Proceedings Report

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Fourth Annual Clinician Scientist Trainee Symposium at the Schulich School of Medicine & Dentistry

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Abstract

The Annual Clinician Scientist Trainee Symposium (CSTS) gathers the local medical research community at the Schulich School of Medicine & Dentistry, including research trainees at the medical student, resident and fellow levels. Trainees showcase their current and upcoming work, and leaders in the community impart their perspectives on the importance and future of research in medicine. At the 4th Annual CSTS, perseverance and cautious optimism emerged as the characteristics that trainees should foster through their future careers as clinician scientists. This was echoed by the challenges and encouraging findings presented by trainees, who conducted their work as part of research projects within the MD, MD/PhD and clinical investigator programs. The four oral presentations and 10 three-minute thesis presentations covered the full breadth of medical disciplines across the spectrum of translational medicine, from fundamental sciences through knowledge translation. The CSTS concluded with the keynote presentation by Michael Strong, current president of the Canadian Institutes of Health Research, who gave a glimpse into his decades-long path of overcoming and overturning dogmatic views in the world of amyotrophic lateral sclerosis research, demonstrating how roadblocks in research can become an impulse for stronger science.

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The Clinician Scientist Trainee Symposium (CSTS) at the Schulich School of Medicine & Dentistry is an annual gathering of medical students, residents, fellows and staff where current and emerging research accomplishments are presented and celebrated by the clinician scientist community. The proceedings of the 4th annual CSTS affirmed the importance and value of training clinician scientists for bettering the future of healthcare. Two key themes emerged across the talks of the day: perseverance and cautious optimism. Perseverance in research was emphasized by the symposium's keynote speaker and current Canadian Institutes of Health Research President, Michael Strong, who encouraged trainees to develop confidence in their observations and instincts to overcome dogmatic rejection, challenges in publishing and difficulties in obtaining funding. Strong told attendees that perseverance should not be seen as mere grit, but rather a means towards better science. Concurrently, David Litchfield, Vice Dean of Research & Innovation at Schulich, argued that there has never been a more exciting time to be doing medical research. As a biochemist, Litchfield views biochemistry as the language of life, and believes that the incredible advances in genome sequencing, CRISPR, bioinformatics and artificial intelligence achieved in recent years will allow us to study and master this language of life like never before, taking us to the cusp of revolution in all medical disciplines.

Crucial to actualizing the potential of these tools, Litchfield advocated for the growth of formal programs for training clinician scientists. This view was strongly echoed in the remarks by both Strong and James Lewis, Director of Schulich's Clinical Research Training programs. To this end, Schulich leadership continues to support and develop the Summer Research Training Program (SRTP), the Schulich Research Opportunities Program (SROP), MD/PhD and the Clinician Investigator Program (CIP). The SRTP and SROP support medical students in pursuing research during the summers of pre-clerkship and longitudinally over the four years of medical school, respectively. The MD/PhD program supports students in completing a doctoral research degree either before the start of the pre-clerkship or the clerkship portions of the medical school curriculum. Lastly, CIP supports residents in pursuing research projects and advanced degrees including the MSc, PhD and now MBA, through a variety of schedules. These programs aim to help fulfill the institution's strategic plan to "optimize life-long health through innovations in research, education and active engagement with our communities". The programs engage the first-year medical student through the "faculty ready" researcher and are all directed by Lewis, an established clinician scientist himself, which has been especially

important for promoting mentorship across all levels of training and a continuity of clinician scientist training. Given the success of these programs and advances by the greater community of translational medicine, Litchfield concluded that "our future is bright, but we're not there yet—we need the continued commitment and leadership to achieve these goals."

Oral presentations

Showcasing the accomplishments made possible through each of the four major clinician scientist training programs, four trainees presented their recent research breakthroughs. Jonathan Hu, SRTP trainee supervised by Craig Campbell and Bekim Sadikovic, walked the audience through an expedition of pediatric neuromuscular diseases that had prompted innovative and targeted molecular investigations. During his summer research training, he participated in several challenging diagnoses, including a congenital myasthenic syndrome patient with novel LRP4 variants and the first two cases of congenital neuromuscular disease with uniform type 1 fiber to be associated with mutations in type 6 collagen. Jonathan also discussed his ongoing research on whole genome methylation profiles of patients with Duchenne muscular dystrophy in relation to disease severity and progression.

