

## Michael Pollak to co-lead Metastatic Breast Cancer Dream Team

**Dr. Michael Pollak**, Director of the Cancer Prevention Centre at the Segal Cancer Center, and **Dr. Nahum Sonenberg**, of the Goodman Cancer Research Centre at McGill University, are leading the new pan-Canadian Stand Up To Cancer (SU2C) Canada Metastatic Breast Cancer Dream Team. The strength of this team lies in the close collaboration between clinicians and basic scientists that will translate fundamental research into effective treatment options for patients.

Over the next two years, the Dream Team will work to develop a translational cancer research project that addresses prevention strategies for those at risk of metastatic cancer, and to gain a mechanistic understanding of metastatic progression. Great progress has been made in the treatment of breast cancer and disease that remains localized can be treated successfully in most cases. However, truly curative treatments are not yet available for metastatic disease that has spread to the lungs or the bones or other organs.

Metastatic breast cancer is driven, in part, by unregulated production of proteins by the cancerous cells. This happens when the basic machinery of the cell that translates genetic instructions carried by messenger RNA (mRNA) into living protein becomes dysfunctional. The Dream Team is taking a new, small-molecule inhibitor of the kinases MNK 1 and 2, enzymes that are key regulators of the mRNA translation process, and using it to block this out-of-control production of proteins.

The agent being tested - eFT508 (tomivosertib) - is known to inhibit this process, but has never before been applied to metastatic breast cancer. It will be given, in combination with paclitaxel or nabpaclitaxel, to patients for whom the standard of care has not been effective, in the hope that the combination will halt or slow down the metastatic process. Approximately forty patients will participate in the trial.

"This is an opportunity to give patients access to the latest results of our laboratory studies," said Dr. Pollak. "This is a Phase I trial, so the patients will be carefully

**Dr. Michael Pollak** has been elected a fellow of the Royal Society of Canada, which recognizes remarkable contributions to the arts, humanities and sciences. "This is recognition by other scientific leaders that I've made a contribution that they consider significant," he said. "I feel this really represents recognition for our entire team, to whom I am very grateful."

monitored for safety profile and to verify that the therapy performs as anticipated. The way the trial is designed, we are going to learn a great deal about how the drug works, and be able to refine our approach so that we make progress in treating metastatic disease by examining the patients' blood, immune system, and tumor biopsies throughout the course of the trial."

SU2C Canada, the Canadian Cancer Society (CCS), and the Canadian Institutes of Health Research (CIHR) are investing up to \$6 million in this novel effort.

"We are very grateful for the support being given to this project, and appreciate that our work is recognized by the funding agencies as having a high priority," said Dr. Pollak. "The JGH and McGill now count among the elite group of institutions supported by Stand Up 2 Cancer."

Other Dream Team members from the LDI include Drs. **Wilson Miller**, **Sonia del Rincon**, and **Claudia Kleinman**. Other key collaborators are at the University of Alberta (Edmonton) and the Cancer Control Agency of British Columbia (Vancouver).



Left to right: Dream Team co-leaders Nahum Sonenberg and Michael Pollak; Marc Müller, Parliamentary Secretary to the Minister of Crown-Indigenous Relations; and Suzanne Fortier, Principal and Vice-Chancellor of McGill University.

## Second phase of funding for CCNA

The Canadian Consortium on Neurodegeneration in Aging (CCNA) has received a second round of funding, totaling \$46 million over the next five years, from the CIHR, along with eleven partner agencies – including the Alzheimer Society of Canada (ASC), the Centre for Aging + Brain Health Innovation (CABHI), Brain Canada, and the *Fonds de recherche du Québec – Santé* (FRQS). The CCNA brings together over 310 researchers from 39 universities in eight provinces across Canada.

Established at the Lady Davis Institute in 2014, CCNA's mission is to foster inter-disciplinary research collaborations on age-related cognitive decline and dementia, which impact over 400,000 Canadians today and will impact as many as 1.5 million by 2031.

Among its most recent initiatives are:

- the Canadian Aging and Neurodegeneration Prevention Therapy Study Using Multi-dimensional Interventions for Brain Support – Unified Platform (CAN-THUMBS UP). The infrastructure and master protocol being created for this large-scale dementia prevention study will test combination therapies and lifestyle changes, such as physical activity, cognitive training, and diet, on individuals who are at higher risk of developing dementia as they age; and
- the Comprehensive Assessment of Neurodegeneration and Dementia (COMPASS-ND), one of the few cohort studies in the world collecting a wealth of data on seniors with different types and severities of dementia. To date, 800 people have been included in this study across Canada, with Québec playing a leading role—27% of the total participants originate from nine Québec-based recruitment sites.

