Supplementary Figure 1

Coimmunoprecipitation of SIRT1 and DBC1 from mouse isolated liver nuclei. Nuclei were isolated from 4 different mice (1-4) and the nuclear protein lysates were immunoprecipitated for DBC1. The amount of SIRT1 that was immunoprecipitated, along with DBC1, was compared with the total amount of SIRT1 in the nuclear lysates (Input). The ratio between total and DBC1-bound SIRT1 was calculated by densitometry. Error bars represent standard deviation (SD).

Supplementary Figure 2

Glucose tolerance test in WT and DBC1 KO mice under normal diet or after 12 weeks of high-fat diet. Mice were starved for 24 hours. After that period, glucose (1.5 g/kg) was injected i.p. (n = 6 in each group). Error bars represent standard deviation (SD).

Supplementary Figure 3

Twenty-four physical activity and energy expenditures were measured in DBC1 KO (n = 5, regular diet; n = 4, high-fat diet [HFD]) and WT (n = 5) mice before and after at least 6 months on an HFD. (**A**) Both groups of mice gained weight on the diet, but the KO mice gained more. (**B**) Both groups of mice showed a significant decrease in VO_2 after high-fat feeding. There was a trend toward a significant difference between WT and KO mice in VO_2 on the regular diet (P = 0.10). (**C**) Energy expenditure corrected for metabolic body weight ($g^{0.75}$) showed the same effect. (**D**) Whole-mouse energy expenditure significantly increased after high-fat feeding, as would be predicted because of their increased body weight. (**E**) The HFD also caused a decrease in the respiratory exchange ratio (RER) in all mice. High-fat feeding caused a decrease in 24-hour horizontal (**F**)**,** vertical (**G**), and ambulatory (**H**) activity in all mice. There was a trend

toward an interaction (P = 0.0562) between diet and group in vertical activity. Error bars represent standard deviation (SD).

Supplementary Figure 4

(**A-B**) Semiquantitation of mRNA levels for fatty acid synthase (FAS) (**A**) and SREBP1c (**B**) in WT and DBC1 KO mice livers after 20 weeks of a high-fat diet (HFD). (**C**) Western blot for FAS in WT and DBC1 KO livers of mice fed normal chow diet and after 20 weeks on a HFD. (**D**-**E**) Western blots for phosphorylated acetyl-CoA carboxylase (pACC) (**D**) and pAMPK (**E**) in WT and DBC1 KO liver of mice fed a normal chow diet. Total ACC and AMPK were used as controls. Values are presented as means. Error bars represent standard deviation. Each group consisted of at least 4 mice.

Supplementary Figure 5

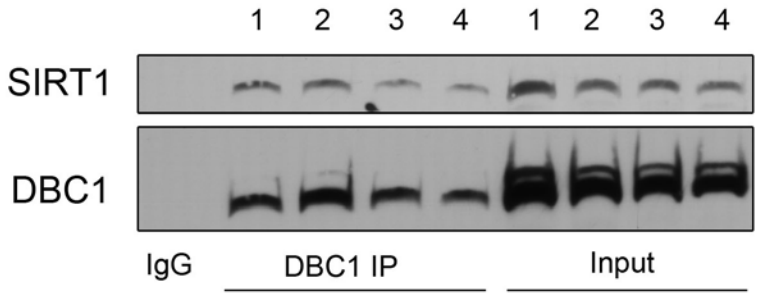
LPS-induced TNF release in Kupffer cells. Kupffer cells were isolated from WT and DBC1 KO mice fed a normal diet. Cells were seeded in a 12-well plate and incubated for 24 hours in DMEM + 10% FBS. Cells were then incubated with increasing doses of LPS (0-10 μg/ml) for 4 hours. TNF-α release into media was measured with an ELISA kit (eBioscience) following the manufacturer's instructions. Values are presented as means. Error bars represent standard deviation. *P < 0.05, t test (n = 3).

