Mannose's unexpected effects on the microbiome and weight gain

September 18 2018

Hudson Freeze, Ph.D., director and professor of the Human Genetics Program at Sanford Burnham Prebys Medical Discovery Institute (SBP). Credit: Sanford Burnham Prebys Medical Discovery Institute (SBP)

Scientists continue to unravel links between body weight and the gut microbiome. Now, researchers from Sanford Burnham Prebys Medical Discovery Institute (SBP) report an unexpected finding: mice fed a fatty diet and mannose, a sugar, were protected from weight gain, leaner, and more fit—and this effect tracked with changes in the gut microbiome. The study published today in *Cell Reports*.

"Obesity and related diseases, such as nonalcoholic steatohepatitis (NASH), are on the rise—and scientists are on the hunt for new treatments, particularly for individuals who are unable to exercise," says Hudson Freeze, Ph.D., senior author of the paper and director and professor of the Human Genetics Program at SBP. "Better understanding of mannose's effects on the gut microbiome may lead to new therapies for treating obesity."

Freeze and his team were studying mannose in the context of a rare disease called a congenital disorder of glycosylation (CDG). People with a specific form of the disease can be treated with mannose. While conducting their research, the scientists observed the anti-obesity effects of mannose feeding.

A closer look revealed the mice were also protected from typical negative effects of a fatty diet. They had less body fat, reduced fat in their liver, stable blood sugar—and even improved fitness. Surprisingly, these benefits were only seen when the mice received mannose early in life—older mice didn't benefit from mannose.

"The gut microbiome is very dynamic in early life," says Vandana Sharma, Ph.D., lead author of the paper and staff scientist in Freeze's laboratory. "Because only young mice that received mannose exhibited leaness, we thought the microbiome might be involved."

Despite eating the same amount of fatty food, mannose-fed mice absorbed fewer nutrients-and instead excreted them. Further work showed the gut microbial composition mirrored that of lean mice fed a regular diet. When mannose was removed, the mice on the fatty diet regained weight, and their gut microbiome composition shifted to resemble that of the obese mice that ate fatty food but didn't receive mannose. The scientists also found that the gut microbes of the mannose-fed mice were less efficient at processing carbohydrates—an energy source.

"These findings further confirm the important role of the gut microbiome in metabolism," says Freeze. "The microbiome partially explains the beneficial effects of mannose, but how exactly it affects the body's metabolism remains a mystery."

More information: *Cell Reports* (2018). DOI: 10.1016/j.celrep.2018.08.064

Provided by Sanford Burnham Prebys Medical Discovery Institute

Citation: Mannose's unexpected effects on the microbiome and weight gain (2018, September 18) retrieved 19 April 2024 from https://medicalxpress.com/news/2018-09-mannose-unexpected-effects-microbiome-weight.html

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