

We are extremely pleased to announce the winners of the inaugural Translational Institute of Medicine (TIME) Incubator Grant competition.

With \$300K in funds provided by the members of the Department of Medicine (DOM), 11 PI's from DOM assembled teams spanning 10 departments. Ten applications went forward for review by external experts from Ottawa University and the University of Alberta. Based on the recommendations of these reviewers, we are pleased to announce that the following five teams were funded:

Multimodal molecular phenotyping for subtype discovery in septic shock: Translational extension of a randomized trial

PI: Dr. David Maslove (DOM)
Co-PIs: Dr. Patricia Lima (DOM), Dr. Gordon Boyd (DOM)
Collaborator: Dr. Charlie Hindmarch (DOM)

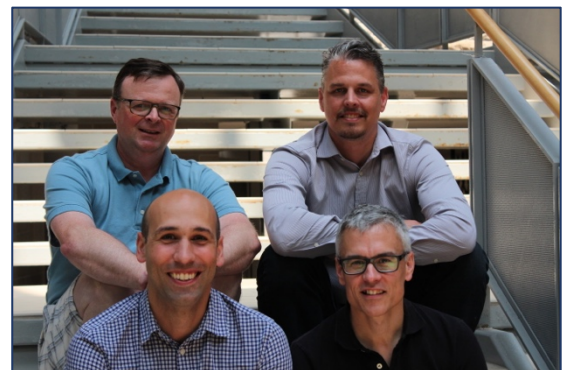


For some people, an infection means little more than a day or two of rest, and a course of antibiotics. But in some cases, infection can lead to life-threatening organ dysfunction, a condition known as *sepsis*. Sepsis is a major public health concern, as it is both common, and serious. In fact, it has been estimated that 1 out of every 18 deaths in Canada involves sepsis. The care of patients with sepsis is largely supportive; despite decades of research, no specific treatments exist. One potential reason for this is that no two patients with sepsis are alike, and a treatment that might work for some may be ineffective for others.

Our research is focused on identifying individual patient traits that can be used to personalize sepsis care. This involves taking a close look at a specific type of white blood cells called neutrophils, using a state-of-the-art laboratory technique called mass cytometry. Tremendous quantities of data are generated that are then processed using machine learning algorithms, in order to identify distinct subtypes of sepsis that might respond differently to a particular treatment. By personalizing sepsis care in this way, we aim to deliver the right treatment to the right patient, at the right time. This is the promise of precision medicine, a paradigm that stands to increase the efficiency of sepsis care, and save lives.

Psychological stress-food antigen triggers IBS symptoms via loss of oral tolerance

PI: Dr. David Reed (DOM)
Co-PI: Dr. Andrew Craig (DBMS, CRI)
Collaborators: Dr. Mark Ormiston (DBMS), Dr. Charlie Hindmarch (DOM)



Irritable Bowel Syndrome (IBS) is a gastrointestinal disorder characterized by abdominal pain associated with diarrhea and/or constipation. A large majority of patients identify food as a trigger of their symptoms yet the underlying mechanisms are unknown. In a preclinical mouse model, we have evidence that when a normally well tolerated food is given at the same time as a psychological stressor, re-exposure to that food at a later time point causes increased pain in the gut. This increased pain appears to involve a local immune response in the gut without activating a more generalized

immune response throughout the body, as is seen in food allergy. Therefore, the goal of this project is to determine if stress and a food trigger interact to activate a specific immune response that leads to increased pain when that food is re-introduced. We will explore this concept using state-of-the-art technology in both our pre-clinical mouse model and in tissue samples from a subgroup of IBS patients. Collectively, these studies will enable us to better understand the causes of IBS and identify new therapeutic targets in food-induced symptoms in IBS patients.

Characterizing Fatty Liver Disease in Adolescents and Young Adults: A Prospective Feasibility Study

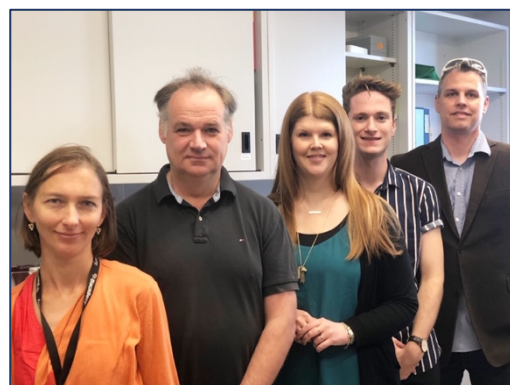
PI: Dr. Jennifer Flemming (DOM)
Co-PIs: Dr. Mohit Kehar (Pediatrics),
Dr. Prameet Sheth (DPMM)



