Particle-Based Delivery Systems for Antigen-Specific Tolerance and Symptomatic Reversal in Multiple Sclerosis (MS)

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TBIOMD 492

Introduction

Multiple Sclerosis (MS) is an autoimmune disease characterized by immune-mediated damage on the central nervous system (CNS).

- Autoreactive T cells target myelin proteins > inflammation and neurodegeneration
- Current disease modifying therapies (DMTs) broadly suppress immunity
- Multi-epitope structure introduced antigen-specific approaches
- Antigen-specific tolerance therapies aim to retrain the immune system without compromising immunity

MS Tolerance Therapies & Direct Comparison

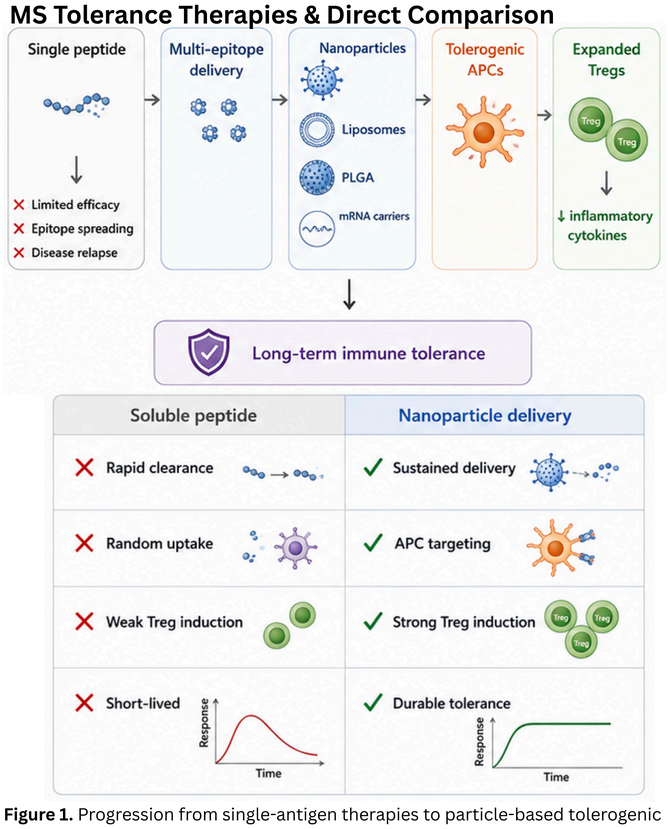

Figure 1. Progression from single-antigen therapies to particle-based tolerogenic delivery platforms. Comparative analysis of original peptide to nanoparticle delivery systems. antigen-presenting cells = APC. Figure generated by ChatGPT.

Methods

Literature review of particle-based antigen-specific tolerance strategies and symptomatic reversal of MS.

- Reviewed >30 peer-reviewed studies examining tolerogenic delivery platforms

Compared: nanoparticles, liposomes, antigen-loaded carriers, and cell-based approaches
Evaluated: immune tolerance mechanism, therapeutic outcomes, and limitations of clinical translation

Results

Mechanism of Nanoparticle Tolerance

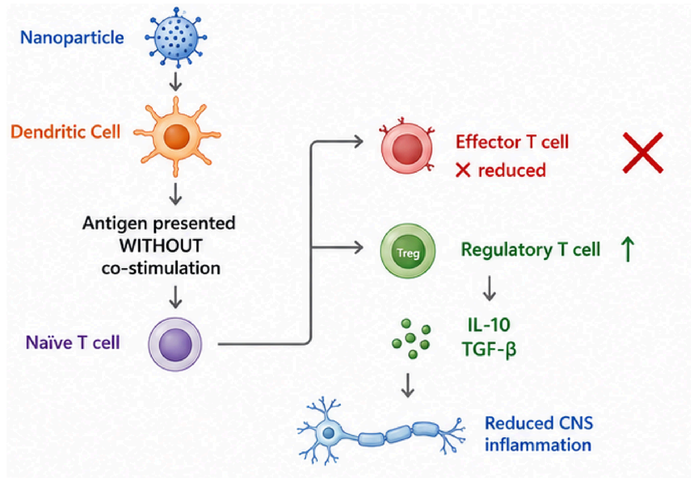

Figure 2. Mechanism of nanoparticle tolerance and immune reprogramming to reduce inflammation. Effector T cell = Teff. Regulatory T cell = Treg. Figure generated by ChatGPT.

