

LDI Annual Research Awards

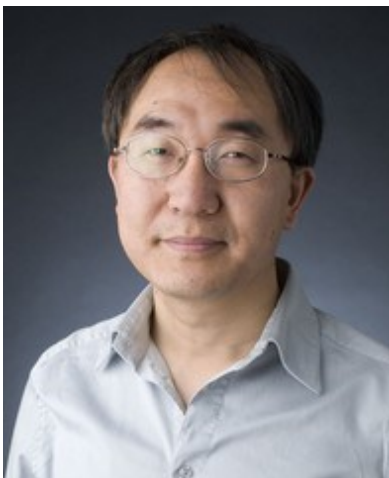
The Lady Davis Institute's annual research awards acknowledge the high regard in which the winners are held by all members of the LDI community.

Dr. **Chen Liang** of the Molecular and Regenerative Medicine (MRM) Axis received the Award for Excellence in Basic Research. Dr. Liang's research is dedicated to discovering the cellular mechanisms that restrict HIV-1, with the ultimate goal of contributing to the development of novel approaches to curing the infection. He also serves as Acting Director of the McGill AIDS Centre and Associate Director for Faculty at the LDI.

Dr. **Susan Kahn**, of the Epidemiology Axis, was honoured with the Award for Excellence in Clinical Research. Dr. Kahn is the founder and director of the JGH's brand new Centre of Excellence in Thrombosis and Anticoagulation Care (CETAC), a state-of-the-art facility that serves as a hub for research, clinical care, and training for thrombosis and its associated complications.



Award for Excellence in Clinical Research: **Dr. Susan Kahn**



Award for Excellence in Basic Research: **Dr. Chen Liang**



Research Leadership Award:
Dr Koren Mann

The recipient of the Research Leadership Award was **Dr. Koren Mann**. This honour is intended to recognize outstanding leadership and significant contributions to the institution, above and beyond her own research program. Dr. Mann was cited for her exceptional efforts as the inaugural head of the MRM Axis and for

fostering new collaborations within the institute.

Two PhD candidates were acknowledged for Trainee Paper of the Year: **Brooke Levis**, of Dr. Brett Thombs's group, for "Accuracy of Patient Health Questionnaire-9 (PHQ-9) for screening to detect major depression: individual participant data meta-analysis," [British Medical Journal](#), 2019; and **Qianyu Guo**, of Drs. Sonia Del Rincon and Wilson Miller's labs, for "MNK1/NODAL Signaling Promotes Invasive Progression of Breast Ductal Carcinoma In Situ," [Cancer Research](#), 2019.

Tod Hoffman, the LDI's Research Communication Officer was recognized as Administrative Employee of the Year.

The awards were presented during the 10th Annual LDI Scientific Retreat

Genetic marker offers promise in targeting ovarian and lung cancers

Dr. William Foulkes, with collaborators at the Goodman Cancer Research Centre at McGill University, has shown that a drug currently in use against estrogen positive breast cancer may be effective in treating [small cell carcinoma of the ovary, hypercalcemic type \(SCCOHT\)](#) and [non-small cell lung cancer \(NSCLC\)](#). The results are published simultaneously in two papers in *Nature Communications*.

The breakthrough that launched this research came in 2014 when Dr. Foulkes showed that SCCOHT, a rare but highly fatal cancer which primarily strikes younger women, is caused by mutations in the gene SMARCA4.

The challenge became how to knock out this gene in order to inhibit progression of the tumor. Subsequent work by Dr. Sidong Huang at McGill, identified that targeting the cyclin-dependent kinase 4/6 (CDK4/6) exposed a vulnerability in SMARCA4. "What's clinically exciting about this work is that CDK4/6 inhibitors have been used for years, so they are very well known and their safety profile is established," said Dr. Foulkes.

In the case of SCCOHT, in particular, it is encouraging to find an existing drug that may prove effective because this is such a rare cancer that it is unlikely to be the subject of dedicated drug development. NSCLC is more common and exhibits SMARCA4 mutations, as well. Evidence has been obtained both *in vitro* on human tumor tissue, and *in vivo* on animal models that CDK inhibitors are effective at quelling SMARCA4-induced tumors.

