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Overview of the Canadian Clinician Investigator Trainees' research presented at the 2019 CSCI-CITAC Joint Meeting

Abstract

The 2019 Annual General Meeting and Young Investigators' Forum of the Canadian Society for Clinical Investigation / Société Canadienne de Recherche Clinique (CSCI/SCRC) and Clinician Investigator Trainee Association of Canada / Association des Cliniciens-Chercheurs en Formation du Canada (CITAC/ACCFC) was held in Banff, Alberta on November 8–10th, 2019. The theme was “Positioning Early Career Investigators for Success: Strategy and Resilience”. Lectures and workshops provided knowledge and tools to facilitate the attendees' development as clinician investigators. Dr. Jason Berman (President of CSCI/SCRC), Elina Cook (President of CITAC/ACCFC) and Drs. Doreen Rabi and Zelma Kiss (University of Calgary Organizing Co-Chairs) gave opening presentations. The keynote speakers were Dr. William Foulkes (McGill University) (Distinguished Scientist Award winner) and Dr. Andrés Finzi (Université de Montréal) (Joe Doupe Young Investigator Award winner). Dr. Robert Bortolussi (Dalhousie University) received the Distinguished Service Award for his work as the Editor-in-Chief of Clinical and Investigative Medicine and for being instrumental in the development of the Canadian Child Health Clinician Scientist Program. This meeting was the first to host a panel discussion with Drs. Stephen Robbins and Marcello Tonelli from the Canadian Institutes of Health Research. Workshops on communication, career planning and work-life balance were hosted by André Picard and Drs. Todd Anderson, Karen Tang, William Ghali, May Lynn Quan, Alicia Polachek and Shannon Ruzycki. The AGM showcased 90 presentations from clinician investigator trainees from across Canada. Most of the abstracts are summarized in this review. Eight outstanding abstracts were selected for oral presentation at the President's Forum.

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Introduction to CSCI -CITAC Annual General Meeting and patterns of attendance

In 2019, the Canadian Society for Clinical Investigation (CSCI) and Clinician Investigator Trainee Association of Canada (CITAC) jointly held the Annual General Meeting (AGM) and Young Investigators Forum on November 8–10th in Banff, Alberta. Close to 100 trainees participated in the AGM, including 79 MD+ (MD/PhD, MD and PhD, MD/Masters) and 17 Clinician Investigator Program (CIP) attendees. The AGM, “Positioning Early Career Investigators for Success: Strategy and Resilience”, featured expert-led workshops aimed to introduce aspiring clinician investigators to effective health communication skills, discuss career planning and development, and highlight the importance of wellness and resilience in academia. This meeting was also the first to host a “fire-side” panel discussion with Canadian Institutes of Health Research leaders, Drs. Stephen Robbins and Marcello Tonelli, who discussed the current and future funding landscape for clinician investigator trainees in Canada.

The analysis of attendance at the 2019 AGM was of particular interest, as this was the first CSCI-CITAC meeting held outside of Ontario (Figure 1). The disparity in the number of MD+ and CIP attendees continued to

increase from 2015 (81% MD+, 17% CIP). In contrast, the ratio of male to female attendees improved compared to the previous three years (53:47). The University of Calgary (UofC) had the greatest number of clinician investigator trainees in attendance (n=40), followed by Queen’s University (Queen’s) (n=12) and University of British Columbia (UBC) (n=8). The number of attendees from the University of Toronto (UofT) dropped to seven individuals from the 77–109 attendees over the past five years. Similar to the observations from last year’s AGM, there was a lack of representation of francophones and individuals from eastern-Canadian academic institutions.

Ninety-two percent of attendees submitted abstracts for presentation, which was up from 64% and 67% in 2017 and 2018, respectively (Figure 2). Most of the abstracts are published in summary form as part of this review. Approximately half of the published abstracts were basic science research, 40% were clinical and translational research, and the remainder were clinical epidemiology and medical education. The top four research fields represented were cancer biology (24 abstracts, 32% of total abstracts), neurosciences (27%), clinical and basic pharmacology (21%) and cardiovascular sciences (12%).

