



Diabetes Research: **Ontario**

Since 1971, Diabetes Canada (formerly the Canadian Diabetes Association) has proudly supported outstanding diabetes research in Canada, administering more than \$140 million in research grants, awards and partnerships to scientists and clinicians who have dedicated their careers to the fight against diabetes.

Since Banting and Best's discovery of insulin in Toronto, in 1922, Canadian researchers have made huge strides and key advances in mapping and understanding the physiology, biochemistry and genetics of diabetes. This is why we choose, each year, to fund Canada's most renowned researchers in their quest for new and innovative developments in the prevention, treatment and management of diabetes. And although the research is diverse in its scope, covering a broad range of specialties and topics, the underlying goal of each study remains the same - to improve the quality of life of people living with diabetes and to find a cure.

Every year, our researchers continue a tradition of innovation and discovery. Below is a list of the scientists and clinicians in Ontario who are currently funded by Diabetes Canada.

Research Grants & Awards

Dr. Andrew Advani (Diabetes Investigator Award)

St. Michael's Hospital (Toronto, ON)

Funded: 2017-2022

Title: Non-coding RNA in diabetic kidney disease

Dr. Advani is studying a type of molecule called a non-coding RNA. His work has shown that the amount of a particular non-coding RNA is increased in kidney cells of people with diabetic kidney disease and that blocking the actions of the non-coding RNA can help to protect kidney cells from damage caused by high glucose levels. If Dr. Advani can determine whether blocking the molecule's actions can protect against kidney damage - the most common cause of kidney failure in Canada - it could lead to the development of new treatments to protect people living with diabetes from this complication.

Dr. Fernando Forato Anhê (Post-Doctoral Fellowship)

Supervisor: Dr. Jonathan Schertzer
McMaster University (Hamilton, ON)
Funded: 2018-2020

Title: Determining how microbes lower blood glucose and insulin after bariatric surgery
It is still not understood why some obese people have high blood glucose and others do not and what causes the progression of prediabetes. The bacteria in our gut (i.e. gut microbiota) is now recognized as an important player controlling host metabolism. Bariatric surgery, the most effective intervention to cause remission of type 2 diabetes, is associated with changes in the type of gut bacteria. Bariatric surgery also lowers blood glucose and insulin before weight loss. Nobody has fully tested how gut bacteria within a bariatric surgery patient change glucose and insulin control. Dr. Anhê will use new ways to grow and identify bacteria from the same patient before and after three different types of bariatric surgery. He will also transplant the bacteria to germ-free mice and determine how these microbes can lower blood glucose without the need for weight loss. His findings could lead to new and more effective treatments for type 2 diabetes.

Dr. Satya Dash (New Investigator Award)

University Health Network (Toronto, ON)
Funded: 2017-2020

Title: Targeting the central nervous system for treatment of obesity and metabolic disease in humans

Dr. Dash is currently studying two weight loss treatments that directly target the brain. The first, a magnetic treatment, targets the area of the brain involved in impulse control and helps patients control their urge to overeat. The second is glucagon, a hormone that, when given as a spray through the nose, can reduce hunger and increase energy expenditure in obese patients. If successful, these treatments could lead to sustained weight loss and improve blood glucose levels, cholesterol, and blood pressure in obese patients with prediabetes and diabetes.

Dr. Helen Dranse (Post-Doctoral Fellowship)

Supervisor: Dr. Tony Lam
University Health Network (Toronto, ON)
Funded: 2016-2019

Title: Leptin action in the brain

Dr. Dranse is studying leptin, a hormone that is made by fat and stomach cells but has actions in other parts of the body. She will study how leptin works in the brain to regulate the body's production of glucose and investigate how this changes with obesity and type 2 diabetes. This will help to develop new ways to restore normal blood glucose levels in these diseases.

Dr. Robin Duncan (Operating Grant)

University of Waterloo (Waterloo, ON)

Funded: 2016-2018

Title: Renal-metabolic axes in glucose control

Dr. Duncan and her team are studying the relationship between kidney fat accumulation (which happens with excess weight gain) and diabetes. Using mouse models, they are examining a signalling molecule from fatty kidneys that they believe may cause problems with how insulin is made and used in the body, how fat cells function, and how fat is stored in the liver. She hopes the results from this research may provide key insights into curing both kidney disease and diabetes.

