**SUPPLEMENTAL FIGURE LEGENDS**

**Figure S1.** Biallelic loss of p120 catenin in adult acinar cells results in ADM and pancreatitis. A) For p120 catenin expression and subcellular localization scoring, IHC depicts examples of absent/low, medium, and high p120 catenin expression in primary and metastatic pancreatic tumors. IHC also shows examples of predominant membranous and cytoplasmic p120 catenin subcellular localization. B-D) *p120f/f*, *CiMist1; p120wt/wt*, and *CiMist1; p120f/wt* pancreata displayed normal histology, and IHC showed p120 catenin expression at 2-4 months of age. E) *CiMist1; p120f/f* pancreata 4 months of age showed normal histology and lack p120 catenin expression in acinar cells. *CiMist1; p120f/f* pancreata 12 months of age developed ADM and pancreatitis (n=1/3 mice). Note that the 12 month image contains unusually high mosaic p120 catenin expression in acinar cells, but ADM lack p120 catenin expression, suggesting that these lesions may be forming in a cell autonomous manner. We stained for Alcian blue to suggest the presence of murine PanIN, and did not observe blue staining in *CiMist1; p120f/f* pancreata. F) Alcian blue staining showed the presence of PanIN lesions in *KCiMist1; p120wt/wt, KCiMist1; p120f/wt,* and *KCiMist1; p120f/f*pancreata. Scale bars are 50µm.

**Figure S2.** Pancreatic loss of p120 catenin cooperates with mutant Kras to form a unique cellular stroma. A,B) IHC for p120 catenin showed ubiquitous expression in *KCiMist1; p120wt/wt* and *KCiMist1; p120f/wt*pancreata. C) IHC showed loss of p120 catenin in *KCiMist1; p120f/f*pancreata with minimal mosaicism, which is highlighted with a yellow arrow. D-F) *KCiMist1; p120f/f*pancreata displayed reduction of amylase-expressing acinar cells when compared to *KCiMist1; p120f/wt* and *KCiMist1; p120wt/wt*pancreata. G-I) Trichrome blue staining showed a distinct cellular composition of fibrostroma in *KCiMist1; p120f/f* and *KCiMist1; p120f/wt*pancreata when compared to *KCiMist1; p120wt/wt* pancreata. J-L) *KCiMist1; p120f/f* and *KCiMist1; p120f/wt*pancreata displayed localized areas containing pronounced inflammation. M-O) *KCiMist1; p120f/f*pancreata displayed notable dilated ducts, which were not seen in *KCiMist1; p120wt/wt* and *KCiMist1; p120f/wt*pancreata. P-Q) PanIN in *KCiMist1; p120wt/wt* and *KCiMist1; p120f/wt*pancreata showed very little basement membrane Laminin expression. R) Orange arrows point to regions in which contiguous basement membrane Laminin expression was disrupted in *KCiMist1; p120f/f*pancreata. Single cells expressing Laminin were also seen in the surrounding stroma. Scale bars are 50µm.

**Figure S3.** Characterization of epithelial cell extrusion in *KCiMist1; p120wt/wt*, *KCiMist1; p120f/wt*, and *KCiMist1; p120f/f* pancreata. A) *KPCPtf1aY* mice show decreased ­­expression of p120 catenin and E-cadherin in delaminated cells. B) *KCiMist1; p120f/f* pancreata display abundant apical and basal epithelial cell extrusion 2 weeks post tamoxifen injection. Yellow arrows point to extruded CK19+ single cells. C) Quantification of CK19+ unit size unbiased to direction of extrusion is shown for *KCiMist1; p120wt/wt*, *KCiMist1; p120f/wt*, and *KCiMist1; p120f/f* pancreata (n=7000 cells in 4 animals for each genotype at one month post tamoxifen injection). D) IF for GFP, CK19, and Vimentin showed that basally extruded single cells in *KCiMist1; p120f/f* pancreata were Vimentin negative. Yellow arrows point to single GFP+, CK19+, Vimentin- basally extruded cells. Scale bars are 50µm.

