Supplemental figure legends

Figure S1. (A) Plasma bile acid levels in C57BL/6 mice infused with S4048 or vehicle (n = 7). (B) Plasma and (C) Fecal bile acid composition in L-*G6pc*$^{-/-}$ and L-*G6pc*$^{+/+}$ mice (n = 7-8). (D) Plasma C4 levels in L-*G6pc*$^{-/-}$ and L-*G6pc*$^{+/+}$ mice in either fed state or after an overnight fast (n = 7-8). (E) mRNA expression in IHH cells after low (1 mM) or high (11 mM) glucose exposure for 24 hours (n = 6).

Data represent Tukey boxplots. ***p < 0.001, ** p < 0.01 indicates significance compared to wildtype littermates or low glucose exposure.

Figure S2. (A) Hepatic *Cyp7a1* mRNA levels in L-*FoxO1,3,4*$^{+/+}$ and L-*FoxO1,3,4*$^{-/-}$ mice treated with S4048 or vehicle (n = 7-9). (B) Hepatic mRNA levels in C57BL/6 mice treated with either shChREBP or scrambled shRNA and infused with S4048 or vehicle (n = 6-7). (C) Hepatic mRNA and (D) Protein levels of bile acid synthesis enzymes in L-*G6pc*$^{+/+}$ and L-*G6pc*$^{-/-}$ mice treated with either shChREBP or scrambled shRNA (n = 3-6). Hepatic mRNA levels of transcriptional regulators of *Cyp8b1* in (E) S4048 or vehicle-infused C57BL/6 mice or (F) L-*G6pc*$^{-/-}$ and L-*G6pc*$^{+/+}$ mice treated with either shChREBP or scrambled shRNA (n = 4-7). (G) mRNA expression in IHH cells exposed to low glucose (1 mM) or high glucose (11 mM) or transfected with siChREBP or scramble after high glucose exposure for 24 hours (n = 6). (H) Biliary bile acid composition in mice treated with either shChREBP or scrambled shRNA and infused with S4048 or vehicle (n = 3-7).

Data represent Tukey boxplots. ***p < 0.001, **p < 0.01, *p < 0.05 indicates significance compared to scrambled shRNA. ###p < 0.001, ##p < 0.01, #p < 0.05 indicates significance compared to vehicle controls or wildtype littermates.

Figure S3. (A) *In vivo* ChIP analysis of the putative HNF4 response elements of the hepatic *Cyp8b1* and *L-pk* gene and (B) acetylated histone H3 at the hepatic *Cyp8b1* gene locus in mice treated with either shChREBP or scrambled shRNA and infused with S4048 or vehicle (n = 4-7).

Data represent means ± SEM. *p < 0.05 indicates significance compared to scrambled shRNA. #p < 0.05 indicates significance compared to vehicle controls.

Figure S4. (A) Correlation between *Cyp8b1* mRNA levels and bile hydrophobicity index and (B) correlation between *Cyp8b1* mRNA levels and fecal neutral sterol excretion in L-*G6pc*$^{-/-}$ and L-*G6pc*$^{+/+}$ mice (n = 8). (C) Fecal excretion of coprostanol (Copr), cholesterol (Chol) and dihydroxy-cholesterol (DiH-Col) in L-*G6pc*$^{-/-}$ and L-*G6pc*$^{+/+}$ mice and C57BL/6 mice treated with either shChREBP or scrambled shRNA (n = 7-14). (D) Fecal energy excretion and (E) fecal fatty acid excretion in L-*G6pc*$^{-/-}$ and L-*G6pc*$^{+/+}$ mice and C57BL/6 mice treated with either shChREBP or scrambled shRNA (n = 7-14).

Data represent Tukey boxplots. ***p < 0.001, *p < 0.05 indicates significance compared to wildtype littermates or scrambled shRNA.

