**Immunomodulatory potential of placental mesenchymal stromal cells as a key mechanism for their therapeutic potential**

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Human term placenta has recently revealed to be a source of not only hematopoietic stem cells, but also of mesenchymal stromal cells (MSC). We have shown that MSC from the amniotic membrane (hAMSC) promote functional recovery when applied in a variety of inflammatory-associated diseases, as demonstrated in preclinical models of lung and liver fibrosis, myocardial ischemia, and stroke. hAMSC can also ameliorate the clinical progression of autoimmune diseases in experimental mouse models, such as multiple sclerosis and rheumatoid arthritis. In these studies, donor cells were rarely detected or absent in host tissues, suggesting that placenta-derived cells might exert reparative effects through the release of unknown, paracrine factors. In line with this hypothesis, we found that treatment with conditioned medium from hAMSC reduced the extent, severity and progression of the diseases mentioned above. In vitro studies demonstrated the ability of these cells to modulate immune cells, specifically T cells and macrophages. Altogether these data support the therapeutic role of placenta-derived mesenchymal cells, mainly based on their immunomodulatory, paracrine effects which induce the regeneration by resident cells, and also suggesting possibility of a cell-free treatment.