

New hope for severely ill COVID-19 patients

Dr. Stephen Robbins, incoming Director of the LDI, and **Dr. Donna Senger**, who is joining the Cancer Axis, are the co-founders of [Arch Biopartners](#), which has been awarded up to \$6.7 million from the Canadian government's Strategic Innovation Fund in support of its lead drug candidate, Metablok. This funding will help the company to advance Metablok through Phase II clinical trials to determine its efficacy in preventing acute respiratory distress syndrome (ARDS), acute kidney injury, and other organ injuries caused by inflammation in hospitalized patients with severe cases of COVID-19.

It will also help Arch Biopartners to engage in further studies for optimal dosage; perform chemistry, manufacturing and controls to support the drug's approval as a COVID-19 treatment; and ultimately prepare for a Phase III trial. This project will contribute to the ongoing fight against the coronavirus pandemic as part of Canada's [Plan to Mobilize Science to fight COVID-19](#), which was introduced in March 2020. Through this investment, the Government of Canada is contributing to breakthrough technologies, efforts to advance the development of a treatment for COVID-19, and the commercialization of a made-in-Canada solution.

The promise of Metablok, also known as LSALT, was first revealed in a [2019 Cell paper](#), in which Drs. Robbins and Senger and their colleagues identified dipeptidase-1 (DPEP1) as a major adhesion receptor of white blood cells in the lungs, liver, and kidneys. This enzyme is the target of the LSALT peptide, which blocks DPEP1, thus significantly reducing white blood cell recruitment in these organs, a complication that frequently afflicts patients hospitalized with moderate to severe COVID-19 infections.

"As the world works toward an effective COVID-19 vaccine, we cannot lose sight of the importance of developing treatments to keep those stricken with

the virus alive," said Navdeep Bains, Minister of Innovation, Science and Industry, in announcing the investment. "Our contribution will support Arch Biopartners in taking its promising treatment through clinical trials and subsequent approvals. Once approved, this drug has the potential to be an important tool to save lives, improve long-term health and reduce the strain on Canada's medical system."

"Our research began long before COVID-19 even existed, so this is really serendipitous," said Dr. Robbins, who is currently the Scientific Director of the Canadian Institutes of Health Research Institute of Cancer Research, "and the applications for Metablok extend well beyond this pandemic, as acute lung injury is a leading cause of death in critical care in Canada."

Metablok has received approval from the U.S. Food and Drug Administration and Turkey's Ministry of Health to conduct Phase II clinical trials, and has begun dosing patients in those countries. Having received approval, as well, from Health Canada, dosing at centres in this country will begin shortly.

Susan Kahn appointed to WHO COVID-19 Expert Panel

Dr. Susan Kahn, Director of the JGH Centre of Excellence in Thrombosis and Anticoagulation Care (CETAC) and Senior Investigator with the Centre for Clinical Epidemiology, has been appointed to serve on the Technical Expert Panel on Thrombostasis of the World Health Organization (WHO) Advisory Group on Therapeutics Prioritization for COVID-19.

The expert panels are small committees consisting of inter-nationally recognized health care leaders. They are multi-disciplinary bodies that provide the WHO with expert, impartial and timely advice on candidate drugs for treatment and prevention of COVID-19. Their recommendations are evaluated in WHO-sponsored platform studies, including trials in hospitalized patients as well as outpatients, pre-exposure prophylaxis, and post-exposure prophylaxis. Among the challenges in treating COVID-19 patients is that the virus induces such a wide array of effects, including hyper-coagulability, or the tendency to form blood clots.

New name, new mission for the McGill AIDS Centre

Established in 1990 under the direction of the late Dr. Mark Wainberg, the McGill AIDS Centre has been at the forefront of HIV research. Now, it is transformed into the [McGill Centre for Viral Diseases](#), marking its evolution to the study of other viruses that pose serious threats to global health.

