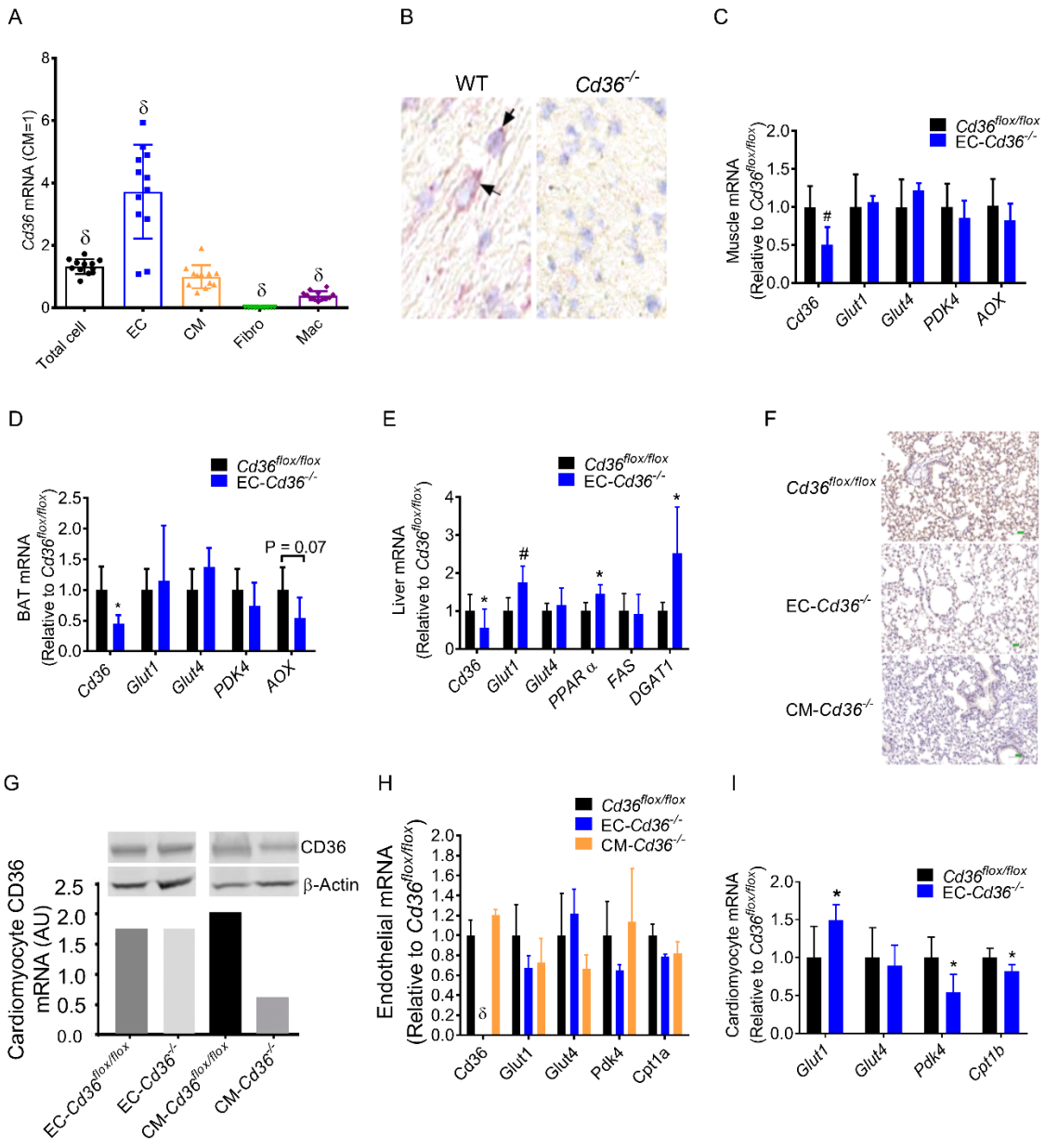


Fig. S1. **Immunostaining and mRNA expression in heart tissue and isolated ECs and CMs from *Cd36*$^{flox/flox}$, EC- *Cd36*$^{-/-}$, and CM-*Cd36*$^{-/-}$ mice. (A)** Sub-organ CD36 mRNA levels in isolated fractionation of female mouse hearts. Data are mean ratios normalized to CM-*Cd36*$^{-/-}$ (set as 1.0). $^{\delta}P < 0.0001$ versus CM-*Cd36*$^{-/-}$ mice. **(B)** In situ identified specific CD36 mRNA in heart tissues (arrow). **(C-E)** mRNA expression in muscle, BAT, and liver of *Cd36*$^{flox/flox}$ and EC- *Cd36*$^{-/-}$ mice. **(F)** Anti-CD36 antibody stained sections from *Cd36*$^{flox/flox}$, EC-*Cd36*$^{-/-}$, and CM-*Cd36*$^{-/-}$ mouse lungs. **(G)** CM *Cd36* mRNA and protein expressions in *Cd36*$^{flox/flox}$, EC- *Cd36*$^{-/-}$, and CM-*Cd36*$^{-/-}$ mouse hearts. **(H)** qRT-PCR analysis of gene expression in ECs from *Cd36*$^{flox/flox}$ and EC-*Cd36*$^{-/-}$ mice and **(I)** CMs from EC-*Cd36*$^{-/-}$ mouse hearts.*P < 0.05 and $^{\delta}P < 0.0001$ versus *Cd36*$^{flox/flox}$ mice. P values were calculated by one-way ANOVA with a Dunnett's multiple comparisons test.

