



Fig. S4. Crocin II improves HFD-induced insulin resistance and hyperlipidemia in mice, referred to Fig. 3. For panel A to C, mouse PHs were pre-incubated with 100 µM Crocin II for 2 h, and then treated with 100 µM Crocin II and 0.4 mM FFAs for 24 h. (A) The relative area and fluorescence intensity of lipid droplets. (B) Intracellular TG contents. (C) The quantitative analysis of protein levels of Fasn, Cidea and Atgl. $n = 3$, $*P < 0.05$ and $**P < 0.01$ v.s. CTL group, $\#P < 0.05$ and $\#\#P < 0.01$ v.s. 0.4 mM FFAs group, one-way ANOVA followed by Bonferroni's *posthoc* test. All values are presented as the mean \pm SD. For panel D to F, mouse PHs isolated from WT and Angptl8^{-/-} mice were pre-incubated with 100 µM Crocin II for 2 h, and then treated with 100 µM Crocin II and 0.4 mM FFAs for 24 h. (D) The relative area and the relative fluorescence intensity of lipid droplets in Mouse PHs. (E) Intracellular TG contents. (F) The quantitative analysis of protein levels of Fasn,

Cidea and Atgl. n = 3, n.s., no significance, $**P < 0.01$ v.s. WT + CTL group, $\#P < 0.05$ and $\#\#P < 0.01$ v.s. WT + FFAs group, one-way ANOVA followed by Bonferroni's *posthoc* test. All values are presented as the mean \pm SD. For panel G to J, mouse PHs were transfected with either Angptl8-overexpressing plasmid or empty vector (pcDNA3.0). 24 h later, cells were pre-incubated with 100 μ M Crocin II for 2 h, and then treated with 100 μ M Crocin II and 0.4 mM FFAs for 24 h. (G) The quantitative analysis of Angptl8 protein levels. (H) The relative area and fluorescence intensity of lipid droplets. (I) Intracellular TG contents. (J) The quantitative analysis of protein levels of Fasn, Cidea and Atgl. n=3, $*P < 0.05$ and $**P < 0.01$ v.s. Vector + CTL group, $\#P < 0.05$ and $\#\#P < 0.01$ v.s. Vector + FFAs group, $\$P < 0.05$ and $\$\$P < 0.01$ v.s. Vector + FFAs +100 μ M Crocin II group, one-way ANOVA followed by Bonferroni's *posthoc* test. All values are presented as the mean \pm SD.