LDI Annual Research Awards

The Lady Davis Institute is proud to honour the achievements of its researchers.

Dr. Prem Ponka of the Molecular and Regenerative Medicine Axis received the Award for Excellence in Basic Research. An internationally recognized scientist who has been at the LDI for more than thirty years, the goal of his research is to enhance knowledge about iron metabolism and heme synthesis in erythroid cells, and to examine the pathophysiology behind some diseases caused by defective hemoglobin formation. Recently, his laboratory provided evidence for his novel hypothesis that, in erythroid cells, iron is directly delivered to mitochondria by endosomes in a “kiss and run” paradigm.

Dr. Kristian Filion of the Centre for Clinical Epidemiology was given the Award for Excellence in Clinical Research. A member of the Canadian Network for Observational Drug Effect Studies (CNODES) team, Dr. Filion uses large, population-based databases to study the safety of commonly prescribed medications, with a particular interest in cardiovascular medications and outcomes.

The inaugural Research Leadership Award was shared by Drs. Bluma Brenner and Thibault Mesplède. This honour is intended to recognize their outstanding leadership and significant contributions to the institution, above and beyond their own research program or professional obligations. Specifically, it rewards their exceptional efforts in taking charge in the wake of Dr. Mark Wainberg’s untimely passing and providing stability and continuity during a difficult time.

The LDIs annual research awards acknowledge the high regard in which the winners are held by all members of the Lady Davis community.
9th Annual Scientific Retreat

More than 300 researchers, trainees, and staff attended the 9th annual LDI Scientific Retreat. This year’s keynote speakers were both from McGill University. Dr. Edouardo Franco, James McGill Professor and Chairman of the Department of Oncology, and Director of the Division of Cancer Epidemiology, spoke on new challenges in scholarly publishing. Dr. Russell Jones, Associate Professor in the Department of Physiology, spoke about novel mechanisms of LKB1-mediated tumour suppression.

Stephane Benhamou, (pictured), the IT manager at the LDI, was recognized as Administrative Employee of the Year.

Trainees have the opportunity to present their research during the retreat by giving talks and displaying posters. The prize for best oral presentation was awarded to Nour Ghaddar of the Koromilas lab for “The adaptive trait of the integrated stress response promotes KRAS lung tumorigenesis.”

Recognition for best posters went to:
- Mingyi Lou (Orthwein lab);
- Thomas Funk (Thiel lab);
- Marisa Cressatti (Schipper lab);
- Elizaveta Solomonova (Zelkowitz lab);
- Michael Dahabieh (Miller/Del Ricon lab).

Dr. Thibault Mesplède was the inaugural recipient of an award from the Mark Wainberg Fund of the Canadian Association for HIV Research (CAHR) which supported his participation in the 2018 Conference on Retroviruses and Opportunistic Infections (CROI) in Boston. Dr. Mesplède presented two posters dealing with HIV drug resistance mutations.

CAHR created the Fund to honour Dr. Wainberg and provide financial support to enable researchers to present their work at Canadian and international conferences.

“It is important for us to show the scientific community that the work Mark started is continuing and advancing,” he said. “One of the strengths of the lab has been to select and identify drug resistance in pre-clinical studies. Our intention now is to work more closely with infectious disease clinicians at the Jewish General Hospital to make our work more translational.”

Dr. Mesplède has also been elected to the “Comité de Direction Scientifique du Réseau SIDA/M” of the Fonds de recherche Québec – Santé for the next four years.

Smoking in patients with heart attack reduced with varenicline

Patients who smoke after an acute coronary syndrome, including a heart attack (myocardial infarction) or unstable angina (reduced blood flow to the heart) are at increased risk of another attack and death if they do not quit.

About 40% of participants in a randomized controlled trial who received varenicline were not smoking at one year, compared with 29% in the placebo group. Reductions in daily cigarette smoking of at least 50% were also higher in the varenicline group (57.8%) compared with the placebo group (49.7%). Rates of adverse events were similar in both groups. The trial was led by Dr. Mark Eisenberg and published in the Canadian Medical Association Journal (CMAJ).

The authors note that if varenicline was used as routine treatment in smokers after heart attack, it would reduce smoking in this group by about 10%.

MAY 31 IS WORLD NO TOBACCO DAY
13th annual JGH Department of Psychiatry Research Day: featuring distinguished speakers from the Lady Davis Institute, focused on the theme Connecting Mind and Body: Psychosocial interventions in the context of treating physical disease. Pictured (left to right) are Dr. David Dunkley of the Institute of Community and Family Psychiatry at the JGH, who coordinates the research day; Dr. Melissa Henry, a psychologist with the Louise Granofsky Psychosocial Oncology Program at the Segal Cancer Centre and an Assistant Professor in the Departments of Oncology and Psychology at McGill University, who discussed her research on meaning-making interventions for patients with advanced cancer confronting existential distress; Dr. Carmen Loiselle, Senior Researcher at the Centre for Nursing Research, Co-Director of the Segal Cancer Center and Professor at McGill’s Ingram School of Nursing, who served as the discussant; Dr. Soham Rej, a geriatric psychiatrist at the JGH and Assistant Professor of Psychiatry at McGill University, who presented new clinical evidence on how mind-body treatments such as meditation, yoga, and Tai Chi can help to treat late-life depression and anxiety; Dr. Karl Looper, Chief of the JGH Department of Psychiatry; and Dr. Brett Thombs, Director of the Scleroderma Patient-centred Intervention Network (SPIN) and Professor of Psychiatry at McGill University, who addressed the unique challenges faced by those living with rare diseases and novel approaches for overcoming insufficient knowledge of their condition and lack of therapeutic options.

