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Journée de la recherche de la Faculté de médecine

Faculty of Medicine Research Day



FACULTY OF MEDICINE RESEARCH DAY

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UOJM: PREFACE

The University of Ottawa Faculty of Medicine was pleased to virtually host the 2021 edition of its annual Research Day on September 24, 2021.

The Faculty of Medicine Research Day was an excellent opportunity for trainees to showcase their outstanding projects covering the full scope of research activities taking place at the Faculty, dans les deux langues, and hone in on their presentation skills. This virtual event also allowed trainees, including graduate and undergraduate students (i.e., TMM students), postdoctoral fellows, medical students, and residents to mingle with trainees outside their specific programs and connect with Faculty members.

This year's keynote speaker is Dr. Kumanan Wilson, a specialist in General Internal Medicine, Professor, Clinical Research Chair in Digital Health Innovation, and CEO and founder of CANImmunize, a science-based technology company specializing in immunization software. He will share his expertise on vaccines and vaccine hesitancy in his talk "Vaccine Wars".

During the workshops participants learned "How to take academic discovery into translation" with panelists Dr. John Bell (Professor, Departments of Medicine and Biochemistry, Microbiology and Immunology and Senior scientist in cancer therapeutics (OHRI), Dr. Chantal Matar (Professor, Department of Cellular and Molecular Medicine) and Dr. Leslie Mitchell (Co-founder and President Neochromosome, Inc.); discovered how to deal with "Misinformation in Research" with panelists Dr. Fatima Tokhmafshan (@DeNovo_Fatima, Research Institute of the McGill University Health Centre) and Dr. Kevin Parent (Social Media Lead at Ottawa Public Health); or how to be "Thriving, not surviving academic life" with panelists Cynthia Abraham and Monica Dobie (Professional Counsellors, Faculty Wellness Program).

Eighteen oral presentations and more than 200 posters have been shared with the research community of the University, in English and French. Among these, 62 abstracts have been published in the present conference proceeding, at the authors' discretion. A scientific committee of evaluators, comprised of faculty members, will review all abstracts and oral presentations to select the winners of the Faculty of Medicine Research Day Awards for best poster and best oral presentation. The winners will receive their awards during the Faculty of Medicine Gala on October 2nd, 2021.

We invite you to peruse this special issue of the University of Ottawa Journal of Medicine that highlights the amazing research conducted at the Faculty of Medicine!

The Organizing Committee
University of Ottawa Faculty of Medicine

JMUO: PRÉFACE

La Faculté de médecine de l'Université d'Ottawa était heureuse d'accueillir virtuellement l'édition 2021 de sa Journée de la recherche annuelle, le 24 septembre 2021.

La Journée de la recherche de la Faculté de médecine était une excellente occasion pour les apprenants de présenter leurs projets exceptionnels couvrant l'ensemble des activités de recherche de la Faculté, in both official languages, et de perfectionner leurs compétences en matière de présentation. Cet événement virtuel permettait également aux stagiaires, y compris les étudiants de premier et de deuxième cycle, les boursiers postdoctoraux, les étudiants en médecine et les résidents, de se mêler aux apprenants qui ne font pas partie de leur programme spécifique et d'entrer en contact avec les membres de la Faculté.

Le conférencier principal de cette année était le Dr Kumanan Wilson, spécialiste en médecine interne générale, professeur, titulaire de la chaire de recherche clinique sur l'innovation en santé numérique, et PDG et fondateur de CANImmune, une entreprise scientifique de technologie spécialisée dans les logiciels de vaccination. Il partageait son expertise sur les vaccins et l'hésitation vaccinale dans sa conférence "Vaccine Wars".

Au cours des ateliers, les participants ont pu apprendre "Comment faire passer les découvertes universitaires à l'étape de la traduction" avec les panélistes Dr John Bell (professeur, départements de médecine et de biochimie, de microbiologie et d'immunologie et chercheur principal en thérapeutique du cancer (IRHO)), Dre Chantal Matar (professeure, département de médecine cellulaire et moléculaire) et Dre Leslie Mitchell (cofondatrice et présidente de Neochromosome, Inc.); à découvrir comment faire face à la "désinformation dans la recherche" avec les panélistes Dr Fatima Tokhmafshan (@DeNovo_Fatima, Institut de recherche du Centre universitaire de santé McGill) et Dr Kevin Parent (responsable des médias sociaux à Santé publique Ottawa); ou encore à "Prosperer et non survivre à la vie universitaire" avec les panélistes Cynthia Abraham et Monica Dobie (conseillères professionnelles, Programme de promotion de la santé à la Faculté).

Dix-huit présentations orales et plus de 200 affiches ont été partagées avec la communauté scientifique de l'Université, en anglais et en français. Les résumés de 62 des projets de recherche présentés ont été publiés dans le présent compte rendu de la conférence, à la discrétion des auteurs. Un comité scientifique d'évaluateurs, composé de membres de la faculté, a examiné tous les résumés et les présentations orales afin de sélectionner les lauréats des prix de la meilleure affiche et meilleure présentation orale de la Journée de la recherche de la Faculté de médecine. Les lauréats recevront leur prix lors du Gala de la Faculté de médecine le 2 octobre 2021.

Nous vous invitons à parcourir ce numéro spécial du Journal de médecine de l'Université d'Ottawa qui met en lumière les recherches étonnantes menées à la Faculté de médecine!

Le comité d'organisation
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Prefrontal cortex network and serotonin dynamics in a novel attentional set-shifting task

Abu Sheikh, M.^{1,2,3}, Maillé, S.^{1,2}, Hsieh, J.^{1,2,3}, Fraser, A.², Gottardi, A.^{1,2,3}, Mulatz, K.^{1,2} BÉique, JC.^{1,2}

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ABSTRACT

Animals need to flexibly adapt their behaviors in dynamically evolving environments. Deficits in behavioral flexibility are associated with psychiatric disorders including schizophrenia and autism. Previous studies have outlined a role for the prefrontal cortex (mPFC) and the midbrain serotonin (5-HT) system in the neural implementation of behavioral flexibility, yet the underlying cellular mechanisms remain poorly understood. We therefore sought to develop a novel attentional set-shifting paradigm that is amenable to multiphoton cellular and network imaging in behaving head-fixed mice. Mice were trained to associate discriminable auditory cues with rewarded behaviors. Auditory cues differed across two dimensions: 1) tone frequency and, 2) location in the azimuth plane; mice learned the relevant (i.e., instructive) dimension through experience. After training, tone-action contingencies were switched, and the resulting adaptation behavior was monitored. Using implantable lenses and genetically encoded calcium indicators, task-related mPFC neuron activity was monitored by multiphoton imaging. Further, a novel optical 5-HT sensor is developed for in vivo imaging of task-related prefrontal 5-HT dynamics. These approaches will allow a detailed analysis of neuronal activity and 5-HT release in mPFC during flexible adaptation to dynamically evolving environments. A deeper understanding of the neural mechanisms underlying behavioral flexibility could provide a framework to improve therapeutic strategies for several psychiatric disorders.

Use of kneeling as a child disciplinary practice by Haitian caregivers

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²Department of Psychiatry & Mathison Centre for Mental Health Research and Education, University of Calgary

ABSTRACT

Background: Use of physical discipline is related to poorer child outcomes. Studies of physical discipline often focus on spanking and overlook non-hitting forms of physical discipline. Kneeling may be an important example but little is known about its use. This study compares the pattern of use of kneeling and spanking by parents in Haiti. **Methods:** Data from the 2016 Demographic and Health Survey from Haiti were used. This survey, composed of a nationally representative sample of households, asked caregivers about use of a standardized set of disciplinary practices on their children 1-14 years of age (n=6004). **Results:** The distribution of the two disciplinary practices differed significantly by child age with spanking more commonly applied to younger children and kneeling more commonly applied to older children, with the latter including 58.1% and 51.5% of children age 5-9 and 10-14 years of age, respectively. The only socio-economic and demographic variables related to exclusive use of kneeling compared to spanking were lower levels of education and older age of the head-of-households, however, this was only found in bivariate analysis. In a multivariate model, only child age remained significantly related to exclusive use of kneeling compared to spanking. **Conclusions:** Given socio-economic and demographic similarities, approaches aimed at reducing reliance on spanking may have relevance for targeting kneeling, however, further study is needed in Haiti and other countries to understand parents' rationale for its use and its impact on children.

Examining the impact of the COVID-19 pandemic on mental health service needs of medical residents

Burhunduli, P.¹, Nikolitch, K.^{1,2}, Sani, M.², Shariati, K.², Carefoot, E.², Saad, M.³, Owsia, K.¹, Talbot, J.^{1,2}, Wiesenfeld, L.⁴, Spilg, E.⁵, Kendzerska, T.⁵, Robillard, R.^{1,3}, Phillips, J.L.^{1,2}

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ABSTRACT

The COVID-19 pandemic has increased demands on medical workers around the globe. Physicians working on the frontlines are at risk of poor mental health outcomes and residents are especially vulnerable through their status as both physicians and learners. This study examined the impact of the pandemic on the mental health service needs of Canadian medical residents. Data was derived from a cross-sectional online survey completed between April 23, 2020, and March 17, 2021. Preliminary descriptive statistics were used to examine psychosocial characteristics. In total, 111 Canadian medical residents (mean age 30, 79.8% female) from 29 specialties completed the survey. Most residents were from Ontario (70.0%) with representation across all levels of training. Over half (56.7%) reported in-person contact with COVID-19 positive patients. Mental health service needs were assessed in a subsample of 51 residents. Within this sample, 32.0% had a current psychiatric diagnosis and 74.5% had worsening mental health symptoms since the onset of the pandemic. Twenty-six residents considered accessing mental health services during the pandemic with more women actively seeking care compared to men ($p=0.034$). Reported reasons for hesitancy to seek mental health services included concerns about confidentiality, stigma and time constraints. While the pandemic is exacerbating existing mental health risks for residents, our findings highlight the importance of addressing medical culture-related barriers to accessing care to ensure mitigation of the impact of the pandemic on resident mental health.

A novel behavioral paradigm to assess learning under uncertainty in a mouse model of autism

Hsieh, W.Z.^{1,2,3}, Maille, S.^{1,2}, Fraser, A.¹, Gottardi, A.^{1,2,3}, Abu Sheikh, M.^{1,2,3}, Mulatz, K.^{1,2}, Beique, J.C.^{1,2}

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ABSTRACT

Autism Spectrum Disorder (ASD) is a developmental disorder characterized by a cluster of traits including cognitive deficits, repetitive behaviors, and difficulties in navigating social and novel settings. Despite a growing understanding of underlying mechanisms, the common etiology of these seemingly unrelated traits remains unclear. Recently, this problem has been approached using a predictive coding framework, in which the brain uses an internal model to generate predictions about future states of the environment. Prediction errors (PEs; i.e., discrepancies between predictions and sensory stimuli) are used to update the model. In probabilistic settings, predictive power is constrained, and PEs must be triaged based on whether they reflect salient shifts (relevant PEs) or statistical noise (irrelevant PEs) in the environment. One predictive coding account, termed the High, Inflexible Precision of Prediction Errors in Autism (HIPPEA) theory, posits that the primary deficit in ASD is a failure to distinguish between relevant and irrelevant PEs. Here, we developed a novel behavioral paradigm to test key predictions of this theory in a mouse model of ASD. We trained mice to associate audio cues with rewarded actions in an operant conditioning task with probabilistic feedback. Following training, we shifted cue-action contingencies and monitored animals' ability to adapt to these shifts under uncertainty. With this work, we endeavor to experimentally validate the HIPPEA model and improve our understanding of the etiology of ASD; this could lead to novel management strategies.

