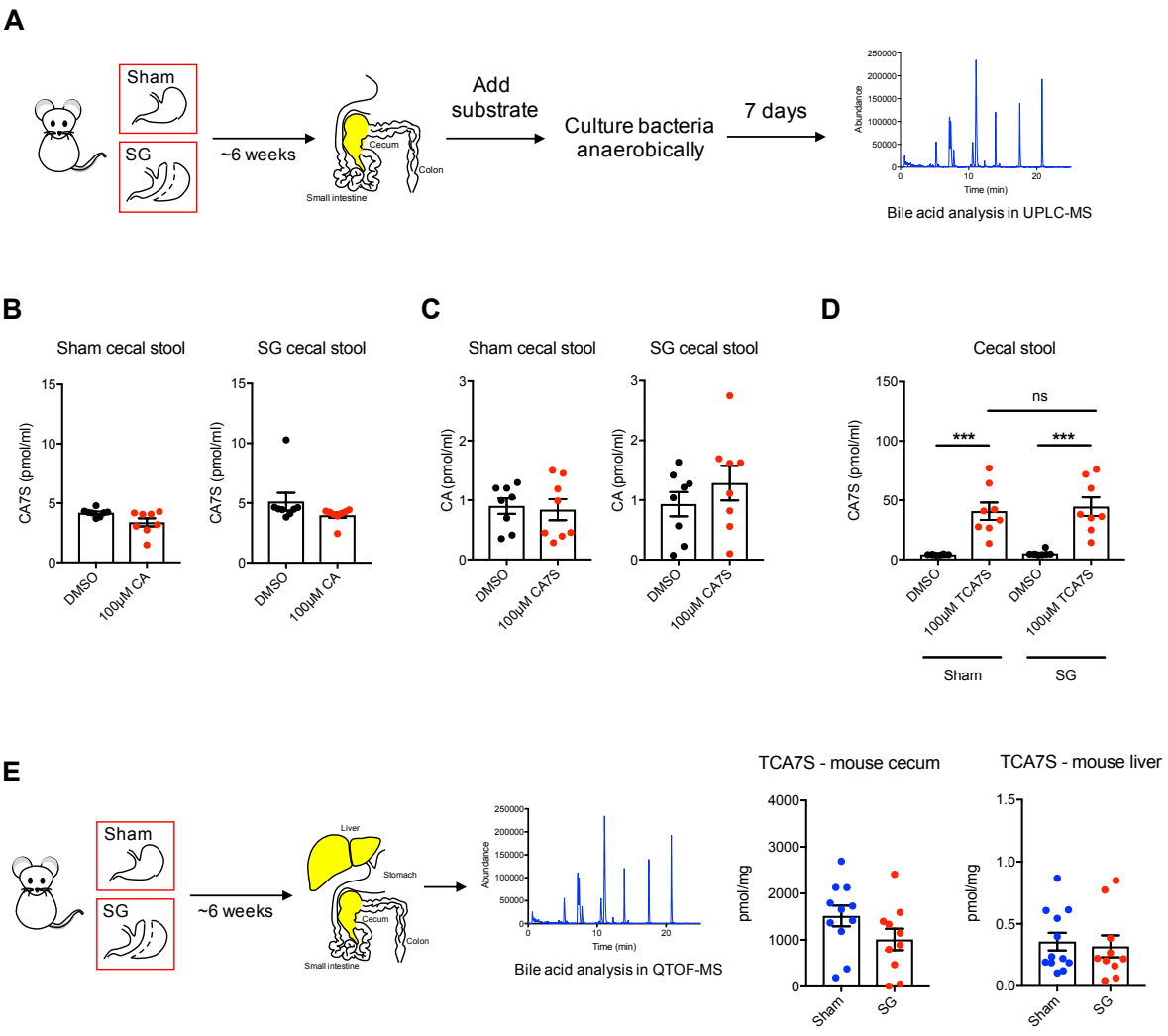

Figure S1, related to Figure 1. Bacteria do not contribute directly to increased CA7S levels post-SG

(**A**) Schematic of bacterial culturing from SG and Sham-operated mouse cecal stool.