FIGURE 1. Number of clinician investigator trainees present at CSCI-CITAC 2013–2019 AGMs

Abbreviations: AGM, annual general meeting; CIP, clinician investigator program and surgeon scientist attendees; CSCI-CITAC, Canadian Society for Clinical Investigation / Clinician Investigator Trainee Association of Canada; female, female attendees; male, male attendees; MD+, MD/PhD, MD and PhD, MD/Masters, MD and Masters attendees

FIGURE 2. Total number of abstracts submitted for presentation at the CSCI-CITAC 2017, 2018 and 2019 AGMs

Footnote: Published abstracts were summarized and included in the 2018 and 2019 Scientific Overview on CSCI-CITAC Annual General Meeting and Young Investigators' Forum and in the current publication (2020).

Abbreviations: AGM, annual general meeting; CSCI-CITAC, Canadian Society for Clinical Investigation / Clinician Investigator Trainee Association of Canada

President's Forum Oral Presentations

In 2019, eight outstanding abstracts were selected for oral presentation during the President's Forum session. Abstracts by Jina Nanayakkara (Queen's), Daniel Kwon (University of British Columbia; UBC), Jonathan Cook (Queen's), Patrick Ciechanski (University of Alberta; UofA), David Guzzardi (UofC), Katelyn Robillard (Louisiana State University), Marc Chretien (Western University; Western) and Theodore Wigle (Western) were selected.

Basic science

Cancer biology

Adam Pietrobon *et al.* (University of Ottawa; UofO), through a combination of three-dimensional cell culture system and high-content imaging, developed a novel drug screening platform to identify potential therapeutic options for lymphangioleiomyomatosis. With this platform, they identified 98 candidate small molecules from an 800-drug library of Health Canada-approved cancer therapeutics.

Alan Blayney *et al.* (State University of New York) were studying the effects of MDM2 and MDMX on p53 protein

expression levels. Using a combined structural and functional approach, they investigated the regulation ubiquitination patterns of p53 by specific interactions in the p53-MDM2-MDMX ternary complex.

Allison Balasko *et al.* (University of Manitoba; UofM) were interested in restoring activity of invariant natural killer T (iNKT) cells in human immunodeficiency virus (HIV) setting by targeting lymphocyte activation gene 3 (LAG-3) and program cell death protein 1 (PD-1)—markers associated with reduced iNKT cell functionality. In HIV-negative donors, there was an increase in the proliferation of iNKT cells when antibodies targeting LAG-3 and PD-1 were administered separately or in combination.

Brian Laight *et al.* (Queen's) were investigating the F-BAR domain of non-receptor tyrosine kinase FER, which is required for metastasis of triple negative breast cancer in mouse orthotopic xenograft models. Through structure-function analysis, they showed that disrupting the active site and the F-BAR domain of FER leads to a reduction of cancer cells to invade *in vitro* and to metastasize *in vivo*.

Daniel Kwon *et al.* (UBC) developed radiotracers for targeting of C-X-C chemokine receptor 4 (CXCR4) in cancer models for use as imaging and therapeutic agents.

Their ^{18}F - and ^{68}Ga -based radiotracers demonstrated imaging capabilities suitable for clinical translation and ^{177}Lu -BL01 agent demonstrated potential for radionuclide therapy targeting CXCR4-expressing cancers.

Hannah Ramsay *et al.* (Queen's) utilized photochemistry to investigate the properties of aqueous silver nanoclusters as potential theranostic candidates in cancer biology. The researchers produced and isolated a pure eighteen atom silver cluster capped by fourteen captopril ligands $\text{Ag}_{18}(\text{Capt})_{14}$ and characterized its optical properties. This will allow future research on the structure-function relationships of new classes of silver nanoclusters for biological use.

Jina Nanayakkara *et al.* (Queen's) used miRNA expression profiles to compare 15 pathological types of neuroendocrine neoplasms (NENs) with 114 non-NEN controls. miR-375 was identified as a mono-analyte marker of NEN tissue differentiation, while miRNA machine-learning models were also applied to separate NENs on developmental and anatomic origins with 97-100% accuracy.

