry of spleen cells from OG mice, PF cells from IP mice, and spleen cells from IP mice revealed no significant differences between groups. Cytokine analysis showed no significant differences in the 36 cytokines and chemokines assessed between groups. Differential gene expression for immunology-related genes was observed between thoracic and lumbar DRGs. Flow cytometry of baseline DRGs revealed that

30.2% of the CD45+ cell population consisted of CD3+ cells.

Conclusion: Preliminary findings suggest that CBD at a dose of 20 mg/kg did not induce any significant alterations in immune cell populations and modulation of the inflammatory response in EM-induced mice compared to controls. Analyzing gene expression in DRGs from different treatment states may uncover inflammation-related differences in gene expression, thereby enhancing the understanding of cannabinoid effects on EM-associated pain pathways.

Funding Source: CIHR

9. Yunfan Li (Experimental Medicine) Investigating Nutraceutical Caffeine and Nicotine Biased GPCR Receptors Transactivating Glycosylated Receptors on Cancer Cells to Induce Epithelial–Mesenchymal Transition of Metastatic Phenotype

Yunfan Li, Myron R. Szewczuk

Chronic inflammation is a critical driver of tumor initiation, progression, and metastasis. G protein-coupled receptors (GPCRs) are key regulators of inflammation and cancer signaling. Our lab has previously shown that GPCRs form functional heteromeric complexes with neuraminidase-1 (Neu1) and matrix metalloproteinase-9 (MMP9), which transactivate glycosylated growth receptors (RTKs) and TOLL-like receptors and promote NF-κB-mediated epithelial–mesenchymal transition (EMT). This study explores how two widely consumed nutraceutical compounds, caffeine and nicotine, modulate this signaling axis as biased GPCR agonists. We hypothesize that caffeine and nicotine enhance Neu1–MMP9–GPCR–RTK/TLR interactions, selectively activating pro-inflammatory and oncogenic pathways. To test this, we use RAW-Blue macrophages, as well as PANC-1 and MDA-MB-231 cancer cell lines to evaluate Neu1 sialidase activity, caffeine/nicotine GPCRs co-localization with Neu1, NF-κB transcriptional activity using SEAP reporter assays, and EMT marker expression. Our preliminary findings suggest that nicotine potentiates EMT and inflammatory signaling via NF-κB activation, while caffeine exerts distinct or opposing regulatory effects. Understanding how these compounds modulate GPCR-biased signaling provides critical insight into inflammation-related cancer mechanisms and identifies new therapeutic targets. These results may guide the development of safe, accessible treatments that mimic or block the effects of common nutraceutical stimulants to manage chronic inflammation and cancer progression.

10. Abdulrahman Yaish (Cancer Research) From Pain Relief to Metastatic Mayhem: Unraveling the Cryptic Role of Opioids in GPCR-Driven Cancer Metastasis

Abdulrahman M. Yaish, Yunfan Li, Aiden H. Yu, Myron R. Szewczuk

Background: Opioid analgesics are indispensable in oncology, yet growing evidence links μ-opioid receptor (MOR) signalling to metastatic progression. We hypothesize that MOR activation engages a previously tested Neuromedin B receptor (NMBR)-matrix metalloproteinase-9 (MMP-9)-neuraminidase-1 (Neu-1) GPCR signalling axis that remodels tumour-cell glycosylation and initiates epithelial-to-mesenchymal transition (EMT). Objective: To determine whether clinically used μ-opioid agonists bind MOR and heterodimerize with NMBR, altering cancer cell metastatic potential. Methods: Human pancreatic (PANC-1) cancer cells were treated with fentanyl (61-1950 pg/mL). Live-cell sialidase activity was quantified using the fluorogenic substrate 4-MUNANA. MOR-induced cascade activation was tested using known inhibitors of NMBR, MMP-9, and Neu-1 (BIM-23127, MMP-9i, and oseltamivir phosphate (OP), respectively). RAW-Blue macrophage reporter cells will be employed to quantify opioid-driven NF-κB activation via secreted embryonic alkaline phosphatase (SEAP) release. Results: Fentanyl displayed significant increases in sialidase activity compared to an untreated control ($p < 0.05$). Furthermore, BIM-23127, MMP-9i, and OP treatment reduced the fentanyl response, confirming NMBR-MMP-9-Neu1 involvement. No cytotoxicity was observed. Conclusion: These preliminary findings identify rapid Neu1 activation as an early molecular consequence of fentanyl exposure in cancer cells, supporting a novel MOR-NMBR-MMP-9-Neu1 signalling platform. Experiments in progress will link MOR-induced NMBR-MMP-9-Neu1 activation to EMT, migration, and NF-κB activation for further evidence. Ultimately, elucidating this mechanism may guide safer analgesic strategies and reveal new anti-metastatic targets.

11. Yun Shi (Inflammatory Bowel Disease) Fecal supernatant from IBD patients direct activated DRG neurons via PAR-signaling pathway

Hannah M Wood, Amal Abu Omar, Corey C Baker, Taylor A Alward, Alexander R Ziegler, Yun Shi, Rita Nakhle, Josue Jaramillo-Polanco, Cintya Lopez-Lopez, Celine Morisette, Laura E Edgington Mitchell, Stephen J Vanner, Prameet M. Sheth, David E. Reed, Alan E Lomax

Background: Abdominal pain is a hallmark symptom of inflammatory bowel disease (IBD), yet its underlying mechanisms remain poorly understood and effective pain therapies are limited. Proteases activate pain-sensing neurons with cell bodies in the dorsal root ganglia (DRG) via the activation of protease activated receptors (PARs). Proteolytic activity is elevated in stool from IBD patients, leading to our hypothesis stool samples from IBD patients excite DRG neurons via PAR activation.
Methods: Stool samples from IBD patients and healthy volunteers (HV) were processed into fecal supernatants (FS; a sterile, cell-free, aqueous fraction containing luminal mediators). Perforated patch clamp recordings from dissociated mouse DRG neurons were used to assess the effect of these FS on neuronal excitability. A decrease in rheobase is indicative of increased neuronal excitability. Results: Overnight incubation of DRG neurons with IBD patient FS significantly decreased rheobase by 55% ($p < 0.0001$). However, incubation with HV FS did not alter the rheobase. Pharmacological antagonism of PAR2, but not PAR1, inhibited the excitatory effects of IBD patient FS. This was validated using a novel proteomic PAR2 cleavage assay, IBD patient FS showed significantly greater PAR2 cleavage by IBD patient FS compared with HV FS ($p < 0.05$). Conclusion: IBD patient FS increases the excitability of DRG neurons by cleavage of PAR2, highlighting a potential therapeutic target for IBD-associated abdominal pain.

12. Alexandra Wodz (Reproduction and Developmental Sciences) Interleukin-33-Activated Regulatory T Cells in Endometriosis Pathophysiology

Alexandra Wodz, Katherine B. Zutautas, Chandra Tayade

Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

Endometriosis (EM) is a chronic inflammatory disease characterized by ectopic (extra-uterine) growth of endometrial-like tissue, most often on the pelvic peritoneum. Interleukin 33 (IL-33), an alarmin and inducer of the T-helper type 2 (Th2) immune response, is elevated in EM and regulates effector cells expressing ST2, which includes regulatory T cells (Tregs). Tregs maintain self-tolerance and homeostasis. Emerging studies suggest that IL-33 and Tregs play pivotal roles in EM pathophysiology, particularly in modulating inflammation, angiogenesis, and EM lesion progression. However, the precise mechanistic contribution of IL-33-stimulated Tregs to EM remains incompletely characterized. Using our established immunocompetent C57BL/6 mouse model of EM with IL-33 priming or PBS control, we address how IL-33-driven Tregs contribute to EM. Flow cytometric analyses showed elevated Tregs in the spleen, peritoneal fluid (PF), and uterus following IL-33 treatment. Multiplex cytokine analysis of PF revealed elevated IL-4 and IL-5, both players in the Th2 immune response, and elevated VEGF, implicating IL-33 in angiogenesis. In vitro studies using murine splenocytes enriched for CD4+ cells, cultured with or without IL-33, illustrate altered proportions of Tregs, Th1, and Th2 cells upon treatment with IL-33, and multiplex cytokine analysis of culturing supernatant again revealed increased Th2-type cytokines including IL-5, IL-9, and IL-13, and elevated VEGF. Together, our findings suggest that IL-33 may exert an immunoregulatory role on Tregs, indicating their potential role in EM pathophysiology.

13. Montserrat Mora-Ochomogo (Microbiology) D-amino acids contribute to increased antibiotic sheltering by β-lactamase-producing bacteria

Montserrat Mora-Ochomogo*, Kristen Mawdsley, Christopher Lohans

β-lactams are the most widely used antibiotics, but their efficacy is being threatened by β-lactamases, enzymes that inactivate the β-lactams, β-lactamase production can also protect neighboring bacteria, a phenomenon known as antibiotic sheltering, which complicates treatment of polymicrobial infections. Our lab has shown that cell-wall alterations in β-lactamase-producing bacteria influence the extent of sheltering.

Bacteria naturally produce D-amino acids for cell-wall synthesis. Peptidoglycan, the major cell-wall component, is cross-linked by D-alanine, but other D-amino acids such as D-tryptophan (D-Trp) and D-methionine can be incorporated and may disrupt outer-membrane and periplasmic interactions. We hypothesized that such incorporation destabilizes the cell wall and enhances antibiotic sheltering.

To test this, β-lactamase-producing E. coli were grown with various D- or L-amino acids, and β-lactamase activity in culture supernatants was quantified using nitrocefin. Certain D-amino acids increased β-lactamase activity, with D-Trp producing a four-fold rise in nitrocefin hydrolysis compared to L-Trp or no supplement. Western blotting confirmed higher levels of FLAG-tagged

KPC-2 β-lactamase in supernatants of D-Trp-treated cultures, indicating increased enzyme release.

Potential synergy between D-amino acids and β-lactam antibiotics was assessed using checkerboard assays against E. coli and Staphylococcus aureus. Several D-amino acids lowered the minimum inhibitory concentrations of the β-lactams tested.

These findings show that specific D-amino acids destabilize the bacterial cell wall, promoting release of periplasmic β-lactamases and enhancing antibiotic sheltering. Microbial metabolites that alter cell-wall stability may therefore influence interbacterial interactions and hinder effective treatment of bacterial infections.

14. Nasry Zane Bouzeineddine (Immunology) Specific inflammatory stimuli that engage innate immune sensors induce novel CD103 expression profiles in macrophages

Nasry Z. Bouzeineddine, Sebastien Talbot, Sam Basta, Katrina Gee

The integrin CD103 is an adhesion molecule that facilitates immune cell retention in epithelial tissues through its interaction with E-cadherin. It is a marker for certain CD8+ T-cell subpopulations and conventional type 1 dendritic cells (cDC1), but its presence on macrophages remains poorly characterized. Macrophage differentiation is influenced by M-CSF and GM-CSF, and we investigated whether macrophages can also express CD103 under inflammatory conditions. We examined baseline CD103 expression in bone marrow-derived macrophages (BMDMs) differentiated in M-CSF or GM-CSF and then stimulated them with pathogen-associated molecular patterns (PAMPs) or examined them following viral infection. We found that CD103 is minimally expressed at baseline but is selectively upregulated in M-CSF-differentiated macrophages after stimulation with endosomal TLR agonists. Mechanistically, p38 MAPK inhibition prevented CD103 upregulation, suggesting that this process is mediated by p38 MAPK signaling. Furthermore, in vivo LCMV infection induced CD103 expression on peritoneal macrophages. These findings demonstrate that macrophages can express CD103 under specific inflammatory conditions, challenging the assumption that CD103 is restricted to T cells and dendritic cells. This study expands our understanding of CD103 beyond its recognized roles in T cells and DCs, providing new insight into its regulation by macrophages.

15. Holly Mackay (Therapeutics, drug development, and human toxicology) Investigating the effects of the flame retardant triphenyl phosphate on estrogen synthesis in an aquatic in vitro model

Holly Mackay[1], Logan Germain[1], Hanna Huska[1], Lihua Xue[1], Louise Winn[1,2]

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Triphenyl phosphate (TPhP) is an organophosphate flame retardant frequently detected in aquatic ecosystems. Although not classified as acutely toxic, TPhP acts as an endocrine disruptor capable of interfering with estrogen synthesis and signaling. This study examined the effects of TPhP on 17β-estradiol production and aromatase protein expression in STE-137, an embryonic steelhead trout cell line. We hypothesized that 80 μM TPhP exposure would decrease estradiol levels and reduce aromatase expression after 24 hours. Estradiol was quantified using a competitive immunoassay, and aromatase expression was analyzed via flow cytometry. TPhP-treated samples showed a modest reduction in estradiol relative to DMSO controls, though differences were not statistically significant. Biological variability was considerable, potentially reflecting the unknown sex and developmental stage of STE-137 cells and the short exposure duration. Flow cytometry indicated specific but weaker anti-aromatase antibody binding in STE-137 cells compared to mouse lymphatic cells, which may result from lower aromatase expression or reduced antibody affinity to fish isoforms. While no significant effects were detected, these findings underscore key methodological considerations in aquatic cell toxicology. Short exposures may miss delayed protein-level changes mediated by epigenetic mechanisms, and antibody validation against fish targets remains critical. Future work should extend exposure durations and refine detection tools to clarify TPhP's impact on endocrine pathways. This study supports the utility of aquatic cell models for investigating flame retardant toxicity.

16. Julia Barilo (Microbes, Inflammation, and Immunity) Extended IL-4 priming of macrophages induces an antiviral state that restricts Lymphocytic Choriomeningitis Virus replication

Julia Barilo, Andra Banete, Bruce Banfield, and Sam Basta

Macrophages (Mϕ) are innate immune tissue sentinels with a variety of functional phenotypes depending on the cytokine microenvironment. Mϕ exhibit distinct activation patterns across a continuum from pro-inflammatory (M1), associated with the Th1 cytokine IFNγ, to anti-inflammatory (M2a), associated with the Th2 cytokine IL-4. Given the critical role of Mϕ in regulating innate and adaptive immunity, it is not surprising that Mϕ activation status directly influences the outcome of viral infections.
Viruses can exploit inflammation to bypass host barriers and support replication. Viruses such as lymphocytic choriomeningitis virus (LCMV) and Lassa virus directly suppress Mϕ activation leading to viral chronicity and severe disease. While the role of M1 Mϕ in viral infections has been defined, the mechanism behind the altered response of M2 Mϕ to virus infections is unknown.
Here, we investigate the response of activated spleen-derived Mϕ (SpM) to LCMV infection to understand how polarization influences the initiation of an immune response. Following infection, polarized Mϕ show an altered resistance to LCMV infection. Protein expression and localization of innate recognition molecules and transcription factors involved in the RLR pathway, including RIG-I, MAVS, STING, and IRFs were evaluated in activated Mϕ, which play a crucial role in the control of LCMV replication and optimal CD8+ T cell priming. Furthermore, MAVS expression on peroxisomes and mitochondria was evaluated. We show for the first time that the altered resistance M1 and M2 Mϕ occurs through distinct mechanisms.

17. Melissa Sadallah (Neuroimmunology) The timing of nerve injury shapes neutrophil responses and pain hypersensitivity

Melissa Sadallah, Anaïs Roger, Ciara O'Conor, Nader Ghasemlou

Neuropathic pain results from injury or disease affecting the somatosensory nervous system. It is characterized by chronic neuroinflammation and manifests as burning sensations, electric shocks, or needles. Pain perception fluctuates throughout the day, and typically diminishes during the active phase. These variations are linked to immune cell activity, which is tightly regulated by circadian rhythms. Neutrophils are among the immune cells displaying rhythmic behavior. They circulate in the bloodstream during the resting phase and infiltrate injured tissues during the active phase. Beyond their role in pathogen clearance, they are essential for resolving inflammation and repairing tissue. However, how their circadian regulation influences the onset and progression of neuropathic pain remains poorly understood.
Because nerve injuries in real life occur unpredictably, it is crucial to investigate how injury timing affects neutrophil migration, neuroimmune interactions, and neuronal excitability. Given that neutrophil behavior and pain perception are governed by circadian rhythms, we hypothesize that the nerve injury timing influences neutrophil-induced inflammation and sensory neuron activation, thereby affecting the severity and progression of neuropathic pain.
Globally, 10–20% of people experience chronic pain, with 7–10% suffering specifically from neuropathic pain. This project seeks to identify how the circadian timing of nerve injury influences immune and neuronal responses, aiming to inform new chronobiology-based strategies for the prevention and management of neuropathic pain and ultimately improve patient quality of life.

18. Hayley Albert (Physiology) Frequency of firing modulates synaptic facilitation in electrically coupled bag cell neurons.

Hayley Albert & Dr Neil Magoski

Gap junctions are intercellular channels that pass ions from pre- to postsynaptic neurons at electrical synapses. In the marine snail, Aplysia californica, reproductive behaviour is controlled by a group of electrically coupled neuroendocrine cells called bag cell neurons. Following a brief cholinergic input, bag cell neurons undergo an ~30-min afterdischarge of synchronous action potential firing. While the overall frequency of the afterdischarge is ~1 Hz, the actual firing pattern is often quite variable. The present study examined the impact of potential differences in spike timing on electrical transmission. Using dual whole-cell recording from pairs of electrically coupled bag cell neurons in culture, a 1-Hz, 10-sec stimulation with regular vs irregular patterning was delivered presynaptically to evoke postsynaptic electrotonic potentials. In agreement with our previous work (J Neurophysiol 130:69-85; 2023), the electrotonic potential underwent use-dependent facilitation. Moreover, the regular input consistently produced significantly larger responses as the stimulus progressed, whereas those evoked by the irregular input were only occasionally different from baseline. Facilitation arises from a progressive increase in postsynaptic input resistance, due to use-dependent run-down of voltage-gated potassium current. Thus, it is likely that the more even timing provided by the regular input leads to greater incremental run-down and thus facilitation. These outcomes highlight the role of spike timing in ensuring maximal signalling efficiency at electrical synapses.

19. Sylvia Shi (Therapeutics, Human Toxicology, and Drug Development) Single-Nucleus Transcriptomic Profiling of Wild-Type and APP/PS1 Alzheimer Mouse Hippocampus

Sylvia Shi, Natalia Lyra E Silva, Thyago Leal Calvo, Gary Bader, Fernanda De Felice
Department of Biomedical and Molecular Sciences, Centre for Neurosciences Studies

Alzheimer's disease (AD) is marked by early hippocampal vulnerability. While the APP/PS1 (APPswe/PSEN1dE9) mouse is a widely used transgenic model, the transcriptomic heterogeneity of its hippocampus remains underexplored. In this pilot study, we optimized a single-nucleus RNA-sequencing (snRNA-seq) workflow on hippocampi from APP/PS1 and WT mice, covering nuclei isolation, library preparation, and downstream analysis. Integration of 1 APP/PS1 and 1 WT hippocampus identified 11 cell populations: 7 excitatory and 2 inhibitory neurons, astrocytes, and oligodendrocytes. Gene set enrichment analysis of upregulated differentially expressed genes suggested that excitatory neurons engage pathways related to oxidative phosphorylation, energy metabolism, and calcium/ion homeostasis, which may reflect a compensatory mitochondrial response to ionic stress induced by amyloid-β pathology. Inhibitory neurons indicated mitochondrial activation and altered lipid/endocannabinoid signaling, potentially disrupting excitation–inhibition balance. We also observed enrichment of amyloid-β and synaptic function pathways, consistent with known AD hallmarks. These findings support the feasibility of using hippocampal snRNA-seq to resolve cell-type–specific transcriptional adaptations in APP/PS1 mice. We will next expand biological replicates to recover microglia, refine pathway-level insights, and investigate cell–cell communication central to AD progression.

Funded by CIHR

20. Megan Cull (Therapeutics, Drug Development, and Human Toxicology) Disrupted Placental Development Following In Utero Benzene Exposure in a Mouse Model

Megan E. Cull, Lauren T. L. Brown, Joy Cheng, Emma Purdy, Perri M. Grant, Lihua Xue, Louise M. Winn

Introduction: Benzene is a widespread environmental contaminant and carcinogen capable of crossing the placenta. In a previous mouse study, we identified that prenatal benzene exposure increased tumour incidence in offspring and altered placental growth, increasing placental weight, with females exhibiting greater placental efficiency than males. Here, we further investigated benzene-induced placental toxicity by evaluating placental morphology.
Methods: Timed-pregnant CD-1 mice received corn oil (control) or 200 mg/kg benzene via intraperitoneal injection on gestational days (GD) 8–14 and were euthanized on GD19. Placentas were collected from consistent intrauterine positions, sexed, fixed, paraffin-embedded, and H&E stained. Using HALO image analysis software, we quantified total placental area, labyrinth area, labyrinth-to-placenta proportion, and placental diameter. Data were analyzed using non-parametric tests in GraphPad Prism.
Results: While no statistically significant differences were observed between exposure groups or sexes (N=24 placentas/group), benzene exposure substantially increased variability across all

metrics. Compared with controls, standard deviation increased 2.25-fold (total area), 1.56-fold (labyrinth area), 2.61-fold (labyrinth proportion), and 3.00-fold (diameter). Female placentas exhibited 166–296% greater variability across all parameters, whereas males showed increased variability only for total area and labyrinth proportion.
Conclusions: These findings suggest that prenatal benzene exposure disrupts placental developmental stability, increasing morphological variability that may have implications for fetal growth and disease susceptibility. Ongoing work will expand the cohort and assess additional placental layers to validate and refine these results.

