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Researchers identify potential target for developing obesity and diabetes treatment

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A newly published study by researchers from the University of Colorado School of Medicine has identified a potential therapeutic target for treating obesity and diabetes.

The scientists studied the biological function of an epigenetic modifier known as histone deacetylase 11 (HDAC11), and determined that deleting it in mice stimulates the formation of brown adipose tissue. The absence of HDAC11 also triggered beiging of white adipose tissue. These changes are important because white adipose tissue stores energy, while brown adipose tissue produces heat, thus expending energy. These findings reveal a regulatory node that could lead to the development of a pharmaceutical-based therapy for obesity and metabolic disease based on increasing energy expenditure.

The details of the study are published in the August 9 edition of *JCI Insight*, a journal published by the American Society for Clinical Investigation.

The first author of the study is Rushita A. Bagchi, Ph.D., a postdoctoral fellow in the laboratory of Timothy A. McKinsey, Ph.D., associate professor of medicine in the Division of Cardiology, who is the corresponding author of the article. Both are part of the Consortium for Fibrosis Research & Translation, a program funded by the School of Medicine to improve understanding of fibrotic diseases across various organ systems.

"The findings uncovered a druggable transcriptional pathway for regulation of energy expenditure, and thus suggest novel approaches for combating the global pandemics of obesity and diabetes based on HDAC11 inhibition," said McKinsey.

Obesity is an increasingly common health problem, with more than one-third of the U.S. population considered obese. Obesity and associated chronic diseases, such as type 2 diabetes, are projected to affect more than a half billion adults worldwide by 2040. Mice lacking HDAC11 were protected from obesity, insulin resistance and other effects of high-fat feeding. The findings suggest a previously unrecognized role for HDAC11, and an associated protein known as BRD2, in the control of adipose tissue.

"Through our investigation we found that inhibiting HDAC11 increases energy expenditure, which highlights its potential as a target in obesity and metabolic disease therapeutic strategies," said McKinsey. "We now need to test the role of HDAC11 in large animal models of metabolic disease and in human cell systems as we attempt to translate these exciting findings to the clinic."

Seventeen authors were listed on the article, "HDAC11 suppresses the thermogenic program of adipose tissue via BRD2." Nine of the authors are members of the CU School of Medicine. The research was supported with funding from the National Institutes of Health, the American Heart Association, and the Canadian Institutes of Health Research.

More information: Rushita A. Bagchi et al, HDAC11 suppresses the thermogenic program of adipose tissue via BRD2, *JCI Insight* (2018). DOI: 10.1172/jci.insight.120159