# Genes unzipped: what our DNA can tell us about MS risk

How do genes affect the risk of developing MS?

## What are genes?

Genes carry information for the body, like the blueprints for different kinds of proteins. When we are born, our genes are passed down from our parents in pairs. You receive one half from your mother, and the other from your father. In those genes, errors or 'variants' often happen. Some gene variants can be helpful like reducing our chance of a disease. Other variants are harmless, changing how we perceive taste, or our ability to handle hot foods like chilli. There are also variants that may increase our risk of diseases like MS.

## Predicting the risk of disease from genes

Some diseases are caused primarily by genetic faults, like Huntington's disease, an inherited disease that damages the brain over time. If one parent has Huntington's disease, their child has a 50 per cent risk of developing the same disease. However, the risk is trickier to predict in MS, as it is thought to be caused by a combination of genetic and environmental factors.

## What is the level of risk if MS runs in the family?

MS is not believed to be an inherited disease. However, the risk of getting MS is higher in relatives of a person with the disease than in the general population, especially in the case of siblings, parents and children.

The risk of developing MS depends on how closely related you are to a family member with MS. In inherited conditions like Huntington's disease, identical twins will either both have MS or neither will because their genes are the same. However, if one identical twin has MS, the risk of the second twin developing MS during their lifetime is 20 to 30 per cent. This is why researchers agree that MS is not simply a genetic disease.

The risk of a sibling developing MS in their lifetime is around 1-3 per cent. Interestingly, non-identical twins who share half of their genes, like siblings, are a different story. If one identical twin has MS, the MS risk of the second twin is about 5 per cent.

Why do non-identical twins have a higher risk compared to ordinary siblings? It could be because non-identical twins share a more similar environment than siblings of different ages. Environmental factors – such as exposure to viruses, vitamin D levels and smoking - account for a large proportion of a person's MS risk.

The higher the number of relatives diagnosed with MS, the higher the risk of family members developing MS over their lifetime. Females also have a higher risk of developing MS compared to males. That being said, MS is not passed directly from parents to their children because is not caused by a single gene. While MS can occur more than once in a family, it is more likely that it won't.

### Certain gene errors may increase MS risk

The worldwide average risk of a person developing MS is 1 in 625, or 0.15 percent, but the risk in some parts of the world may be different due to the environment. Some studies have found that people who live closer to the equator have a lower risk of developing MS, while those living in countries at higher latitudes have a higher risk.

To understand the risk of variants on disease, gigantic genetic studies called genome-wide association studies (GWAS), have been carried out, which help scientists identify genes associated with a particular disease or trait. This is repeated in many people – sometimes up to 100,000 people. If some gene variants are more common in the group of people with MS than in people who do not have MS, then that variant may be involved in increasing the risk of MS.

Genetic variants that increase the risk of MS change how the body interacts with its environment. Many genes have been linked to proteins essential to the function of the immune system. Depending on where the gene variant hits, different proteins and therefore different functions in the body, are affected. For instance, some variants may cause changes to the development and maturation of immune cells such as B cells. Other variants have been found to potentiate B and Th cell activation, which can cause a faulty immune system. In MS, B- and T-cells interact in the peripheral and central nervous system to contribute to the mechanisms underlying the MS disease course.

## Calculating MS risk

More than 200 gene variants have been found. Each variant represents a very small part of overall MS risk. The more of these different genes a person carries, the higher the risk of developing MS.

If you could measure the effect of certain combinations of genetic variants, and combine this with the impact of environmental factors, it may be possible to calculate a person's 'risk score' of developing MS compared to the general population. Studies looking further into risk scores are ongoing (see Further Reading below).

At the moment, genetic tests for MS are not definitive. A person may have a whole group of gene variants that increase MS risk, but they will not develop MS. Therefore, genetic testing for MS is not used in clinics but for research purposes.

## Summary

Genes do play a role in MS, but the risk of MS is more complex. A person's risk of developing MS is the combination of genetic risk and environmental factors such as infections (e.g. Epstein Barr virus), vitamin D levels, smoking, alcohol, and weight during childhood.

In other words, a person carrying risk factor gene variants also needs to be in an environment that triggers the MS.

## Glossary

- **B cell: B** lymphocyte, a group of immune cells, all performing different functions
- **Genome**: the complete set of genetic information in an organism, for instance the human genome
- **GWAS**: a genome-wide association study, is a study of genetic variants or "genetic errors" across the whole genome in many different individuals to see if any variant is associated with a trait
  **Protein**: building blocks of the body. Their structure and function are determined by genes found in living organisms. Proteins are essential for the structure, function and regulation of all the cells in all the organs of our bodies. When gene errors occur (e.g. gene variants), they affect how the protein itself functions.
- **T cell:** T lymphocyte, a group of immune cells. Some types include CD4+ helper, CD8+ killer, and T memory cells, all performing different functions (see cellular response).

## Further reading

- Polygenic risk score association with multiple sclerosis susceptibility and phenotype in Europeans
- Predicting Multiple Sclerosis: Challenges and Opportunities
- Genes and Environment in Multiple Sclerosis project: A platform to investigate multiple sclerosis risk

## What our members say about genes and MS

- MS Australia
- National MS Society (USA)
- MS Society UK
- MS Society Canada
- German MS Society (under Ursachen)