

14th Annual Canadian Undergraduate Conference on Healthcare 2018 “The Future of Healthcare: A Multi-disciplinary Approach.”

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Abstract

The following are abstracts from the research competition at the 14th annual Canadian Undergraduate Conference on Healthcare. The conference was entitled “The Future of Healthcare: A Multidisciplinary Approach,” held on November 9th-11th, 2018 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; Canadian; Undergraduate; Conference; Healthcare; Multidisciplinary; Research; Competition

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Conference Abstracts

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Conference Oral Presentation Abstracts

Oral Presentations in Social Sciences, Epidemiology, and Health Promotion

Temporal trends in living kidney donor candidates

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Background: Living donor kidney transplantation is the preferred treatment for kidney failure, but donation rates in North America have decreased. Living kidney donor (LKD) candidates must undergo rigorous evaluation before they are approved to donate their kidney. Studies on American LKDs show an increasing prevalence of metabolic syndrome which may contribute to the declining donation rates; however, little is known about Canadian LKD candidates. This study evaluates temporal trends in Canadian LKD candidates and identifies characteristics which are predictive of donation.

Methods: All LKD candidates (n=3678) referred to Toronto General Hospital between January 1, 2006 and December 31, 2015 were included in the study; follow-up ended on May 31, 2017. LKD candidate characteristics were evaluated over three time periods: 2006-2009, 2010-2012, and 2013-2015. Multivariable Cox regression models were used to identify candidate characteristics associated with donation.

Results: Donation rates have declined since 2009. The mean age of LKD candidates has increased, the prevalence of comorbidities has risen, and fewer candidates are first-degree relatives of the recipient. Candidates who are Caucasian, married, non-smokers, have a BMI<25, and are first-degree relatives of the recipient are most likely to donate. Candidates over 60 who have comorbidities are least likely to donate.

Conclusion: Despite consistent referral rates of LKD candidates, living kidney donation rates have decreased. This study suggests that the changing profile of LKD candidates over time may explain the decline in donation. Further study is needed to determine specific reasons why LKD candidates do not proceed to donation.

The incidence of hospitalizations in children with nephrotic syndrome

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Background: Childhood nephrotic syndrome (NS) is a relapsing and remitting kidney disease with favorable long-term prognosis. Adverse complications can lead to hospitalizations. However, the incidence and causes of hospitalizations among children with NS are not clear.

Purpose: Determine the incidence rate and causes of hospitalizations among all (steroid sensitive [SSNS] and steroid resistant [SRNS]) childhood NS patients

Methods: In a longitudinal cohort of children with NS ages 1-18 at the Hospital for Sick Children, incidence rate of hospitalization was determined. Cause of hospitalization was classified as either infectious and/or non-infectious. Cox proportional hazards regression model was used to evaluate the hazard of hospitalizations among SSNS and SRNS children.

Results: Among 331 children, the majority were male (62%) with median age at diagnosis of 3.7 (interquartile range [IQR]: 2.7-6.1) years. A total of 122 children (37%) were hospitalized, with a median of 2 hospitalizations (IQR: 1-3). Incidence of hospitalizations was 95 per 1,000 person-years. Median length of stay was 3 days (IQR: 2-6) and median time to hospitalization was 9.1 years. Causes for hospitalizations were infectious (8%), non-infectious (64%), or both (25%). Children with SRNS had 2.5 times higher risk (95% confidence interval: 1.3, 4.6) of hospitalizations compared to children with steroid sensitive NS.

Conclusion(s): One third of all children were hospitalized for adverse complications in NS. Infection was not the most common cause, as historically described. Children with SRNS were hospitalized almost 3 times more often. Future studies are needed to determine factors that lead to increased hospitalization risk.

Safety behaviour use and speech performance in people with public speaking anxiety

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People with public speaking anxiety often use safety behaviours (SBs) to reduce anxiety (e.g., hiding behind a podium, carrying a water bottle) and allow them to stay in feared situations (i.e., delivering a speech). Although SBs contribute to the maintenance of anxiety, new evidence suggests that the judicious use of SBs could enhance the acceptability of exposure therapy while reducing the level of anxiety during this type of intervention. SBs could then facilitate public speaking among speech anxious individuals in the context of treatment that aims to eventually eliminate the use of SBs. This study evaluates whether the use of SBs in people with high speech anxiety results in longer speech duration and less self-reported anxiety during a speech task. High speech anxious undergraduate students were recruited ($N=42$) and deceived in thinking that the study aimed to assess academic achievement. Participants were then asked to deliver a speech in front of a judge who videotaped and evaluated their performance. Participants were randomly assigned to the SB or no SB condition. Their speech duration and self-reported peak anxiety during the task were recorded. Results demonstrated no significant differences in self-reported anxiety and speech duration between groups. In this case, SBs were neither helpful or detrimental for speech anxious participants in delivering a speech. However, the SB options might not have reflected the participants' everyday life choice. Future studies could evaluate the participants' perceived usefulness of SBs during a speech task and willingness to repeat the experience.

Emerging trends in dietetics

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The practice of dietetics has changed remarkably over the years, and it continues to change and evolve. As part of a project on the history of dietetics in Canada over the past 25 years, as well as to inform potential future direction for dietetics, I conducted an online survey (Qualtrics) with follow-up interviews in Summer 2018. I report here on the emerging trends in healthcare that Registered Dietitians are most interested in. The survey was advertised in member updates, through interest networks, and at the national annual conference of Dietitians of Canada. It was open from June 6th to July 15th, 2018. Telephone interviews were conducted with interested people, who were shown the preliminary survey results and asked a series of questions to confirm survey results and identify additional issues, topics, opinions, and possible key informants and reviewers. There were 359 total survey responses, and 51 interviewees. After analysis of the survey and interview data, the results demonstrated that the top emerging trends included the use of technology and telehealth (21% of respondents), dietitians/nutrition in social media (18% of respondents), and dietetics' scope of practice (29% of respondents). Additional topics of interest included Registered Dietitians versus other nutrition titles and health care professionals, and the various practice areas of dietetics. A clear understanding of what the dietitian's role in health care is and what our scope of practice entails is needed in both the professional and public setting to protect our title and provide the best health care possible for patients.

Examining cognitive training and executive function in older adults

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Age-related cognitive decline can greatly impact the health and wellbeing of older adults (OA). As the population of OA grows, so has interest in healthy aging and cognitive decline prevention. The present study investigated whether cognitive training programs (CTP) can lead to improvements in the performance of OA on cognitive tasks. We recruited 35 OA (60-87 years of age) for a 5-week CTP. Before and after training, OA were evaluated on tasks of executive function, including the N-back task of working memory and Flanker task of inhibition. We also recruited 32 young adults (YA; 17-27 years of age), who completed one assessment for baseline comparison with OA. We examined the reaction time (RT) and accuracy of YA and OA on these tasks at baseline, as well as the change in performance of OA pre- and post-training. Repeated measures analysis of variance indicated a reduction of pre- and post-training RT for the Flanker task. There was no post-training change in RT on the N-back task. Although hit rates in OA did not change significantly on the Flanker task between each assessment, they increased in the N-back task. In both tasks, we found significant differences between OA and YA, with YA demonstrating lower RT and accuracy compared to OA. Follow-up studies will reveal whether other factors can also lead to improvement. Determining whether CTP can improve cognitive performance in OA can help determine the potential of such approaches to prevent or rehabilitate age-related cognitive decline.

“Tell it as it is”: How sisom prompts children and parents to discuss their cancer experience

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Background: Sisom is a computerized communication tool shown to improve communication between children and their clinicians. Presented on a computer or tablet, Sisom prompts children to rate the severity of their symptoms. However, what discussions unfolded from using Sisom remained unknown, and may deter implementation into clinical practice.

