Figure S1. Clinical correlation analysis of HMBOX1 and PTPN1. (A and B) The GEPIA2 database was used to analyze the expression of HMBOX1 (A) or PTPN1 (B) in tumor tissues of patients with HCC at different stages. (C and D) The GEPIA2 database was used to analyze the correlation between the expressions of HMBOX1 (C) or PTPN1 (D) and the expression of AFP in the tumor tissues of patients with HCC. (E-H) The cBioPortal database was used to analyze the effects of adjuvant postoperative pharmaceutical therapy (E and F) and ablation embolization tx adjuvant (G and H) on the expression of HMBOX1 and PTPN1 in tumor tissues. HMBOX1, homeobox containing 1; PTPN1, protein tyrosine phosphatase non-receptor type 1; HCC, hepatocellular carcinoma; ns, not significant.

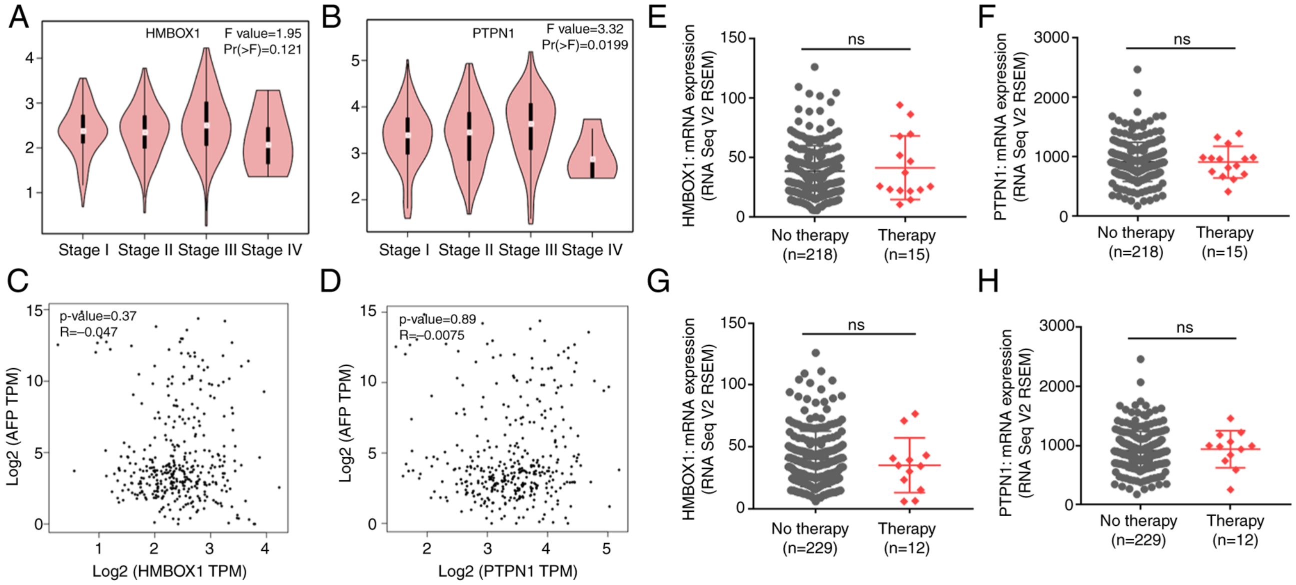


Figure S2. Detection of the effect of intervention on HMBOX1/PTPN1 expression. (A and B) The effect of overexpression of HMBOX1 through lentiviral transfection in HCC was detected by western blotting. (C) The effect of silencing HMBOX1 by siRNA in Huh-7 cells was detected using western blotting. (D and E) The effect of silencing PTPN1 by siRNAs in HCC cells was detected using western blotting. HMBOX1, homeobox containing 1; PTPN1, protein tyrosine phosphatase non-receptor type 1; HCC, hepatocellular carcinoma; siRNA, small interfering RNA; siNC, small interfering negative control.

