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Abstract
The following are abstracts from the research competition at the 13th annual Canadian Undergraduate Conference on Healthcare. The conference was entitled "Medicine in the Modern World", held on November 10th-12th, 2017 at Queen's University. Abstracts are grouped under the categories of oral and poster presentations, with sub-categories based on the general field in which the abstract is found. For more information about the conference, please go to https://www.cucoh.com/.

Keywords: CUCOH; interdisciplinary research; undergraduate research competition

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Conference Abstracts
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Conference Oral Presentation Abstracts

<u>**Oral Presentations in Biochemistry & Applications**</u>

Nano-engineered bio-inspired silver surfaces for tissue engineering

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Nanomaterials have become the new building blocks for regenerative medicine. Nanosilver is amongst the most studied nanomaterials for biomedical use due to its unique electrical, optical and physicochemical properties. When incorporating nanoparticulate silver within regenerative scaffolds, there are still concerns regarding silver surface oxidation, which might lead to toxicity. Increasing evidence points towards the pivotal role of nanoparticle surface modification as the ultimate solution to these problems. In this study, we have explored for the first time the effect of capping agent length and its influence on the spherical nanosilver's stability as well as its suitability for incorporation within 3D-biomimetic matrices. Thus, three novel peptide sequences [CLKGP-Hyp-NH_2, CLKGP-Hyp-GP-Hyp-GP-NH_2 and CLKGP-(Hyp-GP)$_4$-Hyp-NH_2] containing a terminal CLK (Cys-Leu-Lys) anchoring moiety were tested. Our cumulative experimental and computational data indicates that peptide length does indeed have an important effect in the resulting nanosilver's colloidal stability and biological performance. Despite the almost linear structural features of the peptides in solution; the silver surface is able to distort such geometry for peptides of 10 or so amino acids, giving rise to otherwise unseen binding modes. This presents an interesting and original angle for the design of biomimetic composite materials using peptides and their differing lengths as surface modifiers for nanosilver based structures.

A web-based application to easily and more accurately quantify virus infectivity

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The concentration of infectious virus within a sample is typically quantified by plaque or infectious dose (ID) assays. Both assays are performed by infecting wells of cell monolayers with different dilutions of the virus sample. The plaque assay develops under a semisolid overlay so progeny virions only infect adjacent cells, forming plaques of infected or dead cells, identifiable via staining. Each plaque represents approximately one infectious virion from the inoculum, and their count estimates the concentration of infectious virions as plaque forming units (PFU/mL). Plaque counting is subjective, such as when two plaques merge into what appears to be one large plaque. The ID assay focuses on the number of wells infected per dilution, determining only whether infection occurs, which is less subjective than plaque counting. It quantifies virus as the concentration at which half the wells are infected, termed the 50% infectious dose (ID_{50} /mL). Currently, ID_{50} determination relies on one of two mathematical estimates introduced by Spearman-Kaerber (1908|1931) and Reed-Muench (1938). These equations are often misused and the proliferation of incorrect guidelines and online spreadsheets exacerbate the problem. Meanwhile, modern computers would allow for simpler, more accurate estimation via automated nonlinear regression. We have developed such a tool in the form of a web-based app. The app uses nonlinear regression, compares its results against the two traditional estimates, and provides graphs for visual confirmation of all three estimates. It can compute other 50% endpoints, e.g. lethal dose or LD_{50}, and is modifiable for use as a mobile application.

Phosphorylation of ubiquitin at Ser57 hyperactivates parkin

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The ubiquitin (Ub) E3 ligase, parkin, is involved in the clearance of defective mitochondria with its activity stimulated by phosphorylation of Ub at ser65 by its upstream kinase PINK1. Malfunction of parkin leads to errors in the mechanisms of selective degradation of mitochondria and defects in protein quality control associated with Parkinson's disease (PD). We used genetic code expansion to fluorescently label and site-specifically phosphorylate Ub substrates without the need to identify upstream kinases, all of which are largely unknown, with the exception of PINK1. Our focus remained on characterizing the function of Ub phosphorylation site ser57 which has been reproducibly identified in human cells. We quantitatively related the position and stoichiometry of Ub phosphorylation to parkin activation with prominent results that ubiquitin phosphorylated at ser57 (pUb^{S57}) hyper-activates parkin. Our data demonstrates that even in a reaction of 90% un-phosphorylated Ub, parkin can selectively synthesize poly-pUb^{S57} chains. Interestingly, pUb^{S57} was also a competent, and in fact a preferred substrate for parkin in ubiquitination reactions with a native physiological target, Miro-1. We found that pUb^{S65} activates parkin 5-fold above the basal level of auto-ubiquitination seen in un-stimulated and auto-inhibited above the level of the auto-inhibited enzyme. Parkin hyper-activation by pUb^{S57} suggests the function of multiple Ub phosphorylation sites in the activation of parkin and the importance of their roles in the cellular response to oxidative damage in normal cells as well as in cells affected by PD.

Comparison of iPS cells derived from fibroblasts and beta cells in their ability to differentiate into the definitive endoderm and insulin-producing cells

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Type 1 Diabetes (T1D) is characterized by the loss of β-cells leading to hyperglycemia. Islet transplantations such as the Edmonton protocol act as potential therapies for T1D, but islet donor scarcity, failure to generate large amounts of beta cells, and lack in long term insulin production pose as obstacles. Reprogramming of β-cells into Beta cell-derived induced Pluripotent Stem Cells (BiPSCs) serves as a potential solution. The addition of doxycycline to islets obtained from reprogrammable mice (MIP-Cre;rtTA;OKMS-mCherry, MIP-GFP;MIP-Cre-ER;rtTA;OKMS-mCherry) will generate BiPSCs which can then be expanded and re-differentiated back to beta-like cells. Using a reprogrammable system specific to BiPSCs production is needed as these cells likely retain the epigenome, predisposing them to differentiate back into beta-like cells.
Over 50 BiPSCs and fibroblast-derived iPSCs were differentiated as embryoid bodies using ActivinA and Wnt3A. Cells were differentiated into the Definitive Endoderm (DE) state, the first stage of β-cell differentiation from a stem cell. Lines were assessed for relative expression of Sox17 and FoxA2 by qRT-PCR and immunofluorescence imaging, and cell surface markers CXCR-4/c-Kit via flow cytometry. The findings showed that the lines with the highest DE marker expression were derived from BiPSCs, meaning that it is likely that the beta cell epigenome was retained. Clones with the highest expression of DE markers were selected to be differentiated to beta-like cells. After differentiation, the cells can be implanted into diabetic mice and evaluated for insulin production and glucose responsiveness.

Oral Presentations in Molecular Biology

Fin-to-limb transition – Analysis of the cis-acting regulatory elements of the actinodin genes

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The fin-to-limb transition is regarded as a highly important evolutionary step in the colonization of land and diversification of all land vertebrate species. Our lab has identified a gene family in zebrafish, termed actinodin(and), that encodes for structural proteins important for the formation of actinotrichia, rigid fibrils of the teleost fin. This gene family is missing from all tetrapod genomes examined to date and their disappearance may have contributed to the fin-to-limb transition. We proposed that the disappearance of actinodin genes occurred through modifications of its regulation. To study how actinodin1 is regu-

lated we created transgenic zebrafish using a 2kb region (hereafter named 2P) upstream of and1 to drive the expression of a GFP (green fluorescent protein) reporter gene. The 2P element was able to drive reporter expression in a manner that mimicked endogenous and1 expression. Within the 2P element, we have identified and characterized tissue-specific cis-regulatory elements (CREs) responsible for and1 expression in ectodermal and mesenchymal cells in the median and pectoral fins. To test the functionality of the 2P element in tetrapods, we created a transgenic reporter mouse line. In contrast to zebrafish, reporter activity was restricted to the ectoderm of developing limb buds, suggesting that while the regulatory network for and1 ectodermal activation remains intact in mice, there is an absence of regulatory conservation for mesenchymal and1 activity. Mutagenesis of putative transcription factor binding sites within the CREs identified candidate proteins for and1activation in ectodermal and mesenchymal cells. To further validate these putative binding domains as actual and1 CREs, we are using the CRISPR/Cas9 system to mutate the endogenous enhancer sequences and observe the effect on and1 expression. Identifying the transcription factors responsible for and1 activation, coupled with our transgenic mouse results, will allow us to hypothesize on regulatory

Genetic alterations of the Gα13 signaling pathway in primary mediastinal large b-cell lymphoma

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Lymphomas are among the most common cancers affecting patients worldwide. Primary mediastinal large B-cell lymphoma (PMBCL) represents 2-4% of all non-Hodgkin lymphomas and is thought to be derived from thymic medullary B cells. Current chemotherapy treatments are not able to eliminate the cancer for a significant number of patients; therefore, the development of new therapeutic approaches resulting in better treatment outcomes and minimized side effects are critically needed. There is evidence that mutations in genes involved in the Gα13 signaling pathway allow germinal centre B cells (GCB) to leave the germinal centre and spread. These mutations were predominantly found in the GCB subtype of diffuse large B-cell lymphoma (DLBCL), which shows some similarities to PMBCL. Therefore, the purpose of this research is to describe patterns of *GNA13* mutations and analyze the mutational frequencies of associated pathway-genes in PMBCL. We used Illumina next-generation sequencing and Fluidigm arrays followed by SNV prediction algorithms. The results show that there is a high prevalence of mutations in the *GNA13* gene (33.3%) in PMBCL, including hotspot and splice site mutations, indicating that the *GNA13* gene may act as a tumor suppressor. In addition, the mutational frequencies of the Gα13 signaling pathway members *S1PR2* (2.6%), *ARHGEF1* (7.9%), *P2RY8* (15.8%), and *RHOA* (2.6%), were mutated at a similar frequency as observed in GCB-DLBCL. This suggests that this pathway may act as a potential promising target for the treatment of PMBCL in the future.

One in a million variants: Identifying the causative variant in microcephaly-ichthyosis

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In Canada, nearly three million individuals have a rare debilitating disease, with over half the affected being children. The vast majority of rare disease patients do not get proper diagnosis and treatment, which stems from the insufficient amount of research on uncharacterized diseases. CARE4RARE is a national clinical consortium that aims to elucidate the molecular basis of rare genetic disorders in Canadian patients by using next-generation sequencing. Here, we report a CARE4RARE case in an Old Order Amish family, in which a novel genetic disorder affects two second cousins with similar phenotypes consisting of microcephaly, ichthyosis, asymmetric lateral ventricles, colpocephaly and lethality by six months. Through whole-exome sequencing and bioinformatics analysis, we identified a candidate variant in *VPS52* (c.57delG, p.Thr20fs) that co-segregates with the disease status in the family. The variant is a deleterious frameshift deletion in exon one, resulting in a premature stop codon and truncated protein product. Furthermore, the gene has previously been implicated in pluripotent differentiation for ectodermal cell-to-cell interactions in mice, strengthening the association between a null allele in *VPS52* and the phenotypic features of this disorder. Understanding the genetic basis of this novel disorder could lead to improved counselling of the family, and perhaps targeted treatment and better understanding of *VPS52* and its human functionality.

