

Supplementary figure legends

Figure S1. (A) CasRx efficiently silences mCherry expression. 293T cells were transiently transfected by plasmids as indicated. Lipofectamine 3000 was used as described in methods. A fluorescence microscopy (Olympus) was used to capture the image. (B) Sanger-sequencing of Kras mRNA containing the region of G12D mutation. Total RNA was precipitated from indicated cells and reverse transcribed to obtain the cDNA as indicated in methods. Sequences were shown by SnapGene software.

Figure S2. (A-B) Histogram analysis of Kras intensity supplementary to Figure 2C. (C) CasRx overexpression did not affect the cellular Kras protein level. (D) A volcano plot of differentially expressed genes in PANC-1 cells (Kras^{G12D} mutant cell) or (E) in H6c7 cells (Kras wild-type cell) transfected with CasRx+/gRNA+ targeting Kras^{G12D}. Genes with false discovery rate (FDR) <0.05 and |fold change| > 2 were set as differentially expressed genes (DEGs) and highlighted in red. Detailed list of DEGs from Figure S2D-E were shown in Table S1, S2.

Figure S3. CasRx-gRNA system did not affect MIAPaCa-2 cells bearing Kras^{G12C} mutation. (A) RT-qPCR quantification of Kras mRNA. (B) Western-blot analysis of Kras protein. (C) Cell proliferation quantification by using CCK-8 assay. (D) Colony-forming assay in MIAPaCa-2 cells. (E) Gemcitabine IC50 determination in MiaPaCa2.

Figure S4. gRNA targeting mutant Kras^{G12D} transcript silenced mutant Kras^{G12D} transcript in AsPC-1 cells. (A) RT-qPCR quantification of Kras mRNA. (B) Western-blot analysis of Kras protein. (C) Cell proliferation quantification by CCK-8 assay. (D) Colony-forming assay in AsPC-1 cells. (E) Gemcitabine IC50 determination in AsPC-1. (F) RT-qPCR quantification of Kras mRNA in the orthotopic tumor as shown in Figure 4.

Figure S5. Supplementary to Figure 3G. (A) The morphology and Ki-67 staining of PANC-1 tumors. (B) The Mouse weight and (C) tumors weight. (D) CasRx and gRNA targeting mutant Kras^{G12D} dramatically inhibited the 3D-proliferation of PANC-1.

Figure S6. Supplementary to Figure 5. IHC staining of p-Erk expression and the staining score statistics.

