

Segal Cancer Centre partners in national artificial intelligence platform

The federal Minister of Innovation, Science and Economic Development announced an investment of up to \$49 million in the Digital Health and Discovery Platform (DHDP), a network including the Jewish General Hospital that is establishing a cutting-edge, Canada-wide health data platform. The DHDP will accelerate the work of researchers and clinicians to develop new and personalized treatments for disease, focusing initially on cancer, but eventually expanding to include other areas of medicine.

DHDP creates a national infrastructure to collect and amalgamate massive amounts of genomic and proteomic data from tumors samples. The data is then processed through artificial intelligence to generate algorithms that recognize molecular patterns within tumors and their responses to particular treatments.

“The truly revolutionary aspect is that AI can extract nuances in the data that humans can overlook,” said **Dr. Gerald Batist**, Director of the Segal Cancer Centre. “Moreover, AI can learn from itself, meaning that the more data we accumulate, the smarter the AI becomes. We need to enroll as many patients as possible to achieve the necessary scale for the greatest good.”

Led by the Terry Fox Research Institute and Imagia, the network connects 95 partners across nine provinces to establish a more collaborative health care system that is better positioned to maximize medical breakthroughs.

“None of us could achieve alone what we can accomplish together,” said Dr. Batist. “The data we can amass has the potential to reveal intricacies of cancer progression and response that would not otherwise be observable.”

Participating in the **Digital Health and Discovery Platform** positions the JGH at the forefront of a digital revolution in personalized medicine. The initiative fits with the CIUSSS—West Central Montreal’s overall emphasis on digital health and the application of data to improving health care.

Photo credit: Joni Dufour and Owen Egan



Dr. Uri Saragovi (left) is presented the Hakim Famiy Innovation Prize by Dr. Raymond Hakim as part of the McGill Clinical Innovation Competition (CLIC). A Professor of Pharmacology and the founder of RE3 Therapeutics, Dr. Saragovi has developed a simple blood test for quantitative detection of ovarian cancer tumor markers that would allow for earlier detection of disease and offer greater opportunity for curative therapy.

Although therapy for ovarian cancer is 80% effective, the five-year survival rate is only 9% due to late diagnosis and recurrent disease. Early diagnosis—absent to date—would offer greater opportunity for curative therapy. This tumor marker may also detect early recurrence.

CLIC was created to inspire innovative thinkers within the Faculty of Medicine and across McGill to imagine new devices, diagnostics, platforms, programs and processes that will improve health care, in Canada and globally. The Hakim Prize recognizes ideas, new processes or devices in health care with potential to have a tangible and meaningful impact on the lives of patients.

Pioneering clinical trial studies treating breast cancer without surgery

In a radical departure from established treatment protocols, **Dr. Mark Basik**, a surgical oncologist and researcher at the Segal Cancer Centre, is spearheading an international effort that will lead to a clinical trial to forego surgery in breast cancer patients who show no signs of residual cancer following a course of pre-operative chemotherapy.

Dr. Basik is the principal investigator on a National Cancer Institute (NCI) trial that is recruiting 175 patients to test the accuracy of needle biopsies of the breast to detect stray cancer cells after a complete response to therapy. Participants will receive drugs followed by mammograms, ultrasound, and MRIs, as well as a needle biopsy. They will then have a breast lumpectomy as planned.

The trial will determine whether the needle biopsy is sufficiently accurate in determining whether or not there is any remaining cancer so that the idea that surgery may be avoided can be reliably tested in a next clinical trial.

“It doesn’t make sense to perform surgery when the tumor has melted like snow on a summer’s day in response to drugs,” said Dr. Mark Basik

The trial is only open to patients with breast cancers that respond very well to existing chemotherapeutic agents. Dr. Basik says that this applies to approximately 20% of those diagnosed with breast cancer.

