Activation of intestinal human pregnane X receptor protects against azoxymethane/dextran sulfate sodium-induced colon cancer

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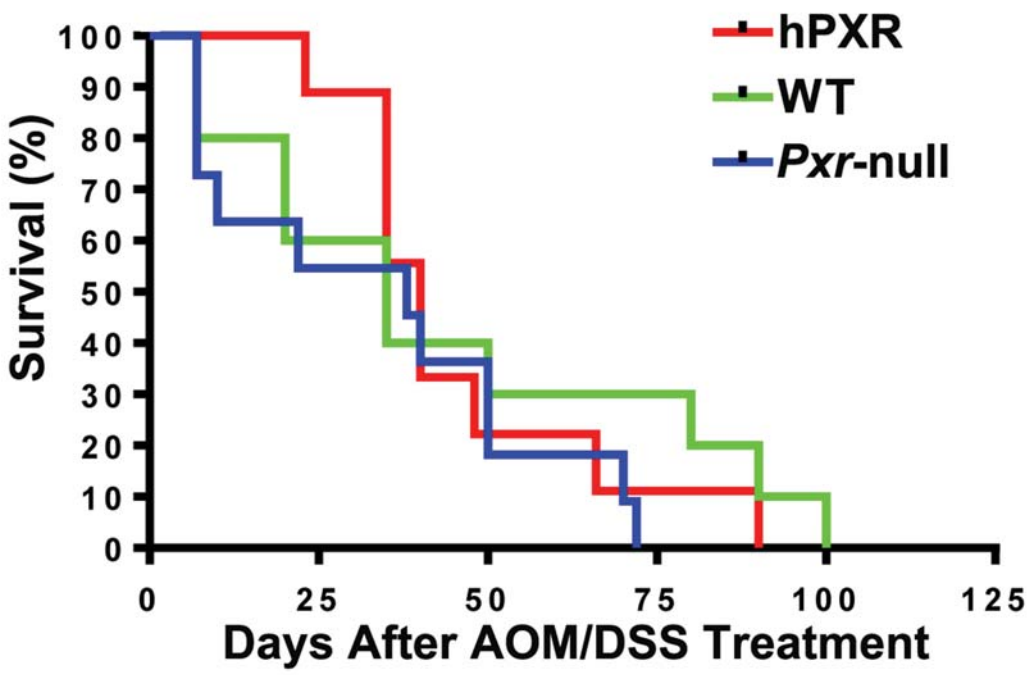
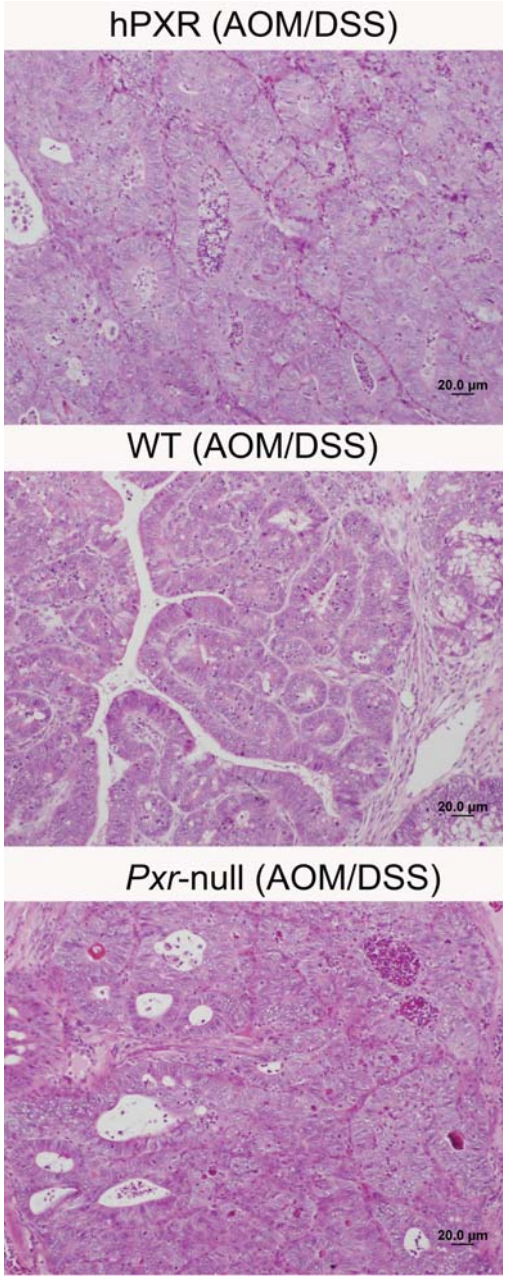
Supplemental Data

