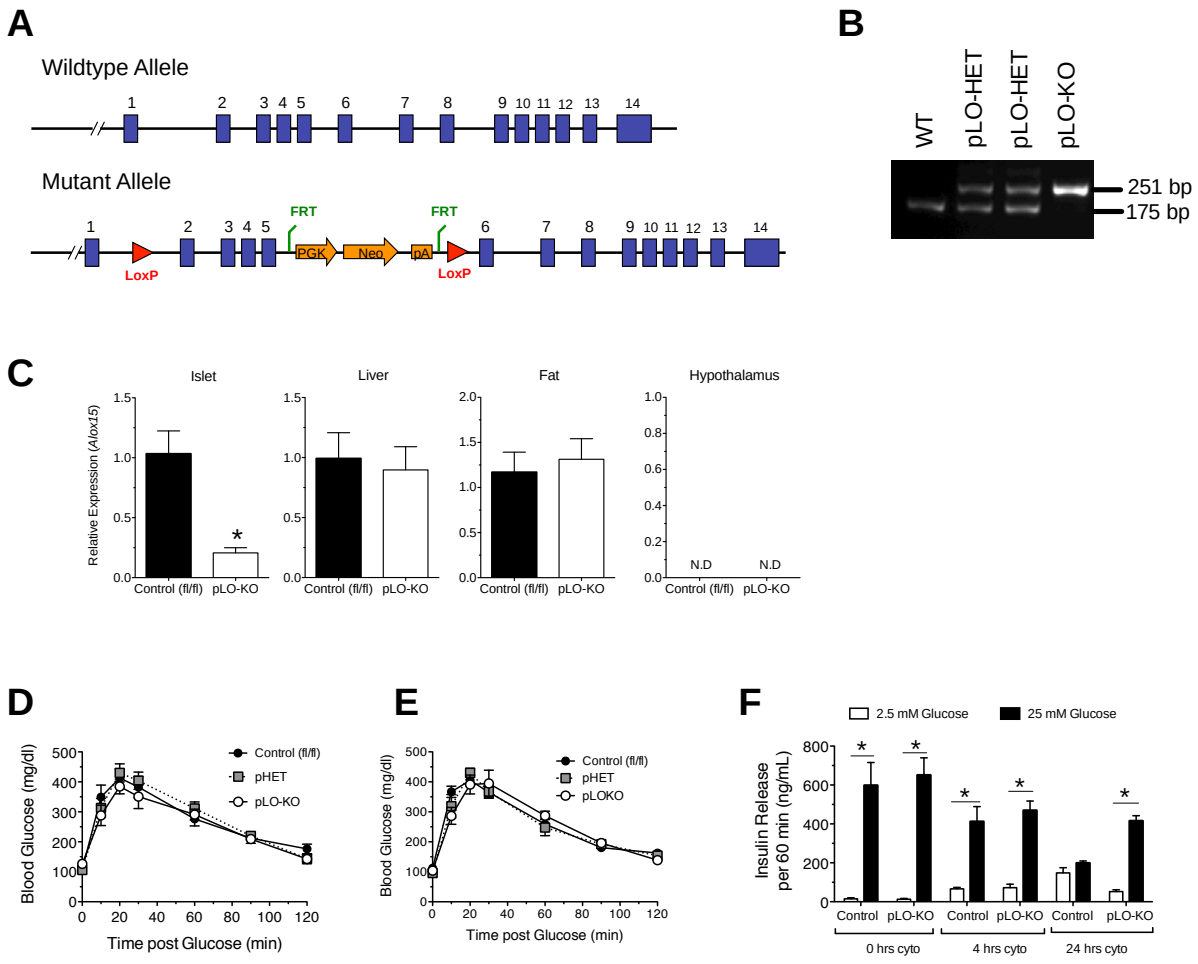
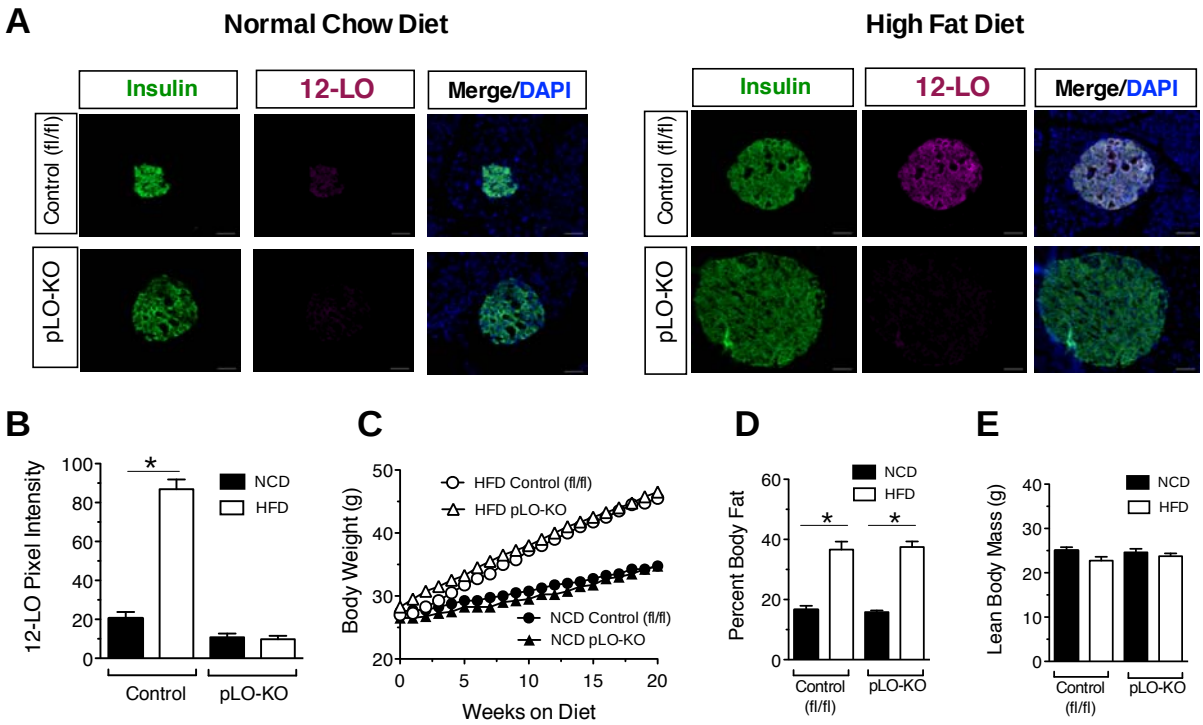
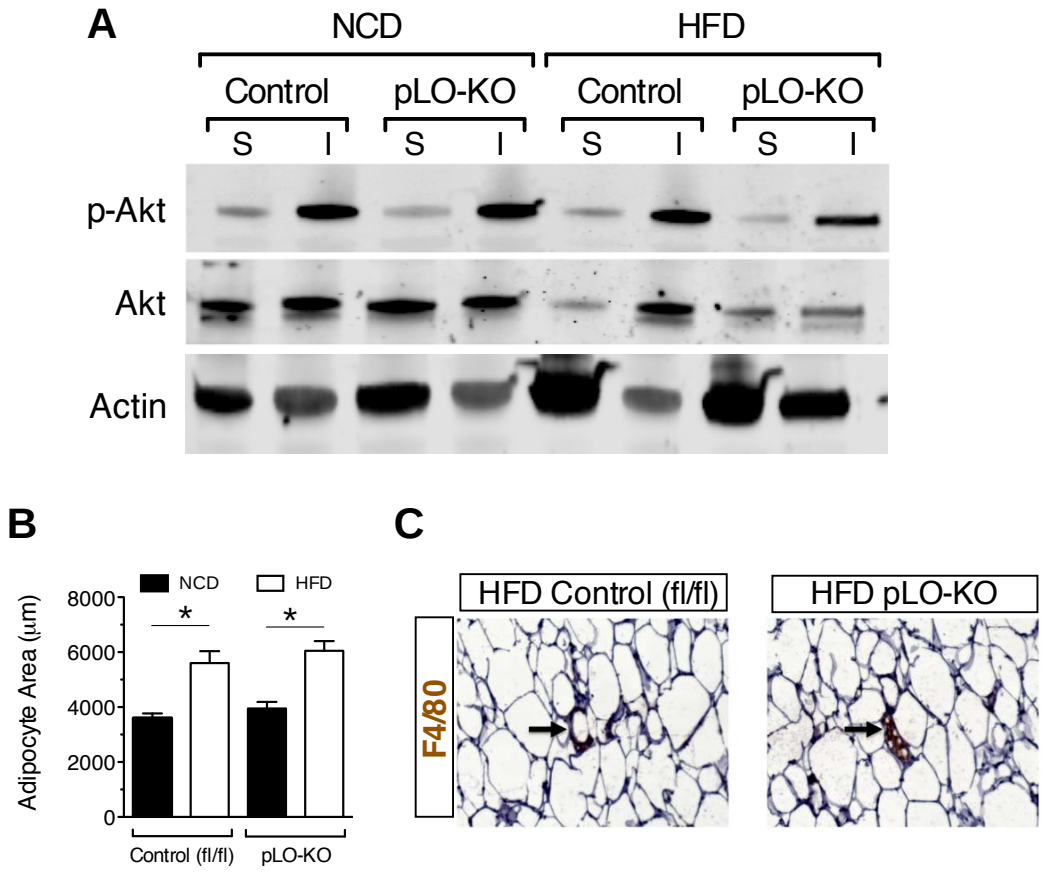


Supplemental Figure 1: Generation and verification of pLO-KO mice. *A*, schematic representations of the wild-type and mutant alleles corresponding to the mouse *Alox15* gene. Numbers and blue rectangles indicate positions of exons. *FRT*, Flp recombinase recognition sequences. *LoxP*, Cre recombinase recognition sequences; *B*, 2% agarose gel showing PCR amplification from genomic DNA of the mutant allele (251 base pair band) and wild-type allele (175 base pair band); *C*, RT-PCR results from RNA isolated from islets, fat, liver, and hypothalamus from control and pLO-KO mice (normalized to *Actb*). *D,* Results of intraperitoneal GTT performed at 12 weeks of age in male mice; *E,* results of intraperitoneal GTT performed at 12 weeks of age in female