

Figure S1 The heatmap of differential genes expressions in GSE107943, GSE26566, and GSE119337.

**annotation**  
 | gene  
 | transcript  
 | CpG island

**data**  
 | RNA-seq v2 (log2)  
 | infinium 450k  
 | slide/clinical data  
 | missing data

**gender**  
 | female  
 | male

**statistics**  
 p Wilcoxon rank-sum test  
 p < 0.05 p ≥ 0.05  
 r Pearson correlation  
 \*\*\* p < 0.001  
 \*\* p < 0.01  
 \* p < 0.05  
 p ≥ 0.05

**sample type**  
 | solid tissue normal  
 | primary solid tumor

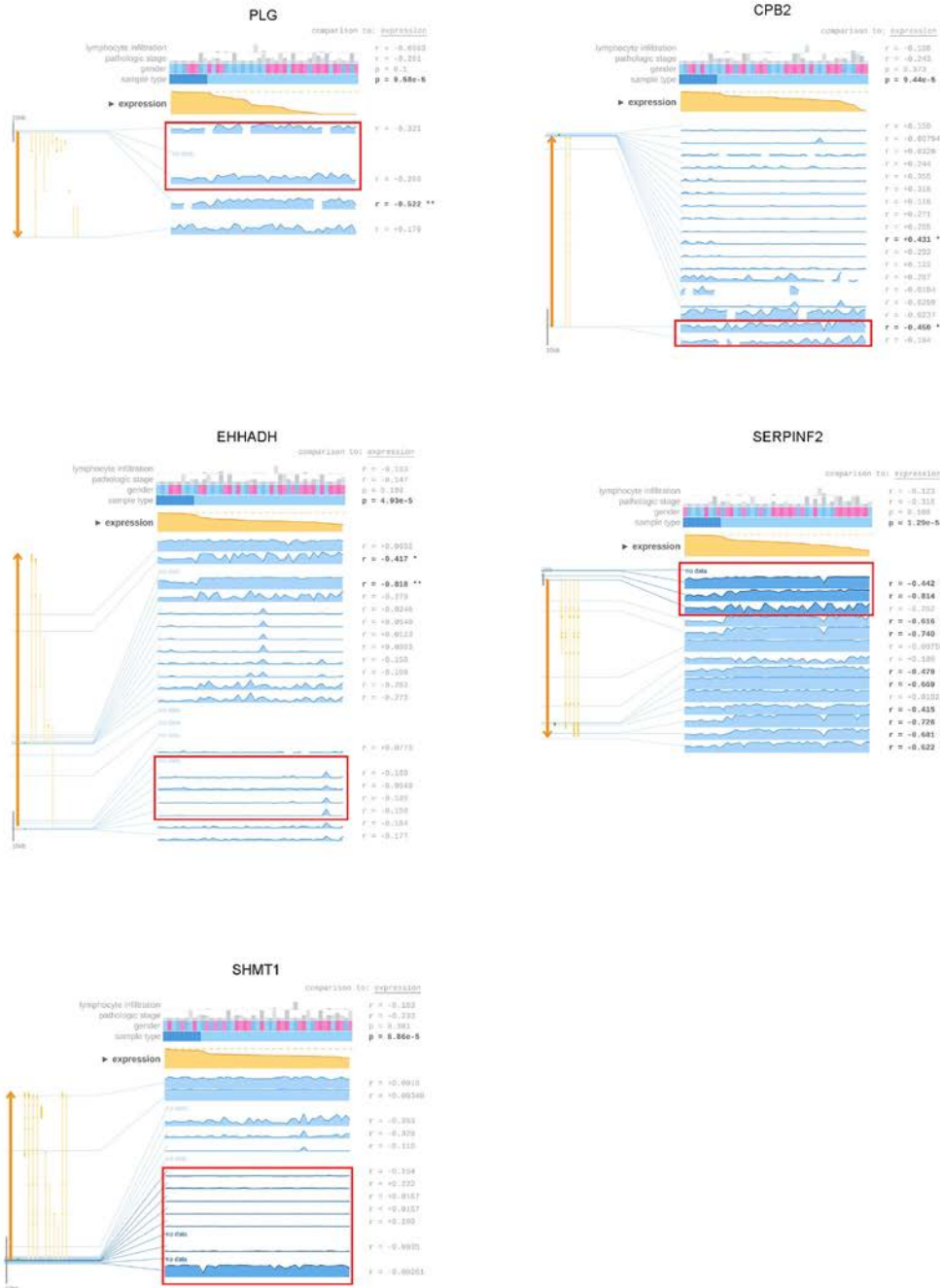


Figure S2 Visualization of the TCGA data for PLG, CPB2, EHHADH, SERPINF2, and SHMT1 in cholangiocarcinoma using MEXPRESS.