Dr. Saifur R. Khan (Post-Doctoral Fellowship)

Supervisor: Dr. Michael Wheeler

University of Toronto (Toronto, ON)

Funded: 2017-2020

Title: Transition of type 2 diabetes from gestational diabetes mellitus: Prediction with high discrimination and novel insight of the type 2 diabetes etiology

Studies show that 20 - 50% of pregnant women with gestational diabetes (GDM) develop type 2 diabetes within 5 years. Dr. Khan believes that the transition from GDM to type 2 diabetes involves the dysregulation of a common subset of metabolites, which are the potential biomarkers for future type 2 diabetes. Using metabolite screening, Dr. Khan will identify the common subset of altered metabolites which can be used to develop a scoring system for type 2 diabetes prediction. This study represents the first metabolomics study of the transition from GDM to type 2 diabetes; providing a rapid, robust diagnostic test to predict future diabetes risk and insight into the mechanism of type 2 diabetes onset.

Dr. Caroline Kramer (Clinician Scientist Award)

Samuel Lunenfeld Research Institute/Mount Sinai Hospital (Toronto, ON)

Funded: 2016-2021

Title: Evaluation of the longitudinal impact of brown adipose tissue on metabolic health in type 2 diabetes

Dr. Kramer is trying to determine if having more brown fat (a type of fat that actually burns energy) in a person's body can lower the risk of metabolic problems in people with diabetes. Better understanding the relationship between obesity and diabetes is an essential first step in helping to prevent type 2 diabetes and diabetes-related complications.

Dr. Lorraine Lipscombe (Diabetes Investigator Award)

Women's College Research Institute (Toronto, ON)

Funded: 2018-2021

Title: Pregnancy as a window of opportunity to quantify and reduce diabetes risk in women

Dr. Lipscombe's goal is to identify and reduce the risk of diabetes after pregnancy. As part of this research program, she will be testing a lifestyle program for new mothers with gestational diabetes (GDM) to reduce their risk of diabetes. She will identify key risk factors that arise around the time of pregnancy and use those to create a prediction tool that estimates a woman's risk of developing diabetes in the next five years. Dr. Lipscombe and her team will use health-care databases in Ontario to examine associations between risk factors and development of diabetes in pregnant women with and without GDM.

These research findings will be used to create and validate risk prediction tools which can be applied shortly after pregnancy to estimate a woman's personal five-year risk of diabetes. This research will help to reduce type 2 diabetes in Canadian women by creating a clinical tool to identify pregnant women who are at highest risk of early diabetes so that interventions can be provided to reduce their risk.

Dr. Yuliya Lytvyn (Post-Doctoral Fellowship)

Supervisor: Dr. David Cherney

University Health Network (Toronto, ON)

Funded: 2016-2019

Title: Blockade of the ace and treatment with empagliflozin - effects on hyperfiltration in type 1 diabetes: The BETWEEN-T1D Study

Dr. Lytvyn is studying kidney damage in people with type 1 diabetes. She wants to know if combining a drug (empagliflozin) that lowers blood glucose levels in type 2 diabetes combined with a drug (ramipril) to treat kidney damage protects the kidneys of people with type 1 diabetes better than using ramipril alone.

Dr. Christopher McGlory (Post-Doctoral Fellowship)

Supervisor: Dr. Stuart Martin Phillips

McMaster University (Hamilton, ON)

Funded: 2017-2019

Title: Mechanisms of insulin resistance during muscle disuse atrophy

Muscle disuse and aging have an enormous impact on health-care costs in Canada . After the age of 50 years, people begin to lose muscle. This muscle loss has a variety of negative impacts on health and the ability to perform activities of daily living. Aging also reduces the muscles' capacity to absorb sugar from the blood via insulin, resulting in high blood glucose levels and the start of diabetic complications. Likewise, periods of muscle disuse, such as those experienced during hospitalization and immobilization, result in muscle loss and impaired blood glucose control. Evidence shows that consuming fish oil changes the type of fat in human muscle and might protect against disuse-induced muscle loss, as well as the onset of diabetes. Dr. McGlory and his team are trying to determine if supplementing the diet of older people with fish oil before being immobilized is protective towards muscle loss and blood glucose control. He will also try to determine if fish oil supplementation improves muscle mass and blood glucose control during recovery from immobilization. The findings from this study could help combat muscle loss and the onset of diabetes complications to improve the health of older adults.

