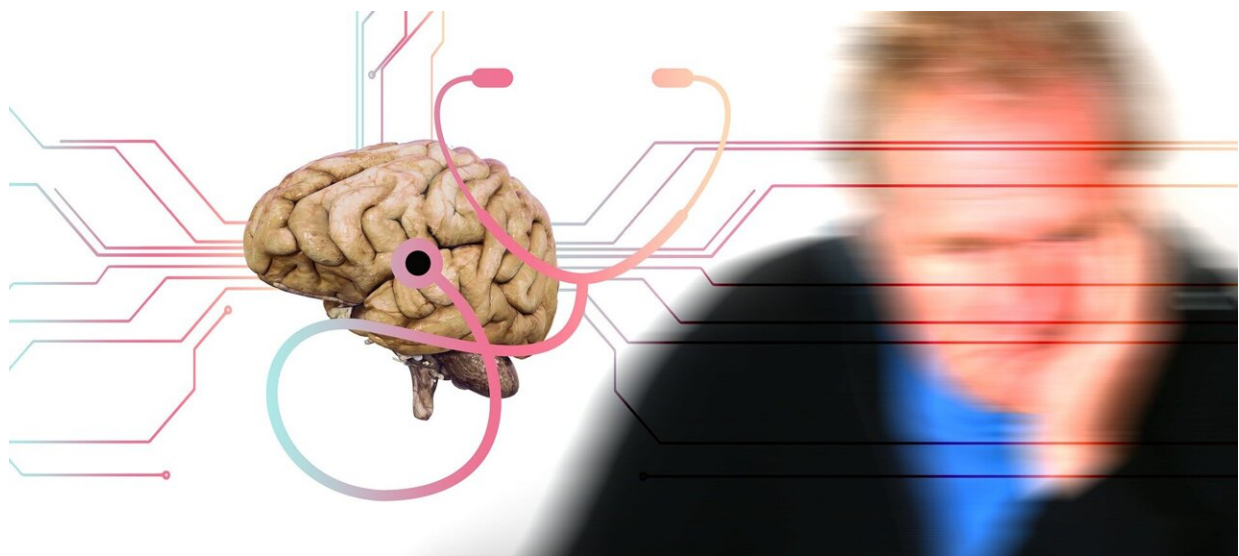# Promising immunotherapy treatment targets multiple pathogenic hallmarks of Alzheimer's disease

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Credit: Pixabay/CC0 Public Domain

Among progressive neurodegenerative diseases, Alzheimer's is one of the most common and most heartbreaking. It robs individuals of their memories and self-sufficiency and can even alter their personalities.

Nearly 7 million Americans over age 65 are living with Alzheimer's, and that number is projected to nearly double by the year 2050 as the population continues to age.

Jonathan Lovell, Ph.D., a professor in the Department of Biomedical Engineering at the University at Buffalo, is developing a novel immunotherapy approach to Alzheimer's treatment. He leads a research team that is working on a vaccine that targets multiple sites within the key polypeptides of both pathogenic hallmarks of the disease: amyloid-beta (Aβ) and tau.

The immunotherapy concept, which was published in the August issue of the journal *Brain, Behavior, and Immunity*, suggests that the body can mount an immune response to multiple epitopes of Aβ and tau, which are parts of those proteins that the immune system can recognize.

"What distinguishes our approach is that we're not just targeting one epitope in Alzheimer's, we're targeting multiple ones," Lovell said. "By targeting multiple epitopes simultaneously, we aim to train the immune system to recognize and attack these problematic proteins more broadly."

He has been working with researchers at the Institute for Basic Research in Developmental Disabilities (IBR), a New York State research entity based in Staten Island, to show that the immunotherapy can prevent and reduce Alzheimer's-like changes in mice that have been genetically modified to develop a condition similar to Alzheimer's.

The team also collaborated with the Buffalo startup POP Biotechnologies, which was co-founded by Lovell, and universities and hospitals in Canada, Japan and Korea.

## Plaques and tangles

In an Alzheimer's patient, the brain has two main disease hallmarks: amyloid plaques, made of mainly amyloid beta (Aβ), that build up outside brain cells, and neurofibrillary tangles of the protein tau inside

the [brain cells](link). Together, they affect memory, the ability to find words, work with numbers, make decisions and follow familiar routes and directions.

"The idea with this immunotherapy is that the patient will make antibodies that will either clear these plaques and tangles or slow their progression," Lovell said. "The ultimate goal of this approach is to reverse disease progression."

The immunotherapy, which Lovell and his team developed, includes epitopes from both Aβ and tau proteins. These are mixed with special liposomes, or tiny fat bubbles, which help deliver the vaccine and boost the immune response.

"What we've found is that the mice that received the immunotherapy early on showed fewer signs of Alzheimer's-related brain damage and performed better in [cognitive tests](link)," Lovell said. "The vaccine appears safe and didn't cause unwanted side effects."

The plan is to eventually get FDA approval to test the vaccine in human trials.

## Longtime study of Alzheimer's

Lovell started working on this immunotherapy concept over five years ago. He recently connected with the researchers at IBR who have expertise in the disease. Now, he and a few graduate students in his lab regularly send different iterations of the vaccine to the institute researchers to test on the mice.

"It was catalytic when we connected with the institute because they have the appropriate experience in the Alzheimer's animal models to test our vaccine," he said. "It's been an exciting collaboration."

IBR researchers have been studying Alzheimer's disease for more than 40 years, noted Cheng-Xin Gong, Ph.D., professor of neuroscience at the institute and one of the corresponding authors of the study.

"Our former chair of the Department of Neurochemistry of IBR discovered tau as the protein constituent of tangles in the 1980s, and since then, we've been working on finding treatments," Gong said. "Immunotherapy has been very hot recently. Almost all of the studies are attacking one single target, which is why this study is unique.

"Most cases of Alzheimer's are sporadic, rather than genetic," Gong explained. "They have more than one cause. If we can target more than one pathological protein, theoretically, this could be more effective."

Currently, no FDA-approved active immunotherapies exist that are specifically designed to treat Alzheimer's disease. Rather, most of the treatments that have recently been approved for Alzheimer's are focused on symptom management and have only shown small to modest gains.

## Moving toward human trials

While the researchers originally administered the vaccine early on, before the mice developed significant symptoms of dementia, they are now testing it on older mice with the disease to see how they fare.

"We're now working to test this active immunotherapy approach in a therapeutic setting," Lovell explained. "We're also working on the logistics of figuring out how we could move this vaccine from mice into humans as soon as possible."

If all goes well, he predicts human trials could become a reality in the next few years and possibly overseas.

"The underlying technology of this [immunotherapy](#) has already been tested in humans in Korea for a COVID-19 [vaccine](#), and we would support working with partners there to advance the translation of the technology there," Lovell said.

The first step is to establish manufacturing standards, he said. Once that is established, they will move forward on improving important metrics such as safety testing prior to human testing.

"Alzheimer's is such a devastating disease that we need bold solutions to address it," Lovell said.

**More information:** Yiting Song et al, A pentavalent peptide vaccine elicits Aβ and tau antibodies with prophylactic activity in an Alzheimer's disease mouse model, *Brain, Behavior, and Immunity* (2024). [DOI: 10.1016/j.bbi.2024.08.028](#)

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