

Gut Microbiota and Obesity

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Between 1,000 and 1,150 bacterial species have potential to colonise the human gastro-intestinal (GI) tract, with each individual harbouring around 160 different species (1). The composition of the gut microbiota has received attention as an etiological factor in the development of obesity. It is sensitive to dietary changes and able to alter composition within hours in both animals and humans (2-5). Independently of diet, the gut microbiota is able to influence host inflammatory responses.

The bacterial components of Gram-negative bacteria, such as lipopolysaccharide (LPS), trigger innate immune responses in the host which can lead to weight gain (6). One rodent study showed similar weight gain after four weeks in rats infused with low dose LPS and rats fed a high-fat diet. When CD14 $-/-$ rats were infused with LPS, no weight gain occurred (7). In much the same way, Toll-like receptor (TLR) 4-deficient mice, which are unable to respond to LPS, are protected from high-fat diet-induced obesity and insulin resistance (8).

Many bacteria produce butyrate, including the *Eubacterium rectale*–*Clostridium coccooides* group and *Faecalibacterium prausnitzii* (9). Butyrate inhibits lymphocyte proliferation, interleukin (IL)-2 and interferon (IFN)- γ (10) – it is this anti-inflammatory action that explains butyrate's therapeutic effects in inflammatory bowel disease (IBD) patients.

Some GI bacteria can suppress host Fasting-Induced Adiposity Factor (Fiaf) and tight junction proteins such as ZO-1 and occludin expressed in the intestinal epithelia. Fiaf plays a central role in triglyceride metabolism (10,11). This glycoprotein inhibits lipoprotein lipase production in adipose tissue and modulates fatty acid oxidation in both adipocytes and skeletal muscle (12). Suppression of tight junction proteins increases intestinal permeability (13).

Evidence suggests that the GI microbiota in the obese is different from the normal weight subject. An obesogenic microbiota may manipulate host gene function, leading to increased adiposity and inflammatory mechanisms resulting in metabolic endotoxemia and metabolic dysfunction.

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