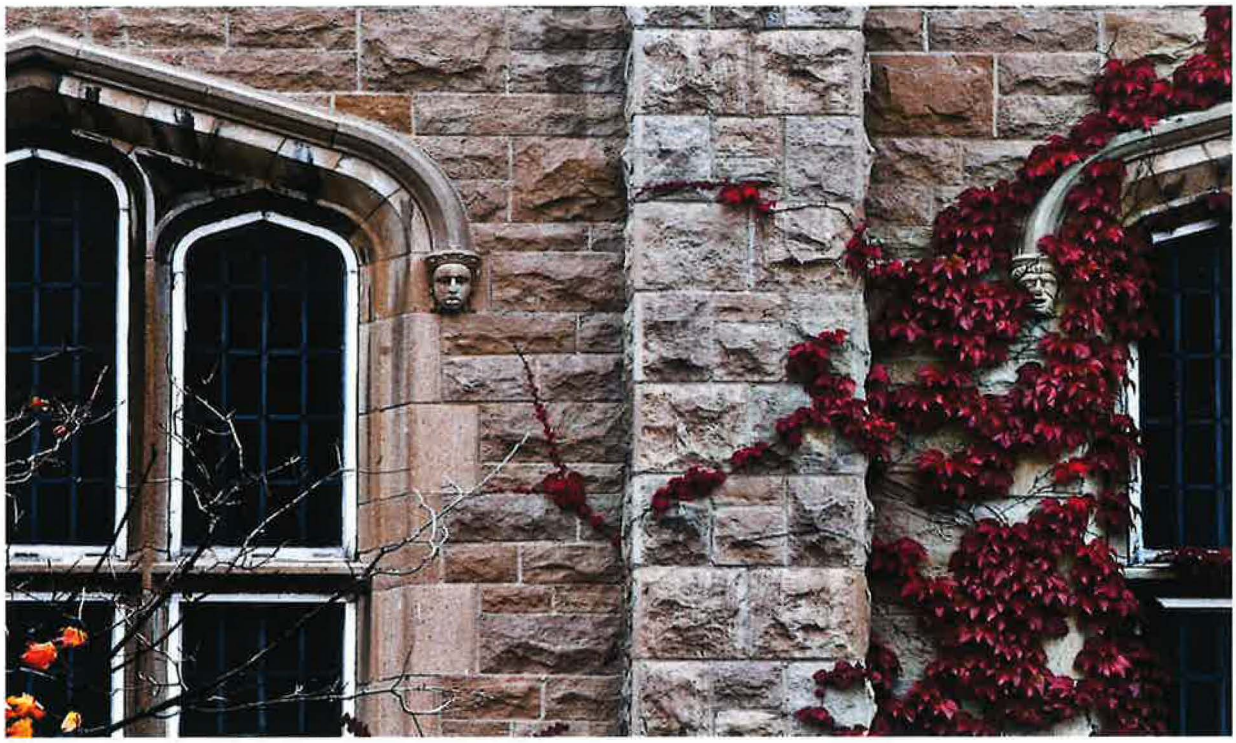
The Twenty-Fourth Annual Scientific Meeting for Health Science Research Trainees
Faculty of Health Sciences
Queen's University

Tuesday, June 28th, 2022
Queen's School of Medicine & BioSciences Atrium



Members of the Organizing Committee

Alan Lomax, Medicine and Biomedical and Molecular Sciences
Anita Lister, Biomedical and MolecularSciences
Andrew Craig, Biomedical and Molecular Sciences
Brian Bennett, Biomedical and Molecular Sciences and Centre for Neuroscience Studies
Chandra Tayade, Biomedical and Molecular Sciences
David Natale, OB/GYN and Biomedical and Molecular Sciences
Gunnar Blohm, Centre for Neuroscience Studies
Katrina Gee, Biomedical and MolecularSciences
Lois Mulligan, Pathology and Molecular Medicine, Division of Cancer Biology and Genetics
Louise Winn, Biomedical and Molecular Sciences
Madhuri Koti, Biomedical and Molecular Sciences and Obstetrics and Gynaecology
Maria Valez, Department of Obstetrics and Gynecology
Mary White, Health Sciences
Michael Rauh, Pathology & Molecular Medicine
Olivia Giovannetti, DBMS GSC President
Peter Greer, Cancer Research Institute
Sam Basta, Biomedical and Molecular Sciences
Sheela Abraham, Biomedical and Molecular Sciences

Session Chairs

Che Colpitts
Michael Rauh
Nader Ghasemlou

Members of the Adjudication Team

Alison McCallion
Brooke DeCarlo
Byron Hunter
Christina Ferrone
Connor Scholl
Daniella Gilmour
Danielle Sisnett
Daria Ostroverkhova
Dominique Hancock
Donya Hayati
Emmanuelle LeBlanc
Ethan Thomas
Farzaneh Afzali
Golnar Taheri
Habibe Dogan
Hannah Wood
Harshavardhan - Lingegowda
Jasleen Jagayat
Juliette Wilson-Sanchez
Katie Dover
Katie Zutautas
Kaylee Punter
Kayne Park
Keegan Turner-Wood
Lauren Brown
Madison Robertson
Manisha Blaskevitch
Matt Jalink
Megan Cull
Mir Sanim Al Mamun
Natasha Iaboni
Navjit Gaurav
Noor Shakfa
Pooja Sridhar
Priyanka Yolmo
Rhiannon Hilton
Richard Nauman
Sadaf Rahimi
Safara Holder
Victoria Lalonde

Oral Presentation Adjudicators

Aurelie Brecier
Jean-Francois Pare
Kshitiz Singh

Acknowledgments

A special thank you to Mary White for her invaluable assistance in organizing this meeting.

