

Table S1 DEGs identified in the liver tissues of CRC patients by comparing the synchronous and metachronous liver metastases

Tag	logFC	AveExpr	t	P value	adj.PVal	B
PAGE2	-1.0588	8.834422	-2.24183	0.03189	0.999863	-3.51181
GRPR	-0.73281	10.40107	-2.68668	0.011006	0.999863	-2.78859
RPL22L1	-0.69118	12.07632	-2.7427	0.009578	0.999863	-2.69361
SLC5A1	-0.69059	13.64516	-2.12049	0.0412	0.999863	-3.6792
PCDHGA10	-0.60875	12.88078	-2.36057	0.024008	0.999863	-3.31814
MAGEC1	-0.51665	10.84899	-3.66535	0.00082	0.999863	-1.00408
CAPN6	-0.50413	12.20878	-2.4412	0.019892	0.999863	-3.19115
SYNPR	-0.48609	10.98673	-2.19649	0.034842	0.999863	-3.56779
FZD3	-0.47134	12.80018	-2.26848	0.029641	0.999863	-3.45974
GDPD1	-0.46835	12.23495	-2.74397	0.009548	0.999863	-2.69144
SNCAIP	-0.4631	12.71017	-2.44112	0.019896	0.999863	-3.19129
CEL	-0.46104	13.4432	-2.09391	0.043655	0.999863	-3.71751
CEP290	-0.45753	12.24604	-2.42035	0.02089	0.999863	-3.22425
GLB1L3	-0.45568	11.07772	-2.89959	0.006445	0.999863	-2.42204
SHISA9	-0.45109	13.05117	-3.49356	0.001323	0.999863	-1.33282
TUBB8	-0.45079	11.062	-2.34694	0.024776	0.999863	-3.33933
KRT40	-0.45029	11.63853	-2.58329	0.01417	0.999863	-2.96093
ANXA13	-0.44575	13.21112	-2.89741	0.006481	0.999863	-2.42586
KLHL32	-0.42718	11.55337	-2.37344	0.023303	0.999863	-3.29805
PPBP	-0.42602	12.54828	-2.11922	0.041314	0.999863	-3.68103
MAGEC2	-0.41789	11.1698	-2.05843	0.047131	0.999863	-3.7681
HRH4	-0.4166	9.241159	-2.32105	0.026295	0.999863	-3.37937
PAQR5	-0.40607	13.23308	-2.21422	0.03349	0.999863	-3.5414
KRT75	-0.38235	11.93962	-3.10741	0.003756	0.999863	-2.05086
OR1A2	-0.36087	11.34791	-2.11318	0.041862	0.999863	-3.68976
OR10A5	-0.34537	11.14506	-2.53951	0.015748	0.999863	-3.03271
C20orf96	-0.34393	12.32322	-2.24036	0.031584	0.999863	-3.50223
ANGPTL5	-0.33751	7.421051	-2.17226	0.036767	0.999863	-3.6036
WFDC11	-0.33615	10.45289	-2.20951	0.033844	0.999863	-3.54842
MUC7	-0.33369	10.82261	-2.10059	0.043025	0.999863	-3.70791
EREG	-0.33121	13.95892	-2.41999	0.020908	0.999863	-3.22483
ZNF214	-0.32956	11.58271	-2.10793	0.042344	0.999863	-3.69734
STXBP4	-0.32221	12.55768	-2.23559	0.031924	0.999863	-3.5094
USP29	-0.31581	10.05404	-2.17741	0.03635	0.999863	-3.59601
TCEAL6	-0.31393	12.38811	-3.44433	0.001515	0.999863	-1.4261
AADAACL2	-0.30081	10.27	-2.14081	0.039406	0.999863	-3.64967
CFTR	-0.29948	14.04541	-2.3174	0.026516	0.999863	-3.38499
