Supplemental Figure Legends

Supplemental Figure 1. Pancreatic immunostaining reveals detection of GATA4 but unreliable detection of GATA6 in primary islets. (a) Immunostaining for GATA4 (white) in *Gata4* control mice. (b) Immunostaining for GATA4 (white) in β-cell inducible *Gata4* knockouts.

Supplemental Figure 2. β-cell inducible deletion of *Gata4* and *Gata6* is efficient. (a) Schema indicating β-cell inducible deletion of *Gata4* or *Gata6*. (b) RT-PCR of cDNA preps from *Gata4* knockout and control islets one week following deletion. (c) Amplification of *Gata4* genomic DNA from equivalent knockouts and controls. (d) RT-PCR of cDNA preps from *Gata6* knockout and control islets one week following deletion. All data are reported as mean ± standard error for 4-5 biological replicates per condition.

Supplemental Figure 3. Several physical and morphometric measures are unaltered following inducible *Gata* deletion. (a) Schema indicating timing of deletion. (b) Measurements of weight change, blood glucose, β-cell area, mass and proliferation are shown for cohorts of at least 4 mice per condition. Data are expressed as mean ± standard error.

Supplemental Figure 4. β-cell inducible *Gata4* or *Gata6* deletion does not severely impact glucose homeostasis. (a) Schema indicating timing of *Gata4* deletion and washout followed by glucose tolerance testing. (b) Glucose tolerance tests from β-cell inducible *Gata4* knockouts and controls. Data are reported as mean ± standard error for 11 knockouts and 5 controls. (c) Schema indicating timing of β-cell inducible *Gata4* or *Gata6* deletion followed by high fat feeding. (d) Glucose tolerance tests from β-cell inducible *Gata4* (left) or *Gata6* (right) mice fed high fat diet for the indicated time. Data

are reported as mean ± standard error for 3 knockouts and 4 controls (*Gata4* deletion) and 7 knockouts and 2 controls (*Gata6* deletion).

Supplemental Figure 5. β-cell inducible *Gata4 Gata6* compound deletion impairs β-cell survival. (a) Schema indicating timing of *Gata4 Gata6* deletion and high fat feeding. (b) Quantification of intra-islet TUNEL positive cells for high fat-fed β-cell inducible *Gata4 Gata6* double knockouts and controls, harvested 11 weeks following deletion. Pancreata from 5 mice per condition (>10,000 β-cells) were machine counted and curated by hand. (c) β-cell mass measurements from high fat-fed β-cell inducible *Gata4 Gata6* double knockouts. 8-12 pancreas sections per mouse, 5 mice per condition were analyzed (d) Glucose tolerance tests from high fat-fed β-cell inducible *Gata4 Gata6* double knockouts. Data are reported as mean ± standard error for 10 knockouts and 5 controls.

Supplemental Figure 6. (a) Schema indicating timing of β-cell inducible *Gata4* deletion followed by gene expression studies. (b) RT-PCR of islet cDNA from β-cell inducible *Gata4* (left) and *Gata6* (right) knockouts. Several genes related to programmed cell death were chosen for analysis. Data are reported as mean ± standard error for 4-5 biological replicates per condition. (c) Schema indicating timing of β-cell inducible *Gata4* deletion followed by low dose STZ treatment. (d) Quantification of intra-islet TUNEL positive cells in *Gata4* deficient islets and controls following treatment with low dose STZ. Note, plotted next to untreated knockouts and control mice from (2c). Pancreata from 4-5 mice per condition (>10,000 β-cells) were machine counted and curated by hand.

Supplemental Figure 7. Thapsigargin induces a robust transcriptional response in β-cells. (a) RT-PCR analysis of cultured wildtype islets treated with 1 uM thapsigargin or DMSO control for various incubation times. Experiments performed in triplicate, with ~30 islets per batch. Data are reported as mean ± standard error.

