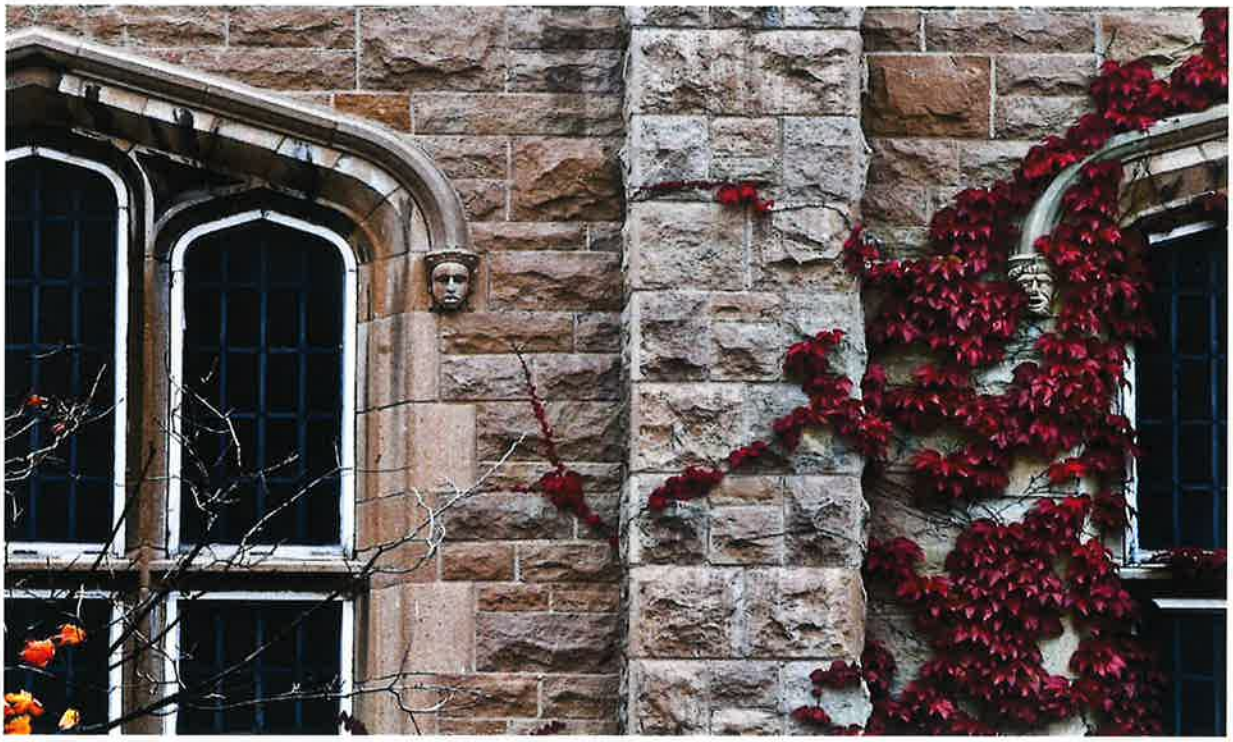
The Twenty-Third Annual Scientific Meeting for Health Science Research Trainees
Faculty of Health Sciences
Queen's University

Thursday, September 23rd , 2021
Four Points by Sheraton Kingston



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Anita Lister, Biomedical and Molecular Sciences
Chandra Tayade, Biomedical and Molecular Sciences
Edmond Chan, Biomedical and Molecular Sciences
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Kat Brennan-Rowcliffe, Biomedical and Molecular Sciences
Katrina Gee, Biomedical and Molecular Sciences
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Rhiannon Hilton
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Aurelie Brecier, Biomedical and Molecular Sciences, Neuroscience
Samantha Benton, Obstetrics and Gynecology, Biomedical and Molecular Sciences

Acknowledgments

A special thank you to Katherine Brennan-Rowcliffe for her invaluable assistance in organizing this meeting.

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Oral/Poster Presentations 2nd floor

8:00 – 8:45 am — ***Registration and Poster Set-Up***

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***

Deconstructing the tumor immune microenvironment: it takes a village!

Dr. Madhuri Koti, Departments of Biomedical and Molecular Sciences and Obstetrics and Gynecology

Recipient of *Mihran and Mary Basmajian Award for Excellence in Health Research 2019*

Oral Presentation - Session 1

Chair: Dr. Katrina Gee

9:35 – 9:47 am	Emmanuelle LeBlanc: **DISRUPTION OF CONSERVED GLYCAN-DEPENDENT ATTACHMENT AS AN ANTIVIRAL STRATEGY FOR EMERGING CORONAVIRUSES**
9:47 – 9:59 am	Safara Holder: **THE IDENTIFICATION OF CELLULAR MOLECULES IN PROXIMITY TO THE HERPES SIMPLEX VIRUS TYPE 2 TEGUMENT PROTEIN UL21**
9:59 – 10:11 am	Rafaella A Gonçalves: **THE EXERCISE-INDUCED HORMONE IRISIN IS REDUCED IN THE CEREBROSPINAL FLUID OF ELDERLY DEPRESSED INDIVIDUALS.**
10:11 – 10:23 am	Rhiannon Hilton: **ENDOTHELIAL *BMPR2* LOSS PROMOTES ALTERED IL-15 SIGNALING, CONTRIBUTING TO IMMUNE AND VASCULAR DYSFUNCTION IN PULMONARY ARTERIAL HYPERTENSION**
10:25 – 10:45 am	***Coffee Break***
10:45 am – 12:15 pm	Poster Presentations (**Odd Numbered** Abstracts)
12:15 – 1:00 pm	Lunch/Poster Set-Up
1:00 – 2:30 pm	Poster Presentations (**Even Numbered** Abstracts)

Oral Presentation - Session 2

Chair: Dr. Neil Renwick

2:30 – 2:42 pm	Noor Shakfa: **IMPROVING CANCER CELL GENOTYPE ASSOCIATED CHEMOTHERAPY RESPONSE IN OVARIAN CANCER VIA CGAS-STING PATHWAY ACTIVATION**
2:42 – 2:54 pm	Nathalia Kim: **COMPREHENSIVE IMMUNE PROFILING OF HUNNER LESIONS IN INTERSTITIAL CYSTITIS USING IMAGING MASS CYTOMETRY: A PROOF-OF CONCEPT STUDY**
2:54 – 3:06 pm	Olivia Lopes: **CLONAL HEMATOPOIESIS AS A RISK FACTOR FOR CHEMOTHERAPY-RELATED COMPLICATIONS IN LYMPHOMA PATIENTS**
3:06 – 3:18 pm	Ayssar Tashtush: **EXCITATION OF VAGAL AFFERENT NEURONS BY FECAL SUPERNATANT FROM PATIENTS WITH INFLAMMATORY BOWEL DISEASE**
3:18– 3:30 pm	Chengying Feng: **A SYSTEMATIC REVIEW AND META-ANALYSIS OF EXERCISE INTERVENTIONS AND USE OF EXERCISE PRINCIPLES TO REDUCE FEAR OF FALLING AMONG COMMUNITY-DWELLING OLDER ADULTS**
3:30 – 3:45 pm	***Coffee Break***

Oral Presentation – Session 3

Chair: Dr. Edmond Chan

3:45 – 3:57 pm	Byron Hunter: **KINESIN-8-SPECIFIC LOOP 2 IS A CONFORMATIONAL SWITCH THAT CONTROLS THE DUAL ACTIVITIES OF THE MOTOR DOMAIN ACCORDING TO MICROTUBULE SHAPE**
3:57 – 4:09 pm	Ananya Chakraborty: **PKC-MEDIATED ENDOCYTIC DEGRADATION OF KV1.5 CHANNELS REGULATED BY BOTH C- AND N- TERMINI**
4:09 – 4:21 pm	Julia Segal: **CIRCADIAN DISRUPTION IN A MOUSE MODEL OF MULTIPLE SCLEROSIS**
4:21 – 4:33 pm	Helen Obilor: **A FEASIBILITY STUDY OF A SOCIAL MEDIA-BASED DIABETIC FOOT ULCER PREVENTION PROGRAM DURING THE COVID-19 PANDEMIC IN CANADA.**
4:35 – 5:00 pm	Concluding Remarks and Awards
5:00 – 7:00 pm	Reception Cash Bar (Small snack will be provided)

Oral Presentations

Cancer Research and Therapy

CLONAL HEMATOPOIESIS AS A RISK FACTOR FOR CHEMOTHERAPY-RELATED COMPLICATIONS IN LYMPHOMA PATIENTS. Olivia Lopes1, Amy JM McNaughton1, Rena Buckstein2, Michael J Rauh1. 1Department of Pathology and Molecular Medicine, Queen's University, Kingston, ON. 2Sunnybrook Health Sciences and Odette Cancer Centre, Toronto, ON.

Clonal hematopoiesis of indeterminate potential (CHIP) is a phenomenon of aging that arises upon the expansion of somatically mutated hematopoietic stem cells. CHIP can cause dysfunctional hematopoiesis and dysregulated immune functions of mature blood cells. CHIP prevalence is >10% in healthy older adults and is associated with hematologic (mostly myeloid) malignancies, cardiovascular disease, and overall mortality. 20% of lymphoma patients over age 70 have evidence of CHIP in their blood cells, although this is not routinely considered and does not currently alter treatment plans. Some lymphoma patients experience chemotherapy-related complications, while others do not, and it remains unknown as to why this occurs. We hypothesized that CHIP may be a risk factor for chemotherapy toxicity in elderly lymphoma patients, related to dysfunctional bone marrow and blood cells. We are applying targeted next-generation sequencing (NGS) to blood for CHIP detection in ~188 lymphoma patients over age 60, prior to starting chemotherapy and at three treatment time points. Upon sequencing 40 lymphoma samples thus far, we found that variant allele frequencies (VAFs) of variants in DNA damage response (DDR) genes increase throughout treatment and new variants in these genes are acquired as therapy progresses. We are currently analyzing if CHIP is associated with chemotherapy complications. Long-term objectives include determining if CHIP is an independent risk factor for therapy-related myeloid neoplasm (t-MN) development or inferior overall survival.

IMPROVING CANCER CELL GENOTYPE ASSOCIATED CHEMOTHERAPY RESPONSE IN OVARIAN CANCER VIA CGAS-STING PATHWAY ACTIVATION. Noor Shakfa, Elizabeth Lightbody, Gwenaelle Conseil, Deyang Li, Juliette Wilson-Sanchez, Afrakoma Afriyie-Asante, Ali Hamade, Stephen Chenard, Kathrin Tyryshkin, Martin Koebel, and Madhuri Koti. Department: Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada

High grade serous ovarian carcinoma (HGSC) is the most lethal gynecologic malignancy with high rates of chemotherapy resistance and poor outcomes. Our previous studies have demonstrated the variable tumor immune microenvironment states that associate with platinum chemotherapy response. We further showed the significance of the interferon (IFN) induced chemokine CXCL10 as a key mediator of tumor infiltrating immune cell recruitment. Using the ID8-Trp53−/− murine model of HGSC, we demonstrated the potential of Stimulator of Interferon Genes (STING) pathway activation in enhancing response of HGSC tumors to carboplatin chemotherapy and sensitizing them to immune checkpoint blockade. Notably, CXCL10 production via IFN1 from STING activation is also governed by genes that regulate cellular DNA damage repair pathways. Evolving evidence indicates a role of BRCA1 and PTEN genes in mediating cellular IFN1 responses. Losses in the function of these genes is widely prevalent in a large proportion of HGSC tumors, where tumors with BRCA1 mutations have higher CD8+ T cell infiltration in contrast to those with loss of PTEN. We hypothesized that HGSC tumors with loss of PTEN expression can be rendered susceptible to immune mediated killing via activating the STING pathway. Tumors generated from ID8-Trp53−/−; Brca1−/− cells and those from ID8-Trp53−/−; Pten−/− cells in C57BL6 mice showed significant immunologic differences. STING agonist treatment significantly increased chemosensitivity and improved overall response in mice implanted with ID8-Trp53−/−; Pten−/− cells compared to those treated with carboplatin alone, altering immune responses. This study is foundational to guide rationalistic combinations of STING pathway activating therapies in HGSC. Supporting Agency: Canadian Institutes of Health Research (CIHR) and Early Research Award from the Ontario Ministry of Innovation Research and Science

PKC-MEDIATED ENDOCYTIC DEGREDATION OF KV1.5 CHANNELS REGULATED BY BOTH C- AND N- TERMINI. Ananya Chakraborty, Wentao Li, Jun Guo, Amanda Paynter, Febri Kurniawan, Mark Szendrey, and Shetuan Zhang. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

Kv1.5 is a voltage-gated potassium channel that is vital in the regulation of atrial action potentials. We previously showed that Protein Kinase C (PKC) decreases membrane expression of Kv1.5 by targeting Thr15 in the N terminus of the channel. Conversely, Kv1.4, a channel found in neurons and cardiac myocytes, is unaffected by PKC activation, even when we replaced its N-terminus with that of Kv1.5. This implicates other parts of Kv1.5 in the action of PKC. We investigated the role of the C-terminus in PKC-mediated endocytosis. Ubiquitin is a signal for endocytosis, and most commonly acts on lysine, and cysteine residues. We removed potential ubiquitination sites by replacing Lys536, Lys565, and Lys565 with Arginine. We found that individually, these do not abolish the effect of PKC, but the removal of all three lysine residues reduces the effect. Since the effect was only partially prevented, we examined cysteine residues in the C-terminal. A point mutation replacing Cys604 with Serine drastically reduced the effect of PKC. Data from channels which combine the triple-lysine mutation and the point C604S mutation, as well as a truncation mutation (ΔC536) which removes triple lysine and C604 completely abolished the effect of PKC. We conclude that an interaction between the N- and C- termini is required for PKC-mediated channel degradation. (Supported by NSERC RGPIN-2019-04878)

Endothelial *BMPR2* loss promotes altered IL-15 signaling, contributing to immune and vascular dysfunction in pulmonary arterial hypertension. L. Rhiannon Hilton[1], Matthew T. Rätsep[1], M. Martin VandenBroek[1], Salema Jafri[2], Melissa Mitchell[1], Anne L. Theilmann[1], James A. Smart[1], Lindsey Hawke[1], Stephen D. Moore[2], Stephen J. Renaud[3], Michael J. Soares[4], Nicholas W. Morrell[2], Mark L. Ormiston[1]
Queen's University Departments of Biomedical and Molecular Sciences, Medicine and Surgery, Kingston, Canada, University of Cambridge Department of Medicine, Cambridge, UK, Western University, Department of Anatomy and Cell Biology, London, Canada, University of Kansas Medical Center, Departments of Pathology and Laboratory Medicine and Obstetrics and Gynecology, Kansas City, Kansas, United States

Rationale: Pulmonary arterial hypertension (PAH) is a disease of pathological vascular remodelling associated with mutations in *BMPR2*, female sex, and immune dysfunction. Natural killer (NK) cells have a documented capacity to mediate vascular remodeling and are impaired in both patients and animal models of disease. While BMP-mediated signaling is known to influence NK cell development, the contribution of *BMPR2* loss to NK cell impairment in PAH remains unknown. We have previously identified that mice bearing a disease-associated *Bmpr2* mutation exhibit decreased NK cells, and reduced pulmonary levels of the interleukin-15 (IL-15)/IL-15 receptor-α (IL-15Rα) complex, a major regulator of NK homeostasis. This work examines the impact of *BMPR2* loss on IL-15 signaling and NK cell homeostasis in two rat models of PAH. **Methods/Results:** siRNA-mediated *BMPR2* silencing of human pulmonary artery endothelial cells significantly reduced IL-15Rα secretion and surface presentation. Confocal microscopy identified a loss of trans-Golgi-network associated IL-15Rα in *BMPR2*-silenced cells. Both male and female NK cell deficient *Il15*$^{-/-}$ rats exposed to the SUGEN/Hypoxia model of PAH developed more severe disease than their wildtype counterparts. In contrast, only male *Il15*$^{-/-}$ rats demonstrated this enhanced severity in the monocrotaline model of disease.
Conclusion: We have identified the loss of IL-15 signaling as a novel *BMPR2*-dependent contributor to NK cell impairment and PAH pathogenesis. Ongoing work will assess the sex differences observed in these models using ovariectomized and castrated rats.

COMPREHENSIVE IMMUNE PROFILING OF HUNNER LESIONS IN INTERSTITIAL CYSTITIS USING IMAGING MASS CYTOMETRY: A PROOF-OF CONCEPT STUDY. Nathalia Kim1, Tiziana Cotechini2, Charles C.T. Hindmarch3,4.5, David Berman6, Charles H. Graham2, J. Curtis Nickel7, D. Robert Siemens7, R. Christopher Doiron7 and Amber Simpson1,2 1School of Computing, 2Department of Biomedical and Molecular Sciences, 3Department of Medicine, 4Translational Institute of Medicine (TIME), 5Queen's Cardiopulmonary Unit, 6Department of Pathology, 7Department of Urology, Queen's University.

Hunner lesions (HLs) are inflammatory lesions of the bladder commonly associated with interstitial cystitis/bladder pain syndrome (IC/BPS). The inflammatory microenvironment of HLs has been poorly described in the literature and there is no agreed upon immune profile diagnostic of a HL. Here we used state-of-the-art, high resolution Imaging Mass Cytometry (IMC) and sophisticated artificial intelligence (AI) algorithms to spatially resolve and profile the cellular immune microenvironment of HLs in a pilot cohort of ten HL-IC/BPS patients. Formalin-fixed paraffin embedded tissue sections were stained using a cocktail of 27 antibodies and images were acquired using the Hyperion™ Imaging System. Multiplexed images were segmented into individual cells using a deep learning/AI approach, single-cell proteomic data were extracted, and a statistical machine learning model was used to phenotype cells. These methods identified 174,903 cells and 17 cell phenotypes across all samples. On average, 49% of all cells within HLs were identified as CD45+ immune cells. Within the immune cell compartment, various populations and activation states of immune cells including macrophages, B cells, CD4+ and CD8+ T cells were identified and spatially resolved. Our data provide an in-depth look into the immune complexity of HLs and provide proof-of-concept data for the use of IMC to study the immune contexture of HLs in a larger cohort of IC/BPS patients.

DISRUPTION OF CONSERVED GLYCAN-DEPENDENT ATTACHMENT AS AN ANTIVIRAL STRATEGY FOR EMERGING CORONAVIRUSES. Emmanuelle V. LeBlanc1, Caleb R. Morin1, Kimberley C. Siwak1, Youjin Kim1, Daniel Whalen2, Chantelle J. Capicciotti1,2,3 and Che C. Colpitts1.
1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Canada, 2Department of Chemistry, Queen's University, Kingston, Canada, 3Department of Surgery, Queen's University, Kingston, Canada

The SARS-CoV-2 outbreak marks the third emergence of a highly pathogenic coronavirus (CoV) in the 21st century. The diversity of CoVs in bats highlights the likelihood of future spillover into human populations. We aim to develop broadly-acting antivirals that prevent CoV infection. Most human viruses, including CoVs, initiate attachment to cells through interactions with complex carbohydrates called glycans. Blocking these initial glycan-dependent interactions is a demonstrated approach to inhibit entry of diverse viruses. We show that the natural product epigallocatechin gallate, which broadly inhibits viral attachment to cellular glycans, inhibits entry of endemic human CoVs (HCoV-229E, HCoV-OC43) as well as highly pathogenic emergent and pre-emergent CoVs (SARS-CoV-2, MERS-CoV, bat WIV1-CoV). However, the specific glycan moieties mediating CoV attachment remain poorly defined. Using targeted glyco-engineering and chemical biology approaches, we show that heparan sulfate glycosaminoglycans contribute to SARS-CoV-2 and WIV1-CoV attachment. Furthermore, CoV spike proteins are themselves highly glycosylated and these viral glycans contribute to entry by interacting with cellular lectins. Using site-directed mutagenesis and enzymatic glycan cleavage, we have produced viral particles with altered spike glycoforms to evaluate the impact on infection of susceptible cell lines which lack or overexpress human lectins. These findings are informing our rational design of potent CoV entry inhibitors to advance the development of pan-coronavirus antivirals that may protect against future emerging CoVs. (Supported by Queen's Rapid Response COVID-19 Funding.)

THE IDENTIFICATION OF CELLULAR MOLECULES IN PROXIMITY TO THE HERPES SIMPLEX VIRUS TYPE 2 TEGUMENT PROTEIN UL21. Safara Holder1, Maike Bossert1, and Bruce Banfield1
1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada

Herpes Simplex Virus Type 2 (HSV-2) is the primary cause of ulcerative genital lesions in humans; however, it is known to cause encephalitis and rare neonatal infections. HSV-2 virions contain a double-stranded DNA genome encased within an icosahedral nucleocapsid. This capsid is enclosed by a glycoprotein studded lipid envelope and between the envelope and the nucleocapsid is a proteinaceous layer called the tegument. In recent years, the Banfield lab has focused on investigating the functions of many tegument proteins during viral replication. Specifically, the unique long tegument protein, pUL21, which has been shown to be involved in multiple aspects of the viral replication cycle and is essential for HSV-2 infection. To further understand the mechanism by which pUL21 enables viral replication, we have utilized a proximity-dependent biotin identification approach (BioID) whereby a bait protein (pUL21) is fused to a non-specific biotin ligase, miniTurbo (mT). In the presence of biotin, mT biotinylates proteins within a 10nm radius, which can be affinity purified and identified by mass spectrometry. We have constructed and characterized a recombinant HSV-2 strain expressing pUL21 fused to mT (HSV-2 pUL21-mT). Our data has demonstrated that HSV-2 pUL21-mT can biotinylate proteins at early and late stages of infection. Future work will aim at identifying biotinylated proteins in proximity to pUL21 during infection to elucidate the roles this protein plays during the HSV-2 replication cycle. (Supported by CIHR grant 407982 and NSERC grant RGPIN-2018-04249)

CIRCADIAN DISRUPTION IN A MOUSE MODEL OF MULTIPLE SCLEROSIS. Julia P. Segal ,a Hailey Gowdy a, Mitra Knezic, a,Ian Gilron a,b,c, Nader Ghasemlou a,b,c, a Department of Biomedical & Molecular Sciences, Queen's University, Kingston, Ontario, K7L 3N6, Canada b Department of Anesthesiology & Perioperative Medicine, Kingston Health Sciences Centre, Kingston, Ontario, K7L 2V7, Canada, c Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, K7L 3N6, Canada.

