Placental Mesenchymal Stem Cells Improve Motor Function in a Rat Unilateral Spinal Cord Contusion Model

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Introduction

Spinal cord injuries (SCI) are devastating with no effective treatments and excessive medical costs. Placental mesenchymal stem cells (PMSCs) are a promising avenue of treatment due to their neuroprotective and angiogenic properties (Kumar, 2019). In addition, extracellular vesicles (EVs) released from these stem cells are an attractive cell-free therapeutic approach.

Extracellular vesicles are approximately 150 nm vesicles released by placental mesenchymal stem cells that contain the proteins, miRNAs and other cargo of the cells themselves (Ramasubramanian 2019).

Methods

PMSCs were isolated from discarded placentas and expanded in a serum-free media. Flow cytometry, nanoparticle tracking analysis, neuroprotection assays and other techniques were used to characterize PMSCs and PMSC-EVs. The *in vivo* studies included injured and uninjured rats. The injured rats underwent a laminectomy at C5, followed by a unilateral spinal cord injury (SCI). The uninjured rats underwent a laminectomy at C5, but did not sustain an SCI.

The injured groups were then treated with either an *extracellular matrix (ECM) patch alone* or *ECM patch with PMSCs* or *ECM patch with PMSC-EVs*. The rats were sacrificed at 8 weeks post injury, after motor testing was complete, for histology.

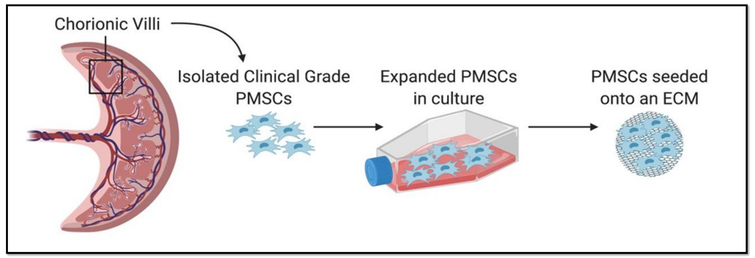

Figure 1: The extraction and expansion of PMSCs

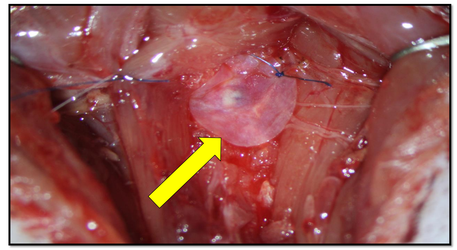

Figure 2: Spinal cord injury repair at C5 vertebra with the arrow pointing towards a PMSC patch

Results

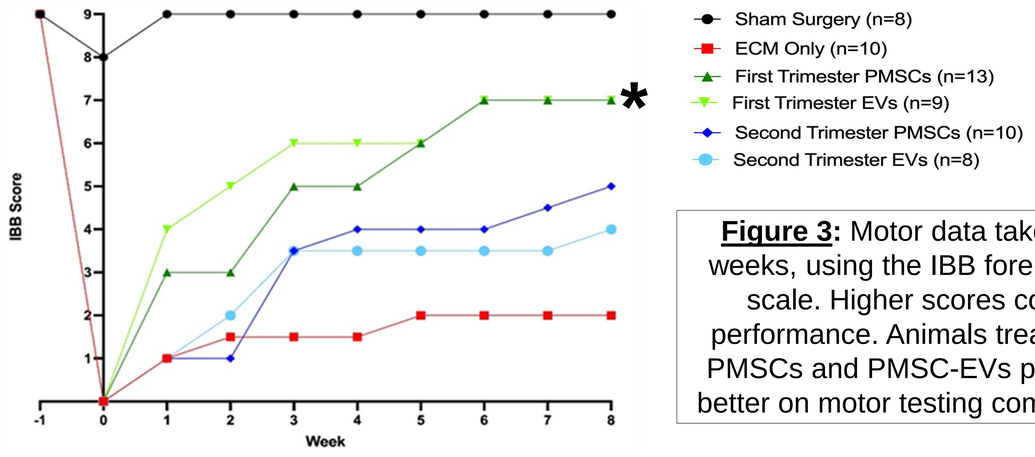

Figure 3: Motor data taken every week, for 8 weeks, using the IBB forelimb recovery scoring scale. Higher scores correlate with better performance. Animals treated with 1st trimester PMSCs and PMSC-EVs performed *significantly* better on motor testing compared with ECM only.

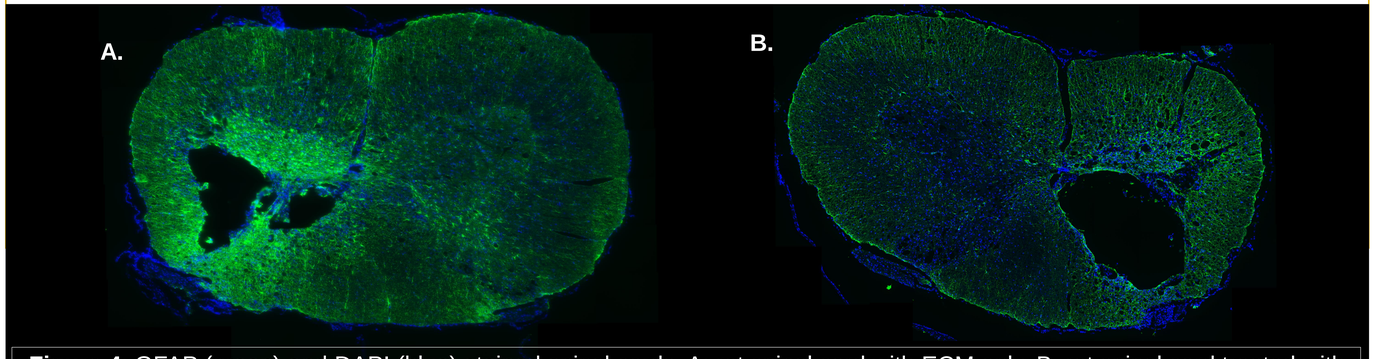

Figure 4: GFAP (green) and DAPI (blue) stained spinal cords. A: rat spinal cord with ECM only. B. rat spinal cord treated with PMSCs + ECM. The brighter green cord correlates with higher GFAP expression and reactive gliosis.

Conclusions

- SCI rats treated with PMSCs and PMSC-EVs show significantly greater motor recovery compared with SCI rats treated with ECM only
- PMSCs and PMSC-EVs provide a novel therapeutic approach to improve motor recovery in SCI
- PMSCs and PMSC-EVs may attenuate reactive gliosis, a harmful inflammatory response inflicted by astrocytes

Further Studies

- Evaluating antibodies specific to neurons, microglia and peripheral macrophages
- Modifying PMSCs and PMSC-EVs for specific targeting or cargo loading

Citations

- Kumar P, Becker JC, Gao K, et al. Neuroprotective effect of placenta-derived mesenchymal stromal cells: role of exosomes. *FASEB J*. 2019;33(5):5836-5849. doi:10.1096/fj.201800972R
- Ramasubramanian L, Kumar P, Wang A. Engineering Extracellular Vesicles as Nanotherapeutics for Regenerative Medicine. *Biomolecules*. 2019;10(1):48. Published 2019 Dec 28. doi:10.3390/biom10010048

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