Relationship between gut microbes and metabolic syndrome

Fredrik Bäckhed, Ph.D.
University of Gothenburg
Wallenberg Laboratory
Bruna Stråket 16
Sahlgrenska University Hospital
Gothenburg 41345 SWEDEN
+46 313427833
Fredrik@wlab.gu.se

The human body is home to microbial ecosystems (microbiotas) whose structure and function differ between different sites in the body. These microorganisms outnumber the number of eukaryotic cells in the human body by at least an order of magnitude. The mammalian gut microbiota has coevolved with its host and has developed metabolic traits that complement the host's metabolism and can thus be regarded as a metabolically active organ located within the mammalian gastrointestinal tract. Evidence is now accumulating to indicate that perturbations of gut microbiota composition/function may play an important role in the development of diseases associated with altered metabolism.

Mice kept under germ-free conditions have reduced adiposity compared with colonized mice. We recently used lipidomics to demonstrate that the gut microbiota has global effects on the host's lipid metabolism, which is characterized by increased hepatic and adipose triglyceride levels, whereas serum triglycerides are reduced compared with germ-free counterparts. This phenotype may be explained by microbial suppression of a lipoprotein lipase inhibitor, angiopoietin-like protein 4 (ANGPTL4) in the intestinal epithelium. Thus, the gut microbiota may affect metabolic diseases by modulating host lipid metabolism.

Increased adiposity is associated with insulin resistance, which precedes type 2 diabetes and cardiovascular disease. Because insulin resistance is associated with an elevated inflammatory tone the gut microbiota may affect insulin sensitivity by promoting a low grade inflammation. Recent data from Cani et al. directly demonstrated that chronic infusion of low levels of lipopolysaccharide impairs glucose metabolism in mice. Interestingly, germ-free mice have a reduced inflammatory tone and improved glucose metabolism. The underlying mechanisms for how the gut microbiota affects glucose metabolism and modulates the low grade inflammation associated with insulin resistance will be discussed.