> complete symptomatic reversal without compromised immunity
> durable tolerance is reliant on regulatory networks
> therapeutic success promotes Tregs, regulatory B cells (Bregs), and myeloid-derived suppressor cells (MDSCs) to maintain long-term immune tolerance while supporting remyelination and CNS repair

Particle-Treatment Groups Show Complete Symptomatic Reversal

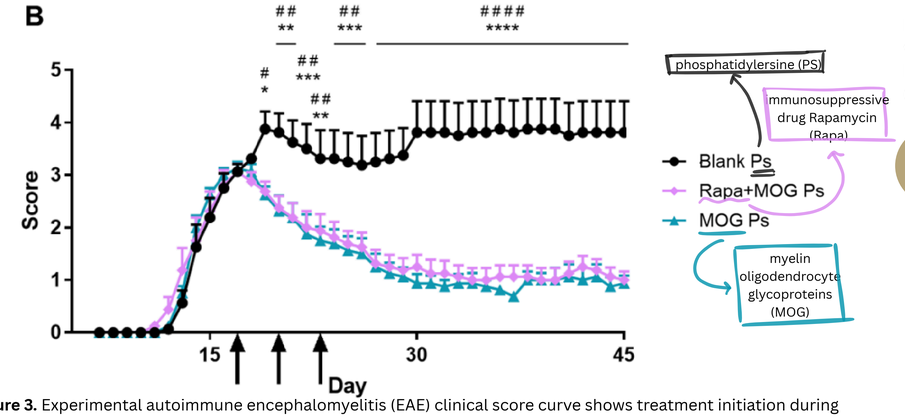

Figure 3. Experimental autoimmune encephalomyelitis (EAE) clinical score curve shows treatment initiation during peak disease, where clinical scores for particle-treated groups (MOG PS and Rapa+MOG PS) sharply decline from 3 (hind limb paralysis) to a score of 1 (functional) proving achieved symptomatic reversal. (Stiepel et al. 2025).

Significance

- **Prospective alternate to lifelong immune suppression in MS**
- **Pathway toward durable tolerance and improved quality of life**
- **Future of MS therapy presents a shift from suppressing immunity > retraining tolerogenic immunity**

Key Findings

1. Particle delivery improves antigen-specific tolerance
   - nanoparticles promote tolerogenic antigen presentation
2. Immune reprogramming succeeds through regulatory networks
   - increased Tregs, IL-10, TGf-β, and reduced Teffs
3. Preclinical models demonstrate functional recovery

> successful reduction of autoimmune response < with maintained immunity

Particle Treatments Present Successful Vaccine Response

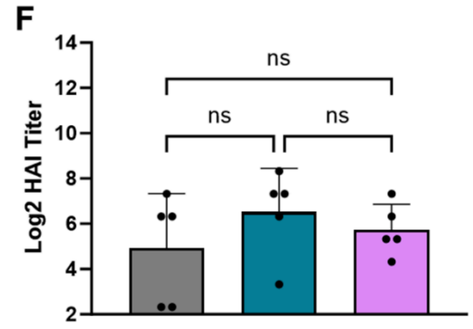

Figure 4. Hemagglutination inhibition (HAI) titers (Standard FDA metric for successful vaccine response) shows mice successfully treated with MS nanoparticles maintained a healthy antibody response to an influenza vaccination, identical to healthy control mice. (Stiepel et al. 2025).

Future Directions

> Improve therapeutic precision with development of multi-antigen platforms
> Advance clinical translation to validate safety and efficacy in human trials
> Long-term goal of durable antigen-specific tolerance

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References