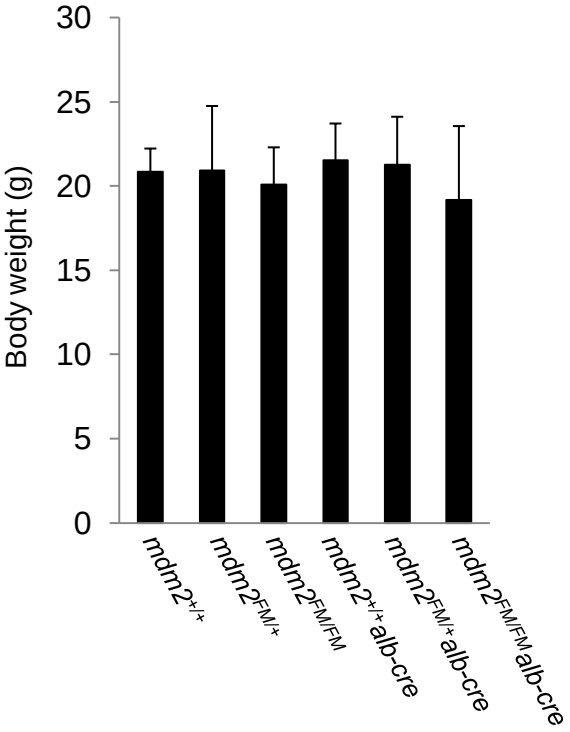
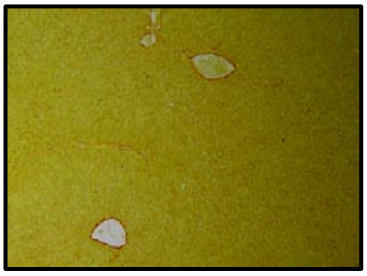
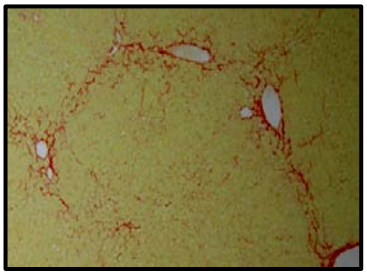


Supplementary Figure 1

Cre(-)



Cre(+)



