

Figure S1. K8 is expressed in glucagon-positive α -cells. Untreated $K8^{+/+}$ mouse pancreas was stained for K8 (green), glucagon (red) and nuclei (blue). a) The white line marks the islet outline, bar = 50 μ m. b) High magnification of islet cells show that K8 is expressed in glucagon-positive α -cells. Bar = 10 μ m.

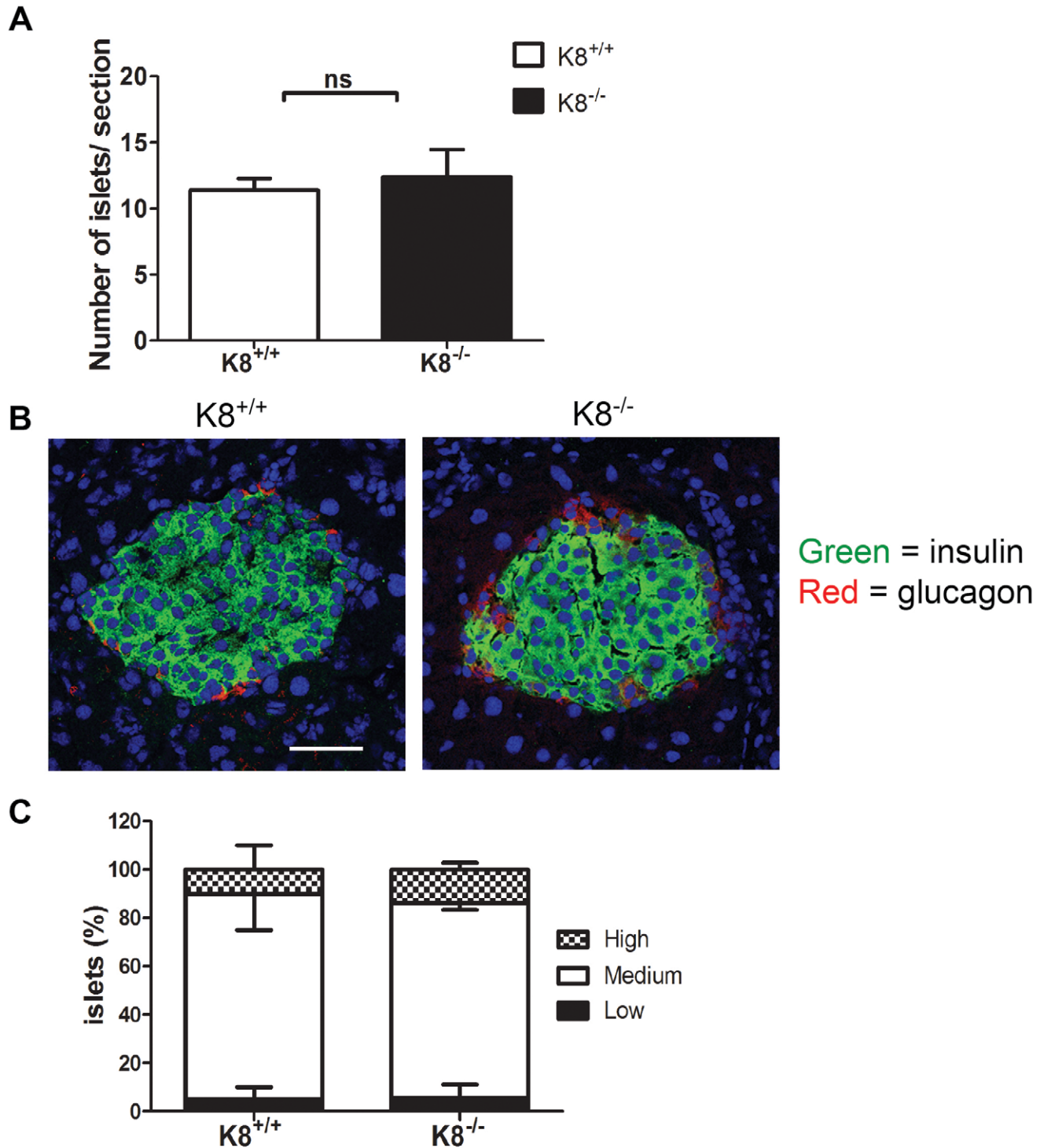


Figure S2. Unaltered number of islets and distribution of α / β -cells after K8 inactivation. A. Islets were counted from 6 longitudinal sections, 150 μm apart, from roughly the middle third of the pancreas obtained from K8^{+/+} and K8^{-/-} mice. Bars represent mean number of islets / section \pm SEM. N = 3 mice /group, ns = not significant. B. Representative staining for insulin (green), glucagon (red) and nuclei (blue) from pancreatic sections from untreated K8^{+/+} and K8^{-/-} mouse. Bar = 50 μm . C. A semiquantitative estimate of α / β cell ratio in untreated K8^{+/+} and K8^{-/-} mice was acquired by scoring the ratio of glucagon to insulin in immunostained pancreatic sections. A 'low' score = < 10%, 'medium' = 10-20% and 'high' = > 20% glucagon positive cells in the islet. The bar graph shows the average per cent islet sections in K8^{+/+} and K8^{-/-} mice with low (black bars), intermediate (white bars) or high (checked bars) glucagon/insulin ratio. N = 2 mice/ group. No significant difference was seen in α / β -cell ratios in K8^{-/-} islets.

