



Lady Davis Institute Research Newsletter



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Segal Cancer Centre joins innovative personalized medicine network

The Segal Cancer Centre is among five Quebec cancer treatment centres partnering with Exactis Innovation to build a coordinated network to match patients who have had their cancer molecularly profiled, with clinical trials based on the characteristics of their tumor through the innovative “Personalize My Treatment” (PMT) digital registry.

“Understanding cancer through its molecular and immune characteristics allows us to target novel medicines to the patient’s disease with the goal of improving treatment response,” said **Dr. Gerald Batist**, Co-Founder and Chief Medical Officer of Exactis and Director of the Segal Cancer Centre at the Jewish General Hospital. “No single cancer centre can identify enough patients of a very specific type eligible for studies using precision medicines. The Exactis PMT program allows us to pool patients from a coordinated network of centres.”

Patients participating in the PMT initiative consent to having their genetic and molecular information about their cancer tumor, as well as clinical data, stored in the Exactis digital registry and agree to be recontacted for potential participation in future research projects, including possible clinical studies of new treatments targeted to their specific type of cancer.

“The Exactis PMT program and its partnership with Quebec’s leading cancer treatment centres is an excellent example of the research community working for the benefit of Quebec patients,” said Dr. Rémi Quirion, Chief Scientist of Quebec and Chair of the Quebec Research Funds.

The Exactis PMT program is a non-profit public-private partnership which receives funding from the federal and provincial governments, research organizations, biopharmaceutical companies and patient groups.

McGill wins \$84 million grant for neuroscience

McGill University will launch an ambitious effort to advance understanding of the human brain and ease the burden of neurological and mental health disorders, thanks to an \$84 million, seven-year grant under the federal government's Canada First Excellence Research Fund (CFREF). The program, Healthy Brains for Healthy Lives, will build on McGill's leading position in neuroscience to make the university a global hub for brain research – one of the major frontiers for 21st century medicine. Healthy Brains for Healthy Lives (HBHL) is designed to transform many brain disorders from terminal or life-long afflictions to treatable, or even curable, conditions. A major focus of the program will be to deepen understanding of individual variations in brain health and susceptibility to illness. **Dr. Lawrence Kirmayer** of the Psychosocial Axis is one of five principal investigators on the project.

Neurological disorders and mental illness take a huge toll in human suffering and economic costs. An estimated 3.6 million Canadians are affected by neurological conditions, and the number of people diagnosed with disorders such as Alzheimer and Parkinson diseases is expected to increase significantly as the population ages in coming decades. The economic burden of neurological and psychiatric disorders combined amounts to \$22.7 billion a year, according to Brain Canada. The World Health Organization forecasts neurological and psychiatric diseases will surpass cancer as the second leading cause of death in Canada by 2040.



Genetic factor behind under-diagnosis of type 2 diabetes in Inuit population

Dr. Brent Richards and his collaborators have found that 27% of Inuit in Nunavik and Alaska have a variant in the TBC1D4 gene that lowers glucose slightly before a meal while raising it after eating. The latter effect is known to be a strong risk factor for complications from diabetes (including heart attack, stroke, loss of limbs, kidney failure, and blindness). Moreover, this curious effect means that diabetes can only be detected if a test known as an oral glucose tolerance test (OGTT) is administered. Less than one-percent of diabetes testing employs this method because it requires that patients wait to have their glucose level tested until two hours after consuming a sugary beverage in the clinic.

“Because of the prevalence of this genetic variant, as many as 10% of all Inuit may have diabetes, or pre-diabetes, without knowing it unless they are administered an OGTT,” Dr. Richards said. “It is, therefore, highly likely that we have underestimated the prevalence of diabetes among this population.”

This genetic change is only manifest among Inuit. One hypothesis is that it was a necessary adaptation that helps their muscles feed off a diet that was traditionally rich in fat and protein, but lacking in glucose. As their traditional hunting and fishing lifestyle has changed and they consume different foods, a genetic evolution that allowed them to survive in a very adverse environment may now be having negative consequences.

“Interestingly,” Despoina Manousaki, the lead author on [the study in Diabetes Care](#), stated, “until recently very few Inuit got diabetes. Now, through the adoption of more processed food, starches, and carbohydrates in their diet, they have matched the rate for the rest of Canada. Given that we now believe we are failing to diagnose many diabetic Inuit, it may be more prevalent in this population than the Canadian average.”