Objective: To describe if and how Sisom prompted children to express themselves, and what discussions unfolded from using Sisom, as well as how parents contributed to shaping these discussions.

Methods: A qualitative descriptive design was used to guide the analysis of interview transcripts derived from the interactions with Sisom of 39 children with cancer between 6 and 13 years old, 31 of which had parent(s) present at the time of interview.

Results: Sisom elicited a verbal response to at least one symptom for the majority of children (n = 33) and prompted the majority of children's parents to interject at least once (n = 23). Sisom prompted children to: (1) discuss their thoughts and feelings; (2) express a spectrum of emotions, ranging from unpleasant to pleasant; and (3) reflect, in varying degrees of certainty and uncertainty, their illness. Parental input was provided in the form of (1) providing clarification, (2) validating their child's responses, (3) guiding their child's responses (4) responding on behalf of their child and (5) making casual remarks.

Discussion: Sisom is a useful tool to prompt children in discussing their illness experience. Meaningful encounters between children and their clinicians may ensue with the adoption of Sisom in practice.

The uptake of the pharmacy-dispensed naloxone kit program in Ontario: a population-based study

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Background: Naloxone is a life-saving antidote for opioid overdose. In June 2016, the Ontario government implemented the Ontario Naloxone Program for Pharmacies (ONPP) to enhance non-prescription access to naloxone. We examined the initial uptake of naloxone through the ONPP and characterized the individuals receiving and pharmacies dispensing naloxone kits.

Methods: We conducted a population-based study of all Ontario residents who received a naloxone kit between July 1, 2016 and March 31, 2018. This involved 1) a cross-sectional analysis of monthly rates of naloxone kits dispensed, individuals accessing naloxone and pharmacies dispensing naloxone; 2) a descriptive analysis of all individuals and pharmacies who accessed and dispensed naloxone, respectively. In each analysis, we stratified individuals according to their opioid exposure as follows: current opioid agonist therapy (OAT) users, current prescription opioid users, past opioid users, and unknown opioid exposure.

Results: The rate of naloxone kit dispensing increased from 1.9 to 54.3 kits per 100,000 residents over the study period. By March 2018, 2,729 community pharmacies dispensed 91,069 naloxone kits to 67,910 unique individuals. Uptake differed between exposure groups, with many OAT users (40.7%) and few current prescription opioid users (1.6%) and past opioid users (1.0%) accessing naloxone. Naloxone dispensing was highly clustered within pharmacies, with one-third (33.74%) of kits being dispensed by 1.0% of naloxone-dispensing pharmacies.

Conclusions: The ONPP led to considerable uptake of publicly-funded naloxone in Ontario; however, uptake among current prescription and past opioid users remains low and access appears to be concentrated among a small number of pharmacies.

Longitudinal analysis of preschool child-parent attachment in association to problematic behaviours in school-aged children

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Prior research suggests that a secure mother-child attachment is imperative for the healthy development of the child's social and emotional skills. However, recent studies presented findings highlighting the importance of a secure father-child attachment and suggested that fathers could play a central role in the formation of behavioural problems in preschool-aged children (Bureau et al., 2017). This longitudinal study aims to determine whether specific patterns of interaction within child-parent dyads detected in the preschool period can predict problematic behaviours occurring in middle childhood. Analyses were conducted with data from 85 intact families participating in this ongoing longitudinal study. In phase one (age 3-5), dyads completed a separation-reunion laboratory procedure used to measure the quality of attachment to each parent separately. In phase two (age 7-9), both parents reported on the child's social behaviour. Results reveal that security towards the father is inversely correlated with externalizing behaviours & hyperactivity, whereas ambivalence towards the father is positively correlated with externalizing behaviours & conduct problems. Furthermore, child punitiveness toward the father is also positively correlated with conduct problems. Regression analyses revealed that these correlations remain marginally significant even after the inclusion of the relevant control variables and the mothers' scores for the corresponding sub-scales of attachment. These analyses extend previous work confirming the unique role of the father in the development of externalized behaviours in school-aged children.

The effect of categorization on perceived word-pair similarity for abstract and concrete words

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The study of categorization in psychology has many implications in a variety of psychological domains. The current study investigates differences in similarity ratings for abstract and concrete word-pairs in natural and ad-hoc categories. With the use of previous research, it was hypothesized that concrete words would be perceived as more similar than abstract words, and words in natural categories be perceived more similar than when in ad-hoc categories, as well as an interaction between concrete words and natural categories. Ten participants were asked to rate the similarity of abstract and concrete word-pairs in natural and ad-hoc categories. A 2x2 within-subjects analysis of variance found a main effect of word-type, where abstract words were rated as significantly more similar than concrete words, $F(1, 9) = 6.60, p = .030, \eta^2 = .423, \text{power} = .629$. The analysis also revealed that word-pairs in ad-hoc categories were rated significantly more similar than words in natural categories, $F(1, 9) = 15.35, p = .004, \eta^2 = .630, \text{power} = .935$. No significant interaction was present, $F(1, 9) = 0.02, p = .906, \eta^2 = .002, \text{power} = .906$. It was suggested that category size and criteria may influence ad-hoc categories to be more specific with category members, leading to more similar features between members in ad-hoc categories than in natural categories. Visual imagery may add a layer of complexity in concrete words leading to poorer similarity ratings when compared to abstract words. Future research should look at the effects of category size and visual imagery with larger samples to confirm these findings.

Oral Presentations in Microbiology and Immunology

Temporal dynamics of dental, tongue, and salivary oral microbial profiles in experimental gingivitis

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Gingivitis is a reversible form of periodontal disease that can progress to periodontitis if left untreated. Periodontitis (PD), the leading cause of tooth loss worldwide, is an irreversible infection that destroys tooth-supporting structures. The experimental gingivitis model (EGM) allows for longitudinal surveillance of oral microbiota during gingivitis induction by eliminating daily oral hygiene practice. Elucidating microbial community shifts using EGM can help to discover indicators for disease risk prediction and timely intervention. The objective of this study was to identify oral commensal and pathogenic bacteria affected by disease transition. We hypothesized that the relative abundance of disease-associated bacteria will increase during gingivitis onset, and decrease as health is restored. 16S rRNA-specific bacterial DNA in subgingival, supragingival, tongue, and salivary samples from 15 healthy individuals was extracted and quantified with RT-PCR at three time points (n=180): 1) baseline, 2) after oral hygiene cessation for three weeks (induced gingivitis state), and 3) after resuming oral hygiene (restored health state). One-way ANOVA was conducted. Of seven species tested, gingivitis induction correlated with significant elevation in *Porphyromonas gingivalis* (PD pathogen), *Streptococcus oralis* (oral commensal), *Synergistes* OT 362 and 363 (novel oral phylotypes) ($p < 0.05$). We conclude that gingivitis induction is accompanied by increased DNA abundances of known and novel health- and PD-associated species, with supragingival plaque serving as a reliable, non-invasive alternative to subgingival sampling. This is the first study that correlates two novel phylotypes with gingivitis induction. Such bacterial indicators can be utilized to develop clinical tools for disease risk prediction and treatment monitoring.

