

Therapeutic Efficacy-Potentiated and Diseased Organ-Targeting Nanovesicles Derived from Mesenchymal Stem Cells for Spinal Cord Injury Treatment.

Abstract

Human mesenchymal stem cell (hMSC)-derived exosomes have been spotlighted as a promising therapeutic agent for cell-free regenerative medicine. However, poor organ-targeting ability and insufficient therapeutic efficacy of systemically injected hMSC-exosomes were identified as critical limitations for their further applications. Therefore, in this study we fabricated iron oxide nanoparticle (IONP)-incorporated exosome-mimetic nanovesicles (NV-IONP) from IONP-treated hMSCs and evaluated their therapeutic efficacy in a clinically relevant model for spinal cord injury. Compared to exosome-mimetic nanovesicles (NV) prepared from untreated hMSCs, NV-IONP not only contained IONPs which act as a magnet-guided navigation tool but also carried greater amounts of therapeutic growth factors that can be delivered to the target cells. The increased amounts of therapeutic growth factors inside NV-IONP were attributed to IONPs that are slowly ionized to iron ions which activate the JNK and c-Jun signaling cascades in hMSCs. In vivo systemic injection of NV-IONP with magnetic guidance significantly increased the amount of NV-IONP accumulating in the injured spinal cord. Accumulated NV-IONP enhanced blood vessel formation, attenuated inflammation and apoptosis in the injured spinal cord, and consequently improved spinal cord function. Taken together, these findings highlight the development of therapeutic efficacy-potentiated extracellular nanovesicles and demonstrate their feasibility for repairing injured spinal cord.

KEYWORDS:

Exosomes; iron oxide nanoparticles; mesenchymal stem cells; nanovesicles; spinal cord injury