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Waste from gut bacteria helps host control weight, researchers report

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A single molecule in the intestinal wall, activated by the waste products from gut bacteria, plays a large role in controlling whether the host animals are lean or fatty, a research team, including scientists from UT Southwestern Medical Center, has found in a mouse study.

When activated, the molecule slows the movement of food through the intestine, allowing the animal to absorb more nutrients and thus gain weight. Without this signal, the animals weigh less.

The study shows that the host can use bacterial byproducts not only as a source of nutrients, but also as chemical signals to regulate body functions. It also points the way to a potential method of controlling weight, the researchers said.

"It's quite possible that blocking this receptor molecule in the intestine might fight a certain kind of obesity by blocking absorption of energy from the gut," said Dr. Masashi Yanagisawa, professor of molecular genetics at UT Southwestern and a senior co-author of the study, which appears online in *Proceedings of the National Academy of Sciences.*

Humans, like other animals, have a large and varied population of beneficial bacteria that live in the intestines. The bacteria break up large molecules that the host cannot digest. The host in turn absorbs many of the resulting small molecules for energy and nutrients.

"The number of bacteria in our gut far exceeds the total number of cells

in our bodies," said Dr. Yanagisawa.

"It's truly a mutually beneficial relationship. We provide the bacteria with food, and in return they supply energy and nutrients," he explained.

Using mice, the researchers focused on two species of bacteria that break up dietary fibers from food into small molecules called short-chain fatty acids. Dr. Yanagisawa's team previously had found that short-chain fatty acids bind to and activate a receptor molecule in the gut wall called Gpr41, although little was known about the physiological outcome of Gpr41 activation.

The researchers disrupted communication between the bacteria and the hosts in two ways: raising normal mice under germ-free conditions so they lacked the bacteria, and genetically engineering other mice to lack Gpr41 so they were unable to respond to the bacteria.

In both cases, the mice weighed less and had a leaner build than their normal counterparts even though they all ate the same amount.

The researchers also found that in mice without Gpr41, the intestines passed food more quickly. They hypothesized that one action of Gpr41 is to slow down the motion that propels food forward, so that more nutrients can be absorbed. Thus, if the receptor cannot be activated, food is expelled more quickly, and the animal gets less energy from it.

Because mice totally lacking Gpr41 were still healthy and had intestinal function, the receptor may be a likely target for drugs that can slow, but not stop, energy intake, Dr. Yanagisawa said.

Source: UT Southwestern Medical Center