Matthew Fung, SROP trainee supervised by Cindy Hutnik, is looking to improve the surgical management of glaucoma and presented his work on an in situ model that mimics physiologic ocular flow parameters using human Tenon's capsule tissue. This innovative model allowed Fung to quantify the impact of TGF1 and flow on fibroblast differentiation, allowing future testing of drugs targeting these factors for the prevention of trabeculectomy failure. Charles Yin, MD/PhD trainee supervised by Bryan Heit, presented his work on the role of macrophages in atherosclerosis and cardiovascular disease. Using atherosclerotic plaque-resident macrophages recovered from the aorta of patients undergoing coronary artery bypass graft (CABG) surgery, he demonstrated that several pathways involved in macrophage removal of apoptotic cells were dysregulated early on during disease development. Yin also discussed two translational projects he is in the process of developing that will focus on the role of macrophages in patient outcomes following CABG surgery and in cardiac reverse remodeling following treatment of end-stage heart failure with left ventricular assist device therapy.

Amanda Berberich, CIP trainee supervised by Robert Hegele, presented her work on the optimization of next generation sequencing for the detection of copy number variations. She has applied this diagnostic tool in a study of

patients with a differential diagnosis of maturity onset diabetes of the young (MODY) but without any of the condition's known genetic mutations. Berberich was able to identify a genetic etiology for several of the patients and revise their diagnosis from diabetes mellitus to MODY. This significantly improved the management of these patients' blood glucose, as MODY patients respond well to sulfonylureas but have limited benefit from other common drugs used to treat diabetes mellitus, such as metformin or insulin.

Three minute thesis presentations

The skilled clinician scientist should be able to communicate effectively not only with content experts in their field but also with laymen and patients. Accordingly, the three minute thesis gives presenters the opportunity to deliver their research narrative to a broad audience in a manner that is accessible and emotionally impactful but still intellectually stimulating [1,2]. As part of the symposium, a friendly competition was held for the best three minute thesis between trainees from across all four Schulich clinical research training programs.

Highlighting the strength of Schulich's programs in Physiology & Pharmacology, Clinical Pharmacology and Precision Medicine, several trainees spoke about their work in drug metabolism, biodistribution and fetal-maternal medication safety. Marc Chretien, CIP trainee supervised by George Dresser, spoke about his research on drug disposition in patients with celiac disease and told a moving story of how he was inspired to pursue clinical pharmacology after witnessing his grandfather's battle with cancer. Theo Wigle, MD/PhD trainee supervised by Richard Kim, presented on his thesis project on utilizing DNA sequencing and precision medicine techniques to guide dosing of fluorouracil in chemotherapy. Wigle's research demonstrated that a precision medicine-guided approach to dosing significantly reduced rates of fluorouracil toxicity. Nick Tonial, MD/PhD trainee supervised by Brad Urquhart, is studying the safety and efficacy of tetrahydrocannabinol (THC) in patients with chronic kidney disease. Tonial's work has shown that THC metabolism is altered in a rat model of chronic kidney disease. Finally, Jake Wihlidal, SRTP student supervised by Qingpeng Feng, discussed his research on the impact of THC exposure during pregnancy on fetal lung development. Using a combination of mouse models and in vitro cell culture experiments, Wihlidal was able to show that THC reduced fetal lung surfactant levels and drove lung fibrosis.

Genetics is another of our institution's strengths, and a number of trainees presented their work in genetics and rare

diseases. Julieta Lazarte, MD/PhD trainee supervised by Rob Hegele, spoke on the contribution of genetics to the etiology of atrial fibrillation. Lazarte performed whole-exome sequencing of 200 patients with atrial fibrillation and identified a number of pathological variants; in particular, variants within genes associated with dilated cardiomyopathy. Fuad Chowdhury, SROP trainee supervised by Tugce Balci, has been working on linking PPR12 variants of unknown clinical significance to patients with a novel genetic syndrome characterized by developmental delay and eye abnormalities. Using Matchmaker Exchange, a service for finding patients around the world with similar rare genetic conditions, Chowdhury has been able to identify over 20 other patients worldwide with similar variants and clinical features.

