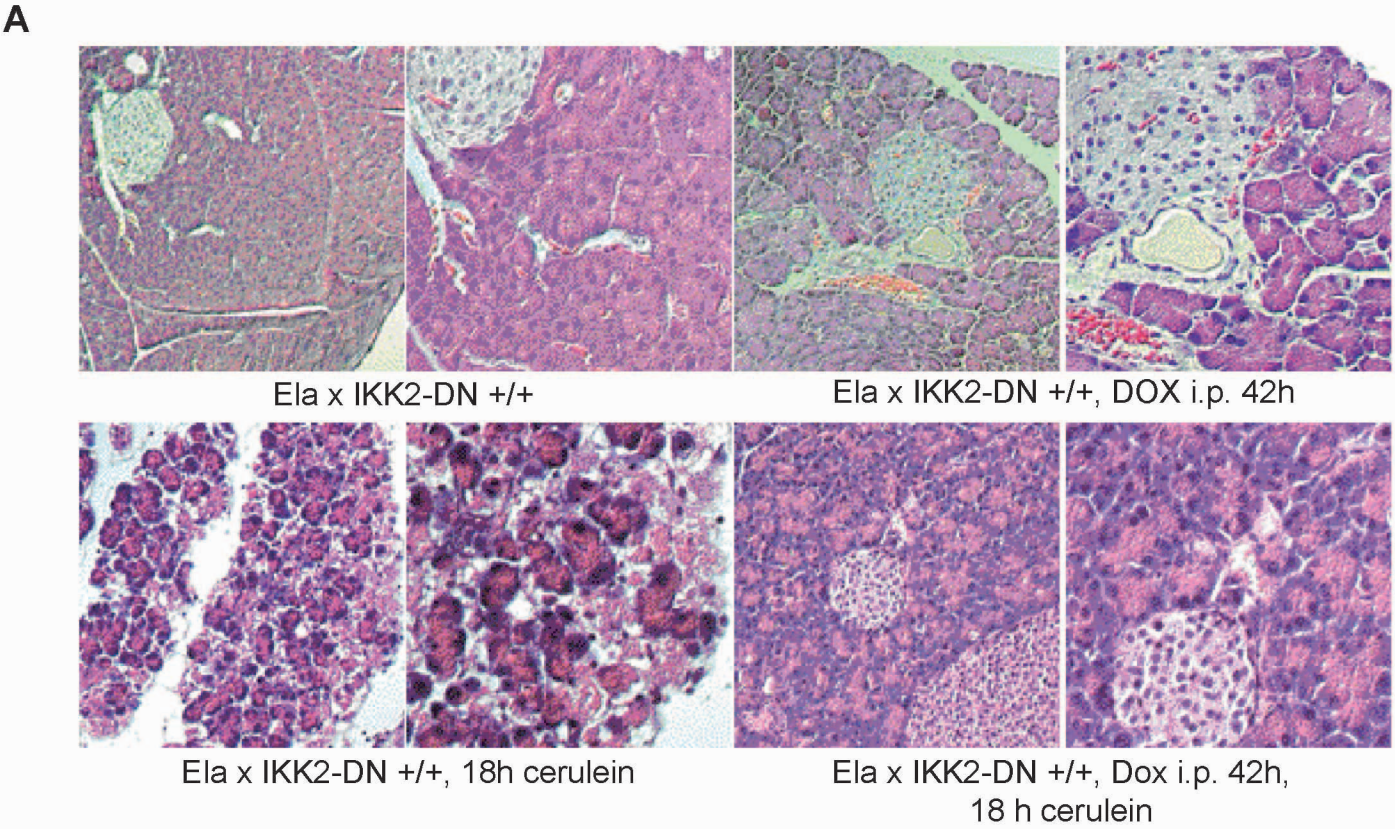
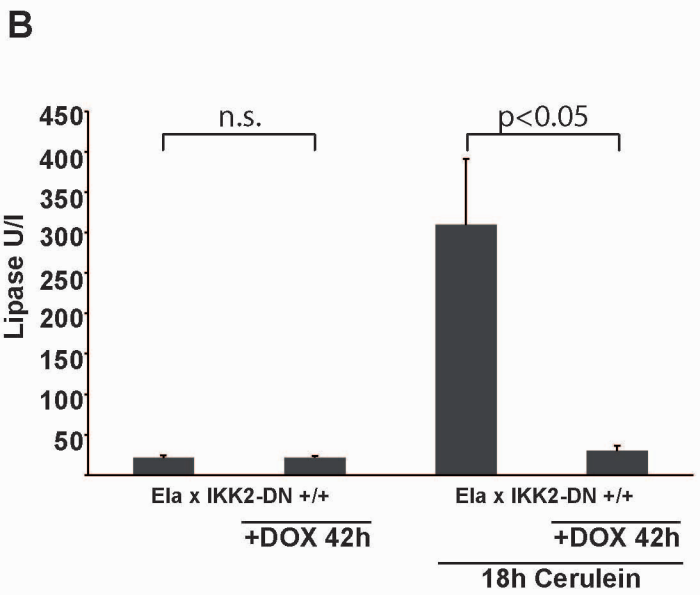
