Figure S1. Concordance of COUP-TFII_V2 IHC score and RT-qPCR results. (A) Scatter plot of concordance of 22 PDAC cases analyzed by IHC and RT-qPCR, clustered according to the concordance of the two techniques. The numbers reported in the graph are the IDs of the samples. The graph is not in an actual scale. (B) Pie charts of the classification of the 22 cases as high- or low-expressing COUP-TFII_V2 tumors by RT-qPCR and IHC. (C) Pie chart of the distribution of the cases according to their classification by RT-qPCR and IHC. (D) Overall agreement of RT-qPCR and IHC in the PDAC classification. Cohen's coefficient was 0.64 (0.32-0.95) and P<0.01, indicating 'substantial/good' concordance between RT-qPCR and IHC. RT-qPCR, reverse transcription-quantitative PCR; IHC, immunohistochemistry; PDAC, pancreatic ductal adenocarcinoma; TF, transcription factor.

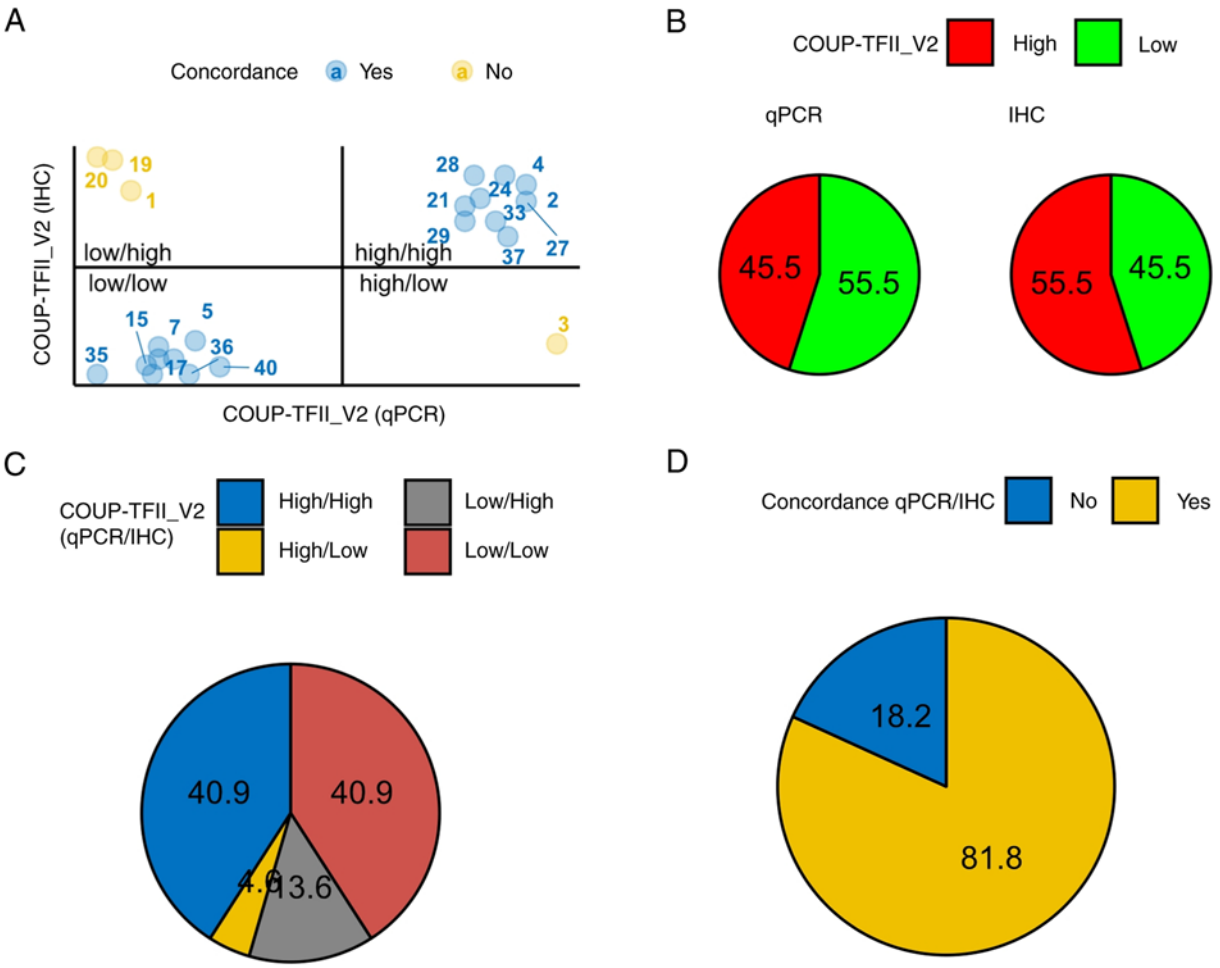


