

Supplemental Figure 1: Effect of E2 on body and fat pad weights in male ZDF rats. (A) Body weight was measured in male ZL, ZDF, and ZDF + E2 rats at the indicated time points \* ZDF vs. ZDF + E2. (B) Fat pads were measured following sacrifice at 16 weeks in rats from part A. Results represent the mean $\pm$ SE (n=4-8 rats). \*p<0.05, \*\*p<0.01, \*\*\*p<0.001.





(A) INS-1 cells were treated with vehicle or E2 ( $10^{-8}$ M) for 24 hrs. Expression of full length ER $\alpha$ 66 and the short ER $\alpha$ 36 isoform was determined by western blotting with three antibodies (HC-20, MC-20 and H222) against ER $\alpha$ . (n= at least two experiments).



Supplemental Figure 3: Glucose stimulates <u>lipid synthesis</u> in INS-1 cells in a dosedependent manner. Effects of increasing glucose concentrations on (A) FAS gene expression (4h) normalized to  $\beta$ -actin, (B) FAS protein expression (24h), (C) FAS enzymatic activity (24h), (D) TG content (24h) in INS-1 cells. Results represent the mean±SE of at least 2 experiments. \* vs. 16mM glucose when not indicated. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001.



Supplemental Figure 4: Phenotypic characterization of male control (ER $\alpha$ lox/lox) and PER $\alpha$ KO<sup>-/-</sup> mice. (A,E&I) Blood glucose concentration and (B,F&J) AUC following an IP glucose challenge [2.0 g/kg, 8 weeks (A&B), 16 weeks (E&F) and 24 weeks (I&J)]. (C,G&K) Fasting and (D,H&L) fed blood glucose concentrations in male mice at 8 weeks (C&D), 16 weeks (G&H) and 24 weeks (K&L). (M) Fasting and (N) fed plasma insulin concentrations in male mice at 12 weeks. (O) Body weight in male mice measured weekly over 24 weeks. (P) Fed plasma leptin concentrations in male mice at 13 weeks. Results represent the mean±SE (n=4-8 for ER $\alpha$ lox/lox and PER $\alpha$ KO<sup>-/-</sup> mice).



Supplemental Figure 5: Effect of HF diet on body weight and fat pad mass in control and PER $\alpha$ KO<sup>-/-</sup> mice. (A) Body weight measured in male control (ER $\alpha$ lox/lox) fed a normal chow diet (NC), control and PER $\alpha$ KO<sup>-/-</sup> fed a high fat diet (HF) at the indicated time points (n=10-21 mice). (B) Fat pads were measured following sacrifice at 11 weeks in the indicated mice from part A (n=9-10 mice). Results represent the mean±SE. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001.

## Supplemental Table 1:

Gene Name	Forward	Reverse
Pdx-1	GAGGACCCGTACAGCCTACA	CGTTGTCCCGCTACTACGTT
Ins1	CAAGCAGGTCATTGTTCCAA	GGACCACAAAGGTGCTGTTT
FAS	TCGAGACACATCGTTTGAGC	TCAAAAAGTGCATCCAGCAG
ΑССα	TACAACGCAGGCATCAGAAG	TGTGCTGCAGGAAGATTGAC
SCD1	CCTTAACCCTGAGATCCCGTAGA	AGCCCATAAAAGATTTCTGCAAA
β-actin	GGGAAATCGTGCGTGACATT	GCGGCAGTGGCCATCTC
<sup>A</sup> FAS	CACAGATGATGACAGGAGATGG	TCGGAGTGAGGCTGGGTTGAT
<sup>A</sup> β-actin	ATGCTCCCCGGGCTGTAT	CATAGGAGTCCTTCTGACCCATTC

Rat and <sup>A</sup>mouse primer sequences used for qRT-PCR

<sup>A</sup>Primers for mouse