WFDC9	-0.29731	10.84212	-2.81509	0.007988	0.999863	-2.56929
OR10G8	-0.29592	12.18128	-2.04379	0.048636	0.999863	-3.7888
ASB14	-0.28425	10.65682	-2.64965	0.012055	0.999863	-2.85077
IL36G	-0.27303	11.93714	-2.49854	0.017368	0.999863	-3.09921
DSC2	-0.26774	13.8035	-2.43185	0.020334	0.999863	-3.20602
GTSF1L	-0.26605	11.07386	-2.08572	0.044436	0.999863	-3.72924
TMEM14EP	-0.26336	11.80761	-2.13798	0.039652	0.999863	-3.65381
ZSCAN5A	0.263856	12.0826	2.251756	0.030783	0.999863	-3.48506
ISL1	0.267669	11.28736	2.289225	0.028278	0.999863	-3.42817
CDCA5	0.268206	13.12138	2.419712	0.020921	0.999863	-3.22526
PXK	0.27467	13.07765	2.088919	0.044129	0.999863	-3.72466
RPTN	0.27978	11.00448	2.412981	0.021254	0.999863	-3.23591
GFPT2	0.281686	12.63883	2.248426	0.031015	0.999863	-3.49008
TEX13A	0.284459	11.87127	2.6339	0.012529	0.999863	-2.87706
NKAIN3	0.288958	10.93199	2.043366	0.048679	0.999863	-3.78939
EPHX3	0.290299	12.66766	2.640093	0.012341	0.999863	-2.86673
FAM167A	0.294564	12.66914	2.185533	0.035701	0.999863	-3.58401
ZNF75D	0.295719	12.36248	2.137618	0.039683	0.999863	-3.65433
IQCF2	0.308313	10.60545	2.62379	0.012842	0.999863	-2.89389
CLEC9A	0.312115	10.75696	2.16988	0.036961	0.999863	-3.60711
ZNF655	0.312992	13.31962	2.621054	0.012928	0.999863	-2.89844
POU4F3	0.316591	11.97574	2.379243	0.022992	0.999863	-3.28898
SNORA77	0.327117	12.8573	3.170393	0.003179	0.999863	-1.93606
TRIM36	0.33054	12.42079	2.089804	0.044045	0.999863	-3.72339
OSBPL6	0.330661	12.60858	2.083214	0.044678	0.999863	-3.73282
SH2D1B	0.335444	10.89708	2.343105	0.024996	0.999863	-3.34528
ADGRE1	0.336423	11.84148	2.407019	0.021552	0.999863	-3.24532
PIWIL4	0.345199	13.45551	2.664765	0.011616	0.999863	-2.82545
KBTBD8	0.345277	11.20389	2.087047	0.044309	0.999863	-3.72734
ARNTL	0.348979	13.09691	4.406286	9.66E-05	0.789844	0.452101
BNIP3	0.352699	13.88717	2.19846	0.034896	0.999863	-3.56792
CRISP1	0.353202	9.863335	2.493978	0.017558	0.999863	-3.10658
NME8	0.358893	9.159359	2.099194	0.043156	0.999863	-3.70992
TRIM48	0.362365	10.71387	3.073574	0.004106	0.999863	-2.1121
GAD1	0.365212	11.90011	2.27235	0.029382	0.999863	-3.45387
PPIL6	0.366826	11.92791	2.426618	0.020585	0.999863	-3.21432
CDC14C	0.367293	10.77132	2.733105	0.00981	0.999863	-2.70995
HUNK	0.381564	12.76172	2.68875	0.01095	0.999863	-2.7851
PLEKHG1	0.3935	12.76051	2.629646	0.01266	0.999863	-2.88415
RNASE3	0.395957	11.72401	2.258932	0.030288	0.999863	-3.47421