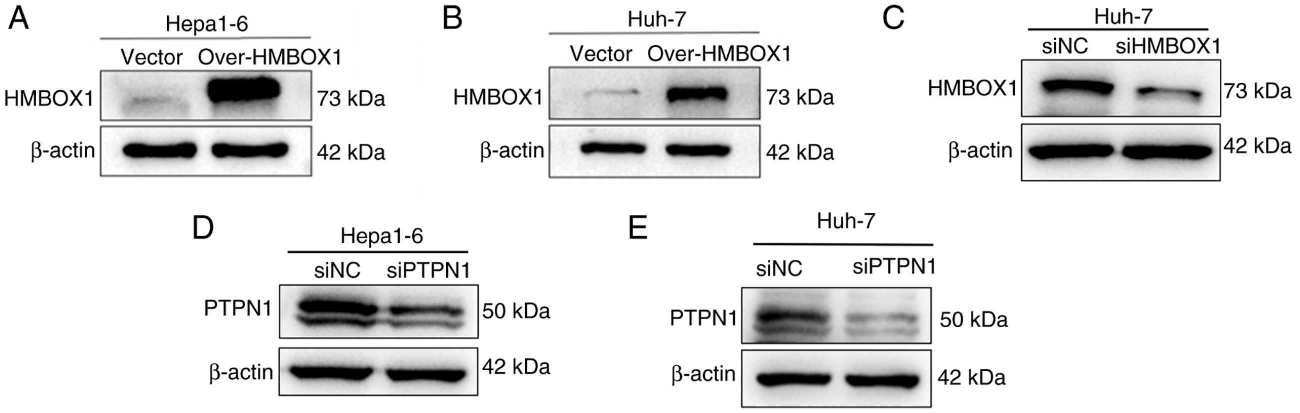


Figure S3. Proteomics differential gene enrichment analysis. (A and B) The Metascape database was used to conduct GO and KEGG pathway enrichment analyses on the differentially expressed genes with up-regulated (A) or downregulated (B) expression screened by proteomics. GO, Gene ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes.

