

Figure S1. Knockdown of *STEAP1* does not induce apoptosis in liver cancer cell lines. (A) HepG2 and (B) Hep3B cells were transfected with non-targeting control siRNA or siSTEAP1. Apoptosis was measured by flow cytometry using Annexin V/7-AAD staining. Data are presented as the mean of triplicate measurements  $\pm$  SD. siRNA, small interfering RNA; STEAP1, six-trans-membrane epithelial antigen of the prostate 1; N.S., not significant.

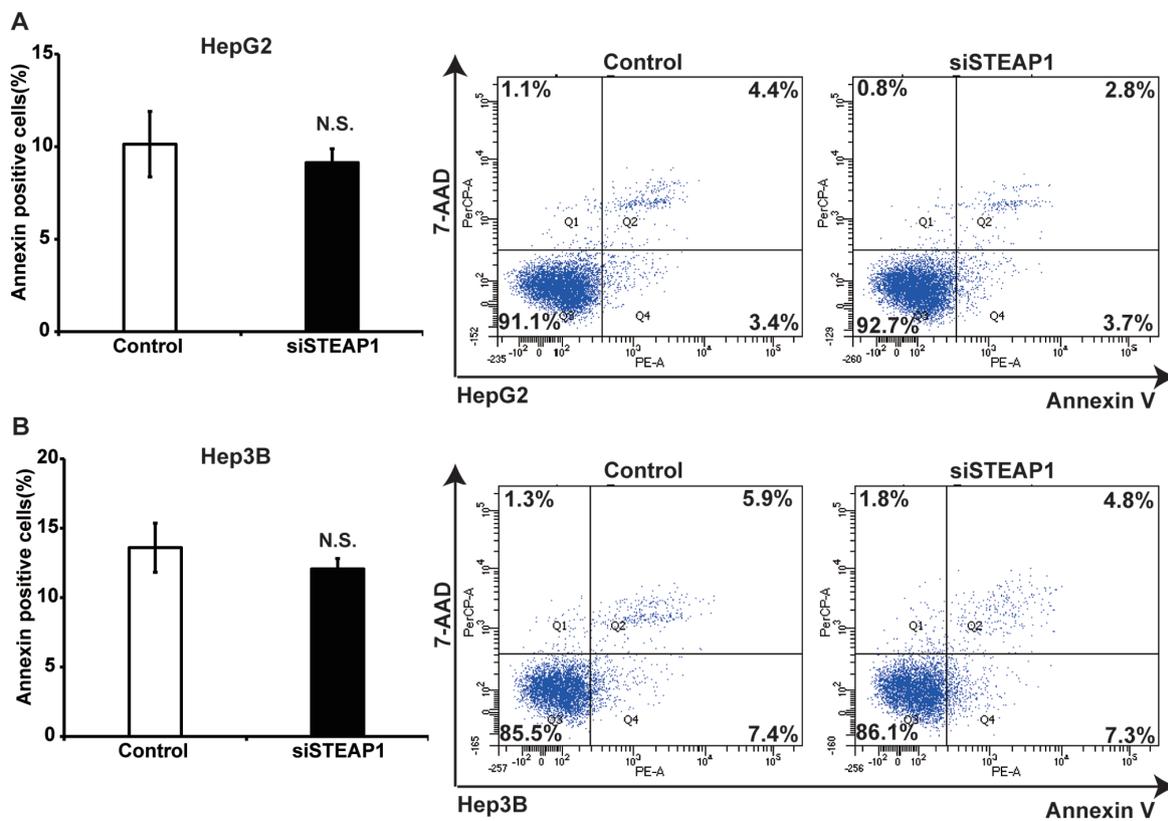


Figure S2. Pathways associated with high *STEAP1* expression were derived from GSEA. GSEA was performed to explore the gene sets regulated by *STEAP1* in hepatocellular carcinoma using the publicly accessible gene expression profiling dataset, GSE14520-GPL3921. Four statistically significant pathways, namely (A) MTORC1\_SIGNALING, (B) MYC\_TARGETS\_V1, (C) UNFOLDED\_PROTEIN\_RESPONSE and (D) REACTIVE\_OXYGEN\_SPECIES\_PATHWAY, are represented as enrichment plots. NOM P-val, nominal P-value; FDR Q-val, false discovery rate Q-value; GSEA, Gene Set Enrichment Analysis; NES, normalized enrichment score; STEAP1, six-transmembrane epithelial antigen of the prostate 1.