The Twenty-Fourth Annual Scientific Meeting for Health Science Research Trainees

Faculty of Health Sciences

Queen's University

Tuesday, June 28th, 2022

Queen's School of Medicine and BioSciences Atrium

Tuesday, June 28th, 2022

8:00 –8:45 am	***Registration - School of Medicine: The Britton Smith Foundation Lecture Theatre (132A) & The David M C Walker Atrium***
	Poster set-up and registration for morning participants - BioSciences Atrium
	Oral Presentations - School of Medicine, Room 132A
8:45 – 9:00 am	*Welcome and Introduction* **Dr. Chandra Tayade, Associate Dean, Graduate and Postdoctoral Education, Faculty of Health Sciences**
	Introductory Remarks **Dr. Jane Philpott, Dean, Faculty of Health Sciences**
9:00 – 9:30 am	***Keynote Speaker*** **Exploiting AI in the Search for Real World Evidence in Cancer** Dr. Amber Simpson, School of Computing and Biomedical and Molecular Sciences

Oral Presentation – Session 1: SOM 132A

Chair: Dr. Che Colpitts

9:35 – 9:47 am	Isabella Pellizzari-Delano: **Characterizing the role of IFNg-inducible guanylate binding proteins in restricting coronavirus replication**
9:47 – 9:59 am	Sono Khan: **Characterizing the interaction between vitamin D and the parathyroid gland in chronic kidney disease**
9:59 – 10:11 am	Kiera Liblik: **The Female Risk factors for post-Infarction Depression and Anxiety (FRIDA) Study**
10:11 – 10:23 am	Keira Frosst: **A DNA Methylation-Based Liquid Biopsy for Monitoring Breast Cancer**
10:25 – 10:45 am	*Coffee Break* - BioSciences Atrium
10:45 – 12:15 pm	Poster Presentations - BioSciences Atrium
12:15 – 1:00 pm	Lunch/Poster Set-Up - BioSciences Atrium
1:00 – 2:30 pm	Poster Presentations - BioSciences Atrium

Oral Presentation – Session 2: SOM 132A

Chair: Dr. Michael Rauh

2:30 - 2:42 pm	Paola Nasute Fauerbach: **Low mammography screening participation by women ages 40 to 49 may contribute to poor breast cancer survival rates in Southeast Ontario**
2:42 - 2:54 pm	Sadaf Rahimi: **Investigating the role of Tumor Associated B cells in Bladder Cancer Progression**
2:54 - 3:06 pm	Courtney Ann Bannerman: **The role of the gut microbiome in spinal cord injury pain and neuroinflammation**
3:06 - 3:18 pm	Shuxiang Li: **DNA methylation cues in nucleosome geometry, stability, and upwrapping**
3:18 - 3:30 pm	James King: **Evidence of transient receptor potential melastatin 3 (TRPM3) channel sensitization in a model of colitis**
3:30 - 3:45 pm	*Coffee Break*

Oral Presentation – Session 3: SOM 132A

Chair: Dr. Nader Ghasemlou

3:45 – 3:57 pm	Parsa Balalaie: **Stimulus-locked muscle responses to visual disturbances are impacted by urgency and certainty to move**
3:57 – 4:09 pm	Megan Cull: **Sca-1 surface expression in trophoblast stem cells identifies multipotent cells that proliferate in response to hypoxia and are phenotypically unique**
4:09 – 4:21 pm	M. Martin VandenBroek: **Circular RNA profiling of human pulmonary artery endothelial cells identifies novel BMPR2-derived regulators of endothelial proliferation and apoptosis**
4:21 – 4:35 pm	Julia Hellas: **Investigating the molecular mechanisms of a putative spreading depolarization activator**
4:35 – 5:00 pm	Concluding Remarks and Awards - SOM 132A
5:00 – 7:00 pm	Reception Cash Bar (Small snack will be provided) - SOM: The David M C Walker Atrium

Oral Presentations

Session One

Characterizing the role of IFN -inducible guanylate binding proteins in restricting coronavirus replication.

(Field: Microbes, Immunity and Inflammation)

Isabella Pellizzari-Delano, Nicole Coman and Che C. Colpitts
Department of Biomedical and Molecular Sciences, Queen's University, Kingston ON, Canada

The COVID-19 pandemic illustrates the urgent need for new therapeutic approaches against emerging pathogenic coronaviruses (CoVs). IFN has direct antiviral activities against multiple viruses, including SARS-CoV-2, although its antiviral mechanisms against CoVs are unclear. For other viruses, the antiviral activity of IFN has partially been attributed to the induction of antiviral IFN -inducible GTPases known as guanylate binding proteins (GBPs). However, whether the antiviral mechanism of IFN against CoVs is associated with the induction of GBPs is currently unknown. We hypothesize that IFN inhibits CoV replication by inducing the expression of antiviral GBPs. Using the endemic CoV HCoV-229E as a model, we show that pre-treatment of A549 human lung epithelial cells with IFN potently inhibits HCoV-229E infection while upregulating GBP2 expression. To evaluate a specific role for GBP2, we used CRISPR/Cas9 to generate GBP2 knockout A549 cells. Notably, the antiviral effect of IFN against HCoV-229E was significantly reduced in the absence of GBP2, suggesting that GBP2 is key in mediating the antiviral effect of IFN against HCoV-229E. Furthermore, GBP2 overexpression inhibits HCoV-229E replication in A549 cells. We are currently characterizing the antiviral mechanisms through which GBP2 antagonizes CoV replication, and whether restriction of CoV infection by GBP2 requires its GTPase activity. These findings may contribute to the development of novel immunomodulatory therapeutic strategies to protect against future emerging CoVs. [Supported by Queen's University and NSERC.]

Characterizing the interaction between vitamin D and the parathyroid gland in chronic kidney disease.

(Field: Therapeutics and Drug Development)

Sono S. Khan1 BScH, Austin P. Lansing1 MSc, Mandy E. Turner PhD1, Emilie C. Ward1, Martin P. Petkovich1 PhD, Rachel M. Holden MD1,2, Michael A. Adams PhD1
1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, K7L 3V6, Canada
2Department of Medicine, Queen's University, Kingston, ON, K7L 3V6, Canada

Secondary hyperparathyroidism (SHPT), which has a major role in promoting cardiovascular disease and mineral bone disorder, is a clinical target in chronic kidney disease (CKD). Use of active vitamin D to address SHPT is a common, but problematic, therapy. This study aims to characterize the interaction between active vitamin D and diseased parathyroid glands to uncover mechanisms of clinical vitamin D resistance and elucidate maladaptive off-target actions.

