Supplemental Material for

The atypical antipsychotic quetiapine induces hyperlipidemia by activating intestinal PXR signaling

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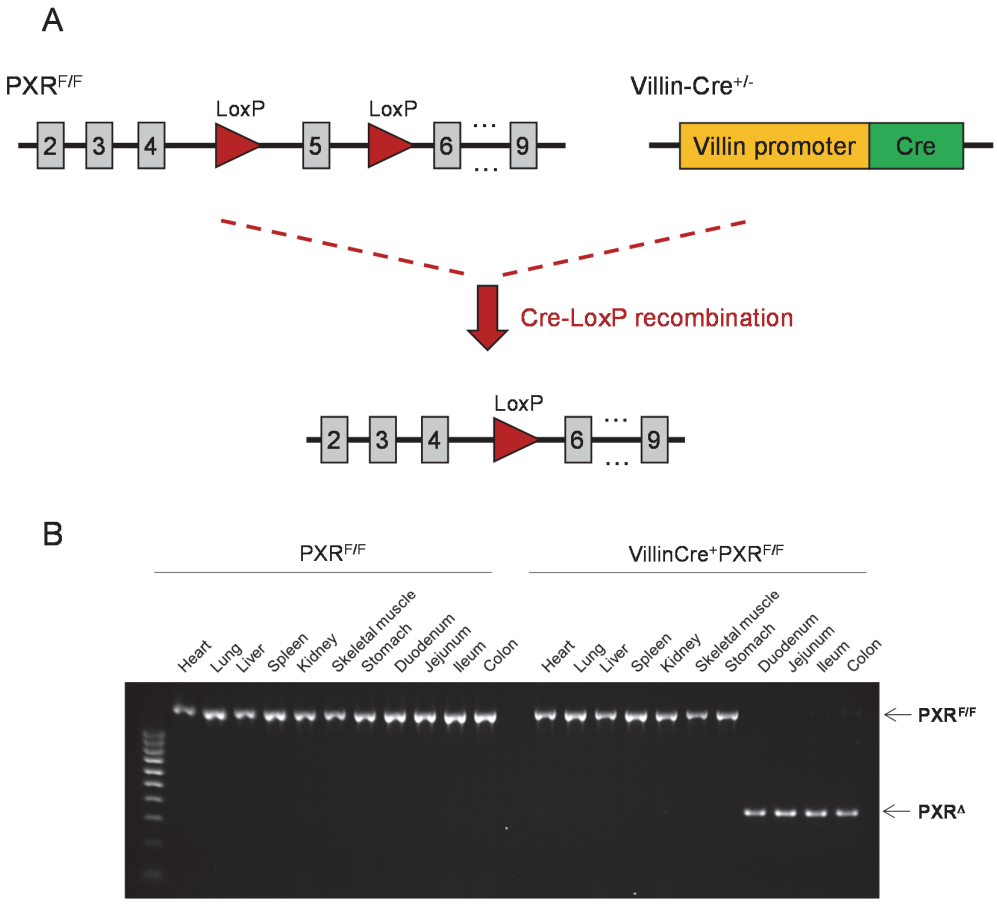
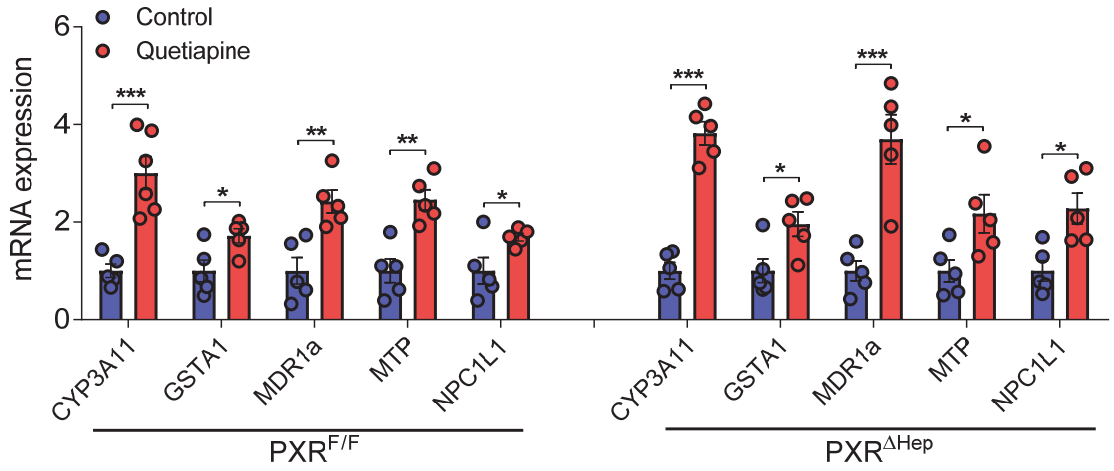
Supplemental Table 1