Dr. Erin Mulvihill (New Investigator Award)

University of Ottawa Heart Institute (Ottawa, ON)

Funded: 2018-2021

Title: Organ cross talk: Heptokines linking inflammation, insulin resistance and cardiovascular disease

All organs in the body are a mixture of distinct cells with different jobs and, when they coordinate their operation, our bodies are healthy. In type 2 diabetes, insulin-producing cells in the pancreas become damaged, but it hasn't been entirely determined how this damage creates miscommunication with other cells in the body, particularly the heart. Dr. Mulvihill and her team have discovered that a protein, DPP4, found in the liver can, in people with metabolic disease, enter the circulation and disturb the exchange of information between cells in adipose tissue and the liver. They now wish to determine if this protein can also signal the heart and, in certain circumstances, cause injury and harm.

Dr. Yoo Jin Park (Post-Doctoral Fellowship)

Supervisor: Dr. Minna Woo

University Health Network (Toronto ,ON)

Funded: 2016-2019

Title: Delineating the role of caspase-8 in adipose tissue inflammation and insulin resistance

Researchers found that people and mice with obesity and type 2 diabetes had high levels of a protein called caspase-8 in their fat cells, and mice with no caspase-8 in their fat cells gained less weight and had lower blood glucose levels, even when they ate a high fat diet. Now, Dr. Park is studying what role caspase-8 plays in regulating blood glucose levels in the body, in hopes of better understanding how obesity and type 2 diabetes develop.

Dr. Jonathan Schertzer (New Investigator Award)

McMaster University (Hamilton, ON)

Funded: 2017-2020

Title: Microbiota control insulin dynamics and sensitivity

Dr. Schertzer's lab has discovered that specific parts of gut bacteria are beneficial and can lower insulin and make insulin work better. The trillions of bacteria in the gut are an untapped source of new drugs/medications. Dr. Schertzer is trying to determine how bacteria are sensed by the immune system to alter insulin. This research will use unique resources in Canada to find out which parts of bacteria can be used to stop or slow prediabetes, which is different from the current drugs that focus on blood glucose management.

Dr. John Sievenpiper (Clinician Scientist Award)

St. Michael's Hospital (Toronto, ON)

Funded: 2015-2020

Title: Relation of food sources of fructose-containing sugars with incident diabetes and cardiometabolic diseases: A series of systematic reviews and meta-analyses of controlled trials to inform dietary guidelines, public health policy, and future trial design in diabetes

To improve the evidence on which clinical nutrition recommendations and public policy are based, Dr. Sievenpiper is studying the relationship between important food sources of sugars that contain fructose and the risk of diabetes, heart disease and other related diseases. There is a lot of controversy about the role of sugars (in particular, sugars that contain fructose) in the development of chronic diseases. As dietary guidance moves away from "nutrient" based dietary advice ("low sugar", "low carb", "low fat", etc.) to more dietary pattern based advice ("Mediterranean diets", "vegetarian diets", etc.), current research is inconclusive in determining whether food sources of added sugars that contain fructose (as

opposed to the sugars, in general) are actually worse than other foods that would replace them. Dr. Sievenpiper wants to get more answers. To do so, he is undertaking a large scale review of all available data from the highest quality controlled human trials on this topic. This technique will allow results from numerous studies to be compared against each other. The review will include research on various food sources of sugars and will explore results in different patient groups. Dr. Sievenpiper's goal is to inform dietary guidelines and public health policy, stimulating the development of healthy products by industry, and shaping future research design.

Dr. Gregory Steinberg (Diabetes Investigator)

McMaster University (Hamilton, ON)

Funded: 2017-2022

Title: Inflammation, metabolism and type 2 Diabetes

Over 50 percent of Canadians have high levels of blood glucose or will have a heart attack or stroke in their lifetime. When the cells of the body that help defend it from infections (immune cells) are active, they create inflammation. It is known that inflammation from cells in the immune system can cause blood glucose levels to rise and lead people to have heart attacks and strokes. Currently, however, it is not possible to know which people with high blood glucose levels will have a heart attack or stroke. In this study, Dr. Steinberg and his team will develop new tests to help predict which people with high blood glucose levels are at risk of having a heart attack or stroke and identify a new therapy aimed at preventing inflammation that will lower people's blood glucose and prevent them from having a heart attack or stroke. This will help lower health-care costs and save people's lives.

Dr. Elodie Varin (Post-Doctoral Fellowship)

Supervisor: Dr. Daniel Drucker

Samuel Lunenfeld Research Institute/Mount Sinai Hospital (Toronto, ON)

Funded: 2016-2019

Title: Role of enterocyte vs. endothelial DPP4 in control of metabolism and inflammation

Gut hormones play a role in controlling blood glucose levels, and two new classes of type 2 diabetes drugs are based on the effects of these hormones. One of them (called DPP4 inhibitors) protects the gut hormones from being broken down by the body. Dr. Varin is studying exactly how and where DPP4 breaks down the gut hormones, in hopes of finding ways to develop new DPP4 inhibitor strategies that could work more efficiently and with fewer side effects than current type 2 diabetes drugs.

