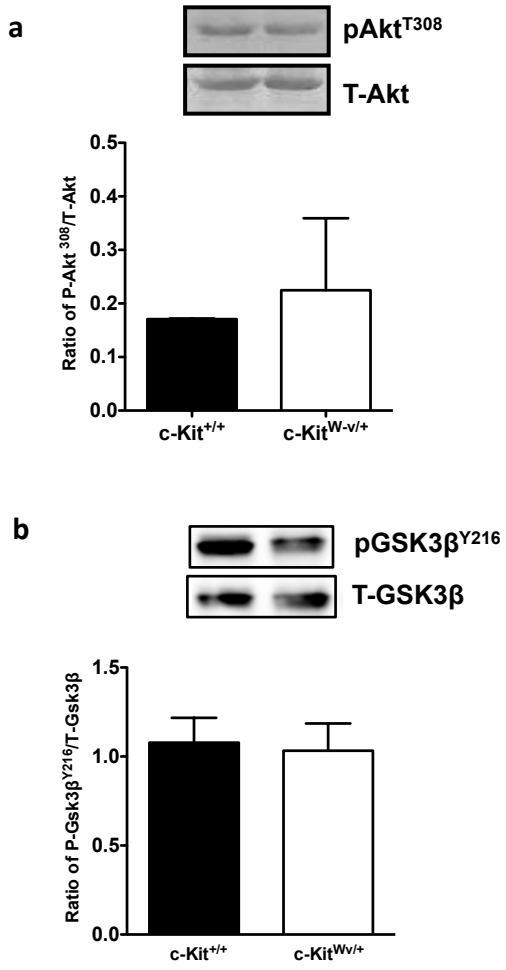
Supplementary Table 1. List of antibodies used for immunofluorescence and western-blot analyses.

Primary Antibody	Dilution	Source
Mouse anti-insulin	1:1500	Sigma, Saint Louis, Missouri, USA
Guinea pig anti-insulin	1:50	Zymed, San Francisco, CA, USA
Mouse anti-glucagon	1:2000	Sigma, Saint Louis, Missouri, USA
Rabbit anti-Ki67	1:200	Abcam Inc.Cambridge,MA,USA
Rabbit anti-PDX-1	1:5000[a]	Dr.Wright, University of Vanderbilt, USA
Guinea pig anti-PDX-1	1:2000	Dr.Wright, University of Vanderbilt, USA
Mouse anti-phospho Akt (Ser473)	1:2000[a]	Cell Signaling Boston, MA,USA
Rabbit anti-Akt	1:3000[a]	Cell Signaling Boston, MA,USA
Rabbit anti-phospho GSK3β (Ser9)	1:2000[a]	Cell Signaling Boston, MA,USA
Rabbit anti-phospho GSK3β (Y216)	1:2000[a]	Abcam Inc.Cambridge,MA,USA
Rabbit anti-GSK3β	1:2000[a]	Cell Signaling Boston, MA,USA
Mouse anti-Cyclin D1	1:2000[a]	Cell Signaling Boston, MA,USA
Mouse anti-Calnexin	1:2000[a]	BD Biosciences Mississauga, ON Canada
Mouse anti-β-actin	1:5000[a]	Sigma-Aldrich; Oakville, ON, CA

