ONLINE APPENDIX – SUPPLEMENTARY TABLE AND FIGURES

SupplementaryTable 1. Mouse primer sequences for Real-Time PCR experiments:

Gene	Primer Sequence
c-met	Forward- 5’CCTTCGAAAGCAACCATTTT Reverse- 5’TTACTGACATACGCGGCTTG
HGF	Forward- 5’TAGGAGCCACAAGGATCTGG Reverse- 5’ACATGAAGCAGGAGGAGGTG
iNOS	Forward- 5'TGAAGAAAACCCCTTGTGCT Reverse- 5’TTGTCTCTGGGTCCTCTGGT
A20	Forward- 5'CGAGAGAGAACCCCAGAAGA Reverse- 5’ATGCATGAGGCAGTTTCCA
Actin	Forward- 5’AGCCATGTACGTAGCCATCC Reverse- 5’CTCTCAGCTGTGGTGGTGAA

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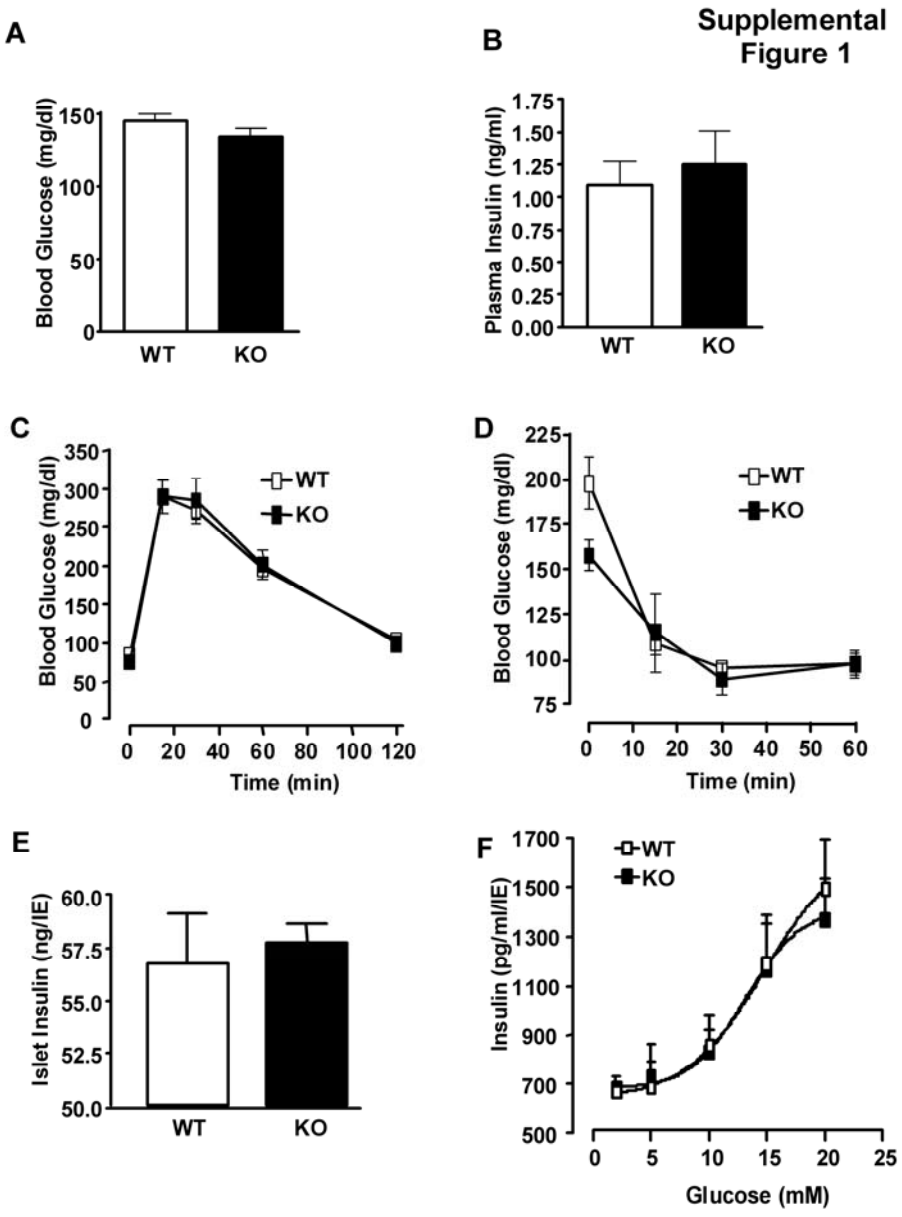
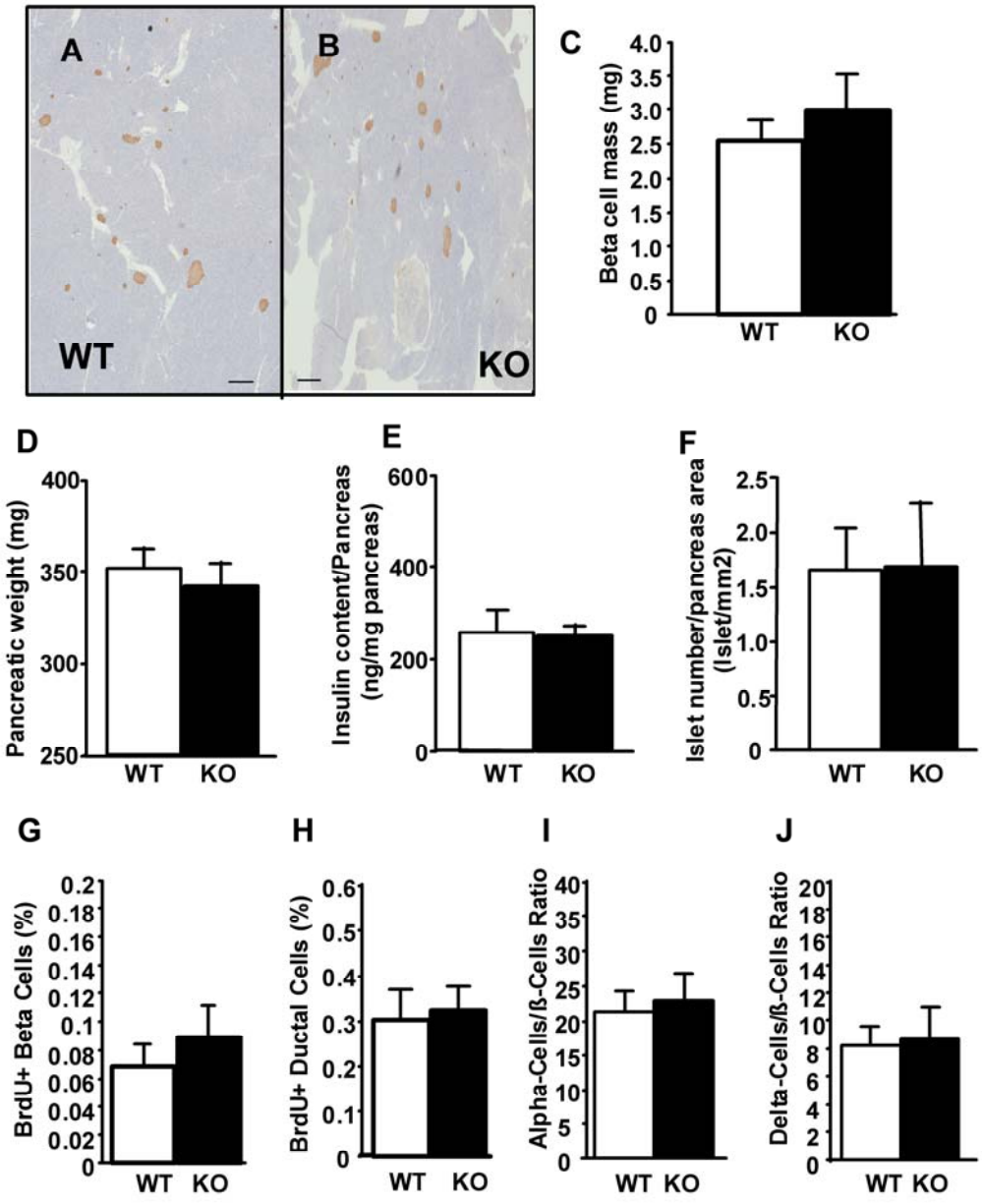
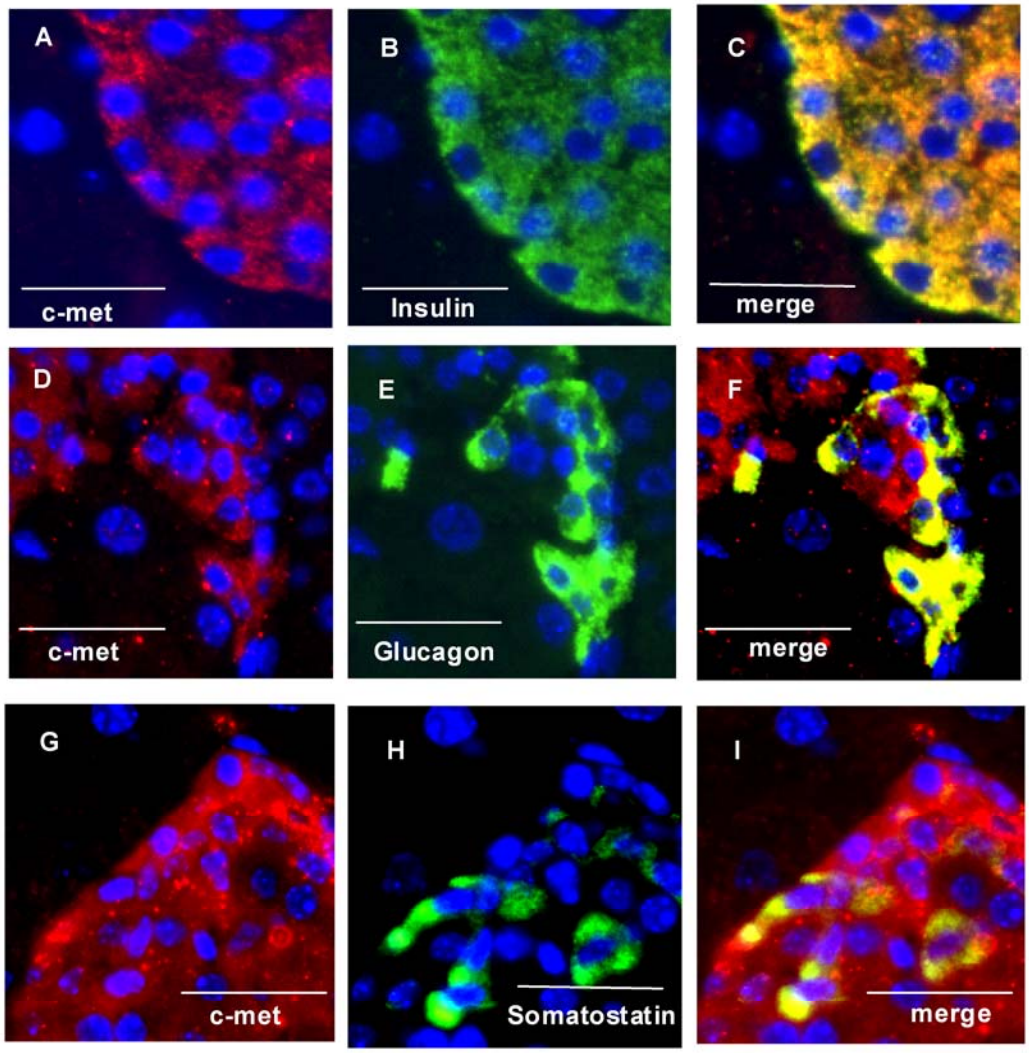
Supplementary Figure 1. Glucose homeostasis is unchanged in adult PancMet KO mice. **(A)** Non-fasting blood glucose, **(B)** plasma insulin, **(C)** intraperitoneal glucose tolerance test and **(D)** insulin tolerance test performed in 10-12 week-old PancMet KO mice (n=10) and WT (n=10) littermates. **(E)** Total insulin content measured in 50 islet equivalents (IE, 1 IE=125μm diameter islet) from PancMet KO (n=6) and WT (n=6) mice. **(F)** Glucose-stimulated insulin secretion measured in isolated islets from PancMet KO and WT mice in 30min static incubations. Results are means±SE of 4 experiments in triplicate. Islets were isolated from 4 mice per group. No significant differences were found between both types of mice in any of these parameters, although a trend in PancMet KO mice to display lower non-fasting blood glucose was observed [p=0.093 in (A) and p=0.070 in (D)].



