**The Gut Microbiome: What Effect Does Our Diet Play in Fracture Healing?**

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**Purpose:** Obesity is a risk factor for delayed fracture healing and nonunion. Associated with this is a recognition of the influence the gut microbiome has on systemic inflammation, which can be altered with prebiotics. Our prior study showed delayed fracture healing with increased adipocytes and decreased biomechanical strength in obese mice compared to lean mice in a tibial shaft fracture model. The purpose of our study was to evaluate the effect of the prebiotic oligofructose on fracture repair and callus morphology in mice fed lean and high-fat diets (HFDs).

**Method:** 20 male mice were fed a lean or high-fat diet for 12 weeks. They were divided into 2 secondary groups supplemented with oligofructose or a control nondigestible fiber for 2 additional weeks. A reproducible tibia fracture was surgically administered and stabilized with an intramedullary needle. At the time of sacrifice (21 days post-fracture), fecal samples were collected and analyzed to determine the bacterial load present using 16S rDNA sequencing. Microcomputed tomography images were obtained to evaluate the volume of mineralized callus. Tibiae were prepared for histological analysis. Histomorphometric analysis of the fracture callus was performed by a blinded observer.

**Results:** In the absence of oligofructose, HFD was associated with a significant increase in % adipocyte area in the callus compared to lean-fed mice. With oligofructose, % adiposity normalized to the phenotype of the lean-fed mice. Histological analysis showed an increased amount of mature, remodeled callus in the lean mice versus the HFD group. Callus size was significantly larger in the mice fed HFDs with cellulose compared to lean fed mice, suggesting delayed callus remodeling. With oligofructose, this normalized to that of the lean mice. The rescue of the phenotype corresponded with a shift in the gut microbiome. Bifidobacterium pseudolongum, a known beneficial microbe, was more abundant in mice fed oligofructose. Several detrimental inflammatory species that were increased in obese mice were suppressed with oligofructose.

**Conclusion:** Oligofructose decreases adiposity and reverses the callus phenotype in obese mice to that of lean mice. Oligofructose resulted in alterations in the gut microbiome favoring a healthy inflammatory environment. Our data suggest that impaired fracture repair in obesity is linked to an inflammatory process driven by an altered gut microbiome, and prebiotic strategies can restore a healthy microbial profile.