

The β -Secretase Enzyme BACE1: A Biochemical Enigma for Alzheimer's Disease

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Abstract: Beta site amyloid precursor protein cleaving enzyme 1 (BACE1) is a rational target in Alzheimer's Disease (AD) drug development due to its role in amyloidogenic cleavage of Amyloid Precursor Protein (APP) in generating Amyloid β ($A\beta$). This β -secretase cleaves not only Amyloid Precursor Protein (APP) and its homologues, but also small series of substrates including neuregulin and β subunit of voltage-gated sodium channel that play a very important role in the development and normal function of the brain. Moreover, BACE1 is modulated at the post-translational level by several factors that are associated with both physiological and pathological functions. Since the discovery of BACE1 over a decade ago, medicinal chemistry and pharmacokinetics of BACE1 small molecule inhibitors have proven challenging for the treatment of Alzheimer's disease.

Key words: Alzheimer's disease; Amyloid Precursor Protein (APP); Amyloid β ($A\beta$); BACE1; palmitoylation; β -pathway.

Link: [https://pubmed.ncbi.nlm.nih.gov/32452328/#:~:text=Beta%20site%20amyloid%20precursor%20protein,generating%20Amyloid%20CE%20\(A%CE%B2\).](https://pubmed.ncbi.nlm.nih.gov/32452328/#:~:text=Beta%20site%20amyloid%20precursor%20protein,generating%20Amyloid%20CE%20(A%CE%B2).)