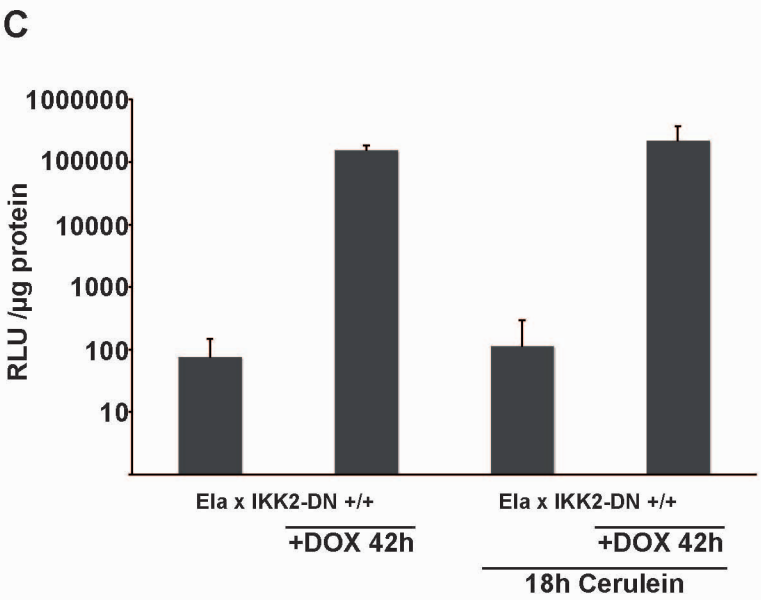
