Figure S1. CRC chromosome copy number amplification and candidate gene extraction. (A) DNA copy number variations across chromosome arm in 621 CRC tissues from TCGA dataset. (B) Schematic diagram of the strategy for selecting candidate genes in CRC. CRC, colorectal cancer; TCGA, The Cancer Genome Atlas.

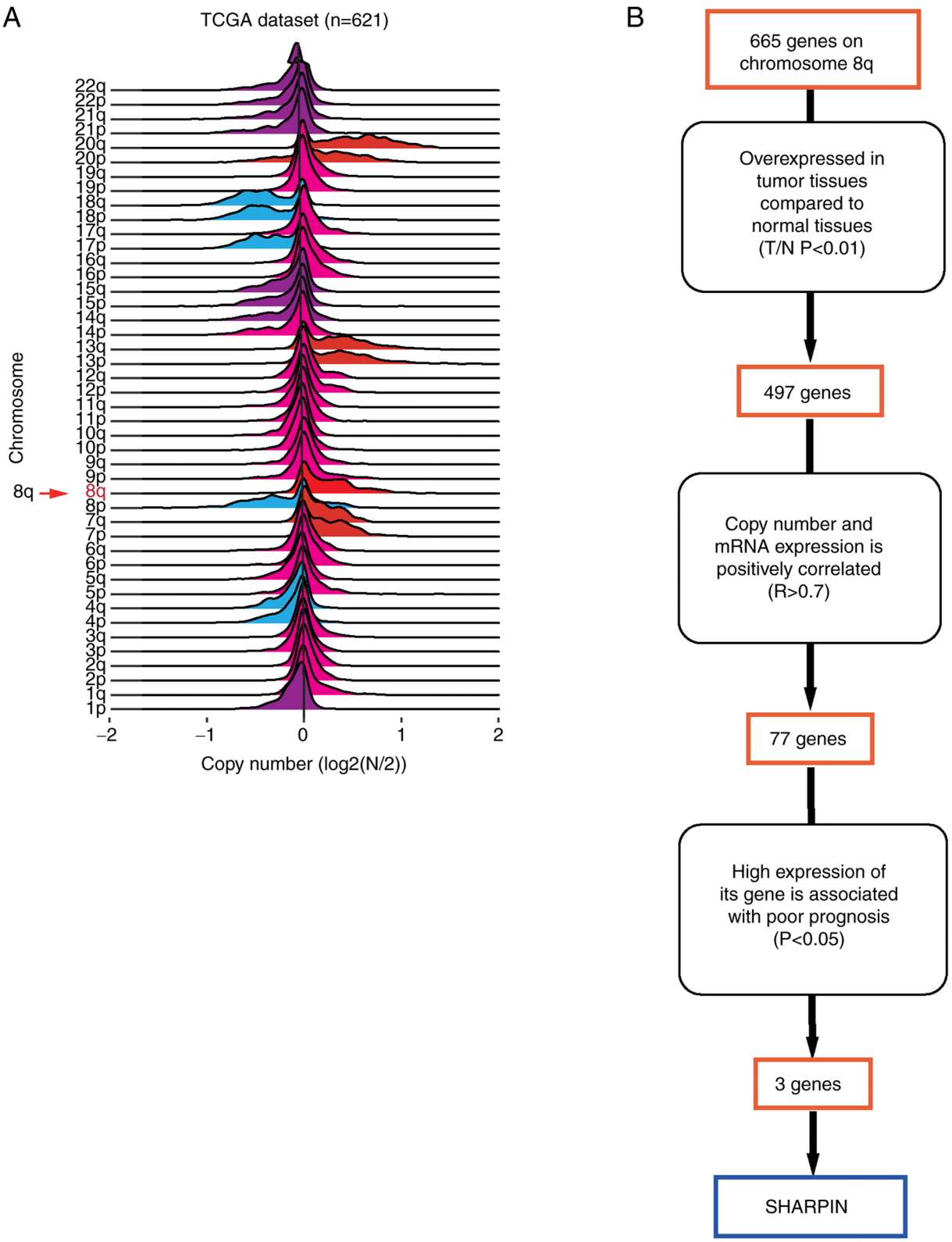

Figure S2. p53 mutation rates in the TCGA dataset and *SHARPIN* expression by p53 status in CRC cases. (A) Pie chart of p53 mutation distribution in CRC cases of the TCGA database (n=380). (B) *SHARPIN* mRNA expression in CRC and normal colon tissue in p53 wild-type cases (left) and p53 mutant cases (right) in the TCGA dataset. The data are presented as the mean ± standard deviation. *P<0.05 and ***P<0.005. TCGA, The Cancer Genome Atlas; *SHARPIN*, shank-associated RH domain interactor; CRC, colorectal cancer.

