**Supplementary Figure Legends**

**Figure S1: Loss of *Rictor* does not prevent pancreatic formation or function**

(A) Schematic showing pancreas specific deletion of *Rictor*. (B) Western blot showing Rictor levels in pancreas tissue lysate from 2-month old mice. α-tubulin is shown as a loading control. (C) Total mouse weight of 2-month old males of indicated genotype. (D) Weight of pancreata isolated from 2-month old males of the indicated genotypes. (E) Average cell area in pancreatic cross section of 2-month old males. (F) Total genomic DNA per pancreas, as an estimation of relative cell number, in 2-month old males (n=4 mice per cohort for C-F). (G) H&E staining, IHC for amylase and glucagon, and IF for insulin in 2-month old males. \* p<0.05, \*\* p<0.01, \*\*\* p<0.001 by student’s t-test. (H) Glucose tolerance test performed on 2 month old males of the indicated genotype (n=3 mice per cohort). Asterisks denote plasma glucose above level of accurate detection (33mmol/L).

**Figure S2: *Rictor* deletion decreases proliferation in PanIN1 lesions**

Immunostaining for Ki67 in the pancreata of (A) 4-month old mice and (B) 8-month old mice of the indicated genotypes. Quantification is shown in the panels on the right. Immunostaining for cleaved caspase 3 in the pancreata of (C) 4-month old mice and (D) 8-month old mice of the indicated genotypes. Quantification is shown in the panels on the right. N=4 for each group. \* p<0.05, \*\* p<0.01 by student’s t-test.

**Figure S3:** ***Rictor* deletion alters CDKI and BMI1 expression and localization**

(A-D) Immunostaining for the CDK inhibitors p16Ink4a, p21Cip1 and p27Kip1 and BMI1 in the pancreata of 4- and 8-month old KC and KC *RictorΔ/Δ* mice (200x magnification). (E) Staining for senescence associated β-galactosidase activity in the PanIN derived cell lines RP 2294 and AH 2375 4 days following *Rictor* knockdown. (F) Western blot for RICTOR, indicated CDKIs, and BMI1 in PanIN derived cell line AH 2375 6 days post *Rictor* knockdown. (G) Quantification of CDKI levels in western blots for the proteins shown in (F) (n=4 for each antibody).

**Figure S4: *Rictor* deletion does not affect response to caerulein-induced pancreatic injury**

(A) H&E staining of pancreata harvested from RictorWT or RictorΔ/Δ mice 2 or 21 days after injection with caerulein or PBS as a control. Note acinar-to-ductal metaplasia (ADM) and increased separation of acinar lobules evident 2 days post-injection of caerulein (middle panels) and fully resolved by 21 days post-injection (lower panels). (B) Quantification of ADM tissue as a percentage of total tissue area in pancreata from KC and KC *RictorΔ/Δ* mice 2 or 21 days post caerulein injection (n=3-4 mice per cohort).

**Figure S5:** **Absence of mTORC2 activity** **increases the nuclear expression of CDKIs in PanIN1 lesions driven by *KrasG12D* and caerulein-induced pancreas injury**

(A-E) Immunostaining for the CDK inhibitors p16Ink4a, p21Cip1 and p27Kip1 and BMI1 and CD45 in the pancreata of KC and KC *RictorΔ/Δ* mice harvested 21 days following caerulein injection (200x magnification). (F) Heatmap of inflammation-associated gene expression changes between untreated or caerulein treated KC Rictorwt, KC RictorΔ/Δ, Rictorwt, and RictorΔ/Δ pancreata as indicated.

**Figure S6: Rictor knockdown impairs the transformed phenotype in murine PDAC cells**

(A, D) Western blot confirming efficient Rictor knockdown in the 9910#1 (A) and 906 (D) murine PDAC cell lines. Total ERK protein levels are used as a loading control. (B, E) Bar graphs showing the impact of Rictor knockdown on PDAC cell proliferation. (C, F) Bar graphs showing the impact of Rictor knockdown on anchorage independent growth as measured by soft agar colony formation. \* p<0.05, \*\* p<0.01, \*\*\* p < 0.001 by student’s t-test.

**Figure S7: AZD2014 treatment blocks signaling downstream of mTORC1 and mTORC2**

(A) Immunoblots showing levels of pAkt, total Akt, pS6, total S6, p4E-BP1, total 4E-BP1 and β-actin in 3 KPC cell lines, untreated, or treated with either vehicle, or 50nM AZD2014. (B) Cytotoxicity assay in K8484 KPC cells (top panel) and MIA PaCa-2 human pancreatic cancer cells treated with gemcitabine (*x*-axis) and AZD2014 (*y*-axis) for 96 hours. Combenefit software was used to analyse the experimental data (left, percentage growth inhibition compared with control), generate predicted inhibition data (middle), and compare for each combination (right). The greater the difference, the more synergistic the combination (shown in cyan and blue).

**Figure S8: AZD2014 and AZD8186 co-treatment blocks downstream mTORC2 targets**

(A) Bar chart showing the effects of AZD2014 (500nM) and/or AZD8186 (3μM) on proliferation of KPC tumor cells. Results are normalized to DMSO treated controls (set at 100%). Bars indicate means of 6 wells per treatment and error bars indicate standard deviation, \* p<0.05 by student’s t-test (compared with AZD2014 alone). (B) Immunoblotting for Rictor, Raptor, pAkt, total Akt, pNDRG1, pS6, total S6, p4E-BP1, total 4E-BP1, p27, cMyc and GAPDH in KPC tumor cells, untreated, or treated with AZD2014, AZD8186 or AZD2014 and AZD8186 at the concentrations indicated.