Profiling lipopolysaccharide-induced neuroinflammation and anxiety- and depressive-like behaviours

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ABSTRACT

Depression and anxiety are a growing concern in Canada, and these are associated with changes in the gut-brain axis (GBA), leading to enhanced neuroinflammation. Therefore, interventions that can attenuate neuroinflammation may play a role in the treatment of mental illnesses. The aim of this study was to establish a mouse model of neuroinflammation that can be utilized to screen dietary interventions for their anti-inflammatory effects leading to reduced anxiety and depression. C57Bl/6 male mice, 6-8 weeks old, were treated with 1mg/kg BW LPS or saline control (n=12/group) by intraperitoneal injection. Sickness behaviours were monitored for 24 hours, after which anxiety/depressive-like behaviours were assessed. All mice were euthanized 48 hours post-injection and brain tissue was isolated for biomarkers of inflammation. Mice treated with LPS showed reduced diet intake, body weight and increased sickness behaviours. Furthermore, LPS induced an increase in the expression of IL-1 β in the medial prefrontal cortex and hippocampus (P<0.05). Despite evidence of LPS-induced neuroinflammation, there were no significant differences observed in anxiety-like (e.g. open field test) or depressive-like behaviours (e.g. splash test). Further involvement of the GBA in LPS-induced neuroinflammation is on-going (e.g. microbial dysbiosis). Thus far, we have validated a model of acute neuroinflammation that will be used for the assessment of the anti-inflammatory effects of dietary interventions, however this model may not be sensitive enough to observe behaviour changes.

Characteristics and CT head findings of TBI patients on antiplatelet or anticoagulant therapy

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ABSTRACT

Traumatic brain injury (TBI) is a major health problem with an annual incidence of 69 million. Increasing number of patients are on anticoagulant or antiplatelet therapy, with an unclear impact on the risk conferred by these medications. This study aims to determine the epidemiology of these patients, as well as preliminary CT head findings in this cohort. This was a retrospective chart review of patients with trauma receiving a head CT in Ottawa hospitals between January 1, 2015 and October 31, 2020. We collected a total of 460 patients, with a mean age of 80.9 + 11 years (231 women, 229 men). Apixaban (48%) was the most frequent medication, then ASA (19%) and warfarin (15%). The most common comorbidities were cardiovascular disorders (86%) and hypertension (70%). The most frequent traumatic etiology was a fall from height (39.7%), followed by an unwitnessed or unclear mechanism (36.9%). Most patients undergoing initial CT (94.3%) had no acute intracranial findings. Of those with acute findings (5.7%), subarachnoid hemorrhage (3%) was the most frequent, then subdural hematoma (2.3%). Of these patients, 56% lacked loss of consciousness and 37% had only mild trauma. Our study identified a greater incidence of TBI than in similar studies. However, de-novo intracranial findings were still rare in our cohort even in those with lesions above the clavicle and there was no clear correlation between severity of CT findings and clinical findings.

Assessing different lipopolysaccharide doses on neuroinflammation & mental health behaviors in mice

Rodrigue, A.F.¹, Livingston, D.¹, Sweet, A.¹, Freije, G.¹, Mahmoodianfard, S.², Kishore, L.², Power, K, A.^{1,2}

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ABSTRACT

Lipopolysaccharide (LPS) is a bacterial endotoxin commonly administered to mice to induce neuroinflammation and a complex range of behaviors, including decreased locomotor activity and exploratory behavior. A number of these symptoms are similar to clinically relevant indicators of depression/anxiety disorders in humans. A single intraperitoneal (I.P.) injection of LPS in mice can thus be used to model neuroinflammation driven anxiety- and depressive-like behaviours, however the dose, housing conditions and strain of mice varies between studies. The purpose of this study is to validate the dose of LPS needed to produce neuroinflammation and resulting anxiety- and depressive-like behaviour in mice. 6–8-week-old C57Bl/6 male mice were single-housed and acclimatized on a basal diet (AIN-93G) for 2-weeks before receiving an I.P. injection (0.5 or 1.0 mg/kg BW) of LPS to induce neuroinflammation and resulting depressive-like (measured by tail suspension test, TST) and anxiety-like (measured by elevated-plus maze, EPM) behaviours before brain and spleen were collected. Mice receiving either dose of LPS displayed increased systemic inflammation, indicated by splenomegaly, and increased neuroinflammation, indicated by elevated brain TNF- α at the gene and protein level. LPS treated mice exhibited increased anxiety-like behaviour (decreased distance moved in EPM), but results for TST were inconclusive. Overall, both doses of LPS assessed are suitable to induce systemic and neuroinflammation, however study-design modification is necessary to see increased depressive-like behaviours.

Methamphetamine use disorder goals and treatments: Defining a clinical pathway (quality improvement)

Boersma, M.¹, Cahill, T.², Binch, J.², Partridge, S.²

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ABSTRACT

Objective: As medical and harm reduction communities have worked hard to cope with and provide treatments for the opioid epidemic that has gripped much of Canada, the treatment options for stimulant use disorder (SUD)—especially methamphetamine (MA) use—has failed to see the same development of treatment options. This project aims to examine both the literature and the charts of patients at the Oasis Clinic in order to better understand the patient population and treatment options for people who use MA. Methods: A literature review was conducted using OVID MEDLINE. A subsequent chart review of n=100 patients of Oasis Clinic who have MA-SUD to better understand the population in Ottawa, ON. Descriptive statistics were run. Results: The review of the literature showed that there are certain predictive factors for patients with SUD, that ADHD and SUD can represent a challenge that should be addressed early on with proper ADHD diagnosis and treatment in adolescence, and that pharmacological treatments remain elusive for MA-SUD while certain psychosocial interventions have proven helpful. The chart review yielded certain areas in which SUD can be addressed more holistically, including a checklist approach for patients who present to clinic with MA-SUD. Conclusions: Adequate treatment of MA-SUD remains a challenge for clinicians. There are certain subpopulations that could benefit from specific care, and by developing a checklist for patient who present with MA-SUD, clinics may be better equipped to care for these patients.

Using electronic consultation data to identify frailty in provider-to-provider communication

Hakimjavadi R.^{1,2}, Karunanathan, S.^{2,4}, Fung, C.^{3,5}, Levi, C.⁶, Helmer-Smith, M.⁷, LaPlante, J.⁸, Gazarin, M.⁹, Rahgozar, A.³, Afkham, A.¹⁰, Keely, E.¹¹, Liddy, C.^{2,3}

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ABSTRACT

Frailty is a complex, multifactorial condition that increases vulnerability to a precipitous decline in health, particularly if left unrecognized. The early identification of frailty is important for improving health outcomes for patients. The use of electronic consultation (eConsult), a secure web-based asynchronous referral platform connecting primary care providers (PCPs) to specialists, has generated a rich source of data containing provider-to-provider communication. Patient-specific language captured on this platform can be used to study frailty and provide the basis for the early identification of this condition in primary care. We aim to determine whether eConsult communication logs between PCPs and specialists can be used to identify patients with frailty. We reviewed the pertinent literature and consulted with clinicians, researchers, and caregivers to compile a list of frailty-related terms. Communication logs from all eConsults in 2019, submitted to the Champlain BASE eConsult Service on behalf of long-term care residents or community-dwelling older adults, were examined to search for frailty-related terms and determine the frequency of their occurrence. The frequencies and percentages of frailty-related terms identified in eConsult communication logs will be reported for LTC cases and community cases (available by September 2021). The identification of frailty through eConsult will offer opportunities to recommend early access to interventions and resources in the primary care setting that may slow progression and reduce adverse outcomes related to frailty.

Risk of prematurity from frozen versus fresh embryos: A population-level study from Ontario, Canada

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ABSTRACT

Motivation and Background: There is limited evidence on the proportion of premature births from pregnancies conceived through assisted reproductive technology (ART) in Canada. Prematurity results in increased childhood morbidities, hospitalizations and caregiver burden. It is also associated with substantial costs to Canadian hospitals. The objective of our study is to evaluate the risk of prematurity between two common methods of ART, fresh embryo transfer (fresh ET) and frozen embryo transfer (FET), compared to naturally conceived pregnancies in Ontario. **Methods:** Large-scale retrospective population-based cohort study using data from the Better Outcomes and Registry Network (BORN). All women who gave birth at a hospital centre in Ontario for whom BORN contains data were included. The data captures ART births from 2013-2016, and non-ART births from 2013-2017. The primary outcome measure was premature births (<37 weeks of gestation). **Results:** There were 525,684 natural cycles, 4,684 cycles of FET and 3,619 cycles of fresh ET resulting in singleton births. The proportion of premature births are 6.6% (95% CI: 6.5-6.7) for natural conception, 9.9% (95% CI: 9.1-10.8) for FET, and 10.7% (95% CI: 9.8-11.8) for fresh ET. **Conclusions:** FET and fresh ET are collectively associated with a higher proportion of premature births compared to natural conception. Our study will help Canadian obstetricians counsel their patients about prematurity risks. The future direction is to include multiple gestations in the outcome analysis.

The tuberculosis patient care pathway in Nunavut, Canada

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ABSTRACT

Canada has a low incidence of tuberculosis (TB) however, its burden disproportionately affects Indigenous populations. In Nunavut, TB incidence rates are 300 times higher than Canadian born non-Indigenous people. Although advances have been made in TB care, it is unknown whether these new measures are more effective. Understanding the epidemiological impact of these methods in reducing TB incidence across Nunavut will provide key information for decision makers. In preparation for model development, the full Nunavut TB care pathway (screening, diagnosis and treatment of latent TB infection and active TB) was mapped using data from the Nunavut TB Program. A TB assessment may be done to identify LTBI/ATB or to document TB status anytime (employment or school screening, TB surveillance). A systematic process is used to ensure all appropriate screening tests are performed based on patient's health history and TB risk-factors. If there are any signs/symptoms, appropriate airborne precautions are implemented before any clinical investigations. Once ATB is diagnosed, a contact investigation is initiated; anyone exposed is categorized based on exposure level and screened accordingly. In Nunavut, all TB patients are treated with directly observed therapy. With risk of non-adherence due to length of treatment and side effects, key messages of support and curability are reinforced. Critical monthly assessments are done to monitor the patient throughout treatment. Understanding the complexity of TB care will provide insight on how to better represent the situation in Nunavut.

The Ottawa Marginalization Index: An adaptation of ON-Marg to quantify marginalization in Ottawa, ON

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ABSTRACT

The Ontario Marginalization Index (ON-Marg) provides a comprehensive tool to quantify marginalization in Ontario but relies on census geographies that may not reflect natural neighbourhoods for accurate public health planning. This study provides an adaptation of this index for Ottawa, ON (named the Ottawa Marginalization Index, OTT-Marg) using previously delineated "natural" neighbourhoods from the Ottawa Neighbourhood Study for more accurate evaluation of marginalization and health outcomes and as a proof of concept for other cities. As per publicly available methodology and communication with ON-Marg developers, the same 18 indicators from the 2016 Canadian Census of Population were extracted for 103 custom geographies in Ottawa. Principal Components Analysis was used to extract four dimensions of OTT-Marg. Factor scores were converted into quintiles with higher quintile scores reflecting a higher degree of marginalization, and an OTT-Marg summary score reflects an average quintile score. Two of 18 indicators loading in different components in OTT-Marg from ON-Marg, allowing similar interpretation of the four marginalization dimensions (residential instability, material deprivation, ethnic concentration and dependency). Differences in amount of variance explained by each dimension reflects differences in Ottawa-specific marginalization from Ontario. The four OTT-Marg dimensions and summary score provide a more relevant, natural measure of neighbourhood-level marginalization in Ottawa, to now be used to evaluate healthcare access and outcomes.