The incidence, prevalence, and mortality from chronic liver disease (CLD) and cirrhosis are increasing in adolescents and young adults (AYAs) in North America at alarming rates. Reasons for this have not been completely determined however, it is hypothesized to be influenced by an increase in fatty liver disease in this population. Fatty liver disease is traditionally dichotomized as either alcohol or non-alcoholic fatty liver disease (NAFLD), both of which are common in AYAs. However, the degree of overlap between these two conditions in AYAs is unknown. If identified before cirrhosis develops, fatty liver disease is potentially treatable with alcohol cessation, dietary modifications, and weight loss. Therefore, there is an urgent need to characterize and understand the natural history of fatty liver disease in AYAs. In this study, we will recruit AYAs with fatty liver disease from both pediatric and adult hepatology clinics at Kingston Health Sciences Centre and use survey data to characterize exposure to alcohol and sugar sweetened beverage consumption. We will also collect stool and saliva samples to evaluate the characteristics of the intestinal and oral microbiome which may be associated with different stages of disease. The overarching goal of this project is to identify, characterize and risk stratify this group to target interventions that can potentially reverse these trends for future generations.

Transcriptional Characterization of the Hemostatic Stress Response in Blood Outgrowth Endothelial Cells from Individuals with Type 1 von Willebrand Disease

PI: Dr. Paula James (DOM)
Co-PI: Dr. Neil Renwick (DPMM)
Collaborator: Dr. Charlie Hindmarch (DOM), Dr Kathrin Tyryshkin (DPMM)



Von Willebrand Disease (VWD) is the most common inherited bleeding disorder and affects ~36,000 Canadians. Some affected patients experience little in the way of bleeding symptoms while others suffer from prolonged and excessive bleeding with menstruation, dental procedures, childbirth or surgery. In the worst cases, blood transfusions or surgical procedures such as a hysterectomy are required. At present, factors that lead to more severe bleeding are not completely understood, and new knowledge in this field could help us more effectively manage patients. In this study, we will specifically test the hypothesis that Type 1 VWD patients who have more severe bleeding, have blood coagulation systems that do not respond adequately to stress. This normal stress response provides an adaptive, evolutionary advantage as it protects against bleeding from injury, but we believe this is disrupted in patients with VWD. We will culture cells from the blood vessels of Type 1

VWD patients and normal healthy controls to examine the differences in how these cells respond when presented with stressors. A new team of researchers has been assembled to carry out this work and the information gathered may reveal important differences that will allow for improved diagnosis and thereby, improved patient care.

The VANGUARD Study: Virtual Histology and Molecular Environment of Atherosclerotic Plaque by a Novel 3D-Guided Ultrasound Tool for Atherosclerosis Risk Detection

PI: Dr. Amer Johri (DOM)
Co-PIs: Dr. Charles Hindmarch (DOM), Dr. Douglas Cook (Surgery) and Dr. Stephen Pang (DBMS)
Collaborators: Dr. David Zelt (Surgery), Dr. Dathan Liblik (Freko Liblik Inc.), Dr. Patricia Lima (DOM)

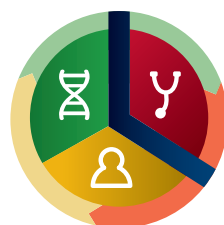


Heart disease and stroke remain one of the most important causes of death in Canada. **How can we detect heart disease and stroke earlier and more accurately to prevent the occurrence of catastrophic cardiovascular events?**

We know that cardiovascular events are caused by deposits in blood vessels known as plaque. If a “vulnerable” plaque, prone to rupture, is detected in one part of the body’s blood vessel network, it may suggest that the patient as a whole is vulnerable to cardiovascular events in the future. Identifying these patients will help us treat them earlier and prevent heart attack and stroke before it occurs.

The VANGUARD Study uses ultrasound as an inexpensive, radiation-free, non-invasive, portable method ideal for imaging vulnerable plaque. Our team at the **Cardiovascular Imaging Network at Queen’s** will be taking 3D ultrasound images from patients undergoing plaque removal by our **Vascular Surgery** department, and analyzing this diseased tissue using advanced, cutting-edge molecular techniques at the **Queen’s Cardiopulmonary Unit**. We will be able to match the pattern of tissue seen on ultrasound with dangerous, or disease-causing cells that suggest risk of cardiovascular events. Our automated ultrasound technology, **IntelliPlaque**, creates a “texture map” of the components of the plaque. We envision applying this to all patients at risk of cardiovascular disease.

The VANGUARDians are a team of physicians, scientists, engineers, and students from several fields, working together to find solutions; supported by a grant from the Translational Institute of Medicine (TIME) program and CINQ (CINQLab.com, twitter [@amerjohri](https://twitter.com/amerjohri)).



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