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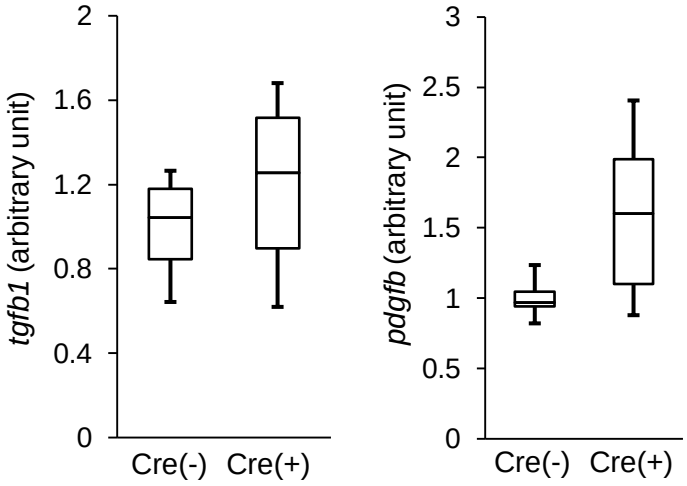
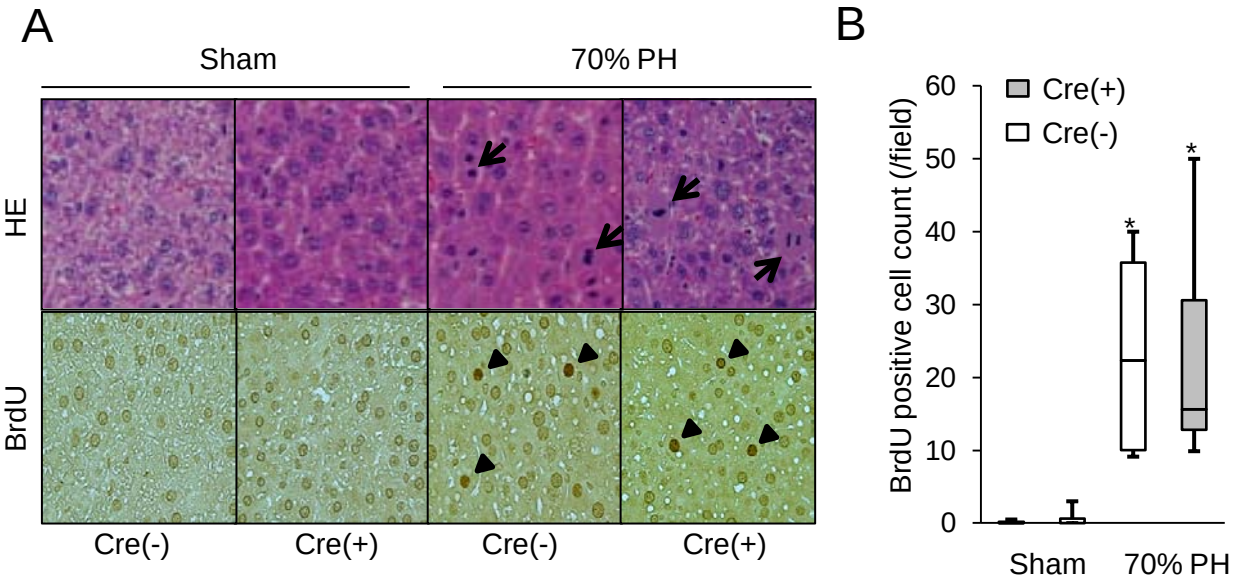
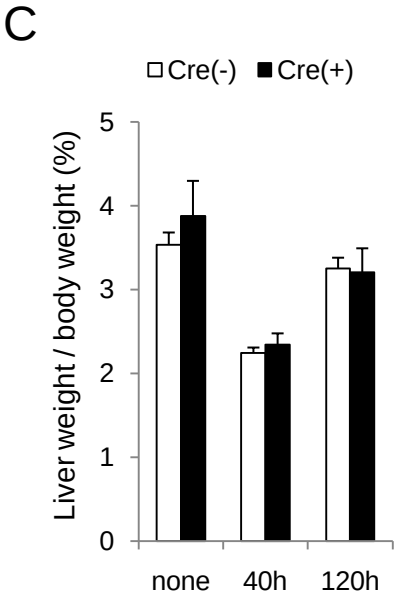


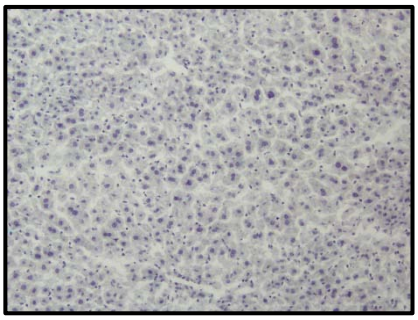
Supplementary Figure 3



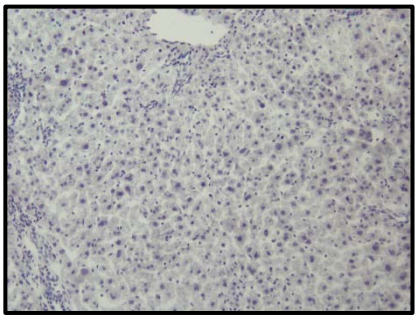


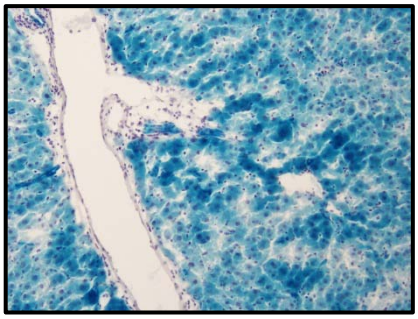
Supplementary Figure 4

Cre(-)



