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.

400

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.

401

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.

403

Epithelial hypoxia maintains colonization resistance against Candida albicans

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