

**HUMAN MESENCHYMAL STEM CELLS ARE NON-HEMATOPOIETIC
“IMMUNE-LIKE” CELLS THAT RESPOND TO INFLAMMATORY SIGNALS**

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Mesenchymal stem cells (MSC) are multipotent nonhematopoietic progenitor cells with the capacity to differentiate into different tissue cell types such as chondrocytes, osteocytes and adipocytes. In addition to this, they display immunomodulatory properties through interaction with a variety of leukocyte subsets. Through mechanisms that are still largely unknown, but seem to involve chemokine directed migration, bone marrow-derived and blood-derived MSC access damaged sites such as inflamed and malignant tissues. In the tissue, MSC are then exposed to local tissue-derived inflammatory mediators. Little is known about the cellular response of MSC to these signals. Therefore, in our study we explored the modulation of MSC immunobiology by prototypic tissue-derived inflammatory cytokines. The present study demonstrates that MSC exert an immunosuppressive effect on activated T lymphocyte proliferation, in which the proinflammatory cytokines IFN- γ and TNF- α did not prevent their suppressive effect. Under unstimulated conditions, blood-derived MSC secrete a distinct set of cytokines, express adhesion molecules on their surface as well as a wide range of chemokine receptors. The functionality of expressed chemokine receptors was demonstrated by migration assays and we showed that RANTES, TARC, 6Ckine, MEC, and SDF-1 α significantly induced MSC migration. Stimulation with inflammatory mediators broadly amplified cytokine production and modulated the adherence to extracellular matrix. Additionally, we demonstrate that IFN- γ and TNF- α upregulate the chemokine receptors expression in blood-derived MSC at mRNA level and significantly increase the migratory response. Our studies define MSC as strongly immunologically active and responsive cells and suggest a potential role for MSC in local tissue immunoregulation.