SUPPLEMENTARY DATA

Supplementary Table 1. Plasma amino acids concentrations in 16h-fasted mice and in fed mice.

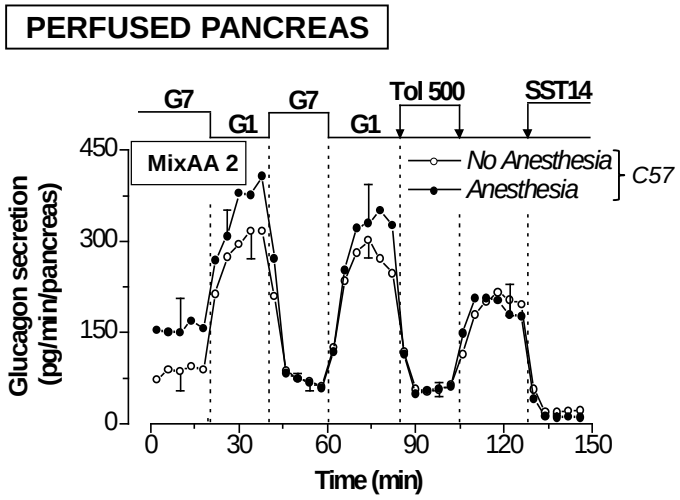
Amino acids	Fasting (µmol/l)	Feeding (µmol/l)
Alanine[#]	145 ± 17	339 ± 35***
Glutamine[#]	421 ± 40	576 ± 13**
Glycine[#]	126 ± 18	232 ± 15**
Leucine[#]	108 ± 9	109 ± 12
Lysine[#]	127 ± 9	218 ± 22**
Serine[#]	57 ± 8	99 ± 8**
Threonine[#]	80 ± 7	121 ± 12*
Valine[#]	145 ± 12	163 ± 12
Taurine	527 ± 37	509 ± 123
Aspartic acid	8 ± 1	10 ± 2
Asparagine	23 ± 7	29 ± 3
Glutamic acid	44 ± 7	36 ± 3
Proline	42 ± 5	72 ± 7**
Citrulline	24 ± 4	40 ± 7
Methionine	28 ± 2	44 ± 4**
Isoleucine	69 ± 6	66 ± 8
Tyrosine	51 ± 10	62 ± 8
Phenylalanine	58 ± 5	55 ± 4
Ornithine	42 ± 11	49 ± 4
Histidine	34 ± 4	45 ± 4
Arginine	41 ± 8	70 ± 8*

[#] refer to amino acids present in the 2 mmol/l mixture (MixAA 2) used for some experiments.

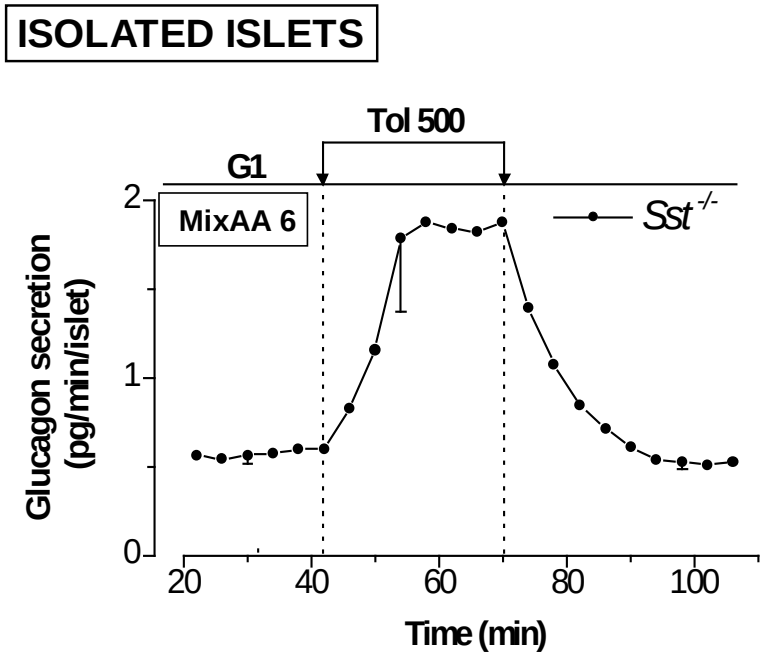
* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ for comparison between different fasting and feeding state.

