



Lady Davis Institute

Research Newsletter



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JGH Awards of Excellence

Basic Research—Gerald Batist

Exceptional infrastructure plays a significant role in summoning the critical mass that “is central to everything we’ve accomplished” at the Segal Cancer Centre, according to its director, **Dr. Gerald Batist**.

“Once you reach critical mass, things develop their own momentum,” he insists. “Given the world class facilities we have, really talented people have been attracted to work here. When you get extremely smart people together, great things start to happen.”

A defining feature of the Segal Cancer Centre is the symbiotic relationship between the clinic and the lab, which is a reflection of Dr. Batist’s own identity as a clinician-scientist. “The clinical experience is essential for guiding the questions you ask in the laboratory, and the laboratory experience helps you determine what has relevance for the clinic. Knowledge constantly moves in a bi-directional fashion, where we use lessons from the lab and the clinical environment to inform our research and how we care for patients.”

Dr. Batist is a pioneering proponent of personalized medicine for cancer, wherein the molecular foundations of a tumor are identified and attacked with targeted therapies. By tracking the patient’s disease over time with sophisticated molecular pathology, genetic changes that drive the cancer can be identified and treatment can be adjusted as indicated.

“It’s clear that cancer is heterogenous and, therefore, we need to identify specific mutations,” he explains.

Even as on-going research reveals the great complexity and variety of cancer, he remains optimistic about the progress being made. “I’ve always been optimistic,” he said. “We get positive reinforcement for our research in the clinic where we see patients have remarkable responses to treatment. As a result, I can envision our being able to cure more and more patients.”

Clinical Research—Howard Chertkow

Dr. Howard Chertkow has experienced the great satisfaction of seeing one of his research projects emerge as the international standard in clinical practice. He and his colleagues developed the Montreal Cognitive Assessment (MoCA), the most accurate diagnostic tool to determine whether a patient is suffering from mild cognitive impairment, a condition that often precedes the onset of Alzheimer’s disease.

Memory is at the heart of his clinical research interests. As Director of the JGH/McGill University Memory Clinic, he investigates early diagnosis of Alzheimer’s disease and how those early signs of memory loss may predict its on-set. He collects data in order to understand the structure, organization, and function of long-term memory and its deterioration in dementia.

Among the most renowned Alzheimer’s researchers in Canada, Dr. Chertkow was most recently chosen to serve as Scientific Director for the new Canadian Consortium for Neurodegeneration in Aging (CCNA), established by the Canadian Institutes of Health Research and other partners, to focus the research of twenty teams across the country on delaying and preventing dementia and related illnesses.

“We hope to accelerate our current progress towards new treatments, better understanding of Alzheimer’s and associated diseases, improved quality of life for our patients and their families, and eventually the cures for these conditions,” he asserts. “The CCNA will be transformative, and offers real hope of a better life for those living with Alzheimer’s and other neurodegenerative diseases.”

The influence of Dr. Chertkow’s extensive publications is evidenced by the frequency with which his work is referenced: twelve of his publications have over 100 citations, three have more than 1,000 citations, while the paper which introduced MoCA has been cited more than 2,000 times.

Mark Wainberg to serve on board of National Cancer Institute

Dr. Mark Wainberg has accepted an invitation to serve on the Board of Scientific Counselors of the National Cancer Institute (NCI) at the National Institutes of Health (NIH), the United States' national medical research agency and the largest source of funding for medical research in the world.

The main function of the Board is to provide advice to NCI leadership on the Intramural Research Program, which consists of two divisions – the Center for Cancer Research and the Division of Cancer Epidemiology and Genetics. Board members participate in site visits to institutions seeking funding, and represent a primary factor in determining the research that will be undertaken by the NCI. Given such responsibility, it is among the most important boards of the NIH.

New prostate cancer screening guidelines

[A new Canadian guideline](#) recommends that the prostate-specific antigen (PSA) test should not be used to screen for prostate cancer based on evidence that shows an increased risk of harm and uncertain benefits, according to the Canadian Task Force on Preventive Health Care, and published in *CMAJ*. Drs. **Roland Grad** and **Brett Thombs** are members of the Prostate Cancer Guideline Working Group.

Based on the latest evidence and international best practices, the guideline balances the possible benefits of PSA screening with the potential harm of false positives, over-diagnosis and treatment of prostate cancer.

