**ESM methods**

*Pancreatic histology*  Rat pancreas specimens were fixed in 10% buffered formalin and embedded in paraffin. Sections were stained with hematoxylin and eosin.

*TUNEL*  Pancreas sections were stained for terminal deoxynucleotidyl transferase (TdT)-mediated dUTP nick end labeling (TUNEL) as per manufacturer’s instructions (Roche); sections were co-stained with insulin to identify beta cell specific apoptosis.

*Antibodies*  For immunofluorescence staining, frozen sections were stained with rabbit anti-rat CD3 (Pharmingen), guinea pig anti-insulin (Dako), rabbit anti-human XBP-1, chicken anti-insulin, and mouse anti-glucagon (Abcam). Secondary antibodies, Alexa Fluor 488 and 592 goat anti-mouse, anti-rabbit, anti-guinea pig, and anti-chicken were from Invitrogen. Isotype controls were from Pharmingen.