Impact of iron chelation on inflammatory parameters in gram-negative sepsis models

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Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection (Singer et al., 2016). The high incidence and mortality associated with sepsis make it a global public health concern. There are currently no approved treatments for immune dysregulation in sepsis. Iron is responsible for the formation of reactive oxygen species (ROS) in response to infection, but overproduction may lead to oxidative stress and tissue damage. Iron chelation has been suggested as a treatment for sepsis due to its ability to reduce both ROS production and the bioavailability of iron for bacterial growth. DIBI is a novel iron chelator which has been shown to be anti-inflammatory in both experimental endotoxemia and polybacterial murine models of sepsis (Islam et al., 2015; Thorburn et al., 2017). In our study, significant reductions in inflammatory parameters were observed in different endotoxemia models by iron scavenging with novel chelator DIBI. Via intravital microscopy, leukocyte adhesion was seen to be significantly reduced in both submucosal V1 and V3 venules of the intestinal microcirculation. Significant improvements were also seen in blood flow within the microvasculature of the intestine. Intestinal histology was also examined in experimental sepsis induced by LPS from *E. coli* and *K. pneumoniae*. Iron chelation may have therapeutic potential for modulating immune dysregulation in clinical sepsis.

Investigating CD3+/CD8+ infiltrates in metastatic pancreatic ductal adenocarcinoma

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Immunotherapy offers a promising outlook for treatment for those with pancreatic ductal adenocarcinoma (PDAC). Immunotherapy treatment targets and inhibits immune checkpoints, preventing anti-tumour immune suppression. Notably, drugs inhibiting CTLA-4 and PDL1 have shown great efficacy in clinical trials, but have been dismal in improving survival rates for patients with pancreatic cancer. Immune infiltration, particularly CD8+ T cells, has shown to be a positive prognostic marker in various cancers, including pancreatic cancer. Given that the liver is the primary region for metastasis in PDAC, we sought to quantify and characterize immune infiltration of liver metastases in pancreatic cancer, and determine the associations between infiltrates and the currently targeted immune checkpoint molecules CTLA-4, PD-L1, and PD-1. To study this, we acquired 70 tumour-annotated immunohistochemistry (IHC) slides of liver metastasis biopsies from the COMPASS trial. We quantified immune infiltrates using HALO Image analysis software, using QuPATH to validate quantification. To further interrogate the immune landscape of these samples and their associations with immune checkpoint molecules, we looked for correlations with FPKM normalized RNA sequencing data (RNAseq) signatures. All statistical analysis was conducted using the R Statistical analysis Software. Results show that both CD3+ and CD8+ immune infiltration is positively correlated with CTLA-4 RNA sequencing expression in liver metastases. Further analysis is being conducted to determine infiltrate differences between primary tumours and metastases, as well as associations with other immunomodulatory molecules. Elucidating the immune landscape in pancreatic cancer may yield novel treatments for patients.

Tumour-infiltrating regulatory T cells express PD-1 and regulate anti-tumour immunity

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Checkpoint inhibitors are becoming increasingly popular in cancer immunotherapy for their ability to target negative regulators of T cell functions. In particular, Pembrolizumab targets the programmed cell death protein 1 (PD1) expressed on activated T cells, preventing engagement of PD1 with its ligand PD-L1, expressed on tumour cells. While anti-PD-1 therapy is classically known to prevent inhibition of the activated T cells, its effect on other cells in the tumour microenvironment is currently unclear. Our lab has recently found that regulatory T (Treg) cells in human ovarian carcinoma express a high level of PD-1, which is associated with a highly suppressive Treg cell phenotype. To elucidate whether Treg cells express PD-1 in murine tumour models, we used the transplantable E.G7-OVA lymphoma model. By performing flow cytometry and histology on the tumours, we found that Treg cells are indeed present in the E.G7-OVA tumour and that these intra-tumoural Treg cells have unique surface expression of CD25, ICOS, and PD-1. Lastly, using the DEREK mouse model whereby diphtheria toxin receptor expressing FoxP3⁺ cells can be depleted through systemic administration of diphtheria toxin, we found that Treg cells also play a functional role in regulating anti-tumour immunity since their absence resulted in complete tumour rejection. These findings suggest that anti-PD1 therapy may also be targeting highly suppressive Treg cells in addition to the effector T cells in the tumour.

Oral Presentations in Neuroscience

microRNA dysregulation in Alzheimer's disease progression

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder that leads to irreversible memory loss and other cognitive impairment. In 2017, nearly 50 million people worldwide were living with AD or a related dementia, and this number is projected to double every 20 years. microRNAs (miRNAs) are small (~22 nucleotide) RNA molecules that negatively regulate

gene expression by targeting complementary messenger RNAs. miRNAs regulate a number of CNS functions, such as development, cognition, and synaptic plasticity, and several studies have found that miRNA expression changes are linked to AD pathology. Our project focuses on the entorhinal cortex (EC) and uses a state-of-the-art assay to investigate the role of miRNAs in AD. We generated expression profiles for 70 total RNA samples, isolated from the lateral EC, medial EC, and cerebellum of human AD patients and age-matched control subjects, through barcoded small RNA sequencing. After data preprocessing to remove the effects of technical variation, high expression analyses show that miR-9 is the most abundant miRNA in all brain samples. Differential gene expression analyses indicate that several miRNAs are dysregulated in the EC of AD patients. Notably, we observed the upregulation of miR-144, which has been associated with aging progression and tumour growth, and downregulation of miR-210, a miRNA that has been implicated in neurogenesis and various human diseases. Our findings are expected to provide insights into the mechanisms of AD progression and identify miRNAs that can be used as adjunct AD tissue biomarkers or therapeutic targets.

Oral Presentations in Genetics, Cytology, and Molecular Biology

Mitochondrial variant detection, annotation and segregation from Whole-Exome Sequencing data

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Reads containing mitochondrial DNA are the most common off-target captures when performing Whole-Exome Sequencing (WES). Even without enriching panels with mitochondrial probes, it is possible to assemble the mitochondrial (MT) genome from off-target reads at relatively high depths; many open-source pipelines and tools have been developed and adapted to this means: MitoSeek, MToolBox, mtDNA-Server, and MitoSuite.

Two alignments to the rCRS of the MT genome were generated with Burrows-Wheeler Alignment Tool (BWA) using cleaned fastq files from Illumina paired-end sequencing. Two alignment protocols for 243 WES samples from 15 Pakistani families containing neuropsychiatric disease subjects and controls were used as input into the MToolbox, mtDNA-Server and LoFreq pipelines. Calls made by the three pipelines were combined and positions present in all three pipeline's variant call files for the entire cohort were extracted, and variant annotation was performed using variants from these common positions. The annotation step was performed using Annovar with an Ensembl gene database, a dbSNP database, and custom-created MitoMap and HmtDB databases. Haplogroups were assigned using the MToolbox pipeline. MitoSuite was used for supplementary graph generation and haplogroup confirmation.

Among the three tested variant callers, MToolbox has the highest concordance with the overlapped variants. A total of 718 MT variants were identified, 25 of which were multi-allelic variants, from 242 of the individuals. 97 variants were classified as non-coding control region variants, 286 were non-coding mt-RNA variants, and 360 were protein-coding variants. 8,955 genotypes were observed using mtDNA-server calls at these positions, of which 40% were homoplasmic variants (>95% heteroplasmy), 5% were heteroplasmic between 50-95% and 55% were heteroplasmic between 0-50%.

Mitochondrial genome assembly from our WES data is possible with reasonable data quality. Variants with varying levels of heteroplasmy and a large number of homoplasmic variants were detected in our data-set, with some variants having potentially interesting biological significance. Variant segregation with disease phenotypes within the pedigrees will be investigated. Incorporation of MT-variant-calling with the selected pipelines and the Annovar annotation step into a larger WES pipeline is underway.