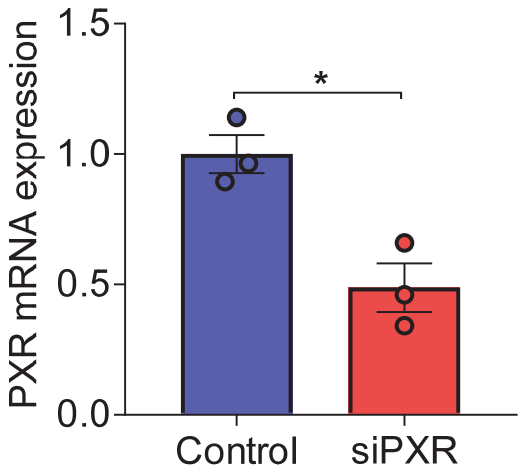


Supplemental Figure 1. Generation of intestine-specific PXR knockout mice.
(A) Schematic diagram of generating intestine-specific PXR knockout mice. (B) PCR analysis of genomic DNA from major tissues showing that Villin-Cre-mediated recombination was specific to the intestine.

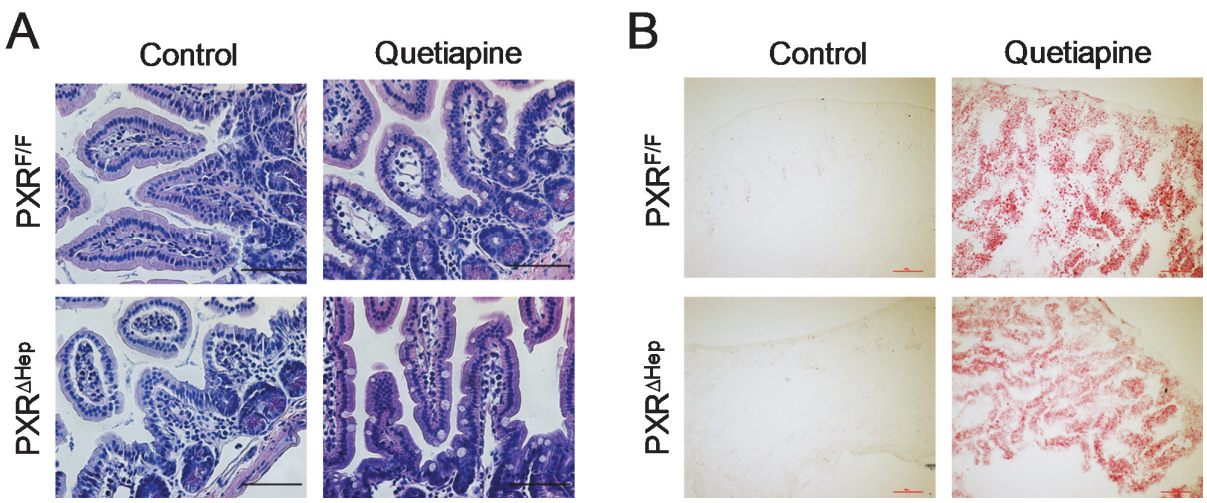


Supplemental Figure 2. Quetiapine stimulates intestinal NPC1L1 and MTP expression in both $PXR^{F/F}$ and $PXR^{\Delta Hep}$ mice

Eight-week-old male $PXR^{F/F}$ and $PXR^{\Delta Hep}$ littermates were treated with vehicle control or 10 mg/kg/day of quetiapine by oral gavage for 1 week. The expression levels of PXR target genes, NPC1L1, and MTP in the intestine of control or quetiapine-treated $PXR^{F/F}$ and $PXR^{\Delta Hep}$ mice were detected by QPCR. (n=5-6, Student's t-test, *P<0.05, **P<0.01, and ***P<0.001).



