Supplementary Information

Figure S1. OCA lowers plasma bile acid levels by activation of hepatic and intestinal FXR. *Fxr*$^{fl/fl}$ mice, *L-Fxr*$^{-/-}$ mice and *I-Fxr*$^{-/-}$ mice were gavaged with either vehicle or OCA for 7 days (n=6). Plasma bile acid levels were determined. * p<0.05, ** p<0.01 compared to the vehicle-treated control group of the same genotype.

Figure S2. OCA induces hepatic SR-BI expression. Wild-type mice were gavaged with either vehicle or OCA (n=6). Hepatic SR-BI mRNA (A) and protein (B) levels were determined. ** p<0.01

Figure S3. OCA treatment does not affect biliary cholesterol secretion but inhibits biliary bile acid secretion through activation of both hepatic and intestinal FXR. (**A-C**) Wild-type and *Fxr*$^{-/-}$ mice were gavaged with either vehicle or OCA for 7 days (n=6). After gallbladder was cannulated, the rates of bile acid secretion (**A**), bile flow (**B**) and biliary cholesterol secretion (**C**) were determined. (**D-F**) *Fxr*$^{fl/fl}$ mice, *L-Fxr*$^{-/-}$ mice and *I-Fxr*$^{-/-}$ mice were gavaged with either vehicle or OCA for 7 days (n=6). The rates of biliary bile acid secretion (**D**) and bile flow (**E**) were determined. * p<0.05, ** p<0.01 compared to vehicle-treated control group of the same genotype.

Figure S4. OCA treatment inhibits intestinal cholesterol absorption through activation of hepatic FXR. *Fxr*$^{fl/fl}$ mice, *L-Fxr*$^{-/-}$ mice and *I-Fxr*$^{-/-}$ mice were gavaged with either vehicle or OCA for 7 days (n=6). Intestinal cholesterol absorption was

determined. * p<0.05 compared to the vehicle-treated control group of the same genotype.

Figure S5. Effect of CYP7A1 and/or CYP8B1 over-expression on cholesterol absorption in wild-type mice. C57BL/6 mice were i.v. injected with Ad-GFP, Ad-rCyp7a1 and/or Ad-mCyp8b1 (n=6-7). On day 8, mice were given [^{3}H]cholesterol and [^{14}C]cholesterol and intestinal cholesterol absorption was performed using dual-isotope plasma ratio method (**A**). Hepatic *Cyp7a1* (**B**), rat *Cyp7a1* (**C**) and *Cyp8b1* (**D**) mRNA levels as well as protein levels (**E**) were determined. * p<0.05, ** p<0.01 compared to Ad-GFP-treated mice.

Figure S6. Effect of CYP7A1 and/or CYP8B1 over-expression on bile acid levels in the intestine, liver and gallbladder. C57BL/6 mice were i.v. injected with Ad-GFP, Ad-rCyp7a1 and/or Ad-mCyp8b1 (n=6-7). After 7 days, bile acids in the intestine (**A**), liver (**B**) and gallbladder (**C**) as well as total bile acid levels (**D**) were determined. * p<0.05, ** p<0.01 compared to Ad-GFP-treated mice.