Irx5 as a major regulator of ventricular myocardium heterogeneity

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For harmonious contraction and relaxation of the heart, the subendocardial (ENDO) and subepicardial (EPI) regions of the ventricular myocardium are physiologically different in nature. The abolition of such heterogeneity is associated with abnormal molecular and electrophysiological properties, leading to heart disease conditions, such as arrhythmias. However, our understanding of the molecular and regulatory mechanisms preserving such differences is comparatively limited. Here, we show the

molecular heterogeneity within the mouse ventricular wall at the genome-wide transcriptome level and reveal that *Iroquois* homeobox gene 5 (*Irx5*), predominantly expressed in the ENDO, is a key transcriptional regulator establishing the transmural heterogeneity. RNA-sequencing followed by bioinformatic analysis showed the enrichment of hypertrophy-marker genes (*Nppa*, *Rcan1.4*), growth factors (*Fgf12*, *Gdf15*) and contractile fiber genes (*Myl1*, *Sdc4*) in the ENDO of wild-type mouse hearts, while potassium channel genes (*Kcnd2*, *Kcna1*) and sodium/hydrogen transporters (*Slc9a2*) were enriched in the EPI. Notably, loss of *Irx5* in mice largely disrupted regional differences across the left ventricle, as the transcript profile of the *Irx5*-null ENDO became similar to that of the EPI. Lastly, gene expression analysis in human ventricle samples also showed the ENDO, MID to EPI gradient of *IRX5* expression, suggesting that *IRX5* likely contributes to the transmural heterogeneity in human hearts, as it does in mouse hearts. Together, our data posit that *Irx5* plays a major role in establishing the ventricle's transmural gradients. Further studies investigating the implications of disrupted regional differences as well as *IRX5* dysfunction in human heart diseases are warranted using this mouse model.

Mechanosensitive ion channel PIEZO1 regulates glioma stiffness and aggression

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Stiffness reflects the rigidity of an object. Stiffness in biological systems varies greatly between different tissue and organ types. Particularly, solid tumors are stiffer than their non-transformed counterparts. Previous studies have shown that increasing the stiffness of the extracellular matrix (ECM) of the cell increases tumor growth. However, the precise molecular sensor and transducer for enhancing tumor growth remains unknown. Glioblastoma multiforme (GBM), a type of glioma, is the most common and aggressive adult solid brain tumor and currently has no effective treatment. Using glioblastoma cell lines as a model, we aim to identify the sensor involved in increasing the stiffness of the tumor and thus the growth. Using patient samples, we identified that the expression of the mechanosensitive ion channel PIEZO1 is increased in human gliomas and inversely correlated with patient survival. Using glioblastoma stem cells, we created an inducible knockdown PIEZO1 cell line. We found that knockdown of PIEZO1 suppressed tumor growth in patient-derived glioma cells *in vitro*. To further investigate this, we xenografted our knockdown patient-derived glioma cells in mouse models. Using bioluminescence imaging, we also found a significant decrease of tumor growth *in vivo*. Our results demonstrate that the PIEZO1 channel is a critical molecular force sensor and transducer in glioma, and targeting PIEZO1 may be a promising therapeutic strategy in the treatment of solid tumors.

Evaluation of mean bone density and volume after stereotactic body radiation therapy to non-spine bone metastases

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Introduction: Stereotactic body radiation therapy (SBRT) has become increasingly prevalent for use on non-spine bone metastases. The primary goal of SBRT is local control and given that patients may be asymptomatic, additional radiographic endpoints are required to assess the efficacy of SBRT to non-spine bone metastases. The objective of my study was to investigate a quantitative technique for measuring response to radiation therapy using the volumetric bony contour.

Methods: A retrospective review was done for 26 patients treated with SBRT to non-spine bone metastases between November 2011 and May 2014. Patients underwent a computed tomography (CT) scan prior to treatment and at least one CT scan after treatment. Density was measured in Hounsfield units and volume was measured in cubic centimetres. Parameters were evaluated at 1-6 months and 7-12 months, if available, post-SBRT.

Results: At baseline imaging, values of mean bone density discriminate between osteolytic lesions and osteoblastic lesions. Osteolytic lesions from renal cell carcinoma (RCC) demonstrate radiological response at later times (7-12 months) compared to osteolytic lesions non-RCC renal lesions which increase in density within 1-6 months. Qualitatively, osteolytic lesions that exhibited an increase in mean bone density also had a corresponding decrease in V. Seven of 8 osteoblastic lesions demonstrated stability to baseline values or a slight decrease in mean bone density and volume.

Conclusion: This method demonstrates an alternate approach toward assessing SBRT response of non-spine bone lesions. The relationship between tumor volume and density changes could lead to more accurate response labels for non-spine bone metastases.

Targeting the glucagon receptor improves cardiac function and enhances insulin sensitivity following a myocardial infarction

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Glucagon's action on cardiac glucose and lipid homeostasis counteract that of insulin's action. In heart failure, the myocardium becomes insulin resistant which influences cardiac metabolism and function. Here we investigated if antagonising glucagon action, using a human monoclonal antibody (mAb A) against glucagon receptor, improves cardiac insulin sensitivity and function post myocardial infarction (MI). Male C57BL/6 mice were subjected to a permanent left anterior descending coronary artery ligation and were treated for 3 weeks with mAb A (4 mg/kg/week). mAb A treatment enhanced cardiac insulin sensitivity and function post-MI. Stimulation of the IRS-1/Akt/GSK-3 β cascade using this approach also improved cardiac insulin signalling, including an increase in insulin-stimulated glucose oxidation rates and its contribution toward tricarboxylic acid cycle acetyl CoA production. Intriguingly, there was a significant reduction in cardiac ketone oxidation rates in the post-MI hearts which were further decreased by mAb A treatment. mAb A treatment also prevented cardiac hypertrophy post-MI which was associated with inhibition of the mTOR/P70S6K signalling pathway. As a result, targeting glucagon signalling is a potential therapeutic approach to improve cardiac function and insulin sensitivity post-MI.

Conference Poster Presentation Abstracts

Poster Presentations in Social Sciences, Epidemiology, and Health Promotion

Prevalence of treatable kidney diseases in African children: a systematic review

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Background: Nephrotic syndrome (NS) is the leading cause of end stage renal disease in African children, however, the burden of treatable forms of childhood NS is not well characterized. We sought to quantify the prevalence of steroid responsiveness and biopsy proven minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS).

Methods: We performed a search using MEDLINE, Embase, African Journals Online and WHO Global Health Library databases to identify primary articles on childhood NS in Africa (January 1, 1946 to January 2018).

Findings: Quality of the studies was low. Among 372 records identified, 315 were excluded, and 18 were supplemented, resulting in 75 papers analyzed. Most countries lacked data, with only 17 countries out of 54 (31%) reporting. Among 3625 children, the pooled prevalence for steroid sensitive NS was 63% (95% CI: 61-64) and 31% (95% CI: 29-32) for steroid resistant NS. Among 3689 children, the pooled prevalence of MCD, FSGS and other histological types was 37% (95% CI: 35-38), 21% (95% CI: 20-22), and 42% (95% CI: 41-44) respectively. Secondary causes were reported in 44% of the cases.

Interpretation: Only one third of African countries had available information. The majority of children studied have a treatable form of kidney disease with a good prognosis. Secondary forms of kidney disease are common and resources to diagnose are limited. The results suggest the need for improved infrastructure to assess burden of disease, trained pediatric nephrologists to improve recognition of primary and secondary forms, and treat accordantly to prevent chronic kidney disease.

