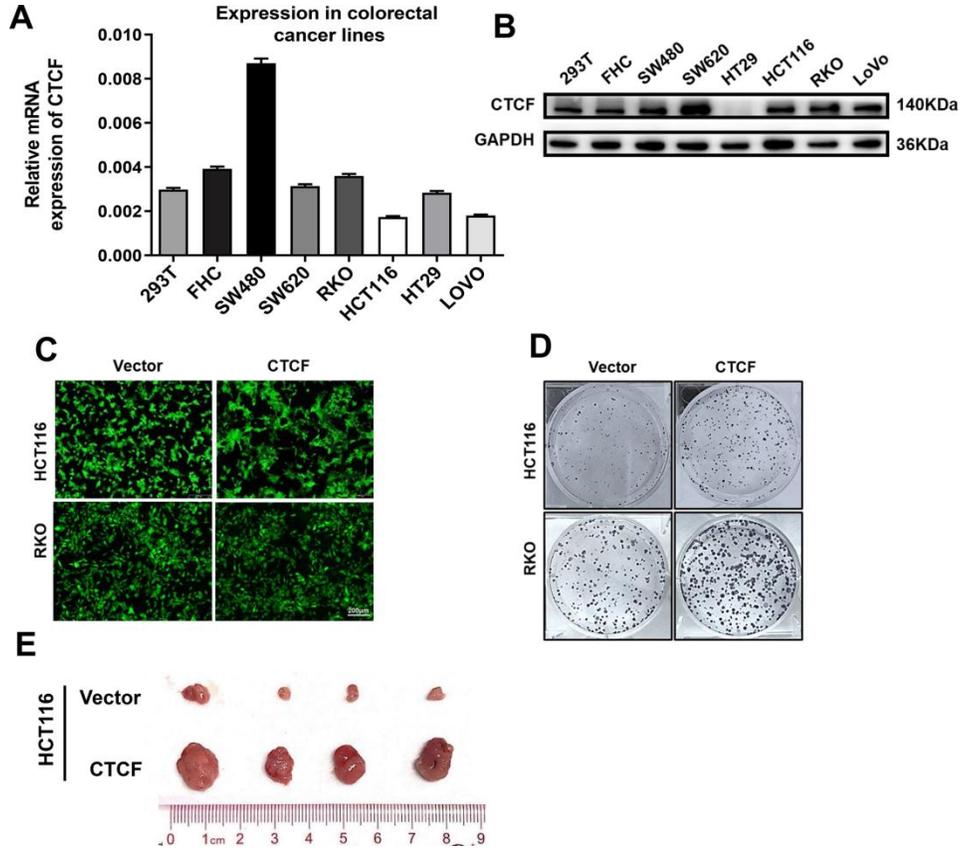
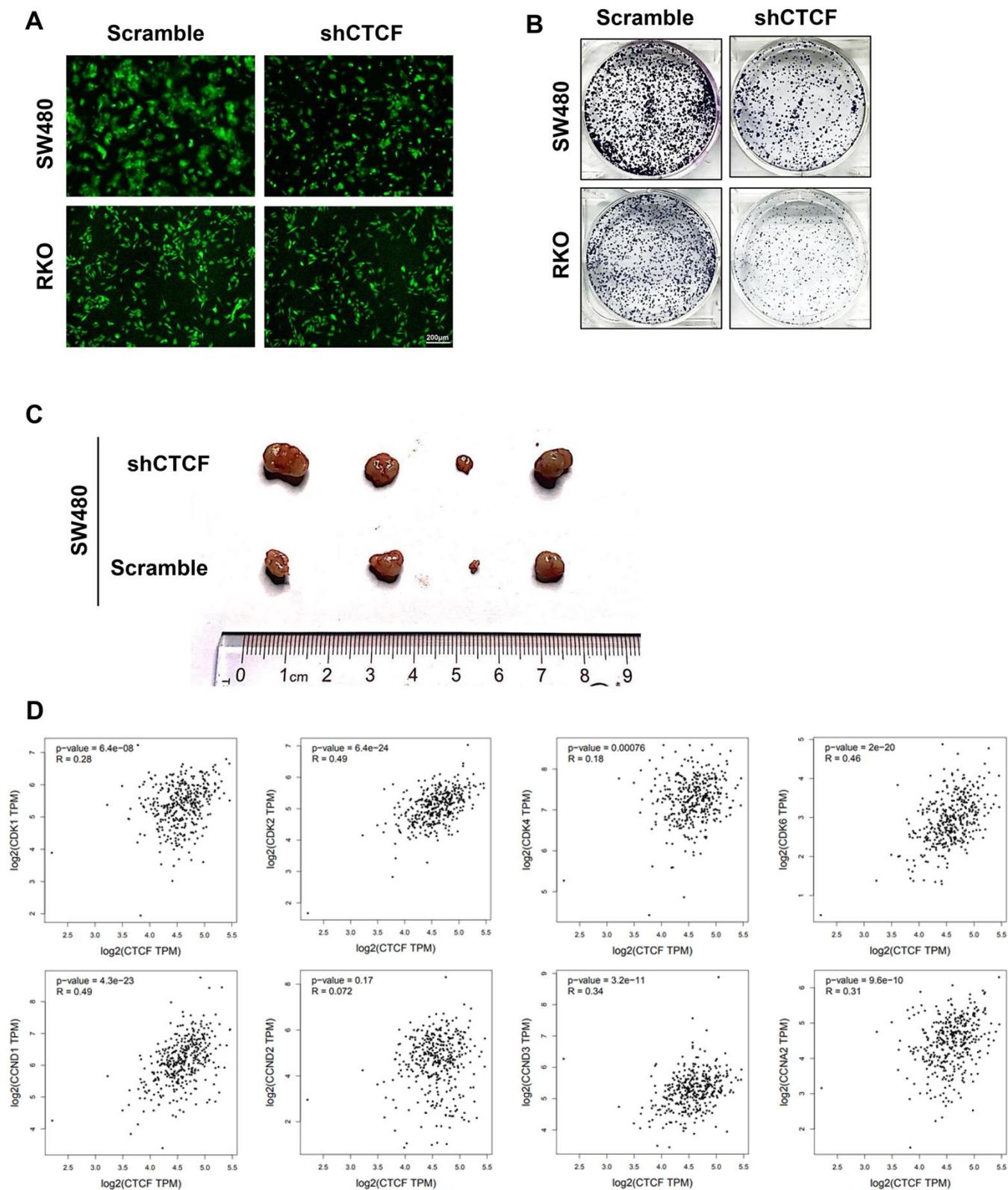


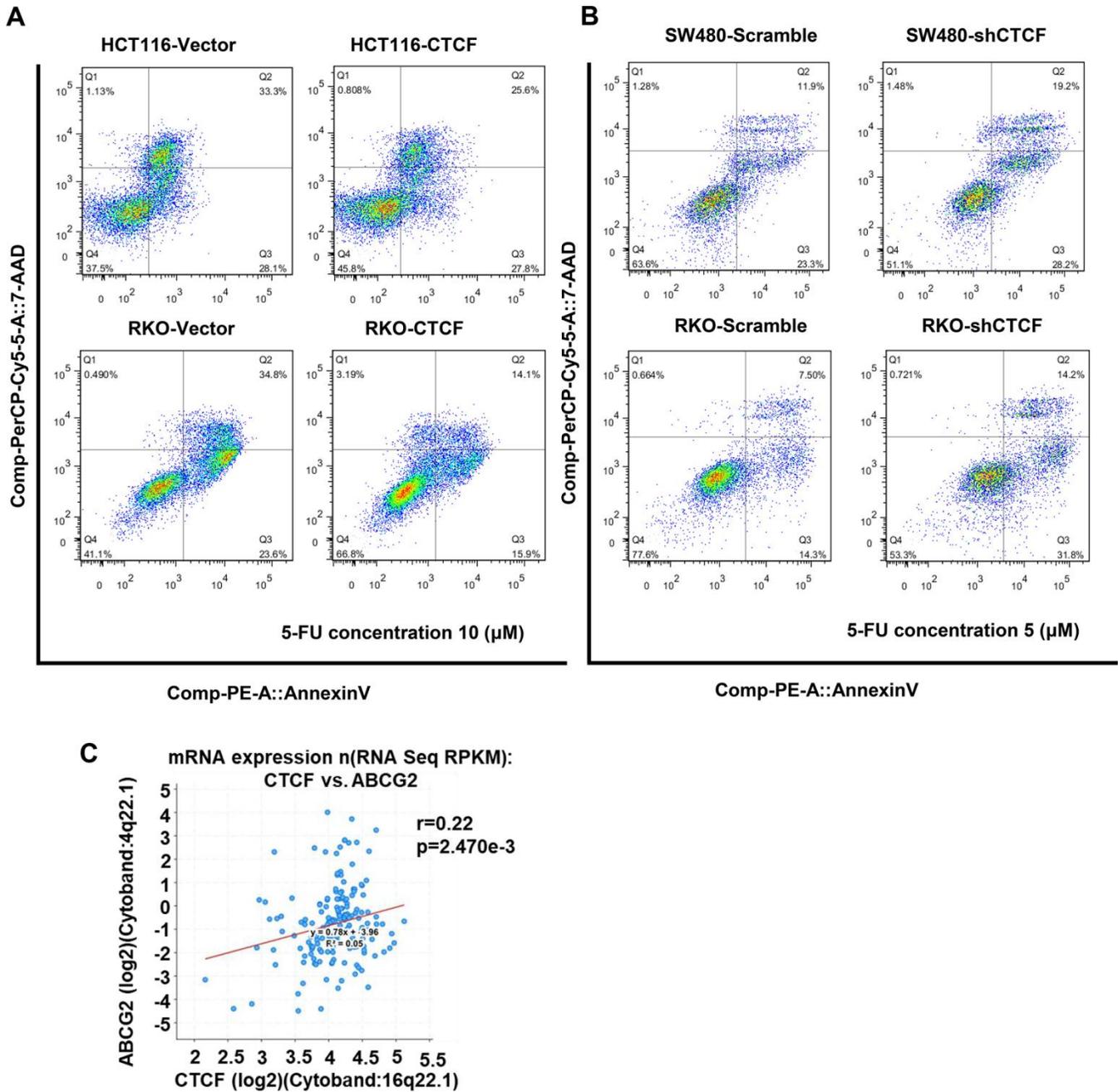
**SUPPLEMENTARY FIGURES**



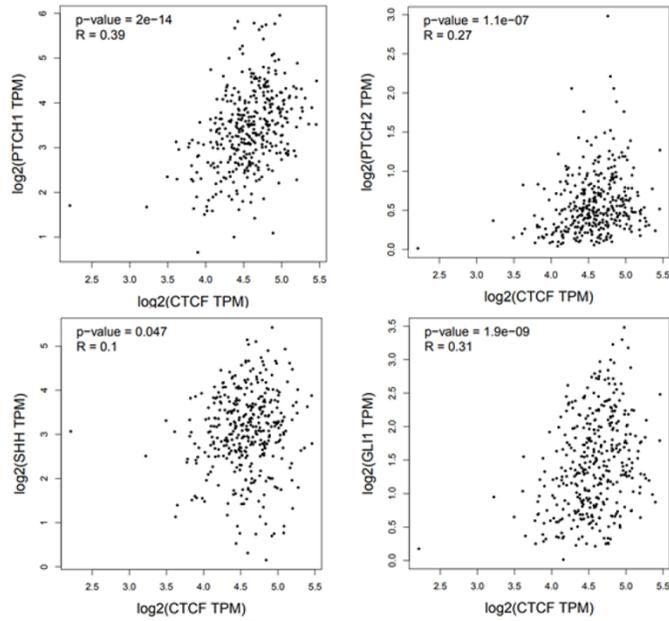
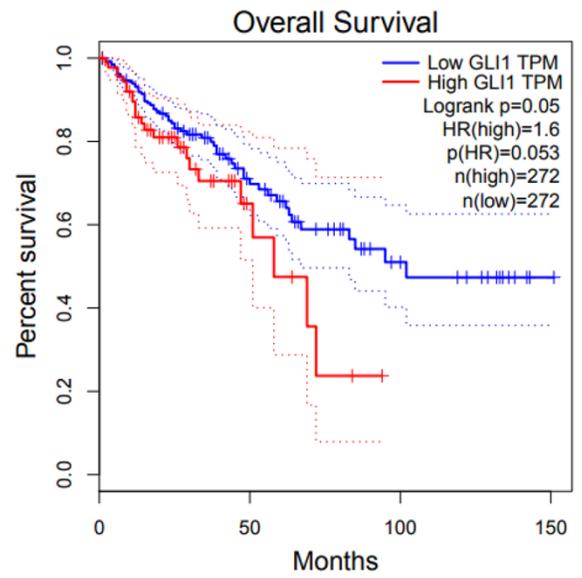
**Supplementary Figure 1. Overexpression of CTCF enhances human CRC cells proliferative capacity.** (A) mRNA level of CTCF in human embryonic kidney cell line (293T), human normal colon epithelial cell line (FHC) and six CRC cell lines. (B) Western blot analysis of human embryonic kidney cell line (293T), human normal colon epithelial cell line (FHC) and six CRC cell lines. The above data are presented as mean ± SEM. (C) Fluorescence assessment of the green fluorescent protein (GFP). Vector represents lentivirus-mediated control groups. CTCF represents lentivirus-mediated CTCF overexpressing groups. (D) The representative images of colony formation assay from different experimental groups are shown. (E) Corresponding cells were respectively injected subcutaneously into the right and left back hips of nude mice (n = 4). Representative images of the tumors are shown. \* P<0.05, \*\*P<0.01, and \*\*\*P<0.001.



