Researcher Profile

UHN Microarray Centre

Dr. Phillipe Gros

Innate susceptibility and resistance to multigenic disease and multidrug resistance

Dr. Phillipe Gros has a broad research programme that encompasses many diseases. His team primarily investigates resistance to anticancer chemotherapeutics and the innate resistance or susceptibility to disease using genetic models.

Dr. Gros and his colleagues also investigate the complex genetic components of diseases such as tuberculosis (TB) and malaria. In a recent study, Drs. Gros and Marquis, and their colleagues, used UHNMAC Mouse 15K cDNA arrays for transcriptional profiling of lung tissue from *M. tuberculosis*-infected mice and uninfected controls with the aim of identifying genes and pathways differentially regulated in response to *M. tuberculosis* in genetically resistant (C57BL/6J) and susceptible (DBA/2J) mice (1). The results of this study identified a number of genes that were differentially expressed between the two strains, including fibrotic response genes (*Sparc*, *Col1a1, Col1a2, Col4a1*, and *Col4a2*) and genes associated with fibrosis (*Mmp2*, *Timp1*, and *Arg1*). These results identify the differential fibrotic response as a pathological basis for the susceptibility of DBA/2J mice to pulmonary tuberculosis. Parallel studies are underway to better understand the molecular mechanism of action and role of these genes and proteins in pathogenesis of TB. Dr. Gros and his colleagues have also used microarrays for transcription profiling in the study of tumour susceptibility (2).

Dr. Gros and his team have found polymorphic variants in the human natural resistance-associated macrophage protein 1 (*Nramp1)* gene that are associated with susceptibility to diseases such as tuberculosis, leprosy, inflammatory bowel disease, and juvenile diabetes (3). His team has shown that the Nramp1 protein plays a pivotal role in macrophages and neutrophils, where it functions as a metal transporter at the membrane of pathogen-containing phagosomes (3). Microarrays have also been used to investigate the role of *Nramp1* on Salmonella infection in mice (4). His team has also used bacterial genome microarrays to identify genes that are differentially regulated in the phagosome in presence or absence of *Nramp1* (3).

Research efforts are also focused on spina bifida, anencephaly, and spinal muscular atrophy. The mouse mutant loop-tail, caused by a mutation in the *Ltap* gene which was cloned by Dr. Gros and his colleagues, is used as a model for the study of neural tube defects (5,6). His team also studies the *Naip* gene which has been shown to affect apoptosis in motor neurons and associated with spinal muscular atrophy in humans (2). Since *Naip* is highly expressed in macrophages, and its expression is further stimulated by phagocytosis of pathogens, the goal now is to understand the role of the Naip protein in pathogenesis and how it regulates microbial-induced apoptosis in phagocytes.

Dr. Gros is a Distinguished Investigator of the CIHR and a Fellow of the Royal Society of Canada. He is affiliated with the Centre of the Study of Host Resistance and the Rosalind and Morris Goodman Cancer Centre at McGill University. He was awarded the 2009 Killam Prize, awarded to distinguished Canadian scholars, in the field of health sciences.

References:

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2. Meunier C, *et al*. Characterization of a major colon cancer susceptibility locus (Ccs3) on mouse chromosome 3. Oncogene 2009, Epub Nov 16
3. McGill University, Department of Biochemistry (2009). Research Interests of Philippe Gros. Retrieved January 15, 2010, from http://www.mcgill.ca/biochemistry/department/faculty/gros/
4. Caron J, *et al*. Influence of Slc11a1 on the Outcome of *Salmonella enterica* Serovar Enteritidis Infection in Mice Is Associated with Th Polarization. Infect Immun 2006, 74(5):2787
5. Kibar Z, *et al*. Ltap, a mammalian homolog of Drosophila Strabismus/Van Gogh, is altered in the mouse neural tube mutant Loop-tail. Nature Genetics 2001, 28:251
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UHN Microarray Centre offers a variety of microarray products and genomics services. The centre also offers bioinformatics services, from experimental design to downstream data analysis and mining, enabling researchers to maximise the success of their genomics projects.