



Lady Davis Institute

Research Newsletter



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Award for Excellence in Fundamental Research

Dr. Andréa C. LeBlanc is the recipient of the 2012 Award for Excellence in Fundamental Research. For almost two decades, she has been honing in on one particular enzyme, Caspase-6, as a potential root cause for Alzheimer's disease, progressing to where she is now recognized as the foremost researcher on this very promising pathway.

"While others were focusing on amyloid plaques as a cause, I considered the possibility that amyloid was a consequence of the disease, and that Caspase-6, of which we find elevated levels early in the emergence of Alzheimer's disease, was an instigator," she says. "Not many people were listening for a long time, but as the evidence has accumulated, interest is growing in the promise that a therapy that inhibits Caspase-6 may hold promise."

Because Alzheimer's is unique to humans, she believed it was essential to examine human neurons in hunting for a cause (and, eventually, a cure). When she did this, she made the breakthrough of observing high levels of active Caspase-6 in those who had been suffering from cognitive impairment. It has taken a great deal of perseverance for the value of her research to be recognized.

In addition to her work at the Bloomfield Centre for Research on Aging, Dr. LeBlanc is James McGill Professor in McGill's Department of Neurology and Neurosurgery. She was recently appointed to the National Institutes of Health's College of Scientific Review. She has been a *Chercheur boursier* and a *Chercheur national* of the *Fond de recherche du Québec - Santé*.

"Over the next ten years, we expect to be able to accomplish what might otherwise take far longer were it not for the support I have received from donors at the JGH, national and international funding agencies, and pharmaceutical companies. Hopefully, we can ascertain whether inhibiting Caspase-6 will be an efficient therapy against Alzheimer's that much sooner," she said.

Award for Excellence in Psychosocial & Clinical Research

Dr. Laurence J. Kirmayer is the recipient of the 2012 Award for Excellence in Psychosocial and Clinical Research. As James McGill Professor and Director of McGill's Division of Social and Transcultural Psychiatry, editor-in-chief of *Transcultural Psychiatry*, and Director of the Culture and Mental Health Research Unit at the JGH, he oversees the development and application of culturally responsive treatments for diverse cultural communities.

"The fact that we see different problems in specific communities demonstrates that we need to examine an individual's culture and incorporate community resources and traditions in the healing process," he says.

Dr. Kirmayer has done significant work with northern Inuit communities which are plagued by teen suicide rates that far exceed the national average, collaborating with local experts to understand the specific challenges faced by Inuit youth.

The Division of Social and Transcultural Psychiatry develops models to address cultural specificities and runs the Cultural Consultation Service, based at the JGH Institute of Community and Family Psychiatry, which sees patients and provides advice to primary care practitioners and other mental health professionals on how to better understand and help the patient within their family, community, and wider social context.

Among his current research projects is the adaptation of a tool kit to enable Aboriginal communities to develop their own mental health promotion programs for youth and families. This work is going on in fourteen First Nations communities across Canada. As well, he is leading an international multi-disciplinary project in Singapore and Nepal to integrate research methods derived from anthropology and neuroscience to better understand common psychiatric problems and the process of healing.

Dr. Schiffrin President of International Society of Hypertension

Dr. Ernesto Schiffrin, Canada Research Chair and head of the Hemovascular Research Axis, has taken over the presidency of the International Society of Hypertension (ISH). The ISH promotes and encourages the advancement of knowledge in the prevention and management of heart disease and stroke in hypertension.

An internationally recognized expert in the field of hypertension, Dr. Schiffrin is the JGH's Physician-in-Chief, Chief of the Department of Medicine, and Director of the Cardiovascular Prevention Centre. He is also a Professor and Vice-Chair (Research) in McGill University's Department of Medicine.

As President, he is responsible for overseeing ISH operations. One aspect of his new mandate of particular personal interest to Dr. Schiffrin is the focus on transferring knowledge from the developed to the developing world, in order to reduce overall morbidity and mortality.

The ISH is the principal international organization dealing with the world-wide epidemic of hypertension

The two primary goals of the ISH are to support younger members and reach out to as many countries as possible. The organization hosts numerous symposiums to improve the exchange of knowledge between health professionals worldwide. It is responsible for the Young Investors Committee, which brings young medical professionals from the Third World to work in top institutions so that they may learn as much as possible about hypertension before returning to their home countries.

“A principle focus of mine is to help develop guidelines for the diagnosis and treatment of patients residing in low and middle-income countries,” Dr. Schiffrin said. “To beat the worldwide epidemic of hypertension, it is essential that we develop evidence-based guidelines that take into account the availability of resources in the developing world, thus making it possible to improve outcomes for those that have fewer resources on hand.”

