MedicalXpress

Researchers identify new functions for autoimmune disease 'risk' gene

July 19 2013

Researchers at the University of Minnesota have identified infection-fighting and inflammation-suppressing functions for a gene associated with human autoimmune disease.

The discovery, centered on a gene known as PTPN22, could set into motion new treatment approaches for autoimmune diseases like lupus, rheumatoid arthritis and type 1 diabetes. The key to these advances may lie with a better understanding of how a variant of PTPN22, known as a "risk variant," impacts autoimmune disease development and the behavior of myeloid cells that act as the body's "first responders."

The study appears in the journal *Immunity*.

In launching their latest research project, University of Minnesota Center for Immunology researchers set out to determine how PTPN22 could regulate immune system function in health and disease.

"Almost a decade ago, researchers at the University of Minnesota and other institutions discovered that people carrying a variant form of the PTPN22 gene bear an increased risk of becoming sick with certain autoimmune diseases. However, we have lacked a deep understanding how the variant creates that increased risk," said Erik J. Peterson, M.D., one of the study's lead authors and a University of Minnesota Medical School associate professor in the Division of Rheumatic and Autoimmune Diseases. "We wanted to understand the molecular basis for PTPN22 association with disease."

Much of the work carried out in the latest study took place in Peterson's laboratory, which utilizes genetic, biochemical, and primary human sample-based approaches to investigate how "risk" genes predispose to development of autoimmune disease.

According to the study's authors, previous research showed that PTPN22 works in immune cells, but few studies had specifically examined PTPN22's function in infection-fighting cells called myeloid cells.

"Myeloid cells are among the body's 'first responders' to a challenge with a virus or bacterium," said Yaya Wang, Ph.D., one of the study's co-first authors and a research associate in the Center for Immunology. "Upon recognizing the presence of an infection, myeloid cells produce chemicals that increase inflammation and help fight the invading microbe. We were intrigued by the idea that PTPN22 and its disease-associated variant might have a role in myeloid cell functions."

Researchers found that both mouse and human myeloid cells carrying the PTPN22 "risk" variant show decreased production of molecules called type 1 Interferons. Type 1 Interferons are needed to boost immune responses to viruses and other infections. In mice lacking the PTPN22 gene, reduced type 1 Interferon production correlates with an impaired ability to fight infections.

But the PTPN22 gene does more than simply fight infection, the study showed.

"Unexpectedly, we also found that PTPN22 suppresses inflammation," said Wang. "Furthermore, we showed that the PTPN22 risk variant is defective in suppressing inflammatory arthritis."

"We anticipate that our findings will open new lines of investigation into how PTPN22 and other autoimmune disease 'risk' genes could work in

infection-fighting and anti-inflammatory processes. Ultimately, we hope that the research will accelerate the drive toward better treatments and cures for autoimmune disorders," said Peterson.

More research is underway to determine the impact of the PTPN22 variant in the function of myeloid blood cells, particularly in patients suffering from lupus. Researchers are also comparing immune responses to influenza A vaccines between carriers and non-carriers of the PTPN22 variant. The goal is to understand the role of the disease-associated variant in mounting a normal response to immunizations against viruses.

Provided by University of Minnesota