

Supplementary Table S1. List of PCR primers.

Gene	Species	Ref Seq	Ref Seq
<i>actb</i>	Mouse	NM_007393	Qiagen
<i>Calca</i>	Mouse	NM_007587	Qiagen
<i>Cdkn1a</i> (p21)	Mouse	NM_007669	Qiagen
<i>Cdkn2a</i> (p16)	Mouse	NM_009877	Qiagen
<i>Tgfb1</i>	Mouse	NM_011577	Qiagen
<i>TgfbR1</i>	Mouse	NM_009370	Qiagen

Actb=actin beta; Calca= calcitonin related polypeptide alpha; Cdkn1a (p21) = cyclin dependent kinase inhibitor 1A; Cdkn2a (p16) = cyclin dependent kinase inhibitor 2A; Tgfb1 = transforming growth factor β 1; TgfbR1: transforming growth factor beta receptor 1.

Supplementary Table S2. Hepatic Bile acids profile (μmol/L).

Bile acids	1 week treatment				2 weeks treatment			
	WT+	WT+TC	α-CGRP ^{-/-} +	α-CGRP ^{-/-}	WT+	WT+TC	α-CGRP ^{-/-} +	α-CGRP ^{-/-}
	BAC	diet	BAC	+ TC	BAC	diet	BAC	+ TC
TwMCA	22 ± 2	0.7 ± 0.5	26.1 ± 25.8	1.3 ± 0.8	15.6 ± 8.2	1.2 ± 0.6	0.5 ± 0.2	1.2 ± 1.5
TaMCA	10.6 ± 4.8	2.4 ± 3.4	12.3 ± 13.	2.9 ± 2.9	3.0 ± 2.0	1.2 ± 0.9	0.5 ± 0.2	1.4 ± 1.2
TbMCA	49.0 ± 21.9	5.7 ± 6.6	79.5 ± 87.7	4.9 ± 2.3	41.9 ± 30.1	4.0 ± 2.2	5.0 ± 1.0	3.0 ± 2.0
TUDCA	2.80 ± 1.2	0.4 ± 0.4	3.3 ± 2.3	0.6 ± 0.7	2.7 ± 1.2	1.2 ± 0.5	0.8 ± 0.4	0.7 ± 0.4
THDCA	3.4 ± 1.0	0.08 ± 0.1 *	1.8 ± 0.9	0.01 ± 0.02 †	1.0 ± 0.7	0	0.09 ± 0.0	0.36 ± 0.0
TCA	124.0 ± 48.0	458.1 ± 541.8	150.1 ± 158.6	1043 ± 211.0 *§	96.51 ± 64.29	477.2 ± 340.6	403.4 ± 47.21	171.9 ± 142.5
ω-MCA	6.7 ± 3.9	0.4 ± 0.7	7.253 ± 8.2	0.7 ± 0.7	13.50 ± 6.6	0.4 ± 0.4 *	0.7 ± 0.7	2.3 ± 3.2
α -MCA	6.9 ± 2.9	0.76 ± 0.0	8.17 ± 8.8	0	10.93 ± 7	0	0.78 ± 0.0	2.34 ± 3
β -MCA	18.8 ± 8	3.16 ± 3.8	40.9 ± 45.5	2.1 ± 2.3	83.6 ± 44.9	3.45 ± 2.2 *	3.88 ± 1.6	12.2 ± 18.6 *
GCA	0.14 ± 0.14	0.16 ± 0.0	0.31 ± 0.36	0.11 ± 0.17	0	0.04 ± 0.025	0	0
TCDCA	5 ± 0.4	1.46 ± 0.7	3.7 ± 2.6	1.5 ± 1	9 ± 2.2	1.2 ± 0.9 *	0.6 ± 0.5	2.01 ± 1.0 *

