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Mesenchymal Stem Cell-derived Extracellular Vesicles: A Novel Approach of Cell-free Regeneration

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Introduction: Mesenchymal stem cells (MSCs) are multipotent progenitors that can be isolated from various tissues. MSCs are of great interest in the field of regenerative medicine because of their unique ability to home to damaged tissue. Much of current interest in therapeutic application of MSCs to various disease settings can be linked to their immunosuppressive and anti-inflammatory properties. One of the key mechanisms of MSC anti-inflammatory effects is the secretion of soluble factors with paracrine actions. Recently it has emerged that the paracrine functions of MSCs could, at least in part, be mediated by extracellular vesicles (EVs). EVs are predominantly released from the endosomal compartment and contain a cargo that includes miRNA, mRNA, and proteins from their cells of origin to recipient cells. Also, EVs have been shown to play a key role in immune modulation and cell-to-cell communication. Furthermore, compared to their parent cells, EVs may have a superior safety profile and can be safely stored without losing function.

Description: Recent animal model-based studies suggest that MSC-derived EVs (MSC-EVs) have significant potential as a novel alternative to whole cell therapies. MSC-EVs were shown to specifically localize to the liver and to alleviate liver fibrosis in carbon tetrachloride (CCl_4)-induced injury by reducing hepatocyte apoptosis and hepatic lobule destruction. MSC-EVs promote hepatocyte regeneration by inducing the IL-6/STAT3 pathway and cell cycle progression. More over, MSC-EVs administration suppressed epithelial to mesenchymal transdifferentiation via reduced TGF-β1 expression and Smad2 phosphorylation.

Discussion and conclusion: These studies have confirmed that MSC-EVs therapy has the potential to promote liver regeneration following acute injury by directly enhancing hepatocyte survival and proliferation. All in all, MSC-EVs have theoretical advantages over intact MSCs as a medicinal product and may, in the future, gain preference over whole cells in the discipline of regenerative medicine.

Key word: *Mesenchymal stem cells, Extracellular Vesicles, Regenerative medicine*