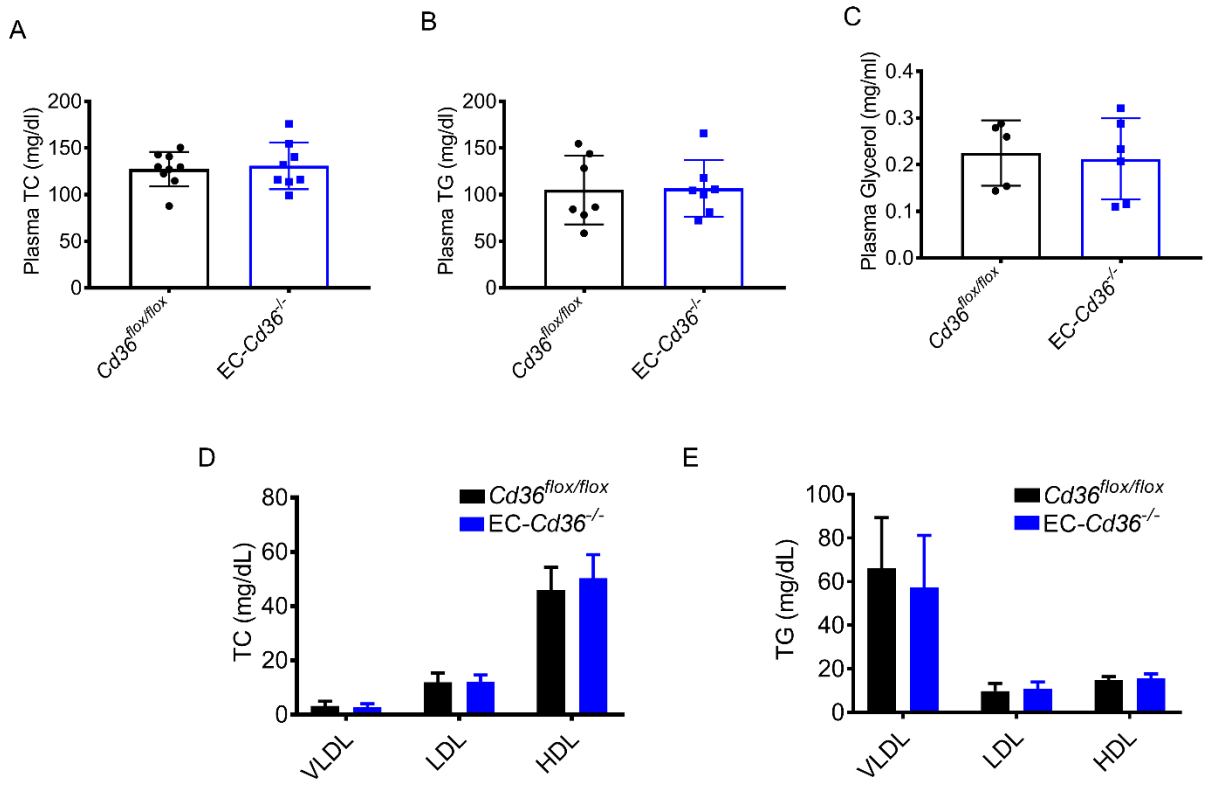


Fig. S2. Plasma lipids, glycerol, and lipoprotein particles in 4-month-old EC-*Cd36*$^{-/-}$ male mice fed chow diet. (A) Plasma TC and **(B)** TG levels in *Cd36*$^{flox/flox}$ and EC- *Cd36*$^{-/-}$, and CM-*Cd36*$^{-/-}$ male mice. **(C)** Plasma glycerol in EC- *Cd36*$^{-/-}$ mice. (**D)** TC and **(E)** TG levels of plasma lipoprotein particles. Data are means ± S.D. (n=5-8). P values were calculated by one-way ANOVA with a Dunnett's multiple comparisons test.