Figure S1

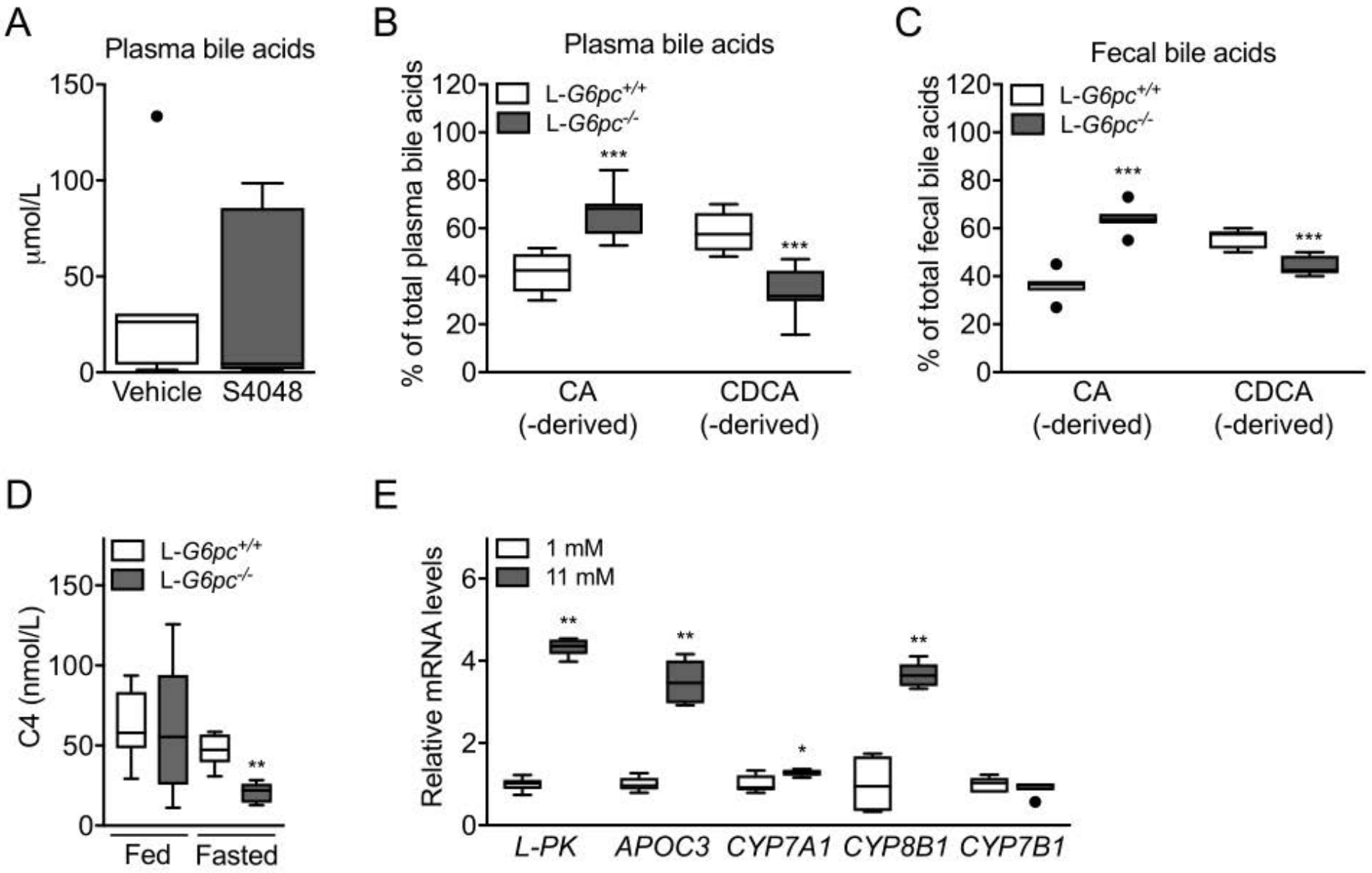
A
Plasma bile acids
µmol/L
150
100
50
0
Vehicle
S4048
B
Plasma bile acids
% of total plasma bile acids
120
100
80
60
40
20
0
L-G6pc+/+
L-G6pc-/-
***
***
CA
(-derived)
CDCA
(-derived)
C
Fecal bile acids
% of total fecal bile acids
120
100
80
60
40
20
0
L-G6pc+/+
L-G6pc-/-
***
***
CA
(-derived)
CDCA
(-derived)
D
C4 (nmol/L)
150
100
50
0
L-G6pc+/+
L-G6pc-/-
**
Fed
Fasted
E
Relative mRNA levels
6
4
2
0
1 mM
11 mM
**
**
*
**
L-PK
APOC3
CYP7A1
CYP8B1
CYP7B1

Figure S2

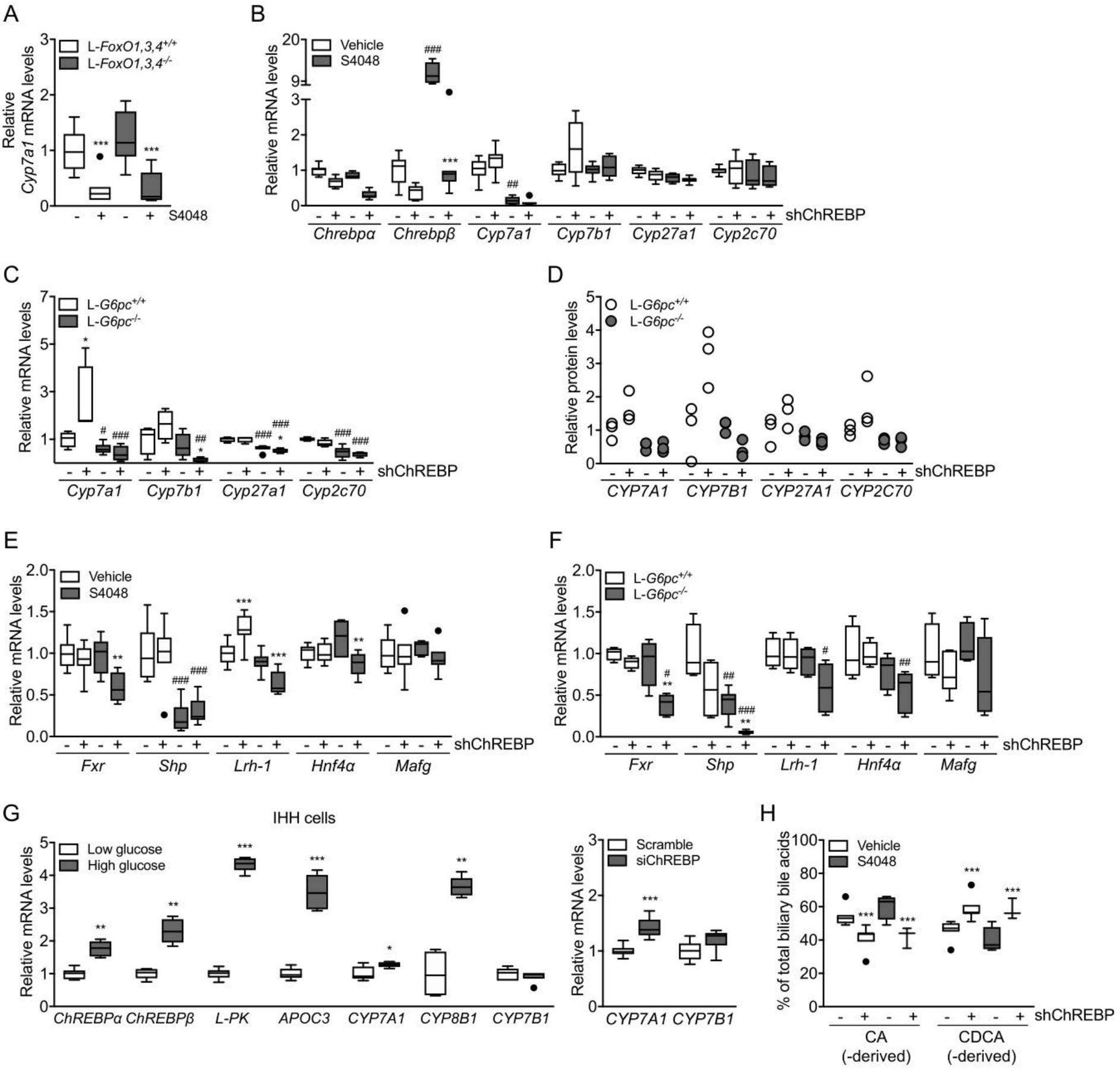
A
Relative Cyp7a1 mRNA levels
L-FoxO1,3,4+/+
L-FoxO1,3,4-/-
S4048
B
Relative mRNA levels
Vehicle
S4048
shChREBP
Chrebpα
Chrebpβ
Cyp7a1
Cyp7b1
Cyp27a1
Cyp2c70
C
Relative mRNA levels
L-G6pc+/+
L-G6pc-/-
shChREBP
Cyp7a1
Cyp7b1
Cyp27a1
Cyp2c70
D
Relative protein levels
L-G6pc+/+
L-G6pc-/-
shChREBP
CYP7A1
CYP7B1
CYP27A1
CYP2C70
E
Relative mRNA levels
Vehicle
S4048
shChREBP
Fxr
Shp
Lrh-1
Hnf4α
Mafg
F
Relative mRNA levels
L-G6pc+/+
L-G6pc-/-
shChREBP
Fxr
Shp
Lrh-1
Hnf4α
Mafg
G
IHH cells
Relative mRNA levels
Low glucose
High glucose
ChREBPα
ChREBPβ
L-PK
APOC3
CYP7A1
CYP8B1
CYP7B1
Relative mRNA levels
Scramble
siChREBP
CYP7A1
CYP7B1
H
% of total biliary bile acids
Vehicle
S4048
shChREBP
CA
(-derived)
CDCA
(-derived)

