

and without neuropathic pain, and those with chronic or acute SCI. Linear regression was performed to explore the relationship between miRNA expression and ISCIBPDS pain intensity ratings. RESULTS/ANTICIPATED RESULTS: In individuals with SCI, significant downregulation of expression of miR-338-5p was present in those with neuropathic pain compared to those without neuropathic pain (fold change = 0.81, $p = 0.04$). A significant relationship between expression of miR-338-5p and highest reported neuropathic pain intensity on the ISCIBPDS was identified ($R^2 = 0.15$, $F = 7.32$, $p < 0.01$). Covariates of sex, age, and years post injury were not found to significantly influence the relationship between miRNA expression and ISCIBPDS intensity ratings. No significant differences in miR-338-5p expression were identified between participants with acute and chronic SCI, or with nociceptive pain ratings, demonstrating specificity of the relationship between miR-338-5p differential expression with pain of a neuropathic nature. DISCUSSION/SIGNIFICANCE OF FINDINGS: These findings, along with validated targets of miR-338-5p in the NF-KB neuroinflammatory signaling pathway, suggest that miR-338-5p may serve a neuroprotective role in modulating neuroinflammation, and that its downregulation may result in maladaptive neuroplastic mechanisms contributing to the development of neuropathic pain after SCI.

76938

Does Decreased Adipose Tissue Eosinophil Content Impair Adipocyte Biology in Human Subjects with Obesity and Insulin Resistance?

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ABSTRACT IMPACT: Extrapolating from mouse data we explored eosinophil content in human adipose tissue and its effect on adipocyte biology potentially leading to the discovery of novel therapeutic targets for treatment of obesity and insulin resistance. OBJECTIVES/GOALS: The interaction between immune cells and adipose tissue (AT) in obesity has not been fully elicited. Mouse models of diet-induced-obesity show AT resident eosinophils (EOS) help preserve insulin sensitivity (IS). As data in human obesity are lacking, here we explored AT-EOS content and their role in AT metabolism in subjects with and without obesity. METHODS/STUDY POPULATION: We recruited lean (L) subjects and patients with obesity (Ob) to undergo abdominal subcutaneous AT biopsy and evaluation of insulin resistance (IR) by determination of HOMA-IR. Circulating EOS were isolated from all participants under fasting conditions and exposed to high glucose (HG) or high lipids (HL) for 4 hrs. AT EOS number was assessed via FACS analysis. Circulating EOS and AT mRNA was assessed by qPCR for multiple genes involved in inflammation and cell migration. To evaluate the effect of EOS on primary human adipocytes, in vitro cultures were exposed for 4 days to either interleukin-4 (IL-4), interleukin-13 (IL-13) or to human EOS. Adipocytes mRNA levels were evaluated for genes involved in adipogenesis and lipid metabolism. RESULTS/ANTICIPATED RESULTS: 16 lean, IS subjects (BMI $22.5 \pm 0.4 \text{ kg/m}^2$) and 22 age-matched IR patients with obesity (BMI: $38.9 \pm 1.0 \text{ kg/m}^2$) participated. We observed a ratio of 2:1 in AT EOS content of L vs Ob subjects ($P < 0.03$). To assess the reduced AT-EOS content in obesity, we evaluated expression of Chemokine-C receptor 3 (CCR3) in

circulating EOS. We show decreased CCR3 mRNA levels in Ob vs L subjects ($P = 0.006$). We expect HL in vitro experiments on peripheral EOS of L subjects to affect CCR3 mRNA levels. In AT of Ob subjects, we found a significant decreased expression of Eotaxin 2, the main EOS chemokine binding CCR3 expressed on EOS. Preliminary data from in vitro primary adipocytes culture suggest for IL-4 and IL-13 to increase mRNA level of Peroxisome Proliferator Activated Receptor Gamma (PPARG), the master regulator of adipogenesis. DISCUSSION/SIGNIFICANCE OF FINDINGS: Comparable to animal studies, we found a decrease of AT-EOS content in patients with obesity. Alterations in CCR3/Eotaxin 2 signaling may be involved. IL-4 & IL-13 are secreted predominantly by EOS and appear to directly regulate gene expression in human adipocytes. These data represent the first evidence for a novel role of EOS in human AT biology.

95332

Intestinal inflammation and altered gut microbiota associated with inflammatory bowel disease render mice susceptible to Clostridioides difficile colonization and infection

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ABSTRACT IMPACT: Use of this novel murine model of inflammatory bowel disease (IBD) and *C. difficile* infection (CDI) will aid in developing new clinical approaches to predict, diagnose, and treat CDI in the IBD population. OBJECTIVES/GOALS: IBD is associated with intestinal inflammation and alterations of the gut microbiota, both of which can diminish colonization resistance to *C. difficile*. Here, we sought to determine if IBD is sufficient to render mice susceptible to *C. difficile* colonization and infection in the absence of other perturbations, such as antibiotic treatment. METHODS/STUDY POPULATION: C57BL/6 IL-10^{-/-} mice were colonized with *Helicobacter hepaticus* to trigger colonic inflammation akin to human IBD. Control mice, not colonized with *H. hepaticus*, were pretreated with the antibiotic cefoperazone to render the gut microbiota susceptible to CDI. Mice were then gavaged with spores of the toxigenic *C. difficile* strain VPI 10463 and monitored for *C. difficile* colonization and disease. The fecal microbiota at the time of *C. difficile* exposure was profiled by 16S rRNA gene sequencing and analyzed using mothur. Statistical analyses were performed using R. RESULTS/ANTICIPATED RESULTS: Mice with IBD harbored significantly distinct intestinal microbial communities compared to non-IBD controls at the time of *C. difficile* spore exposure (14 days post-IBD trigger). Mice with IBD were susceptible to persistent *C. difficile* colonization, while genetically identical non-IBD controls were resistant to *C. difficile* colonization. Concomitant IBD and CDI was associated with significantly worse clinical and intestinal disease than unaccompanied IBD. DISCUSSION/SIGNIFICANCE OF FINDINGS: Patients with IBD who develop concurrent CDI experience increased morbidity and mortality. These studies in a novel mouse model of IBD and CDI emphasize the dual importance of host responses and alterations of the gut microbiota in susceptibility to *C. difficile* colonization and infection in the setting of IBD.