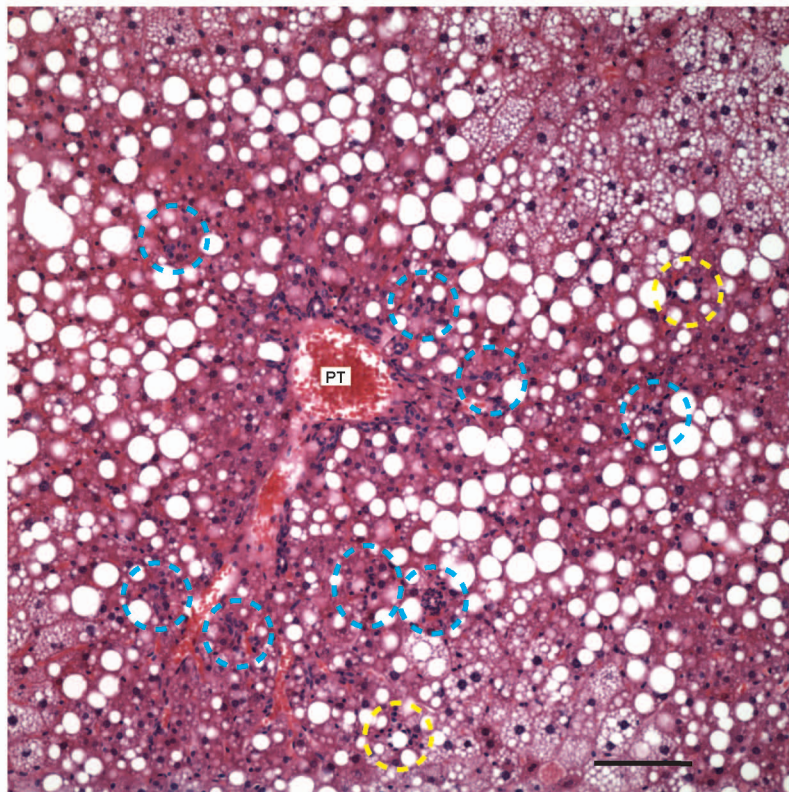


Supplementary Figure 1



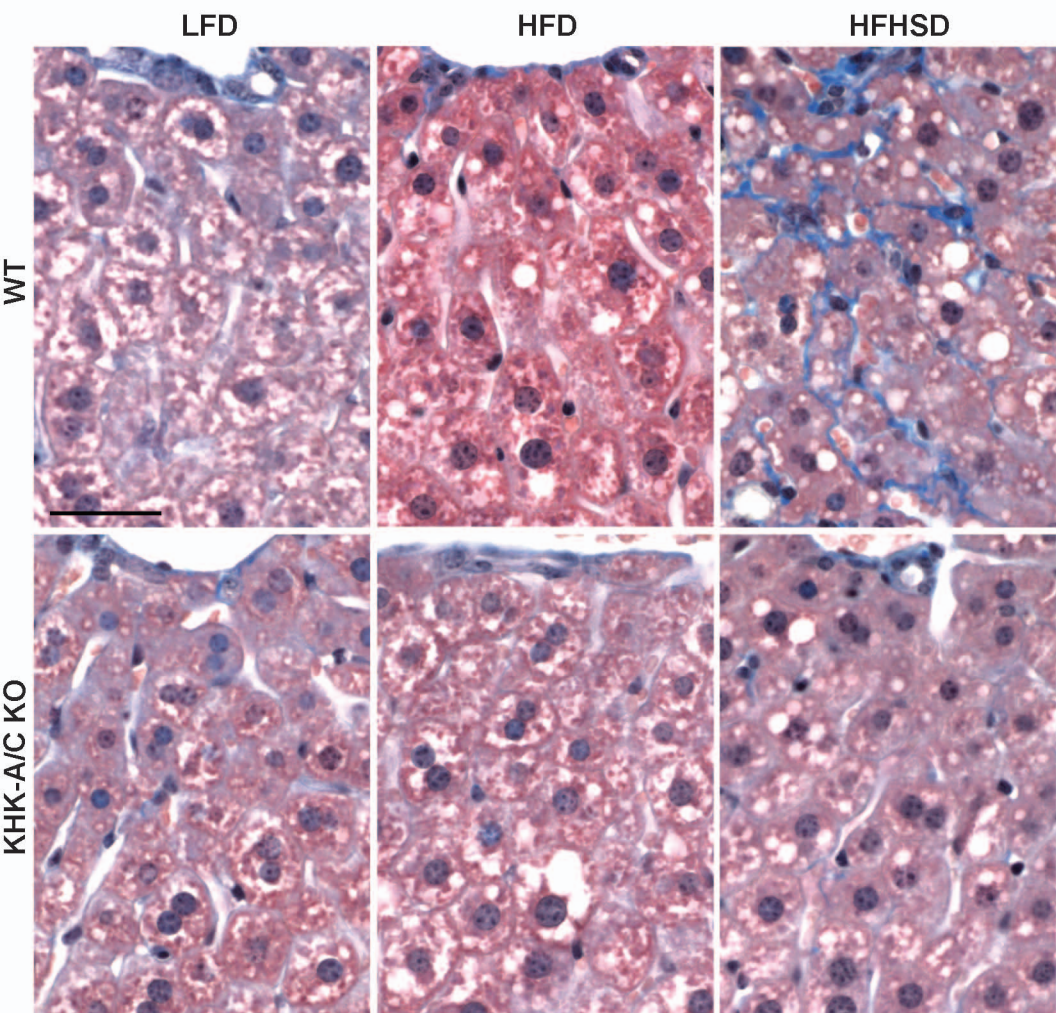
Supplementary Figure 1

(a) A image of H&E staining of the liver from WT fed HFHSD.

Blue circles indicates microgranulomas, and yellow circles indicates small lipogranulomas.

PT, portal triad. CV, central vein. Bar 50 μ m.

