

CanVECTOR Clinical Investigators Group

PROTOCOL STRENGTHENING EXERCISE

May 23, 2019 - Toronto, ON. BMO Education & Conference Centre -
1:00-3:00 p.m.

RSVP TO ATTEND: INFO@CANVECTOR.CA



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NEWS & EVENTS

CanVECTOR is a pan-Canadian, patient-oriented, Community Development Program centered on venous thromboembolism-related research, training, and knowledge translation.

Message from the Directors

Hello CanVECTOR Family,

Spring has finally arrived!

We have been keeping very busy while waiting for the snow to melt away. In February, we also held our Year 4 Pilot Trial competition; the results will be announced in the next To the Point email.

In March, we launched our Spring training award competitions: CanVECTOR's Travel & Research Start-up, Fellowship & Studentship, as well as the Thrombosis Canada CanVECTOR Research Fellowship award. We encourage you to visit our website regularly for all the training resources including the annual funding competitions, training curriculum and academic mentorship program. We'd also like to congratulate all the trainees who received start-up, fellowship/studentship and ERLI awards in our Fall competitions: see page 2 of this newsletter to learn more about their research.

Coming up in May in Toronto, we will hold our 3rd Trainee Boot camp, followed by a new CIG initiative called "Protocol Strengthening Workshop", as well as the 12th meeting of our Scientific Steering Committee. You can find out more about the boot camp and CIG workshop topics and speakers in the News and Events section of this newsletter.

There is much to look forward to at ISTH 2019 in Melbourne, July 6–10, 2019. We look forward to attending, along with many of you. Our partner network, INVENT-VTE, has just closed its "Call for Applications" for their 2nd Annual Dragons' Den

competition, to be held at the ISTH Congress on Tuesday, July 9th at 12:15-1:15 pm – hope to see you there! Three INVENT Judges: Dr. Deborah Siegal; Dr. Simon Noble; Dr. Paul Ockelford (aka INVENT Dragons) will evaluate three research proposals and select a winner who will be awarded a \$35,000(CAD) International Collaboration prize. The presenters will give a 5–8 minute "elevator" pitch, and the audience will get to vote on the trial's potential to change practice.

This year's ISTH social media campaign will highlight our members' presentations and activities during ISTH 2019. **Please remember to send us the titles and presentation dates of your accepted posters and oral presentations, so that we can include these in our social media blitz.** And don't forget to tweet during the Congress, using #CanVECTORatISTH19. It's a long haul to Australia, so remember to get up, stay active and stretch your legs to stay healthy and VTE-free.

As we keep thinking of innovative ways to support Canadian VTE research, we want to hear your suggestions and comments. Please send your thoughts and ideas to info@canvector.ca.

Susan R. Kahn



Susan and Marc

Trainees Spotlight: Fellowship and Studentship Awardees

We are pleased to announce the recipients of the 2019–2020 Fall Research Training awards.

Awardees were selected from a pool of candidates showcasing research activities in the area of thromboembolism, and aligned with one of the network's science or foundational platforms.

Congratulations to the awardees and thanks to all who applied!



Tobias Tritschler
University of Ottawa
awarded *CanVECTOR Fellowship*

PROJECT TITLE: Development and validation of a standardized definition of pulmonary embolism-related death

The adjudication of pulmonary embolism (PE)-related death in clinical trials lacks standardization, despite PE-related death being part of the primary composite endpoint in most venous thromboembolism (VTE) trials. This lack of standardization adds to the difficulty in performing meta-analyses and in comparing results between different studies. Furthermore, recent studies indicate that commonly used definitions of PE-related death may be non-specific and reproducibility of outcome adjudication for PE-related death is poor. The broad objective of the research project is therefore to develop and validate a standardized definition of PE-related death. The specific aims to achieve this objective are 1) to conduct a systematic literature review of existing definitions of PE-related death; 2) to propose a standardized definition of PE-related death as part of a working group of the International Society on Thrombosis and Haemostasis Standardization Sub-Committee on Predictive and Diagnostic Variables; and 3) to validate this definition in an autopsy study. We view this project as an important step to improve internal and external validity of VTE trials.



Siraj Mithoowani
McMaster University
awarded *CanVECTOR Fellowship*

PROJECT TITLE: Toward judicious anticoagulant reversal – can heparin calibrated anti-Xa assays exclude clinically significant drug levels of apixaban or rivaroxaban?

