The role of uncoupling protein-1 in cold-induced bone loss: implications for human climatic adaptation

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Chronic cold exposure causes elevated sympathetic tone that leads to bone loss, which could increase fracture risk in cold-dwelling humans. Nonshivering thermogenesis (NST) via uncoupling protein (UCP1) in brown adipose tissue may reduce bone loss by maintaining body temperature. To test this hypothesis, we studied the effects of temperature and sympathetic inhibition on bone mineral density (BMD) and body composition in male and female UCP1 knockout (UCP1KO) mice vs. wildtype C5BL/6J (B6) mice. We predicted that cooler temperature would lead to lower BMD in UCP1KO compared to B6 mice, and that sympathetic blockade with propranolol (PRO) would prevent bone loss. Mice were pair-housed from 3-12 weeks of age at 26C (thermoneutrality) or at 22C (cool), with or without PRO in drinking water (5 mg/mL). BMD and body composition were measured by peripheral dual-energy X-ray absorptiometry (Piximus I, GE Lunar). Results indicated no differences in BMD due to temperature or genotype in either sex. In female mice at 22C, BMD was lower in PRO-treated B6 and UCP1KO compared to controls. Unexpectedly, body fat was higher in females of both strains housed at 22C vs. 26C; in female UCP1KO vs. B6 at both temperatures; and in PRO-treated vs. wildtype females in both strains. These preliminary results do not support our hypothesis that UCP1-mediated NST reduces cold-induced bone loss. Microcomputed tomography (pending) will show how NST and sympathetic blockade affect trabecular bone microarchitecture and cortical bone geometry. Understanding how cold affects bone is essential for interpreting ecogeographic patterns of skeletal morphology.

Funding for this project was provided by NSF BCS-1638553 to MD.