

BONE
IRISIN BOOSTS BONE MASS

The myokine irisin, which is produced by skeletal muscle in response to exercise, increases both the mass and strength of cortical bone, according to a new study. The findings provide a possible explanation for the beneficial effects of physical activity on the skeleton triggered by skeletal muscle.

In their previous work, the investigators demonstrated that conditioned media from myoblasts isolated from mice after exercise enhanced the differentiation of bone marrow stromal cells into mature osteoblasts, an effect that was abolished by the presence of a neutralizing antibody against irisin. In the current study, the investigators sought to determine whether irisin could also modulate bone mass.

The team injected 2-month-old C57BL/6 male mice with a low dose of recombinant irisin ($100 \mu\text{g kg}^{-1}$) or vehicle once a week for 4 weeks. The dose of irisin—35-fold lower than that known to cause browning of white adipose tissue—was designed to exclude anabolic bone effects of irisin indirectly mediated by expansion of brown adipose tissue, which is itself known to have positive skeletal effects.

Cortical bone mass (determined by micro-CT) and strength (assessed by three-point bending assay and polar moment of inertia measurements) were markedly increased in irisin-treated mice, compared with control mice; no alterations were induced in the trabecular compartment of the same bones. Commensurate with increased cortical bone mass, low-dose irisin suppressed the expression of sclerostin—an inhibitor of the Wnt signalling pathway that is involved in bone formation. While the anabolic action of irisin was primarily mediated by the stimulation of bone formation, osteoclast numbers were substantially reduced, indicating that inhibition of osteoclastic bone resorption probably also contributed to the increase in bone strength.

“Future extension of our work could see irisin being used to treat and prevent osteoporosis during ageing, immobility, muscle wasting (sarcopenia) and absence of mechanical load (microgravity),” speculates lead investigator Maria Grano. “Furthermore, irisin-induced bone anabolism, accompanied by a reduction in white fat mass due to its conversion to healthier brown fat, might be a successful strategy to fight osteoporosis and obesity in one go.”

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