

New key factor identified in the development of Alzheimer's disease

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Inheritance of an extra copy of the gene- β -amyloid precursor protein, APP, in individuals with Down syndrome leads to the inevitable development of early onset Alzheimer's disease, known to be linked to the deposition of Amyloid β peptide or A β in the brain. However, a new study published online by *Proceedings of the National Academy of Sciences* identifies β CTF, a small protein found in APP, as a novel factor for the development of Alzheimer's disease related endosome abnormalities, which have also been tied previously to the loss of brain cells in Alzheimer's disease.

"In the study, using the cells from individuals with [Down syndrome](#) that are genetically predisposed to developing [Alzheimer's disease](#), we showed that elevated levels of β CTF, independent of A β , cause a specific pattern of endosome defects with similar pathology of brain cells in Alzheimer's disease," said Ying Jiang, PhD, lead author and clinical instructor in the Department of Psychiatry at NYU Langone Medical Center. "Our research was successfully able to pinpoint that β CTF causes Alzheimer's disease -related endosome defects and that we could successfully reverse these endosome defects by lowering β CTF levels in the cells."

Endosomes are membrane compartments in cells that support cell survival by absorbing outside nutrients and are crucial in neuronal functions. In Alzheimer's disease, endosome abnormalities are the earliest neuropathologic features to develop, appearing even earlier in cases where one of several major genetic risk factors for the disease in

inherited. Endosomes are also suspected sites of A β production in the cells.

"In the field of Alzheimer's research, we have been questioning whether A β is the only target to better understand the progression of Alzheimer's disease and if lowering A β is the only hoped-for therapy," said Ralph Nixon, MD, PhD, professor, psychiatry and cell biology, director, NYU Center of Excellence on Brain Aging and the Silberstein Alzheimer's Institute at NYU Langone Medical Center. "This study demonstrates that an alternative protein factor, β CTF, derived from the gene APP, is also unequivocally involved in Alzheimer's disease and may be of additional importance for the development of future effective therapies."

Provided by New York University School of Medicine

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