MULTIPLE SCLEROSIS

New gene variants that increase MS risk

Two groups report the identification of new multiple sclerosis (MS) susceptibility loci through the use of genome-wide association studies. The Australia and New Zealand Multiple Sclerosis Genetics Consortium (ANZgene) found two new risk-associated single nucleotide polymorphisms (SNPs), both of which are known to be associated with other autoimmune diseases, on chromosomes 12q13–14 and 20q13. Philip De Jager (Harvard Medical School, Boston, USA) and colleagues identified three new MS susceptibility loci—*TNFRSF1A*, *CD6* and *IRF8*. "Identification of these new loci will, hopefully, provide insights that translate into therapeutic opportunities for people with MS," comments De Jager.

The work by the ANZgene consortium highlights the genetic overlap between autoimmune diseases, and the importance of immune system regulation in MS, notes corresponding author Justin Rubio (University of Melbourne, Victoria, Australia). A link between MS susceptibility and variation in the 25-hydroxyvitamin D-1 alpha hydroxylase gene (*CYP27B1*) on chromosome 12 also provides strong evidence for the importance of the vitamin D pathway in MS. "If fine-scale mapping, deep sequencing and functional studies confirm this association, this is a gene–environment link that could provide the basis for large-scale clinical trials to determine the full impact of the vitamin D system in the prevention and treatment of MS," explains Rubio.

De Jager and colleagues are also currently pursuing the functional dissection of the other three new loci to assess how these genetic variants affect the function of the human immune system. "*IRF8* variants are of great interest since this gene affects responses to interferons, and interferon β is a first-line drug for MS," he says. Knowing more about the gene could be useful for targeting treatment within the MS population. Evidence of an increased risk of MS in people who carry *TNFRSF1A* variants is also fascinating, since many drugs target the tumor necrosis factor (TNF) pathway in other inflammatory diseases. "This could focus interest on evaluating already approved drugs for use in MS, but we have to bear in mind that some TNF blockers are known to exacerbate MS," cautions De Jager.

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Original articles De Jager, P. L. *et al.* Meta-analysis of genome scans and replication identify *CD6*, *IRF8* and *TNFRSF1A* as new multiple sclerosis susceptibility loci. *Nat. Genet.* **41**, 776–782 (2009).
Australia and New Zealand Multiple Sclerosis Genetics Consortium (ANZgene). Genome-wide association study identifies new multiple sclerosis susceptibility loci on chromosomes 12 and 20. *Nat. Genet.* **41**, 824–828 (2009).