

## Supplemental Materials

### **SIRT1 Deacetylates FOXA2 and Is Critical for *Pdx1* Transcription and $\beta$ -Cell Formation**

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The following primers were used:

mPdx1 realF1	gtggatgaaatccaccaaag
mPdx1 real R1	gttcaacatcactgccagtc
mGlut2 real F	tgggctaatttcaggactgg
mGlut2 real R	gccaagtaggatgtgccaat
mPax6 real F	agtgaatgggaggagttatg
mPax6 real R	acttggacgggaactgacac
mNkx2.2 real F	ggtggagcgattggataaga
mNkx2.2 real R	tgccatcaacctttcatca
mMafA real F	ttcagcaaggaggaggtcat
mMafA real R	ctctggagctggcacttctc
Ins2 real F1	tttgtcaagcagcaccttg
Ins2 real R1	ggcttgaaggtcacctgctc
Ins1 real F1	tataaagctggtggcatcc
Ins1 real R1	gggaccacaaagatgctgtt
mGK-f1	aaagatgttgccgacctacg
mGK-R1	ccacgatgtgttccttet
18S(RATMUSHU) F	agtccctgccctttgtacaca
18S(RATMUSHU) R	cgatccgagggcctcacta
Sirt1 F	tttgaagctgttcgtggag
Sirt1 R	ggcgtggaggttttcagta

mPdx1 pF1	ttcgggatctggattgagtc
mPdx1 pR1	ccaagaaagcaaaccatgt
mPdx1 pF4	ttcttttgcaaagcacagc
mPdx1 pR4	caccccaggatgtttgetta
mPdx1 pF6	aggcttacagcgetgagtc
mPdx1 pR6	ctcctttcctcccagtc

## Supplementary Figure legends

**Supplementary Figure 1.** SIRT1 regulates PDX1 and its downstream genes in MIN6 cells. (A) qRT-PCR analysis reveals that overexpression of SIRT1 moderately elevated *Pdx1* mRNA levels. \*  $p < 0.01$ . (B) Western blot shows reduction of PDX1, GK, and GLUT2 due to knockdown of SIRT1.

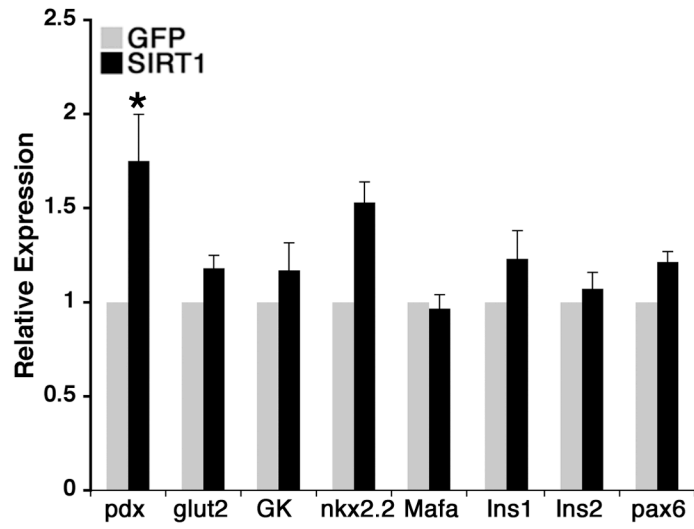
**Supplementary Figure 2.** Pancreas-specific deletion of *Sirt1* using a Cre-loxP-mediated approach. (A) Gene structure showing two loxP sites in intron 4 and 6 of the *Sirt1* gene and the deletion of exons 5 and 6 of *Sirt1* with Cre-loxP mediated recombination. (B) PCR analysis demonstrating *Sirt1* deletion specifically occurred in the pancreas. *Sirt1* floxed and deletion alleles are amplified using primers P1: 5-tccttgccacagtcactcac-3, P2: 5-catctaaactttgttgctgc-3 and P3: 5-acagtcccattcccatacc-3. The PCR product of the floxed allele (P1/P2) is about 592 bp and the deletion allele (P1/P3) is 610 bp. (C) Western blot shows the deletion efficiency of SIRT1 protein in different genotype animals. The corresponding blood glucose level is provided underneath the WB.

