

Supplemental Materials

SIRT1 Deacetylates FOXA2 and Is Critical for *Pdx1* Transcription and β -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.

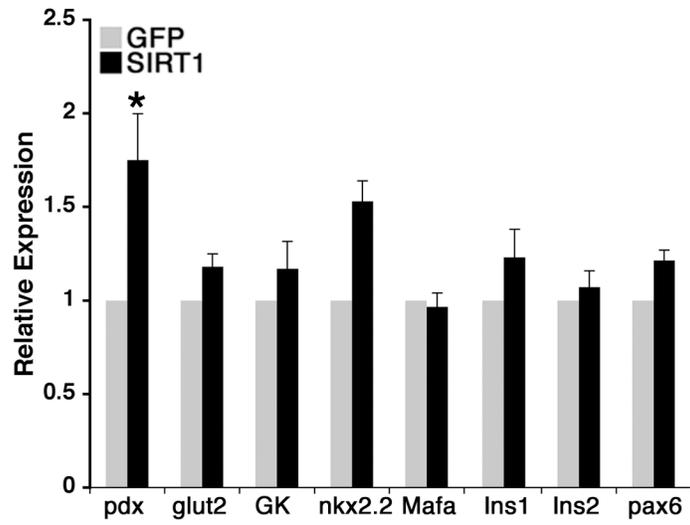
Supplementary Figure 2. Pancreas-specific deletion of *Sirt1* using a Cre-loxP-mediated approach. (A) Gene structure showing two loxP sites in intron 4 and 6 of the *Sirt1* gene and the deletion of exons 5 and 6 of *Sirt1* with Cre-loxP mediated recombination. (B) PCR analysis demonstrating *Sirt1* deletion 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*^{PKO} mice. No obvious inflammatory change was detected by using the markers such as IL-1 β , TNF- α , IL-6, CD3, F4/80, MPO and NF- κ B.

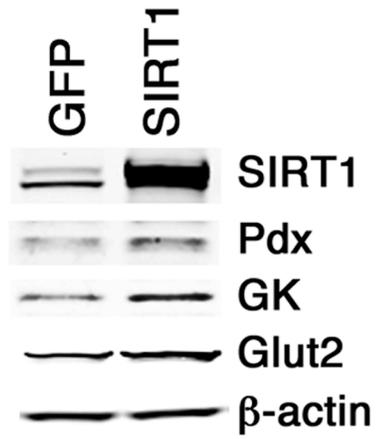
Supplementary Figure 4. Cell lineage analysis using molecular markers. (A) Immunofluorescent staining of α cells (glucagon positive). (B) Immunofluorescent staining of δ cells (somatostatin positive). (C) Immunohistochemistry staining of pp cells (Pancreatic Polypeptide positive).

