

# Cystic Fibrosis Research News

**Title:**

CFTR regulates brown adipocyte thermogenesis via the cAMP/PKA signaling pathway

**Lay Title:**

The CFTR protein impacts energy usage in mouse brown fat

**Authors:**

Kyung-Mi Choi<sup>1,2</sup>, Sung-Hee Cho<sup>1</sup>, Jung Hak Kim<sup>1</sup>, Ae-Rhee Lilian Kim<sup>1</sup>, Xiangmudong Kong<sup>3</sup>, John C. Yoon<sup>1</sup>

**Affiliations:**

<sup>1</sup>Department of Internal Medicine, University of California Davis School of Medicine, Davis, California, USA

<sup>2</sup>Institute of Molecular Biology and Genetics, School of Biological Sciences, Seoul National University, Seoul, South Korea

<sup>3</sup>Department of Surgical and Radiological Sciences, University of California Davis School of Veterinary Medicine, Davis, California, USA

**What was your research question?**

The CFTR (Cystic Fibrosis Transmembrane conductance Regulator) protein forms an opening on the cell surface that lets chloride move out of the cell but it does not work correctly in people with CF. The CFTR protein is best known for its function in the lungs but it is also present in other tissues throughout the body. This study looked at the potential role of the CFTR protein in brown fat, which is a specialized type of fat tissue that burns calories as heat instead of storing it.

**Why is this important?**

People with CF often have a lower body weight than those without CF, partly because they absorb less nutrients and partly because they use more energy, e.g. for fighting chronic lung infections. It has been suggested that people with CF may burn more calories while resting. It has also been reported that a laboratory mouse model with a mutation in the *cftr* gene (F508del) does not spontaneously develop lung infections but still burns more calories than normal mice. We felt it would be of interest to determine whether the CFTR protein present in brown fat impacts the balance between how much energy is absorbed and how much is used.

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## What did you do?

In this laboratory-based study, we first investigated if the CFTR protein is present in brown fat tissue from mice. Then we generated a new mouse model that lacked the CFTR protein in brown fat to determine how this impacted energy usage and weight gain compared to normal mice.

## What did you find?

We confirmed that the CFTR protein is present in brown fat tissue from mice. We found that mice that lack CFTR in brown fat use slightly more energy than normal mice, and the difference is more appreciable under cold-stressed conditions that force the mice to produce more heat. The mice that lack CFTR in brown fat also gained less weight when placed on an obesity-inducing diet compared to normal mice. Brown fat cells removed from the mice that lacked CFTR had a reduced ability to burn energy.

## What does this mean and reasons for caution?

Our study suggests that CFTR in brown fat has a role in regulating energy balance in the body and its loss can contribute to the increased use of energy. It may be that the body adapts to the loss of CFTR in brown fat and develops a greater propensity to burn energy in other tissues such as muscle or white fat.

Brown fat may thus be a site of action for CFTR modulator drugs. However, the mouse model may not perfectly represent what happens in the human body, as there are some differences in the way that heat is produced in humans compared to mice.

## What's next?

It would be useful to understand exactly how the CFTR protein affects how brown fat works and whole-body energy expenditure to try to develop ways to manipulate energy balance in CF.

## Original manuscript citation in PubMed

<https://pubmed.ncbi.nlm.nih.gov/36088207/>