Supplemental Figure Legends

Figure S1 (related to Fig. 1). Exercise induces a PPARδ-dependent shift in muscle energy substrate utilization. (A) Western blot showing the protein levels of PPARδ, PGC1a, Tom20 (mitochondrial marker), and Hsp90 (internal control) in quadriceps from WT or PDmKO mice with or without 4 weeks of exercise. **(B-C)** VO2 and RER in a second set of WT or PDmKO mice with or without exercise (n=5). **(D)** The expression of *Cpt1b* and *Pdk4* in muscle negatively correlates with plasma lactate and RER in 38 BXD mouse lines. **(E)** Cross sections of soleus muscle stained for immuno-histochemical MHC fiber-typing [left panels: type I (blue), IIa (green), IIb (red), and IId/x (unstained)], and mitochondrial complex I activity (right panels). **(F)** mtDNA/nDNA copy number ratio and **(G-J)** mRNA expression levels of four MHC genes in soleus. (n=5, *p < 0.05, **p < 0.01, ***p < 0.001)

Figure S2 (related to Fig. 2). Ligand activation of muscle PPARδ induces substrate shift and boosts endurance. (A-B) VO2 and RER in a second set of WT or PDmKO mice with or without GW treatment (n=5). **(C)** OCR using succinate as the substrate in freshly isolated mitochondria from quadriceps. **(D)** Blood lactate levels. **(E)** Glycogen staining in gastrocnemius and soleus, and **(F)** glycogen content in quadriceps. **(G)** mtDNA/nDNA copy number ratio, **(H)** cross-section staining for mitochondrial complex I (left) and IV (right) activities, and **(I)** mitochondrial complex activities in isolated muscle mitochondria. **(J)** Relative mRNA expression levels of four MHC genes in white quadriceps and **(K)** cross sections of gastrocnemius stained for MHC fiber-typing [type I (blue), IIa (green), IIb (red), and IId/x (unstained)]. **(L)** Blood glucose before and after the endurance test. **(M)** Blood glucose (solid lines) and lactate (dotted lines) in sedentary vs exercised mice during endurance test. **(N)** Blood lactate before and after the endurance test. (n=5, **p < 0.01, ***p < 0.001)

Figure S3 (related to Fig. 3). PPARδ orchestrates opposing changes on fat and glucose metabolism. Gene ontology (GO) analysis of up-regulated **(A)** and down-regulated **(B)** genes in quadriceps that are induced by GW treatment.

Figure S4 (related to Fig. 4). AMPK activation alone has no effect on metabolic shift. (A) Heat map of expression changes of FA metabolism genes induced by GW treatment (GW/Chow) and AICAR (AICAR/CTL) in muscle. **(B)** QPCR verification of key FA and glucose metabolic genes in AICAR treatment. **(C)** VO2 and RER from AICAR (AC) treated mice (8-week 500mg/kg IP) compared to controls. **(D)** Relative mtDNA copy numbers in control (CTL) and PDmKO myotubes treated with DMSO (DM) or AICAR (AC). (n=5, *p < 0.05, **p < 0.01)

