# Some fat cells can feel the cold

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(Medical Xpress)—To survive in cold environments, mammals burn fat to produce heat. The breakdown of fat helps prevent obesity and related metabolic diseases, such as diabetes. Bruce Spiegelman and his colleagues at Harvard Medical School studied how white, beige and brown fat cells respond to cold temperatures. They found that while all three types of fat cells respond to temperature changes when stimulated by certain brain chemicals, white and beige fat cells react to cold temperatures independently of the brain. Their research appears in the *Proceedings of the National Academy of Sciences*.

Mammals break down fat to produce energy, which enables them to maintain a constant body temperature in cold weather. Obesity can occur if fat does not break down and remains stored in the body.

There are three types of fat cells: brown, white and beige. The primary role of brown fat cells is to generate heat in newborns and hibernating mammals, which cannot shiver. Brown fat cells have small molecules and break down easily. While newborns have many of these cells, adult humans retain only a small amount in the interscapular region.

White fat cells store energy. They contain larger molecules than brown cells and do not break down as easily.

Beige cells, like white cells, store energy. However, like brown cells, beige fat cells break down and generate heat in response to cold. Normally when peripheral body cells sense cold, they send this information to the hypothalamus, which then, via the sympathetic

nervous system (SNS), sends norepinephrine (NE) to brown and beige fat cells. The NE attaches to beta-adrenergic receptors in these cells. This causes the expression of genes for thermogenesis.

To study the influence of the brain on heat production, Spiegelman's team exposed mice lacking beta-adrenergic receptors to a temperature of 10 degrees Celsius for 20 hours. Thermogenic gene expression in brown fat was much lower in these mice than in controls. However, thermogenic gene expression in beige and white fat cells increased in both groups, suggesting that these cells, but not brown fat cells, react to cold even without the brain's influence.

The researchers then exposed in vitro fat cells to temperatures ranging from 27 to 33 degrees Celsius for four hours. While brown fat cells reacted to the cold only when NE was added, beige and white cells responded without the addition of NE, indicating once again that they do not require the influence of the brain to generate heat.

Previously, scientists thought fat cells only broke down when beta-adrenergic receptors received signals from the brain. Agonism of the beta-adrenergic system increases the expression of thermogenic genes. However, beta-adrenergic agonists affect many vital organ systems, so their potential for use in treating obesity and related disorders is limited. The discovery that some fat cells respond directly to cold could lead to the development of new treatments for these conditions.

**More information:** Fat cells directly sense temperature to activate thermogenesis, *PNAS*, Published online before print July 1, 2013, doi: 10.1073/pnas.1310261110

**Abstract**
Classic brown fat and inducible beige fat both dissipate chemical energy in the form of heat through the actions of mitochondrial uncoupling

protein 1. This nonshivering thermogenesis is crucial for mammals as a defense against cold and obesity/diabetes. Cold is known to act indirectly through the sympathetic nervous systems and ?-adrenergic signaling, but here we report that cool temperature (27–33 °C) can directly activate a thermogenic gene program in adipocytes in a cell-autonomous manner. White and beige fat cells respond to cool temperatures, but classic brown fat cells do not. Importantly, this activation in isolated cells is independent of the canonical cAMP/Protein Kinase A/cAMP response element-binding protein pathway downstream of the ?-adrenergic receptors. These findings provide an unusual insight into the role of adipose tissues in thermoregulation, as well as an alternative way to target nonshivering thermogenesis for treatment of obesity and metabolic diseases.