Key Points
- **Selective α-site cleavage**
- **Bypasses endogenous inhibition**
- **High substrate specificity**
- **High-efficiency Aβ clearance**
- **Suppression of fibril formation**

Amyloid-β–Degrading Enzymes Derived from Habu Snake Venom

A Highly Selective Amyloid-β Degrader as a Seed for Alzheimer's Disease Therapeutics

Overview

Current Alzheimer's disease therapies provide only limited cognitive benefit, and there is an unmet need for disease-modifying drugs that directly reduce amyloid-β (Aβ) accumulation.

The inventors identified habu snake (*Protobothrops flavoviridis*) venom metalloproteinases (SVMPs), evolutionarily related to non-amyloidogenic APP-processing ADAM proteases, as potent Aβ-degrading enzymes.

In vitro, an SVMP cocktail cleaved secreted Aβ at the APP α-cleavage–equivalent site, converted it to non-toxic p3 fragments, and reduced Aβ levels in culture medium by about 90%.

Among these, the flavoridin-precursor–derived SVMP targets both monomeric and aggregated Aβ and shows higher substrate selectivity than neprilysin with minimal neuropeptide degradation, supporting its potential as a low-toxicity, disease-modifying AD drug lead.

Features・Outstandings

Addition of an SVMP cocktail to the culture medium of Aβ-secreting cells reduced secreted Aβ levels to approximately 10% of those in untreated controls.

Fida Neo analysis indicates that flavoridin acts on Aβ protofibrils.

Product Application

- ☐ A gene therapy product that employs an AAV vector to drive sustained brain expression of the flavoridin precursor gene and thereby promote Aβ degradation.
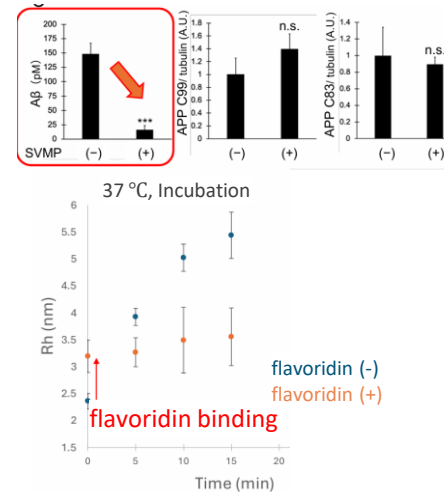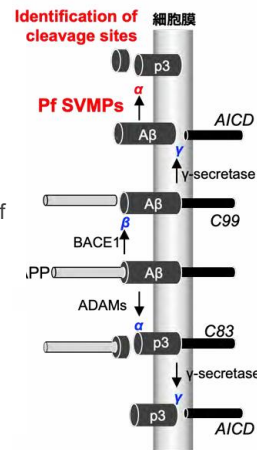 ==in vivo efficacy data to be obtained==

Related Works

[1] Futai et al. A Metalloproteinase Cocktail from the Venom of *Protobothrops flavoviridis* Cleaves Amyloid Beta Peptides at the α-Cleavage Site. *Toxins*. 2023; 15(8):500.

IP Data

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