Immune Therapeutics, Inc.

DESCRIPTION: Dr. Jill Smith has a patent licensing agreement with trials in human NASH. CONFLICT OF INTEREST pHSCs are urgently needed. CCR2 and CCR5 antagonists, BMS-22 remyelination The role of creatine in developmental myelination and drugs that dampen pro-fibrogenic activities of pHSCs. DISCUSSION/SIGNIFICANCE OF IMPACT: Anti-fibrotic Gamt OL during postnatal (P) day P14. Next, we show that knocking out ACTA2); (2) enhancement of a fibrolytic response as measured by qPCR of fibrogenic genes (Col1A1, TIMP1, ACTA2); (2) enhancement of 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.

The role of creatine in developmental myelination and remyelination1

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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 nitrogensous 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.

The Utilization of Polyethylene Glycol Fusion to Improve Facial Reanimation1

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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 transaction of the buccal and marginal mandibular branches of facial nerve. The buccal branch was repaired through 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.

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

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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
CME in preterm infants is limited; optimizing its characterization is a critical step in understanding its impact on vision. METHODS/STUDY POPULATION: In this IRB-approved protocol, 118 preterm infants were imaged in the Duke intensive care nursery (ICN) with a novel lightweight, hand-held, high-speed, SS-OCT system following routine clinical eye exams. SS-OCT images were de-identified, automatically segmented using custom software (DOCTRAP), measured for several retinal layer thicknesses, and reviewed by masked expert graders for the presence and severity of CME. Reliability of SS-OCT measures will be assessed, and the association between CME status and retinal layer thicknesses will be calculated using logistic regression modeling. RESULTS/ANTICIPATED RESULTS: The prevalence of CME overall and by severity will be calculated. The distribution of several retinal layer thicknesses will be reported and compared by infant CME status and, when edema is present, by CME severity. Reproducibility and repeatability will be reported for objective variables, and intra-grader and inter-grader agreement will be reported for subjective variables. Multivariate logistic regression coefficients and odds ratios will be calculated for each retinal layer thickness variable. DISCUSSION/SIGNIFICANCE OF IMPACT: This study will use a novel SS-OCT system to identify retinal thickness measures that may be objective markers of CME status. This will refine the characterization of CME and provide a framework for correlating CME with functional outcomes like visual acuity. CONFLICT OF INTEREST: SC and CT have unlicensed patents on relevant technologies. CT receives royalties from Alcon and Hemosonics and consultation fees from EMMES.