

SUPPLEMENTARY DATA

**Supplementary Table 1.**

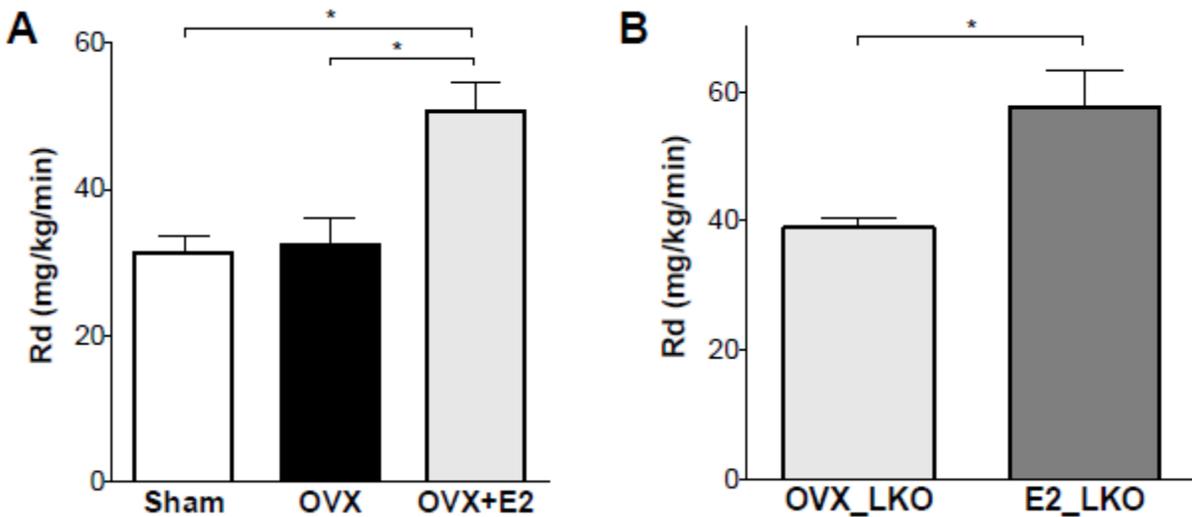
Physiological characteristics of LKO female mice and the littermates

Mice were fed on chow diet for 15 weeks. Body samples were collected after 5 hours fasting (n=5)

	Body Weight (gram)	Adiposity*	Insulin ( $\mu$ U/ml)	Glucose (mg/dl)	Plasma TG (mg/dl)	Plasma Cholesterol (mg/dl)
Littermates	21.8 $\pm$ 1.8	12.3 $\pm$ 1.6	9.7 $\pm$ 2.0	82 $\pm$ 15	62 $\pm$ 5.5	94 $\pm$ 11
LKO	22.5 $\pm$ 2.5	12.7 $\pm$ 1.6	9.1 $\pm$ 0.7	80 $\pm$ 16	53 $\pm$ 4.4	88 $\pm$ 4