Dr. T.M. Zaved Waise (Post-Doctoral Fellowship)

Supervisor: Dr. Tony Lam

Toronto General Hospital Research Institute (Toronto, ON)

Funded: 2018-2020

Title: Interaction of gut microbiota and nutrient sensing

Obesity and diabetes are characterized by a disruption in glucose, lipid and metabolic homeostasis due secondary to an altered microbiota population in the intestine. In this study, Dr. Waise will characterize microbiota and bile acid receptor, farnesoid X receptor (FXR), signaling pathways in the gut that alter glucose metabolism. Specifically, he will aim to identify novel FXR-dependent nutrient sensing mechanisms in the upper small intestine that regulate glucose homeostasis, and determine their therapeutic potential to enhance gut nutrient sensing and restore metabolic homeostasis in obesity and diabetes.

Dr. Alanna Weisman (Post-Doctoral Fellowship)

Supervisor: Dr. Bruce Perkins

University of Toronto (Toronto, ON)

Funded: 2018-2019

Title: Associations between elevated uric acid, allopurinol, and end-stage renal disease in diabetes: Population-based cohort studies

Diabetes continues to be the leading cause of kidney failure, and new medications to prevent kidney disease are required. High uric acid (UA) is a possible cause of kidney disease, and people with diabetes more commonly have high UA than people without diabetes. Allopurinol is a medication used for gout that lowers UA and may prevent kidney failure in people with diabetes.

In this study, Dr. Weisman and her team will use routinely-collected health-care data in Ontario to study the associations of UA and kidney failure (dialysis or kidney transplant), and allopurinol and kidney failure, in people with diabetes. They believe that a higher UA will be associated with a higher risk of kidney failure and use of allopurinol will be associated with a lower risk of kidney failure.

These findings could lead to clinical trials of allopurinol and a wider role for the use of medications that lower UA in people with diabetes to prevent kidney disease.

Dr. Samaneh Yazdanikivi (Post-Doctoral Fellowship)

Supervisor: Dr. Amira Klip

Hospital for Sick Children (Toronto, ON)

Funded: 2017-2020

Title: The microvascular bed in diabetes: Permeability defects, inflammation and potential therapeutic avenues

In this study, Dr. Yazdanikivi will investigate if and how capillary cells are affected by diabetes and diabetogenic conditions. In particular, she will examine if and how exposing human capillary cells to 'diabetic environments' (high glucose, high fat, inflammatory blood components) affects the movement of green-fluorescent insulin glucose. The cellular system will also allow her to screen for chemicals that may improve insulin and glucose movement across the capillary cells. In addition, she will use a novel animal model that was created to have red-fluorescent capillaries, which will allow her to film the distribution of injected, green-fluorescent insulin or green-fluorescent glucose from the blood into the tissues, and examine its possible alterations in diabetes. Eventually, she will use this model to explore if the drugs tested in the cells in culture improve insulin and glucose delivery to tissues in the diabetic mice. This could lead to new and more effective drugs/medications for people living with diabetes.

Dr. Veera Ganesh Yerra (Post-Doctoral Fellowship)

Supervisor: Dr. Andrew Advani
St. Michael's Hospital (Toronto, ON)
Funded: 2018-2020

Title: Inflammation, epigenetics and heart failure in diabetes

Dr. Yerra's objective is to better understand the causes of heart failure in diabetes and to use this new knowledge to develop new treatments. Dr. Yerra has discovered that, in heart failure, a protein in heart muscle cells, called CCR2, signals a series of events that ultimately damage heart muscle cells, especially when diabetes is present. These damaging events involve processes called epigenetic processes, meaning they involve changes in the ways that genes work without causing typical changes in the genetic code. In this project, Dr. Yerra will look to see what the events are that cause heart muscle cell damage by CCR2 and whether medications that block CCR2, or block one of the cell-damaging events it causes, can prevent heart failure in diabetes. These findings will generate important new information about how heart failure occurs in diabetes and possibly lead to the development of new treatments for people with diabetes.

Research Chairs & Partnerships

Strategy for Patient-Oriented Research (SPOR)

Dr. Gary Lewis
Toronto General and Western Hospital Foundation (Toronto, ON)