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TRAINEE SECTION

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Scientific Overview: CSCI-CITAC Annual General Meeting and Young Investigators' Forum 2015

Abstract

The 2015 Annual General Meeting of The Canadian Society of Clinician Investigators (CSCI) and Clinician Investigator Trainee Association of Canada/Association des Cliniciens-Chercheurs en Formation du Canada (CITAC/ACCFC) was held in Toronto November 23-25, 2015, in conjunction with The University of Toronto Clinician Investigator Program Research Day. The theme for this year's meeting was "It takes a village" and the focus was the various support systems necessary to train a successful clinician scientist. The meeting featured an opening presentation by Dr. Vincent Dumez and workshops by Dr. Peter Nickerson, Dr. Jane Aubin, Dr. Kelly Warmington and Dr. Norman Rosenblum, and MD/PhD trainees Nardin Samuel, Kevin Wang and Kirill Zaslavsky. The keynote speakers were Dr. David Malkin (Hospital for Sick Children) who received the CSCI-RCPSC Henry Friesen Award, Dr. Brent Richards (McGill University) who received the Doe Doupe Award and Ernesto Shiffrin (Lady Davis Institute) who received the Distinguished Scientist Award.

As always, the conference showcased outstanding scientific presentations from clinician investigator trainees from across the country at the Young Investigators' Forum. The research topics, which ranged from basic sciences to clinical medicine and translational work, are summarized in this review. Over 90 abstracts were presented at this year's meeting during two poster sessions, with several of the outstanding abstracts selected for oral presentations.

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President's Forum Oral Presentations

Each year, six outstanding abstracts are selected for oral presentation during the President's Forum session. This year, the selected individuals were

- Xin (Kevin) Wang (University of Toronto) (UofT)
- Shari Manga (University of Calgary) (UofC)
- Nayan Madhur (University of Toronto)
- Adam Ramzay (University of British Columbia) (UBC)
- Christopher Wallis (University of Toronto) and
- Kanda Pushpinder (University of Ottawa) (UOttawa).

Xin (Kevin) Wang (UofT) aimed to study medulloblastoma pathogenesis by generating transgenic mice using transposon systems. Model validation using in vitro overexpression and knockdown studies is on-going. Establishing this model would allow scientists to discriminate driver events and passenger events of medulloblastoma. Shari Manga (UofC) presented work on the augmentation of pulse pressure with exercise as a reliable prediction for remodelling post-cardiac resynchronization. Manga found that patients with left ventricle remodelling were more likely to have a > 5mmHg increase in pulse pressure, and that a 5mmHg or higher augmentation of pulse pressure post-exercise predicted favourable left ventricular remodeling with 74% accuracy. Nayan Madhur (UofT) presented epidemiological data evaluating the association between medication exposure (metformin, statins and NSAIDs) and all-cause mortality and kidney cancer-specific mortality among type 2 diabetic patients. Interestingly, he reported that current statin exposure was associated with significantly reduced risk of all-cause mortality and kidney cancer-specific mortality. Neither metformin nor NSAIDs were associated with survival outcomes. Adam Ramzy (UBC) presented work from the Kieffer Lab at UBC that investigated the role of insulin in pancreatic development. Using mice lacking the insulin gene, he showed that insulin is an important signal for alpha-cell maturation, and highlighted the developmental plasticity of the pancreas. Christopher Wallis (UofT) gave a presention on the incidence of treatment-related complications from contemporary treatments of prostate cancer. Complications requiring urological procedures and hospital admissions were common, may occur many years after treatment and are depend on the type of treatment used. This information should be considered when determining a course of treatment. Kanda Pushpinder (UOttawa) explored the mechanism underlying encapsulated cardiac stem cell-enhanced cardiac repair beyond acute retention of transplanted cells. Pushpinder found that encapsulation forces these cells to adopt an invasive migratory

phenotype, promoting invasion, engraftment and therapeutic repair.

