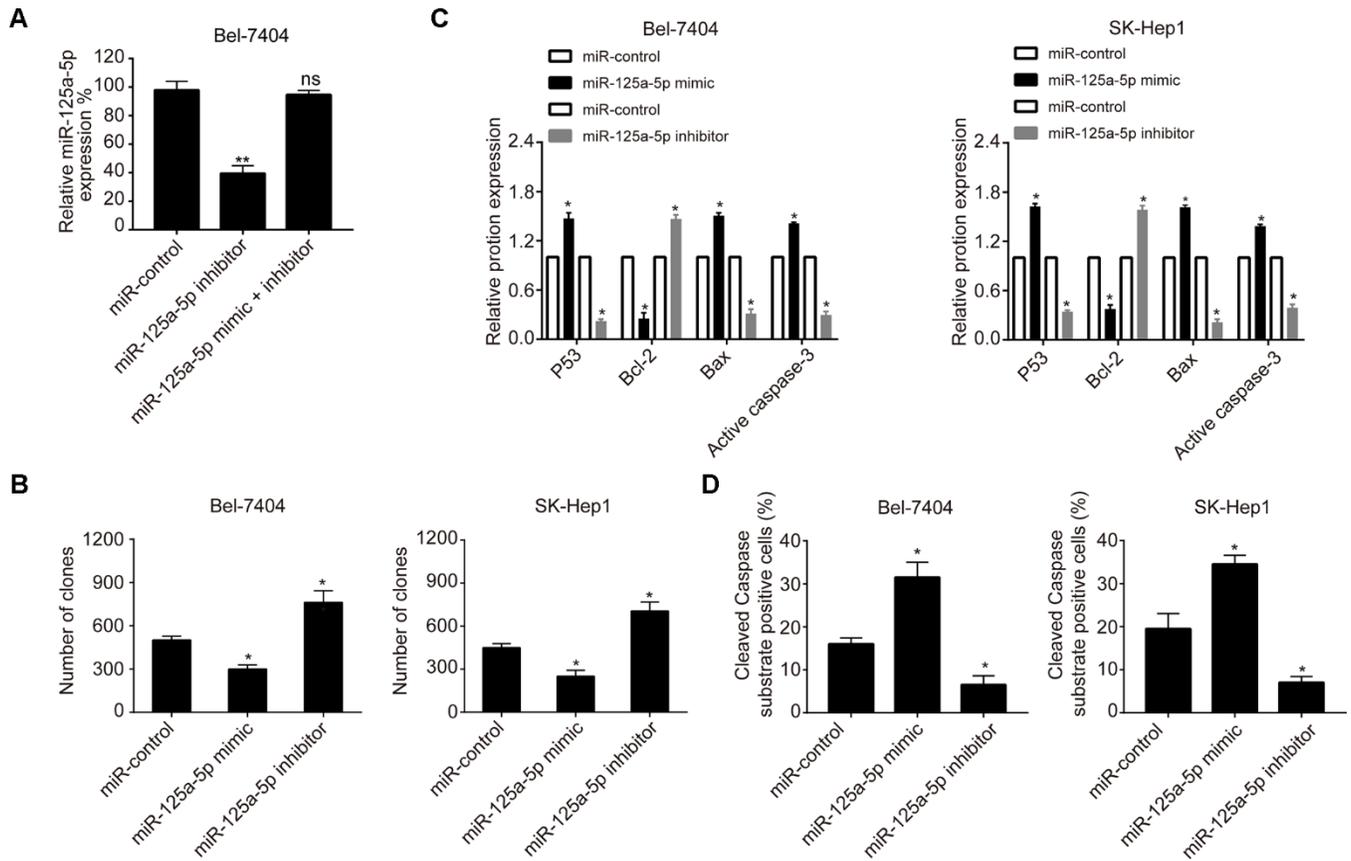
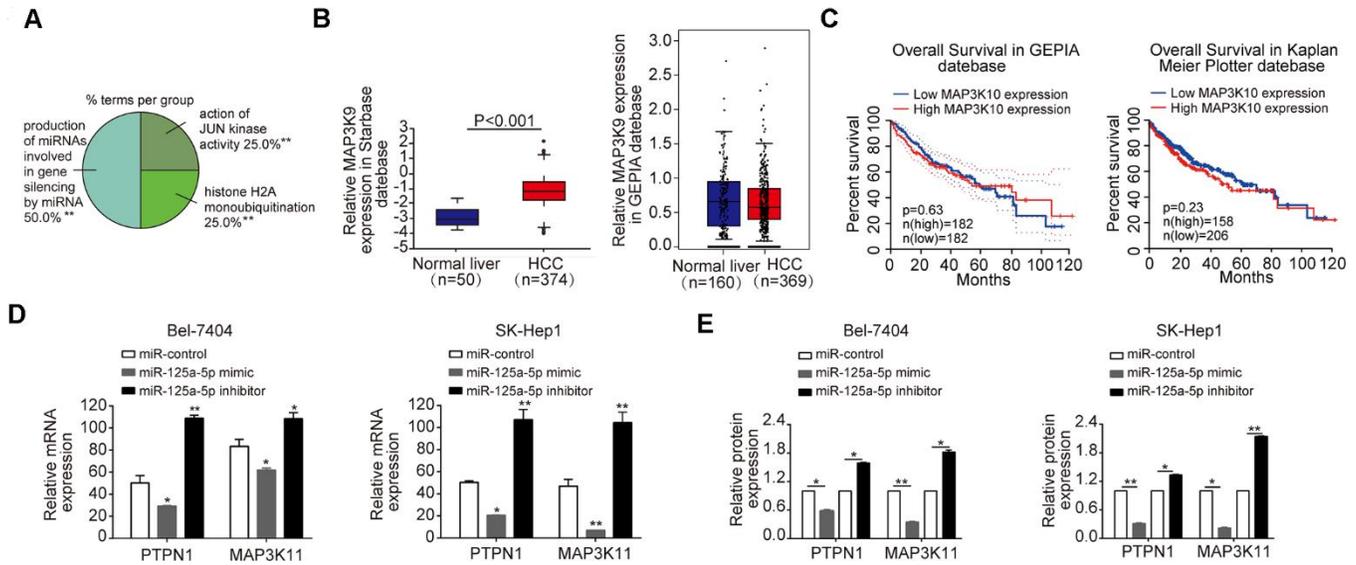


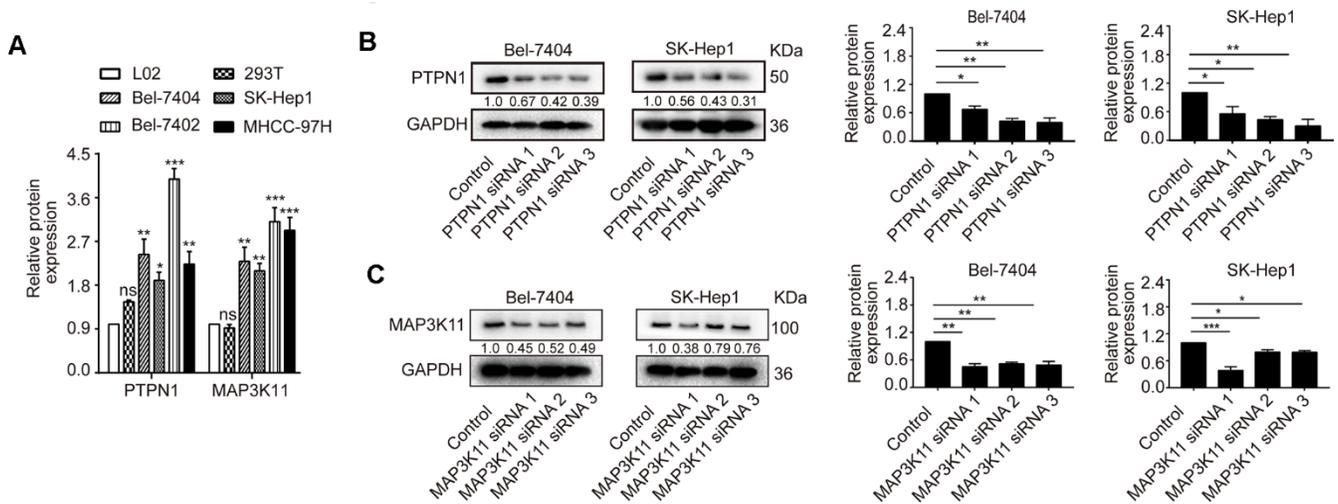
**SUPPLEMENTARY FIGURES**



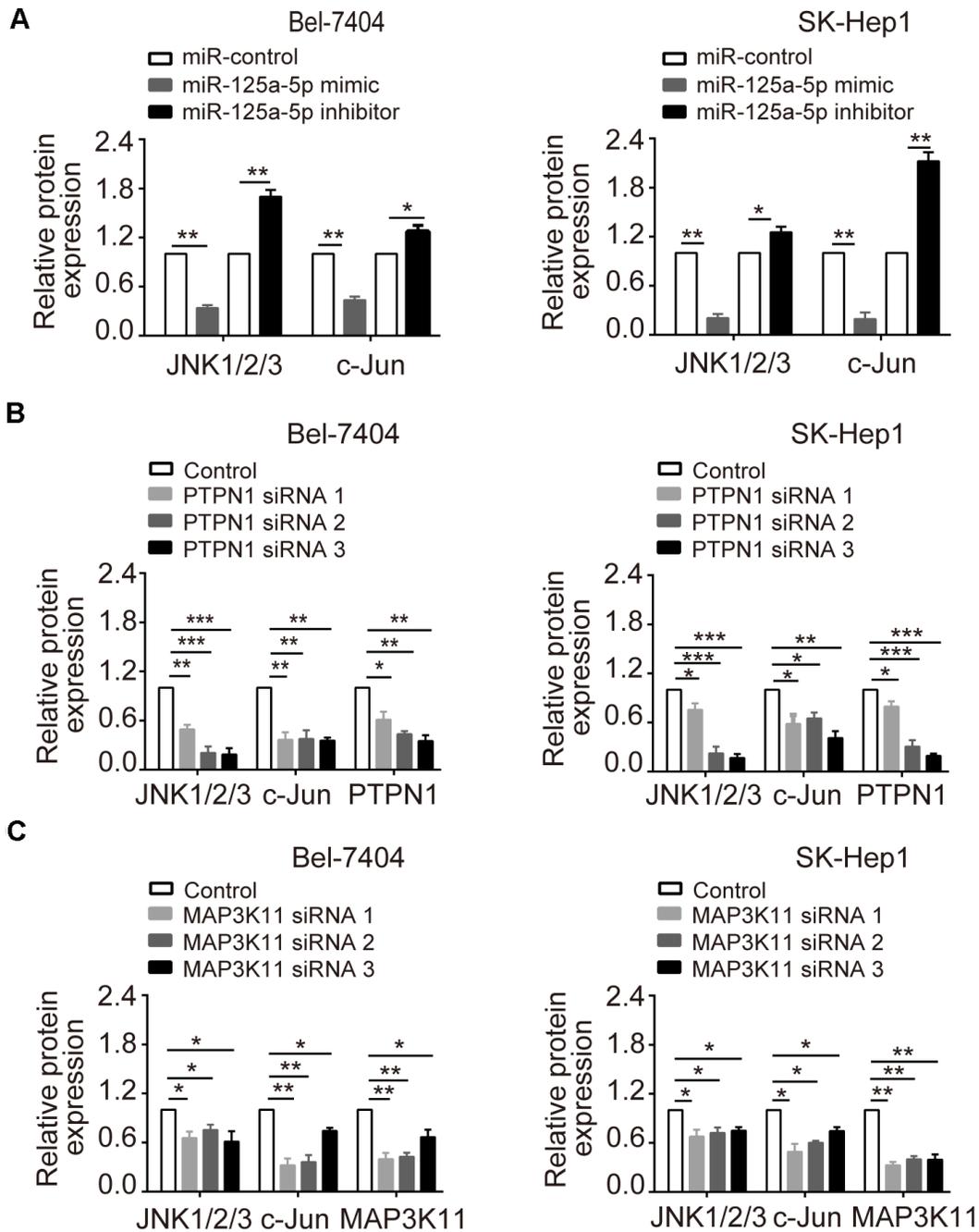
**Supplementary Figure 1. miR-125a-5p suppresses proliferation and induces apoptosis in HCC cells *in vitro*.** (A) Bel-7404 cells were transfected with miR-125a-5p inhibitor and mimic. Student's t-test, mean ± SD, \*\* $P < 0.01$ , ns: not statistically significant. (B) Cell colony numbers in transfected Bel-7404 and SK-Hep1 cells were assessed using Image J. Student's t-test, mean ± SD, \* $P < 0.05$ . (C) Western blots were used to analyze p53, Bax, Bcl-2, and active caspase-3 expression in transfected Bel-7404 and SK-Hep1 cells. Student's t-test, mean ± SD, \* $P < 0.05$ . (D) Cleaved caspase substrate-positive cell numbers were assessed after immunofluorescence staining in transfected Bel-7404 and SK-Hep1 cells using Image J. Student's t-test, mean ± SD, \* $P < 0.05$ .