**Supplementary Figure 3.** Immuno-istochemistry Staining Demonstrates the Absence of Increased Inflammation in the Pancreas from *Sirt1*<sup>PKO</sup> mice. No obvious inflammatory change was detected by using the markers such as IL-1 $\beta$ , TNF- $\alpha$ , IL-6, CD3, F4/80, MPO and NF- $\kappa$ B.

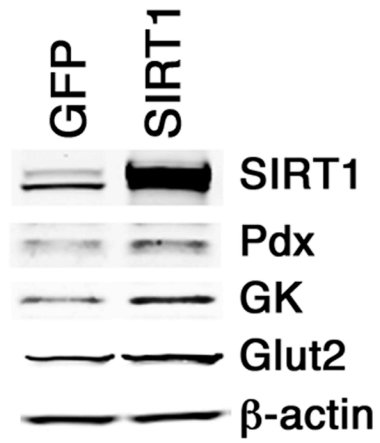
**Supplementary Figure 4.** Cell lineage analysis using molecular markers. (A) Immunofluorescent staining of  $\alpha$  cells (glucagon positive). (B) Immunofluorescent staining of  $\delta$  cells (somatostatin positive). (C) Immunohistochemistry staining of pp cells (Pancreatic Polypeptide positive).

Supplementary Figure 1

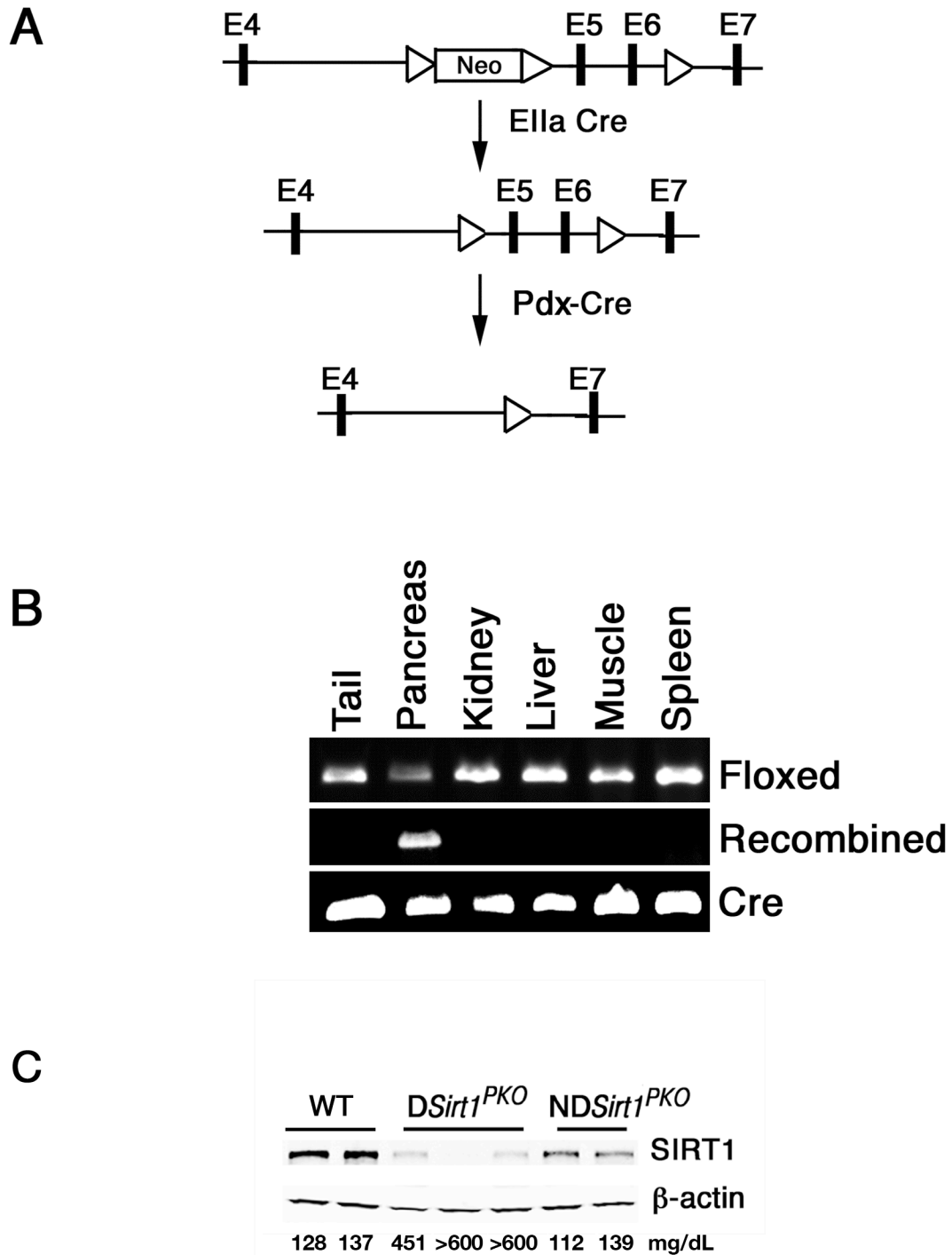
**A**



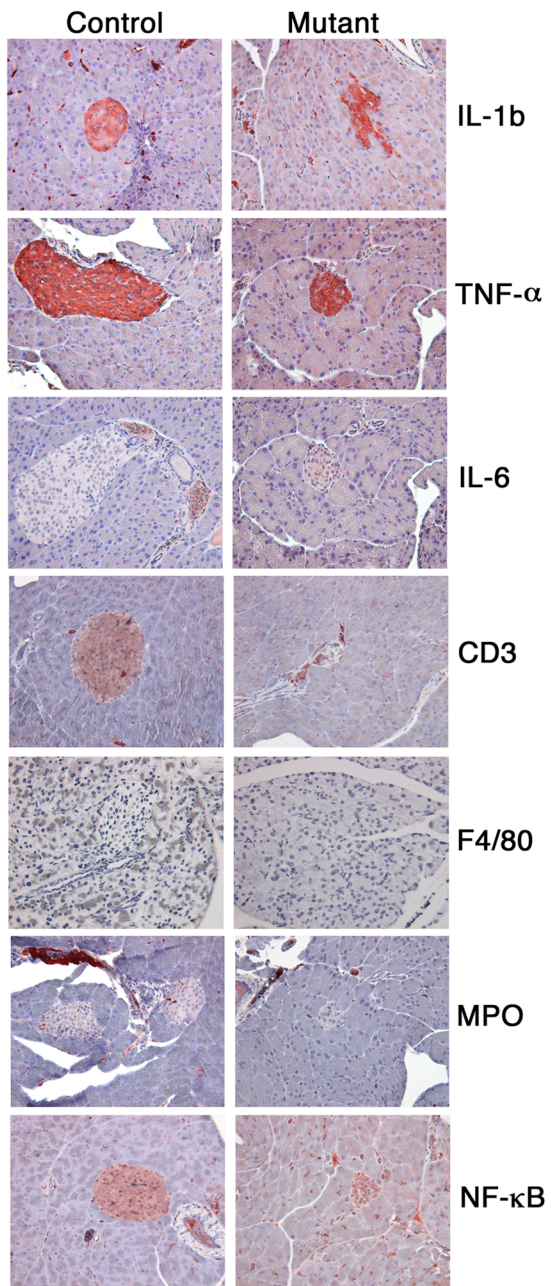
**B**



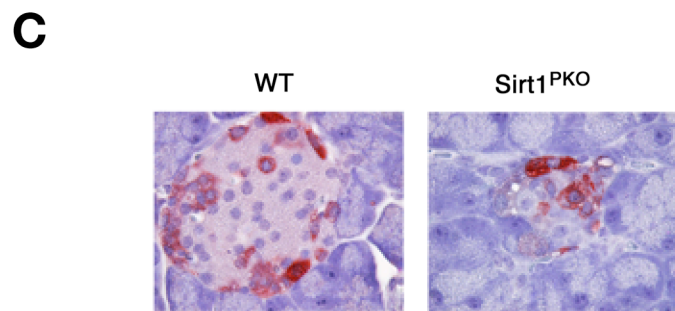
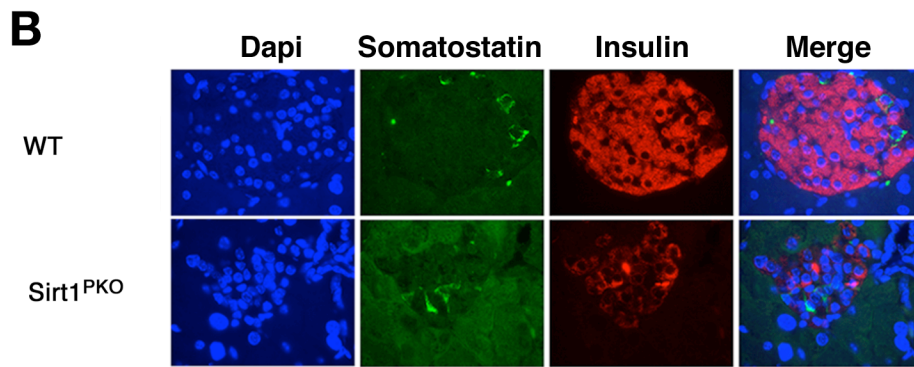
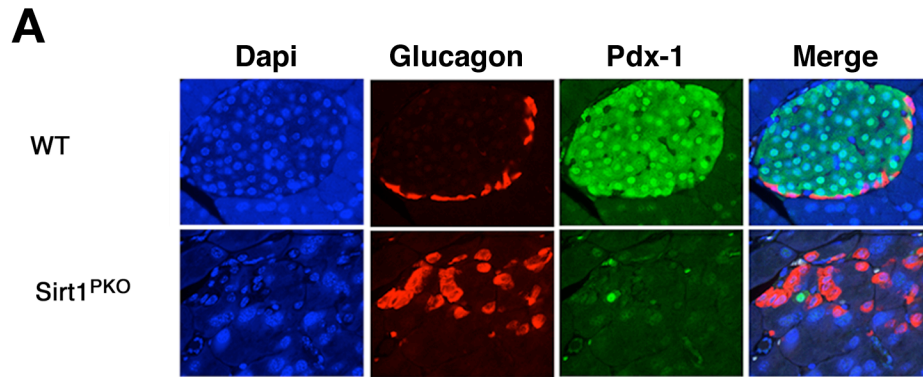
Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4





Supplementary Table 1

**A**  
***DSirt1<sup>PKO</sup>***

Ear Tag	Genotype	P15	P21	6-WEEK	8-WEEK	12-WEEK	16-WEEK
P820	CO/CO/PDX	126	533	>620	>620	>620	>620
P843	CO/CO/PDX	152	459	>620	>620	>620	>620
P846	CO/CO/PDX	184	466	197	192	210	>620
P818	CO/CO/PDX	150	201	171	501	>620	>620
P827	CO/CO/PDX	133	348	371	210	181	346
P822	CO/CO/PDX	121	189	220	316	315	546
P841	CO/CO/PDX	167	156	256	>620	>620	>620
P821	CO/CO/PDX	108	175	159	>620	>620	>620
P828	CO/CO/PDX	124	164	144	574	>620	>620
P845	CO/CO/PDX	137	91	141	258	240	229
P832	CO/CO/PDX	138	164	146	156	166	289
P837	CO/CO/PDX	135	134	185	187	191	205
P851	CO/CO/PDX	115	147	147	180	233	241
P834	CO/CO/PDX	104	104	159	123	142	269
<b>Average</b>	<b>CO/CO/PDX</b>	<b>135</b>	<b>238</b>	<b>253</b>	<b>370</b>	<b>386</b>	<b>462</b>

**B**  
**WT**

Ear Tag	Genotype	P15	P21	6-WEEK	8-WEEK	12-WEEK	16-WEEK
P672	CO/CO	133	166	133	128	122	129
P678	CO/CO	99	170	154	130	120	144
P676	CO/CO	118	174	143	164	137	123
P675	CO/CO	105	170	119	160	135	128
P674	CO/CO	115	144	129	169	120	123
P673	CO/CO	137	162	138	126	121	147
P635	WT/PDX	78	141	157	118	129	141
9027	CO/CO	144	158	134	140	78	123
9029	CO/CO	100	134	120	153	93	123
9028	CO/CO	153	173	152	176	111	133
P677	CO/CO	119	160	122	136	108	145
P645	CO/CO	94	173	149	137	121	122
<b>Average</b>	<b>CO/CO</b>	<b>116</b>	<b>160</b>	<b>138</b>	<b>145</b>	<b>116</b>	<b>132</b>

Fourteen *Sirt1<sup>PKO</sup>* animals (A) and twelve control mice (B) were followed for their glucose level during period of P15 to 4 months. Fourteen *Sirt1<sup>PKO</sup>* animals (A) exhibit hyperglycemia (>200 mg/dL) at various time points during this period. A glucose level of 620 mg/dL is the highest point beyond which, the glucose meter cannot give the exact number.