Drug stimulates brown fat and boosts metabolism

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Researchers publishing in the January 6 issue of *Cell Metabolism* have discovered that a drug FDA-approved to treat overactive bladder may boost brown fat's metabolic powers, making it a promising candidate for combatting obesity. Unlike energy-storing white fat, brown fat burns energy to generate heat, which can help maintain body weight and prevent obesity in rodents.

Previous studies have found that brown fat can be coaxed into action by activating the β3-adrenergic receptor, which is expressed on the surfaces of brown and white fat cells, as well as on cells of the urinary bladder and other tissues. With these findings in mind, investigators wondered whether mirabegron, a drug that targets the β3-adrenergic receptor and was recently approved to treat overactive bladder, might help keep people's weight in check.

In all 12 men enrolled in the study, 200 milligrams of mirabegron led to higher brown fat metabolic activity, and at its peak level in the blood it increased the men's resting metabolic rate by 203 calories per day. While the dose was higher than the 50 milligram dose approved for overactive bladder, the treatment was well tolerated. All of the study participants were young, healthy individuals who had not previously taken mirabegron.

"Brown adipose tissue, or brown fat, produces β3-adrenergic receptor at levels higher than nearly every other organ in the body. We showed that a one-time dose of the drug mirabegron stimulates human brown adipose

tissue so that it consumes glucose and burns calories," said lead author Dr. Aaron Cypess, who conducted the work at Joslin Diabetes Center and Beth Israel Deaconess Medical Center, affiliates of Harvard Medical School, and is now at the National Institute of Diabetes and Digestive and Kidney Diseases, part of the National Institutes of Health.

The findings suggest that drugs that activate the β3-adrenergic receptor may be a promising treatment for obesity. "Prior to our work, the only known way to activate human brown adipose tissue was through cold exposure. While inexpensive, this approach is generally not well tolerated over the long term, and there is significant variability in people's responses," said Dr. Cypess. "In addition, once the cold exposure is removed, the effect usually turns off rather quickly."

Dr. Cypess noted that in addition to attempts to activate brown fat, strategies that produce more of it might also help treat people with metabolic conditions. Other research groups are also generating promising results through the use of drugs to convert white fat cells into brown fat and through discoveries of the pathways and hormones that control brown fat metabolism.

More information: *Cell Metabolism*, Cypess et al.: "Activation of Human Brown Adipose Tissue by a 3-Adrenergic Receptor Agonist" www.cell.com/cell-metabolism/a … 1550-4131(14)00560-9

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