(**B**,**C**) Cecal bacteria from sham and SG mice did not synthesize CA7S by sulfating cholic acid (CA) (**B**) or hydrolyze CA7S to CA (**C**). (Data not marked with asterisk(s) are not significant, n=8 in each group, **B**, Sham p=0.05, SG p=0.17; **C**, Sham p=0.78, SG p=0.33, Welch's t test). Note that the baseline levels of CA7S observed in both the DMSO control and added BA experimental groups resulted from CA7S present in the cecal contents that was resuspended in bacterial media to perform these assays.

(**D**) Cecal bacteria from sham and SG mice deconjugated TCA7S (tauro-conjugated cholic acid-7-sulfate) to CA7S to a similar extent (data not marked with asterisk(s) are not significant, n=8 in each group, Sham ***p=3.00x10^{-4}, SG ***p=1.00x10^{-4}, Sham vs SG p=0.96, ns=not significant, one-way ANOVA followed by Dunnett's multiple comparisons test).

(**E**) TCA7S from sham and SG mouse livers and cecal contents was quantified using QTOF-MS. TCA7S levels did not significantly differ between the two groups (data not marked with asterisk(s) are not significant, TCA7S in cecum, Sham, n=11, SG, n=12, p=0.13; TCA7S in liver, n=10, SG, n=12, p=0.74, Welch's t test).

All data are presented as mean ± SEM.