Figure S3

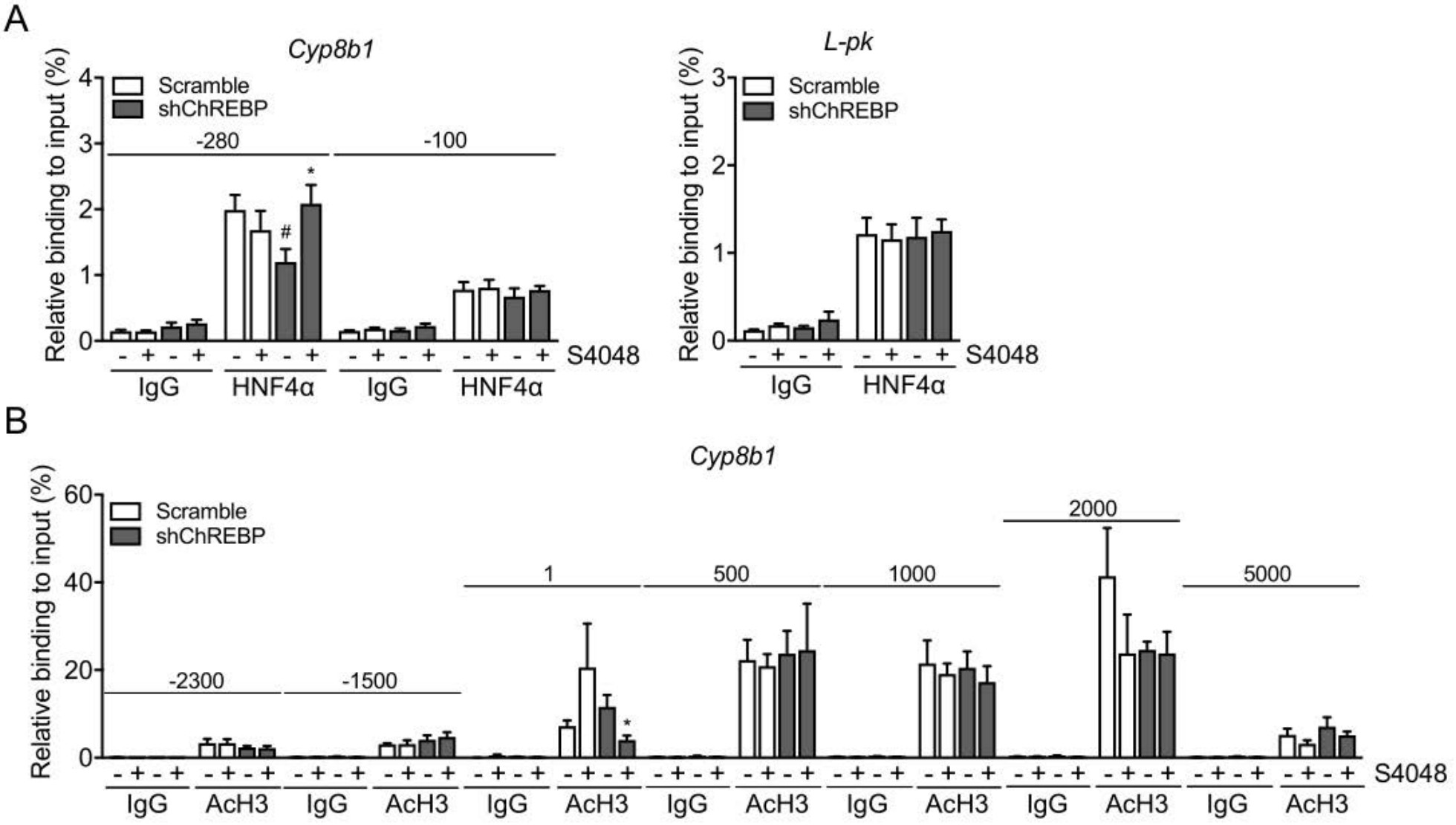
A
Cyp8b1
Scramble
shChREBP
Relative binding to input (%)
-280
-100
S4048
IgG
HNF4α
L-pk
B
Cyp8b1
-2300
-1500
1
500
1000
2000
5000
AcH3