Development of an oral vaccine through agroinfiltration of SARS-CoV2 spike protein subunit in plants

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ABSTRACT

One of the major challenges arising from the COVID-19 pandemic is the engineering of a safe, efficient and convenient vaccine to limit the global spread of the virus. In this project, we attempt to provide a solution through the development of a plant-based orally-administered vaccine. The advantages associated with this vaccine type include but are not limited to: a lower manufacturing time and cost, an easier and efficient administration method not requiring trained personnel, and most importantly: a reliable method of generating mucosal immunity without additional risks of disease spread. Through agroinfiltration into edible plants – such as lettuce and tomato – of GV3103 bacterial strains containing a plasmid coding for the Receptor Binding Domain (RBD) subunit of the SARS-CoV2 spike protein, the inserted gene allows for the transgenic plant to produce the desired recombinant protein. Once extracted, this protein can act as an antigen in the development of an ingestible vaccine capable of generating mucosal immunity. Here, we show through Western blots that the recombinant protein is successfully being expressed in edible plant tissues from lettuce through agroinfiltration. Agroinfiltration in tomato plants was unsuccessful in comparison to control agroinfiltrations in *N. benthamiana*, making this a weak contender for the project. As a result, this provides supporting evidence into the use of certain edible plants in the development of an oral vaccine capable of generating both cellular and humoral immunity.

Development of a CRISPR/Cas9 knockout model of riboflavin transporter deficiency in zebrafish

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ABSTRACT

Introduction: Riboflavin transporter deficiency (RTD) is a rare and progressive neuronopathy with severe sensorimotor and cranial implications. RTD is caused by biallelic mutations in SLC52A2 and/or SLC52A3, encoding RFVT2 and RFVT3, respectively. The primary treatment for RTD patients is high-dose riboflavin supplementation. However, due to the rapid elimination of riboflavin from the body, an alternative or supplemental therapy is needed. **Aim:** To utilize the cost-effectiveness, fecundity, and simplicity of zebrafish models to develop slc52a2 and/or slc52a3 knockouts and use this model to screen for promising therapies. **Methods:** We will generate a CRISPR/Cas9 model of RTD and screen for human RTD-like phenotypes using behavioural and morphological assays including assessment of muscle morphology and riboflavin status. We will then test the ability of riboflavin, probenecid, and antioxidants to improve knockout phenotypes. **Results:** We are testing gRNAs to find efficient targets for producing Cas9-mediated deletions and we have optimized detection of slc52a2/3 via reverse transcriptase PCR. We have also established appropriate behavioural and morphological assays that will allow characterization of RTD-like phenotypes in zebrafish, and toxicity testing of candidate drugs is ongoing in HEK-293T cells and wild-type zebrafish. **Conclusion:** Current models have not been able to comprehensively model the human RTD phenotype. Therefore, a CRISPR/Cas9 model of RTD in zebrafish may help to brighten the future for RTD patients by bringing light to potentially beneficial treatments.

Investigating the role of apoptosis inhibitor of macrophages on promoting necroptosis in foam cells

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ABSTRACT

Necroptosis is a pro-inflammatory mode of cell death dictated by a cell signaling pathway involving the phosphorylation of necrosome components RIPK1, RIPK3 and MLKL. Activated necroptosis leads to cell lysis and during atherosclerosis lead to the development of the necrotic core. Atherosclerosis is a chronic lipid-driven, maladaptive, and non-resolving inflammatory disease of the vessel wall. Macrophage foam cells play a critical role in the development of atherosclerosis. During the late stages of atherosclerosis, foam cells undergo non-apoptotic modes of cell death through necroptosis. In advanced atherosclerotic plaques, macrophage death contributes centrally to the formation of plaque necrosis and necrotic core. Given the previously established transition of macrophage foam cells from apoptosis to necroptosis, and the role of CD5L/AIM on inhibiting apoptosis, we hypothesize that endogenous induction of CD5L in foam cells promotes necroptosis. Using bone marrow-derived macrophages from mice, we first optimized CD5L knockdown using siRNA, and confirmed with qPCR and western blotting. Next, we evaluated the colocalization of CD5L with the marker of active necroptosis (phosphorylated MLKL) in atherosclerotic plaques. Future studies in vitro will focus on assessing whether CD5L knockdown promotes necroptotic cell death as assessed by LDH assay and western blotting. We will also look to explore the relationship between CD5L and necroptosis in vivo by immunofluorescence staining of atherosclerotic plaques from early and late stages.

Developing and characterizing GFPT1-deficient models to mimic the pathology of CMS

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ABSTRACT

Congenital Myasthenic Syndromes (CMS) are a group of early-onset genetic neuromuscular disorders that result from mutations to proteins that are associated with neuromuscular junction (NMJ) function, maintenance, and organization. Glutamine-fructose-6-phosphate transaminase 1 (GFPT1) is the rate limiting enzyme of the hexosamine biosynthetic pathway (HBP), a metabolic signalling pathway which produces the necessary precursor, uridine diphosphate N-acetyl-glucosamine (UDP-GlcNAc), required for N- and O-linked protein glycosylation. Biallelic mutations to GFPT1 in CMS reduces GFPT1 protein expression and enzymatic activity. We hypothesize that a functional impairment in GFPT1 causes a hypo-glycosylation environment at the NMJ resulting in dysfunction to proteins involved in neurotransmission and NMJ maintenance. To test this hypothesis, we aim to develop in vitro and in vivo models of GFPT1 deficiency. Our group previously developed a skeletal muscle-specific GFPT1 knockout mouse model using Cre-LoxP (termed, GFPT1^{tm1d/tm1d}). To characterize the long-term effects of GFPT1 skeletal muscle knockout, a 40-week time course was performed. GFPT1^{tm1d/tm1d} mice exhibited increased muscular fatigue and decreased endurance following grip strength and inverted hanging wire tests, respectively. GFPT1^{tm1d/tm1d} mice exhibited increased fat gain and decreased total activity. Whole muscle mounts of TA, sol and diaphragm stained for NMJs exhibited fragmentation and poor post-synaptic folding. In conclusion the GFPT1^{tm1d/tm1d} exhibit progressive muscle weakness mimicking CMS patients.

Characterization of the cysteine desulfurase SufS related to Crohn's disease

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ABSTRACT

Inflammatory Bowel Disease (IBD) is becoming a growing concern as its burden rapidly increases worldwide. Crohn's disease (CD) is a type of IBD described as a chronic condition with excessive inflammation of the gastrointestinal tract. Current treatments available to CD patients only manage symptoms and prevent its progression. The causality of CD remains debated, however evidence suggests microbial dysbiosis can provoke chronic inflammation in CD patients. Recently, the genera *Atopobium* has been identified as a key microbial producer linked to gut inflammation and CD pathogenesis through the production of H₂S. The *Atopobium* genera contributes to the production of H₂S in the gastrointestinal microbiome through the expression of the cysteine desulfurase SufS. However, the molecular underpinnings of *Atopobium parvulum* SufS (ApSufS) catalysis has yet to be characterized. Using X-ray crystallography, we solved the ApSufS structure and determined that it shares a similar structure to other cysteine desulfurases, where the cofactor pyridoxal-L-phosphate (PLP) forms an aldimine with residue K235. Structure-activity studies reveal H132 forms critical contacts with PLP to help facilitate catalysis, and C375 is required for efficient turnover of ApSufS. Furthermore, a segment of short-chain amino acids is integral to allow for the binding of the cysteine substrate to the enzyme. Investigating the molecular basis surrounding ApSufS function will enable us to analyze a new target for the development of a specific IBD treatment.

How developing mouse oocytes and preimplantation embryos regulate intracellular betaine

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ABSTRACT

Mammalian oocytes and preimplantation embryos are sensitive to extracellular changes in their environment. Cell volume dysregulation impairs maturation in oocytes and induces developmental arrest in preimplantation (PI) embryos. Mouse oocytes and PI embryos utilize a unique mechanism to control cell volume in which organic osmolytes such as betaine are transported into the cell. Significant levels of betaine accumulate in oocytes during meiotic maturation via de novo synthesis by choline dehydrogenase. The origin of betaine in immature germinal vesicle oocytes is a key knowledge gap in mouse oocyte and embryo physiology. Betaine uptake may occur via the γ -LAT2 transporter in follicular somatic cells that are coupled to the oocyte via gap junctions. Endogenous betaine levels will be measured in early oocytes and saturable betaine transport will be measured in follicles. Betaine serves a second role as a methyl donor in blastocysts. Preliminary embryonic DNA methylation patterns that regulate embryo and fetal development are established in the inner cell mass of the blastocyst. The universal methyl donor S-adenosylmethionine (SAM) is utilized by methyltransferases for epigenetic modifications. Significant levels of SAM can be produced from betaine homocysteine methyltransferase (BHMT). Methionine is subsequently converted to SAM. The concentration of intracellular betaine decreases at the blastocyst stage which may be a result of betaine metabolism by BHMT. Endogenous betaine levels will be measured in blastocysts collected from *Bhmt*^{+/+} and *Bhmt*^{-/-} mice, and in blastocysts exposed to a BHMT inhibitor. This project aims to elucidate the mechanisms of intracellular betaine regulation in mouse oocytes and PI embryos.

Molecular and cellular mapping of the postnatal cardiac atrioventricular conduction system

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ABSTRACT

BACKGROUND: The atrioventricular conduction system (AVCS), making up <0.05% of the heart, is a network of specialized cardiomyocytes responsible for coordinated spreading of electrical impulses throughout the heart for synchronized contractions. The AVCS is composed of the AV node (AVN), which delays the electrical signal between atria and ventricles, and the ventricular conduction system (VCS), which rapidly propagates the signal throughout the ventricles. Although these structures were anatomically discovered >100 years ago, their molecular constituents largely remain undefined. **METHODS:** 6855 AVCS cells were isolated and purified from early postnatal fluorescent reporter mouse hearts and were subjected to single-cell RNA-seq. **RESULTS:** Unbiased cluster analysis showed distinct transcriptomic profiles in the AVN, proximal-VCS (His bundle and bundle branches), distal-VCS (Purkinje fibers) as well as a novel cluster of proliferating AVCS cells. Using established markers, such as *Irx3* in the VCS and *Tbx3* in the proximal-AVCS, we identified novel markers of AVN (*Sln*), proximal-VCS (*Lyz2*, *Sfrp5*, *Rspo3*, *Pcp4*) and distal-VCS (*Psd3*). Moreover, we revealed a potential region-specific gene regulatory interaction between transcription factors, *Irx3* and *Tbx3*, mediating their downstream targets, *Gja1* and *Gja5*. Importantly, we recapitulated this observation in cultured neonatal mouse atrial and ventricular myocytes overexpressing *Irx3* and/or *Tbx3*. **CONCLUSION:** Our study provides a comprehensive and high-resolution map of the molecular heterogeneity within the postnatal AVCS in mice.

Homology modelling of ATP10A, ATP10D, Dnf1, and Neo1 using UCSF Modeller

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ABSTRACT

Type-IV ATPases, or P4 ATPases are essential membrane proteins in maintaining lipid homeostasis of living organisms. The objective of this study is to exploit the homology modelling approach and investigate the predicted conformational changes of four novel members of P4-ATPases. UCSF Modeller was used to generate theoretical models of four P4-ATPase homologues (ATP10A, ATP10D, Dnf1, and Neo1). The models were visualized using Pymol. To generate homology models, multiple sequence alignments were performed using bioinformatic approaches, followed by in silico simulation of each P4-ATPase homolog. The best models were selected based on the lowest energy score out of 100 simulated models. The results of this study will be used in the future as theoretical models in comparison with the experimental data by either X-ray crystallography or cryo-electron microscopy. Ultimately, the study aims to elucidate the structure-function relationship of the P4-ATPase phospholipid transporters.

