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Burning extra calories with a 'futile protein cycle'

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A new study in the September issue of *Cell Metabolism* points to a new method for burning off all those irresistible extra calories—by turning on an energy-draining, but otherwise futile, cycle of protein synthesis and breakdown.

Christopher Lynch of The Pennsylvania State University College of Medicine and his colleagues found that they could drive such heightened protein turnover in mice by disrupting an enzyme involved in the metabolism of some amino acids, the building blocks of proteins. The enzyme-deficient animals showed elevated blood levels of the essential amino acid leucine, an important nutrient signal, and became slimmer than normal mice despite eating more food. They also showed "remarkable" improvements in glucose and insulin tolerance, and resistance to becoming obese on a high-fat diet.

"The mice on the outside look normal, just skinnier and smaller," Lynch said. "After looking at their metabolism, we found that for the same activity, they were using more energy."

Moreover, the researchers found that the animals that ate the most food also expended the most energy. "That would be ideal for people who are overweight," Lynch said. "They could continue to eat and just waste the energy and be thin."

Abundant food supplies and a sedentary lifestyle have contributed to the current epidemic of obesity in Western nations, the researchers said.

Obesity results when people consume more energy in their diet than they expend. In both short-term and relatively long-term studies, high-protein and low-fat diets have been found to increase energy expenditure, they noted, while short-term protein intake helps stave off hunger.

The effects of dietary protein are thought to be driven at least in part by leucine and perhaps other so-called branched-chain amino acids (BCAAs). Yet it has remained unclear whether leucine supplementation actually improves or worsens obesity, Lynch said.

In the current study, the researchers generated mice lacking the enzyme BCATm, critical for the first step in BCAA breakdown, which caused their leucine levels to rise by more than 10-fold. As a result of the enzyme deficiency, the animals ate more food but were lean in comparison to normal mice. The researchers traced the effect to an energy-demanding increase in protein turnover that appeared to be directly related to the amount of food the mice ate.

“Unfortunately for dieters, it appears unlikely that the tactic used by the [mutant mice] to avoid weight gain, i.e., a big increase in protein turnover, can be achieved by merely ingesting high-protein diets or leucine supplements,” said Susan Fried and Malcolm Watford in an accompanying commentary. An earlier study found that eating leucine can only increase its levels to twice the normal concentration, they noted. And unlike the enzyme disruption, dietary leucine stimulates protein synthesis while it slows protein breakdown.

Nonetheless, the scientists all agree that the findings could lead to new weight-loss therapies. “It is possible that revving up protein turnover by manipulating BCATm activity through pharmacological means is worth exploring as a treatment for obesity in humans,” Fried and Watford said.

Source: Cell Press