Figure S4

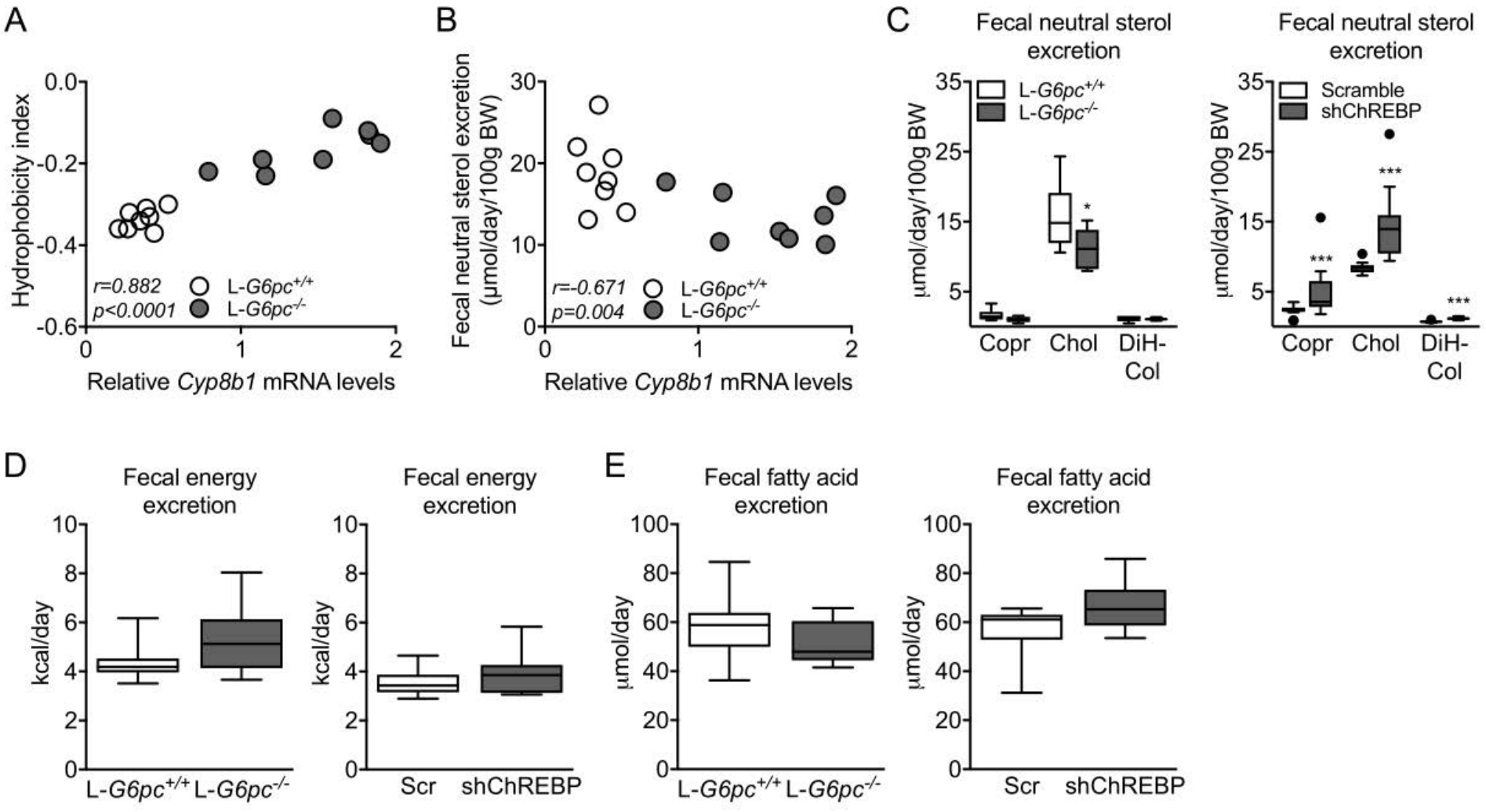
A
Hydrophobicity index
0.0
-0.2
-0.4
-0.6
r=0.882
p<0.0001
L-G6pc+/+
L-G6pc-/-
0
1
2
Relative Cyp8b1 mRNA levels
B
Fecal neutral sterol excretion (µmol/day/100g BW)
30
20
10
0
r=-0.671
p=0.004
L-G6pc+/+
L-G6pc-/-
0
1
2
Relative Cyp8b1 mRNA levels
C
Fecal neutral sterol excretion
µmol/day/100g BW
35
25
15
5
L-G6pc+/+
L-G6pc-/-
*
Copr
Chol
DiH-Col
Fecal neutral sterol excretion
µmol/day/100g BW
35
25
15
5
Scramble
shChREBP
***
***
***
Copr
Chol
DiH-Col
D
Fecal energy excretion
kcal/day
10
8
6
4
2
0
L-G6pc+/+
L-G6pc-/-
Fecal energy excretion
kcal/day
10
8
6
4
2
0
Scr
shChREBP
E
Fecal fatty acid excretion
µmol/day
100
80
60
40
20
0
L-G6pc+/+
L-G6pc-/-
Fecal fatty acid excretion
µmol/day
100
80
60
40
20
0
Scr
shChREBP

Table S1. Metabolic parameters in male C57BL/6 mice treated with S4048 or vehicle and in fasted L-*G6pc*$^{-/-}$ mice and wildtype littermates

	C57BL/6 Vehicle Median (Range)	C57BL/6 S4048 Median (Range)	*p*-value	L-*G6pc*$^{+/+}$ Median (Range)	L-*G6pc*$^{-/-}$ Median (Range)	*p*-value
Body weight (g)	21.3 (20.1 – 23.4)	22.1 (18.7 – 24.9)	0.902	28.4 (21.5 – 29.9)	27.5 (25.3 – 32.5)	0.645
Liver weight (g)	1.0 (0.8 – 1.0)	1.3 (1.0 – 1.4	**0.009**	1.3 (0.8 – 1.5)	1.8 (1.6 – 2.0)	**<0.001**
Liver to body weight ratio (%)	4.3 (3.5 – 5.0)	5.6 (4.8 – 6.2)	**0.009**	4.4 (3.5 – 5.1)	6.7 (6.0 – 7.1)	**<0.001**
Blood glucose (mmol/L)	6.4 (4.1 – 6.9)	2.4 (1.7 – 2.9)	**0.001**	5.0 (3.7 – 8.4)	2.1 (1.7 – 2.4)	**<0.001**
Hepatic G6P (nmol/g liver)	67.1 (59.2 – 83.7)	128.9 (60.6 – 241.0)	0.051	421.7 (264.5 – 483.3)	2585.5 (1980.9 – 3457.3)	**<0.001**
Hepatic glycogen (mg/g liver)	2.2 (1.3 – 2.7)	39.8 (31.3 – 44.4)	**0.004**	17.7 (12.4 – 29.5)	54.2 (46.4 – 62.1)	**<0.001**
Glucagon (pg/mL)	138.4 (78.8 – 200.1)	225.4 (135.2 – 649.9)	**0.017**	112.7 (86.2 – 132.3)	235.9 (136.8 – 581.8)	**<0.001**
Insulin (ng/mL)	0.2 (0.1 – 0.3)	0.2 (0.1 – 0.3)	0.343	0.3 (0.1 – 0.6)	0.2 (0.1 – 0.4)	0.130

