Duodenal nutrient exclusion improves metabolic syndrome and stimulates villus hyperplasia.

Abstract:
Surgical interventions that prevent nutrient exposure to the duodenum are among the most successful treatments for obesity and diabetes. However, these interventions are highly invasive, irreversible and often carry significant risk. The duodenal-endoluminal sleeve (DES) is a flexible tube that acts as a barrier to nutrient-tissue interaction along the duodenum. We implanted this device in Zucker Diabetic Fatty (ZDF) rats to gain greater understanding of duodenal nutrient exclusion on glucose homeostasis. ZDF rats were randomised to four groups: Naive, sham ad libitum, sham pair-fed, and DES implanted. Food intake, body weight (BW) and body composition were measured for 28 days postoperatively. Glucose, lipid and bile acid metabolism were evaluated, as well as histological assessment of the upper intestine. DES implantation induced a sustained decrease in BW throughout the study that was matched by pair-fed sham animals. Decreased BW resulted from loss of fat, but not lean mass. DES rats were also found to be more glucose tolerant than either ad libitum-fed or pair-fed sham controls, suggesting fat mass independent metabolic benefits. DES also reduced circulating triglyceride.
and glycerol levels while increasing circulating bile acids. Interestingly, DES stimulated a considerable increase in villus length throughout the upper intestine, which may contribute to metabolic improvements. Our preclinical results validate DES as a promising therapeutic approach to diabetes and obesity, which offers reversibility, low risk, low invasiveness and triple benefits including fat mass loss, glucose and lipid metabolism improvement which mechanistically may involve increased villus growth in the upper gut.