From the President: Leading Leaders towards a Common Goal
Bruce Carleton, FCP, FISPE (President, CSPT)

Maybe you are wondering, Who is the president and what is he planning for CPST? I think it's more important to ask - Who are the Leaders within CSPT and what are they planning? Jeswald Salacuse wrote a terrific book (Leading Leaders) that I think is particularly pertinent for my first column as president for CSPT's newsletter. The objective of Salacuse's book was to note that great leaders do less leading and more co-leading than less-than-great leaders. “Whether your leadership is innate or thrust upon you, you’re in for a whole new set of challenges when managing other leaders. Think of the qualities that have brought you to a leadership role: your vision, confidence, and charisma, or perhaps your experience, unique skills, expertise, or network of powerful allies. Now remind yourself that other leaders share some or all of these qualities with you. The potential contributions of these elites to any organization are vital, but the likelihood of friction is also high if you don’t manage relationships carefully. In any case, they are people with significant resources -- and strong opinions.”

I suppose one way to “manage” these strong opinions is to control them. To ask for help if and when I want an opinion. But this isn’t keeping with the mandate of either CSPT or of science. Here I am speaking of the importance of collaboration. Instead, we will all be working together - that includes YOU, our members at large, CSPT’s Board of Directors and it’s Executive Committee - to advance our organization to be even more successful in the future.

My goal in leading CSPT these next two years is to share the leadership of the organization with others. We will focus every our attention on seven things:

1. Direction. We will negotiate a common vision for CSPT
2. Integration. We will make all the stars of CSPT into a team focused on our common vision.
3. Mediation. We will resolve conflicts over turf and power that may arise.
4. Education. We will educate each other, even though we are highly-educated people.
5. Motivation. We will move our leaders to do the right thing for CSPT.
6. Representation. We will lead our members while co-leading each other.
7. Create Trust. We will gain and keep each others’ trust, the vital capacity our Society depends on.

So who are the Leaders of CSPT? They are the workhorses of the organization and run the Committees:

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Want to get involved with CSPT? Not sure where to land? Unclear what a committee does? Contact the Leaders and ask your questions, express your interest in joining us. Not sure if you have time? Interview them and find out what they are doing and where their committee is going? Ask about committee meeting frequency and what Committee members are expected to do.

This is OUR organization - meaning that YOU have an important role in where we are going. Get involved. Help us Lead.
Report on the 2021 Scientific Meeting
Dylan Burger, PhD, ISHF (Chair, Publications Committee)

The 2021 Scientific Meeting of the Canadian Society of Pharmacology and Therapeutics: “Not on Mute: Let’s Talk Contemporary Pharmacology” was held from June 7-11, 2021. For the second straight year the meeting was held virtually due to COVID restrictions, however the meeting was greatly expanded compared to 2020 with a sleek virtual interface, networking activities and events, and a strong program featuring keynote speakers.

The meeting opened with presentation of the 2021 awards and award lectures. A list of awardees can be found below. Dr. Abby Collier, Chair of the CSPT Awards Committee noted the diversity of the recipients “Awardees were male and female. Four of six awardees are considered traditionally under-represented communities (women in STEM (1), visible minorities (3)).

Day two focused on the much-anticipated “High Cost Drugs in Pediatrics Summit” a first of its kind gathering of stakeholders to discuss the challenge of high cost drugs in pediatric medicine and to discuss collaborative strategies to ensure equitable access to therapies. The summit attendees included clinicians, discovery scientists, as well as representatives from government agencies, NGOs, and patient advisory groups. Stay tuned for updates on future activities extending from the high cost drugs summit.

Day three opened with a plenary session on Membrane Proteins with a keynote lecture from Dr. Stephen Ferguson (University of Ottawa) “Regulation of Metabotropic Glutamate Receptor Signaling: Role in Alzheimer’s and Huntington’s Diseases” followed by a highly active COVID-19 symposium in the afternoon. The day concluded with a Kahoot trivia networking event that was won by Dr. Goralski.