21. Elijah J Rajsky (Neuronal excitability and secretion, ion channel modulation) Mitochondrial Ca2+ and H2O2 Interact to Control Nonselective Cation Channel Activity in Neuroendocrine Cells

Elijah J Rajsky, Neil S Magoski

The release of intracellular $Ca^{2+}$ can alter neuronal activity by opening ion channels at the plasma membrane. For example, in neuroendocrine bag cell neurons, which control reproduction in the sea snail, Aplysia, collapsing the mitochondrial membrane potential with the protonophore, carbonyl cyanide-4-trifluoromethoxyphenyl-hydrazone (FCCP), releasing $Ca^{2+}$, causes depolarization and action potential firing. Previously, our lab found that FCCP gates a nonselective cation channel, which is sensitive to both buffering of intracellular $Ca^{2+}$ and blocking mitochondrial $Ca^{2+}$ leak. Additionally, hydrogen peroxide ($H_2O_2$), which is produced in these neurons by NADPH oxidase, was shown to trigger a separate nonselective cation channel. Given that the loss of the mitochondrial proton gradient following FCCP can drive a compensatory production of reactive oxygen species, including $H_2O_2$, we examined the potential interaction between these two pathways. Using cultured bag cell neurons and whole-cell recording, the membrane current evoked by FCCP was suppressed upon prior $H_2O_2$ exposure. Conversely, delivering FCCP in advance boosted the $H_2O_2$-induced current, and this was attenuated by buffering intracellular $Ca^{2+}$ with EGTA, suggesting $Ca^{2+}$ dependence. Moreover, the $H_2O_2$-induced current was reduced by the mitochondria-targeted antioxidant, MitoTEMPO. These data indicate that, in conjunction with mitochondrial $Ca^{2+}$, $H_2O_2$ may engage mitochondrial redox to control membrane channels. For Aplysia, neuroendocrine cell activity and the resulting secretion of reproductive hormone, may be influenced by the interaction between reactive oxygen species and mitochondrial $Ca^{2+}$.

22. Lucas Jaryd Iringan Te (Chronic Pain) Developing an Evidence-Based Treatment Pathway for Fibromyalgia: A Systematic Review

Lucas Jaryd Iringan Te; Prisha Adya; Alyssa Labrie; Katie Root-Clarke; Doriana Taccardi; Nader Ghasemlou; Tracy Cupido

Objective: This review aims to evaluate the effectiveness of a comprehensive multimodal treatment pathway for fibromyalgia, integrating pharmacological, physical, nutritional, and psychological interventions.

Methods: A systematic review of literature published since 2019 was conducted across MEDLINE, EMBASE, and Web of Science. Eligible studies included systematic reviews and meta-analyses addressing fibromyalgia interventions. Data were synthesized into five therapeutic pillars: exercise, diet, education/psychotherapy, pharmacology, and complementary modalities.

Results: Exercise and education/psychotherapy consistently improved pain severity, physical function, and quality of life. Dietary interventions showed potential benefits, particularly plant-based diets. Pharmacological agents such as duloxetine, pregabalin, and low-dose naltrexone demonstrated modest efficacy. Complementary therapies showed promise but lacked consistent evidence.

Conclusion: The most effective approach to improve outcomes in fibromyalgia consists of a multimodal treatment pathway emphasizing non-pharmacological interventions as first-line therapies, supplemented by pharmacological and complementary options. Implementation in primary care settings is feasible and warrants further validation.

23. Colin Galarneau (Clinical research/neonatology) Respiratory Support as a Determinant of Oral Feeding Outcomes in Preterm Infants

Colin Galarneau, Amir Ranjbar, Sandra Fucile.

Background: Oral feeding requires coordination of sucking, swallowing, and breathing, dependent on respiratory stability. Evidence is limited on how respiratory status affects feeding outcomes in preterm infants.

Objective: Examine how respiratory support affects attainment of independent oral feeding in preterm infants.

Method: Fifteen infants born at <34 weeks' gestation without congenital anomalies, genetic syndromes, or metabolic disorders were enrolled from the NICU at KHSC. Measures were recorded during the first five minutes of an oral feed with a nipple device containing a pressure transducer. Outcomes: respiratory support, CPAP duration, time to full feeds, suction amplitude, suck-burst and pause duration, and suck count.

Analysis: The multiple linear regression model with sucking measures and infant baseline factors (gestational age and days on assisted respiration) as covariates was performed. Variables demonstrating significance in initial simple linear regression analysis ($p<.07$) were entered into the model.

Results: The number of days on CPAP significantly predicted time to full oral feeding ($B=.354$, $p=0.001$) and pause duration ($B=1.20$, $p=0.044$). Longer CPAP exposure trended toward shorter suck-bursts and smaller amplitudes, though nonsignificant.

Conclusion: Prolonged CPAP affects sucking–swallowing–breathing coordination and delays independent oral feeding. Longer CPAP exposure was linked to extended pauses, suggesting greater respiratory recovery needs. Awareness of these effects may guide earlier, targeted feeding interventions to improve outcomes in preterm infants.

24. Aidan Sander (Diagnostic Radiology) Analysis of Revision Patterns in Resident Radiologist Imaging Reports Using ChatGPT

Aidan C. Sander, Andrew David Chung, Benjamin Y.M. Kwan

Purpose: Quality feedback plays a key role in improving resident radiology reporting skills. Providing detailed narrative feedback on revisions made to draft reports is not always feasible for busy faculty. We assess ChatGPT-4o's ability to identify and provide feedback on revisions between resident draft and faculty-reviewed final imaging reports.
Methods: Three radiology residents submitted five draft and final imaging reports (three CT, two MRI). ChatGPT-4o analyzed these reports using standardized queries focusing on similarities, diagnostic confidence, and organization. Qualitative thematic analysis evaluated ChatGPT's feedback.
Results: ChatGPT-4o highlighted key improvements in the areas of definitive language use, detailed anatomical descriptions, and accuracy of feature measurements. It also identified strengths including report structure and organization, professional tone, correct terminology use, and consistency in diagnostic conclusions.
Conclusion: ChatGPT-4o effectively generated meaningful and actionable feedback on the differences between resident draft and final imaging reports. This pilot study showcases ChatGPT-4o's potential to improve traditional educational workflows by identifying and providing feedback on revision patterns, some of which may otherwise go unnoticed by residents and attendings. By clearly explaining the nature of revisions, this feedback may help learners become more aware of their specific strengths and weaknesses. Future research should explore how trainees and educators can effectively incorporate AI-generated feedback into daily practice and evaluate the integration of these tools within residency programs.

25. Aikam Rai (Epilepsy and Translational Medicine) Arterial Spin Labelling to Lateralize and Localize the Epileptogenic Zone in Presurgical Evaluation: A Scoping Review

Aikam Rai, Gavin Winston

Rationale
Epilepsy is a common neurological condition initially treated with anti-seizure medications. However, these fail in 30% of patients. Focal epilepsy may be amenable to surgical treatment, which requires lateralization and localization of the epileptogenic zone. Arterial spin labelling (ASL) is a non-invasive perfusion magnetic resonance imaging (MRI) technique that may help. This review addresses the role of ASL in the presurgical evaluation of epilepsy.

Methods

The literature search followed PRISMA guidelines using relevant search terms combining epilepsy, localization/surgery, and ASL. Articles published before December 31, 2024, were retrieved from MEDLINE and Embase databases.

Results
42 articles were included and after synthesis, there were four key conclusions: (1) ASL is effective in detecting abnormal cerebral blood flow (CBF) but may show hypo- or hyperperfusion depending on the epileptogenic lesion (2) ASL offers concordant/similar laterality results to other neuroimaging techniques (e.g. EEG, PET, etc.), (3) ASL demonstrates potential for improvement through various methods (e.g. voxel-wise analysis), and (4) ASL can enhance/complement other techniques (e.g. PET, EEG, etc.), by increasing detection of epileptogenic lesions.

Conclusions
ASL demonstrates potential utility as a diagnostic tool in presurgical assessments. However, further studies with larger sample sizes, more MRI negative cases, and a focus on how CBF varies depending on the type of epileptogenic lesion would help validate the use of ASL in broader populations.

Funding: This literature review was supported by Canadian Institutes for Health Research (CIHR) and the Southeastern Ontario Academic Medical Organization (SEAMO) Innovation Fund.

26. Orlin Chowdhury (Palliative Care) Pharmacological Interventions for Anxiety and Depression in Terminal Illness: A Scoping Review of Randomized Controlled Trials

Orlin Chowdhury, BHSc(c); Kristen Kyone, BHSc; Jean Mathews, MBBS, MD

Introduction: Anxiety and depression are highly prevalent among patients with terminal illnesses, contributing to poor quality of life. Clinicians caring for patients with chronic and progressive illnesses need to know how to effectively manage these symptoms at the terminal stage. The objective of this scoping review was to synthesize data on randomized controlled trials (RCTs) of pharmacological interventions for anxiety and depression in terminal illnesses and to identify gaps in the evidence base.

Methods: MEDLINE, Embase, and CENTRAL databases were searched from inception to September 2024. Two reviewers independently extracted data on study design, patient population, pharmacological interventions, and outcomes.

Results: Thirteen RCTs involving 621 participants (average study sample size 48; mean age 57; 58% female) were included. Most trials were conducted in ambulatory settings in high-income countries. Eight studies included patients with advanced cancer, two each of end-stage renal disease and advanced HIV, and one of severe COPD. The most studied drug classes were Selective Serotonin Reuptake Inhibitors and Psychostimulants (5 of each). Overall, 10 of 13 studies reported statistically significant improvement in depression, anxiety, or quality of life.

Conclusion: Pharmacological interventions improved depression and anxiety in terminal illness, though most studies were small and cancer focused. Larger RCTs in non-cancer populations, particularly in advanced heart disease, cerebrovascular disease, and dementia, which represent leading causes of morbidity and mortality globally, are needed.

27. Victoria Mallett (Microbiology and Infectious Diseases) Probiotic Therapies for Salmonella Infections: A Review of In Vitro and In Vivo Evidence to Guide Future Interventions

Victoria Mallett, Dylan Graff, Shu Mei He, Prameet M. Sheth

Salmonella is one of the leading causes of bacterial foodborne illness, responsible for over 95 million infections annually, contributing to significant global healthcare costs and economic losses. Although most Salmonella infections are self-limiting, severe infections can lead to systemic illness and require antibiotic treatment to reduce mortality. However, antibiotics present several limitations in their effectiveness against Salmonella. They do not shorten the duration of clinical illness, they prolong bacterial shedding, and contribute to the emergence of antibiotic-resistant Salmonella. These shortcomings highlight the urgent need for non-antibiotic-based therapeutics for Salmonella. Probiotics offer a promising alternative by improving gut health, modulating the immune response, and competing against pathogens. This review evaluates the current evidence on the efficacy of various probiotic interventions against Salmonella, from both in vitro and in vivo studies. In vitro research demonstrates that probiotics can effectively target key steps in Salmonella pathogenesis, reducing adhesion, invasion, and growth. In vivo studies show that probiotics modulate inflammatory and immune responses, improve systemic outcomes, and maintain the health of the gastrointestinal tract. By synthesizing these findings, this review highlights the diverse mechanisms through which probiotics may offer therapeutic potential in Salmonella infections. It also lays a foundation for advancing basic research into clinical application, aimed at reducing the reliance on antibiotics, limiting the spread of resistance, and improving health outcomes for millions affected by Salmonella.

28. Alisa Quinton (Hemophilia and bleeding disorders) Addressing knowledge gaps around hemophilia-related testing for young girls through the development of an evidence-based infographic

Alisa Quinton1, Megan Chaigneau1, Julie Grabell1, Mackenzie Bowman1, Natalie Philbert, Lisa Thibeault, Laura Wheaton2, Jennifer Leung1, David Good3, David Lillicrap3, Paula James1 1Deparment of Medicine, Queen's University, Kngston, ON, 2Department of Pediatrics, Queen's University, Kingston, ON, 3Department of Pathology and Molecular Medicine, Queen's University, Kingston, ON

Introduction: The misconception that female hemophilia carriers do not experience abnormal bleeding symptoms creates barriers to accessing proper testing, resulting in underdiagnosis and suboptimal care. Prior research highlights a lack of consensus in Canada regarding optimal timing of factor level and genetic testing for carriers. Families impacted by hemophilia have identified a need for consistent testing recommendations and additional education to ensure adequate screening.

Aim: Project aim was to address the knowledge gaps around hemophilia-related testing by developing an evidence-based infographic to support healthcare professionals and advocacy organizations in educating families about early childhood carrier testing for girls who may be impacted by hemophilia.

Methods: Content for the infographic was developed based on a literature review and previously published work by our research group. A review process was conducted with key stakeholders, including physicians, nursing, lab experts, a patient-advocacy organization (Hemophilia Ontario), and patient/family representatives to ensure medical accuracy, clarity, and relevance.

Results: The final infographic tool communicates key information about female hemophilia carrier status, benefits of early testing, implications for procedural and menstruation management, and provides links to further resources and FAQs.

Conclusions: Early childhood testing in girls potentially affected by hemophilia can inform bleeding management and reduce complications. This infographic is a practical tool to support informed decision-making and improve outcomes for girls affected by hemophilia.

29. Tarrah Ethier (Translational Medicine) Estrogen Withdrawal Promotes Interleukin-15-dependent Fibrosis and Failure in the Female Right Ventricle

Tarrah S. Ethier, L. Rhiannon Hilton, Declan J. Gainer, Kimberly J. Laverty, Woo-Yong Lee, Paul Kubes, Stephen Renaud, Michael Soares, Mark L. Ormiston

BACKGROUND: Diseases of right ventricular (RV) failure disproportionately impact women. Although estrogen typically protects the female heart from maladaptive RV remodelling in response to loading, this protection is lost after menopause, leaving the female RV uniquely susceptible to failure.
RESULTS: Using ovariectomy as a model of estrogen withdrawal in menopause, we have discovered that natural killer (NK) cell-deficient interleukin (IL)-15 knockout (Il15-/-) rats are protected from ovariectomy-induced RV fibrosis and failure in two models of RV loading – the monocrotaline model of pulmonary arterial hypertension and the pulmonary artery banding (PAB) model of isolated RV pressure overload. In IL-15 wildtype (Il15+/+) females subjected to PAB and ovariectomy, RV fibrosis was linked to an influx of NK cells into the banded RV, an accumulation of unfolded collagen fragments, and the increased expression of genes linked to TGF-β signalling, collagen deposition and matrix degradation by RV cardiac fibroblasts. Single nuclear RNA-sequencing of RVs from rats subjected to the PAB model also identified a differential induction of inflammatory gene expression in RV macrophages from Il15-/- females following PAB and ovariectomy, when compared to cells from Il15+/+ littermates.
CONCLUSION: Together, these findings point to NK-macrophage interactions as a potential driver

of the Il15-dependent progression to maladaptive ventricular remodelling in Il15+/+ females, providing critical new insights into this significant and understudied issue for women's health.

30. Hertek Gill (Medical Education) Behind the Beard: A Qualitative Study on the Experiences of Medical Learners with Religious Beards Navigating N95 Requirements

Hertek Gill, Angel Gao, Lauren Wamboldt, Jaskarn Dhaliwal, Adna Moalin, Eleftheria Laios, Dr. Wiley Chung

Background: N95 masks are critical for protecting healthcare workers from airborne particles. However, any amount of facial hair can interfere with the proper seal of these masks and decrease efficacy. This creates challenges for medical trainees with religious beards, who are often unable to don N95 masks.
Methods: Medical trainees with religious beards were recruited from medical undergraduate and postgraduate programs across Canada. Semi-structured virtual interviews explored their experiences with accommodations processes and the impact on medical training and career decisions. Interviews were recorded, transcribed and coded using NVivo. Thematic analysis is currently ongoing in an iterative approach.
Results: Preliminary findings reveal that participants commonly experience feelings of frustration and isolation. Many reported inconsistent policies and accommodations across institutions and described how N95-related limitations negatively influenced clinical exposure and specialty choice. Trainees expressed concern over being forced to choose between religious identity and career aspirations. Respondents reported overwhelming support from their peers and instructors in helping navigate unclear protocols. Participants expressed hope for future changes to streamline and consolidate the process for receiving accommodations.
Discussion: This study is the first national exploration of challenges related to religious beards in medical education. Findings highlight the need for standardized, equitable accommodation policies that respect religious practices while ensuring safety. Such policies are essential to promoting inclusivity and equal access to training opportunities for all medical learners.

31. Kawami Cao (Perioperative Management) Intraoperative tissue oxygen saturation as a predictor of post-operative complications in DIEP breast reconstruction

Kawami Cao, Anthony M-H. Ho, Rachel Phelan, Wilma M. Hopman, Jessica Shelley, Elorm Vowotor, Deborah DuMerton, Jessica Xiong, Bethany Smethurst, Michael McMullen, Glykeria Martou, Robert W. Edmunds, Robert Tanzola, Glenio B. Mizubuti

Introduction: The deep inferior epigastric perforator (DIEP) flap procedure is the gold standard technique for breast reconstruction, yet rates for postoperative complications may be as high as 30%. Traditional clinical monitoring for flap surveillance often cannot detect early vascular compromise. Near-infrared spectroscopy (NIRS) enables non-invasive/real-time assessments of tissue oxygen saturation (StO2). We examined the association between intraoperative breast StO2 and postoperative complications following DIEP reconstruction.

Methods: This is a secondary analysis of a randomized controlled trial that evaluated the impact of cardiac output-guided fluid administration and low-dose dobutamine on breast StO2 during DIEP reconstruction. Participants were categorized by breast StO2 45 minutes after arterial clamp removal, as <80% (low) or ≥80% (normal).

Results: The analysis included 38 participants; 24 vs 14 had intraoperative breast StO2s of <80% and ≥80%. Surgical site infections were higher 30 days postoperatively in the low vs normal saturation group (7[29.2%] vs none, P=0.033). There was a trend towards higher overall complications in the low vs normal saturation group at the 30-day follow-up but was not statistically significant (11[45.8%] vs 2[14.3%], P=0.077).

Conclusion: Participants with StO2 <80% experienced higher rates of surgical site infections within the 30-day postoperative period, demonstrating the potential utility of NIRS as a predictive tool for perioperative optimization of graft StO2 and/or prophylactic antibiotic administration to prevent infection, which in severe cases may lead to flap failure.

Supported by the Stuart Vandewater Endowed Studentship

32. Simryn Atwal (Dermatology) Perianal Streptococci Infections and Psoriasis in Adults: A Chart Review

Simryn Atwal, Yuka Asai, MD; Brie Fraser; Chao Xue

Background:
Psoriasis is a chronic inflammatory skin condition affecting over 125 million people worldwide. Subtypes such as guttate and inverse psoriasis have been linked to streptococcal infections, but most research has focused on pediatric populations. Differentiating psoriasis from perianal streptococcal infections in adults is challenging due to overlapping clinical features, and the relationship remains poorly defined.

Objective:
This study aims to characterize the clinical presentation, microbiological profiles, treatment, and outcomes of adult patients with concurrent perianal psoriasis and streptococcal infections.

Methods:
A retrospective chart review will be conducted at Kingston Health Sciences Centre, including adult patients diagnosed with psoriasis and swabbed for perianal streptococci between 2020 and 2024. Data collected will include demographics, comorbidities, clinical presentation, treatment course, recurrence, and streptococcal strain identification. Descriptive statistics will be applied, with further analysis depending on sample size.

Anticipated Results:
We expect to identify patterns in streptococcal strain prevalence, recurrence, and treatment

responses in adults with perianal psoriasis. Findings may clarify clinical overlap between psoriasis and streptococcal infections and highlight implications for diagnosis and management.

Conclusion:
This study will provide much-needed insights into an underreported area of dermatology and infectious disease. Data collection is pending, and the study is currently in the process of obtaining Research Ethics Board (REB) approval.

33. Arshdeep Raul (Cardiology) ECG of Myocardial Infarction with Non-Obstructive Coronary Arteries) ECG Manifestation of Myocardial Infarction with Non-Obstructive Coronary Arteries (MINOCA)

Arshdeep Raul, Shyla Gupta, Annie Hung, Hasan Alturki, Amin Meghdadi, Sebastian Garcia-Zamora, Sanoj Chacko, Martha Gulati, Adrian Baranchuk

Myocardial infarction with non-obstructive coronary arteries (MINOCA) represents a unique subset of acute coronary syndromes where significant coronary artery obstruction is absent. Despite its clinical relevance, the role of the electrocardiogram (ECG) in the diagnosis of MINOCA remains underexplored, with no specific guidelines established. This review examines the current literature to elucidate potential diagnostic markers and guide clinical management. A non-systematic review was conducted using the PubMed database, focusing on literature from 2015 onwards, involving studies that analyze the ECGs of patients with MINOCA. The results revealed that ST-segment elevations are observed in 5-10.5% of MINOCA cases and studies performed on women found ST-segment depression in 15% of cases, T-wave inversions in 45% of cases, prolonged QTc intervals in 28% of cases and 35% present with a normal initial ECG. Recognizing these diverse ECG presentations of MINOCA is crucial for tailoring management strategies to the underlying pathology, thereby minimizing both over-treatment and under-treatment. This review highlights the significance of conducting additional research to develop clear ECG guidelines tailored specifically for MINOCA.

34. Eshal Ali and Shanzey Ali (Medical Education and Health Equity) Health Advocacy Curricula for Emergency Medicine Residents: Enhancing CanMEDS Competency and Social Accountability

Ali, E., Ali, S., Walker, M., Brennan, E., Colmers-Gray, IN.

Background:
Emergency departments often serve as safety nets for patients facing barriers to primary and preventative care, many from equity-deserving groups. Accordingly, emergency physicians must act as health advocates to provide adequate care to these patients. To address calls for stronger advocacy training in medical education, our team developed a longitudinal health advocacy curriculum for emergency medicine (EM) program at Queen's University, incorporating asynchronous modules, small-group case discussions, community organization site visits, and reflective writing. Here we present the curricular evaluation.

Methods:
We used a qualitative approach, analyzing narrative reflections from EM residents at multiple points during the year and reviewing post-curriculum feedback. Evaluation followed the Kirkpatrick framework, examining participation, learning, and behaviour change.