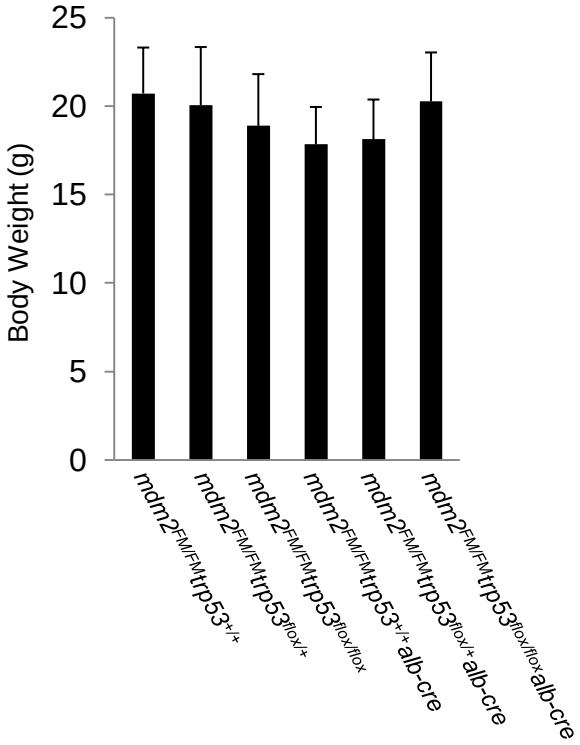
Cre(+)



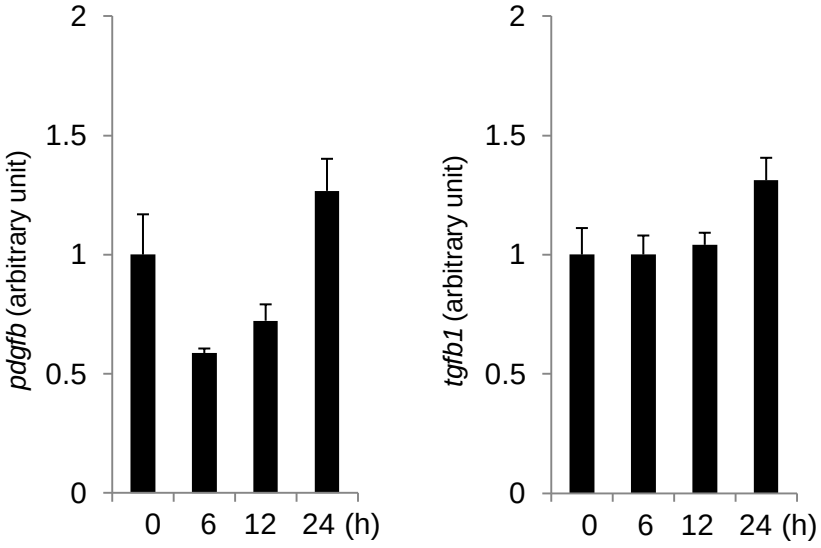


Alb-Cre(+)ROSA26-LacZ(+)

