

SUPPLEMENTARY DATA

Supplementary Table 1. D-[U-¹⁴C]glucose and D-[5-³H]glucose metabolism, and ATP generation in Ncx1^{+/+} and Ncx1^{+/-} islet cells.

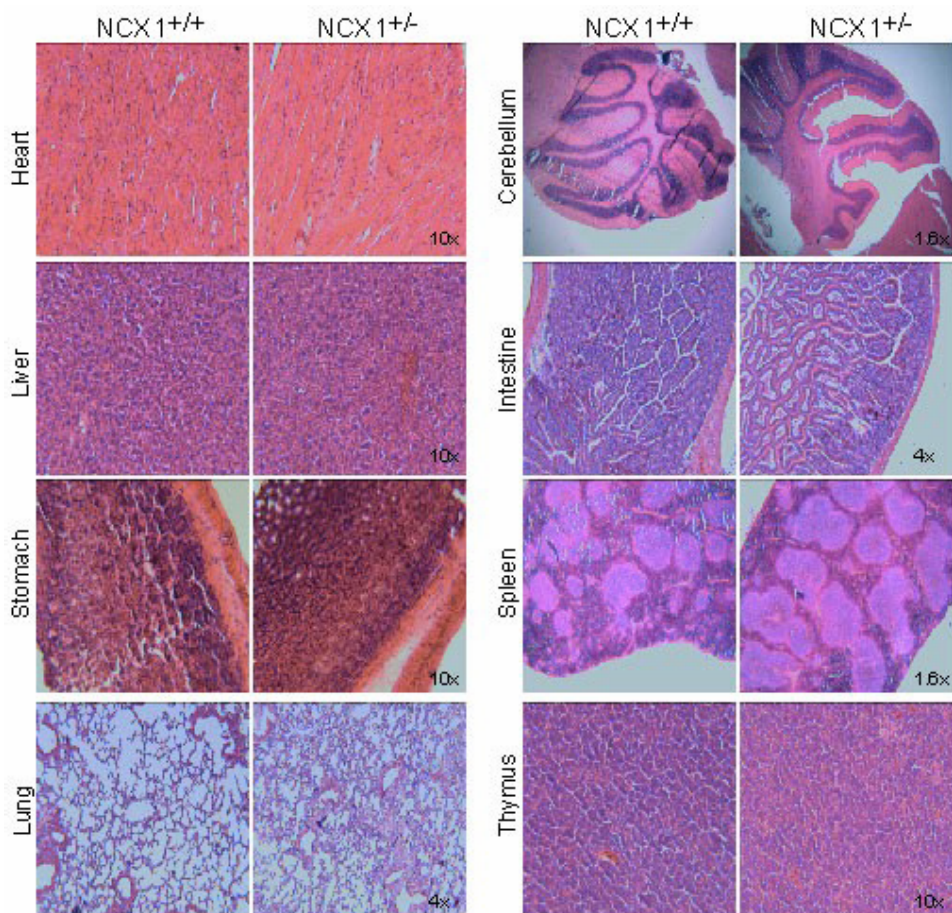
Cells	Ncx1 ^{+/+}		Ncx1 ^{+/-}	
	2.8 mM	16.7 mM	2.8 mM	16.7 mM
D-[U- ¹⁴ C]glucose oxidation	6.80 ± 0.77 (12) ^a	43.40 ± 3.16 (15)	10.34 ± 1.19 (25)	29.79 ± 2.69 (24)
D-[5- ³ H]glucose utilization	64.58 ± 6.40 (17)	293.95 ± 18.54 (19)	93.30 ± 7.76 (25)	305.53 ± 29.02 (21)
¹⁴ C0 ₂ / ³ H ₂ O ratio (%)	10.80 ± 1.19 (10)	16.32 ± 1.72 (15)	11.75 ± 1.12 (25)	11.07 ± 1.10 (21)
ATP generation ^b	363.10 ± 32.40 (10)	2135.10 ± 133.90 (15)	554.00 ± 53.7 (25)	1710.00 ± 148.80 (21)

