

Cancer chemotherapy drug reverses Alzheimer's symptoms in mice

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A drug commonly used to treat cancer can restore memory and cognitive

function in mice that display symptoms of Alzheimer's disease, new UBC research has found.

The drug, Axitinib, inhibits the growth of new blood vessels in the brain—a feature shared by both cancer tumors and Alzheimer's disease, but this hallmark represents a new target for Alzheimer's therapies.

Mice with Alzheimer's disease that underwent the therapy not only exhibited a reduction in blood vessels and other Alzheimer's markers in their brains, they also performed remarkably well in tests designed to measure learning and memory.

"We are really very excited, because these findings suggest we can repurpose approved anti-cancer drugs for use as treatments for Alzheimer's disease," said Professor Wilf Jefferies, the study's senior author and principal investigator at the Centre for Blood Research, Vancouver Prostate Centre and Michael Smith Laboratories. "It could shorten the [clinical development](#) by years."

Alzheimer's disease is estimated to affect 50 million people worldwide. The condition is characterized by cognitive decline, memory loss and dysfunctional changes in the brain.

Potential Alzheimer's treatments have shown promise in animal models before, but failed in [clinical trials](#). Typically, these strategies target a protein called tau or a protein fragment known as beta-amyloid, but the UBC researchers chose a different approach. They left the traditional targets alone and instead focused on curbing angiogenesis, the growth of new blood vessels.

"The vast majority of clinical trials have either directly or indirectly targeted beta-amyloid or tau," said Prof. Jefferies. "Other than some controversial recent results, there's been a paucity of success in these

clinical trials. So, a great deal of effort appears to have been directed toward the wrong targets for reversing Alzheimer's disease."

Setting the stage for the present study, Prof. Jefferies' earlier pioneering work had shown that the proliferation of blood vessels compromises the [blood-brain barrier](#) in patients with Alzheimer's disease. This barrier, made largely of blood vessels, is believed to protect the brain from infection because foreign molecules cannot easily cross it.

Since cancerous tumors also rely on new blood vessel growth to survive and thrive, the researchers reasoned that a proven anti-cancer drug might halt the process in Alzheimer's.

"Axitinib, the anti-cancer drug we used, blocks a receptor in the brain called a tyrosine kinase receptor, which is partly responsible for spurring blood vessel formation," explained Dr. Chaahat Singh, the paper's first author and a postdoctoral fellow working with Prof. Jefferies. "It stops abnormal [blood vessels](#) from growing, which then prevents many downstream effects."

By using Axitinib for just one month, the researchers dramatically reduced blood [vessel](#) growth, restored the [blood](#)-brain barrier, and most significantly, helped mice perform better on cognitive tests.

In a typical test, a mouse is trained how to reach a reward through a maze. A healthy mouse can find its way back to the reward, while an animal with Alzheimer's disease symptoms cannot.

The treatment has only been applied to mice thus far. Clinical trials will be needed to assess the effectiveness of this treatment in patients with Alzheimer's disease, as well as consideration for the long-term use of [anti-cancer drugs](#) in people living with Alzheimer's, who are mostly elders.

Still, the researchers are optimistic. If Axitinib does work well in humans, repurposing an already-approved drug could more rapidly advance its use for Alzheimer's.

"Researchers including myself have been disappointed in observing numerous clinical trials for Alzheimer's [disease](#) fail to reach their clinical endpoints," said Prof. Jefferies. "The therapeutic approach we discovered has an opportunity to revise the clinical treatment of Alzheimer's patients, which I think is absolutely needed at this point for the field to advance."

Prof. Jefferies and his collaborators have shared their findings in *EBioMedicine*, published by *The Lancet*.

More information: Wilf Jefferies et al, Reversing pathology in a preclinical model of Alzheimer's disease by hacking cerebrovascular neoangiogenesis with advanced cancer therapeutics, *EBioMedicine* (2021). [DOI: 10.1016/j.ebiom.2021.103503](https://doi.org/10.1016/j.ebiom.2021.103503)

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