

Breakthrough could lead to new obesity treatments

May 31 2023



Credit: Unsplash/CC0 Public Domain

Researchers at the University of East Anglia and the University of Cambridge have made an important discovery in the race to find treatments for obesity and related diseases, such as diabetes.

A new study published today is the first to reveal the molecular structure of a protein called "Uncoupling protein 1" (UCP1). This protein allows brown fat tissue, or "good fat," to burn off calories as heat—in contrast to conventional white fat that stores calories.

The breakthrough was made by an [international collaboration](#) between UEA, the University of Cambridge, the University of Pennsylvania and the Free University of Brussels.

The team say that their findings provide crucial molecular details that will help develop therapeutics that activate UCP1 artificially to burn off excess calories from fat and sugar. And that this could one day combat obesity and related diseases, such as diabetes.

Dr. Paul Crichton, from UEA's Norwich Medical School, said, "As well as the conventional white fat that we are all familiar with, we can also develop brown fat."

"Brown fat is the good fat—it breaks down [blood sugar](#) and [fat molecules](#) to create heat and help maintain body temperature."

"Most of our fat, however, is white fat, which stores energy—and too much white fat leads to obesity."

"UCP1 is the key protein that allows the specialized brown fat to burn off calories as heat."

"We know that mammals switch on UCP1 activity in brown fat tissue to protect against the cold and to maintain body temperature—especially in newborns, that cannot yet shiver to keep warm."

"Brown fat varies in humans, where it correlates with leanness in the population—and there has been a lot of interest in how to increase

brown fat and activate UCP1 therapeutically, as a potential way to treat obesity."

"A lot of research has been focusing on finding ways to encourage brown fat and how to turn white fat into brown fat—in order to burn more calories and fight metabolic disease."

"But even with more brown fat—UCP1 must still be 'switched on' to gain full benefit. And research has been hampered by a lack of details on the molecular make up of UCP1. Despite more than 40 years of research, we did not know what UCP1 looks like to understand how it works—until now."

Lead researcher Prof Edmund Kunji, from the University of Cambridge, said, "Our paper reveals, for the first time, the structure of UCP1 in atomic detail, and how its activity in [brown fat](#) cells is inhibited by a key regulatory molecule."

Using the Krios G3i, a cryogenic electron microscope at the Penn Singh Center for Nanotechnology, the team were able to view UCP1 in atomic detail.

"This is an exciting development that follows more than four decades of research into what UCP1 looks like and how it works," said Vera Moiseenkova-Bell, an associate professor of Pharmacology and faculty director of the Beckman Center for Cryo-Electron Microscopy.

Prof Kunji said, "Our work shows how a regulator binds to prevent UCP1 activity, but more importantly the structure will allow scientists to rationalize how activating molecules bind to switch the protein on, leading to the burning of fat."

"The activated tissue can also remove glucose from the blood, which can

help control diabetes."

"This is a significant breakthrough in this field," he added.

The research is published in *Science Advances*.

More information: Scott Jones et al, Structural basis of purine nucleotide inhibition of human uncoupling protein 1, *Science Advances* (2023). [DOI: 10.1126/sciadv.adh4251](https://doi.org/10.1126/sciadv.adh4251).
www.science.org/doi/10.1126/sciadv.adh4251

Provided by University of East Anglia

Citation: Breakthrough could lead to new obesity treatments (2023, May 31) retrieved 9 April 2024 from <https://medicalxpress.com/news/2023-05-breakthrough-obesity-treatments.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