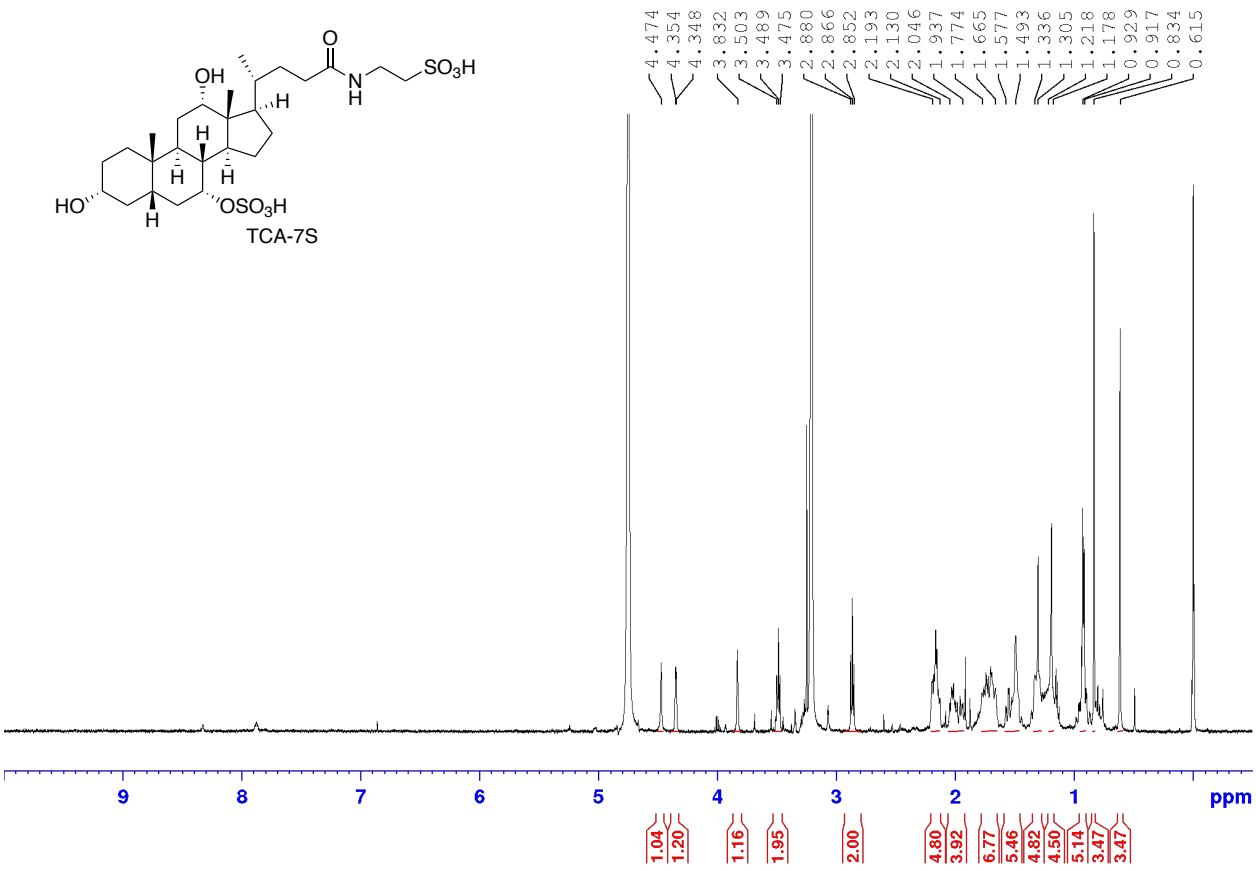

Figure S2, related to Figure 1. NMR of tauro-cholic acid-7-sulfate (TCA-7S)
^{1}H NMR of synthesized tauro-cholic acid-7-sulfate (TCA7S).

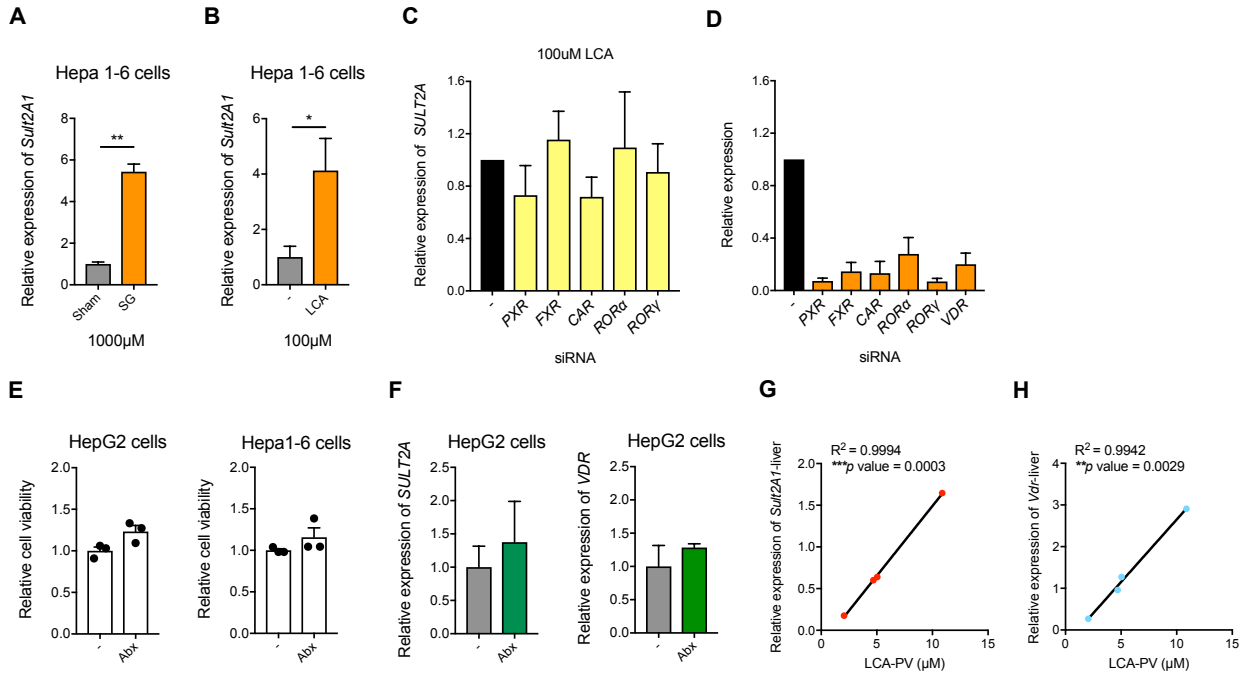

Figure S3, related to Figure 3. LCA induces expression of murine and human *Sult2A(1)* via VDR, that are unaffected by antibiotic treatments.

(**A**,**B**) qRT- PCR quantification of mouse *mSult2A1* expression level in Hepa 1-6 cells treated with (**A**) 1000 μM Sham or SG pool of portal BAs or (**B**) 100 μM LCA normalized to mouse 18S control (3 biological replicates per condition, SG PV bile acids, 1000 μM $^{**}p=4.20\text{x}10^{-3}$, LCA, 100 μM $^{*}p=0.02$, Welch's t test).