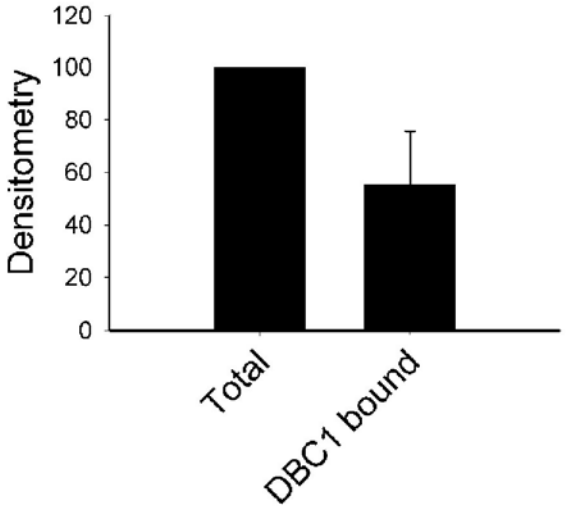
Supplementary Figure 6

(**A**) Mouse embryonic fibroblasts from WT and DBC1 KO stained with Oil red O-hematoxylin after 24 hours of treatment with 1 mM oleate/palmitate (Ole/Pal). Cells were also incubated with 100 μM resveratrol (Ole/Pal+RSV) and 5 mM nicotinamide (Ole/Pal+Nic). Original magnification ×200. (**B**) HEPG2 cells stained with Oil red O-

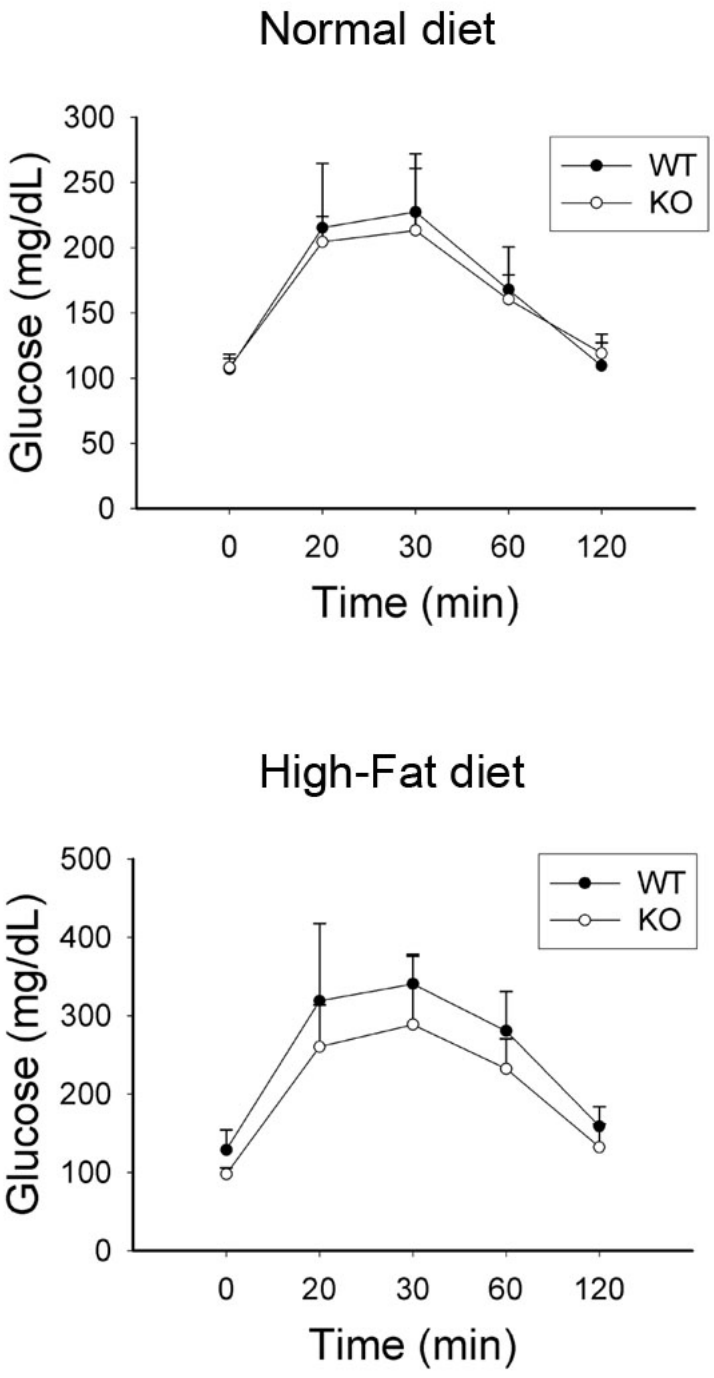
hematoxylin after 24 hours of incubation with 0.5 mM oleate/palmitate. Original magnification ×200. (**C-D**) Western blot corresponding to HEPG2 (**C**) and 293T (**D**) cells transfected either with control plasmid (vector) or Myc-DBC1 plasmid and then treated with different doses of oleate/palmitate. (**E**) 293T cells were transfected with HDAC3, SIRT1, and DBC1 vectors for 48 hours. During the last 24 hours before harvesting, the cells were incubated in the presence of 1 mM Ole/Pal (2:1 ratio). Intracellular lipid content was then measured. Values are presented as means. Error bars represent standard deviation. *$P < 0.05$, ANOVA test ($n = 3$).

