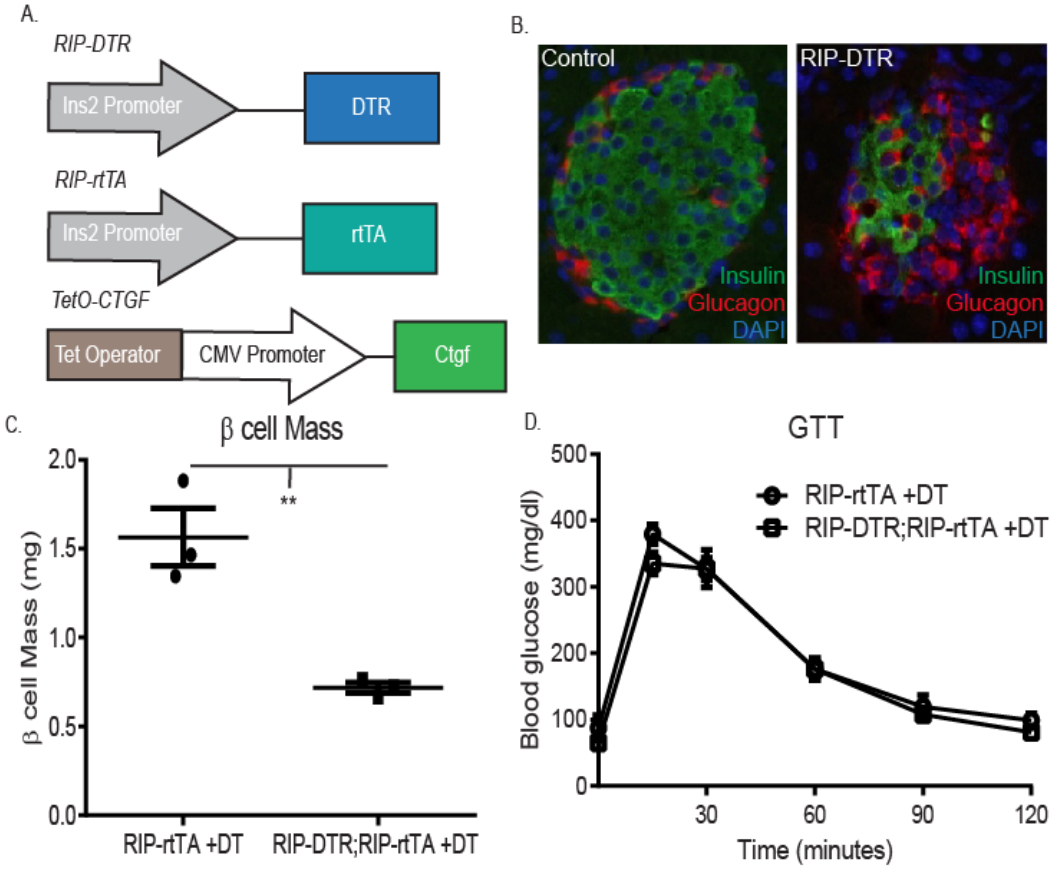
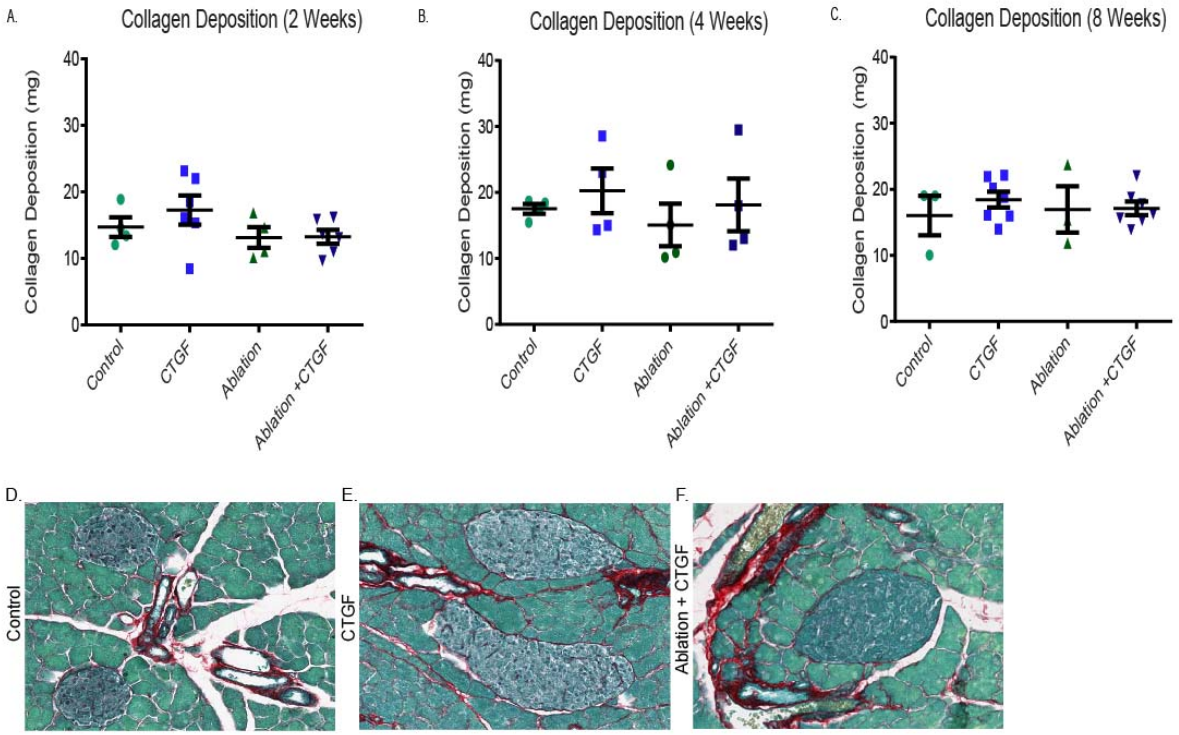
SUPPLEMENTARY DATA