(**C**) qRT- PCR quantification of *hSULT2A1* expression level in HepG2 cells treated with 100 μM LCA and indicated siRNA treatments normalized to human *GAPDH* (≥3 biological replicates per condition, *PXR* (pregnane x receptor) siRNA $p=0.42$, *FXR* (farsenoid X receptor) siRNA $p=0.66$, *CAR* (constitutive androstane receptor) siRNA $p=0.38$, *RORα* (RAR-related orphan receptor alpha) siRNA $p=0.78$, *RORγ* (RAR-related orphan receptor gamma) siRNA $p=0.78$, one-way ANOVA followed by Dunnett's multiple comparisons test).

(**D**) qRT-PCR quantification of indicated receptors followed by siRNA-mediated knockdown in HepG2 cells (related to Figure 3B and Figure S3C).

(**E**) Cell viability in human HepG2 and murine Hepa 1-6 cells when incubated with cocktail of antibiotics (3 biological replicates per condition, not significant, HepG2 $p=0.06$, Hepa1-6 $p=0.29$, Welch's t test).

(**F**) qRT-PCR quantification of *hSULT2A1* and *VDR* expression levels in HepG2 cells treated with cocktail of antibiotics normalized to human *GAPDH* (3 biological replicates per condition, not significant, *hSULT2A1* $p=0.62$, *VDR* $p=0.41$, Welch's t test).

(**G**,**H**) Correlation analysis of LCA levels in the portal vein (PV) and hepatic *mSult2A1* (**G**) and *Vdr* (**H**) expression in SG livers in a single surgical cohort of n=4 mice per group. Linear regression analysis, LCA-PV vs. *mSult2A1*-liver $^{***}p=3.00\text{x}10^{-4}$, $R^2=0.99$; LCA-PV vs. *Vdr*-liver $^{**}p=2.90\text{x}10^{-3}$, $R^2=0.99$.

All data are presented as mean ± SEM.

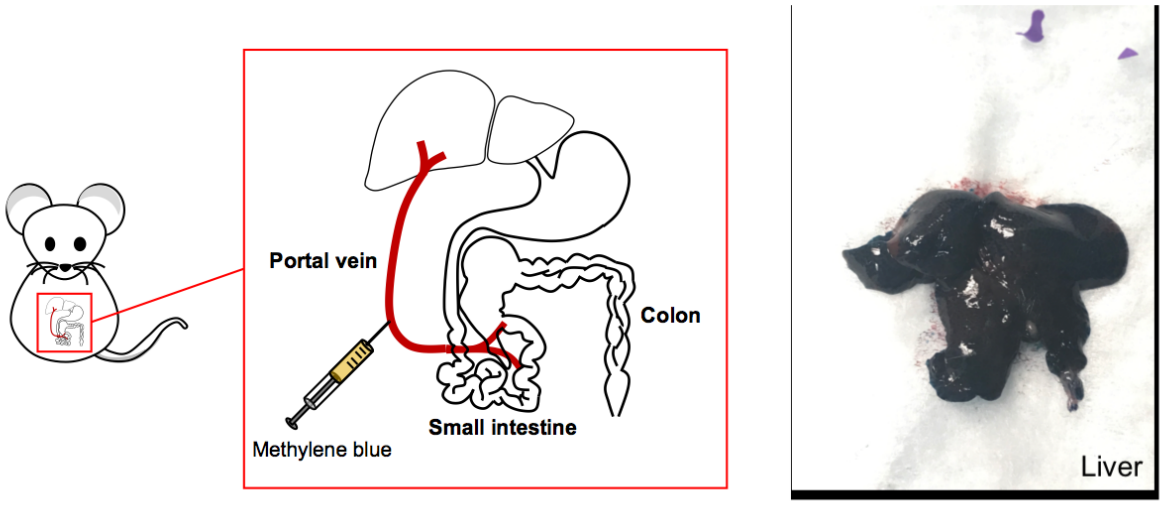

Figure S4, related to Figure 3. Portal injection leads to delivery in all lobes of the liver. Anesthetized mice were subjected to portal injection of methylene blue, a treatment that resulted in delivery of the dye to the entire liver within minutes.