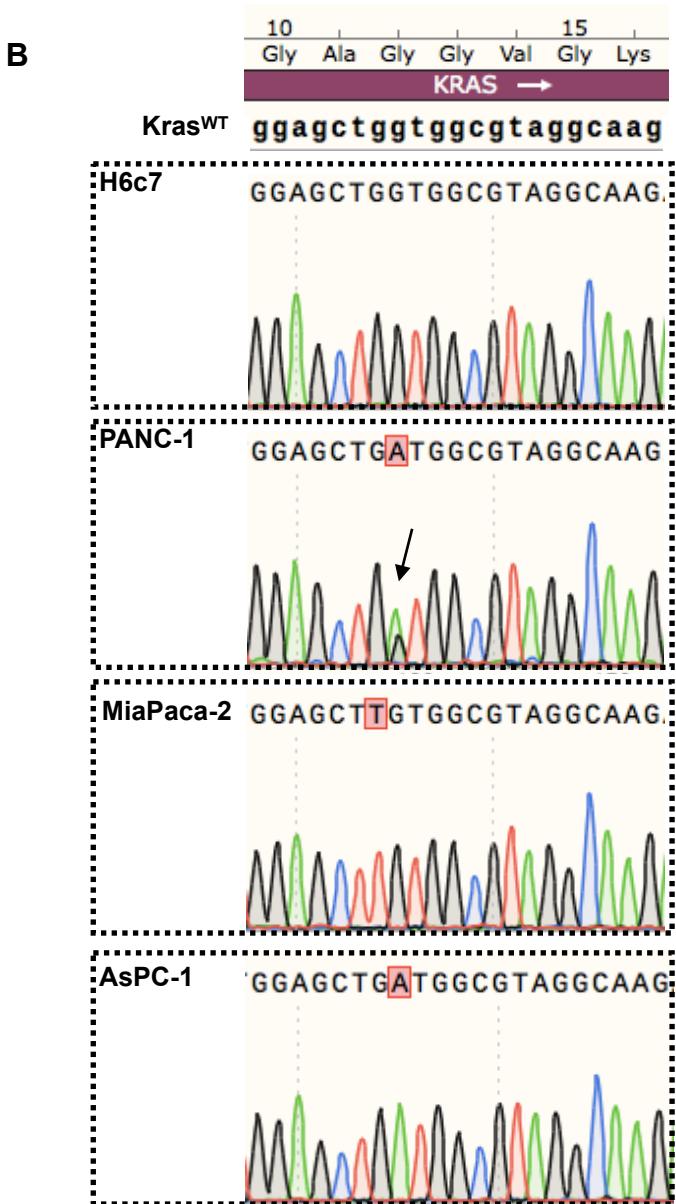
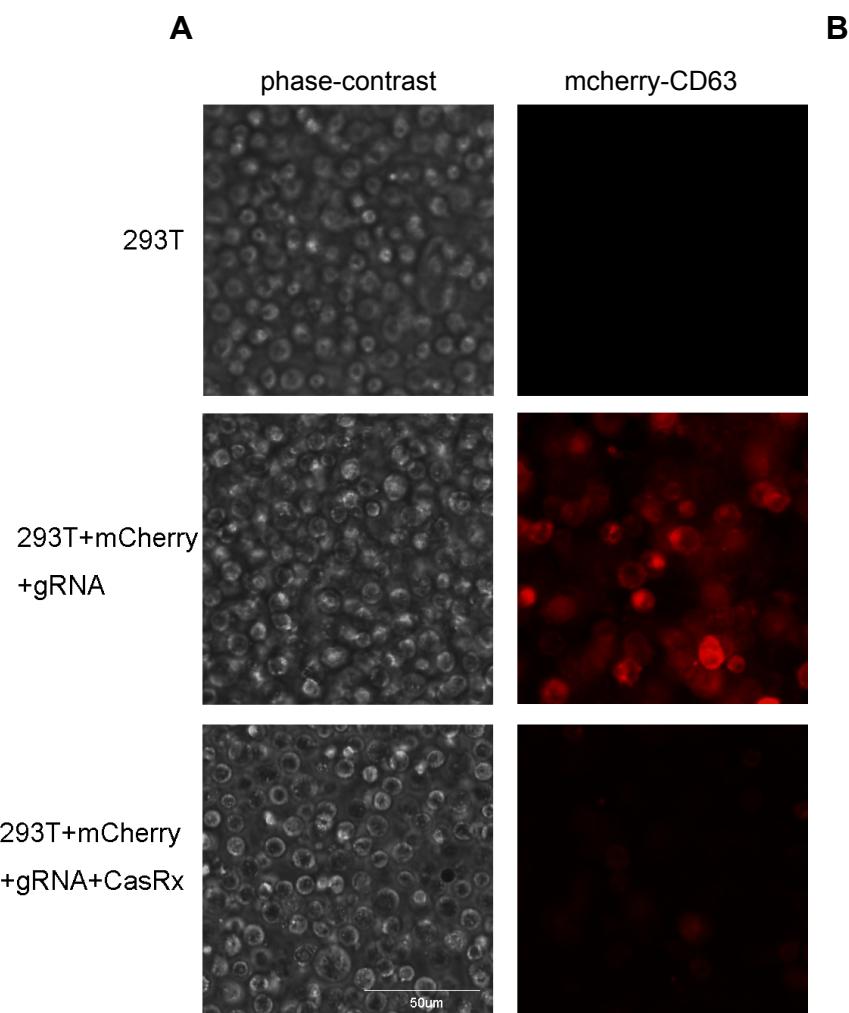