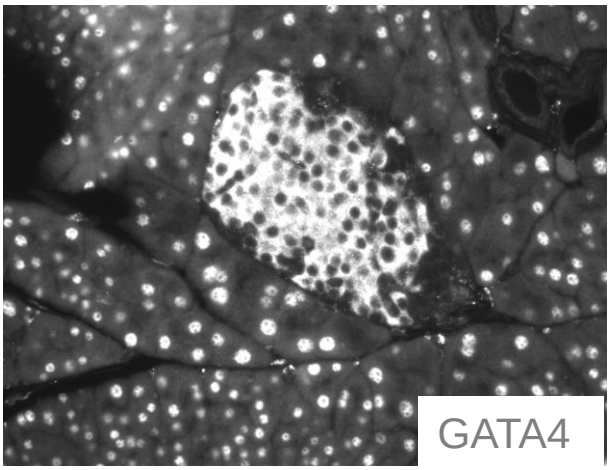
Supplemental Figure 8. β-cell inducible *Gata4* deletion does not affect calcium homeostasis. (a) *Gata4* control (top) and knockout (bottom) islet calcium measurements in response to perifusion in a glucose step gradient. Data are reported as mean ± standard error for 5 replicates.

Supplemental Figure 9. *Gata4* deletion results in a heterogeneous population of sub-cellular abnormalities in β-cells. A range of raw electron micrographs from control (a) and β-cell inducible *Gata4* knockouts (b). Arrows indicated endoplasmic reticulum, arrowheads indicate mitochondria. Scale bars represent 500nM.

Supplemental Table 1. Genotyping and RT-PCR primers used in this study. (a) Forward primer, reverse primer, and probe (with 5' and 3' modifications) used in gene expression and genotyping experiments.