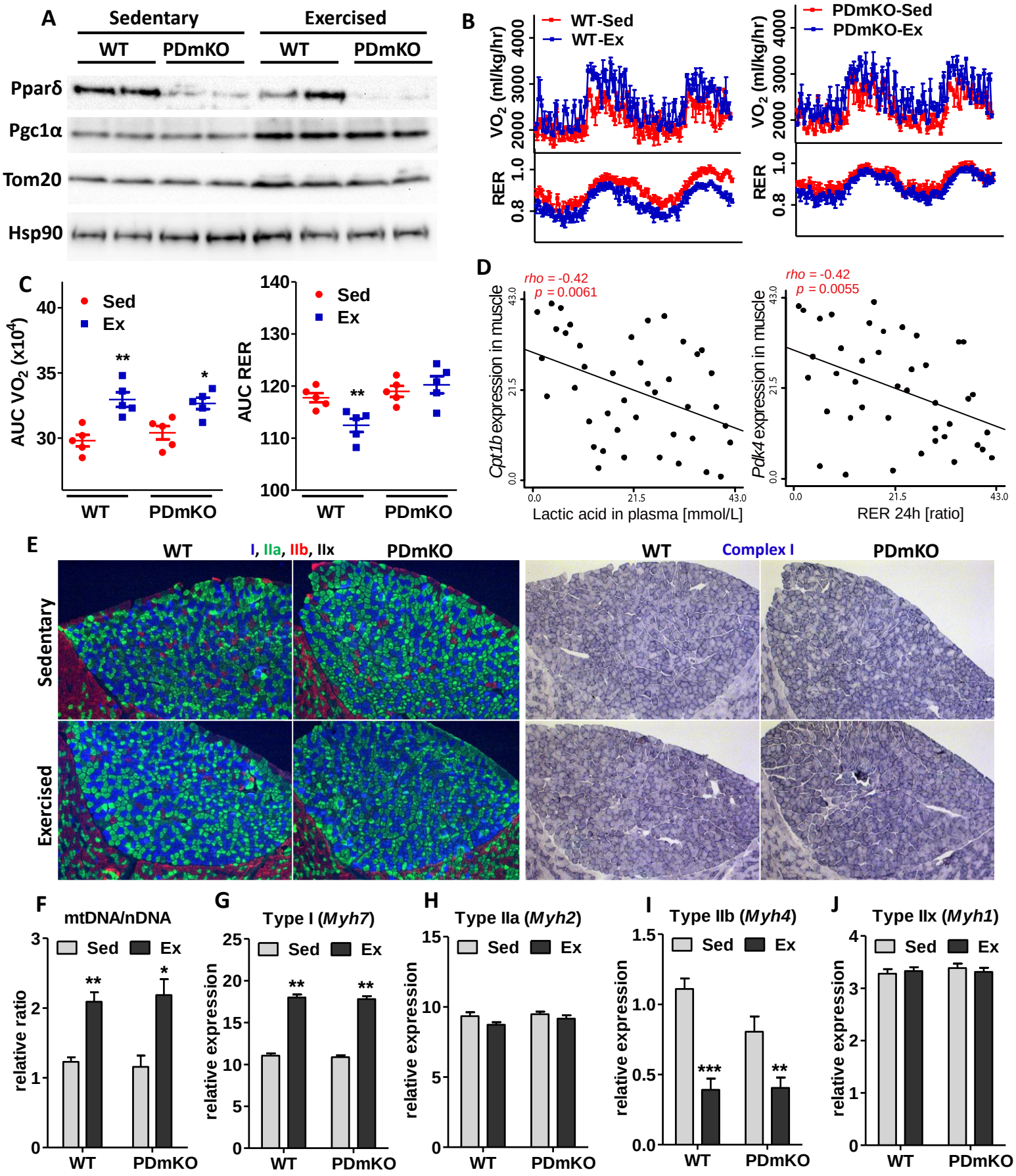

Figure S1. Muscle PPARδ is required for exercise-induced energy substrate shift