Joshua Xu *et al.* (McMaster University, McMaster) completed lentiviral transduction of *PLAGL2* into Lin-CD34+ cord blood stem and progenitor cells to assess its role in myeloproliferative preleukemia initiation and maintenance. They found that upregulation of *PLAGL2* increased erythroid colony output as well as decreased the rate of apoptosis, which suggested the importance of *PLAGL2* in clonal hematopoiesis.

Lori Minassian *et al.* (Queen's) used immunoblot analysis and imaging to assess the role of programmed death protein 1 (PD-1) / programmed death ligand 1 (PD-L1) signalling on chemo-resistance in tumour cells. They found that breast cancer cells exposed to recombinant PD-1/PD-L1 upregulated key mediators of autophagy and that drug resistance induced by reverse PD-1/PD-L1 signalling was causally linked to the increase in autophagy via *in vitro* inhibition.

Madison Turk *et al.* (UofC) conducted intravital microscopy on vesicular stomatitis virus (VSV)-treated tumour cells to evaluate the role of the tumour microenvironment on immune-mediated tumour clearance. They discovered that, when treated with VSV, mouse perivascular cells, but not tumour cells, were infected. This suggests that perivascular cells contribute to microenvironment cytotoxic T cell-mediated tumour clearance.

Matthaeus Ware *et al.* (UofI) were studying how dopamine signalling affects the regulation of glioblastoma stem cells and tumour growth. While dopamine

dysregulation is associated with a variety of brain disorders, the researchers are studying the potential for dopamine signalling to modify the glioblastoma stem cells niche, which may lead to dopamine drugs being redirected toward glioblastoma therapy.

Melanie Finkbeiner *et al.* (UofC) were developing *in vitro* and *in vivo* models to investigate potential benefits of using rhabdoviral vaccine therapy in conjunction with CAR T-cells for treatment of GD2+ tumours. These studies will provide a potential strategy for overcoming current challenges in CAR-T therapy for neuroblastoma.

Nicholas Jette *et al.* (UofC) used a CRISPR/Cas9-engineered ataxia telangiectasia mutated (ATM)-deficient lung adenocarcinoma cell line to investigate the effects of the PARP-inhibitor olaparib, and/or the ATR-inhibitor VE-821 on cancer cell growth and death. They reported that a combination of VE-821 and olaparib was the most effective in inducing cell death and suggested that this combination of therapies could be beneficial for patients with ATM-deficient lung cancer.

Simon Ferguson *et al.* (UofA) compared efficiency of metabolically stabilized bombesin derivatives labelled with various radiometals for PET imaging and radiotherapy in preclinical breast and prostate cancer mouse models. Their study identified methods that have exciting potential for radiolabelling and visualization of tumours.

Stacy de Lima *et al.* (UofC) studied differential expression and proteinase-mediated processing of PAR1 across five urothelial carcinoma lines of varying grades. They found that only high-grade urothelial carcinoma cells expressed functional PAR1, making it an exciting potential pharmacological target.

Cardiovascular sciences

Anum Rahman *et al.* (UofI) developed a novel, cardiac-specific surgical mouse model of hypoplastic left heart syndrome. This model provides a unique platform to interrogate direct effects of cardiac-induced cerebral hypoxia in brain development.

Katrina Besler *et al.* (UBC) investigated the effects of lysosomal acid lipase on cholesterol efflux and homeostatic pathways in human arterial smooth muscle cells. Their preliminary findings indicate that lysosomal acid lipase treatment may have beneficial effects on atherosclerosis progression.

To evaluate the role of human CD34+ cells in cardiac repair following myocardial infarction, Tina Binesh Marvasti *et al.* (UofI) engrafted CD34+ cells from human bone marrow into mice prior to coronary artery ligation. They found that engraftment from patients younger than 65 years

old protected the myocardium from functional decline through increased angiogenesis and regulatory T-cell recruitment.

Cell and developmental biology

Abdullah al-Ani *et al.* (UofC) developed an injectable microtissue delivery system to enhance the survival and integration of retinal pigmented epithelium transplants. Compared with conventional monolayer culture cell suspensions, this approach resulted in improved survival and function of photoreceptors.

Andy An *et al.* (UBC) investigated the role of cellular reprogramming gene *S100A9* in the development of septic immunosuppression using CRISPR knockout macrophages. They were able to induce cellular reprogramming in both knockout and wildtype cells, suggesting that epigenetic mechanisms may contribute to long-term immunosuppression.

