Meta-analysis version 2.2. (Biostat Inc., Englewood, NJ). We conducted fixed or random effects model meta-analyses to assess efficacy outcomes. The quality of studies was assessed using the Newcastle-Ottawa Scale.

We included 11 studies in the single arm meta-analysis. The pooled mean difference in ALS-FRS from the baseline to primary end points was decreased by 3.3 points (95%CI: -5.38 to -1.22) in which ALS-FRS declined 0.4 points per month. In terms of FVC, the pooled mean difference from the baseline was decreased by 14% (95%CI: -19 to -6%), average decline in FVC was 1.2% per month.

According to natural history data, ALS-FRS score was declined 1.01 points and FVC reduced 2.7% and per month in patients with ALS. Compared to natural history stem cell therapy for patients with ALS can be judged as slowing the disease progression based on single arm clinical studies. However, clinical benefits of stem cell therapy for patients with ALS need further investigation and reevaluation to test the clinical efficacy.

191

NEURAL ENGRAFTMENT OF A CORD BLOOD-DERIVED CELL PRODUCT FOLLOWING INTRATHECAL TRANSPLANTATION

R Storms[1], J Lew[1], C Liu[2], T Gentry[1], A Ozamiz[1], B Rusche[1], A Balber[1], J Kurtzberg[1]

[1]Robertson Clinical and Translational Cell Therapy Program, Duke Translational Medicine Institute, Durham, North Carolina, United States, [2]Department of Surgery, Duke University, Durham, North Carolina, United States

We have developed an umbilical cord blood-derived cell product, DUOC-01, as a potential adjunct therapy to facilitate neural repair in patients with leukodystrophies. In clinical practice, DUOC-01 cells will be transplanted by intrathecal injection several weeks after the patient receives a systemic cord blood transplant. To validate this strategy, we developed a preclinical model whereby DUOC-01 cells were transplanted by intrathecal injection into neonatal ($\leq$ 2 days old) NOD/SCID-IL2Rγ^{null} (NSg) mice. In our prior work, we analyzed the tissue distribution of the cells using quantitative PCR to detect human Alu DNA sequences. That work demonstrated that, within the first 24 hours, the DUOC-01 cells were detectable in all mice that had been transplanted (n=5); and, localized to both neural and non-neural tissues, including the brain, spinal cord, lungs and liver. Human cells remained detectable within approximately half of all mice for periods of up to 56 days post-transplantation (n=22); however, from day 7 onward, the cells were only detectable within the brain and spine.

To confirm that the DUOC-01 cells reach the target tissue for this therapy, the current study sought to directly visualize the cells within the brain tissue of transplanted mice. To facilitate their detection in vivo, the DUOC-01 cells were modified with carboxyfluorescein succimidyl ester (CFSE) prior to transplantation. Neonatal NSg mice were transplanted with 10^5 fluorescein-modified cells by intrathecal injection and were sacrificed at 7 days post-transplantation. Using confocal microscopy, the human cells were identified within brain sections based on their green fluorescence and were confirmed by their co-expression of the human nuclear antigen. Using this strategy, human cells were detected at low frequencies within the brains of 6 of 11 mice analyzed. These studies confirmed that, following intrathecal injection, DUOC-01 cells reach the tissue targeted for repair by this cellular therapy.

192

PREPARATION OF AUTOLOGOUS BONE MARROW-DERIVED MESENCHYMAL STEM CELLS (MSCS) FOR MESENCHYMAL STEM CELL THERAPY FOR CANADIANS WITH MULTIPLE SCLEROSIS (MESCAMS) TRIAL

S Khan[1], CSt Germain[1], S Hodgins[1], C Hilliker[2], M Freedman[2,1,3], DW Courtman[1,2,3]

[1]Ottawa Hospital Research Institute, Ottawa, Ontario, Canada, [2]The Ottawa Hospital, Ottawa, Ontario, Canada, [3]University of Ottawa, Ottawa, Ontario, Canada

MESCAMS is a phase IIa "proof-of-principle" study to examine the feasibility, safety and potential benefit of autologous mesenchymal stem cell (MSC) therapy for inflammatory forms of multiple sclerosis (MS). This is a randomized, double-blind, sham-controlled crossover trial using autologous MSCs to treat MS.

Bone marrow (BM) aspirate from donors was transferred to a BioSpherix Xvivo Isolater unit (constantly maintaining and recording critical environmental conditions), diluted in DMEM containing human platelet lysate and plated in T-175 cell bind flasks. Cells were passaged into HYPERFlasks after 7 to 10 days and cultured for a further 7 to 10 days, harvested and resuspended in Plasma-Lyte A containing 5% human albumin and 10% DMSO prior to being cryopreserved.

