

Table S1 Oligo sequences used in the real-time PCR

Gene symbol	Primer sequences
<i>FDX1</i>	Forward: 5'-CTTTGGTGCATGTGAGGGAA-3' Reverse: 5'-CAGCCCAACCGTGATCTGT-3'
<i>LIAS</i>	Forward: 5'-GGGAGGTGGAGAATATGCCA-3' Reverse: 5'-TTGCAATGTGTTCCAGCTCCC-3'
<i>LIPT1</i>	Forward: 5'-GCTCTGAATGCTGTCCAACC-3' Reverse: 5'-GCATTGCTCCTGATCCCTTG-3'
<i>DLD</i>	Forward: 5'-GTTGAAGGAATGGCTGGTGG-3' Reverse: 5'-TGCCCAAGGATCTTCAACCAT-3'
<i>DLAT</i>	Forward: 5'-TCCAACCTCCCCAGCCTTTAG-3' Reverse: 5'-CCATCTGGTCCTGTCCCTTT-3'
<i>PDHA1</i>	Forward: 5'-TGTGTGATGGTCAGGAAGCT-3' Reverse: 5'-ACATGTGCATCGATCCTCCT-3'
<i>PDHB</i>	Forward: 5'-GGGTATGGATGAGGAGCTGG-3' Reverse: 5'-GCACCTACAGCAATCCAGC-3'
<i>MTF1</i>	Forward: 5'-TGTAATCAGGAGGGCTGTGG-3' Reverse: 5'-ACGTTTTCCCTGTGTGAAGC-3'
<i>GLS</i>	Forward: 5'-GAAGGCACAGACATGGTTGG-3' Reverse: 5'-CTGCTTCAGGGCTCAGTACT-3'
<i>CDKN2A</i>	Forward: 5'-CTTCCTGGACACGCTGGT-3' Reverse: 5'-TCAATCGGGGATGTCTGAGG-3'
<i>GAPDH</i>	Forward: 5'-CCAGAACATCATCCCTGCCT-3' Reverse: 5'-CCTGCTTCACCACCTTCTTG-3'

PCR, polymerase chain reaction.