Transcriptomic evaluation of the translatability of new treatments in triple-negative breast cancer

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ABSTRACT

Objective: This study will evaluate the potential of four recently proposed TNBC treatments—which all successfully reduced tumor viability in vitro and/or in vivo—to inhibit genes involved in CSC survival and metastatic metabolomic signature. **Methods:** TNBC cell lines and/or patient-derived xenografts were treated with four different treatments: DCC-2036, 9Gy proton irradiation, miR302b+cisplatin combination, and DFX+doxorubicin combination. Genome-wide mRNA profiling was performed on control and treated groups. We assessed the differential expression of genes associated with CSC growth and metastatic metabolomic signature in TNBC tumors. **Results:** DCC-2036 treatment significantly induced the expression of CSC markers and genes associated with the metastatic metabolomic signature. DCC-2036 showed inconsistent effects on the expression of immunosuppressive markers. 9Gy proton irradiation has mixed effects on the expression of our candidate genes, yet mostly induced the expression of stemness and metastasis markers. Both miR302b and DFX dual-therapy both failed to inhibit the candidate genes, yet without significantly inducing their expression. GSEA analysis confirmed the results obtained for all four treatments. **Conclusions:** Observing cancer rebound in TNBC patients after treatment with traditional cancer drugs is common and often happens when treatments fail to inhibit CSC growth and metabolic pathways associated with metastasis. All four treatments failed to significantly impact the expression of these pathways and will likely not display very positive effects in the clinic.

Unravelling the role of RNAs in RIPK1-mediated necroptosis

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ABSTRACT

With the high burden of atherosclerosis worldwide exists an urgent need to understand its underlying molecular mechanisms. Receptor-interacting protein kinase 1 (RIPK1) is a critical mediator of necroptosis, a programmed form of necrosis that activates within unstable atherosclerotic plaques. Because details on the post-transcriptional control of RIPK1 are unclear, we aim to fill this gap by studying Ripk1 expression in mouse macrophages undergoing inflammation and cell death. Guided by RNA structure prediction software, we designed antisense oligonucleotides (ASOs) and validated their capacity to bind Ripk1 mRNA with RNase H cleavage assays. RNA pull-down assays with biotinylated ASOs were subsequently performed to capture Ripk1 mRNA. RT-qPCR and droplet digital PCR were used to analyze Ripk1 and Tnfa expression, while LDH release assays assessed cell viability following treatments. We saw significant cell death and Ripk1 upregulation when macrophages were induced with TNF- α and pan-caspase inhibitor zVAD.fmk for six hours, and these effects further increased after ten hours. Custom ASOs were confirmed to attach to Ripk1 mRNA upon observing less qPCR detection in samples combined with ASOs and RNase H. Ripk1 expression was markedly higher in samples pulled down with these biotinylated ASOs compared to the scrambled control, which encourages us to proceed with RNA sequencing to reveal and examine key non-coding RNAs interacting with Ripk1. New insights into RIPK1 regulation during necroptosis may eventually lead to the development of targeted therapies for atherosclerosis.

Histological characterization of knee flexion contractures in patients with osteoarthritis

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ABSTRACT

Motivation: Patients with knee osteoarthritis (OA) often present with the inability to fully extend the knee [termed flexion contracture (FC)], associated with worse outcomes. Previous work using small sample sizes has suggested the posterior capsule contributes to FC due to excess stiff collagenous tissue. Using a larger sample size, we histologically characterized the tissue composition (collagenous, synovium, adipose, other) of the posterior knee capsules of patients with end-stage OA, comparing those with, to those without FC. Methods: Knee capsule tissue obtained during knee replacement (n=40 FC, 39 no FC) was embedded in paraffin and sections stained with Masson Trichrome. Collagenous, synovial, adipose, and "other" tissues were determined from digital images. Anterior knee capsule samples served as controls. Results: No difference in the proportion of collagenous (% FC vs % No FC), synovial (% FC vs % No FC), adipose (% FC vs % No FC), or other (% FC vs % No FC; all P>0.05) tissue were observed between patients presenting with versus without KFC. There was a greater proportion of collagenous and lower proportion of adipose tissue in posterior (77.50% ± 2.60% , 15.01% ± 2.44%) versus anterior (57.49% ± 3.56% , 31.44% ± 3.58%) capsule (both P <.01). Conclusion: The proportion of collagenous posterior capsule could not explain the lost knee extension in our FC group. Future research evaluating the contribution of other posterior capsule elements, such as collagen density, as well as non-capsular OA-associated structural changes in OA-associated FC is necessary.

Quantitative assessment of the cryopreservation properties of betaine

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ABSTRACT

The ability to decrease ice growth and recrystallization has become a crucial aspect of cryopreserving biological specimens, such as cells and tissues, for cell-based therapeutics. However, current cryopreservation protocols remain suboptimal and result in loss of cell viability due to cellular damage related to the freezing and thawing process. The use of cryoprotective agents has been effective in increasing post-thaw recoveries and functionality in appropriate models, yet many of these compounds are toxic to cells, preventing their clinical application. Betaine is an organic molecule that has been claimed to function as a cryoprotectant due to its physiological role in the body as an osmolyte. Therefore, the goal of this study was to assess the cryopreservation properties of betaine. Dose response curves obtained from splat cooling assays indicated that betaine could reduce ice crystal growth at concentrations above 200mg/mL but could not completely prevent ice recrystallization. Furthermore, the half maximal inhibitory concentration (IC50) was found to be between 119.9mg/mL and 226.4mg/mL, which is not comparable to cryo-additives used in current cryoprotective protocols. In vitro cytotoxicity studies performed indicated biocompatibility up to 10mg/mL. In summary, our quantitative assessment suggests that the cryoprotective properties of betaine are not sufficient for its use as a cryoprotectant alone. Future directions include assessing the post-thaw viability of betaine and its cryoprotective abilities when combined with another cryoprotectant-like compound.

Improving protein quantification using real-time analysis of MS-based proteomics data

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ABSTRACT

Mass- Spectrometry (MS)-based proteomics can identify and quantify proteins in complex biological samples. Protein differential expression analysis between samples from different experimental conditions can even be accomplished through sample multiplexing using chemical labeling like Tandem Mass Tags (TMT) coupled with MS. However, current approaches do not have the sensitivity to assess the level of differential expression of all proteins in samples. MS methods tend to focus their data collection on the most abundant proteins, collecting large amounts of data for such proteins, leaving low abundance proteins with poor quantification. We proposed a computational method will address this, by assessing protein differential expression in real-time during mass spectrometry analysis and detect when a sufficient data has been collected to quantify a given protein. When this occurs, the software will instruct the mass spectrometer to prevent the additional collection of data for that protein, redirecting saved MS resources for the acquisition of data from less abundant proteins. Our preliminary analysis of MS data from a HEK-293T cell line under two conditions: treated with Torin-1 and a control, shows that our software can redirect 21% of MS resources, while quantifying 98% of the proteins quantified with standard acquisition protocols. Our approach will improve protein quantification using MS and enhance our ability to identify proteins that are differentially expressed in various conditions, providing a better understanding of the biological processes implicated in diseases.

The prevalence of *A. parvulum* in CD and UC patients and correlation with inflammation severity

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ABSTRACT

Crohn's Disease (CD) and Ulcerative Colitis (UC) are two major subtypes of Inflammatory Bowel Disease (IBD). Increasing evidences have shown strong associations between the composition of the gut microbiota and IBD pathogenesis. For instance, *Atopobium parvulum*, a member of the human gut microbiome, has recently been associated with the severity of inflammation in CD patients. To validate this observation, we isolated an *A. parvulum* strain from mucosal-luminal samples of IBD patients. We sequenced the genome of the clinical isolate and designed a strain-specific primer. *A. parvulum* abundance was assessed by qPCR in mucosal luminal samples from CD and UC patients from three different regions of the colon; terminal ileum (TI) proximal colon (PC) and descending colon (DC). *A. parvulum* was significantly more abundant in UC patients with severe inflammation as compared to mild inflammation in the PC and CD regions. Also, the abundance of *A. parvulum* in CD patients was increased with the inflammation severity in all three regions of the colon, but it wasn't significant compared to mild inflammation or inactive disease. However, the results from the UC patients study shows that *A. parvulum* could be used as a biomarker of disease severity in UC and suggests that *A. parvulum* may play a crucial role in IBD pathogenesis.

Stereotactic body radiotherapy in limited-stage small-cell lung cancer

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ABSTRACT

Background: Small-cell lung cancer (SCLC) is an aggressive neuroendocrine tumour that is prone to metastasizing. Stereotactic body radiation therapy (SBRT) is an emerging therapeutic option in limited-stage (LS) SCLC, although without level 1 evidence to support this practice. We aimed to evaluate the use of SBRT in limited-stage SCLC at our institution, in order to expand the evidence base in this area. Methods: With ethics board approval, we performed a review of all cases of LS-SCLC treated with SBRT at The Ottawa Hospital Cancer Centre between 2013-2020. Baseline demographics, diagnostic, and treatment information were collected by retrospective review. Primary outcome was overall survival (OS). Results: During the study period, we identified 26 patients with pathologically confirmed LS-SCLC, representing approximately 10% of all LS-SCLC cases. Data collection has been completed on 20/26. Baseline characteristics: median age 76, median ECOG-PS 1, median Charlson Comorbidity Index 7, 100% current/former smokers. The majority (95%) had very early-stage disease (T1N0). The SBRT dose administered ranged from 48-60Gy in 3-8 fractions; 65% also received chemotherapy, and 25% received prophylactic cranial irradiation (PCI). After a median follow-up of 23.6 months, 50% of patients remained alive without recurrence. The median OS was 45.1 months. Chemotherapy use was associated with a reduced risk of death with hazard ratio of 0.37. Conclusion: Preliminary data from our institution support that SBRT is a useful adjunct for potential cure in patients with limited-stage SCLC.

Characterization of novel viral sensitizers enhancing VSV replication in cancer cells

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ABSTRACT

Oncolytic viruses (OVs) are a class of immunomodulatory anticancer drugs that are designed to infect and kill cancer cells. The viral progeny produced during replication spreads to neighboring tumour cells and activate the adaptive anti-tumour immune response of the host, resulting in the clearance of the remaining tumour tissue. The mechanism behind this therapy has built an interest for pre-clinical and clinical studies in the improvement of OV therapy. Currently, the oncolytic herpes simplex virus-1 (HSV-1) has been approved for clinical use for the treatment of melanomas in the United States, Australia and Europe, while Vesicular Stomatitis Virus (VSV) among other OVs, are at various stages of investigation for many cancer types. Nevertheless, one of the main obstacles that limits the clinical efficacy of OV therapeutics is the poor viral replication in tumour tissue. To counter this problem, a group of compounds known as viral sensitizers have been identified and have shown to be able to enhance viral replication. Our group previously found that the kinase inhibitors BI-D1870 and its analog KA-019, dose dependently enhanced oHSV1 infection in glioblastoma cells. Here, I characterized the effect of KA-019 against the parental drug by examining oVSV infection kinetics by live cell imaging as a measure of viral spread, and replication by western blot to measure viral protein synthesis. The results showed that KA-019 dose dependently potentiates oVSV infection to a greater extent than BI-D1870.

Beyond bare bones: Investigating the history and ethics of anatomical legacy collections

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ABSTRACT

Background: Up until the 1980s, the skeletons mounted in medical schools and the skulls examined by students in anatomy courses were undocumented human remains. They were sold as “specimens” by commercial medical and anatomical supply companies that were supplied almost exclusively by human remains exported from India. **Objectives:** The objectives of this research project were to: (1) investigate the origins of “legacy” anatomical collections in the public and private sectors; (2) identify the role of Canadian anatomical supply companies in medical education; and (3) promote ethical decision-making with regard to the inventory and treatment of educational human bone sets. **Methods:** This research was conducted in collaboration with the Canadian Museum of Nature (CMN), where a human skeleton in the museum’s collection was found to have been purchased from the Canadian Anatomical Specimen Supply Company. Oral histories were conducted with former CMN zoo-archeology staff. Systematic searches were conducted in the archives of Canadian medical schools and North American museums, and in electronic databases. **Results and Conclusions:** Our findings affirm that the trade and collection of undocumented human bones must be considered unethical within scientific and educational pursuits, and recommendations are made for appropriate guardianship of human remains already in the possession of medical schools and museums. Our research illustrates how historical scholarship may facilitate exploration of ethical issues in the curation and administration of medical education.