“Chemotherapy is so effective that, when given before surgery, in many cases, we see tumors shrink to where we can no longer feel anything and it no longer shows up on mammograms or ultrasounds,” he said. “Because of lingering doubts of stray malignant cells, we have been compelled to perform surgery to remove tissue for the sake of absolute certainty.”

The practice of de-escalating medical interventions aims to minimize the invasiveness of treatment. Thus, according to the NCI, in 2015 more than 65% of breast cancer patients over the age of twenty were able to undergo breast-conserving surgeries, while less than 35% had mastectomies. To avoid surgery altogether will be the next evolution in the process.

In-depth tumor analysis presents new treatment options for advanced cancer

The results of the first clinical trial in cancer to add gene expression on top of DNA aberration was published in [Nature Medicine](#). It revealed that combining RNA and DNA profiling gives a far more precise indication of the active biological elements within a tumor, enabling clinicians to more accurately determine which targeted therapies could improve survival among patients with advanced cancer. The Segal Cancer Centre was the only Canadian site in this initiative of the Worldwide Innovative Networking in Personalized Cancer Medicine (WIN Consortium).

“Analyzing the genetic mutations in a tumor doesn’t necessarily isolate the active elements that represent the best clinical targets,” said **Dr. Wilson Miller**, Director of the Segal Cancer Centre’s Clinical Trials Unit and a principal investigator on the study. “Profiling RNA gives us a more accurate picture of the molecules that drive tumor progression in an individual case and, where we can target those molecules, we achieve much better results. Because DNA and RNA are not directly aligned in cancer cells, this added dimension of profiling is very important to personalizing treatment.”

The 107 patients who received treatment in the study had late stage disease for which there was little hope of improvement. All had already received extensive treatments, with one-quarter having had at least five prior lines of therapy. Nonetheless, more than 26% of the participants experienced at least six months of partial or complete response to the new therapies introduced as a result of the combination RNA and DNA profiling. More than 22% experienced survival that surpassed the previously expected norm.

The next phase WINTHER trial will recruit patients earlier in their cancer trajectory in order to further demonstrate the positive effects of precision medicine in cancer. An even deeper level of analysis is to identify the actual proteins underlying the gene expression.

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LDI researchers honoured with FRQS career awards

In the latest career award funding announced by the Fonds de recherche du Québec - Santé (FRQS), LDI researchers enjoyed a 50% success rate.

Dr. Ashley Wazana had his Chercheur-boursier clinicien (CBC) senior award renewed to pursue his project, *Comment l'environnement précoce interagit avec la susceptibilité développementale et le sexe de l'enfant pour modérer la trajectoire de la psychopathologie chez les enfants de 0 à 12 ans - du développement à la pratique.*

Having their Chercheur-boursier junior 2 awards renewed were:

Dr. Claudia Kleinman for, *Modélisation des trajectoires d'expression génique dans le cerveau humain en développement: applications aux tumeurs cérébrales pédiatriques;*

Dr. Christel Renoux for, *Maladies neurovasculaires : facteurs de risque et prévention en population générale.*

Dr. Haim Abenhaim was awarded a CBC junior 2 for, *Programme de recherche compréhensif utilisant des méthodes épidémiologique et d'essais clinique visant à réduire la morbidité maternelle et néonatale.*

CBC junior 2 awards were renewed for:

Dr. Lysanne Campeau for, *Modulation des processus dégénératifs et apoptotiques induits par le proNGF dans les troubles mictionnels reliés au diabète.*

Dr. Isabelle Vedel for, *Intégrer la prise en charge des personnes vivant avec la démence dans le système de santé.*

Dr. François Mercier was named CBC junior 1 to pursue his project, *La génomique fonctionnelle de la leucémie myéloïde aigüe in vivo.*

Dr. Chantal Autexier, Professor in the Department of Anatomy and Cell Biology was awarded the David Thomson Award for Excellence in Graduate Teaching & Supervision from McGill University. This award acknowledges outstanding contributions to promoting graduate student excellence through supervision and teaching by a faculty member who has been supervising for 10 years or more.



