

# Bone-cell control of energy generation is regulated by the protein Atf4

10 August 2009

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Bone cells known as osteoblasts were recently shown to have a role in controlling the biochemical reactions that generate energy via secretion of the molecule osteocalcin. Gerard Karsenty and colleagues, at Columbia University College of Physicians and Surgeons, New York, therefore hypothesized that osteoblasts express a regulatory gene(s) that controls this osteoblast function and then identified Atf4 as this regulatory gene in mice.

Atf4 is a protein expressed predominantly in osteoblasts that is known to regulate many osteoblast functions. The researchers therefore analyzed mice lacking Atf4 and found that they have lower [fat](#) mass and blood glucose (a major source of energy) levels than control mice. The lower blood glucose levels were due to increased expression and secretion of the hormone insulin, which promotes liver, fat, and muscle cells to take up glucose. Sensitivity to insulin in the liver, fat, and muscle was also enhanced.

Several genetic experiments established that lack of Atf4 in osteoblasts was central to these abnormal characteristics of mice lacking Atf4 and further analysis indicated the underlying mechanism. Specifically, Atf4 directly increased expression of the Esp gene, which makes a protein that decreases the activity of osteocalcin. As Atf4 in osteoblasts was already known to regulate bone formation and mineralization, the authors conclude that Atf4 regulates many, but not all, osteoblast functions.

Source: Journal of Clinical Investigation

APA citation: Bone-cell control of energy generation is regulated by the protein Atf4 (2009, August 10) retrieved 5 May 2021 from <https://medicalxpress.com/news/2009-08-bone-cell-energy-protein-atf4.html>

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