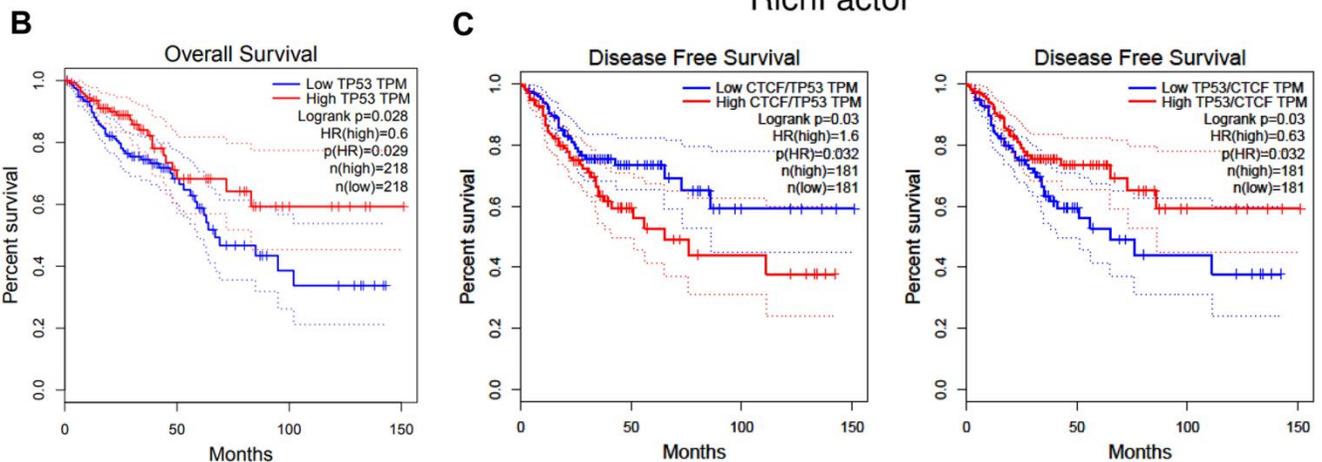
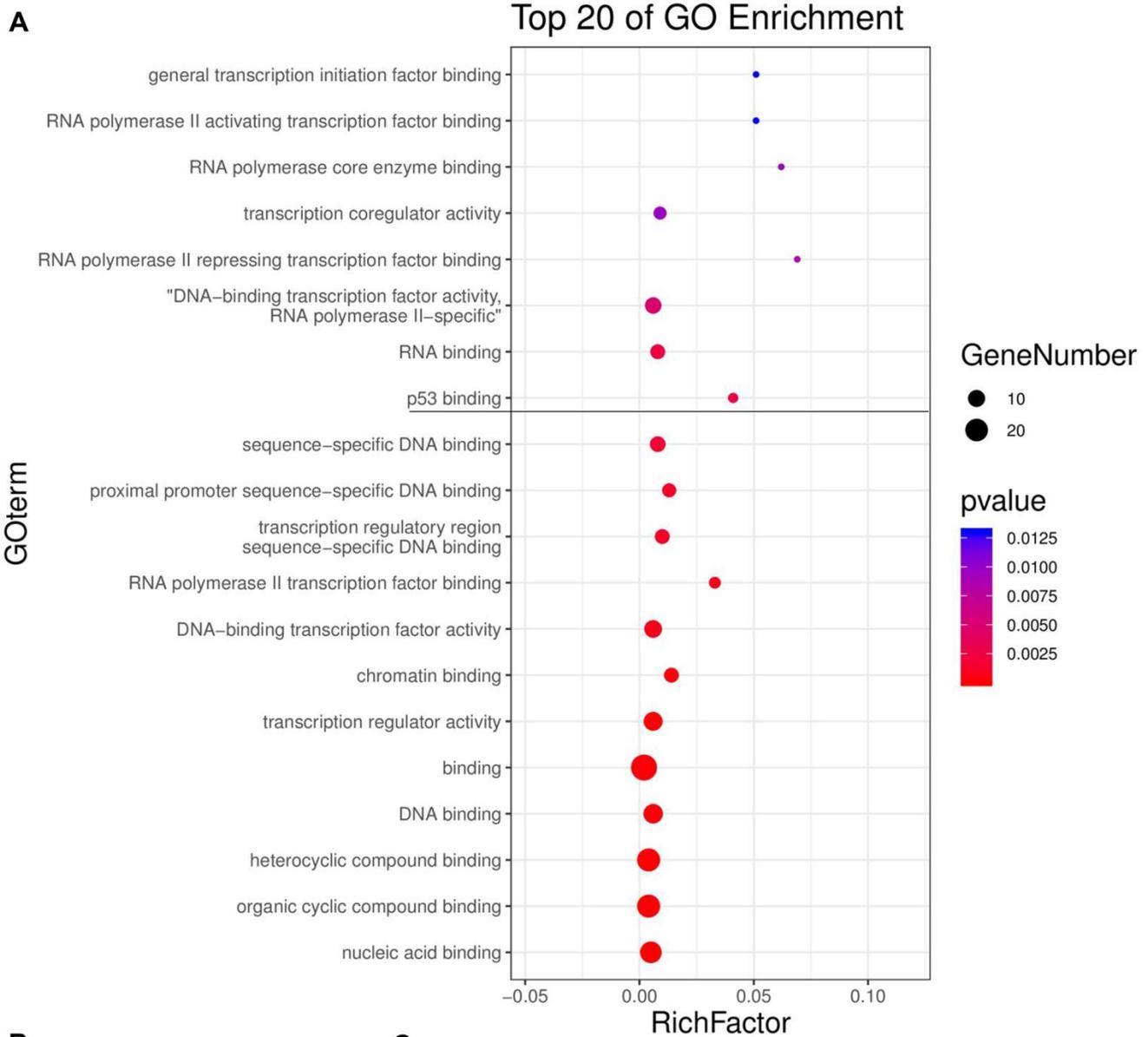
**Supplementary Figure 2. Knockdown of CTCF inhibits human CRC cells proliferation.** (A) Fluorescence assessment of the green fluorescent protein (GFP). Scramble represents lentivirus-mediated control groups. shCTCF represents lentivirus-mediated CTCF silencing groups. (B) The representative images of colony formation assays from different experimental groups are shown. (C) Corresponding cells were respectively injected subcutaneously into the right and left back hips of nude mice (n = 4). Representative images of the tumors are shown. (D) CTCF expression was positively correlated with the expression of CDKs and Cyclins in GEPIA (<http://gepia.cancer-pku.cn/>).



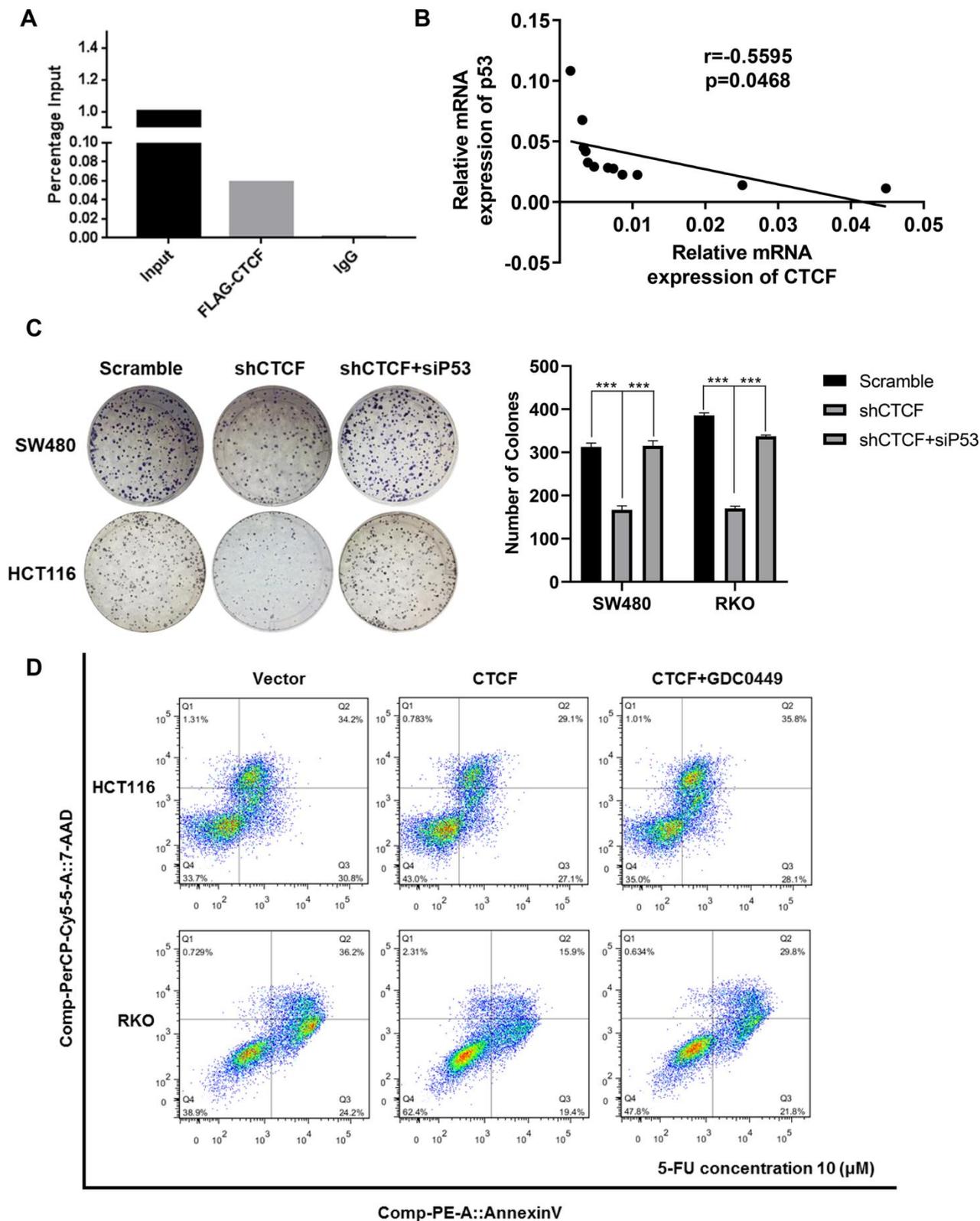
