Supplementary Figures and Table

Supplementary table 1. Primers used for the construction of MafA mutants

C277/293A	C277A-F	5’-gctacgcgcagtcggcccgcttcaagcgggt
	C277A-R	5’-acccgcttgaagcgggccgactgcgcgtagc
	C293A-F	5’-tggagagcgagaaggcccagctccagagcca
	C293A-R	5’-tggctctggag ctgggccttctcgctctcca
C42/59/69S	C42S-F	5’-ggccgagcgcttctcccaccgcctgccgc
	C42S-R	5’-gcggcaggcggtgggagaagcgctcggcc
	C59/69S-F	5’-cagcacgccctcctcctcggtgccctcttcgcccagcttctccgcacccagcc
	C59/69S-R	5’-ggctgggtgcggagaagctgggcgaagagggcaccgaggaggagggcgtgctg

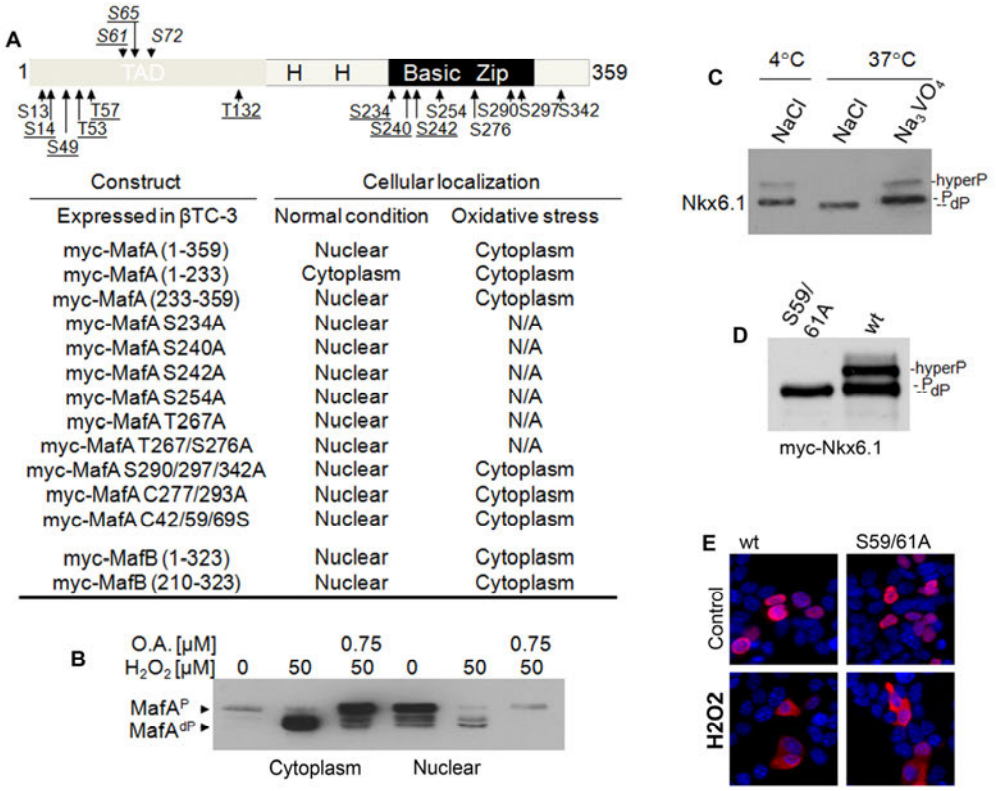

Figure s1. Dephosphorylation is not required for H_2O_2-induced MafA and Nkx6.1 cytoplasmic translocation. A) Summary of cellular localization analysis of myc-MafA and myc-MafB mutants in untreated and H_2O_2-treated βTC-3 cells. N/A: Not Analyzed. B) Okadiac acid (O.A.) prevents H_2O_2-induced MafA dephosphorylation, but not cytoplasmic translocation. βTC-3 cells were pre-treated with 0.75 μM O.A. before H_2O_2 treatment. C) In vitro dephosphorylation of Nkx6.1 in βTC-3 nuclear extract by 2U calf intestinal alkaline phosphatase. Immunoblotting showing that the mobility shift of Nkx6.1 was also inhibited by addition of the sodium orthovanadate (10 mM Na_3VO_4) phosphatase inhibitor. D) Blocking of myc-Nkx6.1 phosphorylation at S59 and S61 results in the disappearance of the hyperphosphorylated form and prevents the mobility shift on SDS-PAGE, but does not affect E) nuclear localization or cytoplasmic translocation under stress conditions. P, phosphorylated; dP, dephosphorylated; hyperP, hyperphosphorylated.