Day four was trainee-focused, opening with the Top 10 Trainee Oral Presentations followed by an afternoon “Practical Pharmacology” session and an evening Career Networking event. The 2021 trainee awardees:

- **Rhoderic Reifenstein Award** – Brendan McKeown - Dalhousie
- **Peter Dresel Award** – Yongjin (James) Lin - Western
- **Ken Piafsky Award** – Brent Tschirhart- Western
- **William Mahon Award** – Kristen Meyer – Toronto

The meeting closed with a plenary session on Cancer Pharmacology with a keynote lecture Dr. Lilian Siu (University of Toronto) “Clinical Applications of Liquid Biopsies for Monitoring of Disease and Response to Therapy” and a Pharmacology Education Workshop “Course Design with Students in Mind – Encouraging Learner Success in Pharmacology”.

In total the meeting had 179 attendees and almost 50 virtual posters.

Feedback from the event has been overwhelmingly positive. Attendees were engaged immediately through by platform’s icebreaking tools and the community remained active throughout the meeting. CSPT immediate past president Kerry Goralski noted that “The Program Chair Thomas Velenosi (University of British Columbia) and his committee can be proud of the tremendous success of the 2021 CSPT Scientific meeting. The virtual platform was easy to navigate, there were many opportunities to socialize and network and the trainee presentations and pharmacology programming was outstanding. The mics were on and the science spoke. See you at CSPT 2022!”
Abby C Collier, PhD – (Chair, CSPT Awards Committee)

Distinguished Service and Education award – Dr. Kerry Goralski
Dr. Goralski is a Professor in the College of Pharmacy at Dalhousie University. He is a long-standing member of CSPT and has recently served as Society President and has undertaken multiple committee roles in the society, including organizing annual meetings on multiple occasions. Dr. Goralski spearheaded CSPT’s affiliation with ASPET and was instrumental in finding sponsorship for ASPET travel awards and continues to contribute to ASPET committees. He has been active in education of trainees (both his own, and promoting multiple workshops for the society) and maintains an outstanding research program. We congratulate Dr. Goralski on his contributions to the Society and to Pharmacology in Canada and abroad and on this well-deserved award.

Senior Investigator Award – Dr. Anna Taddio.
Dr. Anna Taddio is Professor of Pharmacy at the Leslie Dan Faculty of Pharmacy and a Pediatrician at Sick Kids Hospital in Toronto. She has shown outstanding dedication as a clinician, and maintained excellence in her research as demonstrated by her continuing long-term grant success and large number of influential publications (in excess of 200). Her teaching portfolio and the training environment she provides are clearly, also outstanding. Dr. Taddio is an internationally recognized clinician and scientist and CSPT congratulates her on being our 2021 Senior Investigator.

Junior Investigator Award – Dr. Rithwik Ramachandran.
Dr. Ramachandran is an Associate Professor in the Department of Physiology and Pharmacology at the Schulich School of Medicine, Western University. Despite being an early career investigator Dr. Ramachandran has a considerable number of publications and an enviable funding record. He has been uniformly productive as a researcher, and has a strong training environment for his trainees. He also gives back to his department through service on multiple committees and teaching of graduate and undergraduate students.

Post Doctoral Fellowship Award – Dr. Qutuba Karwi.
Dr. Karwi is a post-doctoral fellow at the Cardiovascular Research Centre, Faculty of Medicine and Dentistry, University of Alberta working with Dr. Gary Lopaschuk. He completed his PhD with Dr. Gary Baxter, where he published several papers and won several Fellowship and presentation awards. This has continued into his post-doctoral fellowship with multiple Fellowships including Alberta Innovates, and the American Heart Association. He has published 16 papers in the space of 3 years in the Lopaschuk laboratory, many as first author. Dr. Karwi has shown leadership and mentorship of younger graduate students, sits on several committees and volunteers in the University and wider community. We congratulate him on his success.

