



# Lady Davis Institute Research Newsletter



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## Jonathan Afilalo wins 2012 Royal College Medal Award

Dr. Jonathan Afilalo, a researcher at the Lady Davis Institute and cardiologist at the Jewish General Hospital, has won the prestigious Royal College Medal Award for 2012. He was honoured for his research on gait speed as a predictor of outcomes for elderly patients facing cardiac surgery.

“There are a variety of ways to measure frailty,” Dr. Afilalo explained. “We used walking speed to determine the effect of frailty on how well elderly patients would respond to cardiac surgery. This has important clinical applications because knowing what a patient can tolerate is relevant to prescribing treatment. Before they undergo a very rigorous surgery, we need to be confident that they can withstand the stress.”

His research – for which he has received funding from the *Fonds de recherche de Québec – Santé*, the Heart and Stroke Foundation, and Canadian Institutes for Health Research – seeks an accurate assessment of frailty and to ascertain its impact on how patients are likely to tolerate cardiac procedures.

Dr. Afilalo recently returned to Montreal after completing a two-year fellowship at Harvard University. In addition to his research efforts, he is working with colleagues in cardiology and radiology to build an academic cardiac MRI program that will establish the JGH as a centre of excellence in cardiac imaging.

Winning the Royal College Medal will afford him the opportunity to present his research before the Royal College of Physicians and Surgeons of Canada, as well as to faculties of medicine in Canada as part of the Visiting Medalist Program.

Dr. Afilalo was honoured for his research on gait speed as a measure of frailty to predict outcomes for elderly patients facing cardiac surgery.

## Marc Fabian joins Cancer Research Axis

The recent discovery of small molecules known as microRNAs has given researchers like Dr. Marc Fabian an exciting new avenue to pursue in their quest for innovative cancer treatments.

The hundreds of different microRNAs found in the body have a wide-ranging impact on how protein production is regulated. Under certain circumstances, alterations in these molecules can lead to tumor formation and metastasis.

“There is a great deal of interest in the scientific community about the potential to develop drugs that target cancer cells displaying altered microRNA levels,” said Dr. Fabian, whose newly established lab at the LDI is dedicated to research in this area. “If we can identify microRNA alterations, we may be able to achieve early diagnosis of cancer and clinical intervention before it has a chance to spread out of control.”

The challenges facing researchers are to identify which microRNAs are altered in cancer cells, how these changes contribute to the metamorphosis of a normal cell into a malignancy, and how these cells can be selectively eradicated.

“Once we figure out the roles for different microRNAs, and the cellular pathways that they target, we can use this information to, hopefully, target cancer cells more effectively,” he asserts.

An RNA biochemist, Dr. Fabian spent the last six years completing his post-doctoral work at McGill’s Rosalind and Morris Goodman Cancer Centre. What drew him to the LDI were its first-class research environment and its connection to the JGH.

“Ultimately, what every medical scientist wants is to see their findings from the lab bench applied in the clinic,” he said.

## Changing defense mechanisms improves psychotherapy outcomes

Drs. J. Christopher Perry and Michael Bond, both of the Institute for Community and Family Psychiatry, have completed a study which concludes that defense mechanisms — one of the most durable aspects of personality — ought to be targeted during psychotherapy as an element of treating functionality and symptoms of mental illness.

Defensive behaviours are employed regularly in the course of human interactions — as frequently as once per minute. “They are the building blocks of moment-to-moment personality,” explained Dr. Perry.

“They constitute a psychological process that helps individuals to manage anxiety,” added Dr. Bond. “There are both healthy and less healthy means of employing defense mechanisms.”

Analogous to physical immunological defenses, psychological defenses act as emotional protection. Hence, deficiencies in Psychological defense mechanisms can result in mental illness, as immune deficiencies can bring on physical illness.

Defense mechanisms ought to be considered as a component of psychotherapy when treating the functionality and symptoms of mental illness.

Psychotherapy, and the commitment on the part of the patient to learn about themselves, provides an opportunity to teach appropriate defense mechanisms that help to control anger and impulsive reactions in stressful situations. As a person learns about those elements that act as triggers for them, they can become more comfortable and, therefore, better able to recognize a proclivity to react in a certain way. With practice, they will be able to pause and reconsider their reactions in a more insightful and nuanced light.