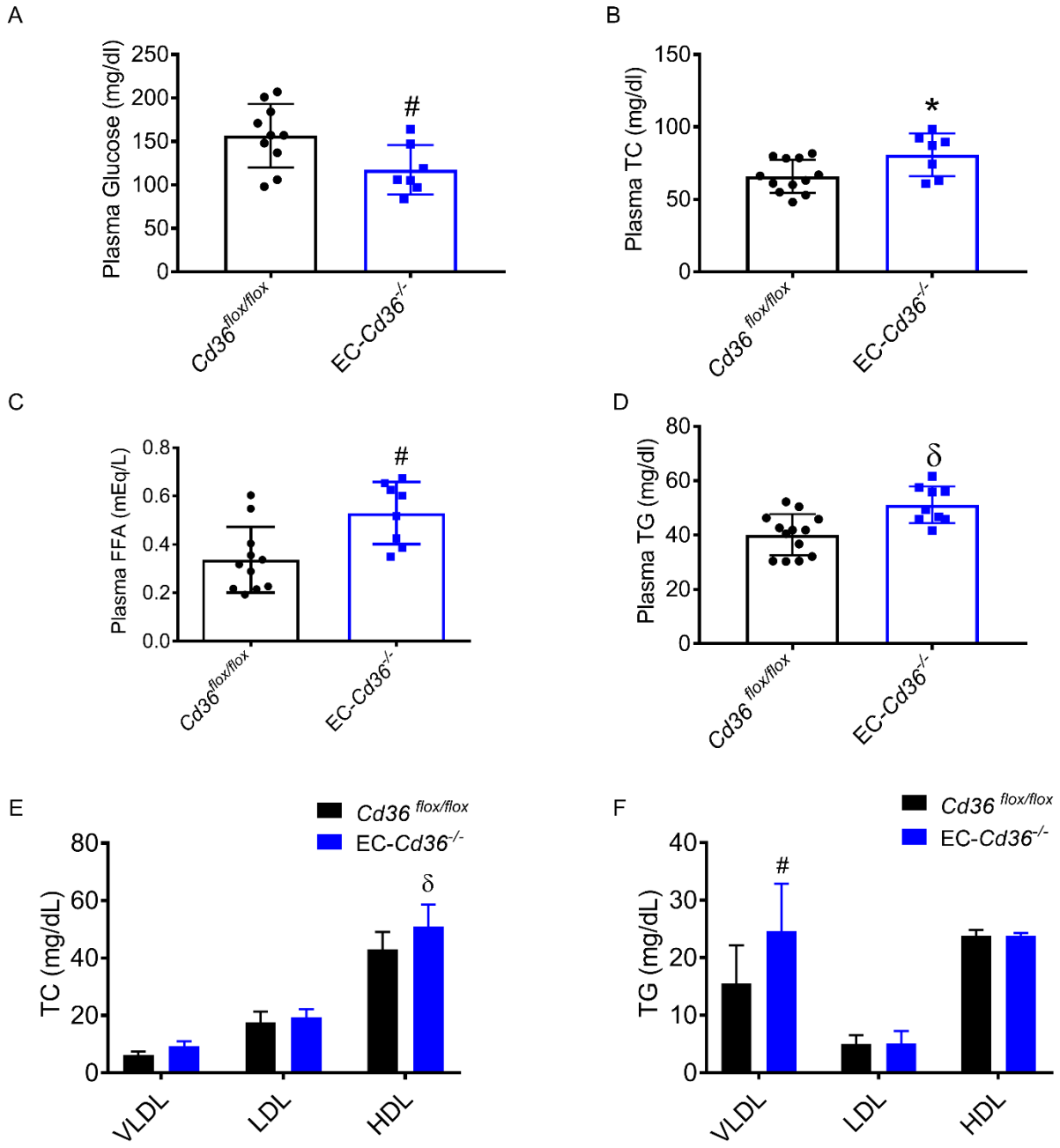


Fig. S3. Increase of plasma glucose, lipids, and lipoprotein particles in 4-month-old EC-*Cd36*$^{-/-}$ female mice fed chow diet. (A) Plasma glucose **(B)** TC, (**C)** FFA, and **(D)** TG. **(E)** TC and **(F)** TG levels of plasma lipoprotein particles. Data are means ± S.D (n=8-10). $^{\#}P < 0.01$ and $^{\S}P < 0.001$ compared to *Cd36*$^{flox/flox}$ mice. P values were calculated by one-way ANOVA with a Dunnett's multiple comparisons test.