Clinical Fellowship Award – Dr. Marc Chretien.
Dr. Chretien is a clinician scientist in the Department of Medicine at Schulich School of Medicine, Western University. He performed his residency in Clinical Pharmacology and Toxicology at Western University. His research contributions revolve around the effect of cytochromes P450 on drug levels and in celiac disease. He is a member of multiple societies and has given national and international talks in both the clinical medicine and clinical pharmacology realms. He has been an active and collegial member of CSPT and the society congratulates him on the Clinical Fellowship award.

Publication Award – Dr. Khaled Abdelrahman
Dr. Abdelrahman is a post-doctoral fellow in the Laboratory of Dr. Stephen Ferguson, Departments of Cellular and Molecular Neuroscience and Neuroscience at the University of Ottawa. He presented a technically outstanding publication for evaluation (Science Signalling, December 2020, DOI: \texttt{10.1126/scisignal.abd2494}), that the
committee felt had excellent impact and reach in the field of Alzheimers and sex-specific etiology. The paper was highlighted by the editors as a top pick of 2020, was downloaded 12,000 times within two weeks of publication and has an Altmetric score in the top 5% of papers. We congratulate Dr. Abdelrahman on his publication and wish him continued success.

EDI Considerations
The awards committee itself is diverse in career stages from student representation through to full professors. There are males and females on the committee, including visible minority representation and representation from multiple provinces (BC, Alberta, Ontario, Quebec, Nova Scotia) and universities (UBC (2), University of Alberta, University of Toronto, Université de Montréal, Dalhousie University). The committee represents a pan-Canadian perspective.

Awardees were male and female. Four of five six awardees are considered traditionally under-represented communities (women in STEM (1), visible minorities (3)). Provinces represented by awardees included Ontario, Nova Scotia and Alberta; and universities represented included universities of Alberta, Dalhousie, Ottawa, Toronto, and Western. The awardees are diverse in career stage, in part because the CSPT awards have been constructed to specify the full range of career stage(s). The committee is pleased to have strong EDI component to awardees, but notes that they can only assess the applications they are sent.

Outstanding research from excellent trainees
Pierre Thibeault, PhD- (Publications Committee)

Poster award winners:
Rhoderic Reiffenstein Award – Brendan McKeown (Dalhousie University)
“Breast cancer affects 1 in 8 Canadian women and 10-20% of advanced breast cancers are triple-negative. Multidrug resistance to standard chemotherapies increases with lengthening treatment duration in triple-negative breast cancer. Jadomycin B is a member of a novel family of drugs which we showed to be effective in killing multidrug resistant human breast cancer cells in vitro. The aim of my research is to investigate the anti-cancer mechanisms of action of jadomycin B through the development of jadomycin B resistant MDA-MB-231 triple-negative, human breast cancer cells. To do this, jadomycin B resistant cells were developed by exposing control MDA-MB-231 cells to increasing concentrations of jadomycin B over a 7-month period. These cells were also resistant to other jadomycins but lacked resistance to anthracyclines. Associated with this increase in resistance was an increase in expression of cyclooxygenase-2 but no change in the expression of drug efflux transporters which is...
typically observed with anthracycline resistance. When cyclooxygenase-2 inhibiting drugs were administered in combination with jadomycin B a synergistic effect was observed, lending further evidence that the cytotoxic effect of jadomycin B is modulated by cyclooxygenase-2 signalling.”

**Peter Dresel Award – Yongjin (James) Lim (Western University)**

“Cisplatin is a highly effective chemotherapeutic medication. The major limitation of cisplatin therapy is toxicity to the kidneys, with cisplatin causing acute kidney injury (AKI) in approximately a third of patients receiving cisplatin treatment. AKI is currently diagnosed by measuring blood levels of creatinine, a waste product that accumulates in the blood when the kidneys are not functioning properly. However, by the time blood creatinine levels rise high enough to diagnose AKI, significant injury has already occurred in the kidneys. Better early diagnostic or predictive markers are necessary for proper intervention/management of cisplatin-induced AKI.

