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# Therapeutic Potentials of Mesenchymal Stem Cells

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**ABSTRACT: Regenerative medicine's main tool is mesenchymal stem cells. Multipotent mesenchymal stromal cells, multipotent stromal cells, medicinal signalling cells, and MSCs are other names for mesenchymal stem cells. The primary immunomodulatory mechanisms by which MSCs exhibit their therapeutic qualities are paracrine action, extracellular vesicle (ECV) secretion, apoptosis-mediated immunomodulation, and mitochondrial transfer of membrane vesicles and organelles. MSCs primarily work by causing functional alterations in immune cells through paracrine signalling. ECVs are vesicles that form via inward or outward budding from the plasma membrane. The process of phagocytic clearance of dying cells, or efferocytosis, contributes to more than just the healing of damaged tissue and the absence of inflammation. A variety of physiological and pathological processes are linked to mitochondrial transport. One of MSC-based therapies' main benefits is their capacity to repair injured tissue, in addition to their intricate immunomodulation processes.**

**Keywords:** Mesenchymal stem cells, Regenerative Medicine, Paracrine action, Mitochondrial transfer, Apoptosis mediated immunomodulation and Phagocytic clearance.

## INTRODUCTION

Regenerative medicine's principal tool is mesenchymal stem cells. Multipotent mesenchymal stromal cells, multipotent stromal cells, medicinal signaling cells, and MSCs are various names for mesenchymal stem cells. (Dominici *et al*., 2006). The primary isolation of human ESC (Embryonic Stem Cells) was evaluated in 1998 (Takahashi and Yamanaka, 2006). In 1968, an osteogenic population of cells with fibroblast-like morphology was extracted from bone marrow, marking the first documented instance of adult multipotent cells, or MSC. Fetal, adult, and embryonic cell types are the different sources of MSCs. (Niess *et al*., 2016).

### *A. Therapeutic Potentials of MSCs*

The primary mechanism by which MSCs attain their therapeutic qualities is through their ability to modulate immune system cells. MSCs exhibit complex immunomodulation activity through apoptosis-mediated immunomodulation, extracellular vesicle (ECV) secretion, paracrine action, and mitochondrial transfer of membrane vesicles and organelles.

### *B. Paracrine Action*

The main way that MSCs work is through paracrine signaling, which alters the way that immune cells-such as dendritic cells, T cells, B cells, macrophages, and natural killer cells-function.

The immunomodulatory effects of MSC have been found to be influenced by a number of variables. Proven effectors like prostaglandin E2 (PGE2), interleukin 10 (IL-10), indolamine-2,3-dioxygenase (IDO), transforming growth factor-beta (TGF-β), and tumor necrosis factor (TNF) are among them (Voga *et al*., 2020).

### *C. Secretion of Extracellular Vesicles (ECV)*

ECVs are vesicles that emerge either inwardly or outwardly from the plasma membrane. They are membrane-protected carriers of proteins, mitochondria, mRNA, and miRNA. Exosomes were shown to be secreted by MSCs. The mechanisms of action of ECVs appear to be comparable to those demonstrated by MSC (Voga *et al*., 2020).

ECVs were also applied to horses and dogs. After treating damaged tendon in a stallion with microvesicles derived from ADMSCs, the use of ECVs increased angiogenesis and its elasticity (Kornicka-Garbowska *et al*., 2019).

Compared to their originator cells, ECVs have been shown to have superior effects on canine vascularization, collagen synthesis, and cutaneous wound healing (El-Tookhy *et al*., 2017).

Through PGE2 activation, exosomes stimulate the production of M2 macrophages, inhibit the proliferation of T-cells via TGF-β and adenosine signaling, and

increase the production of IL-10 (Hyvarinen *et al.*, 2018).

*D. Apoptosis-Mediated Immunomodulation*

In addition to reducing inflammation and repairing damaged tissue, phagocytic clearance of dying cells, or efferocytosis, is involved in the adaptive and immune responses in inflamed tissues (Elliott, 2017).

Following intravenous (IV) administration in mice, monocytes and neutrophils quickly phagocytosed MSCs in the lungs. The process of phagocytosing MSCs results in the expression of regulatory phenotype and polarization of monocytes, which subsequently modulates the adaptive immune system by inducing T-reg cells (De Witte *et al.*, 2018).

Galleu *et al*. (2017) report that following IV infusion, MSCs undergo apoptosis in the presence of cytotoxic cells (CD56+ NK cells and CD8+ T-cells). Macrophages phagocytose apoptotic MSCs, which ultimately results in the delivery of immunosuppressive activity (by generating IDO).

*E. Mitochondrial Transfer*

Apart from transporting molecules through extracellular vesicles, MSCs have the ability to transfer organelles between cells by means of tunneling nanotubes. Given its correlation with a range of physiological and pathological functions, mitochondrial transfer may prove advantageous in the treatment of numerous pathological conditions in the future. The first-ever mitochondrial transfer between somatic cells and MSC was noted in 2006.

Human BMMSC were able to transfer their mitochondria through tunneling nanotubes to alveolar macrophages in a mouse model of pneumonia. This resulted in increased macrophage phagocytosis and an increase in the antimicrobial activity of MSC (Jackson *et al.*, 2017).

*F. MSC Homing*

One of the main benefits of MSC-based treatments is their capacity to repair damaged tissue, in addition to their intricate immunomodulatory processes. Chemical factors like growth factors, cytokines, and chemokines have a strong correlation with MSC homing. Stromal cell derived factor 1 (SDF-1), a chemokine released from injured tissue that sends chemo-attractive signals to cells expressing CXCR4 receptors on the outer membrane, is one of the primary chemical factors involved in MSC migration (Penn, 2010).

The ideal way to administer cells in stem cell therapies is through local MSC transplantation (Nowakowski *et al.*, 2016).

Stem cell homing is influenced by the following FGF-β1, vascular endothelial growth factor, hepatocyte growth factor, insulin-like growth factor-1, and hepatocyte growth factor are examples of growth factors. mechanical factors include microgravity, matrix stiffness, shear stress, and mechanical strain (Fux *et al.*, 2019).

## CONCLUSION

Regenerative Medicine is a budding area in Veterinary Medicine. MSCs are the main tools in the field of regenerative medicine, to use the MSCs properly according to clinical condition it is very important to know the therapeutic potential of MSCs of different origin and different path of action.

**Conflict of interest.** Nil.

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