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Researchers perform large genome-wide analysis of multiple sclerosis

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In a large-scale, genome-wide analysis of more than 110,000 samples, a worldwide consortium of scientists has identified 200 genetic loci associated with multiple sclerosis (MS), an inflammatory and neurodegenerative disease in which a person's immune system attacks the brain and spine, disrupting signaling between the brain and the body. Their findings were presented in a featured plenary session at the American Society of Human Genetics (ASHG) 2016 Annual Meeting in Vancouver, B.C.

Established in 2003, the International Multiple Sclerosis Genetics Consortium (IMSGC) brings together researchers from 30 institutions in 18 countries that study the genetics of MS. By combining data from multiple genome-wide association studies, the consortium assembled genomic data from 47,351 people diagnosed with MS and 68,284 without the condition.

"This is the largest study of this disease worldwide," said Nikolaos A. Patsopoulos, MD, PhD, a principal investigator in the Ann Romney Center for Neurologic Diseases at Brigham and Women's Hospital (BWH), assistant professor of Neurology at Harvard Medical School, and associate member at the Broad Institute, who presented the research on behalf of the IMSGC. "The large sample size provided the statistical power to pinpoint areas of the genome that are likely to be involved in MS, including less common genetic variants that tend to have a larger effect on disease."

By comparing the genomes of people with and without MS, the researchers identified 200 variants that were significantly more common among those with the disease. Most of these variants implicate genes that are associated with immune cells and immune system function, including a few potentially specific to brain-related functions.

"This confirms the complex interplay of different elements of the immune system in MS susceptibility and highlights the role of several different immune cells that contribute to the initiation of this inflammatory disease," explained Phil De Jager, MD, PhD, senior author of the study, director of the Program in Translational NeuroPsychiatric Genomics at the Ann Romney Center for Neurologic Diseases, an associate professor of Neurology at Harvard Medical School, and an associate member at the Broad Institute. "While we now have some hints, the mechanisms that lead this inflammatory disease to target the brain and spinal cord remain unclear," he added.

Interestingly, many of the genes identified were known to also be involved in other autoimmune diseases, such as rheumatoid arthritis, Type I diabetes, and ulcerative colitis. This raises intriguing questions about why these diseases target different organs and have different clinical manifestations.

"The differences and commonalities between MS and other autoimmune diseases are part of our line of research," Dr. Patsopoulos said. "Many of these conditions affect immune system cells, but we believe they change these cells in different ways, leading to different disease outcomes."

This study highlights the power of collaboration, the study authors noted. "None of us could have completed this work on our own," explained Adrian Ivinson, PhD, IMSGC coordinator and executive director of the BWH Institute for the Neurosciences. "Only by sharing our energy and resources have we been able to produce this detailed genetic map of

multiple sclerosis and to share this invaluable data with the rest of the MS research community. Using the same approach, the IMSGC now hopes to turn its attention to the genetic underpinnings of progressive multiple sclerosis, the most aggressive form of MS," added Dr. Ivinson.

More information: Patsopoulos N, on behalf of IMSGC. (2016 Oct 18). Abstract: 200 loci complete the genetic puzzle of multiple sclerosis. Presented at the American Society of Human Genetics 2016 Annual Meeting. Vancouver, B.C., Canada. ep70.eventpilot.us/web/page.ph … =ASHG16&id=160122047

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