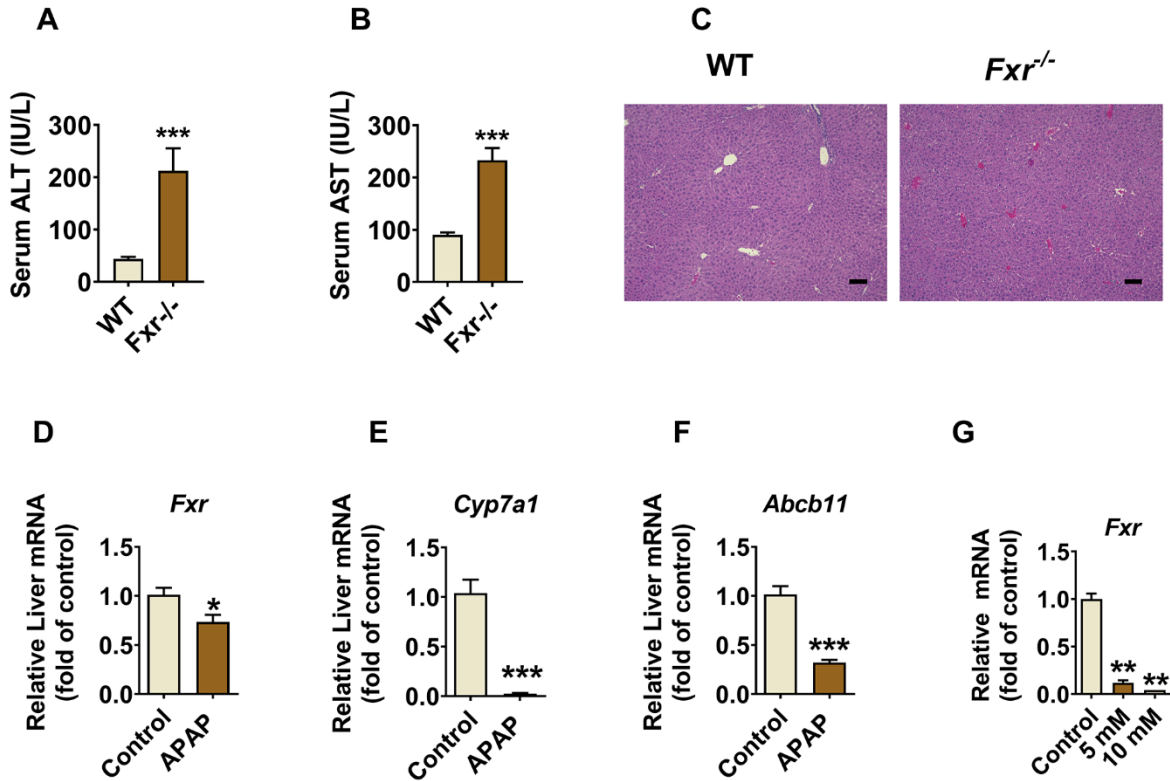


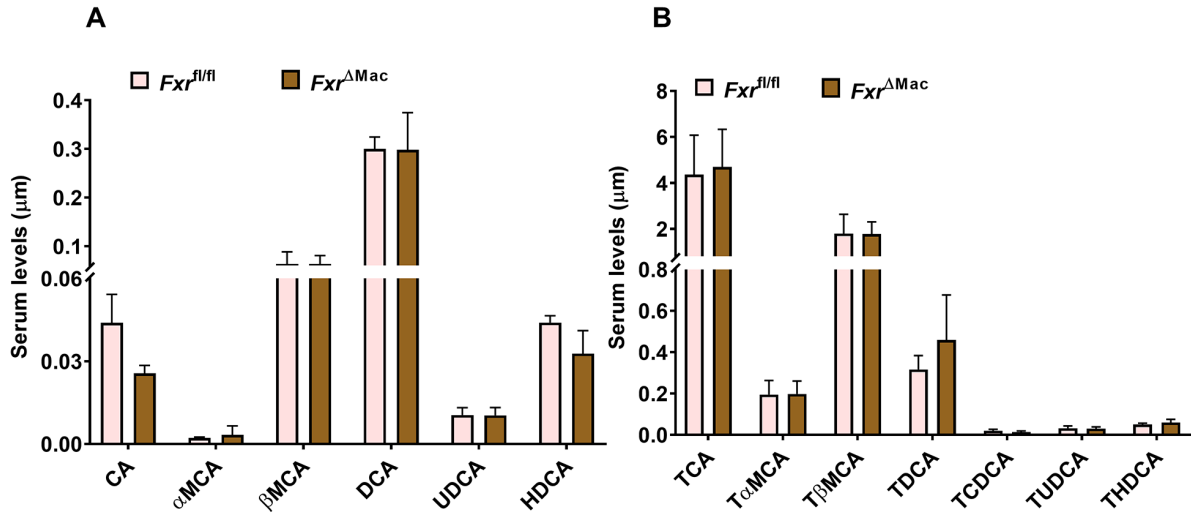
Supplemental Material

FXR-Deoxycholic Acid-TNF α Axis Modulates Acetaminophen-Induced Hepatotoxicity