Plasma levels of (1→3)-β-d-glucan as an alternative biomarker of epithelial gut damage and microbial translocation in HIV-1 infection

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Background: HIV disease progression is linked to changes in the composition of gut microbiota, specifically the decrease of *Lactobacilli* in the distal gut. (1→3)-β-d-Glucan (βDG), a component of several fungal cell walls, represents a potential plasma marker for *Lactobacilli* abundance and thus a novel marker for HIV disease progression. We evaluated βDG as a marker of HIV pathogenesis in comparison to existing markers of disease progression.
Methods: Plasma levels of βDG were measured using the Fungitell Assay®. Markers of epithelial gut damage, microbial translocation, and inflammation including intestinal fatty acid binding protein (I-FABP), lipopolysaccharide (LPS), LPS binding protein (LBP), Kynurenine/Tryptophan ratio, interleukins-1β,6,8 (IL-1β, IL-6, IL-8), and Tumor Necrosis Factor α (TNF-α) were measured in plasma using ELISA in primary (n=74) and chronic (n=30) HIV infected patients and in a sub-group of ART-treated patients, in addition to seronegative individuals (n=18).
Results: βDG in plasma of HIV-1 infected primary (60.5±33.2 pg/mL, p=0.012) and chronic patients (135.6±48.6 pg/mL, p<0.001) are elevated in comparison to seronegative individuals (30.44±5.3 pg/mL). A mean duration of 12 years of ART in chronic patients did not decrease βDG levels (190.7±68.7 pg/mL, p<0.001). A correlation of βDG was observed with viral load (r=0.4301; p<0.001), CD4 counts (r=-0.334; p<0.001), CD4/CD8 ratio (r=-0.2862; p=0.003), IL-6 (r=0.3342; p<0.001), IL-8 (r=0.5055; p<0.001), sCD14 (r=0.3376; p=0.011) and LBP (r=0.4127; p=0.007).
Conclusion: βDG shows promise as an alternative marker for disease progression as it is highly correlated with the markers of HIV pathogenesis including viral load, CD4+ T cell count, LPS, and LBP.

Oral Presentations in Oncology

Screening of young age at onset pancreatic cancer patients for mutations in known and novel cancer susceptibility genes

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Background: Pancreatic cancer is the fourth most common cause of mortality due to cancer globally. Pancreatic cancer has a poor prognosis and is usually diagnosed at later stages when tumor resection is not possible. Heritability for pancreatic cancer is relatively high and clinically significant.
Methods: A group of 24 pancreatic cancer patients with young age at onset from a referral hospital in Tehran University of Medical Sciences were screened for mutations in 710 cancer relevant genes.
Results: Two patients had pathogenic mutations in known pancreatic cancer susceptibility genes, BRCA1/2. Two other patients also had potentially pathogenic mutations in two novel candidate genes including PARP4 and EXO1.
Conclusion: BRCA1/2 genes are the most commonly mutated pancreatic cancer susceptibility genes and they should be considered in all pancreatic cancers cases with young age at onset or family history of cancer. PARP4 and EXO1 are also potential candidate genes for susceptibility to pancreatic cancer. Identifying the hereditary cases of pancreatic cancer will help in

offering more targeted treatment s to the patients and also preventing cancer in family members who might be a mutation carrier.

mTOR inhibition increases lifespan in Li-Fraumeni Syndrome fibroblasts by positively influencing the DNA damage response

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Li-Fraumeni syndrome (LFS) is a classic cancer predisposition disorder commonly associated with germline mutations of the *TP53* tumor suppressor gene. *TP53* mutation carriers are at risk to develop a wide spectrum of early onset cancers with a 75% lifetime risk in males and 93% in females. Interestingly, evidence shows that inhibition of the mTOR signal transduction pathway delays or eliminates tumour onset and increases lifespan in a murine model of p53 deficiency. The mechanism for this mTOR-mediated increase in lifespan is currently unknown. Here, we test the hypothesis that mTOR inhibition increases lifespan of individuals that are predisposed to cancer by positively influencing the DNA damage response (DDR), hence decreasing the rate of the secondary spontaneous mutations responsible for the malignant transformation. To explore this possibility, we make single cell measurements on fibroblasts derived from LFS patients, and measure the correlation of DDR and mTOR activity. Our preliminary data show that the two processes, DDR and mTOR activation, are indeed mutually influencing each other on a single cell basis. These results suggest that pharmacological inhibition of mTOR may serve as a preventative intervention in individuals with cancer predisposition.

Identification of BChE as a novel mediator of radioresistance and aggression in prostate cancer

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Prostate cancer (PCa) is the most prevalent form of cancer among men in Canada, with 1 in 8 men expected to be diagnosed in their lifetime. Advanced PCa has a 31% 5-year relative survival rate, along with a 5-year recurrence rate of 40% following treatment. As Ionizing Radiation (IR) Therapy is the primary treatment of PCa, local recurrences following IR is a pattern of treatment failure attributable to the radioresistance of cancer cells.

RNA screens were performed to identify and characterize the phenotype of RNAs dysregulated in radioresistant (IRR) prostate cancer. mRNA arrays performed in radioresistant cell lines identified several RNAs as candidates that may function to promote tumour survival after IR. The focus of this project is on butyrylcholinesterase (BChE), an mRNA whose levels were decreased by 96% in IRR PCa.

After identification, the dysregulated expression levels of the RNA found in IRR PCa were induced in radiation sensitive PCa cells. Assays were then performed to assess the effects of each RNA on cell proliferation, invasion and migration through extracellular matrices, clonogenic survival, and cell cycle distribution, with and without radiation.

Knockdown of BChE mRNA increases clonogenic survival and cell proliferation following radiation treatment, and increases the invasive capacity of prostate cancer cells. The results suggest that downregulation of BChE in IRR cells is a major contributor of radiation resistance and of the aggressive phenotype.

Dysregulations in the Hippo signaling pathway can cause ovarian cancer

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Epithelial ovarian cancer is the primary cause of death from gynecological malignances among women and its mechanism of onset is poorly understood. The ovarian surface epithelium (OSE) is a single layer of epithelial cells that covers the ovary and

a known site for cancer genesis. The Hippo signaling pathway is important in regulating cell cycle and its chore is a phosphorylation cascade. LATS1 and LATS2 are putative tumor suppressors that are able to phosphorylate YAP. Unphosphorylated YAP is a transcription regulator that affects transcription of proliferation and survival genes. It is reported that Hippo signaling is disrupted in multiple cancers and that LATS1 levels decrease in OSE cells in malignancy. Therefore, we hypothesized that the loss of LATS1/2 contributes to the development of ovarian cancer. We unveiled that the loss of LATS1/2 in OSE cells increases proliferation. Also, deletion of LATS1/2 in OSE cells *in vivo* results in an aggressive ovarian cancer phenotype. By immunohistochemistry, we confirmed the histological subtype to be epithelial high-grade serous carcinoma, because tumors were positive for PAX8, WT1 and CK19. To suppress tumor growth, we treated mice with a YAP inhibitor. Verteporfin prevents YAP from interacting with transcription factors and therefore prevents transcription of targeted genes. We found that treating LATS1/2 deleted mice with verteporfin decreases tumor size. Finally, we showed that YAP is increased in human ovarian cancer cells by western blot. Our results suggest that dysregulations in the Hippo signaling pathway and especially in the phosphorylation cascade can cause OSE cell-derived ovarian cancer.

Oral Presentations in Physiology

Assessment of left ventricular function by cardiac MRI versus MUGA scans in breast cancer patients receiving trastuzumab: A prospective observational study

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Purpose: Little is known about the comparison of multiple-gated acquisition (MUGA) scanning with cardiovascular magnetic resonance (CMR) for serial monitoring of HER2+ breast cancer patients receiving trastuzumab. The association of cardiac biomarkers with CMR left ventricular (LV) function and volume is also not well studied. Our objectives were to compare CMR and MUGA for left ventricular ejection fraction (LVEF) assessment, and to examine the association between changes in brain natriuretic peptide (NT-BNP) and troponin-I and changes in CMR LV function and volume.
Methods: This prospective longitudinal 2-centre cohort study recruited HER2+ breast cancer patients between January 2010 and December 2013. MUGA, CMR, NT-BNP and troponin-I were performed at baseline, 6, 12, and 18 months after trastuzumab initiation.
Results: 41 patients (age 51.7 ± 10.8 years) were enrolled. LVEF comparison between MUGA and CMR demonstrated weak agreement (Lin's correlation coefficient r=0.46, baseline; r=0.29, 6 months; r=0.42, 12 months; r=0.39, 18 months; all p<0.05). Bland-Altman plots demonstrated wide agreement limits in LVEF (pooled agreement limits 3.0 ± 6.2). Both modalities demonstrated significant LVEF decline at 6 and 12 months from baseline, concomitant with increased LV volumes on CMR. Changes in NT-BNP correlated with changes in LV diastolic volume at 12 and 18 months (p<0.05), and LV systolic volume at 18 months (p<0.05).
Conclusions: CMR and MUGA LVEF are not interchangeable, warranting selection and utility of one modality for serial monitoring. CMR is useful due to less radiation exposure and its accuracy of LV volume measurements. Changes in NT-BNP correlated with changes in LV volumes.

Patient-reported outcome measures in pediatric solid organ transplantation: A systematic review

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Aims: Subjective evaluation of disease outcomes and treatment from the patient's perspective has become increasingly important. Patient-reported outcome measures (PROMs) play a significant role in engaging patients in their healthcare and capturing their experiences. This review sought to identify PROMs used in the field of pediatric solid organ transplantation (Tx) and to analyse their health concepts, domains and psychometric properties.
Methods: A systematic review of English language articles was performed on key databases (i.e., MEDLINE, EMBASE, CINAHL, PsychINFO) to identify publications utilizing PROMs in a pediatric Tx population. Screening and study selection were undertaken by two independent researchers. Methodological quality and psychometric properties of instruments validated within pediatric Tx were assessed using COSMIN. The systematic review was prospectively registered with PROSPERO.
Results: The search yielded 3,670 articles with a final data set of 65 articles discussing 48 different PROMs. The PedsQL - Generic Core Scales (n=26) was the most frequently used PROM. PROMs were categorized according to their health concept: quality of life (n=16), psychological (n=23), physical (n=4), or social functioning (n=3), adherence behaviour (n=2). Seven PROMs were validated in a pediatric Tx population, with limited evidence for their psychometric properties.
Conclusions: This systematic review identified PROMs used in the field of pediatric solid organ Tx. As the psychometric properties of PROMs were not adequately assessed within the specific patient population, more extensive validation and evaluation is necessary. This review helps guide methodological decision-making processes for integration of PROMs into clinical care.

