

# Title: Enzymatic Surface Shielding of MSCs Boosts In Vivo Retention and Neuroprotection Against Alzheimer's Disease

Wang Liao, Mengyao Ji, et al.

The Second Affiliated Hospital of Guangzhou Medical University

## Background

Mesenchymal stem cells hold promise for Alzheimer's disease therapy, but their efficacy is limited by poor survival, rapid clearance, and insufficient in vivo retention after systemic administration.

## Strategy

We developed a microbial transglutaminase-mediated single-cell encapsulation strategy to engineer a thin gelatin hydrogel shell around individual MSCs, generating MSC@Gel as a protective cellular interface.

## Key Findings

### 1. Efficient single-cell encapsulation

MSC@Gel formed a continuous gelatin shell around individual MSCs while preserving cell viability and cytoskeletal integrity.

### 2. Enhanced stress resistance

The gelatin shell reduced oxidative stress-induced ROS accumulation, preserved mitochondrial membrane potential and improved survival under shear stress.

### 3. Prolonged in vivo retention

After intravenous administration, MSC@Gel showed markedly prolonged lung-region bioluminescence signals compared with uncoated MSCs.

### 4. Improved cognitive and pathological outcomes

In 5xFAD mice, MSC@Gel improved recognition memory and spatial learning, reduced A $\beta$  plaque deposition, attenuated IBA-1-positive microglial activation, and preserved neuronal integrity.

## Conclusion

Enzymatic surface shielding transforms MSCs into a more persistent and therapeutically effective cell platform, enhancing in vivo retention and neuroprotective efficacy in Alzheimer's disease.

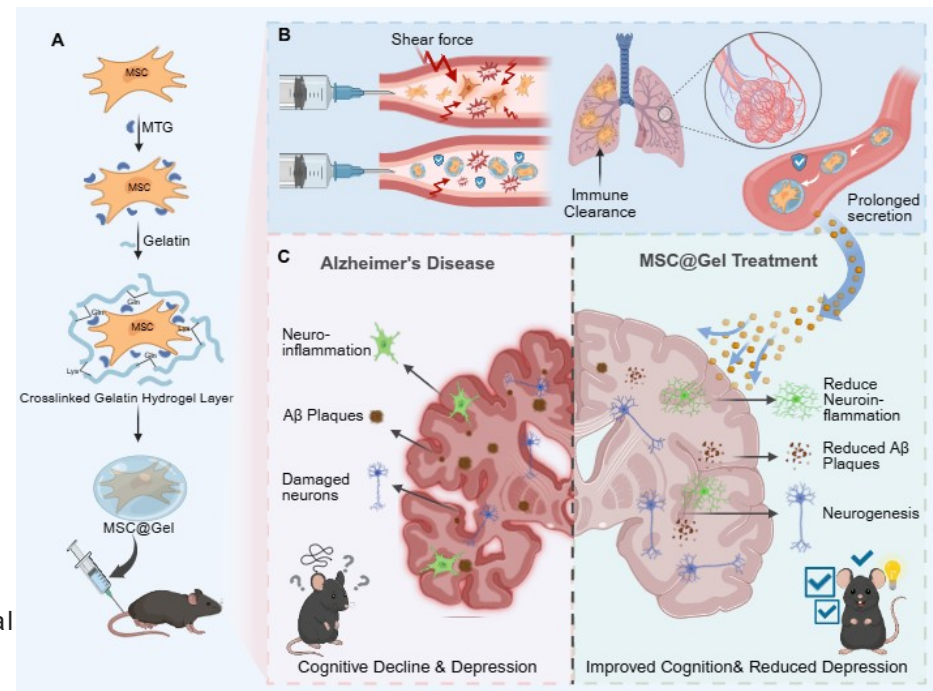


**Figure.** Enzymatic surface shielding enhances MSC retention and therapeutic efficacy in Alzheimer's disease.

MSC@Gel was generated by microbial transglutaminase-mediated gelatin encapsulation, forming a thin protective hydrogel shell around individual MSCs. This coating preserved cell viability, enhanced resistance to oxidative and shear stress, prolonged in vivo retention after intravenous administration, and improved cognitive function while reducing A $\beta$  deposition and neuroinflammation in 5xFAD mice.