Although patients taking Factor Xa (FXa) inhibitors do not require routine coagulation monitoring, it may be helpful to measure plasma drug levels in specific circumstances where anticoagulant reversal is being considered. The ISTH states that FXa inhibitor drug levels of 30–50 ng/mL are sufficiently high to warrant antidote administration in patients who require an urgent intervention or who have serious bleeding. However, laboratory assays specifically calibrated to measure FXa inhibitor drug levels are unavailable in most hospital laboratories. Heparin-calibrated chromogenic anti-Xa assays are more widely available and are known to be highly sensitive to the presence of FXa inhibitors, making them potentially useful for this purpose. In our study, we will collect plasma samples from patients on apixaban and rivaroxaban, and compare heparin-calibrated anti-Xa activities with conventionally measured drug levels. We hope to establish whether heparin-calibrated anti-Xa assays can exclude clinically significant levels of apixaban or rivaroxaban. These findings would be helpful in settings that lack the ability to measure drug levels directly.



Angela Lee
McGill University
awarded *CanVECTOR Studentship*

PROJECT TITLE: Comparison of performance of two clinical scales to assess the post-thrombotic syndrome: Secondary analysis of a multicenter RCT of pharmacomechanical catheter-directed thrombolysis for deep-vein thrombosis

This project is a secondary analysis of the ATTRACT trial (Vedantham S et al., NEJM 2017). We are studying the performance of two different measures used to diagnosis and/or classify the severity of the post-thrombotic syndrome (PTS): the Villalta scale – primarily used by thrombosis researchers – and the Venous Clinical Severity Score (VCSS) – primarily used by vascular surgeons. Scores of these measures at various time points in trial follow-up are compared and analyzed in relation to quality of life (QoL) scores, such as the Short-Form Health Survey-36 version 2 and the Venous Insufficiency Epidemiological and Economic Study-QoL/Symptoms questionnaire, as a benchmark. This secondary analysis of a rigorously conducted multicenter RCT will help to better characterize the relationship of the more objective Villalta scale and VCSS, to the subjective experience seen in the QoL questionnaires. The results will allow for comparison of the performance and value of tools to diagnose and grade the severity of PTS. Overall, the findings will be useful in standardizing the approach to diagnosing, assessing and following PTS in patient populations in the research and clinical setting.



Sahar Sohrabipour
McMaster University
awarded *CanVECTOR Studentship*

PROJECT TITLE: Inhibition of neutrophil-derived procoagulant molecules: a translational study

In recent years, neutrophils have been shown to be indispensable for the initiation and propagation of venous thromboembolism (VTE). Activated neutrophils contribute to VTE through the delivery of neutrophil extracellular traps (NETs), consisting of cell-free DNA (cfDNA), histones, and neutrophil granular enzymes. Both cfDNA and histones have been shown to be procoagulant and antifibrinolytic, as well as exerting many other harmful effects. For example, histones induce endothelial cell death and contribute to vascular dysfunction. However, the mechanisms by which cfDNA and histones are removed from the circulation are not well understood. We hypothesize that the enzymes DNase1 and activated protein C (APC) influence the levels of circulating cfDNA and histones, respectively. By investigating the roles of DNase1 and APC, we hope to achieve a better understanding of the regulation and clearance of neutrophil-derived procoagulant molecules. We also hope that our research can provide useful information about the biological links between neutrophils and thrombosis.





Research Coordinators Working Group – Meet the co-chairs



Elena Shulikovsky

"Hello, it's been 17 years this spring since I joined the Thrombosis team at the Jewish General Hospital – years of a variety of trials (EXCLAIM, RE-COVER, SOX, SOME, Van-Gough, Hokusai, STEP-CAT, COSIMO and many others), years of collaboration with a team of specialists and pharmacists, and academic enrichment through ISTH & CanVECTOR conferences. My role encompasses study coordination and patient coaching. Being appointed the very respectful mission of co-leading the research coordinators working group, I will continue to exercise the following five principles of research practice: compliance, confidentiality, consistency, correctness and collaboration to help make today's investigation into tomorrow's treatment strategy."



Veronica Whitham

"I am a multicentre clinical trials coordinator with the Ottawa Blood Disease Centre. I have worked with the OBDC for the past 2.5 years after 5 years in Emergency Medicine research. My academic accomplishments include a BSc in Kinesiology from Queen's University. My background as a Certified Kinesiologist reflects my commitment to helping others and interest in human physiology."

Talking CanVECTOR Communications



We recently spoke with Caleb MacGillivray – CanVECTOR's Communications Coordinator, about his role with CanVECTOR and what's on the horizon for CanVECTOR's social media and communications.

