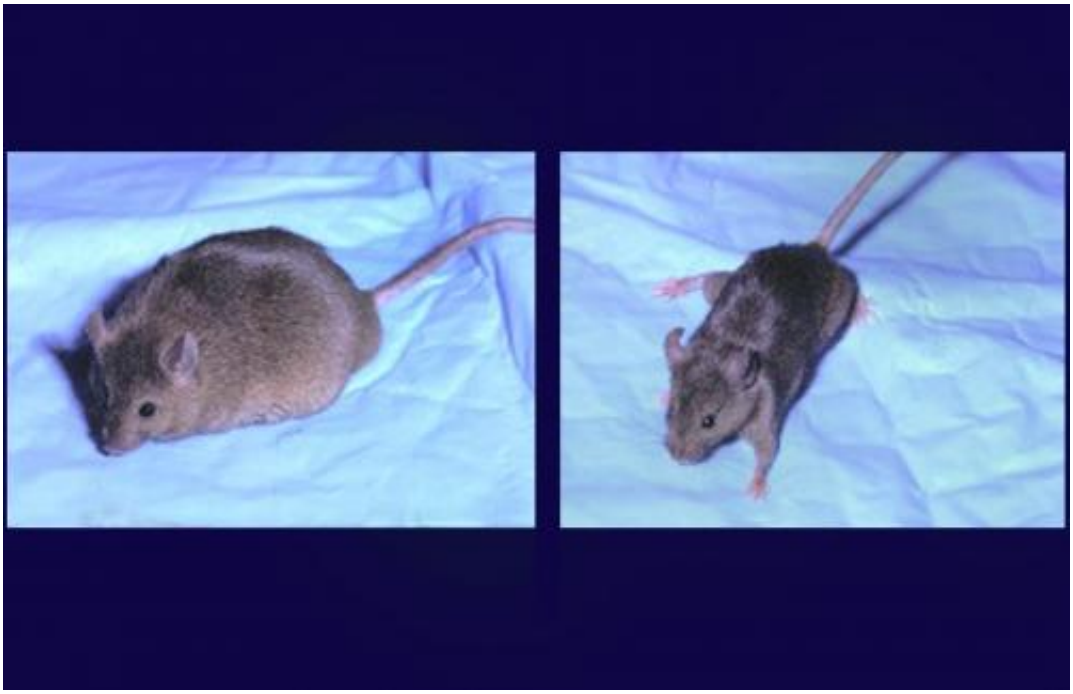
Adjusting bacteria in intestines may lead to obesity treatments

September 24 2013



Tempol significantly reduced the weight gain of the mice compared to the group of mice that were not fed the drug. Andrew Patterson, assistant professor of molecular toxicology at Penn State, said the study indicates that the drug acts on the microbiome and may open up new pathways for medical treatments. Credit: Patrick Mansell, Penn State

A drug that appears to target specific intestinal bacteria in the guts of mice may create a chain reaction that could eventually lead to new treatments for obesity and diabetes in humans, according to a team of

researchers.

Mice fed a high-fat diet and provided tempol, an anti-oxidant drug that may help protect people from the effects of radiation, were significantly less obese than those that did not receive the drug, according to Andrew Patterson, assistant professor of molecular toxicology, Penn State, who worked with Frank J. Gonzalez, laboratory metabolism chief, and James B. Mitchell, radiation biology branch chief, both of the National Cancer Institute.

"The two interesting findings are that the mice that received tempol didn't gain as much weight and the tempol somehow impacted the gut microbiome of these mice," said Patterson. "Eventually, we hope that this can lead to a new line of therapeutics to treat obesity and diabetes."

The microbiome is the biological environment of microorganisms within the human body.

The researchers, who reported their findings in the current issue of *Nature Communications*, said that tempol reduces some members of a bacteria—a genus of *Lactobacillus*—in the guts of mice. When the *Lactobacillus* levels decreases, a bile acid—tauro-beta-muricholic acid—increases. This inhibits FXR—farnesoid X receptor, which regulates the metabolism of bile acids, fats and glucose in the body, according to the researchers.

"The study suggests that inhibiting FXR in the intestine might be a potential target for anti-obesity drugs," said Gonzalez.

The researchers said that tempol may help treat type 2 diabetes symptoms. In addition to lower weight gain, the tempol-treated mice on a high-fat diet had lower blood glucose and insulin levels.

"Previously, Dr. Mitchell observed a significant difference in weight gain in mice on tempol-containing diet," said Patterson. "He approached us to help figure out what was going on, and it had been an interesting journey wading through the complexities of the microbiome."

Other studies hinted at the relationship between tempol, the gut microbiome and obesity, but did not focus on why the drug seemed to control weigh gain, according to Patterson.

The researchers said these studies are demonstrating how integrated the 100 trillion microbes that make up the human microbiome are with metabolism and health and how the microbiome may provide more pathways to treating other disorders.

"There is a tremendous interest in how the microbiome can be manipulated in a therapeutic way," said Patterson. "And we need to look at these microbiome management techniques in a good, unbiased way."

In the study, the researchers dissolved the tempol in drinking water, or delivered it directly to the mice. Within three weeks, tempol reduced the weight gain for the mice in that group. The mice showed significant reduction in weight gain even after 16 weeks.

To further test the role of FXR in obesity, the researchers placed mice that were genetically modified so that they lack FXR on the same high-fat diet. This group was resistant to the effects of tempol and taura-beta-muricholic acid, which further strengthened the importance of FXR in mediating the anti-obesity effect.

Gonzalez said that there are indications that FXR plays a similar role in human obesity and diabetes.

The researchers must now test the treatments to ensure it is effective in

humans, as well as check for any potential side effects, including cancer.

Provided by Pennsylvania State University