Deposition of amyloid β protein (Ab) in the brains is one of the hallmarks of AD pathogenesis. Ab is generated from a larger b-amyloid precursor protein (APP) by sequential cleavages of b-secretase and γ-secretase. Beta-site APP cleaving enzyme 1 (BACE1), the b-secretase in vivo, is essential for Ab production. Despite robust expression of APP gene resulting in high level of APP protein in vivo, Ab production through the amyloidogenic pathway of APP processing is a rare occurrence under normal condition. Previous studies showed that BACE1 can cleave APP both at the ASP+1 site and at the Glu+11 site of Aβ domain. Cleavage at ASP+1 is required for generating full length Aβ and increase in cleavage at ASP+1 site has been considered as one of the major pathological pathways in AD cases. Swedish mutant APP, a genetic defect in APP gene causing early onset of Familial AD, increased BACE1 cleavage at ASP+1 site, resulting in significant increase in Aβ production. To further examine how APP processing and Ab production are regulated by BACE1 and its implication in AD pathogenesis and drug development, several cell lines stably expressing BACE1, wildtype APP and Swedish mutant APP were established. Generation of APP CTFs and Ab species from the stable cell lines and postmortem brain tissues from AD patients were analyzed. We found that BACE1 differentially processed Swedish and wildtype APP proteins. The results suggest that the preferential cleavage site by BACE1 may play an important role in AD pathogenesis under certain pathological conditions.