Figure S1

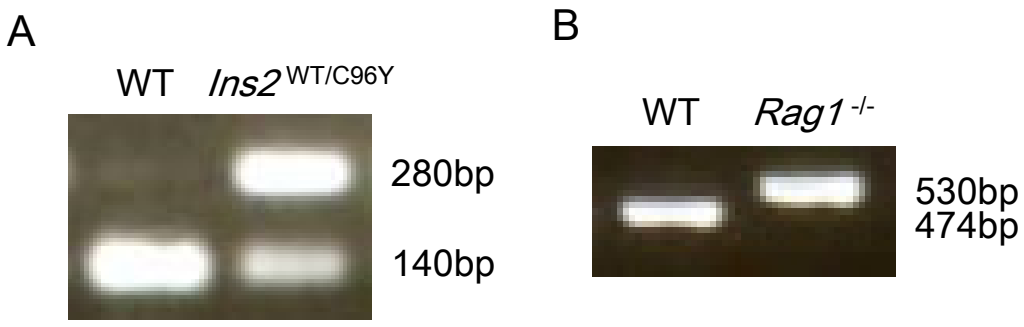
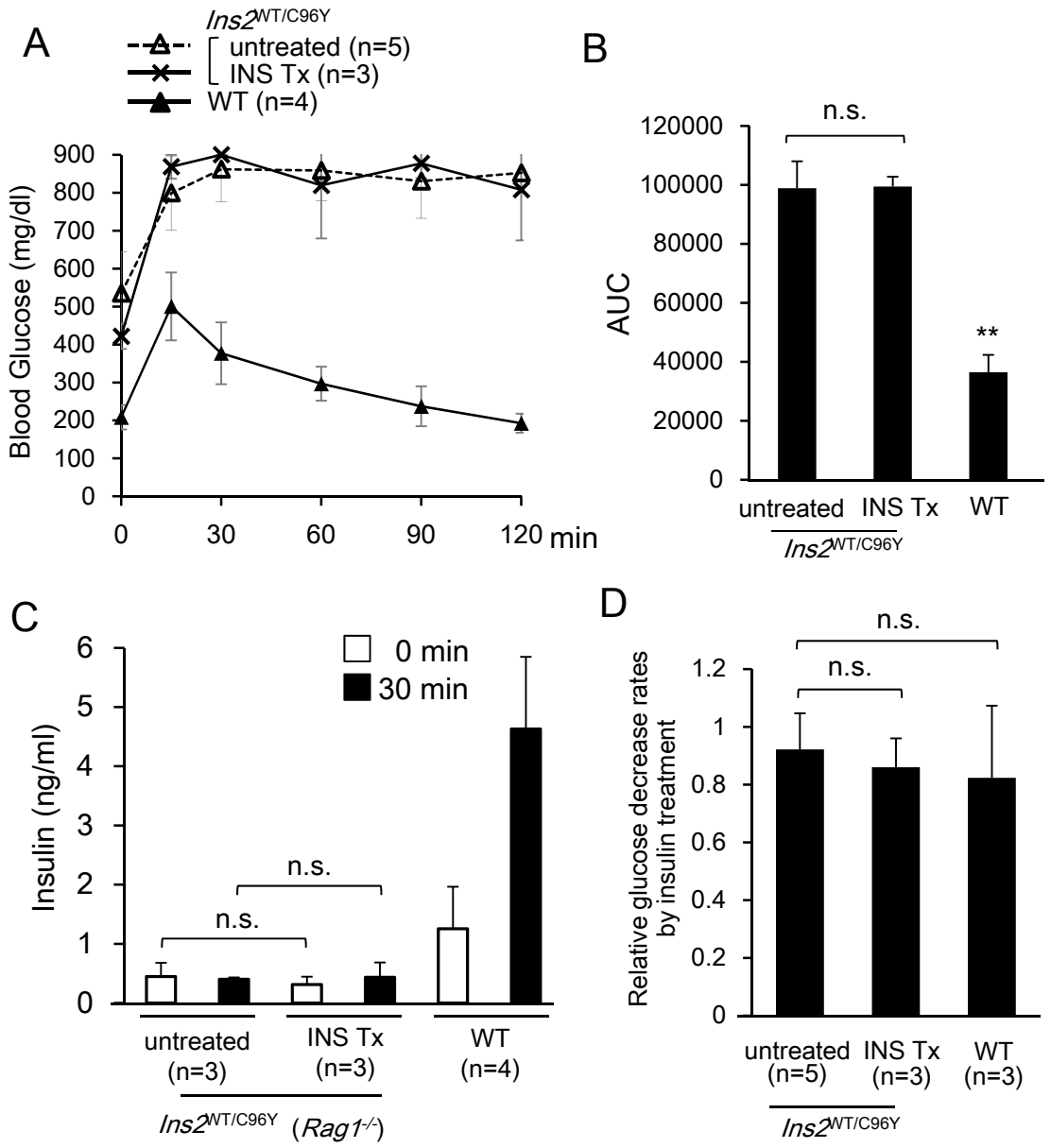


Figure S2


A
Ins2WT/C96Y
untreated (n=5)
INS Tx (n=3)
WT (n=4)
Blood Glucose (mg/dl)
0
100
200
300
400
500
600
700
800
900
0
30
60
90
120 min
B
AUC
0
20000
40000
60000
80000
100000
120000
n.s.
**
untreated
INS Tx
WT
Ins2WT/C96Y
C
Insulin (ng/ml)
0
1
2
3
4
5
6
0 min
30 min
n.s.
n.s.
untreated (n=3)
INS Tx (n=3)
WT (n=4)
Ins2WT/C96Y (Rag1-/-)
D
Relative glucose decrease rates by insulin treatment
0
0.2
0.4
0.6
0.8
1
1.2
n.s.
n.s.
untreated (n=5)
INS Tx (n=3)
WT (n=3)
Ins2WT/C96Y

Supporting Information Legends

Figure S1. Genotyping of Akita mice

(A) PCR analysis of the *Ins 2* gene. The PCR product of the WT gene was evident at 140 bp, whereas the mutant gene was observed at 280 bp. (B) PCR analysis of the *Rag1* gene. The PCR product of the WT gene was evident at 474 bp, whereas that of the mutant gene was observed at 530 bp.

Figure S2. Endogenous islet function was unaffected by insulin treatment

Insulin-treated AKITA mice 1 week after the removal of the insulin implant underwent the IPGTT (A, B), GSIS analysis (C), and ITT (D) to test their glucose and insulin tolerance in comparison to the untreated AKITA mice and WT controls, respectively. (A, B) After discontinuing insulin treatment, AKITA mice were glucose intolerant, similar to the untreated mice (A), also revealed by the AUC shown in (B). (C) The insulin implants contained insulin from different species, which induces anti-insulin antibodies, thus interfering with insulin measurements. Therefore, immunodeficient *Rag1*$^{-/-}$ Akita mice were used to avoid interference. No increase in endogenous blood insulin levels were detected in the Akita mice after insulin treatment was discontinued. (D) The relative rates of glucose decrease as a result of insulin treatment from each basic glucose level. n. s., not significant; $^{**}p<0.01$, two-tailed unpaired Students' *t*-test.