**Supplemental Fig. 1: Alanine is not critical for the activation of hepatic stellate cells. a,** LX2 cells activated by TGFβ-1 (5 ng/mL) and treated with or glutamine (2 mM) or three doses of alanine (1, 2, or 5 mM). *COL1A1*, *COL1A2*, and *COL3A1* gene expression measured by RT-qPCR and expressed as mean ± SEM, relative to TGFβ-1-free cells. **b,** Western blot images for COL1A1, HIF1α, and β-Actin in LX2 cells treated with Gln and HIF1α inhibitor, CAY10585. **c**, The mRNA abundance of *HIF1A* in TGFβ-1-activated LX2 cells expressing scramble or MPC2 shRNA and data expressed as mean ± SEM, relative to TGFβ-1-free scramble-shRNA cells. ns, non-significant, *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001.

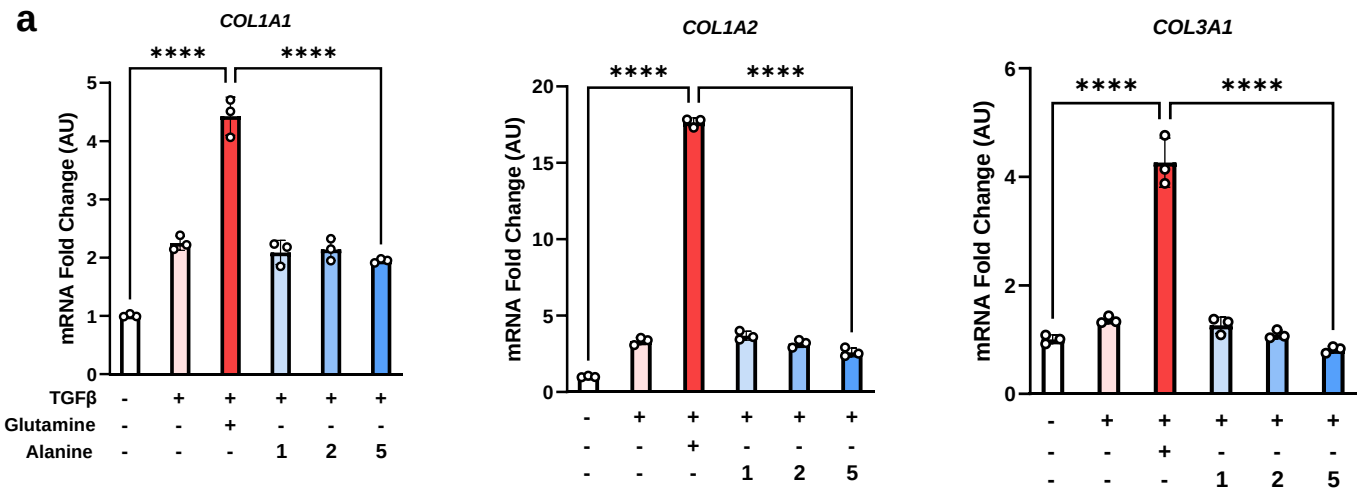
**Supplemental Fig. 2: Stellate cell-specific deletion of *Mpc2* blunts HSC activation in vitro.** *Col1a1*, *Col3a1*, *Acta2*, *Timp1*, *Serpine1*, and *Mpc2* gene expression of isolated hepatic stellate cells (HSC) from wild-type $Mpc2^{fl/fl}$ mice and MPC2-/- littermates that cultured for up to 7 days (Day7). A portion were harvested after 1 day of culture (Day1) for quiescent HSC. Gene expression was measured by RT-qPCR and data are expressed as mean ± SEM, relative to day1 HSC. **p < 0.01, ****p < 0.0001.

