

Lady Davis Institute Research Newsletter



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Introducing the McGill Clinical Genomics Research Program

The Jewish General Hospital is spearheading the launch of the McGill Clinical Genomics Program (McG), a multifaceted research initiative with the potential to improve patient care by applying genomics-based science and medicine in the fight against a wide array of common and rare diseases.

McG aims to collect DNA samples from patients at the JGH, then analyze them and apply the genetic data to help improve physicians' ability to diagnosis the cause of a patient's disease, to more accurately assess their risk for particular conditions, and predict the likelihood of a positive response to a prescribed course of treatment. Genomic technology will be applied to diseases including heart disease, breast cancer, and type 2 diabetes, which represent the biggest causes of mortality and chronic or complex care across Quebec and Canada.

Furthermore, it is expected that the use of state of the art artificial intelligence and big data technologies will contribute to understanding the genetic causes of diseases, identifying an individual's risk of developing a disease, as well as accelerating drug discovery.

"The McG genomics research program sets out to build the infrastructure to support hospital-based clinical genomics services across Montreal, starting with the JGH and wider McGill University affiliated hospital system. Ultimately, we hope it will serve to personalize care for common and rare illnesses," explains **Dr. Brent Richards**, principal investigator on McG. "Identifying the genetic underpinnings of disease will give us the insight to identify pathways for drug development that will directly target risk of disease and deliver better outcomes for patients."

The future ambition is to request that all patients consent to providing DNA samples for 'genomic

"Clinical genomics is the future of our organization" Dr. Lawrence Rosenberg President & CEO, CIUSSS – West Central Montreal

profiling' when they seek treatment at the JGH and across our CUISSS. By amassing extensive DNA data, researchers will be able to identify patterns in the genome and isolate and analyze variations to identify if they are responsible for driving disease progression. Analysis of an individual's genome can help reduce trial and error in determining which drugs and interventions are most likely to improve clinical efficacy, cost effectiveness and reduce side effects.

The aim of the 2-year research study, scheduled to begin in the fall, is to demonstrate that genomic profiling will have a direct impact on clinical care, and it is the ambition of McG to position McGill, Quebec, and Canada as a whole, as a global leader in genomically-enabled medicine.



The other principal investigators on the program are Drs. Vincent Mooser and George Thanassoulis. Dr. Mooser is the Canada Excellence Chair in Genomic Medicine at McGill University. He is a pioneer in the application of genomics-based tools to develop novel targeted therapies. Dr. Thanassoulis is the Director of Preventive and Genomic Cardiology at the McGill University Health Centre. His research focuses on improving care for individuals with a family history of heart disease or cardiometabolic risk factors. Dr. Thanassoulis will work closely with Drs. Anabelle Chen-Tournoux and Lawrence Rudski of the JGH to advance collaborative research across both sites.

For further information, contact: info@mcgillclingen.ca, or visit mcgillclingen.ca

CIHR Project Grants

Twelve CIHR project grants have been awarded to Lady Davis Institute researchers :

- Jonathan Afilalo (\$428,400) to determine whether a comprehensive geriatric assessment and intervention, in addition to usual cardiac care, can improve conditions for frail older adults with a recent hospitalization for heart failure.
- Mark Eisenberg (\$114,750) to conduct a comprehensive knowledge synthesis of interventions and regulations concerning the prevention of electronic cigarette use among youth, and related harm reduction strategies.
- Alexander Thiel (\$579,105) to use the first tropomyosin receptor kinase (TrkB/C) - a potential diagnostic marker in Alzheimer's disease and for plasticity related recovery processes after stroke radiotracer in human healthy controls of different ages to map the concentration of TrkB/C with Positron Emission Tomography (PET).
- Kristian Filion (\$191,250) to develop a personalized dynamic blood pressure control plan to prevent major adverse cardiovascular events among patients with hypertension at low cardiovascular disease risk.
- Antonis Koromilas (\$868,275) to shed new light on the oncogenic mechanisms of KRAS gene mutations, which is activated in 15-25% of nonsmall cell lung cancer cases, through the stress adaptive function of eIF2αP.
- Laurent Azoulay (\$286,875) to conduct a large, international, multi-centre population-based cohort study to assess whether the use of sodiumglucose co-transporter (SGLT-2) inhibitors, the newest pharmacotherapy for the treatment of type 2 diabetes, is associated with an early increased risk of bladder cancer.
- Oriana Yu (\$122,400) to determine whether levothyroxine hormone replacement therapy decreases the risk of adverse cardiovascular events and all-cause mortality among patients with mild subclinical hypothyroidism using a populationbased cohort study.
- Josie Ursini-Siegel (\$975,375) to understand how distinct evolutionary paths are selected during the emergence of aggressive breast cancers.
- Josie Ursini-Siegel (\$948,600) to examine the molecular mechanisms by which p66ShcA reduces responsiveness of certain cancers to PARP inhibitors and identify therapeutic strategies that

augment p66ShcA levels in poor outcome cancers, including triple negative breast cancer, lung cancer and melanoma.

