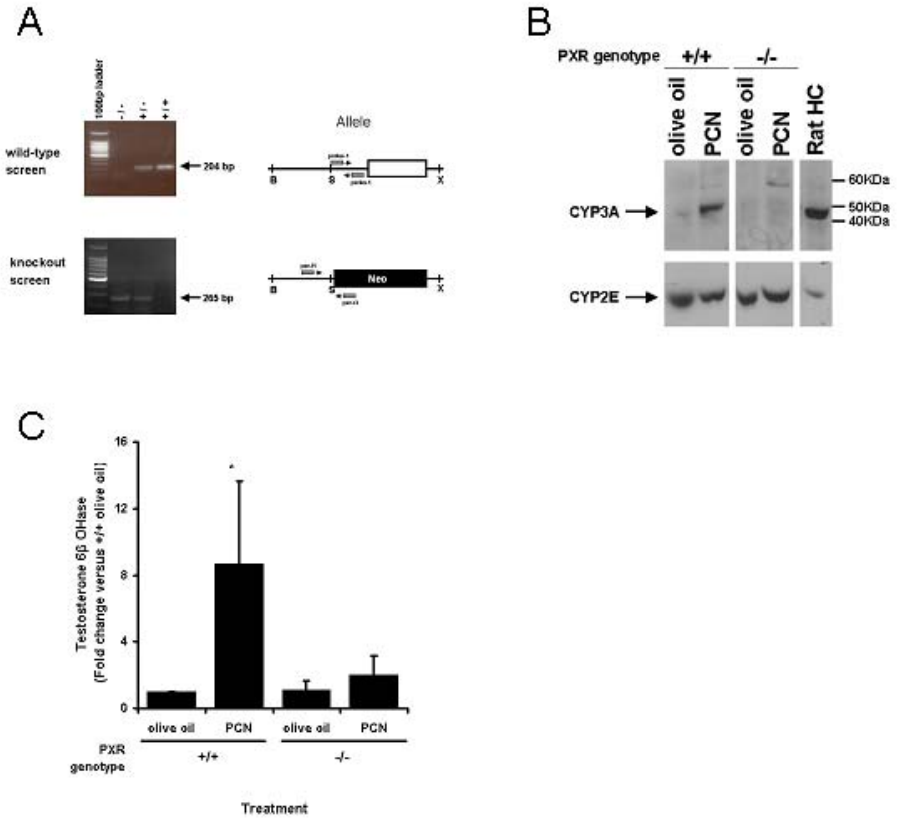
Supplementary Figure legends

Fig. 1. The PXR$^{-/-}$ Mice are Functionally PXR-Deficient as Determined by a Loss of Liver CYP3A Induction by PCN Without Affecting the Expression of CYP2E. A, representative gels of PCR-amplified DNA from tail tip extracted DNA from PXR$^{+/+}$, PXR$^{+/-}$ and PXR$^{-/-}$ mice using the indicated primers (sequences given in Table 1). **B**, Western blot for CYP3A (upper panel) and CYP2E (lower panel) in liver microsomes from PXR$^{+/+}$ and PXR$^{-/-}$ mice administered PCN (100 mg/kg body weight by i.p. injection, suspended in olive oil) daily or olive oil vehicle only. Animals were treated for 3 days and microsomes prepared 24 hours after the last injection. Rat HC - rat hepatocyte extract. The anti-VINGA antibody was raised to the C-terminus of rat CYP3A2 and cross reacts with mouse CYP3A11, CYP3A16 and CYP3A41 which have a related VITGA C-terminal peptide sequence. **C**, CYP3A-mediated testosterone 6β hydroxylase activities in liver microsomal extracts from animals treated as outlined in B above.



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Supplementary Table 1. Rodent Chronic CCl_4 Liver Fibrosis Model - Determinants of Liver Damage and Fibrotic Severity Levels.

A: Haematoxylin and Eosin stained liver sections - damage severity.

Criteria	Damage Severity
Widespread centrilobular necrosis with frequent central-portal bridging of cell loss accompanied by centrilobular collapse. Hepatocytes show degenerating changes (eosinophilia, ballooning) and fatty degeneration. Average cell loss and degenerating area >50% total field of view (with central vein placed in centre of view).	5
Centrilobular necrosis with central-portal bridging of cell loss. Hepatocytes show degenerating changes (eosinophilia, ballooning) and fatty degeneration. Average cell loss and degenerating area between 20 - 50% total field of view (with central vein placed in centre of view).	4
Centrilobular degeneration (eosinophilia, ballooning) and fatty degeneration with some evidence of cell loss. Average cell loss and degenerating area < 20% total field of view (with central vein placed in centre of view).	3
Occasional focal necrosis with evidence of degeneration in surrounding cells.	2
Occasional focal necrosis or evidence of focal degeneration.	1
No abnormalities detected.	0

Liver damage severity was assessed on a scale of 0-5 by a researcher blinded to the treatment groups by visual examination of randomly selected fields using an Olympus CH2 microscope (obj x10; eye x10) using the criteria above. A mean score from each section was determined from at least 20 separate fields.

See main article Fig 1C: group 1 - score 0; group 2 - score 0, group 3 - score 5; group 4 - score 5.

B: α-smooth muscle actin immunostained liver sections - fibrogenic potential severity.

Criteria	Damage Severity
Extensive centrilobular staining with >50% central-portal bridging of stain. Average HSC staining area > 30% total field of view (with a central vein placed in centre of view).	5
Centrilobular staining with 5 - 50% central-portal bridging of stain. Average HSC staining area 10 - 30% total field of view (with a central vein placed in centre of view).	4
Centrilobular staining with central-portal bridging of stain rare (< 5%). Average HSC staining area < 10% total field of view (with central vein placed in centre of view).	3
Majority (>50%) centrilobular regions show some positive but minimal areas of staining	2
Majority (>50%) centrilobular regions normal with no apparent positive staining.	1
No staining within parenchyma - postive staining around periportal vein and artery vessels.	0

Liver fibrosis severity as determined by α-smooth muscle actin immunostaining was assessed on a scale of 0-5 by a researcher blinded to the treatment groups by visual examination of randomly selected fields using an Olympus CH2 microscope (obj x10; eye x10) using the criteria above. A mean score from each section was determined from at least 20 separate fields.

See main article Fig 2A: group 1 - score 0; group 2 - score 0, group 3 - score 5; group 4 - score 2.

C: sirius red stained liver sections - fibrosis severity.

Criteria	Damage Severity
Extensive centrilobular staining with >70% central-portal bridging in randomly selected feilds.	5
Centrilobular staining with 30-70% central-portal bridging in randomly selected feilds.	4
Centrilobular staining with 5-30% central-portal bridging in randomly selected feilds.	3
Less than 5% central-portal bridging. Majority (>50%) centrilobular regions show some positive staining.	2
Less than 5% central-portal bridging. Majority (>50%) centrilobular regions normal with no apparent positive staining.	1
No staining within parenchyma - postive staining around periportal vein and artery vessels.	0

Liver fibrosis severity as determined by sirius red staining was assessed on a scale of 0-5 by a researcher blinded to the treatment groups by visual examination of randomly selected fields using an Olympus CH2 microscope (obj x10; eye x10) using the criteria above. A mean score from each section was determined from at least 20 separate fields.

See main article Fig 2B: group 1 - score 0; group 2 - score 0, group 3 - score 5; group 4 - score 2.