Determination and evaluation of nutrient intake of Canadian toddlers

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This paper outlines the steps taken to determine the nutrient intake of Canadian toddlers in the validation of Toddler NutriSTEP®, and compares the results to the Canadian Dietary Reference Intakes (DRIs) to evaluate diet adequacy. Although the importance of a nutritious diet during toddlerhood has been acknowledged, many international studies draw different conclusions about the adequacy of select nutrients, and Canadian data is limited. This paper brings clarity to toddlers' nutrient intake by being only the second known study to examine Canadian toddlers' nutrient intake, and the first using 3-day food records. The results of this study have important implications for caregivers and health care providers to focus on nutrients of concern, in order to provide a healthy toddlerhood, and avoid health complications in the future.

Erector spinae plane blocks – a panacea or lack of evidence: a systematic review

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Erector spinae plane (ESP) blocks, including thoracolumbar interfascial (TLIF) plane blocks, have shown great promise in improving the pitfalls of traditional analgesic techniques (e.g. transversus abdominus plane block, paravertebral block and oblique subcostal transversus abdominis plane block). While many case reports and case series exist, there are limited RCTs which are needed prior to its global uptake and routine use. In this systematic review, we present a qualitative analysis of the analgesic efficacy of these novel techniques. We searched MEDLINE, PUBMED, Web of Science, SCOPUS and Google Scholar and extracted data regarding changes in pain scores, postoperative narcotic use and emergence of any side-effects. The data was abstracted independently and in duplicate. We included five studies (276 participants) from database creation through to, and including, July 2018. For breast cancer surgery, cardiac surgery, spinal surgery and laparoscopic cholecystectomy, our results confirm the belief that ESP blocks will decrease postoperative pain scores and be associated with better pain scores, without causing additional complications. As shown in our review, ESP blocks not only provide an alternative route to traditional analgesic techniques, but there is also the capacity to modify these techniques to continue to make them simpler and impact patient outcomes. Despite showing great promise in postoperative pain management, further information regarding type of local anesthesia, optimal volume and concentration is required before its routine use.

A retrospective epidemiological study of respiratory risk factors in domestic dogs and cats from the Maritime provinces in Canada

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One Health recognizes that human, animal, and environmental health are all connected. Diseases that are prevalent in humans are also shared by animals. Asthma and Tracheal Collapse are two of the most prevalent respiratory issues in cats and dogs and are shared by humans. There is a gap in the quantitative knowledge regarding the risk factors of these diseases in a Maritime Canadian setting. Therefore, the patients selected were those who presented for treatment of either tracheal collapse or asthma at the University of Prince Edward Island's Veterinary Teaching Hospital between November 2016 and May 2018 inclusively. The data came from the newly implemented electronic medical records (EMR) system. EMR systems are increasing in prevalence in human and animal patient settings. A multivariable logistic regression analysis was done using STATA version 15 on the EMRs. The results produced for the tracheal collapse analysis were that only age, weight, and body condition score proved to be statistically significant. Weight was highly correlated and synonymous for breed size. The population most likely to have

tracheal collapse was small breed size, obese canines older than 10 years. For asthma, the final model included age and species. The population most likely to have asthma was felines older than 10 years old. These findings agree with similar human studies which indicate weight and indoor air pollution are major risk factors to human chronic respiratory diseases. The results also highlighted the benefit of retrospective research projects, which is facilitated through the use of EMRs.

Peer support interventions for individuals with acquired brain injury, cerebral palsy, and spina bifida: a systematic review

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Background: Neurological disorders may negatively impact community integration and/or quality of life. Peer support has emerged as a potential strategy to enhance patients' efficacy in managing their own health. This review examines the key characteristics and impact of peer support interventions for adults with acquired brain injury, cerebral palsy, and spina bifida on community integration and quality of life.

Methods: Eligible studies reported on peer support interventions for adults (16 years of age or older) with acquired brain injury, cerebral palsy, or spina bifida. Only randomized controlled trials published in English in the last 10 years were included. MEDLINE, EMBASE, PsycINFO, and CINAHL were used to conduct the literature search. Two reviewers independently screened studies, abstracted data, and evaluated the risk of bias using the Cochrane Risk of Bias Tool.

Results: The systematic review included 6 trials reporting on acquired brain injury only. Of these studies, 4 reported on stroke and 2 reported on traumatic brain injury. Two studies found significant improvements in quality of life following peer support. No studies reported significant results on community integration. Considerable heterogeneity existed in the key characteristics of interventions.

Conclusions: There is limited evidence on the impact of peer support interventions for adults with acquired brain injury, cerebral palsy, or spina bifida on community integration and quality of life. Standardization of key intervention characteristics may aid the global adoption of peer support as a formalized, evidence-based practice.

A comparison of novel kernel-based association statistics

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Recent advancements in sequencing technologies have made it easier to identify both rare and common genetic variants in the human genome. Along with these sequencing improvements, genetic association studies have become more prominent and are used to test for association between genetic variation and a phenotype of interest such as a disease state. One prospering field of genetic association tests are kernel-based association methodologies. These methodologies first require specification of a kernel function, which outputs a map that describes the degree of genetic similarity between pairs of individuals; many kernel functions have been proposed with strategies ranging from scoring genotype similarity to tree-based approaches. Then, using these maps, a variety of different kernel statistics can be employed to measure the strength of association between genetic similarity with a trait of interest. Due to the rapid expansion of this field, there has been no study that has described and compared the performances of all these different types of kernel-based association statistics in conjunction with the different kernel functions. Through large-scale simulations, we show that the various approaches differ in detecting associations under different phenotypic models.

Suicide presentations of homeless individuals to the emergency department

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Objective: In addition to major psychiatric illnesses such as mood disorders and psychosis, homelessness has been frequently linked to suicide. This study aims to describe and compare the population of homeless and housed individuals presenting to the emergency department with suicide in their demographics, clinical presentation and discharge plans. Research of this nature aims to address this vulnerable population in a novel, directed and effective way.

Method: This project assessed 1306 suicide-related presentations of 2600 (50.2%) to the ED at St. Michael's Hospital in Toronto, Ontario, between April 2013 and March 2015. Medical electronic chart data was used to evaluate demographics, severity of the presentation, as well as follow up plans for the patient. Descriptive statistics and data analyses were conducted using IBM SPSS23.0.

Results: Over a quarter of the presenters to the ED for suicide related behaviour were experiencing homelessness in some way. Individuals experiencing homelessness were more likely to: be male, use substances (namely cocaine, alcohol) and to have attempted suicide. Although individuals experiencing homelessness were not admitted to the hospital less frequently, they had lower follow-up rates with Family Doctors and Psychiatrists, and were more likely to have no documented follow-up.

Conclusions: Individuals experiencing homelessness and housed individuals presenting with suicide to the ED differ in most demographics and drug use patterns, but not in severity of presentation. Relative to counts from the City during the study period, individuals experiencing homelessness are overrepresented in the sample. Although there were targeted programs in place for this vulnerable population, homeless presenters had fewer documented discharge plans overall.

Autism and co-occurring substance use disorder: moving towards best practice strategies for clinical treatment

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Recent research suggests that individuals with Autism Spectrum Disorders (ASD) are at increased risk of developing Substance Use Disorders (SUD). Given the incredible burden of disability that both ASD and SUD create on their own, it is even more imperative that the research community attempt to move towards best practice strategies for clinical treatment of these disorders when they co-occur. Journal articles and case studies were reviewed to compile a description of the clinical features of patients with ASD and co-occurring SUD. Literature was examined for effective treatment strategies for similar issues that co-occur with SUD such as Attention Deficit Hyperactivity Disorder (ADHD), Schizophrenia, and delinquent youth. Similarly, literature detailing effective treatment strategies for ASD and other co-occurring disorders, such as anxiety was reviewed for potential strategies. From this review, ten suggestions for best practice strategies for the treatment of ASD with co-occurring SUD were developed, including: screening individuals with an ASD for suspected drug use as would be done with their non-ASD counterparts, as well as screening for co-occurring mood and anxiety issues, developing a rapport with the patient and his family, being cognizant of the patient's reasons for substance use, being cognizant of the core features of an ASD diagnosis, using a harm reduction approach, involving the patient in goal setting, pacing the therapy sessions based on the learning profile of the patient, targeting skill deficits after substance use stabilization, and ensuring clinician supervision.

