Genes and MS

Our cells contain DNA, which is an extremely long molecule that is composed of four different subunits (called nucleotides) that are linked together in a chain, like beads on a necklace. The DNA contains the instructions for making proteins. Proteins are also long molecules, but they are made up of chains of amino acids. There are 20 amino acids. Three nucleotides code for one amino acid. The segment of DNA that codes for a single protein is called a gene.

When we reproduce, the DNA must be duplicated. This duplication is not always perfect, and the sequence of nucleotides in the children’s DNA may be slightly different from their parent’s DNA. These differences are called mutations. Over the history of humanity we have built up many mutations, creating the great diversity of people. Even individual genes may have different versions of nucleotide sequences coding for a protein.

Large studies have now been done looking for genes that are linked to MS. These studies involve thousands of patients. Blood samples are obtained on these patients and DNA from the samples is evaluated to determine the sequences (or codes) of thousands of genes. Current studies evaluate approximately 500,000 genes on each patient. Different forms (mutations) of each gene can be evaluated to see if that form of the gene is seen more commonly in patients with MS compared to people without MS.

Thus far, approximately 50 gene variations have been found to be more common in MS patients than in those without MS. Most of these are only slightly more frequent in MS patients. To date, only 3 genes are linked to MS tightly enough to be confident of their importance.
The gene with the strongest link to MS is named HLA-DRB1.1501. This is a variant of one of the HLA genes. HLA genes code proteins that are on the surface of lymphocytes and are key to lymphocytes interacting with their targets. This gene accounts for 4% of the variance in the risk of getting MS.

The other two genes that are linked to MS are named IL2RA and IL7RA. Both of the proteins from these genes serve as receptors on the surface of lymphocytes and help determine their activity. Each of these genes accounts for 0.2% of the variance in the risk of getting MS.

Other genes linked to MS explain even less of the risk of getting the disease.

**Importance of genetic studies in MS:**
- Genetic tests cannot currently tell us who is likely to get MS
- These studies have identified only a few genes that are more common in MS patients. This supports our view that MS is not caused by a single gene.
- The genes that have been identified each contribute only a small amount to the risk of getting MS. Altogether they still account for only a minor contribution to the risk of getting MS. This means that the major risk of getting MS is not determined by genetics, but by some environmental risk factor (see section on What Causes MS).
- All of the approximately 50 genes identified with MS involve parts of the immune system. This is reassuring because it suggested that we are not overlooking other possible causes of MS like genetic disorders of myelin formation, myelin health or myelin repair. This suggests that MS is caused by some environmental exposure (perhaps a virus) that interacts with the immune system to cause the disease.