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Award for Excellence in Clinical Research

Dr. Alexander Thiel is the winner of this year's Award for Excellence in Clinical Research. He is Director of the Neuroplasticity Research Program at the LDI and of the Comprehensive Stroke Centre at the JGH. This combination of an acute stroke unit with a non-invasive brain stimulation and imaging laboratory is the first of its kind in Canada, constituting a research facility at the patient's bedside. His specialty is translational research on post-stroke recovery.

Dr. Thiel's lab is the lead study centre for the international (Canada-Germany) NOn-invasive Repeated THerapeutic STimulation for Aphasia Recovery (NORTHSTAR) brain stimulation trial. Its goal is to determine whether repetitive transcranial magnetic stimulation or transcranial direct current stimulation, provided in combination with speech and language therapy will improve the capacity for stroke patients to recover their language expression and comprehension skills. In particular, his research seeks to refine the use of TMS to optimize how the brain selects recuperative pathways to regain lost functionality in the days immediately following a stroke. Thus far, the results of Dr. Thiel's work have been promising. About half of the patients have showed improvement with TMS, and it has caused no significant adverse effects.

His is also the lead centre in a National Health Institutes funded study on neuroinflammation, being conducted with the University of Florida.

His clinical research will be strengthened by the creation of a clinical trials platform on the new integrated neuroscience unit opening at the JGH in December, which will facilitate the systematic evaluation of different stimulation modalities and imaging methods in a clinical context.

Award for Excellence in Basic Research

Dr. William Foulkes is this year's winner of the Award for Excellence in Basic Research. As head of the Cancer Genetics Laboratory at the LDI and Director of the Program in Cancer Genetics at McGill University, he is working toward a deeper understanding of the hereditary components of cancer and of those genes which predispose individuals to developing cancer.

His objective is to uncover the fundamental genetic alterations responsible for the initiation and progression of tumors, as well as those that influence their responses to therapy. In the past year, he has published in each of the following journals - *Nature Genetics*, *NEJM*, *Acta Neuropathologica* and the *Journal of Pathology*.

He is currently:

- Working with Marc Fabian (LDI) to create a model for the DICER1 syndrome, a rare mutation associated with a variety of pediatric cancers, that faithfully represents and reproduces the diseases seen in humans. He intends to build on extensive clinicopathological characterization of DICER1-associated tumors and related conditions.

- Developing new therapeutic strategies for the treatment of the rare small cell carcinoma of the ovary, hypercalcemic type (SCCOHT). To this end, he is working with Michael Witcher (LDI) and Jacek Majewski (McGill) to gain a deeper understanding of the epigenetic changes that underlie SCCOHT. He is collaborating with Sid Huang (McGill, Biochemistry) in the use of synthetic lethal approaches to identify new targets, which he will validate using his lab's very large collection of SCCOHT tumors.

- Identifying, characterizing, and further studying novel cancer susceptibility genes, using tools such as exome sequencing. Dr. Foulkes has been collecting DNA from unique or rare forms of familial cancer for 20 years. He intends to continue using up-to-date discovery tools to identifying the underlying mendelian mutations that are associated with these familial manifestations of cancer.

6th Annual LDI Scientific Retreat

More than 300 researchers, associates, and trainees gathered for the 6th annual LDI Scientific Retreat on June 5 at La Plaza in downtown Montreal. Keynote addresses were given by **Dr. Peter St. George-Hyslop**, of the Universities of Toronto and Cambridge, on the unique discovery of a genetic cause for Alheimer disease in an Eastern European family, and **Dr. Madhukar Pai**, Director of McGill's Global Health Programs, on the difficult process of bringing lab bench discoveries to the populations who need them most.

The technicians of the animal facility were collectively honoured as LDI Employees of the Year. The honourees are (back, left to right) Yvhans Chéry, Tara Thompson, Darleen Element, Kathy Forner; (front, left to right) Julie Labrèche, Goldy Mansourian, Véronique Michaud, and Jenna Mancini. Their efforts to maintain the animal quarters and its related phenotyping and surgery cores serve a significant number of LDI scientists.

Student presentations are an important part of the day. The prize for best oral presentation went to Alicia Bolt of Dr. Koren Mann's lab for "Tungsten enhances breast cancer metastasis to the lung by targeting the tumor microenvironment." Second prize went to Maud Marques of Dr. Michael Witcher's lab for "Targeting aberrant poly-(ADP)-ribosylation in breast cancer."

