

New genetic clue in the development of rheumatoid arthritis

August 14 2011

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."

Provided by Samuel Lunenfeld Research Institute

Citation: New genetic clue in the development of rheumatoid arthritis (2011, August 14)
retrieved 20 July 2023 from <https://medicalxpress.com/news/2011-08-genetic-clue-rheumatoid-arthritis.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.