Parathyroid glands were excised from CKD (0.25% dietary adenine) and control rats. Animals were untreated or treated with either precursor (25-(OH)D3) or active vitamin D3 (1,25-(OH)2D3) for two weeks. Parathyroid glands were studied by immunohistochemistry (IHC). Sections were incubated with primary antibodies against cytochrome P450 (CYP) 27B1, CYP24A1, vitamin D receptor (VDR), and calcium-sensing receptor (CaSR). Histopathological findings were analyzed using HALO (v2.1.13123.139, Indica Labs) and CellProfiler (v2.2.0, http://www.cellprofiler.org/).

Preliminary IHC analyses indicate that the average parathyroid cell area was increased by 2.75- ($p<0.01$) and 3.1-fold ($p<0.01$) in untreated and 1,25-(OH)2D3-treated, but only 2.4-fold ($p<0.01$) in 25-(OH)D3-treated CKD animals compared to healthy controls. Average cell area correlated to circulating in vivo parathyroid hormone (PTH) levels ($r = 0.94$, $p<0.0001$).

CKD seems to induce a hypertrophic response in parathyroid cells, which may be exacerbated by 1,25-(OH)2D3 treatment and associated with PTH hypersecretion. Alterations to parathyroid protein expression and morphology are important considerations for vitamin D-based therapeutic intervention of SHPT.

(Supported by the Canadian Institutes of Health Research and OPKO Health Inc Renal Division)

The Female Risk factors for post-Infarction Depression and Anxiety (FRIDA) Study

(Field: Medicine)

Kiera Liblik BSc, Ricky Hu MASc, Guillaume Foldes-Busque PsyD PhD, Tara Sedlak MD FRCPC, Jacob Udell MD MPH FRCPC, Sharon L. Mulvagh MD FRCPC FACC FASE FAHA, Sarah Blissett MD MHPE FRCPC, Amer M. Johri MD MSc FRCPC FASE
Department: Medicine, Queen's University, Kingston, Ontario, Canada

Several studies demonstrate that female patients are significantly more likely to experience depression and anxiety following acute coronary syndrome (ACS), correlated with higher rates of CV morbidity and mortality. Revised guidelines to address mental health following ACS may be developed with support from studies identifying the CV risk factors and psychosocial determinants of health that elevate female patient risk. We aimed to identify the CV risk factors, demographic, and socioeconomic variables correlated with increased Hospital Anxiety and Depression Scale (HADS) scores at the time of ACS. We further set out to determine whether increased depression and anxiety scores at baseline correlate with three and six-month outcomes (repeated HADS questionnaire, Cardiac Anxiety Questionnaire, major adverse cardiac events, Short Form-12 Health Survey, and Somatic Symptom Scale-8). This prospective multi-center questionnaire-based clinical research study features data collected at baseline and at three and six months plus statistically computed descriptive and inferential values used to observe distributions and significance between groups. We identify a key group of variables associated with HADS-Anxiety≥8 (low income, history of mental illness, and low social support) as well as HADS-Depression≥8 (gender, unemployment, low income, unstable housing, history of mental illness, stress, and low social support). Our results can inform tailored interventions following ACS in primary care and cardiac rehabilitation while understanding identified risk factor correlations can inform prevention at the public health level. (Supported by the Canadian Federation of University Women)

A DNA Methylation-Based Liquid Biopsy for Monitoring Breast Cancer

(Field: Pathology and Molecular Medicine)

Keira Frosst and Christopher R. Mueller. Department of Pathology and Molecular Medicine, Queen's University, Kingston, Ontario, Canada.

One in eight women will develop breast cancer in their lifetime and 33% of these women will develop metastatic disease. In a metastatic setting, treatment response is monitored through CT-scans and CA15-3. Although there are many treatments available for these women, selecting an appropriate line of therapy can be difficult. The mDETECT assay is a DNA methylation based liquid biopsy which uses targeted sequencing of regions specifically hyper-methylated in breast cancer. The mDETECT breast cancer assay contains

79 primers which together recognize all subtypes of breast cancer. The assay has been developed as a one-tube multiplex reaction using novel RNase-H2 dependant primers to improve the assay's efficacy and streamline the mDETECT workflow. These primers have been designed and incorporated into the assay and optimization has been conducted to develop a functional workflow. Next generation sequencing using the novel mDETECT workflow has been carried out on synthetically methylated DNA to allow for balancing of each primer concentration. After further optimization and validation on a cohort of patient plasma samples, this assay could aid in the rapid monitoring of treatment response in the metastatic setting. This would assist in decision making around switching therapies when a patient is not responding to their current course of treatment. This could reduce side effect from ineffective therapies by switching earlier to a more effective therapy, improving outcomes and prolonging lives.

Session 2

Low mammography screening participation by women ages 40 to 49 may contribute to poor breast cancer survival rates in Southeast Ontario

(Field: Medicine)

Paola V. Nasute Fauerbach, Sophia E. Bakyta, Janushan Hariharan, David M. Berman
Department of Pathology and Molecular Medicine and Queen's Cancer Research Institute, Queen's University, Kingston, Ontario, Canada (PVNF and DMB). Faculty of Health Sciences, Queen's University, Kingston, Ontario, Canada (SEB and JH)

Background: The 5-year breast cancer-specific mortality rate of women 40-49 in Southeast Ontario (SEO) is 17.4% versus 8.9% province-wide. Studies show screening mammography reduces mortality ~40% by detecting small asymptomatic cancers. In Ontario, women 40-49 may undergo screening.

Purpose: To identify the proportion of screen-detected cancers in women 40-49 in SEO and its effects on cancer size, treatment, and outcomes.

Methods: Clinicopathological and imaging data from screen-detected, incidental, and clinically-evident (symptomatic) cancers were collected for consecutive women 40-49 who underwent primary breast cancer surgery (2009-2011). Chi-square and log-rank tests were performed.

Results: 57 women met inclusion criteria; four had multicentric or bilateral disease, totaling 61 cancers. Only 3/57 patients (5.3%) had screen-detected cancers and 4/57 (8.7%) had incidental cancers on mammograms for contralateral lesions; 49/57 (86.0%) women had symptomatic cancers. All seven asymptomatic patients had cancers ≤20mm and underwent lumpectomies, contrasting 26/50 (52%) symptomatic women with cancers ≤20mm, and 37/50 (74%) underwent lumpectomies. The remainder had mastectomies. Chemotherapy was administered to 28.6% of asymptomatic and 78.0% of symptomatic women (P=0.006). The 5-year recurrence rate was 12/57 (21%); interestingly, none of the asymptomatic patients had metastases versus 9/50 (18%) of symptomatic women.

