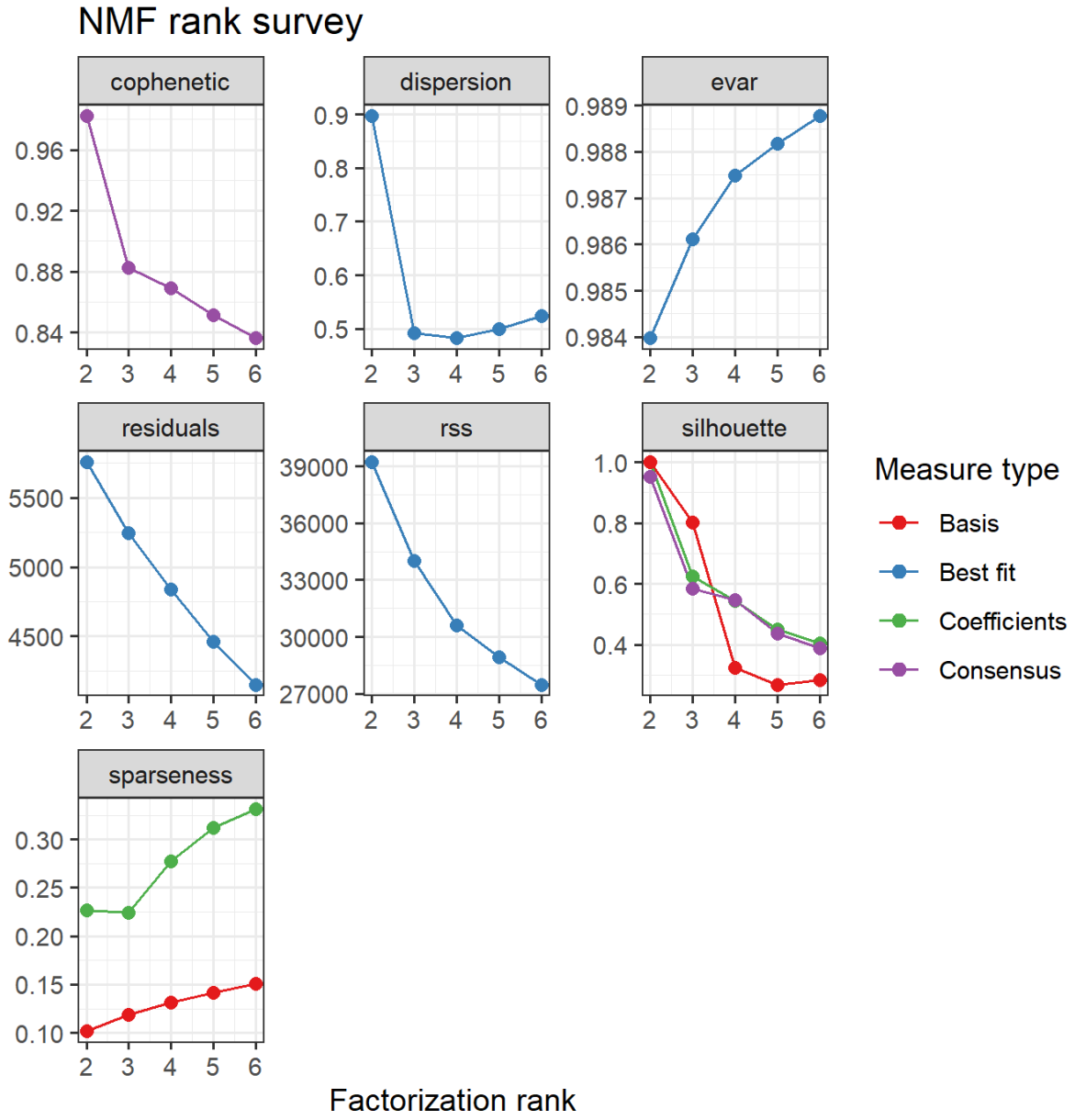

Figure S1 NMF rank survey.