Best poster recognition went to Karine Choquet of Dr. Claudia Kleinman's group, Barbara Gauthier from Dr. Paul Brassard's group, and Laura Hulea, who is supervised by Drs. Ivan Topisirovic and Michael Pollak.

Fackson Mwale prevails in 2015 AmorChem Knock-Out™ Event

Dr. Fackson Mwale emerged as the champion in the second AmorChem Knock-Out™ event, defeating four other challengers to win $500,000 in funding. Dr. Mwale's winning project is ""LINK N peptide as a therapeutic agent to treat intervertebral disc degeneration, arthritis and pain."

Dr. Mwale has demonstrated that the injection of Link N into degenerated discs *in vivo* results in significant repair within two weeks. Moreover, it brings a halt to the process by which the natural function of the peptide is impaired. "Because Link N occurs naturally, there is little or no toxicity associated with injecting it into the body, and it inhibits calcification," he explains. "Furthermore, peptides are very inexpensive to manufacture."

AmorChem, the innovative Quebec-based venture capital seed fund, had conducted a country-wide call for proposals to participate in its KNOCK OUT Event. They will now be working with Dr. Mwale on furthering his innovative research.

"We created this Event to increase the Quebec and Canadian research communities' awareness of AmorChem and reach out to researchers who may not have been aware of the possibility of commercializing aspects of their work," said Elizabeth Douville, General Partner at AmorChem. "This Event definitely reached those goals."

Prepared by the Research Communications Office, Lady Davis Institute at the Jewish General Hospital. Any suggestions with respect to content are welcome.

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

Hans Knecht demonstrates source of telomere damage in Hodgkin's Lymphoma

Dr. Hans Knecht's lab presents the first in vitro model to show how the permanent expression of the latent membrane protein 1 (LMP1), in a setting of a post-germinal B-cell line, leads to downregulation of shelterin proteins, telomeric aggregates and multi-nuclearity. This model, developed in collaboration with the 3D lab of Dr. Sabine Mai in Winnipeg and the basic telomere lab of Dr. Raymund Wellinger in Sherbrooke, largely explains the findings reported in Epstein-Barr virus (EBV) associated Hodgkin's lymphoma.

Downregulation of the shelterins, in particular TRF2, results in exposure of telomeres, the ends of chromosomes. This is dangerous because, without the protection of shelterin proteins, the chromosome ends clash against one another, resulting in recombinated chromosomes and, finally, multinuclearity. The paper was published in *Blood*.

Dr. Knecht has a long track record in clinical, translational and molecular hematology. His most important contribution is the discovery of the transition from the mononuclear Hodgkin to the multinuclear Reed-Sternberg cell, the diagnostic cell for Hodgkin's lymphoma. Presently, his group works, in collaboration with the laboratory of Dr. Nathalie Johnson of the LDI, on the pathogenic mechanisms of Hodgkin's lymphoma refractory to standard treatment.

He has focused his career both on caring for his patients and training numerous basic science and medical students, as well as postdoctoral fellows. His achievements include building and directing the Institute for Clinical Research at the Swiss Paraplegic Center, and his recent job as Professor of Medicine and Director of Hematology Laboratories at CHUS, University of Sherbrooke. He joined the JGH at Chief of Hematology-Oncology on April 1st, 2014.

Dr. Osama Roshdy has received a Canadian Dermatology Foundation Research Grant. Dr. Roshdy's area of interest is cutaneous oncology. Currently, he is investigating the molecular elements of the hypopigmented variant of Mycosis Fungoides, the most common cutaneous T-cell lymphoma.

How the Stat1 protein defends against chemotherapies

Dr. Antonis Koromilas' lab has been striving to understand the role played by the protein Stat1 in the inhibition of tumor cell proliferation and in strategies for tumor treatment with chemotherapeutic drugs. Stat1 is normally activated as an immune response to infection. It is also activated under certain circumstances in response to cancer.

"The odd thing about Stat1 is that it could be activated to inhibit tumors, but once a tumor establishes itself, the protein is somehow modified to protect it," he explains. "From that point, we see that it acts against the drugs that are intended to kill the cancer cells."

He has developed mouse models that are deficient in Stat1 to test traditional and novel anti-tumor drugs in order to determine whether Stat1 will be an effective therapeutic target, in cancers expressing the RAS oncogene, which is found in 33% of human cancers.