SDR42E1	0.417584	12.83105	3.271672	0.002424	0.999863	-1.74943
CYP26A1	0.428998	11.8507	2.2282	0.032458	0.999863	-3.52049
SLAIN1	0.44549	12.2229	2.379446	0.022981	0.999863	-3.28866
OR6C68	0.465618	10.25114	4.291648	0.000135	0.789844	0.224343
CD226	0.484044	11.60287	2.279453	0.028913	0.999863	-3.44307
DPH3P1	0.487039	9.846845	2.097148	0.043348	0.999863	-3.71286
CXorf58	0.501813	9.168746	2.226285	0.032598	0.999863	-3.52336
TAS2R31	0.504158	11.09448	2.5893	0.013966	0.999863	-2.95103
KIAA0319	0.506881	12.32017	2.635829	0.01247	0.999863	-2.87385
RPGRIP1	0.524015	10.06052	2.571256	0.014589	0.999863	-2.98074
SPAG16	0.531744	12.71616	2.487472	0.017831	0.999863	-3.11706
MIR99AHG	0.570395	9.453328	2.132419	0.040138	0.999863	-3.66189
ADGRG2	0.579713	11.264	2.115231	0.041675	0.999863	-3.6868
OR6C1	0.588606	8.623054	2.078193	0.045166	0.999863	-3.73999
ATP12A	0.598017	12.03793	2.148107	0.038779	0.999863	-3.63903
ZDHHC11B	0.633251	12.8559	2.568465	0.014688	0.999863	-2.98533
SPINK7	0.672686	8.644482	2.068891	0.046082	0.999863	-3.75325
CNTLN	0.680737	11.48618	2.691111	0.010886	0.999863	-2.78112
FUT9	0.699768	8.441847	4.407687	9.62E-05	0.789844	0.454887
IL13RA2	0.719021	10.39282	2.628168	0.012838	0.999863	-2.89482
ASPA	0.749501	11.36381	2.245045	0.031252	0.999863	-3.49517
OR5H15	0.750191	8.460118	2.521068	0.016459	0.999863	-3.06273
TAS2R46	0.853411	9.728956	2.104017	0.043163	0.999863	-3.70747
IL5RA	0.907942	11.46483	2.058268	0.047148	0.999863	-3.76833
C19orf18	0.92955	10.87452	2.51537	0.016685	0.999863	-3.07198

DEGs, differentially expressed genes; FC, fold change; CRC, colorectal cancer.

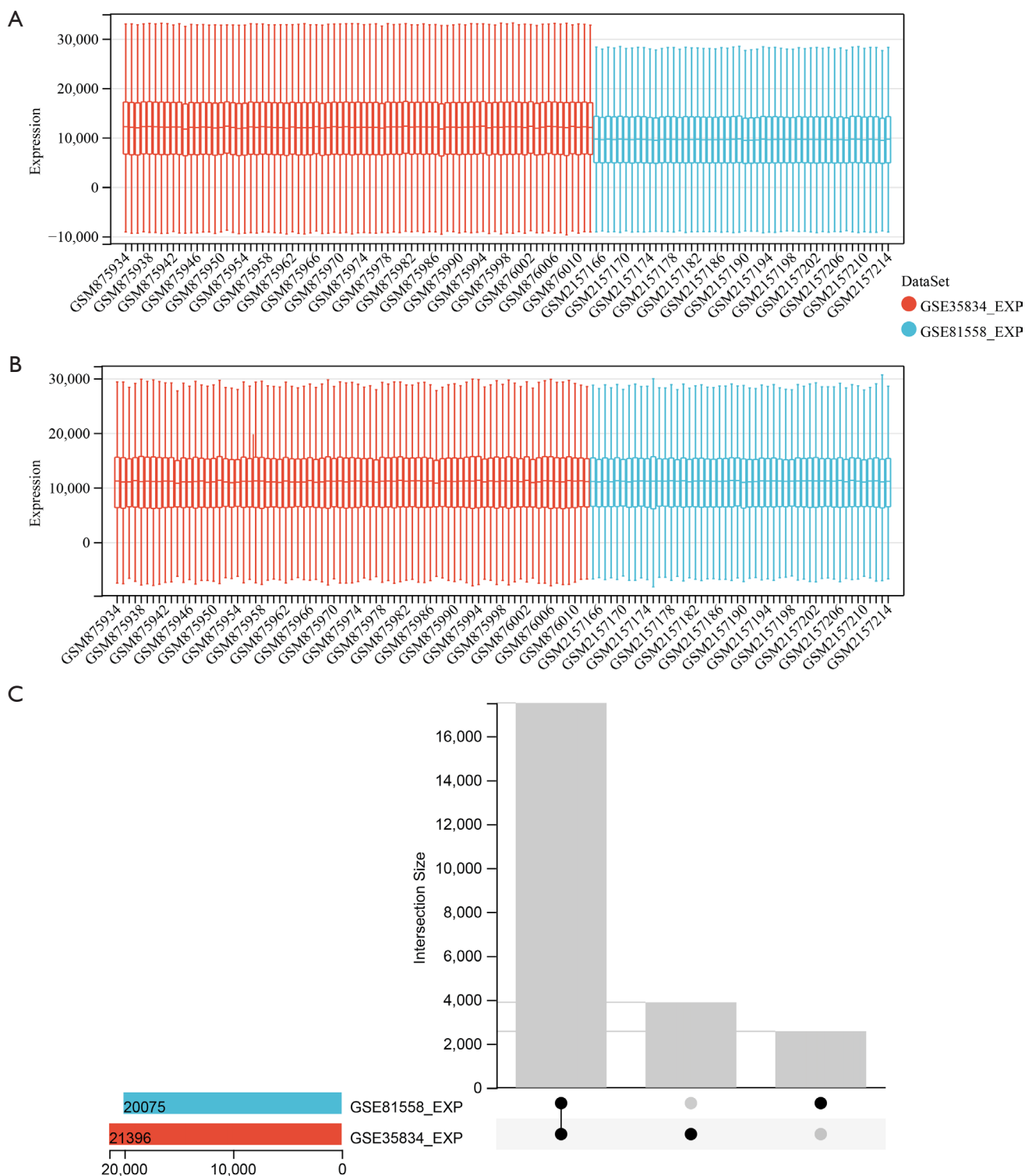


Figure S1 Comparison of GEO data before and after merging. (A) Data distribution plot before removing batch effects. (B) Data distribution plot after removing batch effects. (C) Intersection of genes between the two datasets. The first column represents the number of genes in the two GEO datasets, the second column represents the unique elements of the one set, and the third column represents the element values corresponding to the intersection. GEO, Gene Expression Omnibus.

Table S2 The score of immune cells using the MCP-counter algorithm and the *t*-test results between the primary tumor tissues and metastatic liver tissues in CRC patients

GSE	T cells		CD8 ⁺ T cells		Cytotoxic lymphocytes		B lymphocytes		NK cells		Monocytic lineage		Myeloid dendritic cells		Neutrophils		Endothelial cells		CAFs	
