SUPPORTING INFORMATION

The soluble guanylate cyclase stimulator IW-1973 prevents inflammation and fibrosis in experimental non-alcoholic steatohepatitis.

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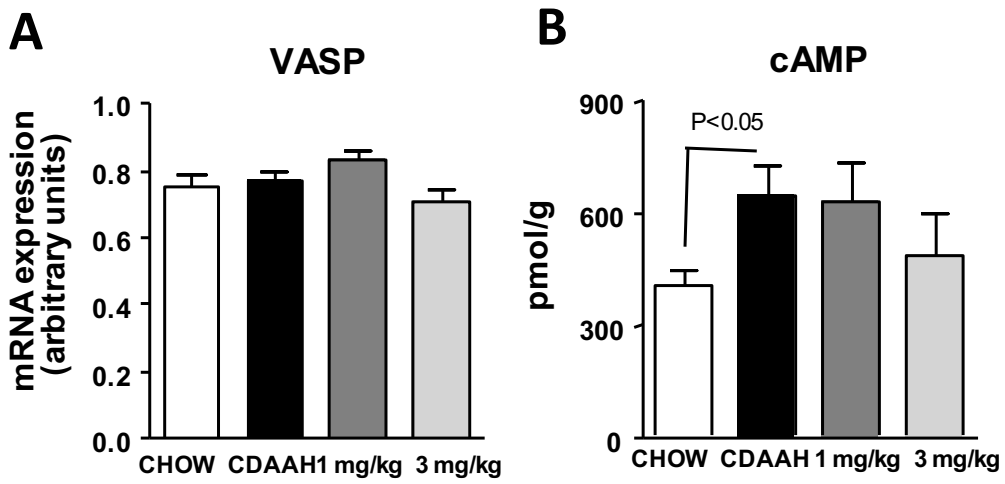
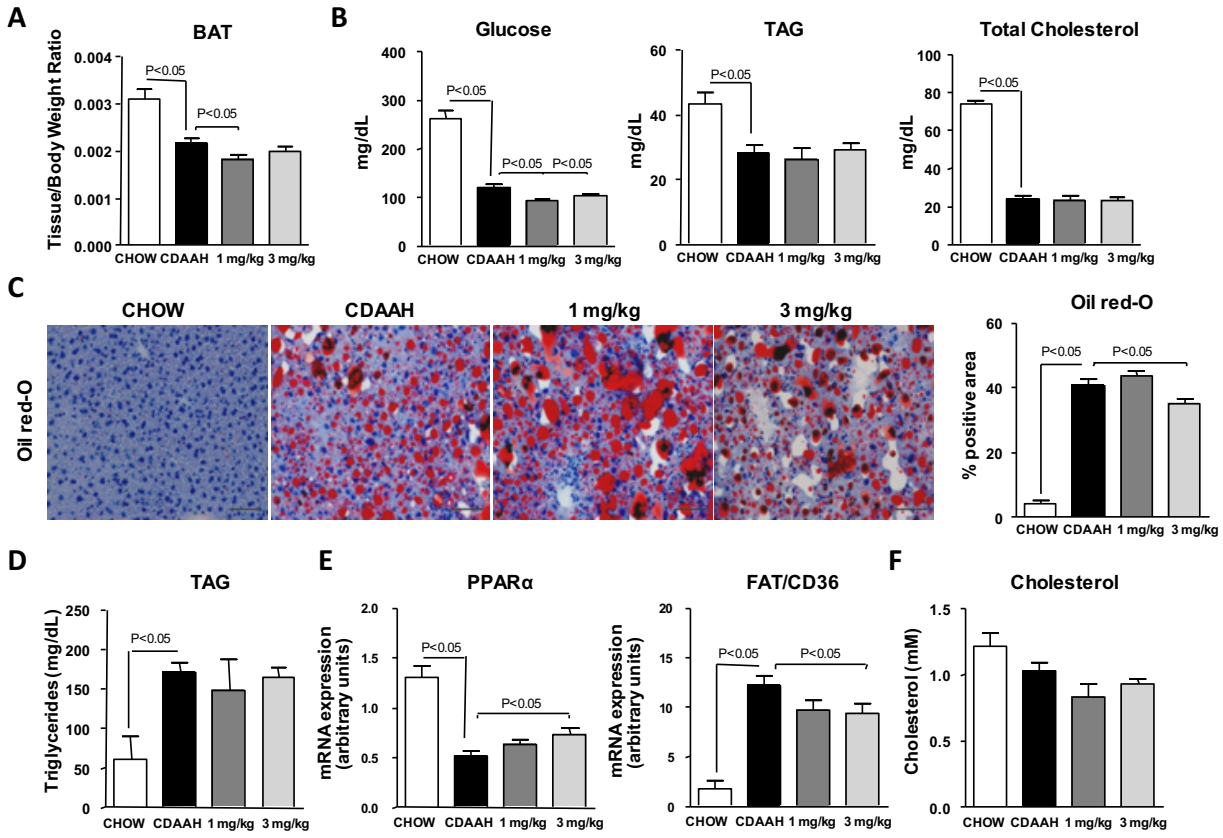
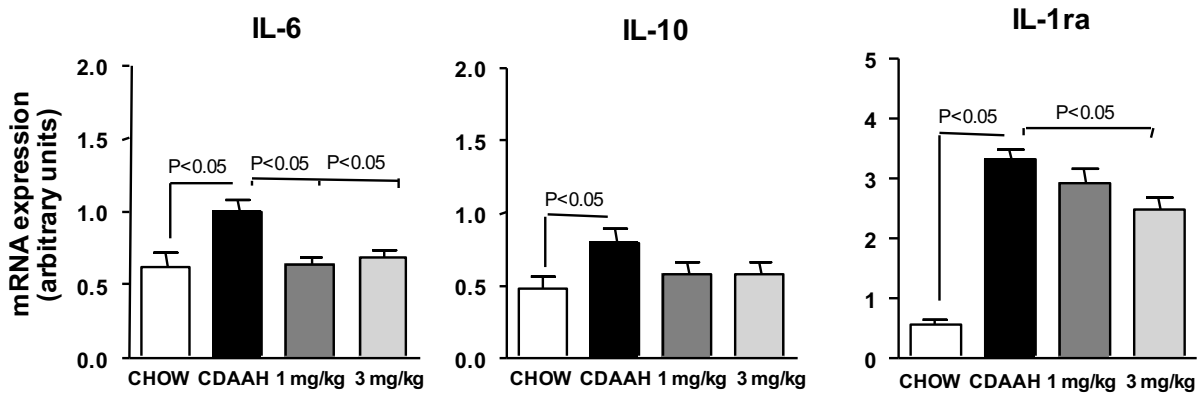