"This is your brain on DHCA": Neurological activity in deep hypothermic circulatory arrest
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Deep hypothermic circulatory arrest (DHCA) is a commonly used technique for cerebral protection during surgical interventions involving the aortic arch. Although the effects of hypothermia on human organs and tissues have been extensively studied, what happens to the brain function as a result of cooling and rewarming is still not understood. We present a review with a particular focus on the current literature regarding DHCA and its effect on brain function assessed via intraoperative neuromonitoring. This presentation was originally featured as a continuing medical education (CME) accredited presentation at the August 2017 Aortic Institute Meeting of the Aortic Institute at Yale-New Haven Hospital at the Yale University School of Medicine in New Haven, Connecticut.

Oral Presentations in Social Sciences

Promoting health equity amongst indigenous populations though acknowledging the social determinants of health: A literature review focusing on cancers
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To achieve true health equity, we must take into consideration one of Canada's deadliest categories of disease – cancers. Cancer incidence varies significantly across the country, with social determinants of health playing an important role. Aboriginal communities had worse outcomes of cancer and unique risk factors that should be considered in prevention programs. Some significant factors were food security, income, diet, land dispossession, alcohol use, smoking behaviour, and environmental pollution. There is much potential to reduce risk and improve disease outcomes. With improvements in health equity and education, Canadians can enjoy a significant reduction in cancer incidence and risk. Today more than ever we understand that social determinants of health are essential for keeping populations healthy and well. This review suggests that applying these principles to cancer, with an equity focus, can be the next big significant improvement to public health. Policy recommendations include: using culturally appropriate health education sources, working with priority population to understand

their needs (and unique drivers of risky behaviour), and focusing on social determinants of health to address risk factors more effectively (ex/ food insecurity or pollution on reserve).

Advice and recommendations given to pregnant elite and high level recreational athletes in the sports community – A survey of coaches

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Introduction: A study of pregnancy and reproductive outcomes in elite and high-level recreational athletes completed in summer/fall 2016 revealed athletes are not receiving adequate information or advice aligned with SOGC guidelines regarding exercise in the antenatal, perinatal and post-partum period. Elite and high-level recreational athletes revealed they often turned to coaches for recommendations in exercise in pregnancy.
Objective: To identify the general knowledge of swimming coaches with regards to exercise in pregnancy, and determine whether advice given to pregnant elite and high-level recreational athletes align with Canadian guidelines.
Study design: Retrospective cohort survey study – data will be collected through a link administered by email to Masters Swimming coaches using Qualtrics survey
Subjects: Swimming coaches for Masters Swimming (n=300) who have coached pregnant swimmers
Observation techniques: Participants were administered a survey of approximately 12 questions. Survey questions will ask about amount of pregnant swimmers, current knowledge of coaches concerning pregnancy, advice and recommendations coaches give their swimmers, and interest in receiving further information on exercise in pregnancy.
Results: Preliminary data (n=14) shows coaches in Canada coach on average 5 pregnancy swimmers per year, and 87% of those coaches have been asked for advice on exercise in pregnancy by their swimmers, but feel only moderately comfortable (on a likert scale of 1-10) providing advice.
Conclusion: All respondants were interested in receiving further information on exercise in pregnancy, demonstrating a clear absence in dissemation of knowledge of exercise physiology in pregnancy from those providing care, in any form, to pregnant athletes. This study warrants further research with an increased sample size. This study may lead to further attempts at educating trainers and coaches about the exercise and pregnancy guidelines.

This is your brain on neoliberalism: Ideology as pathology

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While the "biopsychosocial" approach has become increasingly ubiquitous in clinical psychology, the "social" aspect of this model rarely looks beyond immediate circumstances such as income and family situation. Conversely, the sociological field has spent well over a century examining how large-scale social factors can affect the psychology of the individual. This presentation seeks to marry these two lenses by examining how neoliberalism, the dominant socioeconomic ideology of our time, can have a profound negative effect on mental health. With current and future clinicians in mind, a brief introduction to the isolating tenets of neoliberalism will be followed by an examination of how this ideology produces distinct psychopathologies and damages the mental healthcare system itself. Developing an awareness of the ideology we live under and how it affects practice is critical for any clinician hoping to apply the biopsychosocial approach with greater efficacy and nuance.

Conference Poster Presentation Abstracts

Poster Presentations in Biochemistry

Biophysical studies of novel DNA guanine quadruplex binders with eventual anticancer applications
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Guanine quadruplex is an emerging area of supramolecular research with important implications for regulation of oncogenes. Guanine quadruplexes have been demonstrated to form *in vitro* from Hoogsteen bonding between four guanine base pairs from four strands of DNA. The four guanines form a planar tetrad which can stack on top of other similar tetrads to establish a quadruplex structure. Recent research demonstrated convincing evidence that g-quadruplex forms *in vivo* at key oncogene promoter regions. This current project and the Petitjean group are focused on designing chemical complexes which selectively binds to unique G-quadruplexes. Specifically, this project is focused on stabilizing the c-MYC g-quadruplex which inhibits expression of the c-MYC oncogene, and the human telomeric sequence, 22AG, the formation of which can inhibit telomere elongation which contributes to immortalization in cancer cells. Various biophysical analytical techniques have been employed to study the interactions of these synthesized ligands with G-quadruplexes. Circular dichroism titrations were performed to compare the interactions of different ligands with the c-MYC and 22AG quadruplexes. Any changes brought to the G-quadruplex conformation by ligand interaction could be confirmed in the CD spectra. Moreover, fluorescent intercalator displacement titrations (FID) were performed with the fluorescent agent, thiazole orange, to evaluate the binding constants of ligands to both G-quadruplexes and duplex DNA. Development of mathematical models based on FID results were used to explain and quantify the binding affinity and stoichiometry between ligand and DNA as well as the binding selectivity of the ligand for quadruplex over duplex DNA.

Mesenchymal stem cell transplantation reversed neuropathic pain in rats and mice
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Chronic neuropathic pain (NP) due to disease or lesion of the somatosensory nervous system is one of the most common and most difficult-to-treat pain conditions. Mesenchymal stem cell transplantation (MSC-TP) has shown promise for treating NP but a number of critical parameters need to be determined before clinical trials. We investigated effects of the source of MSCs and route of administration in rats and mice. MSCs were isolated from the bone marrow (BM-MSCs) and adipose tissue (AD-MSCs) from rats and human and characterized by functional differentiation and flow cytometry. Rats and mice with chronic constriction injury (CCI) of the sciatic nerve were transplanted either intravenously (IV) or intrathecally (IT) with BM-MSCs or AD-MSCs. The effects were evaluated by testing paw withdrawal thresholds in response to mechanical and thermal stimuli. MSCs, labeled with Dil dye, were traced after transplantation and immunohistochemistry was performed of the sciatic nerve and DRG. MSC-TP through either IT or IV significantly reversed NP in rats and mice. Similar results were observed between BM-MSCs and AD-MSCs and between human and rat MSCs. MSCs were traced to the injury site of the sciatic nerve after either IV or IT MSC-TP. Inflammation and nerve injury (Aδ and C fibers), induced by the CCI, were significantly reduced after MSC-TP. Signs of toxicity was not observed in any of the vital organs or functions. Thus, MSCs were remarkably efficacious in mitigating NP, promoting nerve repair, and modulating inflammatory processes surrounding the injured sciatic nerve, regardless the source and route of application.

Investigating associations between *MTHFR* and *APOE* genotypes and neurodegenerative disease phenotypes
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The Ontario Neurodegenerative Disease Research Initiative (ONDRI) characterizes five neurodegenerative diseases: Alzheimer's disease/mild cognitive impairment (AD/MCI), amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD), Parkinson's disease (PD), and vascular cognitive impairment (VCI). Genetic variants—including C526T and T388C in *APOE* and C677T in *MTHFR*—contribute to neurodegenerative disease risk. ApolipoproteinE (ApoE) exists in three isoforms—E2, E3, E4. The isoforms are encoded by the *APOE* gene, leading to six genotypes (E2/2; E3/2; E3/3; E4/2; E4/3; E4/4) based on combinations of alleles at C526T and T388C. The *APOE* E4 allele increases risk for AD/MCI. Its protein product does not efficiently clear amyloid ß (Aß) from the brain, accelerating Aß aggregate formation and contributing to neurodegeneration. MTHFR is a rate-limiting enzyme in homocysteine (Hcy) metabolism; the C677T variant has impaired function, causing increased blood Hcy levels, possibly leading to stroke and VCI. We investigated associations between *APOE* and *MTHFR* genotypes and the neurodegenerative diseases under study. *APOE* and *MTHFR* SNPs were genotyped via the ONDRISeq targeted next-generation sequencing panel and confirmed using TaqMan® allelic discrimination assays in 519 ONDRI participants, 192 *APOE* controls, and 110 *MTHFR* controls. Genotype and allele frequencies were compared between cohorts and controls. The *APOE* E4/4 genotype was significantly associated with AD/MCI when compared with FTD, ALS, PD, VCI, and control cohorts. In addition, the *MTHFR* C677T TT genotype was not more associated with VCI than other cohorts or controls. Future studies will analyze genomic data alongside clinical observations and neuroimaging to identify associations between genotypes and specific phenotypes.

Determining how *Helicobacter pylori* Vacuolating cytotoxin (VacA) induces gastric cell damage
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Helicobacter pylori (*H. pylori*) is a gram-negative bacterium that infects gastric epithelial cells leading to peptic ulcer disease and gastric cancer. Vacuolating Cytotoxin A (Vac A) is a bacterial virulence factor associated with a more severe disease outcome. VacA disrupts the host autophagy pathway and membrane trafficking, generating large vacuoles where the bacteria reside. Our laboratory determined that cells deficient in the lysosomal calcium channel TRPML1 phenocopy the effects of VacA, as they display large vacuoles and disrupted autophagy. This led to the hypothesis that VacA impairs TRPML1 activity. If this hypothesis is correct, we reasoned that the inhibition of TRPML1 by other means should mimic the effects of VacA. There is no commercial inhibitor of TRPML1, however, since TRPML1 is activated by PI(3,5)P2, it can be indirectly inhibited by blocking PIKfyve, the sole kinase responsible for synthethizing PI(3,5)P2. Therefore, I compared the effects of apilimod, a novel and specific PIKfyve inhibitor, with VacA on the gastric epithelial cell line, AGS. The cells were treated with Vac A, YM or apillimod. Vacuolation was determined by staining for the lysosomal marker, Lamp1, and autophagy was assessed by LC3 staining and Western blot. We found that apilimod treatment induced vacuolation in AGS cells. Alpillimod also dysregulated autophagy, increasing LC3-II levels. These results further support the hypothesis that VacA toxic effects are a consequence of inhibiting the TRPML1 channel. Elucidating the VacA mechanism of action will lead to the identification of new targets for *H. pylori* treatment.

