The Economist

Microbes and thermoregulation

Cold-weather friends

Body temperature seems, in part, to be controlled by gut bacteria

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WINTER is coming, in the northern hemisphere at least. Time, then, to break out the heavy coats, thick gloves and galoshes—but also time, if a study by Mirko Trajkovski of the University of Geneva is correct, for your gut bacteria to remodel your intestines and make them better at absorbing nutrients before the blizzards arrive. Dr Trajkovski's work, just published in *Cell*, was on mice. But previous experience suggests that in this area of biology what applies to mice applies to men as well. If that is true in this case too, it will mean an important part of the human body's thermoregulation is actually controlled by its companion microbes.

What's bugging you?

Dr Trajkovski's research group studies obesity and insulin resistance—the latter being the cause of the form of diabetes many people suffer from in later life. Past studies have shown that obese animals (people included) have different microbial mixtures, known as microbiomes, in their guts from those found in animals of normal weight. Moreover, in mice at least, modifying the mix can induce obesity without a change of diet. One line of inquiry the group is pursuing therefore involves studying murine microbiomes. And one question they asked themselves is what effect ambient temperature might have.

To find out, they put some mice into one or other of two sets of enclosures for a month. The first set were maintained at 6°C. The second were kept at 22°C (ie, room temperature). The team weighed the animals at regular intervals. They also saved the creatures' faeces and collected blood samples from which they could determine their subjects' sensitivity to insulin. Since insulin stimulates the burning by cells of glucose, the more sensitive an animal is to it, the more glucose it will burn, and the more heat it will generate.

Based on previous findings, Dr Trajkovski expected the mice in the cold enclosures to lose weight as they burned stored reserves to stay warm—and, for the first few days they did. After five to ten days, though, they did something unexpected. In spite of the fact that their rations had not increased, they began to put on weight.

To try to find out why, the team measured the calorific value left in the faeces, to assess how much nutrition the animals had extracted from their food. They also looked at the insulin-sensitivity data.

Mice exposed to the cold, they discovered, became 50% more efficient over the course of the study at absorbing nutrients from their food. Those held at room temperature, by contrast, showed no change in their digestive efficiency. The cold-dwelling mice also became 40% more sensitive to insulin, while those in the room-temperature enclosures did not. That suggested the mice in the chiller cabinets were not only extracting more value from their food, they were also becoming better at burning it, and thus generating heat.

Given its role in obesity, Dr Trajkovski suspected the gut microbiome might be playing a part is these unpredicted results. The team thus reran the experiments and sampled the animals' gut floras. They also looked at the rodents' intestinal walls, to see if the anatomy of these had changed in ways that would make it easier for them to absorb food.

The gut floras of the two groups were radically different. In particular, and intriguingly, the chilled mice lacked a species called *Akkermansia muciniphila* that is often absent from the guts of obese people—an absence that may be involved in their putting on extra weight.

The cold-dwelling mice also had different intestinal anatomy. Their villi, the tiny projections from the intestinal wall that absorb food into the body, were more than 50% longer than those of mice living at room temperature.

Dr Trajkovski and his colleagues then arranged for mice that had been born and raised at room temperature, and in aseptic conditions (and which were thus germ-free), to have bacteria, collected either from cold-dwelling mice or from mice that came from room-temperature enclosures, transplanted into their guts.

After two weeks, those with transplants from cold-dwelling mice resembled the mice the transplants had come from in insulin sensitivity, cold tolerance and the lengths of their villi. The mice with transplants from "room-temperature" mice, by contrast, resembled those.

As a final experiment the team added some *A. muciniphila* to the guts of the mice that had received transplants from cold-dwellers, to see how the bug's reintroduction would shape them. Remarkably, these mice started losing weight and, when the researchers examined their

intestines two weeks later, they found that the villi had shrunk back to the size of those found in room-temperature mice.

How the bacteria cause all these changes Dr Trajkovski has yet to work out. But the bottom line is clear: in mice—and probably in human beings as well—partial control of the body's thermostat is in the hands of subcontractors.

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