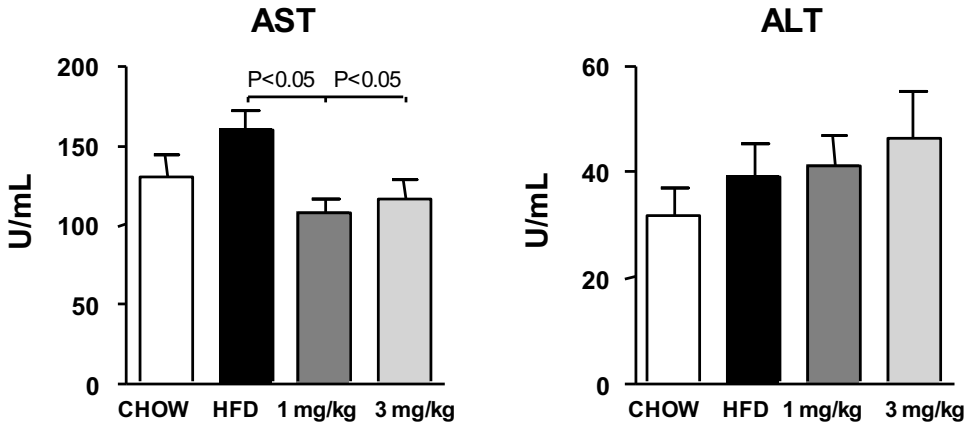
Supplementary Figure 1. Effects of IW-1973 on hepatic cyclic nucleotide pathway. (A) VASP mRNA expression as determined by real-time PCR in liver samples from mice receiving either chow diet (n=10), choline-deficient, L-amino acid-defined, high-fat (CDAAH) diet (n=15), CDAAH plus sGC stimulator IW-1973 at 1 mg/kg (n=10) or CDAAH plus IW-1973 at 3 mg/kg (n=10). **(B)** Hepatic tissue levels of cAMP in these groups of animals as determined by EIA. Results are expressed as mean ± SEM.