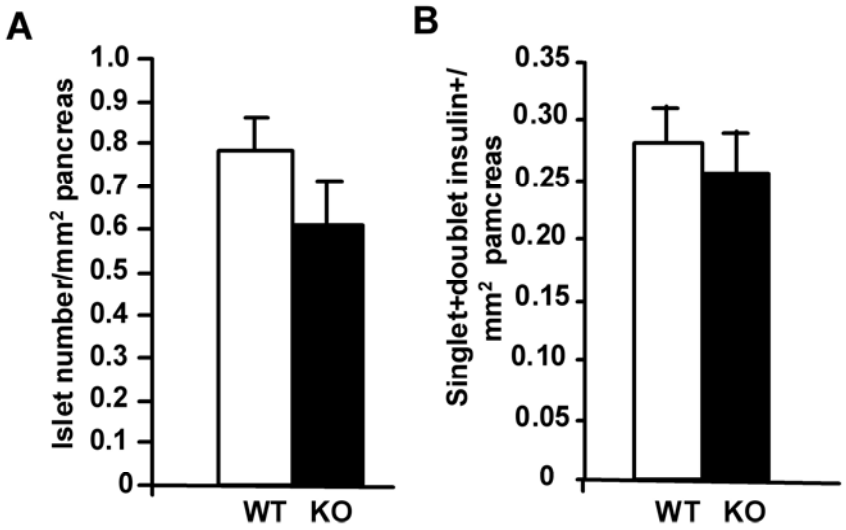
Supplementary Figure 2. Beta cell homeostasis is unchanged in adult PancMet KO mice. **(A-B)** Representative photomicrographs of pancreatic sections of PancMet KO and WT mice stained for insulin (brown). Scale bar=200μm. **(C)** Beta cell mass, **(D)** pancreatic weight, **(E)** pancreatic insulin content, and **(F)** islet number per pancreatic area in PancMet KO (n=6) and WT (n=6) mice . **(G)** Beta and **(H)** ductal cell proliferation in PancMet KO (n=6) and WT (n=6) littermates assessed by BrdU and insulin staining of pancreatic sections obtained from these mice. **(I)** Alpha cell/beta cell and **(J)** delta cell/beta cell ratios per islet were measured in pancreatic sections from PancMet KO (n=6) and WT (n=6) littermates stained for glucagon and insulin or somatostatin and insulin.



