

Molecular Oncology Group

Dr. Rod McInnes is delighted to announce that **Dr. Josie Ursini-Siegel** has agreed to become the new head of the Molecular Oncology Group within the Cancer Axis, effective March 1. She succeeds **Dr. Stephane Richard**. Josie is an Associate Professor in the Department of Oncology and an Associate Member in the Department of Biochemistry at McGill. She received her MSc and PhD from McMaster University, followed by post-doctoral training with Selina Chen-Kiang at Cornell and William Muller at McGill. Josie's research aims to elucidate the mechanisms by which tyrosine kinases promote breast cancer, both by influencing tumor cell intrinsic processes and by facilitating cross-talk with the stromal microenvironment. She has been an outstanding citizen of the LDI, chairing the Organizing Committee of the Annual Retreat since its inception in 2010, and being an active participant as an LDI Internal Grant Reviewer (90 in total). More recently, Josie led a committee to examine the LDI Internal Grant Review process. She is also an active contributor within the broader scientific community and has reviewed for numerous granting agencies, including CIHR, CCSRI, CRS, Alberta Cancer Foundation, NSERC and Susan G. Komen Foundation. As head of Molecular Oncology, Josie intends to foster a culture of research excellence, collaboration and collegiality, and to increase funding success rates (particularly of multi-PI grants) and the number of papers in leading journals.

The LDI is profoundly grateful to Dr. Richard for his excellent leadership of the Molecular Oncology Group over the past eight years. He has made great contributions to the culture of research excellence at the LDI, both by example and by mentoring young faculty.

A James McGill Professor, Associate Director of the LDI and an internationally respected molecular oncologist, Stephane has made pioneering discoveries on RNA binding proteins and arginine methylation, and their links to diseases including ALS, obesity, myelin-disorders, muscle-disorders and cancer. The LDI is proud to have Stephane as one of its leading scientists, a model researcher.



Molecular & Regenerative Medicine

Effective April 2016, **Dr. Koren Mann** was selected as the inaugural head of the new Molecular and Regenerative Medicine (MRM) Axis, a fusion of the HIV/AIDS, Aging, and Hemovascular axes, as well as the four LDI stem cell researchers, which recognizes the commonality of all molecular disease research. The overall focus of the axis is to elucidate the mechanisms that underlie diseases other than cancer, and to develop treatments for them.

Koren is an Associate Professor in the Department of Oncology at McGill. She received her Ph.D. from Boston University in Pathology/Immunology, where she studied environmental immunotoxicology, followed by a post-doc with Dr. Wilson Miller here at the LDI. Her major research goal is to understand the mechanisms of metal toxicology, specifically arsenic and tungsten, an area in which she is a world authority. She is also a member of the Lymphoma Translational Research group, investigating molecular changes in relapsed/refractor diffuse large B cell lymphoma and its treatment. Koren is the Director of the LDI Flow Cytometry Core and was previously the organizer of the weekly PI Meetings. She is an active contributor to both the LDI and the broader research community, and has been a grant panelist at CIHR, the Cancer Research Society, and the Leukemia Lymphoma Society of Canada. In 2015, Koren was made a member of the US National Academy of Sciences panel on Arsenic Risk Assessment. Her initial goals for the MRM Axis are to enhance the research of its members by facilitating research interactions and collaborations between them, and to create an outstanding environment for the training of students and postdocs.

The LDI is greatly indebted to the outstanding leadership of the three former leaders of the axes that now comprise the MRM axis: **Dr. Mark Wainberg** (HIV/AIDS), **Dr. Ernesto Schiffrin** (Hemovascular) and **Dr. Howard Chertkow** (Aging). They led the three axes for a combined 50 years, a remarkable contribution. Reviewing all their accomplishments would take many newsletters, but suffice it to say that they have built a major part of the LDI's worldwide reputation, and continue to be national and international leaders in their fields.

Dr. Mark Wainberg was presented with the Gertrude Elion Distinguished Lecturer Award at the HIV DART & Emerging Viruses conference in Mexico. The award recognizes his invaluable contributions to HIV research. Pictured from left to right are Dr. Raymond Schinazi, Dr. Wainberg, Dr. Charles Boucher, Dr. Rowena Johnston, and Dr. Hiroaki Mitsuya.



Dr. Brent Richards has been elected to the American Society for Clinical Investigation (ASCI), which includes some of the world's leaders in academic medicine and industry who are committed to mentoring future generations of physician-scientists. Members must be 50 years of age or younger at the time of their election, thus reflecting relatively early-career accomplishment.

