

New Alzheimer's Gene Identified

Megan Brooks | October 13, 2015

Researchers have identified a new gene involved in the immune system that increases the risk for Alzheimer's disease (AD), providing a potential new target for prevention and treatment.

They found that older adults at risk for AD and those with the disease who carry a specific variant in the interleukin-1 receptor accessory protein (IL1RAP) had higher rates of amyloid plaque accumulation in the brain over 2 years. The effect of the variant was stronger than the well-known AD risk allele *APOE* ϵ 4.

"These findings suggest that targeting the IL1RAP immune pathway may be a viable approach for promoting the clearance of amyloid deposits and fighting an important cause of progression in Alzheimer's disease," Andrew J. Saykin, PsyD, director of the Indiana Alzheimer Disease Center, Indianapolis, and the national Alzheimer's Disease Neuroimaging Initiative Genetics Core, said in a statement.

The study was published in the October 1 issue of *Brain*.

Novel Association

The researchers conducted a genome-wide association study of longitudinal changes in brain amyloid burden measured by florbetapir positron emission tomography (PET) in nearly 500 individuals. They assessed the levels of brain amyloid deposits at an initial visit and again 2 years later.

Study participants came from the Alzheimer's Disease Neuroimaging Initiative, the Indiana Memory and Aging Study, the Religious Orders Study, and the Rush Memory and Aging Project, all longitudinal studies of older adults representing clinical stages along the continuum from normal aging to AD.

As expected, *APOE* ϵ 4 was associated with higher rates of amyloid plaque buildup. However, they also identified a novel association between a single nucleotide polymorphism in IL1RAP (rs12053868-G) and higher rates of amyloid accumulation, independent of *APOE* ϵ 4.

Carriers of the IL1RAP rs12053868-G variant showed accelerated cognitive decline and were more likely to progress from mild cognitive impairment to AD. They also showed greater longitudinal atrophy of the temporal cortex, which is involved in memory and had a lower level of microglial activity as measured by PET scans, the researchers report.

"This was an intriguing finding because IL1RAP is known to play a central role in the activity of microglia, the immune system cells that act as the brain's 'garbage disposal system' and the focus of heavy investigation in a variety of neurodegenerative diseases," Vijay K. Ramanan, MD, PhD, postdoctoral researcher at the Indiana University School of Medicine, Indianapolis, who worked on the study, said in the statement.

"These results suggest a crucial role of activated microglia in limiting amyloid accumulation and nominate the IL-1/IL1RAP pathway as a potential target for modulating this process," the investigators write.

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