**Supplemental Materials and Methods**

***Animal Experiments***

*Rictorflox/WT*mice were intercrossed to generate RictorΔΔand RictorWT siblings for comparison in PanIN development and caerulein injection studies. In tumor development studies, mice were monitored for symptoms such as abdominal distension, cachexia, jaundice, hunching, reduced mobility, staring coat and diarrhea. For late stage treatment studies pancreatic malignancy was confirmed by abdominal palpation. Mice were euthanized when disease progressed and post mortem tissue was harvested for histological analysis. Survival between cohorts was compared by Kaplan-Meier and Log Rank statistical analysis. Animal experiments were approved by the University of Massachusetts Medical School institutional Animal Care and Use Committee or performed under Home Office regulations and under license approved by the local ethics committee.

***Estimation of cell number and cell size in Rictorwt/wt and RictorΔ/Δ pancreata***

Genomic DNA was isolated using standard phenol-chloroform extraction from pancreas tail. DNA concentration was determined by dividing DNA quantity by the mass of pancreas fragment. The total amount of gDNA was extrapolated by multiplying DNA concentration by the mass of the entire pancreas. Calculations assume that each cell contains an equivalent amount of gDNA.

For estimation of cell size, tissue sections were stained with DAPI, the number of positive cells in 5-8 fields (100x magnification) counted, and divided by the tissue area (ImageJ).

***Glucose Tolerance Test***

Rictorwt/wt and RictorΔ/Δ mice were fasted for 6 hours, and a basal blood glucose reading taken from tail bleed using Accu-Chek Test strips and meter (Roche). Mice were dosed orally with 3g/kg glucose, and blood glucose monitored every 15-30 minutes for 120 minutes post-gavage.

***Histology***

The quadchrome consists of a hybrid protocol derived from Sirius Red staining for collagen and Alcian Blue staining for mucin. Briefly, slides were rehydrated through a graded alcohol series to distilled water. They were then incubated sequentially in Weigert’s Hematoxylin for one hour, Sirius Red for one hour, and Alcian Blue for 30 minutes, with rapid washes in acidified water (15 dips in 0.5% acetic acid) after each incubation. In this stain, collagen appears bright red, mucin is blue, nuclei are black, and cytoplasm is a weak yellow. *Quantification*: Four images were quantified per section representing 1) the area of greatest neoplastic progression, 2) the area of lowest neoplastic progression, and 3,4) areas of the pancreas that were consistent with the average progression for that tissue section. Acini, ducts, PanINs, ADM lesions, and stromal tissue not including blood vessels were manually outlined using ImageJ software and are graphed as the percentage area of all areas quantified.

***Immunohistochemistry***

4- or 5µm formalin-fixed paraffin-embedded (FFPE) sections were deparaffinized and rehydrated by passage through Xylene and a series of graded alcohols. Endogenous peroxidase activity was quenched in 3% hydrogen peroxide, and antigen retrieval was performed using citrate buffer, pH6. Sections were blocked in 5% serum, and then incubated with primary antibody. Sections were incubated in secondary antibody (Vectastain ABC system) and staining visualized using 3,3′-diaminobenzidine tetrahydrochloride (DAB) or NovaRed. For insulin staining, a FITC-conjugated donkey anti-guinea pig secondary antibody (Jackson Immuno, 1:500) was used. Samples were mounted with DAPI containing hard-set (Vector) and observed with a Nikon Eclipse E400 microscope.

***Primary PanIN cell culture experiments***

Primary PanIN lines (isolated in the Bardeesy lab) (29) were grown on Laminin-coated plates as previously described (30). Cells were infected twice at 5h intervals with lentiviruses encoding Rictor or GFP-targeting shRNAs (Table S2), plated at a density of 2.7x104 cells/well in 6-well plates. For protein lysates, cells were plated at 1.3x105 cells/10cm dish.

*Proliferation assay*: Viable cells were counted using trypan blue exclusion. Log2 of cell numbers/well were plotted against time and doubling time was derived from the inverse slope. Differences in doubling time were determined by analysis of covariance (Prism Graphpad).

*Senescence associated* *β-galactosidase staining of PanIN cell lines:*Cells were fixed in PBS containing 2% formaldehyde and 0.2% glutaraldehyde for 10 min at RT, stained (40mM Citric acid 0.1M/sodium phosphate 0.2M buffer pH 6.0, 5mM potassium ferrocynide, 5mM potassium ferricynide, 150mM sodium chloride, 2mM magnesium chloride and 5-bromo-4-chloro-3-indolyl-β-D-galactopyranoside 1mg/ml in water) for 16 hours at 37˚C and counterstained with nuclear fast red (Sigma).

***Nanostring***

RNA was isolated from flash frozen pancreas tissue using an RNeasy midi kit from Qiagen.  Gene expression profiling of inflammatory genes was conducted using the Nanostring platform with the nCounter® Mouse Inflammation v2 probe set.  Raw counts were normalized with six preselected housekeeping genes (Cltc, Gapdh, Gusb, Hprt, Pgk1, and Tubb5) using the nSolver software (Nanostring, Seattle, WA). To remove the low expression genes, the sum of negative controls of each sample was used as a threshold; genes for which raw counts of fewer than 3 samples were below this threshold were removed from the analysis. Heatmaps were produced with log2 expression values using R package pheatmap (<https://cran.r-project.org/web/packages/pheatmap/index.html>). Genes and samples were shown hierarchically clustered by similarity based on Euclidean distance and the complete linkage aggregation algorithm.