The process to formalize expansion of the Centre and redefine its mission to provide solutions to all viral diseases that threaten public health began in 2017. Its scientists have built research programs in areas such as basic virology, immunology, drug discovery, epidemiology, population studies and clinical research.

Dr. Chen Liang is the Centre's Acting Director. He is an internationally renowned HIV researcher whose lab specializes in restriction factors (RFs), innate anti-viral proteins that are the body's first-line defence against viruses. Dr. Liang discovered two of the few known host RFs, which underpin the key innate anti-HIV-1 mechanisms. He also pioneered the study of using the genome editor CRISPR to cure HIV infection. He has recently turned his focus to COVID-19 work, including receiving a grant from the Canadian Institutes of Health Research in their first round of funding and collaborating with McGill engineering professor Stephen Yue on another NSERC Alliance COVID-funded grant. He also played an integral role in launching McGill's two containment level-3 labs for COVID research.

The new Centre, is part of McGill's Interdisciplinary Initiative in Infection and Immunity (MI4). "MI4 has mobilized tremendous resources to support COVID research," says Dr. Liang. "Many members of our Centre have benefited from the support of MI4 through funding and collaboration. We are very fortunate to have this diverse and interdisciplinary environment. With all these, we are better positioned to find solutions to the COVID-19 pandemic."

"This expansion of the McGill AIDS Centre is a tribute to Mark Wainberg and the tremendous team of researchers he assembled and mentored at the LDI," notes Dr. Roderick McInnes, Director of the LDI. "The wonderful contributions they have made to the fight against AIDS are an enduring legacy. The disastrous impact of the coronavirus pandemic is a stark reminder of the essential work they must continue to do."

LDI research among Quebec Science Top 10 discoveries of 2020

Research led by **Dr. Claudia Kleinman**, at the LDI, and Dr. Nada Jabado, of the Research Institute of the McGill University Health Centre, was among 2020's Top 10 Scientific Discoveries in Quebec, as selected by [Québec Science](#). The team's discovery that several types of highly aggressive pediatric brain tumors originate as a result of stalled development of progenitor cells in the pons and forebrain was published in [Nature Genetics](#).

The genetic event that triggers the disease happens in the very earliest phases of cellular development, most likely prenatal. Rather than developing normally, the cells' progress is halted and they transform into malignancies. The condition is analogous to a Peter Pan Syndrome as these cells are in a state of arrested development.

Applying sophisticated single cell sequencing techniques and large-scale data analysis, the researchers compiled the first comprehensive profile of the normal developing forebrain and pons, a major structure on the upper part of the brainstem that controls breathing, as well as sensations including hearing, taste, and balance.

The study has led to novel discoveries, including another publication in [the journal Cell](#), where the developmental atlas at single-cell resolution was used to redefine the origins of a subgroup of lethal glioblastoma, demonstrating they arise in specific neuronal progenitors.

"The cornerstone to fighting these conditions is to identify the biological process at work, which is what our research has achieved," said Dr. Kleinman. "Once we understand the underlying mechanisms, the search can begin for the means to unblock the arrested development of the cells. We are hopeful that the identification of the origin and a specific gene needed for tumour growth could lead to new therapeutics."

Myer Bick, former President and CEO of the JGH Foundation was named [Member of the Order of Canada](#) for his exemplary leadership in fundraising for health establishments as well as for his community service.

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Orthopaedics start-up wins support from adMare BioInnovations

Trepso Therapeutics, based on more than twenty years of scientific research led by Drs **John Antoniou** and **Fackson Mwale** was among six Quebec start-ups selected by adMare BioInnovations, Canada's global life sciences venture, to join its new acceleration program supporting the scale-up and growth of promising life sciences companies. Trepso is developing a best-in-class novel therapeutic, named short Link N (sLN), to reverse the structural deterioration associated with degenerative disc and articular joint diseases, such as osteoarthritis, and to reduce the associated pain and inflammation. Drs. Antoniou and Mwale run the Orthopaedics Research Laboratory at the LDI.

