(*Col1A1), tissue inhibitor of metalloproteinase 1* (*TIMP1),* or *α-smooth muscle actin (ACTA2*). CDAHFD and SD pHSCs were then treated for 48 hours with increasing doses of BMS-22 or MVC (range: 0.3-120ng/mL) to determine (1) the degree of attenuation of the pro-fibrogenic response as measured by qPCR of fibrogenic genes (*Col1A1, TIMP1, ACTA2);* (2) enhancement of a fibrolytic response as measured by qPCR of *matrix metalloproteinases (MMP*) *2, 9* and *13* genes*;* and (3) pHSC migration using the scratch assay. Cell viability and CCR2 and CCR5 gene expression in response to escalating doses of antagonists were also measured. RESULTS/ANTICIPATED RESULTS: Plate- and TGF-b activated CDAHFD pHSCs had a 2-fold greater, dose-dependent attenuation of their pro-fibrogenic activity in response to BMS-CCR2-22 and MVC, when compared with plate- and TGF-b activated SD pHSCs, as measured by reductions in collagen 1α1 (*Col1A1*) and α-smooth muscle actin (*ACTA2*) gene expression. *TIMP1* gene expression was unaffected by drug treatment for 48 hours. Cell viability was not affected up to doses of 30ng/mL of each drug. pHSCs also demonstrated a dose-dependent increase in *CCR2, CCR5* and *MMP-9* gene expression in response to surface receptor antagonism. Migration assays comparing CDAHFD and SD pHSCs in response to escalating doses of MVC and BMS-22 are ongoing and expected to demonstrate a significantly decreased migratory capacity of CDAHFD pHSCs than SD pHSCs in response to therapy, reflecting the increased susceptibility of the "fat-exposed" pHSCs to anti-fibrotic therapy than normal pHSCs. DISCUSSION/SIGNIFICANCE OF IMPACT: Anti-fibrotic drugs that dampen pro-fibrogenic activities of "fat-exposed" pHSCs are urgently needed. CCR2 and CCR5 antagonists, BMS-22 and MVC, respectively, can selectively dampen the pro-fibrogenic response of fat-exposed pHSCs, and must be considered for future trials in human NASH. CONFLICT OF INTEREST DESCRIPTION: Dr. Jill Smith has a patent licensing agreement with Immune Therapeutics, Inc.

4492

The role of creatine in developmental myelination and remyelination†

Lauren Rosko[1], Victoria N Smith[2], and Dr. Jeffrey K. Huang[2]
[1]Georgetown - Howard Universities; [2]Georgetown University

OBJECTIVES/GOALS: Oligodendrocytes (OL) are glial cells of the central nervous system (CNS) responsible for the energy demanding task of generating myelin sheaths during development and remyelination after demyelinating injury. One metabolite shown to significantly increase ATP production in OL is the nitrogenous organic acid, creatine. Creatine plays an essential role in ATP buffering within tissues with highly fluctuating energy demands such as brain and muscle. Interestingly, mature OL, which are the cells capable of myelin production, are the main cells in the CNS expressing the rate-limiting enzyme for creatine synthesis, guanidinoacetate methyltransferase (*Gamt)*. Patients with mutations in *Gamt* display intellectual disabilities, impaired myelination and seizures. Therefore, we hypothesize that creatine may be essential for developmental myelination and improve remyelination. METHODS/STUDY POPULATION: To investigate these hypotheses, we developed a new transgenic mouse model with LoxP sites flanking exons 2-6 of the *Gamt* gene where excision leads to expression of a green fluorescent tag allowing us to track the cells normally expressing *Gamt.* RESULTS/ANTICIPATED RESULTS: In this mouse model, we show a 95% (±0.47%, n = 3) co-localization of *Gamt* within mature OL during postnatal (P) day P14. Next, we show that knocking out *Gamt* leads to a significant reduction in OL in the major CNS white matter tract, the corpus callosum, at P14 and P21 (P14: 0.007, n = 3; P21: 0.04, n = 3). Here, we also investigate whether dietary creatine can enhance remyelination in the cuprizone model of toxic demyelination. DISCUSSION/SIGNIFICANCE OF IMPACT: These studies highlight the important role creatine plays in developmental myelination and investigate whether creatine can provide a therapeutic value during a CNS demyelinating insult.

4362

The Utilization of Polyethylene Glycol Fusion to Improve Facial Reanimation†

Marissa Suchyta[1], Si-Gyun Roh, MD[1], Diya Sabbagh, MD[1], Mohammed Morsy, MD[1], Huan Wang, MD, PhD[1], and Samir Mardini, MD[1]
[1]Mayo Clinic

OBJECTIVES/GOALS: This study's goal is to determine whether intraoperative treatment of facial nerves with polyethylene glycol (PEG) fusion technology improves facial paralysis outcomes. Improved facial nerve regeneration in facial paralysis patients would lead to improved recovery time and effectiveness. METHODS/STUDY POPULATION: 30 rats were utilized; 15 underwent facial nerve regeneration without PEG fusion, and 15 with PEG fusion. Facial paralysis was initiated on the left by transection of the buccal and marginal mandibular branches of facial nerve. The buccal branch was repaired though microsuture technique. Neurorrhaphy sites of rats in the PEG group were exposed to calcium free saline, methylene blue, and polyethylene glycol. Nerve continuity was assessed post-operative in 5 animals in each group through electron microscopy. Functionality was assessed in the other 10 per group by EMG and whisker analysis after surgery, and weekly for 8 weeks. At 8 weeks, nerves and distal muscles were histologically analyzed. RESULTS/ANTICIPATED RESULTS: PEG fusion technology immediately restored axonal continuity following surgery, demonstrated by electron microscopy. Electrophysiology was also similarly restored across the site immediately, determined through intraoperative nerve stimulation, in the PEG fusion group. The nonintervention group showed dramatically reduced functional recovery than the PEG fusion group following surgery, shown by lower whisking activity and poor electrophysiology outcomes. Furthermore, the PEG fusion group showed statistically significant higher fascicle counts, myelination diameter, axonal diameter, and distal muscle fibers histologically. DISCUSSION/SIGNIFICANCE OF IMPACT: This study demonstrates that polyethylene fusion technology may improve facial reanimation outcomes. PEG is already a FDA-approved drug, and thus the pathway to translational clinical application of this work may thus be streamlined, bringing new options to patients with facial paralysis.

4431

Utilization of swept source optical coherence tomography to optimize characterization of cystoid macular edema in preterm infants

Kai Seely[1], Shwetha Mangalesh, Katrina Winter, Vincent Tai, Du Tran-Viet, Stephanie Chiu, and Cynthia Toth
[1]Duke University

OBJECTIVES/GOALS: The goal of this study is to evaluate and optimize the characterization of cystoid macular edema (CME) using an investigational swept source (SS)-OCT system. Our knowledge of

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