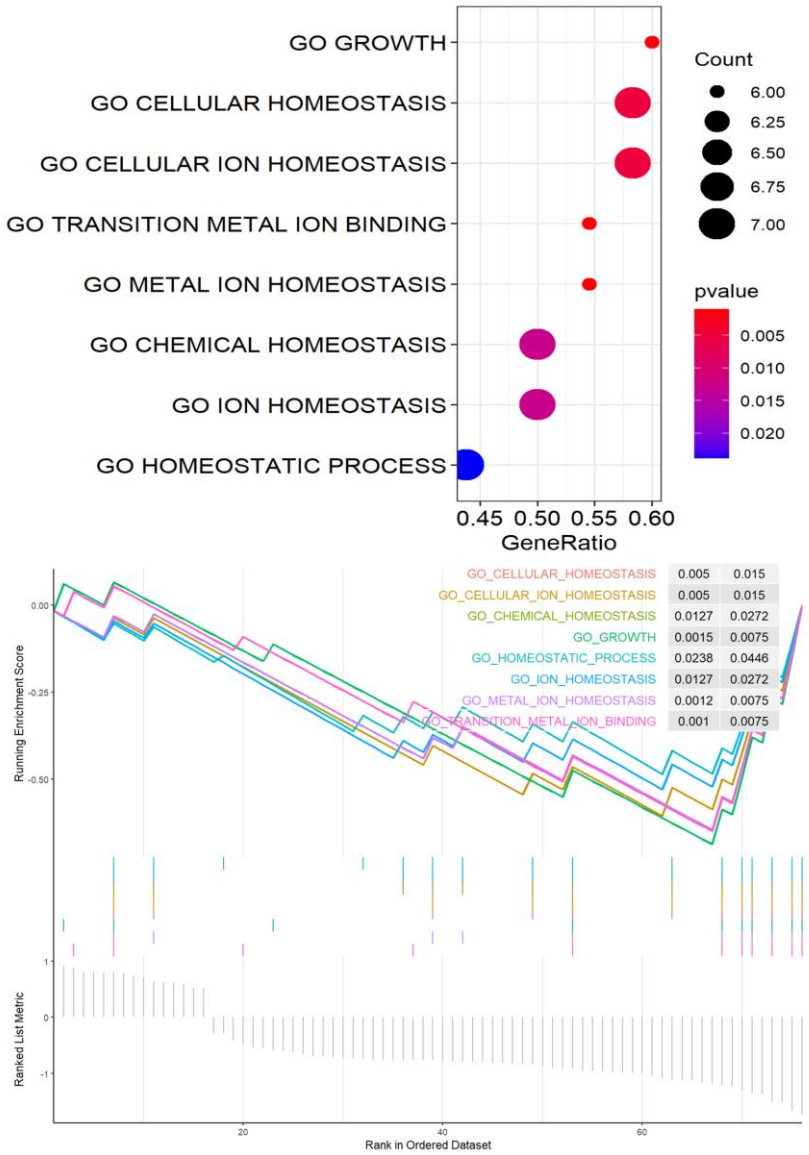

Figure S2 GO items with FDR < 0.05 were identified based on gene set enrichment analysis (GSEA) performed between Cluster 1 and Cluster 2 subgroups.

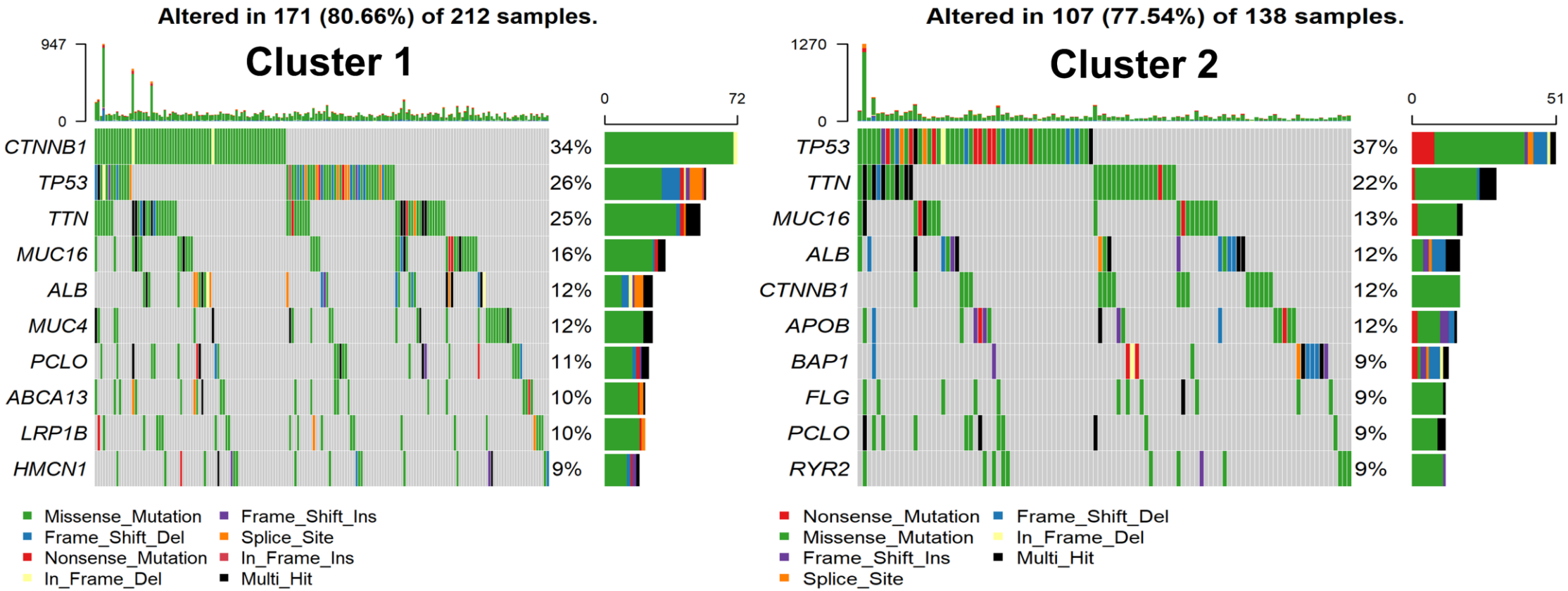

Figure S3 Tumor maps of mutated genes in Cluster 1 and Cluster 2 subgroups.