Figure S1

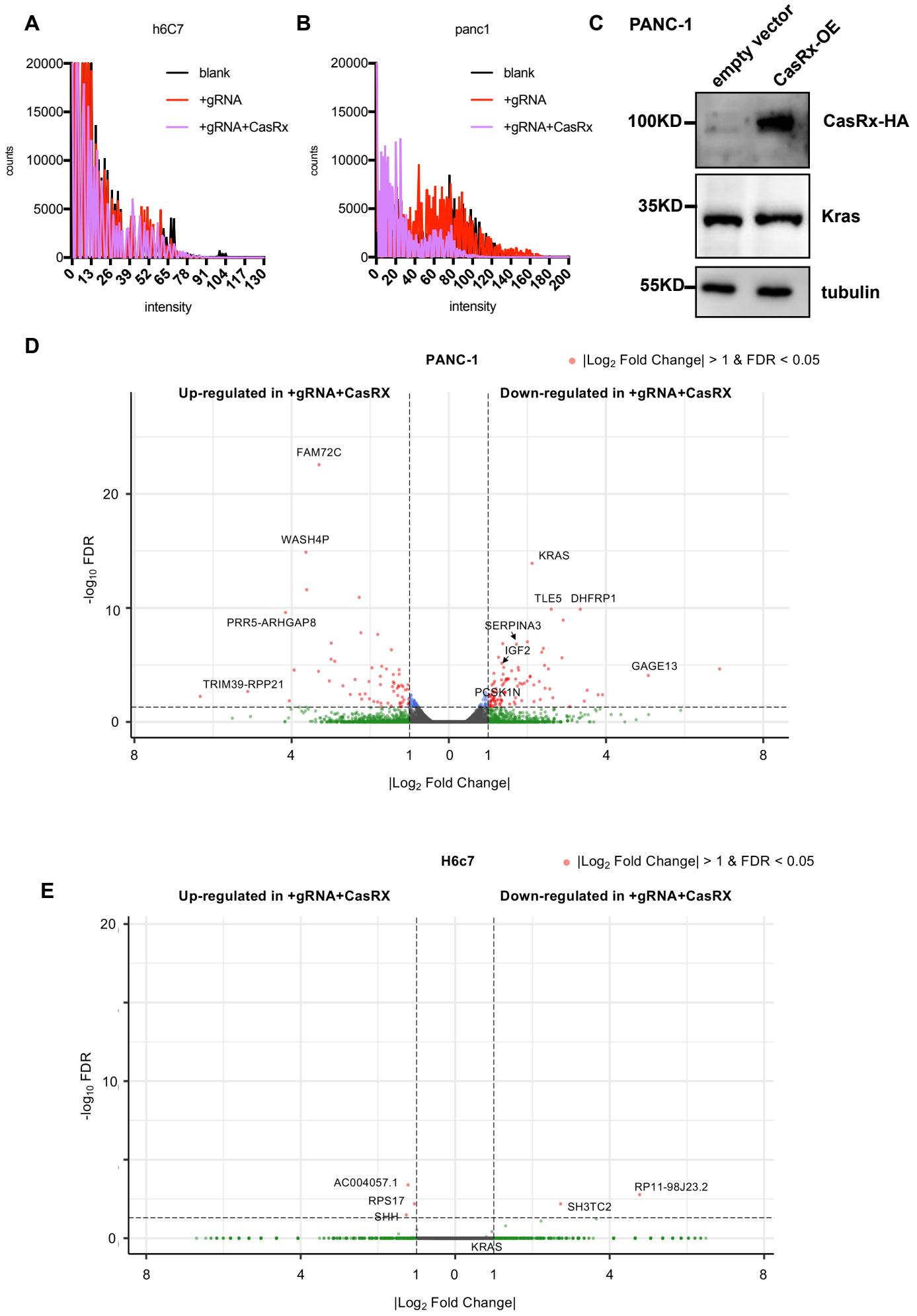


