Sex-Dependent Effects of Irisin on Bone in an Aged Mouse Model

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Irisin is a recently discovered protein that has garnered increasing attention due to its potential impact on metabolic health and disease prevention. This hormone, released from exercising skeletal muscle, is generated through the cleavage of the membrane protein FNDC-5 (fibronectin type III domain-containing protein 5). Irisin has been shown to play a role in the browning of white adipose tissue and serves as a mediator of exercise-induced metabolic improvements. Notably, bone and muscle tissues are known to communicate, influencing each other's physiology. Previous research on Irisin demonstrated that Irisin's effects on bone in response to stress exhibit sex-dependent differences. Specifically, female FNDC-5 knockout (KO) mice were protected from adverse bone phenotypes when subjected to a low calcium diet, while male FNDC-5 KO mice showed worse bone phenotypes at baseline, even before the diet began.

The prior study focused on 5-month-old mice. Our research aims to investigate the effects of FNDC-5 KO in aged mice, both at baseline and under stress conditions. We utilized 18-month-old wild-type (WT) and FNDC-5 KO male and female mice, feeding them a low calcium diet for 2 weeks. Our findings revealed similar results to the earlier study with younger mice: female FNDC-5 KO mice exhibited partial protection against the low calcium diet's adverse effects on bone and skeletal muscle.

These results suggest that age and sex are critical factors in the bone-muscle crosstalk mediated by Irisin, highlighting the need for personalized approaches in nutritional and exercise interventions. Future research should explore the underlying mechanisms and potential therapeutic applications of Irisin in metabolic and musculoskeletal health.