Supplemental Figure 3. SiRNA-mediated PXR knockdown in human LS180 cells.
Human intestinal LS180 cells were transfected with control siRNA or siRNA against PXR (siRXR). PXR mRNA levels in control or siPXR LS180 cells were analyzed by QPCR (n=3, Student's t-test, *P<0.05).



Supplemental Figure 4. Quetiapine enhances intestinal lipid accumulation in both $PXR^{F/F}$ and $PXR^{\Delta Hep}$ mice.

Eight-week-old male $PXR^{F/F}$ and $PXR^{\Delta Hep}$ littermates were treated with vehicle control or 10 mg/kg/day of quetiapine by oral gavage for 1 week. (A and B) Intestine sections were analyzed by hematoxylin & eosin (A) and Oil red O (B) staining. Scale bars, 50 μM (A) and 100 μM (B). (n=5-6).

Supplemental Table 1. Primer Sequences for QPCR, ChIP and EMSA.

Name	Sequence
Mouse primers	F R
ABCG5	5'-TGCCCATTCCTTTAAAAATCC-3' 5'-GATGAACTGGACCCCTTGG-3'
ABCG8	5'-GTAGCTGATGCCGATGACAA-3' 5'-GGGGCTGATGCAGATTCA-3'
CYP3A11	5'-CAGCTTGGTGCTCCTCTACC-3' 5'-TCAAACAACCCCCATGTTTT-3'
GAPDH	5'-AACTTTGGCATTGTGGAAGG-3' 5'-GGATGCAGGGATGATGTTCT-3'
GSTA1	5'-CAGCCTGGCAGCCAGAGA -3' 5'-TCTGTGGCTCCATCAATGCA-3'
MDR1a	5'-CCCCCGAGATTGACAGCTAC-3' 5'-ACTCCACTAAATTGCACATTTCCTTC-3'
MTP	5'-TGAGCGGCTATACAAGCTCAC-3' 5'-CTGGAAGATGCTCTTCTCGC-3'
NPC1L1	5'-TTGCCTTGACCTCTGGCTTAG-3' 5'-AGGGCGGATGAATCTGTGC-3'
PXR	5'-GACGCTCAGATGCAAACCTT-3' 5'-TCTTCTCCGCGCAGCTGCA-3'
Human Primers	F R
CYP3A4	5'-GGCTTCATCCAATGGACTGCATAAAT-3' 5'-TCCCAAGTATAACACTCTACACAGACAA-3'
GAPDH	5'-GGCCTCCAAGGAGTAAGACC-3' 5'-AGGGGAGATTCAGTGTGGTG-3'
GSTA1	5'-CAGCCTGGCAGCCAGAGA-3' 5'-TCTGTGGCTCCATCAATGCA-3'
MDR1a	5'-CCCCCGAGATTGACAGCTAC-3' 5'-ACTCCACTAAATTGCACATTTCCTTC-3'
MTP	5'-ACAAGCTCACGTACTCCACTG-3' 5'-TCCTCCATAGTAAGGCCACATC-3'
NPC1L1	5'-CTTCTACCAGCATAGCTTTGCC-3' 5'-AGAGCCATACACGCCACAC-3'
PXR	5'-GCACCTGCTGCTAGGGAATA-3' 5'-CTCCATTGCCCCTCCTAAGT-3'
UGT1A1	5'-TGCTCATTGCCTTTTCACAG-3' 5'-GGGCCTAGGGTAATCCTTCA-3'
Sequences of MTP oligos for ChIP and EMSA	F R
ChIP (human)	5'-CGAGAGACTACAAACTATAGCCCAC-3' 5'-CAAGGAAGTGACCCTCTTCAG-3'
ChIP (mouse)	5'-CTACAAACTATAGCCCACCTGC-3' 5'-GCAAGGAAGTGACCCTCTTCAG-3'
EMSA	5'-CCTGATTTTGGAGTTTGGAGTCTGACCTT-3' 5'-AAGGTCAGACTCCAAACTCCAAAATCAGG-3'
EMSA mutant	5'-CCTGATTTctaAGTTTatAGTCTGACCTT-3' 5'-AAGGTCAGACTatAAACTtagAAATCAGG-3'