

Breast cancer study among ASCO Clinical Cancer Advances 2016

Research conducted by a team led by **Dr. Richard Margolese** has been selected by the American Society of Clinical Oncology (ASCO) for inclusion in *Clinical Cancer Advances 2016*, the Society's annual review of progress against cancer and emerging trends in the field. The study, a clinical trial of anastrozole versus tamoxifen in postmenopausal patients with ductal carcinoma in situ (DCIS) undergoing lumpectomy plus radiotherapy, is featured as one of the year's major achievements in clinical cancer research and care. The report is published in [the Journal of Clinical Oncology](#).

The outcomes of the study indicated that anastrozole is a "preferable option for treatment of DCIS" because of its favorable safety profile and demonstration of effect among younger women in the study, Dr. Margolese said. "We now have another option for adjuvant therapy for DCIS. Patients can take tamoxifen or anastrozole, and if they're in the right group, it might be preferable to take anastrozole."

The study randomly assigned 3,104 patients to receive 20 mg per day of tamoxifen plus placebo or 1 mg per day of anastrozole plus placebo for 5 years; all patients received breast radiotherapy. Prior to being randomly assigned, patients were stratified by age, younger or older than 60. The primary endpoint was breast cancer-free interval (BCFI). Dr. Margolese said that there was no difference in BCFI between the two treatment groups until about month 96 of follow-up. At 10 years, 93.5% of women in the anastrozole group and 89.2% in the tamoxifen group remained disease free.

When the data were stratified by age there was a clear benefit for anastrozole among women younger than age 60. The better outcomes were "something we can't explain very well," Dr. Margolese said, and the investigators are still looking for an explanation.

Drugs popular for type 2 diabetes do not increase risk of pancreatic cancer

The use of incretin-based drugs is not associated with an increased risk of pancreatic cancer in patients with type 2 diabetes, according to a study published the [British Medical Journal \(BMJ\)](#). The research was conducted by the [Canadian Network for Observational Drug Effect Studies \(CNODES\)](#), which used the health records of almost 1 million patients with types 2 diabetes.

Incretin-based drugs are widely used in the treatment of type 2 diabetes, but there have been concerns that their use may stimulate pancreatic duct cells in a way that might lead to pancreatic cancer. However this, the largest study conducted to date, found no association between these drugs and pancreatic cancer.

"Our study provides some reassurance that the use of incretin-based drugs is not associated with an increased risk of pancreatic cancer," said the study's first author **Dr. Laurent Azoulay**. "However, because pancreatic cancer develops over many years, it will be necessary to re-assess this association in the future."

To conduct the study, CNODES researchers from across Canada examined health records of patients in Canada, the United States, and the United Kingdom. As is its mandate, the network has the ability to analyze a large amount of anonymous patient data to assess questions of drug safety more reliably than would otherwise be possible in smaller trials or epidemiological studies.



Tracking gait for insight into cognitive impairment

As Senior Investigator at the LDI and in his clinical practice at the JGH, **Dr. Olivier Beauchet** studies the connection between gait disorders, which can result in serious falls, and cognitive decline in elderly patients.

“Falling is a major health risk for older people because of the potential for fracture and it is frequently a precursor to a cascade of deterioration,” explains Dr. Beauchet, who holds the Kaufmann Chair in Geriatric Medicine at McGill. “I am working to develop risk assessment tools for falls and a more objective gait analysis that can measure the association between gait disorder and cognitive decline and Alzheimer disease. Age-related gait disorders are a microcosm for aging. Our clinical objective is to improve early diagnosis of dementia.”

Dr. Beauchet is also studying the means by which older patients can be better served by the health care system. As they develop chronic disorders and more complex co-morbidities, it is essential that such individuals be monitored regularly in order to avoid acute crises.

“Our system has placed more emphasis on treating acute events than managing chronic disease,” said Dr. Beauchet. “As our population ages, we are seeing more of the latter so we must improve how we treat these patients. It is important to understand the risk profile for the patient and adopt a treatment plan accordingly”

Dr. Beauchet was Chair of Internal Medicine, Geriatrics and Biology of Aging at Angers University (France), Chief of the Division of Geriatric Medicine and Director of the Memory Clinic at the Center for Research on



Autonomy and Longevity at Angers University Hospital before coming to the JGH. Having arrived at the top of his profession in France he was seeking new challenges and McGill, and the city of Montreal, provided the ideal academic and living environment in which to pursue his career goals.

