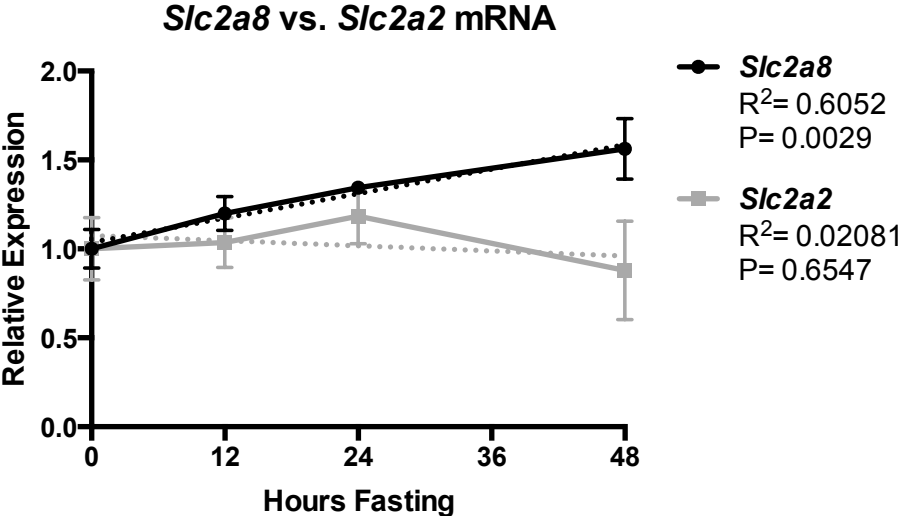


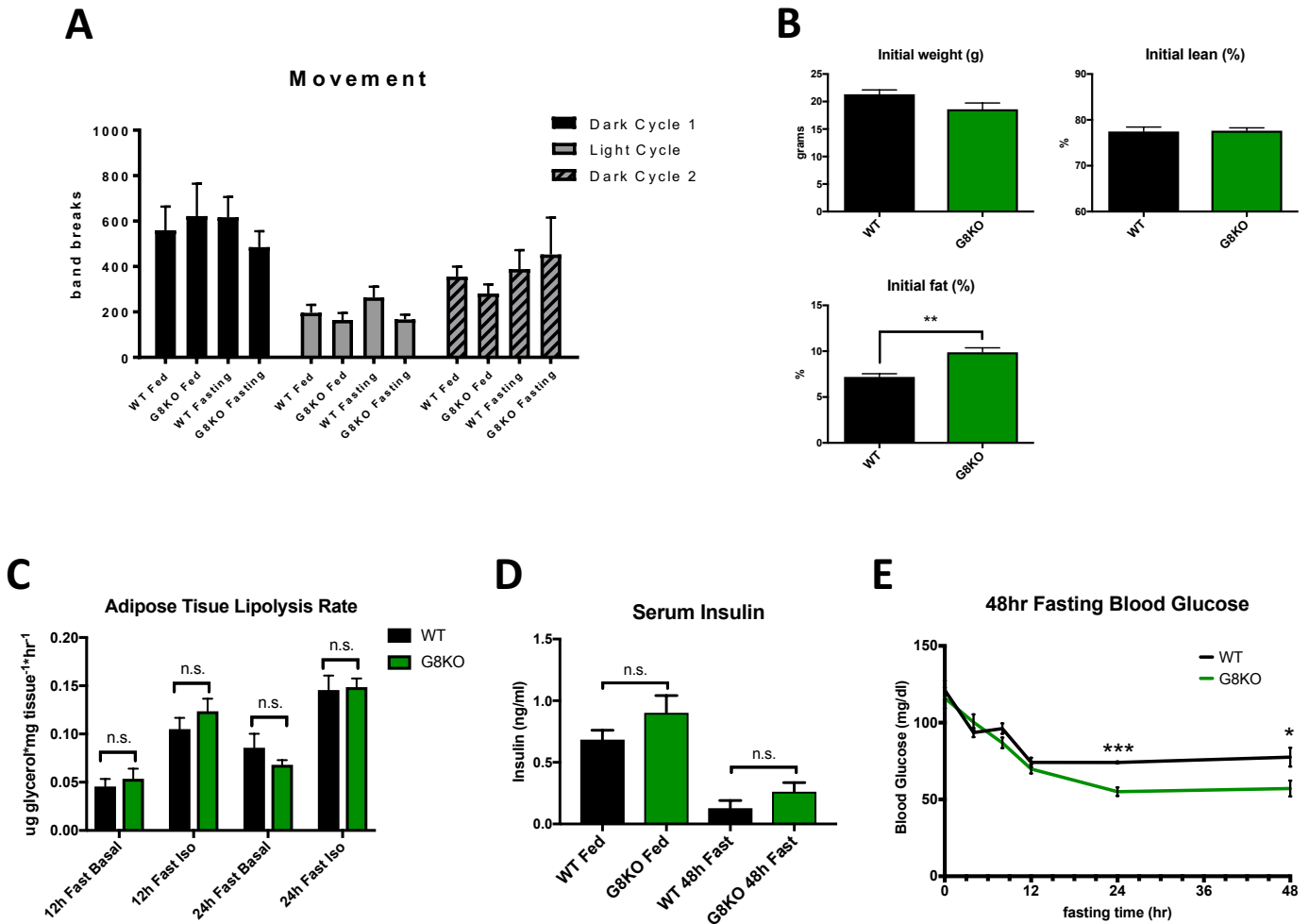
SUPPLEMENTARY MATERIALS

Supplemental Figure 1.



Supplemental Figure 1. Linear upregulation of hepatic GLUT8 mRNA during fasting. qRT-PCR analysis of hepatic *Slc2a8* (GLUT8) and *Slc2a2* (GLUT2) mRNA transcript levels in WT mice over the course of 48 hours of fasting. Linear regression calculated for each mRNA, with R² and p-value indicated. n = 3 mice/group. (Data are presented as mean ± SEM).

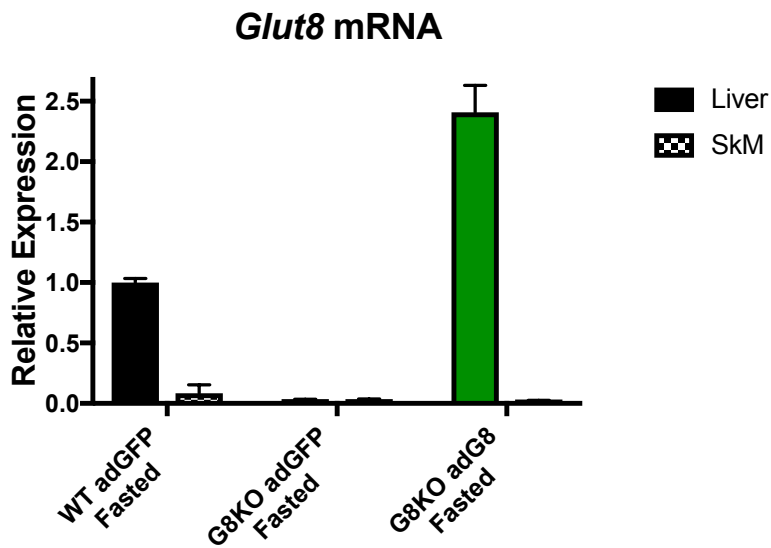
Supplemental Figure 2.



Supplemental Figure 2.

(A) Movement measurements in WT and G8KO mice over a 48 hour period of ad lib chow feeding or fasting. $n = 4$ (WT fed), 4 (G8KO fasted), 6 (WT fasted), 5 (G8KO fasted). (B) EchoMRI quantification of initial weight, initial percent lean mass, and initial percent body fat in WT and G8KO mice prior to fasting. $n = 6$ (WT), 5 (G8KO). (C) Lipolysis rate in white adipose explant tissue from 12 or 24 hour fasted WT or G8KO mice, as assessed by glycerol release in the presence or absence of isoproterenol (Iso). $n = 6$ (12h fast WT basal), 8 (12h fast G8KO basal), 10 (12h fast WT iso), 12 (12h fast G8KO iso), 6 (24h fast WT basal), 4 (24h fast G8KO basal), 8 (24h fast WT iso), 10 (24h fast G8KO iso). (D) ELISA quantification of serum insulin levels in WT and G8KO mice either chow-fed or fasted for 48h. $n = 7$ (WT fed), 8 (G8KO fed), 10 (WT fast), 9 (G8KO fast). (E) Blood glucose measurements taken over a 48 hour fasting time period in WT and G8KO mice. $n = 5$ (WT), 6 (G8KO). (Data are presented as mean \pm SEM; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