**Figure S4.** p120 catenin loss leads to increased susceptibility to pancreatic injury. A,H) On Day 1 post cerulean treatment, no significant difference in injury was observed between *CiMist1; p120f/f* (n=3 pancreata), *CiMist1; p120f/wt* (n=3 pancreata), and *CiMist1; p120wt/wt* (n=2 pancreata) mice. B) IHC showed p120 catenin loss in *CiMist1; p120f/f* pancreata. C,H) Three days post cerulean administration, *CiMist1; p120f/f* mice (n=2 pancreata) showed significantly increased injury when compared to *CiMist1; p120f/wt* (n=4 pancreata, *P*=0.007) and *CiMist1; p120wt/wt* (n=2 pancreata, *P*=0.0063) mice. D,H) Five days after cerulean treatment, *CiMist1; p120f/f* mice (n=3 pancreata) showed significantly increased injury when compared to *CiMist1; p120f/wt* (n=7 pancreata, *P*=0.0007) mice and *CiMist1; p120wt/wt* (n=2 pancreata, *P*=0.0249) mice. E,H) On day 7 post cerulean administration, *CiMist1; p120f/f* mice (n=3 pancreata) continued to display significantly increased injury when compared to *CiMist1; p120f/wt* (n=5 pancreata, *P*=<0.0001) and *CiMist1; p120wt/wt* (n=2 pancreata, *P*=0.0054) mice. F,H) Eleven days after cerulean treatment, *CiMist1; p120wt/wt* mice (n=2 pancreata) showed significantly increased injury when compared to *CiMist1; p120f/wt* (n=4 pancreata, *P*=0.0002) mice. n=5 pancreata for *CiMist1; p120f/f* mice. G,H) On day 15 post cerulean treatment, *CiMist1; p120f/f* (n=4 pancreata)*,* *CiMist1; p120f/wt* (n=7 pancreata), and *CiMist1; p120wt/wt* (n=2 pancreata) pancreata displayed no significant differences in injury and were nearly completely regenerated. I,J) Analysis of FACS-sorted CD45+ pancreatic cells showed significantly increased CD45+ cells in *CiMist1G; p120f/f* mice (n=7 pancreata) when compared to *CiMist1G; p120wt/wt* mice (n=7 pancreata). N=6 for *CiMist1G; p120f/wt* mice. K,L) Treatment with NF-kB inhibitor SN50 significantly reduced the amount of pancreatic area occupied by injury in *CiMist1G; p120f/f* (n=4 SN50 treated mice and 3 dH20 treated mice) and *CiMist1G; p120wt/wt* mice (n=4 SN50 treated mice and 4 dH20 treated mice). Scale bars are 50µm.

**Figure S5.** CK19+ cells that exit pancreatic epithelial structures basally survive. A-C) Immunolabeling showed CK19+ cells that extrude apically express cleaved Caspase-3, and CK19+ cells that extrude basally lack cleaved Caspase-3 labeling in *KCiMist1; p120wt/wt*, *KCiMist1; p120f/wt*, and *KCiMist1; p120f/f* pancreata. Yellow arrows point to basally extruded CK19+ cells, and orange arrows show apically extruded CK19+ cells. Scale bars are 50µm.

**Figure S6.** Basally extruded epithelial cells in *KCiMist1; p120f/f* pancreata display characteristics of malignancy. A) Orange arrows in the H&E stained tissue section point to atypical cells displaying nuclear enlargement in a *KCiMist1; p120f/f* pancreas. The orange arrow in the CK19 IHC image shows a cell with abnormal DNA content in a *KCiMist1; p120f/f* pancreas. The orange arrow in the Feulgan stained image points to an example of an isolated epithelial cell analyzed for DNA content. B,C) The green histogram represents DNA ploidy analysis on gastric epithelial cells (diploid control), and the red histogram shows DNA ploidy analysis on isolated basally extruded CK19+ pancreatic cells. 53 control diploid cells and 253 basally extruded cells were analyzed. The first peak represents cells in the G0/G1 phase of the cell cycle, which have a DNA index of 1.0 and DNA content of 2C (2N or diploid). Cells in the G2/M phase have a DNA index of 2.0 and DNA content of 4C (4N or tetraploid). Cells with greater than 5C (DNA index 2.5) in the red histogram have abnormal DNA content. There are no control diploid cells with ˃5C (green histogram). The peak with DNA index 1.5 in the red histogram represents an aneuploid peak. D) H&E images show histology of *KCiMist1; p120f/f* pancreata. Scale bars are 50µm.

**Figure S7.** p120 catenin expression in isolated epithelial cells in human PDA. A) H&E staining of human PDA shows an isolated epithelial cell, highlighted with an orange arrow (right), and discontinuous epithelium in a lesion, also highlighted by an orange arrow (left). B) CK19 IHC shows isolated epithelial cells in human PDA. C) IF images used to score p120 catenin subcellular localization in isolated CK19+ Vimentin- cells show absent, cytoplasmic, and membranous p120 catenin labeling. D) An analysis of isolated epithelial cells in human pancreatic cancer defined as CK19+ Vimentin- showed 4.74% (12/253) of cells with predominant membranous p120 catenin, 50.20% (127/253) of cells with predominant cytoplasmic p120 catenin, and 45.06% (114/253) of cells with predominant absent p120 catenin. Scale bars are 50µm.

**Figure S8.** Microarray analysis of *KCiMist1; p120wt/wt*and *KCiMist1; p120f/f* mice. A) Sorting strategy for microarray. B) IPA analysis showed significant differentially expressed pathways including pathways involved in organization of actin cytoskeleton (red arrows), inflammatory response (blue arrows), and cell adhesion and migration (green arrows). C-E) *KCiMist1; p120f/f* pancreata showed increased cytoplasmic localization of PKCζ when compared to *KCiMist1; p120f/wt* pancreata and *KCiMist1; p120wt/wt* pancreata. F-K) Adherens junction members E-cadherin and β-catenin were reduced in *KCiMist1; p120f/f* pancreata when compared to *KCiMist1; p120f/wt* pancreata and *KCiMist1; p120wt/wt* pancreata. Orange arrows point to ductal epithelium that expresses p120 catenin. L-N) *KCiMist1; p120f/f* pancreata showed substantial activation of NF-kB in both epithelial and stromal compartments. Scale bars are 50µm.