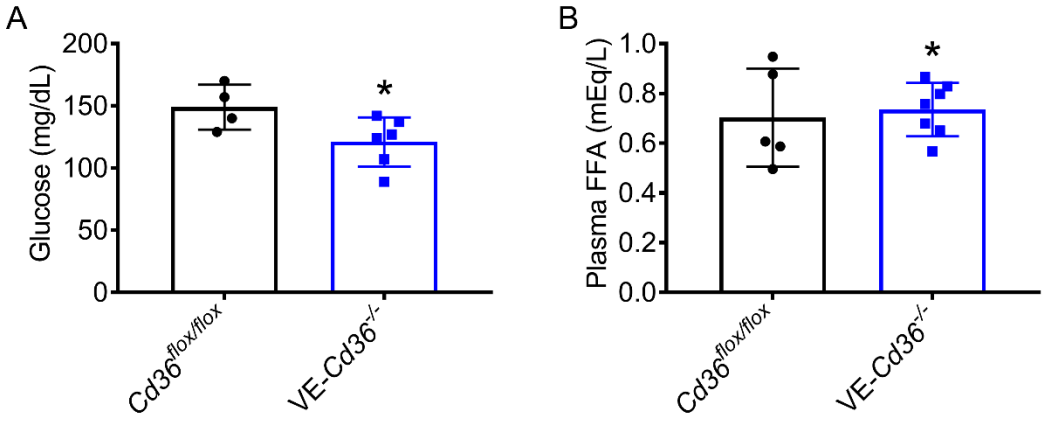


Fig. S4. Decrease of plasma glucose and increase of plasma TC in VE-*Cd36*$^{-/-}$ male mice. **(A)** Plasma glucose and (**B)** FFA in VE-*Cd36*$^{-/-}$ male mice. Data are means ± S.D. (n=4-7). *P < 0.05 compared to *Cd36*$^{flox/flox}$ mice. P values were calculated by one-way ANOVA with a Dunnett's multiple comparisons test.

