Supporting Information

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Table S1. Standards used in this study.

NO.	Analytes	Abbreviation	CAS number	Manufacturer
1	Cholic acid	CA	81-25-4	Yuanye Biology
2	Ursodeoxycholic acid	UDCA	128-13-2	Yuanye Biology
3	Chenodeoxycholic acid	CDCA	474-25-9	Yuanye Biology
4	Deoxycholic acid	DCA	83-44-3	Yuanye Biology
5	Lithocholic acid	LCA	434-13-9	Yuanye Biology
6	Glycocholic acid	GCA	475-31-0	Yuanye Biology
7	Glycoursodeoxycholic acid	GUDCA	64480-66-6	Yuanye Biology
8	Glycochenodeoxycholic acid	GCDCA	640-79-9	Yuanye Biology
9	Glycodeoxycholic acid	GDCA	360-65-6	Yuanye Biology
10	Glycolithocholic acid	GLCA	474-74-8	Yuanye Biology
11	Taurocholic acid	TCA	81-24-3	Yuanye Biology
12	Taurochenodeoxycholic acid	TCDCA	516-35-8	Yuanye Biology
13	Taurolithocholic Acid	TLCA	6042-32-6	Yuanye Biology
14	Taurodeoxycholic acid	TDCA	1180-95-6	Yuanye Biology
15	Tauroursodeoxycholic acid	TUDCA	14605-22-2	Yuanye Biology
16	Lithocholic-d_4 acid (IS)	LCA-d_4	83701-16-0	Sigma-Aldrich
17	Chenodeoxycholic-d_4 acid (IS)	CDCA-d_4	99102-69-9	Sigma-Aldrich
18	Deoxycholic-d_4 acid (IS)	DCA-d_4	112076-61-6	Sigma-Aldrich
19	Glycochenodeoxycholic-d_4 acid (IS)	GCDCA-d_4	1201918-16-2	Sigma-Aldrich
20	Cholic-d_4 acid (IS)	CA-d_4	116380-66-6	Sigma-Aldrich
21	Glycodeoxycholic-d_4 acid (IS)	GDCA-d_4	1069132-37-1	Sigma-Aldrich
22	Tauroursodeoxycholic acid-d_4 (IS)	TUDCA-d_4	2410279-94-4	Sigma-Aldrich

Table S2. List of the selected MRM parameters, declustering potential (DP), entrance potential (EP), collision energy (CE), and cell exit potential (CXP) for each analyte.

Analytes	Q1 Mass (Da)	Q3 Mass (Da)	DP (V)	CE (V)	EP (V)	CXP (V)
CA	535.5	462.4	84.9	11.1	52.0	33.1
UDCA	519.6	446.5	97.9	12.1	57.9	24.1
CDCA	519.6	446.3	80.8	14.3	52.7	23.0
DCA	519.6	446.5	107.1	10.1	52.1	32.1
LCA	503.7	430.0	82.0	10.1	49.2	29.2
GCA	592.7	592.7	87.9	10.7	26.1	14.1
GUDCA	576.7	576.7	138.7	6.1	5.0	15.8
GCDCA	576.7	576.7	118.8	7.7	5.0	18.0
GDCA	576.7	576.7	80.9	10.0	5.0	23.3
GLCA	560.8	560.8	153.9	12.1	5.0	13.1
TCA	514.3	79.9	-130.0	-111.8	-10.0	-13.0

TCDCA	498.3	79.9	-128.3	-103.7	-10.0	-13.8
TLCA	482.3	79.9	-148.8	-114.6	-10.0	-13.2
TDCA	498.3	79.9	-150.0	-109.1	-10.0	-13.0
TUDCA	498.3	79.9	-146.2	-113.7	-10.0	-13.1
LCA-d_4	507.7	434.2	135.9	10.1	54.8	20.8
CDCA-d_4	523.8	450.8	146.0	9.8	56.0	20.0
DCA-d_4	523.7	450.3	129.1	6.8	54.8	15.9
GCDCA-d_4	580.6	580.6	105.7	13.0	5.0	15.9
CA-d_4	539.4	466.4	132.9	53.0	13.8	13.0
GDCA-d_4	580.7	580.7	145.2	12.6	5.0	16.8
TUDCA-d_4	502.3	79.9	-144.8	-123.0	-10.0	-13.7

Table S3. Concentrations of analytes (μg/ml) in rat plasma, liver and intestinal contents samples from healthy control, hepatitis, cirrhosis, HCC and advanced HCC stage.(mean ± SD).The beginning of "P-" represents bile acids in plasma, while the beginning of "L-" and "I-" represent bile acids in liver and intestinal contents.

