Oligofructose alters small intestinal microbiota to improve intestinal nutrient-sensing mechanisms

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The gut microbiota is altered in both obesity and diabetes, recent work has highlighted the therapeutic potential of altering the small intestinal microbiota in metabolic disease. The ingestion of non-digestible carbohydrates, like oligofructose (OFS), represent a non-invasive way to beneficially alter the gut microbiome. Previous studies have shown that OFS can lower body weight and food intake in humans and rodents, although the mechanisms driving these benefits remain poorly understood. Further, no one has examined whether prebiotics alter the small intestinal microbiota, and whether these alterations could impact small intestinal nutrient sensing mechanisms regulating food intake. In this study, high-fat diet (HFD)-fed Sprague Dawley rats were treated with OFS for 6 weeks and food intake, body weight, and adiposity were measured, and rats were tested for nutrient-induced intestinal satiation. Furthermore, expression of small intestinal nutrient receptors and transporters were measured via RT-qPCR, and small intestinal microbiota composition was analyzed by Illumina MiSeq 16S rRNA sequencing. We found that OFS supplementation decreased body weight gain, food intake, and adiposity during HFD. Furthermore, HFD rats treated with OFS increased intestinal nutrient-sensing mechanisms, as evidenced by an increased suppression of food intake following oral nutrient gavage *in-vivo* and increased small intestinal epithelial expression of nutrient transporters SGLT1 and CD36 *ex-vivo*. Lastly, we observed that OFS treatment resulted in a shift in the composition of the small intestinal microbiota in HFD rats. Collectively, these results demonstrate the importance of small intestinal nutrient sensing in mediating the beneficial effects of OFS, and highlight the importance of the small intestinal microbiome in energy regulation.