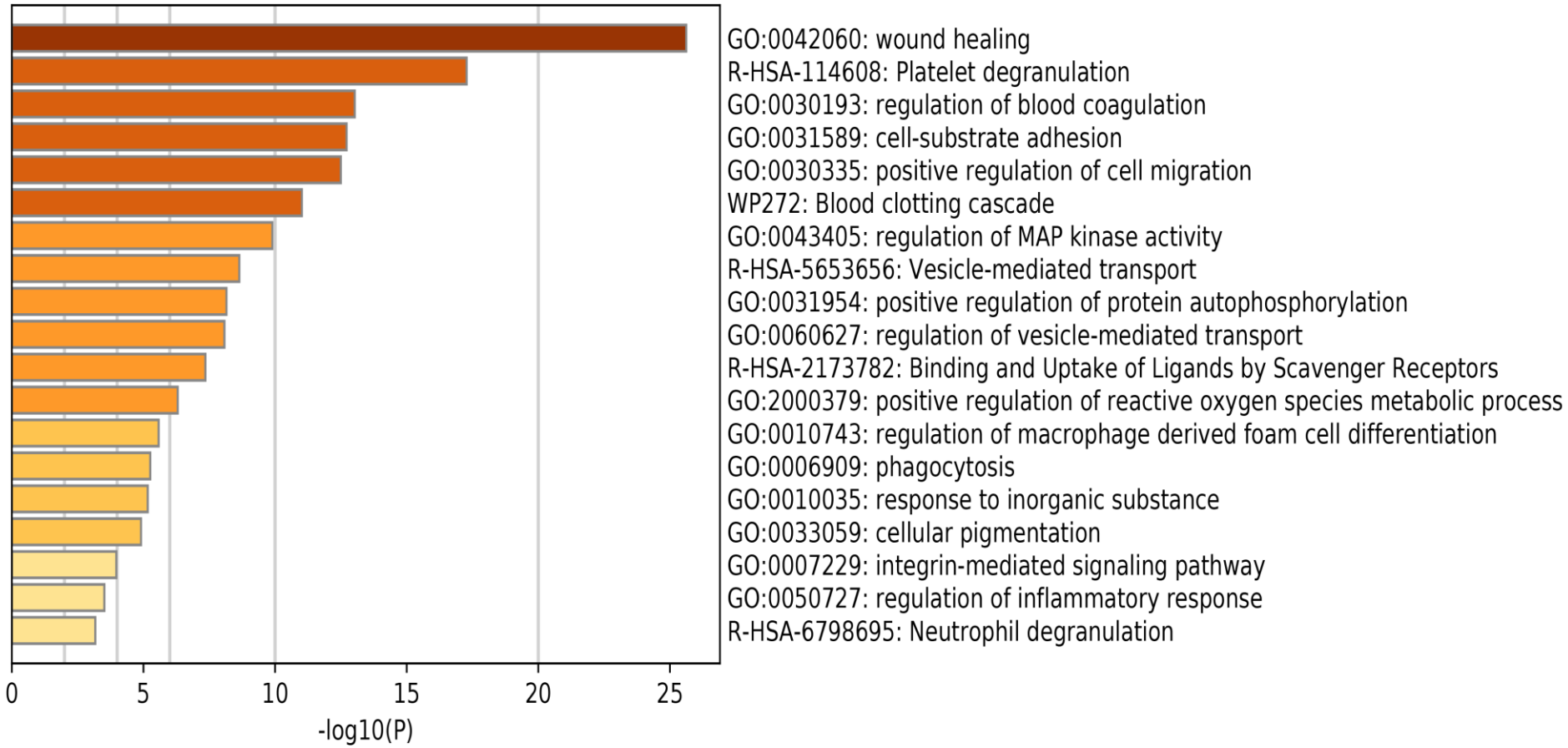

Figure S4 Enriched GO and KEGG items of overlapping genes.