Vitamin D regulation of expression of the IBD susceptibly gene ATG16L1

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Inflammatory bowel disease (IBD) represents a group of complex incurable diseases characterized by chronic gastrointestinal inflammation. Growing evidence from animal and human studies indicate that vitamin D deficiency is an important environmental factor contributing to IBD pathogenesis. Although the exact mechanism is unknown, we hypothesize that vitamin D deficiency downregulates autophagy, a pathway consistently recognized as important in IBD. Previously in our laboratory, we have shown that a vitamin D deficient diet in mice causes a reduction in ATG16L1 and autophagy in the intestine. Therefore, to directly assess the impact of vitamin D on intestinal epithelial cells and autophagy, we employed mouse intestinal epithelial cells. MODE-K cells were incubated with increasing concentrations of active form of vitamin D and lysates assessed via western blotting for autophagy proteins, ATG16L1 and LC3II. Blots were also probed for the vitamin D receptor (VDR), which is a vitamin D responsive gene. A significant increase in expression of VDR was detected in cells incubated with increasing concentrations vitamin D, indicating a dose dependent relationship. A trend towards increased ATG16L1 was also detected in cells incubated with increasing concentrations of vitamin D. Taken together, our findings indicate that vitamin D regulates expression of the IBD susceptibility gene ATG16L1 providing a potential mechanism by which vitamin D deficiency influences IBD.

Activation of the mucolipin transient receptor potential 1 (TRPML-1) channel reverses the damaging effects of the *Helicobacter pylori* toxin VacA

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Helicobacter pylori is a gram-negative bacterium that is known to play a role in the development of peptic ulcers and gastric cancer. The *H. pylori* vacuolating cytotoxin A (VacA) is a virulence factor associated with more severe disease outcomes. It is known to disrupt host autophagy and create large vacuoles which function as an intracellular niche, increasing intracellular *H. pylori* survival in the gastric epithelium. Interestingly, cells deficient in the mucolipin transient receptor potential 1 (TRPML-1) channel mimic the VacA phenotype; displaying large vacuoles and dysfunctional autophagy pathways. Recent work in the lab has shown that overexpression of TRPML-1 and treatment with the TRMPL-1 agonist ML-SA1 reverses VacA phenotype; indicating that VacA inhibits TRPML-1. To verify the results obtained with ML-SA1, I tested the ability of MK-683, another TRPML-1 agonist, to reverse the effects of VacA. Human AGS cells were incubated with either VacA+ or VacA- culture supernatant for four hours before being treated with MK-683, ML-SA1 or the drug vehicle DMSO. Immunostaining and western blot analysis of the autophagy marker LC3 showed that both TRPML-1 agonists restored functional autophagy. Additionally, staining of the lysosomal marker Lamp-1 revealed that MK-683 and ML-SA1 reduced the size and number of vacuoles. I found that two independent TRPML-1 agonists could reverse the effects of VacA and this study further supports the hypothesis that VacA acts by inhibiting the TRPML-1 channel. These findings suggest that activation of the TRPML-1 channel could be used to kill intracellular VacA+ *H. pylori*.

Poster Presentations in Biostatistics

Comparing AMSTAR and ROBIS in quality assessments of systematic reviews for drug treatments for Alzheimer's Disease.

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Background and Objectives: Systematic reviews have been routinely used to evaluate drug treatments for Alzheimer's disease (AD). Policymakers use systematic reviews to help decide whether new drug treatments should be listed on provincial drug formularies. The methodological quality of systematic reviews is important, as policy decisions and current evidence for medical interventions should be based on high-quality reviews. The study aim was to identify all systematic reviews that evaluate the following AD medications: Donepezil, Rivastigmine, Galantamine and Memantine. Afterwards, each systematic review was rated using AMSTAR and ROBIS for methodological quality.
Methods: The electronic databases EMBASE, PubMed, Medline, and Cochrane Library were searched using multiple search terms. Articles included were systematic reviews of randomized controlled trials for Donepezil, Rivastigmine, Memantine or Galantamine medications in AD patients.
Results: 35 studies were identified that matched inclusion criteria. For the AMSTAR Scores (median = 0.81, 25th percentile = 0.63, 75th percentile = 0.83, IQR = 0.20). and ROBIS Scores, (median = 0.74, 25th percentile = 0.66, 75th percentile = 0.81, IQR= 0.15), the variance in index scores were similar, indicating a similarity in methodological quality for both assessment tools. The correlation coefficient was 0.90, indicating a strong positive linear relationship and consistency between AMSTAR and ROBIS high and low scores.
Conclusion: The greater subjectivity and length of the ROBIS checklist required an assessor to spend more time answering questions. The variance index scores between AMSTAR and ROBIS didn't differ substantially. AMSTAR and ROBIS yielded similar quality assessments of systematic reviews.

Poster Presentations in Cellular Physiology

AMPK regulates extravillous trophoblast invasion

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Background: The placenta is involved in transporting and exchanging gases, nutrients and waste products at the mother-fetus interface. Trophoblasts, the primary stem cell lineage in the placenta, play a crucial role in embryo implantation and in spiral artery remodeling during the early stages of pregnancy. Improper progression of these initial stages of pregnancy can lead to a series of adverse effects for both mother and fetus. At a cellular level, AMPK is involved in cellular energy homeostasis but may also contribute to the regulation of cell invasion; an important step in spiral artery remodeling.
Hypothesis: We propose that AMPK function regulates the extravillous trophoblast cell invasion.
Method/Results: By utilizing a transwell invasion assay, our results indicate that Metformin and AICAR increase trophoblast invasion while Compound C decreases the cells ability to invade over a 32 hour period. Reducing AMPK expression, via siRNA technology, results in reduced trophoblast invasion across all pharmacological treatments (Metformin, AICAR, Compound C) as well as the altered expression of genes linked to the trophoblast cell invasion, such as TIMP-1, TIMP-2, MMP-2 and MMP-9.
Conclusion: AMPK is shown to play a role in altered trophoblast invasion through various invasion markers.

Role of Fzd7 in the uptake of exosomal Wnt7a

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Duchenne muscular dystrophy (DMD) is a genetic disease characterized by reduced muscular function and premature death. Despite DMD being one of the most common and devastating forms of muscular dystrophy, a cure has not yet been developed. Our lab has proven that the system of Wnt7a and its receptor Fzd7 represents a mechanism for muscle regeneration. Local injection of Wnt7a in *mdx* mice (a model of DMD) results in an increase of the satellite cell population and myofiber hypertrophy. This data makes Wnt7a a potential solution for DMD. Nonetheless, Wnt7a is hydrophobic, making it incapable of traveling in the bloodstream as a systemic treatment. **Therefore, our main goal is to establish an effective method of transportation for Wnt7a.** To resolve this limitation, we are using exosomes, small vesicles responsible for intercellular communication. Recently, our lab made the exciting discovery that Wnt7a is also secreted through exosomes. Following this

breakthrough, we have begun to study the mechanism of exosomal secreted Wnt7a and comparing with the classical Wnt7a/Fzd7 signaling pathway.

The short-term goal of my project was to evaluate the role of Fzd7 in the uptake of exosomal Wnt7a. To study the function of Fzd7, we started by comparing the uptake of exosomal Wnt7a by wild-type versus Fzd7 knockout primary myoblasts. Subsequently, using confocal microscopy and immunostaining we have proven that the uptake of exosomal Wnt7a is independent of Fzd7 binding. These results provided insights into a new mechanism for Wnt7a uptake and opened different avenues for DMD treatment.

Characterizing TβL1 SUMOylation in Dupuytren's disease
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Dupuytren's disease (DD) is a chronic, contractile fibrosis of the palmar fascia. Treatments are limited to surgical interventions, however disease recurrence rates are high and there is a need for novel therapeutic interventions. One molecular characteristic of DD is increased β-Catenin levels in fibroblasts that induce palmar fascia fibrosis (DD cells). The mechanism of β-Catenin nuclear translocation to transactivate gene expression and promote disease development are unclear. Recently, the conjugation of small ubiquitin-like modifiers (SUMO) to Transducin β-like 1 (TβL1) has been implicated in the nuclear localization of β-Catenin in cancer. We hypothesized that a similar mechanism promotes nuclear translocation of β-Catenin in DD, and there are higher levels of TβL1 SUMO-1 conjugation (SUMOylation) in DD cells relative to fibroblasts derived from non-fibrotic palmar fascia of healthy patients (CT cells). To test this hypothesis, primary DD and CT cells were isolated from three different patients and SUMOylated proteins were immunoprecipitated from cell lysates. Bound and unbound fractions were subsequently immunoblotted for TβL1 and TβL1 SUMOylation levels were quantified by densitometry analysis. To confirm our results, protein lysates from DD and CT cells were also immunoprecipitated with antibodies to TβL1 and subsequently immunoblotted for SUMOylated proteins. Our preliminary findings suggest a trend towards increased TβL1 SUMOylation in DD cells relative to the majority of CT cells assessed. These findings may provide further insights into the molecular basis behind increased β-Catenin levels in DD, and in the future SUMOylated TβL1 may serve as a potential therapeutic target for DD and other fibroses.

Cytoskeletal remodeling in macrophages: The role of RhoA in Slit2-Robo1 signaling
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Rationale: Slit2 is a glycoprotein that has been shown to play conserved roles as a neuronal repellent through interacting with its receptor Roundabout1 (Robo1). In the past, the Robinson group has shown that through Slit2-Robo1 signaling, members of the Rho family of small GTPases, Rac1/2 and Cdc42, are inactivated, inducing changes in the actin cytoskeleton of macrophages. However, this inactivation cannot fully account for all the cytoskeletal changes seen in the macrophages after treatment with Slit2. We recently found that another protein called RhoA, which is also involved in cytoskeletal remodeling, is activated once macrophages are treated with Slit2.

Objective: To determine the molecular events involved in the signaling pathway of RhoA after Slit2 binds to Robo1.

Methods: Using siRNAs, we knocked down the expression of RhoA in RAW 264.7 murine macrophages and treated them with Slit2, finding that the cell rounding effect of RhoA was inhibited. Furthermore, treatment of RAW macrophages with Slit2 and a specific inhibitor of Formin, a key actin polymerization factor in the RhoA pathway, inhibited the cell rounding effects of RhoA in macrophages, illustrating that Formin is involved in the Slit2-Robo1 signaling pathway.