^aAll results are expressed as pmol of D-glucose equivalent per 120 min and islet

^b(pmol/islet over 120 min)

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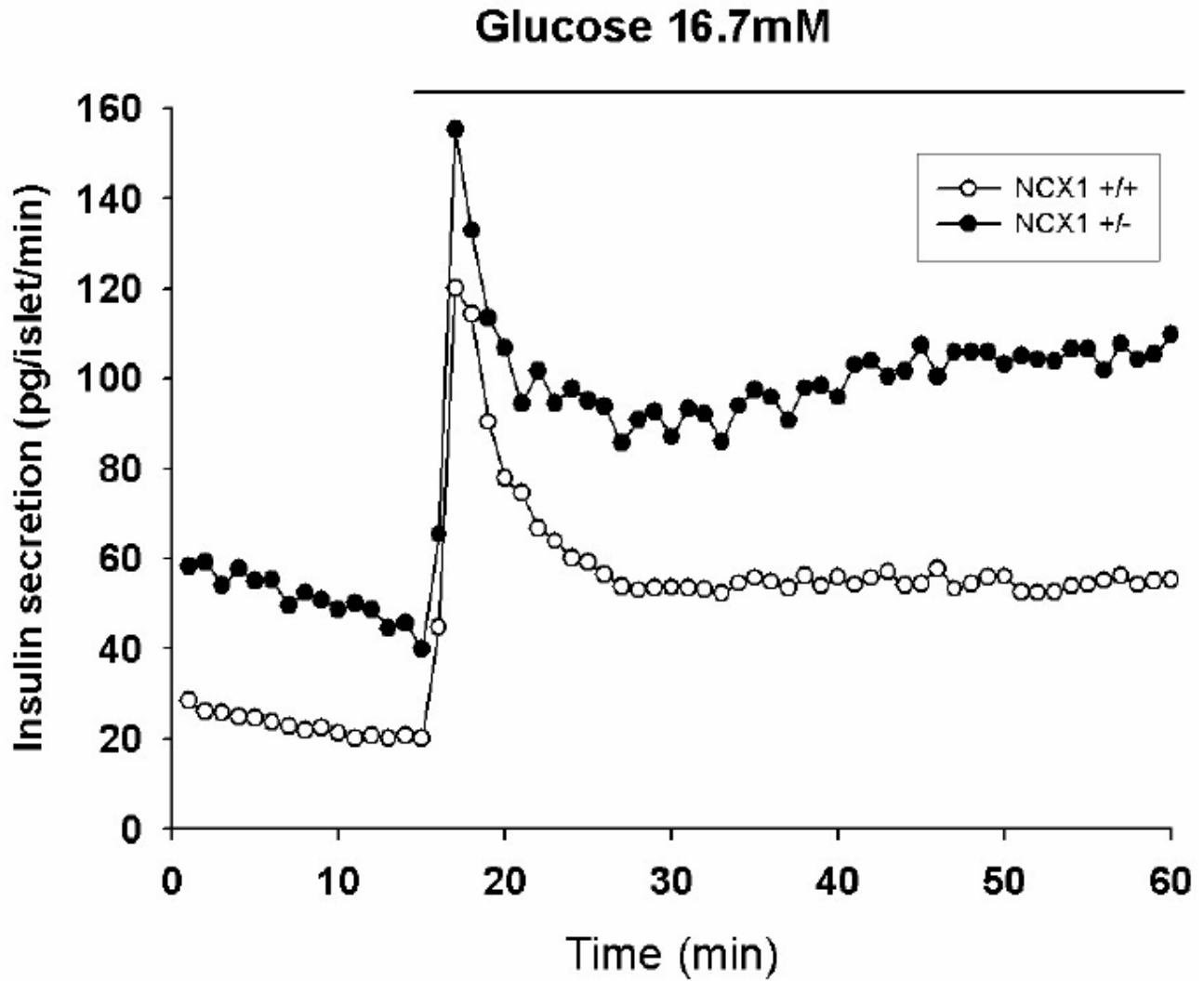
Supplementary Figure 1. Histological and histochemical analysis of main organs (brain, heart, lung, liver, spleen, stomach, intestine and thymus) of *Ncx1*^{+/+} and *Ncx1*^{+/-} mice.