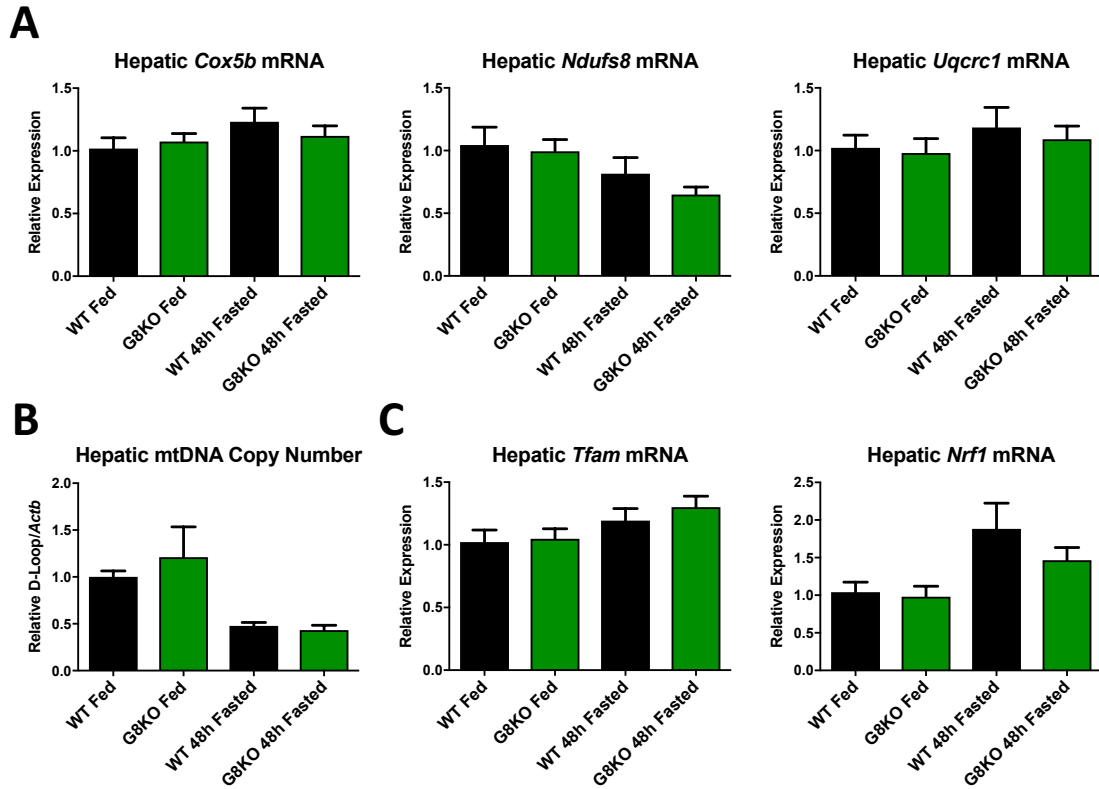
Supplemental Figure 3.



Supplemental Figure 3.

Quantification of *Glut8* mRNA transcript levels in liver and skeletal muscle tissue of WT or G8KO 48-hour fasted mice treated with adenoviral delivery of GFP (adGFP) or GLUT8 (ADG8). n= 2 (WT adGFP), 4 (G8KO adGFP), 4 (G8KO adG8) mice per group. (Data are presented as mean \pm SEM).