Conclusion: These results demonstrate a new signaling pathway for Slit2-Robo1 involving RhoA and several of its downstream effectors. Future studies will include testing more of the downstream effectors of RhoA and their relation to Slit2-Robo1. These pathways are particularly important in inflammatory diseases like atherosclerosis, where cytoskeletal changes of macrophages could significantly affect the progression of the disease.

The role of FGL2 in luteal angiogenesis

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The corpus luteum (CL) is a transient endocrine structure found within the ovaries of female mammals after ovulation. Its primary function is to produce progesterone, a hormone that is essential to the maintenance of a pregnancy. The CL is formed from follicular cells (granulosa and theca cells) that remain in the ovary after ovulation, and undergo a process called luteinization. This process is characterized by changes in gene expression at the cellular level, as well as tissue remodeling and reorganization. While a developing follicle is avascular, angiogenesis occurs during luteinization, forming vasculature that is essential to mature CL function. Macrophages of the M2 lineage drive luteal angiogenesis through the VEGF and FGF pathways, while macrophages of the M1 lineage contribute to luteal regression. Fibrinogen-like protein 2 (FGL2) is an immunomodulator that is known to contribute to macrophage polarization to an M2 phenotype and to promote the VEGF pathway. We therefore hypothesize that FGL2 plays an important role in luteal angiogenesis. Preliminary results show that FGL2 expression is specific to theca cells within the ovary, and is highest around the time of ovulation. Components of the VEGF pathway are expressed immediately after ovulation, suggesting the start of vascularization. FGL2 expression preceding angiogenesis markers supports our hypothesis that it may be involved in the regulation of luteal formation. Using superovulation, timed mating and luteal cell collection in FGL2 knockout mice, we aim to further elucidate the role of FGL2 in luteal angiogenesis through techniques such as quantitative RT-PCR and immunohistochemistry.

Determination of kallikrein 5 hyperactivity in atopic dermatitis

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Within the outermost layer of the epidermis, in the stratum corneum, lies the epidermal barrier. Dysfunction of the barrier may result in its breakdown, leading to disease states such as atopic dermatitis (AD). AD is a chronic, inflammatory disease of the skin characterized by dry, itchy, red lesions, for which there is no known cause or cure. Previously performed quantification by ELISA of Kallikreins, a family of 15 trypsin- or chymotrypsin-like proteases, in the stratum corneum of AD patients demonstrated an overall increase in proteolytic activity accompanying hyper-*expression* of Kallikreins. The objective of this project was to develop an assay to determine if KLK5 specifically is hyper-*activated* in skin lesions with AD. The primary investigative tool used was the fluorescent AMC assay. When the protease of interest cleaves the fluorescent substrate designed with a particular AA sequence, the amount of the fluorescent signal emitted over time indicates protease activity levels in a given sample. Findings were as follows: 500ng was established as the amount of KLK5 necessary to detect activity; antibody 1108 was determined as non-neutralizing for the enzyme; direct ELISAs and Western blots showed specificity of Ab1108 for KLK5 by no cross-reactivity with other recombinant human KLKs. The development of this assay has highly promising clinical applications, as it can be used to compare KLK5 proteolytic activity in lesional vs. non-lesional skin. If KLK5 is observed to be hyper-active in AD skin, the next step would be inhibition of KLK5 with the goal of alleviating symptoms of this condition.

Activated hedgehog signalling in renal stromal cells disrupts pelvis formation and vasculature patterning

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The mammalian kidney develops through complex reciprocal interactions among multiple cells lineages. Renal stroma (*Foxd1+*) gives rise to a connective framework that surrounds nephrogenic elements, signalling with adjacent nephron progenitor and ureteric cells. During development, Hedgehog (Hh) signaling regulates nephrogenesis and ureteric branching, with dysregulation having known contributions to human renal pathologies. We have recently demonstrated that loss of Hh

signalling in *Foxd1+* cells results in aberrant stromal-nephrogenic crosstalk, renal capsule malformation, and decreased nephrogenesis. Here, we tested the role of activated stromal Hh signalling in kidney development.

To further investigate this domain of Hh signalling, we crossed *Foxd1Cre;Ptch1*^{+/-} mice with *Ptch1*[loxP/loxP] mice to remove Hh cell surface receptor *Ptch1* in a Cre-dependent manner. Absence of *Ptch1* renders Hh signaling constitutively active, regardless of Hh ligand presence. Mutant mice (*FoxD1Cre;Ptch1*^{fl/-}) were controlled to wild type (*Ptch1*[loxP/+]) littermates. Hh activation was validated through fluorescence-activated cell sorting and qRT-PCR analysis in stromal cells, which showed significantly increased expression for downstream Hh target *Ptch1*.

Mutant mice with stromal Hh activation displayed renal hypoplasia, characterized by 48% decreased kidney volume and 41% decreased nephron numbers at E15.5, persisting to E18.5. Interestingly, histological analysis of mutant kidneys also revealed defects in collecting duct elongation and pelvis development. Immunostaining further showed that mutants display 22% reduced nephron progenitor domains, 47% fewer intermediate structures, abnormal capsule formation, and spatial defects in vasculature organization. Together, these data suggest that activated Hh signaling in renal stromal cells disrupts normal mammalian kidney development in both cell and non-cell autonomous manners.

Exploring the potential role of KLK inhibitors as therapeutics in skin diseases
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Human tissue kallikreins (KLKs) belong to a family of 15 serine proteases encoded by the largest protease gene cluster. KLKs in the skin serve an important physiological role by promoting skin desquamation, modulating the permeability barrier and participating in the processing of antimicrobial peptides. In the present study we aimed to conduct experiments assessing the efficacy of KLK inhibitory compounds. These substances are chemically synthetic molecules designed to target the serine protease binding site, as potential inhibitors for skin KLKs. Initially, selected screening of skin KLKs inhibition for two compounds (290 and 291) was performed Overall, compound 290 displayed differential inhibition among the skin KLKs and showed preferential inhibition for KLK5, 6, 7, 8. Preliminary Ki and IC_{50} analysis revealed that compound 290 possibly acts as a competitive inhibitor and the cytotoxicity experiments did not show any significant cytotoxic effects in the lower inhibiting concentrations of this compound.

Poster Presentations in Clinical Physiology

Novel national STEM-based early education strategy for improving reporting and outcome in Canadian children diagnosed with juvenile idiopathic arthritis
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Background: Juvenile idiopathic arthritis (JIA) is one of the most common chronic inflammatory diseases of childhood, affecting 1 in 1,000 Canadian children. JIA is a heterogeneous group that includes seven distinct subtypes, including psoriatic arthritis. Up to 10% of JIA can be associated with uveitis (inflammation of the eye). Undiagnosed arthritis and uveitis can lead to irreversible damage to the bones, joints, and sight, with arthritis as a common manifestation. While resources for paediatric arthritis exist in specialized settings, this topic is often overlooked in classrooms. To increase awareness about these conditions, treatment options and specialists involved in diagnosing and treating these diseases, we partnered with Let's Talk Science. This is a national, volunteer-based organization that uses science, technology, engineering and mathematics (STEM) approaches to promote these disciplines and new career options among youth in Canada. Together, we developed a novel STEM-based educational tool to teach children, educators, families and members of the community about arthritis, psoriasis and uveitis in children.

Methods: Workshops on childhood arthritis will be held at community events and Canadian classrooms (grade 3-6). Trained LTS undergraduate and graduate student volunteers will deliver these workshops. Feedback forms for volunteers and partici-

pants will be collected and analyzed. Testing is planned to commence in Waterloo, London, Thunder Bay, Windsor, and Corner Brook.
Conclusion: Educational and advocacy projects driven by undergraduate and graduate students may impact the community by potentially improving outcomes and informing children about new career options.

Risk of chronic kidney disease following acute kidney injury during diabetic ketoacidosis in children with type 1 diabetes

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Background: A recent study demonstrated that 64% of children hospitalized for diabetic ketoacidosis (DKA) presented with acute kidney injury (AKI). Other pediatric populations show AKI to confer an increased risk for chronic kidney disease (CKD).
Objective: To compare the risk of developing CKD in children with T1D three to five years following DKA hospitalization between the groups: those without DKA, those with DKA without AKI, and those with DKA and AKI.
Methods: This is an ambispective cohort study of T1D patients presenting to the BCCH Diabetes clinic from 11/2016 to 07/2017(N=230). Expected baseline creatinine (EBC) was calculated using height and estimated GFR of 120mL/min/1.73m^2. AKI, during DKA, was defined as serum creatinine values $\geq$1.5 times the EBC. Presence of albuminuria, using ACRs, is a CKD risk factor. Current eGFR was evaluated as CKD $\leq$60mL/min/1.73m^2, mildly-decreased as 60-90mL/min/1.73m^2 and hyperfiltration as $\geq$150mL/min/1.73m^2.
Results: Of the 200 subjects, 59.0%(N=115) had DKA, of which 56.8%(N=54) had AKI. In this subset 15.4%(N=2) had mildly-decreased eGFR and 84.6%(N=11) retained normal kidney function. Of those without AKI during DKA, 10.5%(N=2) had mildly-decreased eGFR, 10.5%(N=2) had hyperfiltration, and 79%(N=15) had normal kidney function. The current mean length of follow-up was 3.9±3.3years. Of those without DKA(N=80), 20% have mildly-decreased eGFR(N=6) and 80%(N=24) have normal kidney function. Of 45 subjects with ACRs, 20%(N=9) showed presence of albuminuria.
Conclusions: This is the first study to report CKD in children with T1D. Knowledge translation initiatives are needed to ensure timely management and to develop protocols for renal impairment identification.

Association of low birth weight with clinical outcomes in nephrotic syndrome

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Background: Nephrotic syndrome (NS) is diagnosed in children whose prognosis may vary by birth weight. Barker's theory suggests low birth weight (LBW)/prematurity are risk factors for the development of renal disease.
Objective: Determine the association of LBW/prematurity with outcomes in childhood NS.
Population: Children with NS diagnosed between 1-18 years of age followed from 1996-2016 at SickKids (N=377). LBW/prematurity was determined by parental-reported birth weight of <2500g or gestational age <36 weeks. Normal birth weight (NBW) was defined as birth weight $\geq$2500g.
Results: Median birth weights in LBW/premature (n=46) and NBW (n=331) children are 2098g [1700g-2325g] and 3316g [2977g-3685g], respectively. There was a difference between NBW and LBW/premature children, with more children with LBW/prematurity having initial steroid resistant NS (SRNS), yielding an adjusted odds ratio of 3.78 [95% CI:1.28-11.24]. Upon evaluation of birth weight as a continuous variable, an adjusted odds ratio of 0.92 [95% CI:0.86-0.98] was calculated of having SRNS. Analysis of relapse-free duration yielded an adjusted hazard ratio of 0.79 [95% CI:0.53-1.16], resulting in no significant difference with median durations of 214 and 154 days for the LBW/premature and NBW groups, respectively. Kaplan-Meier analysis of relapse-free duration yielded a log-rank p-value of 0.51.