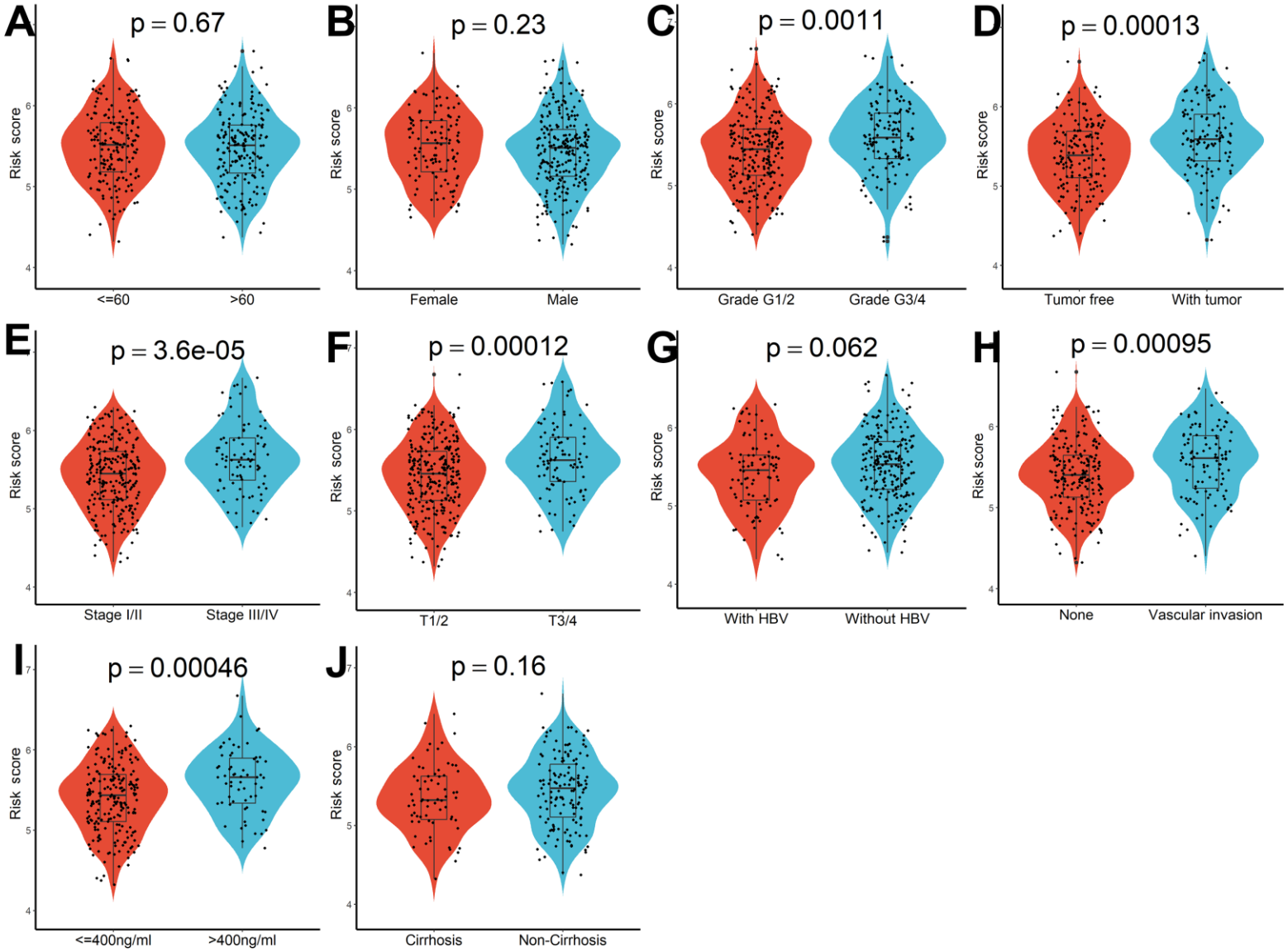

Figure S5 Clinical characteristics evaluation by this classifier. Violin plots showing that higher risk scores were linked to later grade, T stage, advanced TNM stage, recurrence, AFP value, and vascular invasion.

