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RESEARCH/CLINICAL UPDATE

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Genetics Consortium Finds Gene that May Protect Against MS

The International MS Genetics Consortium (IMSGC) has newly identified a gene that may help protect people from developing multiple sclerosis. The group recently published its findings in the *Annals of Neurology* (2007;61(3):228 – 236). The IMSGC is a collaborating group of investigators with expertise in genetics, database design/construction, and clinical assessment and immunology of MS. The National MS Society funded the formation of the IMSGC through a Collaborative MS Research Center Award to Dr. David A. Hafler (Harvard Medical School and Brigham and Women's Hospital).

HLA genes (genes that control how the immune system identifies foreign substances as well as the body's own tissues) have been associated with MS, most strongly, the HLA-DRB1*1501 gene. The IMSGC screened the genetic material in the HLA region in 930 "trio families," which comprise people with MS and their parents (480 from the United Kingdom and 450 from the United States). They excluded families in which either parent carried the HLA-DRB1*1501 gene, to eliminate it as a confounding factor. The results show a significant association between the HLA-C*05 gene and protection from MS. The IMSGC confirmed this association in a group of 721 patients with sporadic MS and 3,660 controls without MS.

The authors note that replication of these findings will be necessary in independent cohorts. If confirmed, these findings may shed new light on the immune attack on the brain and spinal cord in MS. The HLA-C gene family instructs molecules that interact with natural killer cells -- a group of immune cells that home in on and kill viral and cancer cells that have invaded the body. Some research suggests that these cells may play a protective role in MS.

This IMSGC includes Dr. Hafler, Dr. Stephen Hauser (UCSF), Dr. Eric Lander (Broad Institute of MIT and Harvard), Drs. Alistair Compston and Stephen Sawcer (University of

Cambridge), Drs. Jonathan Haines (Vanderbilt University) and Margaret Pericak-Vance (Duke University), Dr. Jorge Oksenberg (UCSF), and others. This multinational effort allows the researchers to compile information on numerous patients, enhancing the statistical power of their findings.

The IMSSGC is currently mapping the genome (all of the genetic material within humans) of MS using a DNA chip that enables investigators to test 500,000 individual genetic locations at one time for possible involvement in MS. The Society committed \$1.1 million to jump-start this effort, and joined with Harvard to raise a total of \$3.63 million to complete the project. The results are expected to be presented at a scientific meeting this year.

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