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Alzheimer's researcher reveals a protein's dual destructiveness—and therapeutic potential

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A scientist at the University of British Columbia and Vancouver Coastal Health has identified the molecule that controls a scissor-like protein responsible for the production of plaques – the telltale sign of Alzheimer's disease (AD).

The molecule, known as GSK3-beta, activates a gene that creates a protein, called BACE1. When BACE1 cuts another protein, called APP, the resulting fragment – known as amyloid beta – forms tiny fibers that clump together into plaques in the brain, eventually killing neural cells.

Using an animal model, Dr. Weihong Song, Canada Research Chair in Alzheimer's Disease and professor of psychiatry, found that disabling GSK3-beta's effect in mice resulted in less BACE1 and far fewer deposits of amyloid in their brains. Song's research, published online today in the Journal of Clinical Investigation, also found that such mice performed better than untreated mice on memory tests.

Previous research had shown that GSK3-beta spurred the growth of twisted fibers inside neurons, known as tangles – another hallmark of AD. Song says his discovery of the protein's dual destructiveness makes it a promising target for drug research.

GSK3-beta, however, is a versatile enzyme that controls many vital physiological functions. The drug used to inhibit GSK3-beta in the mice

is too indiscriminate, and could cause several serious side effects, including cancer.

"If we can find a way to stop GSK3-beta's specific reaction with BACE1, and still leave it intact to perform other crucial tasks, we have a much better chance of treating AD and preventing its progression," says Song, a member of the Brain Research Centre at UBC and the Vancouver Coastal Health Research Institute (VCHRI), and Director of the Townsend Family Laboratories at UBC.

Provided by University of British Columbia