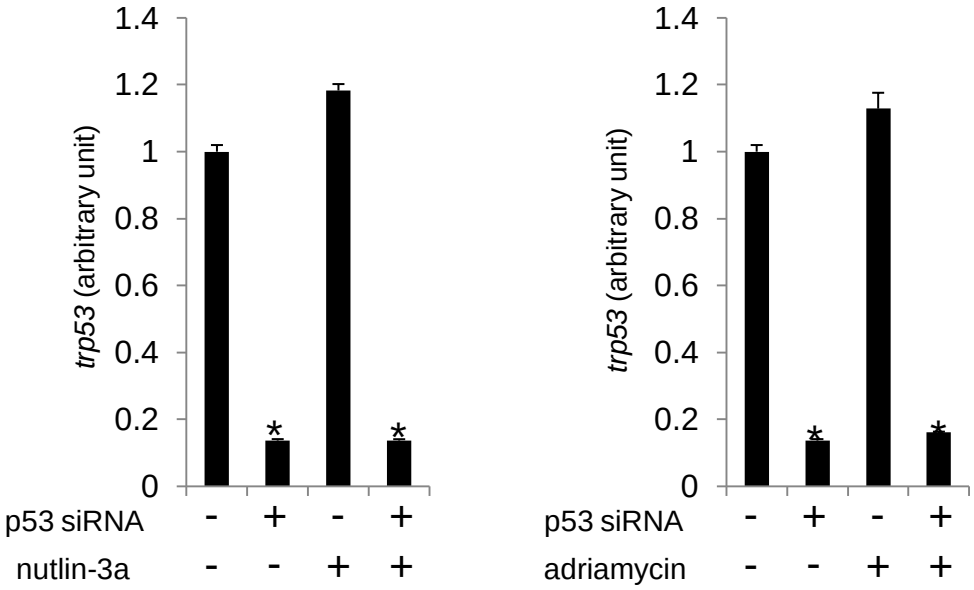
Supplementary Figure 5



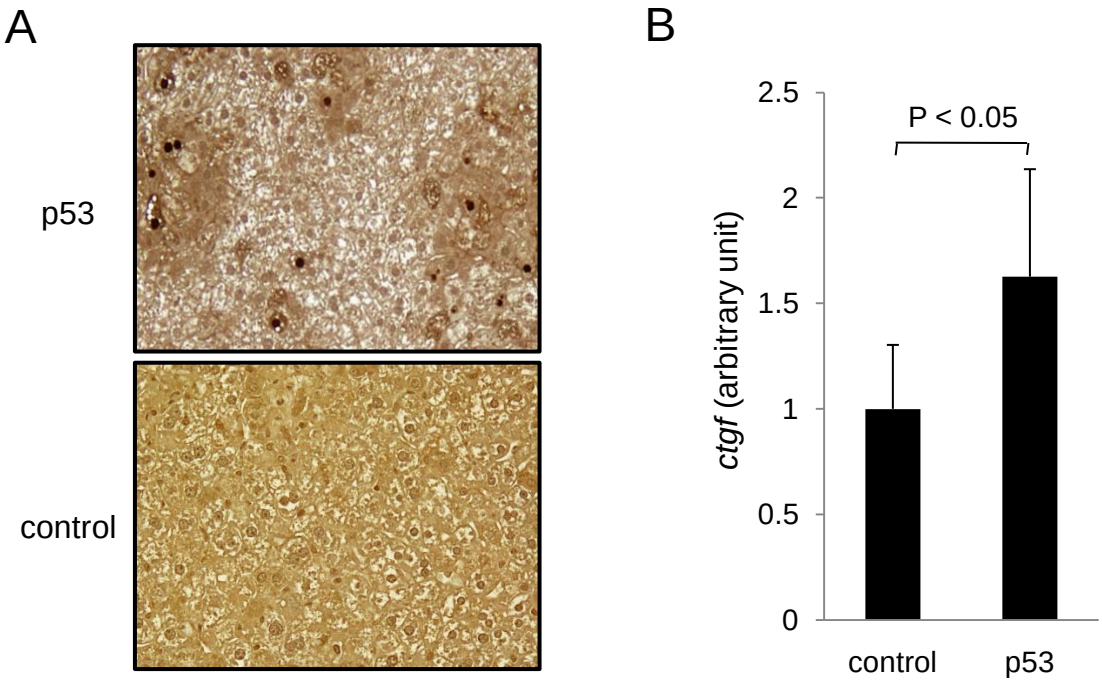
Supplementary Figure 6



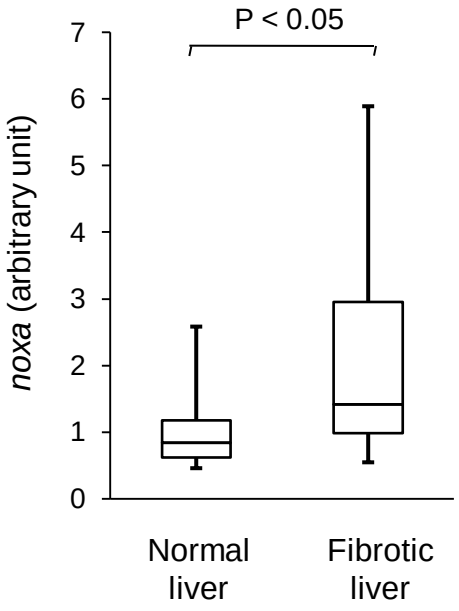
Supplementary Figure 7



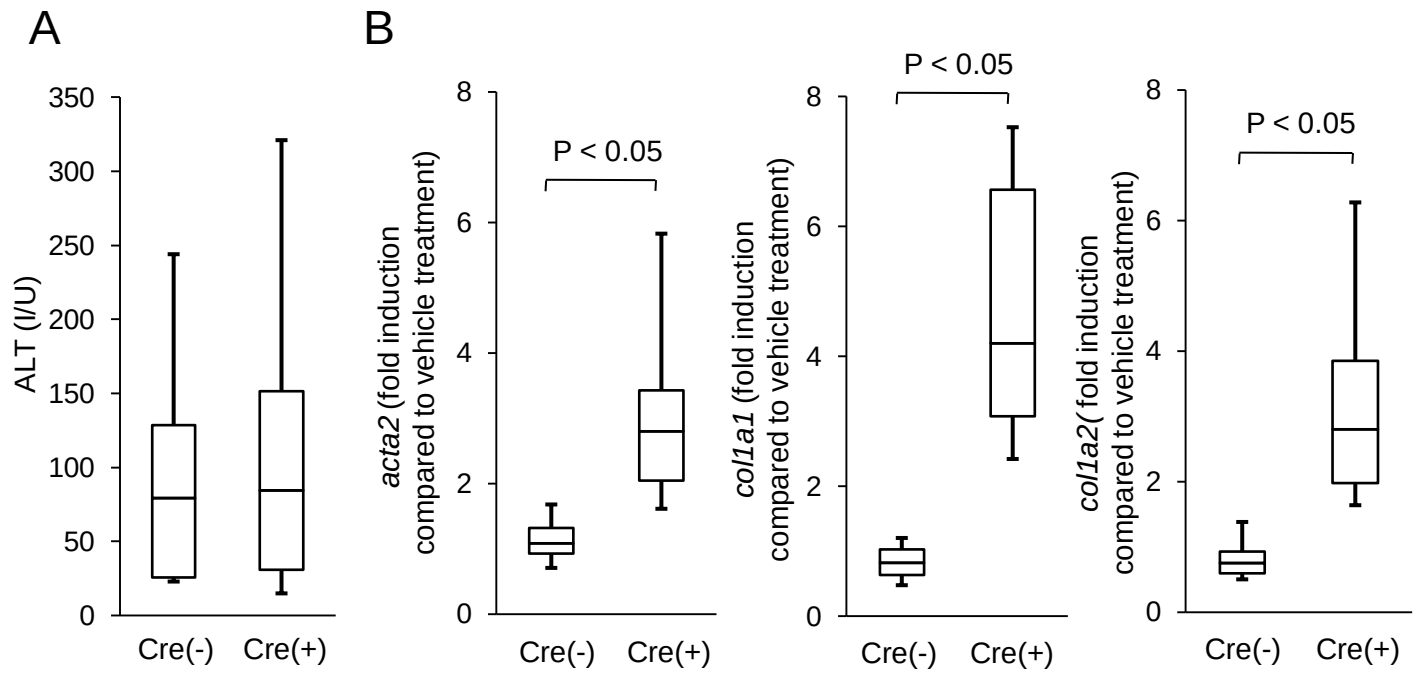
Supplementary Figure 8



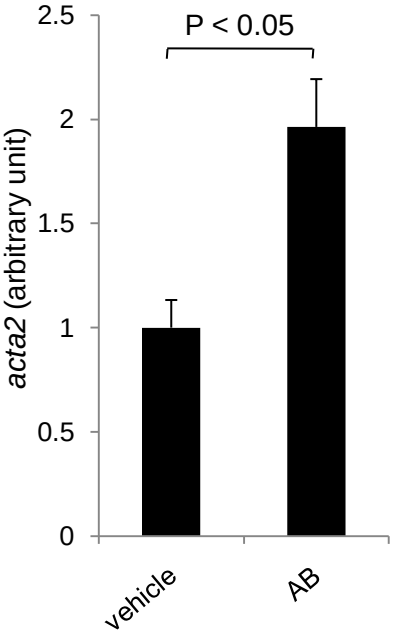
Supplementary Figure 9



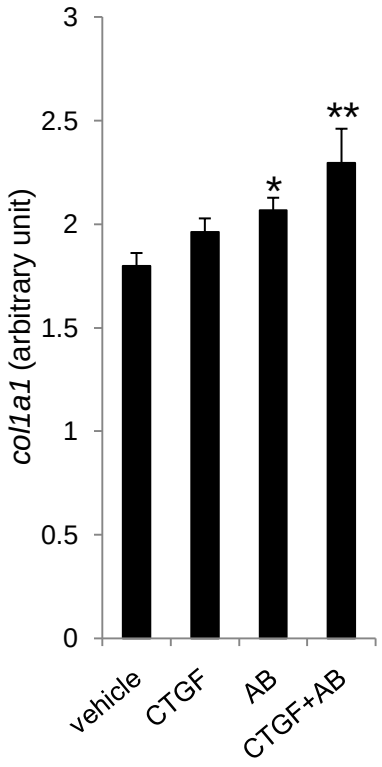
Supplementary Figure 10



Supplementary Figure 11

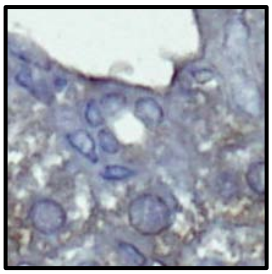


Supplementary Figure 12

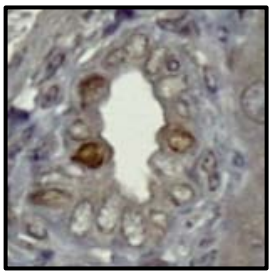


Supplementary Figure 13

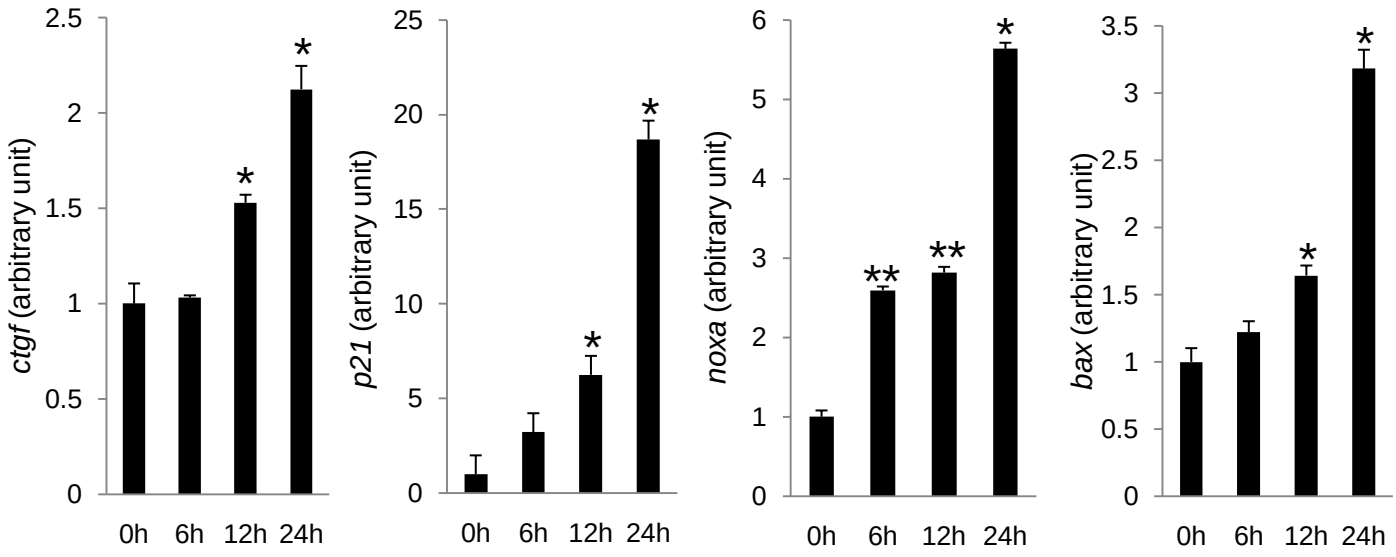
Cre(-)



Cre(+)



Supplementary Figure 14



Supplementary Figure 15

SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1. Body weight of offspring from mating of *mdm2*$^{FM/+}$ *alb-cre* mice and *mdm2*$^{FM/+}$ mice at 6 weeks of age; 7-11 mice per group.

Supplementary Figure 2. Liver fibrosis was evaluated by picrosirius red staining of the liver section from *mdm2*$^{FM/FM}$ *alb-cre* mice and *mdm2*$^{FM/FM}$ mice at 5 months of age. cre(+) and cre(-) stand for *mdm2*$^{FM/FM}$ *alb-cre* and *mdm2*$^{FM/FM}$, respectively.

Supplementary Figure 3. *tgfb1* and *pdgfb* mRNA levels in the liver tissue were determined by real-time RT-PCR at 6 weeks of age; 6 mice per group. cre(+) and cre(-) stand for *mdm2*$^{FM/FM}$ *alb-cre* and *mdm2*$^{FM/FM}$, respectively.

Supplementary Figure 4. (A-B) *mdm2*$^{FM/FM}$ *alb-cre* mice and *mdm2*$^{FM/FM}$ mice were subjected to 70% partial hepatectomy or sham operation at 6-8 weeks of age. After 40 hours, BrdU was intraperitoneally injected 2 hours before the mice were sacrificed; 4-8 mice per group. 70% PH stands for 70% partial hepatectomy. cre(+) and cre(-) stand for *mdm2*$^{FM/FM}$ *alb-cre* and *mdm2*$^{FM/FM}$, respectively. Liver regeneration was evaluated by HE and BrdU staining of liver sections **(A)**; black arrows indicate mitotic cells and black arrowheads indicate BrdU positive nuclei. BrdU positive cell counts of liver sections **(B)**. **(C)** *mdm2*$^{FM/FM}$ *alb-cre* mice and *mdm2*$^{FM/FM}$ mice were subjected to 70% partial hepatectomy. Their liver weight and body weight were measured 40 hours or 120 hours later and are

presented as percent values for liver weight versus body weight; 4 mice per group. cre(+) and cre(-) stand for *mdm2*$^{FM/FM}$ *alb-cre* and *mdm2*$^{FM/FM}$, respectively.

Supplementary Figure 5. Hepatocyte senescence was assessed by senescence-associated β-galactosidase staining of the liver sections. cre(+) and cre(-) stand for *mdm2*$^{FM/FM}$ *alb-cre* and *mdm2*$^{FM/FM}$, respectively. *alb-creROSA26-LacZ* mice were used as the control.