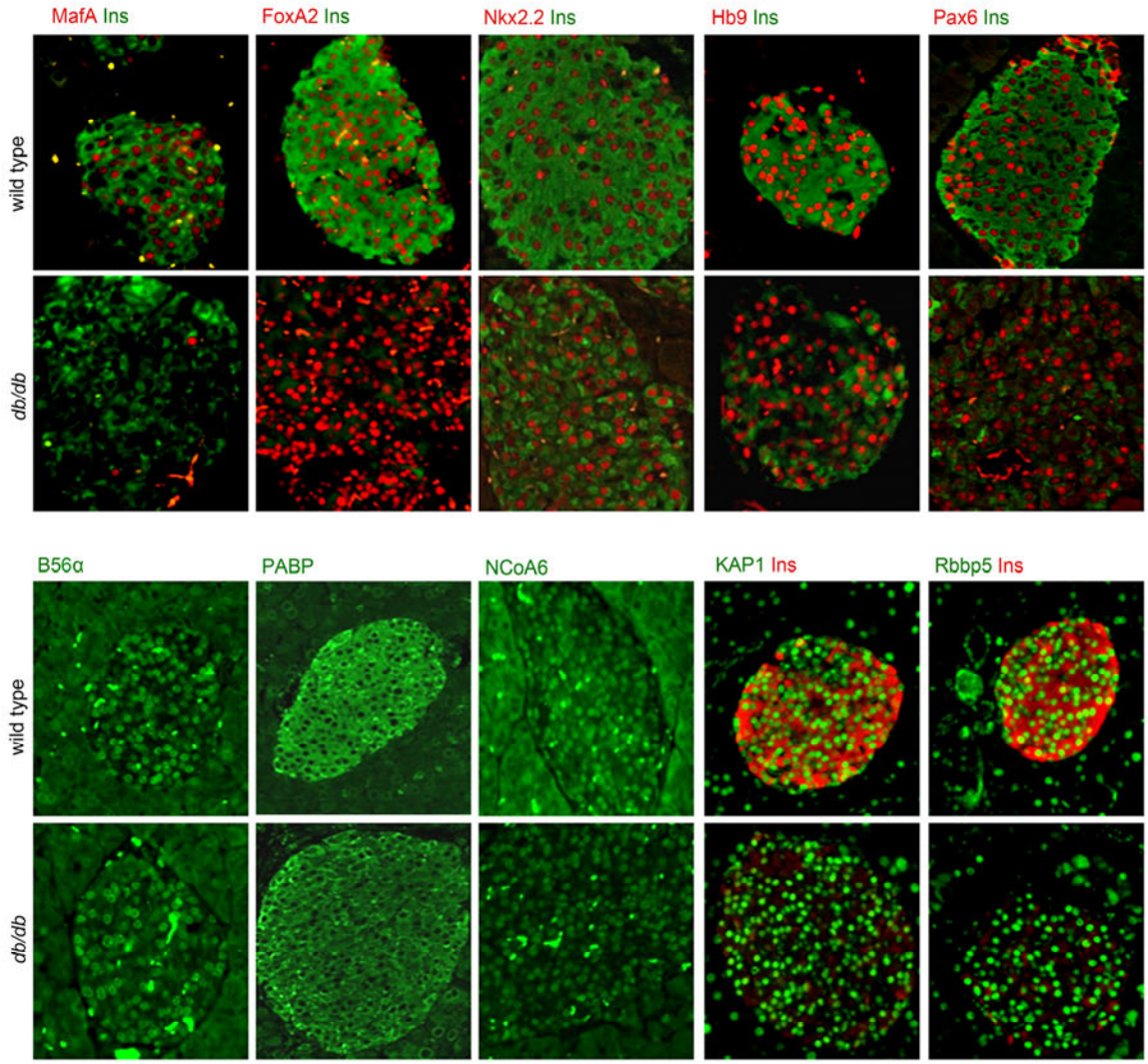

Figure s2. The nuclear levels of most islet-enriched regulators are unchanged under hyperglycemic conditions in the 10 week-old *db/db* islet. MafA immunostaining illustrates the subcellular localization change. B56α is a regulatory subunit of PP2A. PABP is poly-A binding protein. NCoA6, KAP1, and Rbbp5 are widely distributed nuclear regulators.

