CIHR **STAGE**

Strategic Training for Advanced Genetic Epidemiology

Dr. Mathieu Lupien

Scientist, Ontario Cancer Institute
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Investigator, **Ontario Institute for Cancer Research**

Epigenomics Reveal the Function of Genetic Risk-Variants in Cancer

Friday
April 5, 2013
12:00 –1:00 p.m.

The Hospital for Sick Children
CDIU Multimedia Theatre
Room 4132, 4th Floor, Elm Elevators
555 University Avenue, Toronto, ON

Profile: Mathieu Lupien has been scientist at the Ontario Cancer Institute (OCI) and cross-appointed to the Ontario Institute for Cancer Research (OICR) since 2012. He earned his Ph.D. at McGill University in 2005, followed by a post-doctoral training at the Dana-Farber Cancer Institute, Harvard Medical School in Boston, MA as an Era of Hope fellow. Lupien completed his post-doctoral training in medical oncology in 2008. In 2009, Dr. Lupien was recruited as a faculty member at Dartmouth Medical School, in Hannover, NH where he became Director of the Quantitative Epigenomics laboratory. Dr. Lupien has co-authored approximately 30 peer-reviewed publications in his short career, including seminal work reported in high-impact journals including Science, Cell, Nature Genetics and The Journal of the National Cancer Institute. Among other honors, Dr. Lupien is a recipient of the Young Investigator Award from the Ontario Institute for Cancer Research.

Abstract: Genome-wide association studies (GWAS) have identified thousands of SNPs that are associated with human traits and diseases. But, because the vast majority of these SNPs are located in non-coding regions of the genome, the mechanisms by which they promote disease risk have remained elusive. Employing a new methodology that combines cistromics, epigenomics and genotype imputation, we annotate the non-coding regions of the genome in breast cancer cells and systematically identify the functional nature of SNPs associated with breast cancer risk. Our results show that breast cancer risk-associated SNPs are enriched in the cistromes of FOXA1 and ESR1 and the epigenome of histone H3 lysine 4 monomethylation (H3K4me1) in a cancer- and cell type-specific manner. Furthermore, the majority of the risk-associated SNPs modulate the affinity of chromatin for FOXA1 at distal regulatory elements, thereby resulting in allele-specific gene expression, which is exemplified by the effect of the rs4784227 SNP on the TOX3 gene within the 16q12.1 risk locus.

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