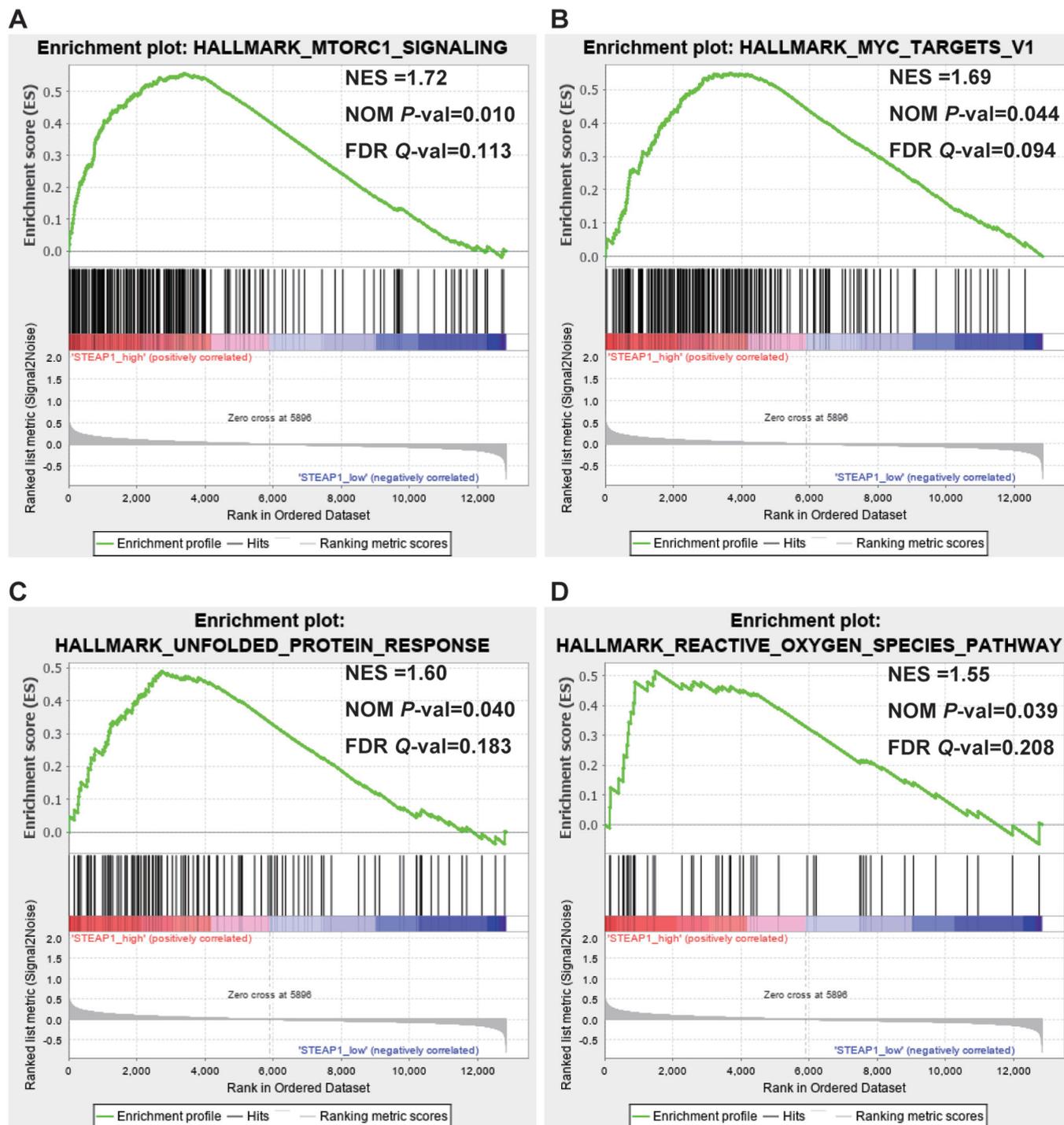


Figure S3. Inhibition of *STEAP1* suppresses c-Myc downstream target genes in HepG2 cells. HepG2 cells were transfected with non-targeting control siRNA and siSTEAP1. c-Myc downstream target genes were evaluated using PCR array. The 84 genes are listed in a (A) chart and (B) heatmap. Blue/purple represents a decreased expression level, and yellow represents no change. The numbers are indicating fold changes. siRNA, small interfering RNA; STEAP1, six-transmembrane epithelial antigen of the prostate 1.

