Researchers find preclinical evidence that a nasal immunotherapy may help treat Alzheimer's disease

September 14 2023

Credit: Unsplash/CC0 Public Domain

Alzheimer's is a debilitating neurodegenerative and neuroinflammatory disease that is difficult to treat. Most existing therapies target the buildup

of amyloid beta (Aβ) plaques in the brain, which requires early intervention and intravenous therapy.

A team of researchers from Brigham and Women's Hospital, a founding member of the Mass General Brigham health care system, tested whether a therapy being tested in multiple sclerosis (MS) patients that dampens immune cell inflammation in the brain could have a positive effect in Alzheimer's mouse models. They found that a nasal immunotherapy—anti-CD3—reduced inflammation and improved cognition independent of Aβ plaques.

In this study, mice were treated three times a week with an intranasal anti-CD3 for five months. The therapy effectively limited the activation of microglia—immune cells responsible for inflammation in the brain. Treated mice performed better in behavioral tests including a water maze, demonstrating improved cognition. Researchers also identified changes in gene expression patterns in the brain and an expansion of regulatory T cells that fight disease in the periphery following treatment. All changes were independent of Aβ plaque levels.

Researchers plan to investigate the use of this immunotherapy in animals in conjunction with anti-amyloid therapies, and expand into human clinical trials. The work builds upon the team's previous studies testing foralumab—the only fully human anti-CD3 monoclonal antibody treatment—in patients with COVID-19 and MS.

"We provide evidence that intranasal anti-CD3 therapy can dampen microglia activation and expand T cells in a murine model of Alzheimer's," said corresponding author Howard L. Weiner, MD, of the Department of Neurology. "This represents a unique approach to treating later-stage Alzheimer's that can be applied to other inflammatory disease conditions as well."

The research is published in the journal *Proceedings of the National Academy of Sciences*.

More information: Juliana R. Lopes et al, Nasal administration of anti-CD3 monoclonal antibody ameliorates disease in a mouse model of Alzheimer's disease, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2309221120

Provided by Brigham and Women's Hospital