

Exercise-induced hormone irisin linked to new mechanisms for bone metabolism

March 3 2017

Two weeks of voluntary wheel running induces higher expression of irisin—a fat-burning hormone that is released during exercise—in bone tissue in mice. In addition, systemic administration of irisin increased bone formation and thickness, mimicking the effects of exercise on the mouse skeletal system. The findings demonstrate a potential new mechanism for the regulation of bone metabolism.

The study was led by scientists from Tufts University School of Dental Medicine (TUSDM) and published in *Bone Research*.

"Our results provide insight into the complex regulatory interplay of muscle, bone and fat tissues. Increased irisin levels in circulation upon systemic administration can recapitulate part of the beneficial effects of exercise in the skeletal system," said senior study author Jake Chen, D.M.D., M.D.S., Ph.D., professor and biological sciences researcher at TUSDM. "Further experimentation will be needed to evaluate the involvement of irisin and other factors increased by exercise and expressed by bone, muscle and fat tissue."

Previous studies have revealed that exercise induces the production of irisin and its precursor molecule, FNDC5 (fibronectin-type III domain-containing 5) protein, which convert white fat tissue into beneficial, calorie-burning brown fat. Irisin has been linked to improved glucose tolerance and weight loss in obese, prediabetic mice. While most studies have focused on irisin produced by muscle tissue, some research has suggested that irisin increases [bone mass](#) in addition to its metabolic

benefits. However, it was unknown whether irisin is secreted by bone upon exercise or whether it regulates [bone metabolism](#).

To investigate, Chen and his colleagues tested a group of five-week-old mice, with two weeks of voluntary wheel running. Compared to a control group without access to a running wheel, mice that had exercised expressed six-fold higher FNDC5 and irisin expression in bone tissue. Irisin expression was observed in several different bone regions, including the growth plate, [trabecular bone](#), [cortical bone](#), articular cartilage and muscle-bone interface.

When mice were injected with irisin or viruses engineered to express irisin, the team found significant increases in bone volume and thickness compared to mice treated with saline. The team evaluated the effects of recombinant irisin in bone cell lines, and found that irisin can directly increase the production of osteoblasts—cells that synthesize bone—and mineralization, while inhibiting the production of osteoclasts—cells that break down bone.

The team's findings demonstrate that irisin produced by bone could have a role in bone metabolism through both direct mechanisms and indirect mechanisms, as the transition from white fat to brown fat has been shown to lead to increased [bone formation](#) by previous studies. In addition, recombinant irisin has also been shown to suppress sclerostin, a protein that is involved in [bone loss](#) during prolonged lack of mechanical load, such as in bed-ridden patients.

"Exercise-induced irisin may not only act as an endocrine factor capable of promoting the browning of white adipose tissue, but could also regulate bone metabolism by autocrine mechanisms," said Chen, who also serves as faculty in the Cell, Molecular & Developmental Biology program at the Sackler School of Graduate Biomedical Sciences at Tufts. "Our results suggest that irisin may have a therapeutic potential in

strengthening bone in [bone](#)-loss-associated diseases, and additional studies are needed to evaluate the underlying mechanisms by which irisin functions."

More information: Jin Zhang et al, Exercise-induced irisin in bone and systemic irisin administration reveal new regulatory mechanisms of bone metabolism, *Bone Research* (2017). [DOI: 10.1038/boneres.2016.56](https://doi.org/10.1038/boneres.2016.56)

Provided by Tufts University

Citation: Exercise-induced hormone irisin linked to new mechanisms for bone metabolism (2017, March 3) retrieved 5 May 2024 from <https://medicalxpress.com/news/2017-03-exercise-induced-hormone-irisin-linked-mechanisms.html>

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