We used metabolomics to investigate the metabolic changes that occur in a mouse model of cisplatin-induced AKI. Metabolomics is the study of all the metabolites present in biological samples such as blood or urine. We administered cisplatin to mice to induce AKI, and collected blood, kidney, and urine samples from these mice from 1-4 days following cisplatin administration.

These samples were used to perform a metabolomic analysis to identify which metabolites could potentially serve as markers for AKI. One such example was the metabolite creatine, which showed an early and sustained rise in both kidney and blood samples in mice treated with cisplatin.”

**Oral presentation award winners:**

**Ken Piafsky Award – Brent Tschirhart (Western University)**

“Sepsis is a dysregulated immune response to infection and the leading cause of mortality globally, accounting for 11 million deaths in 2017. To date, no therapeutics are available to treat the underlying septic response. Previous research from our laboratory has shown that annexin A5 (Anx5) treatment increased survival by 40% in mice with endotoxemia, a model of sepsis. During sepsis, activated platelets (PLTs) release membrane fragments called microparticles with externalization of phosphatidylserine to which annexin A5 binds with a high affinity. We hypothesized that annexin A5 will block the pro-inflammatory response induced by activated PLTs and microparticles in vascular endothelial cells (ECs) under septic conditions. We showed that treatment with annexin A5 lowered expression of inflammatory cytokines and adhesion molecules induced by lipopolysaccharide (LPS)-activated PLTs or microparticles in ECs. Furthermore, annexin A5 treatment improved EC structural integrity and reduced monocyte adhesion to ECs in septic conditions. Our study shows that annexin A5 inhibits EC inflammation in septic conditions, suggesting its potential as a treatment for sepsis. Severe COVID-19 patients develop sepsis. A phase 2 clinical trial on the effects of annexin A5 in critically ill COVID-19 patients with sepsis is currently underway at London Health Sciences Centre.”

**William Mahon Award – Kirsten Meyer (University of Toronto)**

“Bacteria can attach to surfaces and form communities known as biofilms. Staphylococcus aureus excels at forming these biofilms on catheters and other medical devices. Unfortunately, in the biofilm S. aureus is in a metabolically dormant state and very tolerant to antibiotics, a leading cause of treatment failure and chronic infection in patients. I grew S. aureus biofilms on catheter segments and exposed them to different antibiotic regimens. Although we often think more antibiotic for longer is better, I found that by providing a regular break from the antibiotic the treatment was more effective, because the break allowed the dormant and tolerant bacteria to resuscitate and become susceptible. There was a U-shaped response curve around the time of the break. Too short of a break and bacteria do not resuscitate, but too long of a break and the bacteria replicate and resistance is able to expand. With the optimal length of break, treatment was dramatically more effective. This intriguing pharmacokinetic-pharmacodynamic relationship, of antibiotics with bacteria in the physiologically relevant growth state of a biofilm, reveals how to successfully erode biofilm defenses.”
Autoimmune diseases affect many women of childbearing age (Angum, Khan, Kaler, Siddiqui, & Hussain, 2020). Autoimmune diseases are a group of heterogenous conditions attributed to genetic predisposition and environmental factors. T helper 17 (Th-17) cells are major players in the development and progression of these diseases (Waite & Skokos, 2011). While our current knowledge on the effect of Th-17 cytokines and autoimmune diseases on the expression of placental transporters is limited, this mini-review highlights the importance of the findings of our recent research paper entitled “Impact of Th-17 Cytokines on the Regulation of Drug Transporters in the Placenta” (Mirdamadi, Kwok, Nevo, Berger, & Piquette-Miller, 2021).