Results:
Four themes emerged: impact on self, patient, community, and factors affecting learning. Residents reported greater understanding of advocacy, social determinants of health, and barriers to care. They gained confidence in advocacy roles, employing harm-reduction practices, and addressing root causes. Residents also developed awareness of community services, fostering stronger relationships with local organizations. Patient stories and community engagement enhanced learning, while coordinating schedule posed challenges.

Conclusions:
Our EM health advocacy curriculum can strengthen advocacy competencies and support positive outcomes for residents, patients, and communities, offering a model for residency programs across Canada.

35. Aiden H. Yu (Cancer Microbiology/Oncology) Testosterone-GPCR-NMBR Signalling Cascade as a Driver of EMT in Colorectal, Breast, and Pancreatic Cancer

Aiden H. Yu, Abdulrahman M.W. Yaish, Izzah Wahab, Yunfan Li, Myron R. Szewczuk

The majority of colorectal, breast, and pancreatic cancer deaths are due to cancer metastasis. Emerging evidence suggests that through a Neu-1 signalling pathway, testosterone may play a role in this metastasis. Particularly, testosterone can engage with plasma membrane GPCRs that heterodimerize with neuromedin-B receptor (NMBR), activating matrix metalloproteinase-9 (MMP-9), which then unmasks Neu-1 sialidase by cleaving its elastin binding protein (EBP), eventually resulting in NF-κB translocation and promoting epithelial-to-mesenchymal transition (EMT). We investigated this pathway by treating SW620 colorectal, MCF7/MB231 breast, and PANC-1 pancreatic cancer cell lines with testosterone at varying concentrations, alone or with inhibitors of each pathway component. We quantified Neu-1 activity using the fluorescent sialidase substrate, 4-MUNANA. The results showed that there was a significant increase in Neu-1 activity across cell lines when treated with testosterone, whereas cotreatment with inhibitors suppressed this effect. These findings define a novel Neu-1 signalling axis through which testosterone enhances metastatic potential in colorectal, breast, and pancreatic cancers. The suppressive effects of inhibitors highlight therapeutic potentials to block hormone-driven metastasis, while Neu-1 activity could serve as a functional biomarker of metastatic risk.

36. Julia Apolot, Dream Tuitt-Barnes, Heeya Patel, Alisha Higgs, Oluwamisimi Oluwole (Global Oncology) Barriers to Access: Exploring Treatment Challenges Faced By Pediatric Cancer Patients In Uganda

Dream Tuitt-Barnes, Oreoluwapo Maxwell, Ali Haider, Alisha Higgs, Fatima Mohammed, Heeya Patel, Mujeedat Lekuti, Munmeet Paur, Oluwamisimi Oluwole, Rinusha Piranthapan, & Rida Siddiqui

In 2018, the WHO established the Global Initiative for Childhood Cancer, a project advocating for a worldwide pediatric cancer (PC) survival rate above 60 percent by 2030. Many Sub-Saharan African countries, including Uganda, are projected to fall short of this goal. Despite free cancer care, Uganda has a PC mortality rate of 70% compared to 20% in North America. This review explores factors contributing to Uganda's PC survival disparities and suggests practical interventions to improve outcomes.

A 12-member team from Queen's Cancer Kids First searched databases like PubMed, ScienceDirect, and Google Scholar for English-only articles published after 2014 discussing PC care in Uganda. Twenty-five sources were selected, including two non-scholarly articles from The Monitor, a trusted Ugandan newspaper, to provide national insight.

Uganda's high PC mortality is linked to institutional, national, and patient-level barriers. Institutional barriers include limited access to diagnostic facilities, medications, and oncologists. National barriers include the geographic concentration of healthcare services in Kampala and high treatment costs. Patient-level barriers include financial constraints, transportation challenges, and cultural stigma.

Addressing barriers is crucial to survival. Recommendations include using telemedicine to expand diagnostic infrastructure, patient travel support, and stigma reduction. International partnerships can increase medication access and professional training. Cost-effective virtual telementoring may empower rural hospitals to screen for cancers earlier, improving survival.

38. Seerat Waraich (Pediatrics) Adverse Childhood Experiences and Weight Loss in Overweight and Obese Children in a 9-Year Study: A Prospective Cohort Study with Structural Equation Modeling

Seerat Waraich, Hannah Steiman De Visser, Brenden Dufault, Jonathan McGavock

Background: Adverse childhood experiences (ACEs) increase obesity risk in adolescence by 30–50%. Their role in weight loss among overweight/obese children remains unclear.

Methods: Among 8,568 nine-year-olds in the Growing Up in Ireland cohort (2007/2008), 2,210 were overweight/obese and had complete follow-up data at ages 13 and 18. Structural equation and natural effects mediation models examined direct and indirect associations between ACEs before age 9 and achieving healthy weight by 18. Mediators included activity, diet quality, self-image, behavioural difficulties, and BMI at 9.

Results: Of 1,676 adolescents overweight/obese at age 9, 46% reached healthy weight by 18 (56% overweight; 27% obese). 13% had experienced an ACE; 41% were female. ACE exposure was associated with higher BMI Z-scores at ages 9 (0.47 vs 0.36, $p<0.05$) and 13 (0.39 vs 0.29, $p<0.05$), and with 27% lower odds of remission at 18 (OR: 0.73, 95% CI: 0.54–0.99). Exposed children had lower household income, greater behavioural difficulties, and reduced self-concept across all ages. They were 2–3 times more likely to start smoking before 12 and 50% more likely to smoke heavily or vape. Behavioural difficulties, self-concept, and baseline weight, but not smoking or diet, mediated this association.

Conclusion: ACEs reduce the likelihood of achieving healthy weight among overweight/obese children through impacts on early weight, behavioural difficulties, and self-concept. Addressing these mediators may improve long-term weight outcomes.

39. Simran Saxena (Fibrosis) Comparative Effects of PDGF-B and TGF-β on Collagen and YAP/TAZ-Dependent Gene Expression

Simran Saxena (presenting), Aditya Mandapati, Luisa Ulloa Severino, Dr. Darren Yuen

Fibrosis is characterized by excessive extracellular matrix deposition, ultimately leading to tissue scarring and organ dysfunction. Platelet-derived growth factor-B (PDGF-B) and transforming growth factor-β (TGF-β) are two central profibrotic mediators that converge on shared downstream effectors, including Rho, Akt, and MAPK. While TGF-β has long been regarded as the master regulator of fibrosis, the specific role of PDGF-B in modulating fibrotic signaling remains less clearly defined. This study compared the effects of PDGF-B and TGF-β on classical fibrosis markers (COL1A1, COL3A1, COL4A1, ACTA2) and YAP/TAZ-inducible genes (ANKRD1, CTGF, CYR61, PAI1) in NRK49F fibroblasts. Cells were treated with TGF-β, PDGF-B, or vehicle control, and gene expression was assessed by RT-qPCR. Both growth factors induced fibrotic gene expression but with distinct profiles. TGF-β strongly upregulated COL1A1 (~2.8-fold) and PAI1, while PDGF-B induced a moderate COL1A1 response (~1.7-fold) and downregulated PAI1. COL4A1 was increased by both, but PDGF-B uniquely suppressed COL3A1. In YAP/TAZ signaling, PDGF-B more strongly induced ANKRD1 and TAZ, while TGF-β favored YAP and TEAD4 upregulation. These findings suggest that PDGF-B and TGF-β, while both activating fibrogenic pathways, differentially regulate downstream genes, indicating overlapping but divergent fibrotic mechanisms. Future direction includes investigating the serine/threonine kinase NUAK1 as a potential regulator in PDGF-B-mediated fibrosis, building on prior evidence of its role in TGF-β signaling. This may provide insight into novel anti-fibrotic strategies.

40. Brandon Luu (Sleep Medicine) Can Medical Reasoning be Achieved by Artificial Intelligence: A Comparison of Large Language Models' Performance on Medical Licensing Preparatory Exams in Sleep Medicine

Dr. Brandon Luu, Ali Salman Al-Timimi, Dr. Nicholas Fabiano, Dr. Vanessa Martelli

Objective:
To compare the performance of leading large language models (LLMs) on validated sleep medicine board preparatory questions from the American Academy of Sleep Medicine (AASM) self-assessment materials. In addition, the impact of prompting and the capacity for image

interpretation were evaluated.

Methods:
Six LLM's were tested: GPT-5 Thinking (standard and prompted versions), Grok 4, Gemini 2.5 Pro, DeepSeek R1, and OpenEvidence. Models answered 232 AASM questions spanning various sleep medicine domains including sleep-related breathing disorders, insomnia, sleep-related movements and central disorders of hypersomnolence. The question set included 213 text-based and 19 image-based items.

Results:
Grok 4 achieved the highest overall accuracy at 92.7% (215/232), followed by GPT-5 Thinking at 89.2% (207/232), GPT-5 Thinking-Prompted at 87.9% (204/232), Gemini 2.5 Pro at 83.2% (193/232), OpenEvidence at 80.3% (171/213), and DeepSeek R1 at 74.6% (159/213). Image interpretation proved challenging, with accuracy dropping substantially: Grok 4 declined from 95.3% on text to 63.2% on images, GPT-5 from 91.1% to 68.4%, and Gemini 2.5 Pro from 85.9% to 52.6%. GPT-5-Prompted demonstrated the strongest image performance at 78.9%, suggesting prompting benefits for visual interpretation. OpenEvidence and DeepSeek R1 could not process image-based questions.

Conclusions:
Current LLMs show strong but variable performance on sleep medicine board preparatory questions. Performance declined when the LLMs were asked to interpret images in addition to the written questions.

41. Tyonna Ashby (Neuroscience) Establishing saccade, pupil, and blink behaviour during free viewing of dynamic video in non-human primates: translating behaviour to human clinical application.

Ashby. T, Mika. D, Brien. D, Coe. B, White. B, & Munoz. D

The visual system is a highly interconnected circuit where external visual stimuli from the environment, cortical, and subcortical areas provide dynamic input into brain circuitry, shaping oculomotor behaviours such as saccades, blinks, and pupil responses. Dysfunction or deterioration of cortical or subcortical networks results in specific abnormal oculomotor behaviours in psychiatric and neurodegenerative diseases. To understand how to use these oculomotor metrics as a potential biomarker, we are studying non-human primates (NHPs). Previous research has established saccade, blink and pupil behaviour in structured tasks. However, NHP oculomotor behaviour in naturalistic unstructured tasks remains understudied; thus, the neural circuitry involved in the naturalistic, novel tasks has not yet been examined.
The goal of this study is to establish the free-viewing paradigm in NHPs and quantitatively contrast it with human behaviour under similar conditions. Dynamic videos were presented to NHPs on a computer screen, and eye movements were recorded using an Eyelink 1000. NHPs watched 10 minutes of dynamic scenes per session, analogous to someone frequently changing TV channels.

The videos consisted of short clips depicting naturalistic scenes. The changes created visual perturbations influencing saccade, pupil, and blink behaviour. These perturbations elicit specific abnormal oculomotor behaviours in clinical groups, highlighting their importance.
We have uncovered similarities and differences between NHPs and humans. Notably, humans have a well-described gaze distribution on the horizontal plane (horizontal bias) that is much less pronounced in NHPs. Changes in saccade rates induced by clip changes were similar in humans and NHPs. Blink durations were shorter in NHPs. Pupillary responses were very similar in NHPs and humans. As eye tracking becomes increasingly important for diagnosing, tracking disease progression, and evaluating treatment efficacy, understanding the neural circuits underlying these behaviours is essential for linking abnormal behaviour to brain dysfunction in human disease.

42. Scott Davidson (Neuroscience & Mental Health) Examining the Influence of Transcranial Alternating Current Stimulation on Prefrontal Cortex Activity: A Scoping Review

Authors: Scott Davidson, Dr. Felicia Iftene & Dr. Simon O’Brien
Providence Care Hospital, Centre for Neuroscience Study, Queen’s University

Background: Transcranial electrical stimulation is a non-invasive technique that has deservedly garnered much more attention in recent years. It presents an opportunity for modulation of the brain independent of medications. Transcranial alternating current stimulation (TACS) is one method that has shown promise.
Methods: Databases searched were PubMed (7), Embase (9), and MedLine (2) using keywords (“transcranial alternating current stimulation” OR “tACS”) AND (“prefrontal cortex” OR “PFC”) AND (electroencephalogram or EEG). 18 articles fitting criteria were found. Search was conducted in October of 2024, limited to the English language. Only clinical trials from the last 10 years were included, meta-analyses, review articles, and editorials were excluded.
Results: TACS has an impact on the PFC. Three studies found an impact of TACS treatment on memory, another three found an impact of TACS on response times. It is also clear that TACS has an impact on electrophysiology, with several studies finding that TACS impacted spectrograms. Targeted aspects of cognition included memory, learning rate, multitasking, response inhibition, and response latency.
Conclusions: TACS has been investigated across several applications, but consensus has not been reached due to conflicting results, differing electrode montages, and the limited number of studies. This review underscores that TACS is a relatively new method requiring more research and replication to establish effectiveness in specific domains.
Keywords: TACS, PFC, EEG

43. Jennifer Carlson (Psychiatry) Does sex and gender impact risk for metabolic syndrome in schizophrenia?: A scoping review

Jennifer Carlson, Dr Felicia Iftene, Dr. Simon O’Brien

Background: Schizophrenia (SZ) is highly comorbid with metabolic syndrome (MetS), significantly increasing risk of cardiovascular disease and diabetes type II (Mitchell et al., 2018). Considering

sexually dimorphic factors are understood to influence metabolic functioning, this review aims to elucidate the relationship between sex/gender and MetS in SZ (Ding et al., 2006).
Methods: A systematic search was conducted using the terms “schizophrenia” or "schizoaffective disorder" AND "metabolic syndrome" or "glucose metabolism disorders" AND "comorbidity” or "risk factors” AND “sex characteristics” or “sex factors” or “male” or “female” or “gender” from 2019 to present. A search of three databases, Medline (60), Embase (136) and APA PSYC Info (35), yielded 231 results. Twenty articles including data on sex/gender in MetS and SZ were selected.
Results: Eighteen studies were cross sectional, two retrospective and one prospective. Among the included studies MetS criteria (15), lifestyle factors (12), metabolic hormones (5), cognitive functioning (4), inflammatory markers (4), sex hormones (4), and genetic markers (1) were considered as potential associations or risk factors. Five studies included early stage or drug-naïve SZ groups and one studied chronic SZ exclusively.
Conclusion: Most sex/gender findings centered around typical MetS diagnostic components, however a diverse range of risk factors and associations emerged, posing difficulties in drawing meaningful conclusions. This highlights a critical need for more targeted sex/gender focused research elucidating the relationship between SZ and MetS.

44. Kemal Mohammed (Nursing) Cross-Cultural Adaptation and Psychometric Properties: Developing and Validating an Amharic Version of the Compassion Competence Scale for Ethiopian Nurses

Kemal Jemal Mohammed[1,2], Jacqueline Galica[1]

1Queen’s University School of Nursing, Canada,

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Introduction: Compassion is a universal concept, but its expression differs across cultures, shaped by language, values, and social norms. Measures created in one context may not fully reflect their reliability in another setting. Compassion measures are vital indicators of healthcare quality, but no nurse-reported compassion measures currently exist in Ethiopia. Using non-cross-culturally adapted and validated tools risks inaccuracies for research, policy, and clinical judgments. The CCS is a validated and reliable tool used to measure nurses' compassion competence in English-speaking settings. Cross-cultural adaptation of the CCS demonstrates excellent acceptability in new cultural contexts.

Objectives: This study aims to develop a culturally appropriate and psychometrically valid Amharic version of the Compassion Competence Scale (CCS) for Ethiopian nurses.

Methods: The study will follow the cross-cultural adaptation process and psychometric evaluation. The cross-cultural adaptation process will involve the development of an Amharic version of the CCS using forward and backward translation by bilingual translators, reconciling differences, and synthesizing into a single version. A panel of nursing experts used a 4-point Likert scale to determine the content validity index, and a pilot test will be conducted with 30 nurses. Feedback will be incorporated, and the final version will be produced. Finally, a psychometric evaluation will be conducted among 200 nurses recruited from Salale University Hospital, adhering to the rule of thumb of 10 participants per factor for the CCS (17 items). Exploratory and confirmatory factor analyses will be tested to confirm the three-factor structure (communication, sensitivity, insight) and the 17-item construct. Internal consistency, including Test-retest reliability, will be measured using Cronbach's alpha. Convergent validity will be assessed by correlating CCS with the Emotional Competence Scale. Data analysis will be conducted with SPSS and Amos statistical software, with model fit evaluated using indices. Ethical approval will be obtained from both Queen's and Salale University.

Significance: The results will help nurses, researchers, and clinicians use a reliable Amharic version of the CCS to evaluate compassionate care and guide staff training, education, and policy development.

Keywords: Cross-cultural adaptation, tool validation, psychometric properties, compassion measures, Ethiopia

45. Marjan Kekanovich (Nursing) Collaborative research teams: Partnering with an advisory committee in graduate student-led research

Marjan Kekanovich[1], Dr. Danielle Macdonald[1], Dr. Susan A. Bartels[2], Dr. Jacqueline Galica[1]

Affiliations: [1]Queen's University School of Nursing, [2]Queen's University Department of Emergency Medicine and Department of Public Health Sciences

Background: Engaging an advisory committee strengthens research by integrating perspectives of individuals with lived and living experience. This presentation shares my (MK) experience as a graduate research student in partnering with an advisory committee of women with lived or living experience to conduct a qualitative case study about emergency department and urgent care experiences of women who use illegal substances.

Methods: This study includes five planned advisory committee meetings, with two already completed. To date, members have refined the study design, guided sampling, and informed early interpretation of results. They will also co-present findings and co-author manuscripts, ensuring their expertise shapes analysis and dissemination. Throughout, I have used reflexive journalling to document my experiences and reflections about this partnership.

Reflections: Several practices strengthen collaboration: Partnering with community organizations builds trust, co-creating terms of reference clarifies roles and recognizes advisory committee members as integral to the research team, flexible scheduling and participation options allow members to contribute in ways that suit them, financial compensation recognizes members' expertise and affirms their role as researchers, and a welcoming environment encourages participation.

Conclusion**:** Through this work, we demonstrate that graduate student-led research can meaningfully integrate lived experience by engaging an advisory committee as part of the research team. Sustaining this collaboration requires intentional practices that recognize members' expertise, support their participation, and ensure their contributions shape the research process.

This work was supported by the Freda Paltiel Award for Women's Health and Development, the Canadian Society of Addiction Medicine, and the RNAO Nursing Research Interest Group.

46. Sydney Shepherd (Cancer Research) The Earlier Detection of Ovarian Cancer Using an mDETECT Liquid Biopsy

Sydney Shepherd, Keira Frosst, Dr. Josee-Lyne Ethier, Dr. Christopher Mueller

Ovarian cancer is the 5th deadliest cancer for Canadian women, with more than 2000 women dying of the disease each year. It is often diagnosed in late stages when the prognosis is much worse due to its unspecific symptoms and the limitations of the current detection and monitoring tools.
The methylation DETEction of Circulating Tumour DNA (mDETECT) liquid biopsy for ovarian cancer has been developed for the improved detection and monitoring of ovarian cancer. This assay has been validated in 30 tumour and 60 plasma samples obtained from ovarian cancer patients at the current detection timepoint, and has shown high levels of methylation. The assay has also shown low levels of methylation in 60 age-matched healthy control plasma samples, resulting in an assay with a high sensitivity and specificity.
To further validate this liquid biopsy, we are initiating the ORACLE observational pilot study in partnership with Sunnybrook Health Sciences and Kingston Health Sciences Centre. This 2-year study will analyze a single timepoint blood sample from 100 women referred to the gynecological oncologist with suspicious ovarian findings. The mDETECT assay results will be compared to the currently used methods for detection to determine if we can a) accurately detect ovarian cancer at the current diagnosis point or earlier and b) determine the assay's profile in benign ovarian conditions that can be difficult to differentiate clinically.

47. Marco Buttigieg (Cancer, Aging, Genetics, Immunology) Clonal hematopoiesis of indeterminate potential-associated non-small cell lung cancer risk is potentiated by small particulate matter air pollution among non-smokers: a novel somatic variant–environment interaction

Marco M. Buttigieg*, Caitlyn Vlasschaert*, Yash Pershad, Matthew Lanktree, Melinda C. Aldrich, Michael J. Rauh, Alexander G. Bick

Small particulate matter air pollution (PM2.5) is a recognized driver of non-small cell lung cancer (NSCLC), including in non-smokers. Inhaled PM2.5 recruits pro-inflammatory macrophages to the air-lung interface, which promotes malignant lung epithelial cell growth and progression to overt cancer. Smoking is recognized to potentiate this process, though no factors potentiating risk among non-smokers have been identified. We sought to determine whether clonal hematopoiesis of indeterminate potential (CHIP), a common age-related condition characterized by hyperinflammatory macrophages, exacerbates PM2.5-associated NSCLC in non-smokers using genetic, environmental, and phenotypic data from over 650,000 individuals in the UK Biobank and All of Us. In meta-analysis, CHIP was associated with a greater risk of NSCLC in never-smokers (hazard ratio (HR) 1.76, 95% confidence interval (CI): 1.07-2.89). This risk is exacerbated in the

setting of above-median PM2.5 levels (HR 2.51, 95% CI: 1.55–4.05; p-interaction = 0.02). The CHIP x PM2.5 interaction also associated with elevated markers of systemic inflammation (CRP, IL-6, and IL-1β). Altogether, these results suggest CHIP and PM2.5 form a novel somatic gene × environment interaction promoting NSCLC tumorigenesis in non-smokers.

48. Nick Cruickshanks (Epidemiology) Impact of loss to follow-up on treatment effect estimates in Phase III cancer trials

Nick Cruickshanks, Dr. Harriet Richardson, Dr. Wei Tu

Background: Loss to follow-up (LTFU) occurs when we are unable to contact a patient for data submission in a longitudinal study—despite multiple attempts—threatening internal validity and potentially biasing findings. LTFU may be inconsistently reported and managed across trials, and its impact is not fully characterized. The Canadian Cancer Trials Group (CCTG), Canada's largest cooperative oncology group, has conducted over 200 Phase III trials. These include detailed patient-level data and full participation trajectories, providing an unprecedented opportunity to understand LTFU's impact on trial outcomes.