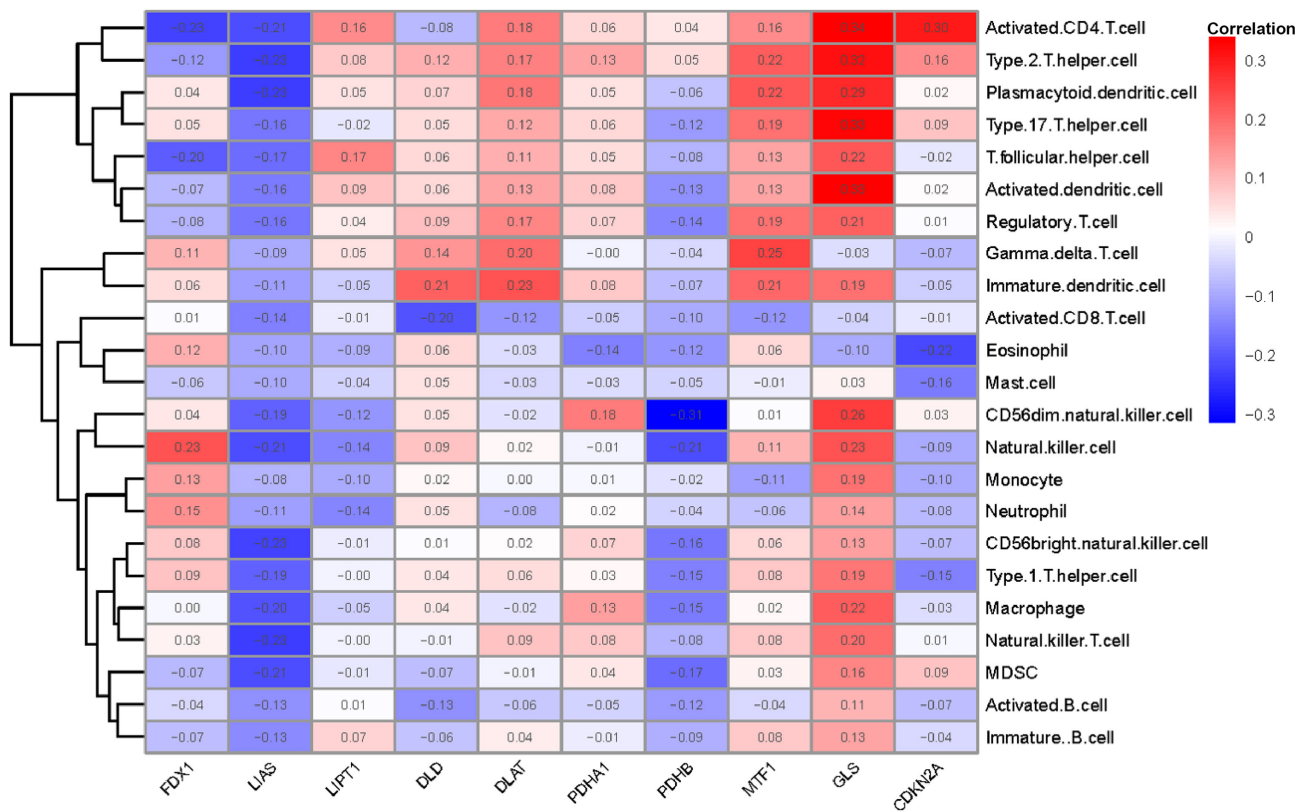


Figure S1 Correlation between the cuproptosis-related regulator in molecular subtypes versus each immune cell infiltrate.

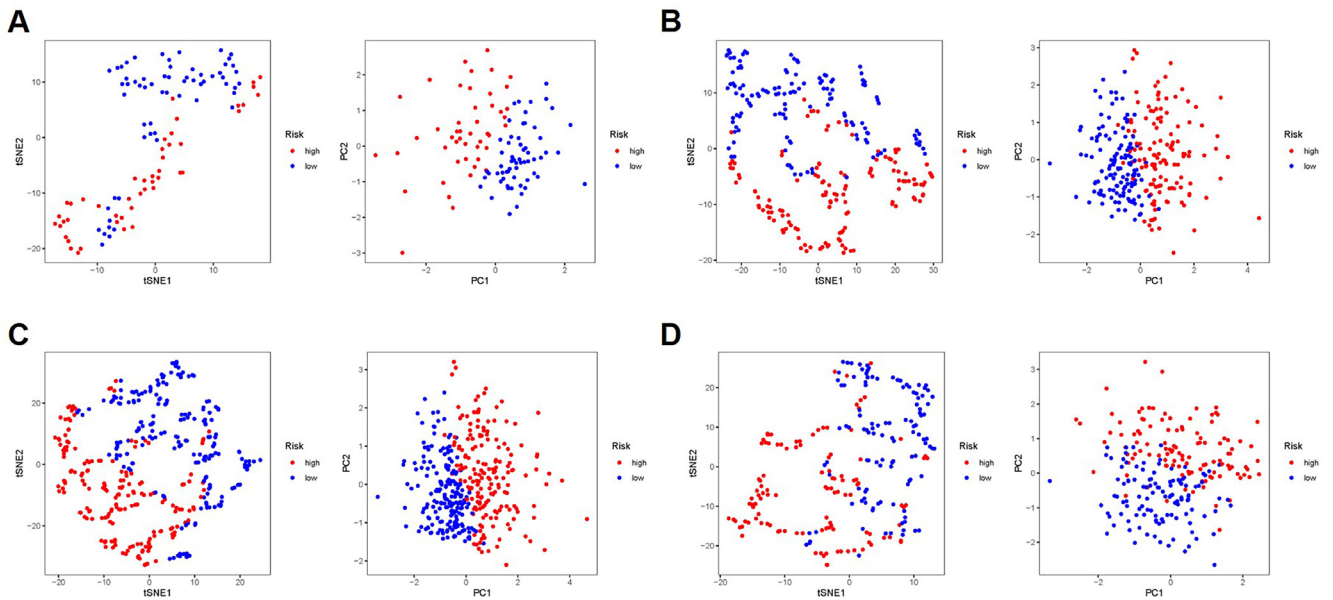


Figure S2 Principal components analysis (PCA) and t-distributed stochastic neighbor embedding (t-SNE) analysis verified the reliable clustering ability of risk scores. PCA analysis and t-SNE plot of (A) The Cancer Genome Atlas (TCGA) train cohort, (B) the TCGA test cohort, (C) The Cancer Genome Atlas Liver Hepatocellular Carcinoma (TCGA-LIHC) full cohort and (D) the International Cancer Genome Consortium Liver Cancer (ICGC-LIRI) cohort.