People living with multiple sclerosis (MS) report daily fluctuations in various symptoms including pain, and some evidence suggests they experience signs of circadian disruption. We therefore sought to identify whether pain and neuroinflammation are under circadian control in experimental autoimmune encephalomyelitis (EAE), a mouse model of MS. It was found that mechanical sensitivity was increased at ZT8 (where ZT0=lights on) compared to ZT2, 14, and 20, suggesting that this pain modality may be under circadian control. Flow cytometric analysis of lumbar spinal cord tissue revealed disrupted rhythms in several immune cell subsets. Furthermore, disrupted clock gene rhythms were identified in the lumbar ventral horn spinal cord of EAE mice, where inflammation is strongest. These findings suggest a potential role for circadian disruption in the pathology of EAE, which led us to investigate the effects of environmental circadian disruption on EAE severity. Housing mice in a 10 hour light 10 hour dark cycle (10:10) for 4 weeks prior to immunization was found to exacerbate EAE symptoms compared to mice housed in regular 12 hour cycles (LD). This increased disease severity was accompanied by increased demyelination as well as CD4+ T cell, macrophage, and monocyte infiltration to the spinal cord. Further investigation may reveal a mechanism underlying circadian disruption as a risk factor for developing MS.

EXCITATION OF VAGAL AFFERENT NEURONS BY FECAL SUPERNATANT FROM PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Ayssar Tashtush, David E. Reed and Alan E. Lomax. Department of Neuroscience, Gastrointestinal Diseases Research Unit, Queen's University, Kingston, Ontario, Canada

Background: The gut-brain axis has received increasing attention recently due to evidence that colonic microbes can affect brain function and behavior. Vagal afferent neurons can sense microbiota signals via the diffusion of bacterial metabolites. However, there is a lack of mechanistic insight into whether dysbiosis of gut microbiota during inflammatory bowel disease (IBD) impacts the function of vagal afferent neurons. Methods: To examine the effect of IBD patients' fecal supernatant (FS) on the excitability of mouse vagal afferent neurons, nodose ganglia (NG) from C57/Bl6 mice were collected, dissociated and incubated overnight with FS from 5 active Crohn's disease (CD) patients,7 active ulcerative colitis (UC) patients, and 5 healthy volunteers (HV) at a 1 in 20 dilution. Current and voltage-clamp recordings were used to assess changes in neuronal activity. Results: CD and UC FS, but not the HV FS, increased the excitability of NG neurons by 40% and 23%, accompanied by a 18% and 34% decrease in the voltage-gated K+ currents respectively. The increase in excitability produced by IBD supernatant was blocked by the cysteine protease inhibitor (E64) (30 nM) but not the serine protease inhibitor (FUT175) (10 μM). The protease-activated receptor 2 (PAR2) antagonist GB83 (10 μM) also blocked the effect of IBD patient supernatant on NG neurons. Conclusion: The dysbiotic microbiota of IBD patients produces cysteine proteases that excite NG neurons by activation of PAR-2. Signaling pathways downstream of PAR-2 activation lead to inhibition of voltage-gated K+ currents. Supported by CIHR

THE EXERCISE-INDUCED HORMONE IRISIN IS REDUCED IN THE CEREBROSPINAL FLUID OF ELDERLY DEPRESSED INDIVIDUALS. Rafaella A Gonçalves and Fernanda G. De Felice. Centre for Neuroscience Studies, Department of Biomedical and Molecular Sciences.

Depression is a common mental disorder with high incidence in the elderly population and pathophysiology still elusive. The identification of new biomarkers associated with disease pathogenesis have important implications for the elucidation of disease mechanisms and therapeutic development. In this cross-sectional study, we measured irisin levels in the plasma and cerebrospinal fluid (CSF) of elderly depressed individuals (n = 25; 16 women [64%]; age 60-83 years) and non-depressed controls (n = 36; 21 women [58.3%]; age 61-85 years). Depression diagnosis was determined using the Geriatric Depression Scale with 15 items, and a cut-off score of 5. Our results indicate reduced irisin levels in the CSF, but not in the plasma, of elderly depressed subjects. We have also observed reduced CSF levels of BDNF in our cohort of depressed individuals, and a positive association between CSF Irisin and BDNF. Moreover, CSF levels of irisin and BDNF positively correlated with Mini-Mental State Exam scores in non-depressed individuals, but not in the depressed group. This may indicate that CSF irisin and BDNF are reduced in depression regardless of cognitive integrity. To our knowledge, this is the first study investigating CSF irisin levels in depression, and our findings suggest that irisin plays a role in disease pathophysiology. Strategies aiming to increase brain irisin levels, such as exercise, might thus be beneficial to depressed individuals. (Supported by CNPq)

Patient Care and Nursing

A FEASIBILITY STUDY OF A SOCIAL MEDIA-BASED DIABETIC FOOT ULCER PREVENTION PROGRAM DURING THE COVID-19 PANDEMIC IN CANADA. Helen Obilor and Kevin Woo. Background. Diabetic foot ulcer (DFU) is a costly complication associated with excessive disability and mortality. Due to the COVID-19 pandemic impact on the healthcare system, recent studies have anticipated an increased DFU incidence among people with diabetes (PWD) (1,2).

Aim. This study aims to determine the PWD acceptance of a social media-based DFU prevention program and its efficacy on foot care outcomes. Method. This feasibility study utilized a partially randomized preference trial design. The study intervention is a patient education-focused support group implemented via Facebook. The study is ongoing, and data collection involves a validated questionnaire administered through QualtricsXM at three time-points with an interview. Results. Thirty-two participants recruited to date (intervention [n= 23] and control group [n=9]). At baseline, 62.5% of the participants had a moderate DFUs' risk level and poor adherence to foot self-care recommendations. The intervention acceptance mean-score was 83.08 ± 9.93 (cut-off point > 70%). The intervention led to significant improvement in only participants' adherence to foot self-care recommendations (p=0.01). Also, the intervention increased participants' awareness of DFUs as a serious diabetes complication. Conclusion. Preliminary findings showed that the social media-based DFU prevention program is acceptable to PWD and could improve foot self-care outcomes.

Department: School of Nursing, Supporting Agency: Wounds Canada 1. Canadian Diabetes Association (2020). The impact of COVID-19 on access to diabetes care, management, and related complications. Retrieve from https://www.diabetes.ca/DiabetesCanadaWebsite/media/Campaigns/COVID-19%20and%20Diabetes/impactcovid.pdf 2. Casciato, D., Yancovitz, S., Thompson, J., Anderson, S., Bischoff, A., Ayres, S., & Barron, I. (2020). Diabetes-related major and minor amputation risk increased during the COVID-19 pandemic. J Am Podiatr Med Assoc, doi: 10.7547/20-224

Protein Structure and Function

KINESIN-8-SPECIFIC LOOP 2 IS A CONFORMATIONAL SWITCH THAT CONTROLS THE DUAL ACTIVITIES OF THE MOTOR DOMAIN ACCORDING TO MICROTUBULE SHAPE. Byron Hunter, Matthieu Benoit, Caitlin Doubleday, Ana Asenjo, Daria Trofimova, Hernando Sosa, and John Allingham. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON Department of Physiology and Biophysics, Albert Einstein College of Medicine, Bronx, New York

Kinesin-8 motors are motile microtubule depolymerizers that regulate mitotic spindle positioning and spindle length. The high-resolution crystal and cryo-EM structures of Candida albicans Kip3 that we report here define a structural mechanism for differential activation of the motility and depolymerization catalytic cycles of kinesin-8. The hyper-elongated loop 2 of CaKip3's motor domain can make extensive interactions with either α-tubulin or the plus end-facing surface of a proximal CaKip3 motor domain, depending on the shape of the tubulin polymer it binds. On a straight tubulin polymer, loop 2 forms bonds with α-tubulin that restrict the motor domain from closing its nucleotide pocket around ATP and initiating neck linker docking and motility. We provide evidence that this loop 2-tubulin interaction limits microtubule-stimulated ATPase and velocity of the motor. On curved tubulin polymers, such as those found at microtubule ends, loop 2 deflects upwards from its position on straight tubulin, allowing the ATP-bound nucleotide pocket to close and the neck linker to dock against the motor domain. This stimulates ATP turnover and appears to be important for microtubule depolymerization activity. These findings implicate the unique loop 2 in the motor domain of kinesin-8s as a conformational switch that enables either movement or microtubule depolymerization activity according to microtubule shape. They also show how kinesin-8s could depolymerize microtubules using a collective force-dependent mechanism. (Supported by the Natural Sciences and Engineering Research Council of Canada and the Canadian Institutes of Health Research)

A SYSTEMATIC REVIEW AND META-ANALYSIS OF EXERCISE INTERVENTIONS AND USE OF EXERCISE PRINCIPLES TO REDUCE FEAR OF FALLING AMONG COMMUNITY-DWELLING OLDER ADULTS. Feng C, Adebero T, DePaul V, Vafaei A, Norman K, and Auais M. School of Rehabilitation Science, Queen's University, Kingston, ON, Canada.

Background: Fear of Falling (FOF) contributes to activity restriction and institutionalization among older adults; exercise interventions are linked to reduction in FOF. Adhering to exercise principles and adapting optimal exercise parameters are fundamental to optimizing the effectiveness of exercise interventions. The purpose of this review was to evaluate the extent to which these interventions followed the exercise principles and reported exercise parameters and quantify the effect of these interventions on reducing FOF. Method: Randomized Controlled Trials (RCTs) of FOF exercise interventions in older adults (≥65 years) were identified from four databases. The methodological quality of RCTs was assessed using the PEDro scale. A random-effect model was used in the meta-analysis. Results: Seventy-five RCTs were included in our review. Regarding exercise principles, specificity was reported in 92% of trials, progression in 72%, reversibility in 32%, overload in 31%, diminished return in 21%, and initial value in 8%. For exercise parameters, 97% of RCTs reported exercise type, 89% frequency, 85% time, and only 25% reported the intensity. The pooled effect of exercise interventions on FOF among all included studies was a standard mean difference of -0.34 (95% confidence interval: -0.44, -0.23). Conclusion: Most exercise principles and intensity of exercises were not adequately reported in included trials. More attention must be given to designing and reporting components of therapeutic exercise programs to facilitate evidence-based practice.

Poster Presentations

Biomedical Engineering

1. **DEVELOPMENT OF A SIMULATION TRAINING CURRICULUM FOR ULTRASOUND-GUIDED VASCULAR ACCESS FOR SUSTAINABLE TRANSLATION TO MAURITANIA.** Sarah GF Ryan1, Tamas Ungi2, Sarah Maxwell3, Melanie Jagger3, Lindsay Patterson3, Parvin Mousavi2, Gabor Fichtinger2. Department of Medicine1, School of Computing2, and Department of Anesthesiology3, Queen's University, Kingston ON.

Cancer Research and Therapy

2. **EFFECT OF ROUTE OF BACILLUS CALMETTE GUÉRIN ADMINISTRATION ON THE TUMOUR IMMUNE MICROENVIRONMENT IN A MOUSE MODEL OF NON-MUSCLE INVASIVE BLADDER CANCER.** Aline Atallah, Arielle Grossman, William Tran, Jean-Francois Paré, Tiziana Cotechini, Charles H. Graham Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Canada

3. **THE POTENTIAL OF TARGETING MITOCHONDRIAL DYNAMICS IN CANCER THERAPY THROUGH UBIQUITINATION AND NEDDYLATION PATHWAYS.** Charles Chu, Brianna Kaplanis, Chelsea Margerum, and Edmond Chan. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada

4. **DIFFERENTIATING COLORECTAL CANCER PATHOLOGICAL REGIONS USING DESORPTION ELECTROSPRAY IONIZATION-MASS SPECTROMETRY IMAGING.** Natasha Iaboni1, David Hurlbut1,2, Kevin Yi Mi Ren1,2, Martin Kaufmann4, Amoon Jamzad3, Vanessa Wiseman4, Parvin Mousavi3, Gabor Fichtinger3, John F. Rudan2,4, Antonio Caycedo-Marulanda2,4 and Christopher JB Nicol1,5 1Dept. of Pathology & Molecular Medicine; 2Kingston Health Sciences Center; 3School of Computing; 4Dept. of Surgery; 5Division of Cancer Biology & Genetics, Cancer Research Institute. Queen's University, Kingston, ON, Canada

5. **SURGICAL MARGIN ASSESSMENT IN LUMPECTOMIES USING COMPUTER AIDED CHARACTERIZATION AND INTERPRETATION OF MASS SPECTROMETRY DATA.** Amoon Jamzad1, Alice Santilli1, Faranak Akbarifar1, Martin Kaufmann2, Kathryn Logan3, Julie Wallis3, Kevin Ren3, Shaila Merchant2, Jay Engel2, Sonal Varma3, Gabor Fichtinger1, John Rudan2, Parvin Mousavi1 1School of Computing, 2Department of Surgery, 3Department of Pathology and Molecular Medicine. Queen's University, Kingston, ON, Canada.

6. **EXAMINING THE IMPACT OF ENDOTHELIAL BMPR2 LOSS ON BMP9-ASSOCIATED ANGIOGENESIS IN A MOUSE MODEL OF METASTATIC BREAST CANCER.** J.A. Harry1, K. Laverty2, P.A. Greer2, V. Hoskin2, D.V. Cole1, M. Mitchell2, Y. Gao2, M.L. Ormiston1,2, 1 Department of Medicine, Queen's University, Kingston ON, Canada, 2Biomedical and Molecular Sciences, Queen's University, Kingston ON, Canada.

7. **IL-27 AND POLY(I:C) SENSITIZE PROSTATE CANCER CELLS TO NK CELL-MEDIATED CYTOTOXICITY.** Olena Kourko[1], Lindsey Hawke[1], Mark Ormiston[1], and Katrina Gee[1] [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston ON, K7L 3N6

8. **SEX DIFFERENCES IN AGING BLADDER IMMUNE PHYSIOLOGY ASSOCIATE WITH DISTINCT PRE-TREATMENT TUMOR IMMUNE STATES IN A MURINE MODEL OF BLADDER CANCER**
   Ali Hamade1,2, Deyang Li1,2, Kathryn Tyryshkin3, Gwenaelle Conseil1, 2, D. Robert Siemens4, Madhuri Koti1, 2, 4 1Queen's Cancer Research Institute, Kingston, ON, Canada, 2Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada, 3Department of Pathology and Molecular Medicine, Queen's University, Kingston, ON, Canada, 4Department of Urology, Queen's University, Kingston, ON, Canada.

9. **REGULATION OF PODOSOME ROSETTE FORMATION FOR FOCAL CONTROL OF SPROUTING ANGIOGENESIS** Charmi S. Shah, Maria B. Umana and Donald H. Maurice, Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

10. **NOVEL TOOLS TO ASSESS AND PREDICT THE RISK OF CANCER-ASSOCIATED THROMBOSIS IN WOMEN UNDERGOING CHEMOTHERAPY FOR BREAST AND GYNECOLOGICAL CANCERS.** Yousra Tera1 (PostDoc), Mihaela Mates2 (MD, FRCPC), Anita Agrawal3 (MSc, MD, FRCSC), Jayachandran Kizhakkedathu4 (PhD), Maha Othman (MD PhD)1,5 1 Department of Biomedical and Molecular Sciences, Queens's University, Kingston, ON, Canada 2 Department of Oncology, Queens's University, Kingston, ON, Canada
    3 Department of Obstetrics and Gynecology, Queens's University, Kingston, ON, Canada
    4 The Centre for Blood Research, University of British Columbia, Vancouver, BC, Canada
    5 Department of Medicine, Division of Hematology, Queens's University, Kingston, ON, Canada 5School of Baccalaureate Nursing, St. Lawrence College, Kingston, ON, Canada.

11. **INVESTIGATING THE OPTIMAL ROUTE OF INOCULATION OF BACILLUS CALMETTE GUÉRIN FOR THE INDUCTION OF INNATE IMMUNE MEMORY IN THE TREATMENT OF BLADDER CANCER.** William Tran, Jean-François Paré, Aline Atallah, Tiziana Cotechini, Charles H. Graham, Department of Biomedical and Molecular Sciences, Queen's University.

12. **TUMOR ADJACENT TERTIARY LYMPHOID STRUCTURES ASSOCIATE WITH POOR RESPONSE TO BCG IMMUNOTHERAPY IN NON-MUSCLE INVASIVE BLADDER CANCER.** Stephen Chenard1,2, Priyanka Yolmo1,2, Danielle Jenkins3, Minqi Xu4, D. Robert Siemens4 and Madhuri Koti1, 2, 4
    1Queen's Cancer Research Institute, Kingston, ON, Canada, 2Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada, 3Department of Pathology and Molecular Medicine, Queen's University, Kingston, ON, Canada, 4Department of Urology, Queen's University, Kingston, ON, Canada

13. **LACK OF DEFINITIVE PRESURGICAL PATHOLOGICAL DIAGNOSIS IS ASSOCIATED WITH INADEQUATE SURGICAL MARGINS IN BREAST-CONSERVING SURGERY.** Paola V. Nasute Fauerbach, MD; Kathrin Tyryshkin , PhD; Silvia Perez Rodrigo, MD; John Rudan, MD; Gabor Fichtinger, PhD; Michael Reedijk, MD, PhD; Sonal Varma, MD; David M. Berman, MD, PhD.**Department:** Pathology and Molecular Medicine, Queen's University, Kingston, Ontario, Canada.

Cardiac, Circulatory, and Respiratory Sciences

14. **ASSESSING THE IMPACT OF BMPR2 LOSS ON PHOSPHOINOSITIDE DYNAMICS AND CELLULAR TRAFFICKING IN ENDOTHELIAL CELLS.** N.J. Chronis1, L.G. Hawke1, M.M. Vandenbroek2, M.L. Ormiston1,2, 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada, 2Department of Medicine, Queen's University, Kingston Ontario, Canada.

15. **GENETIC DELETION OF NATURAL KILLER CELL TGF-B SIGNALING PROTECTS MICE FROM HYPOXIA-INDUCED PULMONARY HYPERTENSION** Kassandra M. Coyle[1], Matthew Rätsep[1], Kimberly Laverty[2], L. Rhiannon Hilton[2], M. Martin Vandenbroek[1], Melissa Mitchell[2], Mark L. Ormiston[1,2] 1. Department of Medicine, Queen's University, Kingston, ON, Canada 2. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

16. **THE PRIMARY CILIUM: A HYPER-LOCALIZED COMPARTMENT FOR CAMP SIGNALLING.** Mikayla Erdelsky, M. Bibiana Umana and Donald H. Maurice, Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

17. **COVID-19 COAGULOPATHIES- SYSTEMATIC REVIEW OF HAEMOSTASIS IMPAIRMENT AND DISEASE OUTCOMES- 18 MONTHS INTO THE PANDEMIC.** Shreya Anil Kumar[1] (3rd year LifeSci), Anushka Pradhan[1] (3rd year BHSc), Abdelrahman Elsebaie[1] (3rd year BHSc), Karina Fainchtein[1] (3rd year LifeSci), Abdelrahman Noureldin[1] (3rd year BHSc), Sajida Kazi[2] (MBBch), Maha Othman[1,3] (MD PhD) [1] Department of Biomedical and Molecular Sciences, Queens's University, Kingston, ON, Canada [2] Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK , [3] School of Baccalaureate Nursing, St. Lawrence College, Kingston, ON, Canada.

18. **PROFILING BMPR2-DERIVED ENDOTHELIAL CIRCRNAS IN PULMONARY ARTERIAL HYPERTENSION.** M. Martin VandenBroek1, Mackenzie C. Sharp2, L. Rhiannon Hilton3, Anne L. Theilmann3, Mark L. Ormiston1,3, 1Department of Medicine, Queen's University, Kingston ON2School of Computing, Queen's University, Kingston ON, 3Department of Biomedical and Molecular Sciences, Queen's University, Kingston ON.

19. **MITOCHONDRIAL DNA-DEPENDENT CHANGES IN LIPID BIOSYNTHESIS AND INSULIN SIGNALLING IN WHITE ADIPOSE TISSUE AND SKELETAL MUSCLE.** Abhishek Shastry, Charles CT Hindmarch, PhD, Kimberly J Dunham-Snary, PhD, Departments of Biomedical & Molecular Sciences and Medicine at Queen's University

20. **DESIGNING A SPLIT LUCIFERASE REPORTER TO ASSESS THE KINETICS OF ENDOTHELIAL BMP9 SIGNALING.** S.I. Skebo1, M. M. VandenBroek2, L. Hawke1, M.L. Ormiston1,2 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston ON, 2Department of Medicine, Queen's University, Kingston ON

21. **WESTERN DIET INDUCES CHANGES IN NUCLEAR GENE EXPRESSION *IN VIVO* THAT ARE MODULATED BY MITOCHONDRIAL HAPLOTYPE.** Mia S Wilkinson[1], Charles C T Hindmarch[2], Kimberly J Dunham-Snary[1,3]. 1 – Department of Biomedical & Molecular Sciences, Queen's University, Kingston, ON. 2 – Queen's CardioPulmonary Unit, Queen's University, Kingston, ON. 3 – Department of Medicine, Queen's University, Kingston, ON.

Health Policy, Population Health, and Epidemiology

22. **ACCURACY OF SELF-ASSESSMENT IN GASTROINTESTINAL ENDOSCOPY: A SYSTEMATIC REVIEW AND META-ANALYSIS.** Michael A. Scaffidi1,2, Juana Li1, Shai Genis1, Elizabeth Tipton3, Rishad Khan1, Chandni Pattni1, Nikko Gimpaya1, Glyneva Bradley-Ridout4, Catharine M. Walsh5,6,7, and Samir C. Grover1.

23. **THE CIRCAPAIN STUDY: EXAMINING CIRCADIAN CONTROL OF CHRONIC PAIN THROUGH A NATIONAL CROSS-SECTIONAL SURVEY.** Hailey Gowdy[1], Mitra Knezic[1], Zihang Lu[4], Gabrielle Pagé[5], Manon Choinière[5], Etienne Bisson[2], and Nader Ghasemlou[2,1,3]. [1]Department of Biomedical and Molecular Science, Queen's University, Kingston, Ontario, Canada. [2]Department of Anesthesiology and Perioperative Medicine, Queen's University, Kingston, Ontario, Canada. [3]Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, Canada. [4]Department of Public Health Sciences, Queen's University, Kingston, Ontario, Canada. [5]Department of Anesthesiology, University of Montreal, Montreal, Quebec, Canada.