Inuit could be offered genetic testing to see whether they have the particular variant of TBC1D4 that causes this glucose anomaly and/or they could be given an OGTT to accurately assess whether they are diabetic.

“A better understanding of the cultural-specific causes under which common diseases occur within indigenous populations can only lead to better care and, in this case, the implementation of precision medicine,” Dr. Richards concludes.

Stem Cell Network funding for two LDI researchers

Drs. Vahab Soleimani and Colin Crist, of the Molecular and Regenerative Medicine Axis, have received funding from the Stem Cell Network. Theirs were among 31 innovative goal-directed projects that will help translate discoveries into improved health outcomes.

Dr. Soleimani received \$200,000 to study how aging changes the genetic wiring of stem cells. “Increased life expectancy comes with an unprecedented challenge of dealing with the epidemic of age-related degenerative diseases. Our study looks at how aging changes the genetic wiring of stem cells. Knowledge gained from this study can further our understanding of what goes wrong with muscle regeneration during aging and provide new knowledge to counter the negative effect of aging on this process,” he explained.

Dr. Crist received \$100,000 for his study. “Muscle stem cells normally reside in a resting state and are poised to activate the muscle differentiation program in response to injury. The resting state of muscle stem cells requires low levels of protein synthesis,” he said. “We will ask whether pharmacological manipulation of pathways preventing protein synthesis can activate muscle stem cells in the body to counteract muscle wasting associated with age and cancer.”

The Stem Cell Network serves as a catalyst for enabling the translation of stem cell research into clinical applications, commercial products and public policy.

Dr. Pierre Ernst has been appointed Deputy Director of Research at Mount Sinal Hospital of the Centre intégré universitaire de santé et de services sociaux (CIUSSS) du Centre-Ouest-de l'Île-de-Montreal. In this new role, he will provide guidance and assess the feasibility of all research projects and, in collaboration with Spyridoula Xenocostas, CIUSSS Associate Director of Research, will ensure that research activities comply with all agency requirements.

Dr. Ernst is an epidemiologist at the Lady Davis Institute and investigator with the Canadian Network for Drug Effect Studies (CNODES), as well as a respiratory physician in the Pulmonary Division at the Jewish General Hospital and Professor of Medicine at McGill University.

Recruiting for clinical study of e-cigarettes for smoking cessation

Smoking still contributes to the death of more than 37,000 Canadians annually. Moreover, only 10 to 20% of smokers will succeed in quitting using current therapies, including nicotine patches, gum, and counselling. The search for novel techniques prompted a clinical study of the effectiveness and safety of e-cigarettes, which is being led by **Dr. Mark Eisenberg**.

“The single most reversible cause of mortality in Canada is smoking,” emphasizes Dr. Eisenberg, a cardiologist and epidemiologist. “The goal of our study is to determine whether e-cigarettes can be used as a transitional tool from smoking conventional cigarettes to quitting completely.”

Participants over the age of 18 who have smoked at least ten cigarettes a day for more than a year and who are motivated to quit are being recruited. Investigators hope to involve 486 people. They will be randomized into one of three groups: nicotine e-cigarettes with individual counselling; non-nicotine e-cigarettes with individual counselling; or individual counselling alone. The treatment period will be twelve weeks, with follow-up for a year to evaluate whether the participants maintain abstinence, and their experience of withdrawal symptoms and side effects.

“Ultimately, multiple trials in multiple populations will be necessary to establish the efficacy of e-cigarettes,” said Dr. Eisenberg, “but ours is a significant first step.”

At the moment, neither Health Canada, nor the US Food and Drug Administration have guidelines concerning e-cigarettes. This trial will provide regulators, health care professionals, and smokers with important information about the efficacy and safety of e-cigarettes for smoking cessation.

For further information contact Shauna McGee, E3 Trial Coordinator, 514-340-8222, ext. 3240 or Shauna.McGee@ladydavis.ca.

