

Targeting fibrillary ApoE4 for treating Alzheimer's disease

Alzheimer's disease (AD) pathology is characterized by neurodegeneration from abnormal protein deposits (neurofibrillary tangles and plaques). Early-stage amyloid- β (A β) accumulation triggers pathological cascade leading to cognitive decline. The growth and aggregation of misfolded proteins like A β are central to the disease process, though the initial trigger is yet unidentified. Genetic studies have found that APOE, especially the APOE4 allele, is a major risk factor for sporadic AD.



Knockout animal models indicate that loss of APOE leads to decreased amyloid plaque buildup, suggesting APOE plays a dual role in plaque biology. Here, we report the use of fibrillary ApoE itself and antigen-binding peptides targeting fibrillary ApoE used individually or in combination to serve in both therapeutic and diagnostic roles.

- 01 Promising preventive therapy pathway for ApoE4 carriers at high risk for AD
- 02 Specific targeting of pathological fibrillary ApoE4 while preserving normal protein function
- 03 Ongoing: generating specific monoclonal antibodies against fibrillary ApoE4 for targeted therapeutic intervention

REFERENCES:

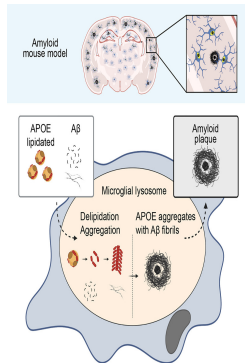


Kaji et al., 2024, Immunity

IP RIGHTS

PCT phase

2025



CHALLENGE

APOE is mainly produced by astrocytes and acts in lipid transportation and cellular repair in the healthy brain. After neural injury or in disease, increased expression of APOE by astrocytes and microglia helps remove lipid debris and shield against cell-toxic molecules. It can paradoxically also co-deposit with A β in plaques and may contribute to their formation and stabilization. Existing treatments for Alzheimer's and similar diseases only address symptoms and fail to halt or reverse disease progression.

INNOVATION

Over 60% of AD patients are ApoE4 carriers and E4 allele carriers face 3x higher AD risk with earlier onset. Fibrillary ApoE aggregates were identified in both AD mouse models and human brain tissue, establishing that fibrillary ApoE seeds A β amyloidosis within microglial cells. Using recombinant proteins fibrillary ApoE4 aggregates were created in vitro and transgenic AD mice expressing human ApoE4 were immunized. A significant reduction in amyloid plaque deposition and insoluble fibrillary ApoE4 in brain tissue was observed without affecting plasma ApoE4 levels.

TRL 08

TRL 07

TRL 06

TRL 05

TRL 04

TRL 03

TRL 02

TRL 01

Technology Readiness Level (TRL)

01 Basic principles observed · 02 Technology concept formulated · 03 Experimental proof of concept · 04 Technology validated in lab · 05 Technology validated in relevant environment · 06 Technology demonstrated in relevant environment · 07 System prototype demonstrated in operational environment · 08 System complete and qualified

