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Pathway to better metabolism discovered in fat cells

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Control over obesity and diabetes may be one step closer thanks to a Hiroshima University study in fat tissue.

The research team of Professor Kazunori Imaizumi, PhD, at Hiroshima University has mapped the activation pathway for a protein responsible for burning excess energy in the body.

If the pathway can be confirmed in living animal studies, control of this pathway may lead to treatments for obesity and related metabolic diseases. Researchers studied mouse fat cells growing in a dish using a combination of chemical treatments and protein measurements.

Part of the pathway involves a protein found only in brown fat cells. Fat cells are classified as either brown or white. White fat accumulates during unhealthy weight gain, but some brown fat is essential for a healthy metabolism.

This protein in brown fat cells, called UCP1, is involved in the process of how warm-blooded animals maintain a stable internal body temperature. This process, called thermogenesis, involves burning excess energy inside the body rather than storing it as fat. More UCP1 means a higher metabolism and less weight gain.

Prof. Imaizumi's team investigated two proteins called IRE1alpha and XBP1 for their relationship to UCP1. When these proteins are active, they can increase the amount of UCP1 inside the cell. Researchers also

identified other molecules that act even earlier in the control pathway.

These results provide strong evidence that somewhere within this cellular signaling cascade is the possibility for precision control of fat cells' metabolic process using UCP1.

Current treatments for metabolic diseases like Type 2 Diabetes and obesity rely on reducing the amount of energy entering the cells. These treatments focus on reducing white fat cells, which store excess calories. Treatments targeting UCP1 would be completely novel by increasing the amount of energy leaving the body. This would require the seemingly counter-intuitive method of increasing the number of the other type of fat cells, brown fat cells, like those used in Prof. Imaizumi's work.

"Brown fat cells dissipate excess energy in the form of heat. Therefore, having a large number of brown fat cells leads to an anti-obesity effect," said Rie Asada, PhD, a postdoctoral fellow in Prof. Imaizumi's lab.

Prof. Imaizumi's research team is currently planning experiments to develop a more detailed understanding of the cellular pathways that lead to UCP1's metabolic actions within brown fat cells.

More information: Rie Asada et al. IRE1α-XBP1 is a novel branch in the transcriptional regulation of Ucp1 in brown adipocytes, *Scientific Reports* (2015). DOI: 10.1038/srep16580

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