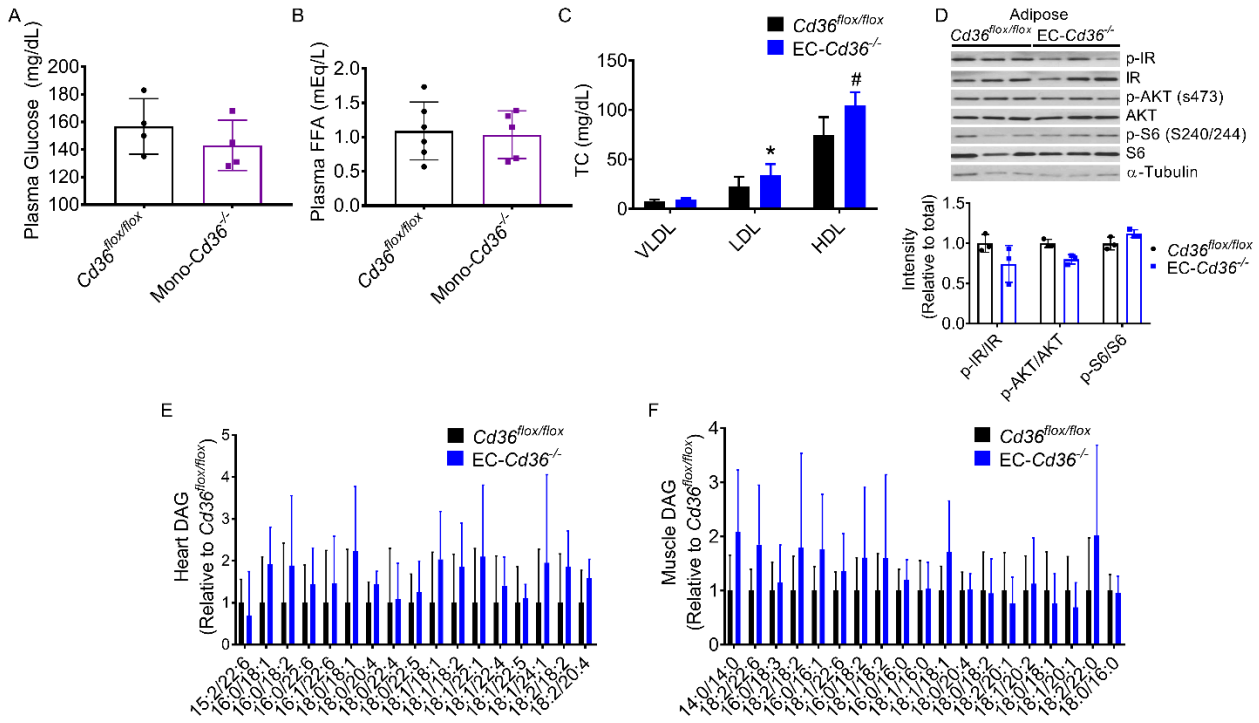


Fig. S5. Plasma and tissue lipids (A) Plasma glucose (n=4) and **(B)** FFA (n=5-6) in Mono-*Cd36*$^{-/-}$ mice (mRNA decreased 70% compared to *Cd36*$^{flox/flox}$ controls) fed chow diet. **(C)** Plasma lipoprotein TC levels in EC-*Cd36*$^{-/-}$ mice fed 3-week HFD. **(D)** Western blots (top) and quantification of p-IR, pAKT, and pS6 protein levels (normalized to total IR, Akt, or S6 signal, bottom) from WAT of HFD-fed *Cd36*$^{flox/flox}$ and EC- *Cd36*$^{-/-}$ mice. **(E)** Individual DAG species in the heart (n=4-5) and **(F)** muscle (n=9-10) of HFD-fed mice. Data are means ± S.D. $^{*}P < 0.05$ and $^{\#}P < 0.01$ compared to *Cd36*$^{flox/flox}$ mice. P values were calculated by one-way ANOVA with a Dunnett's multiple comparisons test.

