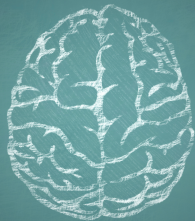


Novel Immuno-therapy Targeting Fibrillary ApoE4

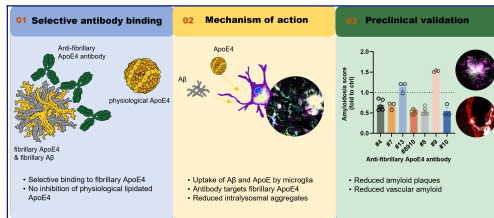
ApoE4 is the strongest genetic risk factor for late-onset Alzheimer's disease (AD), and APOE-directed strategies should preserve ApoE's essential physiological functions, particularly its role in lipid transport. This technology targets the disease-associated fibrillary form of ApoE4, a newly identified seed of amyloid pathology. It offers a differentiated preventive or disease-modifying approach for genetically defined, high-risk AD populations.



Selective ApoE4 aggregate clearance

Fibrillary ApoE4 accumulates in microglial endosomal/lysosomal compartments and promotes A β amyloid deposition. Active vaccination with recombinant fibrillary ApoE4 reduced cerebral fibrillary ApoE4 and amyloid plaque burden in human ApoE4-expressing amyloidosis mouse models, without lowering ApoE4 in plasma. The approach can be developed further with conformation-selective monoclonal antibodies.

- 01 Conformation-selective approach targets pathogenic fibrillary ApoE4 rather than physiological ApoE.
- 02 Disease-upstream intervention addresses a potential trigger of A β plaque formation in microglia.
- 03 In vivo proof of concept shows reduced brain amyloid pathology in human ApoE4 AD mice.



Selective targeting of fibrillary ApoE4 reduces intralysosomal amyloid aggregates and plaque pathology while preserving physiological ApoE4 function.



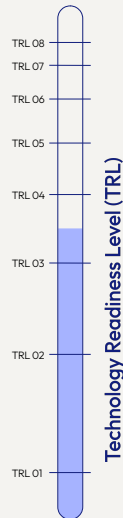
CHALLENGE

Amyloid-targeting therapies address downstream pathology and leave plaque-initiating processes unresolved. Moreover, APOE4 carriers are often excluded because of high risk of side effects, especially ARIA. ApoE4 substantially increases risk and accelerates the onset of late-onset AD, but ApoE is required for physiological lipid metabolism and neuronal support. Broad ApoE inhibition may compromise normal protein function and create safety challenges. A selective strategy for pathogenic ApoE4 species is needed.

INNOVATION

The technology is based on the discovery that fibrillary ApoE aggregates act as microglial seeds for A β amyloidosis. It enables active or passive immunotherapies directed specifically against the pathological fibrillary ApoE4 conformation rather than total ApoE4. In transgenic AD mice expressing human ApoE4, vaccination reduced brain fibrillary ApoE4 and amyloid plaques while preserving plasma ApoE4. This creates a potential precision-immunotherapy platform for ApoE4-associated AD.

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



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