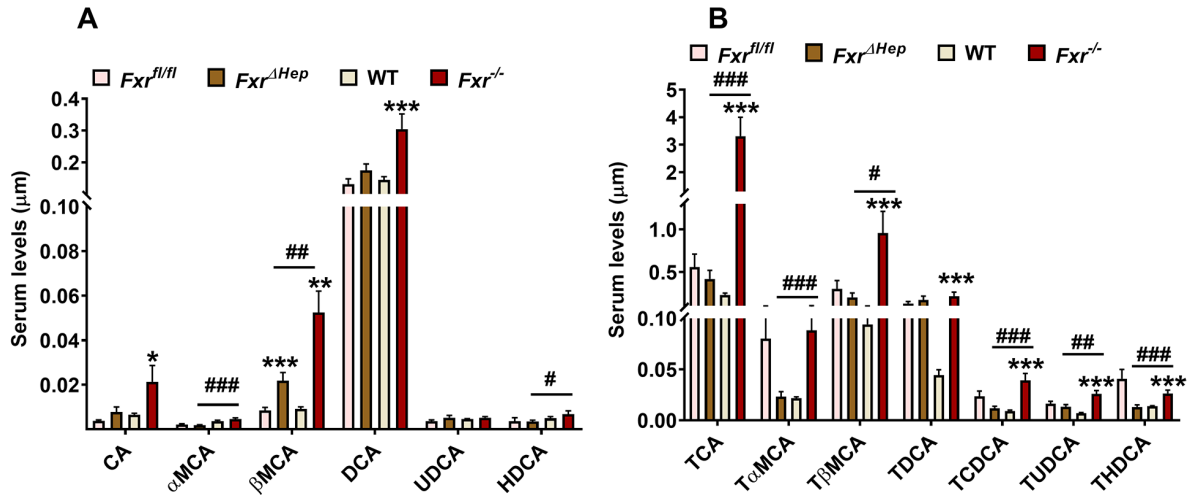
Tingting Yan, Nana Yan, Hong Wang, Tomoki Yagai, Yuhong Luo, Shogo Takahashi, Min Zhao, Kristopher W. Krausz, Guangji Wang, Haiping Hao, Frank J. Gonzalez