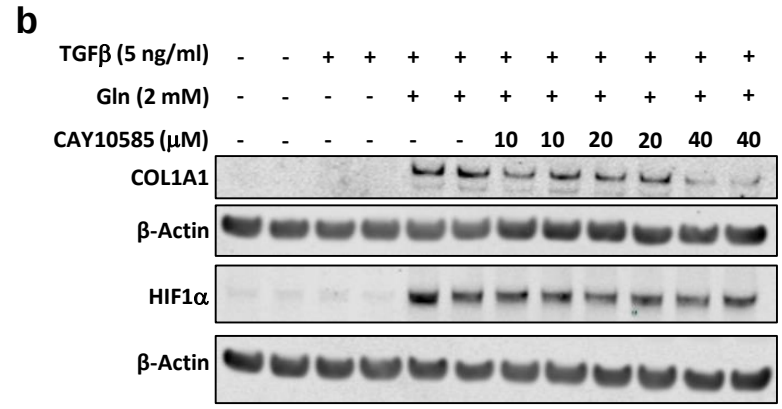
**Supplemental Fig. 3: Plasma lipids were not affected in Lrat-MPC2-/- mice fed a MASH-inducing diet**. At about 8 weeks of age, littermate wild-type (WT) and Lrat-MPC2-/- (KO) mice were placed on either a low-fat diet (LFD) or a diet high in fat, fructose, and cholesterol (HFC) for a period of 12 weeks. **a**, Liver weight, measured at sacrifice, and body composition, determined by EchoMRI, expressed as mean ± SEM (n=7-11/group). **b**, Histological scoring of H&E-stained liver sections assessing steatosis, macrosteatosis, lobular inflammation, and NAFLD activity score expressed as mean ± SEM (n=6-7/group). **c,d**, Analysis of triglycerides

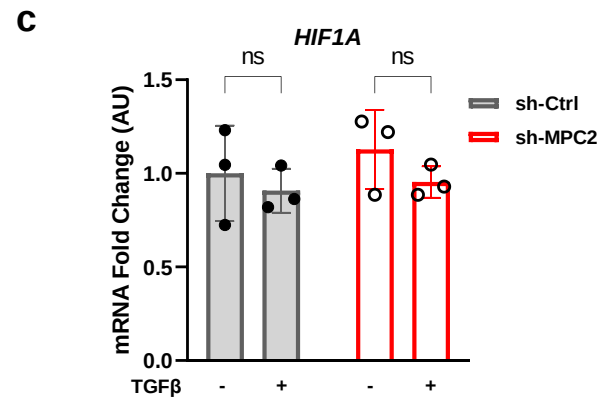
(TG), total cholesterol (TC), and non-esterified fatty acids (NEFA) from liver (**c**) and plasma (**d**), expressed as mean ± SEM (n=7-11/group).

**Supplemental Fig. 4: Diminished expression of HIF1α target genes in Lrat-Mpc2-/- mice on HFC diet**. RNA sequencing was performed on liver tissue from both wild-type (WT) and Lrat-Mpc2-/- (KO) mice and placed on either a LFD or HFC diet (n=5/group). Selected HIF1α target genes from RNAseq data expressed as counts per million (CPM) and represented as mean ± SEM (n=5/group).

