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Placental Mesenchymal Stem Cells (PMSCS) Modulate The Differentiation and Functions of Macrophages in Multiple Sclerosis Patients

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Objective: Multiple sclerosis (MS) is a chronic, progressive inflammatory disorder of the central nervous system (CNS) that results from a destruction of myelin sheath covering axons by autoreactive T cells. Remyelination and restoration of neuronal functions in MS can be achieved via stimulating endogenous neuronal repair mechanism or by transplanting myelinating cells. However, maintaining neuron functions for long term, it requires the regulation of the immunopathogenic process. Mesenchymal stem cells (MSCs) can reduce the encephalitogenic manifestation of MS by inhibiting autoreactive T cell functions. Here, we demonstrated that placental MSCs (pMSCs) can alter the differentiation and functions of macrophages from MS patients.

Design & Method:Monocytes isolated from peripheral blood of MS patients were spontaneously differentiated into macrophages and then co-cultured with pMSCs in the early stages of macrophage differentiation. We then evaluated the effect on differentiation by microscopic examination, flow cytometry and ELISA.

Result: The co-culture of pMSCs with monocytes spontaneously differentiated into macrophages shifted macrophage differentiation from inflammatory M1 macrophages into anti-inflammatory M2 macrophages. This was confirmed by morphological changes typical of M2 macrophages, and by changes in cell surface marker expression including CD14, CD163, CD206 and B7-H4, which are distinctive of M2 macrophages. In addition, pMSCs reduced the expression of the costimulatory molecules (CD40, CD80 and CD86), increased the expression of co-inhibitory molecules (CD273, CD274 and B7-H4) and MHC-II molecules. Furthermore, IL-10 secretion was increased while the secretion of IL-1β, IL-12 (p70) and MIP-1α was decreased; a profile typical of M2 macrophages.

Conclusion: We have shown that pMSCs can change macrophages from an inflammatory M1 into an anti-inflammatory M2 phenotype. This result demonstrates that pMSCs have the potential to modulate the immunostimulatory process in MS, Therefore, pMSCs may have a therapeutic application in treating MS through M2 macrophages, which can suppress autoreactive T cell functions.