1. Could you describe your role and how you became CanVECTOR's social media / communications coordinator?

It was one of those times where you're in the right place at the right time. I was working in an administrative role in the Division of Hematology at the Ottawa Hospital when a part-time role opened at the CanVECTOR network office in Ottawa. I have a journalism and communications background and CanVECTOR required some content curation for the website, so it was a good fit.

My role has evolved over time; now in addition to managing content on our [website](#), I also coordinate digital communications, including social media and email communications.

2. What are some of the highlights or communication achievements you are most proud of since taking on this role?

Our #ResearchSimplified series on social media is one of our major successes. In this campaign we have been able to showcase [Evidence Summaries](#) developed by CanVECTOR trainees and investigators.

This campaign has fostered engagement with new audiences, such as patients, science/medical advocacy organizations, and physicians who do not specialize in thrombosis. At the same time, the weekly posts have resonated with our main target audience: thrombosis physicians, as the posts often reaffirm best clinical practices and/or highlight studies that CanVECTOR members have led or participated in. The campaign has

brought in over 1200 unique click-throughs to the website from over 22 countries.

One of CanVECTOR's main objectives is to enhance our capacity for knowledge translation through a coordinated approach, and I think the dissemination of our members' abstracts and presentations at ASH 2019 through social media was very well received for doing just that. This not only helped to drive traffic to the website and increase our twitter base but has helped to meet one of our communication goals in strengthening our online community of advocates; our social media followers have been more engaged and responsive since this effort.

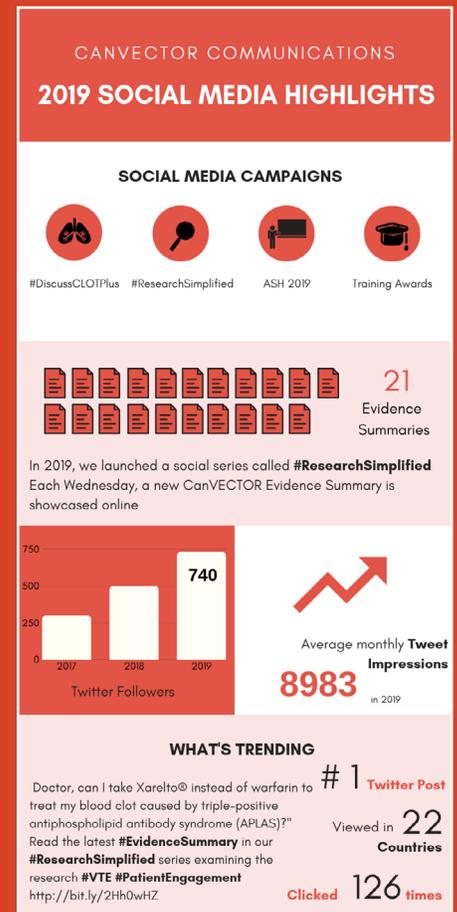
3. What is the biggest communication takeaways you have had since taking on this new role?

You often hear less is more in social media. Though for us, a minimal increase in the frequency of posts and overall activity on twitter, for example, has led to a substantial increase in followers, engagement, and monthly visits to our twitter profile. In fact, in 2017, our twitter posts were visible to approximately 6,500 users each month; in 2018–2019, they showed up in approximately 15,000 twitter feeds every month.

4. Lastly, what can we expect to see in the future in terms of digital communications?

You will continue to see the promotion of CanVECTOR research, though hopefully in some new, attractive ways using alternative forms or tools, such as video and infographics.

In fact, I am currently taking a new course on Digital Strategy, where I'll learn about new tools that I hope to apply to enhance the visibility of the network.





Member spotlight: An Interview with Dr. Paul Kim

Congratulations on receiving CanVECTOR's
2019 Emerging Research Leaders Initiative
(ERLI) Award!

1. Tell us about your career.

I obtained my Ph.D. in Biochemistry at Queen's University in Kingston, Ontario under the guidance of Dr. Michael Nesheim. Following that, I completed a 2-year Heart and Stroke Foundation of Canada Postdoctoral Fellowship under the guidance of Dr. Jeffrey Weitz and then a 3-year CIHR Postdoctoral Fellowship under the guidance of Drs. Weitz and Peter Gross. In 2014, I began my faculty appointment at McMaster University in Hamilton, Ontario, with the lab located at the Thrombosis and Atherosclerosis Research Institute (TaARI). I am the current Chairman of the International Society on Thrombosis and Haemostasis Scientific and Standardization Committee on Fibrinolysis and the Executive Director of the International Society for Fibrinolysis and Proteolysis.