Dr. Schiffrin's Tier 1 Canada Research Chair Renewed

Dr. Schiffrin has been successful in having his Tier 1 Canada Research Chair in Hypertension and Vascular Research renewed for the next seven years for a total of \$1.4 million.

Terry Fox Research Institute funds consortium on colorectal cancer

The Terry Fox Research Institute (TFRI) will provide \$1.2 million over the next 18 months to support the creation of the Canadian Colorectal Cancer Consortium (C4), under principal investigators Dr. Gerald Batist, of the LDI and Segal Cancer Centre, and Dr. Steven Gallinger of Mount Sinai Hospital and the University Health Network in Toronto, in an effort to reduce incidence and mortality while increasing survival and improving quality of life for affected patients.

“The role of the C4 will be to bridge forces among clinicians and scientists from 14 leading cancer care and research centres in six provinces to embrace the entire spectrum of colorectal cancer care, leading to state-of-the-art diagnostics and therapeutics,” said Dr. Batist. It is expected that the project will be extended once the initial work is completed.

Colorectal cancer is the second leading cause of cancer death among Canadians, with one in 14 men and one in 15 women likely to develop the disease. The more advanced it is at the time of diagnosis, the greater the risk of metastasis and resistance to treatments.

Dr. Gerald Batist is one of two principal investigators who will lead the research being undertaken by a national consortium on colorectal cancer.

Research will be conducted along two major axes:

- The Screening Axis will lead to the creation of the Canadian High Risk Colorectal Cancer Registry, and associated familial cancer registries, helping in the development of more effective strategies to promote screening and contribute to efforts to discover novel genetic factors causing high risk CRC.
- The Therapeutic Axis will build on existing efforts of the Quebec—Clinical Research Organization in Cancer (Q-CROC) to develop a biobank of metastatic tissue and longitudinal blood samples to validate biomarkers of resistance related to first-line treatment and continue the discovery of new molecular signatures linked to therapeutic resistance.

“This newly created infrastructure will be an invaluable resource in creating a Canadian niche of excellence in CRC research and providing expertise for the necessary turn towards the implementation of personalized health care in Canada,” says Dr. Batist.

Mechanism for termination of immune response discovered

In an [important study published in *Cell Host & Microbe*](#), S. Mehdi Belgnaoui, a post-doctoral research associate working in the lab of Dr. Rongtuan Lin, identified the protein NEMO as a crucial molecular mechanism in the termination of the body's early immune response. It is the culmination of a discovery made five years ago by Dr. Lin that NEMO acts as a modulator in the innate immune response.

Just as the activation of the immune system is critical to defending against viral infections, the production of antiviral molecules such as interferon must cease once the virus has been eliminated. The researchers demonstrated that the enzymatic addition of small linear chains of ubiquitin molecules to the NEMO protein is a signal that interferes with interferon production and contributes to the proper termination of the immune response. This mechanism is significant because an uncontrolled innate immune response is associated with chronic inflammation and autoimmune diseases.

Dr. Belgnaoui was honoured with an FRSQ *Etudiants-chercheurs étoiles* award in health for work highlighted in his *Cell Host & Microbe* paper.

“Without knowing when to shut down, an uncontrolled anti-viral response will become a destructive force,” Dr. Belgnaoui explained. “NEMO acts to control the body's anti-viral activation along the interferon pathway.”

“This finding surprised us, as we had expected NEMO would serve as an activator, not an inhibitor” added Dr. Lin.

While it remains too early to ascertain the clinical implications, Dr. Lin points out that this discovery increases our understanding of the very early events in the cell's immune response against viruses and could lead to the development of an antiviral drug by targeting linear ubiquitination.

“The field of innate immunity is gaining attention,” Dr. Belgnaoui said. “Diseases like lupus and arthritis are linked to the dysregulation of the innate immunity response. Targeting mechanisms that control this pathway may help people with over-activated inflammatory responses.”

Drs. Batist and Pollak honoured with JGH Clinical Day

The 2012 André Aisenstadt Memorial Clinical Day at the Jewish General Hospital was held in honour of two of the LDI's most renowned cancer researchers, Drs. Gerald Batist and Michael Pollak. They join a distinguished list of past honourees, including former LDI Director Dr. Samuel Freedman, hemovascular scientist Dr. Prem Ponka, and head of the hemovascular axis and Physician-in-Chief at the JGH Dr. Ernesto Schiffrin.