**A**

Layout	01	02	03	04	05	06	07	08	09	10	11	12
A	AIMP2 -3.18	APEX1 -3.36	ATF4 -4.12	BAX -1.7	BCAT1 -1.55	CAD -6.13	CBX3 -1.54	CCNB1 -3.43	CCND2 -1.36	CCT5 -1.41	CDC25A -4.25	CDK4 -5.41
B	CDKN1B -3.74	CDKN2B -1.44	CHEK1 -3.54	CKS2 -1.93	YBX3 -1.92	CSDE1 -2.46	GSTB 1.2	CTSC -3.71	DDX10 -1.14	DDX39B -3.19	DKC1 -2.86	E2F1 -4.08
C	EIF4A1 -2.02	EIF4B -4.5	EIF4E -1.29	ENO1 -8.4	EXOSC8 -1.91	FASN -1.55	GCLC -1.54	GNL3 -2.04	HK2 -5.2	HNRNPA1 -1.87	HNRNPA2B1 -2.42	ID3 -8.45
D	ILK -2.2	ITGB1 -2.14	LTA4H -1.42	MAT2A -4.64	MAX -2.13	MAZ -1.94	MGST1 -1.27	MSH2 -1.86	MTHFD1 -5.94	MYC -2.16	MYCL -1.24	MYCN -5.44
E	NAP1L1 -3.02	NBN -1.08	NCL -3.16	NME1 -1.72	NOLC1 -5.82	NPM1 -2.35	ODC1 -2.83	PA2G4 -1.44	PAICS -3.32	PCNA -2.34	PDK1 -2.99	PHB -2.35
F	PIAS2 -2.43	POLD2 -2.34	PPAT -2.45	PPP2R4 -3.14	PSMG1 -1.7	PTEN 1.31	PYCR1 -3.91	RPL13 -1.27	RPL19 -1.04	RPL23 -1.44	RPL27A -1.15	RPL5 -2.27
G	RPS5 -4.55	SHMT1 -5.68	SNRPB -5.67	SRM -4.96	SRSF1 -3.23	TERT -2.14	TOP1 -3.44	TP53 -2.64	TPI1 -14.16	TYMS -1.82	UBE2C -2.17	ZFP36L1 1.2

**B**

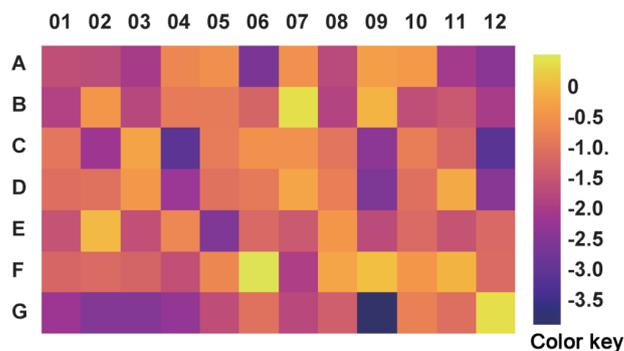


Figure S4. ROS production is increased by *STEAP1*-knockdown, but no statistical correlation between *STEAP1* and *NRF2* expression was observed in HCC. (A) HepG2 and (B) Hep3B cells were transfected with non-targeting control siRNA or si*STEAP1*. Cytosolic ROS levels were evaluated by flow cytometry using CellROX Deep Red. Data are presented as the mean of triplicate measurements  $\pm$  SD. \* $P < 0.05$  vs. control. Correlation between *STEAP1* and *NRF2* expression in HCC samples using the publicly accessible gene expression profiling datasets, (C) GSE14520 and (D) GSE36376, and (E) TCGA. ROS, reactive oxygen species; NRF2, NF-E2-related factor 2; HCC, hepatocellular carcinoma; TCGA, The Cancer Genome Atlas; siRNA, small interfering RNA; STEAP1, six-transmembrane epithelial antigen of the prostate 1.

