Transcript Details

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Uncovering Disease Progression in Multiple Sclerosis

Announcer Intro:
You're listening to *NeuroFrontiers* on ReachMD. On this episode, we'll hear from Dr. Sergio Baranzini, who's a Distinguished Professor of Neurology at the University of California San Francisco and co-senior author of a recent study that, for the first time, has identified a genetic variant associated with faster disease progression in multiple sclerosis. Let's hear from him now.

Dr. Baranzini:
This study was designed by the International Multiple Sclerosis Genetics Consortium, of which I'm part of, and as all the studies that the Consortium designs it takes the participation of several sites around the world, laboratories in the U.S., Europe, Australia, Japan, so it's really an international effort in which all the partners contribute samples from patients and also intellectual input so that we do this as a large collaborative effort.

The goal of this research was to ask the question of whether severity of the disease is influenced by genetics or not. We've known for a long time that risk to develop the disease is genetic, is inherited, and the consortium has been producing a number of studies in the last 20 years uncovering more and more genetic variants that predispose to multiple sclerosis. But the question of when someone is diagnosed with the disease, what kind of evolution will that person have, was always unanswered. We know that some patients after diagnoses follow a rapid decline, unfortunately, and they may be in a wheelchair by five or six years after the diagnosis, but we know there are other patients after 10 years of diagnosis are still running marathons. So what is that difference in disease scores, in disease severity—also at least in part genetically determined—so this is what we set out to study. We only looked at DNA from patients, and this is different from the study design that we have done before. When we were asking about susceptibility, the design was patients compared to healthy controls. In this case, it's only patients, and we have information about their disease progression, about their disease severity, so this is the question that we were trying to answer.

The outcome of this genetic study in which more than 10,000 patients participated in was the discovery of a single DNA variant, which is fairly common in the population, but if you are a patient who has MS and you carry two copies of this variant, you are more likely to develop an aggressive course that will imply a higher severity, and this is very significant. Even though it's a single variant, we think there's more. It's just a matter of statistical power that with 10,000 patients we are scratching the surface of statistical power.

But even though it's the first and the only one so far, we think it's clinically very meaningful. I'm going back to the clinical significance now. Individuals who inherit two copies of this variant will reach an EDSS disease severity of six in the EDSS scale, which severity of the disease is measured. It goes from zero to 10, and six is a landmark because it's a time point at which the patient needs a cane or walker to be able to walk. So patients who have two alleles of these variants are reaching this point of EDSS six almost four years earlier than patients who do not, so we think that this is very, very significant in terms of clinical implications, and it will spare out a search for therapeutic drugs that will manage this aspect of the disease, which so far hasn't been tapped.

There are next steps for the research. On the one hand, this discovery of a variant that confers additional risk to developing an aggressive course is the first one that is not related to the immune system as all the other variants that have been discovered with that influence risk of the disease, which are all related to the immune system and for which very successful and efficient therapies have been developed, but all of those therapies address the inflammatory component of the disease, and some of them are extremely effective at doing that. However, indefinitely, patients transition from an immune-driven disease to a more neurodegenerative form of the disease, and there's nothing for the group of patients or for those patients who transition. We think that with the discovery of this variant, new therapies will be developed that address this component, the neurodegenerative component.

And the discovery of genetic variants always directs the drug development for pharmaceutical industry, so the fact that there is now a genetic target, it will accelerate the development of therapies that will address this part of the disease. So we think that there's more to be discovered, and overall, is extremely good news for people who live with MS.

Announcer Close:
That was Dr. Sergio Baranzini discussing the recent discovery of a genetic variant associated with faster disease progression in patients with multiple sclerosis. To access this and other episodes in our series, visit ReachMD dot com slash Neuro Frontiers, where you can Be Part of the Knowledge. Thanks for listening!