Table S2. Plasma and fecal bile acid profiles in L-*G6pc*$^{-/-}$ mice and wildtype littermates

Bile acid species	L-*G6pc*$^{+/+}$ Median (Range)	L-*G6pc*$^{-/-}$ Median (Range)	*p*-value
Plasma (µmol/L)			
CA	0.41 (0.14 – 2.39)	0.46 (0.08 – 3.19)	1.000
TCA	0.26 (0.08 – 0.35)	0.65 (0.14 – 1.29)	0.281
DCA	0.62 (0.33 – 1.43)	0.30 (0.06 – 1.11)	0.232
TDCA	0.11 (0.06 – 0.18)	0.26 (0.09 – 0.34)	**0.021**
UDCA	0.14 (0.03 – 0.36)	0.09 (0.05 – 0.16)	0.497
TUDCA	0.04 (0.03 – 0.05)	0.05 (0.04 – 0.05)	1.000
CDCA	0.06 (0.02 – 0.14)	0.06 (0.02 – 0.10)	0.648
HDCA	0.07 (0.03 – 0.17)	0.05 (0.03 – 0.14)	0.921
THDCA	0.03 (0.03 – 0.03)	0.03 (0.03 – 0.03)	1.000
α-MCA	0.10 (0.05 – 0.19)	0.04 (0.03 – 0.09)	0.114
Tα-MCA	0.05 (0.01 – 0.07)	0.08 (0.01 – 0.12)	0.106
β-MCA	0.56 (0.14 – 2.63)	0.16 (0.03 – 0.89)	0.093
Tβ-MCA	0.10 (0.04 – 0.26)	0.06 (0.01 – 0.33)	0.649
ω-MCA	1.00 (0.48 – 4.25)	0.43 (0.11 – 1.75)	**0.040**
Total	3.14 (1.51 – 11.41)	2.62 (0.67 – 8.36)	0.232
Feces (µmol/day/100g BW)			
CA	0.57 (0.38 – 0.97)	1.01 (0.49 – 1.69)	**0.028**
UDCA	0.31 (0.19 – 0.51)	0.29 (0.20 – 0.36)	0.645
DCA	2.24 (1.61 – 3.99)	3.22 (1.92 – 4.54)	**0.050**
HDCA	0.23 (0.15 – 0.55)	0.20 (0.11 – 0.26)	0.161
α-MCA	0.66 (0.41 – 1.05)	0.74 (0.44 – 1.16)	0.574
β-MCA	0.96 (0.74 – 1.97)	0.61 (0.43 – 1.05)	**0.005**
ω-MCA	2.61 (1.84 – 4.03)	1.64 (0.78 – 2.00)	**0.001**
Total	7.71 (6.44 – 11.88)	8.14 (4.81 – 9.45)	0.878

Table S3. Biliary and plasma bile acid profiles in male C57BL/6 mice injected with either shChREBP or scramble AAV2/8 and treated with S4048 or vehicle

