

A GUIDE FOR PATIENTS

LITERATURE

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❖ Immunomodulation

➤ Mesenchymal stem cells and immunomodulation: Current status and future prospects

The unique immunomodulatory properties of mesenchymal stem cells (MSCs) make them an invaluable cell type for the repair of tissue/ organ damage caused by chronic inflammation or autoimmune disorders. Although they hold great promise in the treatment of immune disorders such as graft *versus* host disease (GvHD) and allergic disorders, there remain many challenges to overcome before their widespread clinical application. An understanding of the biological properties of MSCs will clarify the mechanisms of MSC-based transplantation for immunomodulation. In this review, we summarize the preclinical and clinical studies of MSCs from different adult tissues, discuss the current hurdles to their use and propose the future development of pluripotent stem cell-derived MSCs as an approach to immunomodulation therapy.

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➤ Human mesenchymal stem cells modulate allogeneic immune cell responses

Mesenchymal stem cells (MSCs) are multipotent cells found in several adult tissues. Transplanted allogeneic MSCs can be detected in recipients at extended time points, indicating a lack of immune recognition and clearance. As well, a role for bone marrow-derived MSCs in reducing the incidence and



severity of graft-versus-host disease (GVHD) during allogeneic transplantation has recently been reported; however, the mechanisms remain to be investigated. We examined the immunomodulatory functions of human MSCs (hMSCs) by coculturing them with purified subpopulations of immune cells and report here that hMSCs altered the cytokine secretion profile of dendritic cells (DCs), naive and effector T cells (T helper 1 [T_H1] and T_H2), and natural killer (NK) cells to induce a more anti-inflammatory or tolerant phenotype. Specifically, the hMSCs caused mature DCs type 1 (DC1) to decrease tumor necrosis factor α (TNF- α) secretion and mature DC2 to increase interleukin-10 (IL-10) secretion; hMSCs caused T_H1 cells to decrease interferon γ (IFN- γ) and caused the T_H2 cells to increase secretion of IL-4; hMSCs caused an increase in the proportion of regulatory T cells (T_{Regs}) present; and hMSCs decreased secretion of IFN- γ from the NK cells. Mechanistically, the hMSCs produced elevated prostaglandin E₂ (PGE₂) in co-cultures, and inhibitors of PGE₂ production mitigated hMSC-mediated immune modulation. These data offer insight into the interactions between allogeneic MSCs and immune cells and provide mechanisms likely involved with the in vivo MSC-mediated induction of tolerance that could be therapeutic for reduction of GVHD, rejection, and modulation of inflammation. (Blood. 2005;105:1815-1822)

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➤ Immunomodulation by Mesenchymal Stem Cells

Mesenchymal stem cells (MSCs) are pluripotent stromal cells that have the potential to give rise to cells of diverse lineages. Interestingly, MSCs can be found in virtually all postnatal tissues. The main criteria currently used to characterize and identify these cells are the capacity for self-renewal and differentiation into tissues of mesodermal origin, combined with a lack in expression of certain hematopoietic molecules

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