



## **USE OF AUTOLOGOUS NEURAL PROGENITORS AS A REPAIR STRATEGY FOR MULTIPLE SCLEROSIS**

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Multiple sclerosis (MS) is a chronic human autoimmune disease of the central nervous system characterized by inflammation-induced demyelination that eventually leads to destruction of oligodendrocytes, axonal loss and progressive irreversible disability. There is an urgent need for therapies that involve neural repair and regeneration to reverse the disability in MS. As a strategy for neural regeneration, we propose using autologous neural progenitors derived from bone marrow mesenchymal stem cells (MSC). Human MSC-derived neural progenitors (MSC-NP) from MS patients exhibit characteristic neurosphere morphology and express increased levels of neural progenitor genes Nestin, Neurofilament-M, GFAP, and CXCR4, and decreased levels of MSC-associated genes Vimentin and SMA. FACS analysis showed that MSC-NPs represent a more homogenous cell population compared to MSCs, suggesting that they may be a more potent cell therapy product. MSC-NPs, but not MSCs, are capable of *in vitro* differentiation into oligodendroglial (O4+) or neuronal ( $\beta$ 3-tubulin+) cell types in the presence of bFGF. In addition, MSC-NPs retain the anti-inflammatory properties of MSCs but lose their differentiation plasticity (i.e. differentiation into osteoblasts or adipocytes). These findings suggest that MSC-NPs are more likely to respond to differentiation cues in the CNS, and in addition can suppress the immune response and provide trophic support for damaged cells. To establish an experimental basis for this repair strategy, we have injected MSC-NPs in EAE. We confirmed that mouse MSC-NPs have similar characteristics to human MSC-NPs. Multiple intracerebroventricular injections of GFP-labeled mouse MSC-NPs into mice with EAE was well tolerated and resulted in decreased disease severity and showed evidence of neural repair. Overall, these data support the rationale to use MSC-NPs in a phase I clinical trial for autologous cell-based therapy in multiple sclerosis.