SAVE THE DATE

FRIDAY JUNE 5, 2015

6th Annual Scientific Retreat

Keynote Speaker: Dr. Peter St. George-Hyslop

Director, Centre for Research in Neurodegenerative Diseases, University of Toronto,
Toronto Western Research Institute
Professor, Experimental Neuroscience, University
of Cambridge

Location: La Plaza, 420 Sherbrooke St. West

Medical physics research optimizes radiation therapy

Medical physicist **Dr. Alasdair Syme** provides essential clinical support to radiation oncology, ensuring that linear accelerators and other radiation machinery is properly calibrated to deliver prescribed dosages to precise tumor sites, maximizing the damage to cancer cells while sparing healthy tissue as much as possible.

Conventional practice is to move the gantry on the linear accelerator around a stationary patient. Dr. Syme, in collaboration with **Dr. Francois DeBlois**, is conducting research on trajectory-based therapy, to determine whether dynamically moving the patient in concert with the gantry will multiply the variety of angles from which to aim the radiation beam at the tumor site. His work will represent a particular improvement in treating deep seated tumors that are difficult to attack, such as metastatic brain or lung tumors. The purpose is to optimize positioning and reduce patient discomfort by decreasing treatment times.

Dr. Syme and his students are analyzing extensive data sets of potential combinations of axes of motion. “We are optimizing the way the algorithm will view combinations of positions, selecting those which are best for the patient, given the location of their cancer. We plot an attack against the tumor site so that the radiation passes through the least healthy tissue in its path.”

He is employing the same motion-capture technology that is used in the video game industry to map patients' positioning and range of motion. Research is in the pre-clinical phase, but the expectation is that it will be employed to capture three dimensional images of each patient to adapt their unique treatment plan.

“We scan the patient as their treatment plan is being developed, then we use this information to rapidly position them exactly as planned at the time of treatment. This will allow for the delivery of high precision radiation therapy with reduced treatment times.”

Since roughly 50% of cancer patients will receive radiation therapy at some point during their care, the work of medical physicists impacts a large population.

Biomarker shows promise for predicting breast cancer outcomes

The protein p66ShcA has exhibited potential to serve as a biomarker that can predict whether or not a breast cancer will have a poor prognosis, according to research directed by **Dr. Josie Ursini-Siegel** and published in [Molecular and Cellular Biology](#).

“We discovered that elevated levels of p66ShcA are strongly associated with expression of numerous epithelial to mesenchymal transition genes in all breast cancer subtypes,” said Dr. Ursini-Siegel, who has a long-standing interest in the role of the ShcA gene in breast cancer.

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Tumor cells lack mature epithelial characteristics, such as the ability to adhere to one another, acting instead like mesenchymal cells, which form loose bonds, move easily into the blood stream and migrate to other organs and tissues, thereby fostering metastasis. This new research reveals that p66ShcA is observable in high quantities in those breast cancers that have undergone an epithelial to mesenchymal transition, and are therefore prone to metastasis and a worse outcome for the patient.

Each subtypes of breast cancers is heterogenous, including those generally associated with good outcomes. Therefore, simple classification alone is not sufficient for prognosis. Within the subset of luminal tumors, which generally have good outcomes, there is no biomarker to indicate likelihood to metastasize. If p66 can be proven to be an accurate biomarker, therapies could be prescribed to patients based on its concentration in the tumor. Similarly, in basal tumors – generally associated with poor outcomes – p66 levels could predict their propensity to behave aggressively.

Dr. Ursini-Siegel became interested in ShcA upon discovering that mammary tumors could be eradicated in transgenic mouse models when the gene was removed from the mammary epithelial cells. In other experiments that modified the function of ShcA, she was able to manipulate a tumor’s blood supply as well as the ability of tumor cells to evade destruction by the immune response. Her work now focuses on discovering the mechanism by which ShcA affects tumorigenesis.

New revelation on how HIV-1 blocks anti-viral response mechanisms

Research led by **Dr. Andrew Mouland** reveals that HIV-1 is capable of resisting stress granules— clusters of RNA and proteins assembled as a protective measure against environmental stresses and viral infections— by blocking the cell’s ability to assemble them to fight off the virus. Moreover, HIV-1 is able to disassemble pre-existing stress granules, which enhances its replicative capacity, further weakening the cell. The finding is published in [Nature Communications](#).