# Supplemental Fig. 1



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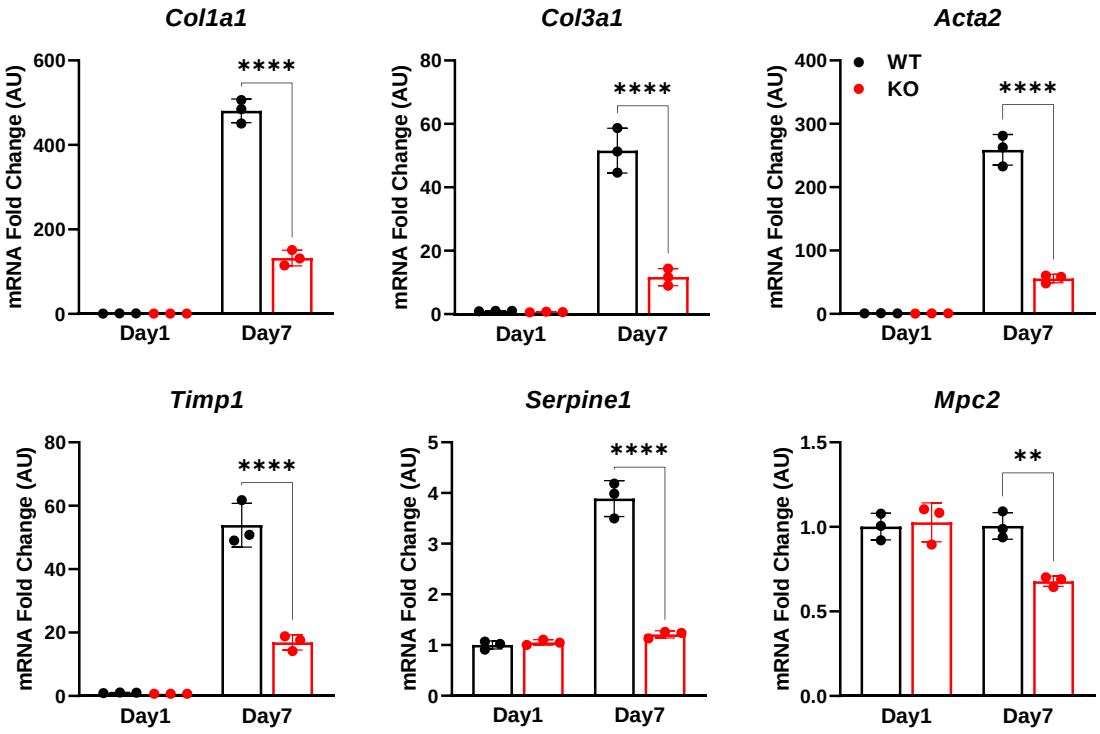
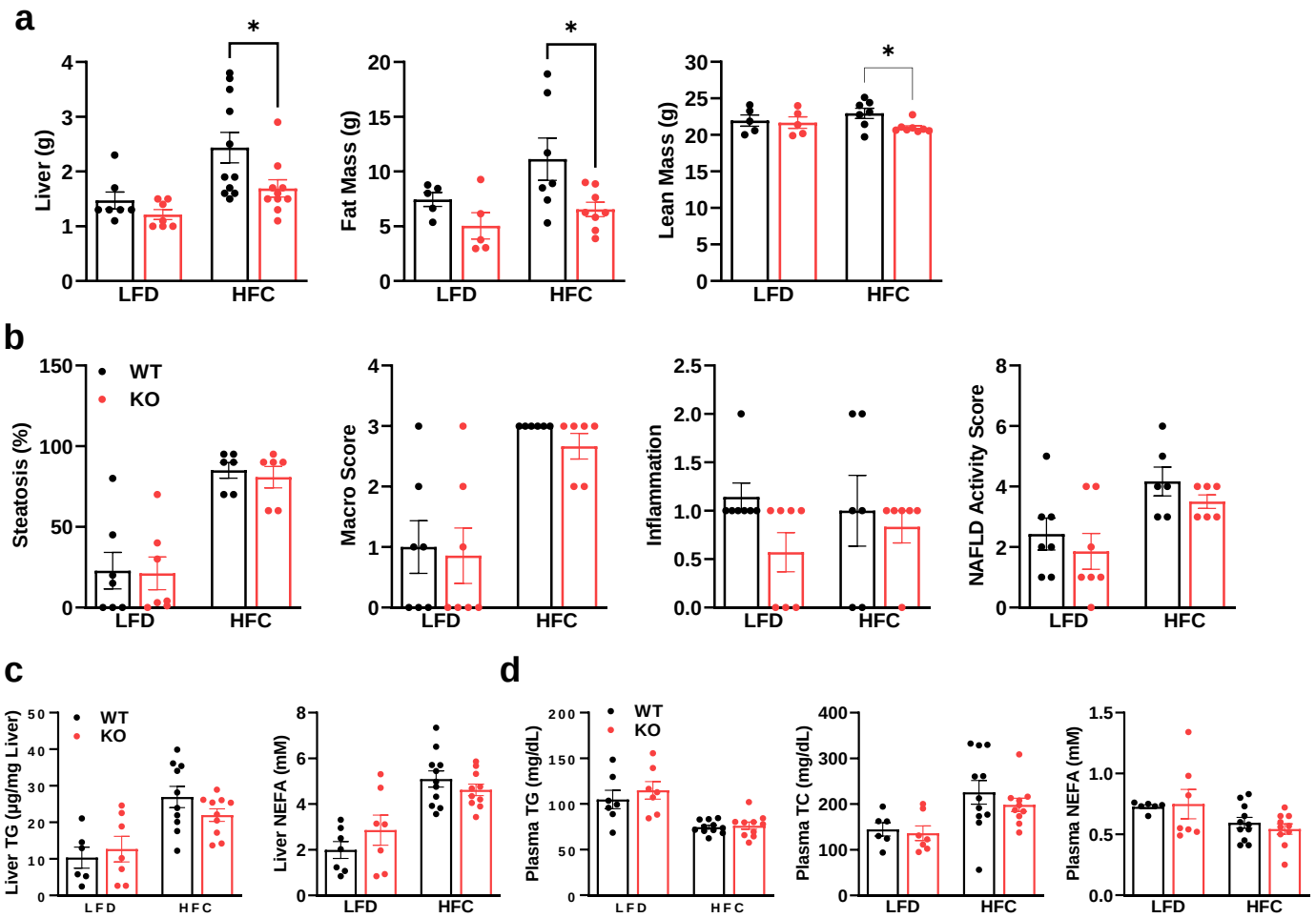


# Supplemental Fig. 3



# Supplemental Fig. 4