SUPPLEMENTARY DATA

Supplementary Figure 1. Anesthesia has no effect on glucagon secretion. C57BL/6 mice were anesthetized or not with Ketamine (100 mg/kg) and Xylazine (16 mg/kg) injected in i.p. Mice that were not anesthetized were killed by cervical dislocation. The period of ischemia was similar for both groups of mice. The pancreas were perfused i*n situ* with a solution containing a 2 mmol/l mixture of amino acids (MixAA 2). The glucose (G) concentration was switched between 1 and 7 mmol/l, and the K_{ATP} channel closer, tolbutamide (Tol, 500 µmol/l) and SST14 (100 nmol/l) were added when indicated. Traces are means ± SE of 7-8 experiments with different mice.

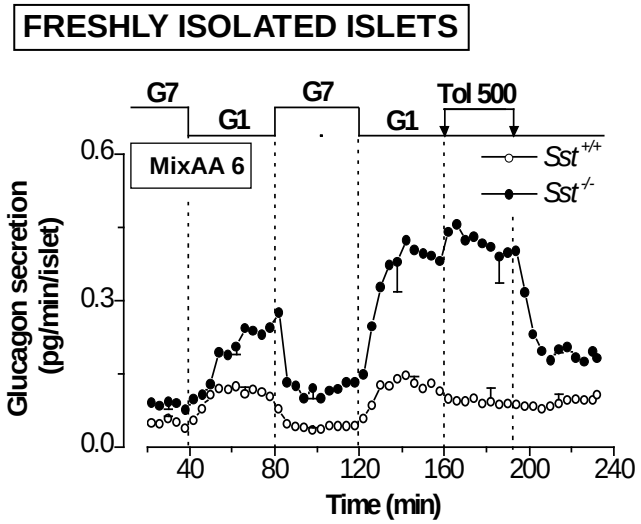


Supplementary Figure 2. Closure of K_{ATP} channels reversibly stimulates glucagon release in islets devoid of paracrine influence of SST. Islets from *Sst*$^{-/-}$ mice were perifused with a 6 mmol/l mixture of amino acids (MixAA 6) and 1 mmol/l of glucose (G1). Tolbutamide (Tol, 500 µmol/l) was added when indicated. Traces are means ± SE for 4 experiments with islets from different preparations.

