77th ASRM Scientific Congress & Expo

October 16-20, 2021 // Baltimore, MD, USA

CHARACTERIZATION OF UMBILICAL CORD TISSUE MESENCHYMAL STEM CELLS BASED ON DONOR SEX FOR PREMATURE OVARIAN INSUFFICIENCY

Katherine S. Brown[1], Erkan Buyuk[2], Mathew L. Skiles[1], Allen Marzan[1], Heather L. Brown[1], Alan Copperman[2], Jaime M. Shamonki[1]

1. Generate Life Sciences, Tucson, AZ
2. Reproductive Medicine Associates of New York, New York, NY

Objective: Umbilical cord mesenchymal stem cells (UCMSCs) are proposed as an intervention to improve fertility in patients with Premature Ovarian Insufficiency (POI) based on their potential to modulate inflammatory and/or apoptotic pathways. Our objective was to examine the influence of the sex of the umbilical cord (UC) donor on the characteristics of UCMSCs isolated by explant outgrowth from cryopreserved umbilical cord tissue.

Materials and Methods: UC tissue from 10 full term neonates (5 female, 5 male) were donated for research by the consenting mothers of the neonates. The UC was prepared for cryopreservation and later isolation of UCMSCs by explant outgrowth as previously described. UCMSCs were expanded to the end of the third passage, 1E5 cells were seeded and cultured for 2 days and culture media collected for analysis of cytokines by ELISA. Average cell yield was calculated at the end of passage zero and normalized to one gram of tissue thawed and cultured. Wilcoxon Rank Sum was used for statistical analyses with $p<0.05$ considered statistically significant.

Results: There was no difference in cell yield, viability, and immunologic characteristics between the UCMSCs from both sexes (Table 1). The average fold increase from P1 to P2, when seeded at 3E4 cells, was similar for both sexes (Table 1). More than 80% viability was obtained in all samples tested. The IL-6, FGF2, and TGF-β secretion were similar in a subset of representative samples (3 female, 3 male), but considerable donor to donor variability was observed. VEGF and TGF-β secretion were observed under hypoxic or hypoxic and activated conditions, respectively, and VEGF may trend towards higher secretion in female UCMSCs.

Conclusion: UCMSCs can be isolated from previously cryopreserved UC and cultured with a relatively high yield. The cells secrete anti-inflammatory, pro-angiogenic and pro-survival cytokines that may positively affect folliculogenesis and prevent germ cell apoptosis. Secretion can be fine-tuned in a donor-specific manner utilizing effect-specific culture conditions. We are initiating in vitro and in vivo studies to elucidate the therapeutic potential of UCMSCs in POI.

	Average Cell Yield/Gr from Thaw (Avg, Std)	Average Expansion P1 to P2 (Std)		Average 7-AAD Viability (%) (Std)		Average Cell Surface Markers (%) (Std)			Median Cytokine Secretion (pg/mL/100,000 cells) (IQR)			
		Fold Increase	Days in Culture	P0	P3	CD73	CD90	CD34/45	IL-6	FGF2	VEGF	TGF-β
Female	4.9E+6 (5.5E+6)	9.3 (0.5)	5.4 (1.5)	90 (6)	94 (3)	99 (2)	95 (5)	1 (2)	720 (321-730)	527 (498-1666)	1057 (833-8535)	747 (609-819)
Male	5.8E+6 (4.7E+6)	9.0 (3.2)	5.2 (1.3)	82 (6)	95 (1)	100 (0)	93 (6)	0 (0)	521 (511-801)	576 (450-905)	115 (75-167)	655 (437-876)
p-value	>0.05	>0.05	>0.05	0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	0.0495	>0.05