DOI: 10.4274/jmsr.galenos.2025.2025.1-1

J Mult Scler Res

LETTER to the EDITOR

The Future of Multiple Sclerosis Research: Unlocking Myelin Repair Through Unified Efforts

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Dear Editor,

A new French foundation for research and patient support, France Sclérose en Plaques, was established on May 15, 2024, by merging the following three major organizations the "Association pour la Recherche sur la Sclérose En Plaques", the "Ligue Française contre la Sclérose en Plaques", and the "Union pour la lutte contre la sclérose en plaques". This new foundation unites the efforts to fund research, support patients, and raise awareness regarding multiple sclerosis (MS), marking a pivotal step in combating the disease.

For the 26th edition of Brain Awareness Week, the France Sclérose en Plaques and French Glial Cells Club organized a conference on MS at the Collège de France to raise public awareness regarding MS. Professor Céline Louapre and Dr. Brahim Nait Oumesmar from Sorbonne University presented the current advancements in MS research and the therapeutic prospects (1). The event also featured information booths and discussions regarding MS, providing a forum for debate between patients and the scientific community.

During this event, the speakers presented actual MS treatment modalities that primarily focused on immunomodulators and immunosuppressants that reduce inflammation and relapses. However, these drugs cannot entirely halt disease progression (Figure 1). Persistent inflammation in older lesions on high-resolution magnetic resonance imaging highlight the need for therapies targeting the underlying disease activity. Although 15 immune-modulating drugs are currently available, no therapy addresses the central nervous system's repair processes (2).

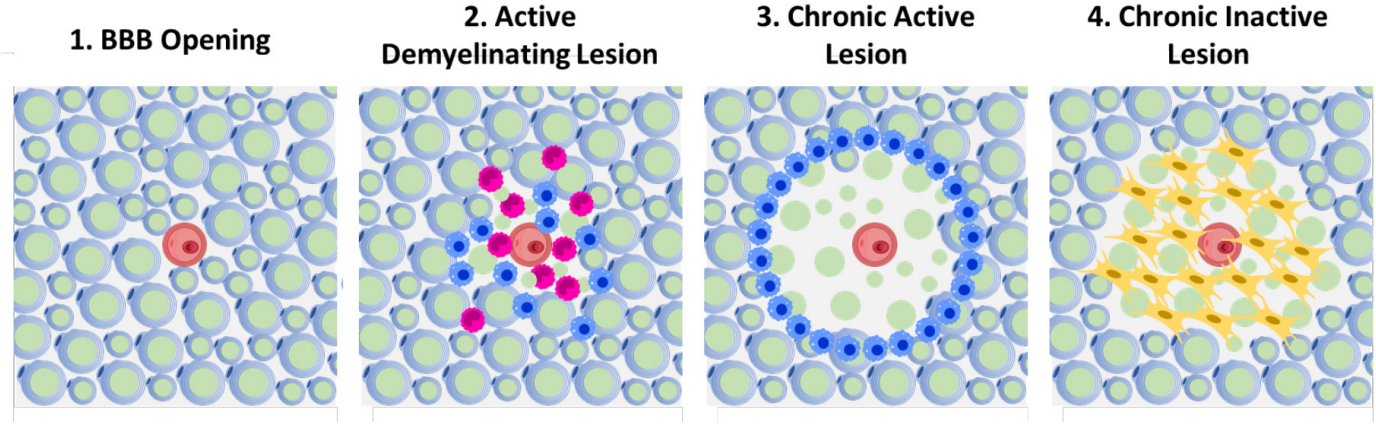

Figure 1. Formation of a chronic inactive lesion. **(1)** Opening of the Blood-Brain Barrier (BBB). **(2)** Immune cell attack. **(3)** Clearance by macrophages. **(4)** Astrocytes proliferate and form a glial scar.

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Received: 04.01.2025 **Accepted:** 24.01.2025 **Epub:** 11.03.2025

Cite this article as: Rancillac A. The future of multiple sclerosis research: unlocking myelin repair through unified efforts. J Mult Scler Res. [Epub Ahead of Print]

Emerging Insights Into Remyelination Studies

Research is progressively moving toward remyelination strategies by examining how oligodendrocyte precursor cells (OPCs) mature and contribute to the regeneration of myelin. Advanced imaging technologies such as positron emission tomography are being used to monitor remyelination dynamics in real-time, offering critical insights into therapeutic efficacy, drug discovery, and stimulating neuronal activity to accelerate repair.

The discovery of promyelinating molecules, via molecular screening, in cultures of OPCs has paved the way for trials using preclinical models of myelin lesions. These molecules, primarily derived by the repositioning of existing compounds, have been selected from among 1,500 candidates using bioinformatics analyses that were designed to predict their effects on myelination and neuroprotection. After being tested in culture, these molecules have been evaluated *in vivo* in mice, which have leading to the identification of promising candidates for promoting remyelination and neuroprotection. Several of these molecules could undergo clinical trials in the near future.

Ortiz et al. (3) demonstrated that neuronal activity *in vivo* following lesion formation enhances functional myelin repair, highlighting the potential of neural stimulation techniques to promote remyelination. A clinical trial is currently underway to explore this avenue. Researchers have also aimed to overcome remyelination decline with age by exploring transcription factors (e.g., Olig2, Sox10, RXR-γ), neurotransmitters, receptors, and external influences such as microbiota and genetics (4).

Future Prospects

Future studies must focus on combining these approaches to create comprehensive strategies for remyelination. Additionally, personalized medicine that leverages patient-specific genetic and microbiome profiles may optimize treatment outcomes. These initiatives highlight the growing understanding of MS and the critical need for innovative approaches to improve patient outcomes.

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