Austin Yan *et al.* (UofO) sequenced the virome of colonic mucosa and stool samples from patients with pediatric ulcerative colitis. Their results demonstrate that the virome at the site of inflammation can be characterized in order to elucidate both the role of viruses in ulcerative colitis and the trans-kingdom relationships of the gut microbiome.

To address the challenge of studying the full viral life cycle of the hepatitis B virus, Connie Le *et al.* (UofA) developed a cell culture system using human serum that exhibits beneficial properties of both immortalized liver cell lines and primary human hepatocytes. They produced a differentiated hepatoma cell line that is suitable for modelling chronic hepatitis B virus infection.

Elise Granton *et al.* (UofC) established a pneumonia model in mice to investigate how the innate immune system is altered during *Pseudomonas aeruginosa* biofilm infection. They demonstrated that mice infected with biofilm-forming bacteria are less clinically sick, have less neutrophil recruitment and better bacterial clearance than mice with non-biofilm lung infections.

Paulina Piesik *et al.* (UBC) investigated the effect of topical immunomodulation using retinoid treatment as a non-invasive treatment option in two mice models of systemic inflammation. Their findings demonstrated a trend towards immunity modulation when pretreating the mice models with topical retinoid.

Sivakami Mylvaganam *et al.* (UofT) used a single-particle tracking and super-resolution microscopy to investigate how endothelial CD44 participate in leukocyte rolling and recruitment. They concluded that endothelial

CD44 limit mobility of bystander adhesion molecules during rolling adhesion to facilitate migrating leukocytes.

Wisoo Shin *et al.* (UofC) investigated the role of hair follicle dermal stem cells in age-associated hair loss. Their work highlighted the importance of functional hair follicle dermal stem cells for regeneration and identified the AP1/Cyr61/p16 pathway relevant in age-associated senescence and stem cell attrition.

Clinical and basic pharmacology

Jonathan Cook *et al.* (UofT) studied the sequence of HIV fusion inhibitor, enfuvirtide, and identified a wide variety of molecular changes that determine the complex mechanism of action of this therapy. They concluded that exploiting the molecular variability in enfuvirtide could help improve the development of resistant HIV viruses and broaden enfuvirtide's clinical utility.

Clinical anatomy

Valera Castanov *et al.* (Queen's) studied the architectural and functional characteristics of extraocular muscles in 14 formalin-embalmed cadaveric specimens using the novel digitization (Microscribe® G2X Digitizer) and 3D modelling (Autodesk® Maya®) methodology. Their findings provided the architectural data for a prototype dynamic model of extraocular muscle function, which can be used to further understand the mechanisms involved in normal and pathologic ocular alignment.

Neurosciences

Albert Yeung *et al.* (UofM) demonstrated that Panx1 channels, often implicated in the pathogenesis of stroke, epilepsy and chronic pain, can be activated with an accumulation of soluble amyloid-beta oligomers in Alzheimer disease. Their work highlights a new mechanism for Panx1 channel activation and a potential therapeutic target in Alzheimer disease.

Daniel Berger *et al.* (UofC) investigated the effects of ionizing radiation, utilized in cranial radiotherapy as brain cancer treatment, on different neural cell lineages. Their findings demonstrated that oligodendrocyte lineage is sensitive to ionizing radiation and could potentially explain the late side effects seen with therapy.

Danielle Weber-Adrian *et al.* (Queen's) used MRI-guided focused ultrasound (MRIGFUS) to target non-surgical transgene delivery through a recombinant adeno-associated virus to the central nervous system in a mouse model of Alzheimer disease. They found that MRIGFUS, along with control of transgene expression under the GFAP promoter,

enhanced the correlation of transgene expression with A β plaque deposition in the central nervous system.

Dennis Dimond *et al.* (UofC) tracked longitudinal changes in axonal density and projection dispersion during childhood, by using the MRI methods neurite orientation dispersion and density imaging and orientation dispersion index. They found that axonal density, but not projection dispersion, increases with age and that variability in neurite orientation dispersion increases may be related to variability in maturational rates of cognitive and behavioural skills.

