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# Integrated Omics Approaches to Characterize a Nuclear Receptor Corepressor-associated Histone Deacetylase in Mouse Skeletal Muscle

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## ABSTRACT

Nuclear receptors regulate gene expression by differential binding to coactivators or corepressors in a ligand-dependent manner, which further recruits a set of epigenome-modifying enzymes that remodel chromatin conformation. Histone acetylation is a major epigenomic change controlled by histone acetyltransferases (HATs) and histone deacetylases (HDACs). HDAC3 is the only HDAC that confers the enzymatic activity to the complexes nucleated by nuclear receptor corepressors NCoR and SMRT. To address the metabolic function of HDAC3, we have deleted it specifically in mouse skeletal muscles. We have performed the following omics profiling in skeletal muscles of these mice: (1) RNA-seq profiling of total RNA; (2) Global nuclear run-on (GRO-seq) analysis of nascent RNAs; (3) Chromatin immuno-precipitation (ChIP-seq) of HDAC3 at both early evening and early morning; (4) proteomics profiling with mass spectrometry; (5) snap-shot metabolomics profiling of water-soluble metabolites at the basal condition; (6) snap-shot metabolomics profiling of lipid species at the basal condition; (7) kinetic fluxomics analysis of glucose utilization using $^{13}C_6$-glucose *in vivo* during treadmill running exercise. These approaches have provided several novel insights into how nuclear receptors regulate circadian rhythm of skeletal muscle fuel metabolism, which has been published elsewhere. Here we present the original datasets and technical details during the execution, analysis, and interpretation of these omics studies.