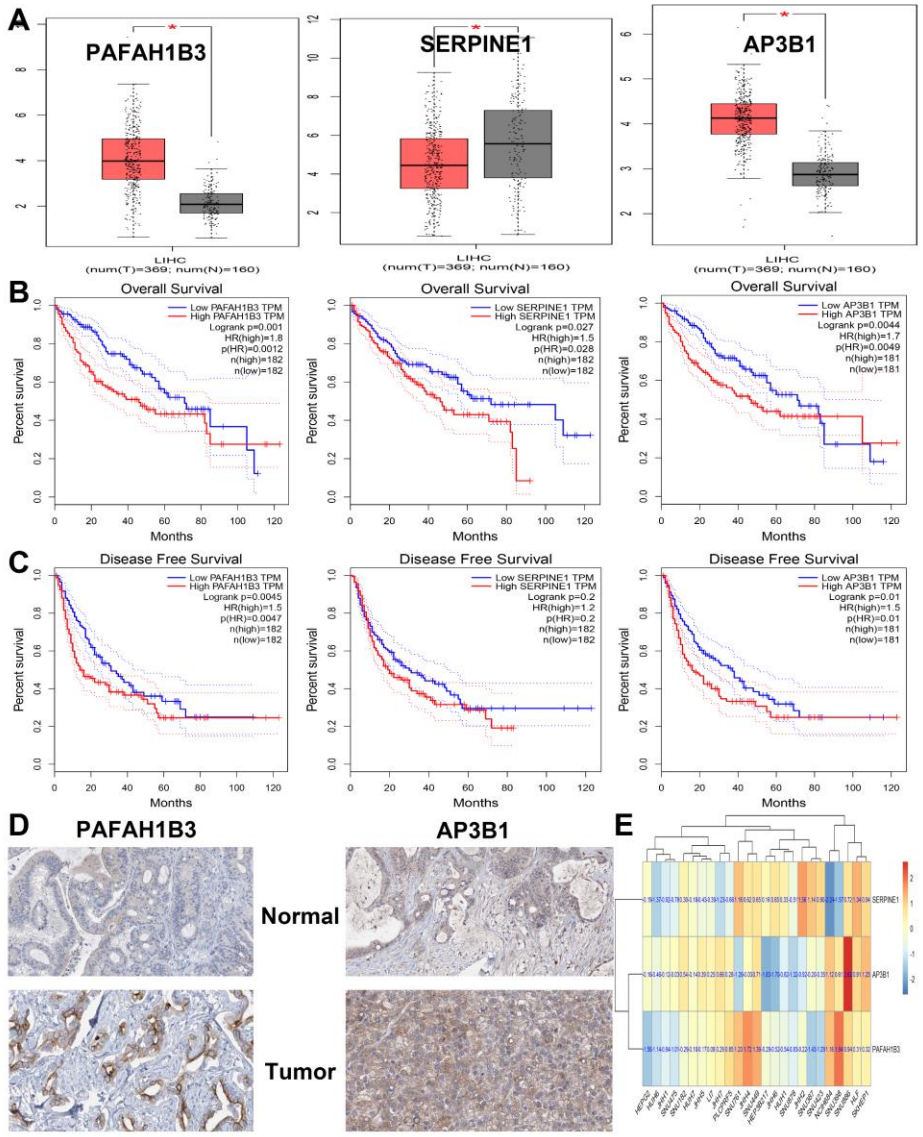

Figure S6 Expression levels of the three molecules explored in GEPIA, HPA, and CCLE database. (A) Expression levels of the three mRNA molecules in GEPIA. (B) Analysis of overall survival rate. (C) Analysis of disease-free survival rate. (D) Protein expression of PAFAH1B3 and AP3B1 in normal and HCC tissues. (E) Expression levels of the three mRNA molecules in CCLE. *Stands for the P value less than 0.05.

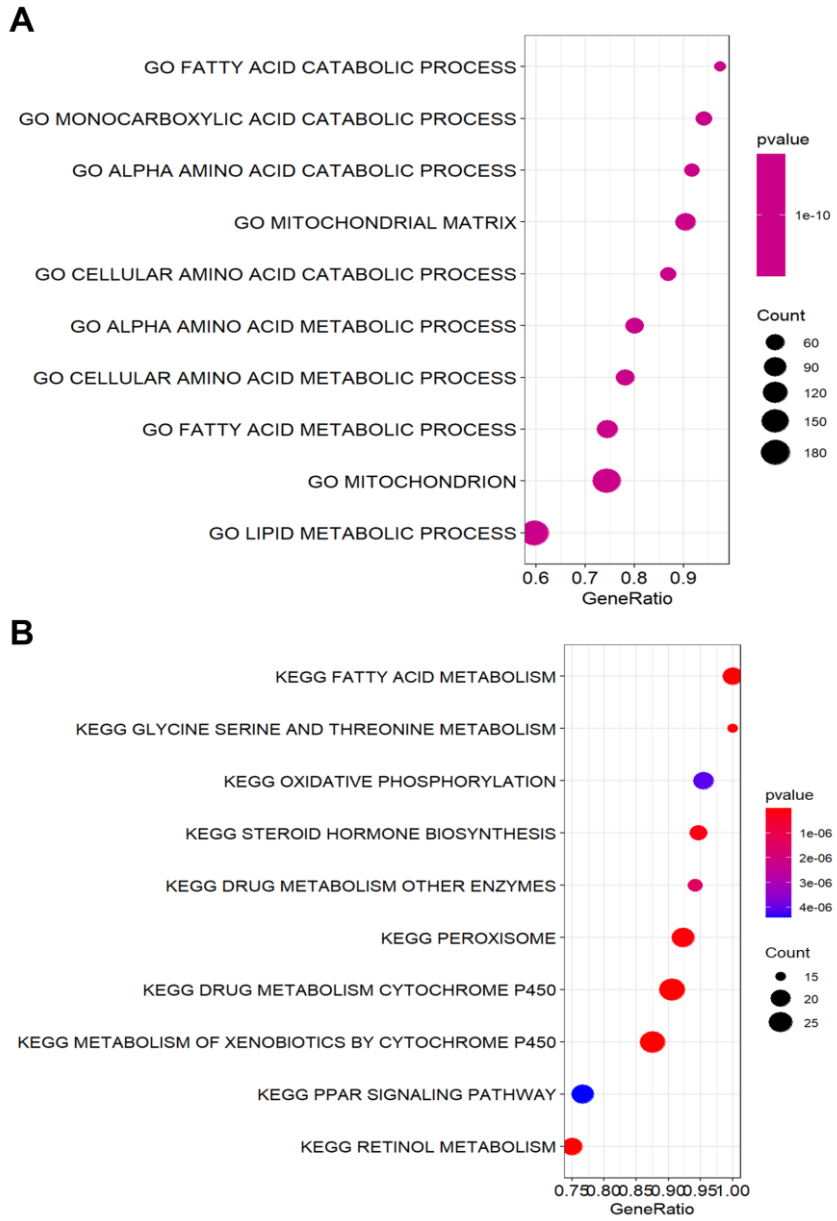

Figure S7 Identification of GO (A) and KEGG (B) items with FDR < 0.05 in the prognostic model.

