

Supplementary Table S1. Serum total thyroxine (TT4) concentrations [$\mu\text{g/dL}$]. Detection limit of 0.5 $\mu\text{g/dL}$. mRNA expression (fold-change) of hepatic deiodinase 1 (*Dio1*) and thyroxine-binding globulin (*Tbg*) under hypo, litho and litho+hypo relative to control conditions by quantitative RT-PCR. *18S* (18S ribosomal RNA), *Ppia* (peptidylprolyl isomerase A, cyclophilin A) and *Rpl13 a* (ribosomal protein L13a) were used as reference genes, efficiency corrected Ct method. Data are presented as mean $\pm$ SEM, one-way ANOVA followed by Bonferroni *post hoc* analysis, ** $p<0.01$, *** $p<0.001$ # $p<0.0001$; n.d.: not detected; §data from Kube et al.; <https://doi.org/10.1055/a-1404-7939>; n=6-8/condition.

Parameter	Time (weeks)	Control	Hypo	Litho	Litho+Hypo
TT4 $\pm$ SEM [$\mu\text{g/dL}$]	2	3.63 $\pm$ 0.29	1.45 $\pm$ 0.40**	6.21 $\pm$ 0.57***	0.89 $\pm$ 0.04***
	4	2.27 $\pm$ 0.26	0.18 $\pm$ 0.01 [#]	4.56 $\pm$ 0.09 [#]	0.50 $\pm$ 0.04 [#]
	6 [§]	3.63 $\pm$ 0.24	0.28 $\pm$ 0.05 [#]	5.03 $\pm$ 0.24 [#]	0.41 $\pm$ 0.05 [#]
hepatic <i>Dio1</i> $\pm$ SEM (fold-change)	2	1.00 $\pm$ 0.12	n.d.	0.38 $\pm$ 0.04 [#]	n.d.
	4	1.00 $\pm$ 0.05	n.d.	0.36 $\pm$ 0.03 [#]	n.d.
	6 [§]	1.00 $\pm$ 0.04	n.d.	0.34 $\pm$ 0.03 [#]	n.d.
hepatic <i>Tbg</i> $\pm$ SEM (fold-change)	2	1.00 $\pm$ 0.13	2.16 $\pm$ 0.19	1.98 $\pm$ 0.21	8.99 $\pm$ 0.77 [#]
	4	1.00 $\pm$ 0.07	4.97 $\pm$ 0.38 [#]	1.63 $\pm$ 0.12	5.48 $\pm$ 0.31 [#]
	6 [§]	1.00 $\pm$ 0.08	8.04 $\pm$ 0.70 [#]	1.09 $\pm$ 0.11	9.32 $\pm$ 0.94 [#]

Supplementary Table S2. Bile acid derivates in bile of 2, 4 and 6 weeks treated female **C57BL/6J** mice.

CA – cholic acid, CDCA - chenodeoxycholic acid, DCA – deoxycholic acid, LCA – lithocholic acid, MCA $\alpha/\beta/\sigma$ – murine cholic acid isoforms $\alpha/\beta/\sigma$, UDCA – ursodeoxycholic acid, T and G prefixes denotes glycine and taurine conjugation. Data are represented as mean in $\mu\text{mol/mL} \pm \text{SEM}$. ULOD: under lower limit of detection; n=4-8/condition.