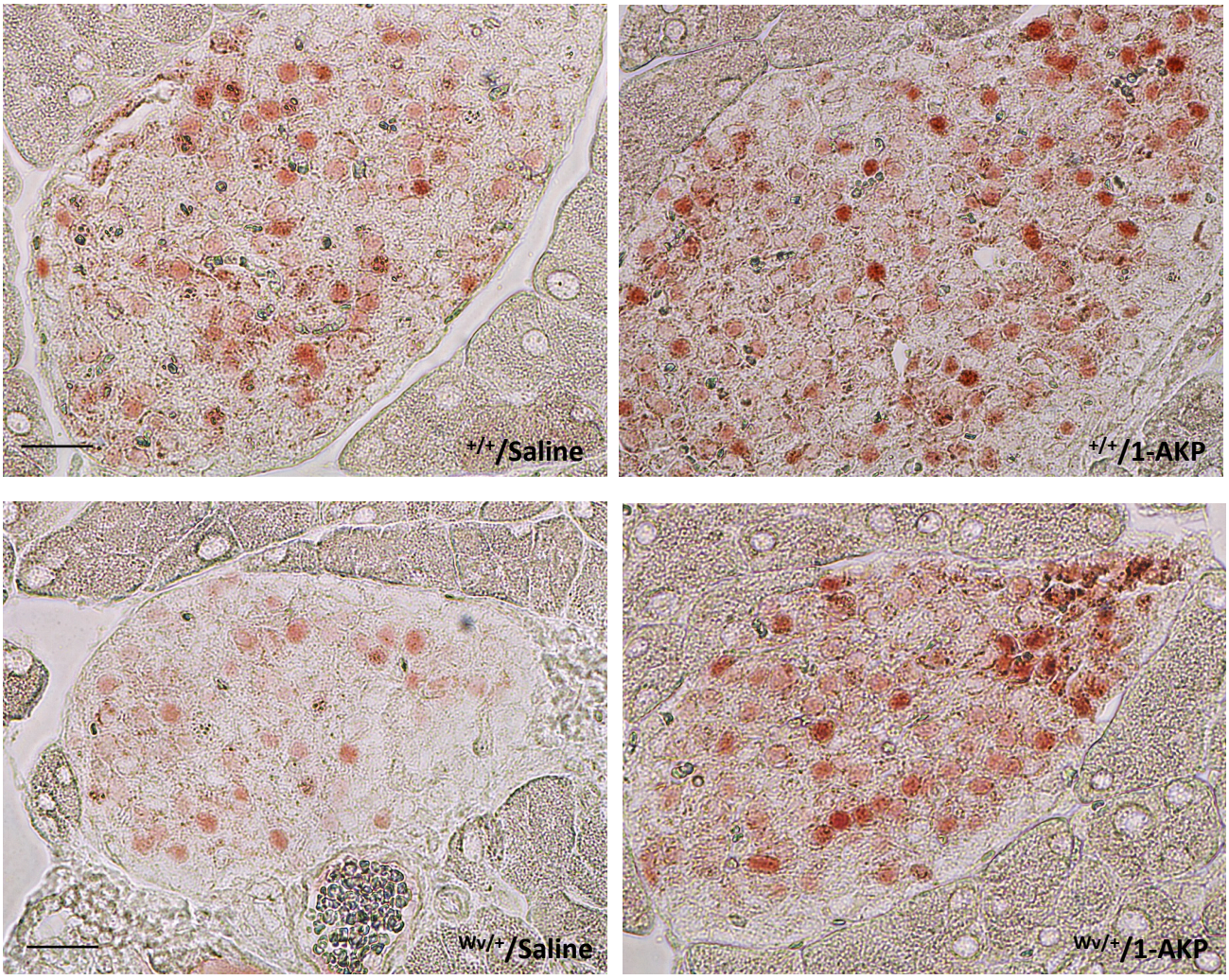
[a]dilution factor applied for western blot analysis.

Supplementary Table 2. Sequences of primers used in real-time PCR

Primer Name	Accession & Definition	Primer Pair Sequence 5'-3'(*Sense/Antisense*)	Location (*nt*)	Fragment Size(bp)
CyclinD1 (Ccnd1)	NM_007631.2	CTG TGC GCC CTC CGT ATC TTA TCG GGC CGG ATA GAG TTG TCA	343-363 636-616	294
Insulin I	NM_008386.3	TGT TGG TGC ACT TCC TAC CC ATC CAC AAT GCC ACG CTT CT	191-210 456-437	266
Insulin II	NM_008387.3	GCA GCA CCT TTG TGG TTC CC GCA GCA CTG ATC TAC AAT GCC	154-173 361-341	208
Mafa	NM_194350.1	AGC GCT TCT CCG ACG ACC AG GGC CCG CCA ACT TCT CGT AT	692-711 976-957	285
Pdx1	NM_008814.2	CCA CCC CAG TTT ACA AGC TCG GTA GGC AGT ACG GGT CCT CT	252-272 575-556	324
18S	NR_003278.1	GTA ACC CGT TGA ACC CCA TTC CCA TCC AAT CGG TAG TAG CG	1577-1597 1727-1708	151



Supplemental Fig. S1: Western blot analysis of phosphorylated (P) Akt T308 and Gsk3β Y216, total (T) Akt and Gsk3β protein level in the isolated islets of *c-Kit$^{+/+}$* and *c-Kit$^{Wv/+}$* male mice at 8 week of age. Representative blots are shown. Data are normalized to either total Akt or Gsk3β protein and expressed as means ± SEM (*n=3 per experimental group*)



Supplemental Fig. S2: Immunohistochemical staining for Mafa (red) of *c-Kit$^{+/+}$/saline*, *c-Kit $^{+/+}$/1-AKP*, *c-Kit$^{Wv/+}$/saline*, and *c-Kit$^{Wv/+}$/1-AKP* mice pancreatic section. An increased Mafa staining intensity was observed in the islet of *c-Kit$^{Wv/+}$/1-AKP* mice when compared to *c-Kit$^{Wv/+}$/saline* treated mice. No counterstaining was applied and nuclei are white transparent. Original magnificant 400x

