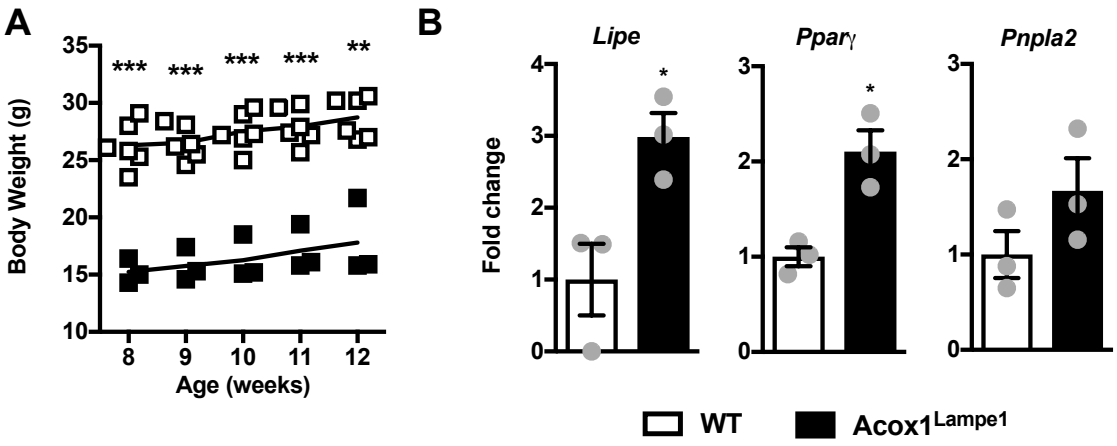
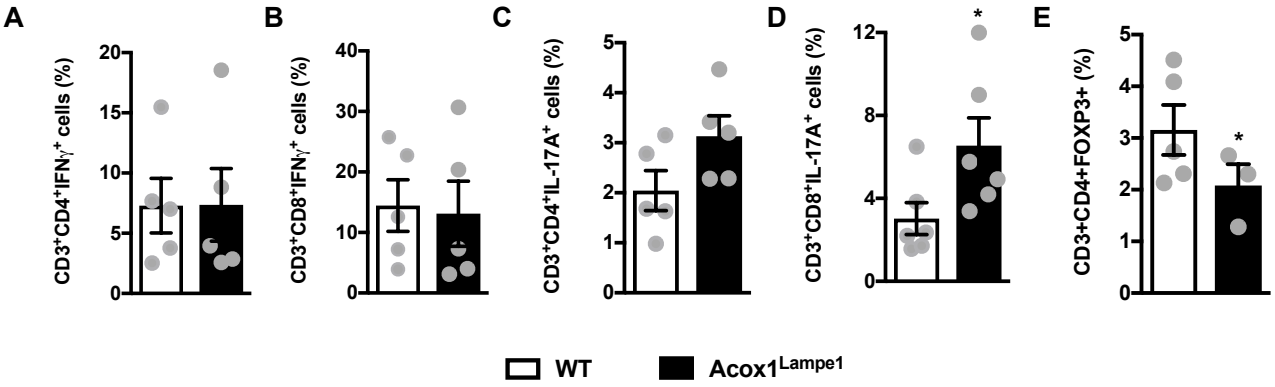
Supplemental Figure 1