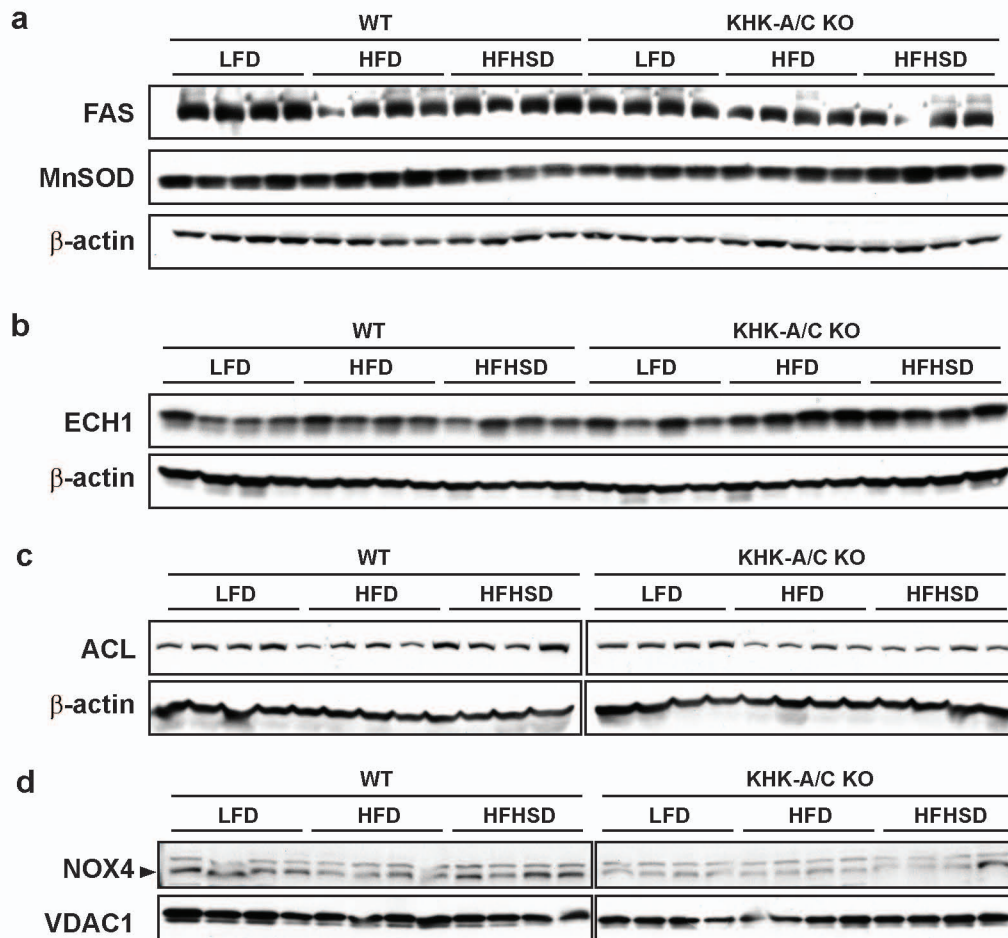
Supplementary Figure 2



Supplementary Figure 2

High-magnification images of trichrome staining of the liver from WT mice and KHK-A/C KO mice given *ad libitum* LFD, HFD or HFHSD for 15 weeks. Large collagen bundles were found in the sinusoids of liver of WT mice fed HFHSD. Bar 50 μm .

Supplementary Figure 3

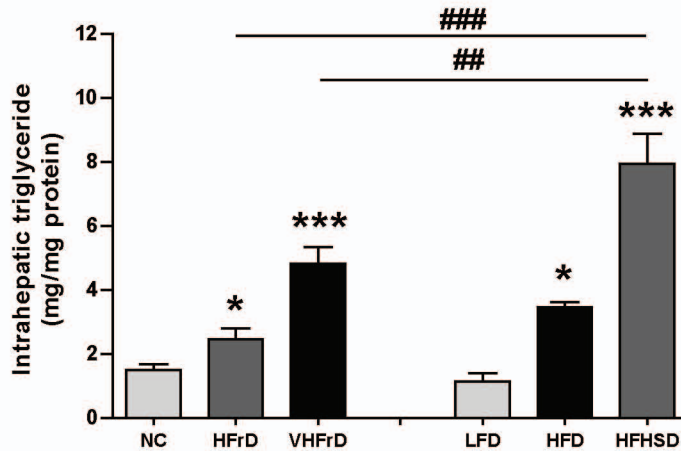


Supplementary Figure 3

WT mice and KHK-A/C KO mice were given *ad libitum* LFD, HFD or HFHSD for 15 weeks.

(a) Images of western blot analysis for fatty acid synthase (FAS), manganese superoxide dismutase (MnSOD) and β -actin in liver from WT mice and KHK-A/C KO mice ($n = 4$). (b) Images of western blot analysis for enoyl CoA-hydratase (ECH1) and β -actin in liver from WT mice and KHK-A/C KO mice ($n = 4$). (c) Images of western blot analysis for ATP citrate lyase (ACL) and β -actin in liver from WT mice and KHK-A/C KO mice ($n = 4$). (d) Images of western blot analysis for mitochondrial NADPH oxidase 4 (NOX4) in liver from WT mice and KHK-A/C KO mice ($n = 4$). Voltage-dependent anion channel 1 (VDAC1) was used as loading control.