24. **THE EXPERIENCES OF PEOPLE WITH A HISTORY OF SUBSTANCE USE AND ALCOHOLISM IN THE EMERGENCY ROOM: A MIXED METHODS STUDY.** Dr. Susan Bartels, Dr. Melanie Walker, Sonal Gupta, Dr. Jodie Pritchard.

25. **TRENDS IN THE PROPORTION OF WOMEN SPEAKERS AT NORTH AMERICAN ALLERGY AND IMMUNOLOGY CONFERENCES OVER A 12-YEAR PERIOD.** Kristin M. Hunt, Mary Foley, Lori Connors, Kyla Hildebrand, Anne K. Ellis. Department of Allergy and Immunology, Queen's University, Kingston, Ontario, Canada.

26. **COVID-19 VACCINE HESITANCY AND UPTAKE IN CANADIAN HEALTHCARE WORKERS.** Sierra Killam, Brenda Coleman, Prameet M. Sheth. Faculty of Health Sciences, Queen's University, Kingston, Ontario, Canada.

Inflammation, Infection and Immunity

27. **A ROLE FOR THE HSV TEGUMENT PROTEIN UL21 IN RETENTION OF VIRAL GENOMES WITHIN CAPSIDS.** Ethan Thomas1 and Bruce Banfield1, 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

28. **INTERLEUKIN-27 INHIBITS INFLUENZA A VIRUS INFECTION IN THP-1 MACROPHAGES.** Heather Amsden, Katrina Gee, and Che Colpitts. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

29. **THE GUT-BRAIN AXIS AND BEYOND: MICROBIOME CONTROL OF SPINAL CORD INJURY PAIN.** Courtney A Bannerman, Katya Douchant, Julia P Segal, Alex Mack, Prameet M Sheth, Nader Ghasemlou. Department: Biomedical and Molecular Science. Funding: Ontario Graduate Scholarship, Craig H Neilsen Foundation.

30. **GPR55-DEPENDENT EXCITATION OF DORSAL ROOT GANGLION NEURONS BY LYSOPHOSPHATIDYLCHOLINE.** Aidan S. W. Bennett, Taylor A. Alward, and Alan E. Lomax. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

31. **CHARACTERIZING THE ROLE OF TRAINED IMMUNITY AND IFNγ IN RESTRICTING CORONAVIRUS REPLICATION.** Isabella Delano, Arielle Grossman, Charles H. Graham, and Che C. Colpitts. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Canada.

32. **EXAMINING THE NASAL MICROBIOTA IN SARS-COV-2, INFLUENZA A VIRUS AND RESPIRATORY SYNCYTIAL VIRUS INFECTED INDIVIDUALS.** Emily Moslinger, Katya Douchant, Kyla Tozer, Calvin Sjaarda, Jesse Kelly, Shu-Mei He, Henry Wong, Prameet M. Sheth. Department of Pathology and Molecular Medicine, Gastrointestinal Disease Research Unit (GIDRU), Queen's University, Kingston, Ontario, Canada.

33. **ENHANCED ANTIGEN PRESENTATION AND PROTECTION AGAINST VIRAL INFECTION THROUGH ACQUISITION OF TRAINED IMMUNITY.** Arielle Grossman, Isabella Pellizzari Delano, Aline Atallah, Tiziana Cotechini, Che Colpitts, Charles H. Graham. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Canada.

34. **ACQUISITION OF INNATE IMMUNE MEMORY IN BONE MARROW MONOCYTES DURING MURINE PREGNANCY.** Nakeisha A. Lodge-Tulloch, Tiziana Cotechini, and Charles Graham. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

35. **TARGETING CYCLOPHILINS TO ENHANCE ANTIVIRAL IMMUNITY AGAINST POSITIVE-SENSE RNA VIRUSES.** John Mamatis and Che C. Colpitts. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Canada.

36. **USING CULTUROMICS TO CHARACTERIZE THE GUT MICROBIOTA OF LOW BIRTH WEIGHT NEONATES.** Jummy Oladipo, Mabel Guzman-Rodriguez, Curtis Noordhof, Shu-Mei He, Katya Douchant, Prameet M. Sheth, Department of Medicine, Gastrointestinal Disease Research Unit (GIDRU), Queen's University, Kingston, Ontario, Canada.

Neuroscience Research

37. **PROTEASE-INDUCED EXCITATION OF DORSAL ROOT GANGLION NEURONS IN RESPONSE TO ACUTE PERTURBATION OF THE GUT MICROBIOTA.** Corey Baker, Jessica L Sessenwein, Amal Abu Omar, Quentin Tsang, Yang Yu, Julia Segal, Nader Ghasemlou, Prameet Sheth, Stephen J Vanner, David E Reed, Alan E Lomax. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

38. **VIGILANCE AND BEHAVIORAL STATE-DEPENDENT MODULATION OF CORTICAL NEURONAL ACTIVITY THROUGHOUT THE SLEEP/WAKE CYCLE.** Aurélie Brécier, Mélodie Borel, Nadia Urbain and Luc Gentet. Centre de Recherche en Neurosciences de Lyon, Bron, France.

39. **THE RELATIONSHIP BETWEEN PAIN CATASTROPHIZING AND QUALITY OF LIFE CHANGES IN CHRONIC PAIN PATIENTS IS MEDIATED BY DEPRESSION AND MODERATED BY PAIN SELF-EFFICACY.** Landon Montag1, Tim Salomons1,2, Rosemary Wilson3,4,5, Scott Duggan4,5, and Etienne J. Bisson1,4,5,6 , 1Centre for Neuroscience Studies, Queen's University, Kingston, ON, Canada., 2Department of Psychology, Queen's University, Kingston, ON, Canada. 3School of Nursing, Queen's University, Kingston, ON, Canada. 4Chronic Pain Clinic, Kingston Health Sciences Centre, Kingston, ON, Canada. 5Department of Anesthesiology and Perioperative Medicine, Queen's University, Kingston, ON, Canada. 6School of Rehabilitation Therapy, Queen's University, Kingston, ON, Canada.

40. **EXCITATION OF MOUSE DORSAL ROOT GANGLIA NEURONS BY FECAL SUPERNATANT FROM IRRITABLE BOWEL SYNDROME PATIENTS.** Samira Osman, Stephen Vanner, David E. Reed and Alan E. Lomax. Gastrointestinal Diseases Research Unit and Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, Canada.

41. **A SCOPING REVIEW ON THE EFFECTS OF PSILOCYBIN IN ANIMAL STUDIES ACROSS BEHAVIOURAL TASK CLUSTERS AND NEUROLOGICAL MEASURES.** Ron Shore, Katrina Dobson, Nigel Barnim, Sandra McKeown, Cella Olmstead, Craig Goldie, and Eric C. Dumont. Department of Biomedical and Molecular Sciences, School of Kinesiology and Health Studies, Department of Medicine, Department of Psychology, Queen's University, Kingston, Ontario, Canada.

42. **EXTRACELLULAR VESICLES CARRYING IRISIN ARE UPREGULATED BY EXERCISE AND RESTORE MEMORY IMPAIRMENT IN MOUSE MODELS OF ALZHEIMER'S DISEASE.** Natalia M. Lyra e Silva1,2*, Tayna Rody3*, Guilherme B. de Freitas1,2, Rafaella A. Gonçalves1,2, Emma L. Robertson1, Isabelle Grenier-Pleau2, Brittney Armitage-Brown1, Andrew Winterborn1, Susan E. Boehnke1, Sheela Abraham2, Margaret Fahnestock4, Sergio T. Ferreira3,5, Douglas P. Munoz1,2, Fernanda G. De Felice1, 2, 6. 1Centre for Neuroscience Studies and 2Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada. 3Institute of Medical Biochemistry Leopoldo de Meis, Federal University of Rio de Janeiro, RJ, Brazil. 4Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, ON, Canada. 5Institute of Biophysics Carlos Chagas Filho, Federal University of Rio de Janeiro, RJ, Brazil. 6Department of Psychiatry, Queen's University, Kingston, ON, Canada.

43. **SKIN-RESIDENT DENDRITIC CELLS MEDIATE POSTOPERATIVE PAIN VIA CCR4 ON SENSORY NEURONS.** Jaqueline R. Silva[1,2], Mircea Iftinca[3], Julia P. Segal[1], Olivia M. Smith[1], Francisco I. F. Gomes[4], Courtney A. Bannerman[1], Atlante Mendes[4], Madeline E. C. Robinson[1], Jelena Petrovic[1], Ian Gilron[1,2,5,6], Thiago Mattar Cunha[4], Christophe Altier[3], and Nader Ghasemlou[1,2,5,] [1]Department of Biomedical and Molecular Sciences, [2]Department of Anesthesiology and Perioperative Medicine, Queen's University, Kingston, Ontario, Canada; [3]Department of Physiology and Pharmacology, University of Calgary, Calgary, Alberta, Canada; [4] Center for Research in Inflammatory Diseases (CRID), Department of Pharmacology, Ribeirão Preto Medical School, University of São Paulo, Brazil; [5]Centre for Neuroscience Studies, [6]School of Policy Studies, Queen's University, Kingston, Ontario, Canada

Patient Care and Nursing Research

44. **PSILOCYBIN AT END-OF-LIFE: A SURVEY OF PLANNED BEHAVIOUR AMONG PALLIATIVE AND HOSPICE HEALTH CARE PROVIDERS IN CANADA.** Nina Thomson, Leann Cunningham, Katie Rideout, Ron Shore, and Eric C. Dumont. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

45. **PEERS IN PATHO: THE ONLINE PLATFORM FOR PEER ASSISTED LEARNING BASED TUTORIALS IN PATHOPHYSIOLOGY.** Karina Fainchtein1 (3rd year LifeSci), Madeline Tripp2 (3rd year BScN), Abdelrahman Elsebaie1 (3rd year BHSc), Asad Taqvi3 (4th year BSc), Sarah Crawford4 (BScN RN), Conner Smith2,5 (BScN RN), Kathryn Osborne2,4 (BScN RN), Maha Othman1,2 (MD PhD)1 Department of Biomedical and Molecular Sciences, Queens's University, Kingston, ON, Canada 2 School of Baccalaureate Nursing, St. Lawrence College, Kingston, ON, Canada, 3 McGill University, Montréal, QC, Canada, 4 Grey Bruce Health Services, Meaford, ON, Canada, 5 Ottawa General Hospital, Ottawa, ON, Canada.

Protein Structure and Function

46. **INVESTIGATING THE ROLE OF A KINESIN-8 REGULATORY DOMAIN IN A FUNGAL PATHOGEN.** Caitlin Doubleday, Byron Hunter, and John S. Allingham1, 1Department of Biomedical and Molecular Sciences.

47. **MOLECULAR BASIS OF KLF15-MEDIATED REPRESSION OF CARDIAC HYPERTROPHY.** Matthew S. Fishman1, Holly L. Spencer1, Marina R. Lochhead1, Keegan B. Turner-Wood 1, Steven P. Smith1, 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, K7L 3N6.

48. **UNDERSTANDING THE MECHANISM OF KINESIN-8-MEDIATED MICROTUBULE DEPOLYMERIZATION.** Michelle Gontcharova, Byron Hunter, Daria Trofimova, and John Allingham. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON

49. **IMPACT OF CARBAPENEMASE MECHANISM ON THE CLINICAL DETECTION OF CARBAPENEM-RESISTANT BACTERIA CHARACTERIZED THROUGH PRODUCT FORMATION.** Rachel. A.V. Gray and Christopher. T. Lohans. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

50. **DEVELOPMENT AND VALIDATION OF A BIOSENSOR-BASED APPROACH FOR THE EVALUATION OF B-LACTAMASE ACTIVITY AND INHIBITION.** Mitchell Jeffs and Christopher T. Lohans. Department of Biomedical and Molecular Science, Queens University, Kingston, Ontario, Canada.

51. **TARGETING POLYPHOSPHATE KINASE ENZYMES TO ATTENUATE PSEUDOMONAS AERUGINOSA VIRULENCE.** Nolan Neville, Nathan Roberge, and Zongchao Jia. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

52. **EXPRESSION AND PURIFICATION OF FUNGAL G PROTEIN-COUPLED RECEPTOR *FG*STE2** Pooja S. Sridhar[1], John S. Allingham[1], Michele C. Loewen[1,2], [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, K7L 3N6., [2]National Research Council of Canada, 100 Sussex Drive, Ottawa, K1A 0R6.

53. **INSPIRED BY THE SEA TO FIGHT CANCER METASTASIS.** Daria Trofimova, Bhavin Pipaliya, Yun Jiang, Andrew Craig, P. Andrew Evans, and John Allingham. Department of Biomedical and Molecular Sciences, Queen's Cancer Research Institute, and Department of Chemistry, Queen's University, Kingston, ON, Canada.

54. **ENGINEERING DESIGNER CELLULOSOMES FOR ENHANCED CARBOHYDRATE DIGESTION** Keegan B. Turner-Wood1, Holly L. Spencer1, Benjamin Pluvinage2, Alisdair B. Boraston2, Steven P. Smith1, 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, K7L 3N6, 2Department of Biochemistry and Microbiology, University of Victoria, Victoria, V8P 5C2.

Rehabilitation Science

55. **DEVELOPMENT OF ANATOMICAL MYOFASCIAL TRUNK AND LIMB EDUCATION MODULES FOR HEALTHCARE PROFESSIONALS IN SPORTS MEDICINE.** Lucy Lu, Dr. Craig Harness, Dr. Mark Lindsay, Dr. Leslie MacKenzie. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

56. **THE ASSOCIATION BETWEEN CAREGIVER'S SOCIAL SUPPORT AND BURDEN OF CAREGIVING FOR PATIENTS WITH HIP FRACTURE: A SCOPING REVIEW.** Cara Sadiq, Varsha Doguparty, Dorothy Kessler, Marcia Finlayson, Vincent DePaul, Mohammad Auais. Department of Health Sciences. Queens University. Kingston, ON.

Reproductive and Sexual Function

57. INVESTIGATING THE DIFFERENTIATION POTENTIAL OF SCA-1$^+$ MOUSE TROPHOBLAST STEM CELLS. Megan Cull[1], Avery McGinnis[1], Bryony Natale[2], Nicole Peterson[2], David Natale[1,2], [1]Dept. of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada; [2]Dept. of Obstetrics and Gynecology, Queen's University Kingston, Ontario Canada.

58. MANAGEMENT OF WOMEN WITH TYPE 2B VON WILLEBRAND DISEASE DURING PREGNANCY-EVIDENCE FROM LITERATURE AND INTERNATIONAL REGISTRY. Abdelrahman Noureldin[1] (3rd year BHSc), Predrag Miljic[2] (MD), Michelle Lavin[3] (MB BCh PhD), Sajida Kazi[4] (MB BCh), Analia Sanchez Luceros[5] (MD PhD), Paula D James[6] (MD, FRCPC), Maha Othman (MD PhD)[1,7] [1] Department of Biomedical and Molecular Sciences, Queens's University, Kingston, ON, Canada
[2] Clinic of Haematology, Faculty of Medicine, University in Belgrade, Belgrade , [3] National Coagulation Centre, St. James' Hospital, Dublin, Ireland, [4] Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK, [5]Hematological Research Institute, National Academy of Medicine, Buenos Aires, Argentina, , [6]Department of Medicine, Division of Hematology, Queens's University, Kingston, ON, Canada , [7]School of Baccalaureate Nursing, St. Lawrence College, Kingston, ON, Canada.

59. EXPLORATION OF THE MECHANISM OF ACTION OF HUMAN OVIDUCT-SPECIFIC GLYCOPROTEIN (OVGP1) IN ENHANCING SPERM CAPACITATION. Sydney C. Vanderkooi (M.Sc. Candidate), Yuewen Zhao (Ph.D), Patricia Lima (Ph.D) and Frederick W. K. Kan (Ph.D). Department of Biomedical and Molecular Sciences & Queen's CardioPulmonary Unit, Queen's University, Kingston, Ontario, Canada.

60. CHARACTERIZATION OF THE FEMALE UROGENITAL TRACT MICROBIOME IN PATIENTS WITH CERVICAL DYSPLASIA. Leah Velikonja, Olivia Giovannetti, Diane Tomalty, and Dr. Michael Adams. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

Therapeutics and Toxicology

61. ALTERATIONS IN CD-1 MOUSE FETAL DNA DAMAGE-RESPONSE GENE EXPRESSION, TOPOISOMERASE IIA ACTIVITY, AND DNA DAMAGE FOLLOWING IN UTERO BENZENE EXPOSURE. Trent H. Holmes and Louise M. Winn.

62. ASSESSMENT OF PLACENTAL EPIGENETICS AND PLACENTAL-FETAL SEROTONIN PATHWAY AS A MECHANISM OF VALPROIC ACID-INDUCED TERATOGENESIS. Brianna L. Jackson and Louise M. Winn. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

63. **LOW-DOSE TACROLIMUS PROMOTES THE MIGRATION AND INVASION OF HUMAN-DERIVED FIRST TRIMESTER EXTRAVILLOUS TROPHOBLAST CELLS AND MODULATES THEIR NITRIC OXIDE SYNTHASE ACTIVITY *IN VITRO*.** Ahmad J.H. Albaghdadi (PhD), Kassandra Coyle (BSc), and Frederick W. K. Kan (PhD). Dept. of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario

64. **A PERIPARTUM VASCULAR ASSESSMENT OF WOMEN WITH PRE-ECLAMPSIA.** Jennifer Armstrong and Dr. Graeme Smith. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

Abstracts

Biomedical Engineering

1. **DEVELOPMENT OF A SIMULATION TRAINING CURRICULUM FOR ULTRASOUND-GUIDED VASCULAR ACCESS FOR SUSTAINABLE TRANSLATION TO MAURITANIA.** Sarah GF Ryan1, Tamas Ungi2, Sarah Maxwell3, Melanie Jagger3, Lindsay Patterson3, Parvin Mousavi2, Gabor Fichtinger2. Department of Medicine1, School of Computing2, and Department of Anesthesiology3, Queen's University, Kingston ON.

As simulation training in medical education becomes more prevalent, it is imperative we share knowledge in resource-limited settings. PerkTutor is an open-source training platform, which allows 3D visualization of ultrasound images and procedural instruments in real-time using electromagnetic tracking1. The platform has been used in multiple procedures including facet joint injection2, lumbar puncture3, and vascular access4,5. We are creating training curriculum using PerkTutor for vascular access, to be implemented in a newly constructed simulation centre in Mauritania. Vascular phantoms were developed using alumisol plastic with 0.1% cellulose poured into a glass container with a wooden dowel that is later removed. Including the one-time cost for the container the phantom costs ~$10, whereas the commercial Blue Phantom costs over $500. Ultrasound training modules will be developed with anesthesiology staff. We will enroll medical trainees at Queen's to test our curriculum. Participants will be split into two groups: the experimental group will have access to PerkTutor, while the control group will only have traditional ultrasound. We will measure metrics of skill proficiency and compare between the groups. This will serve as a proof of concept to guide sustainable implementation of vascular access training in Mauritania, as well as inform the development of future curricula to come. References: [1] Ungi, T., Sargent D., Moult E., Lasso A., Pinter C., McGraw R. C., et al. (2012). Perk Tutor: An open-source training platform for ultrasound-guided needle insertions. IEEE Trans Biomed Eng. 59, 3475-3481. [2] Welch, M., Moult E., Ungi T., McGraw R. C., & Fichtinger G. (2013). Perk Tutor Improves Ultrasound-Guided Facet Joint Injection Training. ImNO2013 - Imaging Network Ontario Symposium. [3] Keri, Z., Sydor D., Ungi T., Holden M. S., McGraw R. C., Borschneck D. P., et al. (2014). A novel technology for teaching ultrasound-guided lumbar puncture with Perk Tutor. Imaging Network Ontario Symposium. [4] Lia, H., Keri Z., Holden M. S., Harish V., Mitchell C. H., Ungi T., et al. (2017). Training with Perk Tutor improves ultrasound-guided in-plane needle insertion skill. SPIE Medical Imaging. 10135, [5] McGraw, R. C., Chaplin T., McKaigney C., Rang L., Jaeger M., Redfearn D., et al. (2016). Development and evaluation of a simulation-based curriculum for ultrasound guided central venous catheterization. Canadian Journal of Emergency Medicine. 18, 405-413.

Cancer Research

2. **EFFECT OF ROUTE OF BACILLUS CALMETTE GUÉRIN ADMINISTRATION ON THE TUMOUR IMMUNE MICROENVIRONMENT IN A MOUSE MODEL OF NON-MUSCLE INVASIVE BLADDER CANCER.** Aline Atallah, Arielle Grossman, William Tran, Jean-Francois Paré, Tiziana Cotechini, Charles H. Graham Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Canada

Bladder cancer is the fifth most common cancer in Canada. The standard of care for high-risk non-muscle invasive bladder cancer (NMIBC) involves intravesical immunotherapy with Bacillus Calmette Guérin (BCG). Unfortunately, most patients do not respond fully to this therapy, and our understanding of BCG's immunotherapeutic effect is incomplete. Using an orthotopic mouse model of NMIBC, we compared the bladder tumour immune microenvironment (TiME) following intravesical versus intravenous (IV) administration of BCG. Compared with intravesical BCG treatment, the TiME of mice treated with BCG intravenously was associated with a significantly higher proportion of CD11b- CD3+, CD3-, and CD4- lymphoid cells, as well as a significantly lower proportion of immature myeloid cells. Furthermore, compared with saline IV treatment, BCG administered IV resulted in a significantly larger CD4- T cell population. There were no significant differences in the TiME of intravesically BCG-treated vs intravesically saline-treated tumour-bearing mice. However, compared with control non-tumour-bearing mice treated with saline intravesically, bladders of non-tumour-bearing mice treated intravesically with BCG had a significantly higher proportion of leukocytes, which consisted primarily of immature myeloid cells. These results provide evidence that the route of BCG administration is an important determinant of the TiME composition. Understanding the link between the TiME and BCG therapy may facilitate the development of new approaches to improve outcomes and reduce recurrence rates in patients with NMIBC. (Supported by CIHR).