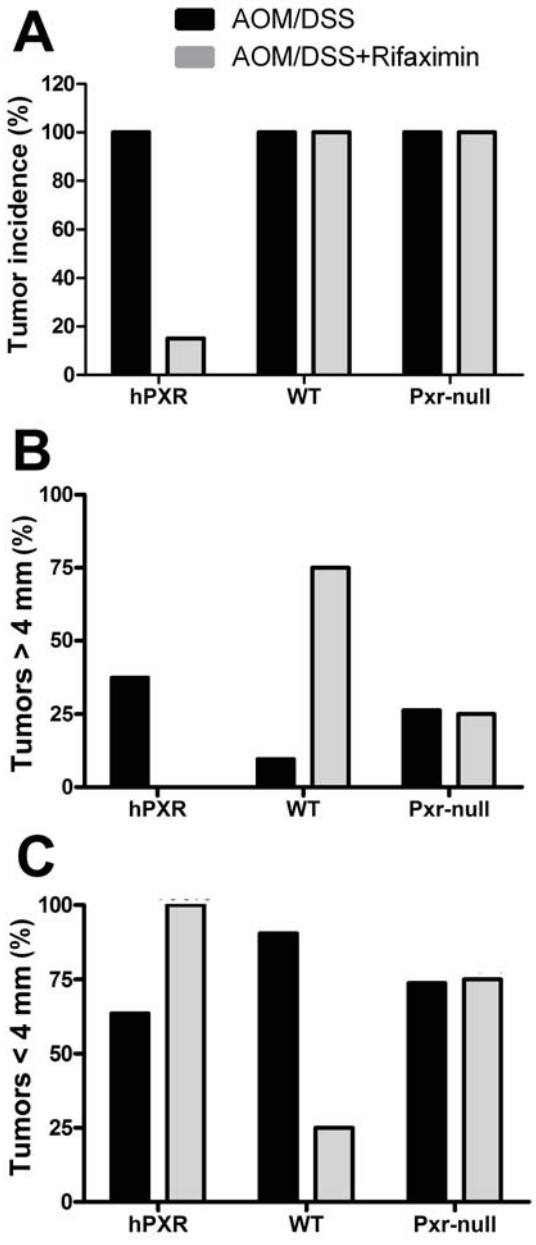
Supplemental Fig. 1 Comparison of survival rates of *PXR*-humanized (hPXR), wild-type (WT) and *Pxr*-null mice after AOM/DSS-induced colon cancer. No significant difference was detected.



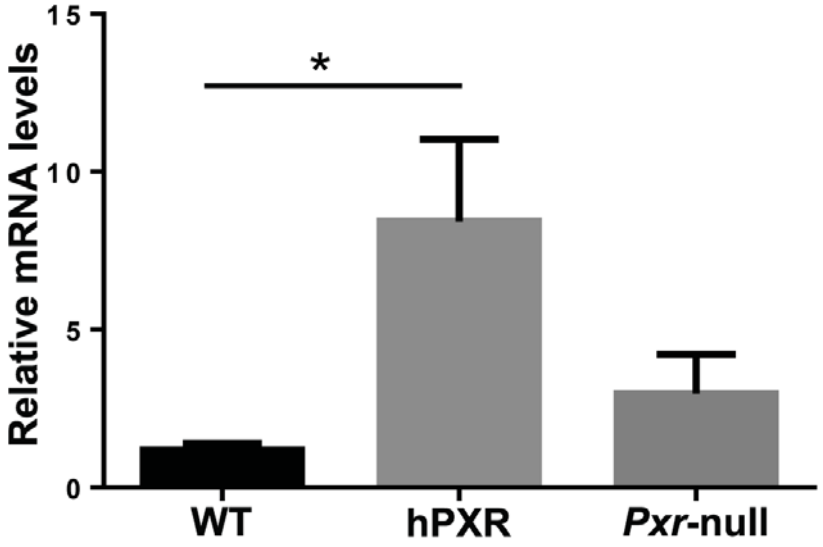
Supplemental Fig. 2 H&E staining of adenocarcinoma in *PXR*-humanized (hPXR), wild-type (WT) and *Pxr*-null mice treated with AOM/DSS.