Basic Science

Given their training trajectory, clinician investigators are well positioned to carry out basic science research in conjunction with the study or practice of medicine. As always, basic science research was well represented at the 2016 CSCI-CITAC Annual General Meeting, and drew from diverse fields.

Microbiology and Immunology

Connie Le (University of Alberta; UofA) presented work 13 investigating the role of chemokines (CKs) in asthma relapse 14 in a mouse model of asthma. Age-matched naïve mice, 15 recovered primed mice, and recovered mice that were 16 re-challenged with allergen were compared with respect to 17 gene expression of 18 CKs and protein levels of three CKs. 18 While naïve and recovered mice demonstrated similar CK 19 gene expression, re-challenged mice had 13 upregulated CK 20 genes. Richard F. Xiang (UofC) studied the role of Rac, Src 21 family kinases (SFK) and integrins in toxicity against 22 cryptococcal fungi. Using various molecular biology 23 techniques, Xiang found that natural killer cell mediated 24 anti-fungal killing initiated by integrin and NKp30 activation 25 of Rac and SFK pathways, respectively. Iiya Mukovozov 26 (UofT) presented work on the role of the Slit family of 27 secreted proteins in influencing clearance of oxidized 28 low-density lipoproteins (oxLDL). The binding and uptake of 29 oxLDL was investigated using fluorescently (DiI)-labeled 30 oxLDL, and quantified by microscopy and flow cytometry. 31 Mukovozov found that both human and murine macrophages 32 express the Slit2 receptor, Robo-1. He also found that 33 treatment with Slit2 inhibited foam cell formation and 34 blocked macrophage binding and uptake of oxLDL (P<0.01).

Robyn Elphinestone (UofT) presented work exploring the 36 role of S-nitrosothiol in improving survival in mice infected 37 with cerebral malaria. She found that T-cells in 38 S-nitroglutatione reductase (GSNOR) knockout mice appear 39 to mediate the protective mechanism by which S-nitrosothiol 40 increases nitric oxide bioavailability. This work suggests that 41 interventions that target GSNOR function may help improve 42 outcomes from severe malaria. Alison Michels (Queen's 43 University; Queen's) presented work aimed at examining the 44 influence of damage-associated molecular patterns (DAMPs; 45 such as histones) on the release of Weibel-Palade bodies 46 (WPBs) and characterizing the association between DAMPs 47 and WPB exocytosis in models of inflammation. She 48

concluded DAMPs can regulate von Willebrand factor levels and function by inducing its release from WPBs. Jason Bau (UofC) presented work exploring the role of Keratinocyte growth factor (KGF) in protecting against C. difficile toxin-medicated cell-death. He found that KGF protected against TxnA and TxnB-induced cell death both in vitro and in vivo and prevented disruption of barrier function as measured by Z0-1 tight junction staining. These data suggest that modulation of KGF activity may hold promise for preventing/treating C. difficile infection.

12 Cardiology

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Jessica Blom (University of Western Ontario; Western) presented a validated adapted surgical model of mammalian cardiac regeneration in a neonatal mouse. This 10-15 minute procedure allows for visualization of the left anterior descending coronary artery and can be used to elucidate mechanisms of mammalian cardiac regeneration after myocardial infarction. Frank M. H. Lee (UBC) studied the role of biochemical cascade to exhibit clot-busting capabilities and found that Xa-K, a modified version of activated clotting factor X, is a viable target for developing novel clot-busting agents.

Neuroscience and Psychiatry

27 Enoch Ng (UofT) presented studies showing that deletion of a neuronal calcium concentration sensory decreased motivation 29 in mice and dopamine release in structures underlying 30 motivation-related behaviour. Jennie Pouget (UofT) 31 investigated whether autoimmunity and schizophrenia shared 32 genetic risk factors. Preliminary findings suggest a shared 33 genetic risk but also suggest that they are likely not major 34 factors to either morbidity. Siddharth Nath (McMaster 35 University) examined the role of ataxin-7 in spinocerebellar 36 ataxia and how mutations to ataxin-7 may alter protein 37 function producing the disease symptoms.