Poster Presentations in Microbiology and Immunology

Role of extracellular vesicles in uropathogenic E. coli infection in an ex vivo model

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Urinary tract infections (UTI) are a prevalent public health concern with a high presence of recurrent UTI in females. The most common cause of UTI is uropathogenic E. coli (UPEC) and the only effective treatment available to date is antibiotics. If

untreated, a UTI can progress up the urinary tract to the kidneys causing pyelonephritis which may lead to permanent renal damage. UPEC is known to subvert antibiotics and the host immune system by invading host urothelial cells and forming intracellular bacterial communities (IBC) (Anderson et. al 2003), which can mature and go on to infect neighbouring cells. With antibiotic resistance on the rise and high recurrence rates of UTI there is a substantial need for research in alternative treatments for UTI. This study aims to understand the role that extracellular vesicles (EVs) play in the pathogenesis of UPEC during different stages of infection. Our Preliminary data shows that pre-treatment of ex-vivo mouse bladders with EVs derived from urine of acutely infected mice leads to a 14.2 fold increase of UPEC titre in bladder tissue vs. ex-vivo bladders infected with the same original titre ($p=0.0252$). This study looks at the effects of EVs derived from acutely infected urine and resolved UTI urine on inflammatory cytokine signalling and UPEC invasion. If pre-treating bladders with EVs from resolved UTI downregulates inflammation and invasion during early stages of infection, it may be a novel therapeutic with potential to decrease formation of IBCs which are a contributor to persistent/recurrent UTI.

Immunotherapy as a promising alternative to chemotherapy for Non-Hodgkin's Lymphoma: current and future treatment options

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Non-Hodgkin's Lymphoma (NHL), a cancer that starts in lymphocytes, is the fifth leading cause of cancer mortality. As of 2017, 8,300 Canadians were diagnosed with NHL with a 5-year net survival of 66%. While its first-line treatment is chemotherapy, multiple immunotherapies are emerging as alternatives. Papers and other publications by public biotech companies regarding the efficacy of currently available immunotherapy options for NHL were reviewed to assess the current pharmaceutical status. Rituximab, a monoclonal antibody targeting CD20, has demonstrated to be a successful treatment on its own and when coupled with chemotherapy or immunoconjugates. Preapproved drugs undergoing the process of clinical trials were also assessed to summarize the future scope of NHL treatments. For example, Lisocabtagene maraleucel, a CD19-directed chimeric antigen is being developed by Celgene Corporation for patients with relapsed or aggressive B-cell NHL. Overall, there are promising immunotherapy treatments coming into the market that will help the prognosis of patients with aggressive NHL, patients who don't respond well to chemotherapy, and finally as a first-line option replacing chemotherapy in the future.

Poster Presentations in Neuroscience

Association of selected genes (HTR2A, ADRA2A) with withdrawn behavior/depressed behavior in an international collaborative sample

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Withdrawn behaviors (WB) are characterised as shy, inhibited, or introverted behaviors, which have been shown to predict anxiety/depression disorders in adolescence and adulthood. Family studies have found that the frequency of behavioral inhibitions increases in children whose parents suffer from agoraphobia and anxiety disorders. This research suggests that genetic variation may play a role in the development of WB phenotypes. Previous candidate gene studies theorize that WB are highly associated with polymorphisms of both the serotonin receptor 2A (*HTR2A*), as well as the adrenoceptor alpha 2A (*ADRA2A*). The study aims to examine the association between SNP rs6314 and withdrawn behaviors in the *HTR2A* gene. The polymorphisms associated with SNP rs6314 result in a missense mutation within locus 442 expressed within the gene. This mutation consequently alters the amino acid histidine, changing it into tyrosine. Additionally, the association between the SNP rs1800544 and withdrawn behaviors will be examined in the *ADRA2A* gene. The polymorphisms associated with the rs1800544 SNP are dependent upon the allele presented in locus 1219. The alleles found in this region can code for C or G within the promoter domain.

DNA was extracted from the saliva of 480 individuals demonstrating a spectrum of withdrawn behaviors using the Oragene DNA Genotek method. DNA was quantified using PicoGreen and genotyped through a TaqMan® assay in order to test whether there are significant associations between withdrawn behaviors and SNPs. Analyses are ongoing, and our preliminary findings

have shown no significant association between SNP rs6314 of serotonin receptor 2A (HTR2A) or SNP 18005444 of the adrenergic receptor (ADRA2A) with the onset of withdrawn/ depressed behaviors. With that being said, this study can be furthered enhanced with the incorporation of other associated genes to evaluate a larger spectrum of genomic variants.

Hippocampal volume in adolescents at high-risk for developing serious mental illness

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Reductions in hippocampal volume (HV) have been reported in serious mental illnesses (SMI) including depression and psychosis. Yet many studies have demonstrated that individuals at risk of developing SMI do not demonstrate this reduction. As part of the Canadian Psychiatric Risk and Outcome (PROCAN) Study, we examined the HV of youth at risk of SMI. A trans-diagnostic clinical staging model was employed to separate the participants into 4 groups; healthy controls (n=37), asymptomatic with risk factors (n=32), help-seeking with symptoms (n=43), and those with attenuated syndromes (n=70). Magnetic resonance imaging scans of 182 participants were manually segmented to calculate HV by two tracers. Tracers were certified using the European Alzheimer's Disease Consortium (ADNI) - Alzheimer's Disease Neuroimaging Initiative (ADNI) Harmonized Protocol (HarP). High interrater reliability between tracers was reported (ICC=0.973 & ICC=0.981, left and right hemisphere, respectively). We used hierarchical multiple regressions to control for intracranial volume and differences between imaging sites. No significant differences in total HV, left HV, right HV, or hemisphere asymmetry were observed between the stages of risk or the healthy controls. No significant HV differences were associated with age, childhood trauma, or depressive symptoms. Our results are consistent with the current literature that individuals at risk of developing SMI do not demonstrate a significant reduction in HV compared to healthy controls. These findings imply HV reduction may represent a biomarker for SMI rather than a risk factor for SMI, as it does not seem to occur prior to the onset of illness.

Is marijuana making the executive decision to harm your executive functioning?

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Canada has the highest rate of youth marijuana use in the developed world. Past brain imaging research has shown that both prenatal exposure to marijuana and teen use can alter the brain's development, negatively impacting the neurophysiological basis of executive functioning. Executive functioning includes such essential cognitive tasks as decision-making, working memory and goal-directed behaviours. A critical period in neuro-maturation occurs in adolescence during which the developing brain is particularly vulnerable to the harmful effects of regular marijuana use. This study examined the effects of marijuana use on working memory in 19-21 year-olds using functional magnetic resonance imaging. Recruited from the longitudinal Ottawa Prenatal Prospective Study, 10 regular marijuana users and 14 non-using controls performed the 2-Back working memory task while fMRI blood oxygen level-dependent responses were measured. Despite similar task performance, marijuana users had significantly greater activation in the superior medial prefrontal gyri and inferior frontal gyri (prefrontal regions) as well as the left middle temporal gyrus. These three regions all contribute to the executive function of working memory. Marijuana users also had greater activation in the right superior occipital gyrus, a region not typically associated with working memory. These results suggest that regular marijuana use significantly impacts neural activity during working memory. Specifically, the brain seemingly engages in compensatory strategies, recruiting additional brain regions in order to complete tasks. With marijuana's legalization in October (predicted to increase use), a better understanding of the impact of cannabis on the developing brain of adolescents and its long-term effects is urgent.

