

Supplementary materials

Table S1. GOBP enriched analysis in BUB1B high-expressions group of HCC.

GOBP Gene set name (BUB1B High group)	NES	NOM p-val	FDR q-val
GOBP_CYTOKINETIC_PROCESS	2.56	<0.001	<0.001
GOBP_REGULATION_OF_SPINDLE_ORGANIZATION	2.38	<0.001	0.033
GOBP_NEGATIVE_REGULATION_OF_CELL_CYCLE_G2_M_PHASE_TRANSITION	2.37	<0.001	0.026
GOBP_CHROMOSOME_LOCALIZATION	2.36	<0.001	0.02
GOBP_REGULATION_OF_UBIQUITIN_PROTEIN_TRANSFERASE_ACTIVITY	2.32	<0.001	0.023
GOBP_REGULATION_OF_CHROMOSOME_ORGANIZATION	2.32	<0.001	0.019
GOBP_METAPHASE_PLATE_CONGRESSION	2.32	<0.001	0.017
GOBP_MITOTIC_CELL_CYCLE_PHASE_TRANSITION	2.32	<0.001	0.015
GOBP_REGULATION_OF_MITOTIC_CELL_CYCLE_PHASE_TRANSITION	2.31	<0.001	0.014
GOBP_CYTOKINESIS	2.31	<0.001	0.012

Table S2. GOBP enriched analysis in RRM2 high-expressions group of HCC.

GOBP Gene set name (RRM2 High group)	NES	NOM p-val	FDR q-val
GOBP_CYTOSKELETON_DEPENDENT_CYTOKINESIS	2.65	<0.001	<0.001
GOBP_CYTOKINETIC_PROCESS	2.64	<0.001	<0.001
GOBP_CYTOKINESIS	2.61	<0.001	<0.001
GOBP_REGULATION_OF_CHROMOSOME_ORGANIZATION	2.59	<0.001	<0.001
GOBP_CHROMOSOME_LOCALIZATION	2.55	<0.001	<0.001
GOBP_MITOTIC_CYTOKINESIS	2.52	<0.001	<0.001
GOBP_REGULATION_OF_MITOTIC_CELL_CYCLE_PHASE_TRANSITION	2.51	<0.001	<0.001
GOBP_MITOTIC_CELL_CYCLE_PHASE_TRANSITION	2.47	<0.001	0.001
GOBP_REGULATION_OF_CELL_CYCLE_PHASE_TRANSITION	2.47	<0.001	0.001
GOBP_DNA_REPLICATION	2.46	<0.001	0.001

Table S3. KEGG enriched analysis in the BUB1B high-expressions group of HCC.

KEGG Gene set name (BUB1B High group)	NES	NOM p-val	FDR q-val
KEGG_CELL_CYCLE	0.7	2.17	< 0.0001
KEGG_OOCYTE_MEIOSIS	0.58	2.1	< 0.0001
KEGG_NUCLEOTIDE_EXCISION_REPAIR	0.51	2.03	0.008
KEGG_DNA_REPLICATION	0.77	2.02	< 0.0001
KEGG_MISMATCH_REPAIR	0.69	1.99	< 0.0001
KEGG_HOMOLOGOUS_RECOMBINATION	0.77	1.91	< 0.0001
KEGG_P53_SIGNALING_PATHWAY	0.52	1.85	< 0.0001
KEGG_BASE_EXCISION_REPAIR	0.5	1.75	0.036
KEGG_PROGESTERONE_MEDIATED_OOCYTE_MATURATION	0.51	1.72	0.004
KEGG_UBIQUITIN_MEDIATED_PROTEOLYSIS	0.3	1.68	0.029

Table S4. KEGG enriched analysis in RRM2 high-expressions group of HCC.

KEGG Gene set name (RRM2High group)	NES	NOM p-val	FDR q-val
KEGG_OOCYTE_MEIOSIS	0.63	2.27	< 0.0001
KEGG_CELL_CYCLE	0.75	2.26	< 0.0001
KEGG_P53_SIGNALING_PATHWAY	0.61	2.15	< 0.0001
KEGG_DNA_REPLICATION	0.79	2.09	< 0.0001
KEGG_HOMOLOGOUS_RECOMBINATION	0.83	2.05	< 0.0001
KEGG_NUCLEOTIDE_EXCISION_REPAIR	0.52	2.03	0.004
KEGG_MISMATCH_REPAIR	0.69	2.02	< 0.0001
KEGG_PROGESTERONE_MEDIATED_OOCYTE_MATURATION	0.58	1.95	< 0.0001
KEGG_BASE_EXCISION_REPAIR	0.54	1.89	0.02
KEGG_RNA_DEGRADATION	0.39	1.86	0.006

Table S5. The relationships between BUB1B expression and patients' clinical features in LIHC TCGA database.