Conclusion: Only 5.3% of patients underwent screening mammography. Symptomatic women had larger tumours, more metastases, and received more intensive therapy than asymptomatic patients, suggesting that low screening participation rates contribute to poor outcomes.

Funding: Paola V. Nasute Fauerbach received the Dean's Doctoral Award, Department of Pathology and Molecular Medicine, Queen's University, Kingston, Ontario, Canada

Investigating the role of Tumor Associated B cells in Bladder Cancer Progression

(Field: Reproduction and Developmental Science)

Sadaf Rahimi1,2, Priyanka Yolmo1,2, Gwenaelle Conseil1,2, Minqi Xu3, D. Robert Siemens4 and Madhuri Koti1,2,4,5
1Queen's Cancer Research Institute, 2Department of Biomedical and Molecular Sciences, Department of Pathology, 4Department of Urology and 5Department of Obstetrics and Gynecology, Queen's University, Kingston, ON, Canada

Background: Bladder cancer can be broadly categorized into non-muscle invasive bladder cancer (NMIBC) and muscle invasive bladder cancer (MIBC), wherein 75% of the incident cases are NMIBC and 25% present with de novo MIBC. Progression to secondary MIBC often occurs in patients with high-risk NMIBC. Our recent study on

whole transcriptome analysis of tumors from 460 patients showed increased expression of B cell associated genes in high-grade tumors. Spatial immune profiling of 332 tumors demonstrated increased density of B cells in patients who exhibited shorter recurrence free survival. We hypothesize that specific B cell subsets expand due to carcinogen induced chronic inflammation in the bladder mucosa promoting tumor progression.

Methods: Female and male mice were exposed to N-butyl-N-(4-hydroxybutyl) nitrosamine (BBN) carcinogen with simultaneous B cell depletion using a panel of B cell depleting antibodies. Systemic immune profiling was conducted at multiple time points using flow cytometry. Whole bladder sections were subjected to hematoxylin and eosin (H&E) and multiplex immunofluorescence staining.

Results: Histologically benign or close to normal urothelium was observed in B cell depleted mice compared to mice injected with isotype control antibodies. These results suggest that long term depletion of B cells in aged mice leads to reduced inflammation in the bladder mucosa and delays disease progression.

Conclusion: Further characterization of specific populations of B cell will define their role in bladder tumor progression.

Research funded by Bladder Cancer Canada

The role of the gut microbiome in spinal cord injury pain and neuroinflammation

(Field:Microbes, Immunity and Inflammation)

Courtney Ann Bannerman, Katya Douchant, Shawna S Kim, Prameet Sheth, Nader Ghasemlou

Spinal cord injuries affect more than 10,000 Canadians every year, with 60-80% developing chronic pain. Recent work has shown that the collection of bacteria in the gut, called the gut microbiome, may play a role in pain processing. Many studies have also shown that the diversity of the gut microbiome is altered after a person experiences a spinal cord injury (SCI). Mice were anesthetized and a partial laminectomy was performed at the vertebral levels T10-11. Moderate contusion (50 kdyn) injury with or without sustained compression (60 seconds) of the spinal cord was carried out on female C57BL/6J mice; sham-injured mice only received a laminectomy. Mice were gavaged with the define microbial community mixture KAT2, water, or an antibiotic mixture (kanamycin, gentamicin, colistin, metronidazole, vancomycin). Mice treated with antibiotics experience gut dysbiosis and with it more severe mechanical hypersensitivity, whereas mice who care treated with defined microbial communities experience less mechanical hypersensitivity. Antibiotic treatment also appears to affect the in infiltration and activation states of macrophages into the spinal cord. This work will also allow for us to better understand the gut-brain axis and its role in pain development and severity.

DNA METHYLATION CUES IN NUCLEOSOME GEOMETRY, STABILITY, AND UNWRAPPING

(Experimental Medicine)

Shuxiang Li1, Yunhui Peng2, David Landsman2 and Anna R. Panchenko1

1 Department of Pathology and Molecular Medicine, School of Medicine, Queen's University, ON, Canada

2 National Center for Biotechnology Information, National Institutes of Health, Bethesda, MD, USA

Cytosine methylation at the 5-carbon position is an essential DNA epigenetic mark in many eukaryotic organisms. Although countless structural and functional studies of cytosine methylation have been reported, our understanding of how it influences the nucleosome assembly, structure, and dynamics remains obscure. Here we investigate the effects of cytosine methylation at CpG sites on nucleosome dynamics and stability. By applying long molecular dynamics simulations on several microsecond time scale, we generate extensive atomistic conformational ensembles of full nucleosomes. Our results reveal that methylation induces pronounced changes in geometry for both linker and nucleosomal DNA, leading to a more curved, under-twisted DNA, narrowing the adjacent minor grooves, and shifting the population equilibrium of sugar-phosphate backbone geometry. These DNA conformational changes are associated with a considerable enhancement of interactions between methylated DNA and the histone octamer, doubling the number of contacts at some key arginines. H2A and H3 tails play important roles in these interactions, especially for DNA methylated nucleosomes. This, in turn, prevents a spontaneous DNA unwrapping of 3-4 helical turns for the methylated nucleosome with truncated histone tails, otherwise observed in the unmethylated system on several microseconds time scale. (Supported by the Natural Sciences and Engineering Research Council of Canada.)