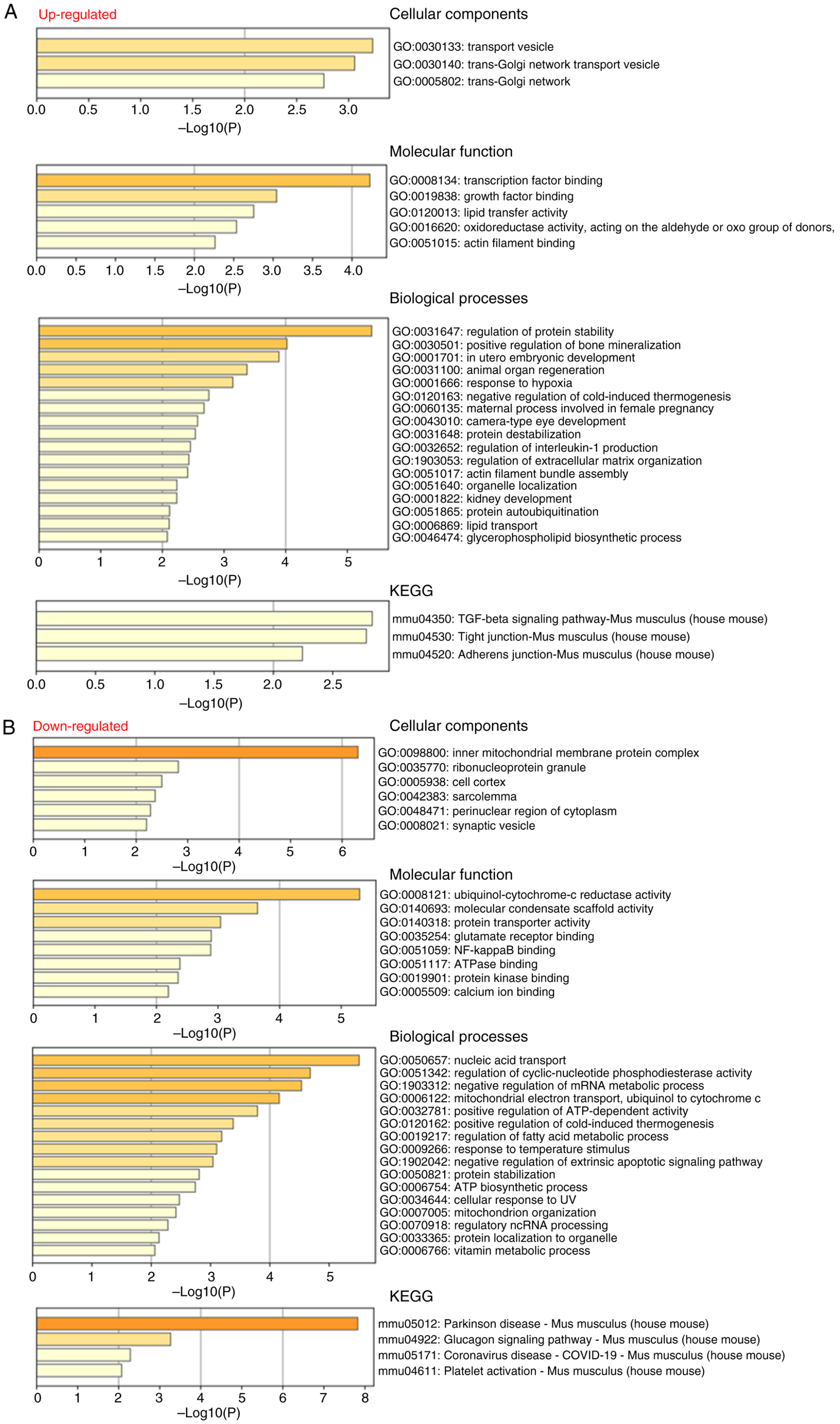
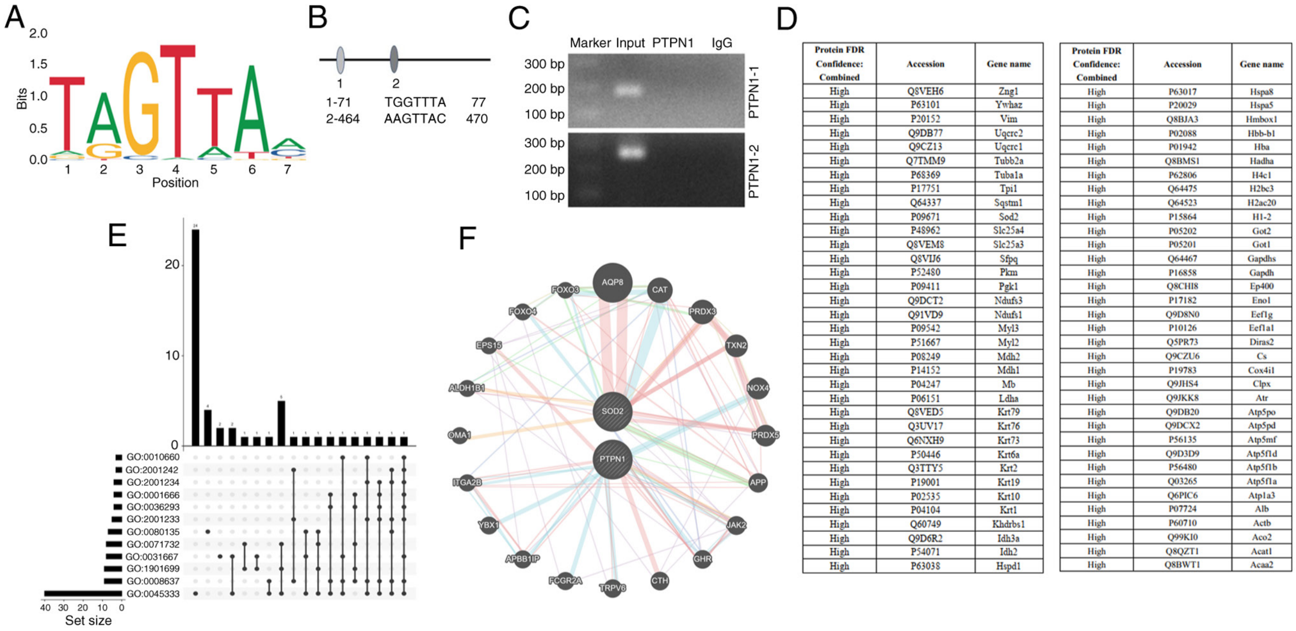