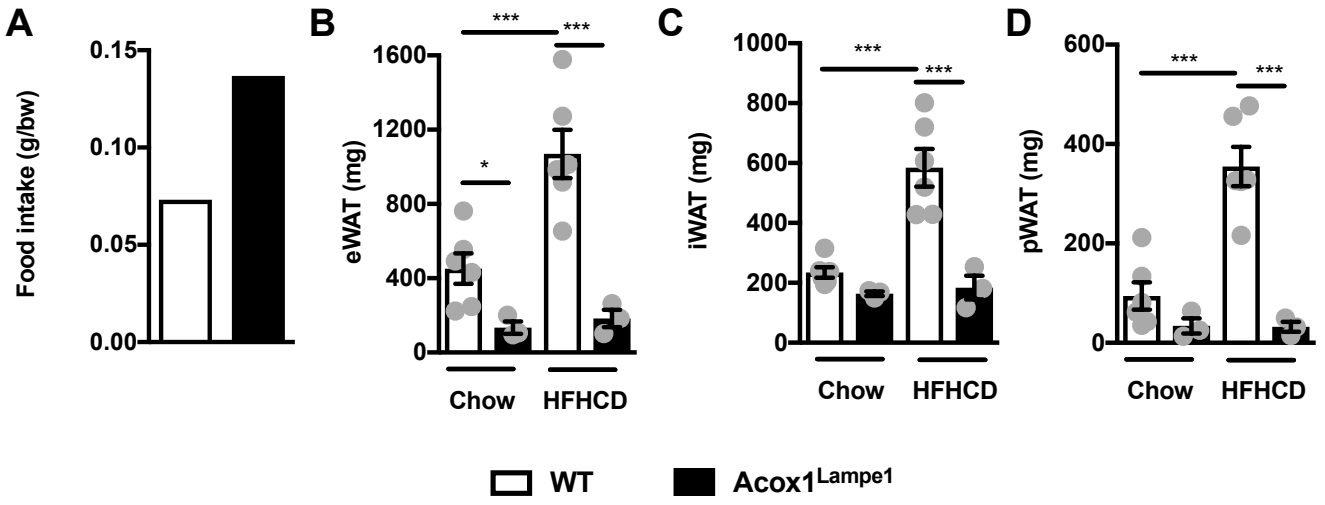
Supplemental Figure 1. Acox1^{Lampe1} mutation impacts weight gain and white adipose tissue (WAT) lipolysis. 8 week old Acox1^{Lampe1} mice and WT littermate controls were fed a chow diet for 4 weeks. (**A**) Body weight. (**B**) mRNA expression of lipolytic genes (*Lipe, Pparg* and *Pnpla2*) in epididymal WAT. Data represent means + SE. Unpaired student's t-test *P < 0.01, **P < 0.01, ***P < 0.001. (**A**) White squares denote WT mice; Black squares denote Acox1^{Lampe1} mice. (**B**) White bars denote WT mice; Black bars denote Acox1^{Lampe1} mice. (**A**) Representative of 3 individual experiments, n = 3-6/condition. (**B**) A single experiment, n = 3/condition. Data combined from two independent experiments.

Supplemental Figure 2



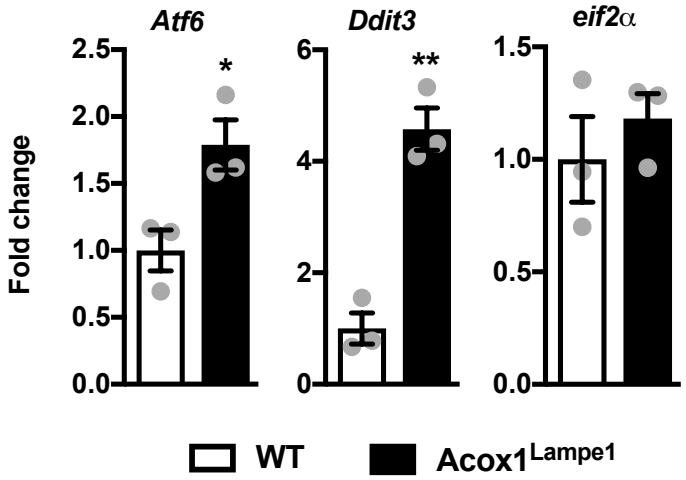
Supplemental Figure 2. Acox1^{Lampe1} mutation alters hepatic immune cell infiltration. 12 week old, chow diet fed, Acox1^{Lampe1} mice and WT littermate controls were examined for presence of hepatic CD4^{+} and CD8^{+} T cell populations. (**A and B**) Frequency of hepatic CD4^{+} and CD8^{+} T cells producing IFNG. (**C and D**) Frequency of hepatic CD4^{+} and CD8^{+} T cells producing IL-17A. (**E**) Frequency of hepatic T_{reg} cells (CD3^{+}CD4^{+}FOXP3^{+}). Data represent means + SE. Unpaired student's t-test *P < 0.05. White bars denote WT mice; Black bars denote Acox1^{Lampe1} mice. Data combined from two independent experiments, n = 6/condition.