BM-derived MSCs from 3 different donors were cultured in our GMP facility with the current MESCAMS protocols. The cells were plastic adherent with a spindle shaped morphology. MSCs displayed 88.3±2.3% viability after being thawed and no significant change in viability after 3h (88±3%) of incubation at room temperature post-thaw. Single nucleotide polymorphism array based genotyping showed genomic stability in BM-derived MSCs. These MSCs were capable of trans-differentiating into both adipocytes and osteocytes; tested positive (>95%) for CD-90, CD-73 and CD-105 and negative (< 2%) for CD-14, CD-19, CD-34, CD-45 and HLA-DR; demonstrated enhanced levels of Indoleamine-pyrrole 2, 3-dioxygenase in response to IFN-γ treatment and an ability to suppress lymphocyte proliferation. Finally, MSCs passed sterility testing (BacT/Alert SA/SN) and displayed endotoxin levels of < 0.2 EU/mL (Endosafe-PTS system).

These results indicate that we have successfully propagated MSCs as a potential therapeutic product in HYPERFlasks with controlled critical cell parameters in a BioSpherix Xvivo Isolator unit and based on this data have been awarded a no objection letter from Health Canada to initiate the clinical trial.

193

HUMAN UMBILICAL CORD PERIVASCULAR CELLS (HUC-PVCs) PROTECT AXONS FROM DEGENERATION IN AN *IN VITRO* PERIPHERAL NERVOUS SYSTEM INJURY MODEL

T Barretto[1], K Park[1], L Maghen[1], S Kenigsberg[1], A Gauthier-Fisher[1], C Librach[1,3,2]

[1]Create Fertility Centre, Toronto, Ontario, Canada, [2]Department of Gynaecology, Women's College Hospital, Toronto, Ontario, Canada, [3]Department of Obstetrics and Gynaecology, University of Toronto, Toronto, Ontario, Canada

HUC-PVCs are novel mesenchymal stromal cell (MSC) therapy candidates for regenerative medicine applications such as neural injuries and neurodegenerative diseases. HUC-PVCs derived from first trimester (FTM) and term cords have previously been shown to exhibit pericyte-like properties. Because of the intimate relationship that exists between pericytes and axons, we hypothesized that HUC-PVCs can prevent axonal degeneration. Axonal degeneration induced by withdrawal of nerve growth factor (NGF) in rat sympathetic cervical ganglia (SCG) neuronal compartment cultures was used as an *in vitro* PNS injury model. Injured axon compartments were treated with ultraculture media or with established lines of fluorophore-labeled HUC-PVCs, bone marrow-derived MSCs (BMSCs) (Lonza) or neonatal fibroblasts (ATCC) and immunostained for βIII tubulin to quantify the proportion of degenerating axons by microscopy. When compared to control conditions (injury alone), treatment with term HUC-PVCs reduced the number of degenerating SCG axons by $40 \pm 6\%$ ($n \geq 4$), first trimester HUC-PVCs by $8 \pm 12\%$, BMSCs by $14 \pm 1\%$ and fibroblasts by $10 \pm 9\%$ (n=3). Term HUC-PVCs had the most profound effect on rescue of SCG axonal degeneration ($p \leq 0.01$).Term HUC-PVCs and axons displayed dynamic interactions and made localized contacts after injury. Western blot analysis revealed an upregulation of pERK and pAKT in lysates of axon compartments treated with Term HUC-PVCs. Blocking experiments indicate that NT3 alone is not required for this effect. Our data suggest that term HUC-PVC-mediated protection against axonal degeneration is dependent on direct HUC-PVC-axon interactions; however, effects of HUC-PVC conditioned media are also being examined. This suggests that local delivery of HUC-PVCs to injured nervous system would be a more effective approach for repairing certain types of neuronal injuries using these cells. The precise mechanism of rescue is currently being investigated.

194

EXPLORING THE SECRETOME OF BONE MARROW MESENCHYMAL AND NEURAL CREST-DERIVED STEM CELLS FOR TREATING SPINAL CORD INJURIES

V Neirinckx, G Agirman, C Coste, B Rogister, R Franzen, S Wislet

GIGA Neurosciences, University of Liège, Liège, Liège, Belgium

Spinal cord injury (SCI) represents a critical issue in clinical research and patient care. Stem cell-based therapies have been proposed worldwide, especially studying stem cells from the adult bone marrow stroma. Previous studies focusing on those cells did not specifically consider their intrinsic embryonic heterogeneity, thus intermingling different stem cells subpopulations to treat experimental SCI or even injured patients.

In this study, we compared adult bone marrow neural crest-derived (NCSC) and mesenchymal stem cells (MSC), and highlight which of their specific properties could be relevant in therapeutic perspectives. We isolated NCSC and MSC from