Bile acid species	Scramble vehicle Median (Range)	Scramble S4048 Median (Range)	*p*-value	ShChREBP vehicle Median (Range)	ShChREBP S4048 Median (Range)	*p*-value
Bile (% of total)						
CA	0.56 (0.22 – 3.16)	2.95 (2.35 – 3.10)	0.073	0.75 (0.09 – 3.78)	1.38 (0.18 – 3.03)	0.833
GCA	0.13 (0.11 – 0.18)	0.18 (0.16 – 0.26)	0.109	0.08 (0.05 – 0.180	0.11 (0.09 – 0.12)	0.833
TCA	48.65 (46.70 – 62.57)	53.93 (43.28 – 56.99)	0.527	38.15 (24.71 – 47.28)	38.37 (32.47 – 45.77)	1.000
TDCA	2.17 (1.35 – 3.66)	3.80 (2.60 – 4.99)	**0.024**	0.58 (0.49 – 0.74)	0.83 (0.68 – 1.23)	0.067
TUDCA	1.00 (0.87 – 1.14)	1.00 (0.96 – 1.41)	0.648	1.09 (0.68 – 1.30)	1.09 (0.59 – 1.20)	0.833
TCDCA	0.98 (0.68 – 1.27)	1.10 (1.02 – 1.76)	0.315	1.57 (1.18 – 1.94)	1.79 (0.63 – 2.23)	0.833
THDCA	0.71 (0.28 – 1.58)	2.65 (0.77 – 3.25)	**0.024**	0.79 (0.16 – 1.69)	0.91 (0.19 – 1.15)	0.833
α-MCA	0.03 (0.00 – 0.38)	0.37 (0.21 – 0.38)	**0.024**	0.05 (0.00 – 0.39)	0.20 (0.00 – 0.64)	0.833
Tα-MCA	6.80 (5.32 – 8.16)	7.82 (6.96 – 8.55)	0.164	7.26 (5.65 – 9.15)	10.14 (4.61 – 10.88)	0.517
β-MCA	0.30 (0.08 – 0.85)	0.43 (0.25 – 0.75)	0.648	0.41 (0.14 – 1.58)	0.65 (0.18 – 0.99)	0.833
Tβ-MCA	35.84 (26.48 – 42.43)	23.65 (20.66 – 39.14)	0.073	45.12 (43.05 – 56.81)	46.89 (37.42 – 49.76)	1.000
ω-MCA	0.34 (0.23 – 1.09)	1.06 (0.59 – 1.72)	**0.042**	0.47 (0.22 – 1.81)	0.64 (0.18 – 2.75)	1.000
Plasma (µmol/L)						
CA	0.24 (0.14 – 0.71)	0.35 (0.11 – 10.10)	0.710	2.37 (0.21 – 44.60)	0.68 (0.25 – 4.65)	0.445
GCA	0.04 (0.04 – 0.16)	0.05 (0.03 – 0.09)	0.686	0.05 (0.03 – 0.24)	0.04 (0.04 – 0.05)	0.857
TCA	13.30 (0.17 – 65.20)	1.80 (0.14 – 37.00)	0.620	3.94 (0.94 – 31.70)	1.95 (0.47 – 17.30)	0.165
DCA	0.11 (0.07 – 0.57)	0.21 (0.10 – 3.08)	0.128	0.26 (0.06 – 0.99)	0.12 (0.05 – 0.46)	0.534
TDCA	0.24 (0.05 – 2.86)	0.14 (0.05 – 2.16)	0.805	0.14 (0.03 – 0.52)	0.12 (0.05 – 0.64)	1.000
UDCA	0.03 (0.03 – 0.05)	0.04 (0.03 – 0.26)	0.250	0.10 (0.05 – 0.52)	0.04 (0.03 – 0.07)	0.015
TUDCA	0.23 (0.03 – 0.87)	0.09 (0.03 – 0.48)	0.662	0.10 (0.04 – 0.63)	0.07 (0.04 - 0.33)	0.318
CDCA	0.05 (0.03 – 0.06)	0.09 (0.04 – 0.29)	0.400	0.12 (0.03 – 1.44)	0.06 (0.03 – 0.14)	0.394
TCDCA	0.20 (0.05 – 0.79)	0.17 (0.03 – 0.36)	0.730	0.08 (0.03 – 1.35)	0.05 (0.03 – 0.33)	0.383
HDCA	0.04 (0.03 – 0.06)	0.04 (0.04 – 0.16)	0.267	0.07 (0.03 – 0.32)	0.06 (0.03 – 0.16)	0.589
THDCA	0.07 (0.03 – 0.41)	0.10 (0.04 – 0.51)	0.445	0.14 (0.05 – 0.45)	0.06 (0.03 – 0.15)	0.101
α-MCA	0.04 (0.04 – 0.13)	0.14 (0.04 – 0.43)	0.229	0.22 (0.04 – 3.83)	0.05 (0.03 – 0.39)	0.836
Tα-MCA	1.36 (0.25 – 5.62)	0.28 (0.03 – 3.56)	0.295	0.83 (0.21 – 7.40)	0.17 (0.07 – 1.68)	0.073
β-MCA	0.22 (0.12 – 1.01)	0.26 (0.06 – 6.88)	0.805	1.53 (0.03 – 18.50)	0.69 (0.35 – 5.28)	0.165
Tβ-MCA	9.66 (0.07 – 52.60)	0.64 (0.11 – 39.80)	0.535	4.52 (1.56 – 59.00)	1.37 (0.31 – 26.50)	0.097
ω-MCA	0.51 (0.25 – 2.46)	0.89 (0.42 – 6.88)	0.318	1.42 (0.10 – 5.97)	1.03 (0.39 – 4.15)	0.535
Total	26.32 (1.27 – 133.43)	4.46 (1.30 – 98.50)	0.620	13.67 (3.80 – 166.63)	6.69 (3.18 – 51.00)	0.383

Table S4. Fecal bile acid profile in chow-fed C57BL/6 mice injected with either shChREBP or scramble AAV2/8

Bile acid species	Scramble Median (Range)	shChREBP Median (Range)	*p*-value
Feces (µmol/day/100g BW)			
CA	1.48 (0.36 – 2.54)	1.03 (0.22 – 2.02)	0.210
DCA	1.55 (0.81 – 2.04)	0.92 (0.49 – 1.27)	**<0.001**
CDCA	0.07 (0.00 – 0.15)	0.00 (0.00 – 0.13)	0.743
α-MCA	0.40 (0.29 – 0.53)	0.31 (0.21 – 0.41)	**0.002**
β-MCA	0.83 (0.47 – 1.40)	0.93 (0.35 – 1.67)	0.210
ω-MCA	1.15 (0.66 – 1.58)	1.11 (0.52 – 1.78)	0.946
Total	5.31 (3.61 – 7.01)	4.61 (2.54 – 5.57)	0.085

Table S5. Biliary and plasma bile acid profiles in chow-fed L-*G6pc*$^{-/-}$ mice and wildtype littermates, injected with either shChREBP or scramble AAV2/8