Poster Presentations in Genetics, Cytology, and Molecular Biology

PRMT5 Inhibitors induce donut shaped nuclei in glioblastoma cells and impede tumor growth

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Glioblastoma (GBM) is a highly malignant brain tumor, but regardless of extensive research, treatment options remain limited and prognosis bleak. Fortunately, Protein arginine methyltransferase enzyme 5 (PRMT5) inhibitors offer an emerging targeted treatment by impairing alternative splicing and the removal of detained introns (DIs). The aim of this project is to identify phenotypic changes associated with PRMT5 inhibitors (PRMT5i) and elucidate the possible mechanism and genes responsible for nuclear morphological phenotypes. Multiple GBM lines were cultured and treated with controls and PRMT5i. The cells were then stained using immunofluorescence stains, imaged, and quantified for phenotypic changes. The lines were also similarly cultured and treated for total RNA purification, cDNA synthesis, semi-quantitative RT-PCR, and gel electrophoresis to analyze alternative splicing events and protein purification for western blots to quantify protein levels. It was found that the proportion of donut shaped nuclei significantly increased upon PRMT5i treatment. A strong negative correlation ($r = -0.68$) between the proportion of donut-shaped nuclei and the total number of cells suggests that the deformed nuclear morphology may play a role in cell cycle and proliferation. Further, the alternative splicing of genes RPAIN, ANAPc16, and PAPOLA was significantly altered in PRMT5i treated cells, which may implicate them in these phenotypic changes. On the protein level, RPAIN was decreased in PRMT5i treated cells, additionally validating the affects of impaired alternative splicing. In conclusion, RPAIN, ANAPc16, and PAPOLA may all be implicated in donut shaped morphology and tumor progression.

Tissue Engineering

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In this article, we will first be looking into the usage of Tissue Engineering (TE) as an alternative treatment option compared to similar treatments such as transplantation, surgical repair and drug therapy to cure organs failure. Cell sources, scaffold structures and growth elements are the three main factors to take into account to ensure a successful organ repair. Living cells are used as the building and engineering material. These cell which should be nondifferentiated ones, are mainly extracted from the target organ or produced in lab, preferably from the same patient body to decrease the chance of rejection. For scaffolding, different materials is discussed in the article ranging from natural polymers to synthetic ones and a blend of the two. Subsequently, main criteria when using a blend of synthetic and natural polymers is discussed. Finally, growth elements which ensures the cell will be developing in a healthy and productive environment are also discussed. At the end of the article, two use cases of the TE methodology will be presented in detail to show how TE is used by scientists as a preferred methodology of organ treatment.

Regulation of STAT5 activation by clathrin-mediated endocytosis

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The epidermal growth factor (EGF) receptor (EGFR) controls many key cellular processes, such as proliferation, survival, and migration. Upon binding growth factor ligands such as EGF, the receptor activates a number of signaling pathways, such as that involving the phosphorylation and nuclear translocation of Signal Transducer and Activator of Transcription 5 (STAT5). The importance of studying EGFR regulation and signalling is underscored by the observation that aberrant EGFR and/or STAT5 signalling drives the growth and progression of a plethora of cancers. Importantly, concomitantly to activation of intracellular signaling upon ligand binding, EGFR undergoes clathrin-mediated endocytosis from the cell surface to endosomes, leading to eventual receptor degradation or recycling.

The mechanism by which EGFR and other receptors phosphorylate and activate STATs is not well understood. Specifically, whether clathrin or endocytosis of the receptor to endosomes are required for activation of STAT5 is not known. We hypothesize that endocytosis of EGFR is required for STAT5 activation, and that STAT5 phosphorylation occurs within endosomal

structures. We used various pharmacological inhibitors and siRNA gene silencing to perturb specific stages of clathrin-mediated endocytosis and intracellular trafficking to determine which of these stages are required for STAT5 activation. To complement this approach, we used immunofluorescence microscopy to observe the localization of phosphorylated STAT5 upon EGF stimulation. We find that EGF-stimulated STAT5 phosphorylation requires clathrin-mediated endocytosis, providing a new understanding of the molecular mechanisms leading to STAT5 activation. Understanding the mechanisms by which STAT5 is regulated has numerous implications in impacting both current and future cancer treatments.

Nutrigenomics: The effect of DNA on nutritional metabolisms – mutations in TMPRSS6 gene alter the iron absorption leading to Iron type anemia.

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Goal: DNA is the fundamental database when addressing human nutrition.

Studies: Iron is a vital nutrient for the human body. In fact, Iron bonds to the Heme group, that are the building blocks of human Hemoglobin. Hemoglobin is a quaternary protein that transports oxygen to molecules such as Myoglobin that further stores oxygen in muscles. Myoglobin additionally uses Iron to further store Oxygen for regulation. Oxygen is essential for human metabolism and energy resolution. The mutation of the gene TMPRSS6 gene causes the overproduction of Heparin. Heparin commands Iron absorption. The absorption of Iron towards digestive organs is much inferior due to the presence of this hormone.

Matriptase-2 is the protein that is produced when the TMPRSS6 (chromosome 22) gene is translated; this protein engages the control of the Heparin levels. Indeed, forty mutations lead to the malfunction of this gene, including SNPs; i.e. T-C substitution

Results: Nutrigenomics a growing field specializes in the study of the connection between human DNA and nutrition. Discoveries such as the TMPRSS6 gene impact on nutrition signify a clear indication that human nutritional metabolism is guided by DNA.

Conclusion: Many researchers and scientists started studying approaches to enhance general nutrition through human DNA. In sum, the ideal human diet can be constructed based on the genetic expression. The future of healthcare is becoming further based on the understanding of molecular biochemistry.

Differences in the genetics of severe hypertriglyceridemia across ethnicities

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Background: Individuals with extremely elevated levels of triglyceride (TG) within the blood are diagnosed with hypertriglyceridemia (HTG). When TG levels surpass 10 mmol/L, individuals are considered to have “severe” HTG. While there are both genetic and environmental factors that can influence HTG, genetic factors have a prominent role. Mutations in genes involved in TG metabolism can have large impacts on TG levels. In contrast, while single nucleotide polymorphisms (SNPs) associated with TG levels have small impacts on TG levels, in aggregate, can confer susceptibility to severe hypertriglyceridemia (HTG). A comprehensive genetic analysis—assessing both mutations and SNP accumulation—was performed in Caucasians with severe HTG but has never been performed in non-Caucasians. The objective of this study was to compare the genetic determinants of HTG in patients of different ethnicities.

Study Design: 719 severe HTG patients of 7 different ethnicities were sequenced using a custom next-generation sequencing panel that targets 73 genes and 185 SNPs associated with abnormal lipid levels and metabolic disorders. Patients were screened for mutations in TG metabolism genes (*LPL*, *APOC2*, *APOA5*, *LMF1* and *GPIHBP1*), and were tested for SNP accumulation using a polygenic risk score.

Findings: The Hispanic patients with severe HTG had a significantly different genetic profile compared to Caucasians. When considering both mutations and SNP accumulation, Hispanics were 2.80-fold more likely to present with one of these genetic determinants compared to Caucasians.

Conclusion: Of the studied ethnicities, the Hispanic patients with HTG showed a significantly different genetic profile compared to Caucasians. This demonstrates that the genetic basis of HTG is unique between ethnic cohorts.