Supplemental Figure 3



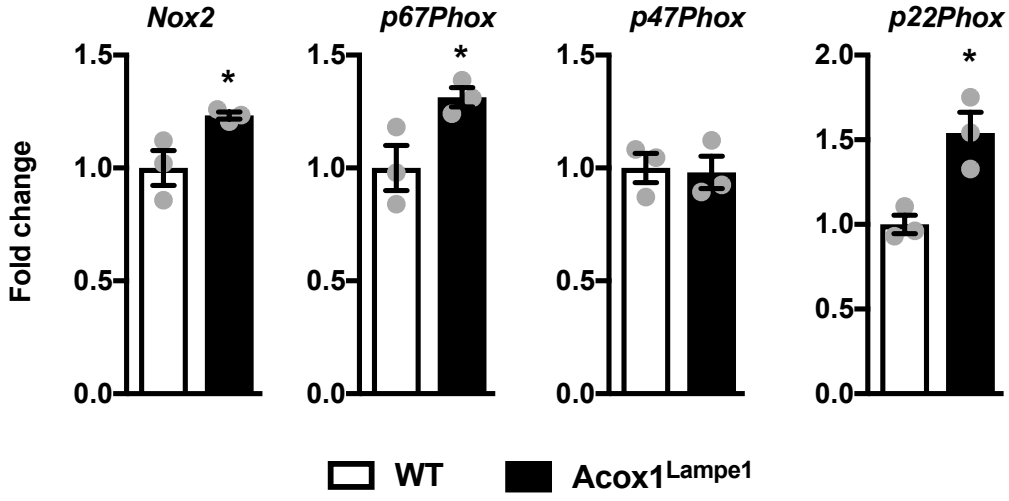
Supplemental Figure 3. Additional parameters from Acox1^{Lampe1} mice and WT littermate controls fed a chow or HFHCD. 8 week old Acox1^{Lampe1} mice and WT littermate controls were fed a HFHCD or chow diet for 4 weeks – continuation of findings depicted in Figure 4. (**A**) Food intake. (**B-D**) White adipose tissue weights: (**B**) epididymal (eWAT), (**C**) inguinal (iWAT) and (**D**) perirenal (pWAT). Data represent means + SE. (**B-D**) ANOVA followed by Tukey's correction *P < 0.01, **P < 0.01, ***P < 0.001. (**A-D**) White bars denote WT mice; Black bars denote Acox1^{Lampe1} mice. (**A**) Representative of 2 individual experiments, n = 3/condition. (**B-D**) Data combined from two independent experiments, n=3/condition.

Supplemental Figure 4



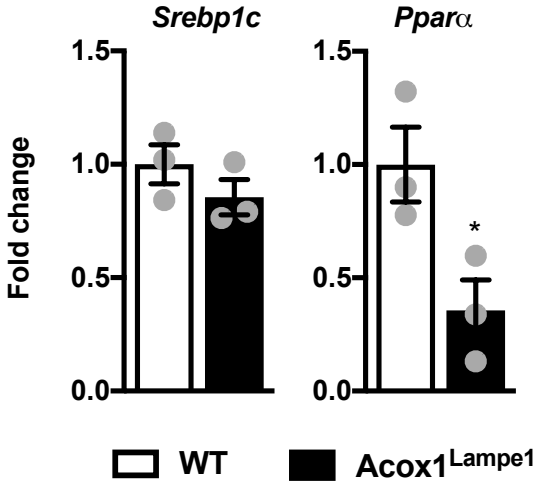
Supplemental Figure 4. Acox1^{Lampe1} mice exhibit increased hepatic mRNA expression of ER stress-associated genes following HFHCD feeding. 8 week old Acox1^{Lampe1} mice and WT littermate controls were fed a HFHCD for 4 weeks. Hepatic *Atf6, Ddit3* and eif2A mRNA expression. Data represent means + SE. Unpaired student's t-test *P < 0.05, **P < 0.01. White bars denote WT mice fed HFHCD; Black bars denote Acox1^{Lampe1} mice fed HFHCD. A single experiment, n = 3/condition.