The study found a correlation between psychiatric problems and lower defensive functioning. With improved defensive functioning, a patient’s vulnerability to illness decreases. In order for this to be enduring, considerable time and effort is required and the patient must commit themselves to a process for recovery.

[The paper, “Change in Defense Mechanisms During Long-Term Dynamic Psychotherapy and Five-Year Outcome,” is published in the high-impact \*American Journal of Psychiatry\* and is available on-line.](#)

## Elizabeth Jones bridges gap between engineering and medicine

A couple of hundred years ago, a physicians’ study of how blood circulates established some of the fundamentals of principles of fluid dynamics in engineering. Today, the flow has been reversed, with chemical engineers like Dr. Elizabeth Jones applying their discipline to health sciences.

“I began looking at embryonic vascular development during my graduate and post-doctoral work, which brought me from traditional engineering to the medical side,” she explains. After four years in the Canada Research Chair in Embryonic Biomechanics at McGill’s Department of Chemical Engineering, she has joined to the LDI for the opportunity to further her research in a hospital setting.

She seeks to explain the role of physiological signals in the formation of new blood vessels, a process known as angiogenesis. This has important implications in cancer, for example, where tumor growth is fed when new vessels sprout to provide it with a nourishing flow of blood.

One theory suggests that cancer growth could be arrested by starving it of its blood supply.

Similarly, macular degeneration, the most common cause of blindness in the elderly, is caused by an overgrowth of blood vessels. In other cases, such as when a patient has suffered a heart attack or stroke, it would be beneficial to be able to induce new avenues of blood flow into damaged tissue.

“Blood flow is so fundamental to many conditions,” said Dr. Jones. “Ultimately, we would like to prevent or induce the development of new blood vessels at will, depending on the condition being treated.”

Dr. Jones is applying the principles of flow dynamics from chemical engineering to the study of vascular development within the hemovascular axis at the LDI. Applications for her work include cancer and cardiovascular diseases.

## Call for new guidelines in reporting medical research

An international team, led by Dr. Brett Thombs and graduate student Michelle Roseman, warns that a lack of guidelines governing how financial conflicts of interest are reported in systematic reviews of drug studies may leave doctors, patients, and policy-makers without important information necessary for properly evaluating such studies. Their paper, [“Reporting of conflicts of interest from drug trials in Cochrane reviews.”](#) appears in the *British Medical Journal* and is available online.

An analysis of 151 systematic reviews published in the highly respected *Cochrane Database of Systematic Reviews* found that only 20% reported the funding source of all of the drug trials under consideration. Less than 10% reported any information on whether employees of pharmaceutical companies may have authored the reports of drug trials that were reviewed.

Absence of guidelines for reporting financial conflicts of interest may deny readers of systematic reviews of drug studies the information they need to evaluate findings.

“There are no standards, however, that require authors of these reviews to clearly reveal financial conflicts of interests in the drug studies they evaluate,” explained Dr. Thombs. “The goal of a systematic review is to amalgamate the broadest and most comprehensive trial data available. However, the way it is currently done, it becomes very unclear who was funding what.”

The present study confirms the findings of previous research by this team, also led by Thombs and Roseman, which was published last year in the *Journal of the American Medical Association*. That study examined 29 systematic reviews that were published in top medical journals and found that only two mentioned the funding sources of the drug trials they cited.

“Together, these studies highlight the urgent need for reform of guidelines that govern the conduct of systematic reviews,” said Roseman. “Otherwise, critical information may be hidden from people entrusted to make important decisions about our health care.”

## McGill Cardiology Research Day

Three students were recognized for their presentations at McGill’s Cardiology Research Day. Tied for third place in oral presentations were Greg Star of Dr. Langleben’s lab (for “Knockdown of bone morphogenic protein receptor–II by siRNA increases in vitro endothelin-1 synthesis by human pulmonary microvascular endothelial cells”) and Stefania Simeone of Dr. Lehoux’s lab ( for “Shear Stress-induced Atherosclerotic Plaque Regression is Reversed By Matrix Metalloproteinase Inhibition”). Second prize for poster presentations went to Talin Ebrahimian of Dr. Lehoux’s lab (for “Inhibition of Four-and-a-Half Lim domain protein 2 increases survival and migratory capacity of human early outgrowth endothelial progenitor cells through upregulation of sphingosin kinase-1: Implications for endothelial regeneration”).