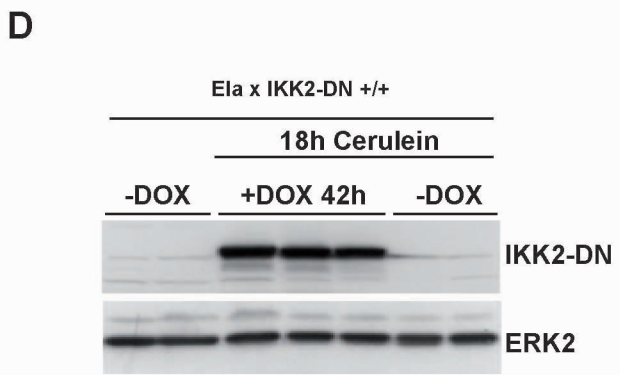
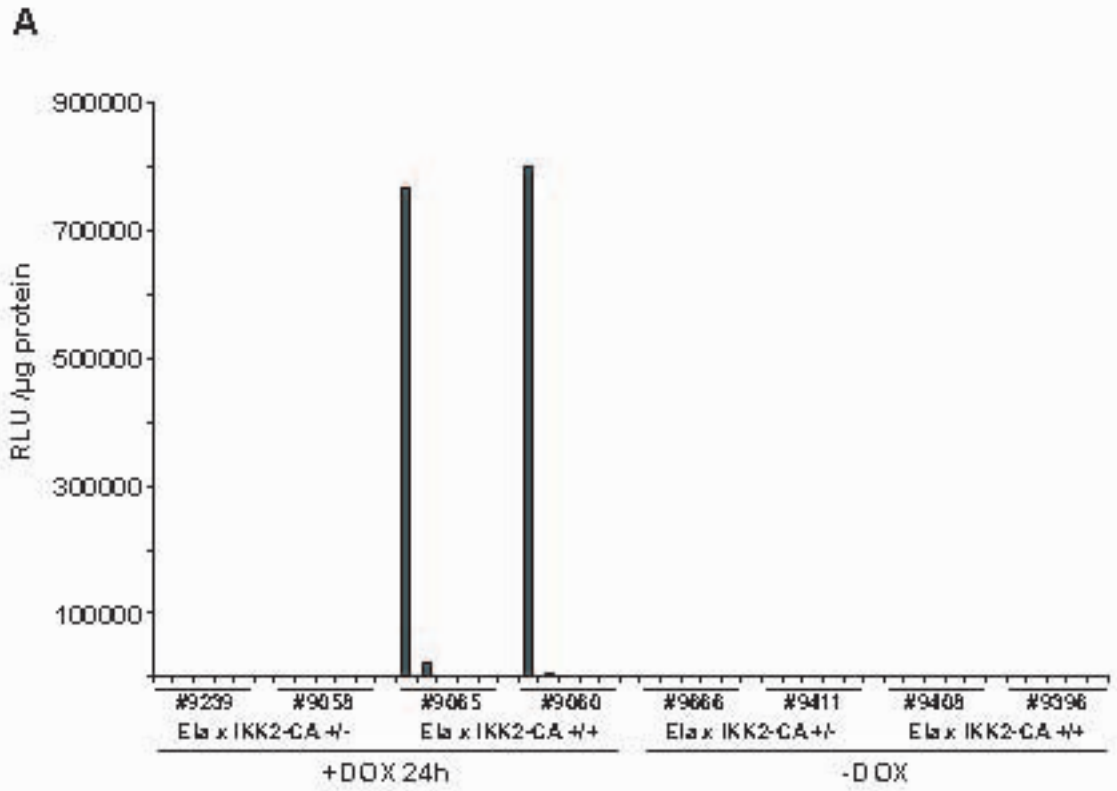