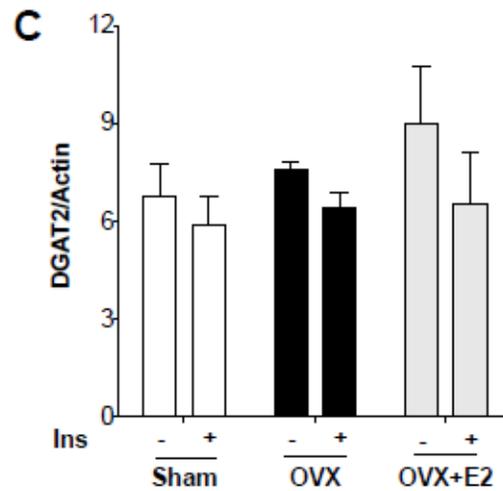
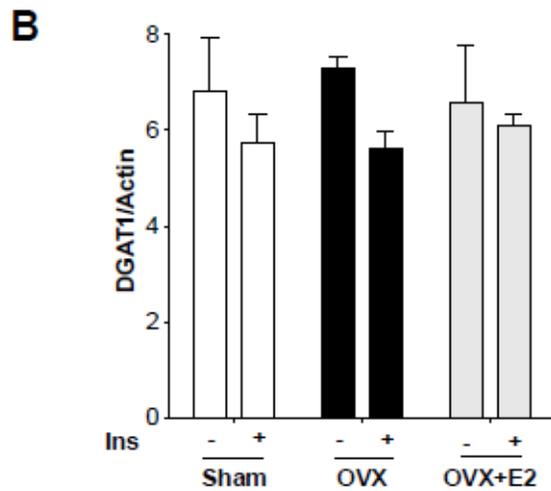
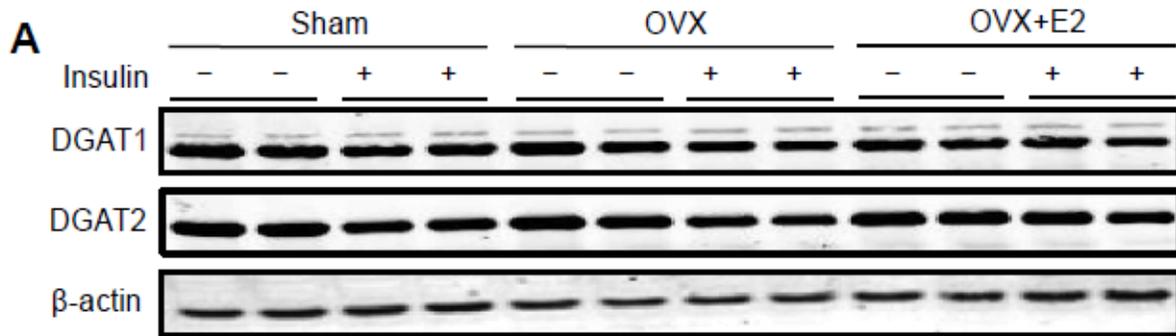
\* Adiposity was presented as the percentage of body weight.

**Supplementary Figure 1.** Glucose disappearance rate (Rd) during clamp: Rd was determined using non-steady state equation for wild-type C57Bl/6J mice (**A**) and liver ER $\alpha$  knock out LKO mice (**B**). \* p < 0.05. Differences between groups were determined by ANOVA followed by Tukey's post hoc tests.



