Tohoku Univ. Technology

CSL2 Lectin for Alzheimer's Drug Discovery

A Novel Mechanistic Approach Through Modulation of Intracellular APP Trafficking

Overview

Alzheimer's disease therapeutics with novel mechanisms are needed to complement or replace existing treatments. Aβ production from APP occurs predominantly in lipid rafts. Previous research showed that a nontoxigenic form of Shiga toxin 2 binds Gb3 (Galα[1–4]-Galβ[1–4]-Glcβ-ceramide), a lipid raft glycosphingolipid, inducing lysosomal APP degradation and suppressing Aβ production (*1).The inventors investigated Gb3-binding chum salmon lectins (CSLs) and found that CSL2 reduces APP, C99, and Aβ levels, accompanied by strong co-localization of CSL2 and APP in lysosomes. Cryo-electron microscopy revealed its distinctive 24-mer architecture. This technology offers a novel approach to suppressing amyloid production through APP lysosomal degradation. Further studies will assess brain delivery, safety, and efficacy toward therapeutic development.

*1 Biochemical and Biophysical Research Communications,557,2021,P247-253

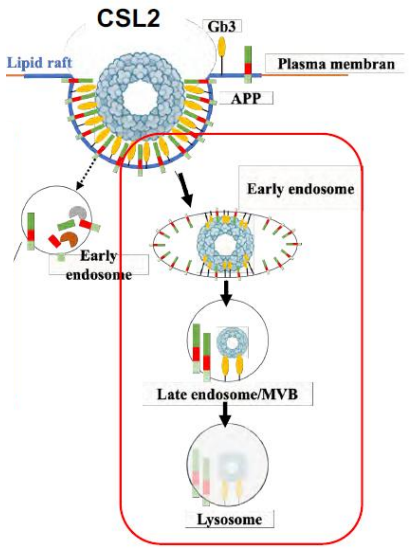
Product Application

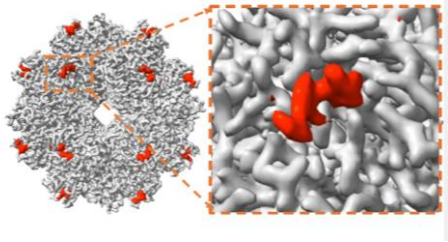
- Protein therapeutics that promote lysosomal trafficking and degradation of APP, or gene-based therapeutics that express such proteins in vivo.

IP Data

IP No.	:	JP2025-146968、PCT/JP2026/031961
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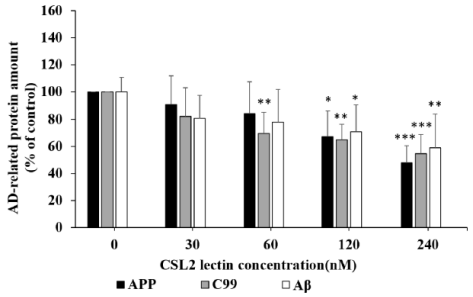
Features・Outstandings

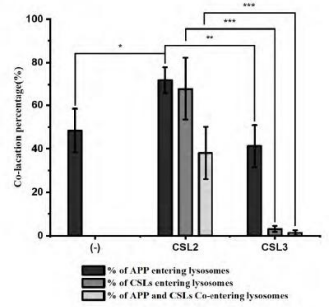




Left: CSL2-mediated lysosomal degradation pathway of APP/Aβ
Above: Gb3-binding sites in the CSL2 24-mer

Through multivalent binding, the 24-mer structure of CSL2 induces Gb3 clustering, triggering lipid raft-dependent endocytosis and trafficking to lysosomes
→ Promotes lysosomal degradation of APP





CSL2 significantly reduced APP, C99, and Aβ in a dose-dependent manner(**Left**) and also exhibited strong co-localization with APP(**Right**).

Contact

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