- Tricia Peters (\$105,000) to determine the protective role of physical activity against polycystic ovary syndrome (PCOS).
- Celine Gelinas (\$524,025) to validate the Nociception Level (NOL) index a numeric value obtained from multiple parameters for ICU pain assessment where self-reporting is often not feasible due to critical care conditions.
- Celine Gelinas (\$684,675) to implement and evaluate the effectiveness of an intervention aimed to Manage Pain in Collaboration in the ICU (MPIC-ICU) in university-affiliated hospitals in Quebec and Ontario to improve patient outcomes.

15th JGH Psychiatry Research Day

STRESS AND COPING IN DIVERSE CONTEXTS: Implications for assessment and treatment of mental health problems

FRIDAY, MARCH 27, 2020 8:30 AM – 12:30 PM

Click here for details

11th Annual LDI Scientific Retreat

Thursday May 7, 2020 8:30—16:30 Gelber Conference Centre 5151 Côte Ste Catherine (2 Cummings Square)

Keynote Speaker: Gustavo Turecki, MD, PhD

Scientific Director, Douglas Research Centre Chief of Psychiatry, CIUSSS Montreal West Island Chair, Department of Psychiatry, McGill University Director, Réseau québécois sur le suicide, les troubles de l'humeur et les troubles associés (RQSHA)

CLICK HERE TO REGISTER

Deadline for Abstract Submission: April 1 Deadline to Register: April 20

Saliva promises simple, efficient biomarker for Parkinson's disease

Parkinson's disease (PD) has resisted accurate diagnosis, most particularly in its earliest stages. There exists no diagnostic biomarker available for use in clinical settings. However, **Dr. Hyman Schipper** has noted that dysregulation of distinct microRNAs, miR-153 and miR-223, is evident in PD. Encouraged by initial observations in a mouse model of the disease engineered in the Schipper lab, his team found that levels of these microRNAs are significantly decreased in the saliva of PD patients in comparison with nonneurological (healthy) control subjects. The research was published in <u>Movement Disorders</u>.

The accuracy of the test separating controls (77 people) from PD patients (83 individuals) was estimated at 79% for miR-153 and 74% for miR-223. This suggests that a simple, non-invasive salivary test may prove to be a useful tool for diagnosing PD, an important achievement given that the disorder affects 2% of the world population over the age of 65.

The research was prominently highlighted in <u>Nature</u> <u>Reviews Neurology</u>.

"The identification of a biomarker would be of great benefit to our patients because it would offer the opportunity of initiating treatments earlier as we develop more effective medications. It may also allow for distinguishing whether a patient has PD or some other degenerative or non-degenerative movement disorders," said Dr. Schipper. "That we can observe the biomarker in saliva is very useful because saliva is easy to collect and relatively inexpensive to analyze."

Dr. Schipper is co-director, along with Dr. Mervyn Gornitsky, of the LDI/JGH Saliva Databank, the largest biobank of its kind in Canada. With more than 2,000 samples in its collection to date, the JGH biobank is proving a useful repository for the testing of biomarkers in a number of important medical conditions.

"Validation of an easily quantifiable salivary biomarker of idiopathic PD in large-scale trials would address a major unmet clinical imperative by facilitating rapid and accurate diagnosis," wrote Marisa Cressatti, the first author on the paper and a PhD candidate in McGill's Integrated Program in Neuroscience.

Rossy Cancer Network wins Ministry of Health Prix de cancérologie

The Rossy Cancer Network (RCN) is proud to announce that its oncology urgent care initiative was honoured with the 2019 Prix de cancérologie (Organisation des services) from the MSSS's Programme québécois de cancérologie.

The project titled HOPE, Helping the Oncology Patient Experience through rapid symptom intervention, was developed in collaboration with the RCN's three partner hospitals -- the Jewish General Hospital (JGH), St. Mary's Hospital Centre and the McGill University Health Centre (MUHC). This project addresses the fact that recent literature demonstrates that for patients with cancer, the management of early symptoms improves quality of life, adherence to treatment and ultimately increases survival.