Supplementary Figure 1

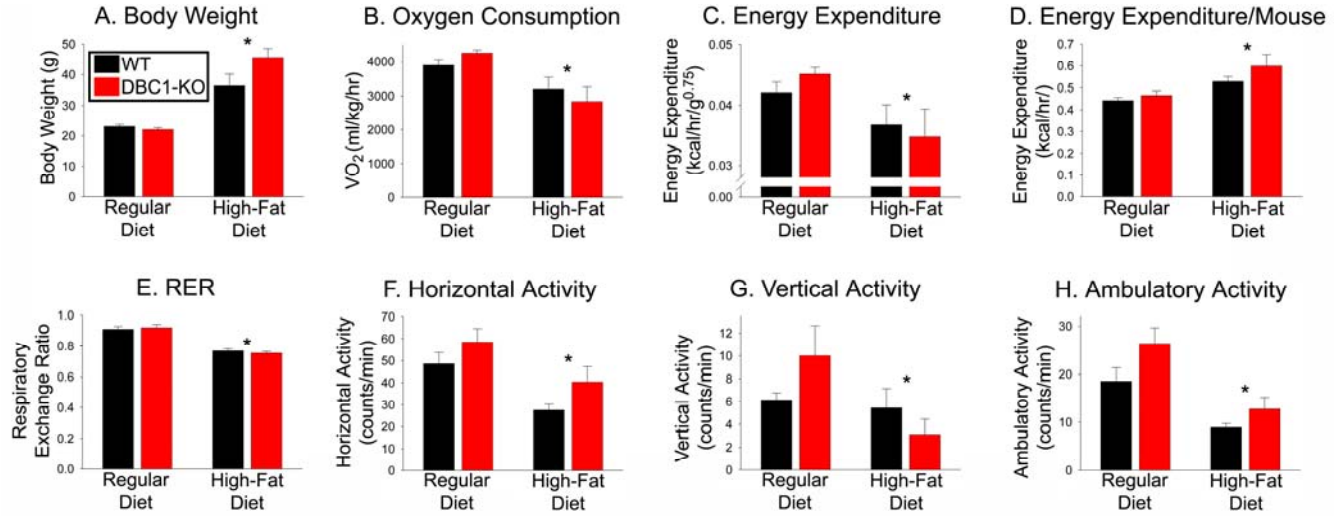




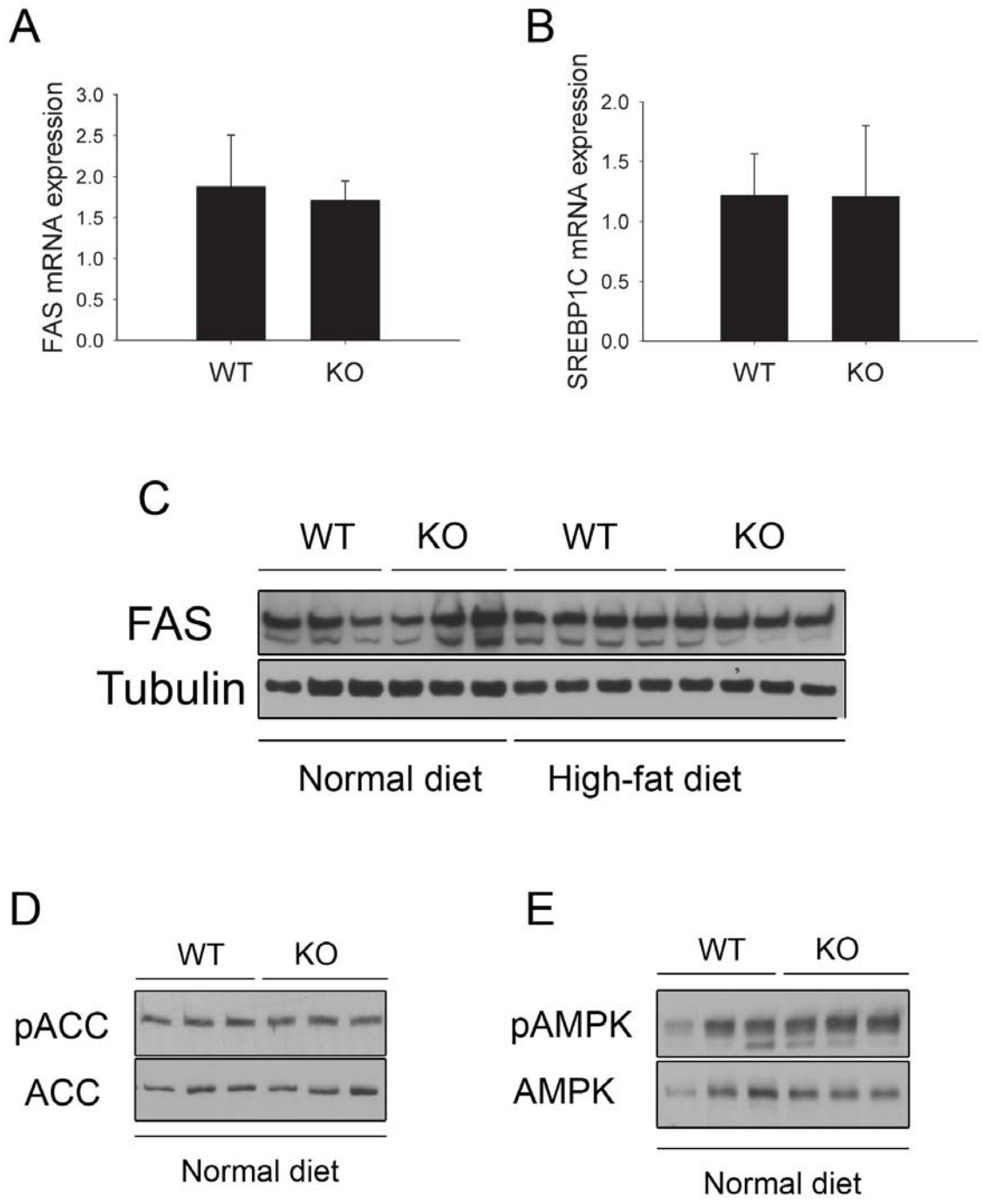
Supplementary Figure 2