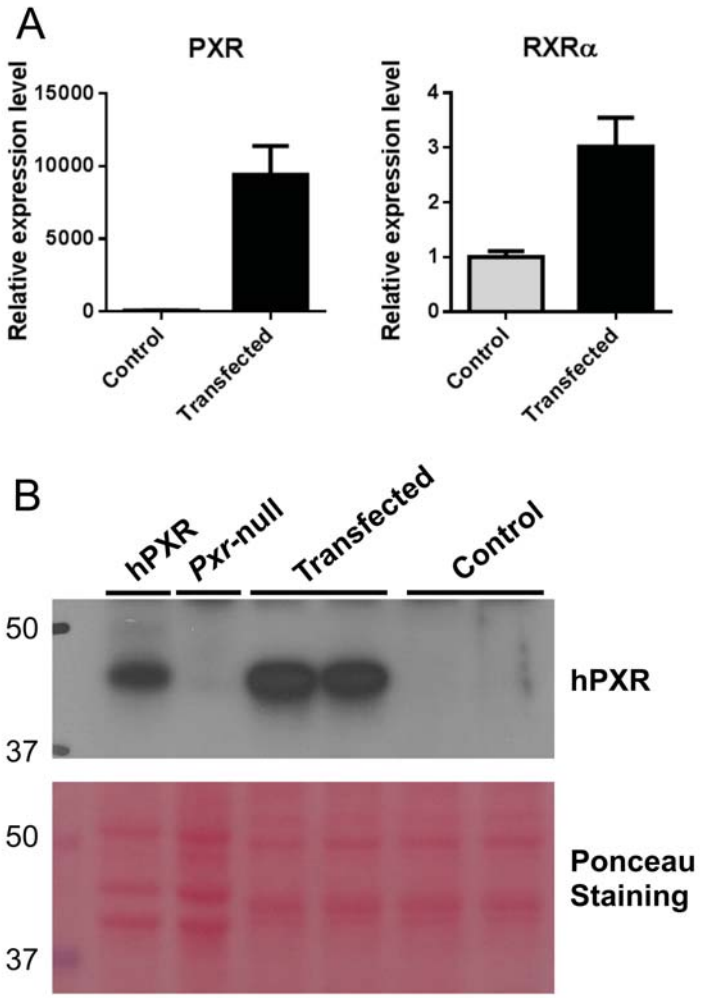
Supplemental Fig. 3. Tumor incidence in cohort 2 of *PXR*-humanized (hPXR), wild-type (WT), and *Pxr*-null mice with or without rifaximin treatment in AOM/DSS-induced colon carcinogenesis (n=10 per group). A. Total tumor incidence in hPXR, WT, and *Pxr*-null mice with or without rifaximin treatment in AOM/DSS-induced colon cancer. B. Percentage of tumors with diameter > 4 mm in hPXR, WT, and *Pxr*-null mice with or without rifaximin treatment. C. Percentage of tumors with diameter < 4 mm in hPXR, WT, and *Pxr*-null mice with or without rifaximin treatment.



Supplemental Fig. 4. Activation of human PXR after treatment with rifaximin for 1 week. The expression of *Cyp3a11* mRNA was determined in *PXR*-humanized (hPXR), wild-type (WT) and *Pxr*-null mice (n=5).*, $P<0.05$.



Supplemental Fig. 5. Analysis of mRNA and protein to demonstrate the transfection efficiency of human PXR and RXRα expression vector plasmids. (A) qPCR of mRNAs encoding human PXR and human RXRα. Human PXR-Forward: GGCCACTGGCTATCACTTCAA, Reverse: TTCATGGCCCTCCTGAAAA. Human RXRα-Forward: ACCGGAACAGCGCTCACA, Reverse: CTCCGTCTTGTCCATCTGCAT. Note that the primers for human *RXRA* mRNA do not amplify the mouse *Rxra* mRNA. (B) Western blotting of human PXR in nuclear extracts prepared from *PXR*-humanized (hPXR) and *Pxr*-null mouse livers and PXR/RXRα-transfected HT29 cells. Twenty μg of protein were loaded in each lane. Nuclear extracts from livers of *PXR*-humanized (hPXR) and *Pxr*-null mice were used as a negative and positive control, respectively. The human PXR in liver has a different mobility than the recombinant PXR. The mechanism of this difference is unknown but may be due to splicing differences of the PXR transcript in the liver.



Supplemental Fig. 6 (A) The apoptosis and cell cycle (% G0/G1) for rifaximin-treated RXRα-transfected cells. (B) Representative flow cytometry data;