Supplementary Figure 1

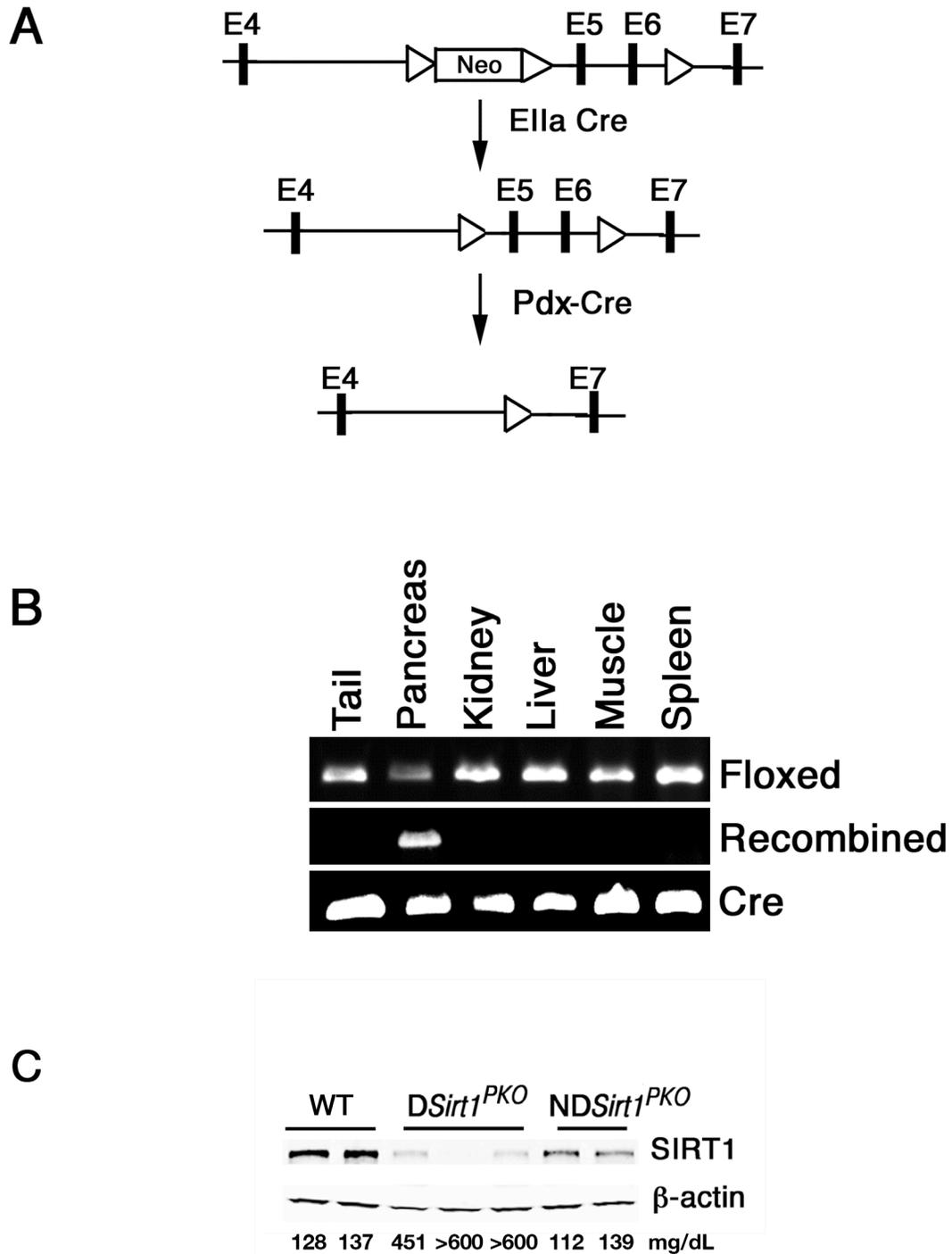
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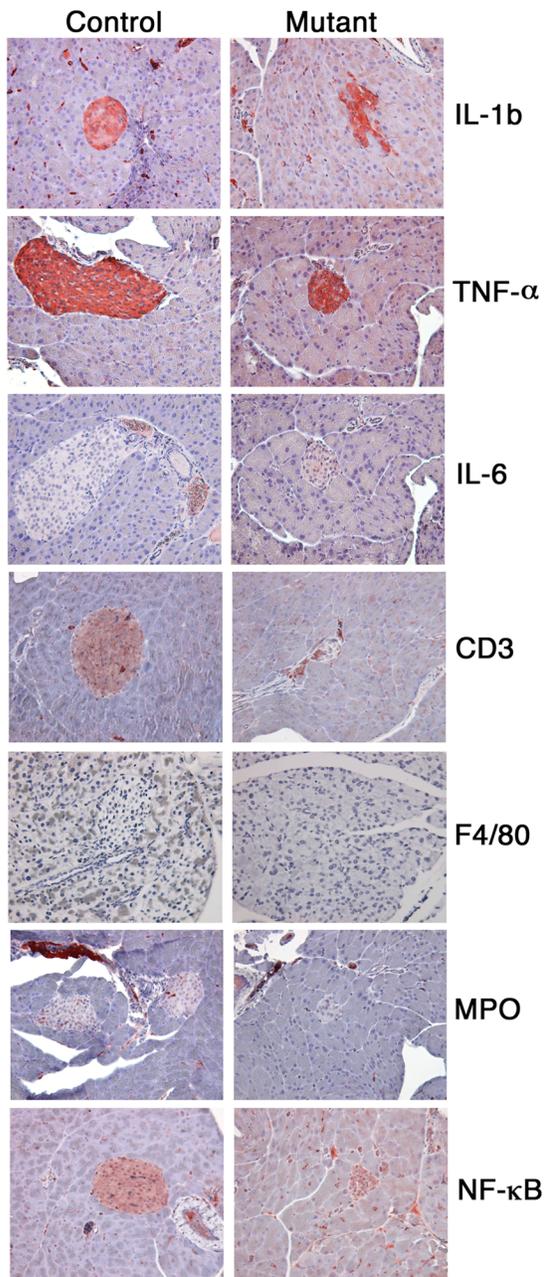
B