Figure S2

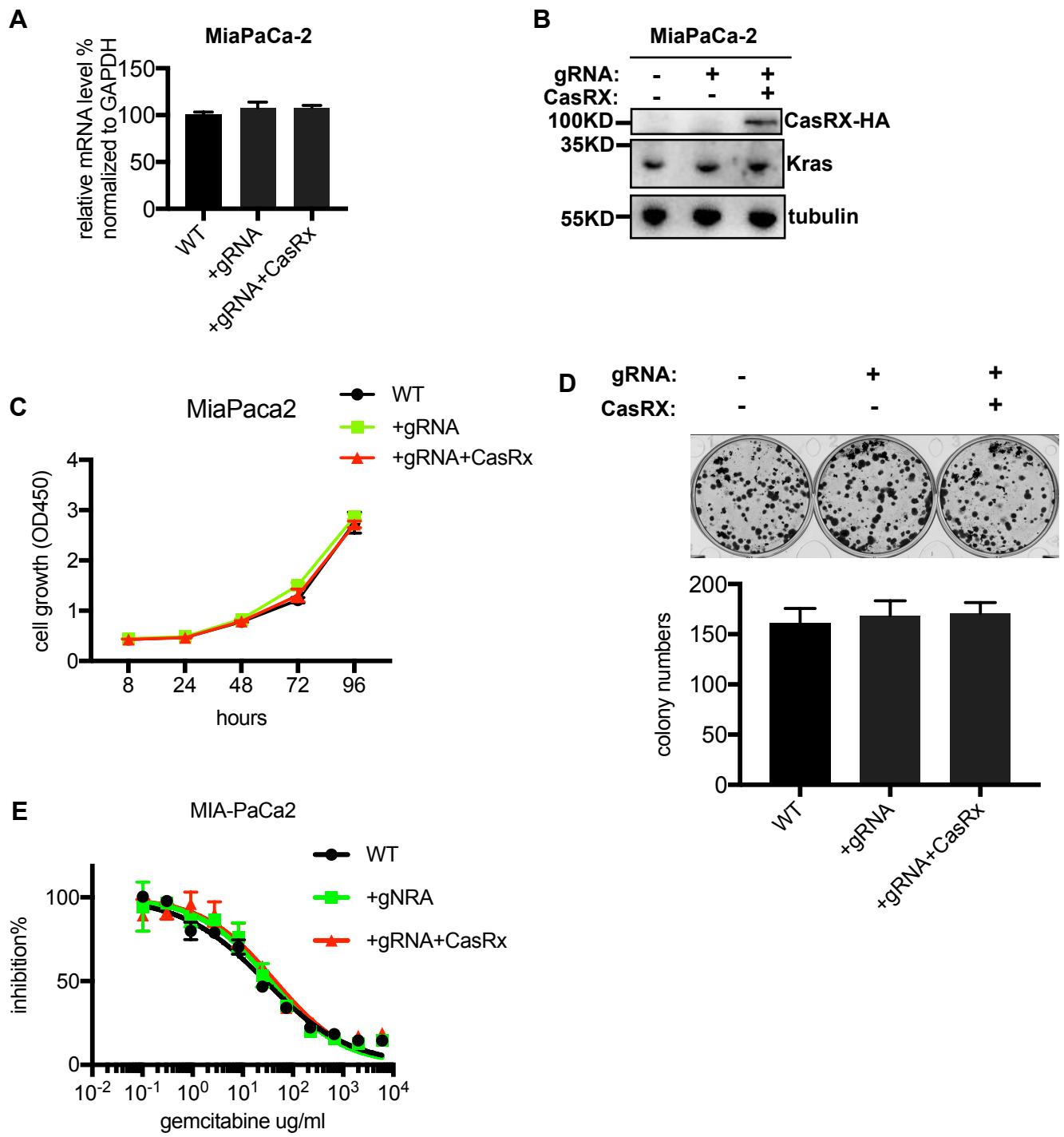


