Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/neurofrontiers/genetic-pathways-in-ms-the-clinical-impact-of-a-chromosome-2-variant/32820/

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Genetic Pathways in MS: The Clinical Impact of a Chromosome 2 Variant

Announcer:
This is *NeuroFrontiers* on ReachMD. On this episode, Dr. Sergio Baranzini will be discussing the identification of a genetic variant associated with disease severity in multiple sclerosis, which he spoke about at ECTRIMS 2025. Dr. Baranzini is a Distinguished Professor of Neurology at the University of California San Francisco Weill Institute for Neurosciences. Let's hear from him now.

Dr. Baranzini:
After we were quite successful as part of the International MS Genetics Consortium in mapping all the genetic variants that contribute to MS susceptibility or to MS risk, the next stage of our research involves the genetics of disease progression or the genetics of the disease severity.

In this context, the latest large study that was conducted by the IMSGC involved 10,000 patients. And we screened more than six million DNA variants in them, and we conducted a genome-wide association study to identify one locus in chromosome 2 that we know now is the first locus to be associated with disease severity. What this means is that individuals inheriting two of these variants in a homozygote fashion—so inheriting the variant from both the maternal and paternal chromosomes—puts these individuals at a higher risk of developing a more severe disease.

We're interested in trying to understand the biology of the genes that sit nearby and, in particular, how computational approaches can also help us make sense of the biological implications and eventually come up with ideas and hypotheses to analyze this locus in more detail to develop countermeasures, including potential therapies that target these genes, to address this unmet need of disease progression in multiple sclerosis.

So the main finding of this study is that there is this locus, this region in chromosome 2 that when patients inherit this variant, they are more likely to develop an aggressive form of MS. And the main implication, if we can figure out what is the mechanism and the targets that could be approached therapeutically, is this could result in drugs that are more effective against this second stage of multiple sclerosis, which is the neurodegenerative component to which there is no known effective therapy today. So we think that mapping those regions of the genome is the necessary first step to be able to identify targets and ultimately develop effective therapies for patients with progressive MS.

The next steps are multi-pronged. We in my group are taking some of these approaches, but this information is public already, so many labs around the world are following with different strategies and capitalizing on this knowledge that we produced as a consortium. One of the steps forward that we're following up on is trying to understand from what is available today—experiments that have been performed that are already available publicly—what might be the implications on the targets, which might be the genes or proteins, and in which cell types these proteins might be expressed so that we can understand better how to design a therapeutic approach.

Other groups are following up on the biology of this information. For example, they're trying to create cell lines or mouse lines in which this gene has been altered, and they are trying to address it therapeutically what drugs can counteract the effects of this gene variant. So we think that both computational approaches and experimental approaches will be very important in the next few months to identify solid targets to which to direct new and novel therapies.

MS is a very complex disease. It's very difficult to understand, and if it's not from the help of patients who help and participate in research studies, this type of research could not be possible, so my gratitude to them. We feel really privileged and honored to be working towards a cure for MS.

Announcer:
That was Dr. Sergio Baranzini discussing his research into genetic variants in MS, which he presented at ECTRIMS 2025. To access this and other episodes in this series, visit *NeuroFrontiers* on ReachMD.com, where you can be part of the knowledge. Thanks for listening!