Characteristics	Categories	BUB1B expression		p value
		High expression	Low expression	
Gender	male	132	119	0.987
	female	63	57	
Adjacent hepatic tissue inflammation	No	59	59	0.219
	yes	57	61	
Age	> 60	91	104	0.017
	≤60	105	73	
Fibrosis Ishak score	No fibrosis	28	47	0.006
	With fibrosis	31	28	
	Cirrhosis	43	37	
Grade	G1, G2	97	138	< 0.001
	G3, G4	99	39	
T Stage	T1	81	108	< 0.001
	T2	57	50	
	T3, T4	58	19	
Survival status	Alive	119	124	0.059
	Dead	77	53	
Race	Asian	97	62	0.037
	Non- Asian	99	105	
Tumor stage	I	78	94	0.02
	II	50	37	
	III, IV	56	34	

Table S6. The relationships between RRM2 expression and patients' clinical features in LIHC TCGA database.

Characteristics	Categories	BUB1B expression		p value
		High expression	Low expression	
Gender	male	139	113	0.345
	female	73	48	
Adjacent hepatic tissue inflammation	No	59	59	0.434
	yes	65	53	
Age	> 60	95	100	0.001
	≤60	117	61	
Fibrosis Ishak score	No fibrosis	32	43	0.092
	With fibrosis	34	25	
	Cirrhosis	47	33	
Grade	G1, G2	114	121	< 0.001
	G3, G4	98	40	
T Stage	T1	86	98	0.001
	T2	65	31	
	T3, T4	61	32	
Survival status	Alive	129	113	0.061
	Dead	83	48	
Race	Asian	107	52	0.001
	Non- Asian	101	104	
Tumor stage	I	84	88	0.007
	II	58	29	
	III, IV	58	32	

Table S7. Univariate analysis and multivariate analysis of factors of overall survival OS of LIH TCGA in BUB1B expression.

Variables	Category	Univariate analysis			Multivariate analysis		
		HR	95%CI	P value	HR	95%CI	P value
BUB1B	Low vs High	1.200	1.100–1.400	<0.001	1.239	1.107- 1.386	0.00019
Age	≤65, >65	0.810	0.570–1.100	0.230			
Gender	Male vs Female	1.100	0.780–1.600	0.500			
Adjacent hepatic tissue inflammation	Yes, NO	0.640	0.400–1.000	0.076			
Fibrosis ishak score	Cirrross	0.870	0.650–1.200	0.350			
Grade	G1-G2 vs G3-G4	0.970	0.670–1.400	0.880			
Tumor stage	Stage I- II vs III -IV	1.200	0.790–1.800	0.420			
T Stage	T1-T2 vs T3-4	1.600	1.100–2.400	0.009	1.631	1.116-2.38	0.011
N Stage	N0 vs N1	1.500	1.000–2.200	0.035	1.443	0.840-2.478	0.183
M Stage	M0 vs M1	1.600	1.100–2.300	0.013	1.367	0.797-2.344	0.255

Table S8. Univariate analysis and multivariate analysis of factors of overall survival OS of LIH TCGA in RRM2 expression.

Variables	Category	Univariate analysis			Multivariate analysis		
		HR	95%CI	P value	HR	95%CI	P value
RRM2	Low vs High	1.300	1.100–1.500	<0.001	1.289	1.126- 1.47	0.00022
Age at initial pathologic diagnosis	≤65, >65	0.810	0.570–1.100	0.230			
Gender demographic	Male vs Female	1.100	0.780–1.600	0.500			
Adjacent hepatic tissue inflammation	Yes, NO	0.640	0.400–1.000	0.076			
Fibrosis ishak score	With Fibross, complete and incomplete cirrhoss	0.870	0.650–1.200	0.350			
Neoplasm histologic grade	G1-G2 vs G3-G4	0.970	0.670–1.400	0.880			
Vascular tumor cell type	Male, Female	1.100	0.720–1.700	0.650			
Tumor stage diagnoses	Stage I- II vs III -IV	1.200	0.790–1.800	0.420			
pathologic _T	T1-T2 vs T3-4	1.600	1.100–2.400	0.009	1.623	1.110- 2.37	0.0124
pathologic _N	N0 vs N1	1.500	1.000–2.200	0.035	1.349	0.83- 2.49	0.28
pathologic _M	M0 vs M1	1.600	1.100–2.300	0.013	1.438	0.830- 2.49	0.194

Table S9. Univariate analysis and multivariate analysis of factors of disease specific survival DSS of LIH TCGA in BUB1B expression.