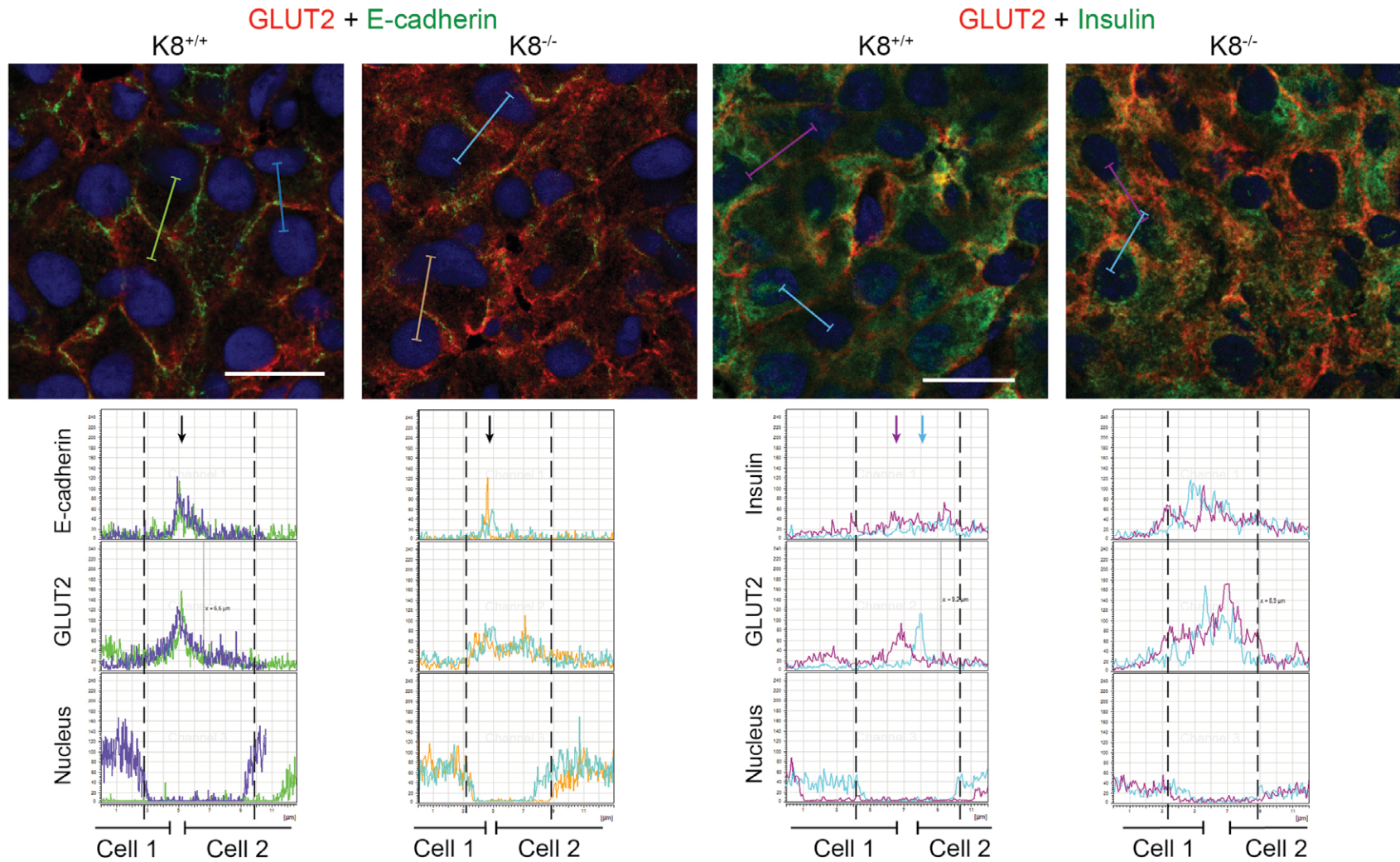


Figure S3. Figure S3. GLUT2 co-localises exclusively with the plasma membrane marker, E-cadherin in K8^{+/+} but not K8^{-/-} β-cells. The figure shows representative immunostainings for GLUT2 (red) with E-cadherin (green) and GLUT2 (red) with insulin (green) from K8^{+/+} and K8^{-/-} pancreatic sections. Nuclei are stained blue, scale bars = 15μm. The histograms below demonstrate co-localisation of GLUT2 and E-cadherin in K8^{+/+} but not in K8^{-/-} β-cells. The histogram y-axes present immunofluorescence intensity and x-axes show the distance of the analysed line. Insulin, was used as a cytosolic marker and co-localised almost entirely with GLUT2 in K8^{-/-} but not in K8^{+/+} β-cells, where GLUT2 shows a narrow fluorescence peak. Arrows above histograms indicate the location of the plasma membrane and the space between the dotted lines indicates roughly the area between nuclei of two adjacent cells (cell1 and cell 2). The histograms are colour-coded to identify the analysed area (same colour in the confocal image as in the histogram below).