	Colon	Liver	Colon	Liver	Colon	Liver	Colon	Liver	Colon	Liver	Colon	Liver	Colon	Liver	Colon	Liver	Colon	Liver	Colon	Liver
GSM875949	9492.66	8637.84	3693.20	4080.81	4803.36	4569.50	8065.97	6431.44	4789.10	6077.04	11749.03	8513.35	5118.98	4768.10	8079.20	8102.92	9690.91	8212.87	16875.99	14451.03
GSM875961	7765.78	8587.02	3091.83	2810.58	4573.58	4569.23	6112.37	6595.73	5169.89	6055.82	9303.02	9765.86	4363.34	5346.13	7849.02	8832.61	8431.24	8693.21	16190.20	14005.01
GSM875951	8342.42	9365.74	3406.83	2841.26	6646.76	8171.18	5959.64	6576.60	6605.05	5533.79	8333.74	15971.09	4468.91	6397.20	8838.85	9625.56	9329.17	9821.49	16215.43	15960.41
GSM876001	7366.96	9877.54	3465.13	3719.79	4243.84	5136.33	5747.41	6626.74	4348.40	5782.70	9079.73	13262.40	4260.90	5033.66	8018.96	9481.70	9001.80	8815.40	15406.68	16142.36
GSM875953	7607.24	8130.31	3301.49	3663.54	4065.95	4773.36	5677.82	6254.73	4636.21	5239.75	7951.48	10675.24	4519.26	5145.72	8091.63	8116.45	8762.41	8917.77	15295.46	15175.63
GSM875962	8536.45	8498.39	3075.47	2878.08	3928.01	4016.84	7606.82	6088.89	5106.47	4388.43	9586.65	14443.02	4900.99	5275.43	7899.25	9465.82	8747.16	9108.08	12474.54	15436.15
GSM875956	8456.24	8226.21	3473.31	3146.04	4253.95	4764.65	6268.97	6407.26	4325.25	5471.09	10445.89	12042.05	5164.56	4926.88	8515.18	8820.36	8776.67	9025.85	15630.20	15120.82
GSM876003	8414.17	8473.72	3090.81	2530.35	4738.99	4848.27	7367.74	6403.97	5423.01	5554.09	7817.05	12503.13	5180.39	5521.63	8535.21	8259.33	9149.07	8888.64	14552.67	15912.07
GSM875959	8002.73	7993.15	3256.49	2229.67	4470.12	4751.31	6459.34	6014.25	5386.25	5556.68	8456.24	10480.94	5213.45	5097.59	8369.02	8518.32	8926.32	8801.55	14499.52	15618.29
GSM875990	7641.90	7431.30	3231.94	4517.52	3916.58	4290.41	6019.57	5489.87	4923.79	4780.07	7510.15	9808.47	4329.74	4470.32	8641.31	9078.01	8319.57	8746.40	13873.95	15043.24
GSM875980	8568.10	8065.26	2611.15	1552.62	4347.07	4366.81	6638.04	6021.03	5738.92	4242.70	11146.44	10636.59	5758.87	4461.42	8250.64	9743.16	8187.24	8013.54	11252.59	15326.19
GSM875955	8245.78	8116.54	3636.95	3382.29	4841.37	4547.25	6420.76	6301.37	4541.80	5201.98	12104.25	11160.45	4503.52	4601.75	9390.85	9317.31	10073.56	9082.54	17229.45	14451.41
GSM876008	8064.57	8155.04	3739.22	3161.38	4930.35	4418.99	6091.91	5309.12	4891.42	4964.04	8483.12	6762.10	4837.52	3781.93	7962.51	8263.94	8304.09	7704.38	13370.22	11899.34