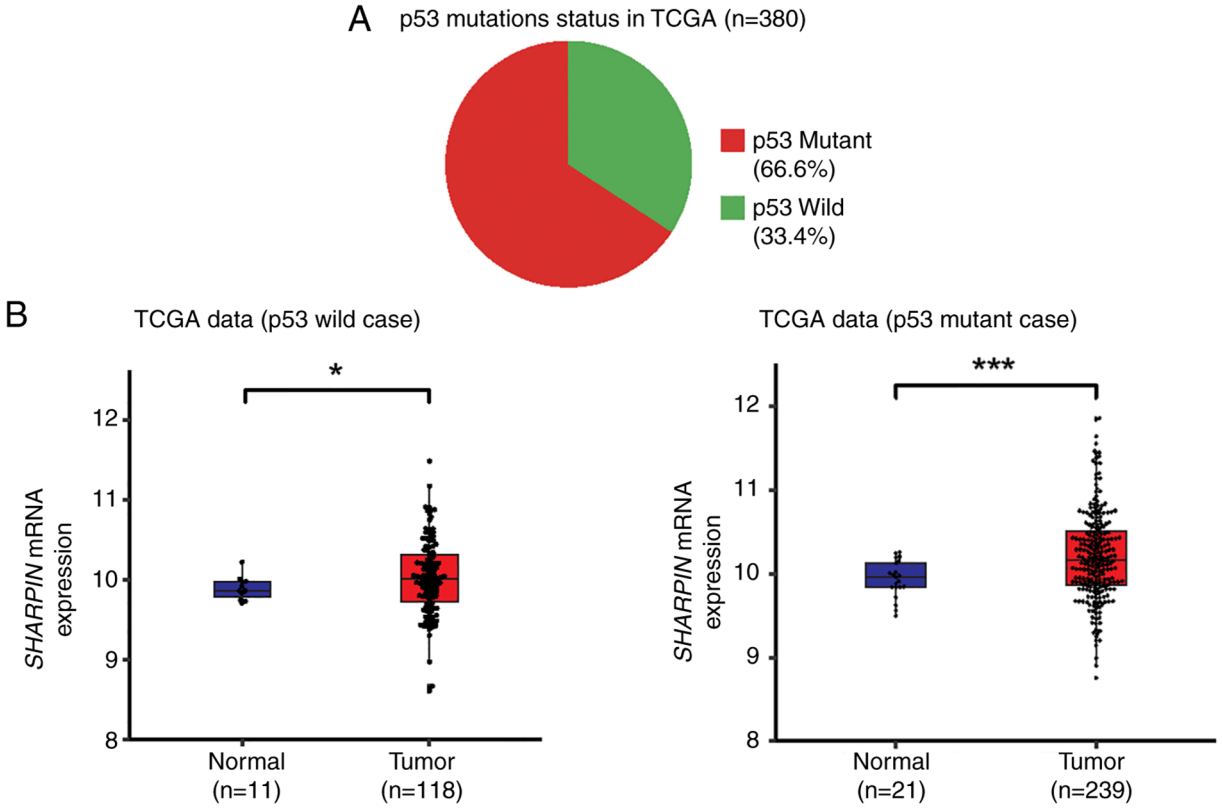

Figure S3. Spatial distribution of various cell types in tissue sections. The spatial transcriptome and single-cell RNA sequencing data were integrated to map the spatial localization of different cell types in the tissue section. The heatmaps represent the predicted contribution of individual cell types to each spatial spot in the spatial transcriptome. The color intensity indicates the predicted relative abundance of each cell type across the spatial spots, with higher intensities representing higher predicted cell type contributions. Tumor Epi, Tumor epithelial cells; Normal Epi, Normal epithelial cells; TCD4, $CD4^+$ T cells; TCD8, $CD8^+$ T cells; NK, Natural Killer cells; ILC, Innate Lymphoid Cells; B, B cells; Plasma, Plasma cells; Mast, Mast cells; Macro, Macrophages; DC, Dendritic cells; Mono, Monocytes; Fibro, Fibroblasts; Endo, Endothelial cells; Smooth Muscle, Smooth muscle cells; Granulo, Granulocytes.