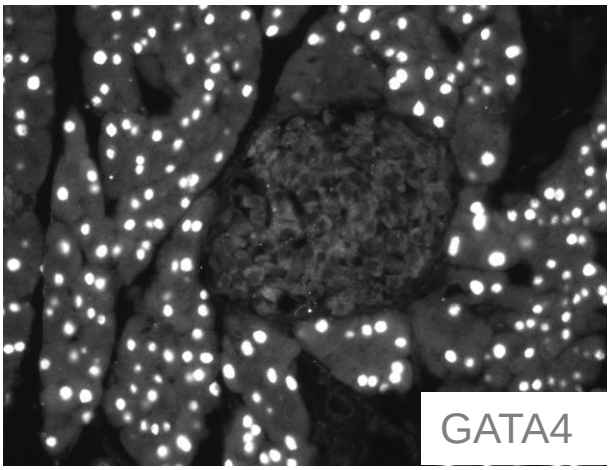
a

Gata4 Control

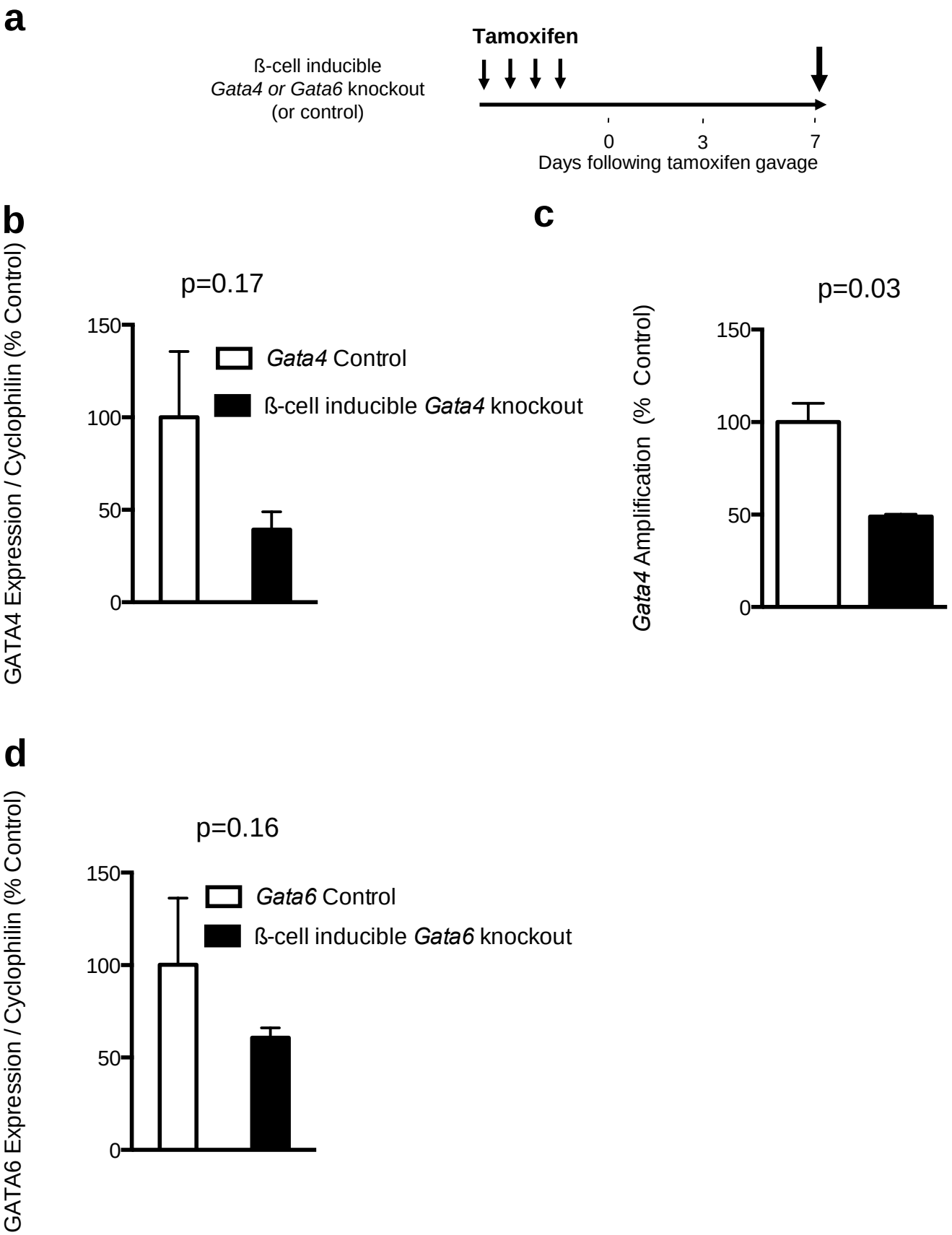


b

ß-cell inducible *Gata4* knockout

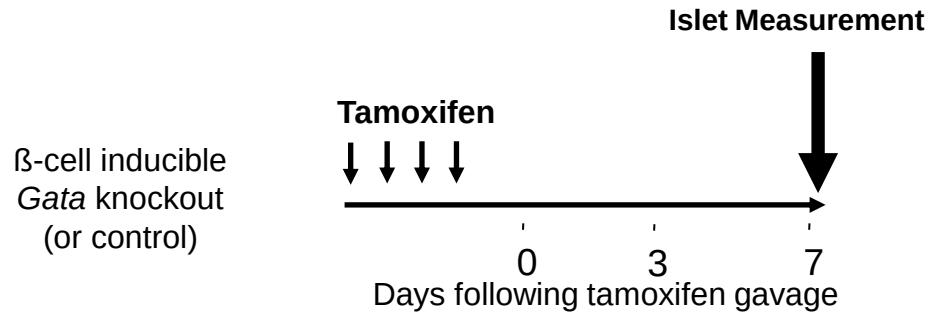


Supp Figure 1, Sartori et al



Supp Figure 2, Sartori et al

a

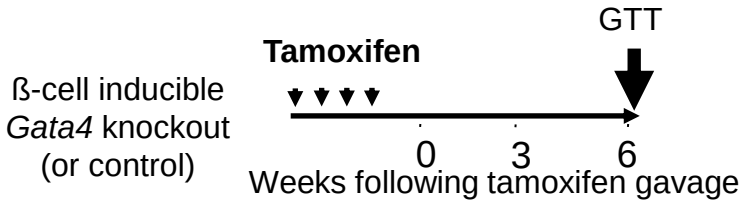


b

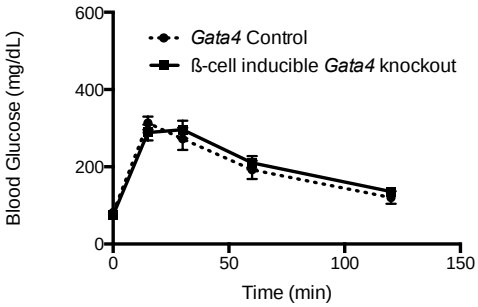
		Physiological Observations					Islet Measurements		
Group		**Weight (g)**	**Weight at harvest**	**Blood glucose (mg/dL)**	**Blood glucose at harvest**	**ß-cell area (%)**	**ß-cell mass (mg)**	**ki67+ ß-cells (%)**	**IDU + ß-cells (%)**
***Gata4* control (*Gata4* loxP/loxP)**	average	25.02	22.73	158.33	141.5	0.48	0.12	0.95	4.04
	std error	2.44	2.08	9.85	10.6	0.05	0.01	0.34	0.87
ß-cell Inducible *Gata4* Knockout (*Gata4* loxP/loxP Ins2-CreERT)	average	27.03	24.8	169.14	156.57	0.59	0.12	1.43	2.93
	std error	2.05	1.83	13.9	13.25	0.05	0.04	0.39	0.77
***Gata6* control (*Gata6* loxP/loxP)**	average	29.90	26.43	135.25	128.75				
	std error	1.94	2.11	12.13	3.82				
ß-cell Inducible *Gata6* Knockout (*Gata6* loxP/loxP Ins2-CreERT)	average	28.33	26.72	129.00	140.00				
	std error	2.04	6.76	2.10	10.16				
***Gata4* control (*Gata4* loxP/loxP)**	average	21.58	22.87	155.33	124.17				
	std error	1.82	1.81	15.27	8.21				
Whole Body Inducible *Gata4* Knockout (*Gata4* loxp/loxp*Ubc-CreERT2)*	average	20.88	22.82	144.20	155.60				
	std error	1.59	1.70	11.97	13.07				