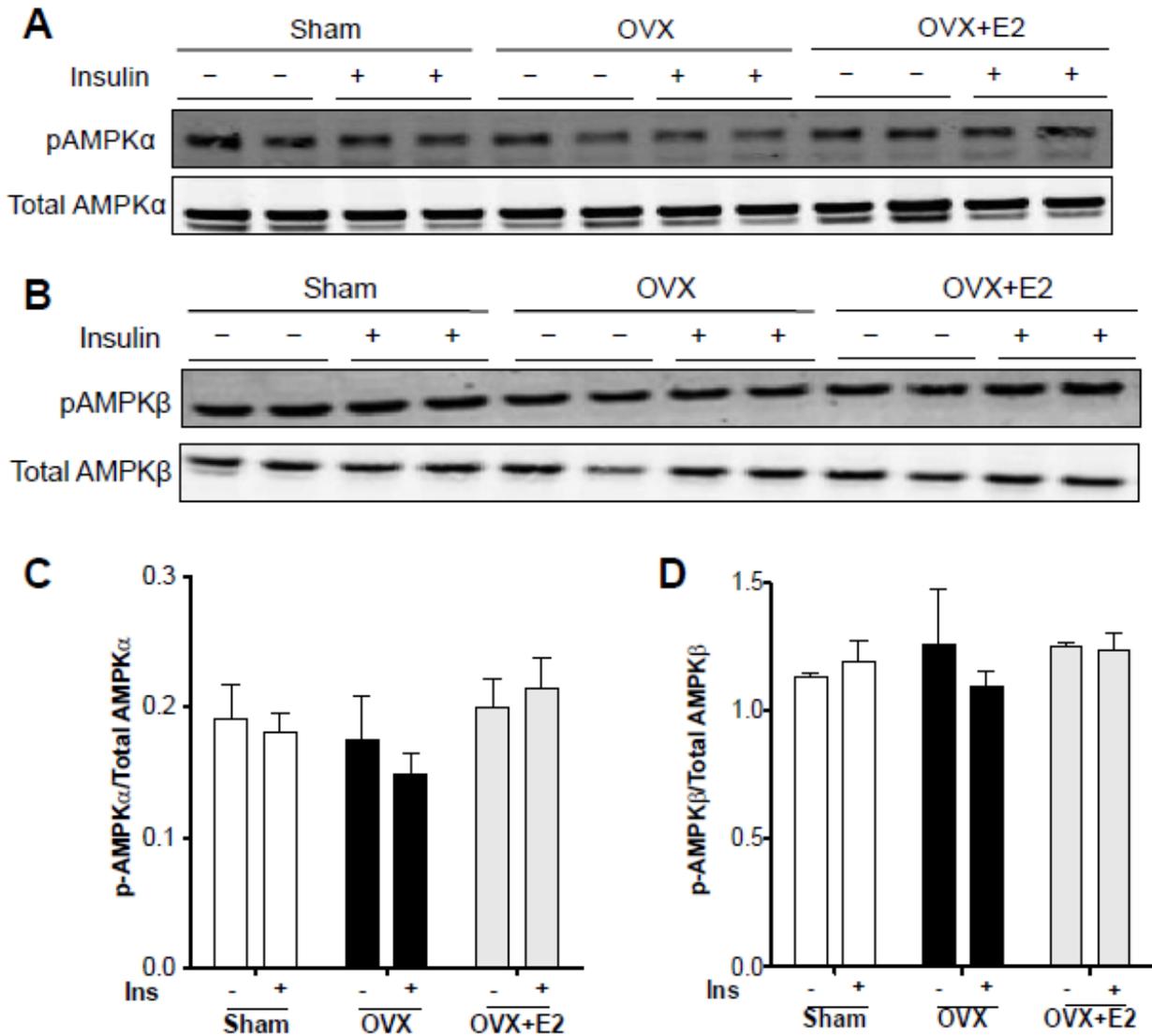
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**Supplementary Figure 2.** Liver DGAT1/2 expression: Livers from mice excised at after fasting (Ins -) or after hyperinsulinemia clamp study (Ins +) were used for protein extraction. Western blotting for DGAT1/2 is shown in panel **A**; expression of  $\beta$ -actin and Panseau S staining were used as loading control; the ratio of DGAT1/actin and DGAT2/actin was quantified in **B** and **C**, respectively.