**Supplementary Figure 3. CTCF causes CRC cells to be insensitive to 5-FU-based chemoresistance.** (A, B) The representative images of apoptotic assays from different experimental groups are shown. Scramble and shCTCF cell lines were treated with 5-FU with a 5µM concentration, and the other cell lines were treated with 5-FU with a 10µM concentration. (C) Positive correlation between CTCF expression and ABCG2 by spearman correlation analysis in cBioPortal (<http://www.cbioportal.org/>).

**A****B**

**Supplementary Figure 4. CTCF activates Hedgehog signaling pathway.** (A) Positive correlation between CTCF expression and the key molecules of Hedgehog signaling pathway by spearman correlation analysis in GEPIA (<http://gepia.cancer-pku.cn/>). (B) Kaplan-Meier survival analysis revealed that CRC patients in the GLI1 high expression group have shorter survival time in GEPIA.



**Supplementary Figure 5. CTCF might regulate P53 in CRC.** (A) GO-molecular function enrichment analysis of the top 30 similar genes of CTCF in GEPIA is shown. (B) Kaplan-Meier survival analysis revealed that CRC patients in the TP53 high expression group have good prognosis in GEPIA. (C) Kaplan-Meier survival analysis showed that the ratio of CTCF/TP53 is positively related to disease free survival time.



**Supplementary Figure 6. CTCF facilitates CRC progression via P53-Hedgehog axis.** (A) ChIP-qPCR results for CTCF on the CBS in HCT116 cells. (B) Spearman correlation analysis between relative CTCF and P53 mRNA expression in 13 fresh human CRC specimens. (C) Cell proliferative capacity was tested by colony formation assays and the representative images of colony formation assays from different experimental groups are shown. (D) The representative images of apoptotic assays from different experimental groups with or without administration of GDC-0449 are shown. The above data are presented as mean  $\pm$  SEM. \*  $P < 0.05$ , \*\*  $P < 0.01$ , and \*\*\*  $P < 0.001$ .