mice; *F,* insulin secretion at 2.5 mM glucose (2.5G) and 25 mM glucose (25G) from isolated islets from male mice after 0, 4, or 24 hours of cytokine treatment; Data in *panels C*, *D*, and *E* represent the average from 3 mice per genotype. In *panel F*, N=4 independent experiments.



Supplemental Figure 2: 12-LO staining, body fat distribution and adipocyte size after high fat diet feeding. At 8 weeks of age Control (*fl/fl)* and pLO-KO male mice were placed on a normal chow diet (NCD) or a 42% kcal from fat high fat diet (HFD) for 20 weeks (N=8 animals per group). *A*, Pancreas sections from control and pLO-KO mice fed a NCD or HFD for 20 weeks were immunostained for 12-LO (*red*), insulin (*green*), and DAPI (*blue*). Magnification *x200*; *B*, Quantitation of 12-LO staining shown in *panel A*. *C*, Weekly body weight measurements in NCD-fed and HFD-fed mice; *D*, Percent body fat after 20 weeks feeding, as determined by dual x-ray absorptiometry; *E*, lean body mass after 20 weeks feeding, as determined by dual x-ray absorptiometry; **P<0.05* for the comparisons indicated.



Supplemental Figure 3: Insulin sensitivity and adipocyte size and macrophage infiltration after high fat diet feeding. At 8 weeks of age Control (*fl/fl)*, and pLO-KO male mice were placed on a normal chow diet (NCD) or a 42% kcal from fat high fat diet (HFD) for 20 weeks (N=8 animals per group). *A*, Results of immunoblots for phosphorylated Akt, total Akt, and Actin in gastrocnemius muscle from mice 5 min post insulin injection; *B,* Epididymal adipocyte size following 20 weeks feeding; *C*, Representative images of epididymal fat immunostained for F4/80+ macrophages (*brown*) and counterstained using hematoxylin (*blue*). Magnification *x100*. **P<0.05* for the comparisons indicated.