

March 2022 Newsletter



Understanding Factors Affecting MS Onset

While MS is not an inherited disease, there are genetic factors that predispose people to it. One of the strongest genetic risk factors for MS is a mutation in the [HLA-DRB1 gene](#) called [HLA-DRB1*15:01](#). The HLA-DRB1 gene provides instructions for making a protein that plays a critical role in the immune system. It is part of a family of genes called the human leukocyte antigen (HLA) complex. The HLA complex helps the immune system distinguish the body's own proteins from proteins made by foreign invaders such as viruses and bacteria. About [200 genetic variations](#) outside the HLA complex have also been associated with MS.



A [recent study](#) conducted by Drs. Elina Misicka and Farren Briggs at Case Western Reserve University and their collaborators found that people with a higher genetic risk of MS (those that have more genetic variations) are likely to develop the disease at an earlier age. Participants' first MS symptom appeared at a mean age of 32. Investigators looked at data from 3,495 adults with MS, most of whom (71%) were women. Data for 1,268 participants came from the [ACP Repository](#). The remaining 2,227 participants were from Biogen-sponsored clinical trials, including the [ADVANCE trial](#), the [ASCEND trial](#), and

the [DECIDE trial](#). About 45% of all participants were positive for the HLA-DRB1*15:01 genetic variant. Genes are usually found in two copies (called [alleles](#)). Each copy is inherited from one parent. Results showed that people with the highest genetic risk (HLA-DRB1*15:01 in both gene copies plus other high-risk gene variants) were on average five years younger at disease onset than those with the lowest genetic risk (some disease-associated genetic variants but no copies of HLA-DRB1*15:01).



This is the first time that the genetic variants related to developing MS have been associated with an earlier age of onset. This finding is key to achieving better outcomes for people with MS. Those diagnosed with the disease earlier in life tend to experience more extreme symptoms over the course of the disease. If a person knows they

are at a higher risk for early onset, they and their healthcare team can be more aggressive with treatment (for example, make the decision to start MS disease modifying therapy (DMT) at a younger age).

Facilitating research such as this is central to ACP's mission. In 2018, ACP [announced](#) a collaboration with the [Regeneron Genetics Center](#) that sequenced the entire exome region of all DNA samples in the ACP Repository. The exome is the protein-coding region of the human genome, which represents under 2 percent of the genome, but contains a majority of the known inherited genetic variants associated with all diseases. According to ACP's data return policy, this information was added to the ACP Repository database for the benefit of future research. These data were instrumental in the Case Western study findings. Drs. Misicka, Briggs and their collaborators are taking a deeper dive into these data as their work toward better understanding the genetic factors related to MS onset continues.