Supplemental Figure 5



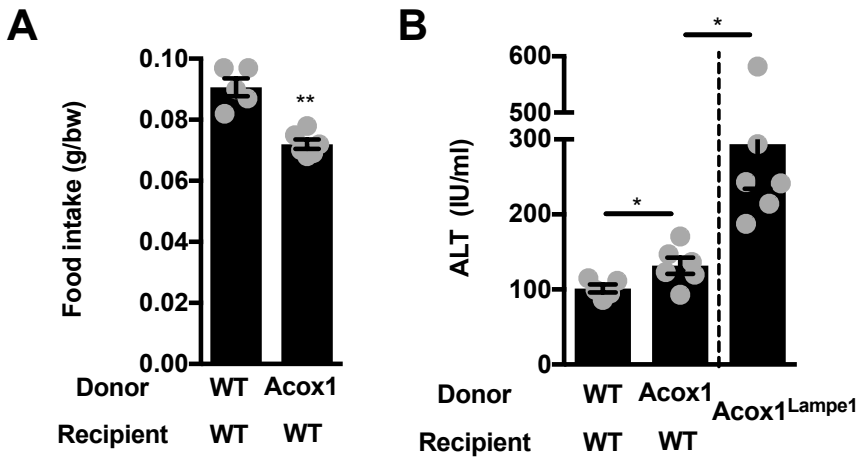
Supplemental Figure 5. Acox1^{Lampe1} mice exhibit increased hepatic mRNA expression of ROS-associated enzymes following HFHCD feeding. 8 week old Acox1^{Lampe1} mice and WT littermate controls were fed a HFHCD for 4 weeks. Hepatic *Nox2, p67Phox, p47Phox* and *p22Phox* mRNA expression. Data represent means + SE. Unpaired student's t-test *P < 0.05. White bars denote WT mice fed HFHCD; Black bars denote Acox1^{Lampe1} mice fed HFHCD. A single experiment, n = 3/condition

Supplemental Figure 6



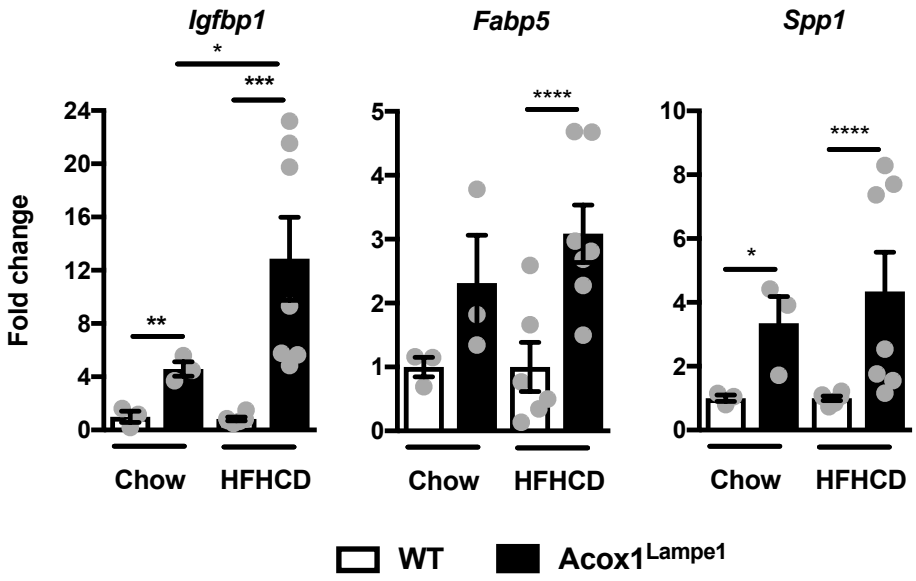
Supplemental Figure 6. Acox1^{Lampe1} mutation partially modulates expression of markers associated with fatty acid oxidation in context of HFHCD feeding. 8 week old Acox1^{Lampe1} mice and WT littermate controls were fed a HFHCD for 4 weeks. Hepatic *Srebp-1c* and *Ppara* mRNA expression. Data represent means + SE. Unpaired student's t-test *P < 0.05. White bars denote WT mice; Black bars denote Acox1^{Lampe1} mice. A single experiment, n = 3/condition.

