### **Supplemental Information**

Cell Metabolism, Volume 11

# Specific Roles of the p110 $\alpha$ Isoform of Phosphoinositide 3-Kinase in Hepatic Insulin Signaling and Metabolic Regulation

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#### Figure S1. Acute and Chronic Deletion of $p110\alpha$ in Liver

(A) Western blot of liver protein lysates from mice with acute deletion of p110 $\alpha$ . p-Akt/PKB represents phosphorylation of Akt on amino acid serine 473 and threonine 308. Vinculin, loading control.

(B) Western blot of liver, muscle, WAT, and brain protein lysates from mice with chronic deletion of  $p110\alpha$ .

(C) PI3 kinase activity from liver lysates immunoprecipitated with  $p110\beta$  of fasted mice of indicated genotype. Data are representative of 5 independent experiments.

### Figure S2. Insulin Response during GTT and Leptin Levels

Mice with acute deletion of  $p110\alpha$ .

(A) Serum insulin levels of 8- to 10-week-old male mice on regular chow diet during glucose tolerance test (n = 8); asterisks indicate p < 0.05.

(B) Serum leptin levels of mice 2 weeks after adenovirus injection and quantitative RT-PCR analysis of mRNA levels of leptin receptor from mouse livers 3 weeks after adenovirus administration (n = 6-7). Data represent the mean  $\pm$  SEM, \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001, compared to Flox + LacZ controls.

Mice with chronic deletion of  $p110\alpha$ .

(C) Serum leptin levels and liver leptin receptor gene expression in p110 $\alpha$  flox and L-p110 $\alpha$  KO mice at 18 weeks. Expression is normalized to 18S. Data represent mean ± SEM (n = 8-10), \*p < 0.05

#### Figure S3. Lipid Expression and aPKC Activity

Mice with acute deletion of  $p110\alpha$ .

(A) Serum triglycerides, cholesterol, and free fatty acids in mice of the indicated genotype (n = 8-9, bars equal mean  $\pm$  SEM, \*p < 0.05 compared to flox).

(B) Quantitative RT-PCR analyses of lipogenic gene expression. Relative gene expression of control mice is set to 1 (dashed line). Bars represent means  $\pm$  SEM, n = 7–8, \*p < 0.05 compared to flox.

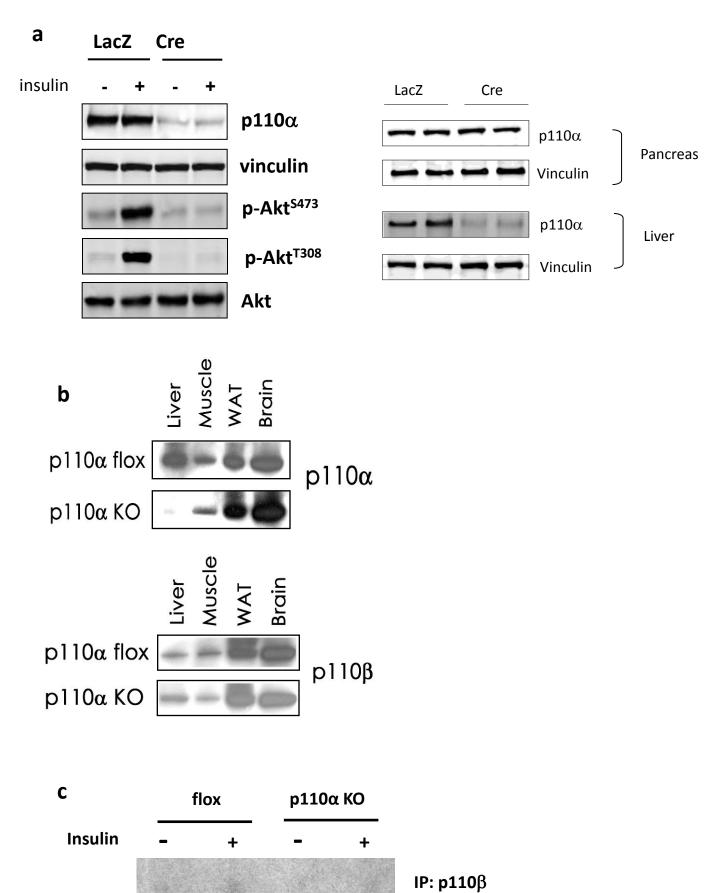
(C) Liver triglyceride (TG) levels (mg/g liver) of 8- to 10-week-old male mice on regular chow diet. Bars represent means  $\pm$  SEM (n = 8 for each genotype, <sup>\*</sup>p < 0.05 compared to flox). Mice with chronic deletion of p110 $\alpha$ .

(D) Hematoxylin and eosin staining and oil red O staining of liver sections from 10- to 12week-old p110 $\alpha$  flox and L-p110 $\alpha$  KO mice. Data are representative of liver sections from 3-7 individual mice.

(E) Quantitative RT-PCR analysis of lipogenic genes from livers of p110 $\alpha$  flox and L-p110 $\alpha$  KO mice in the fed state. Relative gene expression of p110 $\alpha$  flox mice is set to 1 (dashed line). Expression is normalized to 18S. Data represent mean ± SEM (n = 6-10), \*p < 0.05.

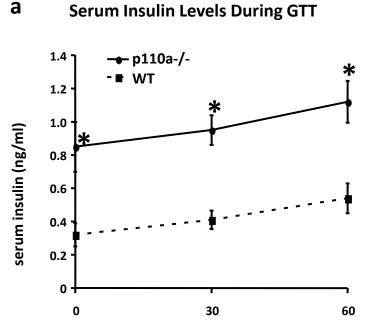
(F) PKC $\lambda/\zeta$  activity from liver lysates of fasted mice of indicated genotype (n = 3-4), \*p < 0.05.

## Supplementary Fig. 1

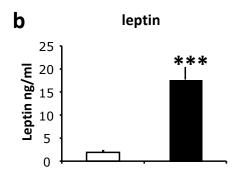


## **Supplementary Fig. 2**

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Minutes after glucose administration





mRNA/GAPDH