Perception of synthetic lesions in PET images for evaluation of trainee performance

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ABSTRACT

Purpose: Perception studies of software-generated lesions inserted into patient images have recently shown the potential to characterize observer limits of detection based on lesion and image parameters. We hypothesize that the performance of trainees can be evaluated using these methods, as a tool for standardization and quality control of nuclear medicine training programs. **Methods:** The in-house developed Lesion Synthesis Toolbox was used to generate spherical lesions of varying sizes and intensity levels inserted throughout the thorax and abdomen of normal whole-body FDG PET/CT studies. Ten observers of different levels of experience (untrained, in-training, and trained) participated in one-hour virtual perception studies, involving a free-response localization task of synthetic lesions using a randomized set of images. Observers freely scrolled through 3D images using clinical software (Hermes) to localize lesions and report their confidence level. The results were analyzed to identify performance metrics that stratify observers’ level of experience. **Results:** Preliminary results showed that the rate and accuracy at which observers detected lesions were correlated to their level of training, but the proposed model of using limits of detection to characterize performance in terms of lesion size, activity, and contrast was underpowered. **Conclusions:** Perception studies of synthetic lesions may be able to evaluate trainee performance in the task of lesion detection, but further optimization of the methods is required to characterize performance in terms of limits of detection.

Analyzing recent trends in Ophthalmology CaRMS data: One of Canada's most competitive specialties

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ABSTRACT

Introduction: The primary aim of this study is to provide Ophthalmology program directors and medical students with an analysis of the latest trends in Ophthalmology match statistics. **Methods:** This is a retrospective review of CaRMS data focusing primarily on Ophthalmology from 2013 to 2020 for Canadian Medical Graduates (CMGs). **Results:** Since 2013, there has been a statistically significant ($p < 0.05$) increase in the number of applicants applying for, ranking, and going unmatched after applying for Ophthalmology. The supply of seats available has remained relatively stagnant and the likelihood of matching after choosing Ophthalmology as a first choice discipline has decreased. Despite substantial progress, gender differences continue to persist, and certain medical schools are more likely to have its medical students successfully match than others. An Ophthalmology applicant is 11.96 and 4.25 times more likely to rank only Ophthalmology when compared to a Dermatology and Plastic Surgery applicant, respectively. An Ophthalmology applicant is also 4.12 times more likely than a Dermatology applicant to go unmatched. **Conclusion:** The finding of this study reinforces the notion that Ophthalmology is one of the most competitive residency programs in Canada.

Implementation and evaluation of a Project ECHO™ on pediatric palliative care in Nepal

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ABSTRACT

Background: Limited pediatric palliative care (PPC) training is a significant barrier to improving PPC in low- and middle-income countries (LMICs). Project ECHO (Extension of Community Healthcare Outcomes) is a distance education program that connects experts to local healthcare providers (HCPs). **Objective:** Project ECHO PPC targeting HCPs in Nepal was developed, implemented, and evaluated, exploring participants' 1) changes in knowledge, self-efficacy, and attitudes towards PPC, 2) learning experiences, 3) program acceptability, and 4) recommendations for program improvement. **Intervention:** A needs-based curriculum was developed, with each session including a didactic lecture from a specialist followed by case presentation and discussion with an emphasis on clinical practice change. **Methods:** A mixed methods approach utilized surveys at baseline, followed by surveys and qualitative interviews upon program completion. Interviews were recorded and transcribed, and emergent themes were identified. **Results:** 53 HCPs participated in 21 ECHO sessions. Program acceptability scores were consistently high. HCPs reported improvements in knowledge and self-efficacy (in all 22 domains) and improved attitudes towards PPC (in 6 of 8 domains) with demonstrated statistical significance ($p < 0.05$). In interviews, three major themes were identified: support for clinical practice change, networking with colleagues and experts, and satisfaction with the ECHO training format. **Conclusion:** Project ECHO is an effective tool to support PPC education, which can support increased access to PPC in LMICs.

H.O.U.S.E. CSL manual: A handbook for student-led homeless health education

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ABSTRACT

Background: The unique needs of homeless and precariously housed populations necessitate training of healthcare professionals who can utilize skills of connection, empathy, trust, and support as well as understanding of social determinants of health. Community Service Learning (CSL) is a pedagogy that allows medical students to work directly with vulnerable populations and apply theoretical knowledge in the context of community engagement. A CSL program led by medical student leaders has an important role in nurturing the next generation of homeless health experts. **Objective:** To develop a handbook detailing the steps for operation of a student-led homeless health CSL program. **Methods:** Core homeless health training competencies were determined based on the 'H.O.U.S.E.' mnemonic and homeless health education framework developed by the Homeless Health Research Network. Various CSL resources and journal articles were examined to identify best ways to organize a CSL program. In order to create CSL activities, we consulted with a local community organization and homeless health scholars to identify the needs of the stakeholders and determine the feasibility and effectiveness of proposed CSL activities. **Results and Conclusions:** A manual describing the organization and operation of a H.O.U.S.E. CSL program was developed. Using plain language and graphics, this manual illustrates different components of the H.O.U.S.E. CSL program and presents a detailed guide for student-led homeless health education in a practical context.

Identifying race-based generalizations of Black Individuals in a medical school curriculum

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ABSTRACT

Background: Recent evaluations have highlighted the lack of representation of Black individuals in medical curricula. Studies have shown that race is a poor proxy for genetic variation and its use as a biological proxy in medicine is harmful and not evidence driven. Consequently, this lack of representation may result in erroneous treatment and medical errors. Such errors can lead medical professionals to experience psychological effects such as anger, guilt, inadequacy, depression, and suicide. The objective of this project was to identify race-based generalizations and gaps within the pre-clerkship undergraduate MD program curriculum at the University of Ottawa. **Methods:** 16 student volunteers reviewed the pre-clerkship curriculum and flagged areas deemed as culturally insensitive, holding race-based generalizations, or lacking diversity. All comments were reviewed by two independent raters to ensure inter-rater reliability. **Results:** A cumulative total of 713 lectures, self-learning modules and case-based learning sessions were reviewed. There were 221 (31.0%) lectures flagged for concern regarding anti-Black racism and among those, 19% perpetuated negative stereotypes against Black individuals. **Conclusion:** Our findings show that the MD program curriculum includes negative portrayals of Black individuals which will adversely affect patient care. A curriculum reform is necessary to change the portrayal of Black individuals in medicine and reduce bias. This will increase physician competency and confidence and reduce medical errors when treating Black patients.

Parents' views to strengthen partnerships in newborn intensive care

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ABSTRACT

Background: Parental involvement in their newborn's neonatal intensive care reduces stress and helps with the parent-child attachment, transition to home, and future development. However, parents' perspectives are not often sought or considered when adapting family-centered care in neonatal intensive care units (NICUs). **Aim:** To identify what parents believe helps or hinders their involvement in their newborn's care when admitted to our Level 3B NICU. **Methods:** Between August and October 2018, nine mothers and one father were interviewed during three 60- to 90-minute audiotaped focus groups using a semi-structured interview tool. From the content analysis of the verbatims, three reviewers identified key themes that affected how involved parents could be in their newborn's care. **Results:** Parents provided examples of factors that facilitated or restricted their involvement. The analysis identified themes: 1) parent-staff interactions, 2) supportive/trustworthy healthcare professionals, 3) consistency in care and caring staff, 4) family, couple, and peer support, 5) newborn status, 6) resources and education for parents, 7) the NICU environment, and 8) academic and research participation. **Conclusion:** We identified a conceptual framework to allow our NICU team to prioritize working strategies to strengthen parental involvement in newborn care. In addition to implementing ways to involve parents, we need to address parents' satisfaction with their participation. These findings may help other investigators explore parents' expectations toward their NICU experience.

Differentiating primary from secondary lung cancer with FDG PET/CT and extra-pulmonary tumor grade

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ABSTRACT

Purpose: In patients with known extrapulmonary cancer presented with a pulmonary nodule, differentiate primary lung cancer from a metastatic disease could be challenging. FDG PET is commonly performed for lung nodules before biopsy. Considering that FDG uptake is related to tumor aggressiveness, we hypothesize that a mismatch between FDG uptake of pulmonary nodule and extrapulmonary tumor grade could allow us to make the differentiation. **Methods and Materials:** This is a retrospective study. Data on FDG uptake of solitary lung nodule, measured by SUVmax and scaled by liver uptake, as well as nodule size, were obtained. Pathology of the nodule were obtained and served as the gold standard. Data for extrapulmonary tumor, including tumor grade, were also obtained. The number of cases consistent with the prediction was identified. **Results:** 65 patients (age:70.4, 36F, 29M) with extrapulmonary tumor grades of low (37), moderate (12) and high (16) were included. Assuming the range of the SUVmax ratio at <0.9 for low, 0.91-1.99 for moderate and >2.0 for high grade tumors, there are 41 patients in the mismatched (e.g. low uptake with high grade) and 24 patients in the matched group (e.g. low uptake with low grade), respectively. Of the 41 patients in the mismatched group, the origin of lung nodule (primary versus metastasis) was predicted correctly in 29 patients (71%) and incorrectly in 12 patients (29%). **Conclusions:** The FDG uptake of solitary pulmonary nodule and extrapulmonary tumor grade could be used to predict the pathology of lung nodules.

Validation and pilot testing of an asthma knowledge questionnaire for children & caregivers

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ABSTRACT

Background: Asthma knowledge of children with asthma and caregivers can be measured using knowledge questionnaires. However, currently available asthma knowledge questionnaires are outdated and/or have not been validated for use in a North American setting. **Objective:** We aimed to develop and assess the validity of a tool for measuring asthma knowledge of caregivers of children, and adolescents with asthma. **Methods:** Our tool was developed from 3 previously validated asthma knowledge questionnaires, and assessed for face validity by our team, 8 asthma experts, and 20 asthma patients/caregivers who provided feedback. The tool is now being pilot tested on caregivers and adolescents admitted to CHEO for an asthma exacerbation, with comparison of knowledge scores before and after attending a CHEO asthma education session. The tool will be administered again 2 weeks later to assess test-retest reliability (i.e., consistency of responses). We will conduct interviews at 3 months and 6 months post-education to assess quality of life, asthma symptom scores, and frequency of emergency/hospital visits which will be correlated to the knowledge scores. **Results:** The current tool consists of 3 sections: demographics, asthma severity and the knowledge component consisting of 24 True/False questions. Pilot testing of the tool before and after asthma education is underway, with 10 responses received so far. **Discussion:** A validated asthma knowledge tool will allow us to more easily identify and fill knowledge gaps of patients and caregivers of children who are admitted to CHEO for their asthma.

Retrospective evaluation of chest radiography and computed tomography in patients with sarcoidosis

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ABSTRACT

Purpose: To assess diagnostic accuracy between chest radiography (CXR) and computed tomography (CT) in patients with sarcoidosis. **Methods:** Retrospective study where patients were classified as “presumed” sarcoid (positive imaging) or “definite” sarcoid (positive biopsy). The CXR and CT scans of patients were categorized as: consistent with sarcoidosis (CWS) or tagged with a non-sarcoid diagnosis. We then calculated the diagnostic sensitivities, cost-effectiveness, and prediction of cumulative radiation. **Results:** Of 34 patients, 8 were excluded, 16 were classified as “presumed” sarcoid and 10 were classified as “definite” sarcoid, based on the IWOS classification. A total of 23 patients received CXR, with 4 CWS (sensitivity = 17.39%). 25 patients received CT, with 20 CWS (sensitivity = 80%). Of those with “definite” sarcoidosis: 7 received CXR, with 1 CWS (sensitivity = 12.5%); all 10 received CT, with 7 CWS (sensitivity = 70%). Cost-effectiveness and cumulative radiation analyses revealed that routine CXR screening would be justified if >20% and >1% of patients avoided subsequent CT, respectively. **Conclusions:** The data supports that CT is more sensitive than CXR in identifying sarcoidosis. It is routine practice at The Ottawa Hospital for sarcoidosis patients to receive CT scans of the chest regardless of CXR results, which may not be justified from cost-effectiveness or radiation dose perspective. Furthermore, considering the extra cost of administration, technical personnel fees and time, CT may be a superior screening method in uveitis cases of suspected sarcoidosis.