Chronic back pain remains an under-served, highly prevalent condition and a leading cause of functional disability worldwide, consistently ranking among the top five reasons for doctor visits, surgery and hospitalization. Chronic lower back pain caused by degenerating discs is a significant contributor to today's opioid epidemic.

Most current pharmacologic treatments address the associated pain and inflammation, rather than the underlying pathophysiology. The benefits of such treatments are generally short in duration, have limited effect as the disease worsens, and patients often end up resorting to surgical intervention.

sLN is the bioactive portion of an endogenous peptide that acts as a growth factor and key regulator of normal spinal disc and cartilage extracellular matrix turnover. It not only blocks inflammatory pain signaling and possibly the ingrowth of pain-sensing fibers, but may preserve and restore the integrity of the degenerating tissue. The potential for sLN to truly be disease-modifying would be of tremendous value to the millions of patients suffering from disc disease and articular cartilage diseases, reducing the number of costly and risky surgeries.

Thanks to contributions from the Government of Quebec, through Start-Up Québec funding from the Ministère de l'Économie et de l'Innovation and the City of Montreal, Trepso will benefit from \$150,000 in customized access to adMare resources, such as laboratories and offices, scientific and business support, and training. With the support of BIOQuébec and Montréal InVivo, it will also access unique networking and mentoring opportunities to increase their visibility in Quebec's life sciences community.

"These promising companies will thus be able to better structure themselves, become more mature, and even more attractive to investors. Ultimately, the entire life sciences and health technology sector will benefit from the scientific breakthroughs advanced by this program," said Pierre Fitzgibbon, Minister of Economy and Innovation, in making the announcement.

Multicultural Mental Health Resource Centre launched

Bell Let's Talk, McGill University, the LDI and The Neuro (Montreal Neurological Institute-Hospital) launched the [Multicultural Mental Health Resource Centre](#) (MMHRC) website, a unique resource to improve the quality and availability of mental health services for people from diverse cultural and ethnic backgrounds, including new Canadians, refugees and members of established ethnocultural communities.

Supported by a \$250,000 donation from Bell Let's Talk, MMHRC is led by **Dr. Laurence Kirmayer**, who has pioneered efforts to approach mental health within the cultural context of those who are being treated and the communities in which they live.

"Addressing issues of language, culture, religion and other aspects of diversity, the MMHRC will promote greater equity in mental health care," said Dr. Kirmayer. "Mental health is often viewed differently in different cultures, which requires culturally responsive approaches to meet the needs of those seeking help. With the generous support of Bell Let's Talk, we have drawn on our extensive research to strengthen and develop our online platform in order to better reach out to those in need and make this resource more accessible."

The MMHRC has developed information and tools for several different groups:

- For patients and their families – multilingual information on mental health issues and treatments, information about how to find culturally appropriate mental health services, and ways to help family members maintain their well-being.
- For health care professionals – information on cultural-assessment tools and methods, access to interpreters and culture brokers, and recommendations for culturally adapted treatment interventions.
- For community organizations – materials for educators about support programs for people living with mental health issues, and advocacy and stigma reduction.
- For policy makers, planners and administrators – information on health disparities, recommendations to improve cultural competence in organizations, and models of mental health services and interventions to address diversity.

Partnership with NRC to develop machine learning for COVID-19 care

The CIUSSS West Central Montreal (CIUSSS-CCOMTL) is partnering with the [National Research Council of Canada \(NRC\)](#) to fund an initiative to develop and assess an explainable machine learning (ML) prototype tool that improves transparency and the applicability of the decisions that it helps to make. The outcome will be to introduce ML to clinical informatics and enhance confidence in its accuracy.