Hailey Pineau *et al.* (UofA) utilized prion organotypic slice culture assay, a technique for modelling strain-specific pathology in prion disease, in whole-brain coronal slices and assessing the usefulness of this technique for modelling strains of Alzheimer disease. Successful development of this *ex vivo* model will help with disease pathogenesis and treatment studies.

Laura Palmer *et al.* (UofC) used whole-cell patch clamp electrophysiology and 2-photon microscopy in rodent hippocampal slices to measure excitotoxicity during ischemia in an Alzheimer disease model. They found that the Alzheimer disease-associated protein, A β , regulates Panx1 opening by mGluR1, and that A β production could therefore attenuate ischemia-related excitotoxicity.

Neil Rasiah *et al.* (UofC) aimed to provide causal links between the activity of corticotropin-releasing hormone (CRH) neurons of the paraventricular nucleus (CRH^{PVN}) and unrestrained behaviour. Using CRH-Cre;Ai148 mice expressing GCaMP6f in CRH-expressing neurons, they found that CRH^{PVN} responded heterogeneously, but that correlated activity between subpopulations of CRH^{PVN} emerged during stress.

Siddharth Nath *et al.* (McMaster) presented a novel variant of spinocerebellar ataxia that results, in part, from Q35P mutation within the multi-functional protein ataxin-7. Using Forster resonance energy transfer (FRET) studies, they found that the Q35P mutation drastically altered ataxin-7 protein structure. Patient cells and a *Drosophila* model both displayed increased nuclear localization of ataxin-7 and altered mitochondrial function, which they proposed contributes to disease.

Translational research

Cancer biology

Alvin Qiu *et al.* (UBC) profiled seven synovial sarcoma tumours from mouse models to study histone modifications, transcriptomes and methylomes compared with control and SSX knockdowns in human SS cell lines. Their results suggested that neither the shared synovial

sarcoma enhancer nor the expression of associated genes were altered after knockdowns of the fusion oncoprotein cell lines. These results have important implications for future therapeutic strategies for these tumours.

Daniel Newsted *et al.* (Queen's) used ovarian cancer cell lines and an ovarian cancer syngeneic mouse model to study their sensitivity to clinical grade immune checkpoint inhibitor LY2157299; alone and in combination with TGF β inhibition (anti-CTLA4 or anti-PD-1 antibodies). Their study provided preliminary evidence that TGF β signalling causes a barrier to effective immune checkpoint inhibitor responses in preclinical ovarian cancer models.

David Kramer *et al.* (UofA) performed mass spectrometry-based proteomic characterization of a panel of 19 human ER+ tumours relative to known disease outcome. Cluster analysis revealed three distinct populations of tumours based on protein abundance profiles, and several protein markers have been validated with immunohistochemistry, leading to exciting potential for predicting prognosis at time of diagnosis.

Mina Aziz *et al.* (McGill University; McGill) showed that poly(methyl methacrylate) (PMMA) containing mesoporous silica nanoparticles can release up to 1.53 times more doxorubicin than the standard PMMA, having important consequences for drug delivery and drug release to tumours.

Sophie Marcoux *et al.* (Université de Montréal) used a forensic medicine-validated immunosenescence biomarker associated with ageing (i.e., SJTREC) to study the extent of accelerated aging in a cohort of childhood acute lymphoblastic leukemia survivors. Results showed that a younger age at diagnosis was a strong predictor of the important difference between chronological and biological age; an insight that may be targeted to prevent the apparition of late adverse effects in this population.

Cardiovascular sciences

Elina Cook *et al.* (Queen's) performed RNASeq on ribo-depleted blood samples from people older than 65 years of age to investigate leukocyte inflammatory gene signatures. They found that clonal hematopoiesis of indeterminate potential (CHIP) may affect neutrophil function or phenotype; therefore, leukocytes may contribute to comorbid disease of CHIP.

Julieta Lazarte *et al.* (Western) utilized whole exome sequencing to assess the association between genetic variants related to ventricular cardiomyopathies with lone atrial fibrillation (occurrence at younger than 60 years of age, without clinical risk factors). Their data demonstrated

that individuals with lone atrial fibrillation were enriched for pathogenic truncating variants in cardiomyopathy genes.