Audit of inpatient parenteral nutrition practice at The Ottawa Hospital

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ABSTRACT

Background: Parenteral nutrition (PN) is a complex therapy used to support patients with intestinal failure or inaccessible gastrointestinal tract. Although potentially lifesaving, PN is invasive, costly, and its inappropriate use can lead to infections, metabolic abnormalities, and high medical costs. Objectives: The purpose of this quality assurance audit is to assess the current practice of PN at The Ottawa Hospital (TOH) in order to identify areas for improving the quality, cost and safety of PN practice. Methods: A prospective chart review was conducted on patients admitted to TOH who initiated PN between June 14 and August 13, 2021. Data collected included PN indication, appropriateness of use and timing, PN composition, as well as patient caloric goals, laboratory biochemical parameters, infections and wastage of PN solutions. Data was collected for the duration of PN infusion. Results: 70 patients were included (mean age=62 ± 16, 33 (47%) male). Of these, 22 (31%) were severely malnourished. 47 patients received central and 23 received peripheral PN. 29 patients (41%) started PN on their ideal start date. Patients on central PN spent an average of 14 ± 10 days on PN, compared with 5 ± 3 days for those on peripheral PN. A total of 28.5 PN bags were wasted. Further analysis including infection rates and metabolic abnormalities is in progress. Conclusion: The preliminary results of this audit provide valuable information on the current PN practice at TOH, including gaps in care and unnecessary waste. The data will be used for quality improvement initiatives.

Non-transplant hepatic sinusoidal obstruction syndrome in pediatric oncology: A systematic review

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ABSTRACT

Hepatic sinusoidal obstruction syndrome (SOS) is a rare and potentially fatal liver disease often seen in pediatric patients. SOS is a common sequelae of conditioning regimens for hematopoietic stem cell transplantation (HSCT) with well described epidemiology and pathophysiology. However, there is a paucity of literature examining non-transplant SOS, secondary to chemotherapy. We will describe the etiology, management, and outcome of non-transplant SOS through this systematic review. Four databases were searched for non-transplant SOS in pediatric cancer patients between 2000–2021. Two reviewers each performed screening and full text review before data abstraction. Articles were retained if they included pediatric patients with cancer who experienced non-transplant SOS/VOD. We screened 2301 records and reviewed 195 full-texts. Of these, 47 articles were included, yielding preliminary data from 78 patients with SOS: 9 (12%) female, 14 (18%) male, and 55 (71%) patients of unknown sex. Mean age was 5.45 years with an age range of 0.25 to 15 years. Underlying diagnoses included Wilms tumour (80%), ALL (12%), rhabdomyosarcoma (1%), and AML (1%). Most patients received chemotherapy with vincristine (92%), actinomycin-D (77%), cyclophosphamide (65%), and doxorubicin (65%). SOS was treated with supportive therapy in 17 (22%) patients. Sixty-two patients resolved, four patients died due to SOS, two patients died due to cancer, and 10 had unknown outcomes. With limited data in this field at present, this review hopes to demystify and demonstrate trends in non-transplant SOS.

HOUSE Manual: Medical Learner Homeless Health Guide

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ABSTRACT

Objectives: The purpose of this project is to improve the health outcomes of individuals with precarious housing by educating medical students about early identification and a team-based approach to supporting vulnerable populations. The students will participate in the development of the HOUSE App, Housing Outcomes Understanding income Start case management for mental illness and Evaluate substance use, in collaboration with the Homeless Health Research Network. The key objective is to train leaders to launch outreach programs to assess and help precariously housed people and improve their health outcomes

Methodology: This project will build on the recent student homeless health curriculum framework. Step 1: The students will update and map practical evidence from existing systematic reviews and guidelines on best practices in improving health outcomes for individuals with precarious housing. The summary will be used as a guiding framework when working with individuals with lived experiences to develop practical algorithms detailing initial assessment and support. Step 2: The students will collaborate with various stakeholders including experienced educators, health professionals, and individuals with lived experiences to develop content for the e-learning modules. Step 3: The content will be evaluated and published to stakeholders for use and feedback. Outcome: (1) Through knowledge synthesis and translation, the student will develop a handbook on practical algorithms detailing initial assessment and steps needed to address precarious housing for other learners and clinicians.

A community medicine mentorship program: Increasing student exposure to community internal medicine

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ABSTRACT

Background: The majority of learning opportunities available to uOttawa medical students are based in academic centres. Unless independently sought by students, no opportunities currently exist to network with community-based internal medicine (IM) physicians. A student survey we conducted in Jul 2020 demonstrated significant interest from students wanting to learn more about community IM. Moreover, there was interest from physicians desiring to showcase their community practice. **Methods:** We designed a novel “Community Medicine Mentorship Program” pairing 13 second-to-fourth year uOttawa medical students with community-based IM physicians for one-on-one mentorship alongside hosted group sessions from Sep 2020 to May 2021. Using surveys and structured phone interviews, we assessed whether our program influenced interest in community IM and effectively addressed students’ questions. We also aimed to identify areas of program improvement. **Results:** Overall student interest in community IM increased post-program. Mentees most commonly reported practice flexibility and fewer teaching/research opportunities as advantages and disadvantages of community IM, respectively. 84.6% of mentees reported a favourable mentorship relationship. The most common suggestion for program improvement was to increase the number of group sessions. **Conclusion:** This mentorship program was effective at addressing students’ questions regarding community IM. Implementing similar programs in other Canadian medical schools may play an important role in improving community IM exposure for medical students.

Knowledge gaps in gay men's health

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ABSTRACT

Many gay, bisexual and other men who have sex with men (GBMSM) experience worse health outcomes than heterosexual age-matched peers. While healthcare providers (HCPs) intend to provide optimal care to GBMSM, they often lack knowledge due to limited curriculum on health of sexual and gender minorities during formative training years. The aim of this project is to evaluate HCPs knowledge of GBMSM health across multiple categories: mental health, physical health, sexual practices, HIV, gay identity and gay seniors. This project was developed within a larger study to determine the effectiveness of learning modules to teach HCPs about GBMSM health. The pre-test (a self-administered 25 item questionnaire) was used as an evaluation of 29 participants' baseline knowledge. We found that participants had the least knowledge regarding physical health and caring for gay seniors (53.4% and 39.7% mean scores respectively) and had the most knowledge regarding mental health and sexual practices (72.4% and 80.5% mean scores respectively). Significant misconceptions around anal intercourse were identified. In addition, 79.3% of participants grossly underestimated the prevalence of HIV among gay men in Ottawa and fewer than 50% of participants correctly answered questions on preventative medicine guidelines. Such misconceptions have potential to negatively impact patient health outcomes. These findings highlight the need for increased education on sexual and gender minority health as well as the need for clinical practice guidelines to assist HCPs in their intent to provide optimal care.

Unattached patients: A preliminary search of solutions

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ABSTRACT

Unattached patients are those who do not have a regular family physician. Given that there are many benefits to having a family physician, including preventative and chronic care, it is imperative to ensure everyone has equitable access to high-quality primary care from a regular provider. Hence, we strove to find solutions to the problem of unattached patients through a literature review. To find relevant terminology to describe the "unattached patient" to maximize the scope of our search we conducted searches of government websites and international agencies and contacted health leaders in other English-speaking countries to inquire about terminology. We conducted searches in PubMed, Google, and Google Scholar as new key terms were discovered. Key terms were connected using Boolean operators. Our search yielded 49 resources, grouped into key themes. First, financial interventions such as incentives for physicians to enrol new patients. Second, policies such as government mandates to attach patients to a regular primary care provider. Third, systems organization to support multidisciplinary teams to increase capacity by delegating tasks to multiple health professionals. Four, leveraging health informatics and digital health solutions to increase capacity and better understand attachment trends through data. Five, educational initiatives to increase the number of graduates choosing to practice family medicine in rural regions. Successful models were those that incorporated multiple of the aforementioned elements and were aligned the dimensions of the patient medical home.

Lessons and challenges faced in implementation research: Reflections from the FAST Package Project

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ABSTRACT

Female genital schistosomiasis (FGS) is a chronic manifestation of schistosomiasis, a neglected tropical disease, that impairs the urogenital and reproductive health of women and girls. FGS affects an estimated 56 million women and girls in Sub-Saharan Africa. The FGS Accelerated Scale Together (FAST) Package is an implementation research study that assesses the impact of four scaled-up interventions to address FGS in Ghana and Madagascar. It works through the collaboration of public and private organizations from Canada, the United States, Ghana, the United Kingdom, Switzerland, and Madagascar. The global nature of the team has resulted in many challenges (i.e., COVID-19 lockdowns, changes in senior Ministry of Health personnel, funding cuts). Coordinating ethical approvals across Ghana, Madagascar, and Canada, mandated management of protocol revisions and feedback that spanned six months. Launching the project during a pandemic illustrated the complexities of planning reports, research tools and program activities in virtual settings and multiple languages. Network connectivity discrepancies impacted fieldwork and online health worker training in Ghana and Madagascar and highlighted the need for adaptability for the activities. The project is dependent on collaboration. As such, critical reflection on the power dynamics between and within the collaborating organizations was crucial to ensure equitable partnerships. The FAST package project offers a unique perspective as a global implementation research project that requires coordination of opportunities and challenges.

Image-guided approach to learning physician skills development

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ABSTRACT

Physician Skills Development (PSD) is a mandatory component of the UGME pre-clerkship curriculum where medical students learn and practice clinical skills within a small group setting. Booklets were developed to enhance this learning. These booklets are separated into major curriculum components such as cardiovascular, neurology, dermatology; etc. The format of current booklets is written text with some referenced illustrations without any clinical photos. Clinical images along with text can assist in memory coding and pattern recognition. The purpose of this project was to provide clinically relevant images to supplement the PSD booklets with a goal of enhancing student learning. Medical databases that allowed image searching via copyright claims were used, allowing integration of images that do not require permission when cited. When images were deemed inadequate using this method, the guidelines for "Fair Dealings" through University of Ottawa were followed. A brief questionnaire with booklet excerpts was sent to the MD2023 anglophone class (116) for feedback. Of 27 (23%) responses, 25 (93%) agreed that the changes were an improvement compared to the previous format; 24 (89%) felt they are more likely to use the booklets, and 24 (89%) felt more confident in their ability to identify clinical findings. The positive response indicates that our approach will enrich PSD learning by making it more illustrative and engaging for students. The future direction is to upload these booklets onto the UGME website for student's use.

Review and validation of undergraduate medical education pre-clerkship formative exam questions

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ABSTRACT

Background: Formative exams are a means to help medical students gauge their preparedness for summative exams, as they serve to identify content areas to focus their studying on. The benefit of formative exams lies in the relevance of the content they test in relation to examinable objectives. Aim: This project aims to appraise the pre-existing formative exam questions available across the five main units of the pre-clerkship curriculum. This content has not been updated for close to a decade. Revised questions will be available to students for the first time via the Elentra platform. Methods: A question revision template, which included the objectives, content areas, and content experts for each respective question, was prepared for every exam. A summer student was tasked, in liaison with content experts, to review each question for accuracy of content, relevance to the unit, and ambiguity. Tracked changes were made accordingly. The student then returned the updated revision templates to an exam coordinator for review and translation into French before being uploaded to Elentra. Results: 10 full-length formative exams were updated, with 315 questions being assessed in total. Within these questions, 22 were removed, 3 questions were added, and 10 were moved to different units. Conclusions: The successful completion of this project allows for updated formative exams to be available for students in the upcoming academic year. This updated content will now be used to pilot test an online formative exam that is being developed in Elentra.

