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Current Updates in Gene Therapy for Multiple Sclerosis

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Background: Multiple sclerosis (MS) is the most common demyelinating disease affecting predominantly young adults. The underlying pathogenesis isn't fully understood although autoimmune attacks against proteins in the CNS is the most accepted theory. Oligodendrocytes seem to be the most involved resulting in demyelinated axons. Currently, the management of MS focuses on relieving symptoms during acute attacks and preventing disease progression using disease-modifying agents such as interferon-beta, dimethyl fumarate, natalizumab, and fingolimod. Studies have proven long-term improvement on these drugs. However, possible side effects and curatively inducing or improving the repair process are major challenges.

Objectives: The objectives of this review are to provide a comprehensive overview of gene therapy for MS and highlight the promising future options for MS management.

Methods: A literature review on PubMed and Google Scholar databases up to January 2023 was carried out and yielded a total of 15 articles that were included in this narrative review.

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Results: Novel gene-based therapies were found to be attractive alternatives in terms of efficacy and safety. For instance, IFN-β fusion proteins containing galectin-9 have demonstrated fewer side effects in comparison with standard IFN-β alone. Similarly, TREM2-transduced myeloid precursor cells limited tissue damage and enhanced repair in murine models with experimental autoimmune encephalomyelitis (EAE). Administration of AAV8-soluble interleukin-23 receptor into the CSF showed maintained clinical improvement and no evidence of demyelination in EAE mice. Other promising approaches for EAE include administering myelin oligodendrocytes glycoprotein (MOG) and hepatocyte growth factors, overexpressing anti-inflammatory cytokines in Wharton's jelly stem cells, and targeting mitochondrial dysfunction.

Conclusion: Therapeutic options for MS have taken leaps in the past years. Yet, a longer patient life span is associated with increased disabilities and complications. Some approaches in gene therapy have proven efficacious among animals. Thus, further research on gene-based therapy is warranted to lay the foundation for the much-anticipated breakthrough.

Keywords: Multiple Sclerosis; Demyelinating; Gene Therapy; Interferon; Oligodendrocytes.

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