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New genetic links to MS also play roles in other autoimmune diseases

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Results of the largest genomics study of multiple sclerosis patients ever undertaken have identified more than two dozen new genetic variants linked to disease risk, including some previously implicated in other autoimmune diseases.

The study, conducted by an international consortium of researchers from the Yale School of Medicine and 129 other institutions, appears in the Aug. 11 issue of the journal *Nature*. Common genetic links between multiple autoimmune diseases were also confirmed in a second study by Yale and Harvard University researchers in a second study published contemporaneously in the journal PLoS Genetics.

"We have known for some time that many devastating diseases of the immune system must have common genetic causes," said Chris Cotsapas, assistant professor of neurology and genetics at Yale and lead author of the PLoS paper. "Now we have the outline of a map that tells us where we can look for common treatments."

In the *Nature* study, researchers studied the DNA from 9,772 individuals with multiple sclerosis and 17,376 unrelated healthy controls. They were able to confirm 23 previously known genetic associations and identified a further 29 new genetic variants as well as five strongly suspected of conferring susceptibility to the disease.

A large number of the genes implicated by these findings play pivotal roles in the workings of the immune system, specifically in the function

of T-cells, which mount an immune response against foreign substances in the body, and interleukins, chemicals that facilitate interactions between different types of immune cells. One-third of the genes identified in this research have previously been implicated in playing a role in other autoimmune diseases such as Crohn's disease and Type 1 diabetes.

The PLoS research paper found that nearly half of the 107 genetic variants previously linked to an autoimmune disease are also found in at least one other autoimmune disease, such as MS, Crohn's disease, psoriasis, rheumatoid arthritis, lupus, celiac disease and Type 1 diabetes.

"These findings will help focus future research to find new ways to intervene in the course of MS and other diseases," said Yale's David Hafler, the Gilbert H. Glaser Professor of Neurology and professor of immunobiology, chair of the department of neurology and an author on both papers.

Authors of the *Nature* paper are the International Multiple Sclerosis Genetics Consortium along with the Wellcome Trust Case Control Consortium 2, which brought together hundreds of scientists from 130 institutions to help conduct this ground-breaking genome-wide analysis of patients with MS. The IMSGC was founded by Hafler while he was at the Harvard Medical School and the Broad Institute, along with Alastair Compston of the University of Cambridge and Stephen Hauser from the University of San Francisco.

"Our research settles a longstanding debate on what happens first in the complex sequence of events that leads to disability in multiple sclerosis, and has important implications for future treatment strategies," said Compston, a senior author of the work.

While it is clear that these common genetic variations are one critical

component underlying the multiple sclerosis, environmental factors also play a role in the onset of the disease. For instance, previous research has shown vitamin D deficiency may lead to increased risk of MS.

"It is not that there are bad genes or necessarily a bad environment, but instead a disconnection between the interaction of genes with the environment," Hafler said.

Provided by Yale University