AMPK regulates lipid accumulation in skeletal muscle cells through

FTO-dependent demethylation of N^6 -methyladenosine

Weiche Wu¹, Jie Feng¹, Denghu Jiang¹, Xihong Zhou², Qin Jiang¹, Min Cai¹, Xinxia

Wang¹, Tizhong Shan^{1*}, Yizhen Wang^{1*}

¹ College of Animal Science, Zhejiang University; Key Laboratory of Animal

Nutrition & Feed Sciences, Ministry of Agriculture; Zhejiang Provincial Laboratory

of Feed and Animal Nutrition; No. 866 Yuhangtang Road, Hangzhou, Zhejiang,

310058, P. R. China

² Institute of Subtropical Agriculture, The Chinese Academy of Science, Changsha,

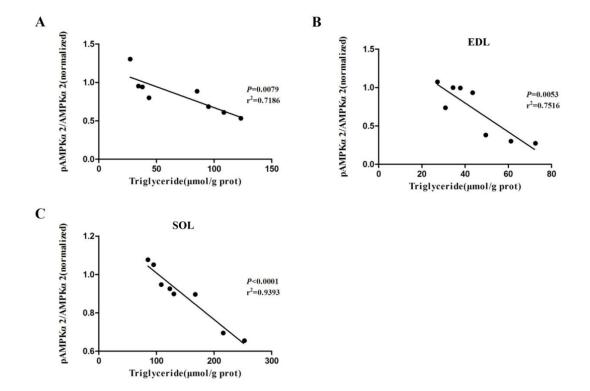
Hunan 410125, P. R. China

*Corresponding author:

Email: tzshan@zju.edu.cn, yzwang321@zju.edu.cn

Fax:+86-0571-88982729

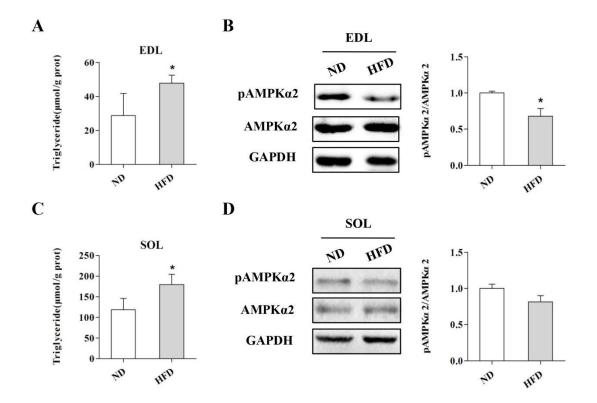
Tel.: +86-0571-88982729



Supplemental Figure 1

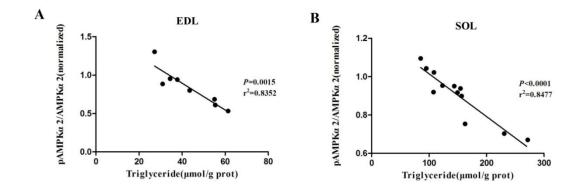
Correlation between pAMPK levels and triglyceride content in muscle. (A)

Correlation in the EDL and SOL of WT mice. (B, C) Correlation in the EDL (B) and SOL (C) of WT and OB mice. P value and R squared are presented in the graphs.



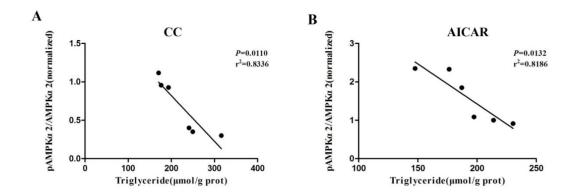
Supplemental Figure 2

The expression of AMPK in skeletal muscle is inversely correlated with lipid content. (A) The triglyceride content in the EDL of the HFD group and ND group. (B) The p-AMPK α 2 levels in the EDL of the HFD group and ND group. (C) The triglyceride content in the SOL of the HFD group and the ND group. (D) The p-AMPK α 2 levels in the SOL of the HFD group and ND group. The results are presented as the mean \pm SEM. n=4-6. *p< 0.05.



Supplemental Figure 3

Correlation analysis between pAMPK levels and triglyceride content in the EDL and SOL of ND- and HFD- fed mice. (A)Correlation in EDL. (B) Correlation in SOL. P value and R squared are presented in the graphs.

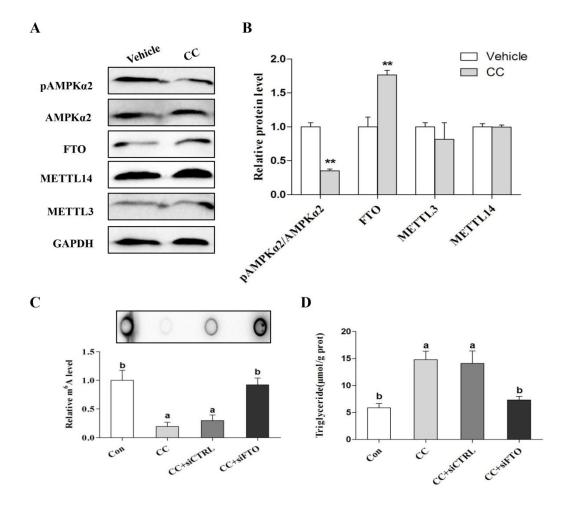


Supplemental Figure 4

Correlation between pAMPK levels and triglyceride content in C2C12 cells.

(A)Correlation in the Vehicle and CC groups. (B) Correlation in the Vehicle and

AICAR groups. P value and R squared are presented in the graphs.



Supplemental Figure 5

Compound C upregulates FTO expression and decreases m^6A methylation in C2C12 cells.(A, B) The protein levels of p-AMPK α 2, AMPK α 2, FTO, METTL3 and METTL14 in C2C12 cells after CC treatment. (C, D) m^6A methylation (C) and the triglyceride content (D) after combined treatment with CC and siFTO. Data are presented as the mean \pm SEM. n=3. *p<0.05, **p<0.01.