Objectives: (1) Describe overall LTFU % in CCTG cancer trials, and LTFU % stratified by various trial-level. (2) Elucidate patient-level characteristics associated with LTFU in select trials. (3) Estimate the effect of LTFU on treatment estimates under various assumptions of LTFU in select trials.

Methods: We will analyze Phase III CCTG-led cancer trials whose analysis occurred after internal harmonization of LTFU definitions. LTFU will include those withdrawn with consent and those truly LTFU, and will also be analyzed separately. LTFU % will be reported by trial-level and patient-level characteristics, and by LTFU timing. We will use statistical methods to see which factors are linked to LTFU and to estimate how much LTFU might change treatment results.

Significance: This understudied issue has major implications for clinical trial reporting, drug approval, and bias evaluation in cancer research.

49. Bailey Milne (Perinatal Epidemiology) Subfertility and risk of congenital anomalies: a systematic review and meta-analysis

Bailey Milne, Tristan Derry, Dr. Susan B Brogly, Dr. Maria P Velez

Objective: Infertility itself, independent of fertility treatment, might be associated with adverse offspring outcomes, including congenital anomalies. Thus, we aimed to assess risks of congenital anomalies for infants born to patients diagnosed with infertility who conceived without fertility treatment (i.e subfertility) compared to patients without infertility.
Methods: Systematic searches were performed on OVID MEDLINE and Embase databases for studies published from earliest availability-April 31, 2024. Search terms included combinations of the following medical subject headings and keywords: congenital anomalies, subfertility, and fertility treatment. All stages of screening and data extraction were completed by two reviewers

independently. Effect estimates for congenital anomalies, singleton or multiple births, were pooled in a random-effects meta-analysis. The Newcastle-Ottawa scale was used to for bias assessment.
Results: Of 3,902 unique records identified, 23 studies met inclusion criteria and 13 contributed to the meta-analysis of any anomaly; there was increased risk observed among infants born to patients with subfertility compared to those without (OR:1.19; 95%CI:1.15–1.23). There was increased risk for cardiovascular (OR:1.12; 95%CI:1.02–1.24) and gastrointestinal anomalies (OR:1.31; 95%CI:1.13–1.50). Subgroup analysis restricted to singletons did not change the results in any meaningful way. There was no evidence of publication bias.
Conclusion: Our findings suggest a small increased risk of any anomalies, for infants born to patients with subfertility. Future studies should focus on delineating risks between different infertility diagnoses.

50. Nicole Vorko (Health services, cancer policy) Trends in Health Canada Approvals of Adult Solid Cancer Medicines (2009-2025)

Nicole Vorko[1,2], Brian Shkabari[1], Wesley Geerlinks[3,4], Claire Diana-Gonsalves[1], Bishal Gyawali[1,2,5]

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As the cancer landscape in Canada evolves, so too do the approvals of cancer medicines to reflect the needs of patients and the health system. Health Canada (HC), the regulatory body that determines which cancer drugs are marketed in Canada, must balance timely access and high-quality evidence for new therapies. In this study, we investigated the trends of adult solid cancer drugs approved by HC from 2009 to 2025 to characterize the changes in approval landscape and strength of evidence supporting the decision-making process. Approvals were extracted from the Health Canada Notice of Compliance (NOC) database using 2 independent reviewers. During this timeframe, 256 unique approvals were extracted with 224 given a NOC and 32 given NOC with conditions. Most cancer drugs were approved for lung (n=70), breast (n=35), prostate (n=20), and melanoma (n=18). The median improvement in overall survival (OS) was 3.10 months (HR=0.70), and progression free survival was 3.90 months (HR=0.55). The proportion of drugs given NOC based on OS decreased by 7.4% from the 2009-2020 to 2021-2025 period. Consequently, 63.3% of all cancer drugs from 2009 to 2025 were granted HC approval based on surrogate primary endpoints, with 70.7% in the last five years alone. Our results suggest that cancer drugs receive HC approval based on lesser quality of evidence and lesser magnitude of benefit in recent years compared to the past.

51. Alison Wu (Rehabilitation) "Disidentifactory Occupational Practices".

Authors include Benjamin Ma, Sydney Grant, Zoha Butt and Alison Wu.

Queer and Cuban-American performance studies theorist José Esteban Muñoz introduced the concept of "Disidentification" as "the survival strategies the minority subject practices in order to negotiate a phobic majoritarian public sphere that continuously elides or punishes the existence of subjects who do not conform to the phantasm of normative citizenship" (1999). Concerning clinical practice, I theorize that these defense mechanisms are essential to understanding how an occupational therapist may begin to understand the extent to which dominating social ideologies identify and call attention to barriers surrounding occupational performance. Furthermore, Muñoz writes how the learned (re)performed behaviours create legitimate worlds for the performer, creating a sense of accomplishment through "successful" social navigation. Occupational therapists recognize how Flow Theory enables a sense of immersion in an activity that leads to pleasurable emotions, however, for the minority culture, I question if 'pleasure' can be attained or if the autonomous practice of pleasing the dominant culture strips one's ability to reach that "immersive" state. In this panel, I offer the use of performance studies (through Muñoz and Schechner) as a Frame of Reference by which one may begin to understand how human behaviour, as it relates to occupational participation and its barriers. Furthermore, this panel strives to offer a different perspective on human behaviour and occupational behaviour as a survival strategy within a dominant sphere, raising the stakes for occupational participation as a survival instinct concerning systemic injustices that control clinical practice.

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52. Sarah Thompson and Bridget Moors (Physical Medicine and Rehabilitation. Concussion treatment and rehabilitation) Treatment of Post-Concussive Sleep Disturbances in Children and Adults: A Scoping Review

Sarah Thompson, Bridget Moors, Jessica Trier

Treatment of Post-Concussive Sleep Disturbances in Children and Adults: A Scoping Review

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Background: a concussion is a type of brain injury caused by direct trauma or rapid movement of the head. Up to 25% of individuals who sustain a concussion develop a post-injury sleep disturbance. Sleep disturbances contribute to prolonged recovery from concussion and poorer long-term outcomes. Thus, identifying effective treatments for post-concussive sleep disturbances is essential in reducing the incidence of persistent post-concussive symptoms. The objective of this scoping review is to provide a summary of existing literature that describes treatment options for post-concussive sleep disturbances in children and adults.
Methods: a literature search was conducted in MEDLINE, Embase, CINAHL, Web of Science, and ProQuest Dissertations & Theses Global. Two reviewers screened titles and abstracts, then full text articles against the inclusion and exclusion criteria. Primary studies that analyze at least one treatment for post-concussive sleep disturbances will be included.
Preliminary results: of the 3660 articles yielded from the search, 1332 duplicates were removed, and 2258 articles were excluded during title and abstract screening. The remaining 70 articles are currently undergoing full text review.
Next steps: included articles will undergo data extraction. Data extraction fields will include study title, author, study design, participant demographics, intervention type, intervention frequency/dose/duration, outcome measures, and key findings. The results of this review will be used to identify gaps in the literature to guide future research in this field.

53. Biniyam Abebe (Primary Health Care) Defaulting: PHC institutional processes and actions influencing access to care for adults with disabilities in rural and urban slum settings in Ethiopia- a grounded theory

Biniyam Abebe, Catherine Donnelly, Adhanom Baraki, Mikyas Abera, Nicole Bobbette

Most adults with disabilities (AwDs) in Ethiopia experience complex barriers to access to Primary Healthcare (PHC) services. Despite promising efforts, the problem remained; yet, while existing studies have examined barriers and facilitators of access for this group, there is limited knowledge about how current institutional processes and practices within PHC shape access to care. This study examines existing service delivery processes and actions within PHC facilities to understand the institutional factors that influence access to care for AwDs in rural and urban-slum contexts in Ethiopia. The objective of this study is to develop a framework to understand and improve

institutional processes that influence access to primary health care for adults with disabilities in rural and urban-slum areas of Ethiopia.

We employed Constructivist Grounded Theory methodology. Twenty-nine intensive interviews with 21 health service providers were conducted in 13 PHC facilities spanning four rural and three urban slum settings. We also conducted non-participant observation to explore physical accessibility and accommodation patterns.

The study results showed that current PHC service delivery in the study area involves three main institutional processes for improving access to care for AwDs: *designing services and delivery systems, compensating for lack of accessibility, and sharing or transferring responsibility.* These processes become standardized "defaults," manifested as typical organizational responses to the issue of access to care for the study population. Based on the findings, we developed a substantive theory and introduced the concept of "*defaulting*" as a critical framework to analyze how these processes unfold. The theory challenges negative, exclusionary institutional defaults such as *disappearance default*, *compensatory default*, and *outsourcing default*, and proposes alternative, positive service delivery "system-defaults." The theory aims to help identify and address commonly overlooked practices that are often concealed under the broad concept of inclusion.

54. Bernice Yamoah (Immigrant Mental Health) Centering Intersectionality and Cultural Safety: A Community-Based Participatory Framework for Engaging African Immigrant Men in Mental Health Program Evaluation.

Bernice Yamoah

African immigrant men experience the lowest engagement rates in community mental health services, facing intersecting barriers including anti-Black racism, precarious immigration status, masculinity norms discouraging help-seeking, and cultural stigma around mental health. Single-axis interventions cannot address the complexity of intersectional marginalization. Traditional evaluation approaches fail to capture how these overlapping systems of oppression create unique experiences that differ across country of origin, language, religion, and immigration pathway. This research provides an integrated evaluation framework that centers intersectionality and cultural safety while employing community-based participatory approaches to meaningfully engage African immigrant men in mental health program evaluation. The study integrates three complementary frameworks: Cultural Safety Evaluation, Intersectionality-Based Policy Analysis, and Community-Based Participatory Evaluation. Analysis examined how intersecting identities shape service experiences while identifying culturally safe mechanisms for community partnership and power-sharing in evaluation processes. The integrated framework establishes Community Advisory Committees with decision-making authority, implements intersectional data collection matrices disaggregating experiences by multiple social locations, and employs culturally resonant evaluation methods including oral traditions and peer facilitation. Key elements include strength-based indicators, multilingual community brokers, and transparent data governance agreements that prioritize community ownership. Centering intersectionality and cultural safety transforms evaluation from extractive institutional practice to collaborative knowledge creation. This framework provides a practical pathway for building trust-based partnerships while generating nuanced understanding of African immigrant men's diverse experiences and mental health needs.

55. Melkitu Melak (PhD in Rehabilitation Science) “It Feels Like My Spine is About to Break”: Experience and Support Needs of Family Caregivers of Children with Cerebral Palsy in Ethiopia

Melkitu Melak, Solomon Mekonnen, Afolasade Fakolade, Beata Batorowicz

Background: Due to the complex and long-term care needs of children with Cerebral Palsy (CP), caregivers often face an overwhelming caregiving burden, and they experience physical and psychological strain. Few studies in Sub-Saharan Africa have indicated that caregivers face financial difficulties and limited access to formal support services. However, evidence is scarce in Ethiopia.
Objectives: This study aimed to explore the caregiving experiences and support needs of family caregivers of children with CP in Ethiopia.
Method: An exploratory descriptive qualitative design was used in this study. A purposeful sampling method was employed to identify and select 13 family caregivers of children with CP. A face-to-face, in-depth interview was conducted in the local language, Amharic. Reflexive thematic analysis was used to analyze the data.
Results: Four themes were identified: the emotional journey of caregivers, daily caregiving demands, impact of caregiving, and support systems and support needs. Caregiving for children with CP negatively affected the emotional, physical and social well-being of caregivers. Caregivers indicated a need for financial support, psychological support, adequate healthcare services, access to assistive devices, and education for their children with CP.
Conclusion: The findings emphasize the urgent need for interventions that address the financial vulnerabilities of caregivers, provide targeted psychosocial support, and enhance access to healthcare, assistive devices and education for children with CP.
Keywords: Cerebral Palsy, Caregiver, Support, Wellbeing, Health

## ***Afternoon Session***

1. Reginald M. Smyth (Cardiorespiratory Pathophysiology) A novel physiology-imaging platform to investigate the effects of single inhaler, co-suspension triple therapy on small airway function, operating lung volumes, and neuromechanical dissociation (SOUND): Consequences for exertional dyspnea in hyperinflated patients with COPD - a protocol.

Reginald M. Smyth, Matthew D. James, Sandra G. Vincent, Maddison M. Coyle, Nicolle J. Domnik, J. Alberto Neder

Background: Dyspnea is the key complaint of individuals suffering from chronic obstructive pulmonary disease (COPD). Symptom alleviation is contingent upon improving distal small airway function, which may lead to lower operating lung volumes and improved neuromechanical dissociation (NMD). There is a need to develop robust platforms to investigate these interrelated

phenomena simultaneously.

Aims: To investigate the effects of single-inhaler, co-suspension triple therapy (combined long-acting beta-agonist / long-acting muscarinic antagonist / inhaled corticosteroid) on small airway function, NMD, and dyspnea during exercise in hyperinflated COPD patients.

Methods: This double-blinded, placebo-controlled crossover study will involve 25 hyperinflated patients (functional residual capacity≥120% predicted). Visit 1: Includes standard pulmonary function tests (PFT) and a symptom-limited cycle exercise test. Visit 2&3: Randomization (placebo or bronchodilator), pre- and post-intervention PFTs, and incremental cycle exercise with an esophageal catheter for respiratory manometry and inspiratory neural drive, and impulse oscillometry for small airway function. Visit 4&5: Randomized interventions, PFTs, and functional magnetic resonance imaging (PREFUL) at rest and during light exercise to evaluate ventilation distribution.

Anticipated Results: Triple therapy, compared to placebo, will improve small airway function, decreasing operating lung volumes, NMD, and exertional dyspnea.

Conclusion: This study may establish a novel exercise-based physiology-imaging platform to assess the role of existing and emerging pharmacological agents in improving small airway disease and its deleterious sensory-mechanical consequences in patients with COPD.

2. Amanda Zacharias (Experimental Medicine) Site- and cell-type-specific miRNA and mRNA genes and networks across the cortex, striatum, and hypothalamus

Amanda M. Zacharias, Ciara D. O'Connor, Danai G. Topouza, Zhi Yi Fang, Helia Ghazinejad, Hanlin Chen, Qingling Duan & Nader Ghasemlou

Biological rhythms control gene expression, but effects on central nervous system (CNS) cells and structures remain poorly defined. While circadian (24-hour) rhythms are most studied, many genes have periods of greater and less than 24-hours; these fluctuations can be both site- and cell-specific. Identifying patterns of gene rhythmicity across the CNS is necessary for both the study of chronobiology and to make sense of data obtained in the laboratory. We now identify cycling mRNAs, miRNAs, gene networks and mRNA-miRNA co-expression pairs in the cortex, hypothalamus, and corpus striatum of male C57BL/6J mice using high-dimensional datasets. A searchable catalogue (https://www.ghasemloulab.ca/chronoCNS) helps refine the analysis of cellular and molecular rhythmicity across the CNS (using the liver as a control). Immunofluorescence confirms the rhythmicity of key targets across cells in these structures, with strong cycling signatures in resting oligodendrocytes. Our study sheds light on the contribution of diurnal, ultradian, and infradian rhythms and mRNA-miRNA interactions to CNS function.

3. Kristin MacLeod (Experimental Medicine) The Potential Impact of Sleep Quality on Functional Capacity in Health and COPD: a CanCOLD Cohort Study

Kristin E MacLeod, Alexandra McCartney, Tetyana Kendzerska, J. Alberto Neder, Nicolle J Domnik, CanCOLD Collaborative Research Group

Physical activity engagement improves health outcomes and functional capacity, but there are complex barriers to maintaining functional abilities, like walking. This may be especially true in older adults or individuals with respiratory disease, groups in whom poor sleep quality is common. However, potential associations between poor sleep quality and functional capacity are underexplored in these populations.

The Canadian Cohort of Obstructive Lung Disease (CanCOLD) was used to investigate associations between sleep quality (Pittsburgh Sleep Quality Index [PSQI]) and functional capacity (6-minute walk test distance [6MWD]). Analyses included adjusted multiple regression to determine correlations between 6MWD and PSQI total score, controlling for reported respiratory disease and COPD, diabetes, cardiovascular disease, cancer, current smoking, age, sex and BMI.

Data for n=729 individuals were analyzed (298 poor sleepers; age 66.5±9.5 years; 58% male). 6MWD was significantly negatively associated with total PSQI score, both in absolute terms and as % of predicted distance (6MWD (m): $\beta$ =-3.993, SE =1.051, p = <0.001, 95% CI =-6.056. R2 for the overall model was 35.6%; 6MWD % predicted: $\beta$ = -0.662, SE = 0.192, p =<0.001, 95% CI =-1.04. R2 for the overall model was 13.8%).

Our findings support a negative association between sleep quality and functional capacity in the CanCOLD cohort. Further investigation is needed to determine the impact of poor sleep on daily physical activity in individuals with/without COPD.

4. Bill Turner & Marissa Shemuel (Cardiopulmonary Physiology) The Effects of Habitual Non-Tobacco Nicotine Consumption on Resting Autonomic Cardiovascular Control in Young Adults: A Pilot Study

William G. Turner, Marissa Shemuel, Elizabeth M. Bignell, Nicole Lewis, Daniel Abdelmalek, Stephanie Adeseiye, Matthew D. James, J. Alberto Neder, Martin Kaufmann, Sebastián Rodríguez Llamazares, Nicolle J. Domnik

Introduction: Non-tobacco nicotine (NTN) consumption methods, like e-cigarettes and oral nicotine pouches, are gaining in popularity. The cardiovascular consequences of long-term tobacco smoking are well-established, but potential shorter-term effects of NTN remain unknown.

Objectives: To investigate whether NTN consumption impacts cardiovascular function in young adults, and whether 24-hours of nicotine abstinence could restore physiological responses.

Methods: 20 control (CTRL: 10m:10f, 20.8+0.9 years old) and 3 nicotine-using (NIC: 2m:1f, 21.7+1.5 years old; 1-8 years NTN use history) participants completed two in-lab visits separated by a one-week monitoring period, with NIC completing a third visit following 24-hours of nicotine abstinence (ABS). Visits measured heart rate (HR), HR variability (HRV), and blood pressure (BP). Nicotine

exposure was quantified through urinalysis by liquid chromatography-mass spectrometry.

Results: HR was elevated in NIC (n=3) (81.2±18.3 bpm) vs CTRL (n=19) (70.5±10.7 bpm). Standard deviation of normal inter-beat intervals (SDNN) was lower in NIC (n=3) (46.9±11.9 ms) vs CTRL (n=18) (63.0±25.1 ms) while BP was elevated in NIC (n=3) (125.9+17.0 mmHg) vs CTRL (n=19) (114.3+4.9 mmHg). NIC cardiovascular indices partially normalized post ABS. NIC (n=3) had higher nicotine (360+375 ng/mL) and cotinine (844+424 ng/mL) concentrations vs CTRL (n=5) (<13.8 ng/mL), with NIC concentration reducing during ABS.

Conclusion: Preliminary findings suggest NTN use is associated with altered cardiovascular function in young adults, illustrating a need for research into NTN health effects. Participant recruitment continues.

5. Richard Nauman (Immunology; Cancer) Clinical Bacillus Calmette-Guérin Strains Induce Distinct Trained Immunity Profiles

Richard W. Nauman and Charles H. Graham

Introduction: Bacillus Calmette-Guérin (BCG) immunotherapy remains the standard of care for higher-risk non-muscle invasive bladder cancer (NMIBC), despite an incomplete understanding of its immunotherapeutic mechanism. Trained immunity (TI), a form of innate immune memory, is thought to be involved. It is well known from the tuberculosis literature that the various BCG strains have distinct immunogenic properties, yet there has been no direct comparison of TI profiles in NMIBC clinical strains. We assessed TI acquisition and secondary responses following administration of BCG-Russia or BCG-TICE.

Methods: C57BL/6 mice received a single intravenous injection of BCG-Russia or BCG-TICE, leading to acquisition of TI in bone marrow progenitor cells. After 4 weeks, bone marrow was collected for flow cytometric analysis of hematopoietic stem and progenitor cell (HSPC) populations, generation of bone marrow-derived macrophages, functional assessment of TI, and transcriptomic profiling.

Results: Macrophages from mice treated with BCG-TICE exhibited significantly higher production of several proinflammatory cytokines upon secondary activation. BCG elicited expansion of HSPCs independent of strain. BCG-TICE was linked to upregulation of key proinflammatory genes and enrichment of functionally relevant pathways.

Conclusions: TI is emerging as crucial to the mode of action of BCG therapy in NMIBC. Understanding whether certain strains produce limited immune responses is important to ensuring optimal and consistent therapeutic efficacy for NMIBC patients.

Funding: Canadian Institutes of Health Research (CIHR), Terry Fox Research Institute (TFRI)

6. Phillip Stachera (Reproductive Immunology) Placental factors induce innate immune memory in bone marrow-derived macrophages.

Phillip Stachera, Christina Ferazzutti, Charles H. Graham, and Tiziana Cotechini

Background

Innate immune memory describes the ability of myeloid cells to undergo epigenetic reprogramming following exposure to pathogen- and danger-associated molecular patterns (PAMPs and DAMPs) resulting in long-lasting altered immunological responsiveness. During both uncomplicated pregnancy and inflammation-associated pregnancy complications (e.g. pre-eclampsia [PE] and fetal growth restriction [FGR]), the placenta releases factors including DAMPS. We demonstrated evidence of innate immune memory in peripheral blood circulating monocytes collected from women with PE/FGR compared with uncomplicated pregnancies. It is not known whether this memory is specific to pregnancy complications and if it is retained during differentiation to macrophages. We hypothesize that release of placenta-derived factors during both uncomplicated and complicated pregnancy induces innate immune memory in macrophages.

