Researchers at the University of South Florida have developed a novel peptide for treating or slowing the progression of Aβ-related disorders including Alzheimer’s disease (AD).

Beta-secretase (BACE1) is one of two enzymes responsible for amyloid-β (Aβ) generation, a pathology of AD and other Aβ-related disorders. This knowledge has been used to develop inhibitors of this enzyme that will reduce Aβ production. However, clinical trials of previous BACE1 inhibitors have demonstrated the difficulty of this task due to the ubiquitous nature and multiple substrates of BACE1. Thus, there is still a need to find a way to modulate this enzyme without incurring adverse off-target effects.

University of South Florida scientists have developed an APP-Tat fusion peptide (TAT-APPsweBBP) to attenuate Aβ production and prevent or treat the onset of Aβ-related disorders. APPsweBBP has an anti-amyloidogenic effect that is mediated through selective and specific inhibition of the APP β-secretase-cleavage, an amyloidogenic pathway for APP processing normally found in AD individuals. Preliminary studies have demonstrated reduced Aβ production as well as improved hippocampal-dependent learning and memory in 5XFAD mice. This peptide holds great potential as an improved therapy for various disorders including Alzheimer’s disease, HIV-associated neurocognitive impairment, Lewy Body Dementia, cerebral amyloid angiopathy, inclusion body myositis, and mild cognitive impairment.

**ADVANTAGES:**

- Higher affinity for BACE than native APP
- Markedly reduces Aβ deposits
- Minimizes adverse side effects
- Improves learning and memory

**Novel BACE1 Inhibitor Peptide**

**3-D Structures of APP-Based BACE1 Inhibitors**

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