	L-*G6pc*$^{+/+}$ Scramble Median (Range)	L-*G6pc*$^{+/+}$ shChREBP Median (Range)	*p*-value	L-*G6pc*$^{-/-}$ Scramble Median (Range)	L-*G6pc*$^{-/-}$ shChREBP Median (Range)	*p*-value
Bile (% of total)						
CA	5.69 (1.97 – 7.32)	0.53 (0.00 – 3.46)	0.057	4.47 (3.64 – 7.80)	0.04 (0.00 – 0.22)	**0.016**
GCA	0.27 (0.11 – 0.30)	0.00 (0.00 – 0.11)	**0.029**	0.23 (0.21 – 0.39)	0.01 (0.00 – 0.09)	**0.016**
TCA	52.81 (46.69 – 59.94)	16.57 (10.70 – 29.58)	**0.029**	64.54 (50.90 – 68.52)	30.42 (25.20 – 41.08)	**0.016**
TUDCA	1.77 (1.01 – 2.35)	0.61 (0.21 – 1.19)	0.057	1.71 (0.46 – 2.10)	0.10 (0.00 – 0.22)	**0.016**
TCDCA	1.20 (0.48 – 1.79)	0.83 (0.45 – 1.11)	0.686	1.70 (0.38 – 1.94)	0.06 (0.00 – 0.13)	**0.016**
TDCA	1.83 (0.92 – 2.79)	0.06 (0.00 – 0.60)	**0.029**	1.22 (0.62 – 2.19)	0.01 (0.00 – 0.04)	**0.016**
THDCA	0.67 (0.45 – 1.16)	0.14 (0.00 – 0.39)	**0.029**	0.43 (0.24 – 0.68)	0.03 (0.00 - 0.07)	**0.016**
α-MCA	0.22 (0.06 – 0.53)	0.14 (0.00 – 0.34)	0.486	0.33 (0.14 – 0.72)	0.00 (0.00 – 0.01)	**0.016**
Tα-MCA	5.34 (3.30 – 8.70)	2.54 (0.76 – 4.80)	0.114	7.26 (2.71 – 7.98)	0.50 (0.42 – 0.68)	**0.016**
β-MCA	1.08 (0.31 – 1.74)	2.22 (0.00 – 4.40)	0.686	0.41 (0.32 – 1.07)	0.05 (0.00 – 0.49)	0.111
Tβ-MCA	26.41 (24.28 – 36.30)	75.66 (53.19 – 86.35)	**0.029**	19.37 (13.24 – 24.00)	68.67 (58.49 – 72.89)	**0.016**
ω-MCA	0.73 (0.25 - 2.19)	0.91 (0.00 – 1.93)	0.886	0.35 (0.23 – 0.77)	0.01 (0.00 – 0.13)	**0.016**
Plasma (μmol/L)						
CA	2.48 (1.51 – 3.44)	0.19 (0.19 – 0.19)	0.221	2.78 (2.03 – 3.28)	0.84 (0.82 – 24.00)	0.513
TCA	2.63 (0.73 – 4.54)	6.75 (6.74 – 6.76)	0.121	4.19 (1.63 – 5.14)	159.00 (39.20 – 250.00)	**0.050**
GCA	0.03 (0.02 – 0.03)	0.03 (0.02 – 0.04)	0.683	0.03 (0.02 – 0.04)	0.69 (0.27 – 1.42)	0.083
DCA	0.71 (0.42 – 1.00)	0.02 (0.01 – 0.03)	0.121	0.33 (0.29 – 0.52)	0.03 (0.02 – 0.03)	**0.050**
TDCA	0.14 (0.07 – 0.21)	0.03 (0.03 – 0.03)	0.121	0.11 (0.09 – 0.14)	0.11 (0.08 – 0.29)	1.000
UDCA	0.35 (0.27 – 0.43)	0.03 (0.03 – 0.03)	0.221	0.24 (0.17 – 0.33)	0.03 (0.03 – 0.03)	0.180
TUDCA	0.09 (0.05 – 0.14)	0.12 (0.11 – 0.14)	0.439	0.08 (0.06 – 0.10)	0.58 (0.35 – 0.82)	**0.050**
CDCA	0.13 (0.09 – 0.17)	0.04 (0.04 – 0.04)	0.221	0.13 (0.10 – 0.15)	0.01 (0.01 – 0.01)	**0.037**
TCDCA	0.05 (0.01 – 0.08)	0.21 (0.21 – 0.22)	0.121	0.07 (0.05 – 0.11)	0.53 (0.32 – 0.84)	**0.050**
GCDCA	0.01 (0.01 – 0.01)	0.01 (0.01 – 0.01)	0.121	0.01 (0.01 – 0.01)	0.02 (0.01 – 0.04)	**0.050**
HDCA	0.14 (0.10 – 0.17)	0.01 (0.01 – 0.01)	0.221	0.10 (0.08 – 0.11)	0.01 (0.01 – 0.03)	**0.046**
GHDCA	0.00 (0.00 – 0.00)	0.01 (0.01 – 0.010	0.121	0.00 (0.00 – 0.00)	0.10 (0.07 – 0.21)	**0.050**
THDCA	0.05 (0.03 – 0.06)	0.04 (0.04 – 0.04)	1.000	0.03 (0.02 – 0.07)	0.26 (0.17 – 0.35)	0.083
α-MCA	0.20 (0.07 – 0.32)	0.02 (0.02 – 0.02)	0.221	0.20 (0.17 – 0.21)	0.05 (0.02 – 0.08)	0.083
Tα-MCA	0.41 (0.14 – 0.68)	0.45 (0.35 – 0.55)	1.000	0.41 (0.14 – 0.42)	2.06 (1.41 – 4.28)	**0.050**
β-MCA	1.81 (1.27 – 2.35)	0.87 (0.15 – 1.60)	0.439	0.93 (0.93 – 1.62)	4.46 (1.43 – 18.70)	0.121
Tβ-MCA	1.24 (0.23 – 2.24)	36.80 (21.30 – 52.30)	0.121	0.93 (0.23 – 1.02)	322.00 (130.00 – 353.00)	**0.050**
ω-MCA	2.15 (1.46 – 2.84)	0.56 (0.09 – 1.04)	0.121	1.04 (0.87 – 1.16)	1.24 (0.38 – 8.58)	0.513
Tω-MCA	10.09 (3.78 – 16.40)	97.25 (70.50 – 124.00)	0.121	4.73 (2.48 – 5.77)	524.00 (168.00 – 1110.00)	**0.050**
Total	22.68 (10.26 – 35.09)	143.28 (102.51 – 187.05)	0.121	17.55 (10.11 – 18.20)	1012.28 (346.47 – 1772.22)	**0.050**