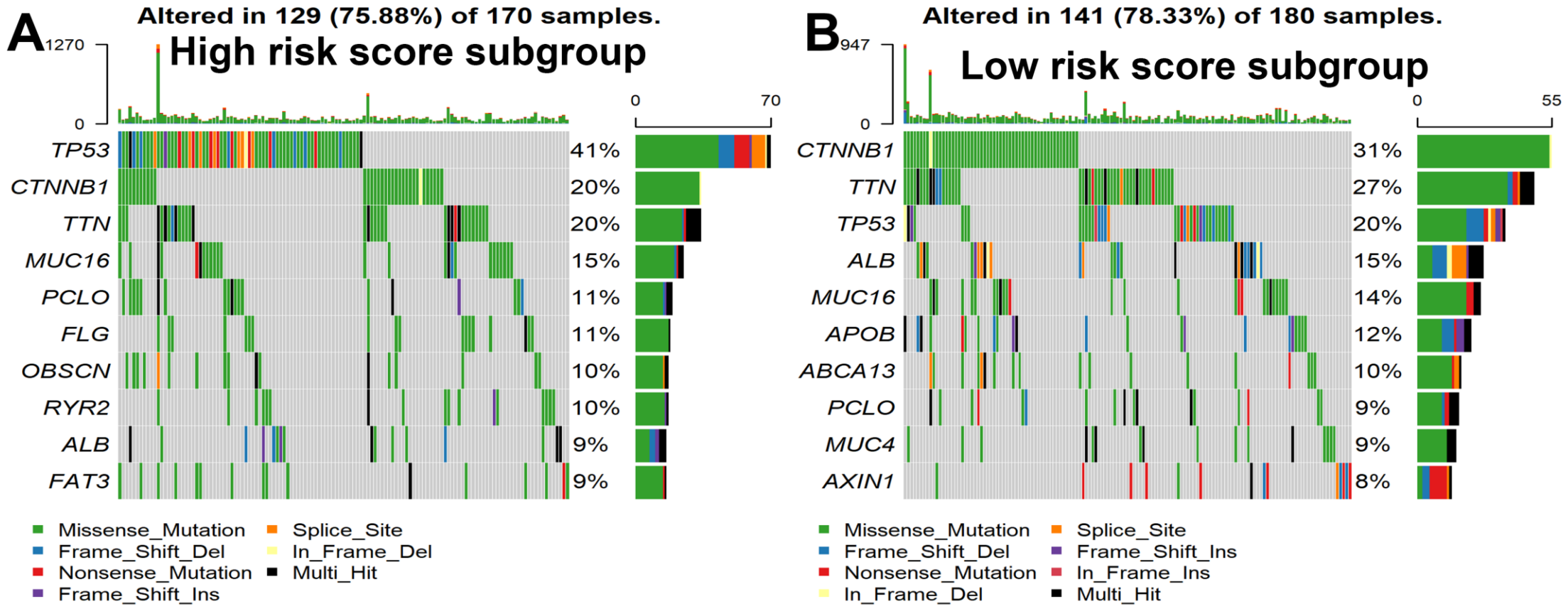

Figure S8 Tumor maps of mutated genes in high- (A) and low-risk (B) score subgroups.

