Supplementary Figure Legends

Supplementary Figure 1
Bmi1 expression is upregulated in the exocrine pancreas at early time points after caerulein injury

Immunofluorescence for amylase, GFP, and DAPI in the pancreas of adult *Bmi1*$^{GFP/+}$ mice 4, 8, and 24 hours after last caerulein injection.

Supplementary Figure 2
Impaired acinar regeneration is persistent in *Bmi1 KO* mice after caerulein injury

Control or *Bmi1 KO* mice were injected with caerulein and sacrificed 21 days post-injection.

(A) Macroscopic views of pancreas (outlined with dashed lines), showing hypoplastic pancreas in *Bmi1 KO* mice 21 days post-injection.

(B) Relative pancreatic weight normalized to body weight. N = 4 mice, each. Means ± SD. ** $p < 0.01$.

(C) H&E staining and co-staining for amylase/cytokeratin19/DAPI showing impaired exocrine pancreas regeneration with increased duct-like structures and reduced acinar area in *Bmi1 KO* pancreas compared to *control* mice 21 days post-injection.

Supplementary Figure 3
Impaired acinar regeneration after CDE diet induced pancreatitis in *Bmi1 KO* mice

Female *control* and *Bmi1KO* mice were fed with a choline-deficient DL-ethionine-supplemented (CDE) diet for 4 days followed by normal chow. Mice were sacrificed at day 4 and 8 after starting the CDE diet.

(A) H&E staining showing disorganized acini and edema in *control* and *Bmi1 KO* pancreata at day 4 after beginning of the CDE diet.

(B) Analyses of *Bmi1*$^{GFP/+}$ pancreata at day 4 after starting the CDE diet. Costaining for clusterin/GFP/DAPI in sections from *Bmi1*$^{GFP/+}$ mice shows coexpression of GFP and clusterin. Immunohistochemistry for Bmi1 or Sox9 shows Bmi1 and Sox9 expression in damaged acinar cells.

(C) Analysis of *control* and *Bmi1 KO* pancreata at day 8 after starting the CDE diet. H&E staining and co-staining for amylase/CK19/DAPI showing impaired exocrine pancreas regeneration in *Bmi1 KO* pancreas compared to *control* mice. Co-staining for cleaved Caspase 3/E-cadherin/DAPI reveals presence of apoptotic cells in *Bmi1 KO* pancreata. Arrows indicate cleaved casase3/E-cadherin double positive cells.

Supplementary Figure 4
Characterization of initial stage of pancreatitis in *Bmi1 KO* mice

(A) H&E staining showing duct-like structures in *control* and *Bmi1 KO* pancreata on day1 and day2 post-caerulein injection.

(B) Co-staining for amylase/CK19/DAPI in *control* and *Bmi1 KO* pancreata on day1 and day2 post-caerulein injection.

(C) Co-staining for clusterin/Sox9 in *control* and *Bmi1 KO* pancreata on day2 post-caerulein

injection.

Supplementary Figure 5
Initial pancreatitis severity appears to be comparable between *Bmi1 KO* and *control* mice after caerulein injury
(A) Serum level of amylase in *control* and *Bmi1 KO* pancreata before caerulein injury and on day1 post-caerulein injection.
(B) H&E staining in *control* and *Bmi1 KO* lung on day1 and day2 post-caerulein injection.
(C) Co-staining for CD45/myeloperoxidase (MPO) with DAPI in *control* and *Bmi1 KO* lung on day2 post-caerulein injection.

Supplementary Figure 6
Initial pancreatic inflammation appears comparable between *Bmi1 KO* and *control* mice after caerulein injury
Immunohistochemistry for CD45 and F4/80 in *control* and *Bmi1 KO* pancreata on day1 and day2 post-caerulein injection.

Supplementary Figure 7
Reconstituted *Bmi1 KO* chimera mice after *WT* bone marrow transplantation
Wild type bone marrow was transplanted into irradiated *Bmi1 KO* mice at 6-8 weeks of age. 8 weeks after bone marrow transplantation, the reconstituted *Bmi1 KO* chimera mice were subjected to caerulein pancreatitis. Mice were sacrificed 7 days after caerulein treatment.
(A) Flow cytometry analysis of chimeric spleens in *WT* reconstituted *Bmi1 KO* chimera mice contain abundant WT, non-GFP positive, CD45-positive cells.
(B) Genotyping PCR reveals presence of *Bmi1* wild type alleles in splenic cells isolated from the reconstituted *Bmi1 KO* chimera mice (N = 3)