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Irisin injected mice display increased tibial cortical mineral density and polar moment of inertia

Graziana Colaianni[1], Concetta Cuscito[1], Teresa Mongelli[1], Paolo Pignataro[1], Cinzia Buccoliero[1], Loris Sartini[2], Maria Severa Di Comite[1], Giorgio Mori[3], Giacomina Brunetti[1], Silvia Colucci[1], Saverio Cinti[2], Maria Grano[1]

[1] Department of Basic Medical Science, Neuroscience and Sense Organs - Section of Human Anatomy and Histology, University of Bari, Bari, Italy - [2] Department of Experimental and Clinical Medicine, University of Ancona, Ancona, Italy - [3] Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy

It has been recently reported that, after physical activity, the skeletal muscle releases Irisin, the newly identified myokine able of driving transition of white adipocytes into brown [1]. This result supported the role of skeletal muscle as endocrine organ, suggesting that it could target other tissues besides adipose tissue. In our previous work, we demonstrated that conditioned media collected from primary myoblasts of exercised mice were able to increase OB differentiation and this effect was Irisin-mediated [2]. Here we show that Irisin has positive effect on cortical mineral density and geometry in vivo. Young male mice were injected with r-Irisin and cortical bone adaptation was analyzed by micro-CT at tibial midshaft. Our results show that cortical tissue mineral density is significantly increased in Irisin-injected mice compared to vehicle-injected littermates (+7.15%; $p<0.01$). Furthermore, this higher density of calcium hydroxyapatite at cortical site is accompanied by increase in periosteal circumference (+7.5%; $p<0.03$) and polar moment of Inertia (pMOI +19,21%; $p<0,01$). A greater pMOI indicates stronger resistance of a long bone to torsion and, together with higher bone mineral density, suggests higher protection against fracture. The effect of Irisin is fully comparable to the effect of physical activity that is widely accepted method for increasing bone mineral density and bone size in healthy populations.

In view of further proving the involvement of Irisin in bone metabolism, we validate its direct effect on osteoblasts in vitro. Phosphorylation of the MAP kinase ERK and the expression of Atf4 were significantly increased after Irisin treatment, as well as ALP and pro-Collagen I mRNA expression.

Our data highlight a novel link in muscle-fat-bone axis demonstrating that Irisin targets bone tissue directly, driving positive effects on cortical mineral density and geometry in vivo. These findings would expand the research of exercise-mimetic drugs that might be widely used to treat osteoporotic patients who are suffering from immobilization and cannot perform physical activity.

References

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Keywords
Myokine; bone; muscle; osteoporosis; sarcopenia; physical activity.