Inhibiting Platelet Micro-Clots to Treat Alzheimer's Disease (AD) and Cerebral Amyloid Angiopathy

An effective therapeutic that targets the vascular contributions to Alzheimer's disease (AD), particularly cerebral amyloid angiopathy (CAA), which affects nearly all AD patients and accelerates neurodegeneration.

Technology

Researchers at NYU Langone Health have discovered a novel therapeutic strategy targeting platelet-mediated amyloid aggregation—a vascular mechanism strongly implicated in AD progression. Using a triple transgenic mouse model of AD subjected to a high-fat diet to mimic atherosclerosis, they demonstrated that vascular platelet micro-clots significantly exacerbate CAA, memory decline, tau hyperphosphorylation, and neuroinflammation. Treatment with a humanized antibody targeting GPIIIa49–66, a cryptic epitope on activated platelets, effectively disaggregates micro-clots, reduces fibrillar Aβ formation, and improves vascular permeability and cognitive function *in vivo*. This therapy offers a first-in-class disease-modifying approach to address AD and CAA through vascular intervention.

Background

Alzheimer's disease is projected to affect 150 million people globally by 2050. Despite decades of research, current therapeutics targeting Aβ or tau pathology remain insufficient to halt or reverse disease progression. Almost all AD patients exhibit cerebral amyloid angiopathy (CAA)—amyloid deposition in cerebral blood vessels—which worsens cognitive decline and neuronal loss. The vascular role of platelets, rich in amyloid precursor protein (APP), has been underexplored until now. This technology bridges cardiovascular disease (e.g., atherosclerosis) with neurodegeneration by demonstrating that platelet micro-thrombi act as sites of Aβ aggregation, particularly under chronic vascular stress.

Development Status

The technology has been validated *in vivo* in a triple-transgenic AD mouse model on a high-fat diet and demonstrated mechanistic efficacy via reduction of fibrillar Aβ, improvement in cognitive and vascular outcomes. Humanized single-chain antibody A11 was developed and tested in proof-of-concept studies.

Applications

Technology ID

WIS02-24

Category

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Learn more

- **Alzheimer's disease (AD):** Disease-modifying therapy targeting platelet-mediated Aβ aggregation.
- **Cerebral Amyloid Angiopathy (CAA):** Therapeutic to reduce vascular amyloid burden and preserve blood-brain barrier integrity.
- **Atherosclerosis-related dementia risk:** Early intervention strategy for patients with high cardiovascular burden and cognitive risk.

Advantages

- **First-in-class approach:** Targets vascular Aβ aggregation, an underexplored but central contributor to AD pathology.
- **Mechanism-based therapy:** Reduces amyloid deposition, tau hyperphosphorylation, neuroinflammation, and vascular permeability.
- **Broad therapeutic window:** Potential use in both pre-symptomatic at-risk patients and those with established disease.
- **Humanized antibody:** Demonstrated efficacy *in vivo* using the A11 anti-GPIIIa49–66 antibody.

Intellectual Property

NYU has filed a U.S. non-provisional patent application covering the use of antibody-based therapies targeting GPIIIa49–66 to treat AD and CAA.