## Effects of recombinant Irisin on the musculoskeletal system of hind-limb suspended mice

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We previously showed that Irisin, a myokine released from skeletal muscle after physical exercise, plays a central role in the control of bone mass, driving positive effects on cortical mineral density and geometry in vivo (1). Here we demonstrated that r-Irisin treatment prevents bone loss in hind-limb suspended mice when administered during suspension and recovers bone mass when mice were injected after a suspension period (4 weeks) during which they developed bone loss. Micro computed tomography of femurs showed that r-Irisin treatment positively affected both cortical and trabecular bone. As expected, unloaded mice treated with vehicle displayed a remarkable decrease of cortical and trabecular bone mineral density (BMD), whereas in Irisintreated unloaded mice no loss of BMD was observed with respect to control mice kept under normal loading. Likewise, by treating mice after they already developed disuseinduced bone loss, r-Irisin was able to restore the damaged mineral component. Furthermore, trabecular bone volume fraction (BV/TV), which dramatically decreased in unloaded mice, was prevented by r-Irisin therapy. In particular, r-Irisin treatment preserved the number of trabeculae (Tb.N) and the fractal dimension, an index of optimal micro-architectural complexity of trabecular bone.We also showed that r-Irisin treatment protects muscle mass suffering from atrophy during unloading. Thus, unloaded mice treated with vehicle displayed a severe loss of muscle mass, as confirmed by ~ 60% decline of vastus lateralis weight and ~33% decrease of fiber cross-sectional area. Conversely, Irisin-treated unloaded mice showed no loss of muscle weight and similar fiber cross-sectional area to control mice. Our data reveal for the first time that r-Irisin treatment prevents and retrieves disuse-induced bone loss and muscle atrophy. These findings may lead to develop an Irisin-based therapy for the prevention and treatment of osteoporosis and sarcopenia in all patients who cannot perform physical activity, as occurs during aging and immobility, and it could also represent a countermeasure for astronauts exposed to microgravity during space flight missions.

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## References

[1] Colaianni et al. (2015) PNAS;112(39):12157-62.

Keywords

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