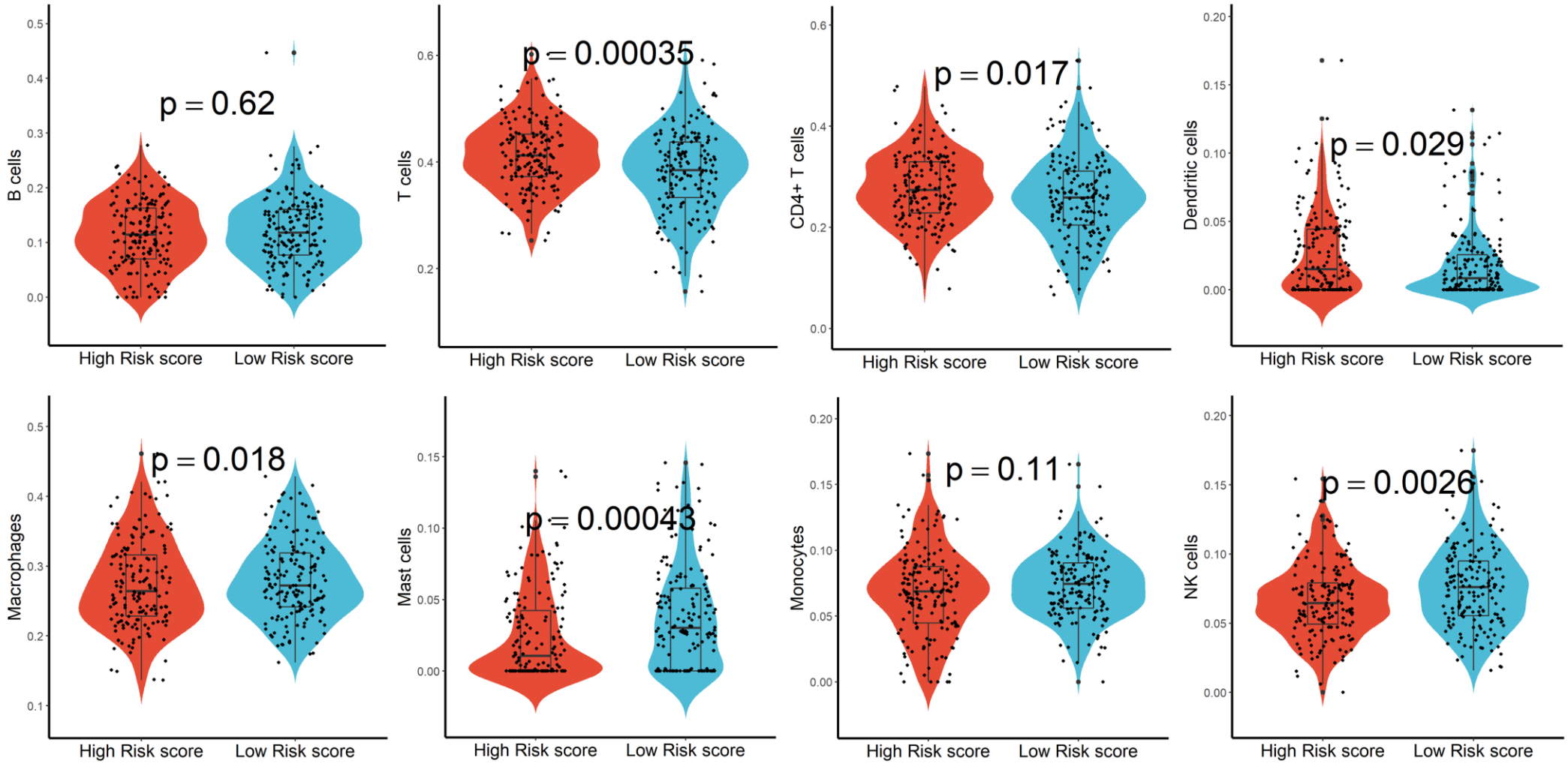

Figure S9 Abundance differentiation of TIICs in high- and low-risk score subgroups.

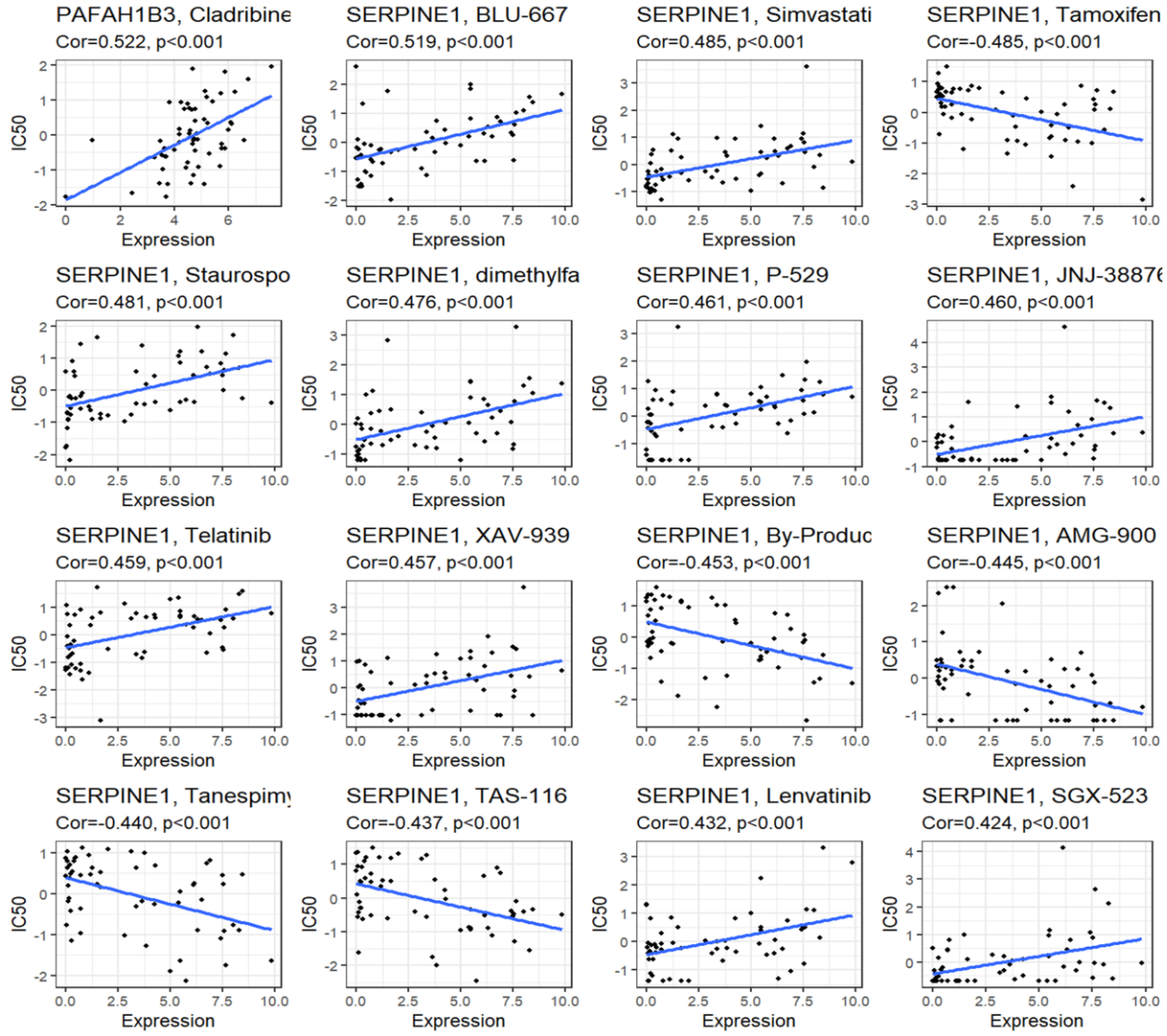

Figure S10 The top 16 most significant tumor-sensitive drugs obtained from correlation analysis of mRNA molecules in this classifier.

Table S1 Clinical characteristics of HCC patients involved in TCGA, ICGC, GSE14520, and the small size clinical cohort.