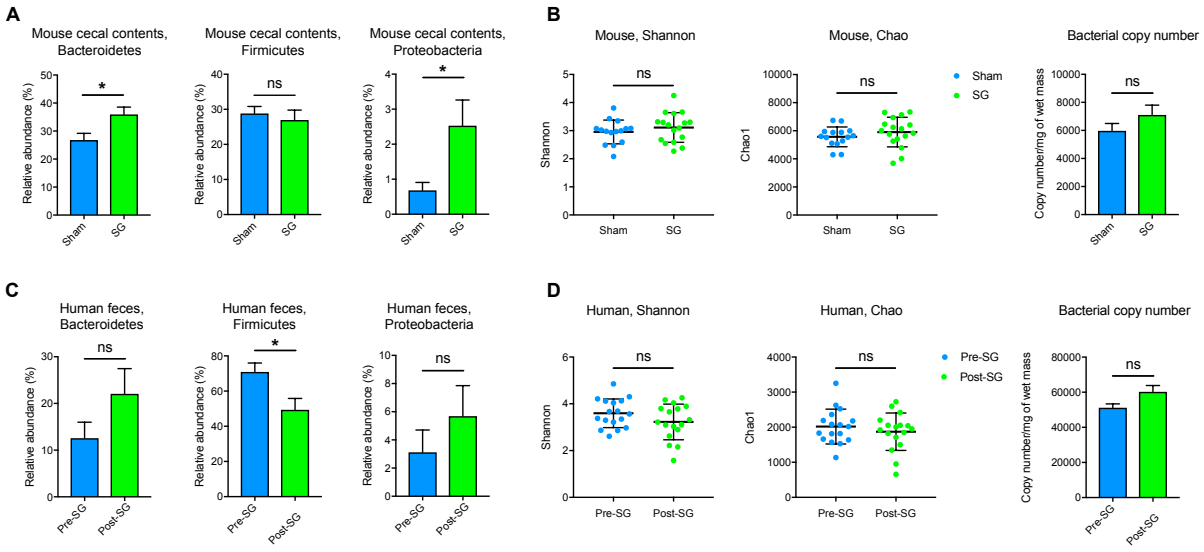

Figure S5, related to Figure 4. 16S rRNA sequencing of post-SG samples

(**A**) Relative abundances of indicated bacterial phyla in Sham and SG mouse cecal stool (Sham, n=15; SG, n=17, ns=not significant, Bacteroidetes **p*=0.01, Firmicutes *p*=0.59, Proteobacteria **p*=0.02, Welch's t test).

(**B**) Sham and SG mouse cecal 16S rRNA sequencing Shannon (*p*=0.35) and Chao (*p*=0.29) indices and copy numbers (*p*=0.20), Welch's t test.

(**C**) Relative abundances of indicated bacterial phyla in pre- and post-SG human feces. (n=17 patients, ns=not significant, Bacteroidetes *p*=0.15, Firmicutes **p*=0.01, Proteobacteria *p*=0.19, paired t test).

(**D**) Pre- and post-SG human fecal 16S rRNA sequencing Shannon (*p*=0.32) and Chao (*p*=0.17) indices and copy numbers (*p*=0.06), paired t test.

All data are presented as mean ± SEM.