Cell and developmental biology

Danielle Lynch *et al.* (UofC) detailed the contribution of ribosomal gene, *RPLP2*, in Nager syndrome and the spliceosomal gene, *SNRNPB*, in cerebro-costo-mandibular syndrome. The genetic contribution to the pathophysiology of these conditions, which are associated with malformation of the jaw and ears, can provide insight to normal development and etiology of related developmental disorders.

Rozlyn Boutin *et al.* (UBC) investigated the contribution of the fungal microbiota to risk and severity of asthma. They demonstrated that expansion of *Pichia kudriavzevii* (yeast) was associated with increased risk and severity of asthma in Ecuadorian infants and in mouse models, and could be mitigated with short chain fatty acids in the latter.

Neurosciences

Joseph Nashed *et al.* (Queen's) used longitudinal functional resting state magnetic resonance imaging to investigate the dynamics of stroke recovery in non-human primates. Their results indicate that recovery from stroke is strongly associated with pre-stroke brain configurations.

Katelyn Robillard *et al.* (Louisiana State University) used a transgenic mouse model of Usher syndrome Type 1C (USH1C), an inherited form of deaf-blindness, to evaluate curative genetic therapeutic strategies. Subretinal injection of an adeno-associated virus vector carrying non-mutant *Ush1c* resulted in successful expression of the transgene in the murine retina.

Robert Taylor Moore *et al.* (UofC) examined how stroke subjects and controls adapted their reaching movements upon encountering a visual disruption to their movements. Their findings show that stroke subjects displayed less motor learning relative to controls and that motor learning was associated with better functional ability. This suggests neurorehabilitation programs that optimize motor learning may help improve stroke recovery.

Rohit Singla *et al.* (UBC) presented their work on measuring medication-induced tremor in renal transplant recipients. Using a simple phone app, they reported potential utility for quantified tremor to be a biomarker for drug levels, in turn allowing for agile dosing and remote monitoring.

Sociology, philosophy and ethics

Laura Rivera *et al.* (UofC) presented their work on the prevalence and predictors of driving under the influence of marijuana in Alberta and Ontario. They showed that 1) a higher prevalence of driving under the influence of marijuana in Alberta 2015–16 than in Ontario 2017–18 and 2) the highest rate of driving under the influence of marijuana in the past year was noted for males aged 15–24 years.

Clinical epidemiology

Cancer biology

Alexandre Bazinet *et al.* (McGill) used a 10-color flow cytometry panel to diagnose and monitor minimal residual disease (MRD) in chronic lymphocytic leukemia (CLL). They concluded that a single-tube diagnosis/MRD approach for typical CLL was feasible and cost-effective.

Cardiovascular sciences

In their meta-analysis, Jamie Benham *et al.* (UofC) showed that cardiovascular events are reduced in participants with type 2 diabetes mellitus treated with sodium-glucose co-transporter-2 inhibitors compared with placebo. They did not find a significant relationship between blood pressure reduction with sodium-glucose co-transporter inhibitors and a reduction in the relative risk of cardiovascular outcomes.

Kevin Kim *et al.* (McMaster) performed a systematic review to determine the effects of heart valve replacement on outcomes in patients with end-stage renal disease. Studies suggested that mechanical valves were associated with decreased risk of mortality (RR=0.80) but increased risk of bleeding (RR=1.89) and stroke (RR=1.62).

Clinical and basic pharmacology

Andrew Stewart *et al.* (UofC) performed a network meta-analysis to review the effects of inflammatory bowel disease treatment on rates of infection in pediatric patients. Preliminary analyses suggested that use of corticosteroids was a risk factor for infection, while there was no consensus on the risk of immunomodulators or biological response modifiers.

Neurosciences

Sophie Hu *et al.* (UofC) conducted a prospective cohort study to ascertain the odds of cognitive decline in pre-dementia patients with mild behavioral impairment (MBI) or subjective cognitive decline (SCD). Patients with MBI

had higher odds of incident cognitive decline (OR=4.76), but patients with MBI and SCD (OR=8.15) had the highest odds of cognitive decline, suggesting that both neuropsychiatric symptoms and cognition were early indicators of cognitive decline.

