Gut microbe battles obesity

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(Medical Xpress)—*Akkermansia muciniphila* is one of the many microbes that live in our intestines. This bacterium, which feeds on the intestine's mucus lining, comprises between 3 and 5 percent of the gut microbes of healthy mammals. There is an inverse correlation between body weight and abundance of *A. muciniphila* in mice and humans. In a paper published in the *Proceedings of the National Academy of Sciences*, Patrice Cani of the Catholic University of Louvain in Belgium and his colleagues reveal that levels of this bacterium are very low in mice genetically predisposed to obesity. Restoring *Akkermansia* to normal levels leads to fat reduction and reduced insulin resistance.

Cani and his team found that genetically obese mice had 3,300 times less *A. muciniphila* in their intestines than healthy mice. When they fed mice, regardless of body weight, a high-fat diet, levels of the bacterium fell 100 times.

The researchers were able to restore normal Akkermansia levels to mice on a high fat diet by feeding them live *Akkermansia* or by giving them oligofructose prebiotics.

When normal levels were established, the mice lost weight and developed a better fat to lean mass ratio. Insulin resistance and adipose tissue inflammation, all associated with obesity and type 2 diabetes, also decreased. Metabolic endotoxemia, another related condition, was abolished, while fasting hyperglycemia was reversed. There was an increase in levels of endocannabinoids, which help control blood glucose levels, the gut barrier and inflammation.

Intestinal mucus, which normally erodes with weight gain, became thicker. The mucus that lines the intestines acts as a barrier to harmful microbes, so *A. muciniphila* could play an important role in preventing inflammation and other disease triggers.

Feeding the mice heat-killed *Akkermansia* had no effect.

Cani believes *Akkermansia* sends a signal to the cells of the intestinal lining that causes them to produce more mucus and more anti-microbial molecules. This results in a mutually beneficial relationship between the bacterium and its host; the host provides Akkermansia with food, and *Akkermansia* protects the host from infection.

Although a high fat diet had a strong effect on gut microbiota composition, giving the mice *A. muciniphila* did not significantly affect the overall microbiota profile. This indicates that this species alone was probably responsible for the beneficial changes that occurred.

When the researchers gave obese mice *Lactobacillus plantarum*, a bacterium often found in probiotics, there was no effect.

Cani says scientists should study whether *A. muciniphila* could help treat obesity and related metabolic disorders in humans.

More information: Cross-talk between Akkermansia muciniphila and intestinal epithelium controls diet-induced obesity, *PNAS*, Published online before print May 13, 2013, doi: 10.1073/pnas.1219451110

Abstract
Obesity and type 2 diabetes are characterized by altered gut microbiota, inflammation, and gut barrier disruption. Microbial composition and the mechanisms of interaction with the host that affect gut barrier function during obesity and type 2 diabetes have not been elucidated. We recently

isolated Akkermansia muciniphila, which is a mucin-degrading bacterium that resides in the mucus layer. The presence of this bacterium inversely correlates with body weight in rodents and humans. However, the precise physiological roles played by this bacterium during obesity and metabolic disorders are unknown. This study demonstrated that the abundance of A. muciniphila decreased in obese and type 2 diabetic mice. We also observed that prebiotic feeding normalized A. muciniphila abundance, which correlated with an improved metabolic profile. In addition, we demonstrated that A. muciniphila treatment reversed high-fat diet-induced metabolic disorders, including fat-mass gain, metabolic endotoxemia, adipose tissue inflammation, and insulin resistance. A. muciniphila administration increased the intestinal levels of endocannabinoids that control inflammation, the gut barrier, and gut peptide secretion. Finally, we demonstrated that all these effects required viable A. muciniphila because treatment with heat-killed cells did not improve the metabolic profile or the mucus layer thickness. In summary, this study provides substantial insight into the intricate mechanisms of bacterial (i.e., A. muciniphila) regulation of the cross-talk between the host and gut microbiota. These results also provide a rationale for the development of a treatment that uses this human mucus colonizer for the prevention or treatment of obesity and its associated metabolic disorders.