"A review of existing structures at the JGH found that 50% of cancer patients had symptoms severe enough to present to the emergency department within 30 days of treatment and that, of those, 40% were hospitalized," explains Erin Cook, project lead, and clinical administrative coordinator for oncology at the JGH. The project team created an early symptom management program to address this.

The initiative includes a telephone triage line staffed by specially trained nurses, as well as oncology urgent care clinics being developed at each site. These measures allow patients to bypass the long waits and exposure to infection of a crowded emergency department (ED) and to receive reassurance and timely treatment of their symptoms, either at home or in a dedicated oncology-specific context.

"This is one of the RCN's most transformational projects," says **Dr. Wilson Miller**, RCN Clinical Lead. "It allows cancer patients to have access to the urgent care they need in a setting that is better suited to their cancer-related problems. And this can be done much more efficiently than in our overcrowded EDs, thus relieving stress both from the EDs and from the inpatient the units."

The early phase of the project at the JGH has already shown a 10% decrease in ED visits.

<u>Watch the video</u>

New diagnostic standard for pulmonary embolism

A clinical trial has revealed that a higher threshold for D-dimer - a protein indicative of blood clot formation should be employed when evaluating patients with a low probability for pulmonary embolism (PE) than has heretofore been the standard. The results appear in <u>The New England Journal of Medicine</u>. The clinical leads at the Jewish General Hospital (JGH) were **Dr. Marc Afilalo**, Chief of the Emergency Department, and **Dr. Andrew Hirsch**, Chief of Pulmonary Medicine.

Typically, outpatients with a low risk for PE who have D-dimer levels of less than 500 ng per milliliter were deemed not to have a PE, and required no further testing. Those with higher D-dimer were given CAT scans before a PE would be definitively ruled out. This current study evaluated more than 2000 patients and concluded that those with a D-dimer level of up to 1000 ng per milliliter could safely be diagnosed as not having PE without further testing.

"Because PE can be difficult to diagnose and, should it go undiagnosed and untreated, can be very serious, even fatal, we were ordering a lot of scans in order not to miss anything," said Dr. Hirsch.

This can be particularly true in Emergency, where patients often present with non-specific symptoms. Being subject to CAT scans carries potential consequences, including exposure to radiation and allergic reactions to the tracer injections. Moreover, reducing the number of diagnostic tests represents a significant cost saving for the health care system.

"By upping the threshold, we can reduce the number of patients we send for scans by thirty-percent," said Dr. Afilalo, "which will improve patient flow and lessen over-crowding in our Emergency, which is crucial to how efficiently we treat our patients."

The JGH had more patients participating in this trial than any other centre, the result of a collaborative effort that included emergency and pulmonary medicine, along with the Centre for Excellence in Thrombosis and Anticoagulation Care (CETAC), directed by Dr. Susan Kahn, and the Canadian Venous Thromboembolism Clinical Trials and Outcomes Research (CanVector) network, which was instrumental in assembling researchers from across Canada.

Award-winning research on seeing the person behind the cancer diagnosis

A paper written by a team led by **Dr. Carmen Loiselle**, and published in the <u>Canadian Oncology Nursing</u> <u>Journal</u> was honoured as Best Publication this past fall by the Canadian Association of Nurses in Oncology (CANO) at its annual conference.

The publication, which underscores the importance of person-centred care that attends to the hopes, needs and unique qualities of individuals affected by cancer, as well as their caregivers, was voted one of the two most significant pieces of Canadian research to have made a major clinical contribution in the previous year.

"Even the term 'cancer patient' does not sit well with the study participants we spoke with," says Dr. Loiselle, Co-Director (Academic) of the Segal Cancer Centre and Scientific Director of Hope & Cope. "Individuals undergoing treatment told us they were much more than their cancer, so we refer them as 'individuals with cancer.""

Although more personalized approaches to care make good sense, more research is necessary. "The strength of our research is that the questions we ask are solidly grounded in the realities of various clinical settings," she notes. "I'm delighted that person-centred care is increasingly being informed by evidence and is becoming an inherent part of day-to-day care.

Dr. Loiselle says. "By documenting and disseminating the findings, we give legitimacy to patients' voices. We are also re-sensitize healthcare providers to the importance of humanizing care. This can easily be forgotten in busy, fast-changing oncology settings, but it remains a crucial matter for patients. Integrating the voices of patients and significant others individuals in our cancer care initiatives can only be a win-win for everyone."

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To submit information or for media enquiries, contact: Tod Hoffman at: tod.hoffman@ladydavis.ca; 514-340-8222, ext. 28661

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