Supp Figure 3, Sartori et al

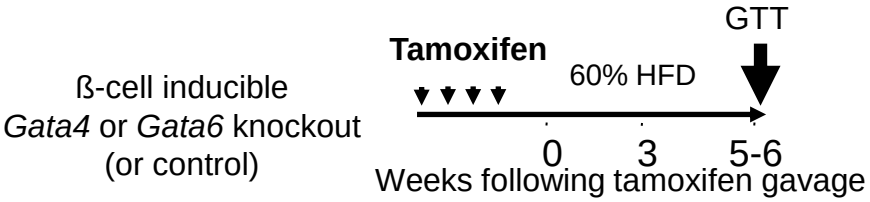
a



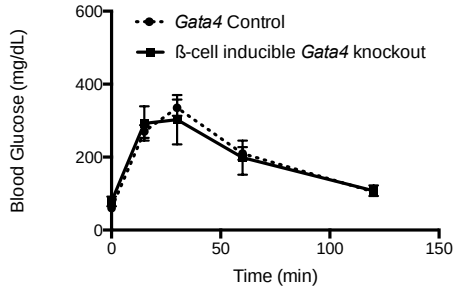
b

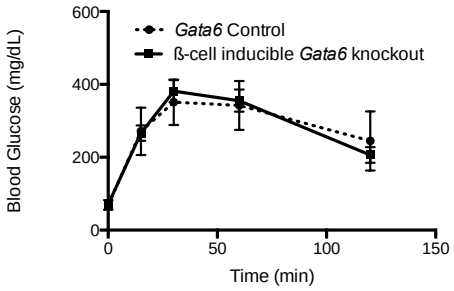


c

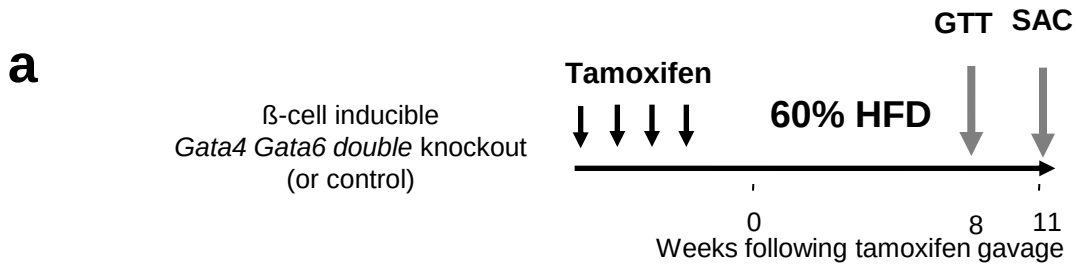


