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A sugar made by a gut bacterium may help the body burn visceral fat

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Duke-NUS and Duke University researchers found that a bacterial sugar increased energy expenditure in visceral fat in preclinical experiments, pointing to a potential avenue for obesity drug development



Scientists from Duke-NUS Medical School and Duke University School of Medicine have discovered that a sugar produced by a gut bacterium increased energy expenditure in visceral fat, reduced weight gain and improved metabolic health in preclinical experiments. The findings point to a potential new approach to treating obesity. Visceral fat, which accumulates around internal organs, is closely linked to metabolic diseases such as type 2 diabetes and cardiovascular disease.

The findings come amid growing concerns over rising obesity rates. Half of the world's population is projected to be overweight or obese by 2035, and more than 12 per cent of Singapore's population is living with obesity.

In the study, published in Cell Host & Microbe, the researchers identified a sugar molecule known as an exopolysaccharide (EPS) produced by the gut bacterium Clostridium immunis (C. immunis). The sugar required a small chemical group called phosphocholine for its activity. The researchers found that the phosphocholine-modified sugar reduced weight gain and visceral fat in their experiments.

The team also examined existing metagenomic data from 4,145 people worldwide. People with obesity had fewer copies of a gene involved in adding phosphocholine than people with a body mass index (BMI) below 25. This association does not establish that the bacterial sugar has the same effects in humans.

First author Dr Tan Chin Yee began the research as an MD-PhD student at Duke-NUS and Duke University School of Medicine's Department of Molecular Genetics and Microbiology. He is now with the SingHealth Internal Medicine Residency Programme.

"What surprised us was that this bacterial sugar did not work by reducing food intake or increasing activity. Instead, it changed how visceral fat used energy. That gives us a completely different way of thinking about how gut bacteria can influence metabolism," said Dr Tan.

How a bacterial sugar changes energy use in visceral fat

The researchers found that phosphocholine-modified EPS reduced levels of interleukin-22 (IL-22), a protein that helps the immune system communicate with tissues in the small intestine and visceral fat. This was accompanied by an increase in the number of cells containing UCP1, a protein that helps fat cells release energy as heat.

The increase in energy expenditure occurred specifically in visceral fat, which is typically resistant to signals that prompt fat cells to burn energy. The researchers found that reduced food intake or increased physical activity did not account for the change.

"Our findings reveal how some gut bacteria are able to uniquely communicate with the human body—they generate distinctive molecules by chemically modifying the sugars they produce. This opens up a new perspective on how the microbiome can influence human metabolism and points to new opportunities for developing treatments for metabolic diseases," said senior author Assistant Professor Neeraj Surana, from Duke University School of Medicine's Department of Pediatrics and the SingHealth Duke-NUS Paediatrics Academic Clinical Programme.

Professor Sheemei Lok, Interim Vice-Dean for Research at Duke-NUS, said: "This study moves us beyond simply knowing that the gut microbiome is associated with obesity. It identifies a specific molecule, a specific mechanism and a potential therapeutic pathway. That is the kind of translational insight needed if we are to turn microbiome science into new ways of preventing or treating metabolic health and tackle obesity."

The researchers have filed a patent relating to C. immunis and the sugar it produces. They are planning clinical trials in the US to evaluate whether targeting the bacterium could be an effective approach to treating obesity.