SUPPLEMENTARY DATA

Supplementary Figure 1. Reduced number of islets in p44tg mice. Islet number was counted for at least 3 pancreas sections per mouse from 3 independent mice at each age in each group. * p<0.05 for p44tg versus control mice. # p<0.05 for 3 versus 12/14 month-old control mice.

Supplementary Figure 2. Normal β-cell proliferation in p44tg mice prior to 2 months of age. (A) Triple co-immunostaining for insulin (blue), somatostatin (green) and glucagon (red) in pancreas sections from control and p44tg mice at 2 months of age as described in Methods. Two representative islets for each group at magnification 40x are presented. (B) β-cell proliferation was quantified by co-immunostaining for pHH3, insulin, and DAPI in pancreas sections from Control and p44tg mice at 2 months of age as described in Methods.
Supplementary Figure 3. No significant increase in apoptosis in p44tg islets with age. β-cell apoptosis was quantified with TUNEL and co-immunostaining for insulin, and DAPI in pancreas sections from Control and p44tg mice at 3 and 14 months of age as described in Methods. (A) A representative islet for each group at magnification 40x are presented. (B) Quantification of TUNEL+ β-cell expressed in % of total β-cells. Arrows point to TUNEL+ cells. ND: not detectable.
Supplementary Figure 4. No significant difference in proinflammatory cytokine levels in serum, liver and white adipose tissue (WAT) of p44tg mice. (A) Proinflammatory cytokine levels were measured in serum of control and p44tg mice at 2 months versus 4/5 months of age by Luminex from Millipore following the manufacturer's instructions. (B) Real time RT-PCR on RNA extracted from liver (upper panel) and WAT (lower panel) of 2 month-old control and p44tg mice. Results are normalized to TBP and expressed relative to control mice.
Supplementary Figure 5. Gene expression in liver and white adipose tissue (WAT) of p44tg mice. Real time RT-PCR on RNA extracted from WAT (A) and liver (B) of 2 and 16 month-old control and p44tg mice. Results are normalized to TBP and expressed relative to control mice. *, p<0.05 p44tg versus control mice at 17 months.
Supplementary Figure 6. Age-dependent increase in p16 and p19 gene expression in p44tg islets. Real time RT-PCR on RNA extracted from islets of 3 and 10/12 month-old control and p44tg mice. Results are normalized to TBP and expressed relative to control mice. * p<0.05 for p44tg versus control mice.
Supplementary Figure 7. Decreased osteocalcin level is not related to hypoinsulinemia in p44tg mice. (A) Osteocalcin level was measured in serum of control and p44tg mice at 2 months versus 4/5 months of age by Luminex from Millipore following the manufacturer's instructions. (B) Real time RT-PCR on RNA extracted from islets of 3 and 10/12 month-old control and p44tg mice. Results are normalized to TBP and expressed relative to control mice.