Can genes predict the clinical course of MS?

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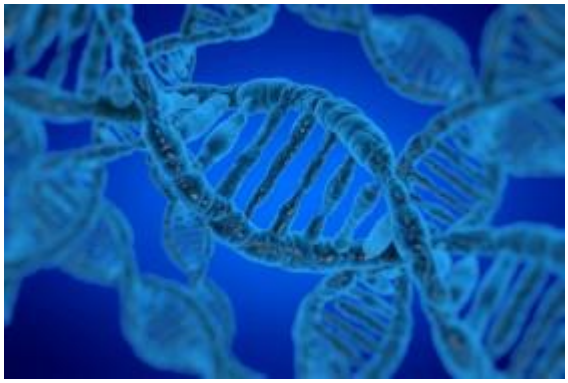

It is known that MS results from a combination of genetic and environmental factors. A huge amount of research both in Australia and internationally, has contributed to the identification of over 110 genes which contribute to a person's risk of developing MS. We know that MS is a varied disease that affects people differently, with a myriad of symptoms and different rates of accumulating disability but we don't know why. Scientists have attempted to determine whether genes also play a role in the way a person's MS develops over time. The ability to predict the future severity of the disease in a person is vital to improve counselling and decision making about appropriate treatments.

A new study from Australian researchers led by Professor Bruce Taylor at the Menzies Institute for Medical Research Tasmania has looked at the role of genetics on the clinical course of MS. The study used the Ausimmune/Auslong cohort, a resource that was established in 2002 and supported by MS Research Australia, and has underpinned a great number of studies into the factors that influence a person's experience of MS. The Ausimmune/Auslong cohort comprises a group of patients who had experienced a first demyelinating event that have been followed over many years. This group had a high chance of developing MS and this study aimed to determining whether the genetic makeup of the individuals played a role in their conversion to MS and the symptoms and disability they experienced over five years.

The study, published in the *Journal of Neurology, Neurosurgery and Psychiatry*, examined 127 people from the original cohort and concentrated on 116 genetic changes that have already been shown to increase the risk of developing MS. They found that of these, there was a group of seven genetic changes which increased a person's likelihood of converting to a full diagnosis of MS usually based on the development of a new relapse or new lesion on MRI and their subsequent relapse risk.
A different group of seven genetic changes predicted whether disability would significantly worsen over time. People who had a greater number of the seven genetic variations were more likely to have higher levels of disability. For example, people who had six of the seven genetic changes were much more likely to have disability progression than those who only had two of the changes.

These interesting results suggest that there are two genetic pathways at work in MS, one driving the inflammatory manifestations of MS (relapses) and another relating to neurodegeneration and disability progression in people with MS. This suggests the underlying processes are likely to be different and implies that different approaches to treatment may be warranted.

Another recent international study also looked at the role of genes in how severe a person's MS might be. This study, published in *Neurology Genetics*, which also included Professor Bruce Taylor and his colleague Associate Professor Ingrid van der Mei as authors, looked at MS patients from around the world, including Australia. This study used a base of 52 genetic changes which have been shown to be involved with MS and examined 7125 people including 204 from Australia. They found some evidence for the overall genetic makeup playing a role in disability accumulation over time. However, when the

analysis was restricted to people who had had MS for over ten years or more, they found that there was no effect of genes on the clinical outcomes.
There were a number of differences in the two studies, most significantly, the amount of time that people included in the study had been diagnosed with their MS. Other differences included the way that disability accumulation was measured, whether or not the people had a full diagnosis of MS and the analysis techniques used, including the genetic changes they chose to focus on.

Taken together the papers suggest that genetics play a role in disability progression in the mid-term but over the longer term of the disease, the role of genetics in disability outcomes seems to become less important. The Australian study calculated that even in the shorter five-year period, genes contribute only a third of the overall risk of increasing disability. This implies that other factors, such as environmental and lifestyle factors as well as treatment decisions, are playing a significant role in a person's MS experience. It is known for example that whether or not a person continues to smoke, after a diagnosis of MS, can influence their level of disability over time.

Professor Bruce Taylor commented, *'Studying factors that are associated with the disease course in MS is very difficult as there is significant variation in the rate of progression between individuals and even during the disease course of the individual. Therefore, having cohorts such as the Ausimmune/AusLong who have been followed for nearly 10 years allows us for the first time to start answering these important questions. If we know what drives a faster or slower rate of progression, we may be able to target these factors either by medication, behavioural or lifestyle changes to improve outcomes for people with MS'*.