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To submit information or for media enquiries, contact: Tod Hoffman at: thoffman@jgh.mcgill.ca;

Men have a lot to learn about their own fertility

The first large-scale study of its kind has revealed that Canadian men generally lack knowledge about the risk factors contributing to male infertility. Research led by **Dr. Phyllis Zelkowitz**, and published in [Human Reproduction](#), found that men could only identify about 50% of the potential risks and medical conditions that are detrimental to their sperm count, and, thus, their prospects to father children. While risk factors such as cancer, smoking, and steroid use were more commonly known, other modifiable risks like obesity, frequent bicycling, and frequent use of a laptop on your lap, were not on their radar. Nonetheless, about a third of the men surveyed expressed concerns about their fertility, and almost 60% wanted to learn more about this issue.

Most men express the desire for fatherhood at some point in their lives. “Infertility can be devastating for people,” Dr. Zelkowitz says. “When men can’t have children, or have to undertake very expensive treatments, it can have a grave psychological impact. It can lead to depression and put severe stress on relationships.” With rates of infertility having increased in the past 20 years, greater awareness of risk factors and medical conditions associated with infertility can lead to early and preventive interventions to enable men to achieve their reproductive goals.

By shedding light on the issue, the researchers hope to stimulate a dialogue about male fertility and inspire health educators and health care practitioners to provide universal public education to promote reproductive health among men from a young age so that they can take the necessary steps to protect their fertility.

SAVE THE DATE

FRIDAY MAY 12, 2017

8th Annual Scientific Retreat

Keynote Speaker: Dr. Peter Zandstra

University Professor, Biomaterials & Biomedical Engineering
Canada Research Chair, Stem Cell Bioengineering
University of Toronto

Details to follow

Spotlight on Fellows

Kathleen Klein – Epidemiology Axis

Kathleen Klein fulfills two roles at the LDI: as research associate working with Dr. Celia Greenwood, who focuses on brain development and mental health, and as biostatistics and bioinformatics consultant for all researchers. In the former role, she concentrates on testing and developing new methodologies, while the latter provides opportunities for direct clinical application.

“I enjoy math and biology, so I was fortunate to be able to combine them,” she says of her ability to apply her graduate work in genetics, which she completed at McGill, with biostatistics. “Bioinformatics allows us to digest vast amounts of data from which we can extract incredible information. Big data requires sophisticated statistics, along with extensive computer power and programming to crunch the numbers.”

Sequencing large regions of DNA that once took years of work to decipher can now be accomplished in the span of several hours. There are cases where tens of thousands of pieces of data must be sorted in order to diagnose affective mutations. This is where bioinformatics is crucial for teasing out the information that is pertinent to prescribing a course of therapy. The capacity to quickly characterize particular mutations has a direct impact on patients.

For example, it is known that BRCA mutation status should be considered when making prevention and treatment decisions for breast cancer. However, other genes may have a similar impact on survival, chemo-resistance and prevention.

“Our goal is to identify these genes (gene signatures) from tumor biopsies or chemo-resistant tumors to aid in deciding treatment options,” she said. “The exciting part of working at the Lady Davis is the direct interaction



between the clinician, the scientist, and the statistician. These collaborations are extremely rewarding, and together we add to our understanding of how cancer behaves.”

Two post-doctoral fellows were honoured with Abstract Achievement Awards by the American Society of Hematology at its recent annual meeting in San Diego:

- **Dr. Amel Hamdi**, a postdoctoral fellow in Dr. Prem Ponka’s laboratory, gave a talk entitled “*Endosome-Mitochondria Interface Controls Intracellular Iron Trafficking in Erythroid Cells*”
- **Dr. Adi Klil-Drori**, a post-doctoral fellow in pharmacoepidemiology and medical oncology, made a presentation on the risk of major bleeding with low-molecular-weight-heparins for venous thromboembolism in dialysis patients.



Dr. Susan Kahn was presented with the Canadian Society of Internal Medicine’s (CSIM) 2016 Dr. Davis Sackett Senior Investigator Award by Dr. Stephen Hwang, President of the CSIM (above). This award recognizes excellence in research by a senior general internist in Canada. As well, Dr. Kahn has been elected a Fellow of the Canadian Academy of Health Sciences.

She is the founder and director of the Centre of Excellence in Thrombosis and Anticoagulation Care (CETAC) at the Jewish General Hospital and Co-Director of the Canadian Venous Thromboembolism Clinical Trials and Outcomes Research (CanVECTOR) Network.