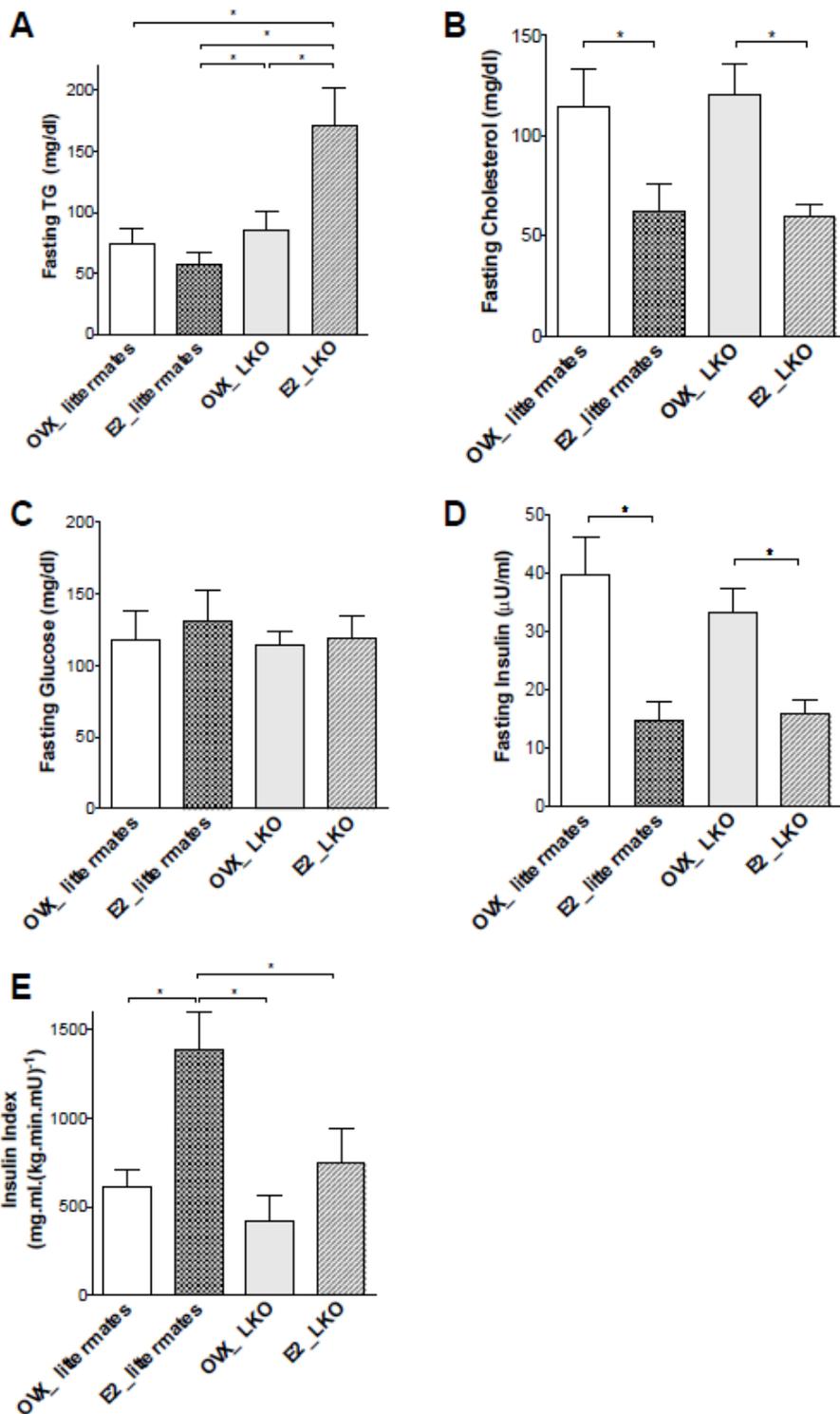
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**Supplementary Figure 3.** Liver APMK $\alpha/\beta$  expression and phosphorylation: Livers from mice excised at after fasting (Ins -) or after hyperinsulinemia clamp study (Ins +) were used for protein extraction. **A:** Western blotting for phosphorylation of AMPK $\alpha$  (pAMPK $\alpha$ ) and total AMPK $\alpha$ . **B:** blots for p-AMPK $\beta$  and total AMPK $\beta$ . Expression of  $\beta$ -actin and Ponceau S staining were used as loading control. **C:** The ratio of pAMPK $\alpha$ /AMPK $\alpha$ . **D:** The ratio of pAMPK $\beta$ /AMPK $\beta$ .



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**Supplementary Figure 4.** Fasting serum chemistry and insulin index for LKO mice and their littermates: **A:** Estrogen treatment did not reduce hypertriglyceridemia in LKO mice. **B:** Estrogen treatment decreased fasting cholesterol levels independent of liver ER $\alpha$ . **C:** Fasting glucose did not change between groups. **D:** Estrogen treatment decreased fasting insulin in wild-type littermates and LKO mice. **E:** Estrogen treatment improved insulin index in wild-type littermates but not in LKO mice. \*,  $p < 0.05$ , differences between groups were determined by ANOVA followed by Tukey's post hoc tests.



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**Supplementary Figure 5.** Quantification of the Western blots in Figure 6E: \*,  $p < 0.05$ . Differences (+) or (-) insulin were defined by student's t-test.