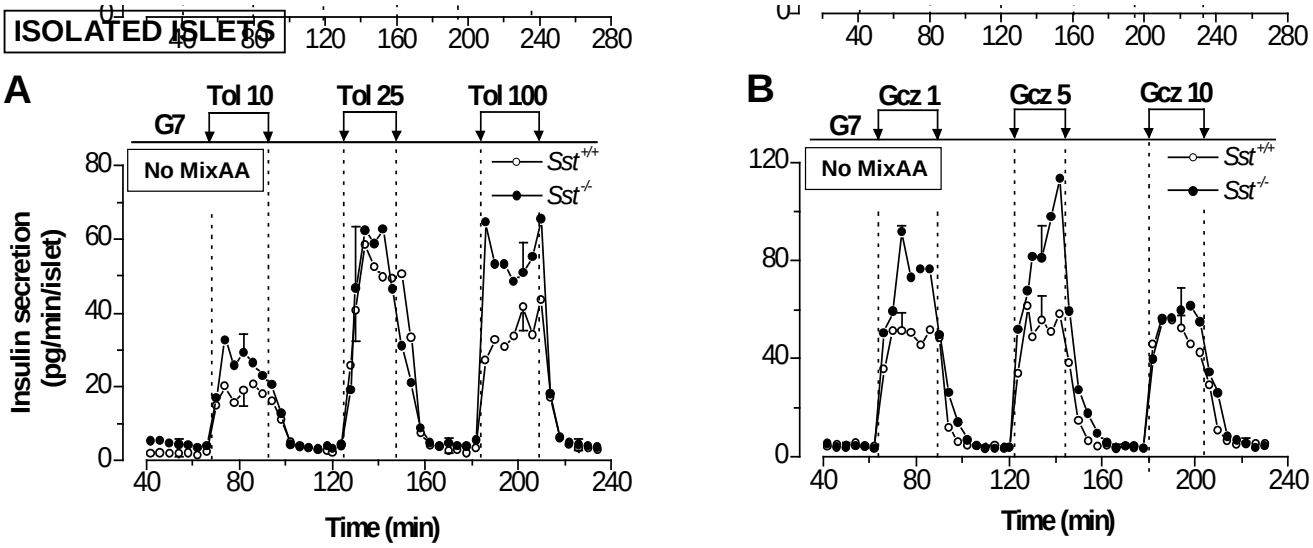


SUPPLEMENTARY DATA

Supplementary Figure 3. Effect of tolbutamide on glucagon release by freshly isolated islets of *Sst*$^{+/+}$ and *Sst*$^{-/-}$ mice. Islets from *Sst*$^{+/+}$ and *Sst*$^{-/-}$ mice were perifused 1 h after they were isolated with a 6 mmol/l mixture of amino acids (MixAA 6). The glucose (G) concentration was changed between 7 and 1 mmol/l, and tolbutamide (Tol, 500 µmol/l) was added when indicated. Traces are means ± SE for 3 experiments with islets from different preparations.

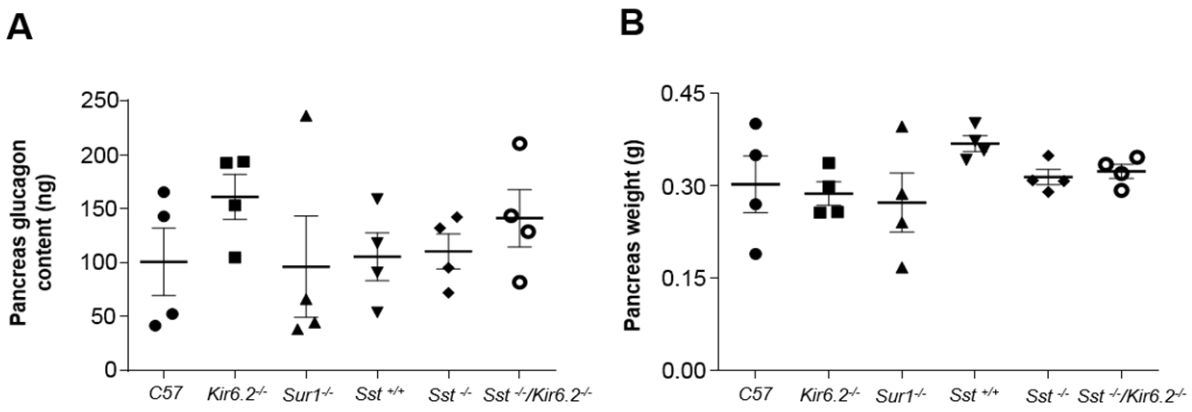


Supplementary Figure 4. K_{ATP} channel blockers stimulate insulin secretion even at low concentrations and similarly in *Sst*$^{+/+}$ (***A***) and *Sst*$^{-/-}$ islets (***B***). The islets were perifused with a medium without amino acids (No MixAA) but containing 7 mmol/l glucose (G7) as in Fig. 5 C-F of the article. Various concentrations of tolbutamide (Tol, 10, 25, 100 µmol/l) or gliclazide (Gcz, 1, 5, 10 µmol/l) were added when indicated. Traces are means ± SE of 3-4 experiments with islets from different preparations. The insulin content was similar in both types of islets. (*Sst*$^{+/+}$: 85.1 ± 9.3 ng/islet, n=4 and *Sst*$^{-/-}$: 91 ± 4.1 ng/islet, n=4).



SUPPLEMENTARY DATA

Supplementary Figure 5. Glucagon content and weight of the pancreas of the different mouse models used for *in situ* perfused pancreas experiments. ***A***: Glucagon content of whole pancreas of C57BL/6, *Kir6.2*$^{-/-}$, *Sur1*$^{-/-}$, *Sst*$^{+/+}$, *Sst*$^{-/-}$, *Sst*$^{+/+}$*/Kir6.2*$^{-/-}$ mice. ***B***: Weight of the same pancreas of these models. Results are shown as univariate scatter plots of data from 4 pancreas for each model.



Supplementary Figure 6. SSTR antagonists reverse the inhibitory effect of tolbutamide on glucagon secretion in the presence of 1 mmol/l of glucose. Pancreases from C57BL/6 mice were perfused *in situ* with a solution containing a 2 mmol/l mixture of amino acids (MixAA 2). The glucose (G) concentration was changed between 1 and 7 mmol/l. The K_{ATP} channel closer, tolbutamide (Tol, 500 µmol/l), SST14 (100 nmol/l) or SSTR antagonists H6056 (H, 1 µmol/l) and CYN154806 (CYN, 300 nmol/l) were added when indicated. Traces are means ± SE of 3-4 experiments with different mice.