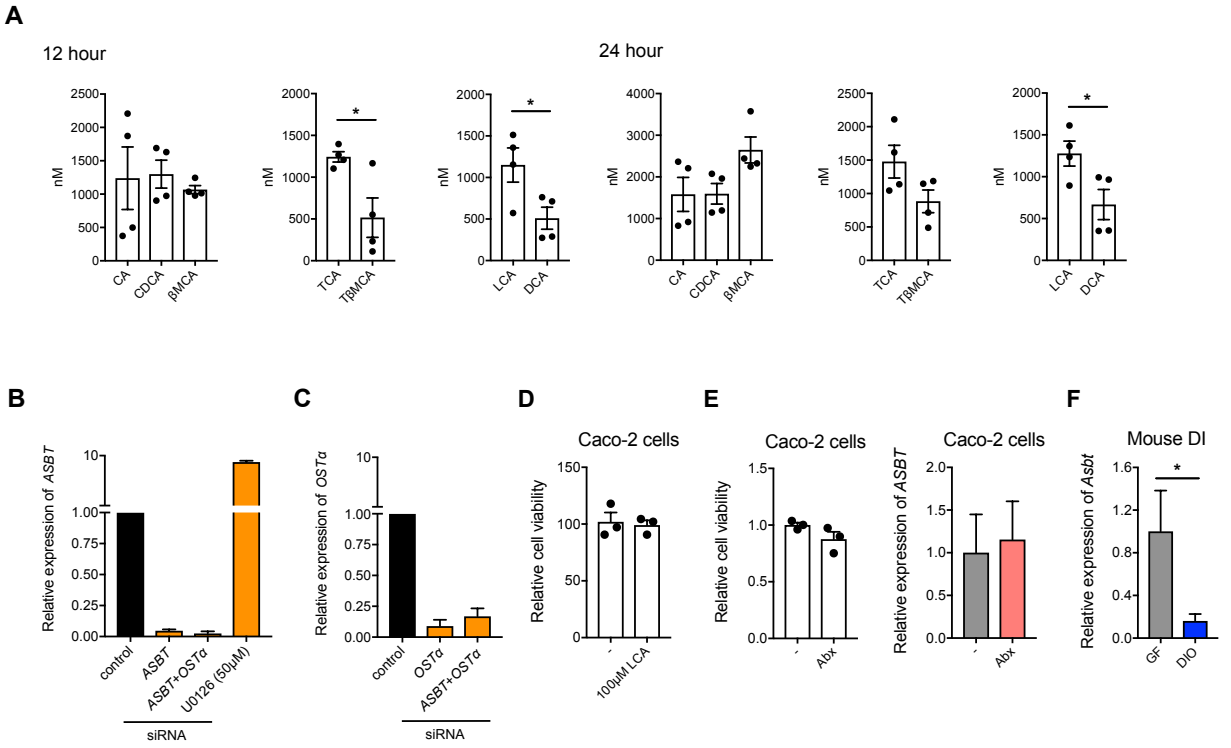

Figure S6, related to Figure 5. BA transcytosis and modulation of *ASBT*, *OSTα* expression levels in differentiated Caco-2 cells.

(**A**) Total transport of indicated BAs after 12 and 24 hours from the apical to the basolateral chamber of differentiated Caco-2 cells in transwells as quantified by UPLC-MS (data not marked with asterisk(s) are not significant, 4 biological replicates, 12 hour CA vs. CDCA p=0.98; CA vs. βMCA p=0.91; CDCA vs. βMCA p=0.84; one-way ANOVA followed by Dunnett's multiple comparisons test; TCA vs. TβMCA *p=0.04; LCA vs. DCA *p=0.04, Welch's t test; 24 hour CA vs. CDCA p=0.99; CA vs. βMCA p=0.10; CDCA vs. βMCA p=0.11; one-way ANOVA followed by Dunnett's multiple comparisons test; TCA vs. TβMCA p=0.09; LCA vs. DCA *p=0.04, Welch's t test).

(**B**) qRT-PCR quantification of human *ASBT* expression levels in differentiated Caco-2 cells treated with indicated siRNA or U0126 (50 μM). Expression levels were normalized to human *GAPDH* (≥3 biological replicates per condition).

(**C**) qRT-PCR quantification of human *OSTα* expression levels in differentiated Caco-2 cells treated with indicated siRNA conditions. Expression levels were normalized to human *GAPDH* (≥3 biological replicates per condition).

(**D**) Cell viability in human Caco-2 cells when incubated with 100 μM LCA (3 biological replicates per condition, not significant, p=0.77, Welch's t test)

(**E**) Cell viability and qRT- PCR quantification of human *ASBT* expression levels in Caco-2 cells treated with cocktail of antibiotics normalized to human *GAPDH* (3 biological replicates per condition, not significant, Cell viability p=0.19, *ASBT* expression p=0.81, Welch's t test).

(**F**) qRT- PCR quantification of mouse *Asbt* expression levels in GF and DIO mouse intestines normalized to mouse 18S (3 biological replicates per condition, *p=0.04, Welch's t test).

All data are presented as mean ± SEM.

