

International Scientific Advisory Board praises progress at the LDI

The International Scientific Advisory Board (ISAB), chaired by Dr. Alan Bernstein, paid its third visit to the Lady Davis Institute over the course of two days in May. This was a follow-up to its last meeting in 2015, and comes at an important juncture, as a search is launched for a successor to Dr. Roderick McInnes, whose term as Director ends in June 2020.

The ISAB's report was highly favourable with respect to the current state and direction of the LDI. The ISAB wrote, "During his tenure as Director of the LDI, Dr. McInnes has taken the LDI to the next level."

It commended the reorganization that saw the reduction in the number of axes from six to four, with the creation of the Molecular and Regenerative Medicine Axis and the new emphasis on stem cells within that axis.

As the LDI embarks on the search for a new director, the ISAB concluded, it is appropriate to reflect on how new leadership will build on existing strengths and further advance the Institute's mission. It suggested that fostering even closer connections between the clinical and basic research activities would only enhance the LDI's reputation for translational success.

Distinguished members of the ISAB who participated in the review of the LDI included, **Alan Bernstein**, chair, (President, Canadian Institute for Advanced Research), **Arthur Slutsky**, co-chair (St. Michael's Hospital, Toronto), **Dan Drucker** (University of Toronto), **Benedikt Fischer** (University of Auckland), **Jeremy Grimshaw** (University of Ottawa), **Mark Levine** (McMaster University, Hamilton) **Ronan Lyons** (University of Swansea), and **Carol Prives** (Columbia University, New York).

Pregnancy complications can affect long-term cardiovascular health

Few systematic studies have been conducted of the long-term health effects of complications experienced during pregnancy. **Dr. Robert Platt** and his colleagues undertook a review of 84 studies, incorporating nearly 29 million patients with a median follow-up of seven-and-a-half years post-partum to determine pregnancy's impact on cardiovascular disease (CVD) related morbidity and mortality. Their results appear in [Circulation](#).

"This paper is part of a longer term project to develop a predictive model for women's long-term cardiovascular health based on complications during pregnancy," said Dr. Sonia Grandi, the first author on the paper. "We appreciate that there is no one-size-fits-all and that personalized medicine applies to a wide range of medical issues, including the fact that women face particular risk factors for cardiovascular disease."

The authors searched for observational studies of the association between the hypertensive disorders of pregnancy, placental abruption, preterm birth, gestational diabetes mellitus, low birth weight, small-for-gestational-age birth, stillbirth, and miscarriage and CVD. They concluded that women with an array of pregnancy complications, including placental abruption and stillbirth, are at increased risk of future CVD.

"The hypothesis is that pregnancy is a stressor to the cardiovascular system and, therefore, pregnancy and its complications may help identify women at risk for subsequent cardiovascular disease," said Dr. Kristian Filion, another of the study's authors.

The authors conclude, "Our findings highlight the need to consider detailed obstetric history in the assessment of CVD risk in women and the importance of initiating follow-up for risk-factor screening and management in women with a broad range of pregnancy complications beyond the post-partum period."

Richard and Edith Strauss Foundation supports stem cell research at the LDI

The JGH Foundation hosted a reception to honour the Richard and Edith Strauss Foundation for its generous contributions to the Lady Davis Institute (LDI) at the Jewish General Hospital (JGH). Recognizing the important potential of stem cell research and regenerative medicine, the Strauss Foundation has been a supporter of research at the LDI since 2015.

“Stem cell research is an integral part of modern medicine, and we have been making a determined effort to develop our capacity in this field,” said Dr. Roderick McInnes, Director of the LDI.

The Strauss Foundation has provided financial backing to the work of three researchers:

- **Vahab Soleimani**, who focuses on muscle stem cells;
- **Francois Mercier**, who investigates blood stem cells; and
- **Colin Crist**, who is doing research on skeletal muscle stem cells.

The reception celebrated the memory of Seymour Cramer, CPA, CA, who, as Secretary of the Strauss Foundation championed funding for the JGH.

Mr. J. Dennis Bell, Chairman of the Board & CEO of the Strauss Foundation, commented on the satisfaction it derives from supporting and engendering collaboration between researchers within both the McGill University community and other institutions, saying, “It is an honour and a pleasure to see how our funding is supporting such tremendous and impactful research in the area of regenerative medicine.”