GSM876006	13072.24	7620.47	6160.03	1664.10	6821.51	4247.19	13634.70	5977.20	5810.47	4019.43	12065.16	11638.45	6002.90	4722.13	8325.46	7877.79	8899.59	7758.81	16479.91	14015.57
GSM875979	7723.34	8137.29	2999.78	3047.85	4325.09	4448.68	6240.83	6759.17	5103.29	5180.10	10389.76	10801.57	4405.83	4803.52	9083.64	9963.15	9379.77	9128.80	16782.19	15750.07
GSM875992	8275.59	8706.32	2548.76	3259.56	4014.67	3818.27	5869.99	6327.07	4471.36	4306.95	8785.85	11946.87	4962.05	4998.67	7883.79	8890.78	9123.02	9305.13	16138.06	14636.56
GSM2157173	8516.17	7922.34	2773.90	3070.54	4256.06	4288.03	6966.02	6221.15	6553.47	6319.96	9157.22	9492.13	4566.81	4952.81	8413.29	8302.66	9086.56	9307.16	15743.41	16110.13
GSM2157174	8281.11	7498.82	2577.09	2738.72	5212.38	4321.42	6476.33	6432.52	6506.76	5871.11	12129.17	9997.23	4775.13	4162.19	8102.29	7694.13	9465.35	8027.84	17023.89	13666.21
GSM2157175	8487.52	10967.74	3257.85	2308.97	4401.72	4406.07	7252.60	7711.57	4626.37	6697.50	9244.95	9951.46	5022.10	4610.88	8813.66	9711.49	8704.65	8905.59	15712.25	14125.90
GSM2157176	8223.18	8540.23	3197.00	3023.01	3654.61	4583.65	7325.38	6591.76	4362.47	4856.30	8233.08	10659.28	5002.81	5272.41	8160.38	9690.20	8769.97	8551.72	15356.06	15055.01
GSM2157177	8884.69	8892.60	2507.68	3601.08	3876.30	4944.24	6040.71	5994.38	4702.91	5271.00	10675.24	12619.35	5976.50	6816.07	8241.53	10265.68	9804.74	9246.40	16950.17	15507.74
GSM2157178	10991.48	8018.98	5249.73	2800.52	5905.21	4445.38	11055.48	5989.94	5416.73	6724.73	13802.44	9272.11	6755.67	4156.01	8527.72	8497.02	10338.15	7905.14	16726.85	13555.75
GSM2157179	8500.72	9610.88	2778.66	3617.24	4630.72	4965.35	8490.84	6919.02	4968.59	5341.41	10698.25	11924.25	5148.86	6699.79	9097.93	11243.99	9953.01	9355.29	16859.53	15379.03
GSM2157180	7354.14	7530.65	2757.74	3268.31	3494.55	4346.73	6193.02	6502.41	5090.98	4952.86	10787.48	12204.62	4198.66	4402.44	8300.30	8478.66	9162.11	8164.59	15572.12	13107.06
GSM2157181	8197.95	12564.21	3753.20	4584.18	4017.06	7951.54	6969.19	8410.65	4790.76	5000.45	8026.88	16381.18	4138.76	6823.90	7780.35	9699.68	7949.48	11448.54	12571.91	17916.91
GSM2157182	8690.36	8119.06	3055.33	4183.91	4369.93	3969.18	6399.34	6304.24	4738.28	4839.08	10220.74	11512.75	5201.41	5061.80	8331.84	8557.64	9083.77	9050.01	15397.24	15265.02