Table S2 Clinical and pathological parameters of patients in TCGA train and test cohort

Characteristics	Group	TCGA train (n=262)	TCGA test (n=108)	P value	Method
Albumin (g/dL) mean (SD)		28.82 (357.7)	4.72 (6.5)	0.5354	Wilcoxon test
Child Pugh Classification Grade, N (%)	A	158 (60.31)	58 (53.70)	0.2591	Fisher's exact test
	B	15 (5.73)	6 (5.56)		
	C	0 (0)	1 (0.93)		
	NA	89 (33.97)	43 (39.81)		
Creatinine (mg/dL) mean (SD)		2.03 (8.1)	4.72 (18.3)	0.0803	Wilcoxon test
Fetoprotein (ng/mL) mean (SD)		16289 (146602.4)	8050 (32355.1)	0.6259	Wilcoxon test
Platelet (/mm ³) mean (SD)		22671 (76489.74)	29170 (82782.6)	0.5154	Wilcoxon test
Prothrombin time (s) mean (SD)		3.933 (5.00)	4.296 (4.75)	0.5604	Wilcoxon test
Body mass index (BMI) (kg/m ²) mean (SD)		26.02 (9.23)	26.42 (6.20)	0.6405	Wilcoxon test
Height (cm) mean (SD)		166.7 (11.07)	168.8 (9.65)	0.0896	Wilcoxon test
Weight (kg) mean (SD)		71.79(19.36)	75.44 (19.58)	0.1168	Wilcoxon test
Relative family cancer history, N (%)	Yes	78 (29.77)	34 (31.48)	0.433	χ^2 test
	No	153 (58.40)	54 (50.00)		
	NA	31 (11.83)	20 (18.52)		
Race demographic, N (%)	American Indian or Alaska Native	1 (0.38)	1 (0.93)	0.5318	Fisher's exact test
	Asian	118 (45.04)	39 (36.11)		
	Black or African American	12 (4.58)	5 (4.63)		
	White	125 (47.71)	59 (54.63)		
	NA	6 (2.29)	4 (3.70)		
Sex, N (%)	Male	182 (69.47)	66 (61.11)	0.1202	χ^2 test
	Female	80 (30.53)	42 (38.89)		
Age (years), N (%)	≤ 65	150 (57.25)	53 (49.07)	0.1507	χ^2 test
	> 65	112 (42.75)	55 (50.93)		
Histological grade, N (%)	G1	41 (15.65)	16 (14.81)	0.73	Fisher's exact test
	G2	126 (48.09)	53 (49.07)		
	G3	82 (31.30)	37 (34.26)		
	G4	8 (3.05)	2 (1.85)		
	NA	5 (1.91)	0 (0)		
Clinical stage, N (%)	I	125 (47.71)	47 (43.52)	0.784	Fisher's exact test
	II	59 (22.52)	24 (22.22)		
	III	57 (21.76)	29 (26.85)		
	IV	3 (1.15)	2 (1.85)		
	NA	18 (6.87)	6 (5.56)		

Table S2 (continued)

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Characteristics	Group	TCGA train (n=262)	TCGA test (n=108)	P value	Method
Pathologic T, N (%)	T1	132 (50.38)	50 (27.78)	0.79	Fisher's exact test
	T2	64 (24.43)	27 (25.00)		
	T3	54 (20.61)	27 (25.00)		
	T4	9 (3.44)	4 (3.70)		
	TX/NA	3 (1.15)	0 (0)		
Pathologic N, N (%)	N0	171 (65.27)	82 (75.93)	0.039	Fisher's exact test
	N1	2 (0.76)	2 (1.85)		
	NX/NA	89 (33.97)	24 (22.22)		
Pathologic M, N (%)	M0	186 (70.99)	81 (75.00)	0.327	Fisher's exact test
	M1	2 (0.76)	2 (1.85)		
	MX	74 (28.24)	25 (23.15)		
Survival status, N (%)	Alive	177 (67.56)	68 (62.96)	0.3956	χ^2 test
	Dead	85 (32.44)	40 (37.04)		

TCGA, The Cancer Genome Atlas; NA, not applicable.

