

Mount Sinai Hospital researchers first worldwide to discover pivotal new clue in the development of rheumatoid arthritis and other autoimmune diseases

Findings will help lead to personalized therapies for common, complex illnesses characterized by abnormal immune responses

(August 14, 2011-Toronto, ON) Scientists at Mount Sinai Hospital, in collaboration with researchers at the University of Toronto, University Health Network and McGill University have obtained significant new insights into the causes of rheumatoid arthritis (RA) and other autoimmune disorders including type 1 diabetes, lupus and Graves disease. The findings represent a key initial step in realizing the full potential of genomics and personalized medicine.

In a study published online today in *Nature Genetics*, Dr. Katherine Siminovitch and her team identified the exact means by which an alteration in the gene *PTPN22* increases risk for RA and other autoimmune disorders. The study used advanced genomics technologies that enable testing of millions of genetic markers in a single experiment to identify genes, such as *PTPN22*, that confer risk for disease. The team then generated a mouse genetic model to show how the *PTPN22* gene mutation impairs immune cell function and then validating their findings in humans, taking their discovery from the laboratory bench to the clinic.

The result: a more accurate understanding of how autoimmune conditions develop, and how new diagnostic tests and targeted therapies can be designed for better symptom control and potential cure.

“Our findings are particularly exciting because this study sets a new precedent for studying arthritis and other autoimmune disorders,” said lead author Dr. Siminovitch, Senior Investigator and the Sherman Family Research Chair in Genomic Medicine at the Samuel Lunenfeld Research Institute of Mount Sinai Hospital, a professor at the University of Toronto, and Director of the Fred A. Litwin & Family Centre in Genetic Medicine. “This is one of the first studies in which we have traced the steps that connect a specific genetic lesion to the development of a common, complex autoimmune condition.”

Led by Dr. Siminovitch, the group used genetically modified mice in which *PTPN22* had been altered to mimic a genetic mutation found in many RA patients. The effects of this change on immune cells were observed in the mice, and the studies were then repeated in human blood samples from patients with and without RA. By this means, the group honed in on the impact of a key protein called Lyp/Pep that—in healthy cells—prevents the hyper-immune responses that lead to autoimmune disorders. The group found that this gene mutation leads to decreased levels of Lyp, thereby removing a natural brake that normally prevents the inflammatory processes underlying RA and many other autoimmune conditions.

“Measuring levels of this protein will help us monitor disease severity in patients with autoimmune disorders, test the effects of various therapies including new drugs, and determine which treatments work best in specific patients,” said Dr. Edward Keystone, co-author of the study and Director of the Rebecca MacDonald Centre for Arthritis and Autoimmune Disease at Mount Sinai Hospital. “We are truly seeing genomics in action with this study, and the results give us new hope for improving patient outcomes.”

Dr. Keystone emphasized the importance of this type of research to the practice of medicine in general, noting that advances in genetics knowledge are allowing for earlier diagnoses and more personalized treatments that give patients better outcomes.

“Using the powerful genetic tools now available, previously cryptic diseases are being dissected and their underlying causes identified,” said Dr. Jim Woodgett, the Lunenfeld’s Director of Research. “Drs. Siminovitch and Keystone are at the leading edge of employing these genomic approaches for the benefit of patients, seamlessly combining their research skills with clinical insights.”

Millions of Canadians are affected by autoimmune disorders that are a common cause of long-term pain and/or disability.

The study was funded by Canadian Institutes of Health Research, the Canadian Arthritis Network, and the Ontario Research Fund.

-30-

About Mount Sinai Hospital

Mount Sinai Hospital is an internationally recognized, 472-bed acute care academic health sciences centre affiliated with the University of Toronto. It is known for excellence in the provision of compassionate patient care, innovative education, and leading-edge research. Mount Sinai’s Centres of Excellence include: Daryl A. Katz Centre for Urgent & Critical Care; Lawrence and Frances Bloomberg Centre for Women’s & Infants’ Health; Christopher Sharp Centre for Surgery & Oncology; Centre for Inflammatory Bowel Disease; Centre for Musculoskeletal Disease and the Samuel Lunenfeld Research Institute. For more information about Mount Sinai Hospital, please visit www.mountsinai.ca.

About the Samuel Lunenfeld Research Institute of Mount Sinai Hospital

The Samuel Lunenfeld Research Institute of Mount Sinai Hospital, a University of Toronto affiliated research centre established in 1985, is one of the world’s premier centres in biomedical research. Thirty-six principal investigators lead research in diabetes, cancer biology, epidemiology, stem cell research, women’s and infants’ health, neurobiology and systems biology. For more information on the Samuel Lunenfeld Research Institute, please visit www.lunenfeld.ca.

Media Contacts

NOTE: IF RESPONDING TO THIS AFTER THURSDAY AUGUST 11, PLEASE CALL ROB MCMAHON:

Rob McMahon
Media and Communications Specialist
Mount Sinai Hospital
(416) 586-3161
RMcMahon@mtsinai.on.ca

Karin Fleming
Communications Specialist - Research
Mount Sinai Hospital
(416) 586-4800 Ext. 2046
fleming@lunenfeld.ca