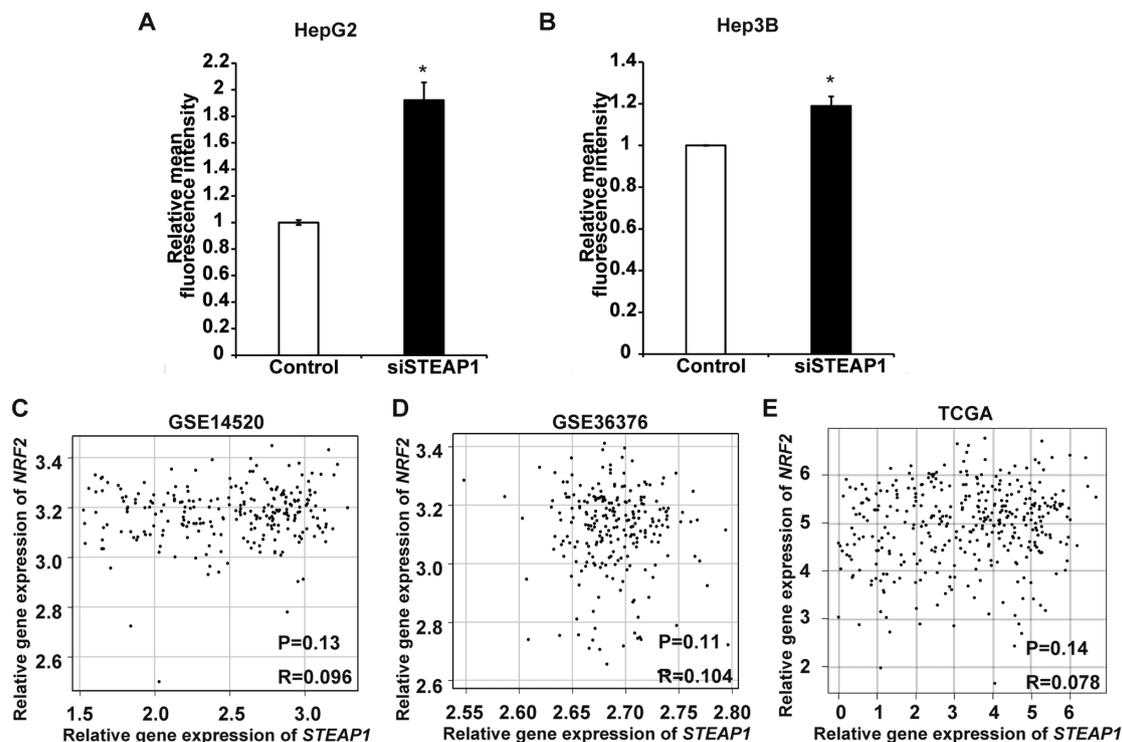


Table S1. List of enriched gene sets derived from Gene Set Enrichment Analysis in STEAPI-upregulated liver cancer using the publicly accessible gene expression profiling dataset, GSE14520-GPL3921.

