Inhibitory effects of dipeptide analogue, DAPT, on γ-secretase causing decrease in amyloid-β concentration in neuroblastoma cells

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Abstract

Alzheimer's disease is a very common type of dementia that destroys memory and other important mental functions. It is a neurodegenerative disorder which affects over 5 million people in the United States alone. In fact, it is the 6th leading cause of death in the United States, and on average, an American is diagnosed with Alzheimer's disease every 66 seconds. This can be a familial or sporadic disease which is primarily caused by the destruction of neurons which starts from the hippocampus and spreads throughout the brain (cerebellum is spared). The apoptosis of the countless neurons seems to be caused by a multitude of factors including amyloid-beta plaques, Tau tangles, and neuronal loss. For the sake of this investigation, there will be a primary focus on the amyloid-beta plaques because the accumulation or buildup of neurotoxic plaques on the neurons seems to be a key factor in Alzheimer's disease. Enzymes called γ-secretase and β-secretase cleave a protein called an amyloid precursor protein (APP) to form these amyloid-beta peptides which can accumulate and form neurotoxic plaques. Previous studies have found that DAPT, a dipeptide analogue, is effective in inhibiting γ secretase thus decreasing amyloid-beta concentration in the brain. This study confirms the efficacy of DAPT in inhibiting γ-secretase, but also investigates the alternative inhibitory effects of other drugs like Activase® rt-PA (alteplase), a tissue plasminogen activator typically used for treatment of stroke, and clonazepam (E64), a pill used to treat panic disorder and anxiety. Although the goal was to see the effects on Aβ40 (40 amino acid amyloid-beta chain) and Aβ42 (42 amino acid amyloid-beta chain) production, only the effects of Aβ40 production were examined due to possible contamination in the Aβ42 tests.

Biography:

Arnav Gupta is passionate about exploring causal relationships of drugs commonly used to treat neurodegenerative disorder. Arnav is interested in pursuing a career in neuroscience. His passion in studying the brain and memory has inspired him to do research about Alzheimer's disease. This common disorder presents so many unanswered questions, and Arnav is motivated to do further research in the future to answer some of these questions.

Research Interests: Neuroscience, Alzheimer disease, Stem Cells, neurodegenerative disorder

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