

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

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

of amyloid beta ($A\beta$) 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 $A\beta$ 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 $A\beta$ 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](https://doi.org/10.1073/pnas.2309221120)

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