Transcript Details
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MS Research: Using Epigenetic Clocks and Biomarkers to Assess Biological Aging

Announcer:
You're listening to *NeuroFrontiers* on ReachMD. On this episode, we'll discuss how we can use epigenetic clocks and biomarkers to assess biological aging in multiple sclerosis patients with Dr. Yinan Zhang. Dr. Zhang is an Assistant Professor of Neurology at Ohio State University. He also presented a session on this exact topic at the 2024 ACTRIMS Forum. Let's hear from him now.

Dr. Zhang:
So my session at ACTRIMS is focused on the study of biological aging in people with multiple sclerosis, and the reason why we're studying biological aging in MS is we know that chronological age is the biggest driver of disease progression in MS early on. People usually present with the relapsing-remitting stage of MS, followed by a higher risk of conversion to secondary progression with age. And we know that chronological age plays a role in this, but not so much the underlying cellular, molecular, and genetic effects of aging, which we call biological age.

And there are some ways that we can measure biological aging in MS by looking at what we call the pillars of aging. There are things like cellular senescence, epigenetic DNA methylation changes, oxidative stress, and so forth, but in this study, we chose two of the currently validated and popular biomarkers looking at cellular senescence and epigenetic alterations. And we measured these biomarkers prospectively in a cohort of patients with MS to see if they differ between the different MS phenotypes and also whether they differ compared to controls.

So there are two biomarkers that we're using in the study. One of them is called P16, which is a tumor suppressor marker in response to cellular senescence triggers. And the other biomarker that we're using is called the epigenetic clock. This is an algorithm that's kind of derived from DNA methylation patterns that's used to predict chronological age as well as age-related outcomes, like mortality, aging phenotypes, and so forth, and both of them are measured in blood. And, in fact, in our study, we're measuring it in peripheral blood T cells because P16 is most robustly expressing T cells, and for the epigenetic clock, we're measuring the same subtype.

So we present the data from about 95 patients with MS, including relapsing-remitting MS, secondary progressive MS, and primary progressive MS as well as a few dozen controls without MS, and what we have seen is that with the measurements of epigenetic clock, there appears to be a signal that epigenetic age acceleration is increased in people with the different MS phenotype. So what that means is that according to this biomarker, people with MS are aging faster than people without MS. Of course, the final results are still in progress, so we will have to wait until the study is over to be able to have adequate power calculations and such to make a conclusion.

And then in regards to the P16 measurements, normally what we see is that P16, which is a marker of cellular senescence, its expression increases logarithmically with age. So when a person gets older, their levels of P16 as measured in peripheral blood T cells also increase. So we see that in our healthy controls without MS, but to our surprise so far, we have not been able to find that chronological age correlation in P16 expression in the people with MS. So basically in young versus older patients with MS, their P16 levels all fluctuate, and that relates to the heterogeneity of the MS disease itself, so that kind of beckons some next steps to look at the associations between the biomarkers that we're looking at in our study and the different MS outcomes.

So the implications of this study is that if we can adequately assess and conclude that biological aging is contributing in some way to disease progression in MS, then we can potentially target aging mechanisms as a way to further treat MS. Right now, there is a big need in the treatment landscape for progressive forms of MS and especially in older adults with MS, but we're taking a new perspective at tackling the issue of aging. And this kind of goes along with a view called the geroscience hypothesis, which posits that many age-

related chronological diseases have a common denominator, which is aging itself, and by targeting aging processes, you can slow down and mitigate a lot of chronic conditions that are caused by aging.

Announcer:
That was Dr. Yinan Zhang talking about his presentation at the 2024 ACTRIMS Forum that focused on assessing biological aging in patients with multiple sclerosis. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!