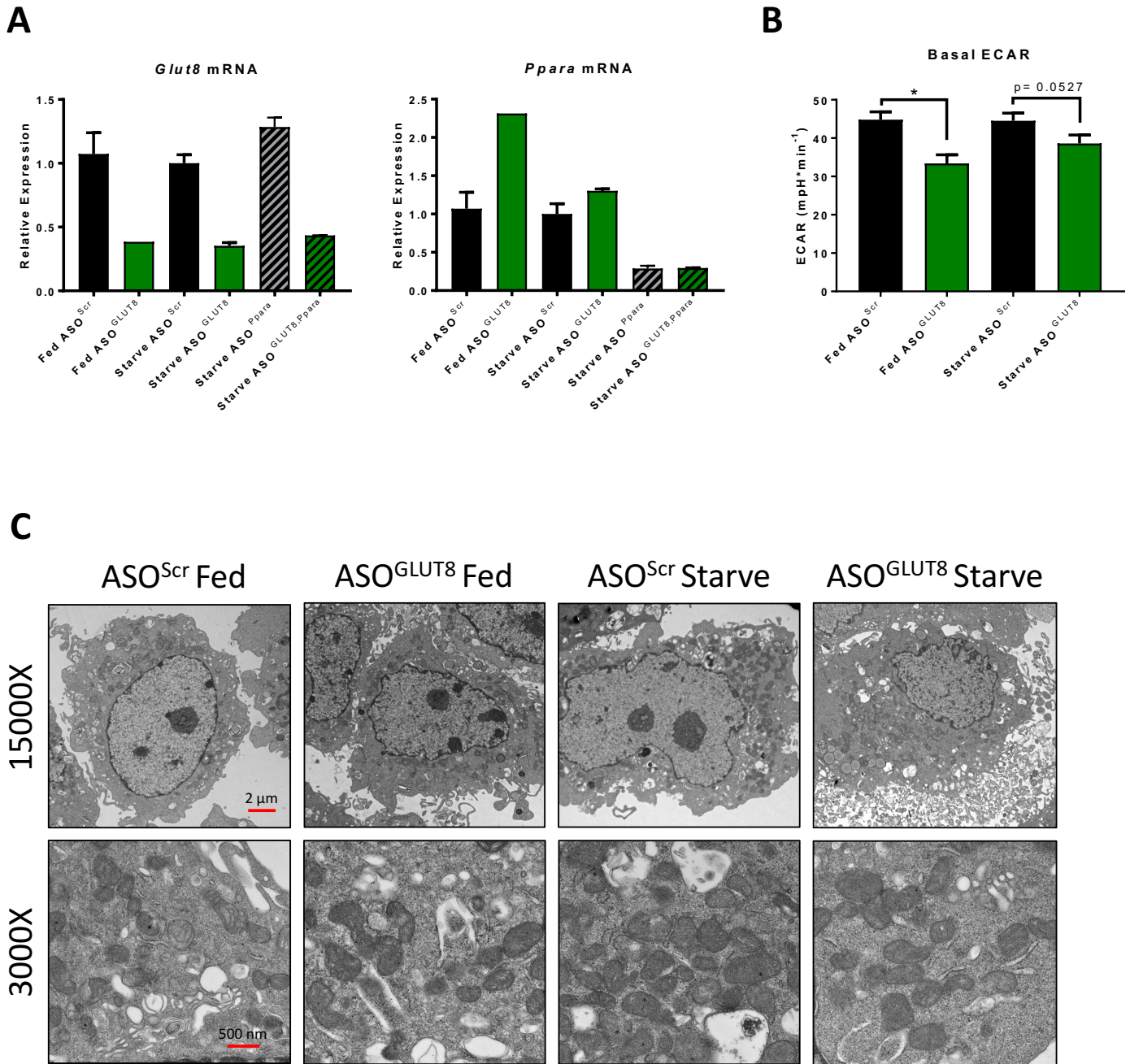
Supplemental Figure 4.



Supplemental Figure 4.

(A) qRT-PCR analysis of mRNA encoding electron transport chain proteins COX5b, NDUFS8, and Uqcrc1 in livers from fed and 48h fasted WT and G8KO mice. $n = 6$ mice/group. **(B)** qRT-PCR analysis of mtDNA copy number in liver from WT and G8KO fed or 48h fasted mice, quantified as the ratio of mitochondrial DNA (D-loop) to genomic DNA (ACTB). $n = 3-5$ mice/group. **(C)** qRT-PCR analysis of mRNA encoding mitochondrial biogenesis transcription factors TFAM and NRF-1 in livers from fed and 48h fasted WT and G8KO mice. $n = 6$ mice/group. (Data are presented as mean \pm SEM).