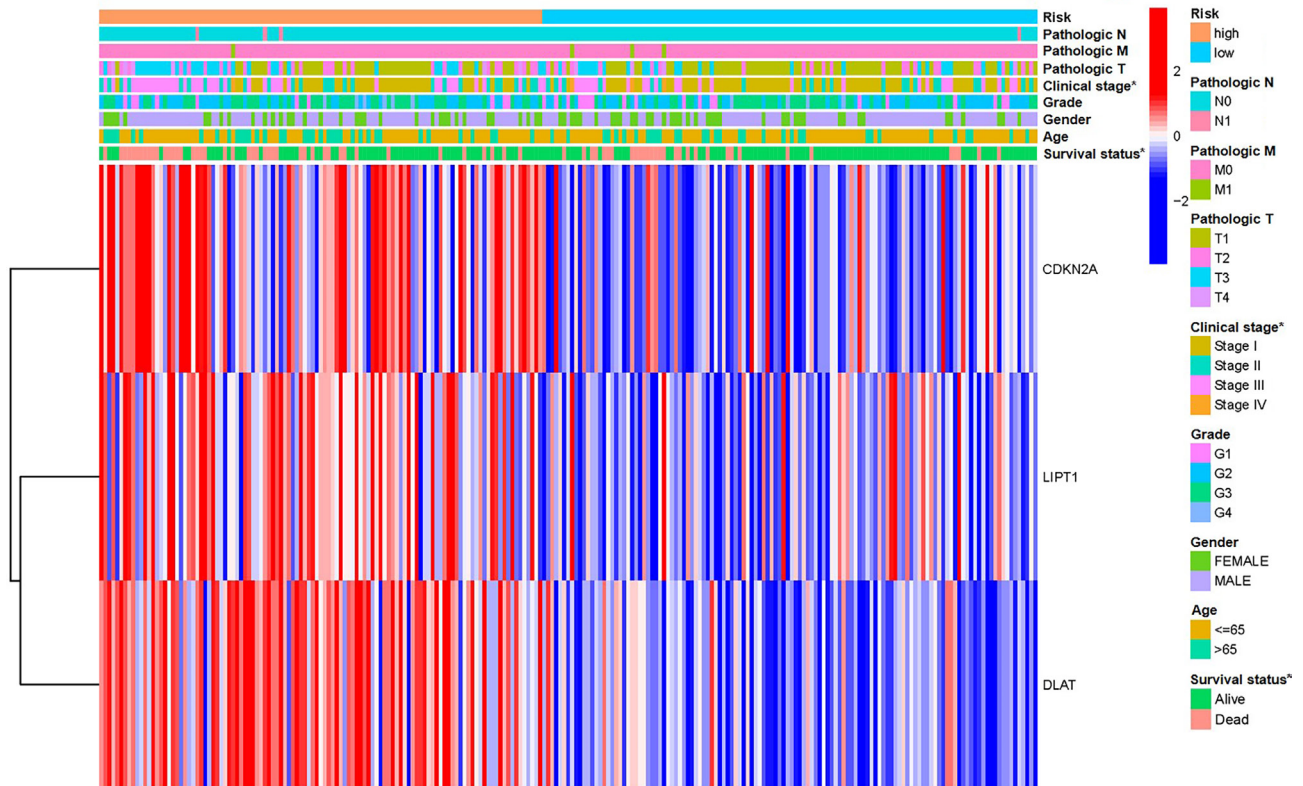


Figure S3 Heatmap of the three cuproptosis related regulatory genes in low- and high-risk groups. The distribution of clinicopathological characteristics was compared between low- and high-risk groups. *, $P < 0.05$.