

# Mapping reveals 110 genes that increase the risk of MS

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Researchers have mapped genetic variations associated with an increased risk of multiple sclerosis (MS) and myasthenia gravis (MG). This may help improve methods of treatment.

Autoimmune disorders result from reactions by the body's immune system which in turn attack and destroy healthy cells.

"Our understanding of the causes of these diseases remains limited, but we do know that the immune system plays a key role in the debilitating processes that occur," explains Hanne F. Harbo, professor at the University of Oslo and head of the clinical science group at Oslo University Hospital.

"MS attacks the central nervous system, causing inflammatory processes that lead to a variety of neurological symptoms including paralysis, loss of sensory function, and problems with vision and bladder function. MG affects the transmission of signals between the peripheral motoric nerve cells and muscles, resulting in muscular fatigue in the patient."

The Norwegian researchers have taken part in an international cooperative effort to map 110 genetic variations that increase the risk of MS and MG. Most of these genetic variations have been mapped in recent years.

"Rapid advances have been made in this area of research," says Harbo.

## Genetic and environmental factors linked

Approximately 8 000 Norwegian are afflicted with MS. MG is far less prevalent, with only around 500 Norwegians affected.

One element preventing a better understanding of these disorders is that they are caused by a mix of genetic and environmental factors. They arise due to the unfortunate combination of genes that are associated with the disorders along with common factors occurring in the environment.

Viral infections - especially the Epstein-Barr virus – along with low levels of vitamin D in the blood and smoking are presumed to be moderate risk factors contributing to MS.

## Finding new risk genes using genetic testing

Participating in large international research projects, Hanne Harbo and colleagues have helped to identify a number of new risk genes for MS and MG. This has contributed significantly to a breakthrough in the genetics of MS.

The most important finding was that over 110 common risk variants show some sort of link to the risk of developing MS.

“We know that most of these risk variants on their own play little role in the development of MS. But mapping the collection of genes associated with MS represents an important advance in efforts to identify the key mechanisms behind its development,” says Harbo.

“Once we gain more insight into the mechanisms behind this disorder, it will be easier to shut down the pathways that trigger the disorder in cells,” she concludes.

### **Common among the population**

Approximately 150 of 100 000 inhabitants in Norway have MS, with the disorder afflicting more women than men and typically affecting young adults. The risk variant mostly highly associated with MS (HLA-DRB1\*1501) triples the risk of developing the disorder.

“We know that the risk variant HLA-DRB1\*1501 is common among the population and that its occurrence differs significantly among those who have MS and those who do not,” explains Harbo.

The Norwegian study of myasthenia gravis covers 370 MG patients and 650 healthy control subjects. The risk variant HLA-B\*08 showed the highest risk for developing MG among young persons while HLA-DRB1\*1501 posed the greatest risk among the elderly.

### **Genetic analyses solely as a research method**

Genetic testing is not currently part of the clinical treatment of patients with MS or MG, and is only used as a research method for uncovering causal mechanisms.

“Risk gene studies have provided new knowledge that is important to those working in the field. We will now move on to studying molecular mechanisms and how risk genes affect the clinical expression of the disorder,” Harbo explains.

The researchers have also examined environmental factors behind the incidence of MS and MG. Certain factors such as smoking appear to increase the risk of developing these disorders.

### **Targeting better treatment**

There is no existing treatment to completely cure MS or MG, but new medications are constantly emerging that reduce inflammation and the role it plays in the disorder.

“We hope to use our research findings to improve the knowledge base for developing more effective methods of treatment,” Harbo concludes.

 [8 000 Norwegian are afflicted with MS. \(Illustration photo: Colourbox\)](#) [5]

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Glenn Wells/Carol B. Eckmann

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