		TCGA cohort (N=365)	ICGC cohort (N=227)	GSE14520 cohort (N=216)	Independent cohort (N=59)
Gender	Male	119	61	187	45
	Female	246	166	29	14
Age	≤60 years	173	49	178	27
	>60 years	192	178	38	32
Grade	G1/2	230			35
	G3/4	130			24
	unknown	5			
TNM Stage	I/II	254	140	167	42
	III/IV	87	87	49	17
	unknown	24	0	0	0
Vascular Invasion	Yes	106			
	No	205			
	unknown	5			
Recurrence With tumor		122		120	29
	Tumor free	161		96	30
	unknown	82			0
Cirrhosis	With	68		198	6
	Without	141		18	53
	unknown	156		0	0
HBV or HCV Infection					
	Yes	149		209	41
	No	203		6	18
	unknown	13		1	0
Child-Pugh	A	216			57
	B	21			2
	C	1			0
	unknown	127			0

Table S2 The sequences of the qPCR primers used in this study.

Gene	Forward primer	Reverse primer
PAFAH1B3	ACATCCGGCCCAAGATTGTG	GGGCTGTCGCTCATTCACC
SERPINE1	ACCGCAACGTGGTTTTCTCA	TTGAATCCCATAGCTGCTTGAAT
AP3B1	GGCCTCTTTAGCAGCGATTTG	CATCCCAACAATCCGCTTCATA
β-ACTIN	CGTGGGCCGCCCTAGGCACCA	TTGGCTTAGGGTTCAGGGGGG

Table S3 102 tumor-sensitive drugs targeting mRNA molecules in this classifier.

Gene	Drug	cor	P value	Gene	Drug	cor	P value	Gene	Drug	cor	P value
PAFAH1B3	Cladribine	0.521753	2.26E-05	*SERPINE1*	AS-703569	0.37018	0.003904	*SERPINE1*	MPC-3100	-0.34799	0.006919
SERPINE1	BLU-667	0.518548	2.59E-05	*SERPINE1*	DOLASTATIN 10	-0.36972	0.003952	*SERPINE1*	EMD-534085	-0.34711	0.007072
SERPINE1	Simvastatin	0.485434	9.74E-05	*SERPINE1*	spebrutinib	0.368105	0.004125	*SERPINE1*	Belinostat	-0.34617	0.007238
SERPINE1	Tamoxifen	-0.48479	9.98E-05	*AP3B1*	ZM-336372	0.367926	0.004145	*PAFAH1B3*	tfdu	0.345015	0.007448
SERPINE1	Staurosporine	0.4806	0.000117	*SERPINE1*	Pazopanib	0.36524	0.004449	*PAFAH1B3*	Asparaginase	0.342274	0.007967
SERPINE1	dimethylfasudil	0.475587	0.000141	*SERPINE1*	Momelotinib	0.3642	0.004572	*SERPINE1*	SNX-5422	-0.341	0.008218
SERPINE1	P-529	0.461383	0.000235	*SERPINE1*	Bleomycin	0.362245	0.004812	*SERPINE1*	ARQ-680	-0.3399	0.008441
SERPINE1	JNJ-3887618	0.45954	0.000251	*SERPINE1*	Rocilinostat	-0.35707	0.005501	*SERPINE1*	ulixertinib	-0.33835	0.008764
SERPINE1	Telatinib	0.458724	0.000258	*PAFAH1B3*	Clofarabine	0.356497	0.005581	*AP3B1*	SAR-20347	0.337952	0.008849
SERPINE1	XAV-939	0.457396	0.00027	*SERPINE1*	BGB-283	-0.3557	0.005696	*PAFAH1B3*	Milciclib	-0.33703	0.009048
SERPINE1	By-Product of CUDC-305	-0.45343	0.00031	*SERPINE1*	R-306465	-0.35524	0.005764	*SERPINE1*	Bafetinib	-0.33701	0.009052
SERPINE1	AMG-900	-0.44549	0.000407	*PAFAH1B3*	Nelarabine	0.354665	0.005848	*SERPINE1*	SB-202190	-0.33593	0.009291
SERPINE1	Tanespimycin	-0.43964	0.000494	*SERPINE1*	4SC-202	-0.35037	0.006519	*SERPINE1*	VX-944	-0.33447	0.009621
SERPINE1	TAS-116	-0.43712	0.000537	*PAFAH1B3*	Gemcitabine	0.350338	0.006524	*PAFAH1B3*	Sapacitabine	0.381235	0.002891
SERPINE1	Lenvatinib	0.432311	0.000628	*SERPINE1*	SB-590885	-0.34978	0.006616	*SERPINE1*	Midostaurin	0.377187	0.003231
SERPINE1	SGX-523	0.423714	0.000826	*SERPINE1*	HYPOTHEMYCIN	-0.34891	0.006761	*SERPINE1*	B-7100	-0.37512	0.003418
SERPINE1	IDH1-Comp 301	0.422977	0.000845	*SERPINE1*	Dasatinib	0.404415	0.001489	*SERPINE1*	Alvespimycin	-0.37484	0.003444
SERPINE1	Nilotinib	-0.42014	0.000924	*SERPINE1*	CUDC-305	-0.40016	0.001688	*SERPINE1*	Volasertib	-0.37477	0.00345
SERPINE1	JNJ-38877605	0.41876	0.000964	*SERPINE1*	PKM2 (9)	0.390994	0.002199	*SERPINE1*	AT-13387	-0.4053	0.001451
SERPINE1	IDH-C227	0.410715	0.001233	*SERPINE1*	Vorinostat	-0.39006	0.002259	*PAFAH1B3*	CNDAC	0.389006	0.002327