GSM2157183	9226.14	7643.32	3110.48	3249.29	5501.47	4338.43	7718.10	5555.22	5038.44	4727.62	12878.90	9608.54	5386.96	4268.01	8630.73	8163.59	9910.63	7959.13	16618.08	13365.89
GSM2157184	8075.91	8116.72	2751.08	2714.00	4369.51	3610.87	6942.60	6635.36	4915.46	4812.66	7451.59	14061.41	3692.61	4814.31	8469.20	8215.77	7916.90	9783.16	12669.70	15900.01
GSM2157185	8258.06	9437.04	3365.29	2467.75	4389.32	4861.81	6424.50	6570.24	5722.80	5992.31	12742.84	12754.64	4944.56	5274.91	9781.99	10673.85	9425.77	9246.81	16169.27	15121.73
GSM2157186	8564.86	8314.38	3478.43	2752.03	5908.45	4624.65	6016.48	6116.94	4109.01	4581.03	13431.93	13797.67	6774.20	6684.28	8363.69	7999.98	9205.22	9066.95	17043.81	15093.77
GSM2157187	9103.11	8342.29	3065.79	3082.90	4656.51	3994.08	7268.40	5980.68	5033.10	4500.43	13452.63	12057.29	5855.82	4787.83	8950.02	9450.47	10926.09	8144.19	17588.11	14432.97
GSM2157188	9757.40	8541.03	2688.33	3797.89	5682.56	5283.51	7605.03	6847.68	5378.31	4580.92	15952.05	12791.41	6374.61	4331.88	9045.12	8638.39	10251.78	8029.59	18112.33	13732.39
GSM2157189	8437.55	8977.80	2909.86	3499.34	4411.56	5470.58	7019.65	8308.94	4446.68	6293.94	9232.69	12301.71	4703.26	5361.04	8135.88	9795.80	8743.37	9551.55	15331.90	16313.41
GSM2157190	9590.90	9174.88	2112.16	2529.55	3901.10	4001.06	7211.63	7261.42	6308.11	5815.04	8599.62	9241.47	5463.15	4577.56	8755.19	8389.76	9814.61	9535.48	15954.32	16371.47
GSM2157191	8423.35	8550.50	5687.09	2694.99	6122.66	4652.70	5934.31	7366.82	4802.78	5394.63	12617.23	9167.44	5623.90	3944.26	8543.76	8282.37	9528.44	8380.10	17654.70	15687.66
<i>t</i> Stat	0.038496296		1.053208564		-0.173136213		1.782060816		-1.203729721		-2.062928077		0.192223258		-3.761478906		1.662788425		1.718682233	
P (one-tailed test)	0.48475857		0.14983653		0.431785498		0.041836379		0.118504062		0.023411769		0.424355422		0.000318927		0.052773957		0.047383376	
<i>t</i> (one-tailed test)	1.690924255		1.690924255		1.690924255		1.690924255		1.690924255		1.690924255		1.690924255		1.690924255		1.690924255		1.690924255	
P (two-tailed test)	0.96951714		0.299673061		0.863570996		0.083672759		0.237008124		0.046823539		0.848710844		0.000637855		0.105547913		0.094766752	
<i>t</i> (two-tailed test)	2.032244509		2.032244509		2.032244509		2.032244509		2.032244509		2.032244509		2.032244509		2.032244509		2.032244509		2.032244509	

CRC, colorectal cancer; MCP, Microenvironment Cell Populations; GSE, gene set enrichment; CAFs, cancer-associated fibroblasts; NK, natural killer.

