

Researchers test sugary solution to Alzheimer's

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(Medical Xpress) -- Slowing or preventing the development of Alzheimer's disease, a fatal brain condition expected to hit one in 85 people globally by 2050, may be as simple as ensuring a brain protein's sugar levels are maintained.

That's the conclusion seven researchers, including David Vocadlo, a Simon Fraser University chemistry professor and Canada Research Chair in Chemical Glycobiology, make in the latest issue of [Nature Chemical Biology](#).

The journal has published the researchers' latest paper Increasing O-GlcNAc slows neurodegeneration and stabilizes [tau](#) against aggregation.

Vocadlo and his colleagues describe how they've used an inhibitor they've chemically created — Thiamet-G — to stop O-GlcNAcase, a naturally occurring enzyme, from depleting the protein Tau of sugar molecules.

“The general thinking in science,” says Vocadlo, “is that Tau stabilizes structures in the brain called microtubules. They are kind of like highways inside cells that allow cells to move things around.”

Previous research has shown that the linkage of these sugar molecules to proteins, like Tau, in cells is essential. In fact, says Vocadlo, researchers have tried but failed to rear mice that don't have these sugar molecules attached to proteins.

Vocadlo, an accomplished chess player in his spare time, is having great success checkmating troublesome enzymes with inhibitors he and his students are creating in the SFU chemistry department's Laboratory of Chemical Glycobiology.

Research prior to Vocadlo's has shown that clumps of Tau from an Alzheimer brain have almost none of this sugar attached to them, and O-GlcNAcase is the enzyme that is robbing them.

Such clumping is an early event in the development of Alzheimer's and the number of clumps correlate with the disease's severity.

Scott Yuzwa and Xiaoyang Shan, grad students in Vocadlo's lab, found that Thiamet-G blocks O-GlcNAcase from removing sugars off Tau in mice that drank water with a daily dose of the inhibitor. Yuzwa and Shan are co-first authors on this paper.

The research team found that mice given the inhibitor had fewer clumps of Tau and maintained healthier brains.

"This work shows targeting the enzyme O-GlcNAcase with inhibitors is a new potential approach to treating Alzheimer's," says Vocadlo. "This is vital since to date there are no treatments to slow its progression.

"A lot of effort is needed to tackle this disease and different approaches should be pursued to maximize the chance of successfully fighting it. In the short term, we need to develop better inhibitors of the [enzyme](#) and test them in mice. Once we have better inhibitors, they can be clinically tested.

More information: www.nature.com/nchembio/index.html ,
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