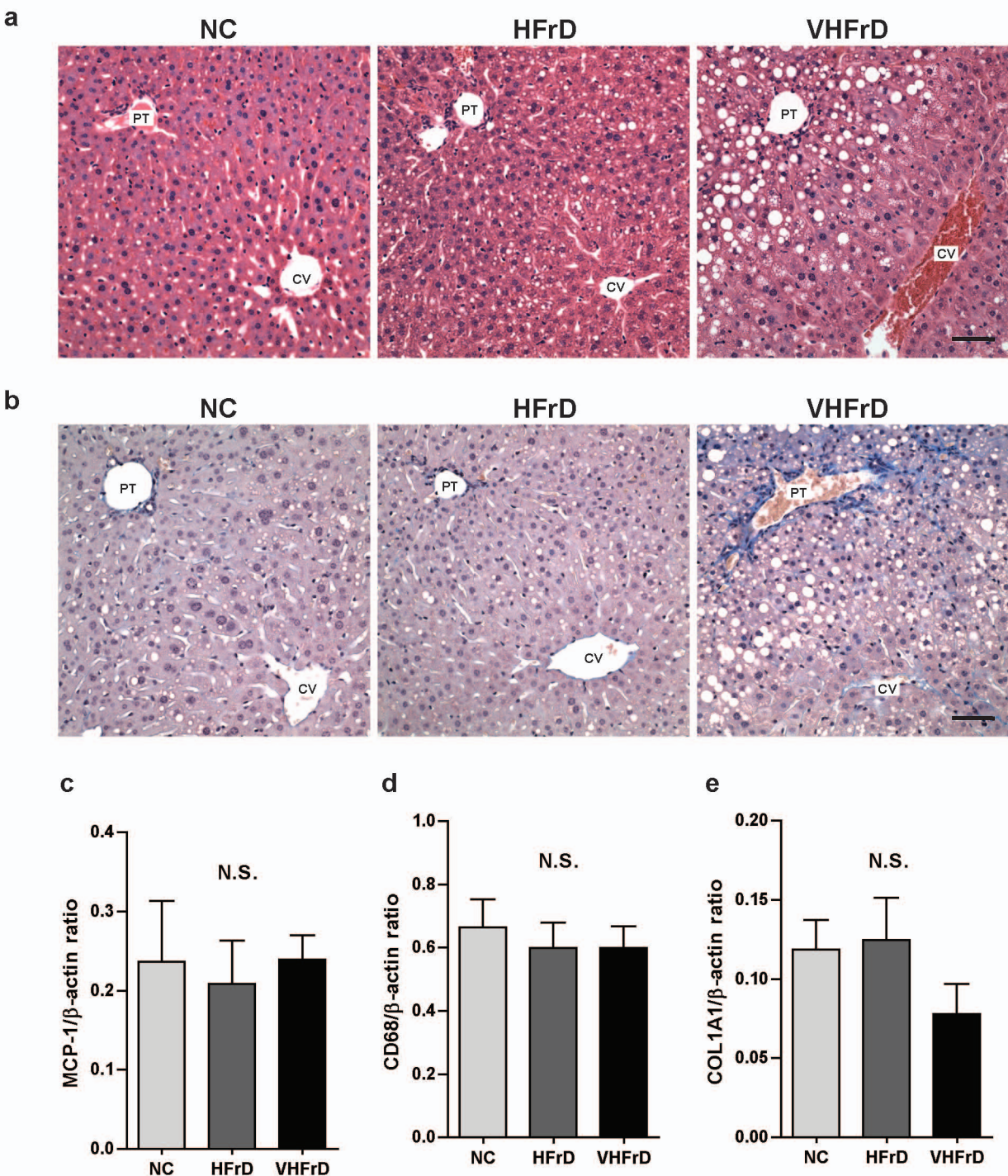
Supplementary Figure 4



Supplementary Figure 4

Intrahepatic triglyceride levels of WT mice given *ad libitum* normal chow with tap water (NC), with 15% fructose water (low fat high fructose, HFrD) or 30% fructose water (low fat very high fructose, VHFrD) for 25 weeks ($n = 6$), and those of WT mice fed *ad libitum* LFD, HFD or HFHSD for 15 weeks ($n = 6$). Data represent means \pm s.e.m. * $P < 0.05$, *** $P < 0.001$ vs. WT fed LFD. ### $P < 0.01$. #### $P < 0.001$.

Supplementary Figure 5



Supplementary Figure 5

WT mice were given *ad libitum* normal chow with tap water (NC), with 15% fructose water (low fat high fructose, HFrD) or 30% fructose water (low fat very high fructose, VHFrD) for 25 weeks. (a) Representative images of H&E stained liver. Bar, 50 μ m. (b) Representative images of trichrome stained liver. Bar, 50 μ m. (c-e) Quantitative real-time PCR for mouse MCP-1 (c), CD68 (d) and collagen type I (COL1A1, e). ($n = 7-8$). β -actin was used as an internal control. Data represent means \pm s.e.m. N.S., no significant. CV, central vein. PT, portal triad.