Evidence of transient receptor potential melastatin 3 (TRPM3) channel sensitization in a model of colitis

(Field: Neuroscience)

James W. King1, Aidan S.W. Bennett1, Corey Baker1, Hannah Wood1, David E. Reed1, Alan E. Lomax1
1Gastrointestinal Disease Research Unit, Queen's University, Kingston, Ontario, Canada

Abdominal pain is a primary symptom of inflammatory bowel disease (IBD). Opioids provide relief from IBD-associated pain, but they are addictive and associated with excess mortality in IBD patients. Thus, there is a need to develop safe and efficacious therapeutics. The mechanosensitive ion channel transient receptor potential melastatin 3 (TRPM3) is upregulated by inflammation and contributes to pain from inflamed joints and cystitis. We hypothesized that TRPM3 may be involved in colonic mechanosensation and may participate in IBD-associated pain. We used ratiometric Ca2+ imaging to determine the effects of pharmacological activation or inhibition of TRPM3 on T13-L5 dorsal root ganglia (DRG) neurons. Furthermore, the effects of TRPM3 activation in healthy mice and mice with dextran sulphate sodium-induced colitis were compared. The TRPM3 agonist, CIM-0216 (0.1-10µM), concentration-dependently increased intracellular Ca2+ concentration in mouse DRG neurons and this was blocked using the TRPM3 inhibitor isosakuranetin (5µM; $p<0.0001$, Mann-Whitney Test). CIM-0216 (5µM)-induced increases in intracellular Ca2+ were significantly larger in neurons from mice with colitis (326±16% of baseline) compared to neurons from healthy mice (257±13% of baseline; $p<0.01$, Kruskal-Wallis with Dunn's Multiple Comparison Test). The percentage of neurons responding to CIM-0216 was also significantly increased in mice with colitis (79%) compared to healthy mice (62%; $p<0.001$, Fischer's Exact Test). Thus, TRPM3 may be sensitized during colitis and future experiments will explore this further.

Session 3

Stimulus-locked muscle responses to visual disturbances are impacted by urgency and certainty to move

(Field: Neuroscience)

Parsa Balalaie, Kayne Park, Stephen H. Scott
Centre for Neuroscience Studies, Queen's University, Kingston, Ontario

The human brain can produce rapid motor responses in less than 100ms when responding to a visual stimulus. These Stimulus-Locked Responses (SLR) are difficult to elicit and are more prevalent under predictable conditions and when the reach is toward a moving target. We used a fast-feedback interception task (FFIT) in which the subjects intercepted a ball moving towards them. In some trials, the ball was randomly jumped to the left or right at different times, requiring different speeds of motor-correction (urgency). Electromyographic activity was recorded from shoulder and elbow muscles. There were different numbers of trials in each block in which the ball did not jump (no-jump), making participants uncertain about the need to move (certainty). For the same level of certainty, SLRs occurred earlier, with bigger magnitudes for trials with greater urgency. For the same level of urgency, higher certainty about the need to move led to greater prevalence and larger SLRs. In the second experiment, jumps with different urgencies were combined in the same blocks with two levels of certainty. When subjects were sure they needed to move, they could modulate their response based on the urgency, like the previous experiment. Co-contraction was a common strategy when expecting a jump. However, uncertainty reduced co-contraction. Our results highlight SLRs are more prevalent at higher certainty and urgency to respond to attain behavioral goals.

Sca-1 surface expression in trophoblast stem cells identifies multipotent cells that proliferate in response to hypoxia and are phenotypically unique

(Field: Reproduction and Developmental Science)

Megan Cull1, Bryony Natale2, Avery McGinnis1, Heejeong Kim3, David Natale1,2. 1Deptartment of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada; 2Deptartment of Obstetrics and Gynecology, Queen's University, Kingston, Ontario, Canada; 3Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Diego, La Jolla, CA USA.

Stem cell antigen-1 (Sca-1/Ly6A), is increased in a late-gestation mouse model of fetal growth restriction and hypoxia and identifies trophoblasts that are proliferative and multipotent when removed from the placenta. Whether Sca-1 is associated with terminally-differentiated trophoblast and whether undifferentiated Sca-1 positive(POS) and negative(NEG) cells from trophoblast stem cell (TSC) cultures are phenotypically unique is unknown. This study aimed to 1) confirm that Sca-1 does not colocalize with differentiated trophoblasts, using transgenic Sca-1-GFP reporter placentae and 2) assess whether Sca-1POS/NEG TSCs have altered phenotypes, expression of TSC markers, self-renewal and proliferative ability; and does hypoxia alter these responses. I hypothesize that Sca-1 is only associated with undifferentiated trophoblast and that Sca-1POS TSCs respond to hypoxia with increased proliferation. Results showed that differentiated trophoblast did not express Sca-1. FACS-isolated Sca-1POS TSCs had increased expression of TSC genes (Cdx2 and Esrrb), with both populations able to self-renew in normoxia and hypoxia over multiple passages. In response to hypoxia (72hrs), Sca-1POS cells had increased proliferation and Sca-1 surface expression when compared with Sca-1NEG hypoxia and Sca-1POS normoxia groups. Surprisingly, Sca-1NEG TSCs gained Sca-1 cell-surface expression and both populations became heterogeneous after 72hrs. Results

support Sca-1 identifying multipotent trophoblasts. While Sca-1POS TSCs responded to hypoxia with increased proliferation, maintaining homogeneous Sca-1NEG proved challenging, suggesting Sca-1 may be required for self-renewal with some plasticity within the population. Funding: NIH/NICHD.

Circular RNA profiling of human pulmonary artery endothelial cells identifies novel BMPR2-derived regulators of endothelial proliferation and apoptosis

(Field: Biochemistry and Cell Biology)

M. Martin VandenBroek1, Mackenzie C. Sharp2, Anne L. Theilmann3, Mark L. Ormiston1,3
1Department of Medicine, Queen's University, Kingston ON
2School of Computing, Queen's University, Kingston ON
3Department of Biomedical and Molecular Sciences, Queen's University, Kingston ON

Background – Pulmonary arterial hypertension (PAH) is characterized by endothelial dysfunction and is strongly linked to mutations in BMPR2, the gene encoding the bone morphogenetic protein type II receptor (BMPR-II). While the impact of linear BMPR2 transcripts on disease progression has been well studied, the role for BMPR2-derived circular RNAs (circRNAs) in the endothelium has not.

Methods and Results – Ultra-deep (~625 million reads/sample) RNA sequencing of human pulmonary artery endothelial cells (HPAECs) identified 425 circRNAs (0.5% of all known or proposed human circRNAs) that are abundantly expressed in HPAECs. This list includes two novel circRNAs derived from the BMPR2 gene, hsa_circ_0003218 (circ3218, from exons 2 and 3 of BMPR2) and hsa_circ_0005078 (circ5078, exon 12). Functionally, siRNA silencing of circ3218 increased HPAEC apoptosis, while circ5078 loss enhanced HPAEC proliferation by 2.02-fold. The proliferative effect of circ5078 silencing, which was eliminated by co-silencing of linear BMPR2 transcripts, was found to be mediated by CAPRIN1, an RNA-binding protein and cell cycle regulator that recognizes a binding site within this circRNA.

