

## Supplemental Material and Methods

**1. Effect of high fat high sucrose (HFHS) diet on histidyl dipeptides in skeletal muscle.** To assess the effect of HFHS on histidyl dipeptides levels within the skeletal muscle, we fed low-fat diet (LFD TD.08485) and HFHS diets (TD.88137) to WTC57/Bl6 mice (age 8 weeks) for 14 weeks. Gastrocnemius muscle isolated from the LFD and HFHS fed mice were analyzed for the histidyl dipeptides carnosine and anserine by LC/MS as described previously[1] .

1. Hoetker D, Chung W, Zhang D, Zhao J, Schmidtke VK, Riggs DW, Derave W, Bhatnagar A, Bishop DJ, Baba SP: **Exercise alters and beta-alanine combined with exercise augments histidyl dipeptide levels and scavenges lipid peroxidation products in human skeletal muscle.** *J Appl Physiol* (1985) 2018. 2018, 1767-1778, 125, doi.org/10.1152/applphysiol.00007. 2018