Primary BAs	BA derivate	Time	Control [$\mu\text{mol/mL}$]	Hypo [$\mu\text{mol/mL}$]	Litho [$\mu\text{mol/mL}$]	Litho+Hypo [$\mu\text{mol/mL}$]	Secondary BAs	BA derivate	Time	Control [$\mu\text{mol/mL}$]	Hypo [$\mu\text{mol/mL}$]	Litho [$\mu\text{mol/mL}$]	Litho+Hypo [$\mu\text{mol/mL}$]
hydrophilic	TCA-S	2 wks	0.15 $\pm$ 0.02	0.14 $\pm$ 0.04	0.04 $\pm$ 0.003	0.01 $\pm$ 0.003	hydrophilic	ω MCA	2 wks	0.58 $\pm$ 0.15	0.29 $\pm$ 0.03	0.04 $\pm$ 0.009	0.009 $\pm$ 0.002
		4 wks	0.17 $\pm$ 0.01	0.02 $\pm$ 0.002	0.05 $\pm$ 0.004	0.003 $\pm$ 0.001			4 wks	0.52 $\pm$ 0.13	0.04 $\pm$ 0.008	0.03 $\pm$ 0.007	0.006 $\pm$ 0.001
		6 wks	0.56 $\pm$ 0.07	0.007 $\pm$ 0.0009	0.06 $\pm$ 0.01	0.001 $\pm$ 0.0001			6 wks	0.54 $\pm$ 0.15	0.09 $\pm$ 0.03	0.06 $\pm$ 0.02	0.03 $\pm$ 0.01
	CA-S	2 wks	0.05 $\pm$ 0.02	0.04 $\pm$ 0.009	0.01 $\pm$ 0.002	0.005 $\pm$ 0.001		TUDCA	2 wks	6.82 $\pm$ 0.92	6.23 $\pm$ 0.86	0.83 $\pm$ 0.05	0.31 $\pm$ 0.01
		4 wks	0.05 $\pm$ 0.003	0.003 $\pm$ 0.0002	0.008 $\pm$ 0.001	0.001 $\pm$ 0.0005			4 wks	8.12 $\pm$ 0.41	3.01 $\pm$ 0.47	0.92 $\pm$ 0.19	0.29 $\pm$ 0.01
		6 wks	0.09 $\pm$ 0.02	0.001 $\pm$ 0.0006	0.008 $\pm$ 0.002	ULOD			6 wks	7.37 $\pm$ 0.38	2.55 $\pm$ 0.15	0.95 $\pm$ 0.08	0.24 $\pm$ 0.02
	TMCA	2 wks	93.31 $\pm$ 10.71	75.21 $\pm$ 11.07	13.41 $\pm$ 1.44	2.91 $\pm$ 0.18		UDCA	2 wks	0.005 $\pm$ 0.001	0.003 $\pm$ 0.001	ULOD	ULOD
		4 wks	89.24 $\pm$ 4.62	27.23 $\pm$ 2.96	13.03 $\pm$ 2.93	2.59 $\pm$ 0.15			4 wks	0.004 $\pm$ 0.001	0.001 $\pm$ 0.0004	ULOD	ULOD
		6 wks	130.38 $\pm$ 8.31	29.22 $\pm$ 2.34	14.25 $\pm$ 0.95	3.15 $\pm$ 0.16			6 wks	0.004 $\pm$ 0.001	0.003 $\pm$ 0.001	0.002 $\pm$ 0.001	0.003 $\pm$ 0.001
	α MCA	2 wks	1.53 $\pm$ 0.47	0.72 $\pm$ 0.14	0.06 $\pm$ 0.02	0.03 $\pm$ 0.01		HDCA	2 wks	0.005 $\pm$ 0.002	0.002 $\pm$ 0.001	ULOD	ULOD
		4 wks	1.01 $\pm$ 0.15	0.13 $\pm$ 0.02	0.05 $\pm$ 0.01	0.03 $\pm$ 0.008			4 wks	0.006 $\pm$ 0.002	ULOD	ULOD	ULOD
		6 wks	1.09 $\pm$ 0.30	0.37 $\pm$ 0.21	0.15 $\pm$ 0.06	0.05 $\pm$ 0.02			6 wks	0.004 $\pm$ 0.001	0.004 $\pm$ 0.003	ULOD	ULOD
	β MCA	2 wks	1.41 $\pm$ 0.43	0.51 $\pm$ 0.06	0.12 $\pm$ 0.05	0.03 $\pm$ 0.01							
		4 wks	0.78 $\pm$ 0.16	0.07 $\pm$ 0.01	0.06 $\pm$ 0.01	0.01 $\pm$ 0.004							
		6 wks	1.72 $\pm$ 0.49	0.13 $\pm$ 0.06	0.22 $\pm$ 0.09	0.03 $\pm$ 0.01							
	7-DHCA	2 wks	1.55 $\pm$ 0.47	0.69 $\pm$ 0.13	0.47 $\pm$ 0.12	0.37 $\pm$ 0.09							
