

The Therapeutic Potential of Placental Mesenchymal Stem Cells and their Exosomes for the Treatment of Neurodegenerative Diseases

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Background

Stem cell therapy has emerged as a valuable tool for the treatment of numerous diseases, including those driven by neurodegenerative processes. There are a wide variety of stem cells that have been identified for therapeutic use, including but not limited to embryonic stem cells, induced pluripotent stem cells, mesenchymal stem cells(MSCs), and neural stem cells(10). In recent years, placental mesenchymal stem cells have been identified as a unique source of therapy that are relatively less difficult to acquire and don't pose the same ethical concerns regarding harvest and use(6).

Methods

- The literature review was narrowed to papers published between 2010-2021
- Search terms included placental mesenchymal stem cells, their use in neuroprotection, and the role of exosomes
- Included articles looking at human PMSCs applied to various animal models, as well as review articles summarizing previously published data

Summary of Research

Placental Mesenchymal Stem Cells (PMSCs)

- PMSCs can be harvested from both preterm placentas, such as those discarded from procedures, as well as from term placentas at birth(6)
- They have been shown to be a source of multiple types of stem and progenitor cells
- There is evidence that PMSCs can be induced to differentiate into all 3 germ layer lineages: ectoderm, mesoderm and endoderm(10)
- Proposed mechanisms of action include replacement of compromised cells or induction of processes that lead to the healing or protection of tissues involved in various diseases

Replacement of damaged neural cells

- Studies have shown that PMSCs can be induced to differentiate into a neural-like morphology, specifically through inhibition of Rho kinase using Y-27632(8) and alternative induction mechanisms that that involve cytoskeletal rearrangement
- However, other studies looking at IV transplantation of PMSCs into rats with ischemic damage show that although many PMSCs migrate to the zone of ischemic damage following IV administration, most of them die(9)

Evidence for a paracrine mechanism of action

- Experiments in a rat model of recovery following ischemic infarction showed that recovery of cerebral tissue may be occurring through PMSC stimulation of resident stem and progenitor cells within the brain(2)
- PMSCs have been shown to secrete high amounts of neurotropic factors such as BDNF, HGF, and VEGF(4)
- PMSCs promoted recovery of hind limb motor function in an ovine model of spina bifida through decreasing the number of apoptotic cells at the site of injury(3)

Looking at the Role of Exosomes and Emerging Research

There has been emerging research suggesting a paracrine mechanism of action behind the neuroprotective effects achieved by PMSCs. Recent research has been striving to characterize this secretory profile, and among this line of exploration, there has been some work done looking at the functions of exosomes derived from PMSCs(3).

In a murine model of autoimmune encephalomyelitis(used to simulate multiple sclerosis(MS)), high doses of PMSC-derived extracellular vesicles (EVs) demonstrated improved motor function outcomes relative to the control. This research identified that the mechanism of action of PMSCs could be due to the secretion of EVs, suggesting that PMSC-derived EVs could be a feasible alternative to cellular based therapies for MS(1).

References

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