Conclusion: We found that LBW/premature children were more likely to develop SRNS, but do not have a difference in relapse-free duration with NBW children. This indicates that LBW/prematurity may be suggestive of an unfavourable course of NS. Physicians can use this information to follow patients closer from time of birth to ensure prompt assessment.

The effects of transcranial direct current stimulation (tDCS) on emotional processing strategies as assessed via the late positive potential electrocortical index
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Transcranial direct current stimulation (tDCS) is a non-invasive neuromodulation technique that uses either anodal (excitatory) or cathodal (inhibitory) low current stimulation to modulate cortical excitability. This technique has shown promise in enhancing cognitive control and executive functioning by stimulating the left dorsolateral prefrontal cortex (DLPFC). In the current study, twenty minutes of excitatory, inhibitory or sham tDCS is applied to the left DLPFC. Few studies have assessed tDCS on emotional re-appraisal strategies, despite tDCS being studied as a potential treatment for mood disorders, which are characterized by emotional dysregulation.

The Late Positive Potential (LPP) is an electrocortically-derived biomarker or event related potential, that has been found to be a reliable index of sustained attention to emotional stimuli (i.e. an index of emotional engagement). The LPP amplitude, which occurs 300 ms after emotional stimuli onset, will be analyzed to assess the response to negative or neutral images while different emotional regulation strategies are employed after the twenty minutes of excitatory, inhibitory or sham tDCS administration. Given that prefrontal stimulatory tDCS has been associated with enhancing cognitive regulation, it is expected that it will also modulate corresponding LPP amplitudes.

Study design and Methods: 32 healthy participants (males and females with no psychiatric or major medical issues), aged 18-40 years, will be recruited and tested across three sessions. Each of the three sessions will include task-based electrophysiological recordings to measure and collect LPP data, after excitatory, inhibitory or sham tDCS stimulation has been applied. Electroencephalograms (EEG), will be used to measure electrophysiological activity, in which LPP event-related potentials will be extracted and analyzed.

Poster Presentations in Epidemiology

Rising fall-related death among seniors: Cause and effect of a policy change?
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To classify deaths more accurately and consistently, the BC Coroners Service implemented a policy change in 2010 to support the identification of individuals whose death was related to a previous fall. These fall-related cases typically involved hospitalized elderly patients who eventually succumb to pneumonia. Prior to 2010, these deaths were classified as natural with pneumonia as the underlying cause of death; however, following the policy change the fall became the underlying cause of death and these cases were classified as accidental. The aim of this study was to determine how changes in reporting practice influence mortality statistics.

BC Vital Statistics mortality data was analyzed from 2001-2015, for cases among seniors 65+ with ICD-10 fall codes W00-W19. Fall-related mortality rates among seniors aged 85 and over increased after 2010, peaked in 2012 at approximately 838 per 100,000 deaths, and decreased from 2012-2014. No significant difference in fall mortality rates for specified fall subcauses between 2007-2009 and 2012-2014 was found, suggesting that mortality rates post-2012 were approaching rates prior to 2010. A lack of documentation of the fall event was indicated by 69.8% of falls being classified as unspecified fall (n = 5,902).

Time trends and key informant communication suggest there may be an unofficial reversion to previous reporting practice among certifiers in British Columbia. As such, further emphasis should be placed on accurately identifying the mechanism of death and implementation of educational interventions and quality assurance measures to allow development of targeted injury prevention initiatives and accurate mortality data.

An evaluation of privatized healthcare in an urban Chicago eye institute

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Purpose: This study aimed to look at vision and medical care outside of Canada in a privatized healthcare setting.
Method: Surveys were distributed to patients waiting to be seen in the urgent and primary eye care clinics at the Illinois Eye Institute (IEI) over a 6 day period. Questions included patient demographics, level of insurance coverage for eye and medical exams, time since last eye and medical exams, and known chronic medical and ocular conditions.
Results: Of the 275 patients surveyed, 234 were seen in IEI's primary eye care clinic, while 32 were in the urgent eye care clinic. The patient population was 64% female, with a mean age of 52.2 years (18 – 89 years), and the majority identified as African-American (73%). 67% of patients had full medical coverage, compared to 64% with full eye care coverage. Most patients had an eye exam within the last two years (86%) and a medical exam within the last year (78%). Of the patients surveyed, 40% had known ocular disease (most common glaucoma), and 54% had chronic medical conditions (most common diabetes). There was no statistical difference in last eye exam between primary care and urgent care eye exams ($p=0.145$).
Conclusion: A high percentage (86%) of patients in an urban Chicago setting receive adequate eye care in a private healthcare setting. Providing adequate eye care services to reduce visual impairment and to provide early detection of systemic and ocular diseases is an important element of delivering primary health care.

Maple syrup urine disease: A retrospective chart review

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Background: Maple syrup urine disease (MSUD) is a rare genetic disorder characterized by the accumulation of the branched-chain amino acids (BCAAs), resulting in the manifestation of phenotypes such as developmental impairment and metabolic decompensation when left untreated. In 2014, the Hospital for Sick Children (HSC) introduced a dried blood spot (DBS) home monitoring system to allow patients to track BCAA levels without the inconvenience of travelling to the hospital.
Objective: This study assesses the impacts of the implementation of DBS monitoring, as well as characterize parameters of the HSC MSUD population including age, biochemical control, and monitoring and hospitalization frequency.
Methods: Retrospective chart review was conducted using data from all HSC MSUD patients followed between 1991-2017 (n=15).
Results: Monitoring frequency was negatively correlated with average leucine level in the newborn period of 0-6 months ($r=-0.74$, $p=0.037$) and positively associated with the proportion of levels within target range ($r=0.68$, $p=0.046$). Correlation strength decreased with age. Monitoring frequency increased by an average of 159% per patient following DBS monitoring implementation (8.6 in 2014 to 22.3 in 2015). Younger patients were most likely to be admitted to the ICU for metabolic decompensation, with an average peak leucine level 9.65 times greater than the maximum recommended threshold of 300 µmol/L (2895 µmol/L).
Conclusions: DBS monitoring has resulted in a sharp increase in monitoring frequency, which, in turn, is associated with a greater degree of biochemical control. Younger patients are most greatly impacted by changes in monitoring frequency and are most likely to be hospitalized.

Characterizing the natural progression of cirrhosis, portal hypertension, and timing of liver transplantation in children with biliary atresia: A competing risks analysis.

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Background: Cirrhosis progresses through stages of increasing severity characterized by different clinical complications. We describe the course of cirrhosis in biliary atresia (BA) using a multistate model and hypothesize that this framework, previously only used in adult cirrhosis, will be applicable to this population.

Methodology: We reviewed medical charts of 59 consecutive children diagnosed with BA between 2001-2012 to identify episodes of compensated cirrhosis (CC), clinically significant portal hypertension (CSPH), decompensated cirrhosis (DC), late decompensation (LD), liver transplantation and death. Data defining stages of cirrhosis were collected from time of Kasai hepatoportoenterostomy (KP) until death or last follow up, including variceal bleeding and ultrasound evidence of ascites, splenomegaly, or portosystemic collaterals.

Results: At time of KP, 54% of patients were not cirrhotic and the rest CC. At final evaluation, 59% were transplanted and alive, 2% were not cirrhotic, 5% CC, 17% CSPH, 10% DC, 2% LD, and 5% were dead. The median duration (days) of stages was 88 for non-cirrhosis, 70 for CC, 775 for CSPH, 173 for DC, and 91 for LD. Among patients with cirrhosis at time of KP, 82% required transplantation, compared to 47% of patients with no cirrhosis at KP. Total duration of in-patient stay was greater in more advanced stages of cirrhosis.

Conclusion: The description of cirrhosis in BA with a multistate model shows the high proportion of patients who pass through stages of decompensation to liver transplantation. The model reflects clinical severity measured by length of in-patient stay and prediction of need for transplantation.

Systematic review: Stimulant medications and induced suicidality in youth with ADHD
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In 2015, Health Canada issued a warning linking stimulant medications with suicidal thoughts and behaviour in youth with ADHD. To the best of our knowledge, there are no peer-reviewed studies presenting such a correlation, and it is possible that the warning is based primarily on anecdotal evidence. In order to correct this gap in psychopharmacological knowledge, we are conducting the first systematic review of research associating suicidality, stimulants, and ADHD. Our preliminary findings have been unable to show a statistically significant association between pediatric suicidality and stimulant medications. That said, two major outcomes are still possible: the discovery of a positive correlation, or no detectable signal. The contribution of this study would be substantial in both cases, either supporting or challenging Health Canada's statements. Accurate pharmacological information is essential for effective treatment and minimizing risks to patients.

Poster Presentations in Health Promotion

Association between maternal vitamin D status during pregnancy and antenatal and postpartum depression: A systematic review
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A recent systematic review revealed a positive relationship between lower 25-hydroxyvitamin D (vitamin D) status and depression in adults (Ju et al). Vitamin D has also been implicated in antenatal depression and postpartum depression (PPD) in many studies; however, results have been inconsistent results due to the complexity of this association. The aim of this study is to systematically review current literature addressing associations between vitamin D and antenatal depression or PPD, and conduct a meta-analysis. Four electronic databases were searched for studies examining the association between vitamin D and PPD or antenatal depression with no date or language limits. Two independent authors reviewed titles and abstracts of the search results and selected studies for full review based on inclusion criteria. Data were extracted and a quality rating was done using the Newcastle-Ottawa Scale (NOS) on the selected studies. A total of 239 studies were identified and after the removal of duplicates 143 were reviewed for titles and abstracts. Ultimately, 21 eligible studies were assessed, and 14 of these were included in the review. When using the NOS, the quality assessment of the included studies ranged from moderate to high. Of the studies on PPD, 4 of the 7 showed an association between vitamin D and PPD. Five of 7 studies on antenatal depression showed an association with vitamin D status. Among these studies there was variation in adjusting for confounding factors. To date, the effect of vitamin D on PPD and antenatal depression remains inconclusive. Meta-analytic techniques to be employed on the existing data have the potential to provide clearer understanding of associations.