		4 wks	1.35 $\pm$ 0.23	0.21 $\pm$ 0.05	0.25 $\pm$ 0.09	0.36 $\pm$ 0.12							
		6 wks	0.81 $\pm$ 0.28	0.15 $\pm$ 0.07	0.42 $\pm$ 0.14	0.44 $\pm$ 0.15							
	12-DHCA	2 wks	0.55 $\pm$ 0.14	0.19 $\pm$ 0.02	0.06 $\pm$ 0.01	0.04 $\pm$ 0.004							
		4 wks	0.51 $\pm$ 0.14	0.08 $\pm$ 0.02	0.03 $\pm$ 0.002	0.03 $\pm$ 0.004							
		6 wks	0.23 $\pm$ 0.05	0.09 $\pm$ 0.03	0.05 $\pm$ 0.007	0.03 $\pm$ 0.008							
hydrophobic	GCA	2 wks	0.13 $\pm$ 0.03	0.31 $\pm$ 0.02	0.57 $\pm$ 0.04	0.56 $\pm$ 0.08	hydrophobic	TDCA	2 wks	5.92 $\pm$ 0.88	4.76 $\pm$ 0.91	34.52 $\pm$ 5.26	42.13 $\pm$ 2.79
		4 wks	0.12 $\pm$ 0.01	0.18 $\pm$ 0.02	1.56 $\pm$ 0.89	1.11 $\pm$ 0.18			4 wks	8.37 $\pm$ 0.47	2.52 $\pm$ 0.67	32.79 $\pm$ 1.62	46.13 $\pm$ 3.29
		6 wks	0.24 $\pm$ 0.02	0.08 $\pm$ 0.006	1.84 $\pm$ 0.62	0.94 $\pm$ 0.28			6 wks	6.87 $\pm$ 0.85	2.65 $\pm$ 0.24	32.31 $\pm$ 4.23	31.03 $\pm$ 3.44
	TCA	2 wks	53.74 $\pm$ 8.18	77.19 $\pm$ 7.88	139.89 $\pm$ 7.01	107.93 $\pm$ 7.33		DCA	2 wks	0.005 $\pm$ 0.002	ULOD	0.02 $\pm$ 0.006	0.06 $\pm$ 0.02
		4 wks	56.94 $\pm$ 2.84	61.39 $\pm$ 5.20	136.38 $\pm$ 6.79	109.99 $\pm$ 6.05			4 wks	0.004 $\pm$ 0.001	ULOD	0.007 $\pm$ 0.001	0.04 $\pm$ 0.008
		6 wks	72.88 $\pm$ 4.40	54.98 $\pm$ 4.29	142.86 $\pm$ 5.18	85.94 $\pm$ 4.79			6 wks	0.003 $\pm$ 0.001	ULOD	0.04 $\pm$ 0.01	0.08 $\pm$ 0.04
	CA	2 wks	4.19 $\pm$ 1.55	4.03 $\pm$ 0.48	5.00 $\pm$ 1.28	5.44 $\pm$ 1.71		TLCA	2 wks	0.09 $\pm$ 0.007	0.06 $\pm$ 0.006	0.01 $\pm$ 0.002	0.01 $\pm$ 0.0008
		4 wks	2.62 $\pm$ 0.33	1.43 $\pm$ 0.48	1.87 $\pm$ 0.89	3.73 $\pm$ 1.17			4 wks	0.11 $\pm$ 0.01	0.04 $\pm$ 0.02	0.02 $\pm$ 0.002	0.02 $\pm$ 0.001
		6 wks	4.44 $\pm$ 1.16	2.45 $\pm$ 1.49	5.88 $\pm$ 2.28	6.56 $\pm$ 3.01			6 wks	0.08 $\pm$ 0.009	0.03 $\pm$ 0.004	0.02 $\pm$ 0.002	0.02 $\pm$ 0.002
	CDCA	2 wks	0.003 $\pm$ 0.001	0.002 $\pm$ 0.001	0.0006 $\pm$ 0.0002	ULOD		LCA	2 wks	ULOD	ULOD	ULOD	ULOD
		4 wks	0.001 $\pm$ 0.0003	0.0009 $\pm$ 0.0003	ULOD	ULOD			4 wks	0.0006 $\pm$ 0.0006	ULOD	0.0004 $\pm$ 0.0001	ULOD
		6 wks	0.002 $\pm$ 0.0005	0.003 $\pm$ 0.001	0.001 $\pm$ 0.0004	0.001 $\pm$ 0.0005			6 wks	0.0006 $\pm$ 0.0002	ULOD	ULOD	ULOD
	TCDCa	2 wks	4.05 $\pm$ 0.64	4.02 $\pm$ 0.60	0.76 $\pm$ 0.05	0.39 $\pm$ 0.02							
		4 wks	3.78 $\pm$ 0.07	3.46 $\pm$ 0.59	0.91 $\pm$ 0.17	0.47 $\pm$ 0.04							
		6 wks	4.91 $\pm$ 0.41	3.15 $\pm$ 0.43	1.15 $\pm$ 0.09	0.36 $\pm$ 0.03							

