

Orexin: A hormone that fights fat with fat

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Devanjan Sikder, D.V.M, Ph.D., is senior author of the study and assistant professor in Sanford-Burnham's Diabetes and Obesity Research Center, located in Orlando's Medical City at Lake Nona. Credit: Sanford-Burnham Medical Research Institute

The fat we typically think of as body fat is called white fat. But there's another type—known as brown fat—that does more than just store fat. It burns fat. Scientists used to think that brown fat disappeared after infancy, but recent advances in imaging technology led to its rediscovery in adult humans. Because brown fat is so full of blood vessels and mitochondria—that's what makes it brown—it's very good at converting calories into energy, a process that malfunctions in obesity. In a study published October 5 in *Cell Metabolism*, researchers at Sanford-Burnham Medical Research Institute (Sanford-Burnham) discovered that orexin, a hormone produced in the brain, activates calorie-burning brown fat in mice. Orexin deficiency is associated with obesity, suggesting that orexin supplementation could provide a new therapeutic approach for the

treatment of obesity and other metabolic disorders. Most current weight loss drugs are aimed at reducing a person's appetite. An orexin-based therapy would represent a new class of fat-fighting drugs—one that focuses on peripheral fat-burning tissue rather than the brain's appetite control center.

"Our study provides a possible reason why some people are overweight or obese despite the fact that they don't overeat—they might lack the [orexin](#) necessary to activate brown fat and increase energy expenditure," explained Devanjan Sikder, D.V.M, Ph.D., senior author of the study and assistant professor in Sanford-Burnham's Diabetes and Obesity Research Center, located in Orlando's Medical City at Lake Nona.

Since the best way to determine something's function is to see what happens when it's missing, Dr. Sikder's team, which included postdoctoral researchers Dyan Sellayah, Ph.D. and Preeti Bharaj, Ph.D., looked at mice genetically engineered to lack orexin. These mice weighed more than their normal counterparts, but they actually ate less, suggesting that overconsumption was not the cause of their obesity. Rather, the orexin-deficient mice lacked diet-induced thermogenesis (heat production); in other words, when fed a high-fat diet, the mice failed to dissipate the extra calories as heat the way that normal mice (and people) do. Instead, they stored that energy as fat.

This finding prompted the team to look at the mice's brown fat—a source of thermogenesis. What they found is that brown fat in mice lacking orexin didn't develop properly at the embryonic stage. This shortage had lasting effects on energy expenditure and weight even in adulthood.

Taking the opposite approach, the researchers then gave the defective mice more orexin. With the [hormone](#) present, brown fat developed properly before birth and continued to be active into adulthood. What's

more, adding orexin to stem cells in a laboratory dish caused them to differentiate (specialize) into [brown fat](#) cells, creating more of this fat-burning engine.

"Without orexin, mice are permanently programmed to be obese. With it, brown [fat](#) is activated and they burn more calories," said Dr. Sikder. "We're now taking the next steps in determining how orexin—or a chemical that has the same effect—might be used in humans to therapeutically prevent or treat obesity."

According to the Centers for Disease Control and Prevention, about one-third of U.S. adults (33.8 percent) are obese. As a person becomes overweight or obese, he or she is at increased risk for type 2 diabetes, coronary heart disease, stroke, and certain cancers.

Provided by Sanford-Burnham Medical Research Institute

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