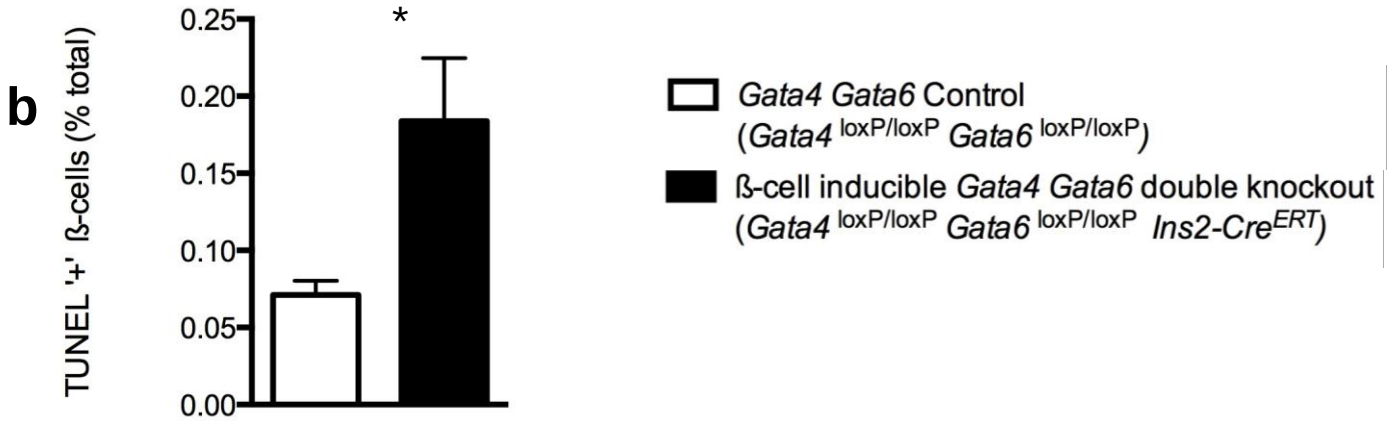
d

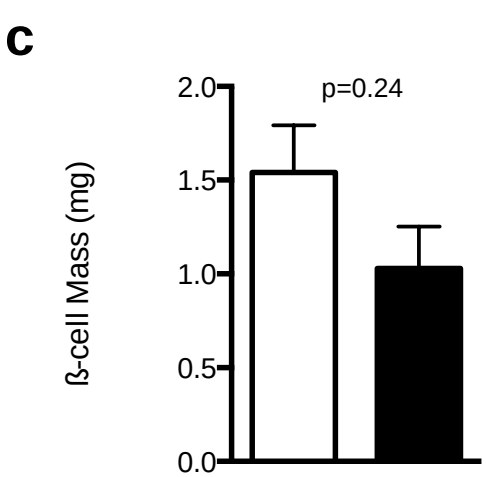


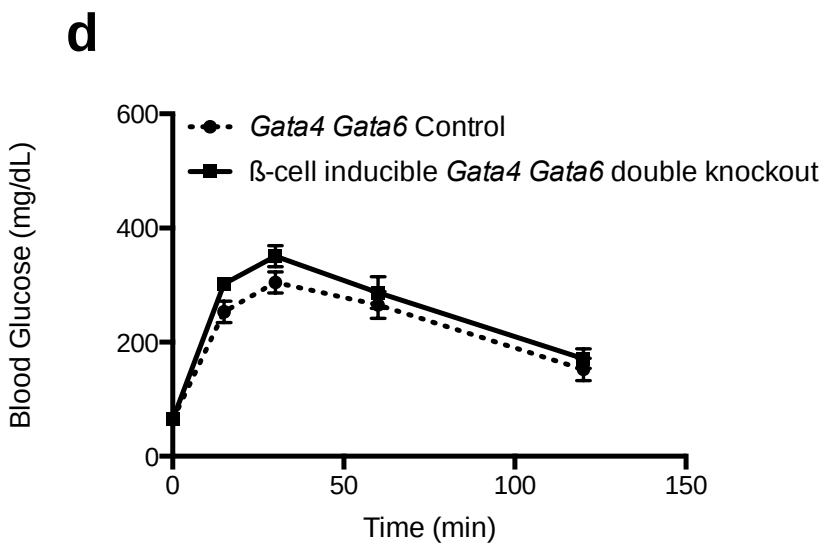


Supp Figure 4, Sartori et al

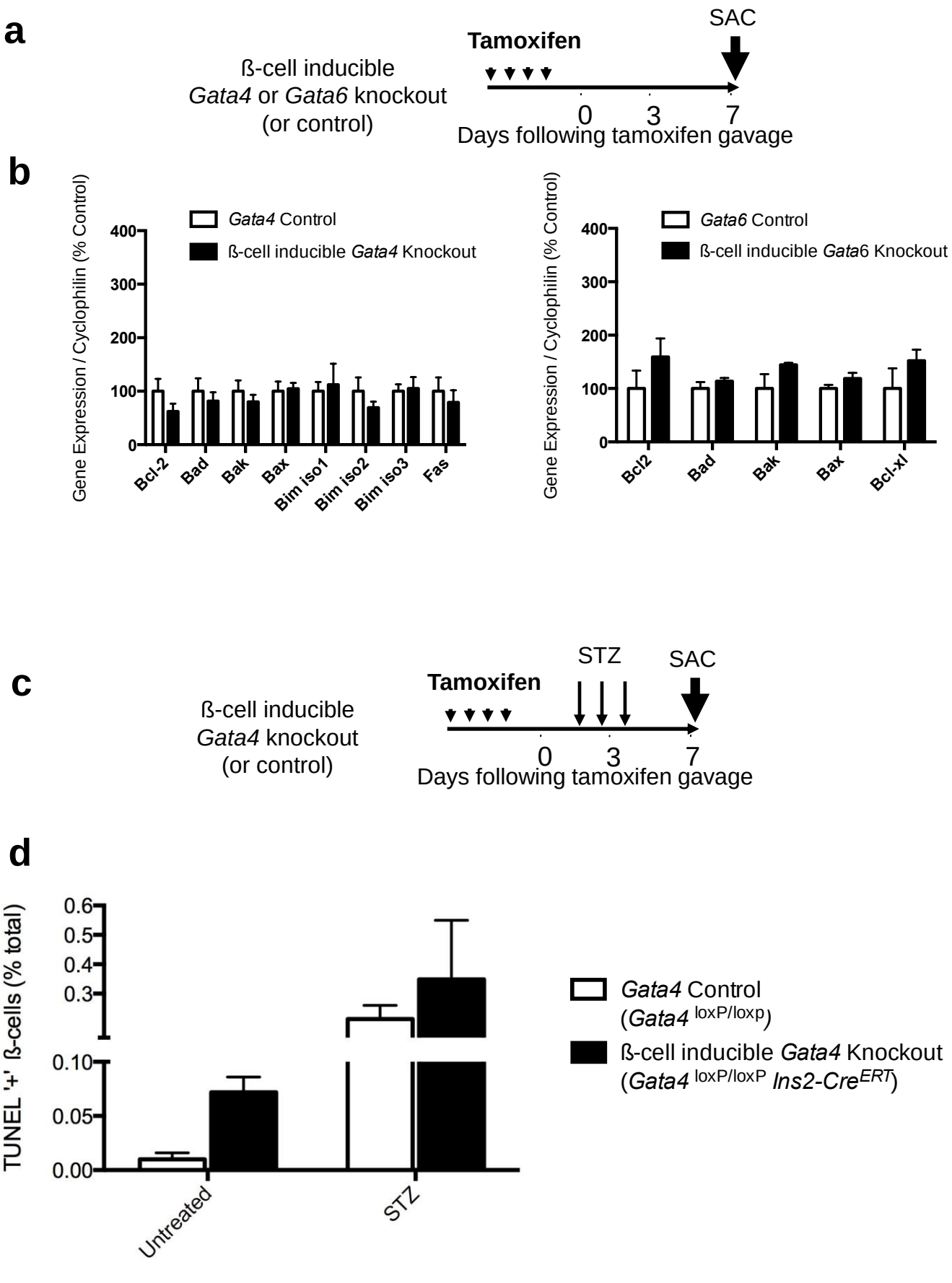






