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Researchers double number of genes associated with multiple sclerosis

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Scientists have identified 29 new genetic variants linked to multiple sclerosis, providing key insights into the biology of a very debilitating neurological disease. Many of the genes implicated in the study are relevant to the immune system, shedding light onto the immunological pathways that underlie the development of multiple sclerosis.

The research, involving an international team of investigators led by the Universities of Cambridge and Oxford and funded by the Wellcome Trust, is published today, 11 August, in the journal *Nature*. This is the largest MS genetics study ever undertaken and includes contributions from almost 250 researchers as members of the International Multiple Sclerosis Genetics Consortium and the Wellcome Trust Case Control Consortium.

Multiple sclerosis is one of the most common neurological conditions among young adults, affecting around 2.5 million individuals worldwide. The disease results from damage to nerve fibres and their protective insulation, the myelin sheath, in the brain and spinal cord. The affected pathways - responsible in health for everyday activities such as seeing, walking, feeling, thinking and controlling the bowel and bladder – are prevented from 'firing' properly and eventually are destroyed. The findings announced today focus attention on the pivotal role of the immune system in causing the damage and help to explain the nature of the immune attack on the brain and spinal cord.

In this multi-population 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 (and an additional five that are strongly suspected) 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 (one type of white blood cell responsible for mounting an immune response against foreign substances in the body but also involved in autoimmunity) as well as the activation of 'interleukins' (chemicals that ensure interactions between different types of immune cells). Interestingly, 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) indicating that, perhaps as expected, the same general processes occur in more than one type of autoimmune disease.

Previous research has suggested a link between Vitamin D deficiency and an increased risk of multiple sclerosis. Along with the many genes which play a direct role in the immune system, the researchers identified two involved in the metabolism of Vitamin D, providing additional insight into a possible link between genetic and environmental risk factors.

Alastair Compston from the University of Cambridge who, on behalf of the International Multiple Sclerosis Genetics Consortium, led the study jointly with Peter Donnelly from the Wellcome Trust Centre for Human Genetics, University of Oxford, said: "Identifying the basis for genetic susceptibility to any medical condition provides reliable insights into the disease mechanisms. Our research settles a longstanding debate on what happens first in the complex sequence of events that leads to disability in multiple sclerosis. It is now clear that multiple sclerosis is primarily an immunological disease. This has important implications for future

treatment strategies."

Peter Donnelly, who leads the Wellcome Trust Case Control Consortium, added: "Our findings highlight the value of large genetic studies in uncovering key biological mechanisms underlying common human diseases. This would simply not have been possible without a large international network of collaborators, and the participation of many thousands of patients suffering from this debilitating disease."

More information: The paper 'Genetic risk and a primary role for cell-mediated immune mechanisms in multiple sclerosis' will be published in the 11 August edition of *Nature*.

Provided by University of Cambridge