Clinical research

Cancer biology

Sapna Oberoi *et al.* (UofM) performed a systematic review to evaluate the efficacy of mindfulness-based interventions on anxiety in cancer patients. Mindfulness was found to have significantly reduced the severity of short-term (1 month; SMD= -0.51) and medium-term (1–6 months; SMD= -0.43) anxiety and depression, and improved health-related quality of life in the short- and medium-term but not in the long-term (6–12 months).

Yiming Qian *et al.* (UofC) conducted a retrospective study of patients with post-hepatectomy liver dysfunction (PHLD) to identify intraoperative factors associated with poor prognosis. Of the 110 (10.9%) patients with PHLD, age ($p=0.015$), duration of surgery ($p=0.030$), blood loss ($p=0.010$) and the need for blood transfusion ($p < 0.001$) were associated with adverse outcomes.

Cardiovascular sciences

Vishnu Vasanthan *et al.* (UofC) conducted a retrospective cohort study comparing outcomes of stented and stentless bioprosthetic aortic valve replacements (AVR). Patients who underwent stented AVR had higher AVR-related reoperation (8.6% vs. 4.3%) while those with stentless AVR had higher all-cause mortality (25.2% vs. 16.0%), with no differences in re-operative mortality, cross-clamp time or cardiopulmonary bypass time.

Clinical and basic pharmacology

Daniel You *et al.* (UofC) employed serial thrombelastography analysis to determine hypercoagulable state duration following hip fracture surgery. They demonstrate that over 50% of patients remain hypercoagulable 6-weeks post-fracture despite thromboprophylaxis and suggest thrombelastography analysis may better predict risk of venous thromboembolism.

Jennifer Héroux *et al.* (Université de Sherbrooke; Sherbrooke) conducted a systematic review to evaluate the impact of peripheral nerve block on functional recovery after upper limb surgery. Of the five studies passing inclusion criteria of the review, three studies reported

functional recovery with a non-statistically significant superiority of locoregional anesthesia versus general anesthesia.

Marc Chretien *et al.* (Western) tested the hypothesis that bioavailability of the probe drug, felodipine, a substrate of CYP3A4 that is expressed at lower levels in celiac patients, is increased commensurate with celiac disease severity. They identified that patients with severe celiac disease did indeed have increased oral felodipine availability and who may be at risk of serious overdose toxicity associated with numerous grapefruit-affect drugs.

Theodore Wigle *et al.* (Western) sought to demonstrate the feasibility of a chemotherapy pretreatment pharmacogenetics testing service for dihydropyrimidine dehydrogenase (DPYD) genotypes in the context of fluoropyrimidine-based therapy. They determined that toxicity-related costs for prospectively screened patients were significantly less than for retrospectively assessed patients; emphasizing that pretreatment DPYD genotype-guided dosing of fluoropyrimidine-based therapies is feasible and benefits both patients and hospitals.

Neurosciences

Cynthia Kahl *et al.* (UofC) sought to determine the safety, tolerability, and possible effects of low-frequency repetitive transcranial magnetic stimulation (rTMS) on the severity of tics in children with Tourette syndrome. Evidence generated from an open-label trial with ten pilot participants provided suggestive data of efficacy and tolerability, emphasizing rTMS interventions as feasible and in need of further trials.

Hayden Danyluk *et al.* (UofA) performed a retrospective cohort study on patients undergoing microvascular decompression for medically-refractory trigeminal neuralgia in order to investigate the relationship between subcortical brain structure and treatment outcomes. Their results suggest that preoperative hippocampal and trigeminal nerve volume, measured on standard clinical magnetic resonance images, may predict early non-response.

Jeffrey Kenzie *et al.* (UofC) conducted a case (stroke patients) vs. control (age-matched healthy individuals) study evaluating the correlation between MRI functional connectivity and upper limb proprioception, as measured with a robotic exoskeleton. Findings suggested a strong inverse association between functional connectivity between the right supramarginal gyrus and various lobes and proprioceptive impairment following a stroke.

Lauran Cole *et al.* (UofC) reported results from a prospective cohort study evaluating the short- and long-term impact of intensive motor learning therapy on

sensorimotor function in pediatric patients with hemispheric cerebral palsy secondary to perinatal stroke. Robotic exoskeleton-evaluated upper limb sensorimotor function seemed to improve for up to six months following a two-week course of intensive motor learning therapy.

