Protein regulates enzyme linked to Alzheimer's disease

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Researchers at Tufts University School of Medicine have zeroed in on a protein that may play a role in the progression of Alzheimer's disease. The team found that increasing levels of the protein (called GGA3) prevented the accumulation of an enzyme linked to Alzheimer's. The strategy may lead to new treatments for the neurodegenerative disease. The findings were published online May 18 in the *Journal of Biological Chemistry*.

People with Alzheimer's disease typically have higher levels of an enzyme called BACE1 in their brains. BACE1 produces a toxin that researchers have pinpointed as a cause of Alzheimer's, and now, researchers have found a way to prevent BACE1 from accumulating in the brain.

"We have identified the protein that takes this enzyme to the cell's garbage disposal for removal. Increasing levels of the protein allows more of the enzyme to be eliminated, possibly preventing the high levels seen in people with Alzheimer's disease," said senior author Giuseppina Tesco, MD, PhD, assistant professor in the department of neuroscience at Tufts University School of Medicine (TUSM).

Tesco and colleagues previously discovered that levels of the GGA3 protein were significantly lower in the brains of Alzheimer's patients than those free of the disease. In the current in vitro study, the team also found, unexpectedly, that the GGA3 protein must bind with the regulatory protein ubiquitin in order to lower enzyme levels.

"This insight advances our understanding of the molecular mechanisms of Alzheimer's disease. We hope that our approach will lead to new therapies that treat and prevent Alzheimer's, which currently affects as many as 5.1 million Americans," said Tesco. Tesco is also a member of the neuroscience program faculty at the Sackler School of Graduate Biomedical Sciences at Tufts, leading the Alzheimer's disease research laboratory.

Alzheimer's disease is a progressive neurodegenerative disorder that results in loss of memory and cognitive function. It is the most common cause of dementia in adults age 65 and over. Currently, prescription drugs are available that may slow the progression of the disease, but none of these medications are effective in stopping the progression of Alzheimer's.

More information: Kang EL, Cameron AN, Piazza F, Walker KR, Tesco G. Journal of Biological Chemistry. 2010. "Ubiquitin Regulates GGA3-Mediated Degradation of BACE1." Published online May 18, 2010, doi:10.1074/jbc.M109.092742

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