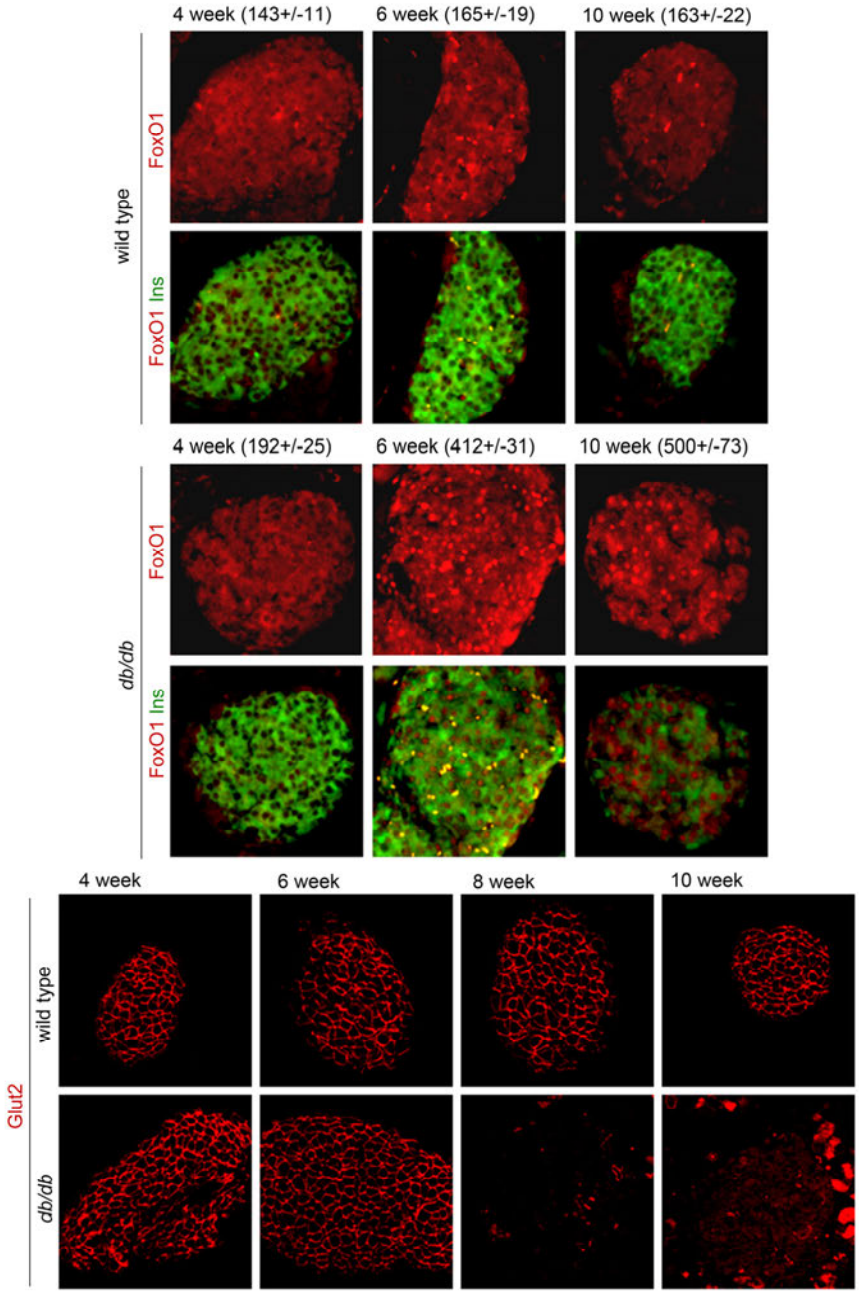

Figure s3. The change in FoxO1 nuclear content and Glut2 levels under hyperglycemic conditions in aging *db/db* mouse islets. The reduction in the Glut2 immunostaining signal closely parallels loss of MafA (Figure 7A).

