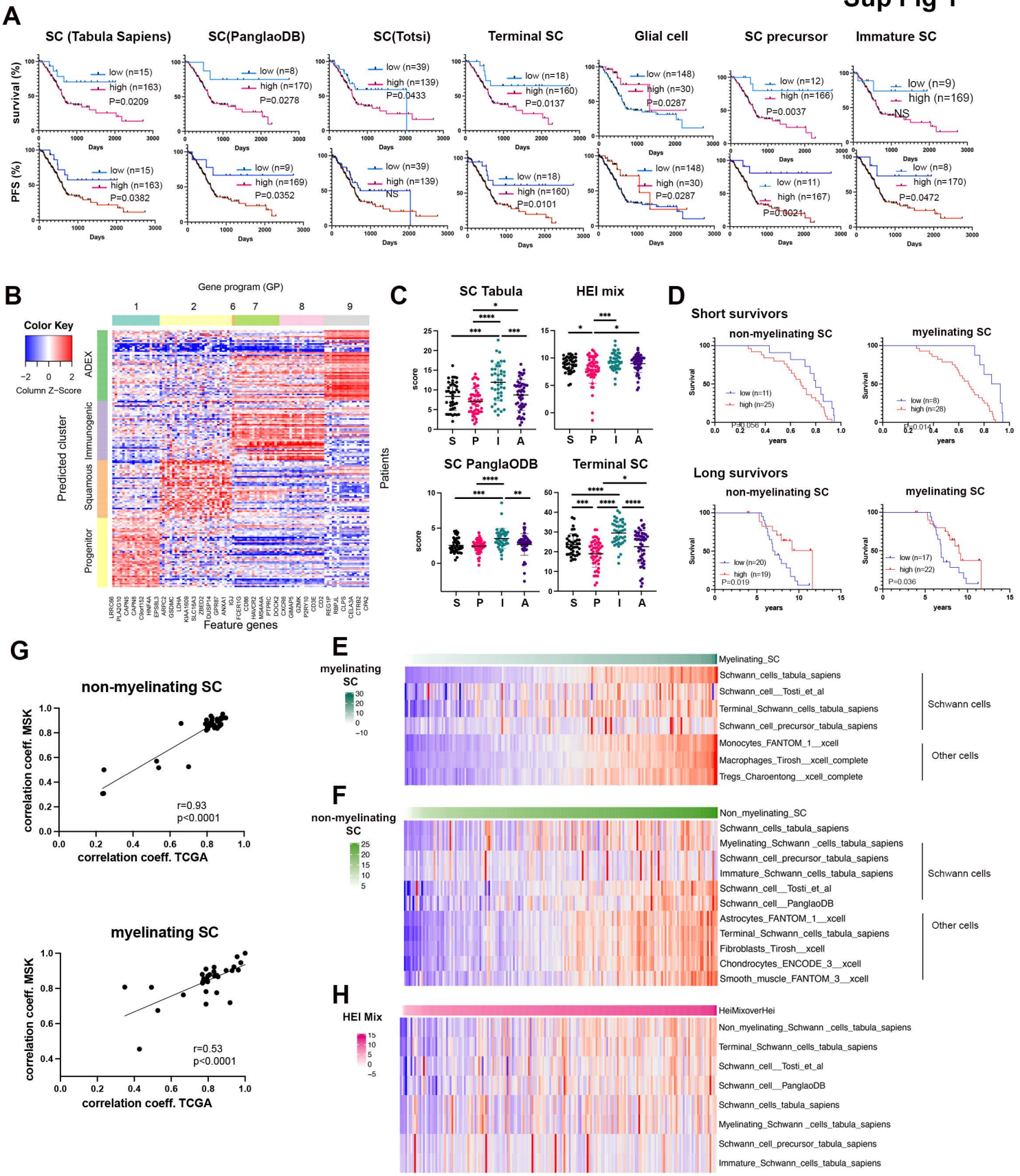
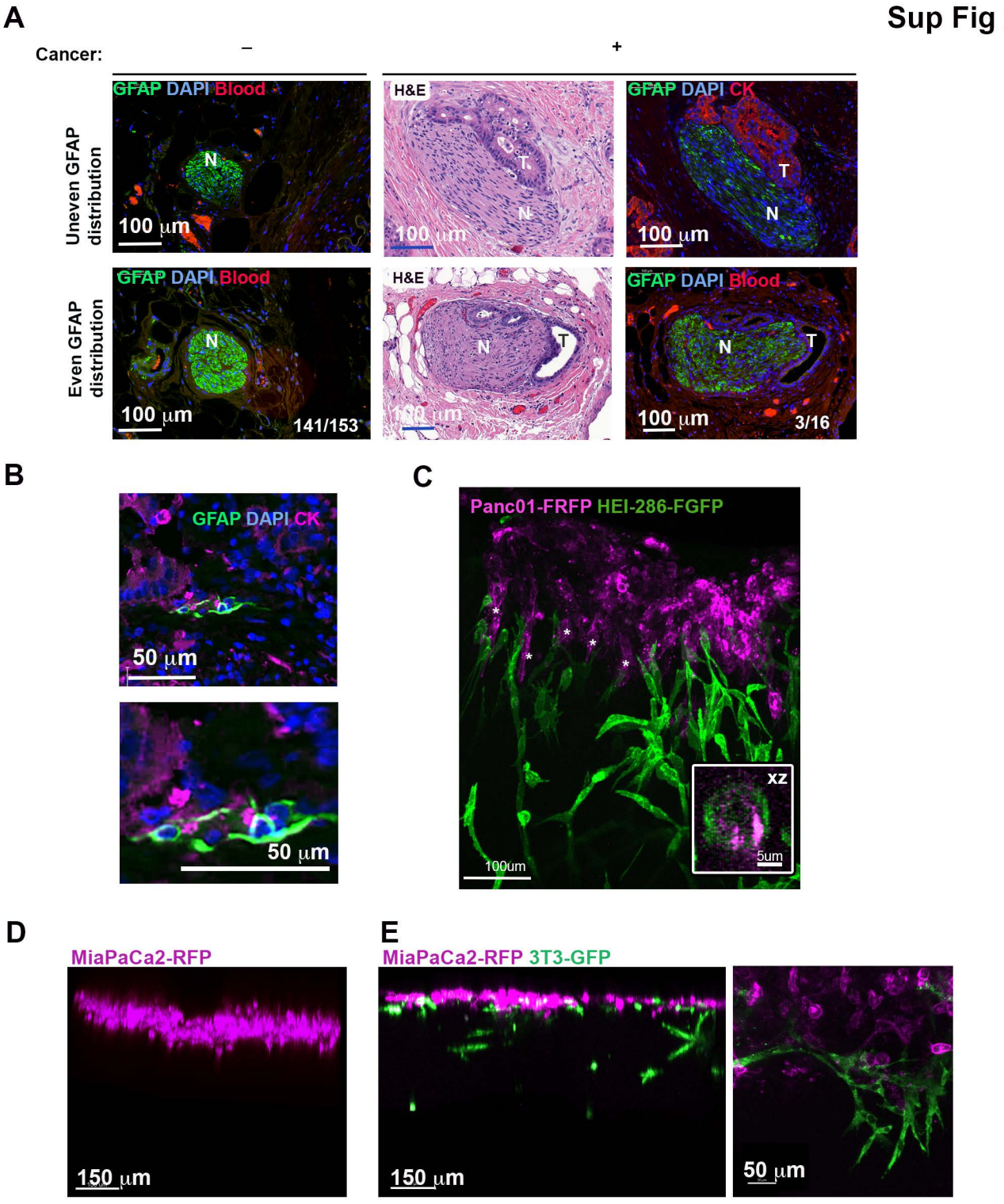
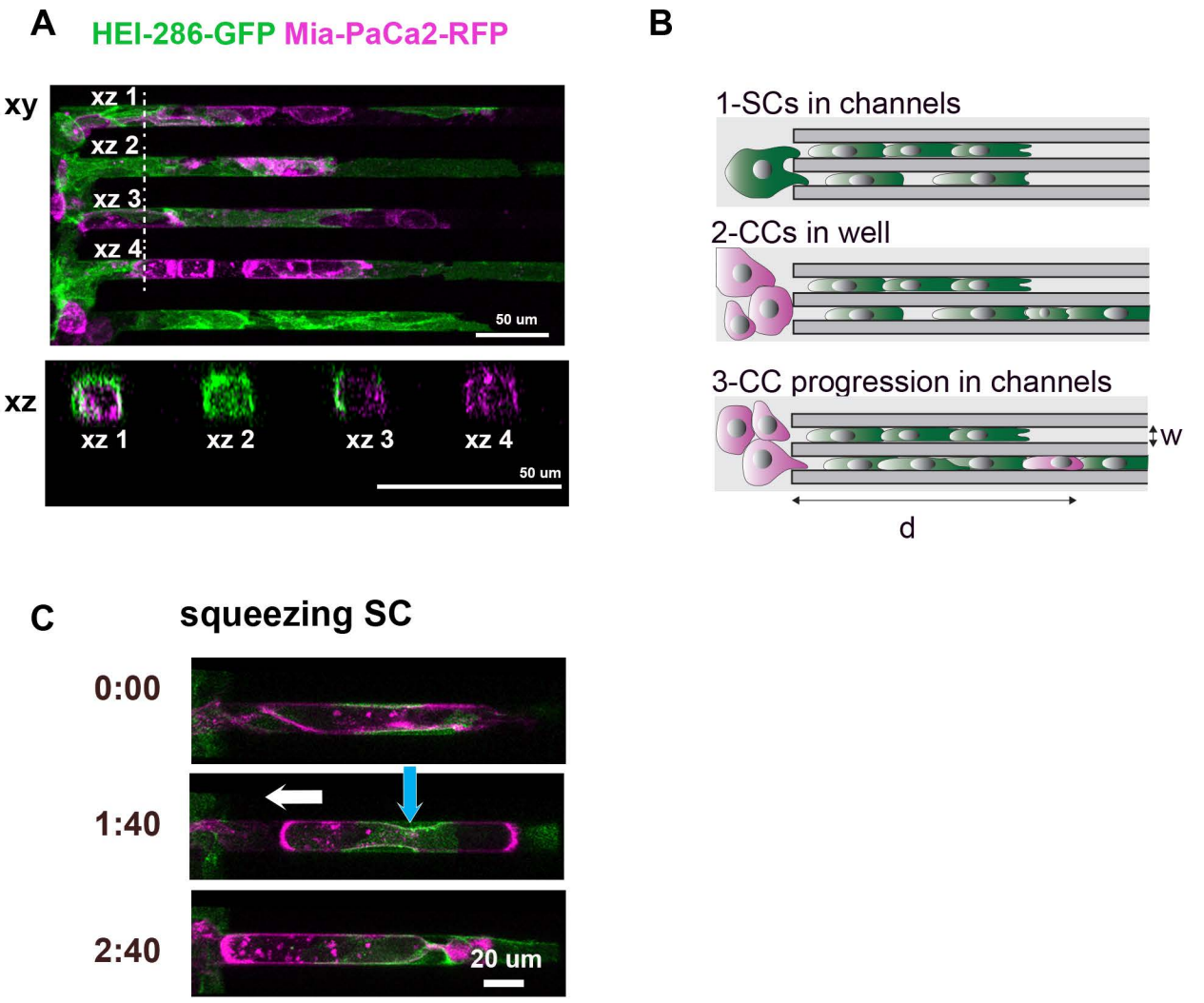


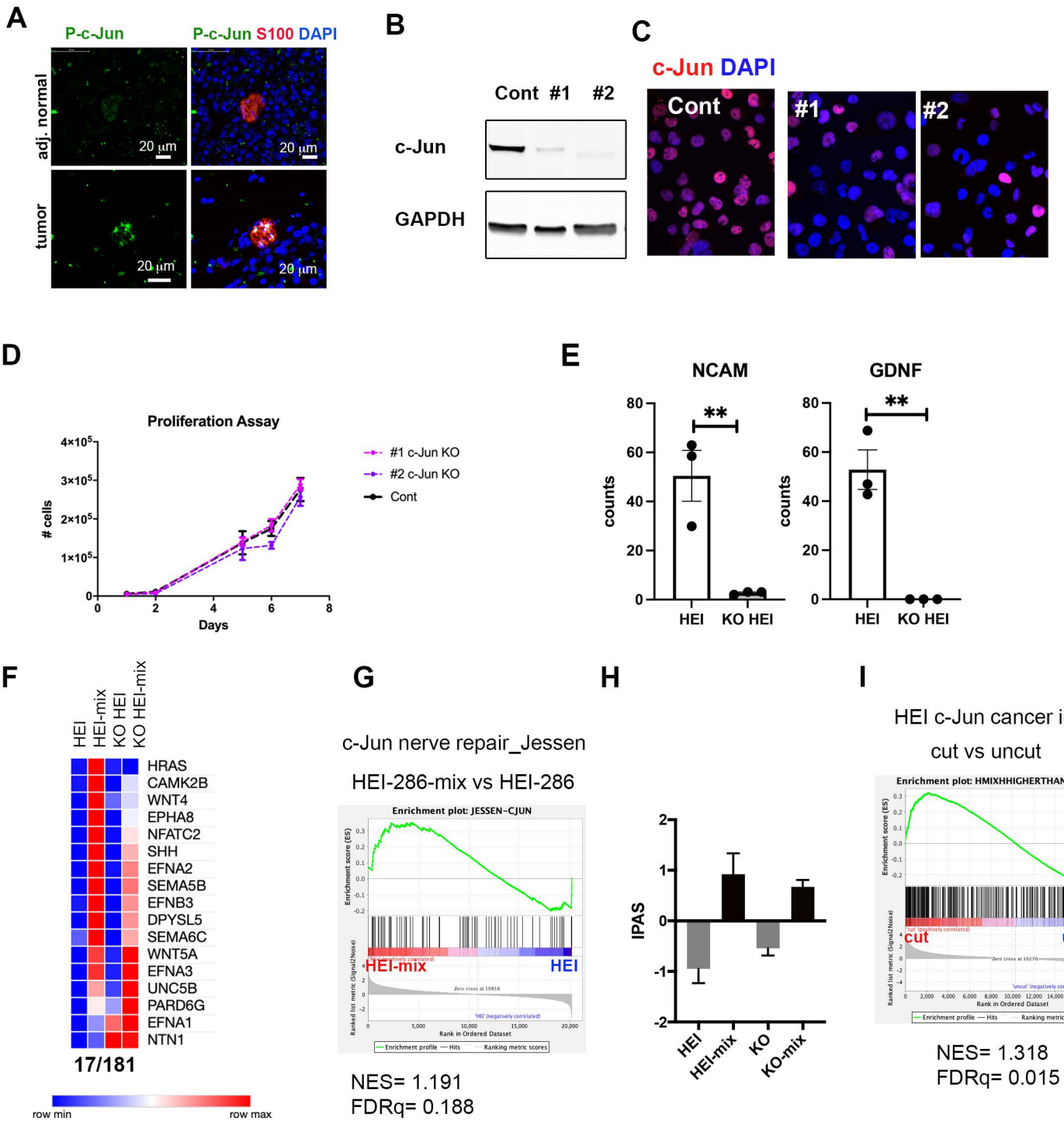
Supplementary Fig. 1 | Correlation of SC signatures and overall survival in patients with PAAD. **A**, Kaplan–Meier curves of overall survival (OS) and progression free survival (PFS) with high or low scores for different signatures of SC in 178 TCGA PAAD patients. **B**, Heatmap showing clustering of TCGA patients into 4 subtypes. **C**, SC signatures scores in the subtypes of the TCGA patients (S: squamous, P:progenitor, I:immunogenic, A: ADEX). **D**, Kaplan–Meier curves of overall survival (OS) with high or low scores for non-myelinating and myelinating SC signatures in short and long survivors MSK patients. **E, F**, Heatmaps of cell signatures correlating with scores for myelinating SC signature (E) and non-myelinating SC signature (F) in TCGA PAAD patients. **G,** Coefficient correlations between SC signature gene set and other gene sets in MSK and TCGA patients correlate with each other. **H**, Heatmaps of cell signatures correlating with scores for HEImix signature in TCGA PAAD patients.