SEAMO Ontario BASE™ eConsult pilot

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Background: The Champlain BASE™ eConsult service is a secure online application that improves communication between primary care providers (PCP) and specialist physicians. Initial results based on one health region, demonstrated positive impact on improving access and reduction of face to face referrals, however, it is unknown if these early successes can be spread and scaled whilst achieving the same impact.
Objective: To evaluate the feasibility of replicating and implementing the Champlain BASE™ eConsult service model in a new region (South East Local Health Integration Network (LHIN).
Setting: Municipalities in the Kingston area (South East LHIN) that have 3.6% of Ontario's population.
Methods: A multi-method approach was used including a cross-sectional analysis of eConsults submitted (February - June 2017) and three focus groups (20 Jun 17) with PCPs and specialists.
Results: User adoption exceeded initial targets with 54 PCPs registered, and 345 eConsult cases submitted to 24 specialty groups. Median response time was 2 days. All patients received enhanced access to specialist care and in 2/3 of all cases a face-to -face referral was not needed. Six main themes emerged from the focus groups: positive impact on patient care and enthusiasm by patients for timeliness of the service; ease of use and intuitive; continuing professional development opportunities; improved collegiality, improved patient flow and an increased sense of trust.
Conclusion: This pilot implementation was successful and demonstrates the potential the Champlain BASE™ eConsult model offers jurisdictions wishing to improve patient care and the provider experience.

Exploring gender differences in concussion awareness through the evaluation of a BC Hockey training mandate for on-ice officials

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Background: Female athletes demonstrate concussion rates similar or higher than males, and are more likely to experience poorer outcomes following concussion. As the number of women and girls participating in sport continues to increase, a greater understanding of how concussion awareness and response differ by gender is required. The Concussion Awareness Training Tool (CATT) is an accessible online educational tool providing training on concussion recognition, response and management. In 2016, BC Hockey mandated CATT training for all on-ice officials (approximately 15,000) prior to the 2016-2017 season.
Objectives: To assess the effectiveness of the BC Hockey mandate of CATT, and explore gender differences in perceptions and actions towards concussion awareness.
Methods: An online survey distributed by BC Hockey solicited feedback on CATT as mandated training. Quantitative and qualitative analysis were performed on the data.
Results: The survey had a >10% response rate (n=1,735). CATT training led to a significant increase in self-reported concussion knowledge amongst respondents ($p < 0.001$). Female officials rated CATT significantly higher with regards to organization, relevance and satisfaction of the content included, as well as the potential of recommending CATT to others as compared to male officials ($p < 0.02$). Mandating CATT training for parents was supported by 68.4% of respondents, with females being significantly more in favour as compared to males ($p < 0.02$).
Conclusions: Significant gender differences were observed, with female BC Hockey officials significantly more satisfied with the mandated CATT training. Females were also more likely to recommend CATT to others, and support a mandate of concussion training for parents.

The role of dietary factors in inflammatory bowel disease: A clinical food guide for patients

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Inflammatory Bowel Disease (IBD) are a group of intestinal disorders of which the two main diseases are ulcerative colitis and Crohn's disease. IBD is multifactorial, and while it is suspected that dietary components play an important role in the disease, there are limited data regarding the impact that specific dietary components have on clinical and endoscopic activity, and the patient-targeted dietary recommendations that are available are overly-restrictive and are very conflicting.

In this study, we identified recurring links between certain dietary factors and specific IBD outcomes by conducting extensive literature searches and validating these findings by collecting primary patient data. The goal of the study was to use this knowledge to develop a clinical tool that would provide patients with accurate, safe, and explicit dietary recommendations.

First, we conducted an extensive PubMed search, from which 71 articles met our inclusion criteria. The articles were assembled into a hierarchy based on the quality of the study and of the outcome measurements, to facilitate the comparison of papers that reported conflicting outcomes.

Second, 69 Patients with IBD from two tertiary care centers in Toronto, Canada completed a 3- to 4-day food diary prior to their scheduled colonoscopies. Differences in nutrient composition associated with clinical and endoscopic activity were analyzed by generalized linear models in a univariate analysis, while accounting for disease type.

The data from the literature search, substantiated by the primary patient data, were used to develop a concise food guide for patients which will be distributed at Mount Sinai Hospital.

A systematic review of international comparison studies on physical/sports activity participation and cultural consumption

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Background: Although complex, international comparisons are scientifically useful and necessary for a thorough understanding of leisure practices from one country to another. In Canada and France, the histories, cultures, sociopolitical structures, and demographics, albeit similar in some respect, remain distinct and tend to produce specific inequalities in sporting commitment.

Objective: The purpose of the review was to explore the theory, methodology, and quantitative results of international comparison studies relating to participation in physical sports activities (PSA) and cultural consumption in different national contexts.

Methodology: A systematic electronic search was conducted using the following databases: SPORTdiscus, PsycINFO, and Sociological Abstracts. Specific inclusion criteria were outlined relating to publication date, language, and research design. The selection process involved a keyword search, title scan, abstract review, and a complete reading of the articles.

Results: Of the 4922 reviewed studies relating to PSA participation comparisons, 6 were selected for inclusion. Of the 7515 reviewed studies relating to international comparisons on cultural consumption, 32 were selected for inclusion. Altogether 24 studies utilized international survey data comparison methods, 10 utilized cross-national survey data comparison methods, and 2 utilized a combination. No direct comparison studies between Canada and France were identified.

Conclusion: An abundance of international survey data was identified in comparison to cross-national survey data, suggesting that international surveys are advantageous for PSA participation/cultural consumption comparison study purposes. The information and methods identified in the selected studies allow for a better future analysis of the various factors affecting PSA participation rates in Canada and France.

Poster Presentations in Immunology

Evaluation of TGFb and IFNb cytokine induced polarization of neutrophil-like HL60 cells

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After cataract surgery, an intraocular lens (IOLs), commonly made of PMMA, is inserted to replace the removed natural lens. However, posterior capsular opacification (PCO) can occur as a complication of cataract surgery, also known as secondary cataracts. Neutrophils are the body's first response cells at a site of infection or intrusion by a foreign material. Neutrophils are found to polarize into one of two forms, N1 (pro-inflammatory) and N2 (anti-inflammatory). The purpose of the experiment is to evaluate TGFβ and IFNβ cytokine induced neutrophil polarization through measuring TNFα on ELISA, which is expressed at high levels in N1, and low levels in N2.

Cell viability assays using Alamar blue reveal that samples that were pre-activated for 24 hours with 50 nM PMA, and then incubated with 24 hours of cytokine, showed less cell activated viability than samples that were incubated with PMA and cytokine simultaneously. TNFα, which is expected to be released by N1 and N2 phenotypes at different levels, were quantified using ELISA. Samples treated with 5 ng/mL and 10 ng/mL IFNβ did not show significantly higher concentrations of TNFα than samples treated with TGFβ. However, TGFβ added with 50 nM PMA simultaneously showed significantly larger TNFα concentrations than if TGFβ and PMA were added a day apart (p=0.0316). HL60s activated with 50 nM PMA in the absence of cytokines still showed a high concentration of TNFα (14-20 pg/mL), suggesting that a serum starved trial may reveal the true effect of TGFβ and IFNβ on TNFα concentrations.

Measuring myelin-specific t-cell cytokine responses in multiple sclerosis (MS) using ELISPOT

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Introduction: Myelin-reactive T cells of T helper 1 (Th1) and Th17 types are thought to be pathogenic in MS. GM-CSF is a cytokine that is produced by pro-inflammatory Th1 and Th17 cells and has been understudied in MS. IL-11 is another cytokine that is poorly understood in the context of autoimmunity, but was recently shown to be the most highly up-regulated cytokine in the cerebral spinal fluid of MS patients.

Objective: To conduct a broad-scale profiling of T cell cytokine production in response myelin antigens in MS patients using ELISPOT assays.

Methods: Thus far, we have collected blood samples from MS patients (22 females, 4 males) and a limited number of healthy controls (4 females, 1 male). Peripheral blood mononuclear cells (PBMCs) were isolated from these samples and then were plated together with either myelin basic protein (MBP), proteolipid protein (PLP), myelin oligodendrocyte glycoprotein (MOG), peptides encoding parts of these proteins, or control antigens on ELISPOT plates. Cytokine (IL-5, IL-10, IL-11, IL-17, TNFα, IFNγ, GMCSF) spots were developed after 48 hours of culture and detected using an ELISPOT reader.

Results: To date, we have analyzed data for GM-CSF and IL-11 responses. For GM-CSF, we have observed a higher frequency of cytokine-producing cells in MS patients versus healthy controls in wells that were stimulated with MBP, a PLP peptide pool that encodes determinants in the second hydrophilic domain of the protein, and MP4 (a fusion protein of MBP and PLP hydrophilic domains). We also detected a higher frequency of GM-CSF spots in MS patients versus controls in the media control wells (contained PBMCs, but no antigen). For IL-11, we saw that IL-11 producing cells were present at a higher frequency in the media control wells in the MS patients versus healthy controls, but that this number did not appreciably increase with the myelin stimuli, with the exception of the MP4 wells.

Conclusion: Patients have a higher frequency of GM-CSF and IL-11 producing cells in peripheral blood than healthy controls. GM-CSF-producing T cells are more reactive to MBP and PLP.

Investigating the repolarization capacity of macrophages and its implications in wound repair

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Despite being part of multiple disease pathogeneses, fibrosis has been evolutionarily conserved, as the production of scar tissue is imperative in the wound healing process. Wound healing can be separated into two phases, beginning with an initial inflammatory phase aimed towards removing the injury, and a later fibrotic phase characterized with extracellular matrix deposition and scar formation. Although fibrosis is generally reversible, when the balance between inflammation and fibrogenesis is dysregulated, or when injury becomes chronic, pathological scarring can occur. A range of macrophage subpopulations have been associated with different aspects of the wound healing process. The inflammatory phase is flush with classically activated macrophages (CAM/M1). Then during the later fibrosis phase, the macrophage population becomes alternatively active (AAM/M2), which are shown to promote fibrosis. We have found that mature M2 macrophages have the capaci-

ty to downregulate their M2 phenotype towards a more M1-like phenotype when repolarized with M1-inducing cytokines. We anticipate that this repolarized macrophage population may have an effect on fibroblast to myofibroblast differentiation and collagen production, providing a potential therapeutic route to decrease the progression of fibrogenesis. Although previous research has utilized variety of pathways to inhibit fibrogenesis, we have directed our view towards macrophage polarization, as macrophages are a crucial factor in both immunity and the wound healing process.

