Microbial menagerie: Junk food binge alters community of microbes in the gut in less than a day

11 November 2009, By Caroline Arbanas

(PhysOrg.com) -- Switching from a low-fat, plant-based diet to one high in fat and sugar alters the collection of microbes living in the gut in less than a day, with obesity-linked microbes suddenly thriving, according to new research at the School of Medicine. The study was based on transplants of human intestinal microbes into germ-free mice.

Switching from a low-fat, plant-based diet to one high in fat and sugar alters the collection of microbes living in the gut in less than a day, with obesity-linked microbes suddenly thriving, according to new research at Washington University School of Medicine in St. Louis. The study was based on transplants of human intestinal microbes into germ-free mice.

Over time, humanized mice on the junk food diet became obese. Their weight gain was in lock step with dramatic shifts in the types of intestinal bacteria present compared to mice on a low-fat diet. Using the latest DNA sequencing technology, the researchers found that mice on the high-fat, high-sugar diet had more microbes and microbial genes devoted to extracting calories from their "western" diet. These microbial genes were turned on when the mice were switched to the diet high in fat and sugar.

The new study, published in *Science Translational Medicine,* documents the intimate relationship between diet and the dynamic variations in the community of intestinal microbes that can influence metabolism and weight. The research also paves the way for using humanized mouse models to tease apart the contributions of human intestinal microbes and human diets to obesity and its converse, malnutrition.

"Pinpointing triggers of obesity or malnutrition in humans is hard because there's a host of factors - genetic, cultural and environmental, such as diet - that are extremely difficult to control," says senior author Jeffrey I. Gordon, M.D., director of Washington University's Center for Genome Sciences. "Recreating the human gut ecosystem in mice gives us a way to control these variables. The information gained from these studies allows us to develop hypotheses that we can test in humans."

Researchers can use these humanized mice to discover the types of microbes that bloom in response to particular diets, with the goal of identifying a new class of probiotics that aid in the digestion of certain foods and nutrients, he adds.

Gordon's pioneering research first established a possible link between obesity and the trillions of friendly microbes that live in the intestine and help to digest food. His group's studies have suggested that the nutrient and caloric value of foods is not absolute but depends, in part, on the mix of microbes that inhabit our intestines.

Obesity affects an estimated 300 million people worldwide, according the World Health Organization. The condition increases the risk for a host of illnesses, including type 2 diabetes, heart disease, stroke and certain cancers.

In the new research, Gordon and graduate student Peter Turnbaugh, together with lab members Vanessa Ridaura and Jeremiah Faith, created an animal model of the human gut ecosystem by transplanting an adult's gut microbial community (obtained from a stool sample) into the guts of germ-free mice. The mice ate low-fat, plant-rich diets in the weeks leading up to the transplants.

The mice continued to eat a low-fat, plant-based diet for one month, and their stool samples were analyzed one day, one week and one month after the microbe transplants. By sequencing the microbes' 16S rRNA gene, which is found in all microbes and can be used to catalog the species present in a microbial community, the researchers found that the microbe transplants were remarkably successful: the mice carried a collection of bacteria that mimicked the human donor's.

After one month on the low-fat, plant-based diet, half the mice were switched to a high-fat, high-sugar "western" diet. Stool samples from all the mice were analyzed 24 hours after the diet change and then again weekly for two months.

"We were surprised to see the rapid shift in the microbial communities of mice on the high-fat, high-sugar diets," says Turnbaugh. "Assuming it takes four to six hours for microbes to move through the intestine, this means that the initial shift in the microbial community occurred 18 to 20 hours after exposure to a western diet."

Compared to mice on the low-fat, plant-based diet, mice on the western diet had a significantly greater proportion of two classes of gut bacteria, Erysipielotrichi and Bacilli, which both belong to a phylum of intestinal microbes called the Firmicutes, and a reduction in members of another phylum known as the Bacteroidetes - changes that Gordon's earlier studies have linked to obesity in mice and humans.

Further, by sequencing the microbial DNA, the researchers determined that mice on the high-fat, high-sugar diet had a greater representation of microbial genes devoted to breaking down and processing simple sugars and other components of a western diet. They also showed these genes were activated in the mice eating the unhealthy diet.

Interestingly, when the researchers transplanted the gut microbial communities of humanized obese mice to germ-free mice, the recipient mice gained weight and fat, even though they ate a low-fat, plant-based diet. The researchers also showed that gut microbes and their genes can be passed don from generation to generation, suggesting that it is possible for motheres to pass their microbial communities to their children.

In other research, Gordon and members of his group are already using the humanized mouse model to understand how communities of human gut microbes may be altered in malnourished children, in work funded by the Bill & Melinda Gates Foundation. In this line of investigation, the humanized mice are created by transplanting microbes from children living in areas of the world where malnutrition is common, and then the mice are fed diets typical of those at risk for the condition.

"By analyzing the microbial communities, we hope to identify the microbial deficiencies that explain why some children and not others suffer from malnutrition," he says.

The researchers also noted that microbial communities could be transplanted successfully into the mice using either fresh or frozen stool samples from a human donor. The ability to use frozen stool samples has broad implications, since it means that humans around the world, who are obese or suffer from malnutrition or other conditions that affect gut microes, could have their stool samples stored and analyzed.

More information: Turnbaugh PJ, Ridaura VK, Faith JJ, Rey FE, Knight R, Gordon JI. The Effect of Diet on the Human Gut Microbiome: A Metagenomic Analysis in Humanized Gnotobiotic Mice. *Science Translational Medicine*. Nov. 11, 2009.

Provided by Washington University School of Medicine in St. Louis