Th-17 cells of CD4+ T cells are major players in the development of various autoimmune diseases such as rheumatoid arthritis (RA), multiple sclerosis (MS), psoriatic arthritis (PsA), Systemic lupus erythematosus (SLE), psoriasis, inflammatory bowel diseases (IBD), and many others (Gaffen, 2008; Huber et al., 2014; Ivanov S. & Linden, 2009; Komatsu N. & Takayanagi H., 2012). Activation and differentiation of Th-17 cells by autoantigens leads to the secretion of other pro-inflammatory cytokines including IL-17A and IL-22. A sequence of signalling of T cell receptors (TCR), transforming growth factor-β (TGF-β), IL-6, IL-23, and activation of retinoic acid-related orphan receptor (ROR-γt) are involved in the differentiation of Th-17 cells leading to extracellular defense, allograft transplantation, and autoimmunity (Sutton et al., 2009).

ATP-binding cassette (ABC) and solute carrier (SLC) transporters are the two main families of transporters distributed in several barriers such as blood brain barrier, intestine, liver, blood-testes barrier and blood placenta barrier. Membrane transporters play a crucial role in the pharmacokinetic of drugs. Drug transporters play an important role in the absorption, distribution, metabolism, and elimination (ADME) of various drug substrates. A wide variety of endogenous and exogenous substances are substrates, inducers or inhibitors of ABC and SLC transporters. In addition, regulation of drug transporters is affected by acute and chronic inflammation in several organs and tissues. Changes in the regulation (expression and activity) of drug transporters impacts the efficacy of drugs, toxicity or lack of efficacy (Evers et al., 2018).

Using human term villous explants, this study demonstrated that the expression of several placental drug transporters is significantly impacted by Th-17 cytokines. Specifically, the mRNA and protein expression of OATP2B1 was significantly downregulated in IL-23 treated placental explants. Subsequently, the accumulation of OATP2B1 substrate was significantly lower in IL-23 treated JAR cells. Similarly, IL-17A and IL-22 imposed a significant downregulation on the mRNA expression of OATP2B1. OATP2B1, a SLC transporter expressed in the liver, placenta, heart, brain, kidneys, lungs, and small intestine, contributes to the transport of various clinically important drugs such as statins, sulfasalazine, glyburide and endogenous substances such as bile acids and steroid hormones (Kusuhara et al., 2012; Ogura, J. et al., 2020; Windt et al., 2019). Located on the basal membrane of the placenta, OATP2B1 facilitates the uptake of fetal-derived unconjugated (sulfated) estrogens such as estrone-3-sulfate (E3S), E1S, and DHEA-S for de novo synthesis of steroids within the placenta. The observed lower expression and activity of OATP2B1 in placental explants may carry important clinical ramifications as reproductive hormones play a crucial role in the growth and development of the fetus (Kaludjerovic & Ward, 2012).

Similarly, the mRNA expression of BCRP was significantly reduced in term placental explants exposed to either IL-23 or the combination of IL-17A, IL-22 and IL-23 (Mirdamadi et al., 2021). Regulation of breast cancer resistant protein (BCRP), an important clinical transporter, is affected by inflammation in several other tissues. For example, intestinal BCRP is 50% less expressed in patients with HIV (Alam, Whyte-Allman, Omeragic, & Bendayan, 2016). In the
placenta, inflammation-induced dysregulation of BCRP has been documented in preeclampsia and chorioamnionitis (Kojovic, Workewych, & Piquette-Miller, 2020; Petrovic, Kojovic, Cressman, & Piquette-Miller, 2015).

The mRNA expression of OCT3 was increased after 24-treatment of term placental explants with a combination of IL-17A, IL-22 and IL-23 (Mirdamadi et al., 2021). OCT3 is one of the highly abundant SLC transporters in basolateral membrane of several tissues including renal proximal tubules, neurons, placenta, uterus, ovaries, hepatocyte sinusoidal membrane, and small intestine enterocytes. In the placenta, OCT3 plays a role in the clearance of catecholamines from the fetal circulation (Staud et al., 2012). In addition, apical SERT transporter and basolateral OCT3 facilitate maternal-fetal transport of serotonin (Kliman et al., 2018). Impaired expression of OCT3 may lead to increased fetal exposure to toxic compounds. In an OCT3 knock-out mice model, Zwart et al (2001) demonstrated that the concentrations of the OCT substrate, MPP+ were significantly lower in the fetus after maternal serum administration of the compound. (Zwart, Verhaagh, Buitelaar, Popp-Snijders, & Barlow, 2001).