Raphael Schneider (UofT) presented studies on the use of exosomal microRNAs in the cerebrospinal fluid as diagnostic do biomarkers in ALS. Several microRNAs were found with different expression levels in ALS patients compared to controls. His work could yield new diagnostic markers. Devon L. Johnstone (UOttawa) presented work on the genetic mechanism and therapies for a novel epileptic encephalopathy. Johnstone found that a patient who died with intractable epilepsy at 1 month of age had a rare homozygous frameshift deletion in PROSC; a highly conserved gene with unknown function. They will now knockout this gene in zebrafish and

produce iPS-derived neurons to characterize the gene's functions and identify potential treatments.

Tianwei (Ellen) Zhou (McGill) investigated inflammatory 3 changes present in retinopathy of prematurity; a serious 4 complication in premature infants. She investigated the visual 5 functions of animal models with oxygen-induced retinopathy 6 in order to study the functional impacts of inflammation 7 mediated changes in the retina. Kirill Zaslavsky (UofT) 8 investigated a method to produce more consistent cultures of 9 induced pluripotent stem cell-derived neurons. This method 10 may help to address the issue of heterogeneity and impact the 11 application of this potential therapeutic avenue in autism 12 spectrum disorder. Alexander Levit (Western) developed an 13 animal model that overexpressed mutant human 14 amyloid-precursor protein to test the hypothesis that a genetic 15 predisposition for Alzheimer's disease can be triggered by 16 hypertension.

Nabeela Nathoo (UofC) presented high resolution MRI 18 of a multiple-sclerosis mouse model and detected previously 19 unseen neuroanatomical changes within the brains of these 20 mice. This work demonstrated the utility of advanced imaging 21 tools to understand disease and structural changes in animal 22 models of neurological diseases. Michael Richards (UofT) used 23 maximum likelihood estimation (MLE) to study the process of 24 multisensory integration. He examined adults with amblyopia 25 and his findings suggested that normal visual experience may 26 be required for proper development of multisensory 27 integration and can, thus, have a lifelong influence on 28 neurological function. Allan R. Martin (UofT) used 29 multimodal MRI to study patients with degenerative cervical 30 myelopathy. He found various advanced MRI metrics that 31 correlate well with white matter injury and disease-related 32 impairment. These methods may help to identify novel 33 imaging biomarkers and improve diagnostics for this disease.

Jonathan Keow (UOttawa) investigated the neurotoxic 35 effects of rotenone, a commonly used pesticide, on zebrafish. 36 They found that zebrafish embryos treated with rotenone 37 displayed a 50% reduction in dopamine neurons in the ventral 38 diencephalon, and a logarithmic increase in markers of 39 oxidative damage. Dopamine neuron loss in zebrafish treated 40 with rotenone may provide a useful tool for studying 41 environmental causes of Parkinson's disease. Jeremiah Hadwen 42 (UOttawa) presented on establishing a database for 43 repurposing clinic-ready small molecules for rare neurological 44 disorders. Hadwen treated mouse cortical neurons with over 45 200 drugs at therapeutic dose and harvested neuronal RNA, 46 which was converted to mRNA sequencing libraries for 47 drug-gene interaction analysis. Heather Leduc-Pessah (UofC) 48

explored the role of microglial P2X7 receptors in morphine tolerance in mice. Leduc-Pessah reported a causal involvement of P2X7 receptors in the development of morphine analgesic tolerance, with repeated morphine leading to increased total microglial expression that, in turn, induced a potentiation of P2X7 receptor function. She concluded that these receptors represent a potential therapeutic target in the management of morphine tolerance.

Mark Chandy (UofT) presented work on microRNA lo biomarkers of vascular cognitive impairment in mice. They hypothesized that in a mouse model of type-2 diabetes, which results in the development of vascular cognitive impairment, anti-inflammatory microRNA in circulating microvesicles is reduced and vascular cognitive impairment pathogenesis is promoted.