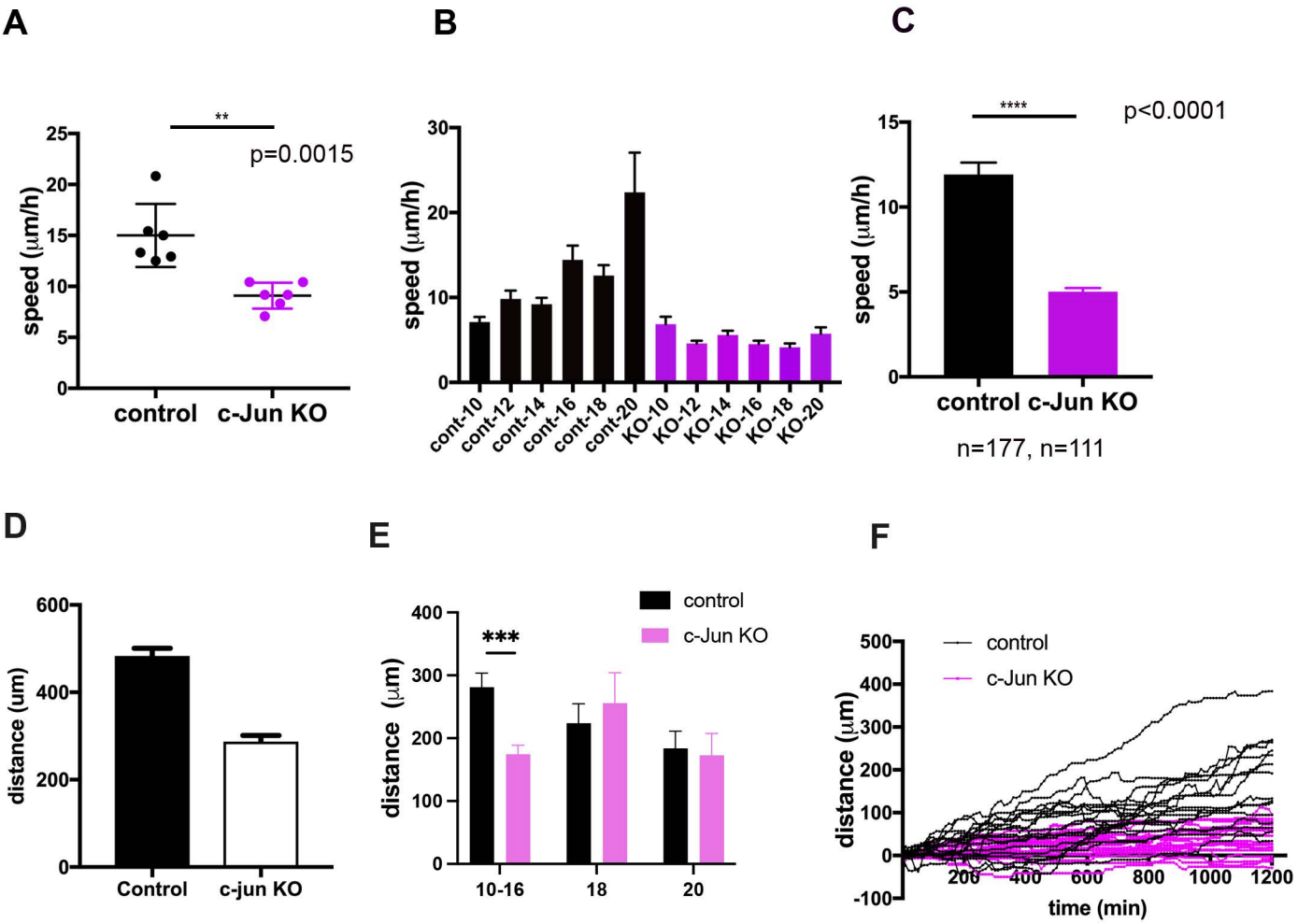
Supplementary Fig. 2 |Cancer cells are closely associated with SCs in PDAC specimens and do not invade in absence of SCs in a 3D assay. **A**, Examples of uneven (top) and even (bottom) distribution of GFAP (green) staining in nerves of PDAC specimens. Nerves without (left) and with (right) visible cancer cells. Middle images are H&E of adjacent sections of right images. Ratios (bottom right corner) indicate number of specimens with even GFAP distribution over the total number of specimens **B**, GFAP+ SC (green) wrapping cytokeratin (CK) expressing cancer cells (magenta) in PDAC specimen **C**, Confocal images showing Panc01 cancer cells (magenta) lined up with HEI-286 SCs (green) in Matrigel (see*). Inset: transverse image showing HEI-286 SCs wrapping around a Panc01 cancer cell. **D-E** Absence of chain of cancer cells in absence of SCs or with NIH 3T3 fibroblasts. **D,** Confocal images of MiaPaCa2-RFP cells seeded on top of a Matrigel chamber and imaged after 6 days. **E**, Confocal images of MiaPaCa2-RFP cells taken 6 days after adding them on top of a Matrigel chamber previously seeded with NIH 3T3-GFP fibroblasts for 5 days.