3. **THE POTENTIAL OF TARGETING MITOCHONDRIAL DYNAMICS IN CANCER THERAPY THROUGH UBIQUITINATION AND NEDDYLATION PATHWAYS.** Charles Chu, Brianna Kaplanis, Chelsea Margerum, and Edmond Chan. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

The mitochondria are well known for their role in maintaining proper cell function through aerobic respiration and coordination of metabolic pathways. The overall function and fitness of mitochondria are furthermore maintained through mitochondrial dynamics, substantiated by balanced membrane remodeling via fusion and fission. Mitochondria compensate for defects content mixing through fusion, while fission achieves mitochondrial repopulation post cell division and also segregates damaged mitochondria for removal through mitophagy. In cancer, altered mitochondrial dynamics have been proposed to represent an underlying factor promoting metabolic plasticity or drug resistance. Here, we hypothesize that protein post-translational modification (PTM) regulators co-amplified with mitochondrial dynamics factors optic atrophy 1 (OPA1) and mitofusin 1 (MFN1) could serve to reprogram mitochondrial dynamics in cancer cells. In this summer project, we investigated potential roles of defective in cullin neddylation protein 1-like protein 1 (DCUN1D1) and ubiquitin regulatory x domain-containing protein 7 (UBXN7) in the regulation of mitochondrial dynamics, stress responses, and cancer cell transformation. The PTM gene regulators were silenced using shRNA in breast cancer cell models followed by biochemical and morphological analysis of mitochondria. Our research findings could serve as groundwork in the development of therapeutics for aggressive breast cancer by targeting and leveraging DCUN1D1 and UBXN7 protein PTM pathways. (Supported by NSERC CRSNG Canada).

4. **DIFFERENTIATING COLORECTAL CANCER PATHOLOGICAL REGIONS USING DESORPTION ELECTROSPRAY IONIZATION-MASS SPECTROMETRY IMAGING.** Natasha Iaboni1, David Hurlbut1,2, Kevin Yi Mi Ren1,2, Martin Kaufmann4, Amoon Jamzad3, Vanessa Wiseman4, Parvin Mousavi3, Gabor Fichtinger3, John F. Rudan2,4, Antonio Caycedo-Marulanda2,4 and Christopher JB Nicol1,5 1Dept. of Pathology & Molecular Medicine; 2Kingston Health Sciences Center; 3School of Computing; 4Dept. of Surgery; 5Division of Cancer Biology & Genetics, Cancer Research Institute. Queen's University, Kingston, ON, Canada

Colorectal cancer (CRC) is the third most diagnosed cancer and second leading cause of cancer-related deaths in Canada. While genetic and molecular aspects of CRC are heavily studied, under-investigated metabolomic profiles of CRC may provide rapid insights to improve patient diagnosis or prognosis. We employ desorption electrospray ionization-mass spectrometry imaging (DESI), a rapid, non-destructive technique that detects small molecules/lipids using spectrums of mass to charge (m/z) ratios, facilitating sample characterization. We hypothesize DESI profiles will differentiate tumour from non-tumour regions of human CRC specimens. To test this, we performed a study using locally accrued human CRC and accompanying biopsy specimens (n=10). DESI was conducted on 10μm fresh frozen sample sections and analyzed in negative ionization, scanning mode. Subsequently, the same sections were H&E stained and annotated for tumour and non-tumour regions by pathologists. Multivariate statistics using PCA/LDA of the 50-1000 m/z range was performed on selected regions of interest per pathological region. Our initial analyses support our hypothesis, and suggest DESI profiles of CRC tumour or biopsy samples distinguish and closely align with pathologist-annotated tumour and non-tumour CRC regions. Current analyses to identify and validate significant ions of interest are underway. These studies will expand our understanding of CRC, and may identify novel biomarkers to facilitate rapid detection and improve patient outcomes. (Supported by Britton Smith Chair in Surgery Research, KHSC)

5. **SURGICAL MARGIN ASSESSMENT IN LUMPECTOMIES USING COMPUTER AIDED CHARACTERIZATION AND INTERPRETATION OF MASS SPECTROMETRY DATA.** Amoon Jamzad1, Alice Santilli1, Faranak Akbarifar1, Martin Kaufmann2, Kathryn Logan3, Julie Wallis3, Kevin Ren3, Shaila Merchant2, Jay Engel2, Sonal Varma3, Gabor Fichtinger1, John Rudan2, Parvin Mousavi1 1School of Computing, 2Department of Surgery, 3Department of Pathology and Molecular Medicine. Queen's University, Kingston, ON, Canada.

PURPOSE: Difficulties associated with detection of cancer in surgical margins can result in incomplete tumor resection in lumpectomies. The iKnife is an intraoperative mass spectrometry modality that provides surgeons with real-time metabolite signatures of tissues. Reinforcement of iKnife with high prediction power and interpretability of artificial intelligence and deep models, can eliminate the need for revision surgeries and improve patient outcome. Here, we propose a framework for classification and visualization of surgical iKnife data using Graph Transformer model to empower the interpretability of breast surgical margin assessment. METHODS: 144 iKnife spectra were collected from breast specimens and converted to multi-level graph structures. A Graph Transformer model was developed and the intermediate attention parameters of the network were extracted in addition to the final prediction. Beside ablation and prospective study, multiple attention visualization approaches were proposed to facilitate the interpretability. RESULTS: In a 4-fold cross validation experiment, an average classification AUC of 95.6% was achieved, outperforming baseline models. Distinguishable spectra patterns were reveals in the proposed visualization, as cancerous and normal burns gather more attention in the lower and higher subbands of the spectra respectively. Looking as cancer subtype prospectively, a pattern of cancer progression was also observed in the attention features. CONCLUSION: Graph Transformers are powerful in providing high network interpretability. When paired with proper visualization, they can be deployed for computer assisted interventions.

6. **EXAMINING THE IMPACT OF ENDOTHELIAL BMPR2 LOSS ON BMP9-ASSOCIATED ANGIOGENESIS IN A MOUSE MODEL OF METASTATIC BREAST CANCER.** J.A. Harry1, K. Laverty2, P.A. Greer2, V. Hoskin2, D.V. Cole1, M. Mitchell2, Y. Gao2, M.L. Ormiston1,2, 1 Department of Medicine, Queen's University, Kingston ON, Canada, 2Biomedical and Molecular Sciences, Queen's University, Kingston ON, Canada,
Background: Angiogenesis, the process of new blood vessel development from pre-existing vasculature, has been implicated in the growth, progression, and metastasis of cancer. Bone morphogenic protein (BMP) signaling has been identified as a potential target for novel anti-angiogenic therapies. Recent work has demonstrated that BMP9 acts as a vascular quiescence factor in healthy endothelium, but promotes angiogenesis when its type-II receptor, BMPR-II is lost. We hypothesize that BMP9 will prevent tumour angiogenesis in wildtype animals but will promote tumour vascularization and growth in animals with an endothelial selective deletion of BMPR-II (Bmpr2EC-/-). Methods: RFP-expressing E0771 cancer cells were implanted orthotopically into the mammary fat pad of female Bmpr2EC+/+, Bmpr2EC+/- and Bmpr2EC-/- mice and allowed to establish a primary tumour and lung metastases for up to 4 weeks. Lung metastases continued for an additional 4 weeks after primary tumour resection, at which point tumour burden was assessed in the lungs using in vivo imaging for RFP. Immunofluorescent imaging was used to analyze the density and distribution of vascular networks within metastatic tumours. Conclusion: Current findings indicate that animals lacking Bmpr2 in their pulmonary endothelium display increased metastatic burden in their lungs. Future work will use a tail vein injection model to determine if endothelial Bmpr2- loss enhances the rate of lung metastases, and will investigate the impact of recombinant BMP9 on metastatic growth in the lung.

7. **IL-27 AND POLY(I:C) SENSITIZE PROSTATE CANCER CELLS TO NK CELL-MEDIATED CYTOTOXICITY.** Olena Kourko[1], Lindsey Hawke[1], Mark Ormiston[1], and Katrina Gee[1], [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston ON, K7L 3N6

Patients with advanced prostate cancer (PC) may benefit from therapies that aim to "re-awaken" the immune system. NK cells are suppressed in patients with PC and effective NK cells in patients with disease is associated with a better prognosis, highlighting the importance of NK cells in cancer progression. Adjuvants, such as cytokines, may enhance cancer therapies and immune surveillance. IL-27 has demonstrated anti-tumour properties in addition to upregulating TLR expression and function on immune cells. We have previously demonstrated that when combined with TLR3 agonist, poly(I:C), IL-27 is able to enhance cytokine/chemokine production, including IFN-β and CXCL10, from advanced PC models, PC3 and DU145 cells, in parallel with inducing cell death. These PC cells normally evade killing by NK cells; therefore, we investigated whether IL-27/poly(I:C) impact the ability of primary human NK cells to target these treated PC cells for killing. Our results indicate that PC cells treated with IL-27/poly(I:C) are more sensitive to NK cell-mediated cytotoxicity. This enhanced NK cell-mediated cytotoxicity is dependent on the ability of the PC cells to secrete IFN-β in response to IL-27/poly(I:C). Thus, we have identified that the secretion of IFN-β from the PC cells activates the cytotoxic function of NK cells. This work provides mechanistic insight to how using IL-27 and poly(I:C) can improve cytotoxic function of NK cells to target cancer cells that have developed immune-evading strategies. Supported by the Prostate Cancer Fight Foundation and the Ride for Dad, CIHR Project Grant, and NSERC.

8. **SEX DIFFERENCES IN AGING BLADDER IMMUNE PHYSIOLOGY ASSOCIATE WITH DISTINCT PRE-TREATMENT TUMOR IMMUNE STATES IN A MURINE MODEL OF BLADDER CANCER.** Ali Hamade1,2, Deyang Li1,2, Kathryn Tyryshkin3, Gwenaelle Conseil1, 2, D. Robert Siemens4, Madhuri Koti1, 2, 4 1Queen's Cancer Research Institute, Kingston, ON, Canada, 2Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada, 3Department of Pathology and Molecular Medicine, Queen's University, Kingston, ON, Canada, 4Department of Urology, Queen's University, Kingston, ON, Canada

The incidence of bladder cancer is four times higher in males than females, however, females tend to present with a more aggressive disease, a poorer response to Bacillus Calmette-Guérin (BCG) therapy in non-muscle invasive bladder (NMIBC) cancer, and suffer worse clinical outcomes. We recently reported the existence of sexual dimorphism in the tumor immune microenvironment of non-muscle invasive bladder cancer (NMIBC). Bladder cancer is mostly diagnosed in individuals over 65 years of age and the bladder mucosa undergoes significant immune alterations with biological aging.
Current pre-clinical modeling approaches do not integrate age and sex in experimental design, which may be affect optimal clinical translation. Towards improved pre-clinical modelling and to further our current understanding of mucosal immune responses within the bladder microenvironment, bulk-RNA sequencing and multiplex immunofluorescence based spatial immune profiling of healthy bladders from male and female mice spanning young to older age groups, was performed. A highly altered innate and adaptive immune landscape that exhibited sex and age-related differences, particularly in the context of B cell associated responses was observed. Characterization of the pre-treatment tumor immune microenvironment of the carcinogen N-butyl-N-(4-hydroxybutyl) nitrosamine induced syngeneic murine bladder cancer model, revealed significant sex and age specific differences. Findings from this study will augment better pre-clinical modeling approaches employed in the therapeutic development of immunomodulatory agents for NMIBC. This research is supported by funding from Bladder Cancer Canada.

9. **REGULATION OF PODOSOME ROSETTE FORMATION FOR FOCAL CONTROL OF SPROUTING ANGIOGENESIS** Charmi S. Shah, Maria B. Umana and Donald H. Maurice, Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

Gradients of angiogenic factors (e.g. TGFβ) stimulate endothelial cells (ECs) to adopt a proliferative-migratory phenotype, and subsequently invade tissues. This requires extracellular matrix remodeling through the coordinated release of matrix metalloproteinases (MMPs). One mechanism of MMP expression involves the ability of ECs to form podosomes, or the larger podosome rosette superstructures, and use these short-lived, actin-based structures, to "target" MMP-mediated matrix remodeling. Our lab previously revealed that the cAMP-effector, protein kinase A (PKA), reduces the invasive capacity of ECs by antagonizing podosome rosette formation. Mechanistically, this effect was attributed to PKA's ability to phosphorylate RhoGDIα and to promote its associated inhibition of cdc42, a positive regulator of EC podosome rosette formation. Interestingly, while most angiogenic agents, including TGFβ, promote cdc42-mediated podosome rosette formation downstream of src-dependent signaling events, the ability of PKA inhibition to promote cdc42-dependent rosettes was src-independent., We hypothesize that PKA regulates podosome rosette formation by acting on a "pool" of cdc42 not regulated directly by src. Further, since evidence suggests that the cdc42 GEF, faciogenital dysplasia protein 1 (FGD1), localizes with RhoGDIα in ECs, we propose that PKA regulates specifically this "pool" of cdc42. Our preliminary findings show that RNAi-based silencing of FGD1 reduced TGFβ-induced podosome rosette formation in ECs. We suggest that our data may help identify mechanisms through which EC podosome rosette formation and invasion may be more selectively regulated.

10. **NOVEL TOOLS TO ASSESS AND PREDICT THE RISK OF CANCER-ASSOCIATED THROMBOSIS IN WOMEN UNDERGOING CHEMOTHERAPY FOR BREAST AND GYNECOLOGICAL CANCERS.** Yousra Tera1 (PostDoc), Mihaela Mates2 (MD, FRCPC), Anita Agrawal3 (MSc, MD, FRCSC), Jayachandran Kizhakkedathu4 (PhD), Maha Othman (MD PhD)1,5 1 Department of Biomedical and Molecular Sciences, Queens's University, Kingston, ON, Canada 2 Department of Oncology, Queens's University, Kingston, ON, Canada. 3 Department of Obstetrics and Gynecology, Queens's University, Kingston, ON, Canada. 4 The Centre for Blood Research, University of British Columbia, Vancouver, BC, Canada. 5 Department of Medicine, Division of Hematology, Queens's University, Kingston, ON, Canada 5School of Baccalaureate Nursing, St. Lawrence College, Kingston, ON, Canada

Cancer associated thrombosis (CAT) is a common occurrence. Chemotherapy increases the risk of venous thromboembolism (VTE) by 6.5-fold. Methods to assess VTE risk are lacking but important for implementation of preventative or early therapeutic interventions. Currently used tools, such as the Khorana score, are limited in validation of many cancers. The identification of a test or a biomarker with high predictive value would be ideal for the administration of more targeted, effective and safe anticoagulation in cancer patients. This study proposal aims to assess the utility of: 1-Global hemostasis test (Thromboelastography; TEG), 2-Novel procoagulant marker (polyanionic cell-free DNA), 3- D-dimer; in quantifying the risk of thrombosis in cancer patients under chemotherapy. We will recruit 100 cancer patients (Breast, Ovarian, Endometrial) who are already planned for chemotherapy. Blood will be collected at first, second and third chemotherapy visits and 6 and 12-month follow up. Citrated whole blood will be used for TEG and plasma will be used to assess cell free DNA and D-dimer. Khorana scoring will assess baseline risk of thrombosis. Clinical records will be examined during follow up for any symptomatic VTE, and disease progression. If our proposed approach (TEG testing combined with D dimer and polyanionic DNA) proves to offer high predictive value, this could be added to the Khorana risk assessment score to improve its applicability and help apply safe and effective thromboprophylaxis. Keywords: Thrombosis; Khorana scoring; Thromboelastography.

11. **INVESTIGATING THE OPTIMAL ROUTE OF INOCULATION OF BACILLUS CALMETTE GUÉRIN FOR THE INDUCTION OF INNATE IMMUNE MEMORY IN THE TREATMENT OF BLADDER CANCER.** William Tran, Jean-François Paré, Aline Atallah, Tiziana Cotechini, Charles H. Graham, Department of Biomedical and Molecular Sciences, Queen's University.

Intravesical administration of Bacillus Calmette Guérin (BCG) is an important tool for the treatment of patients with non-muscle invasive bladder cancer. Unfortunately, up to 70% of patients suffer from recurrence. Recent studies suggest that the mechanism of anti-tumour action of BCG involves the acquisition of innate immune memory, or trained immunity (TI) by myeloid cells such as monocytes. TI is acquired via exposure to pathogen- or damage-associated molecular patterns and manifests as enhanced cytokine release following exposure to a secondary non-specific stimulus. Here we hypothesize that alternative routes of BCG inoculation will result in better acquisition of TI. Therefore, this study will compare the extent of TI acquisition following intravenous (IV), intraperitoneal (IP) and intravesical inoculation of various doses and dosing frequencies of BCG to immunocompetent mice. Bone marrow monocytes collected from to C57BL/6 mice inoculated with IV, IP, or intravesical BCG or saline will be isolated and subject to a secondary in vitro challenge using lipopolysaccharide. Extent of TI acquisition will be assessed by measuring TNF-α, IL-6, IL-12 and IL-1β levels in the supernatants of these cultures using multiplex ELISA. This work will reveal the optimal route and dosing frequency of BCG inoculation to maximize BCG-induced TI and could thereby improve anti-tumour therapeutic efficacy of BCG. Research supported CIHR

12. **TUMOR ADJACENT TERTIARY LYMPHOID STRUCTURES ASSOCIATE WITH POOR RESPONSE TO BCG IMMUNOTHERAPY IN NON-MUSCLE INVASIVE BLADDER CANCER.** Stephen Chenard1,2, Priyanka Yolmo1,2, Danielle Jenkins3, Minqi Xu4, D. Robert Siemens4 and Madhuri Koti1, 2, 4
1Queen's Cancer Research Institute, Kingston, ON, Canada, 2Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada, 3Department of Pathology and Molecular Medicine, Queen's University, Kingston, ON, Canada, 4Department of Urology, Queen's University, Kingston, ON, Canada

Tertiary lymphoid structures (TLSs) are emerging indicators of prognosis and therapeutic efficacy specifically in the context of immunomodulatory therapies. TLSs mimic germinal centers located in secondary lymphoid organs and are primarily constituted by subsets of B cells, T cells, macrophages and follicular dendritic cells. TLSs form at mucosal sites such as the gastrointestinal, respiratory and urogenital tracts as a result of biological aging, following exposure to normal commensal and pathogenic microbes, chronic inflammation, and cancer, and generally evolve to provide local immune protection. Therapy induced TLSs have also been shown as predictive biomarkers in muscle invasive bladder cancer. Given the widespread presence of TLSs in bladder mucosa as a result of biological aging or urinary tract infections or cancer, we hypothesized that tumor associated pre-treatment TLS may inform response to locally administered Bacillus Calmette-Guérin (BCG) in non-muscle invasive bladder (NMIBC) cancer. Using a multiplexed immunofluorescence assay, we characterized lymphoid aggregates/TLSs in tumors from patients with NMIBC who either responded to or failed BCG immunotherapy. Various stages of pre-existing TLSs were present in tumors from both groups of patients. Higher number of mature TLSs were located in peri-tumoral regions in tumors from patients deemed as BCG non-responders. Findings from this study demonstrate the significance of pre-treatment TLSs as prognostic indicators in NMIBC and will potentially help in the early identification of BCG non-responsive patients. This research is supported by funding from Bladder Cancer Canada.

13. **LACK OF DEFINITIVE PRESURGICAL PATHOLOGICAL DIAGNOSIS IS ASSOCIATED WITH INADEQUATE SURGICAL MARGINS IN BREAST-CONSERVING SURGERY.** Paola V. Nasute Fauerbach, MD; Kathrin Tyryshkin , PhD; Silvia Perez Rodrigo, MD; John Rudan, MD; Gabor Fichtinger, PhD; Michael Reedijk, MD, PhD; Sonal Varma, MD; David M. Berman, MD, PhD.Department: Pathology and Molecular Medicine, Queen's University, Kingston, Ontario, Canada.

Purpose: To determine the impact of definitive presurgical diagnosis on surgical margins in breast-conserving surgery (BCS) for primary carcinomas; clinicopathological features were also analyzed. Methods: This retrospective study included women who underwent BCS for primary carcinomas in 2016-2017. Definitive presurgical diagnosis was defined as having a presurgical core needle biopsy (CNB) and not being upstaged at surgery. Biopsy data and imaging findings were retrieved. Inadequate surgical margins (IM) were defined per ASCO/ASTRO guidelines. Univariable and multivariable analyses were performed. **Results:** 360 women (median age, 66) met inclusion criteria with 1 having 2 cancers. 82.5% (298/361) were invasive cancers while 17.5% (63/361) were ductal carcinoma in situ (DCIS). Biopsies were US-guided (284/346, 82.0%), mammographic (60/346, 17.3%), and MRI-guided (2/346, 0.6%). US and mammographic CNB yielded median samples of 2 and 4, respectively, with 14G needles. 15 patients (4.2%) lacked presurgical CNB. The IM rate was 30.0%. In multivariable analysis, invasive cancers >20 mm, dense breasts, and DCIS were associated with IM (p=0.029, p=0.010, and p=0.013, respectively). Most importantly, lack of definitive presurgical diagnosis was a risk factor for IM (OR=2.35; 95% CI=1.23-4.51; p=0.010). In contrast, neither patients <50 nor aggressive cancer features were associated with IM. Conclusion: Lack of definitive presurgical diagnosis was associated with a two-fold increase of IM in BCS; other risk factors were dense breasts, invasive cancers >20 mm, and DCIS. Supported by: Queen's University Faculty of Health Sciences, Dean's Doctoral Award (PVNF), Canada Research Chair of the Natural Sciences and Engineering Research Council of Canada (GF).

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14. **ASSESSING THE IMPACT OF BMPR2 LOSS ON PHOSPHOINOSITIDE DYNAMICS AND CELLULAR TRAFFICKING IN ENDOTHELIAL CELLS.** N.J. Chronis1, L.G. Hawke1, M.M. Vandenbroek2, M.L. Ormiston1,2, 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada, 2Department of Medicine, Queen's University, Kingston Ontario, Canada

Background: Pulmonary arterial hypertension is associated with mutations in the BMPR2 gene encoding the bone morphogenetic protein type II receptor. Our lab previously demonstrated that BMPR2 silencing induces dysregulation of PALD1, the gene encoding phosphoinositide phosphatase, Paladin, which converts PI(4,5)P2 to PI(4)P and influences angiogenesis. PI(4,5)P2 mainly resides in the cell membrane while PI(4)P is localized to the endosomes and trans-Golgi network (TGN). Furthermore, our lab has linked BMPR2 loss to TGN disorganization and potential defects in intracellular trafficking. These findings form the basis for our investigation of the effects of BMPR2 loss on phosphoinositide dynamics and cellular trafficking in endothelial cells (ECs). Methods/Results: PI(4,5)P2 and PI(4)P were tracked in ECs using fluorescently-tagged probes. Plasmids encoding each probe were transfected into primary ECs by nucleofection or jetPRIME transfection reagent, either with concomitant siRNA silencing of BMPR2 (jetPRIME) or a separate BMPR2 silencing step (nucleofection). The two-step nucleofection/siRNA protocol achieved >95% BMPR2 knockdown and 20-30% double plasmid transfection, confirmed by RT-qPCR and flow cytometry, respectively. With jetPRIME, gene knockdown was ~70%, and ~14% of cells expressed both plasmids. Conclusions: Current findings suggest that a two-step nucleofection/siRNA protocol is the optimal transfection method for primary ECs. We are working to image live transfected ECs to assess changes in PI(4,5)P2/PI(4)P dynamics following BMPR2 knockdown, with and without stimulation with bone morphogenetic protein 9 and vascular endothelial growth factor.

