# **Supporting Information**

# Liu et al. 10.1073/pnas.1211611109

Fig. S1. All genes involved in lipid metabolic pathways with at least 2 fpkm were visualized with the GenMAPP program (Version 2.1) (1). Genes up-regulated >20% in adiponectin KO mice (KO/WT > 1.2) are highlighted with a red box, and genes down-regulated >20% in adiponectin KO mice (KO/WT < 0.8) are highlighted with a blue box. Gene changes <20% in KO mice are highlighted by a gray box. Genes not found in RNA-Seq are highlighted by a white box. (A) Fatty acid synthesis pathway. (B) Triglyceride synthesis pathway. (C) Cholesterol synthesis pathway. (D) Fatty acid beta oxidation pathway.

#### Fig. S1

1. Salomonis N, et al. (2007) GenMAPP 2: New features and resources for pathway analysis. BMC Bioinformatics 8:217.

Fig. S2. All genes involved in glycolysis and gluconeogenesis pathways (A) and in TCA pathway (B) with at least 2 fpkm were visualized with the GenMAPP program, with the same criteria described in Fig. S1.

#### Fig. S2

Fig. S3. All genes involved in the mitochondrial electron transport chain with at least 2 fpkm were visualized with the GenMAPP program, with the same criteria described in Fig. S1.

#### Fig. S3

Fig. S4. H&E staining of skeletal muscle and adipose tissues of male WT and adiponectin KO mice (age 18–20 wk), after fed a control diet or a HFD for 10, 20, and 30 d.

#### Fig. S4

Fig. S5. H&E and Oil Red O staining of livers of male WT and adiponectin KO mice (age 10–12 wk) and after being fed a control diet or a HFD for 10, 20, and 30 d

#### Fig. S5

Table S1. The expression levels (fpkm) of rate-limiting or critical genes in hepatic glucose and lipid metabolism, energy production, and detoxification functions in WT and KO mice from RNA-Seq analysis (a pool of RNA from 9 or 10 mice). The fold change in mRNA expression for each gene is expressed as a ratio of KO/WT. The genes in bold were validated by RT-PCR and are presented in Fig. 1. The rate-limiting enzymes in glucose and lipid metabolic pathways and detoxification were retrieved from the Rate-Limiting Enzymes database (RLEdb) (ref. 1; http://rle.cbi.pku.edu.cn)

## Table S1

1. Zhao M, Chen X, Gao G, Tao L, Wei L (2009) RLEdb: A database of rate-limiting enzymes and their regulation in human, rat, mouse, yeast and E. coli. Cell Res 19:793–795.

Table S2. The expression levels (measured by fpkm) of TFs expressed in liver from RNA-Seq analysis (a pool of RNA from 9 or 10 mice). TF with fpkm > 2 in both WT and KO mice are shown. The fold change of the expression level for a gene is expressed as a ratio of KO/WT. The genes validated by RT-PCR are in bold

### Table S2