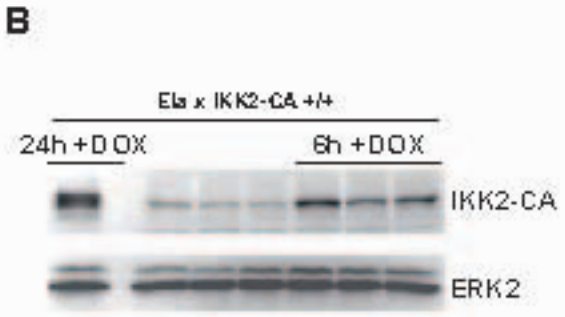


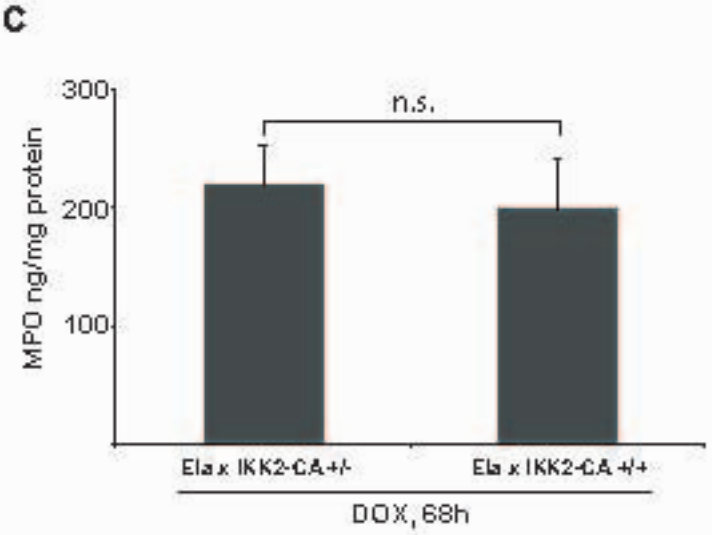




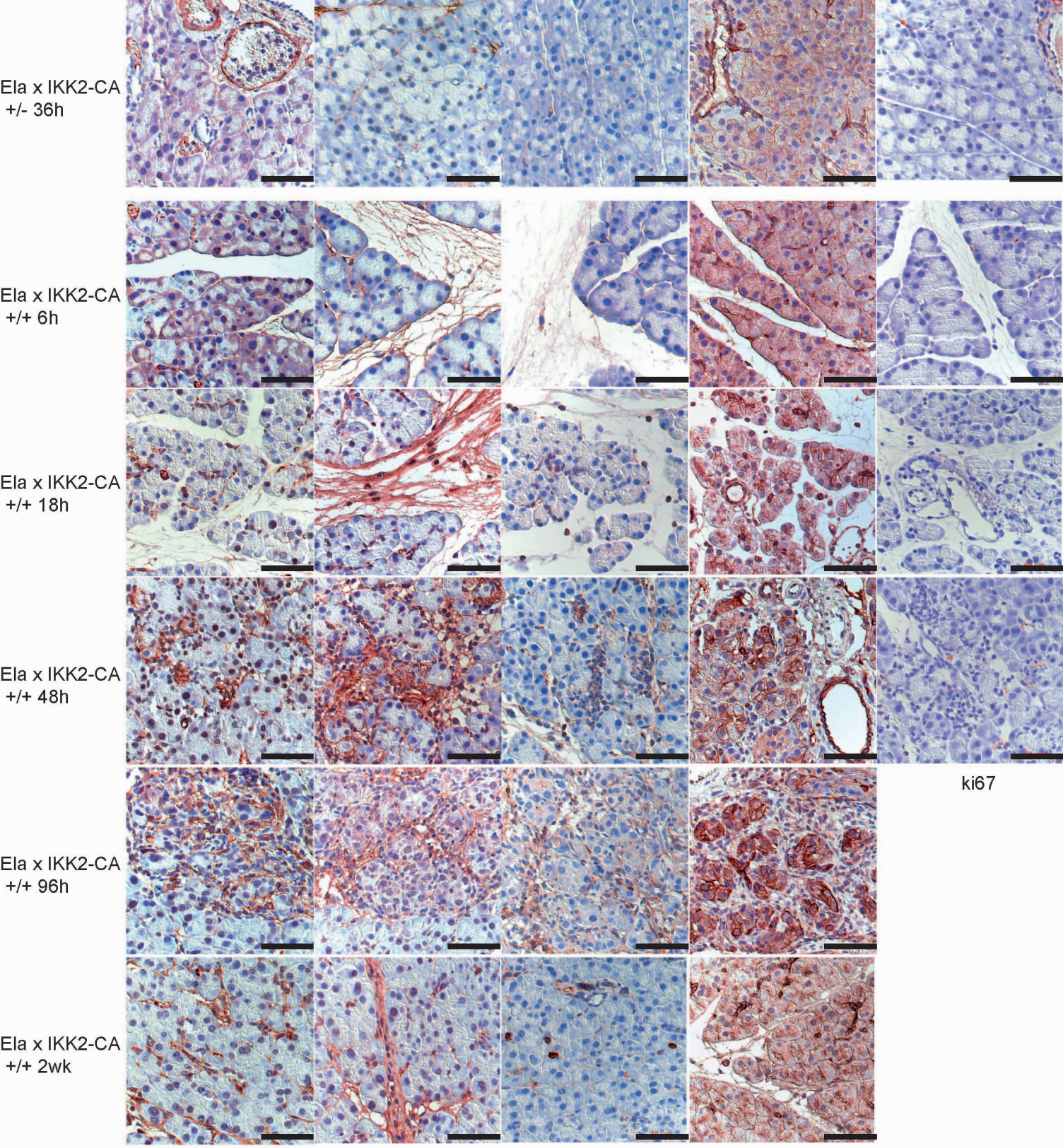
supplementary figure 1







supplementary figure 2



supplementary figure 3

Supplementary Figure legends

Supplementary Figure 1: Cerulein-induced pancreatitis is ameliorated in Dox treated, double transgenic Ela.rtTA x IKK2-DN mice.