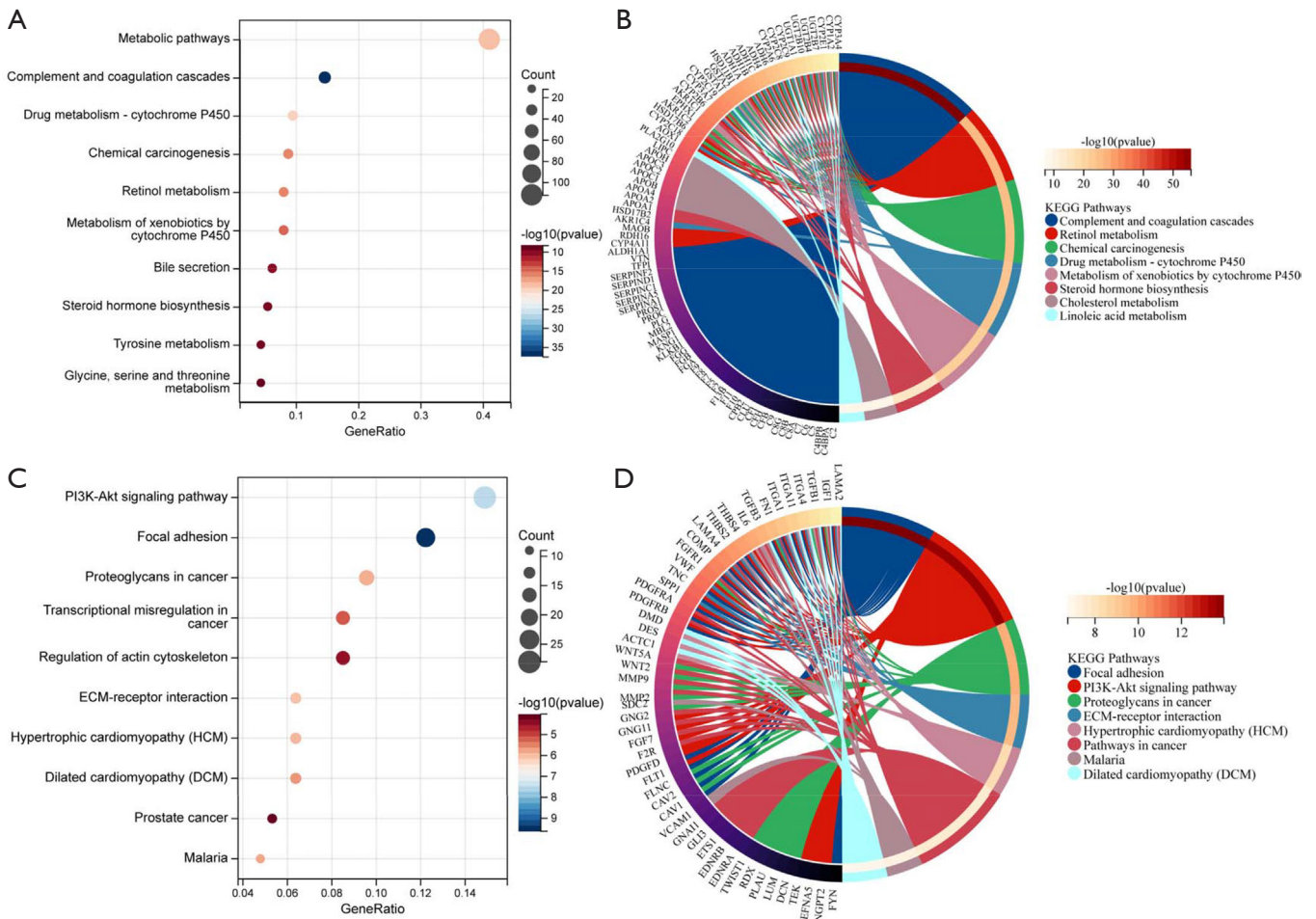


Figure S2 Functional enrichment analysis of genes in candidate modules. Top 10 enrichment results of pathway analysis by KEGG analysis for co-expressed genes in yellow (A) and brown (C) modules. Top eight enrichment results of genes by KEGG analysis in the PPI network of yellow (B) and brown (D) modules. The shade of colour of the inner ring represents the P value. KEGG, Kyoto Encyclopaedia of Gene and Genome; PPI, protein-protein interaction; PI3K, phosphoinositide 3-kinase; ECM, extracellular matrix.