**Supplementary Figure 2. PTPN1 and MAP3K11 are direct targets of miR-125a-5p in HCC.** (A) 131 target genes were analyzed with ClueGO and CluePedia in Cytoscape. (B) MAP3K9 was up-regulated in the Starbase database, but down-regulated in the GEPIA database. (C) Overall survival of HCC patients was not associated with MAP3K10 expression level in Kaplan Meier Plotter and GEPIA databases. (D) PTPN1 and MAP3K11 mRNA expression was detected by qRT-PCR in transfected Bel-7404 and SK-Hep1 cells. One-way ANOVA, mean  $\pm$  SD, \* $P$ <0.05, \*\* $P$ <0.01. (E) PTPN1 and MAP3K11 protein expression was detected by Western blot in transfected Bel-7404 and SK-Hep1 cells. Student's  $t$ -test, mean  $\pm$  SD, \* $P$ <0.05, \*\* $P$ <0.01.

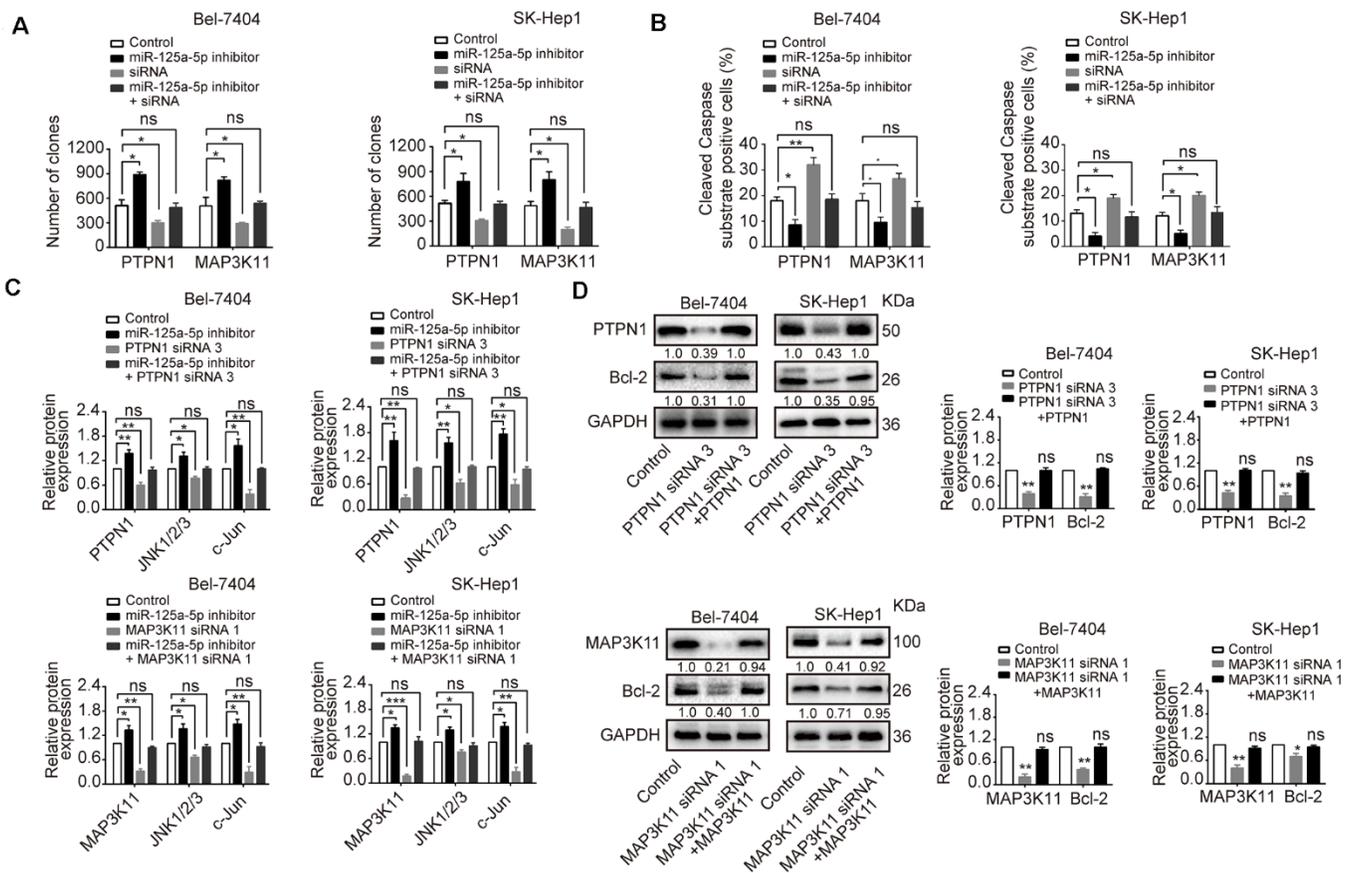


**Supplementary Figure 3. PTPN1 and MAP3K11 are up-regulated and negatively correlated with the expression of miR-125a-5p in HCC.** (A) Western blots indicated that PTPN1 and MAP3K11 were up-regulated in HCC cell lines. One-way ANOVA, mean  $\pm$  SD, \* $P$ <0.05, \*\* $P$ <0.01, \*\*\* $P$ <0.001, ns: not statistically significant. (B and C) Western blots indicated that PTPN1 and MAP3K11 knockdown decreased PTPN1 and MAP3K11 protein expression. One-way ANOVA, mean  $\pm$  SD, \* $P$ <0.05, \*\* $P$ <0.01.



**Supplementary Figure 4. miR-125a-5p suppresses PTPN1 and MAP3K11 expression via the MAPK signaling pathway in HCC.