Newly identified region for telomerase recruitment to telomeres

In more than 85% of cancers, the survival and uncontrolled replication of cells relies on the activation and recruitment of telomerase to the telomere, the protective structure at the end of the chromosome that serves to prevent abnormal activation of DNA damage repair mechanisms. When functioning normally, progressive telomere loss triggers cell death and prevents carcinogenesis. When over-expressed, telomerase leads to cellular immortality characteristic of cancer.

Dr. Chantal Autexier's paper in [Molecular and Cellular Biology](#) marks the first demonstration that a particular region of telomerase known as the insertion in fingers domain (IFD) has a crucial role in the recruitment of telomerase to telomeres using the protein TPP1. The role of TPP1 is to protect the telomere and modulate telomerase and the process of its localization at the telomere.

“IFD is located on the surface of the protein,” Dr. Autexier explains, “so it is potentially more accessible as a therapeutic target, which might conceivably minimize off-target effects. The secret we need to unlock is how to disrupt those activities of telomerase that can be exploited by cancer without interfering with telomere protection.”

The paper's first author, Tsz Wai (Josephine) Chu, wrote, “Our results provide the first evidence that the IFD can mediate enzyme processivity and telomerase recruitment to telomeres in a TPP1-dependent manner.”

7th Annual LDI Scientific Retreat
FRIDAY JUNE 3, 2016

SUBMIT ABSTRACT by April 15
REGISTER by May 1

Keynote Speakers:

Dr. John Bell, Professor
Ottawa Hospital Research Institute;
Leader of the National Centres of Excellence
in Biotherapeutics for Cancer Treatment

&

Dr. Jay Kaufman, Professor
Epidemiology, Biostatistics and Occupational
Health, McGill University

Location: La Plaza, 420 Sherbrooke St. West

Discovery of mechanism regulating activity of skeletal muscle stem cells

Muscle stem cells are normally in a dormant state, only becoming active when they are needed to perform their reparatory function; for example, in response to injury. Research by **Dr. Colin Crist**, published in [Cell Stem Cell](#), reveals a particular pathway regulating protein synthesis that is required for this dormancy. The same pathway is necessary to maintain the stem cells in a primitive state, which is crucial to having them retain their unique properties as stem cells that can repair muscle tissue and also replicate themselves when called upon to do so.

“There is great interest in stem cell based therapies, but because adult stem cells are a rare cell type, we need to be able to expand them outside the donor tissue,” Dr. Crist says.

“However, when we remove them today, they immediately lose their stem cell properties and regenerative capacity.”

“With pharmacological manipulation of this pathway, we can manipulate the cells *ex vivo* in culture and preserve them in their primitive state, retaining their regenerative capacity to repair muscle and replicate themselves.” This latter function is critical, otherwise damage may be repaired once, but the process will not be repeated, which is essential because muscle must continually be repaired.

“Real progress in stem cell based therapies, especially with the goal to achieve a life-long graft, will certainly require a better understanding of the biology of the stem cell. How do they maintain dormancy? How do these cells replicate themselves when responding to injury? We are working to answer these fundamental questions,” Dr. Crist goes on.



Psychiatry Research Day: Youth at Risk

The theme for the 11th Annual Psychiatry Research Day is *Youth at Risk: New Directions in Promoting Resilience*.

“An estimated 1.2 million Canadian children and youth are affected by mental illness, but less than 20% will receive appropriate treatment,” points out **Dr. David Dunkley**, of the Institute of Community and Family Psychiatry (ICFP) at the JGH, who coordinates the event. “Thus, *Youth at risk* is a crucial topic because promoting mental health and optimal development among young people can be expected to have a positive impact on disease prevention, diagnosis, and care. We need ‘new directions’ to better capture the perspectives of troubled youth and to find innovative solutions for improving the mental health services we offer them.”