17 Cancer

Paul Savage (McGill) probed single-cells from breast cancer patients to identify cell subpopulations. Savage found multiple subtypes and is working to strengthen these preliminary findings. Allen W. Zhang (UBC) studied the genomic heterogeneity present in high-grade serous ovarian carcinomas in order to investigate treatment resistance and therapeutic options. In particular, his work focused on the spatial variability in tumour infiltrating lymphocyte composition with the aim of elucidating the role of immune response to cancer.

Eric Zhao (UBC) presented on the merits of genomic mutational signature of BRCA1/2 deficiency in breast cancer as a potential predictive marker of platinum-based therapy response. He found that the signature is associated with improved radiological responses and time to treatment failure of platinum-based chemotherapies. Ashton Connor (UofT) presented on metachronous pancreatic ductal adenocarcinoma tumour evolution examined with whole genome sequencing. Connor found that metachronus lesions share a common ancestor, and that low allele frequency mutations drive metastases. David Twa (UBC) studied the link between programmed death ligand 1 (PDL1) and genomic structural rearrangements in non-Hodgkin's B-cell lymphomas. Through DNA sequencing, Twa identified a number of rearrangement partners, allowing the comprehensively characterization of the landscape of PDL rearrangement mechanisms.

A m a n d a D a n c s o k (UBC) performed immunohistochemical assays on 57 human synovial sarcomas, an aggressive cancer of young adults. She found that expression of KDM2B was associated with improved overall survival at 15 years. Rola Saleeb (UofT) presented data on expression of miR-200 family of microRNAs in Clear Cell Renal Cell

Carcinoma. Saleeb found that when these microRNAs are over expressed, patients have a worse survival and that this 2 overexpression could be used as a prognostic marker. Jack 3 Brzezinski (UofT) investigated the loss of imprinting (LOI) at 4 five imprinting centers in Wilms Tumour, adjacent renal tissue 5 and cells sloughed into urine. Brzezinski described, for the first 6 time, a prevalent LOI at 14q32 and its association with 11p15 7 LOI in the somatic tissue of Wilms Tumour and the detection of 11p15 LOI in urine from sloughed somatic tissue.

Matthew G.K. Benesch (UofA) presented data on the role 10 of autotaxin, a secreted enzyme that produces 11 lysophosphatidate (LPA) from lysophosphatidylcholine. 12 Benesch found that malignant thyroid tumours had higher 13 levels of tumour autotaxin and LPA, and that LPA increased 14 thyroid cancer cell inflammatory mediator and autotaxin 15 secretion. Xenograft thyroid tumour mice treated with 16 autotaxin inhibitor showed reduced tumour volume, 17 angiogenesis and inflammation. Alexandra Kuzyk (UofM) 18 presented work examining telomere organization in 19 neuroblastoma. Using 3D quantitative fluorescence in situ 20 hybridization, she identified four subgroups, each with a 21 distinct level of genomic instability based on telomere 22 organization. Interestingly, subgroups correlated with patient 23 characteristics such as histology, age of diagnosis, MYCN 24 amplification and MYCN expression. Moreover, the number 25 of short and long telomeres increased with MYCN 26 transfection. These findings suggest that genomic instability in 27 neuroblastoma may be mediated through changes in telemeter 28 organization due to MYCN overexpression.

Laura Forrest (UOttawa) presented studies on the 30 relationship among estrogen (E2), GREB1 and E2-stimulated 31 proliferation of ovarian cancer cells. The role of GREB1 in 32 ovarian cancer progression was validated via proliferation 33 assays, using Esr1 (estrogen receptor 1) + and - ovarian cancer 34 cells (+/- E2 treatment). qPCR data supported the hypothesis 35 that GREB1 may promote ovarian cancer progression via 36 modulation of ESR1-mediated signalling. Xiao Zhao (UofT) 37 studied the role of adipose stromal cells in reversing the 38 formation of radiation fibrosis. Zhao found transplanting these 39 cells reduced fibrosis, which may be useful in mitigating 40 sequelae following cancer remission.