2. Why did you choose to study the role of TAFI in thromboembolism?

I always had an interest in TAFI ever since being introduced to it during my graduate studies. Dr. Nesheim was one of the pioneers in discovering and identifying TAFI. I have published a few papers characterizing its biochemical properties over the years and we have always felt that there is more to TAFI than what is already known in the literature.

3. Describe the research you will do using the ERLI award.

We are interested in identifying how TAFI influences blood clot structure and composition. It is uncertain what conditions lead to increased risk of embolism once a blood clot has formed, and its downstream complications. Characterizing how TAFI influences clot properties and behaviour may lead to more effective and safer strategies to resolve these clots and reduce unwanted embolic events.

4. What are the outcomes of your research project?

We want to identify how TAFI directly influences blood clot structure and the consequent biophysical properties of these clots. By correlating the clot structure with embolic events using a newly described model of venous thromboembolism in mice that lack TAFI, we can uncover the underlying mechanism that renders certain clots more susceptible to embolism. Furthermore, based on our clot composition findings, we will target these key components to resolve these clots more effectively and safely.

5. You are a biochemist working with clinician scientists in venous thromboembolism. How do you think the basic science and clinical research interrelate in thrombosis research? Tell us about your approach when collaborating with clinicians.

Synergy between clinicians and basic scientists is critical for the overall advancement and translation of our findings. This proposed project is also a collaborative effort with Dr. Peter Gross, who is a clinician scientist that specializes in the use of intravital microscopy; the main technique we will use to observe and measure blood clot embolization. Being a member of TaARI provides me with ample opportunities to interact with key clinical and basic research scientists that foster collaboration. While good science is crucial for finding precise answers, having the perspectives of clinician scientists are also important to ensure that our resources and efforts are directed towards answering clinically relevant questions. This is my perception of how the two sides should ideally interact and collaborate.

6. In the long run of your career, what would you aim to accomplish in thrombosis research?

Should I be fortunate enough to stay funded and relevant for a lengthy career in research, it is my life goal to be able to contribute even the smallest tidbit in defining the overall picture of thrombosis and haemostasis. I am certainly hoping to leave a mark in the world of TAFI research and defining its role in, but certainly not limited to, thrombosis and haemostasis.

7. Tell us something about yourself outside of your work.

I am a family man first with a beautiful and understanding wife and a 3 and a half year-old daughter. Most of my time away from work is spent with my family. I love sports, especially hockey. I love traveling with my family. We have a speed demon of a daughter and discovered during our recent vacation that downhill skiing is the perfect fit for her. This bodes well as we are all skiers. I am also a big fan of Islay single malt Scotch; the more peat the better.

News & Updates



We are pleased to announce the winners of the CAEP-CanVECTOR Research Abstract awards. These will be presented at the CAEP 2019 Conference in Halifax (May 26–29), NS. Congratulations to:

Vidushi Swarup for her abstract entitled: Identifying patient values and expectations for pulmonary embolism CT scanning in the emergency department

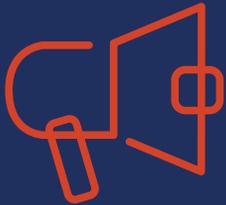
Dr. Leila Salehi for her research abstract titled: Variability in utilization and diagnostic yield of Computed Tomography (CT) scans for pulmonary embolism among emergency physicians.



We are holding our third Trainee and Early Career Investigators Research Boot camp on May 23, in Toronto. This will be a full-day boot camp with an interactive session on **"How to plan a randomized trial 101: Statistics and pilot trial design"** led by Dr. Sameer Parpia and Dr. Clive Kearon. The attendees will join CIG's Protocol Strengthening Workshop in the afternoon to witness and engage in peer review of three pre-selected clinical research protocols.



CanVECTOR' member and CIG Chair Dr. Kerstin de Wit was awarded the [2019 CAEP Top New Investigator Abstract Award](#) for her research abstract titled "Prevalence and clinical predictors of intracranial hemorrhage in seniors who have fallen." Dr. de Wit will be the 3rd Plenary Presentation at the [2019 CAEP Conference](#) in Halifax on Tuesday, May 28th.



The 4th CanVECTOR Annual Conference will be held on October 17–18, 2019 in Toronto, ON at the InterContinental Hotel on Front Street. Invitations will be sent out by early summer, along with the draft program. Abstract Submission will open on June 1st, 2019!

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