Figure S1

Figure S2

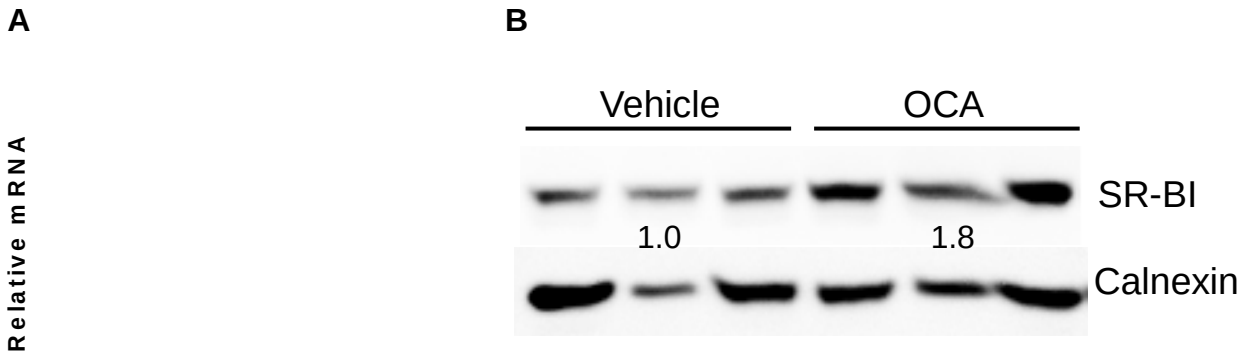


Figure S3

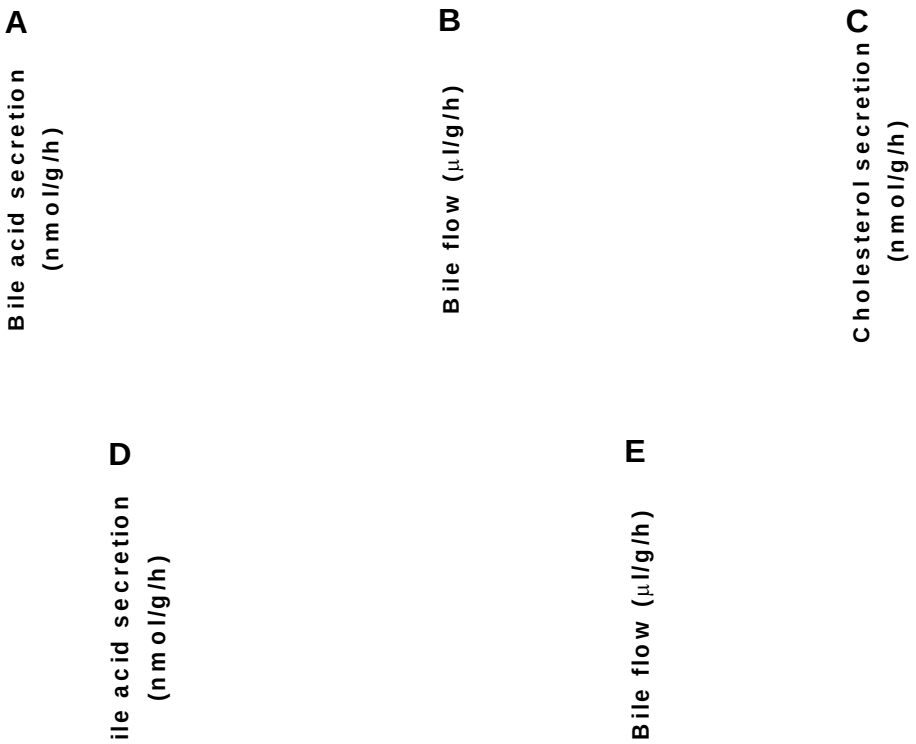

A
Bile acid secretion (nmol/g/h)
B
Bile flow (μl/g/h)
C
Cholesterol secretion (nmol/g/h)
D
Bile acid secretion (nmol/g/h)
E
Bile flow (μl/g/h)

