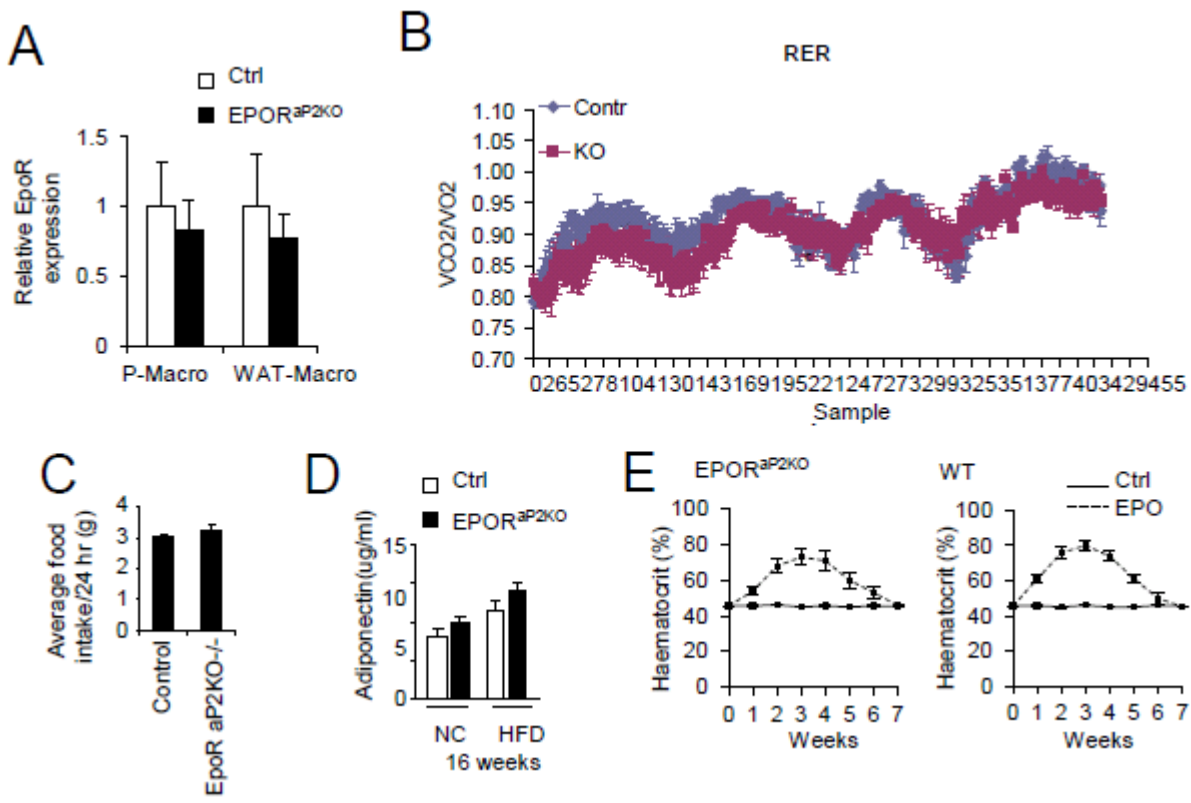


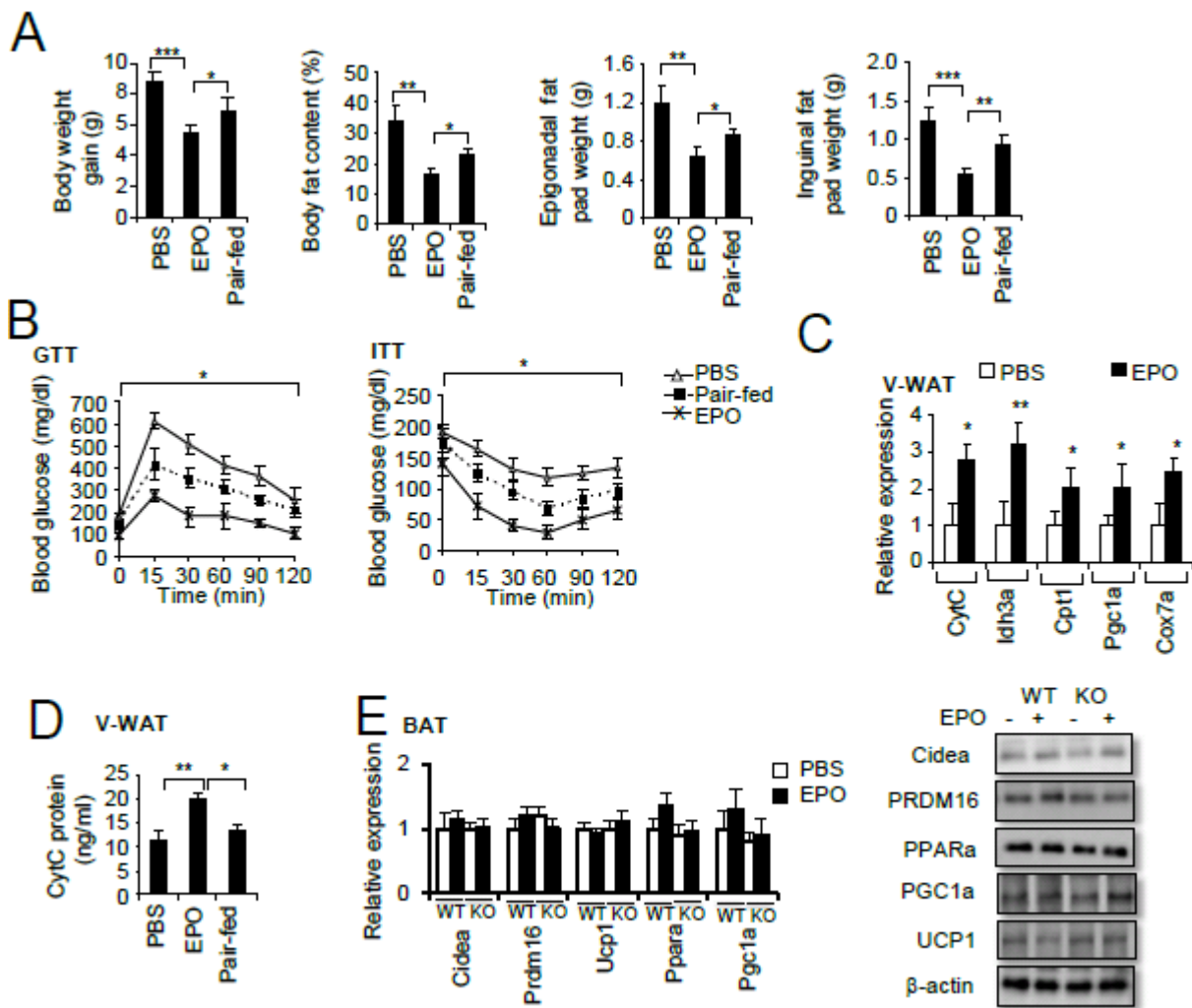
SUPPLEMENTARY DATA

**Supplementary Figure 1.** Energy metabolism in EpoRaP2KO and littermate control mice. A. EpoR expression level in macrophages isolated from WT control and EpoRaP2KO mice (peritoneal macrophage: P-Macro;white fat tissue macrophage:WAT-Macro). B. Total respiratory exchange ratio (RER) in WT and EpoRaP2KO mice. C. Food intake was determined in WT- and EpoRaP2KO mice between 3 month and 4 month of age (n=6). D. Serum adiponectin level was measured in EpoRaP2KO mice and littermate control (Ctrl) on NC and HFD food (n=6). E. EpoRaP2KO and WT mice (8.5 month of age) fed a normal diet were treated with EPO (dashed line) or saline (solid line) for 3 weeks (n=4). Hematocrit were monitored weekly for up to 4 weeks after treatment. Data are presented as mean±s.e.m., and Student's t-test was used for single comparisons. \*P < 0.05 and \*\* P < 0.01.



SUPPLEMENTARY DATA

**Supplementary Figure 2.** EPO protects from diet induced obesity and improves glucose intolerance and insulin resistance. A- B. Mice on high fat diet (HFD) were treated saline (PBS) or with EPO (3000U/kg; 3 times/week for 5 weeks) beginning at 4 weeks of age or were paired-fed. Body weight gain, body fat content, epigonadal