Other topics

John Soleas (UofT) examined the mechanical forces during lung development and how they guide the fate of cells during differentiation. Soleas demonstrated a tissue-engineering model that examined geometric cues to guide cell differentiation. Ranita Manocha (Western) worked to quantify the effect of bracing on elbow stability after elbow

lateral collateral ligament injury using cadaveric specimens. Manocha reported that when the arm was dependent during daily activities, a brace might enhance elbow stability. Chris Walsh (UofT) presented data on microRNA and mRNA levels in critically ill patients with muscle weakness. Walsh found genes with increased expression, which could provide a pathway framework for future drug discovery studies.

In BTBR mice, which model autism spectrum disorders, Chris Newell (UofC) found that a ketogenic diet altered 10 mitochondrial function in liver cells. Cynthia Luk (UofT) 11 explored the role of focal adhesion kinase (FAK) in adipocytes, particularly in the setting of obesity-associated insulin 13 resistance. Adipose tissue-specific FAK knockout mice were 14 studied in the setting of obesity, which was induced through a 15 high fat diet. Luk's findings suggested that FAK is required for 16 adipocyte survival and maintenance of insulin sensitivity.

18 Clinical Research

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With dedicated training in study design and research methodologies, many clinician investigator trainees are carrying out high quality clinical research studies. These studies range from case series and epidemiological surveys to randomized controlled trials. Grouped by medical topics, this section explores the wealth of clinically-focused research carried out by Canadian clinician investigator trainees.

Population Health and Epidemiology

29 Amrita Roy (UofC) examined the ability of health service systems to meet the needs of pregnant aboriginal women. By 31 conducting interviews with multiple stakeholders, Roy 32 determined that reducing stigma and barriers to access such as 33 transportation, and increasing training and 34 culturally-appropriate services are needed. Rebecca Rich 35 (UofT) reviewed recommended performance and quality 36 indicators for use in circumpolar maternity care systems. When completed, this review will highlight the extent and 38 nature of research and policy-related activities on the performance of maternity care systems.

Jonathan Fuller (UofT) presented data showing that 41 randomization does not necessarily balance all confounding causes in a randomized control trial. His work highlighted the reasons why randomized controlled trials often have internal validity metrics. Ben Ouyang (UofT) determined the 45 incidence of needle stick injuries among medical trainees, and 46 the distribution of needle stick injuries across the medical specialties. Ouyang reported that needle stick injuries posed a

common risk to medical trainees at Toronto East General Hospital.

Mohamad Hussain (UofT) assessed the validity of carotid 3 endarterectomy and carotid artery stenting coding in Ontario 4 administration databases by comparing them to procedures 5 documented in charts through a blinded review. This analysis 6 demonstration that these codes accurately identified patients, 7 so researchers can confidently use administrative data to 8 conduct population-based studies. Aleksandra Leligdowicz 9 (UofT) presented a study on biomarkers of endothelial 10 dysfunction and mortality prediction in Ugandan children 11 hospitalized for acute febrile illness. Their preliminary results 12 suggest that adding biomarkers of endothelial dysfunction can 13 independently predict mortality and improve discrimination.

Given the recent availability of HPV vaccination, Karla 15 Willows (University of Manitoba; UofM) performed a 16 meta-analysis to determine whether a 2- or 3-dose schedule was 17 more effective in girls aged 9-14. Willows found that two doses 18 of HPV vaccination resulted in inferior immunogenicity 24-35 19 months post vaccination; however, longitudinal data on these 20 cohorts is missing and it is unknown whether booster shots 21 may be necessary for those that have received only two shots. 22 Julie Lovshin (UofT) presented data on whether inequities in 23 retinopathy screening and treatments were present for 24 immigrants to Ontario with type 2 diabetes. Immigrants had 25 lower screening rates compared with long-term residents; 26 however, access to treatment was similar for both groups. 27 Nater (UofT) aimed to identify key survival predictive factors 28 in surgical metastatic epidural spinal cord compression 29 (MESCC) patients. Nater found that slow tumour growth 30 rate, absence of visceral metastasis and lower degree of 31 preoperative physical disability were predictive factors for 32 longer survival in selected surgical MESCC patients.

