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CAR MACROPHAGES FOR TARGETED DEGRADATION OF PATHOGENIC SUBSTANCES

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Value proposition: *Self-sustaining chimeric macrophages as a novel approach to target amyloid plaques resulting in improved efficacy and survival in patients.*

Technology Description

Researchers from Washington University in St. Louis have engineered macrophages to express an Aβ-targeting chimeric antigen receptor (CAR-Ms). Several monoclonal antibodies that selectively target aggregated forms of beta amyloid (Aβ), have been shown to reduce amyloid plaques and in some cases, mitigate cognitive decline in early-stage AD patients.

The CAR-Ms can significantly bind and resorb beta-amyloid in culture and are able to degrade intracellular amyloid.

Above: (Left) Ex vivo examples of HJ3.4 (red) and X-34 (blue) immunostaining where CAR-Ms can significantly decrease plaque load. In vivo proof of concept obtained where CAR-Ms can persist for at least 1 month without exogenous cytokines and naturally expands in the brain microenvironment. Currently, CAR-Ms can significantly decrease plaque load from the hippocampus after intrahippocampal injection (right) in APP/PS1 mice.

Stage of Research

Tested in the brains of mice.

Publications

- Chimeric antigen receptor macrophages target and resorb amyloid plaques. JCI Insight (2024)

Applications

- Alzheimer’s & amyloid disease treatment

Key Advantages

- Applicable to any pathogenic material through adjusting the scFV domain of the CAR construct.
- Improved efficacy, survival, and proliferation relative to earlier CAR-M prototypes.
- Localize consistently to the treatment site.

Patents

US non-provisional application filed 02/2025.

Related Web Links - Carl DeSelm Profile; DeSelm Lab