suppression. 5 (10.4%) of patients with burst suppression were independent at the time of hospital discharge. Preliminary analyses was performed on 6 patients (24 bursts in total). ROI's determined to be sources in a majority of the burst (>=13) were bilateral superior frontal, rostral middle frontal, parstriangularis precentral, superior parietal, inferior parietal, right post central, superior temporal, lateral occipital, and left middle temporal ROI. A lower mean ADC intensity was associated with a higher EEG power in the bilateral superior frontal ($r = -0.80$, $p < 0.0001$; $r = -0.677$, $p < 0.001$, respectively), left superior parietal ($r = -0.53$, $p = 0.009$), left middle temporal ($r = -0.43$, $p = 0.042$) ROI. DISCUSSION/SIGNIFICANCE: The source of bursts in patients post-cardiac arrest experiencing burst suppression is not well defined. This study will improve our understanding of how burst suppression is a measure of cortical injury, how it may relate to the burden of injury found on ADC imaging, and patient outcomes.

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Investigation of a translational astrocyte-targeted AAV-mediated gene addition therapy in two models of Vanishing White Matter disease

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OBJECTIVES/GOALS: Vanishing White Matter Disease (VWM), is a childhood neurodegenerative leukodystrophy that presents with motor deficits, neurologic decline, and seizures leading to death.There are no treatments. Herein we investigate adeno-associated virus serotype 9 (AAV9) gene addition therapy for VWM. METHODS/STUDY POPULATION: To serve as a baseline for disease correction, we characterized the severe VWM Eif2b5^{I98M} murine model with clinically relevant readouts including motor function, gait mapping and myelin loss through magnetic resonance imaging (MRI). Molecular characterization through the identification of biomarkers was also investigated. To provide targeted disease correction, we designed four gene replacement constructs to drive the rapeutic EIF2B5 expression in astrocytes—a critical cell type for VWM pathology. We are currently evaluating our AAV vectors in two murine VWM models, Eif2b5^{R191H} and Eif2b5^{I98M}, and are monitoring disease progression using traditional and clinically relevant readouts. RESULTS/ANTICIPATED RESULTS: The I98M mice display significant mobility loss, ataxic gait, and demyelination. Molecular characterization also indicates that the integrated stress response is significantly dysregulated, supporting the classic VWM phenotype. Our previous biodistribution study confirmed our ability to efficiently target astrocytes using varying iterations—including one novel—of the glial fibrillary acidic protein (GFAP) promoter. Our data suggests that targeting astrocytes with gene addition delays disease onset, partially rescues motor function, and attenuates myelin loss. Survival of the AAV9-gfaABC(1)D-EIF2B5 treated I98M mice is also significantly increased ($p<0.0001$), currently with a 2-fold extension in life expectancy. DISCUSSION/SIGNIFICANCE: Overall, we anticipate emergence of a lead astrocyte-targeted gene therapy candidate in which the data will be strengthened through the evaluation of clinically relevant measures in two murine models of disease, allowing fortimely translation to the clinic.

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Detecting Hypofibrinolysis in Clinical Coagulation Testing

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OBJECTIVES/GOALS: The goal of this study is twofold: To develop a method for an ex vivo hypofibrinolytic control and second to analyze patterns in standard and recently developed clinical coagulation assays for the detection of hypofibrinolytic states. METHODS/STUDY POPULATION: We analyzed blood samples from healthy patients first under normal conditions and then laced with human recombinant PAI-1 under three different concentrations. We then analyzed both samples using standard clinical assays (PT, aPTT, D-dimer, Fibrinogen), thromboelastography point-of-care tests (Hemosoncs- Quantra system), and with research assays of clot size and aggregation. Our previous research of diagnostic errors showed the patient group with the highest overall risk of these non-identifiable thrombotic complications was post-menopausal women with chronic diseases. We therefore focused our patient population to healthy post-menopausal women who were not using hormone replacement therapy. RESULTS/ANTICIPATED RESULTS: Research assays showed PAI-1 significantly increased clot size and aggregation. Preliminary results of clinical assays showed no detectable difference in hypofibrinolytic samples at any concentration. We anticipate ongoing testing will show similar results. Results on Quantra tests showed much larger differences between control and hypofibrinolysis samples, and we anticipate ongoing testing will achieving statistical significance. It is still unknown whether the mean value for hypofibrinolysis samples on the Quantra Clot Stability assay will be outside of the "normal" reference range. We theorize that this may be due to hypofibrinolytic changes in the overall structure and core density of the clots. DISCUSSION/SIGNIFICANCE: Cellular stress stimulates a concomitant activation of inflammation and coagulation, including decreased fibrinolysis. Unfortunately, current clinical assays do not assess clot breakdown. This connection would account for the increased rate of thrombosis in patients with chronic inflammation without detectable results on clinical tests.