Supplementary Figure 1. Validation of murine transgenic models. **A.** Transgenic models employed. Top: β-cell-specific diphtheria toxin receptor (DTR) is driven by the rat insulin (Ins2) promoter. Middle: β cell-specific reverse tetracycline transactivator (rtTA) is driven by the rat Ins2 promoter. Bottom: Tet-operator sequence binds rtTA to drive CTGF expression in the presence of Dox. **B.** Left- Islet from control DT-injected animal (RIP-rtTA or TetO-CTGF). Right- Islet from experimental DT-injected animal (hemizygous RIP-DTR). **C.** β cell mass (circles) in DT-injected control animals and animals hemizygous for RIP-DTR (squares). **D.** Glucose homeostasis as measured by intraperitoneal glucose tolerance tests. Animals with 50% β cell ablation (squares) and controls (circles). n=3, **p=0.0068.



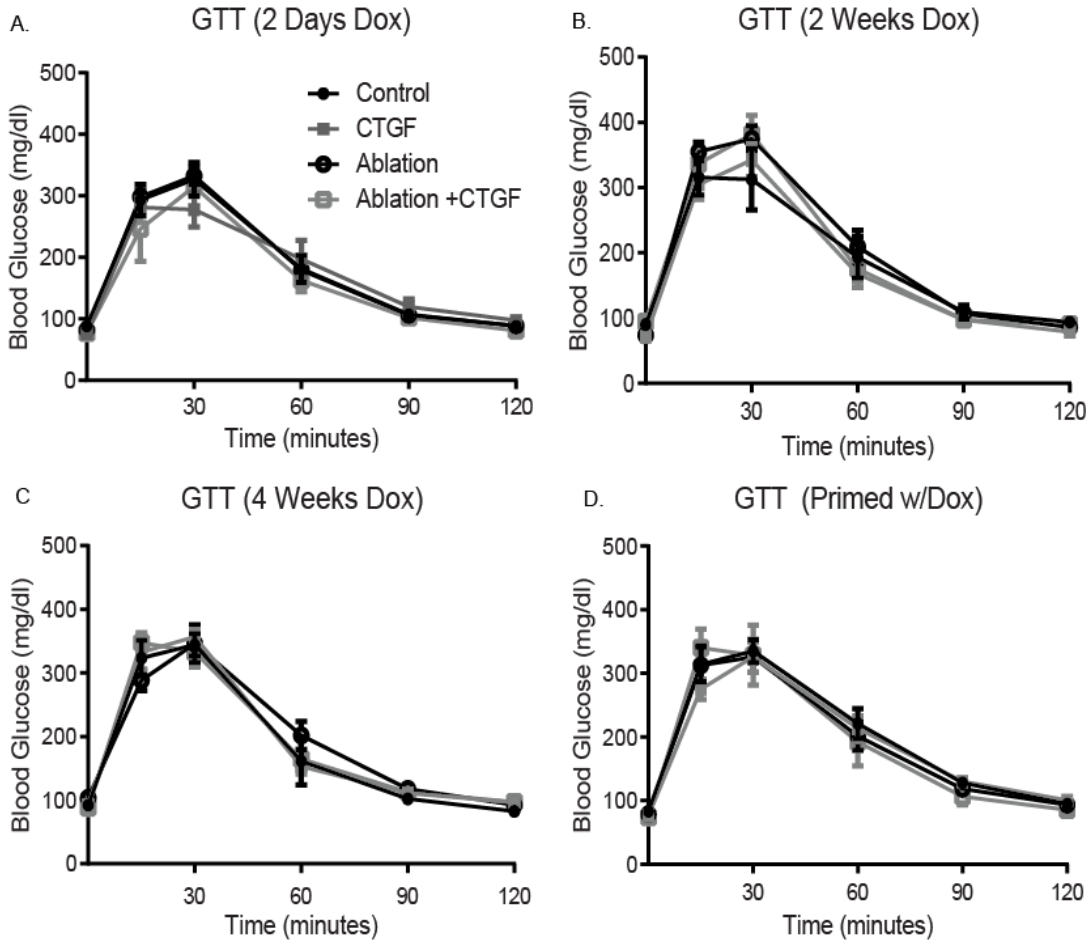
SUPPLEMENTARY DATA

Supplementary Figure 2. Continuous CTGF induction for up to 8 weeks does not promote excess collagen deposition or fibrosis. Quantification of collagen deposition per pancreas at 2 weeks **A.**, 4 weeks **B.** and 8 weeks **C.** of Dox administration. **D-F:** Representative images of collagen staining, with Sirius Red demarking collagen against a pancreatic tissue counterstain with Fast Green. n=3-7.



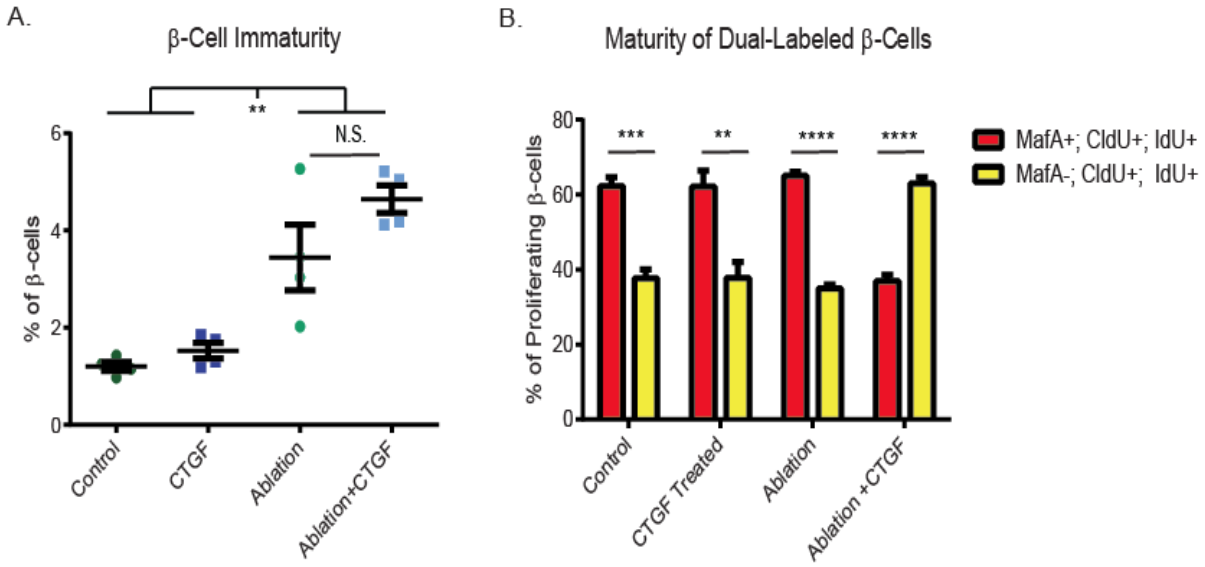
SUPPLEMENTARY DATA