Surgery

Kyle Ricord (UofC) reported the incidence, demographics and outcomes of burns treated at the Burn Unit of Foothills Medical Complex (FMC) in Calgary, Alberta. The majority of patients were young males with facial and neck burns. There was a greater severity of burn injuries sustained during the illegal manufacturing of hash oil; with these burns affecting a greater average body surface area and requiring a longer length of admission than in the general population. David Berger-Richardson (UofT) presented data on the attitude of staff surgeons on changing gloves and instruments during cancer surgery. He found that there is little consensus among surgeons on how gloves and instruments should be handled

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and surgeons rely on clinical evidence for changing gloves and instruments during cancer resections to avoid tumour seeding.

Andras Fecso (UofT) presented survey data on how surgeons distribute "takes" to trainees during a complex laparoscopic procedure. The most important steps were not performed routinely by trainees, and trainee involvement could be improved with defined performance standards. Natashia Seemann (UofT) examined surgeon stress in the operating room. While great inter-surgeon variability was observed, unexpected stressors such as previous complications proved very important. Physiological measures of stress were only interpretable in the context of subjective stress experience and sociocultural aspects (e.g., OR team composition) were an important contributor. Together, these findings suggest that an individualized approach to stress management is important for surgeon wellness.

18 Internal Medicine

Abdul Elkadri (UofT) discussed a novel form of protein losing enteropathy. A patient, who presented at 8 days old with hyponatremia and died at 136 days old from sepsis, was found to have a plasmalemma vesicle-associated protein mutation, which resulted in sieving protein-losing enteropathy and death. Van Woudernberg (UofC) described an ongoing study to test a relationship between infliximab serum levels and clinical outcome in children with ulcerative colitis. Out of 19 children treated with a standard infliximab regimen, 71% were in clinical remission and 59% demonstrated a clinical response by week 8. Although the serum infliximab levels of these children are monitored, further work is required to characterize the relationship between infliximab levels and clinical outcomes.

Dmitry Rosenberg (UofT) examined elderly and more complex patients who were being offered lung transplantation. Two fifths of these patients had skeletal muscle dysfunction resulting in impairments in daily function, and these patients required a longer hospital stay post-transplantation. Ewan Goligher (UofT) presented data on an optimal technique to evaluate sniff airway pressure and diaphragm function. Goligher found that sniff airway with marked airway resistance applied was a valid measure of respiratory muscle function, and that diaphragm thickening was a more reliable method of diaphragm function evaluation than diaphragm excursion.

Husam Abdel-Qadir (UofT) reviewed randomized controlled trials studying interventions for prevention of anthracycline-related cardiotoxicity in adults. Although the data was limited, it suggested that dexrazoxane was better than placebo for effective cardiotoxicity protection. Daniel Kagedan

(UofT) presented an analysis of overall survival following 1 curative-intent resection of pancreatic adenocarcinoma at the 2 Following resection, only patients with 3 population level. negative lymph nodes demonstrated improved overall survival 4 with adjuvant chemotherapy. Helen Cheung (UofT) used 5 preoperative gadolinium-enhanced MRI to predict colorectal 6 liver metastases prognosis post-hepatectomy. Cheung found 7 that patients with weaker MRI enhancement on preoperative 8 gadolinium-enhanced MRI are at a higher risk of 9 disease-specific mortality following colorectal liver metastases 10 resection. Anna Schmidt (UofC) used cardiovascular magnetic 11 resonance to examine the relationship between intra-thoracic 12 fat volume and myocardial function in remaining healthy 13 myocardial tissue patients with known or suspected CAD. 14 Intra-thoracic fat volume was negatively correlated with 15 myocardial function. No such correlation was found with body 16 mass index.