Figure S4

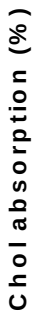


Figure S5

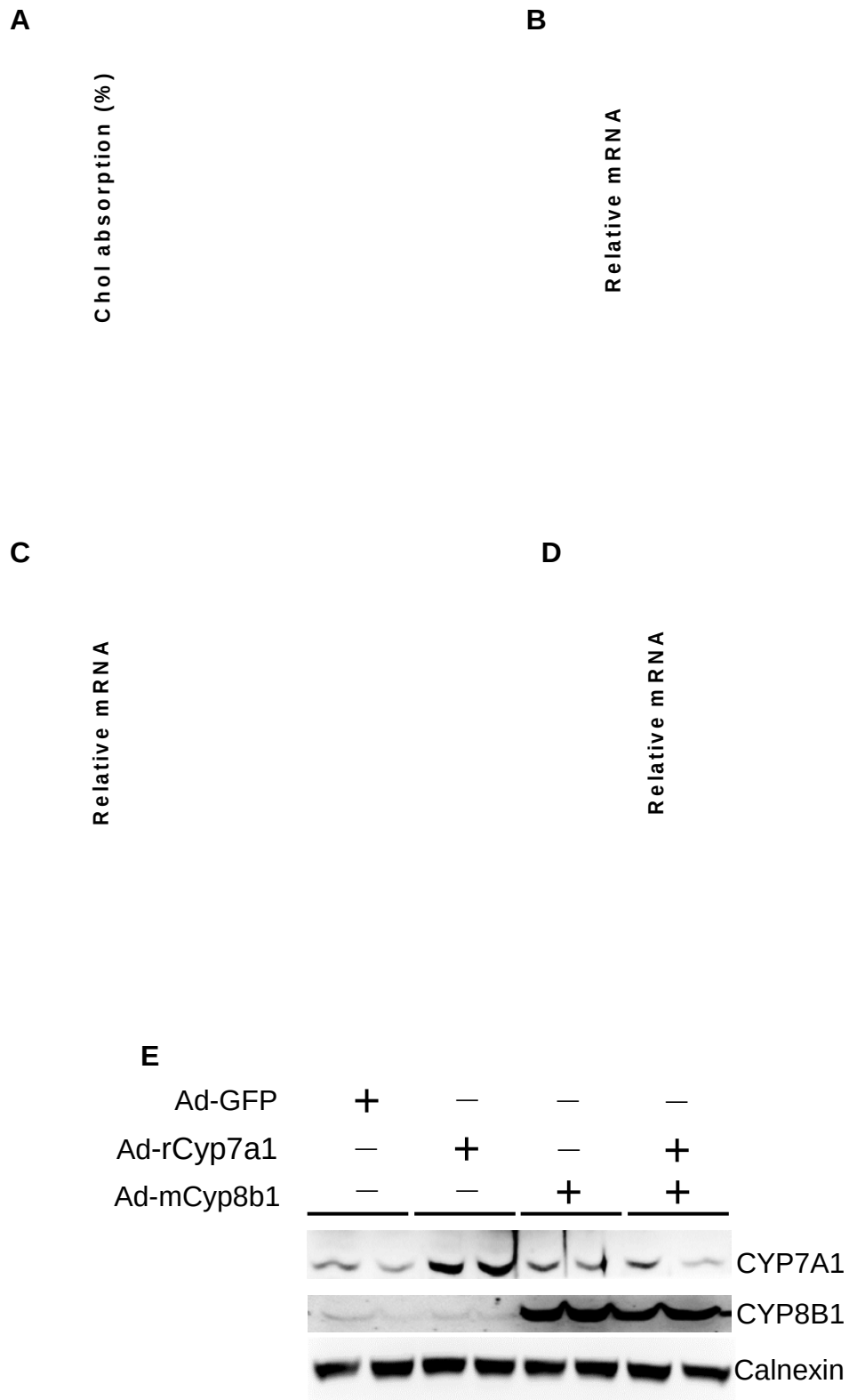
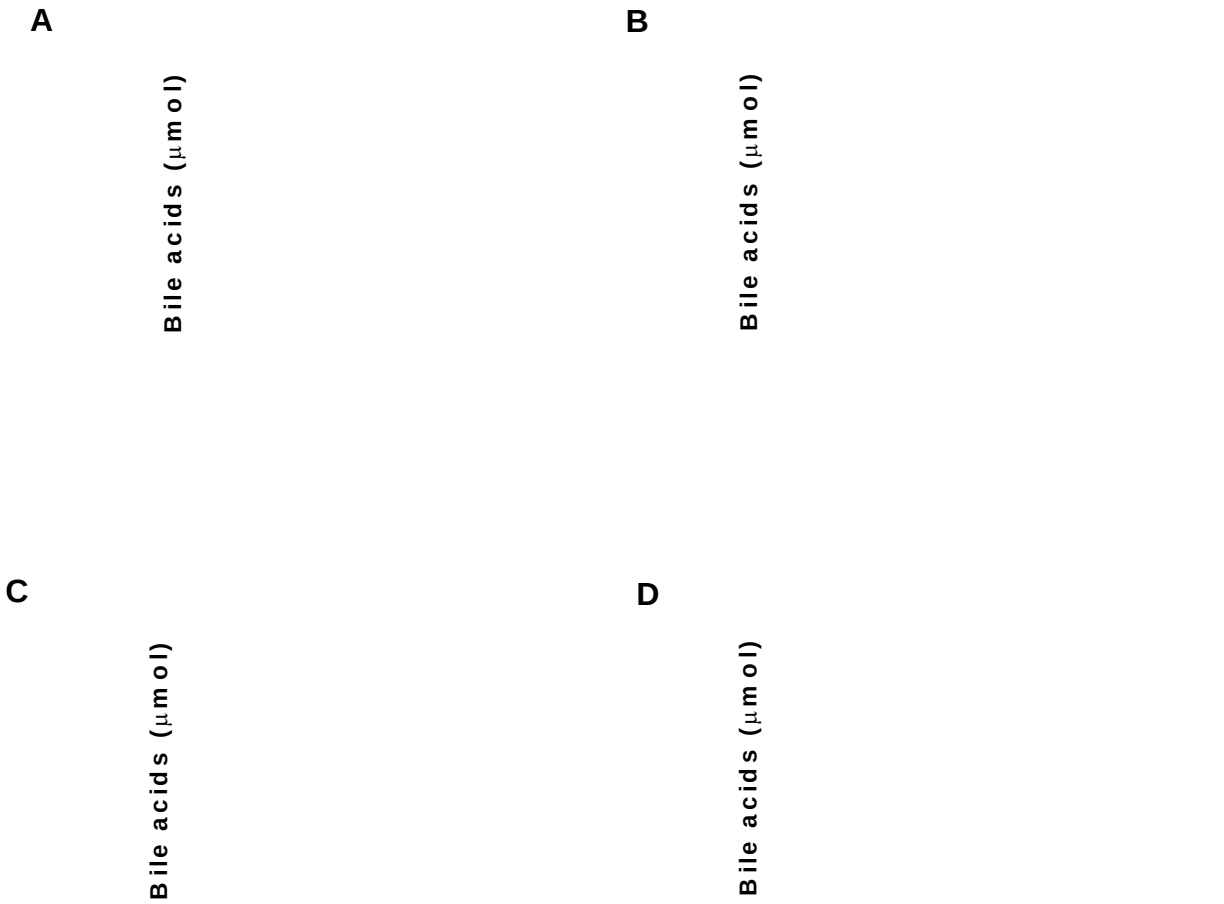

A
Chol absorption (%)
B
Relative mRNA
C
Relative mRNA
D
Relative mRNA
E
Ad-GFP + – – –
Ad-rCyp7a1 – + – +
Ad-mCyp8b1 – – + +
CYP7A1
CYP8B1
Calnexin

Figure S6


A
Bile acids (μmol)
B
Bile acids (μmol)
C
Bile acids (μmol)
D
Bile acids (μmol)