Supplementary Figure 3. Intraperitoneal glucose tolerance tests reveal no difference in glucose homeostasis between Control (filled circles), CTGF treated (filled squares), Ablation (open circles), or Ablation+CTGF (open squares) mice treated with Dox for 2 days **A.**, 2 weeks **B.**, 4 weeks **C.**, or for 1 week prior to, during and 2 days after DT injections **D.** beginning at 8 weeks of age. n=6 for 2 day and primed timepoints. n=8 for 2 and 4 week timepoints.



SUPPLEMENTARY DATA

Supplementary Figure 4. β-cell proliferation characteristics in response to ablation and/or CTGF. **A.** Percentage of immature (MafB+) β-cells. A minimum of 4,000 cells was counted. **B.** Maturity state of CldU/IdU dual-labeled β-cells was determined at 2 weeks of CTGF treatment. All dual-labeled β-cells were quantified as either mature (MafA+; red bars) or immature (MafA-; yellow bars). n=4. **p<0.01, ***p<0.001, ****p<0.0001.



SUPPLEMENTARY DATA

Supplementary Figure 5. Protein levels of total and phospho-Smad3 in response to CTGF treatment and/or ablation. **A:** Isolated islet protein was probed with Smad3, p-Smad3, and β-tubulin antibodies for immunoblot analysis. **B:** Densitometric quanitification of activated p-Smad3 relative to total Smad3 protein provided. n=3 for Control and Ablation, n=2 for CTGF and Ablation+CTGF.