Figure S3

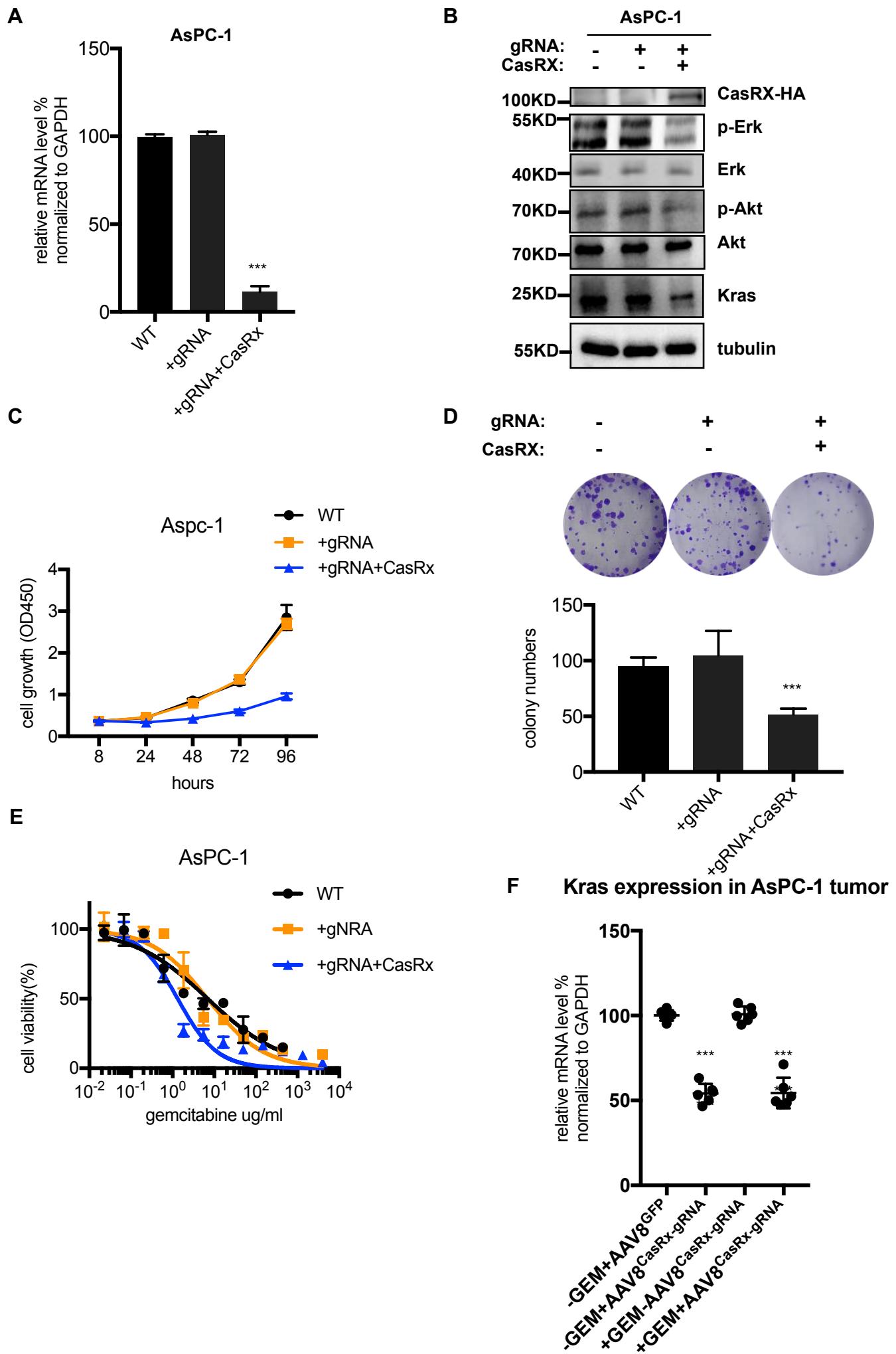