The conference is supported by a grant from the Gustav Levinschi Foundation.

Two LDI trainees—Matthew Laaper (of the Molecular and Regenerative Medicine Axis) and Michael Dahabieh (Cancer Axis) were finalists in McGill’s 3-Minute Thesis competition. Fourteen grad students were the given the opportunity to present captivating and concise summaries of their research.

Dr. Jackson Mwale has been selected to serve as a member of the National Institutes of Health’s (NIH) Musculoskeletal Tissue Engineering Study Section, Center for Scientific Review for a 6-year term beginning July 1. Dr. Mwale has the distinction of being the only non-American on the panel.

President of the Canadian Orthopedic Research Society, Dr. Mwale is co-organizer of the 2019 Combined Meeting of Orthopaedic Research Societies in Montreal.
New therapeutic pathway explored in melanoma

The acral/mucosal subtype of melanoma – which accounts for between 5% and 40% of all cases of melanoma – is less responsive to standard therapies used against cutaneous melanoma. Noting that this variant of the disease is characterized by a mutation of the KIT gene and elevated levels of the MNK / eIF4E proteins has revealed a previously unexplored pathway holding potential for treatment, according to findings from Dr. Wilson Miller’s lab, published in the Journal of Clinical Investigation.

“When mutated, KIT doesn’t require any additional external signals to spawn malignancy,” explained Dr. Sonia del Rincon, Assistant Professor of Oncology. “We showed that the MNK / eIF4E axis was critical to induce this activity. It facilitates downstream synthesis of proteins that have long been associated with cancer.”

KIT mutant melanomas are particularly prevalent among people of Asian descent. Yao Zhan, who obtained her PhD in the lab, played a crucial role in accessing patient samples through the Beijing University Cancer Hospital. These particular melanomas are not associated with sun exposure and are frequently found on the palms and soles of the feet where they may go unnoticed. It is a very aggressive disease.

To this point, the MNK target has not been fully explored. “We propose that MNK1/2 inhibitors could be effective in a molecularly defined cohort of melanoma patients with KIT aberrations, which currently represents a pressing therapeutic challenge,” write the authors.

An MNK inhibitor has been tested on an animal model with KIT mutations. While it doesn’t destroy the melanoma, it was shown to slow its growth and reduce its invasive and metastatic properties. There are clinical trials underway using MNK inhibitors in combination with immunotherapies on different cancers. This is promising because immunotherapies have produced complications due to their toxicity, while the MNK inhibitors are not toxic.

“We see MNK1/2 as a valuable untapped drug target,” said Dr. del Rincon. “We think this is a promising vulnerability in those cancer cells where it is expressed.”

A potential new strategy for treating thalassemia

Thalassemias are a serious form of red blood cell disorder, in which a genetic mutation causes decreased production of hemoglobin. The resulting destruction of large numbers of faulty red blood cells causes anemia. Among genetic disorders, they rank as a major cause of mortality and morbidity, for which there is no optimal treatment or cure available. Dr. Prem Ponka, who is an international leader in the study of heme synthesis and the formation of red blood cells, together with his coworkers, have published the first investigation of heme oxygenase (HO) as a potential target for thalassemia therapy in Blood.

Since genetic therapy is still years away, Dr. Ponka’s lab concentrates on the therapeutic potential of a specific pathway associated with the manufacture of hemoglobin and the regulation of its production.

“We thought we could take an approach that would address the consequences of malfunction of globin chains on the health of developing red cells in the bone marrow”, Dr. Ponka explains. “We contemplated that molecules of heme (red cell pigment) that are associated with free globin chains in excess, are targets for HO-1.”

Hence, Dr. Ponka’s lab looked at HO-1, the enzyme that destroys heme and releases potentially toxic iron from this pigment in developing red cells. The investigators also considered a possibility that abundant HO-1 in macrophages, a type of white blood cell, could play a role in thalassemia pathogenesis. Red cells, after their 50-day (mice) sojourn in the circulation, are engulfed by macrophages that recycle hemoglobin iron.

Dr. Ponka and coworkers have confirmed their hypotheses by showing that blocking the degradation of heme with an inhibitor of HO-1 reduced toxicity and significantly improved the well-being of red cells in thalassemic mice. Additionally, administration of an HO inhibitor to thalassemic animals decreased the amount of iron available for erythropoiesis, consequently ameliorating ineffective erythropoiesis characterized by the premature death of developing red cells in the marrow.

As Dr. Ponka states, “This double-punch strategy stands out as an alternative and advantageous approach for treatment of thalassemia compared to other current procedures and deserves further investigation”.

This article was featured in “This Week in Blood”, a snapshot of the hottest studies from each week’s issue, hand-picked by Editor-in-Chief of Blood.
Upcoming Grants and Awards Deadlines

- May 20, 2018 — LDI Students Travel Awards (up to $1,000 each award), contact janik.jacmain@ladydavis.ca
- June 22, 2018 — Cancer Quality and Innovation Research Fund, Rossy Cancer Network

Selected Bibliography of Papers from the Lady Davis Institute (March—April 2018):

**CANCER**


**Epidemiology**


Molecular & Regenerative Medicine


Psychosocial


