Nutrient-sensing in the GI tract: fat, the gut microbiota and obesity

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The major function of the gut epithelium is to absorb nutrients, ions and water. The epithelium of the gut is involved in sensing meal components by gut enteroendocrine cells (EECs), which *via* humoral pathways and activation of neural reflexes regulates gastrointestinal motor, secretory and absorptive functions to maximize the efficiency of digestion and absorption. These sensory mechanisms also play a major role in the regulation of food intake and other metabolic parameters, such as plasma levels of glucose. These specialized epithelial cells, the EECs, express several different sensing mechanisms, including G protein coupled receptors and nutrient transporters, which when activated *via* nutrients induces release of humoral mediators. Another key component in the regulation of GI function and food intake is the vagal afferent pathway. Recent evidence suggests that these neurons express receptors for many of the variety of GI hormones. Moreover, there is evidence that excitability of these neurons can change depending on exposure to high fat diets and obesity.

The GI epithelium must also balance these absorptive functions with that of protecting the “inside” world from potentially harmful toxins, irritants, bacteria and other pathogens that also exist in the gut lumen. Several recent studies have provided compelling new evidence to suggest that changes in epithelial barrier function and inflammation is associated with and may even lead to altered function in GI sensing mechanisms, including enteroendocrine cells and the vagal afferent pathway, leading to altered regulation of body weight and glucose homeostasis. These have led to the hypothesis that changes in the gut microbiota and alteration of gut epithelial function will perturb the homeostatic humoral and neural pathways controlling food intake and body weight.