Left to right, **Drs. Wilson Miller** (Oncology), **Ernesto Schiffrin** (Medicine), and **Samy Suissa** (Epidemiology, Biostatistics & Occupational Health) have been named Distinguished James McGill Professors by McGill University. This award recognizes a late-career scholar's sustained scholarship of world-class caliber and international leadership. The title it held until retirement.

Controlling blood pressure in elderly patients

With more than 70% of individuals over the age of 75 having arterial hypertension, it is crucial to identify optimal targets for blood pressure in this growing population. **Dr. Antonios Douros** and his collaborators in Germany published an observational cohort study to assess whether treatments to lower blood pressure are beneficial to older hypertensive patients in the [European Heart Journal](#).

“The belief is that lowering blood pressure of hypertensive patients will reduce mortality,” Dr. Douros said. “However, we found that in certain older hypertensive patients normalized blood pressure could actually be associated with an increased risk of death.”

The study involved some 1,600 patients over the age of seventy being treated with antihypertensive drugs, who were followed for an average of 6 years. It concluded that blood pressure below 140/90 mmHg, which is slightly higher than the guidelines by the American College of Cardiology and the American Heart Association set out, was associated with increased mortality among those over the age of eighty or those with previous cardiovascular events.

Of note, the established guidelines on the management of arterial hypertension are based on large-scale randomized trials that generally involve significantly younger patients. Few studies have focused exclusively on older hypertensive patients.

“The idea is that lowering blood pressure can reduce blood flow, which can be problematic in elderly patients for several reasons,” said Dr. Douros. “For example, kidney function may be affected by reduced blood flow in advanced age. Moreover, reduced blood flow could also induce dizziness, which may make an older, frail person prone to falling and the complications that falls can bring on.”

He allows that further studies including randomized trials are necessary before clinical practice is changed. However, it is important for clinicians to consider all facets of a person’s health when determining whether medication to lower blood pressure is indicated. The paper argues for a personalized approach to treatment, rather than a blanket approach that prescribes a single optimal blood pressure for everyone.

Epigenomic data critical to new insights into deadly brain tumors

Dr. Claudia Kleinman and her team performed the comprehensive epigenomic data analysis in order to delve deep into the histone 3K27M driver mutations that characterize more than 80% of high-grade gliomas (HGG), a leading cause of cancer-related death in children and young adults. HGGs are challenging to target because the gene itself serves critical functions so it is not as simple as deactivating gene expression.

Her work was part of a collaboration, including Dr. Nada Jabado of the MUHC, to identify vulnerabilities in the tumor that can be targeted, while avoiding a direct assault on H3K27M. It was published in [Cell Cancer](#).

“The effect we found in these tumors is that areas in the gene that should be silenced become active,” Dr. Kleinman explains. “Endogenous retroviruses that are normally silent become expressed within the cancer, and this is a weakness we can exploit. There are drugs that increase the expression of these dangerous elements and destroy the stressed cells, which may halt the malignant process.”

Using animal models, patient tumors, and patient-derived cell lines, the researchers knocked out the mutation and discovered a side effect of the mutation that caused stress in cells. This revealed a vulnerability that may not be directly related to oncogenic properties, but which may be exploited by existing drugs to interfere with the progression of disease.

This paper illustrates proof of principle for deploying epigenetic therapies against repeat elements as a pathway to combating high-grade gliomas.

“The benefit of profiling the entire genome and layering complementary types of data is that it will reveal information you didn’t even know to be looking for,” said Dr. Kleinman. “We would not have thought to focus on the silent part of the genome, only realizing its potential with respect to these types of tumors when it was revealed through the data.”

Dr. Celia Greenwood, of McGill’s Department of Oncology, has been named a James McGill Professor. This award recognizes a senior scholar’s status as an outstanding and original researcher of world-class caliber and an international leader in their field.

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