Analytes	Health contronl	Hepatitis	Cirrhosis	HCC	Advance HCC
P-CA	158.50±43.80	325.21±109.35*	342.05±97.09*	419.67±121.84**	490.99±129.20**
P-UDCA	22.16±7.71	60.44±8.75**	59.13±11.07**	72.94±14.58**	189.47±54.38**
P-CDCA	50.08±7.33	109.92±19.08**	276.10±71.49**	368.08±42.90**	1035.98±43.16**
P-DCA	30.91±11.22	38.15±12.62	60.64±4.08*	76.55±6.83**	79.63±12.29**
P-LCA	0.34±0.12	0.15±0.06*	0.15±0.04**	0.11±0.04**	0.18±0.09*
P-GCA	5.47±2.52	31.96±6.80**	36.35±9.36**	29.35±10.13**	35.88±6.09**
P-GUDCA	3.04±2.12	8.35±1.81**	4.04±1.02	3.75±1.97	5.10±2.02
P-GCDCA	1.91±0.37	1.94±0.87	1.65±0.44	2.46±1.05	2.00±1.17
P-GDCA	0.31±0.12	0.22±0.05	0.28±0.07	0.23±0.10	0.19±0.06
P-GLCA	0.61±0.20	0.15±0.05**	0.15±0.07**	0.13±0.05**	0.14±0.07**
P-TCA	123.55±41.33	267.44±97.88*	334.35±71.95**	364.49±56.17**	480.73±92.59**
P-TCDCA	51.04±11.27	78.35±18.98*	105.51±18.33**	40.45±19.49	65.26±9.67*
P-TLCA	7.77±2.42	2.62±1.65**	3.04±1.73**	1.69±0.91**	1.87±0.70**
P-TDCA	124.15±11.92	152.92±18.35*	148.36±23.90*	157.83±33.93*	180.00±25.99*
P-TUDCA	102.48±20.62	116.17±12.30	122.58±32.58	112.04±24.24	141.18±33.15*
L-CA	97.00±6.58	243.16±53.76**	265.04±44.33**	393.81±88.39**	493.95±133.45**
L-UDCA	128.84±11.50	60.36±11.96**	46.94±6.55**	49.76±10.97**	38.62±7.27**
L-CDCA	17.72±8.21	64.10±9.79**	68.48±8.16**	75.92±4.10**	94.89±14.16**
L-DCA	29.34±10.86	62.45±9.75*	67.46±6.44*	69.05±13.11*	86.31±5.20**
L-LCA	0.06±0.01	0.04±0.01*	0.05±0.01	0.04±0.01*	0.03±0.01*
L-GCA	23.15±6.49	38.63±14.92	56.42±8.88**	55.04±10.57**	96.12±11.90**
L-GUDCA	9.01±1.95	6.00±2.61	6.93±1.15	7.06±1.95	16.09±1.99**
L-GCDCA	1.95±0.49	1.22±0.38*	2.10±0.48	1.74±0.90	3.89±1.25*
L-GDCA	6.28±2.43	4.49±1.57	8.36±3.03	10.48±2.76	12.06±5.85