Figure S4

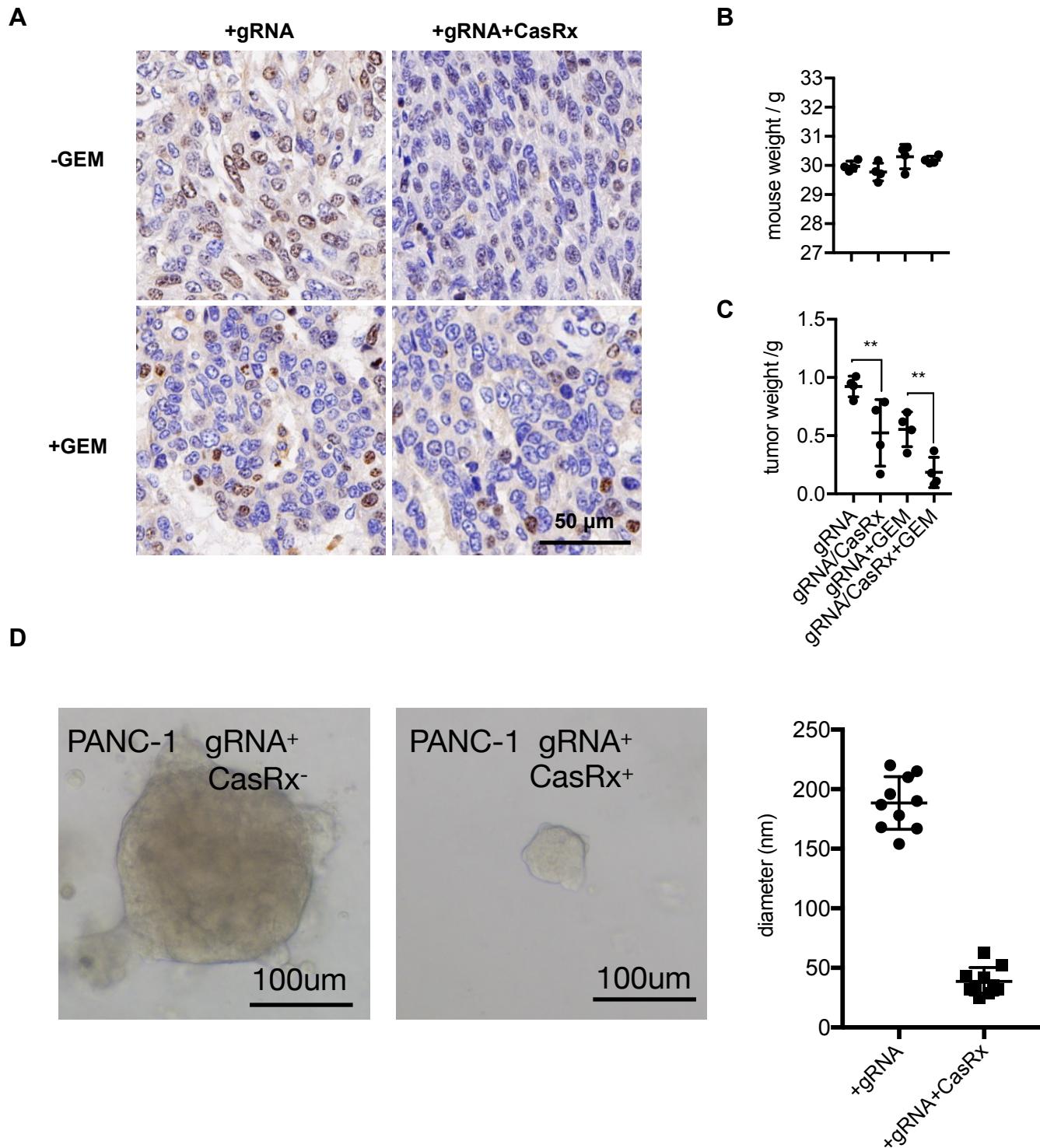


Figure S5