"The fact the drug worked so well was a bit surprising," Dr. Foulkes went on. "Perhaps it works because the protein which is targeted is at critically low levels in the tumor – just enough to keep the tumor alive, but still susceptible to blocking."

The precise mechanism by which these particular inhibitors work in the different cancers is yet to be definitively determined. But, said Dr. Foulkes, this is an academic question; so long as the drugs proves effective, the clinical impact is undeniable.

"The dream would be to cure these cancers, but any hint of a response would be a positive step forward because current treatment for women stricken with SCCOHT have limited effectiveness," he concludes.

Journals fail to enforce reporting standards on clinical trials

Research into health care interventions that are not directly regulated by government agencies - including surgery, rehabilitation, psychological treatments, nursing, and nutrition and diets - is most often published without public registration of any pre-defined primary outcomes. Without this important step, researchers can be selective about the data they report. In many cases, this leads to publication of misleading results about the effectiveness of interventions, but does not accurately reflect what really occurred in a trial.

"There is a long history, unfortunately, of investigators not reporting trial results at all or of reporting skewed versions of what actually happened in a trial," explains **Dr. Brett Thombs**, who led the study, published in [JAMA Internal Medicine](#). "Cherry picking results can distort our understanding of whether or not an intervention benefits patients. Imagine a trial that measures ten outcomes and finds only one positive result out of the ten. If the researcher were compelled to reveal all ten findings, the intervention would be considered a failure. However, if that researcher publishes only the positive finding, it would be deemed a success and probably provided to patients."

His team examined 953 trials of non-regulated interventions published in 254 journals from the areas of surgery, rehabilitation, psychology, nursing, and nutrition. They did not identify any journals that consistently enforced pre-trial registration standards and reported that only 20% of the trials they reviewed had been registered before they were initiated. They found that only 11% of the 254 specialty journals whose contents they reviewed had a stated policy requiring pre-trial registration. However, only 34% of trials appearing in those journals were registered prospectively, compared to 18% in journals with no policy. Most remarkably, only 4% of the 953 trials they reviewed published primary outcomes that could be traced back and were consistent with a pre-trial registration.

"Without transparency there is no way to know which trials accurately represent what would really occur if a treatment is applied," insists Dr. Thombs. "As researchers, we owe it to the public to make sure that they have access to well-conducted, honestly reported science that allows them to make the best possible decisions about their healthcare. We are falling far short of this goal."

14th annual JGH

Psychiatry Research Day:

focused on diagnosis and treatment of the particular mental health problems faced by immigrant populations. How well society responds to new immigrants goes a long way to determining how successfully they will integrate and adapt to their new country.

Pictured (left to right) are **Dr. Eric Jarvis**, Director of the Cultural Consultation Service and the First Episode Psychosis Program at the JGH; Director of Research and the LDI's Psychosocial Research Axis, **Dr. Phyllis Zekowitz**; **Dr. Cecile Rousseau**, an expert in the impact of migration policies; **Dr. Laurence Kirmayer**, Director of the Culture and Mental Health Research Unit at the JGH and of the Division of Social and Transcultural Psychiatry at McGill University; **Dr. Jaswant Guzder**, the recently retired Chief of Child Psychiatry at the JGH; and **Dr. David Dunkley** of the Institute of Community and Family Psychiatry at the JGH, who coordinates the research day.

"We are witnessing a 'compassion inversion,'" Dr. Rousseau explained, "whereas the refugee used to be accepted as the vulnerable party, now the host society is being defined as vulnerable. As a result, the trauma that a refugee experiences does not end with gaining asylum."

Dr. Kirmayer said, "Being stateless is profoundly unsettling. Helplessness is a predisposition for refugee acceptance, yet it is the infusion of capacity and agency that are necessary for resilience, so there is a profound paradox there."

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10th Annual LDI Scientific Retreat

The 10th LDI Scientific Retreat featured keynote presentations by Dr. Brian Drucker, Director of the Knight Cancer Institute at eh Oregon Health & Science University, and Dr. Nada Jabado, Professor of Pediatrics and Human Genetics at McGill University and the MUHC Research Institute.