L-GLCA	7.56±0.87	3.32±0.41**	3.12±0.75**	3.46±0.82**	3.64±1.20**
L-TCA	109.33±28.92	175.25±48.84*	334.35±71.95**	381.07±72.71**	471.05±52.60**
L-TCDCA	41.04±10.49	70.52±8.06**	94.13±17.65**	64.81±9.13**	69.54±6.65**
L-TLCA	6.14±1.72	1.93±0.62**	2.40±1.05**	1.31±0.36**	1.99±0.70**
L-TDCA	168.30±35.93	113.42±24.66	137.83±10.80	238.65±18.37*	218.01±25.42
L-TUDCA	117.74±14.87	88.52±22.58	106.42±10.79	85.36±17.17*	158.86±27.94*
I-CA	78.25±14.33	197.76±20.32**	178.73±11.93**	175.17±31.53**	143.30±20.94**
I-UDCA	207.47±24.44	42.97±11.10**	24.50±7.86**	14.07±8.08**	14.60±7.05**
I-CDCA	7.20±2.92	31.64±4.73**	23.70±8.31**	21.69±6.92**	13.40±3.06*
I-DCA	27.04±4.15	55.18±6.53**	52.39±10.14**	42.69±8.83*	21.73±7.51
I-LCA	10.06±1.22	11.63±2.44	6.75±1.40**	6.20±1.39**	5.64±1.92**
I-GCA	7.83±6.51	23.20±6.14**	16.16±3.84	25.12±6.17**	23.33±6.10**
I-GUDCA	4.90±0.97	2.94±1.07*	1.71±0.41**	1.09±1.13**	0.58±0.76**
I-GCDCA	17.91±5.60	47.36±9.72**	39.12±2.36*	29.82±6.34*	29.76±5.23*
I-GDCA	5.77±3.50	16.33±2.06**	8.58±1.68	13.13±1.38**	13.67±3.10**
I-GLCA	1.64±0.33	1.46±0.41	1.18±0.38	0.55±0.31**	1.37±0.47
I-TCA	127.28±7.98	72.01±6.90**	48.14±15.35**	33.99±13.36**	32.10±4.11**
I-TCDCA	32.84±6.67	15.03±3.22*	7.45±5.09**	6.68±3.45**	10.28±4.63**
I-TLCA	86.27±8.86	78.98±10.31	46.04±16.85**	38.84±13.99**	49.19±7.18**
I-TDCA	22.56±2.57	9.52±1.65**	6.04±3.62**	2.40±0.94**	2.29±0.98**
I-TUDCA	131.77±21.84	93.19±12.23*	37.48±9.80**	16.65±3.96**	14.20±6.41**

*$p < 0.05$, compared with heathy controls; **$p < 0.01$, compared with heathy controls.

Table S4. The classification results by BLDA.

	Groups	Health control	Hepatitis	Cirrhosis	HCC	Advanced HCC	Total
Count	Health control	5	1	0	0	0	6
	Hepatitis	0	6	0	0	0	6
	Cirrhosis	0	1	4	1	0	6
	HCC	0	0	1	5	0	6
	Advanced cancer	0	0	0	0	6	6
%	Health control	83.3	16.7	0	0	0	100
	Hepatitis	0	100	0	0	0	100
	Cirrhosis	0	16.7	66.7	16.7	0	100
	HCC	0	0	16.7	83.3	0	100
	Advanced cancer	0	0	0	0	100	100

Table S5. 15 gene sets with FDR<25%, NES>1.5 and good significance (*P*-value<0.05) of GSEA enrichment analysis for patient samples which collected from TCGA database.