Having obtained a \$2.1 million investment from CCNA, the LDI has nine CCNA-affiliated researchers, three of whom are in leadership roles: Drs. **Howard Bergman** and **Isabelle Vedel** co-lead the team investigating how best to integrate dementia patient care into the health care system; and Dr. **Natalie Phillips** is on the Research Executive Committee and co-leads the team investigating the links between sensory loss and cognitive decline. Other LDI researchers participating in the CCNA include: Drs. **Olivier Beauchet**, **Elizabeth MacNamara**, **Pierre Pluye**, **Uri Saragovi**, **Hyman Schipper**, and **Susan Vaitekunas**.

## 2019/20 TD Studentship Awards

The Lady Davis Institute and JGH Foundation are grateful to TD Bank for supporting our mission to advance health care through the TD Bank Studentship Award. Over the years, funding from TD Bank has had a major impact on our research. Each award is worth \$10,000.

This year's recipients are among the very best trainees pursuing post-graduate degrees at McGill University. Each awardee is currently conducting a research project at the Lady Davis Institute. They include the projects of the following doctoral candidates:

- **Kiran Makhani** on the fetal origins of arsenic-induced atherosclerosis with Dr. Koren Mann;
- **Richeek Pradhan** on the effectiveness and safety of insulin pumps versus multiple daily insulin injections in patients with type 1 diabetes mellitus with Dr. Laurent Azoulay;
- **Hayley Kim** on mTOR regulation of epigenetic modifications in cancer with Dr. Ivan Topisirovic;
- **Maja Jankovic** on the role of beta-galactosylation in AML cells *in vivo* with Drs. Francois Mercier and Alexandre Orthwein.

Master's degree awardees include:

- **Sarah MacKay** looking at self-warmth and self-coldness as distinct pathways towards psychological well-being and distress with Dr. Annette Korner;
- **Yang Yang** on elucidating mechanisms of therapeutic resistance in triple-negative breast cancer by computational analysis of single-cell RNA sequencing with Dr. Claudia Kleinman.

McGill University has promoted the following Lady Davis researchers:

- **Dr. Stephanie Lehoux** to full Professor in the Department of Medicine;
- **Dr. Kristian Filion** to Associate Professor in the Department of Epidemiology, Biostatistics and Occupational Health;
- **Dr. Tamim Niazi** to Associate Professor in the Gerald Bronfman Department of Oncology.

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## Quebec Cancer Consortium to develop new therapeutics and biomarkers

A total of \$27.9 million - \$10M from the *Ministère de l'Économie et de l'Innovation (MEI) du Québec* through its *Fonds d'accélération des collaborations en santé (FACS)* program, and the rest from 12 private, public, and non-profit partners – is being invested in the Québec Cancer Consortium for Novel Therapeutics and Biomarkers (QCC), with the objective of doubling patient recruitment into oncology clinical trials and developing infrastructure to support the development of personalized medicine and immunotherapies.

The Segal Cancer Centre at the Jewish General Hospital is among the founders of the QCC.

“Building a consortium is essential for furthering personalized medicine because you need a critical mass of patients in order to collect enough data to discern patterns that allow you to identify the therapies that will effectively target the genomic or proteomic mutations driving an individual’s cancer,” points out **Dr. Gerald Batist**, Director of the Segal Cancer Centre, and a co-investigator on the initiative.

Collectively, the QCC will have access to approximately 16,000 cancer patients annually, effectively doubling patient recruitment for clinical trials and creating an active biobank of biospecimens collected over the course of clinical trials that will have a major impact on advancing oncology, expanding research opportunities, offering better therapeutic options and outcomes.

QCC researchers and clinicians will collaborate to identify and develop new biomarkers that will serve to better predict responses and adverse effects resulting from personalized treatments and immunotherapies. The development of new biomarkers to optimize treatment decisions will not only increase patient survival and reduce unnecessary treatments but will also curtail healthcare costs in Quebec.

“We’ve long known patients really do benefit from participation in clinical trials. These Quebec institutions working together represents an enormous opportunity to attract more novel experimental therapies for patients and new avenues of inquiry for our excellent scientists,” said Dr. Batist. The Jewish General Hospital boasts the highest level of patient participation in clinical trials of any hospital in Quebec.

## Announcing the Best Trainee Seminars 2018/19 for the Cancer Axis:

MSc category:

**Samantha Worme—(Mercier Lab)**, “Single cell transcriptomics identifies a maturation continuum in acute myeloid leukaemia”

PhD category:

**Jacqueline Ha—(Urisin-Siegel Lab)**, Integration of distinct ShcA signaling complexes promotes breast tumorigenesis

Postdoc category:

**Rajarshi Roy Choudhury—(Saragovi Lab)**, “Carbohydrate-based vaccines for cancer therapy”

Special thanks to the judges, who attending every seminar: Adriana Aguilar, Maud Marques, Andreas Papadakis, Laura Hulea.