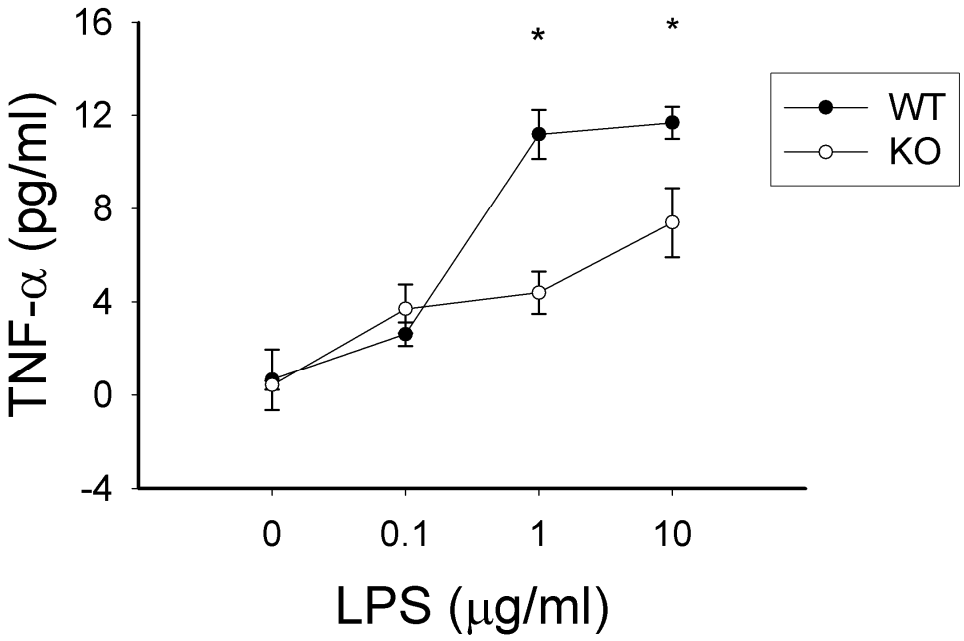
Supplementary Figure 3



Supplementary Figure 4



Supplementary Figure 5



Supplementary Figure 6