Conclusions and Future Directions – We have generated the first ever profile of circRNA expression in the human pulmonary endothelium and identified two novel BMPR2-derived circRNAs as mediators of endothelial function. Future work will confirm the mechanisms through which circ5078-CAPRIN1 interactions regulate the endothelial cell cycle and explore the impact of disease and BMPR2 mutations on circRNA expression.

INVESTIGATING THE MOLECULAR MECHANISMS OF A PUTATIVE SPREADING DEPOLARIZATION ACTIVATOR.

(Field: Neuroscience)

Julia A. Hellas, Chloe A. Lowry, Nikita Ollen-Bittle, Kelly Lee, R. David Andrew.
Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, Canada.

Disrupted cerebral blood flow during stroke or traumatic brain injury prevents neuronal adenosine triphosphate (ATP) production, causes failure of the Na+/K+ ATPase, and promotes spreading depolarizations (SDs). SDs are waves of inactivation that propagate through gray matter and can cause permanent neuronal injury. In live brain slices, SD is induced with oxygen-glucose deprivation. Yet, little is known about the molecular mechanisms promoting SD initiation or recurrence. A marine poison, palytoxin, converts Na+/K+ ATPase into a non-specific channel, thereby inducing SD in brain slices, and hemolysis in red blood cells (RBCs). This study used palytoxin to investigate a proposed humoral SD activator (SDa) that we suspect drives SD in a palytoxin-like manner. We first determined the palytoxin

concentration required to elicit tissue SD and RBC hemolysis. In RBCs, trace amounts of palytoxin seem to prime Na+/K+ ATPase for opening, facilitating hemolysis. This priming was also observed in slices, facilitating SD. Next, fluid containing the SDa was applied to naïve brain slices, eliciting SD with 66 92% frequency. HPLC analysis of SDa samples indicated increased release of low molecular weight molecules ~500 Da. Further, the SDa was purified via a novel RBC binding assay and will be analyzed by mass spectrometry to accurately characterize it. Identification of a humoral SDa and improved understanding of the molecular mechanisms underlying SD will help elucidate novel targets for reducing SDs in clinical populations.

I would like to express my sincerest gratitude to Dr. David Andrew, Dr. Chloe Lowry, Dr. Peter Gagolewicz, and Dr. Paula Germano for their unending guidance and support throughout this project. This project was conducted with financial support from the Boag Family Endowment in Neuroscience, R. S. McLaughlin Fellowship, and New Frontiers in Research Fund.

Poster Presntations

Morning Session

1. Farzaneh Afzali (Field: Experimantal Medicine) - **Adherent independent tolerance of HGSC cell lines where stress and survival meet**
2. Ahmed Al-Baghdadi (Field: Reproduction & Developmental Science) - **Investigating the inositol triphoshate receptor (IP3R)/[Ca2+]i-dependent mechanisms of the tacrolimus-induced migration and invasion of human derived extravillous trophoblast cells in vitro**
3. Mohamed Gamal Abouelyazeed Ali Shehata (Field: Medicine) - I**s Core Muscle Strength Affected in Women Gave Birth by Cesarean Delivery with Several Anaesthetic Types? A Retrospective Cohort Study**
4. Theodore Aliyianis (Field: Neuroscience) - **Robotic assessment of cognitive impairments in adults with focal temporal lobe epilepsy and genetic generalized epilepsy**
5. Alwaleed Aljaser (Field: Neuroscience) - **A Real-world Efficacy and Safety Analysis of Ocrelizumab Treatment in Patients with Primary Progressive Multiple Sclerosis (PPMS)**
6. Reem Al-Rawi (Field: Medicine) - **Determining the Importance of Various gEnders, Races, and body Shapes for CPR Education using manikins: Images in MedIa (DIVERSE II)**
7. Heather Amsden (Field: Microbes, Immunity & Inflammation) - **IL-27 Inhibition of pandemic influenza a virus infection in part relies on type I IFNS**
8. Corey Baker (Field: Experimental Medicine) - **Investigating microbial contributions to the development and treatment of abdominal pain in IBS**
9. Julia Barilo & Erica Smith (Field: Microbes, Immunity & Inflammation) - **Investigating the Susceptibility of IL-4 Treated Spleen and Bone Marrow-Derived Macrophages to LCMV Infection**
10. Aiden Bennett (Field: Experimental Medicine) - **Sex differences in the effect of the microbiota from irritable bowel syndrome patients on abdominal pain**
11. Aurelie Brecier (Field: Neuroscience) - **Sensory Neurons Mediate Activation of Skin-Resident Dendritic Cells in a Model of Postoperative Pain**
12. Alyssa Burrows (Field: Microbes & Immunology) - **Comparing Commercially Available SARS-CoV-2 Immunoglobulin-G Immunoassays to a Clinically Validated Assay to Determine Seroprevalence**
13. Marco Buttigieg (Field: Pathology & Molecular Medicine) - **Characterizing the mutational spectrum of clonal hematopoiesis to develop a comprehensive and cost-efficient NGS screening approach for hematologic cancers**
14. Noah Campagna (Field: Experimental Medicine) - **Differential effects of remdesivir and lumacaftor on homo- and heterotetrameric herg channels**
15. Angela Choi (Field: Experimental Medicine) - **Investigating Biomarkers to Improve Prediction of Patient Outcome to Anti-PD-1 Therapy in Non-Small Cell Lung Carcinoma**
16. Yasmeen Choudhri (Field: Pathology & Molecular Medicine) - **Clonal hematopoiesis of indeterminate potential may increase risk of critical Covid-19 illness**
17. Matthew Cormier (Field: Pathology & Molecular Medicine) - **Mice possess a more limited natural anti-Factor VIII antibody repertoire than humans that is generated primarily by marginal zone B cells**
18. Kassandra Coyle (Field: Medicine) - **Natural Killer Cell TGFb Signaling Influences Pulmonary Vascular Development and Pathological Vascular Remodeling in a Mouse Model of Pulmonary Arterial Hypertension**
19. Paola Dantonio (Field: Medicine) - L**ow mammography screening participation by women ages 40 to 49 may contribute to poor breast cancer survival rates in Southeast Ontario**
20. Mohammad El Diasty (Field: Medicine) - **Building a Proliferative Trainee-Led Research Program in the COVID-19 Era**
21. Eshetu Engeda (Field: Medicine) - **Severe malaria-related disability in African children**
22. Mikayla Erdelsky (Field: Experimental Medicine) - **The primary cilium: A hyper-localized compartment for cAMP signalling**
23. Landon Montag (Field: Neuroscience) - **Low Education and Income are Associated with Worse Pain Outcomes in Adults at an Interdisciplinary Chronic Pain Clinic**