Reed A. C. Siemieniuk (UofT) performed a meta-analysis 18 to examine the impact of corticosteroids on adults hospitalized 19 with community-acquired pneumonia (CAP). Adjunctive 20 corticosteroids reduced all-cause mortality, the need for 21 mechanical ventilation, acute respiratory distress syndrome 22 and the length of clinical stay, suggesting that patients with 23 CAP would benefit from corticosteroid treatment. Jason 24 Elliott (UofT) studied non-invasive genomic analysis of 25 human endometrial receptivity in women with polycystic 26 ovarian syndrome (PCOS). Elliott proposed that ovulation 27 assessment of women with PCOS not actively trying to 28 conceive will be conducted, RNA will be isolated and 29 sequenced from aspirated endometrial fluid and compared 30 with gene-set from women without PCOS to determine gene 31 expression differences.

Neurology and Psychiatry

Alexander Wright (UBC) asked whether the brains of concussed athletes are more vulnerable to rapid blood pressure oscillations. By measuring cerebral blood flow using Doppler ultrasound and blood pressure using photoplethysmography, he observed a trend towards an acute reduction of the ability of cerebrovasculature to buffer blood pressure changes. David Brandman (Brown University) presented on a study using the precentral gyrus to decode common grasps for daily activities in two patients with amyotrophic lateral sclerosis (ALS). Brandman found that the precentral gyrus in humans can be used to accurately predict grasps for daily activities and could potentially be used to enhance prosthetic device utility. Ayan Dey (UofT) investigated whether functional connectivity differed in older adults with cerebral small vessel disease

(CSVD) who self-reported high versus low levels of executive dysfunction in their daily lives. Dey reported that relative to healthy older adults, those with symptomatic CSVD demonstrated reduced functional connectivity within and between critical attention neural networks such as the Default Mode Network and the Dorsal Attention Network.

Andrea Jones (UBC) presented data showing that marginally housed adults were more likely to suffering from psychosis if they had smaller utilized social networks. Utilized social network size may be associated with severity of psychotic illness at presentation. Jiameng Xu (McGill) analyzed the collective narratives of five patients undergoing mental health recovery to understand how these patients strive for their own wellbeing. Fighting and hiding were prevalent narratives, which may reflect patient beliefs about the appropriateness of their symptoms and how patients may choose to manage them.

Kathleen S. Bingham (UofT) characterized the predictive last value of suicidality on treatment outcome in psychotic depression (MDpsy). Bingham reported that baseline suicidality predicts outcome in patients with MDpsy and that patients with suicidality of any intensity did better with combination therapy versus monotherapy. Ingunn Benediktsson (UofC) evaluated standardized anxiety and stress tools in pregnant and postpartum populations for evaluation of psychosocial risk against prospective longitudinal study data collected in Calgary. These generalized tools were found to be appropriate screening tools for pregnant and parenting women at risk for mental distress.

30 Medical Education

With an ever-increasing focus on evidence-based educational practices in medical schools, there is a growing number of Canadian trainees engaged in research focused on improving aspects of medical education.

Cynthia Min (UBC) presented work on the malleability of influences of self-assessment skills of medical students. The use of a checklist after an OSCE station allowing students to score their own performance was found more accurately reflect their performance than students' self-identified strengths. Malika Sharma (UofT) described an ongoing study to characterize how health advocacy is taught in the postgraduate infectious disease curriculum. Because the "Health advocate" CaRMS role is one of the most difficult to teach and appraise, it is necessary to gain a greater understanding of the ways in which advocacy is understood and taught to help health science centres define their commitments to social accountability. Victoria McCredie (UofT) presented data on the effectiveness of a one-day Emergency Neurological Life

Support course by assessing post-course knowledge uptake and 6-month retention by physicians in Nepal. Overall, knowledge 2 had not significantly deteriorated at 6 months compared to the 3 immediate post-course scores, suggesting that this education 4 technique is effective at disseminating evidence-based practice. 5