TDCA	10.55 ± 2.5	77.1 ± 90.5	6.4 ± 5.3	28.6 ± 47.8	9.45 ± 2.7	21.9 ± 10.9	52.8 ± 9.5	28.05 ± 21.1
CA	5.2 ± 4.1	6.0 ± 6.8	6.5 ± 8.6	5.2 ± 4.3	4.5 ± 2.6	7.22 ± 5.3	8.7 ± 5.4	1.8 ± 0.5
TLCA	0.8 ± 0.1	0.7 ± 0.1	0.7 ± 0.05	0.9 ± 0.3	0.9 ± 0.05	0.8 ± 0.02	0.9 ± 0.2	0.8 ± 0.1
CDCA	1 ± 0.4	0.6 ± 0.4	0.6 ± 0.6	0.23 ± 0.1	4.5 ± 2.1	0.4 ± 0.2 *	0.7 ± 0.4	0.5 ± 0.3 *
GLCA	0.2 ± 0.1	0.3 ± 0.1	0.3 ± 0.2	0.3 ± 0.05	0.3 ± 0.06	0.2 ± 0.01	0.3 ± 0.2	0.26 ± 0.1
DCA	0.8 ± 0.4	1.7 ± 2.0	0.9 ± 1	0.7 ± 0.7	0.6 ± 0.2	0.4 ± 0.2	1. ± 0.4	1.2 ± 0.6
LCA	0.09 ± 0.04	0.07 ± 0.03	0.05 ± 0.005	0.07 ± 0.03	0.2 ± 0.09	0.04 ± 0.02 *	0.01 ± 0.006	0.05 ± 0.05 *
CA-7-S	0.41 ± 0.03	0.58 ± 0.0	1.387 ± 1.5	2.73 ± 0.0	0.58 ± 0.0	2.507 ± 0.9	0.5 ± 0.3	0.4 ± 0.1
CDCA- 3- S	0.2 ± 0.03	0.18 ± 0.03	0.1 ± 0.04	0.09 ± 0.09	0.16 ± 0.1	0.1 ± 0.05	0.1 ± 0.05	0.13 ± 0.0781
LCA-7-S	0	0.02 ± 0.02	0.02 ± 0.007	0.01 ± 0.007	0.07 ± 0.04	0.02 ± 0.02	0.02 ± 0.0	0

Abbreviation: TwMCA: Taurine-conjugated ω -muricholic acid; TaMCA: Taurine-conjugated α -muricholic acid; TbMCA: Taurine-conjugated β -muricholic acid; TUDCA: Taurine-conjugated ursodeoxycholic acid; THDCA: Taurine-conjugated hyodeoxycholic acid; TCA: Taurine-conjugated cholic acid; ω -MCA: ω -Muricholic acid; α -MCA: α -Muricholic acid; β -MCA: β -Muricholic acid; GCA: Glycine-conjugated cholic acid; TCDCA: Taurine-conjugated chenodeoxycholic acid; TDCA: Taurine-conjugated deoxycholic acid; CA: Cholic acid; TLCA: Taurine-conjugated lithocholic acid; CDCA: Chenodeoxycholic acid; GLCA: Glycine-conjugated lithocholic acid; DCA: Deoxycholic acid; LCA: Lithocholic acid; CA-7-S: cholic acid-7-sulfate; CDCA-3-S: Chenodeoxycholic acid-3 sulfate; LCA-7-S: Lithocholic acid-7-sulfate; GHCA: Glycine-conjugated γ -muricholic acid; GUDCA: Glycine-conjugated ursodeoxycholic acid; GHDCA: Glycine-conjugated hyodeoxycholic acid; 7keto-DCA: 7-ketodeoxycholic acid; MDCA: Murideoxycholic acid; 3keto-7a-12a(OH)2: 3-Oxocholic acid; HCA: γ -Muricholic acid; UDCA: Ursodeoxycholic acid; HCDCA: Hyodeoxycholic acid; 7keto-LCA: 7keto- Lithocholic acid; isoDCA: isodeoxycholic acid; 12keto_LCA: 12-keto- Lithocholic acid; GDCA: Glycine-conjugated deoxycholic acid; isoLCA: isolithocholic acid; allo_isoLC: allo-iso Licholic acid; 3ketoLCA: 3keto-lithocholic acid; CA-3-S: cholic acid-3-sulfate; DCA-3-S: Deoxycholic acid-3-

sulfate; **UDCA-3-S**: Ursodeoxycholic acid-3-sulfate. Some bile acids were not detectable, including GHCA, GUDCA, GHDCA, 7keto-DCA, MDCA, 3keto-7a-12a(OH)₂, HCA, UDCA, HCDA, 7keto-LCA, isoDCA, 12keto_LCA, GDCA, isoLCA, allo_isoLC, 3ketoLCA, CA-3-S, DCA-3-S, UDCA-3-S. Statistical significance: *p< 0.05 vs. WT+BAC, §p< 0.05 vs. α -CGRP^{-/-} + BAC; †p < 0.05 vs WT+TC; Mean \pm SD.