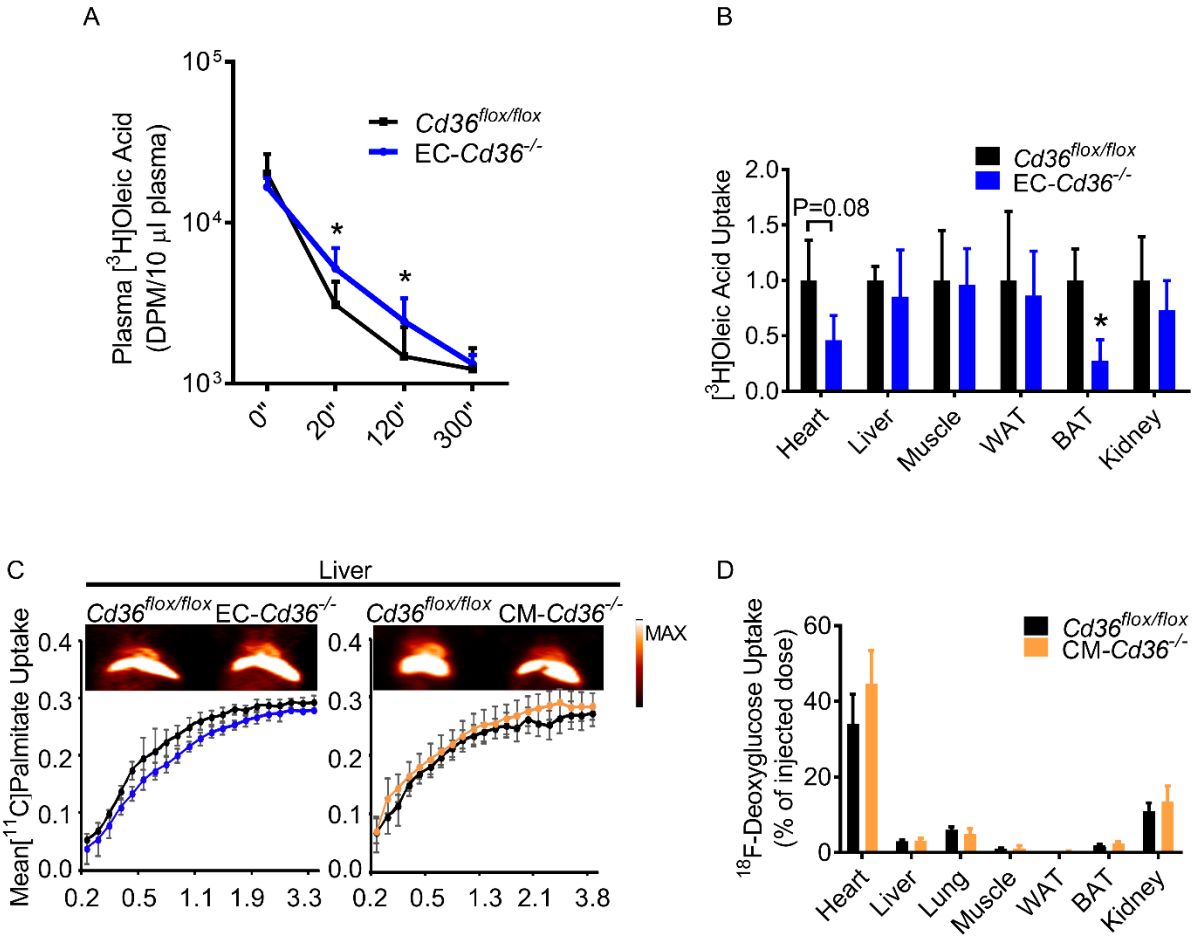


Fig S6. LCFA and [^{18}F]DG uptake in EC-*Cd36*$^{-/-}$ and CM-*Cd36*$^{-/-}$ mice.(A) 4-5 month old female *Cd36*$^{flox/flox}$ and EC-*Cd36*$^{-/-}$ mice (n=5-6) were fasted for 16 hours; plasma radioactivity **(B)** their tissue [^{3}H]oleic acid uptake (n=5-6) were measured at shown time points after intravenous injection of [^{3}H]oleic acid and. **(C)** Real time [^{11}C]palmitic acid uptake into liver of *Cd36*$^{flox/flox}$, EC–*Cd36*$^{-/-}$, and CM-*Cd36*$^{-/-}$ mice. Insert shows representative scans of [^{11}C]palmitate uptake at 2 min after tracer administration. **(D)[**^{18}F]DG uptake in 4-6 month old CM-*Cd36*$^{-/-}$ male mice. Data are means ± S.D. *P < 0.05 compared to *Cd36*$^{flox/flox}$ controls. P values were calculated by one-way ANOVA with a Dunnett's multiple comparisons test.