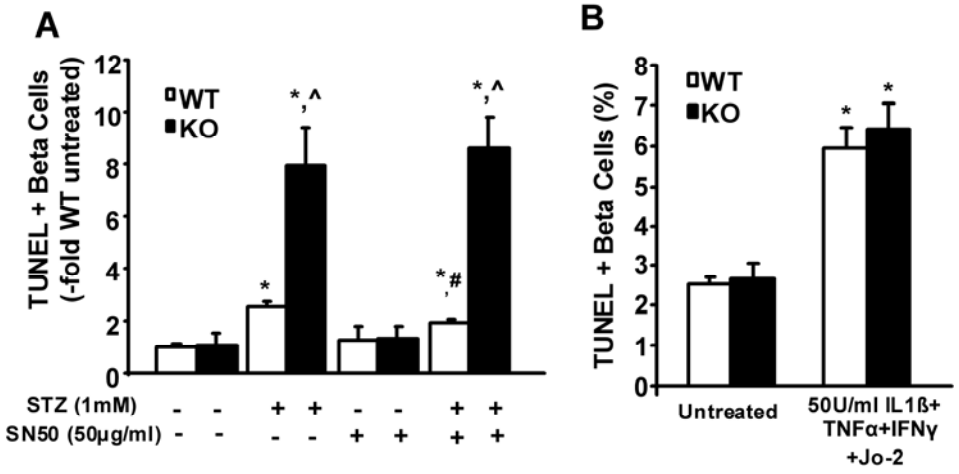
Supplementary Figure 3. (A-C) Insulin, **(D-F)** glucagon, **(G-I)** somatostatin and c-met co-staining in mouse islets. Representative microphotographs of islets in pancreas sections of WT mice stained for islet hormones (green) and c-met (red). Merge of both images (yellow) reveals co-localization of c-met and islet hormones in the islet. Scale Bar=25μm.



Supplementary Figure 4. Islet number and neogenesis are not significantly different in PancMet KO mice compared to WT littermates following treatment with MLDS. **(A)** Islet number, and **(B)** singlet and doublet insulin-positive cells in the pancreas as a potential marker for beta cell neogenesis, were measured per unit of pancreatic area in sections from PancMet KO (n=5) and WT (n=10) littermates 20 days after MLDS.



Supplementary Figure 5. (A) Effect of the NF-kB activation inhibitor SN-50 (50µg/ml) in beta cell death induced by 1mM STZ in WT and PancMet KO beta cells, assessed as in Fig. 6A-D. Three experiments were performed in duplicate and results are means±SE. *P<0.05 vs untreated, ^P<0.05 vs WT and #P<0.05 vs WT treated with cytokines alone. **(B)** Effect of the Fas agonist Jo-2 in beta cell death in primary cell cultures from WT and PancMet KO mouse islets. Cell were treated with 50U/ml IL-1ß, 1000U/ml TNF-α and 1000U/ml IFN-γ for 12h and then 0.2µg/ml Jo-2 (BD-Pharmingen, Franklin Lakes, NJ) was added for an additional 12h period. Four experiments were performed in duplicate and results are means±SE. *P<0.05 vs untreated. No significant differences were found between treated WT and PancMet KO beta cells.



Supplementary Figure 6. HGF does not protect PancMet KO mouse beta cells against cytokine-induced cell death. Quantitation of TUNEL-positive beta cell nuclei in four experiments performed in duplicate in WT and PancMet KO islet cell cultures treated with or without 25ng/ml HGF and 50U/ml IL-1ß, 1000U/ml TNF-α and 1000U/ml IFN-γ for 24h. Results are means±SE. *P<0.05 vs untreated ^P<0.05 vs WT and #P<0.05 vs WT treated with cytokines alone.