continued throughout the experiment. We also tested mice lacking the toll-like receptor adaptor protein, MyD88. Cognitive abilities were tested using spontaneous alternation in a Y-maze. RESULTS/ANTICIPATED RESULTS: We found that minocycline reduces fatigue-like behavior exhibited after irradiation, but had no effect on pre-irradiation activity levels. Similarly, fatigue-like behavior after radiation was partially reversed by genetic loss of MyD88. Y-maze spontaneous alternation performance remained similar in all groups. DISCUSSION/SIGNIFICANCE OF IMPACT: Both pharmacological and genetic anti-inflammatory manipulations increased voluntary activity levels after irradiation. Our results suggest that inflammation is an important factor in the development of fatigue-like behavior. Modulators of inflammatory processes hold potential for alleviating fatigue.

4361

Interim Results of the Effect of Haptoglobin Phenotype on Inflammatory Cytokine Concentrations in Plasma and CSF After Aneurysmal Subarachnoid Hemorrhage

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OBJECTIVES/GOALS: Haptoglobin (Hp) phenotypes may affect inflammatory response after neurologic injury. We are investigating the relationship between patient Hp phenotypes and inflammatory cytokine concentrations in plasma and CSF after aneurysmal subarachnoid hemorrhage (aSAH), a severe form of hemorrhagic stroke. METHODS/STUDY POPULATION: Following IRB approval, all patients with angiographically-proven aSAH and who underwent extraventricular drain (EVD) placement were included. Patients were excluded if they were not expected to survive hospitalization or were on pre-existing anti-inflammatory agents. For all enrolled patients, plasma and CSF samples were taken on post-bleed days 3, 5, 7, and 10, processed and then frozen for later analysis. In this interim analysis, Hp phenotype was assessed through ELISA analysis of plasma samples and cytokine concentrations were determined using multiplex ELISA kits for both plasma and CSF samples. Hp phenotypes were dichotomized to either HP1 (Hp 1-1 or 1-2) or HP2 (Hp 2-2). RESULTS/ANTICIPATED RESULTS: To date, 23 aSAH patients have been enrolled in this IRB-approved study. An interim analysis of the first 13 patients has revealed eight Hp1 patients (Hp 1-1 $n = 1$, Hp 1-2 $n = 7$) and five Hp2 patients. CSF levels of IL-6 and TNF-a were greater than plasma levels in all patients at all time points. CSF levels of IL-6 appear to peak on PBD 5 (1890 ± 767 pcg/mL) and 7 (1612 ± 899 pcg/mL). The CSF IL-6 concentrations in the Hp2 group were lower (1792 ± 806 pcg/mL vs. 1952 ± 791 pcg/mL) on PBD5 but were higher (1635 ± 930 pcg/mL vs 1598 ± 943 pcg/mL) at PBD7; however, these differences did not reach statistical significance. DISCUSSION/SIGNIFICANCE OF IMPACT: This interim analysis demonstrated no statistically significant differences in plasma or CSF cytokine concentrations between patients with different Hp phenotypes. This may be due to the low number of samples or the potential confounding effect of disease-specific secondary neurological injuries.

4126

Intermuscular adipose tissue secretes pro-inflammatory, extracellular matrix, and lipid signals related to insulin resistance and type 2 diabetes

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OBJECTIVES/GOALS: Intermuscular adipose tissue (IMAT) has been associated with insulin resistance and type 2 diabetes, yet mechanistic studies addressing the functional role of IMAT are lacking. The aim of this work was to identify novel mechanisms by which IMAT may directly impact skeletal muscle metabolism. METHODS/STUDY POPULATION: We quantified the secretome of IMAT, subcutaneous adipose tissue (SAT), and visceral adipose tissue (VAT) to determine if there are differences between depots in the secretion of cytokines, eicosanoids, FFAs and proteins that influence metabolic function. SAT and VAT biopsies from patients undergoing laparoscopic bariatric surgery and IMAT extracted from vastus lateralis biopsies of individuals with Obesity were cultured for 48 hours in DMEM, and the conditioned media was analyzed using nanoflow HPLC-MS, multiplex ELISAs and LC/MS/MS for proteins, cytokines and eicosanoids/FFA, respectively. RESULTS/ANTICIPATED RESULTS: IMAT secretion of various extracellular matrix proteins (fibrinogen-β, collagenV1a3, fibronectin) was significantly different than VAT and SAT. Pro-inflammatory cytokine secretion of IFNg, TNFa, IL-8 and IL-13 from IMAT was higher than VAT and significantly higher than SAT ($p < 0.05$). IMAT secretes significantly more pro-inflammatory eicosanoids TXB_2 and PGE_2 than VAT ($p = 0.02$, 0.05) and SAT ($p = 0.01$, 0.04). IMAT and VAT have significantly greater basal lipolysis assessed by FFA release rates compared to SAT ($p = 0.01$, 0.04). DISCUSSION/SIGNIFICANCE OF IMPACT: These data begin to characterize the disparate secretory properties of SAT, VAT and IMAT and suggest a metabolically adverse secretome of IMAT, that due to its proximity to skeletal muscle may play an important functional role in the pathogenesis of insulin resistance and type 2 diabetes.

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Investigating the functional consequences of anaplastic lymphoma kinase (ALK) mutations arising upon Lorlatinib treatment

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OBJECTIVES/GOALS: Neuroblastoma (NB) is an embryonal cancer of the sympathetic nervous system that affects mostly infants and young children. The complex genetic background present across NB patients results in diverse clinical response and difficulty in individualizing therapy. Currently, NB patients undergo a regimen of genotoxic chemotherapeutics, radiation therapy, and new immunotherapy that, while effective, has significant side effects, including excruciating pain. One promising avenue for targeted therapy in neuroblastoma focuses on anaplastic lymphoma kinase (ALK), a cell surface neural receptor tyrosine kinase. We previously identified

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