Methods and Results

Female C57Bl/6 mice mated with male BALB/c mice received a single intraperitoneal injection of lipopolysaccharide (LPS; 10 mg/kg) - to induce FGR - or PBS (control) on gestational day (GD) 10.5. Age- and treatment-matched nulliparous mice were controls. Bone marrow-derived macrophages (BMDMs) generated from pregnant mice (GD 14.5) exhibited significantly decreased IL-6 and increased IL-10 release in response to secondary stimulation (Pam3Cys [10 mg/mL], or LPS [100 ng/mL; 10 ng/mL]) compared with BMDMs from nulliparous controls. Bone marrow from virgin mice cultured in placenta conditioned medium (Pl-CM; collected from GD 14.5 placental explants) prior to differentiation into BMDMs (Pl-CM-BMDM) demonstrated significantly reduced IL-10 release in response to secondary stimulation compared with non-Pl-BMDMs. Lastly, IL-6 release was significantly reduced following secondary stimulation in Pl-CM-BMDMs generated from LPS-treated mice as opposed to PBS-treated controls.

Conclusion

Placental-derived factors induce innate immune memory in bone marrow progenitor cells that persists through differentiation into macrophages.

7. Caitlyn Kirkpatrick (Biomedical Informatics) Modelling Intra-Litter Variability in Response to Developmental Toxicant Exposure: A Mixed Effects Approach Compared to Litter-Averaging Methods

Megan Cull, Lauren Brown, Louise Winn

Developmental toxicology studies in rodent models often rely on litter-averaged outcomes to evaluate fetal responses to toxicant exposures. However, this approach can obscure biologically meaningful variability within litters, such as differences due to fetal sex, uterine position, or placental morphology. As a result, important treatment effects may be overlooked, limiting the reproducibility and interpretability of findings. This project applies linear mixed effects models (LMMs) to reanalyze two complementary toxicology datasets, benzene and valproic acid exposure, while explicitly accounting for the hierarchical nesting of pups within litters. By incorporating both fixed effects (treatment, sex, uterine position) and random effects (litter), the analysis aims to account for variance more accurately and capture intra-litter influences that traditional methods neglect. A parallel analysis using conventional litter-averaging will enable direct comparison of statistical significance, effect sizes, and biological interpretations between approaches. The expected outcome is a methodological framework that highlights the value of mixed effects modelling for capturing intra-litter variability and clarifying toxicant effects across litters and time points. This approach aims to enhance the robustness and reproducibility of developmental toxicology research, while also providing methodological strategies for analyzing hierarchical biological data and supporting more reliable evidence in toxicological risk assessment.

8. Addisyn Smith (Microbes, Inflammation, and Immunity) Isolating Nanobodies Specific for Herpes Simplex Virus 2 pUL21: A Synthetic Nanobody Display Library Approach

Dr. Bruce W. Banfield

Herpes simplex virus (HSV) types 1 and 2 are prevalent human pathogens that infect billions globally, causing lifelong infection and disease. Despite HSV's significant global health burden, no cure has been identified. Nanobodies (Nbs) are camelid-derived small single-domain proteins with antigen-binding capacity. Biochemical modifications enable the stable intracellular expression of Nbs. This novel application may be a valuable tool for investigating intracellular viral protein function, enabling the identification of new targets for therapeutic intervention. A significant barrier to Nb development is camelid immunization. This costly and timely process contributes to the limited repertoire of Nbs, which are typically unable to bind conserved protein regions. Recent advancements have led to the synthetic development of Nbs, eliminating the need for camelid immunization. Using a synthetic expression library, Nbs against HSV proteins will be isolated, purified, and expressed within infected cells. These methods will provide new tools to study the functions of viral proteins and evaluate whether Nb expression inside animal cells during HSV infection interferes with virus replication. Using these techniques, we can further our understanding of mechanisms driving HSV infection and assembly, prompting the development of novel therapeutic strategies through intracellular Nb expression. This approach has the potential to reduce HSV's global health burden and could serve as a “proof of principle” that can be applied to the treatment of infections caused by numerous pathogens.

9. Lauren T. L. Brown (Therapeutics, Drug Development, and Human Toxicology; Reproduction and Development) Valproic Acid Alters Placental Morphology in CD-1 Mice: Junctional Zone Reduction and Sex-Specific Labyrinth Changes

Lauren T. L. Brown, M. Cull, E. Purdy, J. Cheng, L. Xue, and Louise M. Winn

Valproic acid (VPA) is an antiepileptic drug and potent teratogen that can disrupt placental development, yet its effects on placental structure remain underexplored. Because structural abnormalities in the placenta can impair its function and compromise fetal growth, this study investigates whether VPA exposure alters placental morphology and whether these effects vary by sex. Pregnant CD-1 mice were subcutaneously injected with saline, 400 or 600 mg/kg VPA on gestational day (GD) 9. Placentas were collected on GD18. To control for intralitter variability, placentas from the left uterine horn were paraffin-embedded, stained with hematoxylin and eosin, and analyzed using HALO image analysis software. Placental area, diameter, and proportions of the labyrinth and junctional zone were quantified and statistically analyzed in GraphPad Prism. Preliminary findings reveal that placental area did not differ across groups, but placental diameter decreased with 600 mg/kg VPA ($p = 0.0082$). VPA-exposed males demonstrated higher labyrinth proportions compared to saline males (400 mg/kg: $p = 0.0377$; 600 mg/kg: $p = 0.0452$). Junctional zone proportion decreased with VPA exposure in both sexes (all $p \leq 0.0169$). These findings suggest that VPA exposure alters placental morphology in a dose-dependent manner, with some sex differences, particularly in the labyrinth, and a consistent reduction of the junctional zone. Ongoing immunofluorescence analysis will further clarify VPA's impact on the different placental development and its contribution to adverse fetal outcomes.

10. Nakeisha Lodge-Tulloch (Biomedical and Molecular Sciences) Aberrant inflammation during murine pregnancy leads to subsequent pregnancy complications: potential role of innate immune reprogramming

AUTHORS: Nakeisha A. Lodge-Tulloch, Charles H. Graham, and Tiziana Cotechini.

AUTHOR AFFILIATIONS: Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

BACKGROUND: Pregnancy complications, including fetal loss, are associated with aberrant maternal inflammation, release of damage-associated molecular patterns, and an increased risk of subsequent disease. We hypothesize that aberrant inflammation during pregnancy drives innate immune reprogramming, wherein myeloid cells, acquire memory and exhibit an altered secondary, non-specific immune response. Whether inflammation-induced fetal loss leads to such reprogramming and subsequent pregnancy complications remains unclear.

METHODS: C57BL/6 mice were administered 20 μg/kg of lipopolysaccharide (LPS) or saline intraperitoneally on gestational day (GD) 10.5. Dams were euthanized on postnatal day (PD) 7 or bred for a second pregnancy. Litters sizes and pup weights were recorded on PD 0 and 7. Whole bone marrow and isolated bone marrow monocytes harvested on PD 7 were challenged *in-vitro* with LPS or Pam3Cys. Cytokine concentrations in cell-free supernatants were measured using a multiplex platform.

RESULTS: LPS exposure reduced litter size and PD 7 pup weight in the first pregnancy. In a second pregnancy, pups born to dams with prior LPS exposure were significantly smaller. Functionally, whole bone marrow from LPS-treated dams showed altered cytokine production following secondary stimulation, including reduced TNF and IL-10 levels. Similarly, bone marrow monocytes from these dams exhibited increased IL-6 and decreased IL-1β production.

CONCLUSION: Inflammation-induced fetal loss is associated with subsequent pregnancy complications and altered reprogramming of bone marrow and bone marrow monocytes. Further investigation into reprogramming of other innate immune cells and following other pregnancy complications may help identify at-risk mothers and offspring.

FUNDING: This work is supported by Canadian Institutes of Health Research (CIHR).

11. Safara Holder (Biomedical and Molecular Sciences) Proximity Labelling Reveals Proteins Associated with HSV-2 pUL21 at Early and Late Times After Infection

Authors and Department: Safara M. Holder[1], Maike Bossert[1], Renée L. Finnen, and Bruce W. Banfield[1]

[1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada

Herpes Simplex Virus Type 2 (HSV-2) is a widespread human pathogen that infects ~500 million individuals worldwide. HSV-2 virions contain a dsDNA genome encased within an icosahedral capsid, surrounded by a glycoprotein-studded lipid envelope. Situated between the nucleocapsid and viral envelope is a proteinaceous tegument layer, which houses many proteins that promote viral infection. pUL21 is a conserved and multifunctional alphaherpesvirus tegument protein that is critical for both the early and late stages of the HSV-2 lifecycle; however, the mechanism by which pUL21 participates in these activities is poorly understood. To address this, we used a proximity-dependent biotin identification (BioID) approach by constructing an HSV-2 strain encoding pUL21 fused to the non-specific biotin ligase, miniTurbo (pUL21mT). Cells infected with this strain were treated with exogenous biotin at early and late times post-infection, and biotinylated proteins were affinity-purified and identified by mass spectrometry. This approach enabled the identification of many viral and cellular proteins in proximity to pUL21mT at late times after infection, including those involved in cell adhesion and junction organization, the spliceosome, and the nuclear envelope. Given the robustness of this assay, we also utilized this system to identify proteins in proximity to tegument-delivered pUL21mT immediately following viral entry, providing a comprehensive profile of pUL21 proximal interactors at both early and late stages of infection. These proximal interactions were further validated by pUL21 affinity purification experiments, which confirmed that many viral and cellular proteins identified by BioID associate with pUL21. Not only do these findings provide insights into the role of HSV-2 pUL21 during infection, but they also highlight BioID as a powerful tool for investigating virus-host interactions at multiple stages of infection.

12. Olimpia Sienkiewicz (Biomedical and Molecular Sciences) Imaging Mass Cytometry Reveals Altered Immune Cell Spatial Relationships Between During Inflammatory Bowel Disease Exacerbations

Olimpia Sienkiewicz, Dr. Daniel Mulder

Background:

Inflammatory Bowel Disease (IBD) is a chronic, relapsing and remitting autoimmune disease with growing prevalence in North America. It presents with a distinct spatial element, with many patients only having inflammation in specific regions of their gut, with other regions being unaffected.

Objective:

To gain insight into how spatial relations between immune cells differ between inflamed and uninflamed tissue sections, we performed imaging mass cytometry (IMC) using a panel of 33 markers on inflamed and uninflamed colon and ileal tissue biopsies collected from IBD patients (n = 30).

Methods:

Using an unsupervised clustering approach, we phenotyped 324,786 cells based on marker expression. We generated 17 clusters of cell types of immune and structural origin.

Results:

Neighbourhood analysis of all samples revealed classically activated macrophages and neutrophils to be highly associated with proliferating leukocytes, while alternatively activated (M2) macrophages are highly associated with T cells, mast cells, and plasma cells. In both gut regions, spatial interactions of classical macrophages and M2 macrophages differed between inflammation status. In uninflamed tissue, CD4+ T cells, CD8+ T cells, mast cells, plasma cells, and proliferating leukocytes are predominantly associated with M2 macrophages, however in inflamed tissue classical macrophages became predominantly associated with these immune cell types.

Conclusion:

Spatial analysis revealed unique cellular interaction patterns dependent on disease exacerbation and gut location, highlighting potential cellular relationships involved in IBD homeostasis.

13. Sarah Hopkins (Biomedical and Molecular Sciences) Role of the Microbiome in Modulating CAR-T Cell Therapy Responses

Authors: Sarah Hopkins, Maja Jacobsen, Annette Hay, Bethany Monteith, Karine Gauthier, Shu Mei He, Prameet Sheth

Chimeric antigen receptor (CAR) T cell therapy represents a transformative advance in the treatment of hematological cancers such as leukemia, lymphoma, and myeloma. Despite remarkable clinical success, its' broader impact remains constrained by a 60% relapse rate and 65% chance of adverse reactions1,2. Recent studies have highlighted the role of the gastrointestinal microbiome as a critical modulator of T cell immunity, with mounting evidence linking microbiome composition to patient outcomes in cancer immunotherapy. In particular, exposure to antibiotics prior to chemotherapy or immune checkpoint blockade has been associated with inferior responses across multiple cancer types, including lymphoma. These findings suggest that interventions designed to restore or support a healthy microbiome may enhance immune-based cancer therapies. Therefore, we hypothesize that correcting gut dysbiosis will improve the efficacy of CAR-T cell therapy. To test this hypothesis, we are developing a proof-of-concept murine lymphoma model in which we will evaluate the effects of administrating a defined microbial community both alone and in combination with antibiotic exposure. This approach will allow us to assess whether restoring a disrupted microbiome can enhance CAR-T cell responses, as well as whether supplementation in the absence of antibiotics provides additional benefit. Insights from these studies will clarify how microbial interventions influence CAR-T cell function in vivo and inform future patient care, aimed at improving outcomes with this state-of-the-art therapy.

1 Bellal, M., Malherbe, J., Damaj, G. & Du Cheyron, D. Toxicities, intensive care management, and outcome of chimeric antigen receptor T cells in adults: an update. *Crit Care* **28**, 69 (2024). https://doi.org/10.1186/s13054-024-04851-0

2 Smith, M. *et al.* Gut microbiome correlates of response and toxicity following anti-CD19 CAR T cell therapy. *Nat Med* **28**, 713-723 (2022). https://doi.org/10.1038/s41591-022-01702-9

14. Jad Tirani (Biomedical and Molecular Sciences) Sequence and Structural Analysis of the Human Coronavirus OC43 Mutation Clock Using AlphaFold3

Jad Tirani, Kyla Tozer, Henry Wong, Calvin Sjaarda, Shu-Mei He, Danielle Brabant-

Kirwan, Ramzi Fattouh, Robert Kozak, Prameet M. Sheth

Human coronavirus OC43 (HCoV-OC43) is a beta coronavirus that circulates endemically, contributing to recurrent seasonal infections. Although considered low risk, identifying and studying mutations in the S gene which encodes for the spike protein can aid screening for potential outbreaks. In total, 484 (2023: 313, 2024: 171) OC43 clinical samples collected in southeastern Ontario were whole genome sequenced using the GridION platform. Annotations were lifted from a reference genome (GenBank: AY391777.1) and had their S genes extracted and translated into protein sequences. Multiple sequence alignment (MSA) and seasonal stratification enabled analysis of intra and inter-year differences. Conservation, dictated by deviation in amino acid properties per column of the MSA, showed both years individually favour a diverse S1 region. Analyzing samples by year into their most probable consensus sequence showed 26 differing residues, 17 residing within the S1 region. A localized ring of mutations were located around the conserved 9-O-acetylated sialic acid binding site, critical for host attachment and priming the receptor binding domain to interact with target receptors. Structural analysis of these mutations with AlphaFold3 showed shifting to form a more basic, lipophilic surface around the binding site. This work highlights the mutation clock of OC43 and can serve as the basis for understanding how binding affinities for neutralizing antibodies may change as a result.

15. Ananya Chakraborty (Biomedical and Molecular Sciences) Investigating the role of sex in impaired vagal satiety sensing in obesity.

Authors: Ananya Chakraborty, David E. Reed, Alan E. Lomax.

Satiety is conveyed from the gut to the brain by vagal afferent neurons (VANs) that have cell bodies in the nodose ganglion (NG) with axons that terminate in the gut. In obesity, there is evidence of sex-dependent decreases in satiety sensation. Therefore, the aim of this study is to characterise changes in VAN satiety sensing in diet-induced obesity and determine the contribution of biological sex.

Diet-induced changes were studied in male (m) and female (f) mice fed either a high fat diet (HF) or a low-fat diet (LF) [N = 6-8 mice/group] for 5 weeks. *Ex-vivo* recordings were conducted on VAN axons attached to mouse jejunum. Changes in firing frequency were assessed in response to satiety-related hormonal (cholecystokinin, CCK) and mechanical (ramp distension) stimuli.

When compared to their lean counterparts, mHF mice had a 57% decrease in basal discharge rates ($2.97 \pm 0.52$ Hz in mLF vs. $1.42 \pm 0.30$ Hz in mHF, unpaired t-test), 68% decrease in response to CCK (unpaired t-test), and a 43% decrease in distension responses (two-way ANOVA) ($P<0.05$ in each comparison). No differences in VAN excitability were observed between fHF and fLF mice. Across all comparisons, VANs from female mice were more excitable than male counterparts.

Our findings suggest that HF diet contributes to VAN inhibition in obesity in male mice, but female mice may be resistant to this effect.

16. Natalie Wilcox (Biomedical and Molecular Sciences) Tracking immune cells in vivo: use of a photoconvertible mouse to identify tissue-origin for cell migration in inflammatory models

Authors: Natalie C. Wilcox, Nasry Z. Bouzeineddine, Amelia Campbell, Courtney A. Bannerman, Nader Ghasemlou

Accurately mapping the origin and fate of immune cells infiltrating the spinal cord after injury is essential to identify mechanisms that drive secondary damage and chronic pain. The Kikume Green-Red (KikGR) photoconvertible mouse line provides a powerful platform to label and trace cells in vivo by switching fluorescence from green to red upon 405 nm laser exposure. In this work, we developed and optimized tissue-specific photoconversion protocols for multiple immune reservoirs—including skin, spleen, liver, lymph nodes, and intestine. We established ideal laser exposure times, access techniques, and a novel "flip method" for complete small-intestine conversion. Using these optimized procedures, we demonstrated that we can track immune cells migrating from the gut to spinal cord in the acute spinal cord injury stage. Flow cytometry analysis of photoconverted cells revealed that red-labeled cells regain green fluorescence as they divide, producing daughter cells with dimmer red and increasing green signal, thereby validating the dynamic nature of KikGR tracking in proliferating immune populations. Together, these findings establish a standardized in vivo framework for using KikGR mice to dissect immune cell migration and turnover in injury states. Future work will integrate time-lapse imaging of photoconverted cells in vitro to directly visualize cell division and fluorescence recovery, enabling more precise interpretation of cell fate and proliferation during immune responses to injury.

Keywords: Spinal cord injury, immune cells, neuroinflammation, cell migration

17. Aitana Rickert Llàcer (Biomedical and Molecular Sciences) Sensory Neurons Regulate Gut-Derived γδ T Cell Migration and Pain Outcomes After Spinal Cord Injury.

Authors: Rickert-Llacer A, Wilcox NC, Bannerman CA, Dubois RM, Nobis CC, Ghasemlou N

Keywords: spinal cord injury, γδ T cells, sensory neurons, immune cell migration,

neuropathic pain

Spinal cord injury (SCI) induces a rapid influx of immune cells from peripheral reservoirs, which contributes to secondary tissue damage and persistent neuropathic pain. γδ T cells that are normally enriched in epithelial barrier tissues such as the gut and are among the earliest immune cell subsets to reach the injured spinal cord. Using the Kikume Green-Red (KikGR) photoconvertible mouse model, we established optimized protocols to track tissuespecific immune cell migration and demonstrated that a large proportion of γδ T cells originates from the small intestine in the acute post-injury period. Morphological analyses revealed that gut-resident γδ T cells shift toward a more circular, activated phenotype following SCI, with the duodenum and proximal jejunum harboring the highest cell densities. Depletion of sensory neurons markedly increased γδ T cell recruitment to the spinal cord without altering their abundance or morphology in the gut, indicating that neuronal pathways modulate later steps in migration rather than cell priming within the intestine. Collectively, these findings identify a gut-spinal cord axis for γδ T cell traVicking and highlight

sensory neurons as regulators of this process. Future studies will apply single-cell RNA sequencing to gut- and spinal cord-derived immune cells to resolve transcriptional states along the migration trajectory and to identify molecular targets for modulating γδ T cell activity as a means of reducing post-SCI neuroinflammation and chronic pain.

18. Regan Sinden (Biomedical and Molecular Sciences) Patient Perceptions of Physical Activity in Obstructive Sleep Apnea: Impact of Sleep and CPAP Therapy

Introduction: Obstructive sleep apnea (OSA) is associated with daytime symptoms and linked to poor health outcomes. While increased physical activity (PA) promotes health, individuals with OSA often exhibit reduced PA, possibly linked to OSA-related barriers to PA. This relationship, and whether continuous positive airway pressure therapy (CPAP) helps reduce these barriers, is incompletely understood.

Methods: We characterized the lived experiences of individuals with OSA (AHI: 32.6±27.8) through semi-structured interviews before (“pre”; *n*=21, m10:f11) and three months after initiation of CPAP (“3mo”; *n*=9 complete, m6:f3). Responses were analysed through hybrid thematic analysis (NVivo) and compared with quantitative actigraphy (ActivPAL) and 6-minute walk distance (6MWD) data at pre- and 3mo.

Results: Participants reported poor sleep quality and impaired daytime performance pre-CPAP. Lack of motivation and fatigue were the most reported barriers to PA. After 3mo CPAP (5.7±2.3 hours/night), all participants reported improved sleep quality and reduced burden of daytime symptoms. While some participants (*n*=3) reported higher self-perceived levels of PA at 3mo, this was not reflected in quantitative actigraphy outcomes (daily step count: pre 7508.7±4610.1 vs 3mo 6879.3±3664.0); however, functional capacity (6MWD) improved in 7/9 participants at 3mo CPAP.

Conclusions: Preliminary findings suggest that CPAP reduces daytime symptoms and perceived barriers to PA in OSA. Recruitment is ongoing to explore whether this translates to quantitative changes.

