

Sympathetic Inhibition Is Associated with Lower BMD and Higher Body Fat in Young Female UCP1 Knockout and Wildtype Mice

*Maisey Schuler¹, Rebecca Tutino¹, Miranda Cosman¹, Rachel Hurwitz¹, Taylor Spencer¹, Alexis Stokel¹, Isabel Hermsmeyer¹, Cleo Moursi¹, Maureen Devlin¹

¹University of Michigan, United States

Brown adipose tissue (BAT) helps maintain body temperature through nonshivering thermogenesis, in which uncoupling protein-1 (UCP1) releases energy as heat. BAT is correlated with higher bone mass in humans, and experimental studies in adult rodents show BAT may protect the skeleton from cold-induced bone loss due to elevated sympathetic tone. To investigate interactions of cold stress, sympathetic tone, and BAT on body composition and skeletal acquisition in subadults, we studied the effects of housing temperature and sympathetic inhibition in young C57BL/6J (B6) mice and UCP1 knockout (UCP1KO) mice. We hypothesize that 1) cold-housed UCP1KO mice will have lower BMD vs. B6 mice and 2) sympathetic inhibition via the beta-blocker propranolol (PRO) will reduce cold-induced bone loss, particularly in UCP1KO mice. To test these hypotheses, male and female B6 and UCP1KO mice were pair housed at 26C (thermoneutrality) or 22C (mild cold stress) from 3-12 wks of age with food and water ad lib. Half of each group were given PRO in drinking water (0.5 mg/mL) and half were controls (CON) (N=4-11/group). Outcomes at 12 wks of age included body mass, food intake, whole body bone mineral density (BMD, g/cm²), bone mineral content (BMC, g), and percent body fat (%) via PIXImus, and cortical and trabecular bone architecture at the midshaft and distal femur via μ CT (results pending due to research hiatus). In females, BMC was lower at 12 wks and body fat was higher at 9 and 12 wks in UCP1KO at 22 vs. 26C, and in UCP1KO vs. B6 at 22C. In males, there were no significant differences in UCP1KO vs. B6 at either temperature. In B6 PRO females at 22C, BMD was lower at 12 wks, BMC was lower at 9 and 12 wks, and body fat was higher at 9 wks. In UCP-1KO PRO females at 22C, BMD was lower at 6 and 9 wks of age and BMC was lower at 6 wks of age, and body fat was higher at 9 and 12 wks of age vs. CON. In male PRO vs. CON mice, there were no significant differences in bone density or body fat for either genotype or temperature. These data show UCP1KO mice have lower BMC, consistent with a protective effect of BAT on the skeleton. Contrary to our hypotheses, sympathetic inhibition was associated with lower BMD and BMC and higher body fat in both B6 and UCP1KO females, but not in males, suggesting a sex-specific trade-off between bone and body fat. Future work will investigate whether skeletal effects of sympathetic tone differ in subadult skeletal acquisition vs. adult bone maintenance.

Disclosures: Maisey Schuler, None