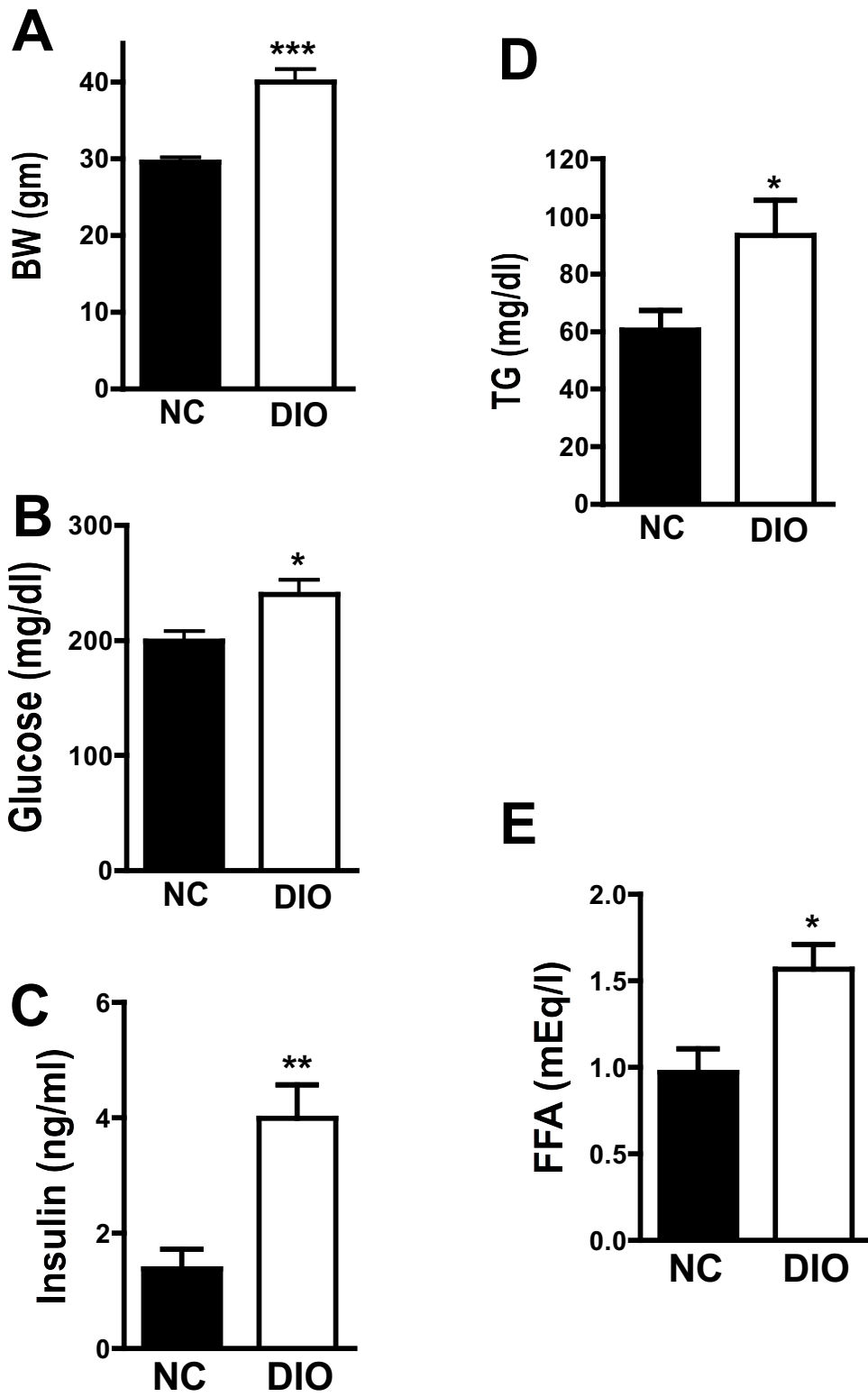


**Supplementary Figure 1:** C57Bl/6J mice were weaned to regular rodent chow (4% fat kcal, NC) or high fat diet (45% fat kcal, DIO) and allowed ad libitum access to diet for 3 months. (A) Body weight, (B) ad libitum fed tail blood glucose, (C) serum insulin levels, (D) serum triglycerides levels, and (E) serum free fatty acid levels were obtained. Data are means  $\pm$  SEM, n= 5 to 8, \*:  $p < 0.05$ , \*\*:  $p < 0.01$ , \*\*\*:  $p < 0.01$  vs. NC.