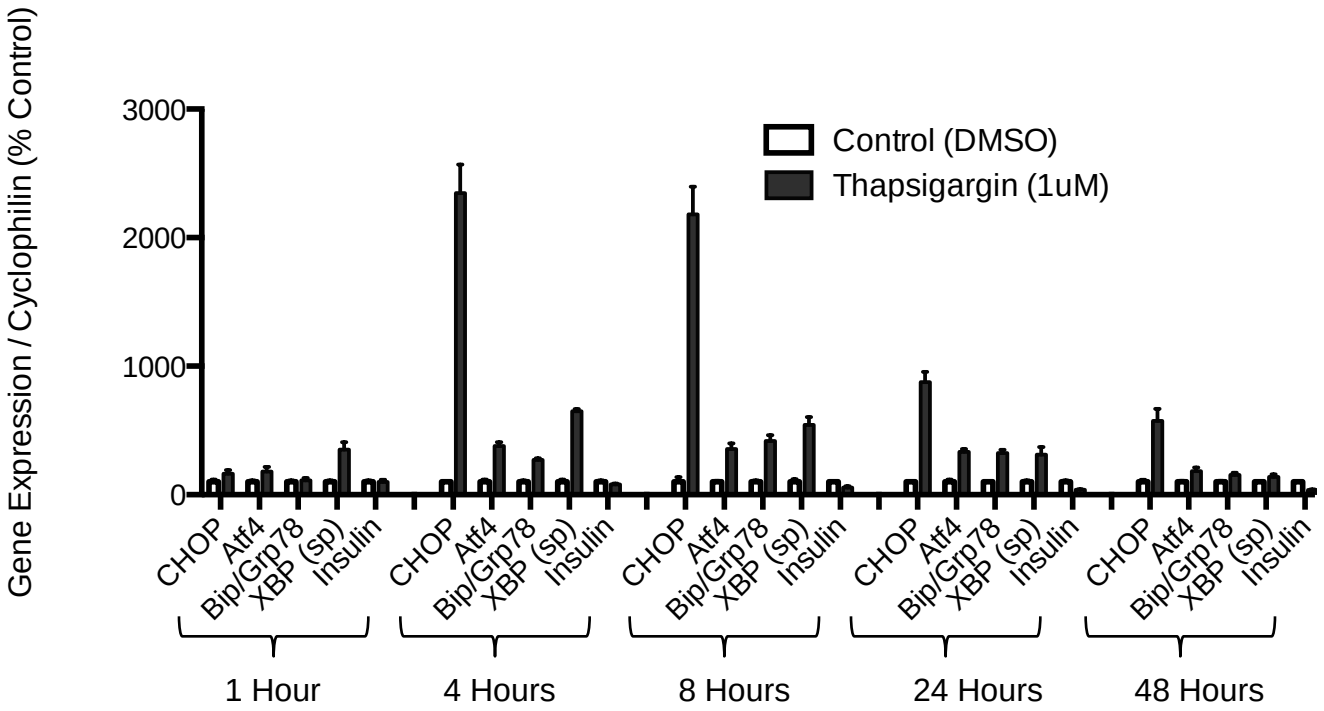


Supp. Figure 5, Sartori et al



Supp Figure 6, Sartori et al

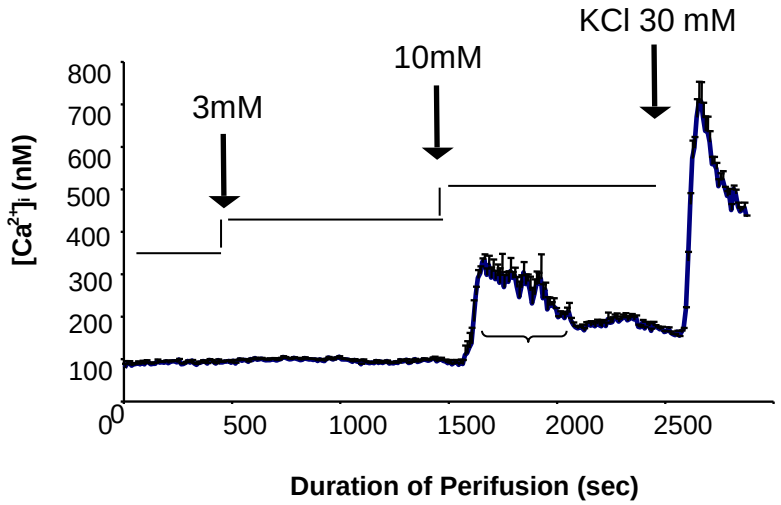
a



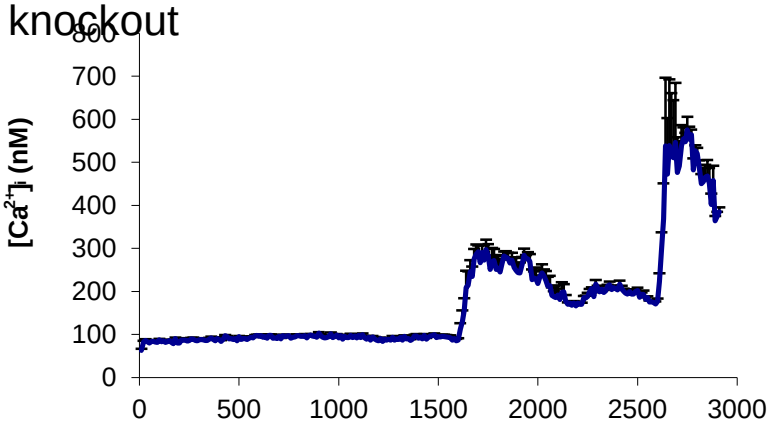