Supplementary Figure 6. Body weight of the offspring from mating of *mdm2*$^{FM/FM}$*trp53*$^{flox/+}$*alb-cre* mice and *mdm2*$^{FM/FM}$*trp53*$^{flox/+}$ mice at 6 weeks of age; 8-12 mice per group.

Supplementary Figure 7. HepG2 cells were treated with nutlin-3a (20 μM) or vehicle for the indicated time courses. Real-time RT-PCR analysis of *pdgfb* and *tgfb1* mRNA expression; N = 3/group.

Supplementary Figure 8. HepG2 cells were transfected with *p53* siRNA or control siRNA for 2 days and then cultured for 24 h with vehicle or nutlin-3a (20 μM) (left) or adriamycin (1 μM) (right). Real-time RT-PCR analysis of *p53* mRNA expression; N = 3/group; **P* < 0.01 *vs.* control siRNA groups.

Supplementary Figure 9. (A-B) Balb/c mice were given hydrodynamic injection of ORF9-mp53 plasmid or an injection of its control plasmid via the tail vein and

sacrificed 2 days later; 4-5 mice per group. p53 and control stand for mice given hydrodynamic injection of pORF-mp53 plasmid and mice given hydrodynamic injection of the control plasmid, respectively. Expression of p53 proteins in the liver sections was assessed by immunohistochemistry examination **(A)**. *ctgf* mRNA levels in the liver tissue were determined by real-time RT-PCR **(B)**, Statistical analyses were performed by the paired *t*-test.

Supplementary Figure 10. A total of 21 non-tumorous human liver samples were subdivided into two groups of normal liver and fibrotic liver based on histological analysis. *noxa* mRNA levels in the liver were determined by real-time RT-PCR. N = 11 (normal liver group) and 10 (fibrotic liver group).

Supplementary Figure 11. (A-B) ABT-737 (100 mg/kg) or vehicle was intraperitoneally administered to *mdm2*$^{FM/FM}$*alb-cre* mice and *mdm2*$^{FM/FM}$ mice, which were examined 2 days later; 4-6 mice per group; Cre(+) and Cre(-) stand for *mdm2*$^{FM/FM}$ *alb-cre* and *mdm2*$^{FM/FM}$, respectively. Serum levels of alanine aminotransferase (ALT) upon ABT-737 administration **(A)**. *acta2, co1a1* and *col1a2* mRNA levels in the liver were determined by real-time RT-PCR **(B)**; data are presented as the fold induction of the ABT-737-treated group compared to the vehicle-treated group.

Supplementary Figure 12. Hepatic stellate cells (HSCs) isolated from C57BL/6J mice were co-cultured with apoptotic bodies derived from UV-treated BNL CL.2 cells for 48 h. AB stands for apoptotic bodies. *acta2* mRNA levels of

HSCs were determined by real-time RT-PCR; n = 4 / group, statistical analyses were performed by the paired *t*-test.

Supplementary Figure 13. HSCs isolated from C57BL/6J mice were co-cultured with apoptotic bodies derived from UV-treated BNL CL.2 cells, with or without recombinant CTGF (100 ng/ml) for 24 h. AB stands for apoptotic bodies. *col1a1* mRNA levels of HSCs were determined by real-time RT-PCR; n = 4 / group.*$P < 0.01$ *vs.* vehicle and CTGF+AB groups, **$P < 0.01$ *vs.* the other three groups.

Supplementary Figure 14. Expression of p53 protein in cholangiocytes was determined by Immunohistochemical analysis. cre(+) and cre(-) stand for *mdm2*$^{FM/FM}$ *alb-cre* and *mdm2*$^{FM/FM}$, respectively.

Supplementary Figure 15. SNU-1079 cells were treated with nutlin-3a (20 μM) or vehicle for the indicated time courses. *ctgf, p21, noxa* and *bax* mRNA levels were determined by real-time RT-PCR; N = 3/group; *$P < 0.01$ *vs.* the other three groups, **$P < 0.01$ *vs.* 0 h and 24 h groups.