

From fetal development and beyond: human term placenta as a source of stem cells for regenerative medicine

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Over the past decade, human term placenta has become more than a vital organ during pregnancy, but also a precious reservoir of cells. An increasing number of studies have shown that these cells harbor beneficial properties. In fact, we and others have reported the therapeutic effects of placental cells in preclinical models of lung and liver fibrosis, sepsis, inflammatory bowel disease, autoimmune encephalomyelitis, cardiac ischemia and hind limb ischemia. Remarkably, the diseases which were most attenuated by placental cell treatment were those with underlying altered immune reactions. We have significantly contributed to the understanding of the immune-modulatory properties of cells from the amniotic membrane *in vitro*, showing that they can reduce the proliferation of T cell subsets, down regulate Th1 and Th17 subsets, and increase T lymphocytes with regulatory functions (Treg). Contributing to their regenerative potential, placenta-derived cells have been reported to secrete a variety of growth factors that could act on progenitor and/or resident cells to favor tissue regeneration. For example, placental cells can release pro-angiogenic factors, such as hepatocyte growth factor, and mediators in extracellular matrix degradation, such as matrix metalloproteinases (MMPs). Moreover, the release of growth factors could stimulate resident stem cells to proliferate, altogether contributing to tissue regeneration. Interestingly, to further substantiate the observation that secreted factors are the main players in the therapeutic properties of placental cells, an increasing number of studies have shown that these beneficial effects are evident when conditioned medium obtained from cell culture is used or when cells are cultured in transwell systems. In conclusion, the placenta is a rich resource of therapeutic derivatives, such as cells, their secreted factors, and also others such as amniotic membrane patches, the latter of which have been successfully used in medicine for over a century. More recently, placental cells and their derivatives are being tested in clinical trials in patients with immune-dysregulated diseases.

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Keywords

Regenerative medicine; human term placenta; stem cells immunomodulation; paracrine effects.