Other clinician scientist trainees have been engaged in clinical outcomes research. Jielin Lu, SRTP trainee supervised by Damir Matic and Sandrine de Ribaupierre, discussed her research on outcomes following total cranial vault reconstruction surgery in pediatric patients with craniosynostosis. Lu showed that infants with syndromic craniosynostosis do not require greater cranial volume expansion during surgery, a finding that was unexpected given the current understanding of the condition. Eric Di Gravio, SRTP student supervised by Anthony Nichols, presented his work on a substudy of the ORATOR trial, an open-label randomized study comparing differences in quality of life between trans-oral robotic surgery versus radiotherapy for oropharyngeal squamous cell carcinoma. Di Gravio's work will better characterize specific patient subgroups that would benefit more from this type of robotic surgery.

Siobhan Smith, MD/PhD trainee supervised by Harry Prapavessis, works on exploring sedentary behaviour as a risk factor for the development of cardiovascular disease and type 2 diabetes mellitus (T2DM). Smith's research has already shown that sedentary behaviour is an independent risk factor for T2DM and that both physical activity and avoidance of sedentary behaviour are required to minimize risk of developing diabetes mellitus. Jake Armstrong, MD/PhD trainee supervised by Cindy Hutnik, recently completed his doctoral work on understanding the balance of inflammation and inflammation resolution in ocular disease. Using scarring of Tenon's capsule as a model system, Armstrong showed that immuno-resolvant drugs and especially pro-resolving molecules are promising means of reducing inflammation and limiting fibrosis.

Keynote presentation

This year's keynote presentation was given by Michael Strong, a former Dean of the Schulich School of Medicine & Dentistry and the current President of the Canadian Institutes of Health Research. Strong spoke on the importance of persistence in the face of scepticism and rejection in medical research, using his own journey as a clinician scientist as an example. Strong is internationally renowned for his description of cognitive symptoms and frontotemporal changes in patients with amyotrophic lateral sclerosis (ALS); however, his early work characterizing degeneration in the frontotemporal region of ALS patients by autopsy examination [3] and brain imaging [4] was met with significant pushback from the neuroscience community, as the dogma at the time held that ALS was purely a motor neuron disease. Subsequent studies demonstrating aberrant Tau phosphorylation and aggregation as a pathological mechanism in the development of ALS were also initially met with rejection from the scientific press. Using these examples from his own career as teaching points, Strong emphasized the importance of not giving up and trusting one's own instincts and observations. A point was made that clinician scientists are uniquely poised to make these observations and have access to tools (e.g., studying the natural history of disease in patients or participating in drug trials) that allow research to continue even when funding is scarce. Ultimately, perseverance in moving research forward is key to success as a clinician scientist. As Strong eloquently summarized, "If you think you are right, beat them with more data."

Conclusion

The 4th Annual CSTS saw the gathering of trainees and staff at all levels to celebrate the work of clinician scientist trainees at Schulich. It was a day showcasing the excellent and innovative research of these trainees who will go on to become part of the next generation of researchers that will push the boundaries of medical science. This symposium has seen significant growth over the years, reflective of the growing importance Schulich has placed on fostering the education of clinician scientists. Since the 2nd Annual CSTS in 2017, the proceedings of which have been published [5], this symposium has expanded to include trainees not enrolled in a specialist dual-degree clinician scientist training program such as the CIP and MD/PhD programs. This change speaks to the importance of not limiting the opportunity to engage in meaningful research training to a select cohort of trainees, but rather allowing for clinician trainees to experience research in a way that suits their own

career goals. It is through initiatives like SRTP, SROP and CSTS, which permit more medical students to engage in research, along with plenty of optimism and persistence, that we can start to shift the culture of medical training to one that truly values research rather than one that views it as a necessary checkmark for career advancement.

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References

1. Copeman P. Three minute theatre. *Int J Res Den*. 2015;6(1):77-92.
2. Ferguson C, Davidson PM. The importance of communicating your research: The 3 minute thesis. *Adv Nurs Dr Educ Res*. 2014;2(1):11-4.
3. Wilson CM, Grace GM, Munoz DG, et al. Cognitive impairment in sporadic ALS: A pathological continuum underlying a multisystem disorder. *Neurology*. 2001;57(4):651-7.
4. Strong MJ, Grace GM, Orange JB, et al. A prospective study of cognitive impairment in ALS. *Neurology*. 1999;53(8):1665-70.
5. Yin C, Blom JN, Lewis JF. The 2nd Annual Clinical Scientist Trainee Symposium, August 22, 2017, London, Canada. *Clin Invest Med*. 2018;41(1): E34-6.