Effect of nanosilver surfaces on peptide reactivity towards reactive oxygen

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In the context of biomedical sciences, a material extensively studied has been silver nanoparticles (AgNPs). These have been of interest due to their antibacterial and pro-regenerative properties. A strategy used for optimizing these characteristics is to chemically modify the surface of the AgNPs using capping agents. Smaller capping agents such as citrate can provide cost-effective stabilization but are still unstable under physiological conditions. Consequently, published studies done by our lab have identified proteins and short peptides that can provide the appropriate colloidal stability while improving biological performance. Yet, in vivo, these capping agents are nonetheless susceptible to endogenous free radicals. Protein oxidation is already a well studied phenomenon; however, what is still unclear is the impact of nanoparticles on the oxidation pathway and whether it is pro or antioxidative. To investigate this, we have used a multidisciplinary approach. A combination of steady state spectroscopy, ultrafast spectroscopy and molecular dynamics experiments were used to study the interaction of short collagen mimetic peptides (bearing a terminal tryptophan moiety) anchored to AgNPs in the presence of peroxy radicals. Our results indicate that the extent and efficiency of the interaction depends on factors beyond peptide length that includes conformation and distance between the terminal tryptophan and the metal surface. Overall, our results contribute to a better understanding of the role nanomaterials in a physiological system.

Study Design: 719 severe HTG patients of 7 different ethnicities were sequenced using a custom next-generation sequencing panel that targets 73 genes and 185 SNPs associated with abnormal lipid levels and metabolic disorders. Patients were screened for mutations in TG metabolism genes (*LPL*, *APOC2*, *APOA5*, *LMF1* and *GPIHBP1*), and were tested for SNP accumulation using a polygenic risk score.

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Conclusion: Of the studied ethnicities, the Hispanic patients with HTG showed a significantly different genetic profile compared to Caucasians. This demonstrates that the genetic basis of HTG is unique between ethnic cohorts.

Poster Presentations in Morphology

Longitudinal changes in cardiac structure and function in pediatric renal transplant recipients

Isabel de Verteuil, BSc. Student [1], Jessica Fitzpatrick, MPH, PhD [1], Ana Catalina Alvarez Elias, MSc., MD [1,2], Tonny Banh, HBSc. [1], Jovanka Vasilevska-Ristovska, MD [1], Bianca Bondi, HBSc. [1] Jordan Brown, BSc., MSc., [1], Wei Hui [3], Cameron Slorach [3], Chia Wei Teoh, MD. [1,2,4], Luc Mertens, MD, PhD [3,4], and Rulan S. Parekh, MD, MS [1,2,3,4,6].

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Background: Cardiovascular disease results in increased morbidity and mortality in pediatric renal transplant recipients.

Objective: Assess the longitudinal changes in cardiac structure and function in pediatric renal transplant recipients.

Methods: We conducted a longitudinal study of children who received their first renal transplant at the Hospital for Sick Children from 2004 to 2015. Children were followed until transfer to adult care, death or censoring on July 11th, 2018. Structural and functional parameters were collected from echocardiograms. Intraventricular septum thickness (IVS), left ventricular end-diastolic dimension (LVEDD) and left ventricular posterior wall dimension (LVPWD) were compared to average values at SickKids matched for body surface area. An adjusted segmented mixed-effect model assessed IVS z-score, LVEDD z-score, LVPWD z-score and fractional shortening over time.

Results: Of 196 children, 59% were male with a median of 3 (Interquartile range [IQR]: 1, 5) echocardiograms during follow-up. Average age at transplant was 10 years. Baseline z-scores for IVS, LVEDD, LVPWD were 0.81 (IQR: -0.03, 1.65), 0.45 (IQR: -0.76, 1.28), 0.63 (IQR: 0.07, 1.43), respectively. Fractional shortening values were 37% (IQR: 34, 41), Structural z-scores significantly improved, reaching normal values at 5.3 years for IVS, 0.9 years for LVEDD and 4.3 years for LVPWD. Fractional shortening was within a normal range and remained constant over time.

Conclusion: Cardiac structural abnormalities improve following a renal transplant and return to normal within the first 6 years. It is important to ensure that the improved cardiac structure is maintained as children age to decrease mortality.

Association of sarcopenia with frailty and mortality risk in end-stage renal disease

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Both frailty and sarcopenia are highly prevalent in end-stage renal disease (ESRD) and independently associated with mortality, yet the combined mortality risk in these patients is unknown. We assessed the association between sarcopenia and frailty, as well as sarcopenia's ability to predict mortality in adults initiating hemodialysis. We conducted a prospective cohort study on 317 adults initiating hemodialysis. Two reviewers independently performed cross-section measurements of three internal intercostal muscles on abdominal computed tomography scans collected at dialysis initiation. Interrater coefficient of variation was 15%. The cohort was divided based on overall median muscle size and classified as sarcopenic or non-sarcopenic. Frailty was assessed at hemodialysis initiation using Fried's criteria. Association of frailty and sarcopenia was estimated using logistic regression. Cox regression was used to assess association of sarcopenia with all-cause mortality. Median age was 56 years at dialysis initiation with 57% male. Median internal intercostal muscle size was 0.23 [interquartile range: 0.20-0.27] cm, 53% were frail, 30% were sarcopenic and frail, and 71% were African-American. Median follow-up time was 3.6 years. Sarcopenia was associated with 1.68-times increased odds of frailty (95% confidence interval [CI]: 1.07-2.62). The adjusted hazard ratios for all-cause mortality of sarcopenia, frailty, and combined sarcopenia and frailty were 0.93 (95% CI: 0.66-1.32), 1.31 (95% CI: 0.92-1.87) and 1.07 (95% CI: 0.78-1.47), respectively. Sarcopenia was significantly associated with frailty among adults

undergoing hemodialysis. Sarcopenia did not increase risk of mortality beyond that of frailty. Close observation of sarcopenic ESRD adults may be beneficial to prevent further health decline.

Reversibility of marrow fat accumulation in a rat model of knee flexion contractures.

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Bone marrow adipose tissue (MAT) accumulation is a natural process associated with aging and can be accelerated by prolonged immobilization. In a previous study investigating fat deposition in a rat model of immobility-induced knee flexion contractures, we documented fat accumulation in the epiphysis of proximal tibia characterized by hyperplasia of small adipocytes following short periods of immobilization while longer durations of immobilization were characterized by adipocyte hypertrophy. The objective of the current research project was to assess reversibility of adipocyte hyperplasia and hypertrophy after remobilization. Eighty Sprague Dawley rat knee joints were immobilized in flexion with a Delrin® plate at a 135° angle for 1, 2, 4 and 8 weeks. Remobilization was initiated by removing the fixation device and allowing rats four varied periods of unassisted recovery. The contralateral knee and age matched groups were used as controls. Histomorphometric analysis was conducted on hematoxylin and eosin stained sagittal sections of knee joint. Light microscopy techniques and ImageJ software were used to collect data from six fields of view in the epiphysis region of each tibia. Preliminary results showed that adipocyte count increased with increasing immobilization (2, 4 and 8 weeks) and hyperplasia was not reversed following remobilization. Adipocyte hypertrophy was not observed at studied durations of immobilization. Findings from this study provide insight into the lack of reversibility of spontaneous mobility on MAT accumulated during immobilization. These results could provide a rationale for preventing or treating marrow fat accumulation by targeting adipocyte hyperplasia rather than hypertrophy.

Conflicts of Interest

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

Authors' Contributions

MA, MBH, and JM equally contributed to the planning of the research competition, assisted in the collection of abstracts and reviewed the abstract submissions. SM and SP provided support in the selection of abstracts as volunteers to the planning committee.

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