15. **GENETIC DELETION OF NATURAL KILLER CELL TGF-B SIGNALING PROTECTS MICE FROM HYPOXIA-INDUCED PULMONARY HYPERTENSION** Kassandra M. Coyle[1], Matthew Rätsep[1], Kimberly Laverty[2], L. Rhiannon Hilton[2], M. Martin Vandenbroek[1], Melissa Mitchell[2], Mark L. Ormiston[1,2] 1. Department of Medicine, Queen's University, Kingston, ON, Canada 2. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada

Background: Pulmonary arterial hypertension (PAH) is a devastating disease of obstructive vascular remodeling that is strongly linked to immune dysfunction. Previous findings support a critical role for NK cell impairment in disease pathogenesis, yet the molecular mechanisms underlying this contribution are unknown. We hypothesize that ***TGFβ signaling in NK cells influences pulmonary vascular development and drives pathological vascular remodeling in PAH.*** **Methods/Results:** Mice lacking the TGFβ type-II receptor exclusively in NK cells (*Tgfbr2*$^{NK-/-}$) and littermate controls (*Tgfbr2*$^{NK+/+}$) were exposed to the chronic hypoxic model of PAH. Assessment of right ventricular systolic pressure by closed-chest cardiac catheterization indicated that male, but not female *Tgfbr2*$^{NK-/-}$ mice are protected from developing pulmonary hypertension relative to sex-matched *Tgfbr2*$^{NK+/+}$ controls (p=0.0028). Transthoracic echocardiography of blood flow in the pulmonary artery confirmed the presence of a protected phenotype in *Tgfbr2*$^{NK-/-}$ males. Immunofluorescent imaging of pulmonary arterioles revealed a decrease in pulmonary vascular density of *Tgfbr2*$^{NK-/-}$ mice of both sexes, suggesting a developmental alteration in these animals. **Conclusion:** These results suggest that the genetic deletion of *Tgfbr2* in NK cells is sufficient to protect mice from hypoxia-induced PAH despite a truncated pulmonary vasculature at baseline. Further work aims to understand how the selective deletion of Tgfbr2 in NK cells affects the development of the pulmonary vasculature and the potential of NK-selective TGFβ blockad
e as a novel therapeutic strategy for PAH. (Supported by the Canadian Institute for Health Research.)

16. THE PRIMARY CILIUM: A HYPER-LOCALIZED COMPARTMENT FOR CAMP SIGNALLING.

Mikayla Erdelsky, M. Bibiana Umana and Donald H. Maurice, Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

Recent evidence indicates that the presence of a primary cilium, and of selective cAMP signalling within this smallest of cellular structures, promotes pre-adipocyte differentiation in vitro and in vivo. Indeed, in this earlier work, activation of a cilial free fatty acid receptor (FFAR4) was correlated with increases in cilial cAMP and omega-3 FA-induced adipogenesis in mice, and in 3T3-L1 pre-adipocytes. While this earlier work reported that the cAMP-effector, exchange protein activated by cAMP (EPAC), acted downstream of FFAR4 in these events, it was silent on the need for primary cilium localized adenylyl cyclases (ADCYs) and cAMP phosphodiesterases (PDEs) in coordinating these hyper-local events. In this context, our studies are assessing IF local primary cilium cAMP PDE activity is required for coordination of these hyper-localized actions of cAMP within the primary cilium of differentiating 3T3-L1 cells. Moreover, since mitotic clonal expansion (MCE) is required for efficient differentiation of 3T3-L1 cells, we further delineate the role(s) of cAMP hydrolysis by PDEs in each MCE and differentiation. Overall, our studies identify a critical role for PDE4, and exclude roles for PDE2, PDE3, or PDE7 PDE-family encoded enzymes in these events. We propose that this work will identify more selective therapeutic targets through which to control adipogenesis, and perhaps differentiation of other stem cells in which the primary cilium is critical.

17. COVID-19 COAGULOPATHIES- SYSTEMATIC REVIEW OF HAEMOSTASIS IMPAIRMENT AND DISEASE OUTCOMES- 18 MONTHS INTO THE PANDEMIC.

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Coagulation impairment was evidenced early in the COVID-19 pandemic. SARS-CoV-2 infection causes an overwhelming inflammation, cytokine storm, endotheliopathy, immune activation and triggers platelet activation and hypercoagulability. Variable rates of venous thromboembolism (VTE) were reported. This systematic review aims to describe published evidence on COVID-19 coagulopathies over the course of the pandemic thus far. MEDLINE, EMBASE, EPUB Ahead of Print were searched from inception to July 2021. Screening of abstracts and full-text review were performed using Covidence software, by two independent reviewers. Studies reporting on severe COVID-19 published in journals with impact factor ≥ 3 were included. Systematic reviews, meta-analyses and letters to the editor were excluded. VTE events, hemostasis lab parameters and anticoagulation data were extracted. Disease outcomes were assessed based on ICU admission and mortality. A total of 113 studies and 33832 patients from 18 different countries were reported. Of all patients, 37% were admitted to the ICU, with an 11% mortality. Almost 50% of studies reported 3 coagulation lab markers (d-dimer, fibrinogen, platelet count) with elevated d-dimer (3226 ug/L) (90/113 studies), elevated fibrinogen (598 mg/dL) (70/113 studies), and normal platelet count (240 10^9 /L) (75/113). 22% of patients had VTE (82/113) and anticoagulation varied greatly among studies. This study shows coagulopathy is a significant problem in COVID-19. Subgroup analyses are underway to examine how the clinical and lab evaluations evolved over the various pandemic waves.

18. PROFILING BMPR2-DERIVED ENDOTHELIAL CIRCRNAS IN PULMONARY ARTERIAL HYPERTENSION. M. Martin VandenBroek1, Mackenzie C. Sharp2, L. Rhiannon Hilton3, Anne L. Theilmann3, Mark L. Ormiston1,3, 1Department of Medicine, Queen's University, Kingston ON2School of Computing, Queen's University, Kingston ON, 3Department of Biomedical and Molecular Sciences, Queen's University, Kingston ON.

Rationale – Pulmonary arterial hypertension is a disease of vascular remodeling and endothelial dysfunction associated with mutations in BMPR2, encoding the bone morphogenetic protein (BMP) type II receptor. As the impact of BMPR2 loss in the pulmonary endothelium remains poorly understood, we set out to explore circular RNAs (circRNAs) as a novel mediator of disease. Methods and Results – Deep RNA sequencing (~600 million reads per sample) was performed on human pulmonary artery endothelial cells (HPAECs), with and without both siRNA knockdown of BMPR2, and BMP9 treatment. Of all known or proposed human circRNAs, 21% (19,353) were detected across 12 samples, but only 0.5% (467) were deemed abundantly expressed. Differential expression analysis identified six circRNAs altered by BMPR2 loss, including hsa_circ_0005078, derived from the BMPR2 locus (formed from exon 12). An additional BMPR2 circRNA hsa_circ_0003218 (exons 2 and 3) was also abundant in HPAECs. Despite decreased expression of their linear counterparts in mutation carrying PAH patients, neither BMPR2 circRNA was altered in disease. Conclusions and future directions – High-depth RNA-sequencing has allowed for the first ever profiling of circRNA expression of the pulmonary endothelium and the identification of novel BMPR2 derived circRNAs. Unlike linear BMPR2 transcripts, these circRNAs are unaltered in PAH, suggesting they are retained to serve alternative functions. Further studies will explore the functional role of these circRNAs and their contribution to endothelial dysfunction.

19. MITOCHONDRIAL DNA-DEPENDENT CHANGES IN LIPID BIOSYNTHESIS AND INSULIN SIGNALLING IN WHITE ADIPOSE TISSUE AND SKELETAL MUSCLE. Abhishek Shastry, Charles CT Hindmarch, PhD, Kimberly J Dunham-Snary, PhD, Departments of Biomedical & Molecular Sciences and Medicine at Queen's University.

Background: Obesity is an increasingly prevalent cardiometabolic disease affecting 1:3 Canadians. While differences in mitochondrial DNA (mtDNA) background have an influence on whole body metabolism and cell signalling, the mechanisms are not well understood. **Methods:** Mitochondrial-Nuclear eXchange (MNX) mice, which have nuclearDNA and mtDNA reciprocally exchanged between two mouse strains, were studied. Adiposity and metabolism were assessed throughout 6-week chow or high-fat diet exposure. Inguinal (subcutaneous) and epididymal (visceral) white adipose tissue (WAT) and gastrocnemius skeletal muscle (SM) were collected and RNA sequencing (RNASeq) was performed. Differential gene expression was profiled in WAT, and analysis of SM RNASeq data will be conducted, targeting insulin signalling and lipid biosynthesis genes to see if the same patterns as in WAT exist. Differentially expressed genes will be validated using RT-PCR. **Results & Conclusions**: Adiposity results in an upregulation of biosynthetic/metabolic pathways in mice having $C57^{mtDNA}$ compared to $C3H^{mtDNA}$ in WAT, whereas insulin signalling is downregulated. We expect these findings to be replicated in SM from mice harboring $C57^{mtDNA}$. We predict lipid/triglyceride synthesis and insulin signalling pathways will be up- and down-regulated, respectively. $C57^{mtDNA}$ increases cellular-metabolic economy, resulting in enhanced lipid biosynthesis and storage in WAT after high-fat diet. SM gene expression will confirm if mitochondrial-bioenergetic processes have lower 'activation thresholds' for lipogenic gene expression compared to those involved in insulin signalling, or if these pathways interact, attenuating expression of insulin-induced lipogenesis genes. Supporting Agencies: American Heart Association, National Institutes of Health, the Garfield Kelly Cardiovascular Research & Development Fund, and the Departments of Biomedical & Molecular Sciences and Medicine at Queen's University.

20. **DESIGNING A SPLIT LUCIFERASE REPORTER TO ASSESS THE KINETICS OF ENDOTHELIAL BMP9 SIGNALING**. S.I. Skebo1, M.M.VandenBroek2, L. Hawke1, M.L. Ormiston1,2 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston ON, 2Department of Medicine, Queen's University, Kingston ON.

Rationale: Bone morphogenetic protein-9 (BMP9) is involved in angiogenesis, the process of sprouting new blood vessels from existing vasculature. Published work has shown BMP9 signalling occurs in oscillatory waves of downstream Smad mediators, affecting the angiogenic response. To assess how altered signaling kinetics impact the angiogenic response to BMPs, this project aims to design an assay to evaluate Smad signaling in real time using the NanoBiT split luciferase reporter system. Methods: HiFi assembly was used to create constructs encoding Smad1 and Smad4, tagged on their N-terminus with either the large (LgBiT) or small (SmBiT) segments of the split reporter. 5-alpha competent E.coli were transformed with a construct and expanded in the presence of ampicillin (0.1mg/ml). Colonies were selected and Sanger sequenced to determine proper plasmid construction. Corresponding LgBiT and SmBiT pairs were transfected into human embryonic kidney (HEK-293) cells via jetPRIME. Overexpression of tagged Smads was confirmed by qPCR and western blotting. Luminescence was monitored in live and lysed cells following the addition of a luciferin substrate. Conclusions: Results suggest that transfection of HEK-293 cells with plasmid constructs induces an upregulation in Smad mRNA levels. Ongoing work aims to determine the optimal configuration of construct pairs to use as the luciferase reporter, with future studies to optimize plasmid and siRNA transfection in human endothelial cells, with the ultimate goal of tracking real-time oscillatory BMP9 signalling.

21. **WESTERN DIET INDUCES CHANGES IN NUCLEAR GENE EXPRESSION *IN VIVO* THAT ARE MODULATED BY MITOCHONDRIAL HAPLOTYPE.** Mia S Wilkinson[1], Charles C T Hindmarch[2], Kimberly J Dunham-Snary[1,3]. 1 – Department of Biomedical & Molecular Sciences, Queen's University, Kingston, ON. 2 – Queen's CardioPulmonary Unit, Queen's University, Kingston, ON. 3 – Department of Medicine, Queen's University, Kingston, ON.

BACKGROUND Cardiometabolic diseases (CMDs) are a leading cause of mortality and current treatments don't address underlying genetic/biomolecular factors impacting disease etiology. Mitochondria, a master regulator of metabolism, play a complex role in CMDs. Mitochondria have their own DNA (mtDNA) encoding key metabolic proteins, and this genome diverged as humans migrated from Africa, resulting in ancestry-dependent *haplotypes*. Susceptibility to CMDs is linked to haplotype, but mechanisms are unclear. Skeletal muscle (SM) is highly metabolically active, but the role of haplotype in SM metabolism and gene expression is unknown. METHODS To isolate haplotype-specific effects, Mitochondrial-Nuclear-eXchange (MNX) mice were developed using mice with differing CMD susceptibility and haplotypes; MNX mice harbor opposite nuclear/mitochondrial genomes. Wild-type and MNX mice were fed high fat (HFD) or chow diet, and RNA sequencing performed on SM and white adipose tissues (WAT). We will assess gene expression in SM in response to diet and haplotype and generate haplotype-specific transcriptome profiles via target validation. Intra-diet comparisons will identify haplotype-regulated targets, and intra-haplotype comparisons will identify diet-regulated targets. RESULTS & CONCLUSIONS In WAT, mice with $C57^{mtDNA}$ exhibited increased differential gene expression on HFD, compared to $C3H^{mtDNA}$. Bioenergetic-metabolic/OXPHOS genes were downregulated, and B-cell receptors/chemokine signalling genes were upregulated. In SM, we expect $C57^{mtDNA}$ will increase differential expression of metabolic process and immune function genes, and we will demonstrate interaction between the mitochondrial and nuclear genomes, confirming a 'Mito-Mendelian' genetic paradigm of CMD. (Supported by the American Heart Association, National Institutes of Health, the Garfield Kelly Cardiovascular Research & Development Fund, and the Departments of Biomedical & Molecular Sciences and Medicine at Queen's University)

Health Policy, Population health, and Epidemiology

22. ACCURACY OF SELF-ASSESSMENT IN GASTROINTESTINAL ENDOSCOPY: A SYSTEMATIC REVIEW AND META-ANALYSIS. Michael A. Scaffidi1,2, Juana Li1, Shai Genis1, Elizabeth Tipton3, Rishad Khan1, Chandni Pattni1, Nikko Gimpaya1, Glyneva Bradley-Ridout4, Catharine M. Walsh5,6,7, and Samir C. Grover1.

Division of Gastroenterology, St. Michael's Hospital, University of Toronto1; Faculty of Health Sciences, School of Medicine, Queen's University2; Institute for Policy Research, Northwestern University3; Gerstein Science Information Centre, University of Toronto4 ; Department of Paediatrics5 and Medicine6, University of Toronto; Division of Gastroenterology, Hepatology and Nutrition, Hospital for Sick Children, University of Toronto7 . Objective: Assessment is necessary to ensure both attainment and maintenance of competency in gastrointestinal endoscopy, wherein this assessment occur with self-assessment. Previous studies, however, have shown that physicians may be inaccurate in their self-assessments. We conducted a meta-analysis to evaluate the self-assessment accuracy of among GI endoscopists. Design: We performed a systematic search and included studies if they were primary investigations of self-assessment accuracy in GI endoscopy that used statistical analysis to determine accuracy. We conducted a meta-analysis of studies using a limits of agreement (LoA) approach to meta-analysis of Bland-Altman studies. Results: We screened 6067 records. We included 16 studies for qualitative analysis and 3 for meta-analysis. We found that the population limits of agreement were wide (-41.0% to 34.0%) and beyond the clinically acceptable difference. Subgroup analyses found that both novice and intermediate endoscopists had a wide population limits of agreement (-45.0% to 35.1% and -54.7% to 46.5%, respectively) and experienced endoscopists had a narrow population limits of agreement (-14.2% to 21.4%). Conclusion: Although gastrointestinal endoscopists are overall inaccurate in self-assessment of their endoscopic competency, experienced endoscopists have demonstrated accuracy of their self-assessment. While we advise against the sole use of self-assessment among novice and intermediate endoscopists, experienced endoscopists could potentially integrate it into their practice. Supporting agency: None. (PROSPERO: CRD42019136375).

23. THE CIRCAPAIN STUDY: EXAMINING CIRCADIAN CONTROL OF CHRONIC PAIN THROUGH A NATIONAL CROSS-SECTIONAL SURVEY. Hailey Gowdy[1], Mitra Knezic[1], Zihang Lu[4], Gabrielle Pagé[5], Manon Choinière[5], Etienne Bisson[2], and Nader Ghasemlou[2,1,3]. [1]Department of Biomedical and Molecular Science, Queen's University, Kingston, Ontario, Canada. [2]Department of Anesthesiology and Perioperative Medicine, Queen's University, Kingston, Ontario, Canada. [3]Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, Canada. [4]Department of Public Health Sciences, Queen's University, Kingston, Ontario, Canada. [5]Department of Anesthesiology, University of Montreal, Montreal, Quebec, Canada.

1 in 5 Canadians have some form of chronic pain, though not all of these people experience it the same way: pain intensity can fluctuate throughout the day in some cases, but remain constant in others. Our 24-hour circadian rhythms have been found to regulate the function of our nervous and immune systems, and therefore may impact our experience of pain. We previously studied the circadian control of chronic pain in a Kingston chronic low-back pain cohort and are now expanding this work nationally with an online survey, for which all adults in Canada with chronic pain are eligible. Following a baseline questionnaire, participants will complete a series of electronic symptom-tracking diaries (ecological momentary assessments), in which they rate their pain, mood, and fatigue on a 0-10 scale at 3 timepoints (8:00AM, 2:00PM, 8:00PM) each day for one week. Using this data, the participants' patterns of pain fluctuation will be identified. We will then investigate associations between specific pain fluctuation patterns and factors such as chronic pain conditions, latitude, and sleep habits. This work will deepen our understanding of pain fluctuations, which may provide insight into how different chronic pain conditions can be more effectively managed. After completing this national pilot, we hope to broaden this work to an international study to further examine the associations seen here. (Supported by the CIHR-SPOR Chronic Pain Network)

24. THE EXPERIENCES OF PEOPLE WITH A HISTORY OF SUBSTANCE USE AND ALCOHOLISM IN THE EMERGENCY ROOM: A MIXED METHODS STUDY. Dr. Susan Bartels, Dr. Melanie Walker, Sonal Gupta, Dr. Jodie Pritchard.

The RECONNECT (impRoving carE experienCes Of equity-deservingiNg groups iN thE emergenCy deparTment) study conducted by the Department of Emergency Medicine is a voluntary, mixed qualitative/quantitative research project to understand emergency department (ED) care experiences among vulnerable populations at the Kingston Health Sciences Centre's ED and Urgent Care Centre. As an equity-deserving demographic, people with a history of substance-related disorders and alcoholism have recounted negative ED experiences, often enduring inequitable treatment and access to care due to stigmatization. RECONNECT aims to analyze populations with substance-related disorders and alcoholism; their emergency room experiences; the projected attitudes of health care workers; the accessibility of health services; and the effects of prejudice in emergency care. A mixed methodological approach using Spryng.io and Canadian literature published in both English and French over the last 15 years was used to conduct this study. Between June and August 2021, 217 participants recruited from the Kingston General Hospital, Urgent Care Centre, Change Health Care, Detoxification Centre and Street Health Centre, identified as having a substance use disordered. In conjunction with data extracted from the literature review, the analysis is underway to understand patients' care experiences, with an emphasis on barriers pertaining to accessibility and judgment within the ED.
Cumulative results from the RECONNECT study will be extracted to implement qualitative improvement strategies to ameliorate the experiences of patients with substance- use disorders or alcoholism. *Keywords:* Substance-related disorders, alcoholism, emergency room care

25. **TRENDS IN THE PROPORTION OF WOMEN SPEAKERS AT NORTH AMERICAN ALLERGY AND IMMUNOLOGY CONFERENCES OVER A 12-YEAR PERIOD.** Kristin M. Hunt, Mary Foley, Lori Connors, Kyla Hildebrand, Anne K. Ellis. Department of Allergy and Immunology, Queen's University, Kingston, Ontario, Canada.

Women in medicine have often been underrepresented at medical conferences. Aurora et al. (2020) examined the proportion of female speakers across multiple specialties and evaluated factors that may have led to this disparity. This study excluded the field of Allergy and Immunology. We thus aimed to examine the distribution of invited speakers by gender over time at three North American conferences including the *Canadian Society of Allergy and Clinical Immunology (CSACI),* American Academy of Allergy, Asthma, and Immunology (AAAAI), and the American College of Allergy, Asthma and Immunology (ACAAI). This retrospective longitudinal analysis used conference programs from 2008 to 2020 to analyze the gender of invited speakers, panelists, and planning committee members. This data was then compared to publicly available data on composition of the specialty by gender in Canada and the US. Preliminary results show that female speakers at CSACI conferences have historically been lower than male speakers, however this gap has been closing over the last decade (21% in 2008 to 50% in 2020). This coincides with the consistent increase in number of women on the planning committee (9% in 2008 to 54% in 2020). This study sheds light on the evolution of women speaker representation at Allergy and Immunology conferences. We hope to identify other contributing factors that may help us to address these gender inequities in the future. (No supporting agency).

26. **COVID-19 VACCINE HESITANCY AND UPTAKE IN CANADIAN HEALTHCARE WORKERS**. Sierra Killam, Brenda Coleman, Prameet M. Sheth. Faculty of Health Sciences, Queen's University, Kingston, Ontario, Canada.