Authors: Regan M.T Sinden1, Kristin E MacLeod1, Rinusha Piranthapan1, Stephanie Ferreira1, Dhara Karvat1, Nicholas G Ricci1, Matthew D James1,2,3, Rayna Rosenblood1, Helen S Driver2,3, Christina Liak2,3, Amirali Mahpour2,3, Vanessa Martelli2,3 Sebastián Rodríguez-Llamazares2,3, Jose Alberto Neder1,2,3, Nicolle J Domnik1,2,3

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19. Ethan Thomas (Biomedical and Molecular Sciences) The HSV-2 Viral Kinase pUs3 Interacts with the Viral Protein VP11/12 During Infection

Ethan Thomas, Michelle Li, Elise Rougier, Maike Bossert, Queens University; Bruce Banfield

pUs3 is a serine/threonine kinase that phosphorylates cellular and viral proteins throughout infection. During infection, pUs3 functions together with the viral protein VP11/12 to maintain mTORC1 activation and sustain virus replication in the face of amino acid insufficiency. How pUs3 interacts with VP11/12 to promote virus replication is not completely understood. We utilized proximity-dependent biotinylation to identify proteins in proximity to either kinase-active, or kinase-dead, pUs3. HSV-2 strains were constructed that express WT pUs3, or kinase-dead pUs3, fused to the promiscuous biotin ligase miniTurbo. Infected human keratinocytes were treated with exogenous biotin from 8-9 hpi to induce biotinylation of pUs3 proximal proteins. Biotinylated proteins were purified and identified by LC MS/MS. The most prominent protein in proximity to both kinase-active and kinase-dead pUs3 was VP11/12. Co-immunoprecipitation analyses of infected cell lysates demonstrated that pUs3 was in complex with VP11/12 and immunofluorescence microscopy demonstrated co-localization between pUs3 and VP11/12 in infected cells. Strikingly, pUs3 and VP11/12 co-localized to discrete small puncta throughout the cytoplasm of WT HSV-2 infected cells and is colocalization was not dependent on pUs3 kinase activity. Our finding that pUs3 and VP11/12 are interaction partners advances our understanding of how these proteins synergize to maintain mTORC1 activity and support virus replication. We hypothesize that pUs3 and VP11/12 support infection by co-localize at a signaling hub that serves to concentrate and promote communication between factors that maintain mTORC1 activity.

20. Michelle Kuriakose (Biomedical and Molecular Sciences) Characterizing inflammasome activation in the aorta of db/db mice

<u>Michelle Kuriakose</u>[1], Mia S Wilkinson[2], Kimberly J Dunham-Snary[1,2]

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<u>Background:</u> Cardiometabolic disease (CMD) is a global health burden strongly linked to chronic inflammation and vascular dysfunction. Type II diabetes mellitus (T2DM) accelerates vascular injury through metabolic disturbances and persistent low-grade inflammation. A central pathway implicated in this process is the NLRP3 inflammasome, which activates caspase-1 and promotes the release of pro-inflammatory cytokines IL-1β and IL-18.

<u>Objective:</u> To determine whether expression of inflammasome-related genes (NLRP3, Caspase-1, IL-1β, IL-18) is altered in the aorta of db/db mice compared to controls.

Methods: All procedures were approved by the Queen's University Animal Care Committee (Protocols 2023-2390 and 2024-2520). Male C57BL/6J mice (n=30) were studied at 6 weeks of age, while leptin receptor-null db/db mice (n=12), a model of genetic diabetes, were studied at 14 weeks. Mice were anesthetized with isoflurane and euthanized via cardiac puncture. Whole aortas were excised, cleaned of perivascular adipose tissue snap-frozen in liquid nitrogen, and stored at -80°C. Total RNA was extracted, reverse-transcribed into cDNA, and analyzed by quantitative PCR (qPCR) for relative expression of NLRP3, Caspase-1, IL-1β, and IL-18, normalized to housekeeping genes.

Expected Results: We hypothesize that db/db mice will exhibit higher expression of inflammasome-related genes in the aorta compared to controls, reflecting vascular inflammatory activation in diabetes. These findings would provide mechanistic insight into the vascular complications of T2DM and lay the groundwork for future studies targeting vascular inflammation in cardiometabolic disease.

21. Christina Ferazzutti (Biomedical and Molecular Sciences) Aberrant maternal inflammation alters the composition and function of uterine macrophage subsets and increases the risk of recurrent pregnancy complications

Christina M. Ferazzutti, Tiziana Cotechini, Charles H. Graham

Department of Biomedical and Molecular Sciences, Queen's University, Kingston ON

Pregnancy loss is often linked to aberrant inflammation. Pregnancies that follow a pregnancy loss carry an elevated risk of recurrent loss, though the mechanisms remain unclear. We hypothesized that inflammation-induced alterations in the uterine macrophage composition and function contribute to this increased risk of pregnancy loss.

BALB/c female mice mated with C57BL/6 males were injected with lipopolysaccharide (LPS; 20 μg/kg, i.p.), or saline, on gestational day (GD) 10.5, resulting in complete fetal loss in 71% of dams. Uterine tissue was collected at GD 14.5 in a separate group of mice or at postnatal day 7. Another cohort with prior LPS exposure underwent a second pregnancy without further challenge to assess persistence of inflammation-induced effects. At both endpoints, uterine macrophages were profiled by flow cytometry, and F4/80$^{+}$ cells were isolated for secondary stimulation with Pam3Cys-LK4 (P3C).

Second pregnancies of dams previously exposed to LPS were characterized by reduced litter sizes and lower pup weights. During first pregnancy, recruited macrophages expanded but declined postpartum. Proportions of tissue-committed proinflammatory macrophages were stable during pregnancy and postpartum yet increased due to inflammation. Functionally, macrophages from pregnant and postpartum uteri exhibited heightened cytokine responses to P3C compared with non-pregnant controls, independent of inflammatory status, indicating pregnancy-induced innate immune memory within the uterine environment.

These findings demonstrate that aberrant maternal inflammation persistently reshapes uterine macrophage populations, compromising subsequent reproductive outcomes. This work highlights a potential immunological mechanism linking inflammation-induced pregnancy loss with recurrent complications, providing a foundation for therapeutic strategies to improve reproductive health.

FUNDING: This work is supported by Canadian Institutes of Health Research and the Cancer Research Society.

22. Vina Li (Anesthesiology) The role of glial cells in disease progression and symptoms in an animal model of multiple sclerosis

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Multiple sclerosis (MS) is a central nervous system demyelinating disease, with over 50% of people with MS (pwMS) citing pain as their primary symptom. PwMS often report a diurnal rhythm to their symptom intensities, including fatigue and pain. When normal circadian rhythms are disrupted by shiftwork schedules and sunlight hour shift at high latitudes, the risk of MS increases significantly. We therefore sought to investigate the role of circadian rhythms in pain and disease progression of MS using the experimental autoimmune encephalomyelitis (EAE) model. Female C57BL/6J mice (7-12 weeks old) were induced with EAE using myelin oligodendrocyte glycoprotein (MOG35-55) in complete Freud's adjuvant (CFA); sham mice received saline instead of MOG35-55. Pain outcomes were assessed at multiple days post-immunization using the von Frey, Hargreaves and acetone assay for mechanical, thermal and cold sensitivity respectively. Pain assays were carried out at multiple timepoints throughout the day (ZT2, 8, 14, and 20; where ZT0 corresponds to lights-on and ZT12 to lights-off). For mice tested only at peak disease, mice were behaviour-tested at ZT2 and 8, given an indomethacin injection, and tested again at ZT14. Flow cytometry, qRT-PCR and immunofluorescence were used to characterize demyelination, immune cell infiltration and immune activation in the spinal cord. The results show that mechanical hypersensitivity oscillates in a circadian pattern, with EAE mice experiencing greatest sensitivity to mechanical stimuli at ZT8. At peak of disease, pro-inflammatory cytokines *IL-1β*, *TNF-α*, *IFN-γ*, *IL-6,* and *CCL2* exhibit a pronounced circadian pattern, with the lowest expression of the cytokines at ZT8. Spinal cord infiltration by activated monocytes and macrophages shows a circadian pattern with its trough at ZT8. Myeloid cell activation in the dorsal horn at peak disease also exhibits a circadian rhythm with lower levels of activation at ZT8 compared to other timepoints. Given the reciprocating circadian oscillations in mechanical hypersensitivity and neuroinflammation, their potential interactions were further validated. After indomethacin injection, EAE mice exhibited increased mechanical hypersensitivity at ZT14, similar to ZT8. Correspondingly, indomethacin injection reduced the inflammatory cytokine expression levels and increased myeloid cell ramifications. Our data shows, for the first time, that symptom and pathology follow a circadian rhythm in the EAE model of MS, which may be regulated by circadian rhythms of neuroimmune interactions. Interactions between the nervous, immune and circadian systems merit further investigation to determine whether modulating circadian rhythm could uncover novel therapeutic targets for managing pain and disease progression in MS.

23. Rinusha Piranthapan (Cardiovascular and Respiratory Physiology / Exercise and Health) A Protocol for Evaluating Metronome-Paced Hyperpnea as a Surrogate for Exercise Testing in COPD

Rinusha Piranthapan, Matthew D James, Reginald M Smyth, Karam Alosta, Patrick J Drouin, Sandra G Vincent, Jose Alberto Neder, Nicolle J Domnik

Introduction: Dynamic hyperinflation (DH) is a marker of disease severity and bronchodilator efficacy in chronic obstructive pulmonary disease (COPD). Cardiopulmonary exercise testing (CPET) is the standard for assessing DH but is resource-intensive and burdensome. Metronome-paced tachypnea (MPT; i.e., voluntary, high-frequency breathing, Cooper 2024 AJRCCM) has been proposed as a lower-burden alternative for inducing DH, but may not adequately replicate key physiological conditions of exercise. We developed a metronome-paced hyperpnea (MPH) protocol that may better mimic CPET.

Methods: 10m:10f aged >40 with COPD and baseline hyperinflation (FRC > 120%pred) will complete three visits. Visit 1: incremental cycling CPET, Cooper's MPT, and our MPH protocol. Visits 2 and 3 (randomized: placebo or bronchodilator (salbutamol sulfate 400 μg + ipratropium bromide 40 μg)): constant work rate CPET (75% of Visit 1 peak), MPT and MPH. Key outcomes include DH, diaphragmatic electromyography as an index of inspiratory neural drive, and ratings of dyspnea.

Hypothesis: We hypothesize the MPH will more closely replicate the DH of CPET than MPT, but that both MPH and MPT will elicit lower dyspnea than CPET. MPH is expected to show greater sensitivity to bronchodilator effects.

Next Steps: Preliminary data collection is ongoing. Our findings will help inform whether standardized, low-resource protocols for assessing DH and bronchodilator efficacy in COPD patients, like MPT and/or MPH, may be feasible in settings where traditional exercise testing is inaccessible.

24. Joshua A Bougadis (Neuropsychology) Mechanistic Outcome Factors Following Litigation Settlement in Patients with Mild Traumatic Brain Injury

Joshua A. Bougadis, Sanghamithra Ramani, and Konstantine K. Zakzanis

Objective:
This study aimed to examine the role of litigation in shaping recovery trajectories after settlement in individuals who sustained a mild traumatic brain injury (mTBI). While prior quantitative studies have linked litigation to prolonged symptom persistence, the underlying mechanistic and experiential factors remain underexplored. This study used qualitative methods to investigate how litigation influences psychological, cognitive, and functional outcomes post-settlement among patients with mTBI.

Methods:
Ten adults (5 male, 5 female; mean age = 48.3 years) with previously litigated mTBIs were recruited

through an independent medical examination referral source. All participants had reached legal settlement and met criteria for uncomplicated mTBI as defined by the American Congress of Rehabilitation Medicine. Semi-structured interviews explored litigation experiences, post-settlement cognitive and emotional recovery, and satisfaction with compensation outcomes. Interviews were transcribed verbatim and analyzed using inductive coding and thematic analysis. Two independent reviewers conducted investigator triangulation to ensure thematic consistency and reliability.

Results:
Five key themes emerged: (1) the burden of litigation, (2) legitimization of symptoms, (3) does money matter, (4) social support, and (5) loss of identity. Participants described litigation as emotionally taxing, with prolonged legal procedures exacerbating psychological distress, delaying recovery, and diminishing self-concept. Financial settlements offered limited relief and were often perceived as insufficient. Strong familial and legal support emerged as protective, while skepticism about symptom validity by institutions intensified emotional distress.

Conclusion:
Litigation significantly affects long-term psychological and functional outcomes in mTBI patients. Findings highlight modifiable post-settlement factors that could inform patient-centred interventions to reduce litigation-related distress and improve recovery.

25. Abed A. Hijleh (Respiratory Physiology) Novel Paradigms for CPET Interpretation in the Investigation of Exertional Dyspnea: Dynamic Assessment of Dyspnea and Ventilation During Exercise (DyVe-X)

Abed A. Hijleh, Danilo Berton, Matthew James, Reginald Smith, Sandra Vincent, Nicolle Domnik, Devin Philips, Denis E. O'Donnell, Onofre Moran-Mendoza, J. Alberto Neder

Exercise limitation due to exertional dyspnea is characteristically multifactorial. Current cardiopulmonary exercise testing (CPET) interpretation relies on a single, discrete metric of ventilatory limitation at peak exercise (ventilatory reserve (VR)peak<15%) to ascertain a role for "the lungs" in eliciting the symptom. We aim to develop a novel CPET data analysis and interpretation software, DyVe-X, linking dynamic changes in dyspnea (Dysdyn) to dynamic dual-mechanism metrics of "excessive" (VRdyn) and "constrained" breathing (inspiratory reserve (IR)dyn). To contrast this novel approach (DyVe-X) with the current standard metric (VRpeak) across a variety of subjects with different pre-test likelihood of abnormality, data from four groups were tested: CanCOLD of ever-smokers without airflow obstruction (n=443), CanCOLD of predominantly mild-moderate COPD (n=426), RIU-SEFICE of predominantly moderate-to-severe COPD (n=359), and mild-to-severe fibrosing interstitial lung disease (n=95). In all instances, a statistically significant disagreement between VRpeak and DyVe-X was found (p<0.01). In each group, DyVe-X revealed abnormalities missed by VRpeak. Moreover, abnormalities in DyVE-X (VRdyn or IRdyn > 75th centile), but not VRpeak, were associated with greater dyspnea and lower exercise capacity (p<0.05). DyVe-X is poised to improve the yield of incremental CPET in detecting ventilatory abnormalities germane to exertional dyspnea in patients with obstructive and restrictive lung diseases.

26. Mia Wilkinson (Translational Medicine) Platelet and skeletal muscle bioenergetics correlate in preclinical type II diabetes.

Mia Wilkinson, Emily Ferguson, Justin Bureau, Dalia Miller, Michelle Kuriakose, Roan Haggerty-Goede, Jennifer Veeneman, Patricia Lima, Chris McGlory, Kimberly Dunham-Snary

Background: Type II diabetes represents a substantial global health burden. Skeletal muscle mediates >70% of systemic glucose clearance. While clinical markers identify established metabolic disease, early biomarkers of muscle metabolic dysfunction prior to overt dysregulation are lacking. Skeletal muscle bioenergetics provide mechanistic insight but require invasive sampling; blood platelets offer a non-invasive surrogate. Building on our prior correlation of platelet and muscle bioenergetics in healthy mice, we investigated whether this relationship persists in preclinical type II diabetes.

Methods: Male C57BL/6J mice (healthy, n=23) and db/db mice (diabetic, n=11) were studied. Platelet and white gastrocnemius fiber respirometry were performed. Pearson correlations were analyzed between platelet and muscle mitochondrial parameters. Group differences were assessed via unpaired t-test or Mann-Whitney test.

Results: Diabetic platelets exhibited elevated basal, ATP-linked, and maximal respiration (all $p<0.05$), while reserve capacity and coupling efficiency (CE) were unchanged. Db/db skeletal muscle displayed blunted OXPHOS and LEAK, but higher CE (all $p<0.05$). Platelet CE positively correlated with muscle CI-OXPHOS ($p=0.02$, $r=0.43$), linking platelet coupling shifts to muscle Complex I deficits. Platelet basal and ATP-linked respiration correlated with muscle CI+CII-OXPHOS (basal: $p=0.02$, $r=-0.45$; ATP-linked: $p=0.02$, $r=-0.44$) and ATP-linked (basal: $p=0.02$, $r=-0.45$; ATP-linked: $p=0.02$, $r=-0.46$) respiration; correlations were negative, reflecting divergent bioenergetic adaptations to diabetes.

Conclusion: Platelet bioenergetics correlate with muscle mitochondrial function in diabetes, supporting their potential as a non-invasive biomarker for monitoring metabolic disease progression.

27. Thomas Rollin (Translational Medicine) A method for assessing mitochondrial bioenergetics in in vitro megakaryocytes

Thomas A Rollin[1], Kimberly J Dunham-Snary[1,2]

Affiliations
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Background: Platelet mitochondrial function has growing potential as a biomarker of metabolic diseases. Mitochondrial and bioenergetic profiling of megakaryocytes (MKs), the precursors to platelets, is largely unexplored. Assessing MK mitochondrial function could contextualize platelet mitochondrial dysfunction in disease, improving their biomarker potential. The DAMI hematopoietic stem cell (HSC) line can be differentiated into MKs with either thrombopoietin (TPO) or phorbol myristate acetate (PMA). DAMI bioenergetics are unexplored and will guide future investigation of primary MKs.
Objective: To optimize a mitochondrial bioenergetic assay for DAMIs with optimal adherence, plating density, cell maturation, and differentiation substrate.
Methods: DAMIs were cultured in RPMI-1640 with 10% FBS and PenStrep. Cells were differentiated with 50μg of TPO, 1μM of PMA, or both, for 2, 4, or 6 days. Mitochondrial bioenergetics were measured using a Mitochondrial Stress Test in a Seahorse XFe24 Analyzer (SXF). Changes in basal, ATP-linked, and maximal respiration in response to varying cell density, maturation status, effector dosage, and differentiation substrates were compared.
Results: Both naïve and differentiated DAMIs produce reproducible mitochondrial respiration traces independent of adherent plate coatings. PMA differentiation resulted in significantly higher maximal respiration than TPO differentiation and untreated cells at day 4 ($P < 0.001$) and day 6 ($P < 0.001$).
Conclusions: Mitochondrial respiration can be reliably measured in DAMIs before and after differentiation, establishing a method to assess bioenergetic changes during MK maturation.

28. Mudia Iyayi (Anesthesiology/Medicine) Perioperative Anesthetic Considerations in Class III Obese Patients Undergoing Minimally Invasive and Robotic Cardiac Surgery: A Narrative Review

Mudia Iyayi, Amit Sekhon, Mohammad El Diasty

Class III obese (BMI>40 kg/m2) patients have an increased mortality risk in the perioperative period due to increased comorbidities and risk of surgical complications. Minimally invasive cardiac surgery (MICS) has emerged as a significant innovation demonstrating a decrease in complication rates compared to the traditional median sternotomy approach. However, it has unique surgical and anesthetic considerations in this patient population. This narrative review aims to provide anesthesiologists with a summary of guiding evidence.

A literature search was conducted on PubMed, Embase, and Google Scholar using relevant keyword searches with scientific articles published since 2000. Additional research articles were reviewed based on relevance and clinical impact, as determined by the authors.

The main preoperative recommendations included a detailed assessment for common obesity-related co-morbidities with optimization and individualized prehabilitation. Difficult airways should be anticipated. Intraoperatively, invasive hemodynamic monitoring, central venous access, and a low tidal volume protective lung ventilation strategy are recommended. Special attention should be paid to anesthetic drug pharmacokinetics as certain agents are dosed with total, ideal, or lean body weight. Postoperatively, early extubation and mobilization are ideal. Regional analgesia techniques such as paravertebral blocks or thoracic epidurals are reasonable to add to a multimodal analgesic regimen.

Further randomized control trials and society guidelines are required to provide focused evidence to guide anesthetists in optimizing their care for class III obese patients.

29. Declan Gainer (Translational Medicine) Targeting natural killer cell TGF-β signaling in preclinical Bronchopulmonary Dysplasia

Declan Gainer, Kassandra Coyle, Matthew Rätsep, Sofia Skebo, Martin VandenBroek, Kimberly Laverty, Yupu Deng, Shawyon Shirazi, Hugh Brady, Jennifer Sucre, Eric Vivier, Niraj Shrestha, Hing Wong, Duncan Stewart, Nicolle Domnik, Mark Ormiston

Rationale: Bronchopulmonary dysplasia (BPD) is a chronic lung disease of prematurity that is linked to impaired pulmonary vascularization, dysregulated transforming growth factor-β (TGF-β) signaling and the accumulation of senescent cells. Despite the documented role for TGF-β for suppressing the senolytic activity of natural killer (NK) cells and promoting vascular remodeling, the contribution of NK cell TGF-β signaling to postnatal lung development and the pathogenesis of BPD remains unclear.
Results: Neonatal mice with TGF-β-insensitive NK cells (Tgfbr2NK-/-) exhibited baseline reductions in pulmonary arteriolar density and alveolar patterning, but were partially protected from lung injury in an acute 3-day model of hyperoxia-induced BPD. Single-cell RNA sequencing linked these changes to the excessive clearance of senescent general capillary cells by NK cells in Tgfbr2NK-/- mice, which is pathological at baseline, but protective in hyperoxia. Lung sequencing data from human infants with BPD confirmed excessive TGF-β signaling and cytolytic impairment in NK cells. Treatment with HCW9218, a bifunctional TGF-β antagonist fused to an IL-15/IL-15 receptor-α complex (10 mg/kg, S.Q.), prevented senescent cell accumulation and rescued lung development in the acute hyperoxia-induced model of BPD.

Conclusions: This work identifies TGF-β as a rheostatic regulator of NK cell activity in the postnatal lung. Excessive NK cell TGF-β signaling contributes to impaired lung development following exposure to neonatal hyperoxia and may serve as a viable therapeutic target for human BPD.

