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PRESS RELEASE

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MONTREAL HEART INSTITUTE RESEARCHERS CONTRIBUTE TO THE DISCOVERY OF A NEW GENE RELATED TO SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND RHEUMATOID ARTHRITIS (RA)

A North-American study reveals a new genetic risk factor for the millions of people with SLE and RA

Montreal and Toronto, August 1st, 2008 – A North-American consortium of clinical scientists and genomics experts, including major contributions from Canadian researchers – Dr. John D. Rioux from the Montreal Heart Institute and Université de Montréal and Drs. Joan Wither and Paul R. Fortin from the University Health Network in Toronto – have identified a novel genetic risk factor for systemic lupus erythematosus (SLE); a disease commonly known as "lupus". Lupus is a chronic "autoimmune" disease in which the body's immune system attacks healthy tissues and organs. Symptoms range from skin rashes and joint pain to strokes, seizures and organ failure. This study shows that genetic variation of a particular gene — known as TNFAIP3 — leads to SLE and Rheumatoid Arthritis (RA). This study also confirmed the identity of an additional four genetic risk factors for SLE: the HLA, IRF5, BLK and STAT4 genes. These findings appear in the August 1st online edition of *Nature Genetics*.

In order to complete this study, the researchers examined the more than 20,000 genes in the human genome by performing over 300,000 genetic tests of DNA samples from 431 patients with SLE and compared the results to those of 2155 healthy individuals. These results were then confirmed in a group of 740 SLE patients and their family members. In healthy individuals, when a virus or bacteria enters a human body, the immune system revs up to fight and expel the invader. Once the invader is gone, the body puts on the brakes to stop the immune response. In lupus patients it is believed that the immune system keeps going at full speed long after the threat is gone, causing damage to the body. "TNFAIP3 can be thought of as a critical brake mechanism for the immune system," said Patrick M. Gaffney, the senior author of the study and Associate Member of Oklahoma Medical Research Foundation's Arthritis and Immunology Research Program.

“It has been suspected for a long time that problems in the regulation of the immune system lead to lupus. The identification of TNFAIP3 and the other genetic risk factors now indicate the specific biological pathways that need to be targeted in order to generate better diagnostic markers and effective therapies.” says Dr. John D. Rioux, Ph.D., Associate Professor of Medicine at the Montreal Heart Institute (MHI) and Université de Montréal, and one of the study’s authors.

“I am excited that our Canadian cohort has revealed its full potential for the identification of important new SLE genes,” says Dr. Paul R. Fortin, co-principal investigator of the CIHR-funded CaNIOS Genetic and Environment SLE (GenES) study and Professor of Medicine at the University Health Network Research Institute and the University of Toronto.

“The observation that genetic variation in TNFAIP3 is associated with both SLE and Rheumatoid Arthritis suggests that some of the risk factors for these two conditions are shared,” says Dr. Joan E. Wither, co-principal investigator of the GenES study and Associate Professor of Medicine and Immunology at the University of Toronto.

About lupus
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.

About the Montreal Heart Institute: www.icm-mhi.org.
About the Université de Montréal: www.umontreal.ca.
About Canadian Network for Improved Outcomes in SLE: www.canios.ca.

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Genetic Variants Near TNFAIP3 on 6q23 are Associated with Systemic Lupus Erythematosus

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