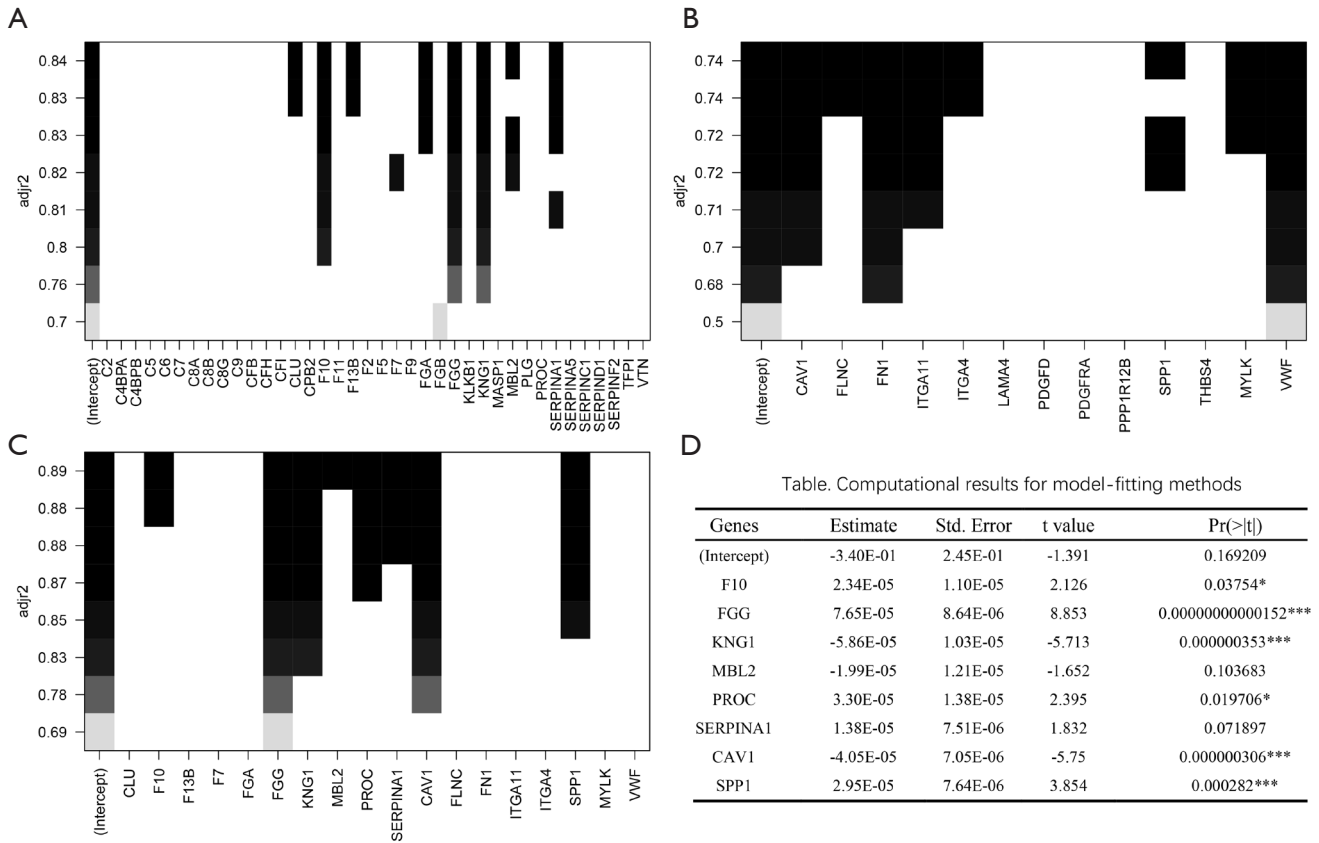


Figure S3 The best-fitting regression model for the analysis of CRCLM. The optimal subset regression of hub genes in the yellow module (A), brown module (B), and further filtering the two (C). The left of the forest plot is the adjusted R^2 value corresponding to the combination of different gene subsets, and the colour of the grid corresponds to the value. (D) The result of the backward stepwise regression. *, $P < 0.05$; ***, $P < 0.001$. CRCLM, colorectal cancer with liver metastasis.