No.	Name	gene	description	collections	source organism	contributor
1	HALLMARK_BILE_ACID_METABOLISM	112	Genes involve in metabolism of bile acids and salts.	H	Homo sapiens	MSigDB Team
2	GOMF_CHOLESTEROL_BINDING	51	Binding to cholesterol (cholest-5-en-3-beta-ol); the principal sterol of vertebrates and the precursor of many steroids, including bile acids and steroid hormones. [GOC:jl, ISBN:0198506732]	C5 GO	Homo sapiens	Gene Ontology Consortium
3	GOBP_BILE_ACID_BIOSYNTHETIC_PROCESS	36	The chemical reactions and pathways resulting in the formation of bile acids, any of a group of steroid carboxylic acids occurring in bile. [GOC:go_curators]	C5 GO	Homo sapiens	Gene Ontology Consortium
4	GOBP_BILE_ACID_METABOLIC_PROCESS	49	The chemical reactions and pathways involving bile acids, a group of steroid carboxylic acids occurring in bile, where they are present as the sodium salts of their amides with glycine or taurine. [GOC:go_curators]	C5 GO	Homo sapiens	Gene Ontology Consortium
5	GOBP_BILE_ACID_AND_BILE_SALT_TRANSPORT	31	The directed movement of bile acid and bile salts into, out of or within a cell, or between cells, by means of some agent such as a transporter or pore. [GOC:dph, GOC:krc, PMID:12663868, PMID:14699511]	C5 GO	Homo sapiens	Gene Ontology Consortium
6	GOBP_REGULATION_OF_CHOLESTEROL_METABOLIC_PROCESS	40	Any process that modulates the rate, frequency, or extent of cholesterol metabolism, the chemical reactions and pathways involving cholesterol, cholest-5-en-3 beta-ol, the principal sterol of vertebrates and the precursor of many steroids, including bile acids and steroid hormones. [GOC:BHF, GOC:dph, GOC:tb]	C5 GO	Homo sapiens	Gene Ontology Consortium
7	REACTOME_SYNTHESIS_OF_BILE_ACIDS_AND_BILD_BILE_SALTS_VIA_7ALPHA_HYDROXYCHOLESTEROL	24	Synthesis of bile acids and bile salts via 7alpha-hydroxycholesterol	C2 CP	Homo sapiens	Reactome
8	REACTOME_SYNTHESIS_OF_BILE_ACIDS_AND_BILD_BILE_SALTS_VIA_27_HYDROXYCHOLESTEROL	15	Synthesis of bile acids and bile salts via 27-hydroxycholesterol	C2 CP	Homo sapiens	Reactome
9	REACTOME_SYNTHESIS_OF_BILE_ACIDS_AND_BILD_BILE_SALTS	34	Synthesis of bile acids and bile salts	C2 CP	Homo sapiens	Reactome
10	WP_FARNESOID_X_RECEPTOR_PATHWAY	19	Farnesoid X receptor pathway	C2 CP	Homo sapiens	WikiPathways
11	KEGG_PRIMARY_BILE_ACID_BIOSYNTHESIS	16	Primary bile acid biosynthesis	C2 CP	Homo sapiens	Kyoto Encyclopedia of Genes and Genomes
12	REACTOME_CYTOCHROME_P450_ARRANGED_BY_SUBY_SUBSTRATE_TYPE	64	Cytochrome P450 - arranged by substrate type	C2 CP	Homo sapiens	Reactome
13	WP_DRUG_INDUCTION_OF_BILE_ACID_PATHWAY	17	Drug induction of bile acid pathway	C2 CP	Homo sapiens	WikiPathways
14	REACTOME_BILE_ACID_AND_BIL	45	Bile acid and bile salt metabolism	C2 CP	Homo sapiens	Reactome

15	E_SALT_METABOLISM REACTOME_RECYCLING_OF_BIL E_ACIDS_AND_SALTS	18	Recycling of bile acids and salts	C2 CP	Homo sapiens	Reactome