Table S6. Taqman and SYBR Green qPCR primer and probe sequences

Gene	Species	Forward primer 5'-3'	Reverse primer 5'-3'	TaqMan probe 5'-3'
Primers for qPCR				
36b4	Mouse	GCT TCA TTG TGG GAG CAG ACA	CAT GGT GTT CTT GCC CAT CAG	TCC AAG CAG ATG CAG CAG ATC CGC
18S	Human	CGG CTA CCA CAT CCA AGG A	CCA ATT ACA GGG CCT CGA AA	CGC GCA AAT TAC CCA CTC CCG A
Cyp8b1	Mouse	AAG GCT GGC TTC CTG AGC TT	AAC AGC TCA TCG GCC TCA TC	CGG CTA CAC CAA GGA CAA GCA GCA AG
CYP8B1	Human	CCT GAG CTT GTT CGG CTA CAC	TGC GGA ACT CCA TGA ATA ACT CTC	CCT GTA GCA GGT CCT GCT CCT TGT CCT T
Cyp7a1	Mouse	CAG GGA GAT GCT CTG TGT TCA	AGG CAT ACA TCC CTT CCG TGA	TGC AAA ACC TCC AAT CTG TCA TGA GAC CTC C
CYP7A1	Human	TCA GCT TGG AAG GCA ATC CTA T	AGC CTC AGC GAT TCC TTG ATT A	CTG GCA GGT CAT TCA GTT CTG CTT GAC TC
Cyp7b1	Mouse	TGA AAT AGG AGC ACA TCA TCT TGG	AAT ACA TTG CCC AGA ACA TAG CTG	CTC TGG GCC TCT CTA GCA AAC ACC ATT C
CYP7B1	Human	CTT GAA ATA GGA GCA CAT CAT TTA GG	GAT AAT ACA TTG CCC AGA ACA TAG TTG	CTC TGG GCC TCT GTG GCA AAC ACT ATT C
Cyp27a1	Mouse	GCC TTG CAC AAG GAA GTG ACT	CGC AGG GTC TCC TTA ATC ACA	CCC TTC GGG AAG GTG CCC CAG
Cyp2c70[a]	Mouse	CCA CAG TGA AAT ATG GGC TTT T	AAT TTA GCT GTG ACT TCT GG	
ChREBPα	Mouse	CGA CAC TCA CCC ACC TCT TC	TTG TTC AGC CGG ATC TTG TC	CCT GGC TTA CAG TGG CAA GCT GGT CTC T
ChREBPα[a]	Human	AGT GCT TGA GCC TGG CCT AC	TTG TTC AGG CGG ATC TTG TC	
ChREBPβ	Mouse	TCT GCA GAT CGC GTG GAG	CTT GTC CCG GCA TAG CAA C	CTC AGT GGC AAG CTG GTC TCT CCC A
ChREBPβ[a]	Human	AGC GGA TTC CAG GTG AGG	TTG TTC AGG CGG ATC TTG TC	
Fxr	Mouse	CGC TGA GAT GCT GAT GTC TTG	CCA TCA CTG CAC ATC CCA GAT	ATG ATC ACA AGT TCA CCC CGC TCC TCT
Shp	Mouse	AAG GGC ACG ATC CTC TTC AA	CTG TTG CAG GTG TGC GAT GT	ATG TGC CAG GCC TCC GTG CC
Lrh-1	Mouse	TGC TGG AGT GAG CTC TTG ATT C	GAT GGT GGA GTA GTC CAC GTG T	CCT TCC TTC CCA TGC GCC ACT TG
Hnf4α	Mouse	ATG CCA AGG GGC TGA GTG AC	GCC GGT CGT TGA TGT AAT CCT	CAC CTG TGA CCG CAG CCG CTT G
L-PK	Human	TGT CTG TGC CAC ACA GAT GCT	CAT TGG CGA CAT CGC TTG TCT	CAT GAT TAC CAA GCC CCG GCC AAC
APOC3	Human	ATG AAG CAC GCC ACC AAG AC	TTG TCC TTA ACG GTG CTC CAG TA	CAC CCA GCC CCT GGC CTG CT
Mafg[a]	Mouse	CAA GGC CTT AAA GGT GAA GCG	TTC AAC TCT CGC ACC GAC AT	
Acly	Mouse	GGA GAA GTT GGG AAG ACC ACT G	CAA TGG CCG TCA TGT GAG TT	ATC CCC ATC CAT GTC TTT GGC ACA GA
Primers for subcloning				
ChREBPα		GCG AAA CTT AAG AGA TCT ATG GCG CGC GCG CT	GCG AAA GCG GCC GCG CTT GGA AAC TTT CAC CAG G	
ChREBPβ		GCG AAA CTT AAG ATG CGC GAA TAC CAC AAG TGG A	GCG AAA GCG GCC GCG CTT GGA AAC TTT CAC CAG G	
Mlx		GCG AAA AAG CTT ATG GCC TAC CCA TAC GAC GT	GCG AAA CTC GAG TCA GTA GAG TTG GTT TTT CAA CTG	

[a]Sybr Green method used

Table S7. SYBR Green primers used for ChIP-qPCR

Region	Forward primer 5'-3'	Reverse primer 5'-3'
L-pk	GCT CTG CAG ACA GGC CAA AG	TCT TGC CAA TGG AAG CCT TG
Cyp8b1 region a[a]	GAG ACG AGG AAA GAG ATG TG	CAC CGA CTG CTC ACA TTC C
Cyp8b1 region b[a]	GAG CTG AAC CTG AAC AGT AG	CAG AGG CTC GGA CGT G
Cyp8b1 region c[a]	ACC ACG TCC GAG CCT CTG	GGA ATT GCT TTA TGT GGC
Cyp8b1 region d[a]	GGT GGG CTC AAG GCA G	GCT GAC TAG AGA GAC GAT G
Cyp8b1 region -2300	CTG CAG GAC AGA TTT CAT CTT G	TCA ACT GCA GAA TGT GTT AGG AC
Cyp8b1 region -1500	AGG CCC CAC AGA TAG ATT CA	CTG AGC ATC TGT CAG GGT GA
Cyp8b1 region -280	TAA GGA GAC ACC GTC TCT AC	GAG ACC TGA CAT CCC TCT AC
Cyp8b1 region -100	TTG CAG AGG ACG ATA CC	AAA GTG CGT GTC TGT G
Cyp8b1 region 1	CAG CGC TGT AGA GCT GAC AA	CAC TGT ACA CCA CAG CGT CA
Cyp8b1 region 500	TCC TGA GCT TAT TCG GCT ACA	CGG AAC TTC CTG AAC AGC TC
Cyp8b1 region 1000	CAG CGG ACA AGA GTA CCA GA	GGG GTC CAT GTG TAC TGA GAG
Cyp8b1 region 2000	CGA TGC CCT TAC TCC AAA TC	CTC GAT TCC ATT GAG CAA CA
Cyp8b1 region 5000	TGG AAG CTG CTG AGA AAG TG	CTC AGG TCC TGG CTT TTG TC

[a]Regions are explained in the manuscript