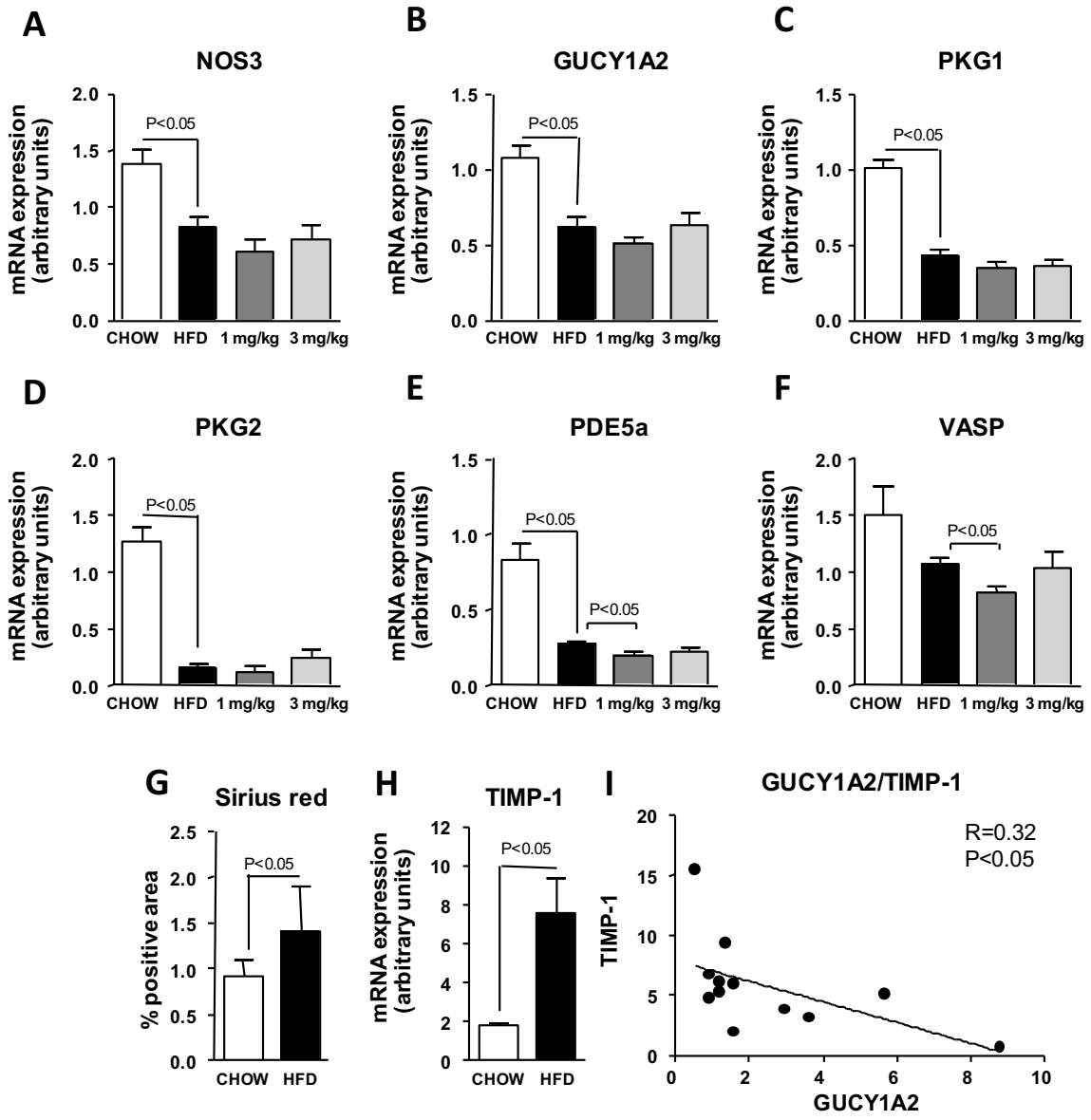
Supplementary Figure 2. Effects of IW-1973 on plasma biochemistry and steatosis. (A) BAT-to-body weight ratio in mice receiving either chow diet (n=10), CDAAH diet (n=15), CDAAH plus sGC stimulator IW-1973 at 1 mg/kg (n=10) or CDAAH plus IW-1973 at 3 mg/kg (n=10). **(B)** Plasma glucose, TAG and total cholesterol levels. (**C**) Representative photomicrographs (200x magnification) of liver sections and histomorphometric analysis of the area stained with Oil red-O. **(D)** Hepatic TAG levels. (**E**) Hepatic PPARα and FAT/CD36 mRNA expression. (**F**) Hepatic cholesterol levels. Results are expressed as mean ± SEM. Scale bar = 50 μm.