H2A.X + insulin + nuclei

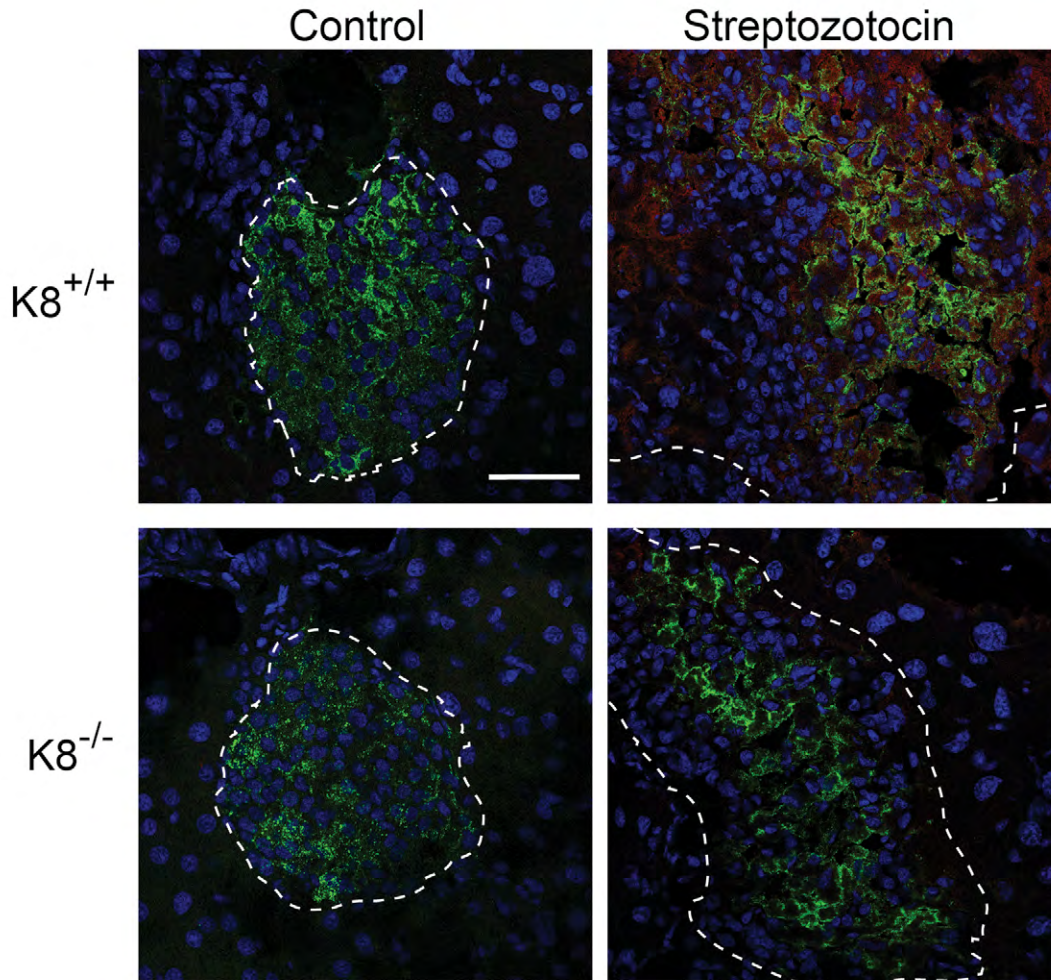


Figure S4. Increased phosphorylated H2A.X in high-dose streptozotocin treated K8^{+/+} compared with K8^{-/-} pancreatic islets. Pancreatic sections from untreated K8^{+/+} and K8^{-/-} mice and streptozotocin (200 mg / kg, i.p.) treated mice were stained for phospho- H2A.X (red), insulin (green) and nuclei (blue). The endocrine islets are indicated with white broken lines. Phosphorylated H2A.X, which is induced in apoptotic cells, was readily observed in the islets of K8^{+/+} mice, but was barely detectable in the K8^{-/-} islets. Untreated control K8^{+/+} and K8^{-/-} pancreas sections were negative for phosphorylated H2A.X. Scale bar = 50 μ m.