Supp Figure 7, Sartori et al

a

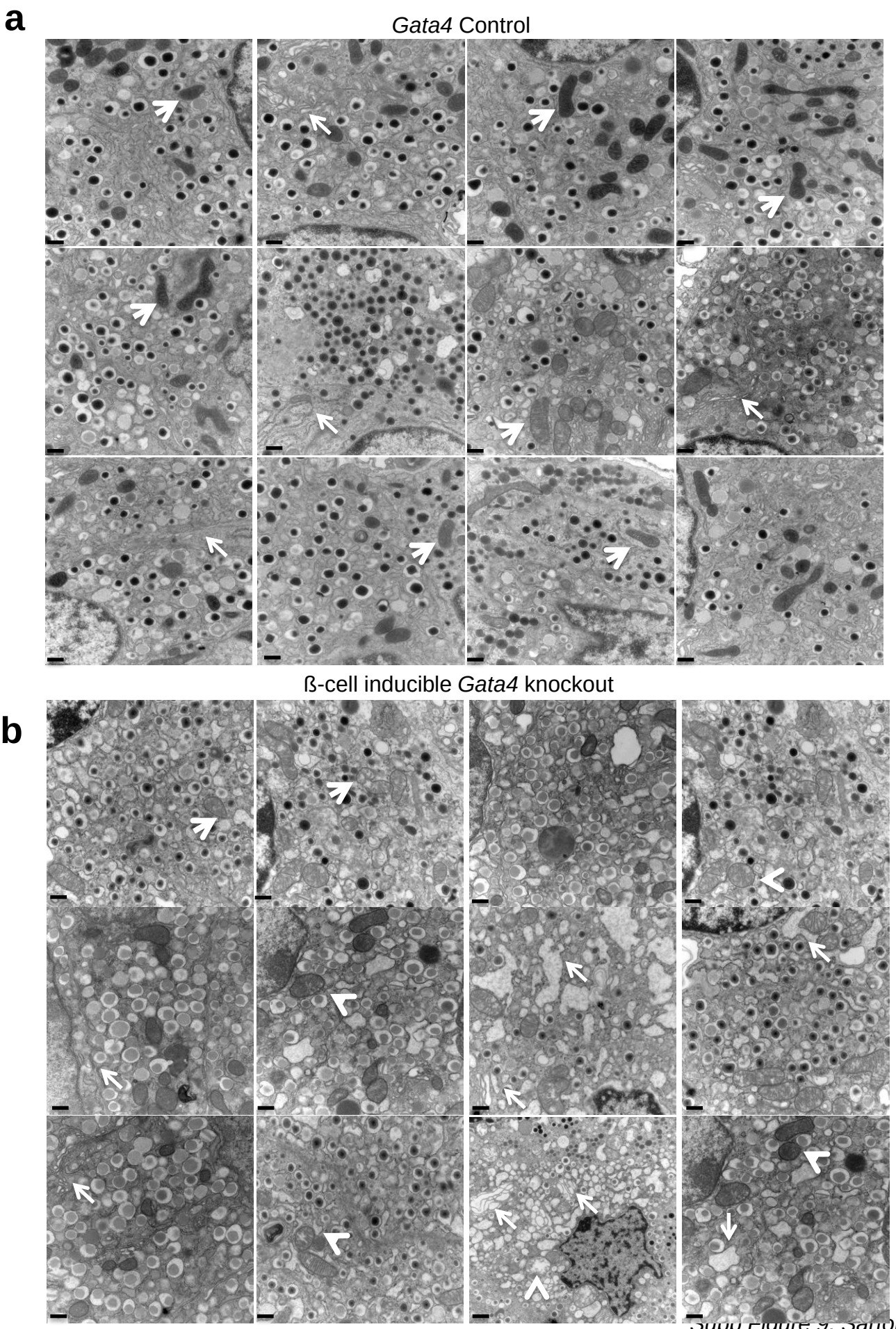
Gata4 Control



ß-cell inducible *Gata4* knockout



Supp Figure 8, Sartori et al



Supp Figure 9, Santori et al