

**Table S1.** Clinical characteristics of patients

Characteristics	Controls (n=85)	Training set/(n=176, ECC=90, ICC=86)	Validation set/(n=225, ECC=116, ICC=109)
Sex (F/M)	42/43	88/88	112/113
Age	46±4	44±5	47±8
BMI(kg/m <sup>2</sup> )	24.31±2.78	24.40±2.59	23.99±3.37
HBsAg(negative/positive)	negative	positive	positive
ALT (U/L)	19.55±6.73	34.45±8.21	36.28±7.67
AST (U/L)	16.97±8.41	36.35±9.04	32.37±10.17
ALP(U/L)	64.25±22.13	94.76 ± 31.01	98.15 ± 29.93
Bilirubin (total) (mg/dl)	0.68±0.422	1.33±0.67	1.63±0.74
Albumin (g/dl)	1.44±0.76	3.50±1.28	3.80±1.21
Serum CEA (ng/ml)	3.08±1.11	5.27±2.24	5.69±3.02



**Table S3.** ROC curve analysis of serum metabolites detected by UPLC-MS

No	Metabolite	AUC	Sensitivity (%)	Specificity (%)
1	21-Deoxycortisol	0.918	92.6	95.2
2	Bilirubin	0.922	97.1	94.3
3	LysoPC(14:0)	0.954	93.7	88.8
4	LysoPC(15:0)	0.927	84.5	91.2
5	four-metabolite panel	0.993	98.5	99.2

**Table S4.** Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis in CC

No.	Pathway Name	Total	Expected	Hits	Raw p	Impact
1	Glycerophospholipid metabolism	39	0.29165	4	0.00015313	0.28685
2	Linoleic acid metabolism	15	0.11217	2	0.005237	0
3	Sphingolipid metabolism	25	0.18695	2	0.014315	0.04292
4	Glycosylphosphatidylinositol(GPI)-anchor biosynthesis	14	0.10469	1	0.10001	0.0439
5	Retinol metabolism	22	0.16452	1	0.15284	0.09322
6	alpha-Linolenic acid metabolism	29	0.21687	1	0.19665	0
7	Methane metabolism	34	0.25426	1	0.22662	0
8	Fatty acid metabolism	50	0.37391	1	0.31559	0
9	Starch and sucrose metabolism	50	0.37391	1	0.31559	0.01265
10	Pentose and glucuronate interconversions	53	0.39634	1	0.33116	0.009
11	Arachidonic acid metabolism	62	0.46365	1	0.37588	0
12	Steroid hormone biosynthesis	99	0.74034	1	0.53174	0.01601
13	Porphyrin and chlorophyll metabolism	104	0.77773	1	0.54973	0.01101

Note: Total is the total number of compounds in the pathway; the Hits is the actually matched number from the user uploaded data; the Raw p is the original p value calculated from the enrichment analysis; the Impact is the pathway impact value calculated from pathway topology analysis.