

Effects of SMDT1 Knockout on Skeletal Muscle Development and Energy Metabolism in Mice

Mengyang Zhao¹, Hefan Shi¹, Zhu Liu¹, Chunbo Cai^{1, 2, *}

¹College of Animal Science, Shanxi Agricultural University, Jinzhong, China;

²Shanxi Key Laboratory of Livestock Genetic Resources Exploration and Biotech Breeding, Shanxi Agricultural University, Jinzhong, China

Email address:

18736361260@163.com (Mengyang Zhao), shihfean0718@163.com (Hefan Shi), 2924554651@qq.com (Zhu Liu), caichunbo@sxau.edu.cn (Chunbo Cai)

*Corresponding author

Abstract

This study aimed to investigate the effects of SMDT1 knockout on skeletal muscle development and energy metabolism in mice. The SMDT1 heterozygous knockout (SMDT1^{+/-}) mouse model was successfully generated using CRISPR/Cas9 gene editing technology; breeding experiments revealed that homozygous knockout resulted in embryonic lethality. Body weight, glucose tolerance, insulin tolerance, and respiratory metabolic capacity were systematically evaluated in SMDT1^{+/-} and wild-type (WT) mice to assess the impact of SMDT1 deficiency on energy metabolism. The expression levels of myogenic differentiation marker genes and muscle fiber type-related genes in the soleus muscle were quantified by qRT-PCR. Furthermore, mRNA transcriptome sequencing was performed on soleus muscle tissues from SMDT1^{+/-} and WT mice to identify differentially expressed genes (DEGs). The results demonstrated that SMDT1^{+/-} mice exhibited significantly increased body weight, impaired glucose and insulin tolerance, and reduced oxygen consumption and CO₂ production, indicating diminished respiratory metabolic capacity compared with WT littermates. The expression levels of myogenic differentiation genes (*Myod*, *Myog*, *Myf5*, *Myhc*) and slow-twitch fiber marker genes (*Myh7*, *Myh2*) were markedly upregulated in the soleus muscle of SMDT1^{+/-} mice, whereas fast-twitch fiber marker genes (*Myh4*, *Myh1*) were significantly downregulated, suggesting that SMDT1 deficiency promotes myogenic differentiation and facilitates the transition from fast-twitch to slow-twitch muscle fibers. Transcriptome analysis identified 1,908 DEGs (942 upregulated and 966 downregulated), which were predominantly enriched in biological processes including skeletal muscle contraction, muscle cell development, glycolysis/gluconeogenesis, the PPAR signaling pathway, and the MAPK signaling pathway. In conclusion, SMDT1 plays a pivotal role in regulating skeletal muscle development and energy metabolism; its deletion transcriptionally reprograms myogenic differentiation and muscle fiber type switching while impairing systemic glucose homeostasis and metabolic capacity. These findings provide novel insights into the molecular mechanisms by which SMDT1 governs muscle growth and meat quality traits.

Keywords

SMDT1, Skeletal Muscle Development, Muscle Fiber Type Switching, Energy Metabolism, CRISPR/Cas9