Implementing a patient safety curriculum in Canadian undergraduate medical education (UGME)

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ABSTRACT

focus in preventing adverse events in Canada. However, there is little published data in this field. The aim of this study is to identify the barriers and facilitators in integrating PSQI training into Canadian UGME. Methods: This was an observational descriptive study using semi-structured recorded telephone interviews with either the Dean, UGME Dean or Undergraduate Curriculum Director of each Canadian medical school. Interview recordings were transcribed and analyzed using inductive thematic analysis. Results: From the 17 Canadian medical schools, 12 participants representing 10 schools took part in the study. Six overarching themes were identified, including Patient Safety Culture, Leadership, Curriculum Change Process, Teaching Resources, Time, and Instructional Method. Key barriers identified include a poor culture of safety in the clinical environment, unclear national standards for PSQI teaching, and time constraints in the curriculum. Facilitators include having sufficient faculty familiar in PSQI content, leadership support, and teaching PSQI through active learning methods rather than didactic lectures. Conclusions: This study will provide a national understanding of the factors that affect the implementation of PSQI into UGME curricula. The findings will be used to generate recommendations for further development of PSQI teaching in UGME, with the goal of advancing health care quality and patient safety in Canada.

A scoping review protocol for digital learning tools in postgraduate family medicine training

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ABSTRACT

Digital learning tools have become increasingly important in postgraduate family medicine education. To integrate existing tools into curricula as well as develop novel effective tools, family medicine departments and developers must have a robust understanding of the use and effectiveness of existing digital tools. The current scoping review aims to explore and organize the literature regarding digital learning tools in postgraduate family medicine training. Following the methodological framework outlined by Arksey and O'Malley, this scoping review will include a search of academic literature (in MEDLINE, ERIC, Education Source, Embase, Scopus, and Web of Science) as well as available grey literature. Identified resources will undergo title and abstract followed by full text screening. In addition to presenting key findings of the included studies, we will conduct a thematic analysis and use natural language processing (NLP) techniques to identify and organize the themes and content of the literature. Finally, we will use NLP to examine research collaborations and co-authorship networks in research on digital tools for postgraduate family medicine education. This scoping review will serve to examine and organize the breadth of literature regarding the design, development, implementation, use, and evaluation of digital learning tools in postgraduate family medicine training. Findings will be used to inform development of effective digital tools that meet the learning needs of trainees and inform future research in this area.

PET imaging of sympathetic denervation in patients with ischemic cardiomyopathy using flubrobenguane

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ABSTRACT

Measurements of cardiac sympathetic function in the myocardium have been shown to be sensitive to early changes in heart failure and ischemic cardiomyopathy (ICM) and may have prognostic value in predicting the risk of sudden cardiac death. The recent PAREPET trial used the established C-11-labeled PET tracer hydroxyephedrine (HED), which is limited in clinical practice due to its short half-life. This study sought to evaluate the ability of a new F-18-labeled PET tracer flubrobenguane (LMI-1195) to measure regional denervation and sympathetic tone in patients with ICM. A subset of patients (N=8; 6 ICM, 2 normals) in the LMI-1195 vs HED validation trial underwent early (30 min) and late (3 hrs) PET-CT imaging upon tracer injection. Regional tracer distribution and percent washout rate were quantified using the 4DM-PET analysis program (9-segment LV model). In normal controls, there was minimal tracer washout over the 3-hour early-late image interval ($4 \pm 4\%$). In patients with ICM, washout was significantly accelerated ($P < .0001$) in regions with reduced perfusion ($21 \pm 10\%$) and in remote regions ($17 \pm 9\%$), suggesting increased sympathetic tone in the whole-LV and within regions of reduced perfusion. These results on the use of flubrobenguane as a marker of presynaptic neuronal function demonstrate accelerated washout in regions of sympathetic denervation in patients with ICM. With its favourable imaging characteristics and capacity for distribution, this would represent a novel and non-invasive method to quantify cardiac sympathetic activity if confirmed in larger studies.

Optimization of isolation and collection methods to enhance the potency of small extracellular vesicles derived from mesenchymal stromal cells for treatment of cardiovascular diseases

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ABSTRACT

Pulmonary arterial hypertension (PAH) is a rare and fatal disorder with no curative treatment. PAH is characterized by elevated pulmonary arterial pressure due to precapillary arterial disease. The increase in global death rates of PAH patients illustrates the pressing need for new therapeutics. Fortunately, mesenchymal stromal cells (MSCs) derived extracellular vesicles (EVs) have shown therapeutic potential. The cell source (rat bone marrow (rBM) vs. human umbilical cord (hUC)), collection method (with or without serum starvation), and isolation technique (ultracentrifugation (UC) vs tangential flow filtration (TFF)) may impact the quality and quantity of small EVs (sEVs). We aim to compare the effect of cell sources, isolation techniques, and collection methods on the potency of EVs products. We hypothesize that TFF and serum starvation will produce the most EVs, and that EVs-hUC-MSC will have greater therapeutic potential. hUC-MSCs and rBM-MSCs were cultured to near confluency and EVs were collected over 24h in exosomes-depleted-serum or serum-free conditions. Sequential UC and TFF were used to isolate sEVs. Nanoparticle tracking analysis demonstrated that sEVs had a consistent median size of 162-167nm regardless of cell source, isolation nor collection methods. Interestingly, preliminary results suggest that EVs-rBM-MSC contain nearly 40-fold more protein per particle than EVs-hUC-MSC, regardless of isolation and collection method. Overall, cell source, isolation and collection methods appear to impact the quantity and quality of EVs produced. Endothelial cell proliferation was measured as a preliminary potency assay to assess therapeutic potential, suggesting that serum-free EV collection resulted in a 1.8-fold increase in EC proliferation rate.

Radiation dose reduction for dynamic SPECT imaging of absolute myocardial blood flow measurement

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ABSTRACT

Recent studies have validated absolute myocardial blood flow (MBF) & reserve (MFR) measurements using full doses of radiotracer (10mSv) & new solid-state CZT cardiac SPECT cameras. In this study, we evaluated the agreement of SPECT MBF measurements using a 50% radiotracer dose reduction compared to full dose. Patients with suspected/known coronary artery disease were recruited for the Multi-Center Evaluation of Feasibility of SPECT Measurement of MBF & MFR (NCT03427749). Data from 60 patients from 2 sites (Ottawa & Singapore) were reanalyzed. SPECT 99mTc-tetrofosmin rest-stress dynamic images were acquired at the time of radiotracer injection. List-mode SPECT data was subsampled to half-count levels to simulate a 50% dose reduction. Motion correction (MC) was applied to half & full dose dynamic SPECT data. MBF & MFR were determined using a 1-tissue-compartment model with a previously determined extraction fraction correction. Bland-Altman analysis compared half to full dose MBF to determine bias (mean % difference) & 95% confidence limits. The Bland-Altman determined the bias & standard deviation between half & full dose global MBF measurements with & without MC as 0.0086+/-0.2477 & 0.016+/-0.2000 & the confidence limits were -0.4768, 0.4941 & -0.3758, 0.4082 respectively. Global MFR with & without MC, bias +/- standard deviation were 0.0195+/-0.2745 & -0.0256+/-0.2339 & the confidence limits were -0.5185, 0.5575 & -0.4329, 0.4329 respectively. Bland-Altman analysis showed good agreement with minimal bias for SPECT MBF measurements with half & full doses of radiotracer.

Development and evaluation of MMP-targeted imaging probes for atherosclerosis

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ABSTRACT

Matrix metalloproteinases (MMPs) are enzymes involved in extracellular matrix remodelling. Up-regulation of MMPs is linked to degradation of the protective collagen cap on atherosclerotic lesions, thus leading to plaque rupture and associated life-threatening events. MMP imaging by positron emission tomography (PET) or optical imaging (OPI) has the potential to identify vulnerable atherosclerotic plaques. Two classes of compounds were evaluated: a dual PET/OPI probe (DPO) combining a MMP inhibitor with a fluorophore and a series of MMP-13 specific quinazoline-2-carboxamide (Q2C) derivatives for PET imaging. Half-maximal inhibitory concentrations (IC50) were determined for several MMPs and imaging ability was assessed by in vitro fluorescence imaging of ApoE^{-/-} mice aortic root sections (DPO) or by PET imaging and a biodistribution study (Q2C). DPO IC50s were found to be in the micromolar range for MMP-2,8,9, and 13 (6-51 μ M), indicating poor inhibition potency occurring with addition of the bulky fluorophore. Fluorescence imaging with micromolar concentrations of DPO revealed non-specific binding. Q2C probes showed nanomolar potencies for MMP-13 but micromolar for other MMPs. Biodistribution studies of Q2C showed hepatobiliary excretion and low accumulation of radioactivity in non-excretory organs, corresponding to PET results. While DPO will not be used in further studies, it served as a useful tool to develop protocols for future probe generations containing a longer linker region. Q2C shows promise as a selective MMP-13 tracer to assess atherosclerotic plaques.

Proper heart development depends on transcription factor expression profile within cardiac cells

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ABSTRACT

The heart, a highly complex organ, requires the coordination of several different cell types to develop into a properly functioning organ. Little is known about the involvement of specific genes and their associated expression levels in this developmental process, and thus this study aims to, based on the data acquired from Li et al., identify the cells found within the embryonic heart at day 10.5, and use bioinformatic tools to analyze the associated gene expression profile. Uniform Manifold Approximation and Projection for Dimension Reduction (UMAP) clustered the cells into six groups, including cardiomyocytes and fibroblasts. Due to similar expression patterns for genes typically expressed in cardiomyocytes, the fibroblasts and cardiomyocytes clusters were combined for further clustering, which yielded three clusters. The major difference between these clusters was the expression levels of transcription factors involved in the cell cycle. More specifically, two of the clusters had an increased expression of cell cycle genes. Iroquois transcription factors had also been of particular interest, and by looking at their expression patterns, the main cell types within this subcluster had been determined to be compact myocardial cells, found in the atria and ventricles, and atrioventricular canal cells. Altogether, findings from this study provide a deeper understanding of the genes involved in heart development and will have meaningful implications in the field of congenital heart diseases by providing an opportunity for research to be conducted in the treatment methods.

A quality assurance protocol to prevent thrombotic disease in hospitalized COVID-19 patients

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ABSTRACT

Background: Patients admitted to hospital with COVID-19 are at increased risk of developing venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE). At the start of the pandemic, high VTE rates of 15-20% were reported in hospitalized COVID-19 patients in China and Europe. Importantly, these events occurred despite use of standard anticoagulation prophylaxis. Based on this increased rate of VTE, an intermediate weight-based dose anticoagulation prophylaxis protocol was implemented at the Ottawa Hospital (TOH) in April 2020 for hospitalized COVID-19 patients. **Purpose:** The objective of this study is to determine the efficacy and safety of this new protocol. **Methods:** A retrospective chart review was conducted of all COVID-19 patients admitted to TOH between April 2020 and January 2021. Data collected included patient demographics, clinical data, thromboprophylaxis received, and outcomes. The primary outcome measure was the rate of VTE (DVT/PE). The safety outcome was the rate of major bleeding. **Results:** Of 369 admitted patients with COVID-19, all received thromboprophylaxis: 14.8% received therapeutic doses, 37.5% received intermediate doses, and 47.7% received low doses. VTE events occurred in 26 patients (7.0%), including 15 DVT (4.0%) and 19 PE (5.1%). Major bleeding occurred in 14 patients. **Conclusion:** An intermediate weight-based thromboprophylaxis strategy in hospitalized COVID-19 patients was effective and safe.

