Published on *American Council on Science and Health* (https://www.acsh.org)

Key for Alzheimer s Treatment May Be Newly-Found Protein

By Lila Abassi — November 18, 2015

[1]

via shutterstock [2]

Alzheimer s disease (AD) is the most common cause of dementia. It is a complex and heterogeneous illness characterized by the progressive loss of brain function. Brain tissues for those diagnosed with AD feature an accumulation of extracellular plaques known as senile plaques or Î²-amyloid (AÎ²) as well as intracellular tangles of proteins called tau. These aberrations induce neurotoxicity and inflammation that cause loss of neurons, eventually impairing key functions of the brain that involve memory, cognition and personality.

A new study published in *Science Translational Medicine* has identified a new protein involved in the plaque formation pathway that can serve as a potential new target for the treatment of AD.

It has long been postulated that altered cholesterol metabolism is a key link to the development of AD. ApoE stands for apolipoprotein E, a protein that operates like a molecular truck that shuttles cholesterol in the brain. A mutation of this molecular truck (APOE genotype) is strongly linked to the development of senile plaques, and it has been shown previously that by deleting the APOE gene it would reduce plaque aggregation in the brain.

A cell surface receptor called the low-density lipoprotein receptor (LDLR) is responsible for binding ApoE. If you increase the amount of LDLR, then you can decrease the presence of ApoE and thus reduce the amount of plaques in the brain. In mouse models, researchers in this study discovered an enzyme they called Idol, which is responsible for degrading LDLR. When they silenced the activity of Idol they observed a rise in LDLR on the cell surface. Downstream of that, more ApoE was cleared away as were the amount of plaques present in mice brain.

In mice with Alzheimer s disease, those with Idol deficiency experienced decreased plaque burden and overall reduced inflammation in the brain as compared to control mice with normal Idol levels. It has been postulated that the loss of Idol stimulates the action of cells in the brain called

microglia (think of them as garbage trucks of the brain) that help clear amyloid plaques and ApoE.

With regard to future therapeutic interventions, this pathway serves as a target for further investigation. Idol inhibition can potentially subdue the formation and/or enhance the clearance of these neurotoxic plaques that will ultimately pave the way for treating people suffering from what is considered an incurable disease.

Links

[1] http://acsh.org/wp-content/uploads/2015/11/shutterstock_103291430.jpg

[2] http://shutterstock.com