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Macrophage-Targeted PEGosomes for Treating Neuroinflammation and Neurodegeneration

Stanford researchers have developed a macrophage-targeted PEGylated liposome ("PEGosome") platform that selectively delivers polyethylene glycol (PEG) to inflammatory monocytes and macrophages driving neuroinflammation in diseases such as multiple sclerosis (MS), Alzheimer's disease, Parkinson's disease, and ALS. These large, ~700 nm liposomes are engineered to accumulate in peripheral monocytes that later infiltrate the central nervous system (CNS), while sparing CNS-resident microglia.

Neuroinflammatory and neurodegenerative diseases remain poorly controlled by current therapies, which largely target adaptive immunity or use broad immunosuppression and often fail to prevent long-term disability. No approved drugs directly and selectively modulate pathogenic macrophages in the CNS.

The inventors' PEGosome composition combines DSPC, DSPE-PEG-NH2-3400, and cholesterol in a defined ratio to create stable, long-circulating particles that preferentially home to inflammatory macrophages. In murine models of experimental autoimmune encephalomyelitis, prophylactic or therapeutic administration of drug-free PEGosomes markedly reduces clinical scores, demyelination, and CNS infiltration of macrophages and T cells, while selectively suppressing macrophage IL-1B secretion without broadly altering M1/M2 polarization or affecting IL-6 and TNF-α. This targeted immunomodulation offers a scalable, drug-agnostic vehicle that can be used alone or loaded with additional agents to treat MS and other IL-1B–driven neuroinflammatory and neurodegenerative disorders.

Stage of Development
Proof of concept – *in vivo* rodent models

Applications

- Disease-modifying therapies for MS and other IL 1B–driven neurodegenerative diseases (Alzheimer's, Parkinson's, ALS)
- Targeted delivery vehicle for immunomodulatory or neuroprotective drugs to inflammatory CNS-infiltrating macrophages
- Platform for non-invasive or minimally invasive formulations (e.g., parenteral, oral, nasal, pulmonary, transdermal, ocular) in future clinical products

Advantages

- First macrophage-targeted PEGosome shown to reverse established EAE and delay relapse with minimal toxicity in vivo
- Selective IL-1B suppression without broad immunosuppression, preserving other macrophage functions
- Simple, scalable liposome formulation compatible with additional payloads and multiple delivery routes for commercial development

Publications

- Muselman, Alexander, Yu, Lewis W., et al. (2026). Macrophage-targeted PEGylated liposomes ameliorate experimental autoimmune encephalomyelitis. *Frontiers in Immunology*, **16**, 1657131.

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