Gene set	Size, bp	ES	NES	NOM P-value	FDR q-value	FWER P-value	Rank at max	Leading edge
HALLMARK_MYC_TARGETS_V2	58	0.69207776	1.8522855	0.004056795	0.037062958	0.025	2609	tags=67%, list=20%, signal=84%
HALLMARK_MTORC1_SIGNALING	198	0.55517286	1.7184767	0.009708738	0.112650275	0.13	3399	tags=64%, list=26%, signal=86%
HALLMARK_MYC_TARGETS_V1	199	0.5485847	1.691135	0.044265594	0.09423097	0.157	3651	tags=57%, list=28%, signal=79%
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	111	0.49010047	1.5956153	0.03968254	0.18295158	0.301	2734	tags=46%, list=21%, signal=58%
HALLMARK_REACTIVE_OXYGEN_SPECIES_PATHWAY	46	0.51548195	1.5508558	0.0390625	0.20838094	0.367	1485	tags=33%, list=12%, signal=37%
HALLMARK_SPERMATOGENESIS	125	0.39619297	1.4034897	0.06036217	0.45093307	0.66	2142	tags=23%, list=17%, signal=28%
HALLMARK_UV_RESPONSE_UP	158	0.39965212	1.4012077	0.025096525	0.39195782	0.667	2467	tags=34%, list=19%, signal=42%
HALLMARK_IL6_JAK_STAT3_SIGNALING	87	0.48076102	1.3984529	0.115530305	0.3493785	0.673	2083	tags=34%, list=16%, signal=41%
HALLMARK_PI3K_AKT_MTOR_SIGNALING	102	0.35231537	1.3757539	0.06994329	0.35343066	0.717	2677	tags=36%, list=21%, signal=45%
HALLMARK_GLYCOLYSIS	188	0.39369822	1.3516054	0.04518664	0.36649844	0.763	1741	tags=29%, list=14%, signal=33%
HALLMARK_G2M_CHECKPOINT	198	0.5125287	1.3197974	0.22132796	0.3985368	0.817	2961	tags=48%, list=23%, signal=62%
HALLMARK_COMPLEMENT	188	0.37945133	1.2343261	0.19165085	0.5467972	0.904	3021	tags=36%, list=24%, signal=46%
HALLMARK_INFLAMMATORY_REJECTION	199	0.45003456	1.2291461	0.2626459	0.518129	0.912	2160	tags=33%, list=17%, signal=39%
HALLMARK_IL2_STAT5_SIGNALING	192	0.4123962	1.2164818	0.22535211	0.5071917	0.921	2541	tags=32%, list=20%, signal=40%
HALLMARK_IL2_STAT5_TARGETS	190	0.50353825	1.2131625	0.32416502	0.4807731	0.924	3011	tags=51%, list=23%, signal=66%
HALLMARK_IL2_STAT5_SIGNALING	176	0.37062678	1.2019329	0.15019011	0.4733342	0.933	1902	tags=32%, list=15%, signal=37%
HALLMARK_PROTEIN_SECRETION	96	0.35899216	1.1633826	0.28070176	0.52060544	0.954	2855	tags=36%, list=22%, signal=47%
HALLMARK_APICAL_SURFACE	34	0.36205694	1.120722	0.2993763	0.58005255	0.976	1708	tags=24%, list=13%, signal=27%
HALLMARK_CHOLESTEROL_HOMEOSTASIS	62	0.42461875	1.1076323	0.34179688	0.575295	0.98	2927	tags=45%, list=23%, signal=58%
HALLMARK_OXIDATIVE_PHOSPHORYLATION	200	0.34020543	1.0903395	0.42114696	0.58114666	0.984	3621	tags=39%, list=28%, signal=53%
HALLMARK_DNA_REPAIR	139	0.31362012	1.0856876	0.35510203	0.56315047	0.984	3269	tags=39%, list=25%, signal=52%
HALLMARK_TNFA_SIGNALING_VIA_NFKB	198	0.3788036	1.0426354	0.4123314	0.6192131	0.988	1380	tags=23%, list=11%, signal=25%
HALLMARK_HEME_METABOLISM	200	0.26369643	1.0405926	0.38649157	0.596399	0.988	2546	tags=25%, list=20%, signal=30%
HALLMARK_ANDROGEN_RESPONSE	100	0.29549375	1.0267878	0.4173077	0.59721136	0.99	2345	tags=27%, list=18%, signal=33%
HALLMARK_FATTY_ACID_METABOLISM	146	0.36947468	1.0193533	0.45724908	0.5859001	0.992	2310	tags=32%, list=18%, signal=38%
HALLMARK_ADIPOGENESIS	180	0.3029539	1.0026596	0.47134936	0.59420824	0.994	2268	tags=24%, list=18%, signal=29%
HALLMARK_ESTROGEN_RESPONSE_LATE	199	0.2794801	0.9988759	0.43796992	0.5792375	0.994	2004	tags=26%, list=16%, signal=30%
HALLMARK_MITOTIC_SPINDLE	178	0.3066864	0.9811845	0.4848485	0.5906945	0.996	1201	tags=17%, list=9%, signal=19%
HALLMARK_KRAS_SIGNALING_UP	196	0.29806554	0.9515187	0.54615384	0.6171569	0.997	2173	tags=27%, list=17%, signal=31%
HALLMARK_INTERFERON_GAMMA_RESPONSE	182	0.3532676	0.9378794	0.5162524	0.6206802	0.997	2377	tags=30%, list=19%, signal=37%
HALLMARK_HYPOXIA	195	0.29013985	0.9182161	0.5803922	0.63247	0.997	1593	tags=21%, list=12%, signal=25%
HALLMARK_APOPTOSIS	159	0.26394483	0.8810248	0.6206226	0.6772358	0.999	2364	tags=26%, list=18%, signal=31%
HALLMARK_INTERFERON_ALPHA_RESPONSE	83	0.3361705	0.8581146	0.62830186	0.69522154	1	2709	tags=34%, list=21%, signal=42%
HALLMARK_P53_PATHWAY	198	0.23427106	0.8421303	0.7685009	0.6997487	1	1911	tags=20%, list=15%, signal=23%
HALLMARK_PEROXISOME	99	0.23860918	0.705571	0.8519924	0.87374604	1	2721	tags=29%, list=21%, signal=37%
HALLMARK_COAGULATION	137	0.2352326	0.688134	0.905838	0.86841744	1	1613	tags=18%, list=13%, signal=20%

STEAPI, six-transmembrane epithelial antigen of the prostate 1; ES, enrichment score; NES, normalized ES; NOM, nominal; FDR, false discovery rate; FWER, family-wise error rate.