

# Human Mesenchymal Stem Cell derivatives promote functional recovery in models of Multiple Sclerosis

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**ABSTRACT:** Previous studies suggest that human mesenchymal stromal cells (hMSCs) promote functional recovery in murine models of Multiple Sclerosis such as (EAE). Cell tracing analyses indicate the transplanted MSCs accumulate in regions of demyelination, raising the possibility that MSCs may have direct effects on neural and immune cells, or that they release neuroactive factors that promote functional recovery. To determine the relative involvement of MSC secreted factors the effects of MSC conditioned medium were assayed. We show that MSC conditioned medium (hMSC-CM) stimulates the development of neurons and oligodendrocytes from neural stem cells in vitro. This neurogenic activity had a molecular mass of 50-100kDa (hMSC-CM<sub>100Kd</sub>). When injected into animals with MOG, induced hMSC-CM<sub>100Kd</sub> reduces disease burden, promotes histological improvement and reduces inflammatory activity. In vitro studies suggest that in cell cultures derived from EAE animals exposure to hMSC-CM<sub>100Kd</sub> increases in the number of nestin<sup>+</sup> NSCs, NG2<sup>+</sup>/A2B5<sup>+</sup> OPCs, O1<sup>+</sup> oligodendrocytes, MBP<sup>+</sup> mature oligodendrocytes and  $\beta$ -tubulin<sup>+</sup> neurons. These data suggest that a significant component of the functional recovery seen in EAE animals treated with hMSCs is a reflection of the release of trophic factors and raise the possibility that they may be a novel therapeutic modality for MS.