Introduction: Vaccine hesitancy threatens the efficacy of vaccine initiatives and hinders efforts to eradicate vaccine-preventable diseases. Healthcare workers (HCWs) were among the first to receive COVID-19 vaccines, however little is known about hesitancy in this population. This study aims to better understand COVID-19 vaccine hesitancy in Canadian HCWs. Methods: A prospective multi-site cohort study in Ontario, Alberta, and Nova Scotia evaluated COVID-19 vaccine motivations and uptake in hospital-based HCWs. HCWs were invited to self-enroll using online questionnaires at baseline examining vaccine intent and vaccination information. Results: 1682 HCWs (85% female, mean age 41) self-enrolled between 06/2020-07/2021. Nurses (35%), allied-health-professionals (30.5%), and physicians (13.3%) represented the three largest occupational groups. Most participants were from Ontario (74.6%) and self-identified as White (70.9%). Of those who filled out an intent-to-be-vaccinated questionnaire, 587/807 (94.9%) had received at-least one vaccine dose or indicated positive intent. The most common reasons for seeking vaccination were to prevent spread of COVID-19 (30.7%), protect family (28.3%), and avoid illness (28.0%). Uncertainty of long-term vaccine side-effects was the top concern in those with negative intent (61.6%). Overall, 1473/1682 (87.6%) reported one dose and 1370/1682 (81.5%) reported two doses by July 1st, 2021. Conclusions: Vaccine hesitancy appears low in this cohort of Canadian HCWs and vaccine uptake was over 80%. Education on long-term vaccine safety may help further motivate hesitant HCWs.

27. A ROLE FOR THE HSV TEGUMENT PROTEIN UL21 IN RETENTION OF VIRAL GENOMES WITHIN CAPSIDS. Ethan Thomas1 and Bruce Banfield1 , 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

Mature infectious herpes simplex virus (HSV) virions are comprised of a double-stranded DNA genome packaged at high pressure within an icosahedral protein shell called a capsid, that is in turn surrounded by a lipid envelope studded with viral glycoproteins. Viral genome synthesis, capsid assembly, and genome packaging into capsids occur in the cell nucleus, whereas final envelopment of capsids into mature virions occurs at cytoplasmic membranes. Thus, large 130nm diameter DNA-containing nuclear capsids must transit to the cytoplasm through a process called nuclear egress (NE). Coupled to NE is a quality-control mechanism that preferentially selects DNA-containing capsids rather than empty capsids lacking DNA for translocation from the nucleus to the cytoplasm. Our lab and others have shown that cells infected with HSV strains lacking the viral protein UL21 have DNA-containing capsids as well as empty capsids lacking genomes in the cytoplasm of infected cells. Two possible explanations for these unexpected findings are: 1) a break-down in NE quality-control in the absence of pUL21; or 2) virion DNA (vDNA) is unstably packaged within pUL21 mutant capsids, leading to its premature ejection. Results of transmission electron and confocal microscopy experiments designed to distinguish between these possibilities suggest that pUL21 facilitates vDNA retention within capsids and NE quality-control is functional in the absence of pUL21. This prompts future capsid composition analyses to elucidate the pUL21-mediated vDNA retention mechanism. (Supported by CIHR grant 407982 and NSERC grant RGPIN-2018-04249)

28. INTERLEUKIN-27 INHIBITS INFLUENZA A VIRUS INFECTION IN THP-1 MACROPHAGES. Heather Amsden, Katrina Gee, and Che Colpitts. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

Influenza A virus (IAV) is a single stranded RNA virus responsible for seasonal respiratory infections with the potential for causing pandemics. Macrophages are one of the first immune cells to respond to IAV infection and are critical for initiating a protective immune response. However, macrophages can become infected themselves and may exacerbate IAV infection. Interleukin-27 (IL-27) is an immunomodulatory cytokine produced by myeloid cells in response to Toll-like receptor (TLR) ligation and IAV infection. Recent evidence suggests IL-27 has potent antiviral effects and inhibits viral replication by stimulating type I interferon (IFN) and interferon stimulated gene (ISG) production in models such as HIV and HCV. IL-27 had a protective effect during IAV infection *in vitro* and in murine models. However, the influence of IL-27 on macrophages during IAV infection has not been studied. It is hypothesized that IL-27 will inhibit IAV infection in macrophages by modulating cytokine and ISG production in a TLR-dependent manner. Using the THP-1 human monocytic cell line to derive macrophages *in vitro*, we demonstrate that IL-27 inhibits IAV replication in a dose-dependent manner and this inhibition correlated with increased production of ISGs. Further investigation into the mechanisms used by IL-27 to modulate IAV infection and resulting immune responses will provide insight into whether enhancing or antagonizing IL-27 activity can be an effective treatment option for viral infections.

29. THE GUT-BRAIN AXIS AND BEYOND: MICROBIOME CONTROL OF SPINAL CORD INJURY PAIN. Courtney A Bannerman, Katya Douchant, Julia P Segal, Alex Mack, Prameet M Sheth, Nader Ghasemlou. Department: Biomedical and Molecular Science. Funding: Ontario Graduate Scholarship, Craig H Neilsen Foundation.

Spinal cord injury (SCI) is a devastating injury to the central nervous system in which 60 to 80% of patients experience chronic pain. Unfortunately, this pain is notoriously difficult to treat, with few effective options currently available. Patients are also commonly faced with various compounding injuries and medical challenges, often requiring frequent hospitalization and antibiotic treatment. Change in the gut microbiome from the "normal" state to one of imbalance, referred to as gut dysbiosis, has been found in both patients and rodent models following SCI. Similarities exist in the bacterial changes observed after SCI and other diseases with chronic pain as an outcome. These changes cause a shift in the regulation of inflammation, causing immune cell activation and secretion of inflammatory mediators that likely contribute to the generation/maintenance of SCI pain. We have shown that pain intensity after injury can be altered through altering the gut microbiome by microbial communities or antibiotics.

30. GPR55-DEPENDENT EXCITATION OF DORSAL ROOT GANGLION NEURONS BY LYSOPHOSPHATIDYLCHOLINE. Aidan S. W. Bennett, Taylor A. Alward, and Alan E. Lomax. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

Inflammatory Bowel Disease can cause visceral hypersensitivity in the GI tract leading to abdominal pain. The epithelial layer of the GI tract is mainly composed of lysophosphatidylcholine (LPC) and has recently been shown to bind to GPR55, a receptor with a role in inflammatory pain. Therefore, this study aimed to investigate whether LPC binds to GPR55 on dorsal root ganglion (DRG) neurons, leading to the excitation of pain pathways. Voltage patch clamp recordings showed that application of LPC (10 μM) to murine DRG neurons depolarised the resting membrane potential ($p = 0.0001$) and rheobase ($p < 0.05$). Using ratiometric Ca2+ imaging using FURA-2 AM, LPC (10 μM) enhanced intracellular [Ca2+]i. This effect was significantly reduced by selective GPR55 antagonist CID16020046 (10 μM) ($p < 0.05$), suggesting the response to LPC is partially mediated by GPR55. The source of the Ca2+ influx following LPC application was elucidated using cyclopiazonic acid (CPA) and a 0-Ca2+ external solution. While both significantly decreased the Ca2+ influx elicited by LPC, the 0-Ca2+ external diminished the effect more ($p < 0.0001$), suggesting the increased Ca2+ concentration elicited by LPC and GPR55 is partially mediated through the release from intracellular stores but is mostly due to influx of extracellular calcium. Therefore, it appears that LPC excites DRG neurons through GPR55 and there is a potential role of voltage-gated Ca2+ channels. (Work supported by grants from CIHR)

31. **CHARACTERIZING THE ROLE OF TRAINED IMMUNITY AND IFNγ IN RESTRICTING CORONAVIRUS REPLICATION.** Isabella Delano, Arielle Grossman, Charles H. Graham, and Che C. Colpitts. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Canada.

The COVID-19 pandemic, caused by SARS-CoV-2, illustrates the urgent need for new therapeutic approaches against emerging pathogenic coronaviruses (CoVs). Interestingly, the BCG vaccine for tuberculosis has been suggested to provide cross-protection against SARS-CoV-2. BCG induces a trained state in innate immune cells, characterized by increased secretion of cytokines IL-1β, TNFα, IL-6, and IFNγ. IFNγ has direct antiviral activities, although its antiviral mechanisms against CoVs are still unknown. For some other viruses, the antiviral activity of IFNγ is at least partially attributed to IFNγ-inducible GTPases known as guanylate binding proteins (GBPs). However, whether IFNγ-inducible GBPs antagonize CoV replication is unknown. We hypothesize that IFNγ, produced by trained innate immune cells, inhibits CoV replication by inducing expression of antiviral GBPs. Using murine (MHV) and human (HCoV-229E) CoV models, we have shown that coculture of CoV-infected epithelial cells with BCG-trained monocytes or alveolar macrophages decreases viral replication (as measured by viral titer and viral gene expression) in comparison to untrained conditions. Notably, pre-treatment of cells with IFNγ, but not IL-1β, TNFα or IL-6, inhibits HCoV-229E replication in human lung A549 epithelial cells. Furthermore, our preliminary data suggests that IFNγ-inducible GBPs restrict HCoV-229E replication. By characterizing the role of trained immunity in regulating antiviral cascades, we provide a basis for new therapeutic strategies to protect against future emerging CoVs. (Supported by Queen's University and the SEAMO COVID-19 Innovation Fund.)

32. **EXAMINING THE NASAL MICROBIOTA IN SARS-COV-2, INFLUENZA A VIRUS AND RESPIRATORY SYNCYTIAL VIRUS INFECTED INDIVIDUALS.** Emily Moslinger, Katya Douchant, Kyla Tozer, Calvin Sjaarda, Jesse Kelly, Shu-Mei He, Henry Wong, Prameet M. Sheth. Department of Pathology and Molecular Medicine, Gastrointestinal Disease Research Unit (GIDRU), Queen's University, Kingston, Ontario, Canada.

Background; Our nasal cavity is home to a diverse community of bacteria referred to as the nasal microbiota (NM). Literature shows that respiratory viruses including Influenza A Virus (IAV) change the NM and result in enrichment of inflammatory bacteria including Streptococci, predisposing individuals with IAV to secondary bacterial infections with S. pneumoniae. Here we aim to evaluate the differences in the NM of individuals infected with SARS-CoV-2, IAV, Respiratory Syncytial Virus (RSV), and uninfected individuals. Methods; Nasopharyngeal (NP) specimens positive for SARS-CoV-2, IAV, RSV and uninfected controls tested by RT-PCR at the Kingston Health Sciences Center were used. Extracted RNA from NP specimens were analyzed using the 16S rRNA Illumina Next Generation Sequencing library protocol. Results; SARS-CoV-2 infected individuals had higher alpha-($p<0.001$) and beta-diversity($p<0.001$) vs. uninfected individuals (n=45 both). SARS-CoV-2 positive individuals had further enrichment of inflammatory genera including Streptococcus and Burkholderia, and depletion of Haemophilus, Pseudomonas and Moraxella vs. RSV-positives ($p<0.001$ for all). SARS-CoV-2 infected individuals had elevated proportions of Streptococcus, and Bifidobacterium, and a decrease in Haemophilus, and Pseudomonas in comparison to IAV-positives ($p<0.05$ for all, n=40). Conclusions; This study demonstrates that NM profiles are unique in respiratory viral infections. Further investigation of the role of the NM in viral infections may provide insight into risks of secondary bacterial infections and viral disease pathogenesis.

33. ENHANCED ANTIGEN PRESENTATION AND PROTECTION AGAINST VIRAL INFECTION THROUGH ACQUISITION OF TRAINED IMMUNITY. Arielle Grossman, Isabella Pellizzari Delano, Aline Atallah, Tiziana Cotechini, Che Colpitts, Charles H. Graham. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Canada.

The term "trained immunity" (TI), or innate immune memory, refers to the process by which innate immune cells acquire memory via epigenetic reprogramming. Acquisition of TI has been linked with protection against viral infection and improved responses to anti-cancer therapy. TI is characterized by enhanced secretion of proinflammatory molecules in response to a secondary non-specific stimulus. However, whether acquisition of TI regulates other innate immune functions is unknown. Using an in vivo model of TI in which mice are injected intraperitoneally (i.p.) with bacillus Calmette-Guérin (BCG), we evaluated whether acquisition of TI modulates antigen processing and presentation capacity of dendritic cells (DCs) and whether trained alveolar macrophages (AMs) are more protected against viral infection compared with non-trained controls. BCG-trained DCs exhibited increased ovalbumin antigen uptake and presentation capacity compared with untrained DC controls. Moreover, viral titers collected from the supernatant of co-cultures consisting of BCG-trained AMs with murine coronavirus-infected fibroblasts were significantly decreased compared with titres collected from co-cultures with untrained AMs. These results demonstrate that acquisition of TI alters innate immune cell functions beyond enhancement of cytokine release and provide a rationale to investigate the downstream effects on adaptive immune responses. Discovering ways to enhance adaptive immunity with non-targeted approaches including BCG vaccination may be beneficial in the treatment of various diseases. (Supported by CIHR and SEAMO COVID-19 Innovation Fund).

34. ACQUISITION OF INNATE IMMUNE MEMORY IN BONE MARROW MONOCYTES DURING MURINE PREGNANCY. Nakeisha A. Lodge-Tulloch, Tiziana Cotechini, and Charles Graham. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

nnate immune memory, or trained immunity (TI), is defined as a functional epigenetic reprogramming of innate immune cells during which cells of the myeloid lineage, including monocytes acquire memory. TI arises following exposure to damage- or pathogen-associated molecular patterns (DAMPs and PAMPS) resulting in enhanced cytokine release following exposure to a secondary stimulus. The physiological inflammatory processes related to normal pregnancy including implantation and placental development are also associated with release of DAMPS. Thus, we hypothesize that pregnancy will result in the acquisition of trained immunity. To examine this, bone marrow monocytes collected from pregnant C57BL/6 mice (N = 12) on GD 15.5 and age-matched non-pregnant controls (N = 12) were exposed to the PAMPS lipopolysaccharide and Pam3Cys *in vitro* for 24h. Increased levels of the pro-inflammatory cytokines TNF-alpha and IL-6 were measured in the supernatant of monocyte cultures collected from pregnant dams compared with non-pregnant mice. Our data reveal that normal pregnancy leads to the acquisition of trained immunity in bone marrow monocytes in mice. These results provide a rationale to investigate whether known inflammation-associated pregnancy complications including pre-eclampsia and fetal growth restriction are associated with enhanced acquisition of TI. (Supported by the CIHR).

35. TARGETING CYCLOPHILINS TO ENHANCE ANTIVIRAL IMMUNITY AGAINST POSITIVE-SENSE RNA VIRUSES. John Mamatis and Che C. Colpitts. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Canada

Cyclophilins (Cyps) are essential host factors for several positive-sense RNA viruses, including hepatitis C virus (HCV) and coronaviruses (CoVs). However, a clear mechanism as to how these viruses exploit Cyps to promote their replication has yet to be elucidated. We previously showed that cyclophilin inhibitor (CypI) treatment of HCV-replicating human hepatoma Huh7 cells induced expression of antiviral genes to inhibit HCV infection, dependent on the transcription factor interferon regulatory factor 1 (IRF1). We show here that expression of IRF1 and IRF1-inducible genes potently restricts HCV replication. We hypothesize similar mechanisms mediate inhibition of CoV replication by CypI. Using HCoV-229E and HCoV-OC43 as models, we show that treatment of infected A549 lung alveolar epithelial cells with the classical CypI cyclosporine A (CsA) inhibits CoV replication. Excitingly, CsA treatment of CoV-infected A549 cells induced expression of IRF1-dependent antiviral genes, such as Mx1 and RSAD2. Importantly, RNAi-mediated silencing of IRF1 reduced the antiviral potency of CsA. Silencing of CypA expression by RNAi or CRISPR inhibited CoV replication, suggesting a specific role for CypA. We propose a model where CypI treatment induces IRF1-dependent antiviral immunity, thus contributing to its broad spectrum of antiviral activity against CoVs and other positive-sense RNA viruses. These findings open perspectives for novel therapeutic approaches against positive-sense RNA viruses, many of which are currently untreatable. (Supported by Queen's University and the Banting Research Foundation.)

36. USING CULTUROMICS TO CHARACTERIZE THE GUT MICROBIOTA OF LOW BIRTH WEIGHT NEONATES. Jummy Oladipo, Mabel Guzman-Rodriguez, Curtis Noordhof, Shu-Mei He, Katya Douchant, Prameet M. Sheth, Department of Medicine, Gastrointestinal Disease Research Unit (GIDRU), Queen's University, Kingston, Ontario, Canada.

Introduction: The neonatal gastrointestinal tract is colonized by a diverse population of bacteria known as the gastrointestinal microbiota (GIM). Metagenomics is commonly used to characterize the GIM however, 'culturomics', the use of specialized media in conjunction with metagenomics has the potential of providing further insight into the isolation and identification of bacterial populations in the GIM. This study aims to better characterize the GIM of low birth weight neonates (LBW) by using selective and differential media in conjunction with NGS to provide insight into the role of fastidious bacteria not previously defined to play a role in the neonatal GIM. Methods: Selective and differential agar including Columbia Blood agar, Colistin/Naladixic Acid, fastidious anaerobic, MacConkey, Bile Esculin, Bacteroides Bile Esculin, de Man, Rogosa and Sharpe, Bifidus agars were used to isolate bacteria healthy adults and LBW neonatal stool. Bacteria were identified using MALDI-TOF or 16S sequencing and community profiles were evaluated using NGS. Results: Bacteria isolated from healthy adult stool as an internal control included Staphylococcus warneri, Streptococcus salivaris, Bifidobacterium spp., Paeniclostridium soredelli, Bacteroides caccae, B.thetaiotamicron, B.uniformis, B.vulgatus, B.ovatus, Parabacteroides distasonis, Actinomyces meyeri, E.coli, and Rombustia sedimentorium. Analysis of neonatal stool identified and isolated S.epidermidis, S.hominis S.lungdunensis, E.coli, and E.faecali and E.faecium. Conclusion: These studies will expand our understanding of the membership of the neonatal GIM and better understand gastrointestinal diseases process in LBW neonates.

37. PROTEASE-INDUCED EXCITATION OF DORSAL ROOT GANGLION NEURONS IN RESPONSE TO ACUTE PERTURBATION OF THE GUT MICROBIOTA. Corey Baker, Jessica L Sessenwein, Amal Abu Omar, Quentin Tsang, Yang Yu, Julia Segal, Nader Ghasemlou, Prameet Sheth, Stephen J Vanner, David E Reed, Alan E Lomax. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

Abdominal pain is a major symptom of diseases associated with microbial dysbiosis. Disruption of the gut microbiota with antibiotics increases visceral pain, and germ-free mice are more prone to pain than conventionally-raised mice. However, the mechanisms underlying microbial modulation of pain remain elusive. We hypothesized that disruption of the intestinal microbiota modulates the excitability of peripheral nociceptive neurons. Patch clamp electrophysiological recordings of dorsal root ganglion (DRG) neuron excitability were obtained from control and treated mice with the non-absorbable antibiotic vancomycin (50µg/ml in drinking water) for one week. Bacterial dysbiosis was verified by metagenomic analysis of stool microbial composition. Mice treated with vancomycin were more sensitive to colorectal distension in vivo, and DRG neurons from vancomycin-treated mice were hyperexcitable in vitro compared to water-treated controls. Interestingly, hyperexcitability of DRG neurons was not restricted to gut projecting neurons, suggesting a widespread effect of gut dysbiosis on pain pathways. Incubation of DRG neurons from naïve mice in serum from vancomycin-treated mice increased neuron excitability, suggesting that microbial dysbiosis alters circulating mediators that influence nociception. The cysteine protease inhibitor E64 (30nM) and the protease-activated receptor 2 antagonist GB-83 (10µM) each blocked the increase in DRG neuron excitability in response to serum from vancomycin-treated mice. Overall, this suggests that microbial dysbiosis within the gut alters pain sensitivity and identify circulating cysteine proteases as a potential mediator of this effect. (Supported by CIHR)

38. VIGILANCE AND BEHAVIORAL STATE-DEPENDENT MODULATION OF CORTICAL NEURONAL ACTIVITY THROUGHOUT THE SLEEP/WAKE CYCLE. Aurélie Brécier, Mélodie Borel, Nadia Urbain and Luc Gentet. Centre de Recherche en Neurosciences de Lyon, Bron, France.

GABAergic inhibitory neurons, through their molecular, anatomic and physiological diversity, provide a substrate for the modulation of ongoing cortical circuit activity throughout the sleep-wake cycle. Here, we investigated neuronal activity dynamics of parvalbumin (PV), vasoactive intestinal polypeptide (VIP) and somatostatin (SST) neurons in naturally-sleeping head-restrained mice at the level of layer 2/3 of the primary somatosensory barrel cortex of mice. Through calcium-imaging and targeted single-unit loose-patch or whole-cell recordings, we found that PV action potential firing activity was largest during both NREM (nonrapid eye movement) and REM sleep stages, that VIP neurons were most active during REM sleep and that the overall activity of SST neurons remained stable throughout the sleep/wake cycle. Analysis of neuronal activity dynamics uncovered rapid decreases in PV cell firing at wake onset followed by a progressive recovery during wake. During NREM sleep spindles, PV and SST activity increased and decreased, respectively. Finally, we uncovered the presence of whisking behavior in mice during REM sleep and show that the activity of VIP and SST is differentially modulated during awake and sleeping whisking bouts, which may provide a neuronal substrate for internal brain representations occurring during sleep.

39. THE RELATIONSHIP BETWEEN PAIN CATASTROPHIZING AND QUALITY OF LIFE CHANGES IN CHRONIC PAIN PATIENTS IS MEDIATED BY DEPRESSION AND MODERATED BY PAIN SELF-EFFICACY. Landon Montag1, Tim Salomons1,2, Rosemary Wilson3,4,5, Scott Duggan4,5, and Etienne J. Bisson1,4,5,6 , 1Centre for Neuroscience Studies, Queen's University, Kingston, ON, Canada., 2Department of Psychology, Queen's University, Kingston, ON, Canada. 3School of Nursing, Queen's University, Kingston, ON, Canada. 4Chronic Pain Clinic, Kingston Health Sciences Centre, Kingston, ON, Canada. 5Department of Anesthesiology and Perioperative Medicine, Queen's University, Kingston, ON, Canada. 6School of Rehabilitation Therapy, Queen's University, Kingston, ON, Canada.