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Epithelial hypoxia maintains colonization resistance against Candida albicans

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OBJECTIVES/GOALS: Antibiotic treatment sets the stage for intestinal domination by Candida albicanswhich is necessary for development of invasive disease, but the resources driving this bloom remain poorly defined. We sought to determine these factors in order to design novel prophylaxis strategies for reducing gastrointestinal (GI) colonization. METHODS/STUDY POPULATION: We initially developed a generalizable framework, termed metabolic footprinting to determine the metabolites C. albicanspreferentially uses in the mouse GI tract. After identifying the metabolites C. albicansutilizes, we usedin vitro growth assays in the presence and absence of oxygen to validate out metabolomics findings. We next determined if a probiotic E. coli that utilizes oxygen would reduce C. albicanscolonization compared to a mutant E. coli that could not respire oxygen. Finding that oxygen was a necessary resource, we utilized germ-free mice to determine if Clostridiaspp. known to reduce GI oxygen would prevent C. albicanscolonization. Lastly, we sought to see if 5-aminosalicylic acid (5-ASA) could prevent C. albicanscolonization. RESULTS/ANTICIPATED RESULTS: We found that C. albicans preferentially utilizes simple carbohydrates including fructo-oligosaccharides (e.g., 1-kestose), disaccharides (e.g., β-gentiobiose), and alcoholic sugars (e.g., sorbitol) and is able to grow in vitro on minimal media supplemented with either of these nutrients. However, in the hypoxic environment that is found in the "healthy" colon, C. albicans cannot utilize these nutrients. We next found that pre-colonization in a mouse model with a probiotic E. coli significantly reduced C. albicanscolonization, but the mutant E. coli had no effect on colonization. We next showed that Clostridia supplementation restored GI hypoxia and reduced C. albicanscolonization. Remarkably, we found that 5-ASA significantly reduced GI colonization of C. albicans. DISCUSSION/SIGNIFICANCE: We have shown that C. albicans requires oxygen to colonize the GI tract. Importantly, we found that 5-ASA can prevent an antibiotic mediated bloom of C. albicans by restoring GI hypoxia, which warrants additional studies to determine if 5-ASA can be used as an adjunctive prophylactic treatment in high risk patients.

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Mechanisms of a Dynamic Stability Protocol for Persons with Thumb Osteoarthritis†

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OBJECTIVES/GOALS: Our aims are to 1) describe changes in thumb Carpometacarpal (CMC1) joint stability following an 8-week clinic-based dynamic stability exercise program using computerized tomography (CAT) and 2) to evaluate the agreement between ultrasound and CAT (reference standard) when quantifying thumb CMC stability. METHODS/STUDY POPULATION: Aim 1: We have enrolled 13/49 participants in a prospective pre-post interventional study of an 8-week clinic-based occupational therapy dynamic stability program. The primary outcome will be change in stability (thumb metacarpal subluxation in mm) when forcefully loading the thumb as per CAT from pre-treatment to post-treatment at 9 weeks. Aim 2: Same 49 participants are undergoing a one-time ultrasound during baseline assessment. Agreement of ultrasound and CAT measurements (thumb metacarpal subluxation in mm) will be assessed by the Bland-Altman method. RESULTS/ANTICIPATED RESULTS: Exercise is a first-line treatment of CMC1 OA yet there is insufficient evidence to support this. Progression of CMC1 OA is characterized by altered joint mechanics. Joint replacement surgery may reduce pain but often worsens thumb mechanics and overall hand function. This study is the first to test the sustained biomechanical effects of non-invasive thumb exercises. Should these benefits exist, this will further support exercise as a first-tier intervention. Should ultrasound be a suitable proxy for CAT, therapists/physicians could monitor thumb CMC mechanics in response to treatment without risk of radiation exposure. We anticipate 1) a statistically significant reduction in thumb CMC subluxation at 9 weeks follow up and 2) high agreement between sonographic and CAT measures of thumb stability. DISCUSSION/SIGNIFICANCE: This study will lay the foundation for future work and may offer critical support for the use of a non-pharmacological and non-surgical approach as first-line treatment of a highly disabling disease. Future study should include controlled trials where hand function, activity limitation, disease progression, and costs are the outcomes in interest.

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A CTS Team Approach to Identifying Risk of Neonatal Hypoglycemia and its Relationship with Endothelial Dysfunction*

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OBJECTIVES/GOALS: Neonatal hypoglycemia is seen in 65% of maternally diabetic pregnancies, and can lead to severe neurological damage. Neonatal glycemia may also be an indicator of placental function in these pregnancies. The purpose of this study is to identify patterns of neonatal glycemia, and associated endothelial dysfunction, by maternal diabetes subtype. METHODS/STUDY POPULATION: Pregnancies with maternal Type 1 (T1DM), Type 2 (T2DM), and gestational diabetes mellitus (GDM) are being enrolled. Maternal hemoglobin A1c (HbA1c) and umbilical cord insulin/glucose are being collected from 20 pregnancies in each group, 10 of which also undergo placental/umbilical cord tissue collection. Following delivery, neonatal blood glucose levels are also collected every 3-4 hours (4+ measurements) to determine rate of glycemic change. Linear regression modeling will be used to determine associations with placental and umbilical endothelial RNA expression, umbilical cord insulin levels, and maternal HbA1c within each diabetic subtype and between normoglycemic and hypoglycemic neonates. Endothelial gene expression will be compared using paired t-tests with Benjamini-Hochberg correction. RESULTS/ANTICIPATED RESULTS: Thus far, 5 T1DM, 10 T2DM, and 13 GDM samples have been collected. Gestational age at delivery and birth weight were similar between groups (38.1 ± 1.05 weeks; 3.6 ± 0.59 kilograms) and delivery method is evenly distributed (Cesarean section or vaginal delivery). Currently, with limited cohort size, no association is evident between maternal HbA1c and