**Dr. Chen Liang’s** term as Interim Director of the McGill AIDS Centre has been extended until June 30, 2020. Professor Liang has been serving in this role since June 2018. Dr. Liang will continue to lead the efforts to launch the Mark Wainberg Centre for Viral Diseases, a new McGill Initiative in honour of Dr. Wainberg. The Centre will unite over 40 talented researchers from across McGill to study viral infections from basic science to clinical research to population health.

**Dr. Howard Bergman** has been appointed to the newly created position of Assistant Dean, International Affairs in McGill’s Faculty of Medicine. In his new role, Dr. Bergman will provide strategic oversight of the international and business development activities in the Faculty of Medicine. He will develop and implement an International Affairs strategy to increase the Faculty’s visibility abroad and explore new collaborations with international partners.

**Dr. Mark Basik** (right) has been appointed the Herbert Black Chair in Surgical Oncology at McGill University, in recognition of his accomplishments and to further his research.



## Genome Quebec invests in next generation cancer assay

A project designed by Drs. **Chrisoph Borders** and **Alan Spatz** to develop the next generation of precision cancer diagnostics has been awarded funding through Genome Quebec's Genomic Applications Partnership Program (GAPP).

In order to apply immunotherapy against a patient's cancer, it is critical that the active proteins blocking the patient's immune system be identified and targeted. PD-L1 is one of these proteins that is widely targeted because it is associated with several cancers, including lung, the leading cause of cancer deaths.

However, existing immunohistochemistry techniques used to measure PD-L1 are often inaccurate. The GAPP funding will be used to develop next generation assays at the Segal Cancer Proteomics Centre that are expected to be far more precise at determining the concentration of PD-L1 molecules in malignant tumors.

"Precision cancer treatment depends on an accurate analysis of the protein that needs to be disrupted," said Dr. Borchers, director of the proteomics centre. "There's no point in giving patients an inhibitor for a protein that isn't fueling the cancer. Our patented technology is very precise, able to determine the concentration of molecules per cell, and, thus, whether a PD-L1 inhibitor will help the patient."

"Proteomics technology gives a more complete analysis of the active proteins in a tumor, thereby functioning as a better guide for treatment options. This will change the landscape of cancer care by improving diagnosis and potentially identifying new drug targets," points out Dr. Spatz, Director of Pathology and the McGill-JGH Dubrovsky Molecular Pathology Centre at the Jewish General Hospital. "Correctly quantifying the biomarker that will predict a clinical response means you don't waste precious time before giving patients the right medication. Moreover, immunotherapies are very expensive, so you must apply them efficiently."

The technology is germane to multiple proteins, known as immune checkpoint proteins, that have been associated with cancer progression. Follow-up with the patient over time will provide a feedback loop that allows clinicians to determine the effectiveness of the treatment. It will also indicate changes in the cancer in the event that resistance develops.

## Certain Antidepressants Linked to Reduced Risk of Stroke

A new study led by **Dr. Christel Renoux** found that certain selective serotonin reuptake inhibitors (SSRIs) and other antidepressants that increase serotonin levels in the brain the most may be associated with a reduced risk of ischemic stroke when compared to antidepressants that increase serotonin levels the least. The study is published [in Neurology](#).

SSRIs are the most commonly prescribed antidepressants. Serotonin is released from a cell when sending a signal and then is naturally reabsorbed back into the cells. SSRIs inhibit the nerve cells from reabsorbing serotonin, thereby making more of it available in the brain, in the gaps between nerve cells, which improves the brain's ability to regulate mood.

"It is not uncommon for people with depression to also have heart disease, a risk factor for stroke, so it is important to investigate whether antidepressants raise or lower the risk of stroke," said Dr. Renoux. "Our study investigated stroke risk in people who take antidepressants that increase serotonin levels the most compared to people who take antidepressants that increase levels the least."

People who used antidepressants that increased serotonin levels the most, had a 12% lower risk of having an ischemic stroke than people who used antidepressants that increased serotonin levels the least. Anti-depressants that increased serotonin levels the most included fluoxetine, paroxetine, and sertraline and the drug duloxetine, which is a selective serotonin and norepinephrine reuptake inhibitor (SNRI).

In the analysis assessing the risk of stroke with drugs that increase serotonin levels the most, among 2,836 people with stroke, 2,277, or 80.3%, took drugs that increased serotonin levels the most, whereas among 80,821 people who did not have a stroke, 66,577, or 82.4%, took drugs that increased serotonin levels the most.

A limitation of the study was that the database listed only antidepressants prescribed by general practitioners, not by specialists. However, Dr. Renoux notes that antidepressants are usually prescribed by general practitioners.

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