(A) Morphological examination of double transgenic mice (Ela.rtTA x IKK2-DN +/+) without Dox and 42h after i.p. injection of Dox revealed comparable histology. Cerulein induced pancreatitis in untreated controls (Ela x IKK-DN +/+) 18h after starting cerulein injection while this phenotype was nearly abolished in Dox treated double transgenic animals (Ela x IKK-DN +/+, Dox i.p. 42h). (B) Serum lipase levels were at base line in double transgenic animals independent of Dox treatment (Ela x IKK2-DN +/+ and Ela x IKK2-DN +/+, Dox 42h). Serum lipase values were elevated in untreated double transgenic animals 18h after cerulein injection (Ela x IKK2-DN +/+, 18h cerulein). In Dox treated Ela x IKK2-DN +/+ mice serum lipase remained at the basal level 18h after cerulein injection (Ela x IKK2-DN +/+, Dox 42h, 18h cerulein). (C) Luciferase activity was induced more than 1000 fold in the Dox treated double transgenic mice in this experiment as compared to the untreated, double transgenic control (note logarithmic scale of the RLU/µg protein). (D) Western blot analysis confirmed the overexpression of IKK2-DN after Dox treatment of double transgenic mice as compared to the untreated, double transgenic control. ERK2 expression served as loading control. Statistical differences were tested with the Mann-Whitney-Wilcoxon test.

Supplementary Figure 2: Characterization of double transgenic Ela.rtTA x IKK2-CA mice.

(A) Transgene expression is tissue-specific and depends on Dox-induction. Luciferase activity as measurement of transgene expression was evaluated in single transgenic (Ela x IKK2-CA +/-) and double transgenic (Ela x IKK2-CA +/+) mice left uninduced (right panels) or after Dox treatment for 24 hours (left panels, +Dox 24h). Tissue extracts of pancreas, spleen, liver, lung and thymus of two individual animals for each condition were examined. Luciferase activity above the baseline level was only observed in the pancreas of double transgenic

animals treated with Dox (animals #9065 and #9060). Low levels of luciferase were sometimes observed in spleen samples and represent most likely contamination with surrounding pancreas tissue. (B) Western Blot analysis of pancreatic extracts showed expression of IKK2-CA already 6h after Dox treatment (Ela x IKK2-CA +/+, 6h Dox+) in double transgenic animals as compared to the untreated, double transgenic control. This expression was further increased 24h after Dox treatment. ERK2 expression served as loading control. (C) Myeloperoxidase activity (MPO) was measured in lung tissue 68h after Dox treatment (at the time point of the most severe pancreatitis) in single and double transgenic Ela.rtTA x IKK2-CA mice as indicator of lung injury. No statistical significant differences were evident between double and single transgenic mice. Statistical differences were tested with the Mann-Whitney-Wilcoxon test.

Supplementary Figure 3: Immunohistochemical characterization of the pancreatitis in Ela.rtTA x IKK2-CA mice.

Tissue sections of a single transgenic control (upper row, 36h after Dox treatment) and of double transgenic Ela.rtTA x IKK2-CA mice 6h, 18h, 48h, 96h and 2weeks after Dox treatment were stained with the indicated antibodies. α-smooth-muscle-actin positive cells dramatically increased in the double transgenic animals 18 to 96h after Dox treatment. α-smooth-muscle-actin positive cells persisted 2 weeks in the pancreas of double transgenic mice after a single induction IKK2-CA with Dox. Collagen I stained deposits of extra cellular matrix were evident 18h after Dox treatment in double transgenic mice. These deposits were still evident after 2 weeks. Staining with CD45-LCA confirmed, that invading leucocytes were only evident from 18h after Dox treatment of double transgenic animals. Interestingly, CD45-LCA positive leucocytes were still seen 2 weeks after the IKK2-CA induction. Immunostaining with cytokeratin 8/18 served as a marker of epithelial cells and to distinguish these cells from mesenchymal cells. Ki67 staining was performed to evaluate possible effects

of the IKK2-CA expression on the proliferation of acinar cells in Dox treated, double transgenic mice. Up to 48h no increase in Ki67 positive was evident in the Dox treated double transgenic animals as compared to the Dox treated, single transgenic control.