30. Sean Lazaro (Neurology) Use of neuroimaging and EEG in asymptomatic patients in the emergency department with syncope and normal neurologic evaluation at Kingston Health Sciences Centre

Sean Lazaro, Sharleen Hoffe, Omar Islam and Gavin Winston

Choosing Wisely recommendations advise against ordering neurologic investigations in patients with typical syncope with no focal neurologic symptoms or examination findings, as these tests are not helpful in determining etiology or management. This study aimed to quantify the use of neuroimaging and EEG in neurologically asymptomatic patients with syncope presenting to the emergency department (ED) at Kingston Health Sciences Centre (KHSC). Retrospective data was collected for a 6-month period (March to August 2024) on the number of CT head, MRI head or EEG tests performed in asymptomatic patients with syncope and normal neurologic examination presenting to the ED at KHSC. Patients who suffered mild head trauma due to syncope were included. Patients with lightheadedness, vertigo, nausea, headache, confusion and focal neurologic deficit were excluded. A total of 457 patients were included. EEG was performed on 6 (1.3%), 3 of which were not indicated. Neuroimaging was performed on 79 (17.3%). Among those, 55 (69.6%) met criteria for clinical decision tools for CT head in the context of trauma. Only 4 CT head tests were not indicated. Obtaining neuroimaging or EEG in asymptomatic patients with syncope and normal neurologic evaluation presenting to the ED at KHSC occurred at an extremely low rate. Educational material on appropriate use of neurologic investigation in this population can be distributed to the referring physicians to provide positive feedback.

31. Tanvi Nandani (Biomedical Informatics) PHELEX- A community research tool for publicly available pulmonary hypertension ‘omics data

Tanvi Nandani, Ben Wood, Prusha Balaratnam, Charles Hindmarch

Pulmonary hypertension (PH) is a heterogeneous group of disorders characterized by an elevated mean pulmonary arterial pressure above 20 mmHg, leading to worsening dyspnea, progressive right heart strain or failure, and often death. While treatments can reduce severity and improve survival, PH remains highly progressive and life-threatening, negatively impacting quality of life and creating a significant economic burden1.

Over the last 15 years, efforts to understand the molecular processes driving PH have expanded through large-scale “omics” data, evident on the Gene Expression Omnibus (GEO)2, which currently hosts 1,165 records related to pulmonary hypertension with 5,765 unique samples (2,282 microarray, 2,888 next-generation sequencing, 466 protein profiling, and 129 genomic samples) from 8 species, totalling to 110 TB of data. However, mining this data requires bioinformatics expertise, multiple software tools and data processing pipelines, limiting many scientists.

To address this issue, we present PHELEX: Pulmonary Hypertension Engine for Linked EXperiments - a web-based R Shiny application with a searchable dashboard that allows users to search and filter GEO data by platform, experiment type, sample type, and species, and view its associated metadata in a clear, accessible format. The dashboard integrates with the Confidence© RNA Sequencing Analysis software3, enabling differential gene expression and pathway analysis with DESeq2, NOISeq, edgeR, or Limma, allowing users to visualize and download results. With PHELEX, scientists can easily access and analyze PH datasets from GEO within a single application, democratizing public data and accelerating discovery.

32. William Redfearn (Medicine) Effects of Music Based Therapies on Depression, Anxiety and Sleep in Patients Admitted to Psychiatry

Authors: Jessica Xiong, Arshdeep Grewal, Luna Han, Christiaan Van Zyl, Rebecca Wood, Victoria Liu, Elvina Chu

Introduction: Passive music listening (PML) and live music listening (LML) have been associated with improvements in mood and sleep in various populations, but evidence in acute psychiatric in-patients remains limited.

Methods: This study evaluated the effects of PML and LML against a on anxiety, depression, and sleep quality compared to a treatment as usual (TAU) group. Depression, anxiety, and sleep quality were assessed at baseline and post-treatment using the Patient Health Questionnaire-9 (PHQ-9), Beck Depression Inventory (BDI), Generalized Anxiety Disorder-7 (GAD-7), Beck Anxiety Inventory (BAI), and Sleep Quality Scale (SQS).

Results: 12 participants in the PML group, 9 in the LML group, and 16 in the TAU group. In the PML group, PHQ-9 scores significantly decreased from severe to moderately severe ($p = 0.02$), and BDI scores significantly decreased from severe to moderate ($p < 0.05$), while anxiety and sleep scores showed non-significant improvements. Post-treatment, LML group reported significantly lower GAD-7 scores than both PML and TAU ($p < 0.01$), and sleep quality had improved significantly ($p<0.05$). In the TAU group, PHQ-9 scores decreased ($p = 0.05$), with no significant changes in any other measures. No other significant between-group differences were observed.

Conclusions: These findings suggest that PML may reduce depressive symptoms and serve as a safe adjunct to standard psychiatric care. LML may have different therapeutic potential, with reduction in anxiety and improved sleep. Larger studies are warranted to confirm these benefits and clarify the distinct roles of PML and LML in acute psychiatric in-patient settings.

33. Oumar El-Aina (Medicine) Envisioning the Future Together: Improving system navigation of pediatric low vision resources in Ontario – Landscape Survey

El-Aina, O; Bona, M; Mann, M; Law, C*

Background
Approximately 1.7 in 1000 children aged 0–19 live with blindness or low vision, defined as impairment not correctable by surgery, medicine, or spectacles. Pediatric low vision significantly affects development, education, wellness, and health. Vision rehabilitation services (VRS) can mitigate these challenges by building adaptive skills and accessibility, but services in Ontario are fragmented, vary across regions and school boards, and lack coordination. This leaves families confused, frustrated, and without needed supports. A centralized Ontario pediatric VRS navigation resource is essential to ensure timely, equitable access.

Methods
We are conducting a cross-sectional Qualtrics survey open for 5 weeks (Sept–Oct 2025), distributed through institutional newsletters, email listservs, and Facebook groups to providers interacting with low vision patients (ophthalmologists, primary care physicians, rehabilitation professionals, and other stakeholders) and patients/caregivers with low vision within Ontario.

Questions are targeted to the individuals role in pediatric low vision to help identify strengths, barriers and experiences with pediatric VRS in Ontario.

Results
Survey responses will undergo descriptive statistical analysis of participant demographics and responses. Responses will also grouped according to the individuals role within vision rehabilitation (patient/caregiver vs health care professional vs service provider). Written responses will be thematically analyzed. Over 120 responses have been collected to date, with more expected during the collection period.

Anticipated Implications
Well-delivered pediatric VRS improve skill acquisition, independence, communication, mobility, motor skills, caregiver–child interactions, as well as caregiver knowledge. Currently, services are fragmented, inconsistent, and difficult to access. The survey will provide a framework to develop the Pediatric Ontario Vision Rehabilitation Resource (POVRR) will define care pathways, improve access and integration, and enhance family and provider experiences.

34. Rami Idris (Medicine) Barriers of Successful Implementation of Discharge Criteria at a Tertiary Heart Function Clinic; a Retrospective Cohort Analysis

Authors: Rami Idris, Ansh Patel BMSc MD, Dhruv Srikanth BHSc, Rebecca Lynn Wood MSc BSc, Drew McLean BHSc, Kelly McNabb NP MScN CCN(C), Samuel Gouett NP MScN CCN(C), Wendy Earle NP MScN CCN(C), Dianne Kirkpatrick NP MScN CCN(C), Sarah Culhane NP MN, Hoshiar Abdollah MB ChB, Joshua Durbin MD MSc, Aws Almufleh MBBS MPH

Department: Medicine

Background: Most heart function clinics cannot absorb their high volume of referrals. Effectiveness of clinic discharge protocols to offload stable patients is understudied. We herein examined predictors and barriers of implementing discharge criteria at our tertiary heart function clinic.

Methods: This is a retrospective analysis of implementation of our developed discharge protocol between August 1st, 2023, and March 31, 2024. The outcomes were successful discharge (primary), and rates of admissions/emergency department visits/mortality within 6-months of discharge (secondary).

Results: Out of 153 patients reviewed, 92 were suitable for discharge, but only 56/92 (60.9%) were actually discharged. Failure to discharge was associated with atrial fibrillation (66.7% in un-discharged patients vs 30.4% among discharged patients; $p<0.001$), having ejection fraction <50% at the last visit (77.8% vs 51.8%; $p=0.012$), having worse kidney function (mean Creatinine at initial visit 101.0 vs 86.5 μmol/L; and at last visit 106.5 vs 99.0 μmol/L) among un-discharged vs successfully discharged patients, respectively. Importantly, patients were more likely to be discharged if seen by providers with >= 10 years of experience (67.1% discharged) vs only 40.9% when seen by less experienced providers; $p=0.028$. Upon thematic analysis, the two most common reasons cited for failure to discharge were providers awaiting an extra left ventricular function assessment (48.6%) or coordinating with other cardiac care teams (27.0%).

Conclusions: Successful discharge rate from our clinic is suboptimal, which impedes timely care for new referrals. We identified several patient- and provider-specific barriers to successful discharge. More studies are needed to explore this important area.

35. Aidan Sander (Diagnostic Radiology) Comparing AI-Generated Podcasts Versus Reading for Radiology Learning

Aidan C. Sander, Benjamin Y.M. Kwan, Andrew David Chung

Background:
Podcasts are a popular educational tool. Artificial Intelligence tools such as Google's NotebookLM can generate structured podcasts from peer-reviewed journal articles.
Purpose:
This pilot study compares the effectiveness of NotebookLM generated radiology research podcasts to reading on knowledge acquisition, retention, and learner satisfaction.
Methods:
Four peer-reviewed radiology articles were converted into podcasts using NotebookLM. Four fourth year radiology residents from a Canadian residency program were assigned two articles to read and two to experience via podcast. Residents completed pre-tests, immediate post-tests, delayed post-tests, and satisfaction surveys adapted from the validated User Engagement Scale (UES).
Results:
For three of the four articles evaluated, immediate knowledge gains from reading were more than twice those observed with podcasts. Residents rated podcasts higher for satisfaction, attention, and reward but lower for usability compared to reading. Qualitatively, podcasts were described as easier to follow, but limited by their disruptive delivery style and lack of technical depth and visual aids. Articles were described as comprehensive and rich in visuals but also lengthy and dense.
Conclusion:
NotebookLM-generated podcasts offer promise as accessible and engaging learning tools but are currently limited by their lack of technical detail, tendency to repeat information, and absence of visuals. Currently, they may better serve as a supplementary learning resource to reading, providing short summaries. Future improvements in AI models may address these limitations.

36. Abby Lee (Translational Medicine) Investigating the role of myoendothelial junctions signaling in smooth muscle cell hyperproliferation in pulmonary arterial hypertension

Abby K. Lee, Julie Choi, Douglas Quilty, Donald H. Maurice, Mark L. Ormiston

Pulmonary arterial hypertension (PAH) is a disease of obstructive pulmonary vascular remodeling that leads to vasoconstriction and right heart failure. Although end-stage disease is primarily characterized by the excessive proliferation of pulmonary artery smooth muscle cells (PASMCs), the genetics of PAH are heavily biased towards disease associated mutations in endothelial-linked genes, such as, ALK1, AQP1, CAV1 and BMPR2, the gene encoding the type II bone morphogenetic

protein receptor (BMPR-II). This work investigates myoendothelial junctions (MEJs) as a potential avenue by which endothelial BMPR-II loss drives a disease phenotype in PASMCs. MEJs are endothelial projections that contact and regulate smooth muscle cell function via fenestrations in the sub-endothelial basement membrane of blood vessels. In an in vitro transwell model, depletion of BMPR-II in human telomerase immortalized human aortic endothelial cells (TeloHAECs) and pulmonary arterial endothelial cells (HPAECs) reduced the number of cellular projections formed through a porous membrane towards a vascular endothelial growth factor (VEGF)-supplemented endothelial growth medium, using both physiological and super-physiological VEGF concentrations. We have also established endothelial-PASMC transwell co-cultures, with and without BMPR-II depletion. Future work will quantify the impact of BMPR-II depletion on MEJ formation, as well as PASMC phenotype and gene expression in these cocultures. This work will contribute to the understanding of PAH, offering an avenue to link the genetic basis of disease to cellular mechanisms in the pulmonary circulation.

37. Freya Shah, Patrick Salwierz (Medical Education) Views from the Frontline: The Perceived Impact of Shorter Resident Call Shifts on Learning

Ashwin Rao, Marina Ivanova, Patrick Salwierz, Eleftheria Laios, Celine Bruce-Lepage, Freya Shah, Rylan Egan, Nancy Dalgarno, Ashly Fraser, Amy Hickey, Wiley Chung

Introduction:

Resident fatigue negatively impacts well-being, cognitive function, and patient care. Reducing duty hours may mitigate these effects. In 2020, the Queen's University General Surgery Residency Program replaced its 24-hour call system for PGY2/PGY3 residents with a Night Float System (NFS), reducing shifts to 16 hours. While evidence suggests that shorter shifts improve patient safety and resident well-being, there is limited data on the impact of NFS on resident learning.

Methods:

A qualitative study using semi-structured virtual interviews was conducted to assess the experiences of those working within the traditional and NFS call schedules. Using snowball sampling, current and former surgical residents at the Queen's University General Surgery Residency Program, and staff physicians employed at KHSC were recruited. Inductive reflexive thematic analysis was used for data analysis with NVivo.

Results:

Twenty-four interviews were conducted (11 residents, 3 former residents, 10 staff physicians). Preliminary analysis identified that views of call schedules are influenced by the following themes: Individual perceptions of wellness and learning, level of training, and medical education culture. These perceptions are backdropped by administrative decisions and program characteristics.

Discussion:

This study highlighted a proliferating perception that operative learning was the most valued learning. Junior residents sought opportunities to observe surgeries, whereas seniors aspired to operate autonomously. Residents resoundingly reported that working nights was hard on their wellness, but many appreciated that NFS expedited night calls.

38. Ranmeet Dulai (Urology) A Mixed-Methods Quality Assessment of the Cyclosporine A Protocol for Refractory Interstitial Cystitis/Bladder Pain Syndrome at Queen's University

Ranmeet Dulai, R. Christopher Doiron

Background: Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic urologic condition marked by pelvic pain and urinary symptoms. The Hunner lesion (HL) subtype is associated with more severe disease and is often refractory to standard treatments. Cyclosporine A (CyA) is an immunosuppressant with evidence for use in refractory HL-IC/BPS, but its adoption is limited by safety concerns and the need for close monitoring.
Objective: To evaluate the safety, feasibility, and perceived value of a structured CyA protocol for refractory HL-IC/BPS implemented at Queen's University.
Methods: A mixed-methods quality assessment was conducted. Adult patients enrolled in the protocol between March 2021 and July 2025 were included. Quantitative data included demographics, laboratory monitoring, symptom scores (ICSI/ICPI), treatment course, and adverse events. Qualitative data were collected via semi-structured interviews with patients and healthcare providers and analyzed for emergent themes.
Results: Nine patients were included. Most experienced stable renal function, minor and transient elevations in serum creatinine, and improvements in symptom scores. Six patients had marked clinical response, while two discontinued due to lack of benefit. Interviews revealed that patients appreciated having a new treatment option, felt supported during care, and valued structured monitoring. Suggestions for improvement included enhanced education and peer support.
Conclusion: The protocol was feasible, safe, and perceived as valuable by stakeholders. Structured implementation may facilitate broader CyA use in urologic practice.

39. Cheyan Athanasiou (Perioperative Medicine) Functional Assessment for Surgery with a Timed Walk

Cheyan Athanasiou, Duminda Wijeysundera, Daniel McIsaac, Rachel Khadaroo, Angela Jerath, Daenis Camiré, Janet van Vlymen

Every year, about 3 million inpatient surgeries are done worldwide. After these surgeries, 1 in 6 adults are expected to have a major complication. These complications can lead to death, poor functional recovery, and increased health care costs. A key risk factor for issues after surgery is fitness level before surgery. The aim of this study is to determine whether the results of a walk test, called the 6-Minute Walk Test, and some other simple tests (MET-REPAIR, NT-proBNP, grip strength) can help identify who is more likely to experience health complications within 30 and 90 days after

major elective non-cardiac surgery. This is a multicenter prospective cohort study that aims to enroll 1672 participants, at hospitals located in and outside of Canada. This trial will be the first head-to-head comparison of low-cost, practical tests that can be implemented in Canadian hospitals. The results of our study hope to provide individualized risk estimates for surgical complications and recovery, improving informed consent, patient satisfaction, and shared decision-making. These risk estimates will also guide more personalized interventions such as prehabilitation, hemodynamic optimization, and enhanced monitoring, leading to cost-effective outcome improvements.
Supporting Agencies: Canadian Institutes of Health Research (CIHR) and PSI Foundation

40. Bisola Olaseni (Medicine) Integrating Anti-Racism in Health Sciences Education: An Evaluation of GLPH 281, a Racism and Health Course at Queen's University

Bisola Olaseni, Giselle Valarezo, Natalie McGuire, Jennifer Carpenter

Systemic racism within health education contributes to persistent health inequities, yet anti-racism training remains inconsistently integrated into undergraduate health curricula in Canada. In response, Queen's University developed GLPH 281: Racism and Health, a semester-long, credit-bearing course designed through student–faculty collaboration. This study documents the co-development, implementation, and evaluation of the course within the Bachelor of Health Sciences (BHSc) program. For data collection, students (n=50) enrolled in the pilot offering, completed pre- and post-course surveys assessing knowledge, confidence, and comfort engaging with racism and health, as well as biweekly reflective assignments capturing perspectives on course content and delivery. Using a mixed-methods design, quantitative data including questions on a likert scale, will be analyzed with descriptive statistics, while qualitative reflections will undergo thematic analysis in NVivo. Preliminary findings are expected to highlight changes in student awareness, attitudes, and engagement relating to systemic racism, as well as best practices for embedding anti-racism education sustainably in health curricula. The feedback collected was used to refine the content and delivery of later iterations of the racism and health course. This research addresses critical gaps in the literature by evaluating a longitudinal, credit-bearing, and co-designed anti-racism course situated in the Canadian socio-historical context. By offering a replicable and scalable model, the study aims to inform systemic curricular reform in health sciences education and contribute to the advancement of culturally safe and socially accountable healthcare training.

41. Sarah Liu (Medical Oncology; Lung Cancer; Immunotherapy) Development of Pneumonitis in Advanced Non-Small Cell Lung Cancer (NSCLC) Patients Treated with Immune Checkpoint Inhibitors (ICIs) - A Retrospective Review

Sarah Liu, Laura Wong, Wilma M Hopman, Mihaela Mates, Andrew G Robinson, Yuchen Li, Pierre-Olivier Gaudreau, Dominique C Dabreo, Aamer Mahmud, Timothy E Owen, Andrea S Fung, Sofia Genta

Objective
To evaluate the incidence of pneumonitis in NSCLC patients treated with ICIs and identify risk

factors contributing to its development.

Methods

This retrospective chart review included patients with metastatic NSCLC who received at least 1 cycle of pembrolizumab at the Cancer Centre of Southeastern Ontario between 2016-2021. Collected data included demographic information, comorbidities, cancer stage and subtype, treatment history, and the presence and severity of ICI-related toxicities.

Results

Among the 159 patients included, 79 (49.7%) were male and the median age was 69 years. Overall, 62 patients (39%) experienced immune-related toxicity of any location and grade. Median time to onset of toxicity was 43 days from pembrolizumab initiation. Pneumonitis of any cause (both ICI-related and radiation-related) was observed in 23 patients (14.5%). Among all pneumonitis patients, 11 (47.8%) were Grade 3 or higher, including 2 cases (8.7%) of Grade 5 (fatal) pneumonitis. There were no statistically significant risk factors identified for pneumonitis, although low FEV1 % predicted (p=0.060), baseline COPD (p=0.063), low DLCO % predicted (p=0.076), and greater smoking pack-years (p=0.088) approached significance.

Conclusion

Our findings suggest that poor baseline lung function may be associated with the development of pneumonitis. However, this study was limited due to low statistical power. Radiation treatment data collection is ongoing to explore the potential effect of radiation dose, fractionation, and technique on the development of pneumonitis.

42. Golnar Taheri (Neuroscience) Improving the NeuroD1-AAV-based gene therapy intracerebral injection protocol for optimal neuronal recovery

Golnar Taheri, Bruce Masotti, Gabriel Ramirez Garcia, Lydia Wan, Maddy Wilson, Douglas J Cook

Ischemic stroke increases the number of glial cells, such as astrocytes, and causes neuronal death, disrupting the neuron-to-glia balance and contributing to neurodegeneration. Prior studies have demonstrated that treatment with NeuroD-adeno-associated virus (NeuroD1-AAV) effectively facilitates astrocyte to neuron transdifferentiation and enhances motor function in animal models. However, to advance towards clinical applications, modifications were necessary in the plasmid structure, resulting in the development of the 001 prototype. The present study examines the therapeutic potential of the 001 prototype, aiming to evaluate its efficacy in comparison to NeuroD1-AAV-based gene therapies while also assessing the effects of gene therapy on the lower spinal cord, particularly in relation to alterations in the cortico-spinal tract. Twelve non-human primates (NHPs) underwent middle cerebral occlusion surgery. Following a fourteen-day post-stroke recovery, subjects received intracerebral injections of the drug at low and high doses. Nine months later, brain tissues were collected and stained with neuronal (NEUN, MAP2, NF) and glial (GFAP, IBA1) markers. Luxol fast blue staining assessed demyelination in the corticospinal tract. Our results indicate that both protocols effectively rebalance the neuron-to-glia cell ratio by decreasing GFAP+ cells in the low-dose and high-dose NHPS ipsilateral hemispheres. Significant demyelination of the corticospinal tract has been observed in the control group, while it appears to be reduced in NHPs receiving the lower dose of the medication.

43. Blake Noyes (Eye movements in depression) Patients with depression gaze less at positive and negative faces than controls in a novel free-viewing video task

Noyes, B.K., Booij, L., Yep, R., Riek, H., Pitigoi, I.C., Brien D.C., White, B.J., Khalid-Khan, S., & Munoz, D.P.