Dr. Hartley Stern, CEO of the JGH, said that honouring two cancer researchers who also perform clinical duties “exemplifies the principle of moving information from the bench to the bedside and highlights the critical role that research plays in enabling the hospital to fulfill its mission.”

The theme was “Recent Advances in Cancer Research and Therapy.” Among the presentations, and esteemed presenters, were Dr. Nahum Sonenberg, of McGill's Goodman Cancer Research Centre, on translational control of cancer; Dr. William S. Dalton, Director of the H. Lee Moffitt Cancer Center and Research Institute in Tampa, on bridging research and care in an evidenced-based fashion; and Dr. Morag Park, Scientific Director of Cancer Research at the Canadian Institutes of Health Research, on new paradigms for cancer control.

The honourees both gave talks on their current research interests. Dr. Pollak addressed the issue of hormones, nutrition, and cancer, while Dr. Batist spoke on the evolving prospects for personalized medicine in cancer.

Dr. Richards' research recognized in *Quebec Science*

In selecting fifty scientific challenges to address by the year 2050, [Quebec Science](#) ranked innovative research into the genetic causes of disease at number fifteen, highlighting research on osteoporosis conducted by Dr. Brent Richards.

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Cancer patients in denial make life difficult for family caregivers **Clinical research on coping with new advanced cancer diagnosis**

Denial is a common coping strategy for patients with advanced cancer, who are unable to come to terms with their progressive decline. In a unique study published in *Palliative and Supportive Care*, Naomi Kogan, an oncology social worker at the Segal Cancer Centre, and colleagues examined how denial increases the burden on the family caregivers of those patients.

Her findings reveal that denial prevents patient and caregiver from discussing issues relating to the illness, blocking the latter from providing adequate care. In some cases they were helpless to do anything even when the patient's refusal to follow treatments placed them in life-threatening situations.

"On the one hand, the caregivers felt obliged to support the denial because it can help patients deal with an intolerable situation that they can't change and to preserve a sense of normalcy," Kogan said. "However, it excluded family members from any dialogue about the nature of the patient's condition leaving them feeling very isolated and powerless."

As a result, the caregivers experienced high levels of anger, frustration or anxiety, and guilt, believing they failed to provide adequate support, which placed them at higher risk for physical and emotional problems later on.

"Caregiving is a difficult job, for which the caregiver has received no training or preparation," said Kogan. "Patients are living longer with cancer and spending less time in a hospital setting, meaning that family members are playing a bigger role in caring for loved ones. As a result, they require support from health care professionals, both in dealing with the patient and with their own needs."

It is for professionals to navigate a narrow course between supporting the patient while letting the caregivers know that the problems they are dealing with are common, and helping them to understand that there are often very real limitations to the help they can provide for their patients.

Kogan co-authored the study, titled "The extra burdens patients in denial impose on their family caregivers," with Dr. Robin S. Cohen of the Lady Davis Institute at the Jewish General Hospital and Michelle Dumas of the Ottawa General Hospital.

Drs. Melissa Henry and Robin Cohen, along with colleagues, have [launched a study](#) to evaluate whether individuals newly diagnosed (i.e., within the previous two months) with advanced (stage III or IV) cancer would benefit from discussing their experience with a health care professional.

"Our objective is to help people re-adjust following their diagnosis and to cope with this new reality in their lives," Dr. Henry explains. "Taking in this kind of news often leads people to contemplate why this has happened to them, to re-evaluate the meaning of their lives, and to define what is truly important to them. Some very profound issues can arise. We want to help people come to terms with what they're going through."

Psychosocial interventions in oncology aim to guide people to a better understanding of the impact of the diagnosis and how they react to it.

"Distress and fear often accompany a cancer diagnosis, and anyone treated at the Segal Cancer Centre can obtain psychosocial support. We think our novel approach, designed specifically for people newly diagnosed with cancer, is particularly relevant for those people with advanced cancer," she said.

Her research interests center around enhancing quality of life for those with advanced cancers, and identifying best practices. Her clinical specialty involves working with individuals with head and neck or thyroid cancer, but this study, which is supported by the Canadian Institutes for Health Research Cancer Institute, is designed to include people with any kind of advanced cancer. The intervention in question could be for an initial cancer occurrence, a progression, or a recurrence in advanced stage.

Patients recently diagnosed with advanced cancer are being recruited for a psychosocial clinical study. For more information, contact Cassy Shitong Wang, research coordinator, at 514-340-8222, ext. 8320.