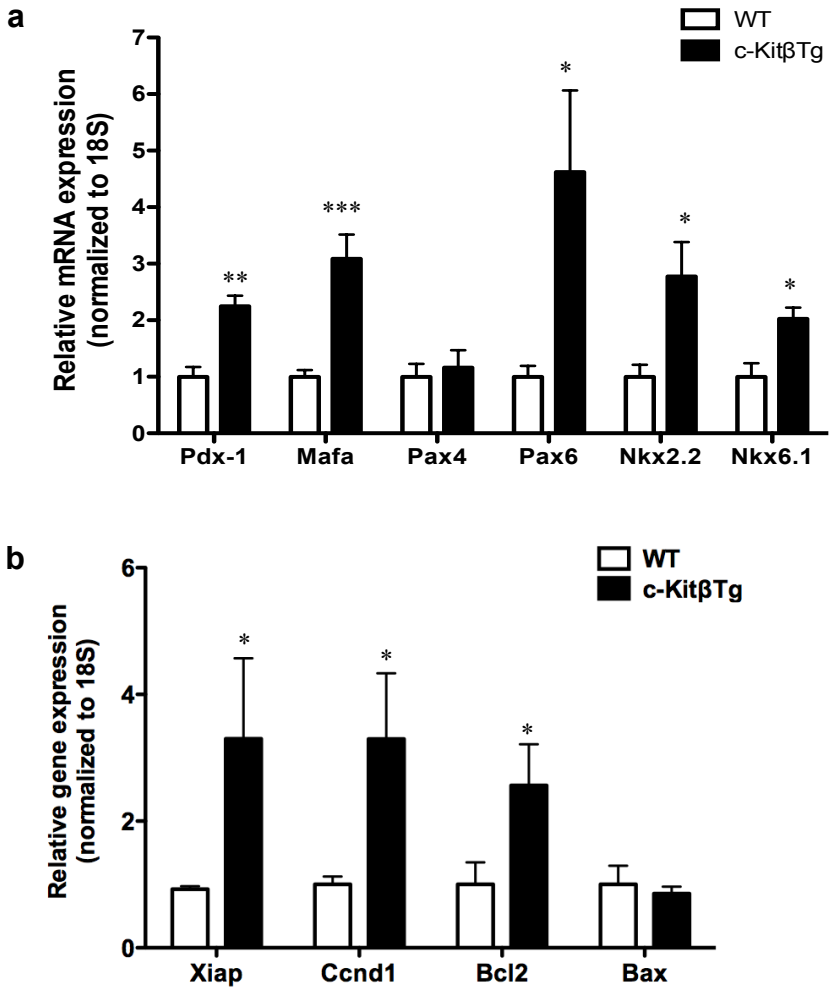


Fig. 1 for review only: Transcription factors and signaling molecules expression in *c-KitβTg* mice. Quantitative RT-PCR analysis of islet transcription factors (**a**) and signaling molecules downstream of Akt/Gsk3β (**b**) in isolated islets of WT and *c-KitβTg* mice at 8 weeks of age. Data are expressed as means ± SEM (*n=4-8*). *p<0.05, **p<0.01, ***p<0.001 vs. WT mice.