Dr. Susan Kahn has been appointed an associate editor for the journal, *Research and Practice in Thrombosis and Haemostasis*, of the International Society on Thrombosis and Haemostasis (ISTH).

Dr. Colin Crist has been reappointed Marjorie & Gerald Bronfman McGill University Chair in Stem Cell Research.

Dr. Laurence Kirmayer will lead a three year project to develop online mental health resources focused on the needs of multicultural communities. The initiative, to be run from McGill's Montreal Neurological Institute and Hospital, is being funded by a \$250,000 donation from Bell Let's Talk. "Mental health is often viewed differently in different cultures, which requires culturally sensitive approaches to reach out to those seeking help," said Dr. Kirmayer. "With this generous gift from Bell Let's Talk, we will draw on our extensive research to support diverse communities and strengthen and develop our online platform, to better reach those in need and make this resource truly national."

HPV Vaccine Awareness

The vaccine to prevent human papillomavirus (HPV) is proven safe and effective. Eliminating the spread of HPV, the most common sexually transmitted infection, is an important public health issue because of its association with cervical, anal, vaginal, penile, vulvar, and oropharyngeal cancers, and genital warts. **Dr. Zeev Rosberger** and his team published a study in *BMC Public Health* about how parents decide whether to vaccinate sons. It was the most read publication from the LDI the week it appeared online, according to ResearchGate.

"The bottom line is that nobody should suffer from an HPV-related cancer," Dr. Rosberger insists. "By including boys and girls in vaccination programs we can ensure the most comprehensive protection for everyone. To achieve this, we need to make sure that parents are well informed of the consequences of not vaccinating and that the provinces make the vaccine available to boys, as well as girls."

The decision to vaccinate against HPV is "a complex process that is influenced by multiple psychosocial determinants," wrote the authors. However, lack of HPV awareness seems to be the most crucial factor. This is particularly so among parents of sons, as those with daughters are generally better informed of the risk. Another factor is that only very recently have six provinces offered free vaccination for boys (all provinces have had programs for girls since 2007).

It isn't sufficient to inform parents. Health care providers, who are the preferred source of information for most parents, need to be proactive in broaching the issue.

Dr. Rosberger expresses frustration with the persistent influence of anti-vaccination advocates, "When a parent chooses not to vaccinate their child, it means greater risk for everyone. As a society, we need to achieve 70-80% vaccination of the population for successful immunization."

Association between certain antidepressants and intracranial bleeding

The most common antidepressant medications are among a class of drugs known as selective serotonin reuptake inhibitors (SSRI). Though very effective and generally well tolerated, these drugs are known to cause gastrointestinal bleeding. A new study conducted by **Dr. Christel Renoux** shows them to increase the risk for spontaneous intracranial hemorrhage (ICH), a rare but potentially serious side effect. The results of her population-based cohort study are [published in JAMA Neurology](#).

“Antidepressants that are strong inhibitors of serotonin reuptake increase the risk of ICH, particularly within the first thirty days of use,” said Dr. Renoux. “Because serotonin reuptake inhibition is not a feature of their effectiveness in treating depression, this factor should be considered by clinicians when deciding which of these medications to prescribe. Furthermore, we believe it makes sense to classify antidepressants according to the strength of their serotonin reuptake inhibition.”

The potential for bleeding is directly associated with the strength of serotonin reuptake inhibition of the SSRI, and antidepressants can be distinguished according to their degree of serotonin reuptake inhibition, something the authors did in their paper. With strong inhibitors, the risk for ICH increased by 25%. ICH can be very serious, as the buildup of blood within the skull can put pressure on, or reduce blood supply to, the brain and can cause stroke.

ICH had not shown up in previous studies due to the rarity of the effect and because they involved small samples. Dr. Renoux studied data from almost 1.4 million patients who began taking antidepressants between 1995 and 2014, from the United Kingdom’s Clinical Practice Research Datalink. Among these were more than 3,000 cases of ICH.



8th Annual LDI Scientific Retreat

FRIDAY May 12, 2017

SUBMIT ABSTRACT by April 3

REGISTER by April 30

Keynote Speakers:

**Dr. Peter Zandstra, University Professor
Biomaterials & Biomedical Engineering
Canada Research Chair, Stem Cell
Bioengineering, University of Toronto**

&

**Dr. Jill Baumgartner, Assistant Professor
Epidemiology, Biostatistics and Occupational
Health, McGill University**

Location: La Plaza, 420 Sherbrooke St. West

12th Annual Psychiatry Research Day

The theme for Psychiatry Research Day is “*There should be an App for That: The Promise of Technology for Mental Health.*” As more and more people search for health information online, there are now thousands of health-related mobile applications available. Researchers at the JGH are embracing this trend, while carefully evaluating how the technology can benefit patients.