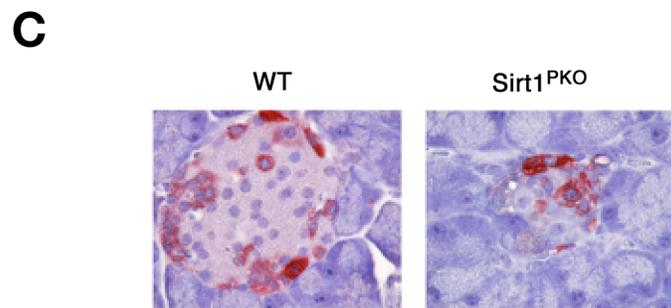
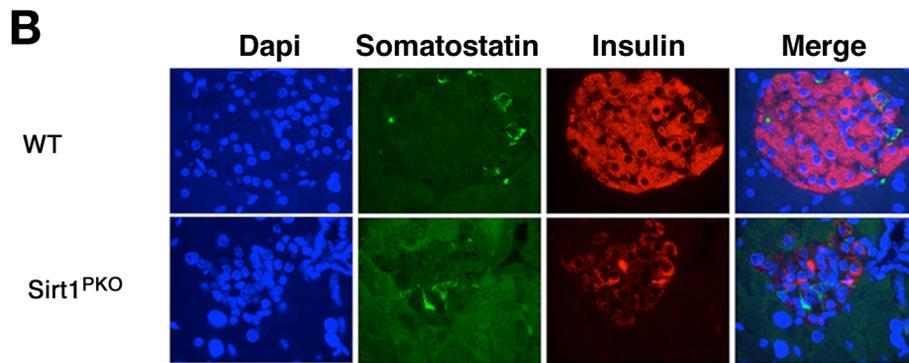
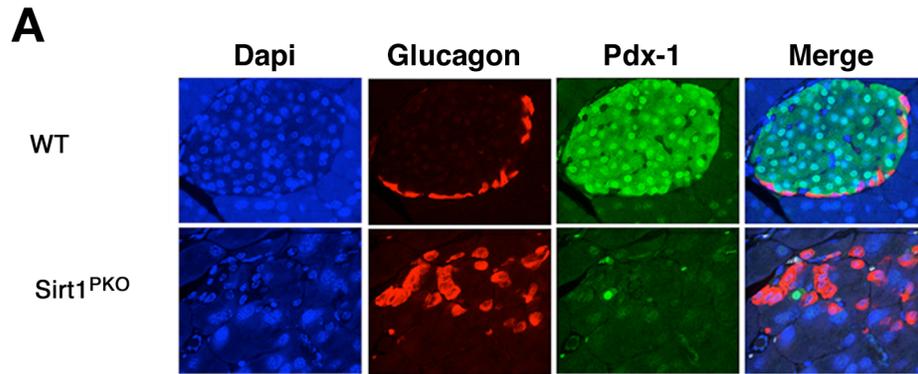
Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4



Supplementary Table 1

A
DSirt1^{PKO}

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
Average	CO/CO/PDX	135	238	253	370	386	462

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
Average	CO/CO	116	160	138	145	116	132

Fourteen *Sirt1^{PKO}* animals (A) and twelve control mice (B) were followed for their glucose level during period of P15 to 4 months. Fourteen *Sirt1^{PKO}* 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.