SUPPLEMENTARY DATA

Supplementary Figure 2. Effect of Ncx1 heterozygous inactivation on glucose-induced insulin release

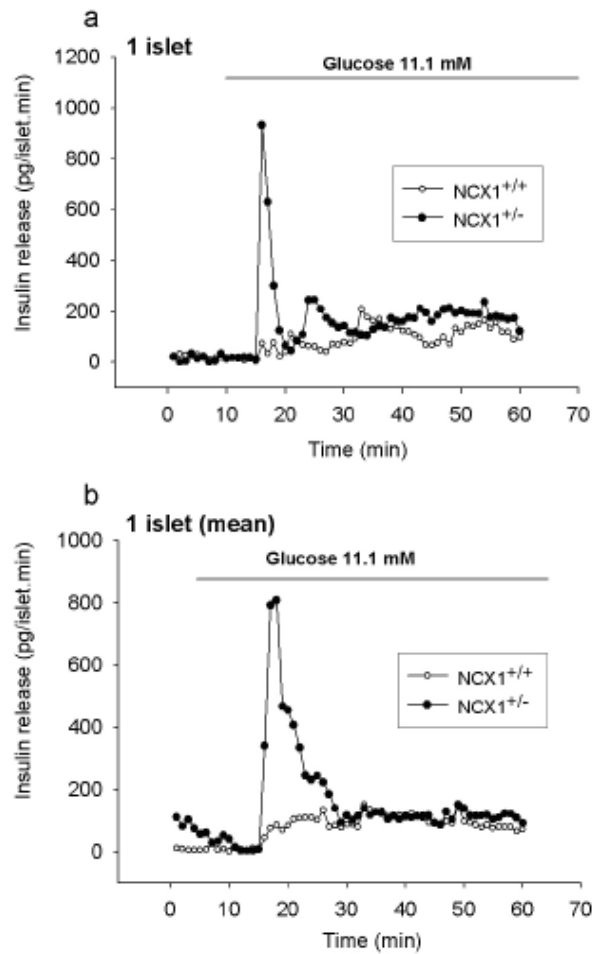
Effect of 16.7 mM glucose on insulin release from groups of 20 islets. Mean of 4 individual experiments in each case. The islets were from different mice.



SUPPLEMENTARY DATA

Supplementary Figure 3. Effect of Ncx1 heterozygous inactivation on insulin release from 1 single islet

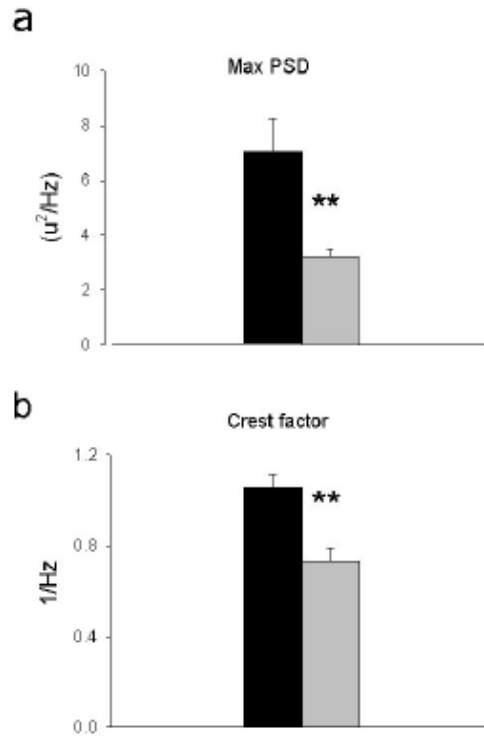
Representative experiment. (b) Mean of 4 experiments. The islets were from different mice.