Variables	Category	Univariate analysis			Multivariate analysis		
		HR	95%CI	P value	HR	95%CI	P value
BUB1B	Low vs High	1.300	1.100–1.500	<0.001	1.307	1.126-1.51	0.0004
Age at initial pathologic diagnosis	<=65, >65	1.200	0.760–1.900	0.420			
Gender	Male vs Female	1.300	0.820–2.100	0.260			
Adjacent hepatic tissue inflammation	Yes, NO	0.630	0.330–1.200	0.140			
Fibrosis ishak score	With Fibross, complete and incomplete cirrhoss	0.920	0.640–1.300	0.640			
Neoplasm histologic grade	G1-G2 vs G3-G4	1.200	0.730–1.800	0.540			
Vascular tumor cell type	Male, Female	1.400	0.790–2.400	0.260			
Tumor stage diagnoses	Stage I- II vs III -IV	1.300	0.790–2.200	0.290			
pathologic _T	T1-T2 vs T3-4	1.900	1.200–3.000	0.007	1.885	1.167-3.04	0.0095
pathologic _N	N0 vs N1	1.700	1.100–2.700	0.028	1.552	0.78- 3.07	0.207
pathologic _M	M0 vs M1	1.800	1.100–2.900	0.016	1.503	0.755-2.99	0.246

Table S10. Univariate analysis and multivariate analysis of factors of disease specific survival DSS of LIH TCGA in RRM2 expression.

Variables	Category	Univariate analysis			Multivariate analysis		
		HR	95%CI	P value	HR	95%CI	P value
RRM2	Low vs High	1.400	1.100–1.600	<0.001	1.375	1.151- 1.64	0.00044
Age at initial pathologic diagnosis	<=65, >65	1.200	0.760–1.900	0.420			
Gender	Male vs Female	1.300	0.820–2.100	0.260			
Adjacent hepatic tissue inflammation	Yes, NO	0.630	0.330–1.200	0.140			
Fibrosis ishak score	With Fibross, complete and incomplete cirrhoss	0.920	0.640–1.300	0.640			
Neoplasm histologic grade	G1-G2 vs G3-G4	1.200	0.730–1.800	0.540			
Vascular tumor cell type	Male, Female	1.400	0.790–2.400	0.260			
Tumor stage diagnoses	Stage I- II vs III -IV	1.300	0.790–2.200	0.290			
pathologic _T	T1-T2 vs T3-4	1.900	1.200–3.000	0.007	1.840	1.135- 2.98	0.0132
pathologic _N	N0 vs N1	1.700	1.100–2.700	0.028	1.537	0.763-3.09	0.2284
pathologic _M	M0 vs M1	1.1	0.68-1.7	0.016	1.467	0.72- 2.968	0.2860

Table S11. Univariate analysis and multivariate analysis of factors of Progression free interval PFI of LIH TCGA in BUB1B expression.

Variables	Category	Univariate analysis			Multivariate analysis		
		HR	95%CI	P value	HR	95%CI	P value
BUB1B	Low vs High	1.200	1.100–1.300	<0.001	1.191	1.08-1.305	0.00018
Age at initial pathologic diagnosis	<=65, >65	1.100	0.810–1.500	0.580			
Gender	Male vs Female	1.300	0.920–1.700	0.150			
Adjacent hepatic tissue inflammation	Yes, NO	0.790	0.550–1.100	0.200			
Fibrosis ishak score	With Fibross, complete and incomplete cirrhoss	0.950	0.760–1.200	0.660			
Neoplasm histologic grade	G1-G2 vs G3-G4	1.200	0.850–1.600	0.350			
Vascular tumor cell type	Male, Female	1.300	0.930–1.800	0.120			
Tumor stage diagnoses	Stage I- II vs III -IV	1.100	0.760–1.500	0.680			
pathologic _T	T1-T2 vs T3-4	1.600	1.100–2.200	0.007	1.498	1.08- 2.07	0.0148

pathologic_N	N0 vs N1	1.200	0.880–1.700	0.250
pathologic_M	M0 vs M1	1.200	0.860–1.600	0.310

Table S12. Univariate analysis and multivariate analysis of factors of Progression free interval PFI of LIH TCGA in RRM2 expression.

Variables	Category	Univariate analysis			Multivariate analysis		
		HR	95%CI	P value	HR	95%CI	P value
RRM2	Low vs High	1.200	1.100–1.300	0.001	0.69	0.51- 0.93	0.016
Age at initial pathologic diagnosis	<=65, >65	1.100	0.810–1.500	0.580			
Gender	Male vs Female	1.300	0.920–1.700	0.150			
Adjacent hepatic tissue inflammation	Yes, NO	0.790	0.550–1.100	0.200			
Fibrosis ishak score	With Fibross, complete and incomplete cirrhoss	0.950	0.760–1.200	0.660	1.21	1.00- 1.45	0.046
Neoplasm histologic grade	G1-G2 vs G3-G4	1.200	0.850–1.600	0.350			
Vascular tumor cell type	Male, Female	1.300	0.930–1.800	0.120			
Tumor stage diagnoses	Stage I- II vs III -IV	1.100	0.760–1.500	0.680			
pathologic_T	T1-T2 vs T3-4	1.600	1.100–2.200	0.007	1.47	1.06- 2.01	0.018
pathologic_N	N0 vs N1	1.200	0.880–1.700	0.250			
pathologic_M	M0 vs M1	1.200	0.860–1.600	0.310			