24. Daniel Espiritu (Field: Biochemistry) - **Elucidating the Impact of Histone Mutations in Cancer**
25. Emmanuel Fagbola (Field: Biochemistry) - **Exploring the Impact of Endothelial BMPR2 Loss on Phosphoinositide Dynamics and the Pathobiology of Pulmonary Arterial Hypertension**
26. Eric Fernandes (Field: Pharmacology & Toxicology) - **In experimental CKD, increases in FGF-23 are associated with left ventricular hypertrophy even without corresponding hemodynamic changes.**
27. Carla Gallardo Flores (Field: Microbes, Immunity & Inflammation) - **Characterizing the roles of cellular cyclophilins in coronavirus infection**
28. Hailey Gowdy (Field: Microbes, Immunity & Inflammation) - **The DouleurCircaPain study: examining circadian control of chronic pain through a national cross-sectional survey**
29. Dominique Hancock (Field: Neuroscience) - **Investigating the role of the TRPV4 channel in neuronal swelling and spreading depolarization**
30. Maaz Haq (Field: Medicine) - **Learning curves in minimally invasive cardiac surgery: A systematic review**
31. Jordan Harry (Field: Experimental Medicine) - **Examining the impact of endothelial Bmpr2 loss on the growth and vascularization of lung metastases in a mouse model of metastatic breast cancer**
32. Donya Hayati (Field: Reproduction & Developmental Science) - **Isolation and Characterization of Extracellular Vesicles derived from Endometriosis Patients**
33. Safara Holder (Field: Microbes, Immunity & Inflammation) - **The Identification and Characterization of Cellular Molecules in Proximity to the Herpes Simplex Virus Type 2 Tegument Protein UL21**
34. Gavin Hughes (Field: Medicine) - **Optimizing Referral Practices for a Newly Established First Seizure Clinic**
35. Natasha Iaboni (Field: Pathology & Molecular Medicine) - **Profiling ductal carcinoma in SITU (DCIS) and invasive ductal carcinoma (IDC) using desorption electrospray ionization (DESI)**
36. Amoon Jamzad (Field: Engineering) - **Improve margin assessment in iKnife cancer surgeries via uncertainty estimation**
37. Natasha Jawa (Field: Neuroscience) - **Identifying neurocognitive outcomes and cerebral oxygenation in criticlly ill adults on acute kidney replacement therapy in the intensive care unit: The incognito-AKI pilot study**
38. Mitchell Jeffs (Field: Biochemistry) - **Development and Application of a Whole-Cell Biosensor for the Discovery of β-Lactamase and Penicillin Binding Protein Inhibitors**
39. Allison Jones (Field: Reproduction & Developmental Science) - **Localization of Cannabinoid Receptors in the Mouse Placenta**
40. Dure Khan (Field: Neuroscience) - **Manipulation of Glioblastoma Microenvironment using Focused Ultrasound & Microbubbles**
41. Olena Kourko (Field: Microbesm, Immunity & Inflammation) - **NK cells induce cell death of IL-27 and poly (I:C) - Stimulated PC3 and DU145 cells in a type I IFN dependent manner**
42. Dhruv Krishnan (Field: Medicine) - **Patterns of RAAS blockade medication use in patients with heart failure, diabetes or hypertension after admission with acute kidney injury: a study protocol**
43. Miles Lambert (Field: Medicine) - **Quality participation experiences among persons with chronic neurological conditions who participate in technology-mediated exercise interventions: Work in progress**
44. Emmanuelle LeBlanc (Field: Microbes, Immunity & Inflammation) - **Characterizing the roles of SARS-CoV-2 spike glycosylation in viral entry and pathogenesis**
45. Vina Li (Field: Microbes, Immunity & Inflammation) - **Circadian Disruption as a Risk Factor for Multiple Sclerosis Pathogenesis**
46. Josephine Liu (Field: Biochemistry) - **Development of a pH Assay to Monitor the Impact of Bacterial Porins on β-Lactamase Activity**
47. Jack Lott (Neuroscience) - **Kinarm-based Assessment of Neurological Impairment in Primary Brain Tumour Patients**
48. Kaylee Punter (Field: Biochemistry) - **Cancer as a Mitochondrial Disease: Targeting the Mitochondrial Fusion Protein, Optic Atrophy 1 (Opa1)**