Figure S2. (A) PC analysis of the differences in PDAC cells lines according to the expression of a selection of genes (including both variants of COUP-TFII); PCA indicates a cluster of COUP-TFII isoforms and SNAIL1 that accounts for the main variability in Su.86.86 cells. (B) Expression and localization of COUP-TFII_V2 in the hTERT-HPNE cell line. Expression of COUP-TFII_V2 was analyzed by immunofluorescence with a COUP-TFII_V2-specific antibody; similar to the results reported in Fig. 1B, the localization of COUP-TFII_V2 was both nuclear and cytosolic with cells expressing alternatively more nuclear COUP-TFII_V2 and cells where COUP-TFII_V2 was predominantly cytosolic (white arrows; scale bar, 10 $\mu$m). (C) MiaPaca2 cells expressing a COUP-TFII_V2-EGFP fusion protein to further confirm the nuclear and cytoplasmic localization of COUP-TFII_V2 (original magnification, x100). (D) Western blot analysis of cellular fractions obtained from MiaPaca2 cells either transfected with a control plasmid (-) or with COUP-TFII_V2, indicating the expression of COUP-TFII_V2 in the cytoplasmic and nuclear fraction. (E) Western blot analysis of cellular fractions of PANC-1, BxPC3 and CAPAN-2 PDAC cells to indicating the nuclear-specific expression of the longest isoform of COUP-TFII, COUP-TFII_V1. PDAC, pancreatic ductal adenocarcinoma; TF, transcription factor; EGFP, enhanced green fluorescence protein; PC, principal component. NR2F2-V1, COUP-TFII_V1; NR2F2_V2, COUP-TFII_V2; N-cad, N-cadherin; Vim, vimentin; β-cat, β-catenin; E-cad, E-cadherin; hTERT, human telomerase reverse transcriptase; ABCG2, ATP binding cassette Subfamily G member 2

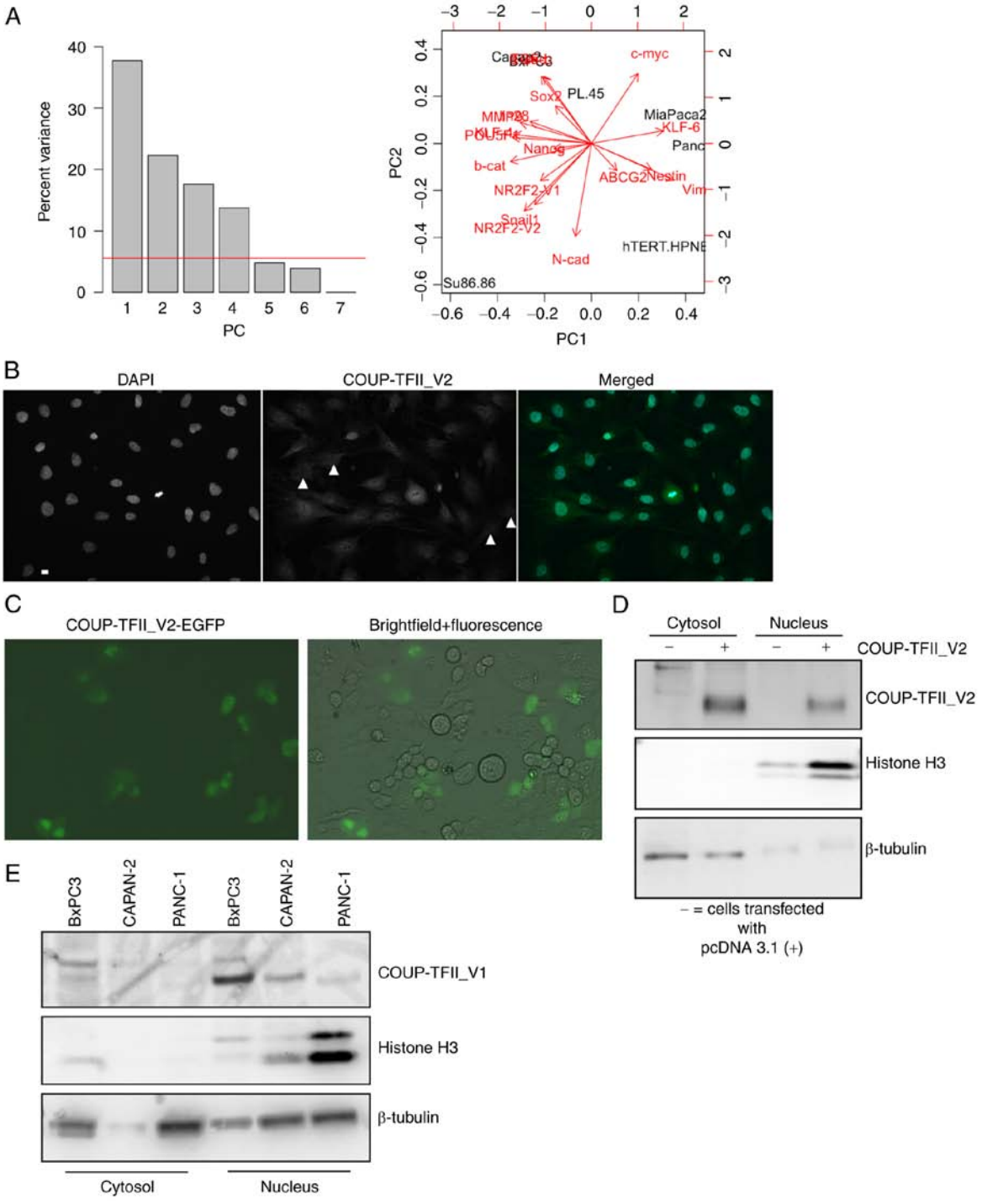
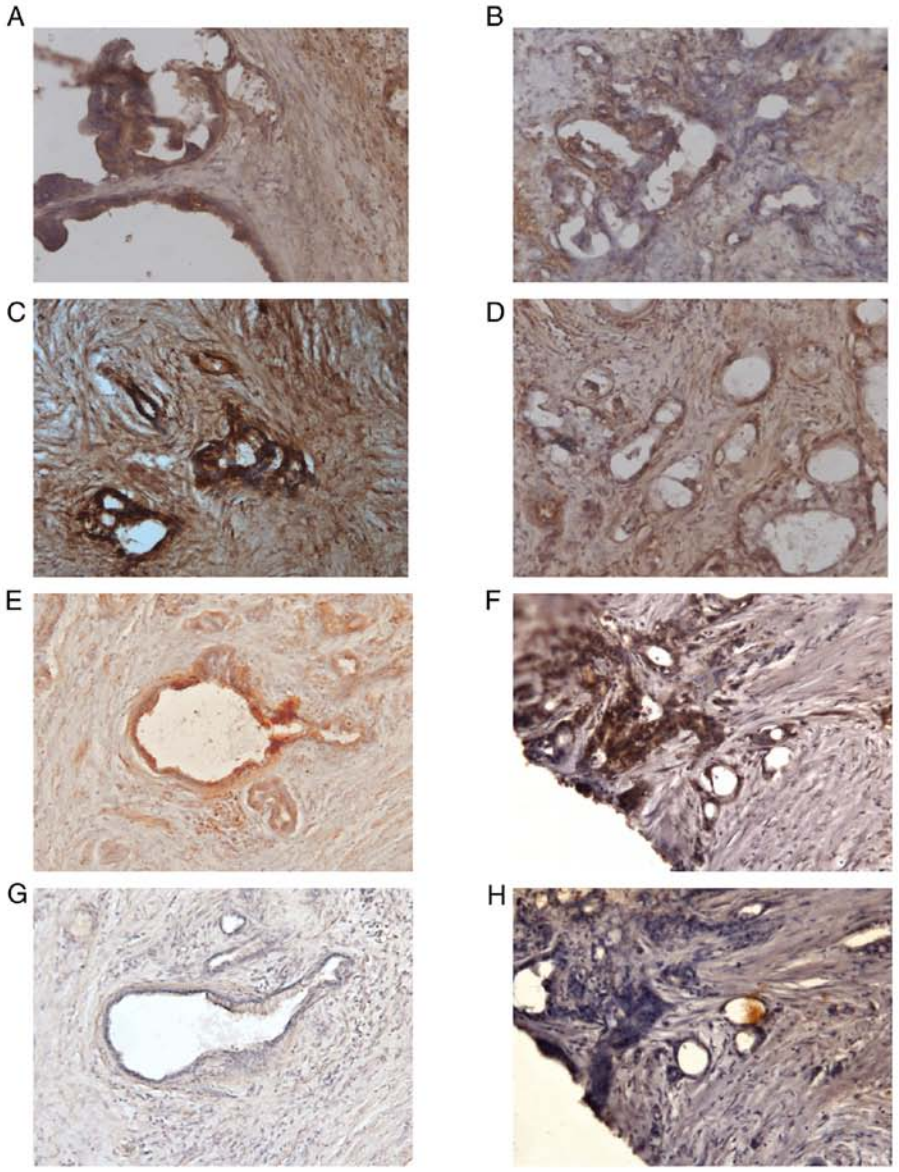


Figure S3. COUP-TFII_V2 and primary PDAC. (A-F) IHC images for COUP-TFII_V2 in selected primary PDAC samples. Positive staining is brown. (G) Negative control IHC of PDAC sample from E. (H) Negative