SUPPLEMENTARY DATA

Supplementary Figure 4. Effect of Ncx1 heterozygous inactivation on 11.1 mM glucose-induced changes in $[Ca^{2+}]_i$

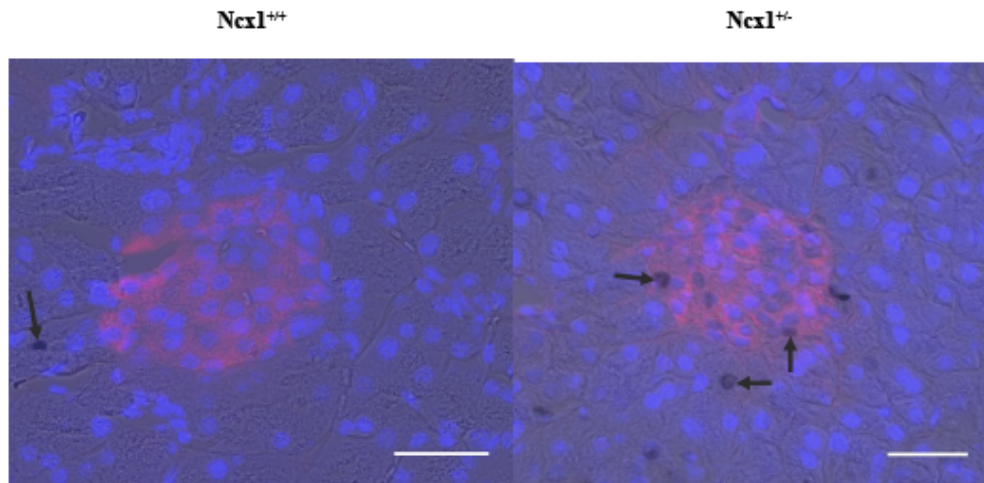
Power spectral density (PSD) analysis of the $[Ca^{2+}]_i$ oscillations of the curves illustrated in Figure 2. (a) maximum of the peak of power spectra and (b) crest factor (ratio of peak/integral), mean \pm SEM of 5 individual traces, in each case. ** $P < 0.003$ vs $Ncx1^{+/+}$ islets. Black: $NCX1^{+/+}$, grey : $NCX1^{+/-}$ islets.



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Supplementary Figure 5. Effect of Ncx1 heterozygous inactivation on β -cell proliferation rate

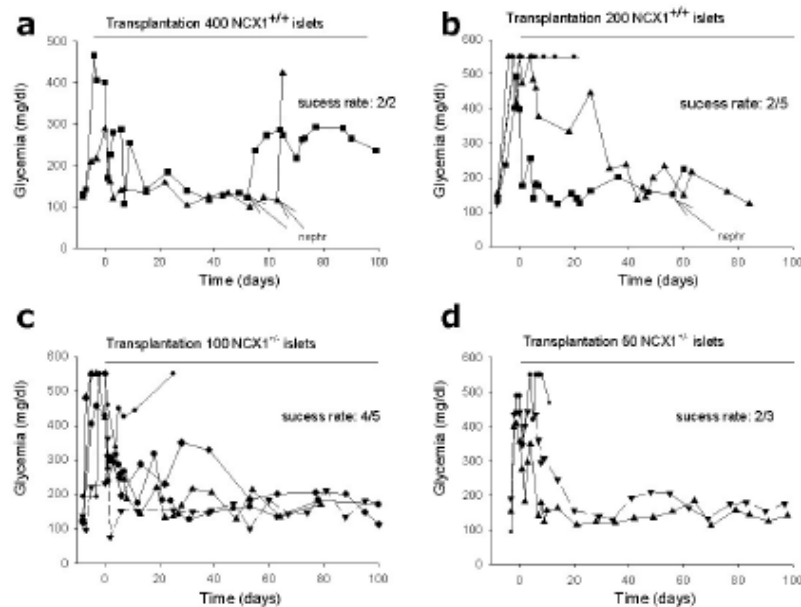
Representative micrographs of proliferation rate measurement from 5 to 6 pancreases per genotype. The arrows show BrdU positive nuclei in endocrine (β -cells coloured in red) and exocrine tissue. Sections were double stained for BrdU in black (immunoperoxidase) and for β -cells in red (immunofluorescence) and counterstained with DAPI (blue nuclei). The micrographs were from pancreatic sections of 12 weeks old Ncx1^{+/+} (left panel) and Ncx1^{+/-} (right panel) mice. Scale bar = 0.2 μ m.



