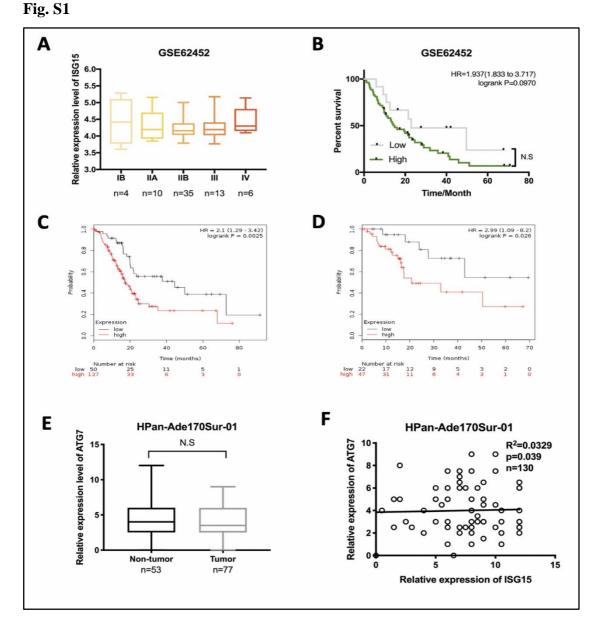
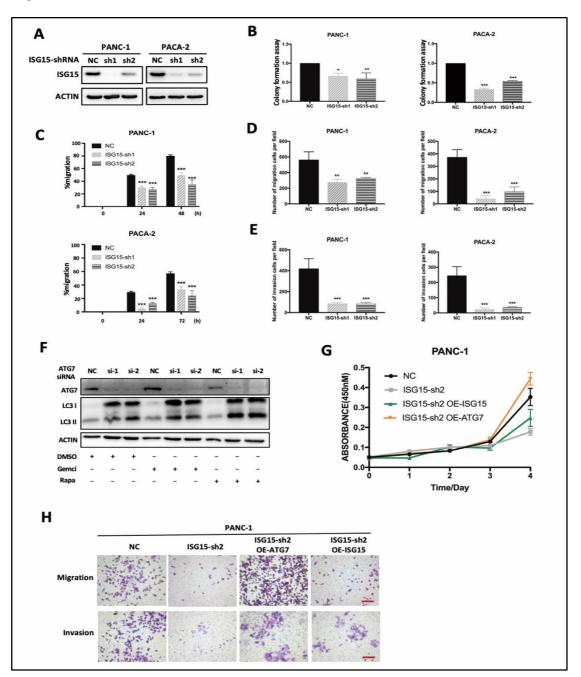
Meng YL` Revised Supplementary Figures and Legends



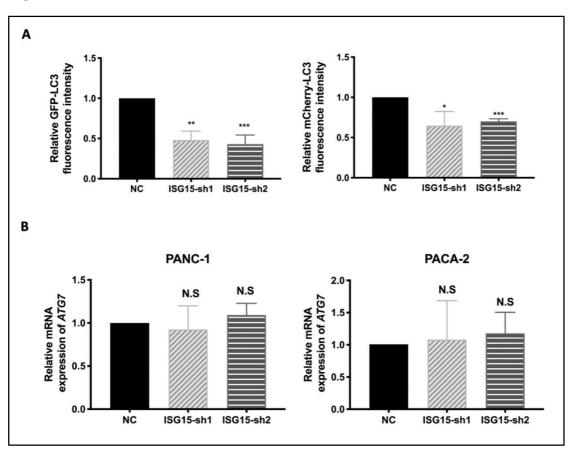
**Fig. S1. A,** ISG15 expression exhibited no significant correlation with the PC stage. Data from dataset GSE62452 were analyzed. **B,** No significant correlation between ISG15 and PC patient survival was shown based on the analysis of GSE62452 dataset. **C-D,** K-M survival analysis was used to analyze the correlation between overall survival (C) and recurrence-free survival (D). **E,** Box-plot of the expression of ATG7 in tumor and adjacent non-tumor tissue sections from PC microarray. Method of H-score evaluation was described in Methods and Materials. **F,** Analysis of the correlation between the expression levels of ISG15 and ATG7 of PC microarray.

Fig. S2



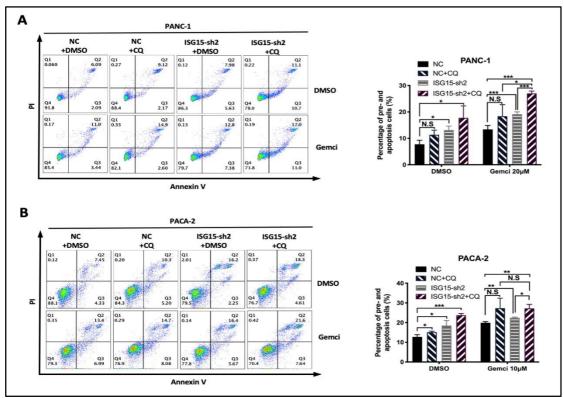
**Fig. S2. A,** ISG15-targeted shRNA significantly reduced ISG15 in both PANC-1 and PACA-2 cells. Representative results of Western blotting are shown. **B-E,** Statistical results of colony formation assays (B), wound healing assays (C), chamber migration (D) and chamber invasion (E) are shown. **F,** Effects of ATG7 knockdown on LC3 II/I ratio. 48h after transfection of ATG7-targeted siRNA, DMSO (as the control), Gemcitabine (Gemci) or Rapamycin (Rapa) was added. **G-H,** Restored expression of ISG15 or ATG7 rescued the effects on cell proliferation (G), migration and invasion (H) in ISG15-depleted cells (scale bar; 50 µm). (\* p<0.05; \*\* p<0.01; \*\*\* p<0.001).





**Fig. S3. A,** Relative fluorescence intensity for the confocal microscopic images of GFP-mCherry-LC3-labeled autophagosomes in ISG15-depleted or control PANC-1cells. **B,** Relative mRNA levels of *ATG7* were assayed by RT-PCR in PC cells with or without ISG15 depletion. *ACTIN* was used as an internal loading control. (\* p < 0.05; \*\* p < 0.01; \*\*\* p < 0.001).





**Fig. S4. A-B,** Apoptosis induced by Gemcitabine (Gemci) or/and chloroquine (CQ) in PANC-1(A) and PACA-2 (B) cells with or without ISG15 depletion was detected with flow cytometry, and the statistical results are shown on the right, with representative pictures shown on the left. (\* p < 0.05; \*\* p < 0.01; \*\*\* p < 0.001).