Adults with chronic pain have lower quality of life (QOL) compared to the general population. The goal of chronic pain treatment is to increase QOL rather than eradicate the pain. This study examined adults with chronic pain after a year of specialized treatment to determine the role of pain catastrophizing, depression, and pain self-efficacy in predicting changes in QOL. Patients in the KHSC Chronic Pain Clinic (N=81) completed measures of pain catastrophizing, QOL, depression, and pain self-efficacy at baseline and one-year later. A moderated mediation was performed, and correlations were completed to understand the relationships between the variables. Baseline pain catastrophizing significantly affected QOL changes (b=0.48, CI95%[0.122; 0.888]). Higher baseline pain catastrophizing was significantly associated with decreased depression (b=-0.23, CI95%[-0.473; -0.021]), and increased depression was associated with decreased QOL (b=-1.16, CI95%[-1.414; -0.821]) while controlling for pain catastrophizing. Furthermore, the relationship between baseline pain catastrophizing and the change in depression was moderated by the change in pain self-efficacy (b=-0.14, CI95%[-0.216; -0.044]). Patients with high baseline pain catastrophizing reported decreased depression, and this effect was greater as pain self-efficacy increased. Our findings highlight the roles of cognitive and affective factors and their impact on QOL in adults with chronic pain. Understanding the psychological factors that predict increased QOL is clinically useful, since medical teams may be able to optimize these positive changes in QOL through psychosocial interventions. (This study was partially supported by the Canadian Pain Network, the 2021-2022 Franklin Bracken Fellowship, and the Alison B. Froese Fund from the Department of Anesthesiology and Perioperative Medicine at Queen's University.)

40. EXCITATION OF MOUSE DORSAL ROOT GANGLIA NEURONS BY FECAL SUPERNATANT FROM IRRITABLE BOWEL SYNDROME PATIENTS. Samira Osman, Stephen Vanner, David E. Reed and Alan E. Lomax. Gastrointestinal Diseases Research Unit and Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, Canada.

Background: Irritable bowel syndrome (IBS) is a common disorder of the gastrointestinal tract which is highly associated with visceral pain. Proteases and their associated receptors have been implicated in the pain that accompanies IBS. However, most of these studies focused on the role of host-derived proteases to the exclusion of any role for proteases produced by the gut microbiota. Therefore, we examined the effect of fecal supernatants (FS) from IBS patients on visceral nociception by assessing changes in the excitability of mouse dorsal root ganglia (DRG) neurons. Methods: Lumbar (L1-4) DRG neurons from C57/Bl6 mice were collected, dissociated, and incubated overnight with a 1/20 dilution of fecal supernatant (FS) from five IBS patients. Perforated current clamp and whole cell voltage-clamp recordings were used to examine the effect of IBS patient FS on DRG neurophysiology. Results: FS from IBS patients led to a significant decrease in rheobase (26.9 ± 4.9 pA) and an increase in resting membrane potential (-52.1 ± 1.8 mV) of DRG neurons compared to vehicle controls (58.5 ± 3.9 pA; -57.3 ± 0.6 mV). The protease- activated receptor 2 (PAR2) antagonist GB-83 (10uM) abrogated the effects seen following treatment with IBS FS. A cysteine protease inhibitor (E64, 30nM), but not serine protease inhibitor (Fut-175, 10uM) blocked the hyperexcitability of DRG neurons in response to IBS-FS. No changes were found in action potential number at 2x rheobase, input resistance, or voltage-gated K+ and Na+ ion current densities. Conclusion: Cysteine proteases can directly impact the excitability of DRG neurons, via PAR-2 activation. The ability of bacterial proteases to modulate afferent signaling could suggest a potential role for the microbiota in visceral pain associated with IBS. **Supported by**: CIHR

41. A SCOPING REVIEW ON THE EFFECTS OF PSILOCYBIN IN ANIMAL STUDIES ACROSS BEHAVIOURAL TASK CLUSTERS AND NEUROLOGICAL MEASURES. Ron Shore, Katrina Dobson, Nigel Barnim, Sandra McKeown, Cella Olmstead, Craig Goldie, and Eric C. Dumont. Department of Biomedical and Molecular Sciences, School of Kinesiology and Health Studies, Department of Medicine, Department of Psychology, Queen's University, Kingston, Ontario, Canada.

A scoping review was conducted to determine the effects of the psychedelic compound psilocybin in animal studies across both behavioural task clusters and neurological measures, to chart what studies have been done and to identify behavioural tests, neurological measures and dosing modalities utilized. Method: The scoping review was guided by an a priori protocol. Given the widescale interest in psychedelics, we scoped the literature for areas relevant to the design of future clinical and pre-clinical studies. Scoping review methodology is indicated where scientific literature is heterogeneous and still emerging. Results: 62 studies from 14 countries were found spanning the time period 1962-2020. Many (older) studies should be interpreted with care given methodological concerns. Studies showed limited investigation of sex-based differences while identifying that timing between conditioning and dosing has significant impact. Some behavioural effects appear to be linearly dose-dependent and biphasic. Many studies used doses exceeding those of contemporary human trials, and some utilized the whole fungal biomass instead of synthetic psilocybin to somewhat stronger outcomes. Specific strains of Psilocybe mushrooms may have effect on behavioural outcomes. Discussion: Animal studies using psilocybin are generally dated and would not meet contemporary ARRIVE guidelines; animal studies may have limited value in translation to human behavior, especially with psychedelics, but study findings pertaining to dosing regime, pre-conditioning and the use of the whole natural fruiting body may contribute to contemporary trial design and to our understanding of the effects of Psilocybe mushrooms and psilocybin.

42. EXTRACELLULAR VESICLES CARRYING IRISIN ARE UPREGULATED BY EXERCISE AND RESTORE MEMORY IMPAIRMENT IN MOUSE MODELS OF ALZHEIMER'S DISEASE. Natalia M. Lyra e Silva1,2*, Tayna Rody3*, Guilherme B. de Freitas1,2, Rafaella A. Gonçalves1,2, Emma L. Robertson1, Isabelle Grenier-Pleau2, Brittney Armitage-Brown1, Andrew Winterborn1, Susan E. Boehnke1, Sheela Abraham2, Margaret Fahnestock4, Sergio T. Ferreira3,5, Douglas P. Munoz1,2, Fernanda G. De Felice1, 2, 6. 1Centre for Neuroscience Studies and 2Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada. 3Institute of Medical Biochemistry Leopoldo de Meis, Federal University of Rio de Janeiro, RJ, Brazil. 4Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, ON, Canada. 5Institute of Biophysics Carlos Chagas Filho, Federal University of Rio de Janeiro, RJ, Brazil. 6Department of Psychiatry, Queen's University, Kingston, ON, Canada.

Exercise is an important lifestyle intervention for Alzheimer's disease (AD). Multiple mechanisms are involved with the beneficial aspects underlying physical activity. Fibronectin type III domain-containing protein 5 (FNDC5) is the precursor of irisin, a hormone upregulated by exercise. Our group showed that AD patients have low levels of irisin in their central nervous system, and boosting irisin availability either centrally or peripherally triggers memory improvements in mouse models of AD. Here we aimed to investigate if exercise increases irisin in EVs and to test the therapeutic potential of EVs containing irisin. We found that irisin is physiologically present in EVs isolated from plasma and cerebrospinal fluid of primates and mice. We further observed that exercise specifically increases EV-associated irisin isolated from plasma of humans and mice. Finally, we demonstrate that treating mouse models of AD with EVs obtained from mice that overexpress FNDC5 prevents memory impairment. Taken together, our findings provide new insights about irisin physiology and propose a new therapeutic approach to increase the levels of irisin and to restore memory function in AD.

43. SKIN-RESIDENT DENDRITIC CELLS MEDIATE POSTOPERATIVE PAIN VIA CCR4 ON SENSORY NEURONS. Jaqueline R. Silva[1,2], Mircea Iftinca[3], Julia P. Segal[1], Olivia M. Smith[1], Francisco I. F. Gomes[4], Courtney A. Bannerman[1], Atlante Mendes[4], Madeline E. C. Robinson[1], Jelena Petrovic[1], Ian Gilron[1,2,5,6], Thiago Mattar Cunha[4], Christophe Altier[3], and Nader Ghasemlou[1,2,5*] [1]Department of Biomedical and Molecular Sciences, [2]Department of Anesthesiology and Perioperative Medicine, Queen's University, Kingston, Ontario, Canada; [3]Department of Physiology and Pharmacology, University of Calgary, Calgary, Alberta, Canada; [4] Center for Research in Inflammatory Diseases (CRID), Department of Pharmacology, Ribeirão Preto Medical School, University of São Paulo, Brazil; [5]Centre for Neuroscience Studies, [6]School of Policy Studies, Queen's University, Kingston, Ontario, Canada

Inflammatory pain, such as hypersensitivity resulting from surgical tissue injury, occurs as a result of interactions between the immune and nervous systems with the orchestrated recruitment and activation of tissue-resident and circulating immune cells to the site of injury. Our previous studies identified a central role for Ly6Clow myeloid cells in the pathogenesis of postoperative pain. We now show that the chemokines CCL17 and CCL22, with their cognate receptor CCR4, are key mediators of this response. Both chemokines are upregulated early after tissue injury by skin-resident dendritic and Langerhans cells and peripheral sensory neurons express CCR4. CCL22, and to a lesser extent CCL17, elicit acute mechanical and thermal hypersensitivity when administered subcutaneously, a response that is abrogated by pharmacological blockade or genetic silencing of CCR4. Electrophysiological assessment of dissociated sensory neurons from naïve and postoperative mice showed that CCL22 was able to directly activate neurons and enhance their excitability after injury. These responses were blocked using C 021 and siRNA targeting CCR4. Finally, our data show that acute postoperative pain is significantly reduced in mice lacking CCR4, wildtype animals treated with CCR4 antagonist/siRNA, as well as transgenic mice depleted of dendritic cells. Together, these results suggest an essential role for the peripheral CCL22:CCR4 axis in the genesis of inflammatory pain via direct communication between skin-resident dendritic cells and sensory neurons, opening new therapeutic avenues for its control.

44. PSILOCYBIN AT END-OF-LIFE: A SURVEY OF PLANNED BEHAVIOUR AMONG PALLIATIVE AND HOSPICE HEALTH CARE PROVIDERS IN CANADA. Nina Thomson, Leann Cunningham, Katie Rideout, Ron Shore, and Eric C. Dumont. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

Multiple clinical trials have shown reductions in anxiety related to terminal diagnosis following psilocybin consumption[1-3]. Additionally, psilocybin has a relatively low physiological toxicity[4-6], a low potential for abuse and dependence[7-9]. We are conducting a study of palliative and hospice healthcare professionals in Canada first to explore the perspectives of a small group (n=25) of nurses, nurse practitioners, and physicians through an elicitation survey. The survey is comprised of open-ended questions relating to the administration of psilocybin-assisted therapy for patients with end-of-life distress who have received a Schedule 56 exemption. The survey is constructed based on the Theory of Planned Behavior so we can understand how attitudes, subjective norms, and perceived behavioral control may influence the intent of health care professionals to participate in the administration of psilocybin-assisted therapy.
Responses will be analyzed for themes with verification by principal component analysis. These results will then inform the development of another survey to be sent to a larger group of health care providers (n=320). We anticipate that the results will contribute to our understanding of the educational needs of health care providers related to this topic, raise awareness of this topic among survey participants and may contribute relevant data to evolving drug policy in Canada.

45. PEERS IN PATHO: THE ONLINE PLATFORM FOR PEER ASSISTED LEARNING BASED TUTORIALS IN PATHOPHYSIOLOGY. Karina Fainchtein1 (3rd year LifeSci), Madeline Tripp2 (3rd year BScN), Abdelrahman Elsebaie1 (3rd year BHSc), Asad Taqvi3 (4th year BSc), Sarah Crawford4 (BScN RN), Conner Smith2,5 (BScN RN), Kathryn Osborne2,4 (BScN RN), Maha Othman1,2 (MD PhD)1 Department of Biomedical and Molecular Sciences, Queens's University, Kingston, ON, Canada 2 School of Baccalaureate Nursing, St. Lawrence College, Kingston, ON, Canada, 3 McGill University, Montréal, QC, Canada, 4 Grey Bruce Health Services, Meaford, ON, Canada, 5 Ottawa General Hospital, Ottawa, ON, Canada.

Peer-Assisted Learning (PAL) models have been integrated into postsecondary education across Canada and internationally. PAL strategies improve the comprehension of course material among students and offer a dynamic support system to help mitigate the anxiety and stress students often feel when immersed in complex courses. The value of peer support has been accentuated during the COVID-19 pandemic with more online learning and students experiencing greater isolation amidst lockdowns. As a multi-institutional team encompassing current students and alumni, we developed an online education platform (currently exists as a functional prototype) to accompany a university-level pathophysiology course. The purpose of this platform is to enhance peer support, access to tutorials and course content, and to facilitate student-led collaborative learning. The foundation of this online platform is a PAL tutorial model developed for a 12-week pathophysiology course over the past five years as well as comprehensive course guide that combines lecture slides and notes with clinical experience and knowledge from former students. The online platform is expected to further develop the tutorial model and allows for the continuous development of a central repository of resources for students and peer facilitators including flashcards, interactive chat, games, and testing, and the ability to create or join online study groups. A quality improvement plan and research study are in development to provide objective evaluation and insights to meet evolving student needs

Protein Structure

46. INVESTIGATING THE ROLE OF A KINESIN-8 REGULATORY DOMAIN IN A FUNGAL PATHOGEN. Caitlin Doubleday, Byron Hunter, and John S. Allingham1, 1Department of Biomedical and Molecular Sciences.

Candida albicans is common commensal colonizer of humans and a normal part of the gut mycobiome. However, immunocompromised individuals are vulnerable to severe skin, mucosal, and systemic C. albicans infections, the latter of which can have a mortality rate in excess of 40%. An important factor in C. albicans pathogenicity is its ability to transition from growth as a budding yeast into long filamentous cells (hyphae) which penetrate host tissue membranes. Establishing and maintaining this morphological switch is heavily dependent on microtubule cytoskeleton remodelling proteins that are crucial for mitosis and distribution of nuclei and organelles in the elongated cells. Our research has shown that a kinesin-8 motor protein, named Kip3, is a critical regulator of microtubule structures, and we have evidence that the catalytic activity of CaKip3 is regulated by a unique non-catalytic domain at its C-terminus. Using structural, biochemical and bioinformatic techniques, we are attempting to uncover the mechanism by which CaKip3's tail domain regulates the catalytic motor. Preliminary results suggest that a subdomain of the tail, called the distal tail, provides an additional microtubule binding site through electrostatic interactions, and that this interface may be dependent on the curvature of the microtubule lattice. Based on these results, we hypothesize that the distal tail of CaKip3 is critical for motor domain localization to microtubule plus ends. (Supported by the Canadian Institutes of Heath Research)

47. MOLECULAR BASIS OF KLF15-MEDIATED REPRESSION OF CARDIAC HYPERTROPHY. Matthew S. Fishman1, Holly L. Spencer1, Marina R. Lochhead1, Keegan B. Turner-Wood 1, Steven P. Smith1, 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, K7L 3N6.

Cardiomyocyte development and function is a highly regulated process orchestrated by a specific network of cardiogenic transcription factors that form precise macromolecular complexes allowing the cardiovascular system to respond to specific stimuli. The dysregulation of these transcription factors can lead to the re-activation of fetal cardiac genes resulting in abnormal myocardial growth, a condition known as cardiac hypertrophy, a key risk factor associated with heart failure. The activity of several cardiogenic transcription factors required for fetal cardiac development are activated by the transcriptional co-activator homologues CREB-binding protein and p300 (CBP/p300). CBP/p300 are multi-modular transcriptional coactivators that increase the rate of transcription by interacting with intrinsically disordered transactivation domains (TADs) of transcription factors, allowing for dynamic associations that lead to the activation or repression of target genes. The transcription factor KLF-15 has been implicated in sequestering CBP/p300's ability to activate fetal cardiac genes, by blocking the protein-protein interaction domains of CBP/p300 through its two TADs. Our current study uses biochemical and biophysical techniques to determine the molecular basis by which KLF-15 regulates fetal cardiac genes through its sequestration of CBP/P300. These studies will provide critical molecular information regarding the role of dynamic complexes involved in regulating cardiac hypertrophy and the detailed structure-function studies will provide key insights that can be used to identify novel risk factors to diagnose heart failure at earlier stages of the disease.

48. UNDERSTANDING THE MECHANISM OF KINESIN-8-MEDIATED MICROTUBULE DEPOLYMERIZATION.
Michelle Gontcharova, Byron Hunter, Daria Trofimova, and John Allingham. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON

Survival of all eukaryotes depends on equal partitioning of their chromosomes between the two newly formed daughter cells during mitosis. Kinesin-8 motors are fundamental to this process. They modulate the length of mitotic spindle microtubules (MTs) by walking to their plus ends, where they catalyze removal of tubulin subunits, resulting in rapid MT shortening. This activity ensures proper positioning of the mitotic spindle and regulation of its length, yet the molecular basis underlying the dual ability of kinesin-8s to traverse and shorten MTs remains unclear. To define its mechanism of tubulin release from MT ends, we have devised a strategy to elucidate a high-resolution structure of kinesin-8 bound to an individual tubulin subunit. By fusing the tubulin-capping protein DARPin to the C-terminus of the kinesin-8 motor domain, we increased the tubulin-binding surface area by ~30%, effectively producing a modified kinesin-8 that binds almost irreversibly to tubulin. Analytical size-exclusion chromatography shows that all the input kinesin-8-DARPin motor complexes with tubulin. Tight tubulin-binding is also evident from the dramatic drop in the ATPase activity of this engineered kinesin-8, which is expected when the motor domain cannot cycle between a tubulin-bound and unbound state. This tight binding interaction should prevent dissociation of the kinesin-8-tubulin complex under most protein crystallization conditions yet allow us to observe the conformation of this intermediate of the kinesin-8's MT-shortening mechanism. (Supported by the Canadian Institutes of Health Research)

49. IMPACT OF CARBAPENEMASE MECHANISM ON THE CLINICAL DETECTION OF CARBAPENEM-RESISTANT BACTERIA CHARACTERIZED THROUGH PRODUCT FORMATION. Rachel. A.V. Gray and Christopher. T. Lohans. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

The combination of excessive administration and incorrect application of antibiotics has drastically accelerated the emergence of multidrug-resistant (MDR) bacterial pathogens worldwide. The production of β-lactamases by MDR bacteria is one of the most common mechanisms for resistance; these degradative enzymes threaten the clinical viability of carbapenems, a group of antibiotics used as a last-resort treatment for infections. The rapid detection of bacteria that produce carbapenemases, β-lactamases that can degrade carbapenems, helps guide the prescription of optimal therapeutics to treat infections. Accurate detection of β-lactamases is especially challenging, as no gold-standard methods currently exist that can detect all classes of these enzymes. In particular, class D carbapenemases (CHDLs) are becoming more clinically significant and yet are substantially more difficult to detect compared to other classes of carbapenemases. We recently found that carbapenem degradation by CHDLs often generates a mixture of hydrolysis and lactone products. Current detection approaches take advantage of the acidic hydrolysis products by incorporating colorimetric pH indicators to detect carbapenem breakdown. However, CHDLs may be missed by these approaches due to their higher levels of lactone formation. By developing an assay that closely mimics commercial identification methods and confirming the types of products formed by NMR, we have found major discrepancies in detection by these lactone-producing carbapenemases. New modes of detection for β-lactamases are critical for the clinical longevity of our antibiotics; we hope to develop and validate innovative techniques that offer improved sensitivity and reliability.

50. DEVELOPMENT AND VALIDATION OF A BIOSENSOR-BASED APPROACH FOR THE EVALUATION OF B-LACTAMASE ACTIVITY AND INHIBITION. Mitchell Jeffs and Christopher T. Lohans. Department of Biomedical and Molecular Science, Queens University, Kingston, Ontario, Canada.

β-lactams are the most commonly prescribed class of antibiotic worldwide. Thus, it is concerning that an array of pathogens have been able to develop resistance mechanisms to render these medications ineffective. When considering gram negative organisms, the production of β-lactamases is the most common form of resistance. These enzymes are capable of inactivating β-lactams by hydrolyzing the central ring structure of the drug. In recent years, new β-lactamases have been discovered that have extremely broad substrate ranges, which include carbapenems (last resort antibiotics for targeting drug resistant pathogens). In response, efforts have been made to develop β-lactamase inhibitors: molecules which are administered alongside an antibiotic to rescue it from enzymatic degradation. Several inhibitors have been approved for clinical use against pathogens producing serine-β-lactamases (SBLs). Unfortunately, no such inhibitors exist for targeting metallo-β-lactamases (MBLs), a subclass of β-lactamases that have disseminated across the globe. To address this need, we have developed and validated a luminescence-based biosensor for studying β-lactamase activity and inhibition. This sensor is based around the detection of peptidoglycan catabolite influx into the bacterial cytoplasm following β-lactam exposure. We hope to apply this platform in the future to study MBL enzymology, as well as for screening compound libraries with the aim of identifying new β-lactamase inhibitors with activity against MBLs. Project supported by Natural Sciences and Engineering Research Council of Canada.

51. TARGETING POLYPHOSPHATE KINASE ENZYMES TO ATTENUATE PSEUDOMONAS AERUGINOSA VIRULENCE. Nolan Neville, Nathan Roberge, and Zongchao Jia. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

In 2017, the World Health Organization deemed *Pseudomonas aeruginosa* a Priority 1 bacterial pathogen in urgent need of new drugs. Polyphosphate (polyP) plays a key role in the virulence and stress response of this bacterium, suggesting an attractive therapeutic target. Uniquely, *P. aeruginosa* encodes four polyP kinase enzymes—PPK1, PPK2A, PPK2B, and PPK2C—which synthesize and consume polyP. PPK2 enzymes can produce sufficient polyP to compensate for the loss of PPK1, and *vice versa*. Here, we present a small molecule that disrupts polyphosphate homeostasis by inhibiting all members of both polyphosphate kinase families (PPK1 and PPK2) encoded by *P. aeruginosa*, demonstrating dual-specificity PPK inhibition for the first time. Inhibitor treatment reduced cellular polyP in WT, Δ*ppk1*, and Δ*ppk2* strains to levels on a par with the Δ*ppk1*Δ*ppk2A*Δ*ppk2B*Δ*ppk2C* knockout control. Inhibitor treatment also phenocopied *ppk1* and *ppk2* deletion to attenuate biofilm formation, motility, and pyoverdine and pyocyanin production, elucidating a hitherto unreported role of PPK2 enzymes in these phenotypes. Most importantly, inhibitor treatment attenuated *P. aeruginosa* virulence in a *Caenorhabditis elegans* infection model while exhibiting negligible toxicity towards the nematodes or HEK293T cells. This work therefore establishes PPK2s, in addition to PPK1, as valuable drug targets in *P. aeruginosa*, and provides a favourable starting molecule for future inhibitor design efforts. (Supported by Cystic Fibrosis Canada and NSERC)

52. EXPRESSION AND PURIFICATION OF FUNGAL G PROTEIN-COUPLED RECEPTOR *FG*STE2 Pooja S. Sridhar[1], John S. Allingham[1], Michele C. Loewen[1,2], [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, K7L 3N6., [2]National Research Council of Canada, 100 Sussex Drive, Ottawa, K1A 0R6.