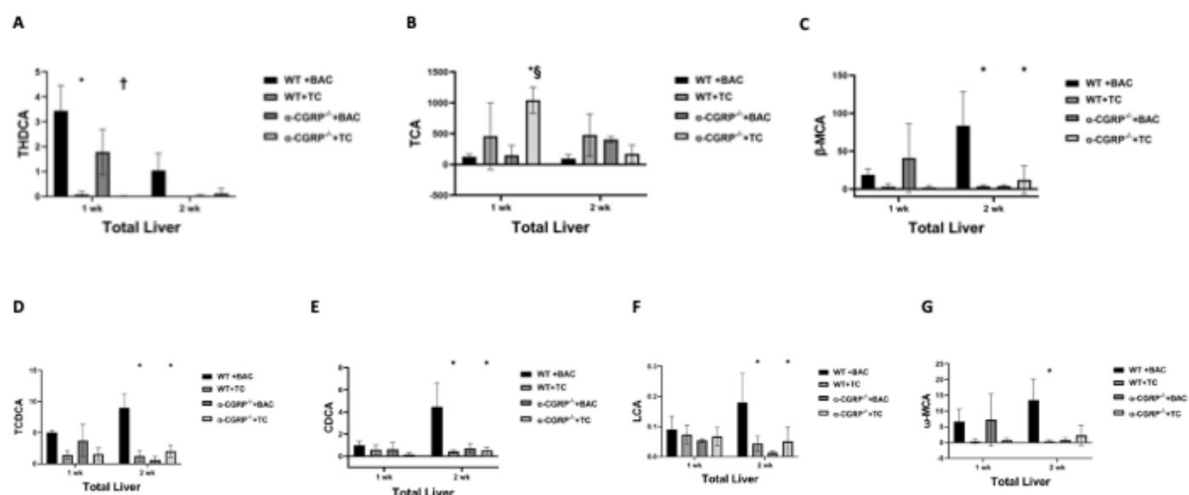
Supplementary Table S3. Hepatic bile acids profile (μmol/L).

Terms	1 week treatment				2 weeks treatments			
	WT+ BAC	WT+TC diet	α-CGRP ^{-/-} + BAC	α-CGRP ^{-/-} + TC	WT+ BAC	WT+TC diet	α-CGRP ^{-/-} + BAC	α-CGRP ^{-/-} + TC
Total BA	268.6 ± 60.58	559.7 ± 656.8	350.7 ± 368.8	1094 ± 277.4	297.6 ± 131.7	523.7 ± 361.7	480.6 ± 63.44	230.3 ± 134.9
Total Primary BA	220.7 ± 59.2	477.8 ± 563.2	302.1 ± 325.6	1060 ± 225.7	253.9 ± 121.4	494.9 ± 348.5	422.7 ± 53.3	195.1 ± 123.0
Total primary conjugated BA	188.8 ± 61.63	467.7 ± 552.4	245.9 ± 262.1	1052 ± 217.9 *	150.4 ± 65.48	483.8 ± 341.1	409.5 ± 48.2	178.3 ± 140.4
Total primary unconjugated BA	31.93 ± 7.5	10.03 ± 10.8	56.18 ± 63.5	7.487 ± 7.8	103.4 ± 56	11.09 ± 7.5 *	13.23 ± 7.0	16.85 ± 21.4
Total secondary BA	47.8 ± 3.2	81.8 ± 94.5	48.5 ± 43.3	34.4 ± 52.2	43.6 ± 14.4	28.8 ± 12.8	57.8 ± 10.4	35.1 ± 16.9
Total secondary conjugated BA	39.75 ± 2.851	79.26 ± 91.48	38.77 ± 33.88	31.87 ± 43.13	28.94 ± 8.804	25.30 ± 11.92	55.31 ± 9.573	31.13 ± 19.17
Total secondary unconjugated BA	7.5 ± 3.5	2.2 ± 2.7	8.2 ± 8.1	1.5 ± 1.4	14.2 ± 6.7	0.8 ± 0.4 *	1.8 ± 1.1	3.6 ± 2.6
Total conjugated BA	229.0 ± 64.4	547.4 ± 643.3	286.2 ± 297.4	1085 ± 268.2	179.8 ± 69.55	511.7 ± 353.8	465.5 ± 57.	209.8 ± 155.4
Total unconjugated BA	39.5 ± 11.0	12.2 ± 13.6	64.4 ± 71.5	9.0 ± 9.3	117.7 ± 62.0	11.9 ± 7.5*	15.1 ± 8.1	20.4 ± 24.0
Ratio of total primary BA to total BA	0.8 ± 0.04	0.9 ± 0.06	0.8 ± 0.03	0.1 ± 0.04 *	0.8 ± 0.06	0.9 ± 0.01	0.9 ± 0.007	0.8 ± 0.05