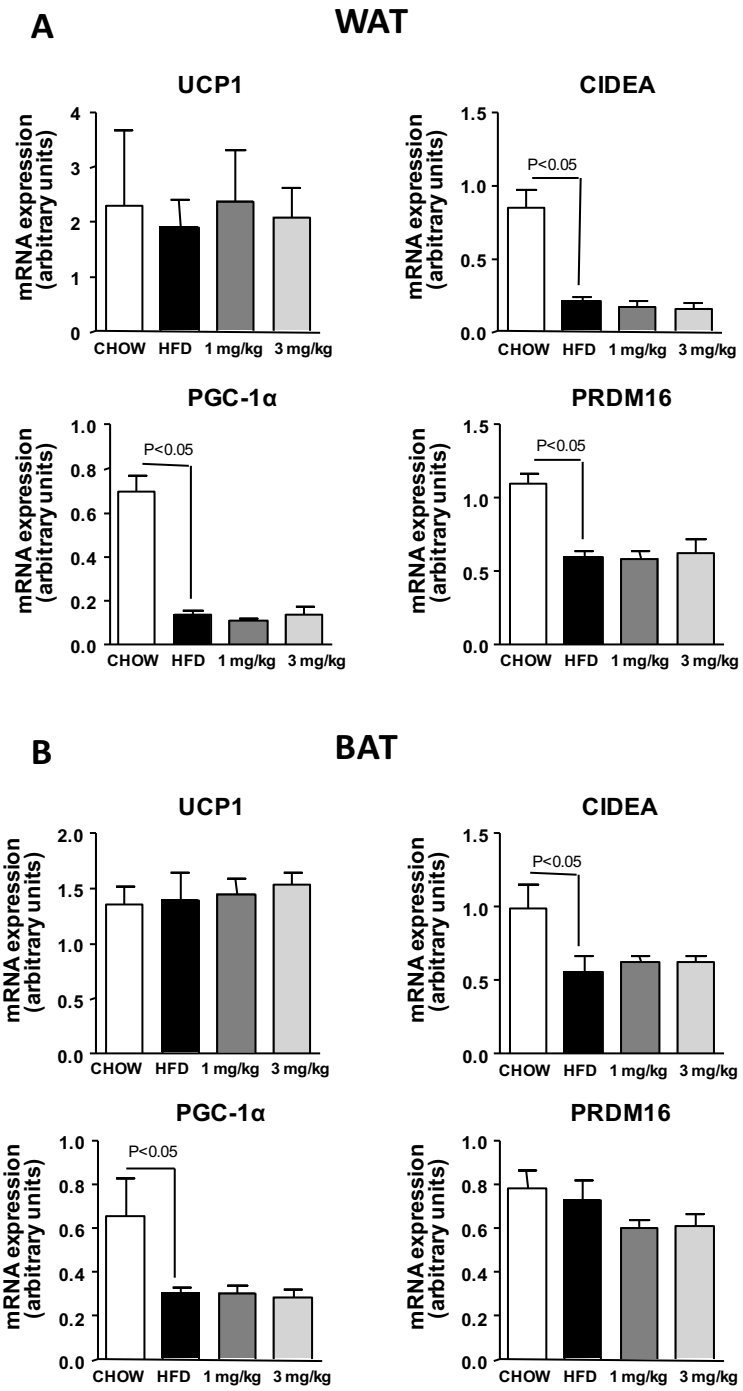
Supplementary Figure 3. Effects of IW-1973 on hepatic cytokine expression. Hepatic IL-6, IL-10 and IL-1ra mRNA expression in mice receiving either chow diet (n=10), CDAAH diet (n=15), CDAAH plus sGC stimulator IW-1973 at 1 mg/kg (n=10) or CDAAH plus IW-1973 at 3 mg/kg (n=10). Results are expressed as mean ± SEM.



Supplementary Figure 4. Effects of IW-1973 on plasma transaminase (i.e. AST and ALT) levels in mice receiving either chow diet (n=5), an obesogenic HFD diet (n=10), HFD plus sGC stimulator IW-1973 at 1 mg/kg (n=10) or HFD plus IW-1973 at 3 mg/kg (n=10). Results are expressed as mean ± SEM.



Supplementary Figure 5. Changes in WAT cGMP pathway and fibrosis in high-fat diet (HFD)-induced obese mice. WAT mRNA expression for NOS3 **(A)**, GUCY1A2 **(B)** , PKG1 **(C)**, PKG2 **(D)**, PDE5a **(E)** and VASP **(F)** in mice receiving either chow diet (n=5), HFD diet (n=10), HFD plus sGC stimulator IW-1973 at 1 mg/kg (n=10) or HFD plus IW-1973 at 3 mg/kg (n=10). **(G)** Histomorphometric analysis of fibrosis by Sirius red staining. **(H)** mRNA expression of the fibrosis marker TIMP-1. **(I)** Correlation between GUCY1A2 and TIMP-1 in human obese WAT. Results are expressed as mean ± SEM.



Supplementary Figure 6. Effects of IW-1973 on adipose tissue thermogenesis. UCP1, CIDEA, PGC-1α and PRDM16 mRNA expression in WAT **(A)** and BAT **(B)** in mice receiving either chow diet (n=5), HFD diet (n=10), HFD plus sGC stimulator IW-1973 at 1 mg/kg (n=10) or HFD plus IW-1973 at 3 mg/kg (n=10). Results are expressed as mean ± SEM.