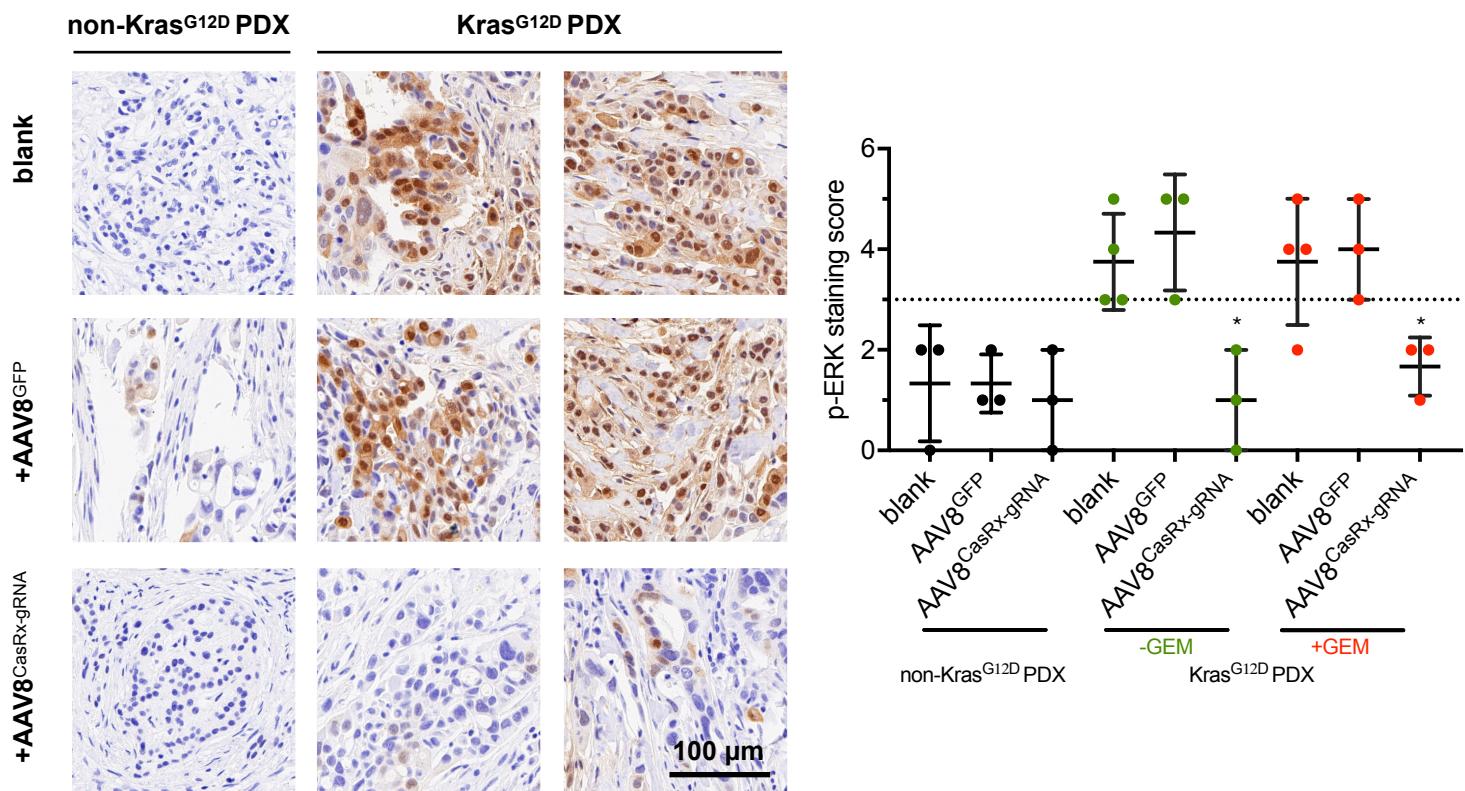


Figure S6