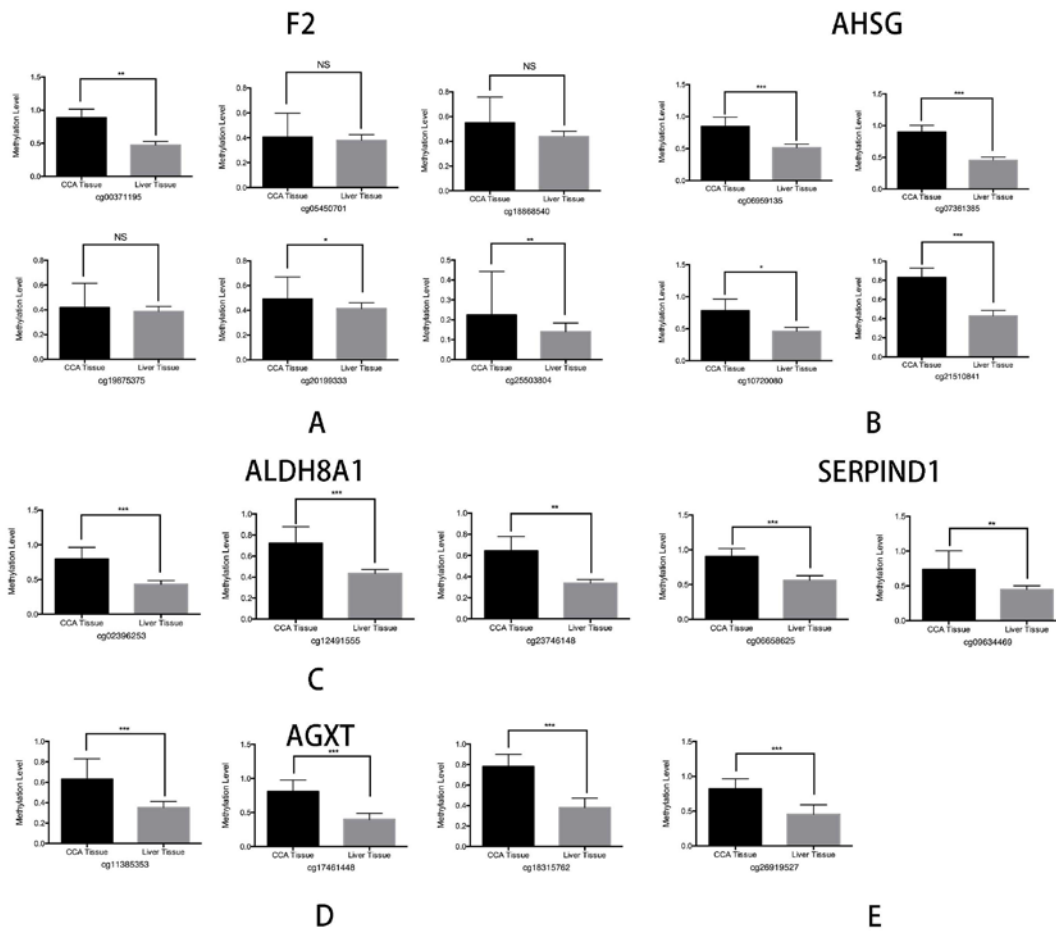


Figure S3 A. The methylation level of F2 in the promoter of CCA and adjacent normal tissues. B. The methylation level of AHSG in the promoter of CCA and adjacent normal tissues. C. The methylation level of ALDH8A1 in the promoter of CCA and adjacent normal tissues. D. The methylation level of AGXT in the promoter of CCA and adjacent normal tissues. E. The methylation level of SERPIND1 in the promoter of CCA and adjacent normal tissues.

Table S1 Primer sequences of 5 target genes

Gene	Sequence (5' -> 3')	Length
F2	CACGGCTACGGATGTGTTCTG (F)	21
	ACCCTCAGCACAGTTACCTTC (R)	21
AHSB	TCCTTGGGGATACAAACACACC (F)	21
	TACCACGGAAAACCTTGCCATC (R)	22
ALDH8A1	ATGGCTGGAACAAACGCACT (F)	20
	CCCTGTTGATGGGTCGTAAGAA (R)	22
SERPIND1	TTCCTCATCATAACATCTGCGTG (F)	23
	TGGAATCCAGTCGTTGGTGAC (R)	21
AGXT	CACCCGATGACCAAGGACC (F)	19
	CTCCCCGTGGGTAAAGAACAG (R)	21