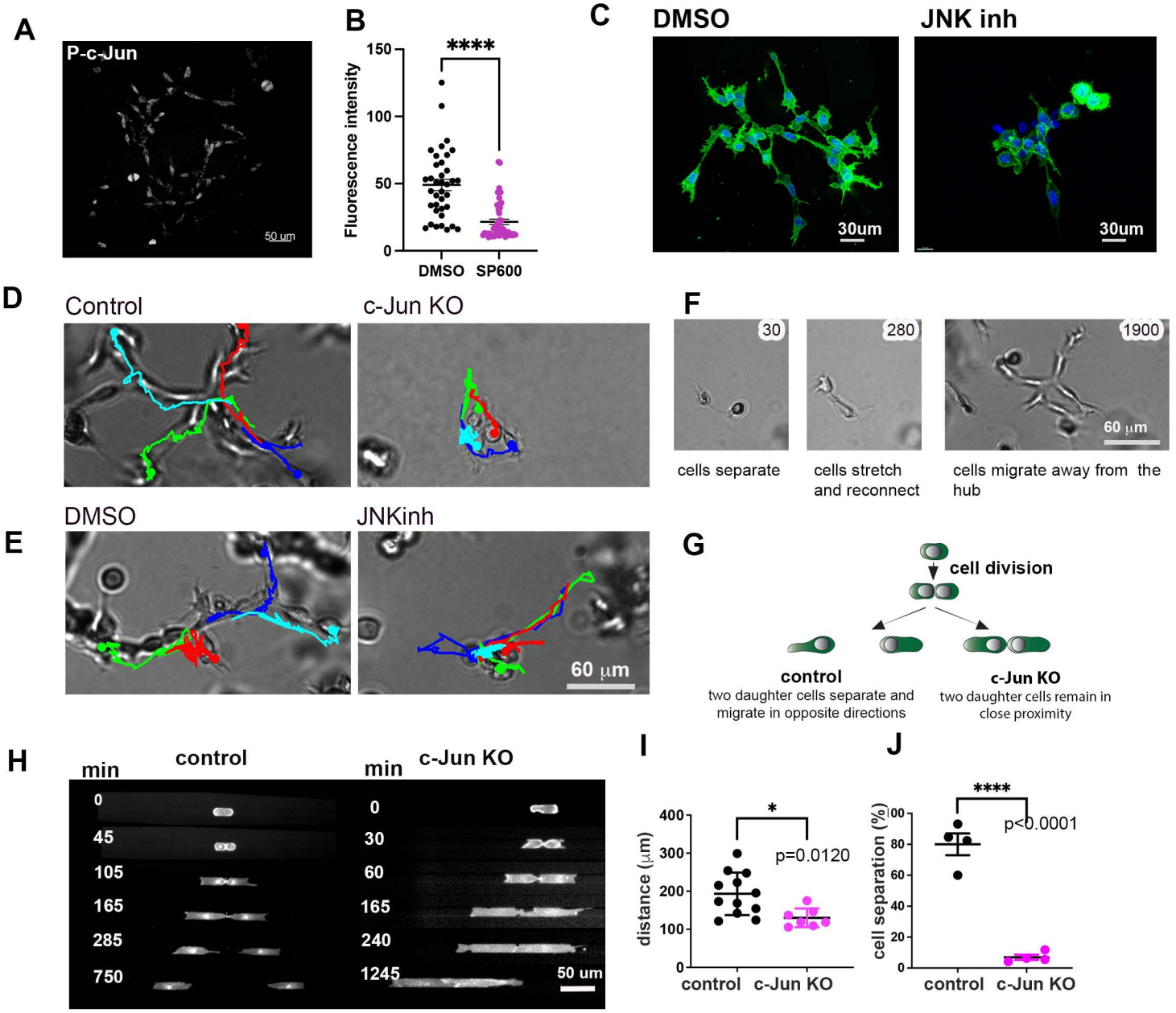
Supplementary Fig. 3 | HEI-286-GFP SCs and MiaPaCa-2-RFP cancer cell microchannel assay. A, Confocal images of HEI-GFP and MiaPaCa2-RFP within microchannels in longitudinal (xy) and transverse sections (xz) showing SCs fully occupying the channel (xz 2) or either wrapping partially (xz 3) or completely (xz 1) a cancer cell. **B**, Schematic showing the microchannel assay sequence. (1) HEI-286 SCs are first seeded in wells and enter microchannels. (2) MiaPaCa-2 cancer cells are seeded in the wells and (3) enter the microchannels occupied with HEI-286 SCs. **C**, Fluorescent images of time-lapse movie showing HEI-286 SCs (green) squeezing a cancer cell (magenta). Blue arrow indicates HEI-286 SC movement and white arrow indicates cancer cell displacement. Time is h:min.