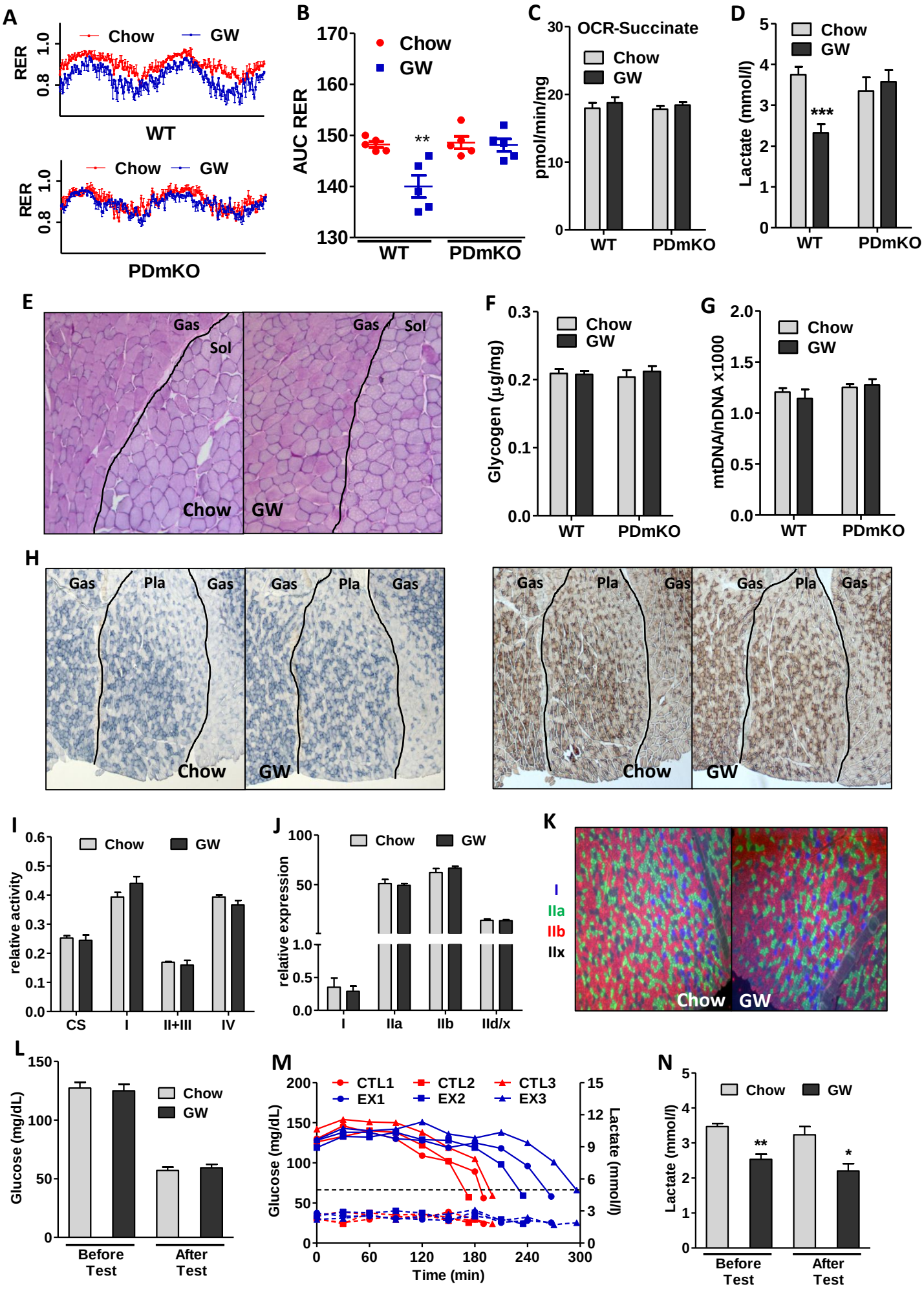

Figure S2. Ligand activation of muscle PPARδ induces substrate shift and boosts endurance