Stat1 functions as a tumor suppressor by inhibiting cell proliferation and mediating anti-tumor responses via immune regulatory and cell-autonomous mechanisms. However, recent findings have shown that once a tumor becomes established, it can hijack Stat1 and exploit it for protection against conventional chemotherapeutic drugs. Once this transition in Stat1 occurs, the cancer becomes far more difficult to treat.

In a recent paper in the *Proceedings of the National Academy of Sciences (PNAS)*, Dr. Koromilas and his team investigated how the protein's function changes within the tumor environment, revealing the pathway through which Stat1 regulates protein synthesis in the tumor, which allows it to defend against those chemotherapies deployed to destroy it.

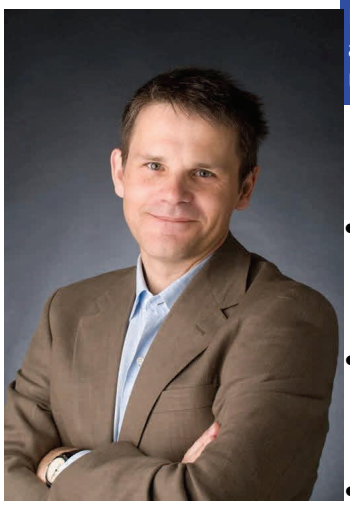
The challenge now is to develop a drug that could maintain the protective properties of Stat1 against tumor formation while suppressing the capabilities of the tumor to turn the protein to its advantage in response to chemotherapies.

"Such drugs may target specific pathways in mRNA translation utilized by Stat1 to convey resistance to chemotherapies," Dr. Koromilas speculates.

Proposal to limit testing for genetic breast cancer susceptibility

Screening for genes whose risk association with breast cancer has yet to be proven is not justified and potentially harmful, argue an international team of leading geneticists and oncologists, including **Dr. William Foulkes**, head of the Cancer Genetics Laboratory, in a paper in the *New England Journal of Medicine*.

"We propose that a genomic test should not be offered until its clinical validity has been established," the authors insist. Moreover, "we believe that failing to require the clinical validation of genomic tests before they are submitted for regulatory approval is likely to lead to substantial misuse of the technology." With genetic screening having become quick and affordable, the authors have noted a trend toward offering women genetic screening tests for breast cancer that are not clinically justified and for genes without sufficient evidence of their association with high or moderate risk for breast cancer.



"In the absence of clinical validity, why would you test?" Dr. Foulkes asks. "It is really a professional duty for physicians and genetic counsellors to limit genetic testing for cancer susceptibility to those circumstances where the results are likely to provide data that you can put into action. Finding out that someone has a particular mutation for which we have not even proven that the variant discovered poses a risk to the woman simply serves no purpose.

"Finding a mutation without knowing its association to breast cancer is the equivalent of a false positive, where the patient ends up suffering anxiety for no reason. This is a form of harm that we, as professionals, should spare them through the exercise of proper judgement," he went on. The paper argues that genetic tests should not be approved until their clinical validity has been proven – this is not without its challenges, but ignoring the need for validation could lead to harm, or at least misinformation.

Carolyn Ells Appointed to Chair Panel on Research Ethics

Dr. Carolyn Ells has been appointed to Chair the Inter-agency Advisory Panel on Research Ethics. The Panel advises the presidents of Canadian Institutes of Health Research (CIHR), the Natural Sciences and Engineering Research Council of Canada (NSERC) and the Social Sciences and Humanities Research Council of Canada (SSHRC) on the ethics of research involving humans. It also provides recommendations regarding the evolution and interpretation of *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*.

Dr. Ells is a philosopher with a specialization in bio-ethics. She is Associate Professor of Medicine, Associate Member of the Division of Experimental Medicine, and Member of the Biomedical Ethics Unit at McGill University, and an investigator at the LDI.

McGill promotions

- **Dr. Andrew Mouland**, of the HIV/AIDS Axis has been promoted to full Professor of Medicine, Microbiology & Immunology.
- **Dr. Brett Thombs**, of the Psychosocial Axis, has been promoted to full Professor in the Department of Psychiatry.
- **Dr. Marie Hudson**, of the Epidemiology Axis, has been promoted to Associate Professor in the Department of Medicine.

Dr. Stephane Richard, of the Cancer Axis had his James McGill Professorship renewed for a further seven year term. He was first appointed in 2003. The award was created to recognize a senior scholar's status as an outstanding and original researcher of world-class caliber in their field.