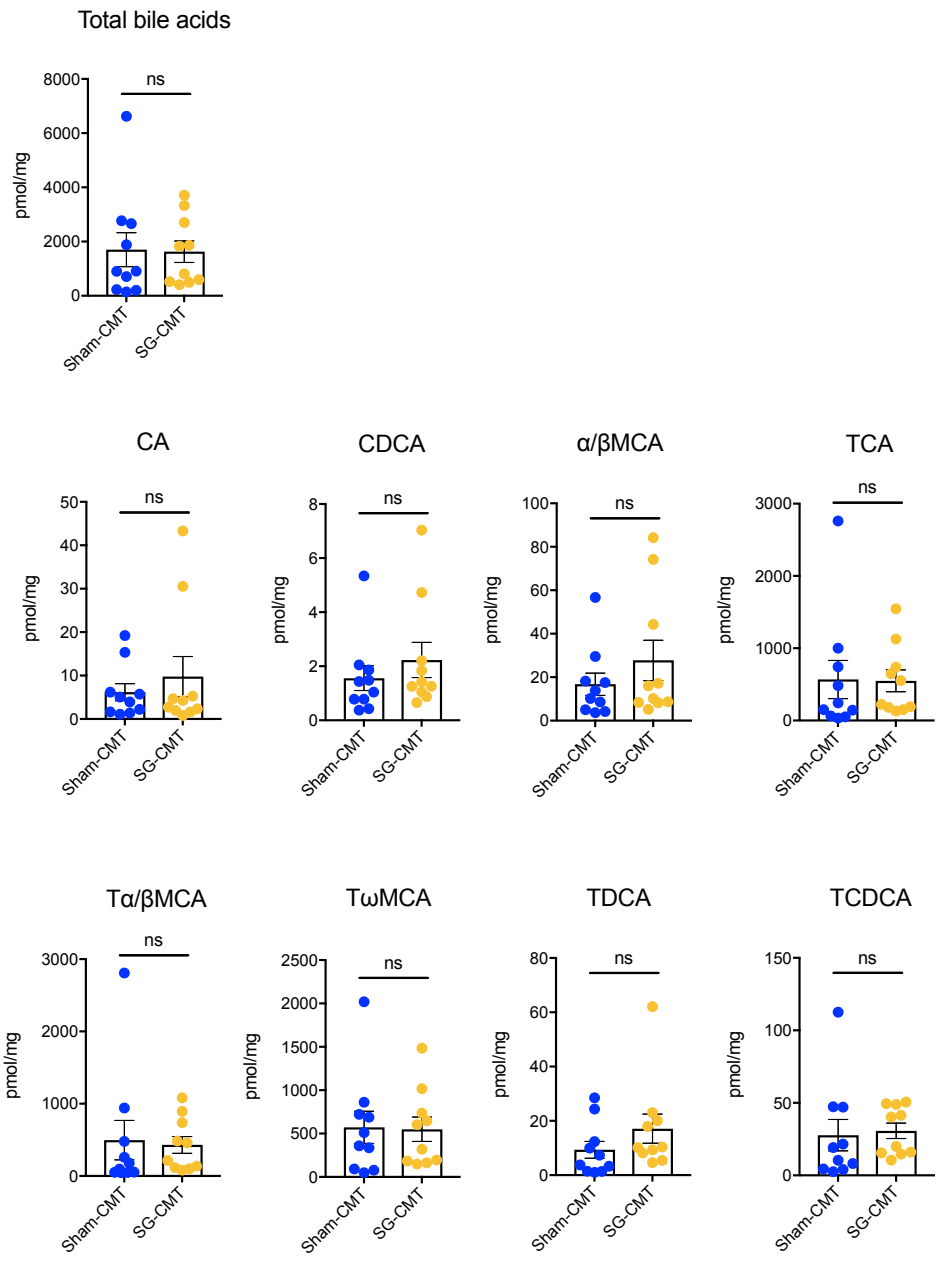

Figure S7, related to Figures 7. Portal BA levels in CMT mice.
Portal vein BAs in Sham-CMT and SG-CMT mice. All bile acids with measurable concentrations above the limit of detection are shown. (n=10 in each group, ns=not significant. Total bile acids, *p*=0.92, CA, cholic acid, *p*=0.49; CDCA, chenodeoxycholic acid, *p*=0.40; α/βMCA, alpha-muricholic acid and beta-muricholic acid, *p*=0.32, TCA, tauro-cholic acid, *p*=0.95; Tα/βMCA, tauro-alpha- and tauro-beta-muricholic acid, *p*=0.82; TωMCA, tauro-omega-muricholic acid, *p*=0.92; TDCA, tauro-deoxycholic acid, *p*=0.23; TCDCA, tauro-chenodeoxycholic acid, *p*=0.80, Welch's t test).
All data are presented as mean ± SEM

Table S1. Oligonucleotide primer sequences for qPCR.

