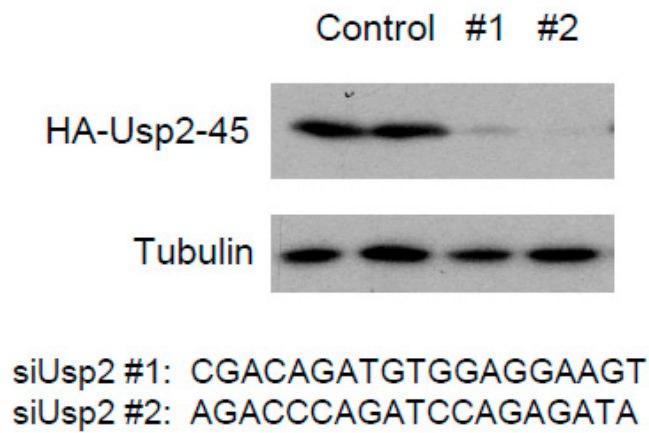
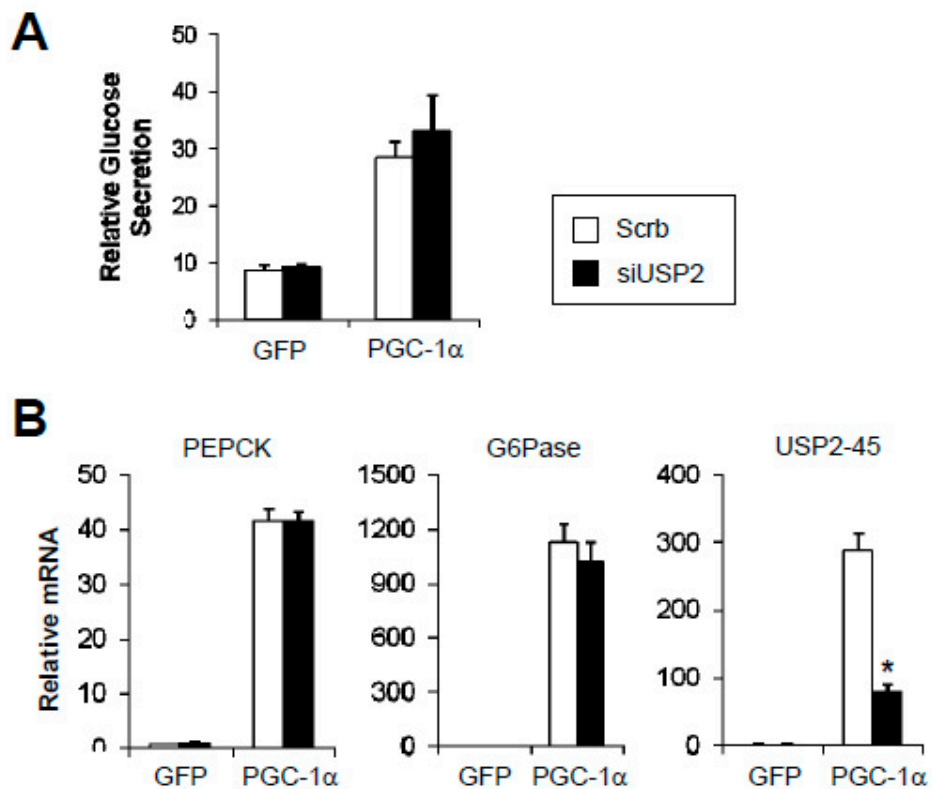


SUPPLEMENTARY DATA

**Supplementary Figure 1.** RNAi knockdown of USP2. Immunoblots of lysates from 293 cells transiently transfected with HA-USP2-45 in the presence of control or two shRNA constructs directed against USP2. The sequences of the shRNA targets are indicated.

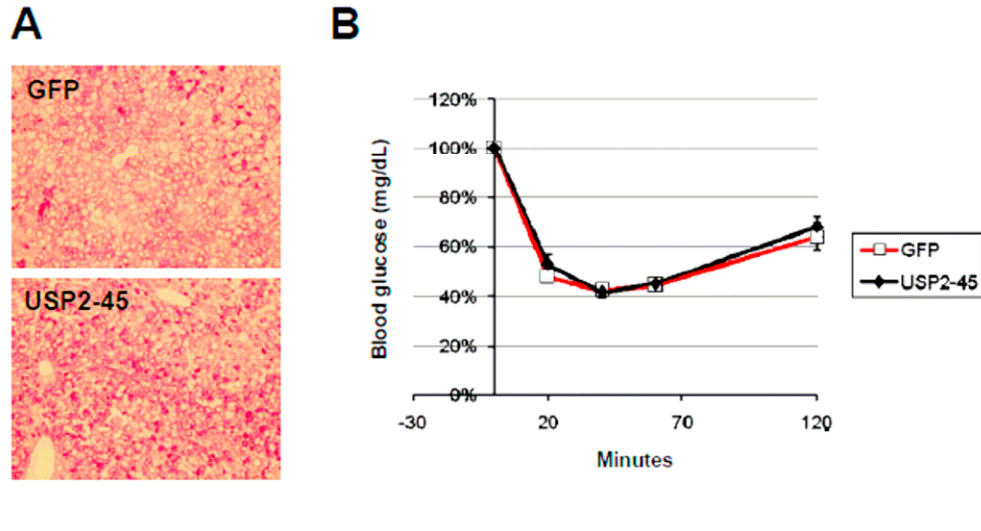


**Supplementary Figure 2.** Effects of USP2 RNAi knockdown on the induction of gluconeogenesis by PGC-1 $\alpha$ . *A*: Glucose secretion assay in hepatocytes transduced with GFP or PGC-1 $\alpha$  adenovirus in the presence of control (Scrb, open) or siUSP2 (filled) adenovirus for 48 hrs. Shown is relative glucose secretion rate in triplicate wells following normalization to respective protein content. *B*: Gene expression analysis in transduced hepatocytes. \*  $p < 0.01$  Scrb vs. siUSP2.