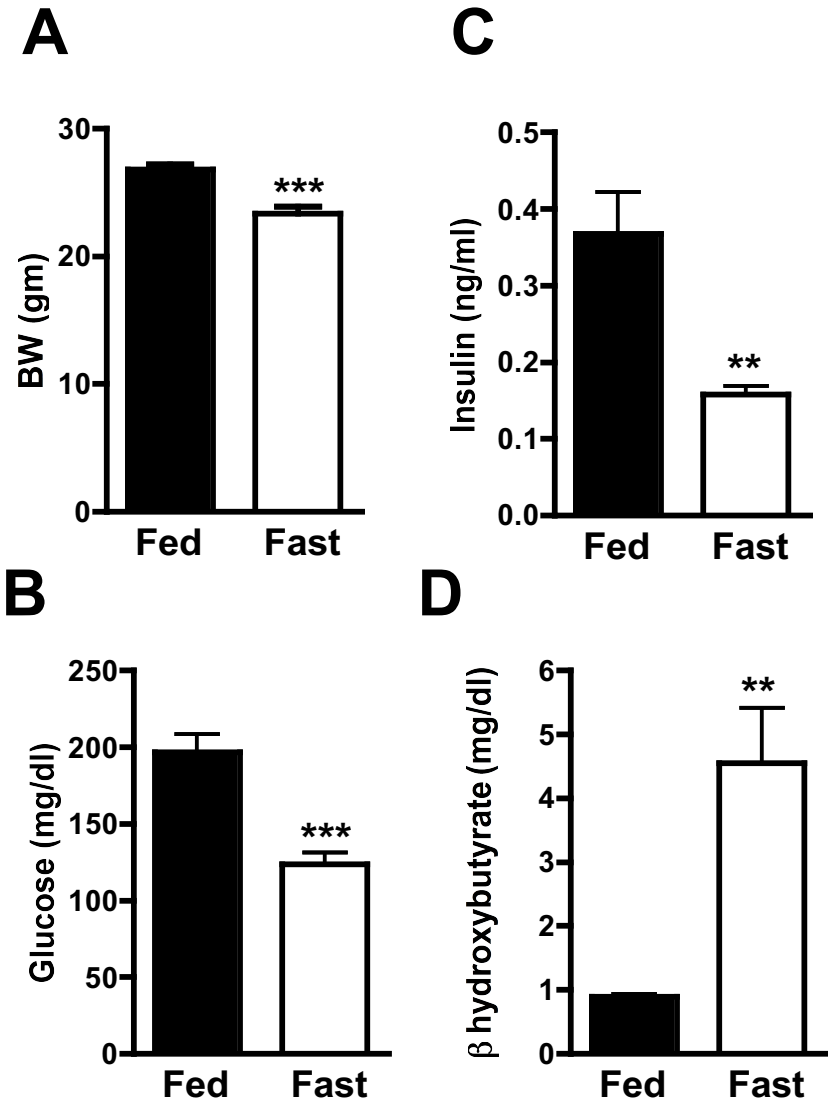
**Supplementary Figure 2:** C57Bl/6J mice were fasted for 24 h. (A) Body weight, (B) ad libitum fed tail blood glucose, (C) serum insulin levels, and (D)  $\beta$  hydroxybutyrate levels were obtained. Data are means  $\pm$  SEM, n=6, \*\*:  $p < 0.01$  vs. ad libitum fed mice, \*\*\*:  $p < 0.005$  vs WT

**Supplementary Figure 3:** MIN6 cells were transfected with non targeting siRNA (Cont si) or siRNA targeting ADFP (ADFP si) and incubated overnight as done in ADFP-ASO experiments. (A) Real time PCR showed that ADFP expression normalized to  $\beta$  actin levels was reduced to 40% of control by ADFP si (\*\*\*;  $p < 0.005$  vs Cont si). (B) Representative western blot showing the reduction of ADFP by ADFP si treatment. (C) Insulin secretion was measured in MIN6 cells transfected with Cont si or ADFP si in the presence of glucose and 0.5 mM palmitic acid for 1 h. Insulin secretion at 25 mM glucose plus 0.5 mM PA was reduced to 55% of Cont si (\*;  $p < 0.05$ ). Data are means  $\pm$  SEM, n= 9 to 12 from 4 independent experiments.

Supplementary Fig. 1



Supplementary Fig. 2



### Supplementary Fig. 3