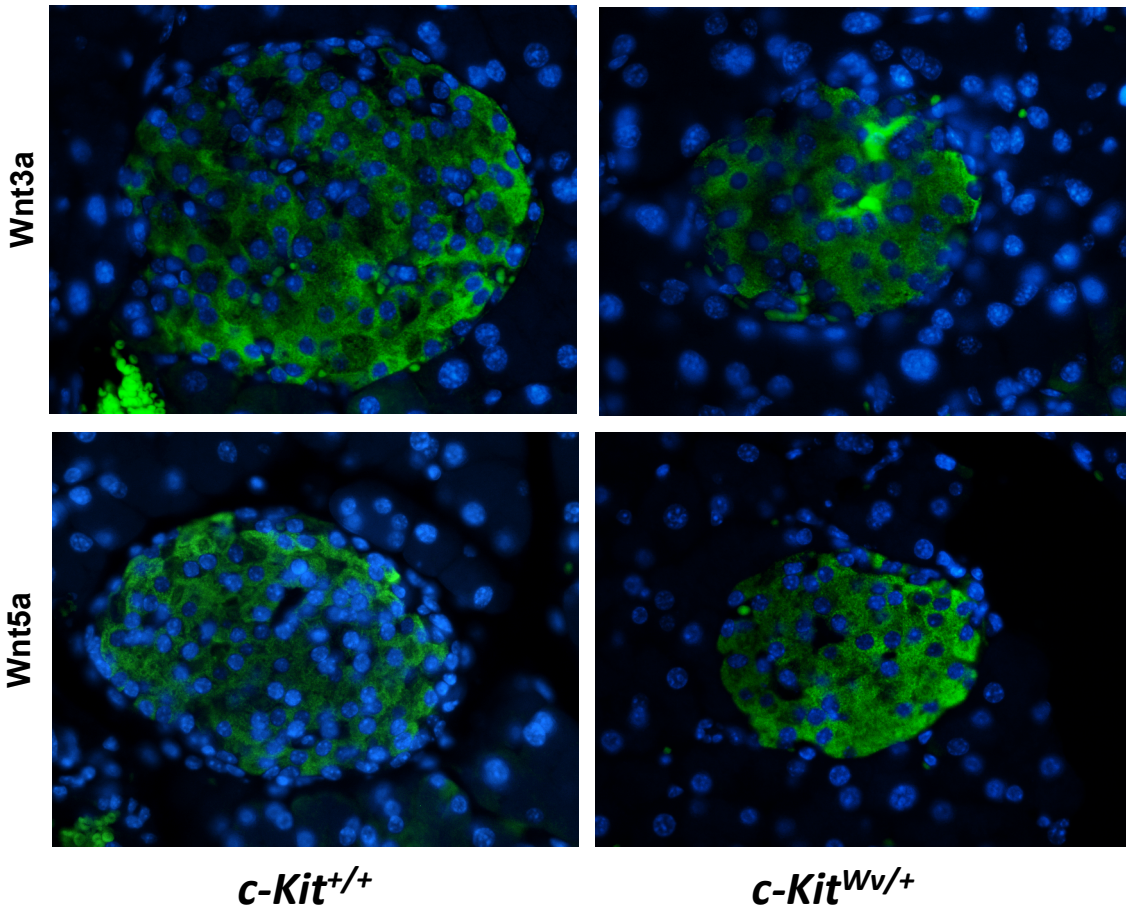


Fig. 2 for review only: Immunofluorescence staining for Wnt3a and Wnt5a (green) of *c-Kit*$^{+/+}$ and *c-Kit*$^{Wv/+}$ mice pancreatic section. A similar staining intensity was observed in the islet of *c-Kit*$^{+/+}$ and *c-Kit*$^{Wv/+}$ mice. Original magnificant 400x

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Improved β-cell proliferation and function in *c-Kit$^{Wv/+}$;Fas$^{lpr/lpr}$ double mutant mice*

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Understanding the molecular mechanisms that control the balance between proliferation and death of pancreatic β-cells has important implications for diabetes. c-Kit receptor and its ligand, stem cell factor, are important for β-cell survival and maturation while Fas (CD95) is a member of the tumor necrosis factor receptor family capable of triggering β-cell apoptosis. Our previous *in vivo* studies of c-Kit deficient (*c-Kit$^{Wv/+}$*) male mice have determined that disruption of c-Kit receptor signaling leads to a severe loss of β-cell mass and function with a significant increase in Fas expression and cell apoptosis. This led us to hypothesize that activation of the c-Kit receptor signaling regulates β-cell survival by down-regulating the Fas-mediated cell death cascade. Using a double (*c-Kit$^{Wv/+}$:Fas$^{lpr/lpr}$*) mutant mouse model, we found that *c-Kit$^{Wv/+}$:Fas$^{lpr/lpr}$* male mice displayed a significant improvement in fasting blood glucose levels ($p<0.01$) and glucose tolerance ($p<0.05$) when compared with *c-Kit$^{Wv/+}$:Fas$^{+/+}$* mice. Glucose-stimulated insulin secretion tests *in vivo* revealed that *c-Kit$^{Wv/+}$:Fas$^{lpr/lpr}$* mice also displayed improved β-cell function and increased β-cell proliferation ($p<0.001$) that was associated with increased islet number and β-cell mass. These *c-Kit$^{Wv/+}$:Fas$^{lpr/lpr}$* mice also showed a significant increase in insulin and Pdx-1 mRNA expression when compared to c-*Kit$^{Wv/+}$:Fas$^{+/+}$* mice. Taken together, these results demonstrate that down-regulation of the Fas pathway in c-Kit-deficient mice results in improved β-cell survival and function. This study shows that cross-talk between the c-Kit and Fas signaling pathways is critical for the regulation of β-cell mass and function.