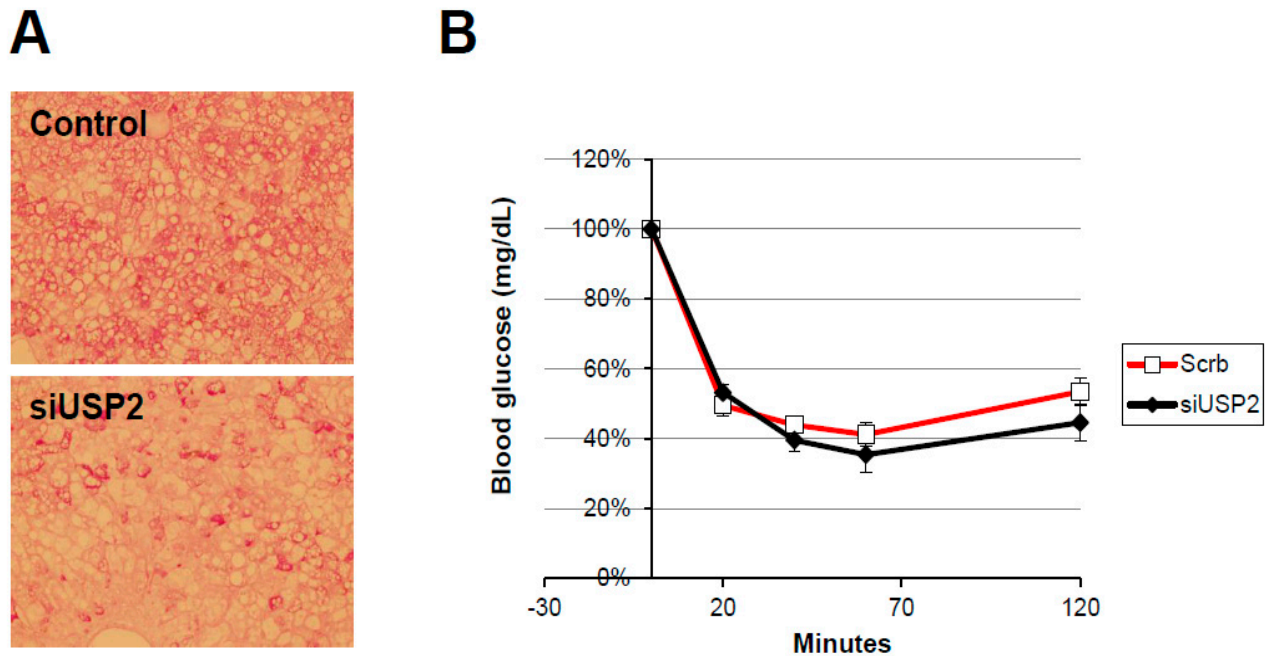


SUPPLEMENTARY DATA

**Supplementary Figure 3.** Hepatic USP2-45 overexpression in high-fat fed mice. *A*: PAS staining of liver sections from mice transduced with GFP or USP2-45 adenovirus. *B*: ITT in transduced mice. Graph represents normalized glucose levels as shown Fig. 4F.



**Supplementary Figure 4.** RNAi knockdown of USP2 in high-fat fed mice. *A*: PAS staining of liver sections from mice transduced with control or siUSP2 adenovirus. *B*: ITT in transduced mice. Graph represents normalized glucose levels as shown Fig. 6E.



SUPPLEMENTARY DATA

**Supplementary Figure 5.** List of qPCR primers.

<i>Gene</i>	<i>Fwd Sequence</i>	<i>Rev Sequence</i>
<b>TSC22D3</b>	5'- CCTCAACACTGACAAGCTGAAC	5'- CCTCAACACTGACAAGCTGAAC
<b>ANGPTL4</b>	5'- GACTCAGCTCAAGGCTCAAAAC	5'- TTCCCCTCGAAGTCTTGTCTAC
<b>DUSP1</b>	5'- GATCCTGTCCTTCCTGTACCTG	5'- GTGACCCTCAAAGTGGTTAGGA
<b>HSD1</b>	5'- GGAGGAAGGTCTCCAGAAGGT	5'- AGAGACAGCGAGGTCTGAGTG
<b>TNF<math>\alpha</math></b>	5'- AGCCCCCAGTCTGTATCCTT	5'- CTCCTTTGCAGAACTCAGG
<b>CCL2</b>	5'- AGGTCCCTGTCATGCTTCTG	5'- TCTGGACCCATTCTTCTTG
<b>IL6</b>	5'- AGTTGCCTTCTTGGGACTGA	5'- TCCACGATTTCCAGAGAAC
<b>USP2-45</b>	5'-GCTTCTGCTCAACAAAGCCA	5'- CTCAGATGGGCTCACCACATC
<b>USP2-69</b>	5'- AGCCAGGACTCATCCGCAGCT	5'-CTCAGATGGGCTCACCACATC