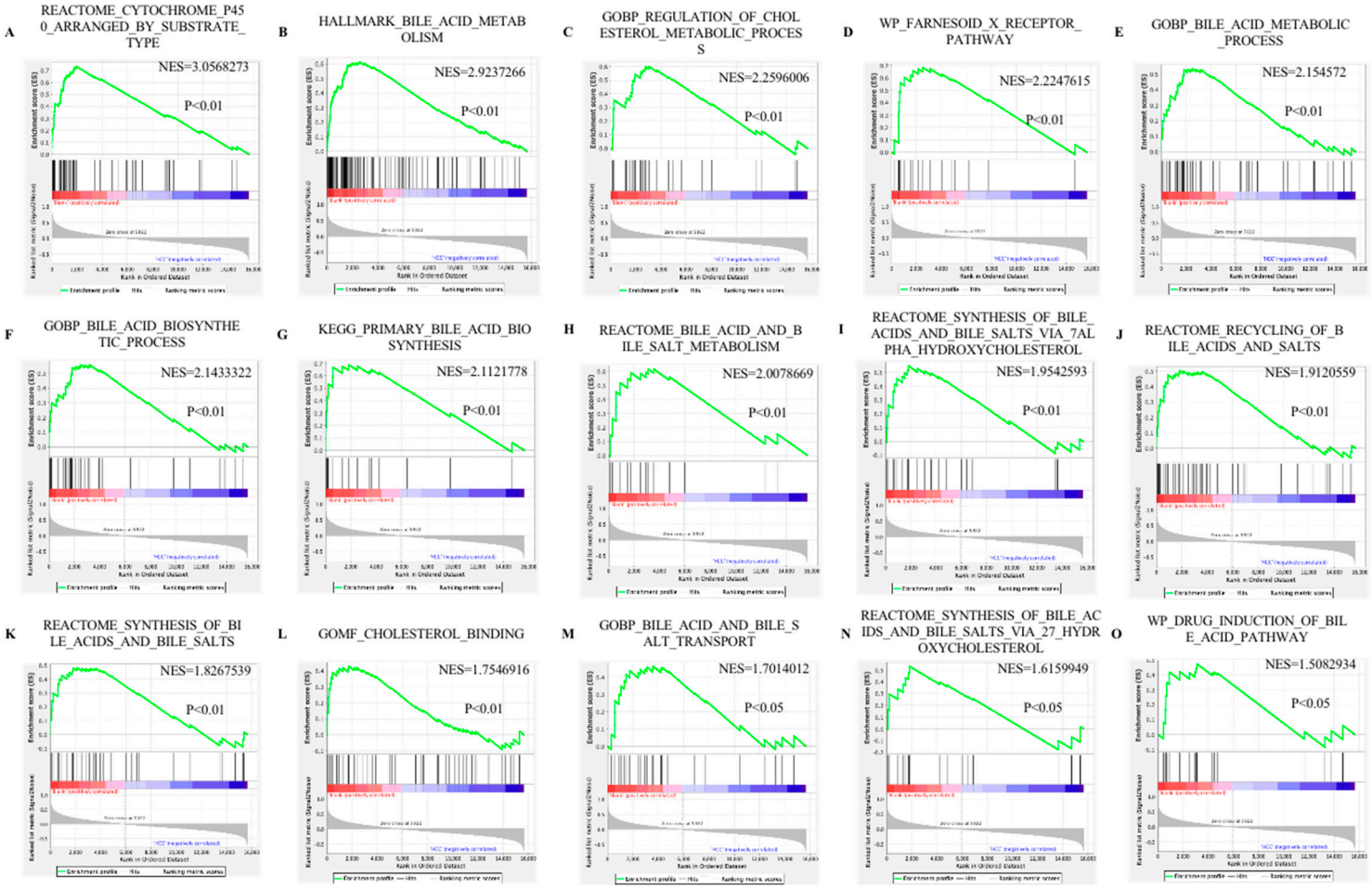

Figure S1. 15 gene sets with FDR<25%, NES>1.5 and good significance (*P*-value<0.05) of GSEA enrichment analysis for patient samples which collected from TCGA database.The order of the gene sets is arranged according to NES value (A-O).

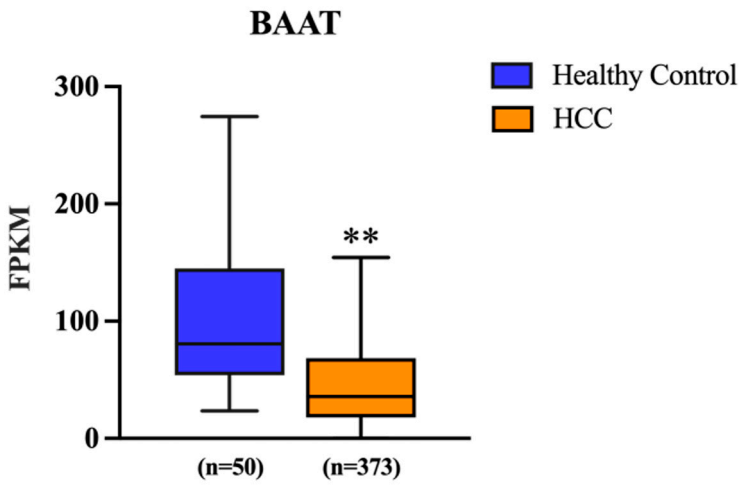

Figure S2. BAAT expression is generally downregulated in human HCC tissues. Expression of BAAT in patients with HCC based on data from TCGA Liver Hepatocellular Carcinoma dataset. FPKM, Fragments Per Kilobase of exon model per Million mapped fragments. Figure indicates statistical significance compared with heathy controls by t-tests, $^{**}p < 0.01$.