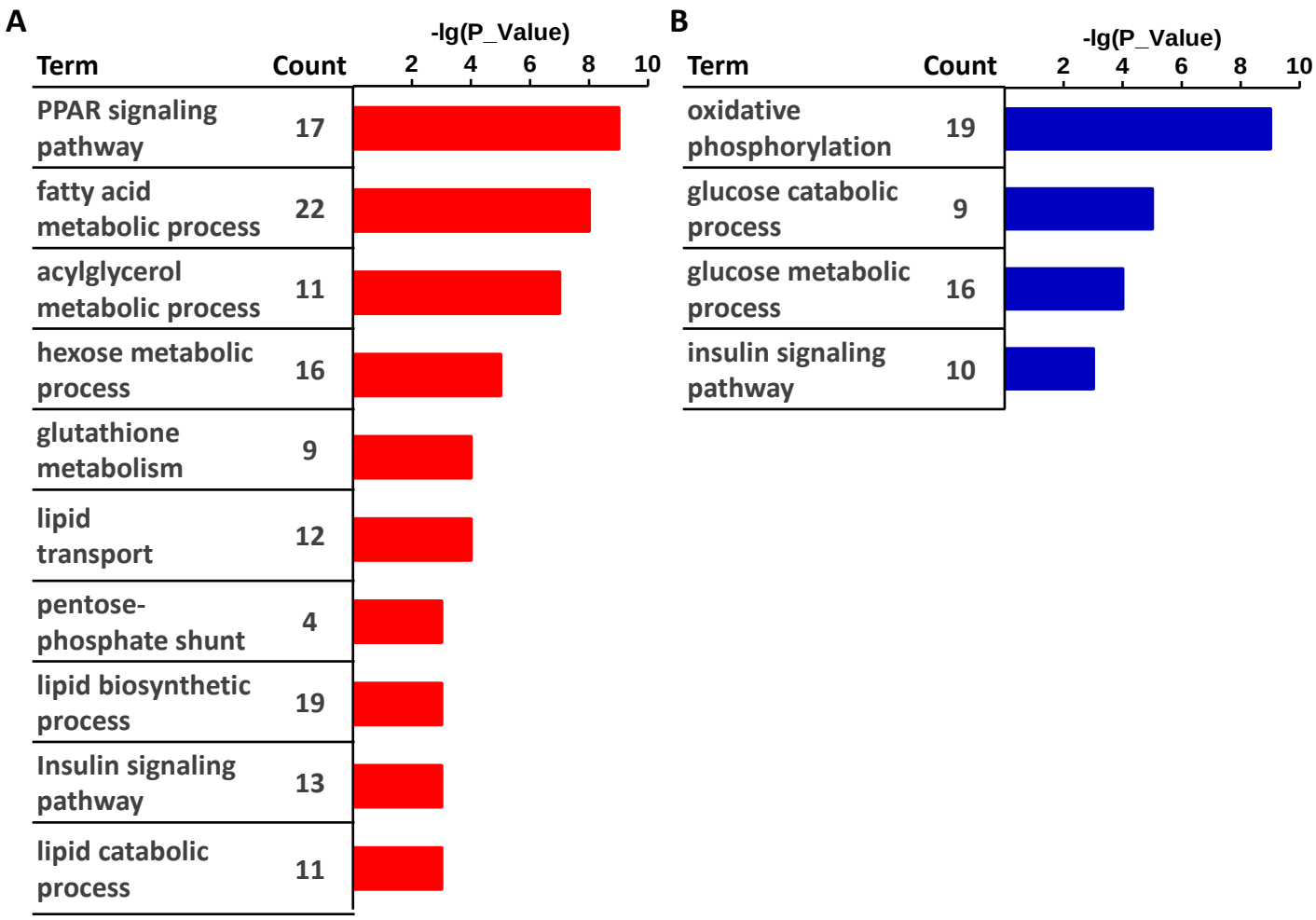

Figure S3. PPARδ gene network orchestrates opposing changes on fat and sugar metabolism

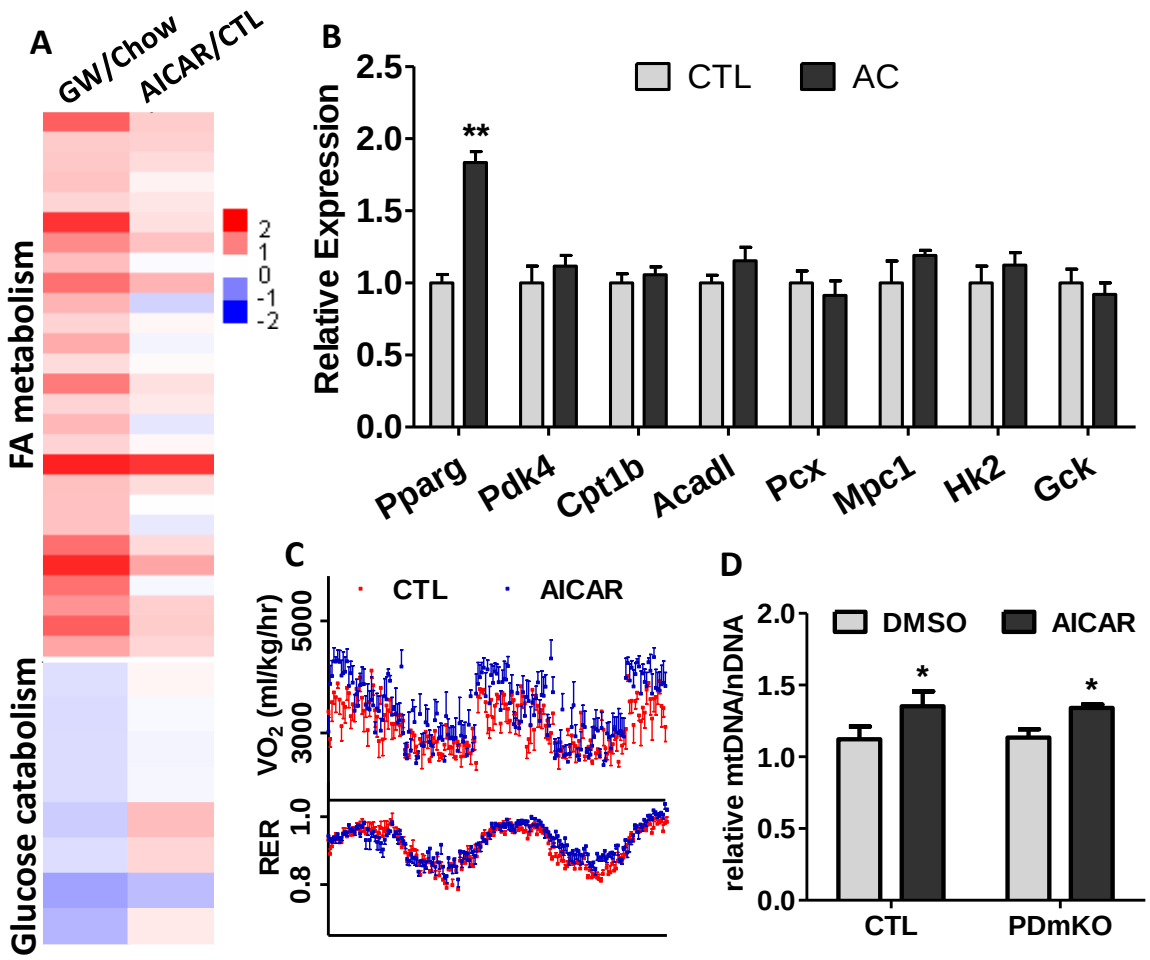

Figure S4. AMPK activation alone has no effect on metabolic shift