Placental drug transporters determine how much drug enters the placenta and fetal circulation. Understanding the interaction between autoimmune diseases and their associated cytokines and placental drug transporters could determine the extent of fetal drug disposition. As flare of autoimmune diseases during pregnancy are not uncommon, the aim of pharmacotherapy is to protect the mother against the major impacts of systemic inflammation. The findings of our recent research study can be a major contribution to preventative medicine to protect the fetus against maternal pharmacotherapy and to increase the quality of life during pregnancy without jeopardizing the physical and mental health of the growing fetus.

**References**


Where our interest in sciences comes from?
Ozgun Varol, BSc (Publications Committee)

To many of us, science has become second nature, a major part of our lives perhaps an instinct even. However, it was not always like that and during our annual conference Not on Mute: Let’s Talk Contemporary Pharmacology we thought we would ask our attendees as an icebreaker what it was that really sparked their first interest in science and pharmacology.

I’ll start with my own, for me I have always been fascinated by the living world around me. I remember being 6 years old digging up worms and just feeling them squiggle in my hands had me so curious as to how they can live under the earth. Later in high school, performing my very first chemistry experiment I was certain that science was the right career for me, and I have not once looked back.

Esther Bonitto, Co-op Research Student:

When I was in grade 8, my science teacher collected some samples of water from a nearby pond and brought them to class one day. He had a few light microscopes in his classroom, and it was the first time in my life that I had the chance to use a microscope. I was fascinated as I watched protozoa swim around and live out their lives in the few drops of water on the slide. I guess I almost always had an appreciation for science, but this moment was what really made me realize that I want to have a career exploring creatures and cells under the microscope.

Dr. Dylan Burger:

First interested in Science? I was always curious about the unknown. When my family got a computer in 1990 I took it apart because I wanted to know how it works (broke the video card in the process). First interested in Pharmacology? My fourth year honours project in the laboratory of Dr. David Freeman at Western. Actually Dr. Urquhart was the grad student I was working with.

Dr. Brad Urquhart:

And you stayed in science after working with me? For me it was either science or business in high school. Science won out (by a landslide) as it provided so many opportunities to explore how to make things better. It’s so interesting to learn how things work and how we can help when they aren’t working properly.

Dr. Abby Collier:

First interest in pharmacology - I was 14 and asked my GP how antibiotics worked. I said “I’m going to do drug research one day”... and here I am.

Dr. Kerry Goralski:

I always had a leaning toward sciences. Biology and chemistry were areas that I excelled in in high school. Absolutely loved the fruit fly genetics experiments in grade 12. However, when I started university I wanted to follow my big brother’s footsteps and go into management. Fortunately I received a "D" in my Calculus pre-requisite course and I was not eligible to apply until I improved my grade. While I was doing that I decided to take chemistry and physics and I was hooked and changed course entirely completed a BSc Hon in Biochemistry and Microbiology.
Dr. Thomas Velenosi:

I had a sick family member go through successful treatment when I was young and became fascinated by the drugs kept them alive. Started working as a pharmacy assistant/technician part time in high school (not sure if that’s allowed anymore) and took the first pharmacology class I could in undergrad. Dr. Urquhart was the course manager.

So, whether our interest in science first stemmed from Dr. Urquhart, discovering the unknown or helping others I think it’s fair to say that we all have a love for science and pharmacology alike. Although, some of us are further into their careers than others it’s nice to recognize that we all came from similar backgrounds and share an appreciation for the greatest topic in the world – science.

Kudos

• Congratulations to longtime CSPT members Michael Rieder (Western University), Anna Taddio (University of Toronto), and Reina Bendayan (University of Toronto) who were recently elected Fellows of the Canadian Academy of Health Sciences. Further details are available here: https://cahs-acss.ca/wp-content/uploads/2021/09/CAHS-2021-New-Fellows-News-Release-EN.pdf