Lianne Cho *et al.* (UBC) prospectively evaluated the diagnostic accuracy of the Beck Depression Inventory (BDI) for depressed mood in a precariously-housed group. The BDI did not demonstrate a strong correlation with other scales and exhibited moderate sensitivity (72%) and high specificity (89%) when a 12 point-threshold was applied.

Nicholas Sader *et al.* (UofC) performed a retrospective before-after cohort study of pediatric patients subjected to a surgical decompression of a Chiari type 1.5 malformation. Sleep-disordered breathing in the cohort was improved post-operatively, with statistically and clinically significant differences in two out of three polysomnographic apnea indices.

Ryan Kirkpatrick *et al.* (Queen's) conducted a case (outpatient adolescents with eating disorders) vs. control (healthy individuals from the community) study to evaluate saccadic eye movements as a biomarker for the disorder of interest. Preliminary results suggested that cognitive control of saccadic eye movements appeared to differ between cases and controls, suggesting their efficacy as a behavioural biomarker for eating disorders.

Reproductive biology and endocrinology

Isabelle Hardy *et al.* (Sherbrooke) conducted a single centre open label randomized controlled trial to assess the impact of lifestyle interventions on the health of the babies of overweight women. If successful, large scale clinical trials will be conducted before implementing this strategy into clinical practice.

Medical education

Alysha Keehn *et al.* (UofC) aimed to assess gender equity in clinical practice, academia and leadership in general surgery and found that despite comprising 60% of medical students, women comprise only 20% of general surgeons in Canada. Ongoing investigations will attempt to address gender inequity factors in this field.

Christopher Newell *et al.* (UofC) sought to examine the effectiveness of the Surgery 101 program—an in-person session to orient families of pediatric surgery patients to the hospital and experience—and to evaluate the best way to enhance its content and accessibility. After establishing its importance, they aim to prepare an online-accessible

version of the Surgery 101 program for those who are unable to attend in person.

Heather Whittaker *et al.* (McGill) aimed to assess and improve the scientific writing of medical trainees, using an interactive seminar, to encourage student contributions to scholarly discourse by writing letters to the editors. Strategies to promote the adoption of these workshops could include incorporating them into a longitudinal curriculum in medical school and integrating them into journal clubs during residency or fellowship, on an annual basis.

Patrick Ciechanski *et al.* (UofA) assessed whether transcranial direct-current stimulation (tDCS), a safe and economical form of non-invasive brain stimulation, can enhance surgical skill learning. They found that surgical training did not alter brain electrical activity; however, surgical training paired with tDCS increased primary motor and premotor area alpha and low-beta frequency band activity.

Concluding remarks

The national 2019 Canadian Society for Clinical Investigation / Clinician Investigator Trainee Association of Canada (CSCI-CITAC) AGM was a highly successful event. In addition to the stellar program, which was put together by the AGM planning committee, it was hosted in a beautiful venue with the majestic Rocky Mountains as the backdrop. The meeting highlighted the continuously evolving landscape of medical research and showcased the groundbreaking work of clinician investigator trainees across Canada.

The CSCI-CITAC AGM is one of the most important events for the clinician investigator trainee community in Canada. It is important that the CITAC executive committee members continue to reflect on the patterns of attendance, address any barriers and/or inequities in participation and promote fair opportunities for all MD+ and Clinical Investigator Program (CIP) trainees to disseminate their research. The continued lack of representation from francophone and eastern Canadian academic institutions may be due to language bias in meeting design, patterns of institutional connectedness and lack of travel funding. Furthermore, the meeting location (in western Canada and outside of Ontario for the first time) may have introduced a shift in representation from geographically-affected programs (e.g., programs that would normally have a large CIP representation at the usual Toronto location). However, the change in location resulted in increased engagement of western Canadian trainees, many of whom had never attended the meeting when it was

held in Ontario due to barriers in cost and accessibility. In summary, even though the total attendance was reduced due to decreased CIP attendance, we are encouraged to host our future meetings across Canada to ensure balanced access and opportunity amongst our trainees across Canada.

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