
In Utero Treatment of Myelomeningocele with Placental Mesenchymal Stromal Cells - Selection of an Optimal Cell Line in Preparation for Clinical Trials.

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Public Summary:

Background We developed a cell culture assay in order to determine if different lines of placenta mesenchymal stromal cells (PMSCs) can protect cultured neurons from dying when a toxin was administered to the neurons. We then examined if these same PMSC cell lines would have the same neuro protective effect in a fetal lamb model of spina bifida. **Methods** PMSC lines were created following culture of three different early age human placentas. The lines were labeled as A, B, and C. Their ability to protect dying neurons in a cell culture model was assessed. Spina bifida was created in 28 fetal lambs, and the lambs were repaired with PMSCs seeded on a clinical grade scaffold from each cell line. The number of lambs treated with each different cell line were: 6 with Line A , 7 with Line B, 5 with Line C, and 10 lambs did not receive PMSCs. The lambs motor function post birth was scored with the establish Sheep Locomotor Rating (SLR) scale. A score of 15 denotes normal motor function, while a score of 0 indicates complete hindlimb paralysis. **Results** Cell culture, Line A and B had a higher neuro protective effect than no PMSCs. Line C did not have a higher neuro protective effect than no PMSCs. Lambs treated with Line A and B had higher motor function scores than lambs that were treated with Line C or with no PMSCs. **Conclusion** The cell culture model used to assess a PMSC line's ability to protect dying neurons in culture can provide insight on the same cell line's ability to protect neurons in a lamb spina bifida model. Thus, the cell culture model can help predict if a PMSC line will aid in restoring motor function in human spina bifida.

Scientific Abstract:

BACKGROUND: We determined whether in vitro potency assays inform which placental mesenchymal stromal cell (PMSC) lines produce high rates of ambulation following in utero treatment of myelomeningocele in an ovine model. **METHODS:** PMSC lines were created following explant culture of three early-gestation human placentas. In vitro neuroprotection was assessed with a neuronal apoptosis model. In vivo, myelomeningocele defects were created in 28 fetuses and repaired with PMSCs at 3×10^5 cells/cm² of scaffold from Line A (n=6), Line B (n=7) and Line C (n=5) and compared to no PMSCs (n=10). Ambulation was scored as ≥ 13 on the Sheep Locomotor Rating Scale. **RESULTS:** In vitro, Line A and B had higher neuroprotective capability than no PMSCs (1.7 and 1.8 respectively vs 1, p=0.02, ANOVA). In vivo, Line A and B had higher large neuron densities than no PMSCs (25.2 and 27.9 respectively vs 4.8, p=0.03, ANOVA). Line C did not have higher neuroprotection or larger neuron density than no PMSCs. In vivo, Line A and B had ambulation rates of 83% and 71%, respectively, compared to 60% with Line C and 20% with no PMSCs. **CONCLUSION:** The in vitro neuroprotection assay will facilitate selection of optimal PMSC lines for clinical use. **LEVEL OF EVIDENCE:** n/a. **TYPE OF STUDY:** Basic science.

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