Afternoon Session

1. Isabelle Mastantuono (Field: Neuroscience) - **Assessing Cognitive, Sensory, and Motor Function in Multiple Sclerosis Patients Using Kinarm Robotics System**
2. Alison McCallion (Field: Reproduction & Developmental Science) - **Mast Cells in the Pathophysiology of Endometriosis**
3. Avery McGinnis (Field: Reproduction & Developmental Science) - **The Relationship between Sca-1 and TGFb in Mouse Trophoblast Stem Cells**
4. Jacob Melamed (Field: Biochemistry) - **Biosynthesis of the O antigen of escherichia coli O157:H7**
5. Mohammad Mohammad (Field: Kinesiology) - **Estimating energy expenditure using wearable sensors during outdoor locomotion**
6. Ramtin Mojtahedi (Field: Engineering) - **Tumor Segmentation in Colorectal Liver Metastasis Using an Optimal Vision Transformer Patch Resolution**
7. Max Moloney (Field: Medicine)- **Determining the Prevalence of Asthma in a Primary Care EMR: Suspected or Confirmed?**
8. Landon Montag (Field: Neuroscience) - **Examining the Effects of Patient Expectations, Pain Sensitivity, and Therapeutic Alliance on Pain Relief Following Intravenous Lidocaine Infusion**
9. Blake Noyes (Field: Neuroscience) - **Using eye-tracking to characterize adolescent depression**
10. Montserrat Mora Ochomogo (Field: Microbiology & Immunology) - **Sheltering of β-lactam-susceptible bacterial strains by β-lactamase-producing strains**
11. Daria Ostroverkhova (Field: Pathology & Molecular Medicine) - **Mutated DNA Polymerase Epsilon Produces Distinct Mutational Landscape in Endometrial Cancer Genomes**
12. Kayne Park (Field: Neuroscience) - **Directional and general impairments in initiating motor responses after stroke**
13. Ryan Peters (Field: Nursing) - **Examining the quality and timeliness of discharge summaries from Kingston Health Sciences Centre (KHSC)**
14. Andrea Petkovic (Field: Biochemistry) - **Dissection of the atpase cycle of kinesin-8 at the microtubule plus end**
15. Aaron Philipp-Muller (Field: Psychology) - **Ketamine and eCBT for the treatment of PTSD**
16. Chinmay Potdar (Field: Microbiology & Immunology) - **Computational approaches to inflammatory bowel disease evaluation: identifying new mechanistic disease classifications**
17. John Mamatis (Field: Microbes, Immunity & Inflammation) - **Cyclophilin inhibitors enhance cell-autonomous antiviral immunity to inhibit coronavirus infection**
18. Doug Quilty (Field: Biochemistry) - **The effect of sFRP1 expression in melanoma is context dependent**
19. Madison Roth (Field: Microbes, Immunity & Inflammation) - **Characterization of the antiviral functions of IL-27 during dengue virus infection of human macrophages**
20. Tyler Rowsell (Pharmacology & Toxicology) - **Calcifying vasculature is protected from acute phosphate accrual by calciprotein nanoparticles**
21. Sanathan Sadh (Field: Patholohy & Molecular Medicine) - **The impact of TET2 on the expression of endogenous retroviral elements (ERV'S and the interferon response**
22. Cara Sadiq (Field: Medicine) - **The Association between Caregiver's Social Support and Burden of Caregiving for Patients with Hip Fracture: A Scoping Review**
23. Olivia Saville (Field: Reproduction & Developmental Science) - **The Impact of Sex on D-Dimer Levels and Disease Outcomes in Hospitalized COVID-19 Patients: A Systematic Review and Meta-analysis**
24. Jaya Sharma (Field: Biochemistry) - **Obesity and metabolic syndrome impair acute phosphate tolerance in females**
25. Abhishek Shastry (Field: Experimental Medicine) - **Mitochondrial DNA-Dependent changes in lipid transport and metabolism in skeletal muscle**

26. Mustafa Sherik (**Field: Biochemistry**) - **Identification of a hemolytic red blood cell-binding domain in a Vibrio cholerae adhesin**
27. Ron Shore (Field: Neuroscience) - **Behavioural Investigations of Psilocybin in Animals: A Scoping Review**
28. Danielle Sisnett (Field: Reproduction &Developmental Science) - **IL-23 and the IL-23/TH17 Axis: A Role in Endometriosis Pathophysiology?**
29. Kimberley Siwak (Field: Microbes, Immunity & Inflammation) - **Elucidating the Role of Cellular Glycans in the Cell Entry of a Pre-emergent Bat Coronavirus**
30. Reginald M. Smyth (Field: Experimental Medicine) - **Exertional dyspnea in patients with mild interstitial lung disease: The role of gas exchange abnormalities**
31. Golnar Taheri (Field: Microbes, Immunity & Inflammation) - **Identification of a novel modulator of neuroinflammation and pain**
32. Susan Thanabalasingam (Field: Medicine) - **Clinical thresholds using risk prediction models in advanced CKD**
33. Ethan Thomas (Field: Microbes, Immunity & Inflammation) - **Herpes Simplex Virus (HSV) Tegument Proteins pUL21 and pUL16 Prevent Nascent Capsids from Docking at Nuclear Pore Complexes During Virion Assembly**
34. Bryanna Thomson (Field: Biochemistry) - **RET receptor-mediated invasion in pancreatic ductal adenocarcinoma**
35. Anh Tran and Danielle Cutler (Field: Experimental Medicine) - **Automatic Segmentation of Malignant Pleural Mesothelioma in Thoracic CT scans using U-Net Architecture**
36. Quentin Tsang (Field: Therapeutics) - **Low-dose combination of cannabinoid receptor 1 (CB1R) and MU-opioid receptor (MOR) agonists synergistically inhibit visceral pain in vivo without adverse side effects or tolerance**
37. Tim Walker (Field: Pathology & Molecular Medicine) - **Altered RET Trafficking Contributes to Oncogenicity in a Model of TMEM127-mutant Pheochromocytoma**
38. Mia Wilkinson (Field: Experimental Medicine) - **Nuclear-mitochondrial DNA mismatch induces tissue-specific gene expression profiles: Transcriptomic analysis of subcutaneous and visceral white adipose tissues in mice**
39. Tristin Wilson (Field: Medicine) - **The abdominal aortic calcium score could increase access to non-calcium based phosphate binders in hemodialysis patients**
40. Juliette Wilson-Sanchez (Field: Pathology & Molecular Medicine) - **Comprehensive characterization of genetically distinct pre-clinical metastatic murine models of high-grade serous ovarian cancer**
41. Amanda Zacharias (Field: Experimental Medicine) - **RNA-sequencing identifies novel circadian genes and pathways regulating neuropathic pain**
42. Emmanuel Zangio (Field: Kinesiology) - **Can rapid onset vasodilation be enhanced by prior priming exercise?**
43. Sasha Zarnke (Field: Medicine) - **Assessing the Impact of the COVID-19 Pandemic on Patients Referred to a Lung Cancer Rapid Assessment Clinic in Ontario, Canada**
44. Katherine Zutautas (Field: Reproduction & Developmental Science) - **Dysregulation of Leukemia Inhibitory Factor in Endometriotic Lesions; Implications for Endometriosis Pathophysiology**