“It is a huge advantage for the virus to be able to prevent the cell from, in effect, summoning reinforcements to help it fight off HIV-1 infection,” he explains. “Using biochemical and genetic analysis, along with advanced microscopy, we uncovered the mechanism by which HIV-1 blocks stress granule assembly,”

Dr. Mouland’s lab examined cells obtained from actual HIV-1-infected patients in order to ascertain that the virus was employing this technique in its arsenal to survive and thrive. The fact that this process has been observed *in vivo* is as strong an indicator as possible that it is important to the biology of the virus.

“We believe that HIV-1 actively elicits these changes to the cell in order to enhance replication,” he said. “Our work proposes to answer the question of how stress granules assemble and how they can be disassembled, two highly significant and elusive questions hanging over our field. Because they are an essential response to so many different stresses on the cell, the knowledge we’re gathering will have relevance for other viral diseases, as well as for neurological conditions including Alzheimer’s, dementia, and amyotrophic lateral sclerosis (Lou Gehrig’s disease).”

As the authors wrote in their paper, “Understanding how HIV-1 counters anti-viral stress responses will lay the groundwork for new therapeutic strategies to bolster host cell immune defences against HIV-1 and other pathogens.”

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Alexander Thiel wins 2014 LDI CliPP Funding Initiative

Dr. Alexander Thiel is the recipient of the LDI's third annual Clinical Research Pilot Project (CliPP) grant, an initiative to provide operating funds to enable investigators to launch clinical research projects. The grant is worth \$25,000. Dr. Thiel's project is "*NON-invasive Repeated Therapeutic Stimulation for Aphasia Recovery In Chronic Patients (NORTHSTAR)*."

Vanier Scholarships for LDI doctoral candidates

Two PhD candidates working in **Dr. Zeev Rosberger's** group in the Psychosocial Axis were awarded CIHR Vanier Canada Scholarships. Samara Perez's project is "The Invisible Son: Understanding the factors that influence parents' HPV vaccine decision-making for their sons." Gilla Shapiro is researching a new technique to measure cancer anxiety and a meditation treatment approach for cancer survivors and their partners.

LDI hosts TanZamBo Workshop on the future of HIV-1 prevention

Drs. **Mark Wainberg, Bluma Brenner, Gerasimos Zaharatos**, and their research teams, along with Dr. Vlad Novitsky of Harvard University, welcomed representatives from clinical and research institutions in Tanzania, Zambia and Botswana (TanZamBo) to the LDI for a three day collaborative workshop that provided research training and technological expertise in the latest advances in phylogenetic surveillance, molecular epidemiology, drug resistance testing and clinical care for HIV-1/AIDS prevention.

The workshop was held as part of a capacity-building exercise to provide expertise in HIV phylogenetics to our African research partners and was chaired by Dr Brenner, a world-class authority on this topic. The workshop was funded through the Global Health Research Initiative (GHRI) of Canada.

Three elected to Canadian Academy of Health Sciences

Three LDI researchers were among 50 new fellows elected to the Canadian Academy of Health Sciences (CAHS) at its annual general meeting in Ottawa in September: Drs. **Francois Béland, Howard Chertkow**, and **William Foulkes**.

Fellows of the CAHS are elected on the basis of their demonstrated leadership, creativity, distinctive competencies, and commitment to advance academic health sciences. Membership is considered one of the highest honours for members of the Canadian health sciences community.

Dr. Béland, Professor at the School of Public Health at the Université de Montréal and Associate Professor in the Department of Geriatrics at McGill, is the co-director of the Solidage—Research Group on Aging and Frailty. He initiated the evaluation of the first home care policy of the government of Quebec. He is a leader on a \$4 million research project funded by the FRQS, Rossy Foundation, and LDI to optimize how critical services are delivered to patients in the most effective and efficient manner. He is a senior editor of *Health-care Policy / Politiques de Santé*.

Dr. Chertkow was just appointed Scientific Director of the Canadian Consortium on Neurodegeneration in Aging (CCNA). He is co-founder and director of the JGH/McGill University Memory Clinic and Director of the Bloomfield Centre for Research in Aging at the LDI. In 2008, he received the Irma Parhad Award from the Canadian Consortium of Centres for Clinical Cognitive Research.

Dr. Foulkes is head of the LDI's Cancer Genetics Laboratory and Director of the Program in Cancer Genetics at McGill. He was the recipient of the 2013 O. Harold Warwick Prize from the Canadian Cancer Society. He was among the leaders of a recent study demonstrating that mutations in the PALB2 gene may be a signature for elevated risk of breast cancer.

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To submit information or for media enquiries, contact: Tod Hoffman at: thoffman@jgh.mcgill.ca; 514-340-8222, ext. 8661.