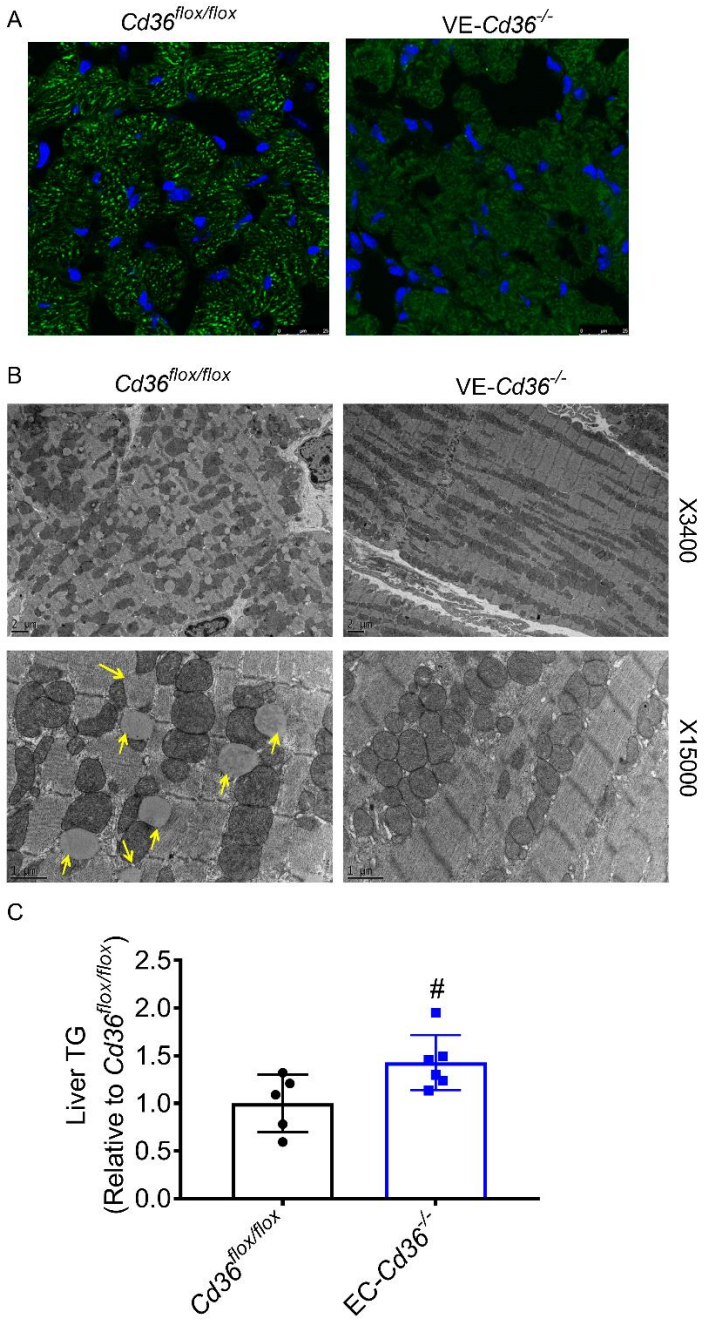
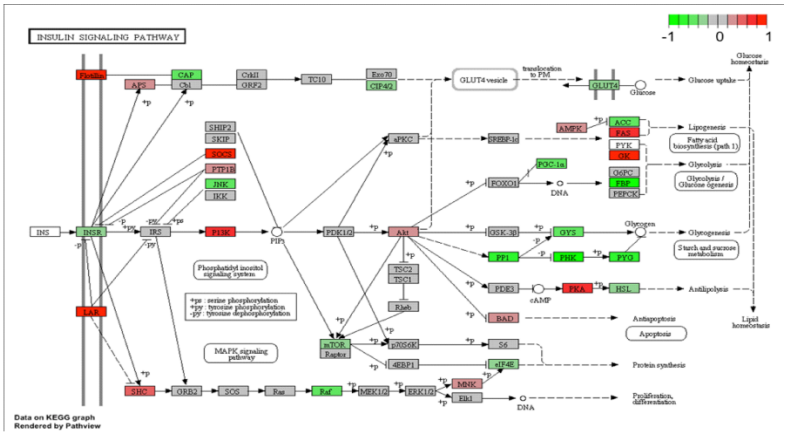
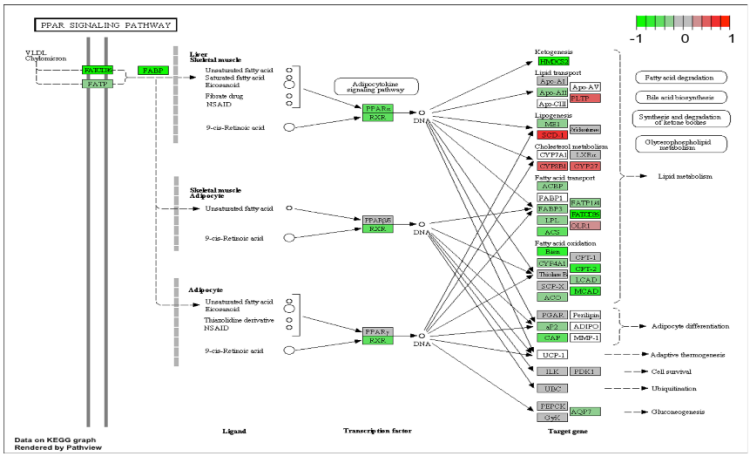