Poster Presentations in Neuroscience

Novel derivatives of kainic acid as inhibitors of neuroinflammation

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Alzheimer's disease (AD) is a neurodegenerative disorder that presents in patients as progressive cognitive decline, invariably resulting in dementia. This manifestation causes severe emotional and financial hardship for AD patients and their families. The diseased brain is characterized by the presence of neuritic plaques and tangles. When microglia, the immune cells of the central nervous system, interact with these pathological structures, the microglia become activated. Chronic microglial activation leads to the continuous secretion of pro-inflammatory mediators, which at high concentrations are damaging to neurons.

The goal of this project was to assess the therapeutic potential of two novel kainic acid chemical derivatives as treatments of AD. The first objective was to determine how these derivatives affect activated microglial functions that negatively impact neuronal cell viability. After treatment with either of the derivatives, microglia were activated and their conditioned media was transferred onto neurons. Neurotoxicity of microglia treated with either of the two derivatives was significantly reduced compared to stimulated untreated cells. The second objective was to determine whether these derivatives alter the microglial secretion of pro-inflammatory mediators. Analysis of the microglia-conditioned media confirmed that treatment with either of the kainic acid derivatives caused a downregulation of the potentially harmful monocyte chemoattractant protein-1, reactive nitrogen species and reactive oxygen species.

AD currently affects 40 million people worldwide. This number is predicted to double by the year 2030 as there is currently no effective treatment. This project unveils potential therapeutic strategies, which could impact the lives of AD patients and their families.

Influence of transcranial direct current stimulation on the posterior parietal cortex in action execution, action observation and action imagination

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Rehabilitation approaches typically incorporate protocols in which the patient executes a series of movements (physical practice). Physical practice can be limited, however, due to fatigue, pain, and other symptoms. For this reason, action observation (observational learning) and imagination (motor imagery) are being considered and incorporated into rehabilitation protocols because these approaches show benefits to performance without the need for executing movements. To maximize the potential of these approaches, a deeper understanding of the neuro-cognitive mechanisms involved in action execution, imagination and perception is needed. The present study was designed to investigate the role of the posterior parietal cortex (PPC) in these tasks. To this end, participants completed action execution, perception, and imagination tasks before and after receiving transcranial direct current stimulation (TDCS) to the PPC. TDCS is a technique that can modulate (increase of decrease) activity in a targeted cortical region. Participants received anodal, cathodal or sham tDCS on different testing days. During each visit, participants executed, imagined and perceived cyclical aiming movements of the hand before and after tDCS (for 20 minutes while they rested). The primary outcome measure was movement time of the executed, perceived and imagined movements and it was found that performance on the tasks was altered following tDCS. These results will be discussed with respect to the role that the PPC plays in motor behavior. Future work will explore the role of PPC in motor adaption or (re)learning following, as well as the potential use of these tasks for better assessing and understanding movement disorders.

Quantitative analysis of spontaneous movement in full-term infants

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Qualitative analysis of spontaneous movements has been validated as a method of predicting the onset of neurodevelopmental disorders. Spontaneous movement are early involuntary movements that begin during fetal development and continue into infancy. Spontaneous movements have been associated with the cortical subplate, a transient zone in the brain that is heavily involved in neurodevelopment. Thus far, literature has focused on determining the accuracy of utilizing qualitative analysis of spontaneous movements as a predictor. The aim of this study is to elucidate the quantitative phenotypes of spontaneous movement in healthy, full-term infants. This proof-of-concept pilot study details the trial methodology conducted over 24 healthy full-term infants. Kinematic data for one infant undergoes frequency and velocity analysis to demonstrate potential methods of data manipulation in future investigation. The protocol generated from this pilot study will inform further work in the predictive capacity of spontaneous movements.

Poster Presentations in Oncology

Efficacy of recombinant wild type vaccinia virus

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The research is aimed for the identification and characterization of cancer killing therapeutic viruses based on selective replication of viruses in cancer cells and their subsequent spread within the tumour while leaving healthy tissues unharmed. The remarkable parallels between cancer propagation and viral infection within mammalian cells has led to the development of oncolytic viruses which are becoming a likely tool for cancer immunotherapies. It has been shown that oncolytic viruses infect and in some cases destroy tumour cells and additionally induce anti-tumour immune response. In this research, we will be testing out the efficacy and cytotoxicity of the recombinant strains of the wild type vaccinia virus in leukemia cells. The screening of L1210, HL60, Hela S3 and 786-0 cell lines will indicate which recombinant viruses are more effective and ensuing the subsequent testing in vivo using L1210 and at t=0, t=6 to observe the vaccine's affect on other organs and it's cytotoxicity. In turn allowing us to conduct a safety-bio distribution profile and potential modification of the recombinant viruses though the application of immune checkpoint inhibitors.

Characterization of the GREB1 interactome in human ovarian cancer cells

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The use of exogenous estrogen, such as in hormone replacement therapy, increases the risk of ovarian cancer. Our lab has demonstrated in a mouse model of ovarian cancer that estrogen treatment resulted in early onset of tumors and significantly decreased survival time. A microarray analysis of the tumors shows that estrogen upregulated 197 genes, with *GREB1* (Growth regulation by estrogen in breast cancer 1) being highly increased. GREB1 is a critical meditator of estrogen-stimulated proliferation and involved in estrogen receptor 1 (ESR1)-related transcription. Estrogen upregulates GREB1 in ovarian cancer through ESR1, though preliminary data in other hormone-stimulated tissues suggest that GREB1 can be upregulated through progesterone receptors (PR). Therefore, we hypothesize that steroid-hormone responsive GREB1 participates in both ESR1 and PR pathways in human ovarian cancer cells. We have characterized a panel of human ovarian cancer cell lines for their response to steroid hormones and identified a subset that upregulated GREB1 upon estrogen or progesterone treatment, with significant increases determined in ovarian cancer cell lines ES-2 and PEO1. To shed light on the function of GREB1 in ovarian cancer, we are currently identifying its binding partners using Biotinylation Identification (Bio-ID), a method used to identify robust and transient protein-protein interactions in living cells. Although how GREB1 functions in

ovarian cancer is unknown, we have shown that both estrogen and progesterone can increase GREB1 expression and identification of its interacting proteins will help to further elucidate its role in hormone-induced actions.

Immunofluorescent image analysis of tumour hypoxia microenvironments

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Solid tumour's hypoxic environment is known to cause dramatic changes in tumor cell phenotypes, such as increased metastasis, radiation resistance, and overall poor survival of patients. Thus, understanding the root causes and molecular mechanisms of tumour hypoxia formation can help target these malignant phenotypes, improve the efficacy of hypoxia-targeted drugs, and extend patient survival.

The current study aims to develop an immunofluorescence image analysis pipeline to accurately quantify the oxygen and proliferation gradients as a function of distance from the nearest perfused blood vessel. Pancreatic cancer xenografts were grown subcutaneously in mice, then excised and embedded in OCT. Serial slices of the tumor were stained with immunofluorescent markers DAPI (nucleus), EF5 (hypoxia), EdU (proliferation), CD31 (vessels), and Hoechst (perfusion), and subsequently imaged. The slices were digitally registered to one another in MATLAB. Image analysis was performed using Definiens, an object-oriented machine learning software. Vessels that were actively supplying oxygen were detected based on morphology and CD31 stain intensity, and each cell in the tumor slice was assigned a "distance to the nearest vessel" value. Mean intensities of the hypoxia and proliferation markers were quantified on a per cell basis, and plotted against their distance to the nearest vessel. Analysis shows an increase in hypoxia and a decrease in proliferation the further a cell is from a vessel. This pipeline could be validated and used in clinical scenarios, such as assessing the patient tumour hypoxic status, which ultimately could be used to improve the efficacy of hypoxia-targeting drugs or radiation treatment.

Poster Presentations in Social Sciences

Risk of bias assessment of randomized controlled trials in high-impact rheumatology journals and general medical journals: A systematic review

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This systematic review investigates the risk of bias in randomized controlled trials (RCTs) published in high-impact rheumatology journals and general medical journals. We also aim to identify factors associated with high risk of bias. Using Ovid MEDLINE (1946-2016), RCTs in the top 3 high-impact rheumatology journals containing RCTs published in the year 2015, were systematically identified and critically appraised for the risk of bias prevalence. To perform the critical appraisal, relevant extracted RCTs were assessed in all domains of bias as defined by the Cochrane Collaboration. A comparison to rheumatology articles from three high-impact general medical journals was performed. Of the 138 records that were screened from rheumatology-specific journals, 113 RCTs met all inclusion criteria and were critically appraised. In total, 32.2% of domains had an unclear risk, 18.6% had a high risk and 50.2% had a low risk of bias. In comparison, rheumatology articles from general medical journals had a higher prevalence of unclear risk (39.0%), lower prevalence of high risk (14.3%) and a lower proportion of low risk domains (46.8%). Similar to our previous study in ophthalmology, more than half of RCTs contained at least one high risk of bias domain, a finding that highlights the need for greater awareness of this issue in the medical scientific community. Given the influence that bias can have on study results, it is necessary that authors and peer reviewers of RCTs closely adhere to published guidelines formulated by the Cochrane Collaboration as a way of minimizing risk of bias.

"The case of the castle": A study abroad strategy of experiential learning and its implications for medical education

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It has been recognized that medical education must adapt to equip healthcare professionals with skills that meet the changing demands of patient-centered care. Experiential learning is a teaching strategy based on Kolb's Learning Theory that encourages proactive learning through practical applications, self-directed reflection, and critical appraisal of evidence. Based on a descriptive phenomenological research design, the lived-experiences of students and faculty at the Bader International Study Centre (n=117) were analyzed qualitatively and quantitatively. Conditions identified by publications as conducive to experiential learning were tested through a Likert-scale survey, and thematic and factor analysis were carried out. Results of the analysis supported that students consolidated information best when new knowledge presented built upon their prior understandings of the phenomenon. Thorough understanding of learning goals prior to the experiential learning opportunity encouraged learner ownership, and subsequently facilitated self-directed, professor-facilitated learning. Problem-based learning (PBL) was most effective in developing transferable skills that are retained when recreated in realistic "life scenarios". The implications from experiential learning for the advancement of medical education therefore can be summarized in the following points: learner-directed instead of professor-directed PBL scenarios may encourage learner responsibility and increase knowledge retention. Valuing the prior knowledge and experiences of physicians (whether situational, vocationally transferable, etc.) may create a stronger foundation for physicians to consolidate new information. Encouraging active reflection and subsequent experimentation through PBL and in realistic 'life scenarios' may increase transferability of professional skills as dictated by the General Medical Council.

Conflicts of Interest
The author(s) declare that they have no conflict of interests.

Authors' Contributions
JSW, BH, CBP, and CL equally contributed to the planning of the research competition, assisted in the collection of abstracts and reviewed the abstract submissions. CM and MA provided support in the selection of abstracts as volunteers to the planning committee.

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