control IHC of PDAC sample from F. (I) Boxplot expression of COUP-TFII_V2 compared among different N stages. Although the COUP-TFII_V2 expression trend was toward an increase from N0 to N2, no statistical significance was reached. Gray-filled dots mark the position of outliers. Original magnification of IHC images was x200, all sections were counterstained with Gill's hematoxylin. PDAC, pancreatic ductal adenocarcinoma; TF, transcription factor; IHC, immunohistochemistry.



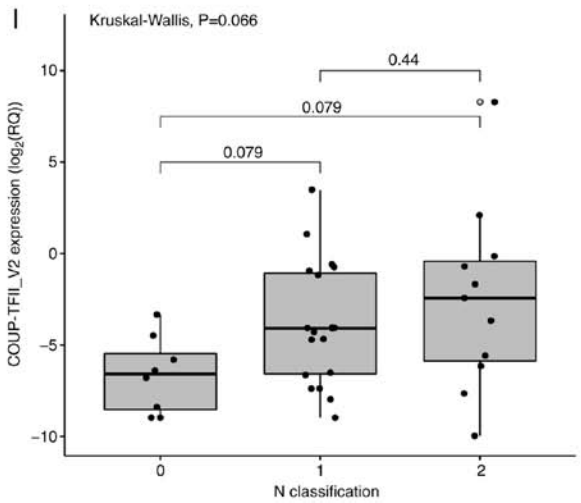



Figure S4. Exploratory correlation analysis. (A) Distribution of gene expression in primary PDAC arrayed in two by two plots, the panel also show Pearson's correlation. (B) Pearson's linear correlation coefficients of genes in the patients with PDAC. PDAC, pancreatic ductal adenocarcinoma. Corr, Pearson's correlation coefficient; V1, COUP-TFII_V1; V2, COUP-TFII-V2; β-cat, β-catenin; nCAD, N-cadherin; eCAD, E-cadherin.