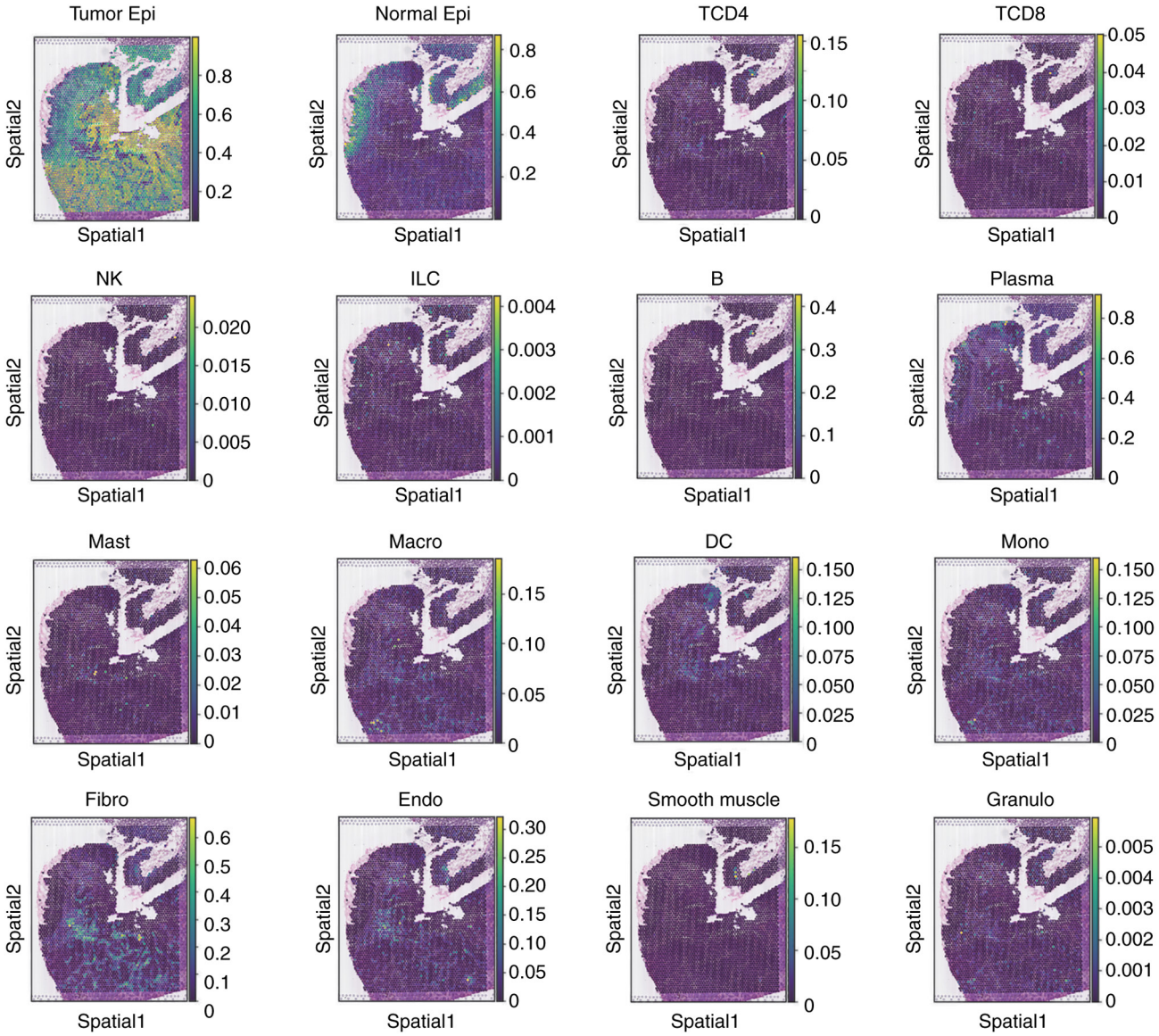

Figure S4. SHARPIN knockdown inhibits cell proliferation in CRC cells through its involvement in regulating MDM2 and p53 expression. (A) *SHARPIN* mRNA expression using RT-qPCR in CRC cell lines. mRNA expression was normalized to 18s. (B) Protein expression using western blot analysis for SHARPIN and β-actin in CRC cell lines. The lower panel quantitatively displays the proteins from the upper panel. (C) *SHARPIN* mRNA expression using RT-qPCR in SHARPIN-knockdown and control cells. mRNA expression was normalized to 18s. (D) Colony formation assays using SHARPIN-knockdown cells. (E) SHARPIN, MDM2 and p53 protein expression using western blot analysis in SHARPIN-knockdown and control cells. β-actin was used as the loading control. The right panel quantitatively displays the proteins from the left panel. The data are presented as the mean ± standard deviation. Statistical differences between groups were determined using a two-tailed unpaired Student's t-test for C and D and one-way ANOVA with Turkey's HSD post hoc test for A. *P<0.05, **P<0.01 and ***P<0.005. *SHARPIN*, shank-associated RH domain interactor; CRC, colorectal cancer; RT-qPCR, reverse transcription-quantitative polymerase chain reaction.