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PRESS RELEASE

For immediate release

AN INTERNATIONAL GROUP OF SCIENTISTS, INCLUDING THOSE FROM THE MONTREAL HEART INSTITUTE, FIND MAJOR SUSCEPTIBILITY GENES FOR LUPUS IN WOMEN

**Discoveries reveal new genetic risk factors
for the millions of people with lupus**

Montreal, January 20, 2008 – An international consortium of clinical scientists and genomics experts, which includes the Montreal Heart Institute, conducted a large-scale genomic study that uncovered multiple new genetic risk factors for systemic lupus erythematosus (SLE), commonly known as lupus. The study is the first comprehensive one of its kind investigating the genetic basis of lupus. These findings appear in the January 20 online edition of Nature Genetics. Dr. John D. Rioux, Ph.D., Associate Professor of Medicine at the Montreal Heart Institute (MHI) and the Université de Montréal, is one of the study's authors.

Systemic lupus can involve the joints, kidneys, heart, lungs, brain and blood. The disease occurs in about 31 out of every 100,000 people and affects women nine times more frequently than men. Scientists believe that lupus is caused by genetic variants that interact with each other and the environment.

The researchers studied the DNA of 720 women of European descent with lupus and 2,337 women without lupus. They scanned the entire genome for more than 317,000 single nucleotide polymorphisms (SNPs), which are locations on chromosomes where a single unit of DNA, or genetic material, may vary from one person to the next. The goal was to identify SNPs linked to lupus. They confirmed these results in another independent set of 1,846 women with lupus and 1,825 women without lupus.

The scientists found evidence of an association to three genes: ITGAM, KIAA1542 and PXX, and to a region of the genome that does not contain any known genes. ITGAM is important for both the adherence of immune cells and for cleaning up pathogens. KIAA1542 is important for translating the DNA code into proteins. PXX encodes a molecule that transmits signals and controls complex

processes in cells. The scientists also found association in genes previously associated with lupus and other autoimmune diseases.

“These results help to delineate the genetic distinctions between rheumatoid arthritis, lupus and other autoimmune diseases, which could lead to earlier, more accurate diagnoses,” said Dr. John Harley, M.D., Ph.D., lead author and SLEGEN director, from the Oklahoma Medical Research Foundation. “They identify biologic pathways that help us understand the condition better and suggest additional genetic and non-genetic triggers.”

“These will now allow us to focus our research on the specific biological pathways and genes identified in this study and to dissect the precise molecular mechanisms by which these genes contribute to the risk for lupus,” added Dr. John D. Rioux.

In fact, these discoveries come only a few weeks following the identification of one of the first genetic risk factors for systemic lupus, published in the January 2008 issue of *Nature Genetics*. “In our previous study, we identified that a gene called TNFSF4, important for the communication between different cells of the immune system, is also involved in the susceptibility to systemic lupus,” said Dr. Rioux. “The technological advances that made these studies possible are truly revolutionizing our ability to identify genetic risk factors for common diseases and these discoveries represent a major advance in our efforts to use genetic information to improve on the diagnosis and treatment of our patients,” concluded Dr. Jean-Claude Tardif, Director of the Research Center of the MHI and Professor of Medicine at the MHI and the Université de Montréal. Dr. Tardif also mentioned that “this remarkable contribution to the advancement of medical knowledge confirms the value of Université de Montréal’s strategy in the field of genetics and genomics, which is based upon targeting important medical questions, supporting world class researchers and their international collaborations, in order to have a significant impact on our health system and on the scientific, social and economic development of Quebec and Canada”.

This work was supported by the Alliance for Lupus Research and the National Institutes of Health of the United States.

About Dr. John D. Rioux

Dr. Rioux, Ph.D., is an Associate Professor of Medicine at the Université de Montréal and at the MHI where he works as a researcher and director of the Laboratory in Genetics and Genomic Medicine of Inflammation (www.inflamngen.org). He is also a visiting scientist at the Broad Institute of MIT and Harvard, and holder of the Canada Research Chair in Genetics and Genomic Medicine of Inflammation.

About the Montreal Heart Institute

Founded in 1954, the Montreal Heart Institute constantly aims for the highest standards of excellence in the cardiovascular field through its leadership in prevention, ultra-specialized care, training of professionals, clinical and fundamental research, and assessment of new technologies. It is affiliated with the Université de Montréal and its clinical outcomes are among the best in the world.

The MHI Research Centre officially came into existence in 1976 and has made enormous strides since its creation. Today, there are approximately 500 employees, students and researchers at the MHI Research Centre. The MHI's outstanding feature is the balance it achieves between basic research, clinical research and clinical care. Its prime focus areas of research are vascular diseases, myocardial function and electrophysiology. MHI researchers also contribute to the advancement of knowledge and medical applications in the fields of genomics (in particular in disease gene discovery and pharmacogenomics), biomarkers and preventive cardiology. To learn more about the Institute, please visit our website at www.icm-mhi.org.

About the Université de Montréal

Deeply rooted in Montreal and dedicated to its international mission, the Université de Montréal is one of the top universities in the world, particularly in the French-speaking world. Founded in 1878, the Université de Montréal today has 13 faculties and together with its two affiliated schools, HEC Montréal and École Polytechnique, constitutes the largest centre of higher education and research in Québec, the second largest in Canada, and one of the major centres in North America. It brings together 2,500 professors and researchers, accommodates more than 55,000 students, offers some 650 programs at all academic levels, and awards about 3,000 masters and doctorate diplomas each year.

- 30 -

Genome-wide association scan in women with systemic lupus erythematosus identifies susceptibility variants in ITGAM, PXX, KIAA1542 and other loci

The International Consortium for Systemic Lupus Erythematosus Genetics (SLEGEN)

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Polymorphism at the TNF superfamily gene TNFSF4 confers susceptibility to systemic lupus erythematosus

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