Figure S4. HMBOX1 regulates PTPN1 expression indirectly. (A and B) HMBOX1 binding motif (A) and two potential HMBOX1-binding sites within the 2-kb region upstream of the transcription start site of PTPN1 analyzed by JASPAR database (B). (C) Agarose electrophoresis for chromatin immunoprecipitation analysis of HMBOX1 binding to the PTPN1 promoter-specific sequences predicted by JASPAR database. The protein molecules bound to HMBOX1 in Hepa1-6 cells which overexpressing HMBOX1 were pulled down using co-immunoprecipitation, and then the protein molecules were analyzed by mass spectrometry. (D) The Metascape database was used to conduct GO enrichment analysis on PTPN1 and the proteins bound to HMBOX1. (E) The GO terms that contain PTPN1 were selected in the enrichment analysis results and the Upset graph was drawn. (F) The protein-protein interaction between SOD2 and PTPN1 was analyzed using the STRING database. HMBOX1, homeobox containing 1; PTPN1, protein tyrosine phosphatase non-receptor type 1; GO, Gene ontology.



Protein FDR Confidence: Combined	Accession	Gene name
High	Q8VEH6	Zng1
High	P63101	Ywhaz
High	P20152	Vim
High	Q9DB77	Uqcrc2
High	Q9CZ13	Uqcrc1
High	Q7TMM9	Tubb2a
High	P68369	Tuba1a
High	P17751	Tpi1
High	Q64337	Sqstm1
High	P09671	Sod2
High	P48962	Slc25a4
High	Q8VEM8	Slc25a3
High	Q8VIJ6	Sfpq
High	P52480	Pkm
High	P09411	Pgk1
High	Q9DCT2	Ndufs3
High	Q91VD9	Ndufs1
High	P09542	Myl3
High	P51667	Myl2
High	P08249	Mdh2
High	P14152	Mdh1
High	P04247	Mb
High	P06151	Ldha
High	Q8VED5	Krt79
High	Q3UV17	Krt76
High	Q6NXH9	Krt73
High	P50446	Krt6a
High	Q3TTY5	Krt2
High	P19001	Krt19
High	P02535	Krt10
High	P04104	Krt1
High	Q60749	Khdrbs1
High	Q9D6R2	Idh3a
High	P54071	Idh2
High	P63038	Hspd1

Protein FDR Confidence: Combined	Accession	Gene name
High	P63017	Hspa8
High	P20029	Hspa5
High	Q8BJA3	Hmbox1
High	P02088	Hbb-b1
High	P01942	Hba
High	Q8BMS1	Hadha
High	P62806	H4c1
High	Q64475	H2bc3
High	Q64523	H2ac20
High	P15864	H1-2
High	P05202	Got2
High	P05201	Got1
High	Q64467	Gapdhs
High	P16858	Gapdh
High	Q8CHI8	Ep400
High	P17182	Eno1
High	Q9D8N0	Eef1g
High	P10126	Eef1a1
High	Q5PR73	Diras2
High	Q9CZU6	Cs
High	P19783	Cox4i1
High	Q9JHS4	Clpx
High	Q9JKK8	Atr
High	Q9DB20	Atp5po
High	Q9DCX2	Atp5pd
High	P56135	Atp5mf
High	Q9D3D9	Atp5f1d
High	P56480	Atp5f1b
High	Q03265	Atp5f1a
High	Q6PIC6	Atp1a3
High	P07724	Alb
High	P60710	Actb
High	Q99KI0	Aco2
High	Q8QZT1	Acat1
High	Q8BWT1	Acaa2