Three experts will present different aspects of their research. **Dr. Jaswant Guzder**, Director of Child Psychiatry and the Childhood Disorders Day Hospital at the JGH, will discuss efforts to promote resilience among high risk children in Jamaica. **Dr. Michael Bond**, Director of Youth Service at the ICFP, will address the long-term accuracy of early psychosis diagnoses. **Dr. Catherine Fichten**, of the Behavioural Psychotherapy and Research Unit at the JGH, will discuss the challenges faced by post-secondary students with disabilities.

The discussant is **Dr. Ashok Malla**, Director of the Prevention and Early Intervention Program for Psychoses at the Douglas Mental Health University Institute and leader of the ACCESS Canada project of Transformational Research in Adolescent Mental Health.

[Click here to register.](#)

Department of Psychiatry Research Day
Friday, April 1, 2016, 8:30 AM and 12:30 PM
ICFP Amphitheatre, 4333 chemin de la Côte Ste-Catherine, Montreal.

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

National Bank Molecular Pathology Fellowship

Below, Yann Jodoin, National Bank's Senior Vice President—Client Strategy, Marketing and Branding (left), joins Dr. Lawrence Rosenberg, CEO of West-Central Montreal Health and Dr. Alan Spatz (right) in awarding the 2016 National Bank Molecular Pathology Fellowship to Dr. Andreas Papadakis.

After completing his PhD in the laboratory of Dr. Antonis Koromilas (LDI) in 2011, Dr. Papadakis was a post-doctoral fellow in Dr. Huang's laboratory at the Goodman Cancer Centre. The National Bank Molecular Pathology Fellowship allows Dr. Papadakis to combine the knowledge and expertise that he has developed in the LDI and Goodman towards deciphering the role of the PP2A phosphatase subunit PR70 in controlling DNA replication and RNA translation in different tumor types, including melanoma and breast cancer. The laboratory of Drs Alan Spatz and Leon Van Kempen has identified a tumor suppressor function of PR70 and validated PR70 expression as a strong prognostic biomarker for cutaneous melanoma. A better understanding of the molecular mechanism allows for a rational design of novel therapies. To this end, the laboratories of Drs. Huang, Koromilas, Spatz and Van Kempen will closely collaborate to identify therapeutic targets to promote the tumor suppressive effect of PR70. Dr. Papadakis will use state of the art technologies and infrastructure at the LDI and Goodman Centre to develop a novel therapeutic strategy based upon a strong prognostic biomarker.

Gas6 has potential for thrombosis prevention in cancer

Venous thromboembolism (VTE) is a significant complication experienced by cancer patients. Known as cancer-associated VTE, it complicates both cancer and many of its treatments. VTE is, in fact, the most common cause of death, save for the cancer itself, in this patient population.

It develops in association with cancer because cancer secretes factors that thicken the blood. Moreover, the nature of tumor growth causes injury to blood vessels. Those in more advanced states lack mobility, which is also a general risk factor for blood clots.

Cancer patients are frequently prescribed anticoagulants to treat venous thromboembolism, the most serious risk from which is uncontrolled bleeding. This is an important problem because cancer patients are already susceptible to bleeding from the cancer and the many interventions they are often subjected to. In addition, they often need to take antithrombotic medications over the course of many years. For those reasons, and because anticoagulants can be difficult to administer and complex to monitor, the search for better antithrombotic agents is important. **Dr. Mark Blostein** has been investigating the protein Gas6, which has demonstrated anti-clotting properties without inducing bleeding.

"This advantage of Gas6 distinguishes it from all current anti-thrombotic treatments," he said. In a paper [published in *Blood*](#), his lab identified a mechanism – the expression of prostaglandin E synthase (Ptges) from the endothelium – triggered by Gas6, which promotes venous thrombosis associated with cancer.

Dr. Blostein, who sees many cancer patients in his clinical practice at the JGH where he manages anti-coagulation in thrombosis, said, "Our hope is that therapies directed against Gas6 will prove to be as effective as existing anti-coagulants, but safer, in particular for those who need such medications on a permanent basis."

