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HOW COLD –AND A BACTERIUM – FIGHT OBESITY

Mirko Trajkovski's team, at the University of Geneva (UNIGE), Switzerland, demonstrated few weeks ago that the absence of gut microbiota can be linked to increased brown fat activation as a mean of limiting obesity. Today, pursuing their research, the scientists show that mice exposed to cold experience a sharp shift in their microbiota composition, rendering them leaner and more sensitive to insulin. Transplantation of this cold-modified microbiota to germ-free mice is sufficient to enable complete tolerance to cold. Indeed, it increases their brown fat levels and thus improves their sensitivity to insulin, even without exposing them to cold. However, prolonged cold exposure can also attenuate the body weight loss as the body takes up more calories from the consumed food. This is due to a disappearance of a key bacterium, *Akkermansia muciniphila*, which acts on the way nutrients are absorbed by the organism. When the bacterium is artificially administered, the weight loss resumes. This discovery, published in *Cell*, may lead researchers to develop new solutions to fight obesity.

Mammals' body temperature is usually rather constant. When exposed to cold, however, the body temperature drops by few degrees, before slowly rising almost back to normal. This adaptive mechanism is mediated by the brown fat, which function is, once activated by cold, to generate heat by burning calories. Therefore cold, as well as exercise, has the effect of favouring the appearance of adipose cells similar to brown fat – the beige fat – within white fat, which protects the body against excess weight and its damaging consequences.

But how this phenomenon interplays with microbiota composition? Could cold be a tool in triggering this anti-obesity mechanism? Over a period of a month, the UNIGE researchers exposed a group of mice to cold – dropping slowly their environment temperature from 20°C to 6°C - and studied how their microbiota changed. They also transplanted this “cold microbiota” to germ-free mice. “The changes we observed in the microbiota composition of the mice living in a cold environment were even more dramatic than the microbiota differences previously observed between obese and healthy individuals, point out Claire Chevalier and Ozren Stojanovic, co-first authors of this study. And strikingly, the cold transplanted germ-free mice became immediately resistant to cold: their body temperature did not drop, as if the transplanted microbiota also modified this adaptive mechanism.” This amazing effect suggests that the microbiota, alone, can confer resistance to cold. Moreover, the transplanted mice showed a better metabolic profile in general, with greater sensibility to insulin and additional beige fat.

The effect of cold on body weight

Normally, mice gain weight regularly, but when exposed to cold, they lose weight because they burn calories in order to convert them into heat. After some time they resume gaining weight, however. This suggests that it is the way nutrients are absorbed that changes. “Otherwise, we would expect the mice exposed to cold to keep on losing weight, because they would continue to burn calories to generate heat, indicates Mirko Trajkovski. We were amazed to observe that the changes in microbiota during cold exposure actually promote increased gut and microvilli lengths.” Microvilli are small projections that protrude from the intestinal wall which enlarge the absorptive surface of the gut and therefore increase the nutrients uptake from the consumed food. This shows that the microbiota has also the ability to regulate the gut morphology.

An amazing bacterium called Akkermansia muciniphila

If the profile of microbiota changes with cold, it is due to the drastic reduction of a bacterium called Akkermansia muciniphila. But when this bacterium is artificially administered, the gut length shrinks to a normal size, showing it is an essential element of this adaptive mechanism. And indeed, when mice exposed to cold were administered Akkermansia muciniphila, they kept on losing weight.

Interestingly, the microbiota of people suffering from obesity seems to lack this same bacterium, which has the ability to regulate the absorption of food nutrients. The next step for the UNIGE scientists will then to further study the effect of this bacterium. If proven to be a valid anti-obesity strategy, it would open a door to completely new ways to treat this metabolic disorder. This discovery goes even beyond its potential as anti-obesity treatment: “The gut is also our largest endocrine tissue, which secretes many hormones acting in different parts of our body. Thus, altering the gut morphology might be one of the ways by which microbiota impacts all other organs, including our brain”, concludes Professor Trajkovski.

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