Supplementary Table S3. Oligonucleotides used for amplification of genes by quantitative RT-PCR. Oligonucleotides were designed using PrimerBlast (NCBI) and synthesized by Eurofins (Eurofins MWG Synthesis, Ebersberg, Germany).

Gene name	Abbr.	Sequence (5'→3') For	Sequence (5'→3') Rev	Product length (bp)	GC (%) For	GC (%) Rev	Tm (°C) For	Tm (°C) Rev
18S ribosomal RNA	<i>18S</i>	CGG CTA CCA CAT CCA AGG AA	GCT GGA ATT ACC GCG GCT	187	55.0	55.0	59.4	59.3
Multidrug resistance protein 3	<i>Abcb4</i>	GAT GGA TCT TGA GGC AGC GA	TTC TCT GCC TTG GTT GCT GA	88	55.0	50.0	59.3	57.3
ATP-binding cassette sub-family G member 5	<i>Abcg5</i>	CTC CGC GGA CTT CTA CAA CA	CAT GAC CTT GGG GTC CTG AA	166	55.0	55.0	59.3	59.3
Aquaporin 1	<i>Aqp1</i>	CTT GCC ATT GGC TTG TCT GTG G	CCA GTG GTT TGA GAA GGT GCG G	123	54.6	54.6	62.5	62.2
Aquaporin 8	<i>Aqp8</i>	TAC CTT GGG GAA CAT CAG CG	TCT GGA CTC ACC ACT TTA GCC	159	55.0	52.4	59.3	59.8
Aquaporin 9	<i>Aqp9</i>	TTG CAA CGG CAG TTG TGA TG	GGC CAT GAG TCC GTC ATA GT	200	50.0	55.0	57.3	59.3
Bile acid-CoA:amino acid N-acyltransferase	<i>Baat</i>	CCT CAC TTC CAT AGA GGA ATG TCT T	CAC TCT CCA TCC TGT ATT TTC T	85	44.0	61.3	44.0	61.3
Bile salt export pump	<i>Bsep</i>	ACA TCT GTA GGG TTG TTG AGT GA	CAA AGA AGC CAA CTC GAG CG	182	45.0	55.0	55.3	59.3
CytochromeP450 Family7 Subfamily A Member 1	<i>Cyp7a1</i>	TTC TGC GAA GGC ATT TGG AC	GAT TTA GGA AGG CCC GGA GG	171	50.0	60.0	57.3	61.4
CytochromeP450 Family27 Subfamily A Member 1	<i>Cyp27a1</i>	TTT AAG GCA TCC GTG TAG AGC	CCT CAC CTA TGG GAT CTT CAT G	132	47.6	50.0	57.9	60.3
Deiodinase Type 1	<i>Dio1</i>	GGG CAG GAT CTG CTA CAA GG	CGT GTC TAG GTG GAG TGC AA	98	60.0	55.0	61.4	59.3
3-Hydroxy-3-methylglutaryl-CoA reductase	<i>Hmgcr</i>	TCG CTG GTC CTA GAG CTT TC	CCA GCG ACT ATG AGC GTG AA	171	55.0	59.4	55.0	59.4
3-Phosphoadenosine 5-phosphosulfate synthase 2	<i>Papss2</i>	CCC ACC TCA CAG ACC TTC AC	GGT GGA TTT TTG CTG GTC TCT TT	187	60.0	43.5	61.4	58.9
Peptidylpropyl isomerase A, cyclophilin A	<i>Ppia</i>	CTT GGG CCG CGT CTC CTT CG	GCG TGT AAA GTC ACC CTG GC	160	70.0	60.0	65.5	61.4
Ribosomal protein L13a	<i>Rpl13a</i>	GGG CAG GTT CTG GTA TTG GA	GGG GTT GGT ATT CAAT CCG CT	162	55.0	52.4	59.3	59.8
Sulfotransferase family 2A1	<i>Sult2a1</i>	ATC TCC AGC TCA AAG ACC AAT TCT	TCC ATG TTG CTG GGG TTC TG	109	50.0	50.0	57.3	57.3
Thyroxine binding globuline	<i>Tbg</i>	TGG GCA TGT GCT ATC TTC A	GAG TGG CAT TTT GTT GGG GC	153	47.4	55.0	54.5	59.3
UDP glucuronosyltransferase family 1 member a5	<i>Ugt1a5</i>	ATG CCC CTA CAA GGA TTA GTG G	AGC ACC TTC TCA CCT TCA GTC	71	50.0	52.4	60.3	59.8