LDI trainees had the opportunity to present their research. Honours for the best oral presentation went to:

- **Samantha Worme** (Mercier/Kleinman lab) for "Single-cell transcriptomics identifies a maturation continuum in acute myeloid leukemia"; and
- **John Heath** (Orthwein lab) for "Emerging roles of ZNF280E in the maintenance of genome stability."

Best poster recognition went to:

- Brandon Shokoples (Schiffrin lab); and
- Selin Jessa (Kleinman lab)

Doctoral candidate **Georgia Mitsa** of Dr. Christoph Borchers' proteomics lab received two awards from McGill University:

- the **Dr. Gerald B. Price Memorial Travel Award** from the Department of Experimental Medicine; and the
- **Grad Excellence Award in Experimental Medicine**

International initiative to improve dementia diagnosis and care

Drs. Isabelle Vedel and **Howard Bergman** are the Canadian leads on an international research effort to design dementia diagnosis and post-diagnostic care toolkits for use in primary care. The three-year project will receive more than \$2.3 million from the Canadian Institutes of Health Research (CIHR), the Public Health Agency of Canada, and the European Union's Joint Programme – Neurodegenerative Disease Research (JPND). They will collaborate with researchers in Canada, Australia, Poland, the Netherlands and United Kingdom to produce material that can be implemented cross-culturally.

"Our objective is to empower primary care physicians to diagnose dementia and work with family caregivers to design a care plan without necessitating arduous and time consuming visits with specialists or, worse still, waiting until a situation has deteriorated to where a visit to emergency is required," said Dr. Vedel, a public health physician and researcher.

When properly trained, family physicians can play a very positive role in assessing a patient for dementia and developing a plan with the participation of patient and caregivers, upon whom so much of maintaining normal daily life will depend.

"Generally, people can sense when they are experiencing cognitive problems, or when a loved one is behaving abnormally, and they feel better when a family doctor is able to provide a diagnosis, explain what is happening to them, and work toward a plan that will maximize their quality of life," Dr. Vedel explains. "We have seen very good results with early diagnosis from primary care doctors who have been trained to recognize the symptoms of Alzheimer disease. And patients show a preference for working with a doctor with whom they are familiar, rather than needing to consult with specialists."

The toolkits that will emerge from this research will offer guidelines for diagnosis and suggest best practices for post-diagnostic care.

In announcing the funding, Minister of Health Ginette Petitpas Taylor said, "This research will help make life easier for people with dementia and their family caregivers by giving them tools to make important decisions and guiding them to resources and support services."

Obesity, not age at puberty, linked with risk of multiple sclerosis

Previous studies have suggested that people who begin puberty at an earlier age have an elevated risk of suffering from multiple sclerosis (MS). However, new research conducted by Drs. **Brent Richards** and **Adil Harroud** found that the link between early puberty and MS is mainly attributable to obesity. The study is published in [Neurology](#).

"It appears that earlier puberty is associated with an increased risk of MS, but this association is influenced by obesity. Our findings do not support a substantial role for the effect of the timing of puberty on the risk of MS independent of obesity," explained Dr. Harroud.

For this study, researchers looked at a genome-wide association study of 329,245 women and 372 genetic variants that are strongly associated with the age when girls have their first menstrual cycle. Previous studies have shown that the genes related to the timing of puberty are well-correlated in girls and boys. Then researchers looked at another genetic study that included 14,802 people with MS and compared them to 26,703 people who did not have the disease to examine whether the age of puberty was associated with risk of MS. Dr. Harroud said they did find that people with an earlier age of puberty were more likely to develop MS, but once they factored in obesity, the effects of earlier puberty importantly decreased.

Canada has one of the highest rates of MS in the world, with one in 385 Canadians affected, according to the MS Society of Canada. What is more, previous studies have indicated that MS rates may be on the rise. "Our results suggest that the current obesity epidemic might explain in part why more people are being diagnosed with MS," he said.

"The findings are important because obesity is something that people can modify," said Dr. Richards. "This means that decreasing rates of obesity could help to reduce the prevalence of MS. Also, most of the complications linked to obesity, like heart disease, tend to manifest only late in life, but MS is a condition that often starts when people are in their 20s and 30s. This can provide more urgency for younger individuals to control their weight."

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