Fusarium graminearum is a pathogenic fungus that causes devastating diseases in cereal crops, leading to food shortages and economic losses. Our laboratory has shown that the fungal G protein-coupled receptor (GPCR) Ste2 in *F. graminearum* (*Fg*Ste2), plays a key role in mediating directed fungal hyphal growth, also called chemotropism, towards a host-derived ligand. However, the molecular basis of the activation of *Fg*Ste2 by its host-derived ligand is currently unknown. Its orthologue in *Saccharomyces cerevisiae* has been extensively studied and its structure was recently solved by cryo-electron microscopy (cryo-EM). The present study aims to determine the structure of *Fg*Ste2 bound to its host-derived ligand to elucidate the molecular basis of its interaction with its ligand. We designed an expression construct containing *Fg*Ste2 tagged with Green Fluorescent Protein and a his-tag for easy capture and detection. This enabled successful recombinant expression and purification from a Sf21 insect cell line. Our ongoing work includes testing its expression in different cell lines and optimizing expression parameters to maximize protein yield. Next steps will include scaling up the purification to obtain large protein yields for either x-ray crystallography or cryo-EM. Understanding the structural basis of the binding of *Fg*Ste2 with its ligand will shed new light on the fundamental mechanisms underlying the pathogenicity of *F. graminearum*, and new potential strategies for combatting this pathogen.

53. INSPIRED BY THE SEA TO FIGHT CANCER METASTASIS. Daria Trofimova, Bhavin Pipaliya, Yun Jiang, Andrew Craig, P. Andrew Evans, and John Allingham. Department of Biomedical and Molecular Sciences, Queen's Cancer Research Institute, and Department of Chemistry, Queen's University, Kingston, ON, Canada.

Macrolides can be important allies in the battle against cancer. A good example is Mycalolide B, a compound isolated from the marine sponge that can suppress proliferation and motility of cancer cells at low nanomolar concentration, giving it promise for preventing metastasis. This effect of Mycalolide B is a consequence of its ability to target and bind the polymer-forming protein actin, leading to the collapse of the actin cytoskeleton and prevention of its reassembly in cells. Without the actin cytoskeleton, cells cannot form membrane protrusions or establish focal adhesions and are unable to contract, making cell motility impaired if not impossible. Unfortunately, Mycalolide B is not easy to obtain from nature and is extremely challenging to synthesize. Therefore, the design of truncated synthetic Mycalolide B analogues that mimic the activities and potency of the natural form is crucial for developing new cancer treatments. Using the X-ray crystal structure of the Mycalolide B - actin complex, we designed and synthesized a library of 30 Mycalolide B analogues. We then evaluated their ability to inhibit G-actin polymerization, induce F-actin depolymerization, and block SKOV3 cell invasion of extracellular matrix. Through these studies, we identified a highly potent truncated MycB derivative whose bioactivity suggests it could be used as a template for designing a new class of drugs to slow or halt cancer metastasis. (Supported by the New Frontiers in Research Foundation and Collaborative Health Research Partnerships (NSERC/CIHR)

54. ENGINEERING DESIGNER CELLULOSOMES FOR ENHANCED CARBOHYDRATE DIGESTION Keegan B. Turner-Wood1, Holly L. Spencer1, Benjamin Pluvinage2, Alisdair B. Boraston2, Steven P. Smith1, 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston, K7L 3N6, 2Department of Biochemistry and Microbiology, University of Victoria, Victoria, V8P 5C2.

Marine polysaccharides represent a functionally limitless reservoir of renewable energy. Microorganisms have evolved specialized carbohydrate-active enzymes (CAZymes) capable of digesting the recalcitrant polysaccharide matrices found within marine biomass. The aquatic bacterium Bacteroides uniformis uses four agarose-specific glycoside hydrolases with complementary activity to efficiently digest agarose into its monosaccharide constituents. These agarases are excreted and function as freely diffusing enzymes in either the periplasm or extracellular environment. In contrast, a subset of terrestrial saccharolytic microorganisms incorporate their CAZymes into a scaffold, leading to the formation of multi-enzyme complexes termed cellulosomes. The enhanced activity of cellulosomes over free enzymes is due to their proximity and ability to target their polysaccharide substrate via a resident carbohydrate binding module (CBM). Assembly of CAZymes onto a cellulosome is mediated by a high-affinity protein-protein interaction between cellulosome-based cohesin modules and enzyme-borne dockerin domains. Despite the increased activity granted through cellulosome formation, no marine organisms have yet adopted this strategy. Our current study uses protein engineering techniques to generate agarose-degrading multi-enzyme complexes with enhanced agarose degrading properties. We've generated a library of chimeric cellulosomes with alternative cohesin arrangements and integrated agarose specific CBMs. Using these designer scaffolds, we assembled multi-enzyme complexes comprising two to four agarases and assessed their enzymatic activities relative to free-enzyme mixtures. These studies are the first to assess the impact of integrating agarose specific CAZymes into chimeric cellulosomes.

Reproduction and Sexual Function

55. DEVELOPMENT OF ANATOMICAL MYOFASCIAL TRUNK AND LIMB EDUCATION MODULES FOR HEALTHCARE PROFESSIONALS IN SPORTS MEDICINE. Lucy Lu, Dr. Craig Harness, Dr. Mark Lindsay, Dr. Leslie MacKenzie. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

The understanding of anatomy is fundamental to healthcare professionals. Insufficient knowledge of anatomy in practicing professionals has been well-documented in allopathic practitioners, with feelings of inadequate preparation cited by senior clinicians and medical trainees. There has been little investigation into the continued maintenance of anatomical knowledge in complementary and alternative medical professionals such as physiotherapists, athletic trainers, and chiropractors, with the subsequent impact on clinical responsibilities. Questionnaires, anatomy assessment tools, and interviews were used to evaluate the efficacy of educational modules piloted to the medical staff of a professional sports team. Quantitative and qualitative findings were compared to 1) identify gaps in anatomical knowledge, 2) demonstrate an improvement in anatomical knowledge after completion of the modules, and 3) compare perceived knowledge gaps of professionals to actual knowledge gaps.

56. THE ASSOCIATION BETWEEN CAREGIVER'S SOCIAL SUPPORT AND BURDEN OF CAREGIVING FOR PATIENTS WITH HIP FRACTURE: A SCOPING REVIEW. Cara Sadiq, Varsha Doguparty, Dorothy Kessler, Marcia Finlayson, Vincent DePaul, Mohammad Auais. Department of Health Sciences. Queens University. Kingston, ON.

Although informal caregiving can be rewarding, individuals who provide care to older adults with hip fracture often experience significant burden. Perceived caregiver resources, such as social support, have been theorized to modulate caregiver burden, yet have been largely overlooked within the context of hip fracture. The aim of this review is to identify social support factors associated with caregiver burden experienced by informal caregivers of patients with hip fracture. Methods: This scoping review followed the Modified York Framework. A search was conducted utilizing the main medical databases (CINAHL, EMBASE, Medline, PsycINFO and Cochrane), from inception to February 2021, for studies investigating caregiver burden and caregiver social support within the hip fracture population. Studies were excluded when they were qualitative/ perspective papers or were not available in English. Results: We identified 41 studies in total and 10 fulfilled our criteria. Caregiver participants were primarily female, and their mean age ranged from 53.1 to 69.2 years old. Evidence of statistically significant associations (p=0.05) between caregiver social factors and burden were found in 80% (n=8) of studies. Factors identified included: Social support (e.g., social contact frequency), social factors (e.g., relation to care receiver), life disruptions (e.g., work) and family factors (e.g., caregiving obligation). Conclusion: Emerging evidence supports that caregiver social factors may have an influence on caregivers' burden, which can impact health outcomes for caregivers and patients.

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57. INVESTIGATING THE DIFFERENTIATION POTENTIAL OF SCA-1$^+$ MOUSE TROPHOBLAST STEM CELLS. Megan Cull[1], Avery McGinnis[1], Bryony Natale[2], Nicole Peterson[2], David Natale[1,2], [1]Dept. of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada; [2]Dept. of Obstetrics and Gynecology, Queen's University Kingston, Ontario Canada

OBJECTIVE: Trophoblast stem (TS) cell contribution to placenta pathology and their adaptive potential is unknown. Stem cell antigen (Sca)-1, a murine cell surface marker, can sort for a TS cell-like population from the mid-gestation placenta and is increased in placental pathology models. Whether Sca-1 alters TS cells proliferation or differentiation potential is unestablished. **DESIGN**: Compare *in vitro* proliferation rate, TS cell marker expression and differentiation potential in Sca-1$^+$ and Sca-1$^-$ TS cell populations. **MEASUREMENTS:** Proliferative mouse TS cells were sorted into Sca-1$^+$ and Sca-1$^-$ subpopulations by magnetic-activated cell sorting (MACS). RNA profiling of stem cell and differentiated trophoblast genes was assessed by qPCR. A serial passage study evaluated proliferation rate to establish both subpopulations self- maintenance ability and their original RNA profile. Statistical analysis utilized multiple T-tests to compare groups and was corrected for multiple comparisons using the Holm-Sidak method. **RESULTS:** TS cell identifying genes are unchanged in the Sca-1$^+$ and Sca-1$^-$ populations. Morphologically, both populations are similar. After preliminary passage numbers, the proliferation profile of both populations is comparable. Differentiation potential analysis is in progress. **CONCLUSIONS:** Preliminary results suggest that the TS cell profile, proliferation, and differentiation potential of Sca-1$^+$ and Sca-1$^-$ subpopulations are similar. Sca-1 as a cell surface marker will be an ideal means to assess TS cell recruitment *in vivo*, in models of placental pathology. Supporting Agencies: NIH/NICHD.

58. MANAGEMENT OF WOMEN WITH TYPE 2B VON WILLEBRAND DISEASE DURING PREGNANCY-EVIDENCE FROM LITERATURE AND INTERNATIONAL REGISTRY. Abdelrahman Noureldin[1] (3rd year BHSc), Predrag Miljic[2] (MD), Michelle Lavin[3] (MB BCh PhD), Sajida Kazi[4] (MB BCh), Analia Sanchez Luceros[5] (MD PhD), Paula D James[6] (MD, FRCPC), Maha Othman (MD PhD)[1,7] [1] Department of Biomedical and Molecular Sciences, Queens's University, Kingston, ON, Canada
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Type 2B von Willebrand disease (VWD) accounts for ~5% of all cases of VWD; the most common bleeding disorder. It results from gain-of function-mutation in the *VWF gene* leading to enhanced VWF-platelet binding. Management of women during pregnancy is challenging due to the associated physiological haemostatic alterations. Best approaches for lab monitoring, choice and goals of therapy remain ill-defined. We aimed to examine diagnostic and management approaches and outcomes of women with this disease during pregnancy via: 1-systematic review of literature, 2-data from an international registry supported by the International Society on Thrombosis and Haemostasis (ISTH). EMBASE was searched from inception-June 2021 and 2312 articles were screened; 101 were selected for full text review and 23 selected for data extraction. Forty-three pregnancies from across the globe were analyzed (literature: 35, registry:8). Genetic testing confirmed diagnosis in only 17(39%) pregnancies. Thirty-reports included bleeding symptoms with no objective bleeding scores. Compared to pre/early pregnancy, platelet count decreased significantly (median=47x10^9/L; p=0.0001) and VWF:RCo levels increased significantly (median=15 IU/dL; p=0.02) in third trimester. Post-partum hemorrhage was reported in 14 patients (32%) and 20 patients (46%) received transfusion in response to acute bleeds during or immediately following delivery (12 received platelets; 4 packed RBCs). Treatment varied between VWF:FVIII, VWF concentrate and antifibrinolytic therapy. 60% of patients received treatment during or after labour with no haemostasis monitoring reported. This data indicates bleeding remains a concern in pregnancy associated with type 2B-VWD. Management practices are variable thus an international guidance is critically needed for better care of this cohort. Key words: Bleeding disorders, Women, VWF. Funding Support: Canadian Hemophilia Society, ISTH.

59. EXPLORATION OF THE MECHANISM OF ACTION OF HUMAN OVIDUCT-SPECIFIC GLYCOPROTEIN (OVGP1) IN ENHANCING SPERM CAPACITATION. Sydney C. Vanderkooi (M.Sc. Candidate), Yuewen Zhao (Ph.D), Patricia Lima (Ph.D) and Frederick W. K. Kan (Ph.D). Department of Biomedical and Molecular Sciences & Queen's CardioPulmonary Unit, Queen's University, Kingston, Ontario, Canada.

To date, there is an increasing number of infertile couples who seek fertility treatment with assisted reproductive technologies, including conventional *in vitro* fertilization (IVF). The mammalian oviductal cells secrete a major glycoprotein known as oviduct-specific glycoprotein (OVGP1). Among many beneficial effects on the sperm and oocytes during fertilization, this glycoprotein has been implicated in enhancing sperm capacitation, a requirement which sperm must complete to become fertilizing competent. Our lab has produced recombinant human OVGP1 (rHuOVGP1) which enhances tyrosine phosphorylation of sperm proteins, a biochemical hallmark of capacitation that occurs in the sperm tail. Progesterone (P4) is known to be involved in calcium influx, an important aspect of capacitation, through CatSper channels in the sperm tail. Here we performed a study in the hope of gaining a better understanding of the mechanism of sperm capacitation by examining if rHuOVGP1 works in synergy with P4 in regulating calcium influx and tyrosine phosphorylation of sperm proteins. The techniques used include flow cytometry, live cell imaging, and Western blot analysis. The results obtained indicate that both rHuOVGP1 and P4 can enhance sperm capacitation through increasing the levels of intracellular calcium influx and protein tyrosine phosphorylation, however, the best results were obtained when they were used in combination. The present research is of significance to the field of infertility as a better understanding of the mechanism that regulates the function of OVGP1 could lead to improvement of the success rates of IVF by supplementing the culture media currently used in fertility clinics with rHuOVGP1. This work was supported by CIHR.

60. CHARACTERIZATION OF THE FEMALE UROGENITAL TRACT MICROBIOME IN PATIENTS WITH CERVICAL DYSPLASIA. Leah Velikonja, Olivia Giovannetti, Diane Tomalty, and Dr. Michael Adams. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

Introduction: Little is known about the female urogenital tract (FUT) and the interactions of their microbiomes, yet thousands of procedures are performed on these regions each year. Given the close anatomical relationship between the vagina, cervix, and urethra, it is possible that dysbiosis from one region can impact neighboring regions. Therefore, it is essential to determine the relationship between FUT microbiomes in women with cervical dysplasia. **Methods:** Patients undergoing the loop electrosurgical excision procedure (LEEP) were recruited. Vaginal swabs, cervical swabs, and urine samples were collected to analyze the vaginal, cervical, and urethral microbiomes, respectively. 16S rRNA analysis was performed to analyze the presence and relative abundance of bacteria in the samples.**Results:** The vaginal microbiome was analyzed for 24 women, and the cervical and urethral microbiomes were analyzed for 25 women and compared to healthy controls from previous literature. Participants with cervical dysplasia showed a decrease in the abundance of *Lactobacilli* and an increase in microbial diversity compared to the reported normal microbiome. **Conclusion:** This study identified a microbial relationship between regions of the FUT in women with cervical dysplasia. These findings may contribute to the growing understanding of the interrelatedness of the female pelvis, specifically the microbiomes of the FUT. It may also form a basis for the development of new therapeutic strategies to manage symptoms of dysplasia associated with microbial changes.

Therapeutics and Toxicology

61. ALTERATIONS IN CD-1 MOUSE FETAL DNA DAMAGE-RESPONSE GENE EXPRESSION, TOPOISOMERASE IIA ACTIVITY, AND DNA DAMAGE FOLLOWING IN UTERO BENZENE EXPOSURE. Trent H. Holmes and Louise M. Winn.

Benzene is an environmental toxicant and known human carcinogen. Recent epidemiological studies have demonstrated a relationship between exposure to benzene in pregnant women and the incidence of childhood leukemias. The hypothesized mechanism of benzene-induced DNA damage is through the inhibition of topoisomerase IIα (topo IIα), in part, to generate DNA double stranded breaks and induction of error-prone DNA repair. This sex-dependent relationship has previously been demonstrated in murine models of transplacental benzene carcinogenicity and consequently, the cellular mechanisms of benzene toxicity require further studies. This study aims to further expand upon previous in vitro findings in murine fetal-derived cell cultures and determine mechanisms of toxicity in vivo. Using the established mouse model of transplacental benzene carcinogenicity, GD14 fetal livers were harvested 2, 6 and 24 hours following final benzene exposure and used to assess DNA damage, repair, and topo IIα activity. Topo IIα activity was assessed in fetal livers, and no significant difference was seen in any timepoint, or between sexes. Genes which express DNA repair pathways were assessed, and significant DNA repair gene expression changes were observed after 24 hours. DNA damage, measured by levels of modified histone H2AX (γH2AX), showed a significant increase in benzene exposed pups, with sex-dependant significance seen only in female pups. Preliminary data from comet tests shows DNA damage in fetal livers.

62. ASSESSMENT OF PLACENTAL EPIGENETICS AND PLACENTAL-FETAL SEROTONIN PATHWAY AS A MECHANISM OF VALPROIC ACID-INDUCED TERATOGENESIS. Brianna L. Jackson and Louise M. Winn. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

Valproic acid (VPA) is a medication used to treat neurological and psychiatric disorders. Administration of VPA during pregnancy is associated with a 3-fold increase in the development of neurodevelopmental disorders in children, including autism spectrum disorder (ASD). The mechanisms exerting VPA's teratogenicity remain unclear, though it is now evident that the placenta plays a prominent role in influencing the development and function of the fetal brain. Specifically, the production and secretion of serotonin in the placenta is critical for fetal forebrain wiring; impairments to placental function can disrupt this system and has been implicated in ASD. As a potent histone deacetylase inhibitor, VPA may elicit placental dysfunction by modifying the epigenetic landscape and altering gene expression in the placenta. In this study, CD-1 mice will be administered VPA using an established dosage regime that produces offspring with an ASD-like phenotype. Placentae and fetuses will be harvested at 1-, 3-, and 24-hours post-dosing and on gestational day 18. Epigenetic modifications in the placenta, including histone acetylation/methylation and DNA methylation, will be quantified by immunohistochemistry. Furthermore, potential alterations to the placental-fetal serotonin signaling pathway will be investigated by Western blotting and high-performance liquid chromatography. Information from this study will contribute to a body of knowledge that seeks to understand the mechanisms driving VPA-induced teratogenesis, and aid in the development of safer therapeutics for women of childbearing potential.

63. LOW-DOSE TACROLIMUS PROMOTES THE MIGRATION AND INVASION OF HUMAN-DERIVED FIRST TRIMESTER EXTRAVILLOUS TROPHOBLAST CELLS AND MODULATES THEIR NITRIC OXIDE SYNTHASE ACTIVITY *IN VITRO*. Ahmad J.H. Albaghdadi (PhD), Kassandra Coyle (BSc), and Frederick W. K. Kan (PhD). Dept. of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario

Objectives: To test the hypothesis that, independent of its immunosuppressive properties, the macrolide immunosuppressant tacrolimus can influence uterine spiral artery remodeling (SAR) through the promotion of migration and invasion of human first-trimester extravillous trophoblast (EVT) cells and the modulation of their Nitric Oxide Synthase (NOS) enzyme activity. **Study methods:** HTR8/SVneo cells were treated with low-dose tacrolimus (10 ng/ml) in the presence and absence of the NOS inhibitor N^{ω}-Nitro-L-Arginine methyl ester (L-NAME) (50 mM). The protein expression of eNOS, p-eNOS-Ser 1197, p-eNOS-Tyr495, STAT3 and pSTAT3 was analyzed by Western blot after 12-, 24- and 48-hours post-treatment. IncuCyte zoom-monitored wound scratch and transwell invasion assays were performed. NO production in treated cells was analyzed by fluorescent microscopy and flow-cytometry using the NO sensitive fluorescent probe DAF-FM. **Results:** Low-dose tacrolimus significantly ($p < 0.001$) stimulated the migration and invasion of the HTR8/SVneo cells and abrogated the suppressive effect of L-NAME likely through the activation of STAT3. Moreover, tacrolimus prevented L-NAME-induced suppression of NO and stimulated the phosphorylation of the eNOS activation domain p-eNOS-Ser1179 in treated HTR/SVneo cells. **Conclusions:** Our data suggest an immune-independent mode of action of tacrolimus in positively influencing SAR, at least in part, through promoting the migration and invasion, and NO release of human-derived first-trimester EVT cells. Further research into the use of low-dose tacrolimus in complexed gestations featuring defective uterine SAR is warranted. **Funding source:** This work was supported, in part, by CIHR.

64. A PERIPARTUM VASCULAR ASSESSMENT OF WOMEN WITH PRE-ECLAMPSIA. Jennifer Armstrong and Dr. Graeme Smith. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

Pre-eclampsia (PE) is characterized as new-onset hypertension in pregnancy (>140mmHg systolic or >90mmHg diastolic), along with proteinuria. Although the symptoms associated with PE typically disappear after delivery, women who have experienced PE are at a higher risk of developing cardiovascular disease (CVD) later in life. In women with PE, the development of capillary rarefaction, defined as a reduced spatial density, occurs more severely than in healthy pregnancies and continues into the puerperium. It is reasonable to connect capillary rarefaction to microcirculation function as PE is a systemic disease that affects the microcirculation. Thus, it is hypothesized that capillary rarefaction visualized with nailfold-video capillaroscopy (NVC) will be more severe in women with PE and will persist after delivery. To investigate this hypothesis, both control participants and women with PE are assessed using NVC both within a week of delivery and 24-hours post-partum. Evidence of persistent microvascular alterations post-partum may provide an impetus to surveillance patients with a history of PE for future CVD and intervene through lifestyle modifications or therapeutics.