Brandon Girardi (UofT) showed that a novel 2-week 6 intensive simulation skills course for all first year surgical 7 residents significantly improved structured assessments of basic 8 surgical skills, enabling residents to begin clinical practice with 9 much greater technical skills. Peter Szasz (UofT) examined 10 international perspectives with respect to technical 11 competence assessments in surgical training. By analyzing 12 seven responses to an open-ended survey from academic health 13 centres around the world, he showed that while technical 14 competence assessments were valued across all aspects of 15 training, these assessments were rarely implemented during 16 selection or certification of trainees both because of a lack of 17 evidence for their use and because of financial limitations. Dale 18 Podolsky (UofT) presented a proposal for developing a robotic 19 approach to cleft palate repair using a phantom model created 20 from an infant CT scan. Both staff surgeons and fellows were 21 successful in performing a cleft palate repair using the phantom 22 simulation. Moreover, all steps of the repair protocol were 23 deemed feasible using the da Vinci Surgical System. Further 24 modifications to the instruments and methodology to improve 25 safety and efficiency of the procedure were recommended. 26 Vivek Bodani (UofT) attempted to improve the training of 27 neurosurgical residents in endoscopic colloid cyst resection. 28 Bodani developed a patient-specific colloid cyst simulator and 29 future work was needed to conduct validation studies.

Applied Science and Biomedical Engineering

Another theme this year was a growing number of trainees engaged in applied science research with the aim of elucidating tissue biomechanics or improving therapeutic approaches.

Kyle Eastwood (UofT) attempted to increase the use of minimally invasive neuroendoscope. Eastwood proposed a method using the established single burr-hole ETV/ETB procedure. This study established a platform for estimating the shape of curved dextrous tools, capable of targeting multiple intraventricular points, to guide future instrument design. Philip Edgcumbe (UBC) introduced the Pico Lantern, a miniature projector for minimally invasive surgery, with an intention to improve surgical navigation and reduce surgical complications. Edgcumbe showed that the proof-of-concept Pico Lantern offers sub-millimeter surface reconstruction accuracy and detection and display of subsurface pulsatile vessel motion.

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Amanda Khan (UofT) investigated the amount of crush

force a tissue can take before cellular injury occurs. At the conclusion of this study, Khan hoped to determine how much force can be safely exerted on each gastrointestinal tissue without causing damage. Carlyn Figueiredo (UofT) presented work investigating the use of gold nanoparticles (GNPs) in the detection and treatment of glioblastoma tumours. He demonstrated that using an enhanced Raman scattering signature to track GNPs allowed for in vitro and in vivo 10 delineation of tumour boundaries. This work highlights the 11 potential of GNPs to serve as cancer therapeutics. Cameron 12 Kaye (UofM) reported on the use of microwave imaging for 13 biomedical applications. Kaye successfully reconstructed 14 experimental data collected from simple 2D targets with 15 dilutions of magnetic nanoparticles using microwave imaging.

17 Knowledge Translation

Very important to patient-oriented research are large scale efforts at knowledge translation that can improve the way clinicians apply findings from scientific studies to their practice. Paul Kudlow (UofT) presented the results of a trial studying the effect of a novel, post-publication dissemination strategy on article page views at six weeks. Randomly-chosen articles distributed across the TrendMD network had 87% more views compared with control articles, and no differences were observed by article type or medical discipline. Laveena Munshi (UofT) investigated strategies for mechanical ventilation in acute respiratory failure (ARF). Using the Premier Database, she looked at findings from 514,809 patients for the use of various ventilation strategies and correlated actual practices against findings from landmark trials. She found that strategies used did not always reflect published evidence, and concluded that research such as this may help to improve knowledge translation.

Concluding Remarks

The landscape of clinician investigator training in Canada is continually shifting; however, two facts are clear: (1) trainees are engaged in a wide variety of high quality research endeavours; and, (2) the community is experiencing gradual but consistent growth. The work presented at the CSCI-CITAC Annual General Meeting provides an exciting glimpse at a set of research questions at the interface of health and science – a set of questions that clinician investigators are especially well positioned to tackle. As such, we are grateful that the Young Investigator's Forum continues to provide a forum for the exchange of ideas and the mentorship and career development of these promising young scientists.

Acknowledgements

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