fat pad and subcutaneous inguinal fat pat weight were measured (n=10) (A) and glucose tolerance test (GTT) and insulin tolerance test (ITT) were determined (n=6) (B). C. Mitochondrial function related genes without (PBS) and with EPO treatment in viceral WAT were determined. D. CytC protein level without (PBS) and with EPO treatment in viceral WAT were determined. E. Brown fat depot were isolated from the EPO and saline treated WT and EpoRaP2KO mice and indicated genes and protein were determined. For A, B and E, one-way ANOVA was used. All other statistics were performed using Student's t-test, and bar graphs are mean±s.e.m. \*P < 0.05. \*\*P < 0.01. \*\*\*P < 0.001.



SUPPLEMENTARY DATA

**Supplementary Figure 3.** Gene and protein level analysis. A-B. Mice on HFD were treated beginning at 4 weeks with PBS or with EPO (3000U/kg) for 3 weeks and the body weight gain was determined in Figure S2F (n=6). GTT and ITT were determined in Figure 1G (n=6). Data are presented as mean±s.e.m., and Student's t-test was used for single comparisons. C. PGC-1α was overexpressed in 3T3-L1 adipocytes, confirmed by Western blotting. D. Validation of Sirt1 knock down by Western blotting. Data are presented as mean±s.e.m., and Student's t-test was used for single comparisons. \*P < 0.05. \*\*P < 0.01.