SUPPLEMENTARY DATA

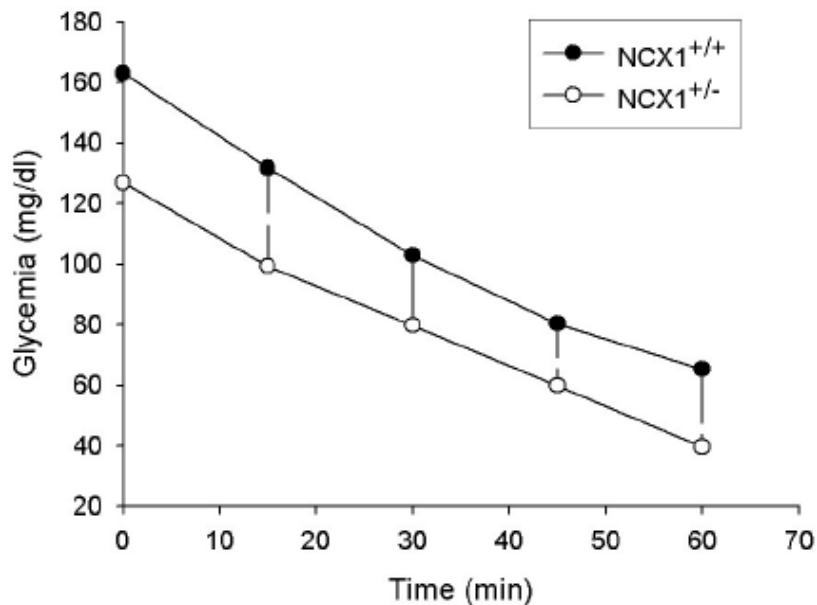
Supplementary Figure 6. Effect of Ncx1 heterozygous inactivation on the ability of islets transplantation to cure diabetes

Effect of transplanting grafts of (a) 400, (b) 200, (c) 100 and (d) 50 islets from Ncx1^{+/+} or Ncx1^{+/-} mice on non-fasting blood glucose levels. The success rate of diabetes cure (blood glucose level <220 mg/dl) was 2/2 and 2/5 for 400 and 200 Ncx1^{+/+} islet, respectively, and 4/5, 2/3 for 100 and 50 islets Ncx1^{+/-} islets, respectively.



Supplementary Figure 7. Effect of Ncx1 heterozygous inactivation on intraperitoneal insulin sensitivity test.

Insulin was injected intraperitoneally at a dose of 0.52 U/ Kg body weight, in the fasting state (2h). n = 5 in each case.



SUPPLEMENTARY DATA

Supplementary Figure 8. Effect of Ncx1 heterozygous inactivation on ER Ca²⁺ content.

Effect of thapsigargin (2 μ M) on [Ca²⁺]_i in Ncx1^{+/+} and Ncx1^{+/-} islets. Mean of 6 individual experiments in each case. The period of exposure to thapsigargin is indicated by a bar above the curves.