Gene	Primers	Identifier
Mouse *Sult2A1*	F-CCTCAAAGGAAATGTTCTATTCGGA	This study
	R-CCATTCTCTCATGGACAGCCA	
Mouse *Sult2A2*	F-GAATAGGTGTCCTCGGCTGG	This study
	R-CAGCCAGTTCGTTCCTGACT	
Mouse *Sult2A8*	F-AGATTCTCCCGACCTTACTCCA	This study
	R-GATGCACACAGGTGCTTTGAG	
Mouse 18S	F-ATTGGAGCTGGAATTACCGC	This study
	R-CGGCTACCACATCCAAGGAA	
Human *SULT2A*	F-TGTGACATGCTGGGACAAGG	This study
	R-GTTTCAACTGTAGCCACCGC	
Human *VDR*	F-ATGAAGCTAACGCCCCTTGT	This study
	R-GTGAGGAGGGCTGCTGAGTA	
Human GAPDH	F-GAAGGTGAAGGTCGGAGT	This study
	R-CATGGGTGGAATCATATTGGAA	
Mouse *Vdr*	F-CCATTCAGGACCGCCTATCC	This study
	R-CCTCTAGCACAAGGGGTGTG	
Human *PXR*	F-CTGTGACAAGGCTACGCTGA	This study
	R-AGGCAGGCACTTTCATACCC	
Human *FXR*	F-TACATGCGAAGAAAGTGTCAAGA	This study
	R-ACTGTCTTCATTCACGGTCTGAT	
Human *CAR*	F-GGGAGCAGCTGTGGAAATCT	This study
	R-GTGTTCCAGGTGAGCGATCC	
Human *RORα*	F-AGATAGAGGGAGTCTCGGAGC	This study
	R-CCGGAGCTGACTCCATGTTT	

Human *RORγ*	F-AAGAAGACCCACACCTCACA	This study
	R-GGATCCCAGACGACTTGTCC	
Mouse *Asbt*	F-TGGGGTGCAATGTGGAAGTC	This study
	R-GAGGCATCATTCCAAGGGCA	
Mouse *Ostα*	F-CTAACAGTGGGCAGATCGCT	This study
	R-GGCTTTGAGTGCTGAGTCCA	
Mouse *Ostβ*	F-CCAGGGCCAGAAACATCTCAA	This study
	R-TGTTTCTTTGTCTTGTGGCTGC	
Mouse *Oatp1*	F-GCCAACGCAAGATCCAACAG	This study
	R-GGGCCAACAATCTTCCCCAT	
Mouse *Oatp2*	F-CCACGTCTGTAGTTGGGCTT	This study
	R-GGCCCATAACTGCACATCCT	
Mouse *Oatp4*	F-ATGCAAGGCACTAGGTGGAG	This study
	R-GAAATGTGGCAACGCAGTCA	
Mouse *Mrp1*	F-AGCAACTCGTCTTCCCACAG	This study
	R-TTCGCCTGAGTCCCATTGAC	
Mouse *Mrp2*	F-TTGCCTGTTATTCGGGCCTT	This study
	R-AGGGCGTTGGACAGAACAAA	
Mouse *Mrp3*	F-GTGGACTCTCATGTGGCGAA	This study
	R-GTCCACCAGCAAGCACAATG	
Human *ASBT*	F-TGTCGTATTCACCTTCCCGC	This study
	R-AAACGATGACTCTGGCTCCG	
Human *OSTα*	F-TTCCTGGAGGATGCCGTCTA	This study
	R-ACGAGGGATCCAGAGACCAA	

Bacteria *baiCD*	F-GGWTTCAGCCCRCAGATGTTCTTTG	*(Wells et al., 2003) doi: 10.1016/s0009-8981(03)00115-3*
	R-GAATTCCGGGTTCATGAACATTCTKCKAAG	
Bacteria *16S*	F-TCCTACGGGAGGCAGCAGT	This study
	R-GGACTACCAGGGTATCTATCCTGTT	