“New technology brings the promise of making services more accessible to patients, empowering patients to play a more active role in their own care in partnership with health care professionals, and enhancing personalized care through assessments of a patient’s daily life experiences,” said Dr. David Dunkley, who coordinates the event.

When: Friday, March 10, 8:30 am to 12:30 pm

Where: ICFP Amphitheatre, 4333 Côte Ste-Catherine

[The program and registration is available on-line.](#)

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To submit information or for media enquiries, contact:
Tod Hoffman at: thoffman@jgh.mcgill.ca;
514-340-8222, ext. 28661

Spotlight on Fellows

Alicia Bolt – Molecular & Regenerative Medicine Axis

After researching arsenic for her PhD in environmental toxicology at the University of Arizona, Alicia Bolt decided to study tungsten at the Lady Davis Institute with Dr. Koren Mann.

“Tungsten is an emerging toxicant about which little was known,” said the final year post-doctoral fellow. “Since tungsten alters immune cells and accumulates in bone, one of the primary places where immune cells and their progenitors reside, we believe it can have broad health implications.”

She is looking at how tungsten affects bone biology and its impact on B-cell development, given that high levels of tungsten were discovered in drinking water near three pediatric leukemia clusters in the United States. She also participated in a study of a cohort of women exposed to an interoperative shield made of tungsten that was supposed to protect them against the impact of radiation therapy for breast cancer. However, the shield broke down inside the patients and tungsten could be detected in the blood and urine even years following the treatment. She launched an animal study to look at the effects of tungsten on breast cancer tumor progression and found that tungsten significantly enhanced breast cancer metastasis to the lung.

“Our work is aimed at identifying the ramifications of exposure to tungsten in humans,” Dr. Bolt explained.

One of the advantages of the LDI that she notes is the translational aspect of the research. “The diversity of the LDI is a huge strength,” she says. “It gives me the opportunity to learn about cancer, aging, and stem cells all at the same time. The overlap between clinical and fundamental research has given me a much better understanding of how our research impacts patients. Looking at a toxicant that impacts bone, for example, I can find people here who know a great deal about bone biology, which gives me a broader outlook on the mechanisms at work.”

This spring, Dr. Bolt will be taking up a position at College of Pharmacy at the University of New Mexico.



Notable advance in explaining gender disparity in melanoma prognosis

Though it has been shown that men who get melanoma are twice as likely to die from the disease as women, the biological explanation for this is poorly understood. Research led by **Dr. Alan Spatz**, Director of Surgical and Molecular Pathology at the Jewish General Hospital and head of the “X chromosome and cancer” lab at the Lady Davis Institute, reveals that the decreased expression of the X chromosome gene PPP2R3B and its protein PR70 are positively linked to tumor progression in this aggressive form of skin cancer. The finding is published in [Science Translational Medicine](#).

“We focused on the machinery of the X chromosome because we postulated that the inactivation of one of the two X chromosomes in women, as opposed to men who have an X and a Y, and the way this mechanism is regulated, may have deep implications on the cell biology of cancer cells” explains Dr. Spatz. “We believe that the genetic specificity of the X chromosome plays a significant function in the gender difference we observe in melanoma. We see unique regulation of tumor suppressor genes and oncogenes in the X chromosome.”

Dr. Spatz and Dr. Leon van Kempen, COO and Scientific Director of the Molecular Pathology Center, have extensively studied the gene PPP2R3B, which is located on the X chromosome in females, but on the Y in males. The expression of this gene has been independently correlated with more favourable progression in melanoma and is important because its expression is higher in females. PPP2R3B codes for the PR70 protein, which decreases melanoma growth by negatively interfering with DNA cell replication and, therefore, acting as an X-linked tumor suppressor. PR70 is at the forefront of controlling the cell replication cascade. From a clinical perspective, this research suggests there could be potential anti-cancer therapies in actioning the proteins linked to PR70.

“I believe this discovery advances our understanding of the specific role of the X chromosome genetics in modulating the expression of genes that are critical in cancer progression,” Dr. Spatz said. “Specifically, this is a new avenue for exploring X-linked tumor suppressor genes and oncogenes. I’m confident that we will eventually be able to exploit this discovery to pursue new therapeutic avenues against cancer.”