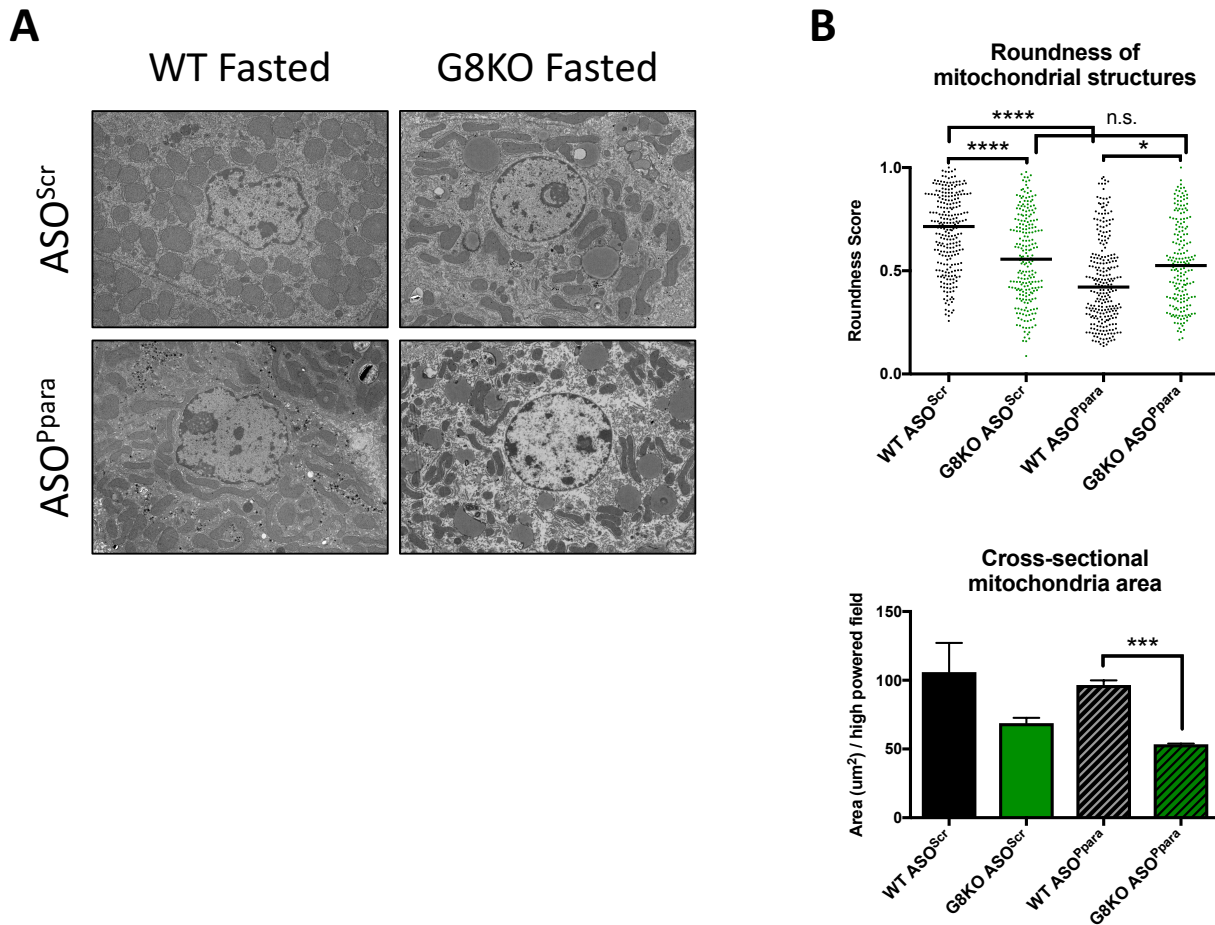
Supplemental Figure 5.



Supplemental Figure 5.

(A) Quantification of *Glut8* and *Ppara* mRNA transcript levels in fed or fasted AML12 hepatocytes treated ASO^{Scr}, ASO^{GLUT8}, or ASO^{Ppara} and cultured in fed or starve media for 24 hours. (B) Basal extracellular acidification rate of AML12 hepatocytes treated with ASO^{Scr} or ASO^{GLUT8} and cultured in fed or starve media. (C) Electron micrographs of cells as in B. (Data are presented as mean ± SEM).

Supplemental Figure 6.



Supplemental Figure 6. Mitochondrial morphology in livers with or without PPAR α knockdown.

(A) Electron micrographs of representative liver sections from WT or G8KO 48h hour fasted mice after treatment with control (ASO^{Scr}) or PPAR α -targeted (ASO^{Ppara}) ASOs. **(B)** Quantification of mitochondrial cross-sectional area and roundness score of mitochondrial structures. n = 2-3 mice/group. Quantifications from 3 representative images per group. Komogorov-Smirnov test was used to analyze distribution of roundness scores. (Data are presented as mean \pm SEM; *p<0.05, ***p<0.001, ****p<0.0001).