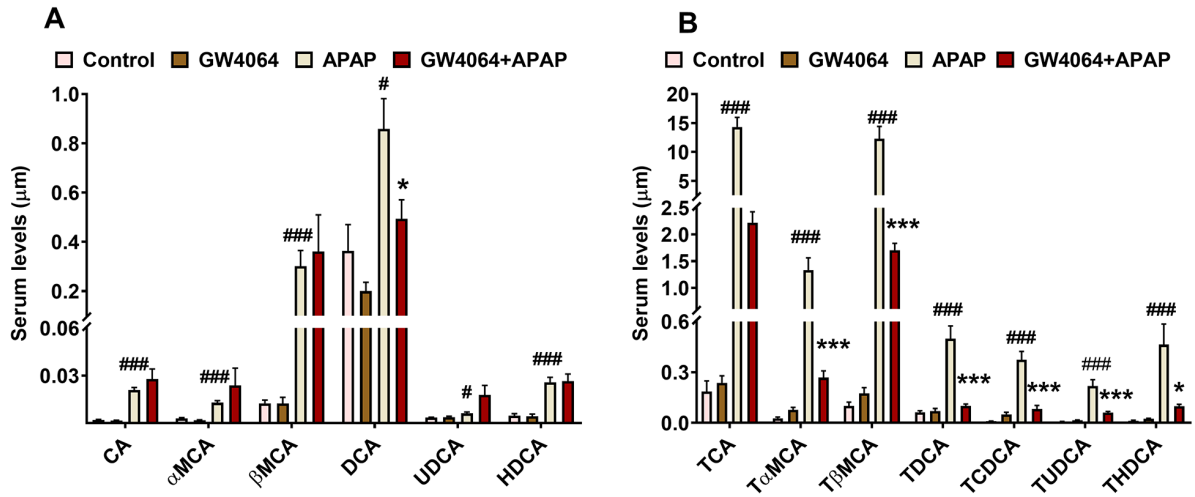
Supplementary Figure 1: Hepatic function parameters of untreated global *Fxr*^{-/-} mice and effect of APAP in hepatic FXR signaling. A-C, Serum ALT levels and AST levels of untreated control global *Fxr*^{-/-} mice and WT mice. C, Liver H&E staining for untreated control WT mice and *Fxr*^{-/-} mice, scale bar 50 μ m. D-F, mRNA levels of genes, *Fxr*, *Cyp7a1*, *Abcb11* in APAP-treated livers; D, *Fxr* mRNA levels in primary mouse hepatocytes treated with 0 (Control), 5 mM or 10 mM of APAP. * $P < 0.05$, ** $P < 0.01$ and *** $P < 0.005$ compared with the control group. *Abcb11*, ATP binding cassette subfamily B member 11.



Supplementary Figure 2: Bile acid levels showed no significant difference between *Fxr*^{ΔMac} and *Fxr*^{fl/fl} mice after APAP dosing. A, serum-free bile acids after APAP dosing. B, serum-conjugated bile acids after APAP dosing. N=5 mice per group. Data are presented as means ± SEM. Full names of abbreviated bile acids were listed in the Figure 4 legend.



Supplementary Figure 3: Bile acid levels were more significantly accumulated in untreated control global *Fxr^{-/-}* mice than in *Fxr^{ΔHep}* mice. A, basic serum free bile acids. B, basic serum conjugated bile acids. N=5 mice per group. Data are presented as means ± SEM. *P<0.05, **P<0.01 and ***P<0.005 compared with the WT group. #P<0.05, ###P<0.01 and ####P<0.005 compared with the *Fxr^{ΔHep}* group. Full names of abbreviated bile acids were listed in Figure 4 legend.



Supplementary Figure 4: Bile acid levels were decreased in GW4064/APAP-treated WT mice. A, serum free bile acids. B, serum conjugated bile acids. N=5 mice per group. Data are presented as means \pm SEM. * P <0.05, ** P <0.01 and *** P <0.005 compared with the APAP group. # P <0.05, ## P <0.01 and ### P <0.005 compared with the control group. Full names of abbreviated bile acids were listed in the Figure 4 legend.

Supplementary Table 1. List of primers:

Primers	Forward 5'-3'	Reverse 5'-3'
<i>Actb</i>	AAGTGCTTCTAGGCGGACTGTT	TTTTCTGCGCAAGTTAGGTTTG
<i>Abcb11</i>	AAGGACAGCCACACCAACTC	TGGATCAACAGCTCCTTCAA
<i>Fxr</i>	CTGAGAACCCGCAGCATTTC	GAGCGGGGTGAACTTGTGAT
<i>Cyp7a1</i>	GCTGTCCGGATATTCAAGGA	AGCTCAGCTCTGGAGGGAAT
<i>Tnfa</i>	CCACCACGCTCTTCTGTCTAC	AGGGTCTGGGCCATAGAACT