Selection of reference region for quantitation of 99mTc-pyrophosphate uptake in cardiac amyloidosis

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ABSTRACT

99mTechnetium-pyrophosphate (99mTc-PYP) imaging with single-photon emission tomography (SPECT) is a non-invasive tool used to diagnose transthyretin cardiac amyloidosis (ATTR-CM). Visual analysis has significant observer variability, especially for low uptake levels. Quantitation of 99mTc-PYP is being developed to improve observer variability and for following progression of disease. Many studies use left ventricular blood pool (LVBP) as a reference region to normalize myocardial radiotracer activity, but LVBP may be increased by myocardial scatter. To optimize quantitation, we evaluated several blood pool regions and their effect on diagnostic accuracy of PYP imaging. Mean radiotracer activity from 7 normal and 13 abnormal 99mTc-PYP SPECT studies was quantified in each of the 17 myocardial segments using 10 blood pool reference regions to calculate target to background ratios. Diagnostic accuracy of each blood pool region was measured as the area under receiver operator characteristic curves (AUC) using visual grading as a reference standard (0-3: no myocardial uptake, <, =, or > rib uptake, respectively). The AUC for LVBP (0.898) was less than the AUCs (0.997 to 1.0) using left atrium, pulmonary artery (main, right, left) and aorta (ascending, descending and arch) regions (P value <0.0001). LVBP activity correlated with myocardial uptake ($r=0.975$, P value <0.0001) consistent with myocardial scatter into the LVBP. The left atrial, pulmonary artery and aortic regions are superior to LVBP as reference regions for the quantitative assessment of myocardial 99mTc-PYP uptake.

Rôle du sécrétome du muscle dans le développement de la résistance à l'insuline musculaire au cours du diabète de type 2

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ABSTRACT

Avant même le développement du diabète de type 2 (DT2), le métabolisme énergétique des muscles squelettiques est altéré chez les individus à risque pour cette maladie. En effet, les muscles de patients DT2 présentent une résistance à l'insuline entraînant une diminution de l'entrée du glucose dans ce tissu à l'état postprandial et favorisant l'accumulation du glucose dans le sang (i.e. hyperglycémie). Les cellules musculaires sécrètent des peptides que l'on appelle myokines qui peuvent modifier le métabolisme et la fonction du muscle ou voyager dans la circulation pour influencer la fonction d'autres tissus. La sécrétion des myokines dans le muscle des patients DT2 est altérée et de façon intéressante, le milieu conditionné (MC) provenant de cellules musculaires différenciées (myotubes) issues de patients DT2 induit la localisation anormale d'un transporteur d'acides gras à la membrane de myotubes sains, un défaut métabolique typique du DT2. Notre hypothèse est que les myokines pourraient être à l'origine d'autres défauts métaboliques musculaires chez le patient DT2, telle la résistance à l'insuline. Pour étudier ce phénomène, j'ai exposé des myotubes sains au MC de myotubes DT2 pendant 24h, puis j'ai traité ces cellules à l'insuline et mesuré la transduction de la voie de signalisation moléculaire de l'insuline et l'entrée du glucose. La phosphorylation de protéines de la cascade de l'insuline ainsi que l'entrée du glucose étaient diminuées en réponse au traitement dans les myotubes sains préalablement exposés 24h au MC de myotubes DT2. Ces résultats suggèrent que des facteurs inconnus sécrétés par les muscles de patients DT2 peuvent induire la résistance à l'insuline dans des cellules musculaires saines. La prochaine étape est de quantifier les myokines contenues dans le MC de cellules DT2 pour déterminer si elles sont réellement à l'origine du développement de ce défaut métabolique.

Réfléchir à une faculté de médecine satellite au Nunavut : Obstacles et solutions

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ABSTRACT

Contexte: La littérature suggère qu'en milieu rural, un établissement de formation médicale améliore le recrutement et la rétention des professionnels de la santé, améliorant la qualité et l'accès à des soins de santé primaire. Les facultés de médecine reconnaissent davantage l'importance et l'intérêt de décentraliser leurs activités en créant des programmes satellitaires. Cependant, il n'existe présentement aucun pôle universitaire de formation en médecine dans les trois territoires. L'objectif du projet était d'initier une demande pour développer le premier programme satellitaire en médecine au Nunavut afin d'améliorer la rétention du personnel et l'accès aux soins. Méthodes: Une revue de la littérature et des discussions avec le Bureau de la responsabilité sociale et le Programme autochtone de la Faculté de médecine de l'Université d'Ottawa ainsi que des médecins de l'hôpital général Qikiqtani à Iqaluit (QGH) ont généré des données probantes et bonnes pratiques sur la médecine rurale et en milieu minoritaire. Ces connaissances seront utilisées pour formaliser une demande pour un programme satellitaire au Nunavut. Résultats: 76% des programmes de médecine canadiennes ont des places réservées aux étudiants autochtones, mais aucune spécifiquement réservée aux Inuits. Au-delà de la création de telles places réservées, un plus grand engagement communautaire dans le Nord, dès l'école primaire, par le biais d'ateliers ou programmes de mentorat longitudinaux, pourrait susciter un plus grand intérêt pour la médecine afin de développer un éventuel site satellite. Conclusion: Il s'agit d'une première étape d'un processus rigoureux pour développer l'infrastructure adéquate pour soutenir la formation médicale dans le Nord. Les prochaines étapes comprennent finaliser la demande et renforcer des collaborations durables avec une sensibilisation culturelle adéquate pour établir le futur site satellite.

Vers un site web adaptatif pour l'orientation des apprenants à Iqaluit

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ABSTRACT

L'orientation dans les divers milieux cliniques est souvent le parent pauvre de la formation médicale. Trop souvent, les étudiants et les résidents se retrouvent dans de nouveaux milieux et il est tenu pour acquis qu'ils sauront s'orienter. Pourtant, chaque milieu a ses spécificités, notamment dans l'Arctique canadien. La littérature souligne qu'il est important que les étudiants et résidents commencent leur stage en ayant une base de compréhension des différences culturelles et des spécificités sur les pathologies rencontrées dans le lieu du stage. Actuellement, un document d'orientation est offert aux nouveaux apprenants qui arrivent en stage à l'hôpital Qikiqtani d'Iqaluit. Un projet mené précédemment par l'équipe de recherche a souligné que le guide d'orientation devait être plus interactif et inclure des informations culturelles et cliniques, en plus des détails logistiques. À l'ère de la technologie, toutes ces informations conciliées dans un site web ne pourront qu'être bénéfiques pour les stagiaires. Un site web adaptatif a donc été conçu à l'aide de l'application Wix. Ce site web contient notamment : des informations logistiques, culturelles et historiques, des ressources utiles pour les soins adaptés aux traumatismes, un profil de santé et maladies de la région et des perles cliniques pour une pratique clinique dans le Nord. Un pilotage du site web sera effectué auprès des membres de l'équipe et des stagiaires qui seront présents à Iqaluit durant l'automne 2021. Il y a un nombre croissant d'étudiants et de résidents en médecine au Nunavut. En vue de les préparer pour leur stage en Arctique, il est primordial qu'ils bénéficient de la meilleure orientation possible.

Les facteurs influençant l'admission et la poursuite des études médicales par les étudiants de minorités ethniques

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ABSTRACT

CONTEXTE Les minorités ethniques notamment noires restent sous représentées dans les effectifs d'admission en médecine au Canada. Selon la loi canadienne sur les droits de la personne, l'ethnicité ne doit pas restreindre l'accessibilité à la profession médicale pour tous candidats méritants. Les facultés de médecine canadiennes prônent l'équité, la diversité et l'inclusion dans leurs mandats. Cependant, ces notions restent à être concrétisées dans leur processus d'admission et à être activement promues au sein des facultés. Ce projet visait à identifier les facteurs influençant l'admission en médecine et la poursuite des études médicales par les minorités ethniques. **MÉTHODOLOGIE** À travers une revue narrative de la littérature dans les bases de données Medline (PubMed), PsycINFO, CINAHL, Education source, Eric et Google Scholar, 152 documents en anglais publiés entre 1994 et 2021 ont été répertoriés et traités dans les logiciels Zotero et Covidence. 45 articles ont été retenus et analysés. **RÉSULTATS** Sur les 45 articles analysés, 34 (75,5%) traitent de ce sujet chez des étudiants noirs. Seul 1 article se rapporte au contexte canadien. Les barrières identifiées incluent : une préparation insuffisante des étudiants, des préjugés des administrateurs, le manque de mentors, le manque de ressources financières et de connaissances préalables sur le métier de médecin. Des facilitateurs ont également été identifiés, notamment : des programmes visant à augmenter la diversité en médecine, des programmes de mentorat offrant une exposition et sensibilisation précoce à la profession, du soutien financier et du support académique. **CONCLUSION** Ils existent plusieurs barrières et facilitateurs à l'éducation médicale pour les minorités ethniques, plus particulièrement noires. D'autres recherches sur le sujet au Canada permettraient de mieux cerner cette problématique à l'échelle nationale.

La santé maternelle des femmes d'Afrique subsaharienne et des Caraïbes à l'hôpital Montfort: Stratégies de recrutement

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ABSTRACT

Bienfondé : La recension des écrits rapporte la réticence que les personnes issues de la communauté noire ressentent vis-à-vis le recrutement associé à la recherche. Étant des populations sous-représentées, il existe des défis quant au recrutement. Au cours d'un projet explorant les expériences et le parcours obstétrical des femmes d'Afrique subsaharienne et des Caraïbes nous avons dû modifier nos stratégies de recrutement à plusieurs reprises. Objectifs : Explorer les défis et solutions associés au recrutement des femmes de la communauté noire afin d'optimiser la participation à la recherche et répondre à leurs préoccupations. Méthodologie : Depuis août 2020, de multiples méthodes de recrutement ont été utilisées: rejoindre groupes et associations communautaires, et leaders religieux; utilisation des réseaux sociaux; méthode boule de neige; affichage dans les hôpitaux. Des rappels périodiques, par courriel, ont aussi été employés selon la méthode Dillman. En dernier recours, nous avons collaboré avec les archives médicales qui ont contacté des femmes afin d'atteindre le seuil de participation prévue. Des stratégies spécifiques ont aussi été employées pour atténuer les inquiétudes envers le projet de recherche (emphasis mis sur la confidentialité, l'anonymat et la formation en éthique de l'équipe de recherche entière). Résultats attendus: Amélioration de notre recrutement par des approches proactives, dans lesquelles les participantes ont été contactées de manière personnelle. Ces approches se sont avérées plus prometteuses que les approches passives. Ceci pourrait servir à orienter les recherches futures en prêtant attention aux raisons pour lesquelles les communautés marginalisées hésitent à prendre part à la recherche.

PoCUS de l'aorte abdominale: un livret numérique pour les étudiants de premier cycle en médecine

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ABSTRACT

L'un des changements récents dans la pratique de la médecine est l'avènement de l'échographie au point d'intervention (aussi connue sous le nom de PoCUS). Le PoCUS est utilisé avec l'examen physique traditionnel pour obtenir une évaluation plus complète lors d'un examen clinique et offre plusieurs avantages, tels que des meilleurs taux de spécificité et sensibilité diagnostiques et une sécurité accrue pour les patients (Blooms, B & Gibbons, R, 2017). Dans le cas des anévrismes aortiques abdominaux (AAA), le PoCUS réduit le temps de diagnostic et améliore le taux de survie (Salyer, 2007). Malgré ces avantages cliniques, notamment dans la gestion et le dépistage des AAA, l'enseignement du PoCUS pendant le premier cycle des études médicales est peu répandu, car les programmes manquent de ressources éducatives pour les étudiants (Maclsaac J, 2018). Notre but est de combler cette lacune en créant un livret numérique (e-book) didactique sur la façon de réaliser un examen PoCUS de l'aorte abdominale (AA), avec une emphase particulière sur les AAA. À cette fin, nous avons procédé à une analyse documentaire afin de synthétiser les informations pour le livret numérique. À partir de ces informations, nous avons créé le livret numérique avec des objectifs d'apprentissage ainsi que des chapitres couvrant une introduction au PoCUS et à la knobologie, l'anatomie de l'AA et des AAA et comment faire et interpréter l'échographie de la AA. Nous souhaitons mettre tester l'utilité et l'efficacité de cette ressource à l'automne 2021 pour les étudiants en pré-externat à l'Université d'Ottawa.