Supplementary Fig. 4 | c-Jun and P-c-Jun in SCs. **A**, P-c-Jun staining in S100-labeled nerves from PDAC specimens that are close to tumor as compared with nerves from adjacent normal tissue. **B**, Western-Blot of HEI-286 SCs showing loss of c-Jun expression using either construct. **C**, Immunofluorescence of c-Jun in HEI-286 SCs showed diminished nuclear c-Jun expression with either construct. **D**, Proliferation of control and c-Jun KO HEI-286-SCs. **E**, mRNA expression level of NCAM1 and GDNF in HEI-286 and c-Jun KO HEI-286. **F**, Heatmaps of expression of axon guidance genes that are upregulated in co-cultured HEI-286 cells (HEI mix) as compared to HEI-286 grown alone (HEI). Each value is the mean of three biological replicates. **G**, Gene set enrichment analysis (GSEA) assessing upregulated c-Jun nerve-repair genes (27) in co-cultured HEI-286 compared to HEI-286 SCs. NES is normalized enrichment score. **H**, Inferred Pathway Activation/Suppression (IPAS) scores for the murine c-Jun nerve repair genes signature (27). **I**, GSEA assessing upregulated c-Jun genes in co-culture HEI versus grown alone HEI-286 in cut sciatic nerves compared to uncut sciatic nerves (27). NES is normalized enrichment score.



Supplementary Fig. 5 | SC c-Jun supports both SC and cancer cell migration. A, Quantification of control and c-Jun KO HEI-286-SC speed in two dimensions. **B**, Quantification of control and c-Jun KO HEI-286-SC speed in three dimensions in microchannels of sizes from 10 to 20 μm. **C**, Quantification of control and c-Jun KO HEI-286-SC speed in three-dimension. **D**, Quantification of length of columns formed by MiaPaCa-2 combined with WT HEI-286 SCs or with c-Jun KO HEI-286-SCs. **E**, Quantification of distance migrated by Panc01 cancer cells in microchannels of different widths, and occupied by HEI-286 SCs (n=18-35 cells per channel size). **F**, Individual tracks of cancer cells in microchannels occupied by control vs. c-Jun KO HEI-286 SCs. (n=21 in each group).



Supplementary Fig. 6 | WT and c-Jun KO SCs behavior. A, Confocal images of phospho-c-Jun (P-c-Jun) staining in HEI-286 GFP SCs in Matrigel. **B**, Effect of SP600125 on P-c-Jun expression in HEI-286 GFP SCs. **C**, Confocal images of HEI-GFP-SCs treated with JNKi SP600125 or DMSO in Matrigel showing lack of SC organization in JNKi-treated cells. **D-E**, Images of cells from 72h time-lapse movies of control and c-Jun KO HEI-286 SCs (D) and DMSO or JNK inhibitor treated HEI 286 SCs (E) grown in 3D Matrigel with colored cell tracking. **F**, Images of WT SCs from time-lapse movies showing formation of a branched organized structure in 3D: cells separate after division (1); cells stretch and reconnect, reestablishing contacts (2); cells divide, organize in a structure that spreads out (3). Time in minutes **G**, Schematic show the separation and positioning of two daughter HEI-286 SCs after mitosis in Matrigel is c-Jun-dependent. **H**, Time-lapse images of a dividing control and c-Jun-KO HEI-286 SCs and the two daughter cells in microchannels. **I**, Quantification of (H), the distance between two daughter cells following mitosis for control vs. c-Jun KO HEI-286 SCs in a 400 min time period (control n=16, c-Jun KO n=12, mean ± SEM). **J**, Quantification of percentage of daughter cells that separate following mitosis for control versus c-Jun KO HEI-286 SCs. (4 independent experiments, n>20 cells per condition in each experiment, mean ± SEM)