Previous research has investigated the extent to which depressed individuals display attention bias to emotional stimuli during free-viewing (FV) tasks – typically finding a decrease in attention to positive stimuli, and an increase to negative stimuli. However, the majority of such research is conducted in adult samples and utilizes static images. This poses a problem because 1) depression typically emerges in adolescence, thus research within this age group is imperative and 2) videos as opposed to images offer more translation to real-world context. To investigate attentional biases of adolescents with depression we developed a novel FV task, which includes 10 minutes of neutral clips (e.g., cityscapes, nature) and 10 minutes of clinical-oriented clips (including positive/neutral/negative faces). The study sample included 50 adolescents with depression (mean age [M]=15.93, 40 female) recruited from a local psychiatric outpatient program and 66 age- and sex-matched healthy controls (M=16.01, 51 female) recruited from the community. All participants completed FV and self-report questionnaires for psychiatric symptoms. We found that depressed adolescents gazed at faces less overall and had a decrease in gaze towards all face valences – positive, neutral, and negative – contradictory to prior research. This distinct pattern in viewing behaviour demonstrates that eye tracking is a feasible technique to distinguish adolescents with depression from healthy adolescents and could identify potential eye movement markers for detection purposes.

44. Amin Jalali (NeuroImaging, Epilepsy) Multi-Method Quantification and Spatial Visualization of Brain Asymmetry from ASL Perfusion Data

Amin Jalali, Gavin Winston

Brain hemispheric asymmetry assessment is crucial for understanding neurological conditions, including epilepsy, stroke, and neurodevelopmental disorders. We developed an open-source Python toolkit for quantifying cerebral perfusion asymmetries from FreeSurfer parcellated Arterial Spin Labeling (ASL) data using standardized MRI segstats output processing. The framework implements mathematical algorithms, including laterality indices, statistical effect size measures (Cohen's d and z-scores), a volume-corrected normalization algorithm, robust median-based calculations, and information-theoretic approaches, such as entropy differences and fold-change analysis. Automated bilateral region pairing processes subcortical and cortical anatomical structures, maintaining FreeSurfer SegID ordering for reproducible cross-study analysis. Spatial visualization generates NIfTI maps compatible with FSLeyes, MRIcroGL, and AFNI software, with multi-method heatmaps utilizing consistent colormaps for intuitive interpretation. Comprehensive statistical validation incorporates multiple significance thresholds (|LI| > 0.1 for clinical significance), inter-method correlation analysis, and automated quality control frameworks with outlier detection. This standardized computational framework addresses needs for objective, reproducible asymmetry quantification in neuroimaging research, enabling seamless integration with established FreeSurfer workflows across clinical and research institutions. All code, documentation, and example datasets are made freely available to the neuroimaging community.

45. Cassidy Bretney (Critical Care Medicine) Investigating Patterns of Cerebral Oxygenation in ICU Patients with Delirium using fNIRS: A Feasibility Study

Cassidy Bretney, Dr. Gord Boyd

Delirium is an acute state of altered consciousness affecting perception, cognition, and memory. It occurs in up to 80% of Intensive Care Unit (ICU) cases and is associated with worse outcomes, including prolonged hospitalization, ventilation, higher readmission rates, and increased mortality. Despite its prevalence and impact, evidence-based therapies remain limited, mainly due to gaps in the understanding of the pathophysiology.

Cerebral oxygenation, as measured by Near-Infrared Spectroscopy (NIRS), has been shown to be lower in critically ill patients with delirium compared to non-delirious patients. Additionally, functional NIRS (fNIRS) studies in children demonstrated widespread frontal lobe suppression during postoperative delirium. However, fNIRS has not yet been used to investigate delirium in critically ill adults.

This study aims to address this gap by employing fNIRS alongside the standard CAM-ICU delirium screening tool in ICU patients. The objective is to advance understanding of delirium pathophysiology by exploring cerebral oxygenation patterns. Specifically, this feasibility study has three aims: (1) to determine the practicality of using fNIRS in critically ill patients, (2) to examine changes in cerebral oxygenation patterns and their association with delirium, and (3) to assess whether fNIRS can provide early insights into delirium duration and severity.

This work seeks to establish fNIRS as a novel tool to investigate delirium in the ICU and to inform future development of targeted management strategies.

46. Matthew Suppa Modrusan (Epilepsy) Automated and Interpretable Detection of Hippocampal Sclerosis (AID-HS) for Presurgical Assessment: Implementation at a District Epilepsy Centre

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In patients with temporal lobe epilepsy (TLE), resective surgery can render many seizure-free. However, hippocampal sclerosis (HS)—a common TLE pathology—often eludes detection on MRI, causing surgical delays. Advanced MRI postprocessing can improve detection but requires real-world validation. We introduced AID-HS—a tool that quantifies hippocampal morphology to generate probabilities for left HS, right HS, or no asymmetry—into our presurgical pathway to assess its utility.

After initial case review in epilepsy surgery rounds, patients underwent 3T MRI. Scans were subsequently postprocessed with AID-HS. Findings and concordance were recorded for retrospective cases (with histopathology) and prospective cases under review.

In the retrospective cohort (n=8), AID-HS correctly predicted unilateral HS in both confirmed cases. It also flagged bilateral HS in 5 patients without histopathological evidence of HS. In the prospective cohort (n=9), bilateral HS was flagged in 4 cases. Across cohorts, bilateral HS warnings were associated with 10% lower total brain volume (TBV) (1046 $cm^3$ vs 1165 $cm^3$), suggesting hippocampal volume loss in the context of global brain atrophy.

AID-HS is useful for unilateral HS detection. However, global brain atrophy may produce spurious bilateral HS warnings. Ongoing work aims to train models that incorporate additional imaging data and TBV correction.

Southeastern Ontario Academic Medical Organization Innovation Fund.

47. Evelyn Yach (Pathology) Quantitative Nuclear Grading Features from Whole Slide Non-Muscle Invasive Bladder Cancer Images

Evelyn Yach, Katherine Lindale, Betty Wang, Susie Choi, T. Regan Baird, Ava Slotman, Amber Simpson, David M. Berman.

Non-muscle invasive bladder cancer (NMIBC) patient interventions are titrated to each patient's needs based, in part, by cancer grading. Pathologists grade bladder cancer by evaluating prognostically relevant features across whole slide images (WSIs). However, subjectivity and unclear guidelines in current grading methods undermine reproducibility and prognostic power. To assist pathologists, we are developing efficient image processing techniques to objectively measure grading features in digital whole slides and relate them to patient outcomes. Using a cohort of patients with stage Ta NMIBC, 163 WSIs were processed using imaging software (Visiopharm, Hørsholm, Denmark). A U-Net deep learning algorithm was trained to automatically isolate regions of interest (ROIs) enriched for cancer cells. We detected cancer cell nuclei and mitotic figures within ROI, and measurements for 12 quantitative grade-based nuclear features were digitally collected. These features were used to train a random survival forest (RSF) to predict patient recurrence. In testing ROIs, initial image processing models identified mitotic nuclei with 80% or greater accuracy, frequently identifying mitotic figures that manual feature annotation missed. RSF models run in small ROIs achieved a testing C-index of 0.70 (95% CI: 0.66-0.70). In future work, we will validate these models on external NIMBC cohorts and develop models to predict cancer progression. This work aims to transform NMIBC grading by providing accurate and clinically applicable information for both pathologists and their patients.

48. Flourish Adebayo (Neuroendocrine Neoplasms: Data Science Approaches) Fuzzy Classification for Discriminating Neuroendocrine and Non-Neuroendocrine Tissues

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Neuroendocrine neoplasms (NENs) are diverse group of tumors and cancers characterized by the expression of specific molecular markers. Established neuroendocrine markers include chromogranin A (CHGA), synaptophysin (SYP), and insulinoma-associated protein 1 (INSM1), as well as the loss of Yes-associated protein (YAP). Recently, microRNA-375 and microRNAR-7 have emerged as novel diagnostic markers of NENs. Using The Cancer Genome Atlas (TCGA), we investigated the expression of these six markers across NEN and non-NEN tissues. Stable reference genes and microRNAs were identified through locally estimated scatterplot smoothing (LOESS) modelling and variability filtering to enable robust cross-cancer comparisons. A Mamdani Fuzzy Inference System was then developed, integrating the six markers as inputs to predict NEN status. Membership functions were optimized using multiple curve-fitting approaches and evaluated with 10-fold cross-validation. Rule-based systems were constructed and defuzzied, with the centroid method providing the most consistent performance. The fuzzy classifier distinguished NEN from non-NEN tissues yielding AUROC = 1.00 and Accuracy = 99.15% (Precision = 1.00, Recall = 0.98, F1-score = 0.99), but also showed cases where negative samples were misclassified as positive and vice versa. These observations will be further examined with additional datasets to clarify their biological and clinical significance .

Keywords: neuroendocrine neoplasms, fuzzy classification, miRNA, mRNA, TCGA

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49. Maria Avgeropoulos (Hematology) Assessing the Utility of Genomic Testing to Achieve Specific Diagnoses in Patients with Bleeding Disorder of Unknown Cause

Maria Avgeropoulos, Mackenzie Bowman, Megan Chaigneau, Julie Grabell, David Good, David Lillicrap, Andrea Guerin, Jennifer Leung, Paula James

Achieving a clear diagnosis in patients with suspected bleeding disorders is often challenging, with 50% of patients being labelled as bleeding disorder of unknown cause (BDUC). BDUC is a diagnosis of exclusion, used to label patients who have a positive bleeding phenotype yet lack confirmatory hemostatic laboratory testing. The aim of this study was to address the diagnostic gap and evaluate the utility of integrating early genetic testing in achieving a clear diagnosis in patients with a BDUC phenotype. A total of 25 patients, all female, (mean age 44.8 years), with BDUC, were recruited from Hematology clinics at Kingston Health Sciences Centre. Patients underwent a molecular testing

first strategy by having sequencing of known bleeding disorder genes on a whole genome backbone. Variants were filtered and underwent expert review, identifying at least one or more relevant pathogenic, likely pathogenic and/or uncertain significance variants in seventy-two percent of patients. Following analysis by a multidisciplinary team, thirty-two percent of patients were classified as having found a complete or a partial explanation for their bleeding phenotype, and sixty-four percent had a possible or no explanation for their bleeding phenotype. Results are encouraging regarding the utility of molecular diagnostics in these previously undiagnosed patients. Further study is needed to clarify the contribution of variants that could potentially impact the patient bleeding phenotypes.

50. Ana Maria Vera Rodriguez (Oncology and Immunology) Immunosenescence Characterises Failure of Bacillus Calmette-Guérin Therapy in Patients with Non-Muscle Invasive Bladder Cancer

Ana Vera-Rodríguez, Andrew Garven, Jean-François Paré, Alexandra Robins, Rohan Sampy, Richard Nauman, Madhuri Koti, Lynne-Marie Postovit, Andrew Craig, Peter Greer, Robert Siemens, Tiziana Cotechini, David Berman, Amber Simpson, and Charles H. Graham

Introduction: A majority of bladder cancer patients are initially diagnosed at a stage where the cancer remains confined to the bladder mucosa, designated as non–muscle invasive bladder cancer (NMIBC). Intravesical administration of Bacillus Calmette–Guérin (BCG) is the gold standard therapy to mitigate recurrence risk following surgical resection of high–risk NMIBC. While BCG is established as a clinically beneficial immunotherapy, around 50% of patients recur or progress to more aggressive muscle–invasive cancer. Unfortunately, reasons why some NMIBC patients fail BCG therapy remain unknown. Our research aims to fill this knowledge gap.

Methods: Peripheral blood mononuclear cells were isolated from two blood draws of 16 patients with intermediate– and high–risk NMIBC, the first preceding treatment and the second following the fifth BCG intravesical instillation (n = 32 samples). Patients were classified as non–responders (n = 8) experiencing disease recurrence within one year and responders (n = 8) having no recurrence within two years. Single–cell RNA sequencing data was analyzed using differential expression and pathway enrichment analysis to compare across responders and non–responders.

Results: Monocytes of non–responders displayed an immunosenescence phenotype, characterized by a pro–inflammatory state and preparatory metabolic activation that may underlie treatment resistance ahead of BCG initiation. BCG responders demonstrated attenuated immune activation prior to therapy followed by heightened activation of immune and metabolic pathways post–BCG.

Conclusion: BCG non-responder patients exhibited immune dysfunction characterized by metabolic and inflammatory disturbances.

52. Julia Schuurmans (Multiplex Immunofluorescence, Tumour Microenvironment) Optimization of a Pan-Membrane Marker for 9-Plex Multiplex Immunofluorescence Using Opal-TSA Technology: Addressing Challenges of Stripping, Cross-Reactivity, and Blocking

Julia Schuurmans, Logan Engle, Andrew McLellan, Eman Radwan, Michael Fotheringham, Ben Green, Joel Sunshine, Mide Olanrewaju, Katie Brewer, Janis Taube, Tricia Cottrell

Background
Multiplex immunofluorescence (mIF) enables spatial profiling of the tumour microenvironment (TME), but extraction of single-cell data requires precise cell segmentation. This is often suboptimal for large, irregular tumor cells, leading to inaccurate quantification and missed membrane-localized proteins (e.g., PD-L1). AI-based segmentation algorithms leverage membrane and nuclear signals for accurate performance, but inconsistent membrane staining limits their application. We aimed to optimize a pan-membrane marker for consistent membrane delineation in mIF.
Methods
A CD44, CD45, and ATPase antibody cocktail was designed with board-certified pathologists (JT/TRC) to label tumour and lymphocyte membranes. Fluorescent signal optimization involved titration of primary, secondary, and fluorophore reagents. Once optimized in single-plex, the cocktail was incorporated into a 9-plex mIF panel; PD-1, PD-L1, FoxP3, MPO, CD8, CD163, pan-cytokeratin (pan-CK), and DAPI. Validity was defined as <5% difference in positive staining vs IHC.
Results
Pan-membrane was optimized in single-plex at dilute concentrations (CD44: 0.066 μg/μL; CD45: 0.156 μg/μL; ATPase: 0.007 μg/μL). Cross-reactivity to pan-CK was resolved by adjusting the staining order. Membranous PD-L1/PD-1 stains partially blocking the cocktail were merged for segmentation algorithm input. Combination yielded more accurate cell boundaries than pan-CK-dependant segmentation (32.5% ±10% increase in mean cell area). Positive Pixel-based validation showed ±4% concordance between mIF and chromogenic IHC.
Conclusion
Our approach demonstrates a validated strategy for improving membrane delineation in mIF–critical for TME spatial analysis and AI-assisted segmentation.

53. Timothy Nunes and Alexandra Hauser (Healthcare Teamwork and Patient Safety) Team Resilience and Adaptability Beyond the Operating Room: A Scoping Review

Timothy Nunes*, Alexandra Hauser*, Eleftheria Laios, Wiley Chung. *These authors contributed equally to this work.

Resilience and adaptability are essential for healthcare teams working in high-pressure environments. Team resilience is the collective capacity of healthcare teams to adapt, recover, and sustain safe performance when unexpected deviations occur in the delivery of patient care. While prior studies have examined these dynamics in operating room (OR) teams, less is known about resilience in non-OR team settings—such as emergency departments, intensive care, and palliative care. This scoping review aims to map existing research on team resilience and adaptability across non-OR healthcare environments, identify gaps, and synthesize insights for novel team resilience frameworks to optimize patient safety.

Searches were conducted in MEDLINE, Embase, APA PsycInfo, and CINAHL, yielding 1092 unique references. Title and abstract screening removed 904 studies, with 160 moving to full-text review, which is ongoing. Included studies examine resilience, adaptability, or related human factors in non-OR patient care teams with respect to patient safety. Screening and extraction stages are conducted in duplicate according to Joanna Briggs Institute and PRISMA-ScR review guidelines.

The results will provide a high-level assessment of the contexts and extent to which resilience has been studied in healthcare teams, including analysis of existing conceptual models and frameworks. This review will highlight commonalities and unique challenges across clinical environments and contribute to evidence-based strategies for strengthening resilience, collaboration, and patient outcomes.

54. Jaya Pardy (Indigenous Health Scholars Network) Mapping Indigenous Health Research at Queen's University: Building Toward a Collaborative Scholars Network

Jaya Pardy

This project aims to systematically identify and describe the landscape of Indigenous health research at Queen's University and affiliated institutions. Through interviews with key informants engaged in Indigenous health scholarship, the study will document areas of focus, along with the use of Indigenous health policy frameworks and ethical guidelines used to guide research engagement with Indigenous Peoples. The objective is to assess current strengths and gaps in institutional research practices related to Indigenous health. Insights from this work will inform the development of an Indigenous Health Scholars Network at Queen's University to support collaboration, resource-sharing, and the advancement of community-informed, culturally safe research.

55. Abbey Politeski (Immunology) Tissue Resident Macrophages Expand in Skeletal Muscle Regeneration

Abbey L. Politeski, Jasleen Kaur, Jiarui Che, Sarah A. Dick

Skeletal muscle is essential for locomotion, force generation, metabolism, and thermoregulation. Under normal conditions, muscle damage is efficiently repaired through regeneration driven by satellite cells, the resident muscle stem cells. Disruptions in homeostasis from traumatic injury or muscular dystrophies impair regeneration and muscle function, diminishing quality of life. Macrophages are key regulators of homeostasis, inflammation, and repair, but how their dysregulation contributes to pathology and fibrosis in muscle wasting diseases remains unclear. To explore macrophage heterogeneity in healthy and regenerating muscle, we analyzed publicly available single-cell RNA sequencing datasets following acute cardiotoxin injury. We identified diverse monocyte-derived macrophage (MDM) populations and three subsets of tissue-resident macrophages (TRMs) in healthy muscle, which were ontogenetically and functionally distinct from MDMs. TRM functions in regeneration remain poorly defined, largely due to challenges distinguishing them from infiltrating MDMs.
We found TRMs change dynamically during regeneration and engage in ligand-receptor interactions with myoblasts, fibroblasts, endothelial, and immune cells. Using a TRM-specific fate-mapping

mouse model, we tracked TRMs following injury, observing a proliferative burst in the early-intermediate regenerative phase, which coincided with MDM phenotype shifts. Overall, these findings describe the temporal kinetics of macrophage subsets during muscle regeneration, highlighting previously understudied TRMs. Ongoing work with a TRM depletion model will directly assess their functional role, with the long-term goal of informing therapies to enhance regeneration in chronic injury and degenerative disease.

56. Rachel Di Iorio (Global health; Sexual and reproductive health) Reducing Contraceptive Stigma and Promoting Sexual Health Empowerment Among Adolescent Girls in Tanzania

Di Iorio, Rachel; Yeates, Karen; Kiwelu, Anisia; Mruma, Doreen; Ngolle, Elizabeth; Jumanne, Mwasiti; West, Nicola; Logie, Carmen; Butler, Lisa; Mmbaga, Blandina

Background
Despite free access to contraceptive services in Tanzania, adolescent girls and young women (AGYW) often avoid clinics due to stigma and perceived promiscuity. These barriers undermine reproductive autonomy and sexual empowerment. Interventions targeting contraceptive stigma are understudied; therefore, a participatory workshop program was adapted for stigma reduction among AGYW.
Methods
Building on the London School of Hygiene and Tropical Medicine's HIV stigma-reduction guide, we piloted a culturally adapted program targeting sexual and reproductive health (SRH) and contraceptive stigma among 40 AGYW in urban and rural Kilimanjaro. Workshops combined interactive activities with peer discussion. Mixed-methods evaluation included pre/post surveys (Contraceptive Use Stigma [CUS], Adolescent SRH stigma [ASRH], and Sexual Double Standards [SDS] scales) and thematic analysis of focus group discussions.
Results
Workshops were feasible, acceptable, and fostered strong engagement. Quantitative findings suggest reductions in CUS ($p < .001$) and internalized stigma ($p = .029$), with more supportive attitudes toward condom use and fertility. Enacted stigma scores increased ($p = .001$), which may indicate greater recognition of community-level discrimination. Qualitative findings suggest improved confidence discussing SRH, more supportive views of contraception, and critical reflection on gender norms.
Conclusion
This pilot suggests that stigma-reduction workshops are a promising approach to improving SRH attitudes, reducing contraceptive stigma, and fostering empowerment among AGYW. Findings will guide the development of a larger-scale trial to strengthen reproductive autonomy and gender equity in Tanzania.

57. Maya Baloula (Pediatric Developmental Disability Research) Short-Term Effects of Creative Movement-Based Interventions on Social Reciprocity and Motor Coordination in Children with Autism Spectrum Disorder: A Literature Review

Maya Baloula (1), Ben Yang (2), Akshaya Adabala (3) , Vera Qian (4) - (1) Health Sciences, Queen's University, Kingston, ON, Canada (2) Department of Psychology, University of Toronto Mississauga, Mississauga, ON, Canada (3) Central Peel Secondary School, Brampton, ON, Canada (4) Oakville Trafalgar High School, Oakville, ON, Canada

Children with Autism Spectrum Disorder (ASD) frequently experience difficulties in social reciprocity, motor coordination, and behavioral regulation, limiting participation in traditional physical education. Creative Movement-Based Interventions (CMBIs)—including dance, yoga, martial arts, and music-based activities—have been proposed as accessible alternatives aligning with sensory and regulatory needs. This systematic review, conducted in accordance with PRISMA guidelines, synthesized studies published between 2000 and 2025 that included children under 18 years of age with a formal ASD diagnosis, incorporated creative movement delivered in-person or via telehealth, and reported short-term outcomes in motor, social, or behavioral domains. Thirty studies met inclusion criteria with 10 reported moderate-to-high improvements in social communication (e.g., eye contact, imitation, peer engagement), 9 reported moderate-to-high motor improvements (e.g., balance, bilateral coordination, sequencing), and 8 reported moderate behavioral regulation gains (e.g., emotional control, attentional focus). Randomized controlled trials generally reported stronger outcomes, although some found no clinically significant differences in motor improvements compared with general movement interventions. While findings suggest CMBIs are engaging and beneficial for children with ASD, heterogeneity in study design, intervention content, and outcome measures limits generalizability. Future research should incorporate standardized assessments and longitudinal designs to establish the sustained impact and generalizability of CMBIs.

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