Mr. Cramer’s wife, Dr. Jane Gellert, spoke of his dedication to making extremely well-informed decisions about how best to invest on behalf of the Strauss Foundation for the purpose of ensuring that their contributions would have the greatest possible impact.



(Left to right) Dr. Roderick McInnes, Dr. Jane Gellert, Dr. Francois Mercier, Mr. Robert Cowling, President of the Strauss Foundation, and Dr. Vahab Soleimani. Not pictured, Dr. Colin Crist and Mr. J. Dennis Bell.

Two LDI researchers were elected fellows of the Canadian Academy of Health Sciences, one of the highest honours within the Canadian health sciences community:

- **Carmen Loiselle**, an internationally recognized expert in person-centred cancer care, who is Co-Director (Academic) of the Segal Cancer Centre and Scientific Director at Hope & Cope at the JGH. She has received over \$43 million in research funding and has published 140 scientific works. She led a 12-year CIHR-funded research training initiative in psychosocial oncology that provided stipends for promising trainees pursuing transdisciplinary cancer research.
- **Cécile Rousseau**, whose clinical and research career has been dedicated to understanding and preventing the effects of organized violence on children, families and communities. She has developed school-based prevention programs for refugee children. Consulting to governments, she presently implements clinical and prevention programs to address the sensitive issue of violent radicalization

Dr. William Foulkes has been honoured with the 2019 Distinguished Scientist Lecture and Award by the Canadian Society for Clinical Investigation. This distinction is conferred on a clinician or medical scientist – of which, Dr. Foulkes is both - who has made significant contributions to new knowledge and is generally recognized in their field as expert, innovative, and in the forefront of research endeavors. He delivered his lecture at the CSCI Annual Meeting in Banff, Alberta.

Funding for new research to counter drug resistance in cancer

Research designed by **Drs. Gerald Batist and Jian Hui Wu** is one of four projects to win financial support from the LeadAction-Onco competition, supported by Quebec's Ministry of Economy and Innovation and the federal government through IRICoR, as well as Merck and the FRQS through Oncopole.

The major problem in treating metastatic cancer is that tumors eventually become resistant to therapies that were initially effective. Drs. Batist and Wu have identified a sub-population of tumors, those with a Keap1 mutation, that can be re-sensitized to treatment, prolonging the effectiveness of those medications to which the cancer is responsive by delaying the onset of, or reversing, resistance. Keap1 mutations are found in several cancers, and have been identified as a key component in therapeutic resistance.

"We will explore the chemical correction of this mutation to overcome resistance," explains Dr. Batist. "This will change the face of cancer therapeutics in that it is a personalized approach to sensitizing tumors to therapies, putting off the process by which they become resistant, and thereby extending patient survival."

The project will receive \$600,000 over two years. The LeadAction-Onco competition gives Canadian researchers an opportunity to greatly accelerate the transformation of their projects in oncology, for the benefit of patients. IRICoR, based at the Institute for Research in Immunology and Cancer of the Université de Montréal, accelerates the discovery, development, and commercialization of novel therapies. Oncopole was created by the FRQS to serve as a Quebec hub for research, development and investment to advance the fight against cancer.

"The LeadAction-Onco competition is an exceptional opportunity to support creative projects that ensure the development of new treatments for people with cancer. This competition also helps Québec attract foreign investments that generate significant spin-offs for our life sciences industry," said Pierre Fitzgibbon, Minister of Economy and Innovation, in announcing the results of the competition.

[View the video of the drug resistance research project.](#)

Age-old debate in pulmonary medicine resolved

Dr. David Langleben and his colleagues have resolved an important physiological question: how does normal pulmonary circulation absorb large increases in blood flow during exercise with only small increases in pulmonary arterial pressure?

Two competing answers have been proposed. One argued that all pulmonary blood vessels are employed in normal circulation and simply stretch to accommodate added pressure, a process known as distention. The other said that only a portion of available capillary capacity is used during normal activity and that reserve function is recruited when necessary.