## CliPP results announced

The results for the first Clinical Research Pilot Project (CliPP), a program to provide operating funds to LDI scientists for pilot clinical research projects, have been announced. The purpose of CliPP is to enable principal investigators to obtain preliminary data that will increase their ability to attract external peer-reviewed funding for clinical research. Three applications were selected following a competitive review:

AZOULAY, Laurent: Creating of a Mother-Child Registry using Large Electronic Medical Databases from the United Kingdom.

EISENBERG, Mark J.: Administration of Fixed Dose versus Weight-Based Dose of Heparin in Patients with ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention.

HUDSON, Marie: Epigenetic signatures of systemic autoimmune rheumatic diseases – A Pilot Study.

The next CliPP competition will be in early 2013.

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## Research launched into optimizing delivery and efficiency of patient care

Funding totalling \$4 million has been granted by the Fonds de recherche du Québec – Santé (FRSQ), the Rossy Foundation, and the LDI to support research into optimizing how the hospital can deliver critical services to its patients in the most effective and efficient manner.

“Health care is a very dynamic profession and it is essential that we evaluate how to enhance our operations while ensuring that patients receive the best care,” explained Dr. Lawrence Rosenberg, Director of the JGH’s Transformational Change Initiative and Chief of Surgical Services, who will lead the project along with Dr. François Béland.

Much of the study will be undertaken at the Segal Cancer Centre.

This research initiative fits within the hospital’s Transformational Change program, which aims to make improvements that will continue to enhance

patient access to timely care and increase workplace efficiency. It will enable the JGH to learn best practices for providing multi-disciplinary health services. The JGH is committed to decreasing waiting times and to improving patient care and safety. This will be achieved by deploying available resources to maximum effect.

“By operating in a more logical and consistent way throughout the hospital, we can cut expenses, keep our budget in line, and reinvest the savings directly into patient care,” said Dr. Hartley Stern, Executive Director of the JGH. “It’s simply not the nature of the JGH to accept the status quo. Whenever something needs improvement—whether in clinical services, administrative operations or any other area—we go ahead and do it. Ultimately, it’s our patients who benefit from these changes.”

“This is important research that cuts to the very heart of how best to deliver health care to patients at a time when treatments are increasingly sophisticated and expensive while resources are limited,” added Dr. Roderick McInnes, Director of the LDI.

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## CIHR Master’s Scholarship

Amanda Lovato, a second year Master’s student working in Dr. Michael Witcher’s lab, has been awarded the Canadian Institute for Health Research’s Frederick Banting and Charles Best Canada Graduate Scholarships for the 2012-13 academic year. Her work seeks to clarify how tumor suppressors are silenced, thereby allowing cancer cells to proliferate uncontrolled. Specifically, she is looking at the over-expression of PARG, which inhibits the work of tumor suppressors, in breast cancer.

“If we can show that PARG blocks tumor suppressors, we may be able to target it with drugs that will prevent its activity and allow for reactivation of suppressors that will control tumor growth,” Lovato explained.

She added, “This scholarship is a great motivator because it validates the promise of my research and reaffirms that we are going in the right direction and have the potential to make a meaningful contribution to treating cancer.”

## Research associate awarded Diamond Jubilee Medal

Dr. Myrna Lashley, a research associate on Dr. Lawrence Kirmayer’s team at the Culture and Mental Health Research Unit has been awarded a Diamond Jubilee Medal for her contributions to Canada. The Medal commemorates the 60th anniversary of Queen Elizabeth II’s accession to the throne.

Dr. Lashley is an Assistant Professor of Psychiatry at McGill. She has played a major role in sensitizing police to cultural issues, serving as Chair of the Cross Cultural Roundtable on Security, as well as Vice-chair of the board of the École Nationale de Police du Québec, as well as the Comité expert en matière de profilage racial of the Service de police de la Ville de Montréal. She has authored two training manuals on intercultural issues in the workplace and has received several awards including the 2006 Friends of Simon Wiesenthal Award for Holocaust Studies; the 2004 Martin Luther King Legacy Award; and the 1995 Merit Award for the Kahnawake Native Survival School. Her current research interests include cultural aspects of youth mental health, and cultural aspects of radicalization leading to violence. She is also Barbados’s Honorary Consul to Montreal.