“During the COVID-19 pandemic, clinicians were provided with a deluge of models to address forecasting, contact tracing, screening and patient care. Many algorithms show tremendous promise, but further work is required to optimize their application as effective clinical tools,” explained **Dr. Michael Shulha**, Associate to the Director of Digital Health for the CIUSSS-CCOMTL and an investigator at the LDI. “With this project, our objective is to improve the association between machine learning and its implementation in clinical interfaces. Accordingly, these cutting-edge tools will gain wider acceptance and have a more meaningful impact on clinical decision-making while ensuring consistency in clinical practice.”

In the first wave of the COVID-19 pandemic, health care institutions were faced with the challenge of rapidly adapting care systems and services to cope with the surge of patients. While tremendous efforts were made to adapt facilities, care protocols, care modalities, and infection protocols, the capacity to quickly implement ML tools aimed at patient care was limited. Much of this challenge is related to the lack of a comprehensive framework for implementing explainable artificial intelligence within the Jewish General Hospital. The science of machine learning explainability is still in its infancy, as is the link between explainability methods and new design paradigms for user experience in clinical interfaces.

Within the scope of this project, a prototype machine learning tool will be designed with input from clinicians who have spent significant time on the front lines caring for COVID patients in the wards and the intensive care unit of the Jewish General Hospital. This is an opportunity for AI and actual clinical practice based on nearly a year of experience in dealing with the pandemic to learn from each other.

The first phase of the project will seek to answer:

1. What are the most potentially relevant machine learning algorithms that could be implemented to aid in the continuing response to COVID-19?
2. What explainability methods would be most appropriate to apply to these algorithms?
3. What is the state of the art in representing explainable machine learning in user interfaces?
4. What is the most appropriate scientific methodology for studying end user acceptability of explainable machine learning tools?

Studies clarify effectiveness and safety of new medications for type 2 diabetes

The Canadian Network for Observational Drug Effect Studies (CNODES) has published a series of papers about sodium glucose co-transporter 2 (SGLT-2) inhibitors, a class of drugs that has been used for second- or third-line treatment of type 2 diabetes in Canada since 2014. One looked at their effectiveness in preventing cardiovascular events. The others addressed potential safety concerns, including diabetic ketoacidosis (DKA), below-knee amputation, and serious urinary tract infection (UTI).

“SGLT-2 inhibitors are a relatively new therapy for type 2 diabetes,” explains **Dr. Kristian Filion**, who contributed to all four studies. “They performed well in clinical trials, but their real-world safety and effectiveness, based on the experiences of hundreds of thousands of people, have yet to be confirmed. It’s always essential to ascertain the effects of drugs beyond the controlled setting of a clinical trial.”

With respect to cardiovascular events research published in [BMJ](#), concluded that their use was associated with a decreased risk of serious cardiovascular events. “These drugs became popular after demonstrating that they reduce the risk for myocardial infarction, heart failure, renal failure, cardiovascular mortality, and potentially all-cause mortality in patients with type 2 diabetes in randomized controlled trials,” points out Dr. Filion, “so this represents important confirmation of their benefits in everyday clinical practice.”

The researchers found that, compared with dipeptidyl peptidase-4 (DPP-4) inhibitors, SGLT-2 inhibitors were associated with an almost 3-fold increased risk for DKA, a rare but potentially life-threatening complication of diabetes. This finding was published in the [Annals of Internal Medicine](#). The results suggest that the risk of this adverse effect could be higher among patients with less advanced disease. However, further studies are needed to corroborate this finding. “This risk should be interpreted in the context of the cardiovascular and renal benefits of SGLT-2 inhibitors,” points out **Dr. Antonios Douros**.

With respect to below-knee amputation, reports have been “inconsistent,” according to **Dr. Oriana Yu** in the paper published in [Diabetes Care](#). “While these findings provide some reassurance,” she wrote, “studies with longer duration of follow-up are needed to assess potential long-term effects.” Following up on warnings from the FDA of an increased risk of serious UTI in patients with type 2 diabetes treated with SGLT-2 inhibitors, the study published in [Diabetes, Obesity and Metabolism](#) found no such association.

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