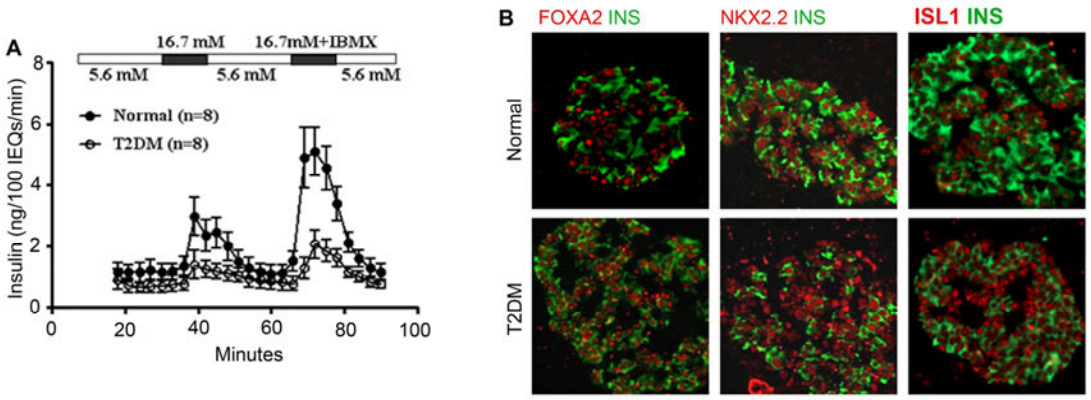

Figure s4. The insulin secretion response is severely blunted in human T2DM islets. A) Islet perifusion assays were performed on normal and T2DM islets. B) There was no apparent difference in the nuclear levels of the islet-enriched FOXA2, NKX2.2 and ISL1 transcription factors between normal and T2DM islets.

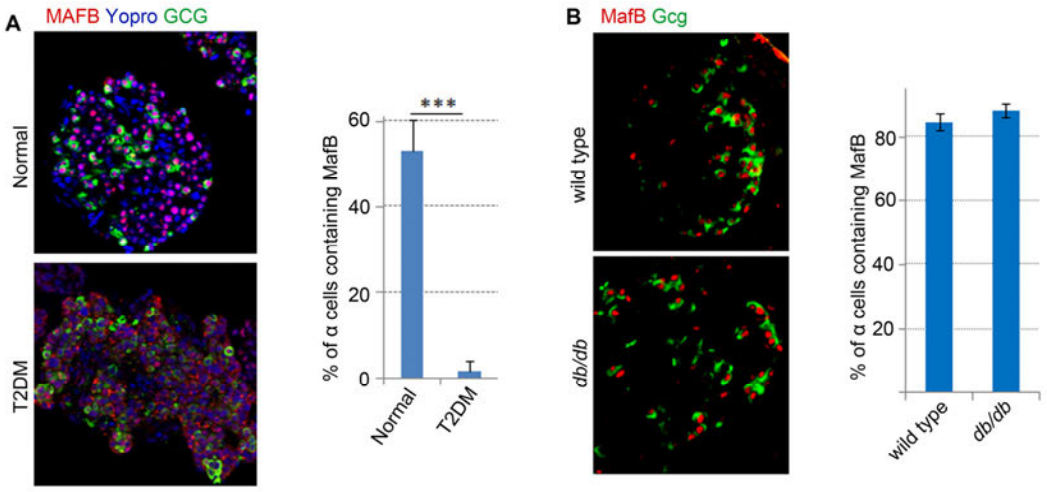

Figure s5. Islet α-cell MafB levels are only reduced in human T2DM, but not 10 week-old hyperglycemic *db/db* mice. MafB and Glucagon immunostaining in A) T2DM and B) *db/db* mouse islets. Quantification of the percentage of glucagon^{+} α-cells containing nuclear MafB is shown.