

The leptin activator: New study reveals brain receptor key to burning brown fat

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Some call it baby fat. But recent research has shown that adults have it too—which is a good thing. Brown fat, the so-called good fat that can protect against obesity and associated health risks, like cardiovascular

disease and diabetes, is located in small pockets throughout the body. Most mammals use brown fat (and its closely related cousin beige fat) to stay warm.

"In mice and humans, if you have more brown or beige fat, you are more protected from metabolic disease," says Liangyou Rui, Louis G. D'Alecy Collegiate Professor of Physiology at U-M Medical School, whose lab studies the molecular and physiological mechanisms of obesity, diabetes and fatty liver disease.

In a new study published in *Nature Communications*, Rui, first author Lin Jiang, Ph.D. and their colleagues reveal a pathway by which the [hormone leptin](#) contributes to weight loss.

Leptin regulates body weight by controlling appetite and energy expenditure, but exactly how has been a mystery. What is known, says Rui, is that leptin activates brown and beige fat. The new study elucidates a molecular accelerator of leptin action in the brain called Sh2b1.

His team has found that Sh2b1 in the hypothalamus, an important brain region controlling body temperature and hunger among other functions, promotes the stimulation of the sympathetic nervous system. The sympathetic nervous system sends signals to brown and beige fat to activate it, thus maintaining body weight and metabolism.

The team demonstrated this proof-of-principle by creating two mouse models. Mice that lacked the Sh2b1 gene in the leptin receptor neurons "had an incredibly reduced sympathetic drive to the brown/beige fat and reduced capability to promote energy expenditure," says Rui.

This reduced the ability of brown fat to be metabolized into heat, lowering the mice's core body temperature. What's more, the mice also

developed obesity, insulin resistance and a fatty liver. In contrast, mice with extra expression of Sh2b1 in their brains were protected from obesity.

"No one knew that Sh2b1 in the brain controls the sympathetic nervous system or was required for leptin to activate [brown fat](#) to increase [energy expenditure](#)," notes Rui. As for how this finding could be applied to humans, he says the hope is to eventually find a way to increase expression of Sh2b1 or its ability to enhance leptin signaling and fat burning.

More information: Lin Jiang et al, Leptin receptor-expressing neuron Sh2b1 supports sympathetic nervous system and protects against obesity and metabolic disease, *Nature Communications* (2020). [DOI: 10.1038/s41467-020-15328-3](#)

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