Dr. Langleben initiated a clinical trial of ten adults who engaged in varying amounts of physical activity – seven exercised regularly, of whom three had run a marathon or half-marathon in the past three years. Five were ex-smokers. The participants were monitored with a cardiac catheter while pedaling a stationary supine bike following the injection of a protein tracer that allows for measuring functional capillary surface area.

"As flow increased, we clearly saw that previously unused capacity was recruited as blood flow increased," said Dr. Langleben. "Distention occurs only after recruitment has been maximized. It takes far less pressure to recruit than to distend, which is why we don't see pulmonary arterial pressure rising with increased circulation."

From an evolutionary standpoint, this is a far more efficient use of the lungs. Since the human lung contains an estimated 300 million capillaries, with a surface area of 400 square centimetres, it has tremendous reserve capacity while we are at rest, which enables it to adapt to increasing blood flow without being further stressed.

"The make-up of this study was very practical, so we are confident that it is conclusive," said Dr. Langleben. "Furthermore, since our systems generally have redundancies, it makes sense that while in repose we wouldn't be engaging the entire pulmonary circulatory system, but would have plenty in reserve to accommodate activity."

The study results are published in the [American Journal of Physiology – Lung Cellular and Molecular Physiology](#).

It is with deep sorrow that we announce the sudden passing of **Dr. Premysl Ponka**, a distinguished scientist, beloved mentor and colleague, respected teacher, and valued friend. Dr. Ponka was an internationally renowned expert in the field of iron metabolism and had made many unique contributions to understanding the many roles of iron in human health.

He came to McGill in 1979, where he joined the Department of Physiology, becoming a full Professor in 1987. Since 1984, he had conducted his research at the Lady Davis Institute.

[Click here to read his obituary.](#)

Dr. Prem Ponka (right) was awarded the Presidential Prize for Life Achievements by the International Society for the Study of Iron in Biology and Medicine for more than fifty years' contribution to the understanding of iron-sulfur protein biogenesis (the prize was awarded at the 2019 Bioiron Conference, ACT-EMBL Heidelberg, May 2019).



McGill University has re-appointed **Dr. Celia Greenwood** as Program Director of the Quantitative Life Sciences Program, an interfaculty, inter-departmental, and interdisciplinary graduate program in which the latest mathematical, statistical, computational and/or quantitative approaches are used to address the most important and challenging problems in biology, medicine, and the environment.

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Aripiprazole and psychiatric worsening

A study led by **Dr. Christel Renoux**, published in [JAMA Psychiatry](#) has shown that concerns regarding the severe exacerbation of psychiatric symptoms among patients who are given aripiprazole following treatment with other anti-psychotic drugs are largely unfounded.

Reports that aripiprazole was associated with reactions leading to hospitalization, self-harm, or suicide were alarming because, since coming on the market in 2005, it has become a popular treatment option as it induces fewer side effects than first generation anti-psychotics, most notably with respect to weight gain and metabolic adverse events.

“There is always concern when a patient changes medication, and there were anecdotal indications of abrupt and severe worsening with aripiprazole,” said Dr. Renoux. “In those cases, the patients had been on high-dose, long-term treatment before switching. So, we wanted to determine whether serious treatment failure is a significant risk in these instances.”

Dr. Renoux and her post-doctoral trainee, Dr. Francois Montastruc, used a population-based cohort of more than 1600 patients, comparing them with patients who started use of a different anti-psychotic drug.

“We are very cautious in our findings to specify that we did not find an increased risk of hospitalization, self-harm or suicide, which are at the extreme end of clinical worsening,” Dr. Renoux points out. “Our data did not allow us to study less severe clinical worsening that can be managed in an out-patient setting. Also, our data included patients treated by general practitioners, not those who are only followed by a psychiatrist.”

Aripiprazole has a different mechanism of action than other anti-psychotics – though it acts on the same receptor in the brain – and this factor may explain why it sometimes has the paradoxical effect of worsening the patient’s condition following a change in medication.

While these results should reassure physicians who intend to introduce patients to aripiprazole, the authors recommend replication in larger population-based studies. Furthermore, study is warranted to see whether less serious psychiatric episodes may be associated with switching to aripiprazole.

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