Ratio of total primary BA to total secondary BA	4.6 ± 1.2	7.6 ± 4.8	5.6 ± 1.2	150.8 ± 118.6 *†	5.8 ± 2.5	16 ± 4.2	7.4 ± 0.5	5.6 ± 2.1
Ratio of total primary conjugated BA to total primary unconjugated BA	6.3 ± 3.2	42.4 ± 6.0	4.9 ± 1.1	241.0 ± 150.6 *†	1.6 ± 0.3	44.0 ± 5.9	39.8 ± 26.1	37.1 ± 36.0
Ratio of total conjugated BA to total unconjugated BA	6.3 ± 3.3	41.7 ± 6.7	5.0 ± 1.4	196.4 ± 113.0*†	1.6 ± 0.4	42.9 ± 6.4 *	39.8 ± 26.1	29.5 ± 26.5
Ratio of total secondary BA to total BA	0.2 ± 0.04	0.1 ± 0.06	0.1 ± 0.02	0.02 ± 0.04*§	0.2 ± 0.06	0.06 ± 0.01	0.1 ± 0.007	0.2 ± 0.06
Ratio of total secondary conjugated BA to total secondary unconjugated BA	6.295 ± 3.564	40.80 ± 29.47	6.037 ± 3.006	12.76 ± 13.03	2.239 ± 0.8819	34.08 ± 19.83	39.08 ± 19.83	14.23 ± 11.78

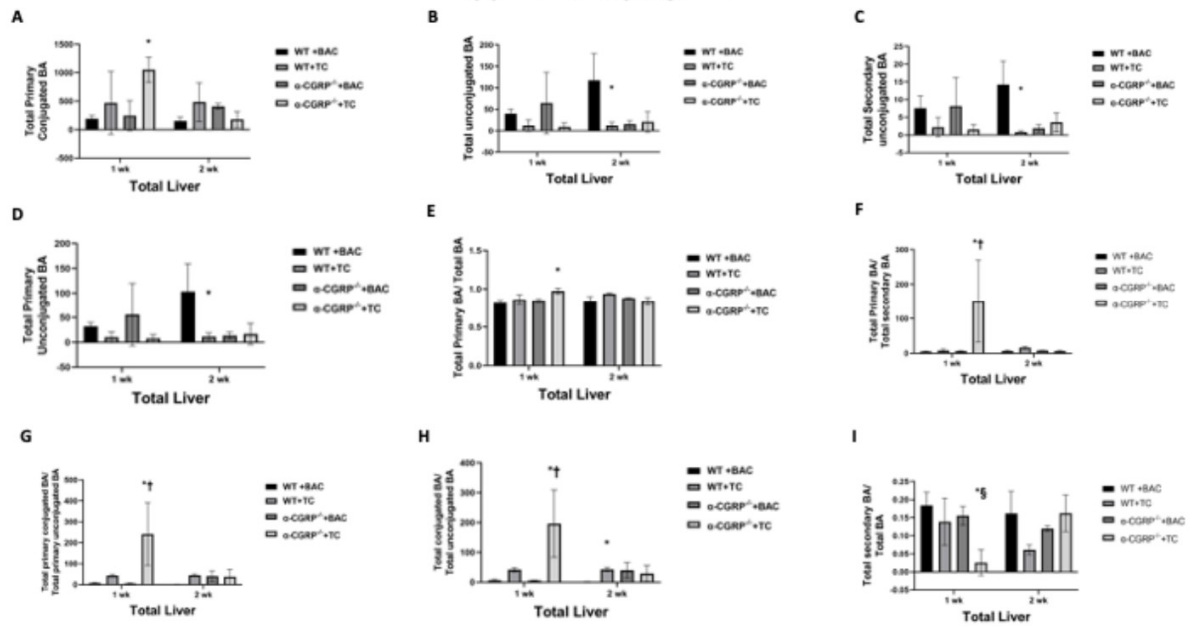
BA: Bile acids; BAC: Bile acid control diet; TC: Taurocholic acid diet. Statistical significance: *p<0.05 vs. WT+BAC, §p<0.05 vs. α -CGRP^{-/-} + BAC; †p<0.05 vs WT+TC; Mean ± SD.

Supplementary Figure 1



Supplementary Figure S1. Graphic expression of Supplementary Table S2.

Supplementary Figure 2



Supplementary Figure S2. Graphic expression of Supplementary Table S3.