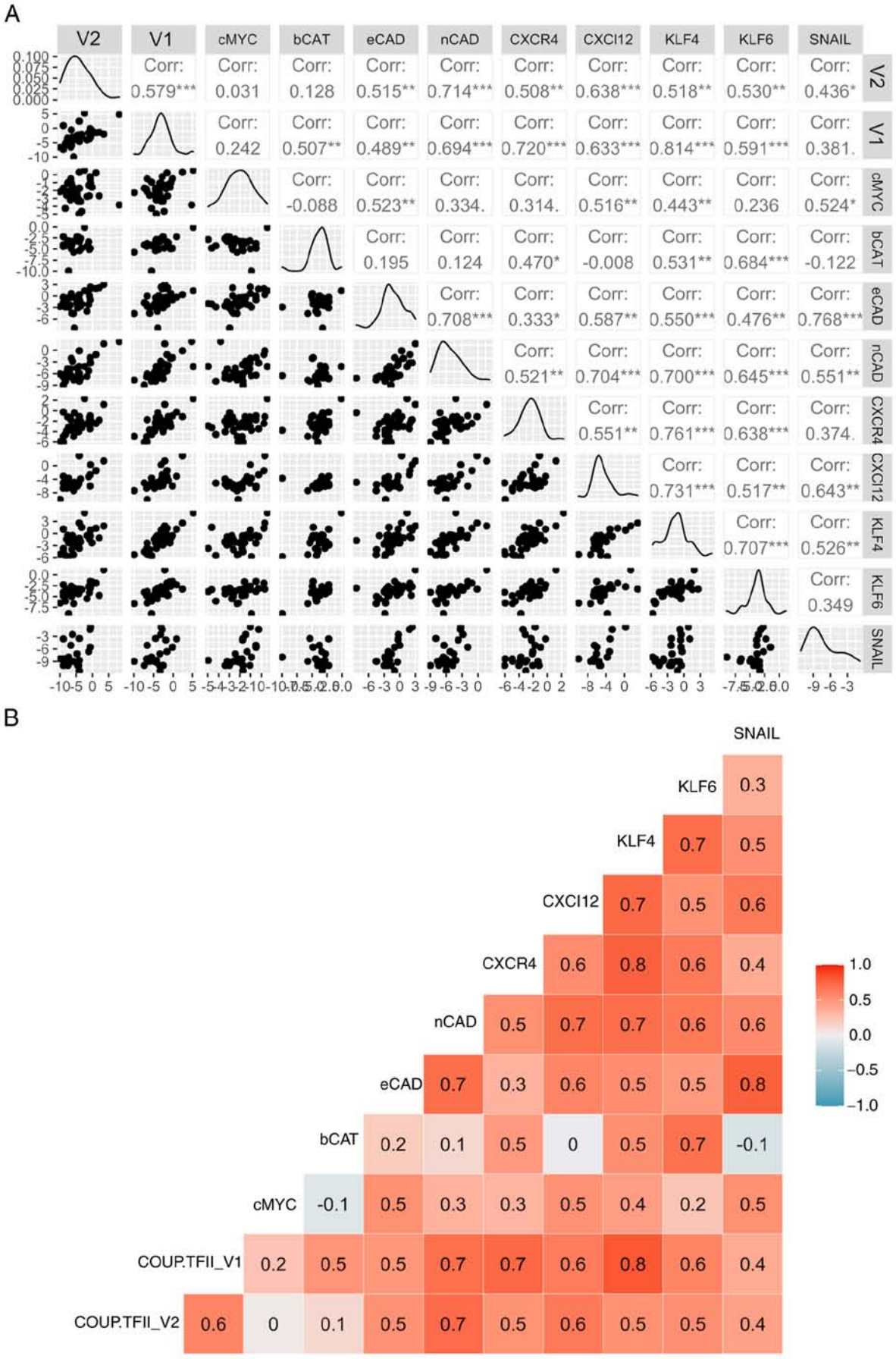


Figure S5. Kaplan-Meier survival analysis of the study population according to (A) N status, (B) degree of differentiation, (C) age (≤70 vs. >70 years), (D) T stage and (E) sex. It was indicated that patients with stage N2 and poorly differentiated PDAC had a shorter overall survival. These data agree with the epidemiology of PDAC, demonstrating that the present PDAC population is a good representation of the general population. PDAC, pancreatic ductal adenocarcinoma.