Fig S7. Reduced heart lipid droplet accumulation in VE-*Cd36*$^{-/-}$ mice. (A) BODIPY (493/503) staining of intramuscular lipid droplets in *Cd36*$^{flox/flox}$ and VE–*Cd36*$^{-/-}$ hearts. (B) EM images of *Cd36*$^{flox/flox}$ and VE–*Cd36*$^{-/-}$heart tissues. **(C)** Liver TG content in EC- *Cd36*$^{-/-}$ mice (n=5-6). Data are means ± S.D. $^{\#}P < 0.01$ compared to *Cd36*$^{flox/flox}$ mice. P values were calculated by one-way ANOVA with a Dunnett's multiple comparisons test.

A



B



C

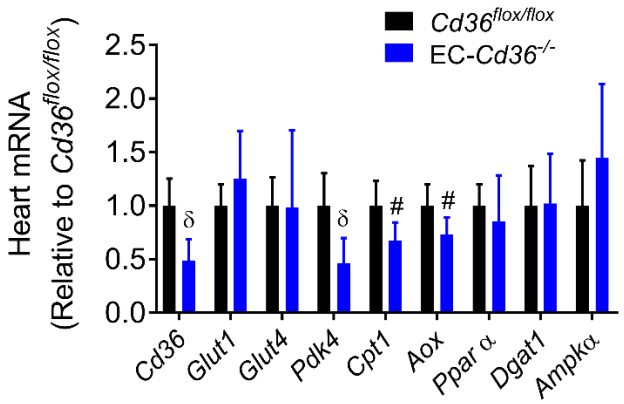


Fig S8. CM-*Cd36*$^{-/-}$ KEGG analysis and female mouse heart mRNA expression. (A) KEGG analysis of insulin signaling and **(B)** PPAR pathways in CM-*Cd36*$^{-/-}$ mouse hearts. **(C)** qRT-PCR analysis of mRNA expression in 4-5 month old female *Cd36*$^{flox/flox}$ and EC-*Cd36*$^{-/-}$ mice with 16 hours fasting (n=7-9). Data are means ± S.D. $^{\#}P < 0.01$ and $^{\delta}P < 0.001$compared to *CD36*$^{flox/flox}$ controls. P values were calculated by one-way ANOVA with a Dunnett's multiple comparisons test.

	Primer sequences	Amplification size (base pair)
Primer 1	Sense: 5'-attggcatctgtgtagcgctcttggc -3' Antisense: 5'-tgctactatgcactccatgcaggc -3'	WT: 289 bp Cd36 floxed allele: 372 bp
Primer 2	Sense: 5'-attggcatctgtgtagcgctcttggc -3' Antisense: 5'-tcaggaccatagcaagtaggc -3'	WT: 2116 bp Cd36 null allele: 420 bp
Primer 3	Sense: 5'-aacactgtgattgtacctg-3' Antisense: 5'-tcaataagcatgtctccgac -3'	WT: 160 bp Cd36 null allele: undetectable

Supplementary Table 1. Primers used for PCR amplification to detect DNA and mRNA from wild type, *Cd36*$^{flox/flox}$, and *Cd36*$^{-/-}$ mice.