**

(A) Western blots showed that miR-125a-5p overexpression reduced, while miR-125a-5p knockdown increased, JNK1/2/3 and c-Jun expression in Bel-7404 and SK-Hep1 cells. Student's t-test, mean  $\pm$  SD, \* $P$ <0.05, \*\* $P$ <0.01. (B and C) Western blots indicated that PTPN1 and MAP3K11 knockdown decreased JNK1/2/3 and c-Jun expression in Bel-7404 and SK-Hep1 cells. One-way ANOVA, mean  $\pm$  SD. \* $P$ <0.05, \*\* $P$ <0.01, \*\*\* $P$ <0.001, ns: not statistically significant.



**Supplementary Figure 5. miR-125a-5p suppresses cell proliferation and induces apoptosis in HCC by targeting PTPN1 and MAP3K11 via the MAPK signaling pathway.** (A) Cell colony numbers were assessed in transfected Bel-7404 and SK-Hep1 cells using Image J. One-way ANOVA, mean  $\pm$  SD,  $*P < 0.05$ , ns: not statistically significant. (B) Cleaved caspase substrate-positive cell numbers were assessed after immunofluorescence staining in transfected Bel-7404 and SK-Hep1 cells using Image J. Student's t-test, mean  $\pm$  SD,  $*P < 0.05$ ,  $**P < 0.01$ , ns: not statistically significant. (C) Western blot experiments were used to analyze PTPN1, MAP3K11, JNK1/2/3, and c-Jun expression in transfected Bel-7404 and SK-Hep1 cells. One-way ANOVA, mean  $\pm$  SD,  $*P < 0.05$ ,  $**P < 0.01$ ,  $***P < 0.001$ , ns: not statistically significant. (D) PTPN1 and MAP3K11 CDS were inserted into pCDNA3.1(+) vectors to confirm acceptable rescue efficiency and to rule out off-target siRNA effects via Western blot. One-way ANOVA, mean  $\pm$  SD,  $*P < 0.05$ ,  $**P < 0.01$ , ns: not statistically significant.