Supplemental Figure 7



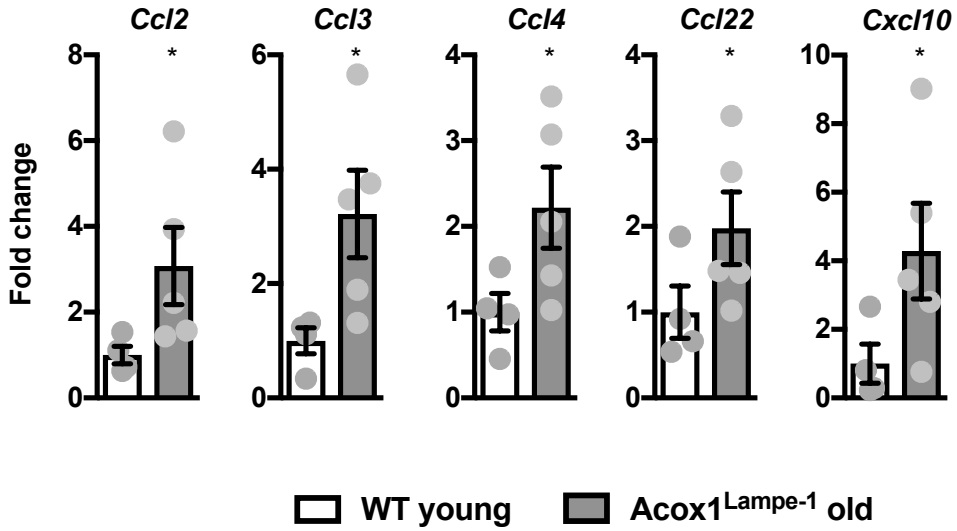
Supplemental Figure 7. Additional parameters from bone marrow transfer studies. 8-10 week old WT mice were lethally irradiated and subsequently reconstituted with bone marrow (BM) from WT or Acox1^{Lampe1} mice, as depicted in Figure 5. Following successful immunological reconstitution mice were fed a HFHCD for 4 weeks. (**A**) Food intake. (**B**) Comparison of serum ALT levels between bone marrow transplanted mice and Acox1^{Lampe1} mice (total body mutants; as depicted in Figure 4) fed a HFHCD for 4 weeks. Data represent means + SE. Unpaired student's t-test *P < 0.05, **P < 0.01. A single experiment, n = 5-6/condition.

Supplemental Figure 8



Supplemental Figure 8. Additional parameters from studies focused on hepatic gene expression in Acox1^{Lampe1} mice and WT littermate controls fed a chow or HFHCD. 8 week old Acox1^{Lampe1} mice and WT littermate controls were fed a HFHCD or chow diet for 4 weeks, as depicted in Figure 7. Hepatic *Igfbp1*, *Fabp5*, and *Spp1* mRNA expression. Data represent means + SE. ANOVA Tukey's correction **P < 0.01, ***P < 0.01. White bars denote WT mice; Black bars denote Acox1^{Lampe1} mice. Data combined from two independent experiments, n = 3-6/condition.

Supplemental Figure 9



Supplemental Figure 9. Acox1^{Lampe1} mutation spontaneously induces hepatic chemokines expression with age. 59 weeks old Acox1^{Lampe1} mice and 12 weeks old WT controls (n=3-4/condition) were fed chow diet. Hepatic *Ccl2, Ccl3, Ccl4, Ccl22, and Cxcl10* mRNA expression. Data represent means + SE. Unpaired student's t-test *P < 0.05. White bars denote young WT mice; Gray bars denote old Acox1^{Lampe1} mice. A single experiment, n = 3-5/condition.