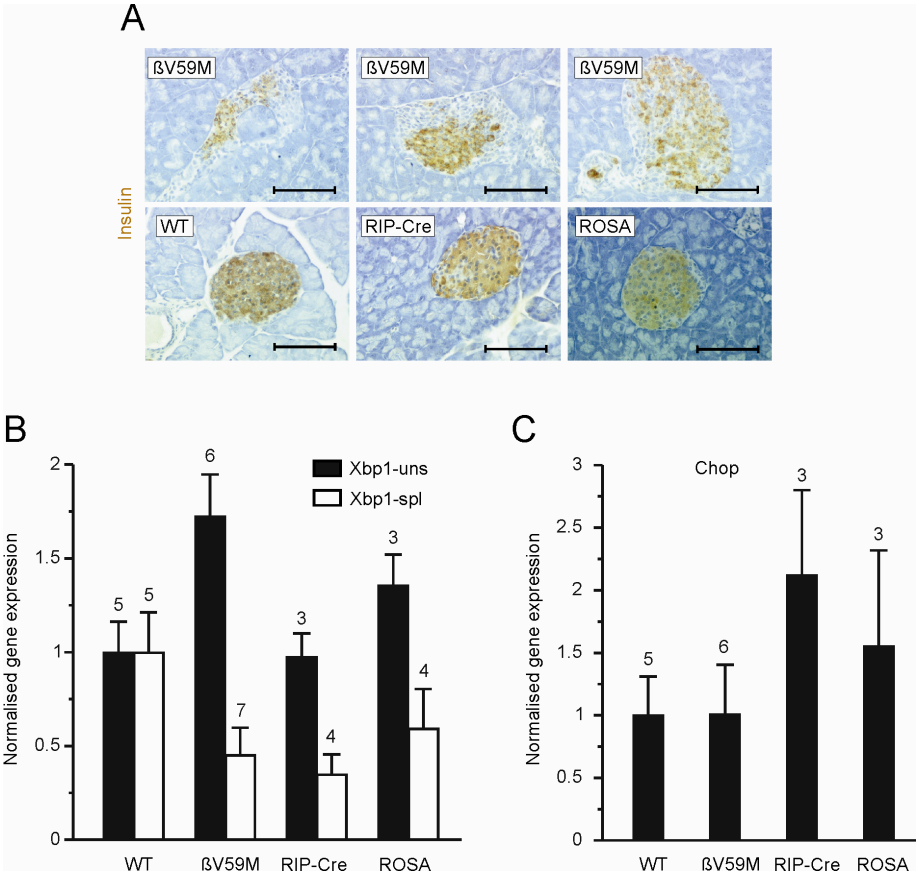
SUPPLEMENTARY INFORMATION

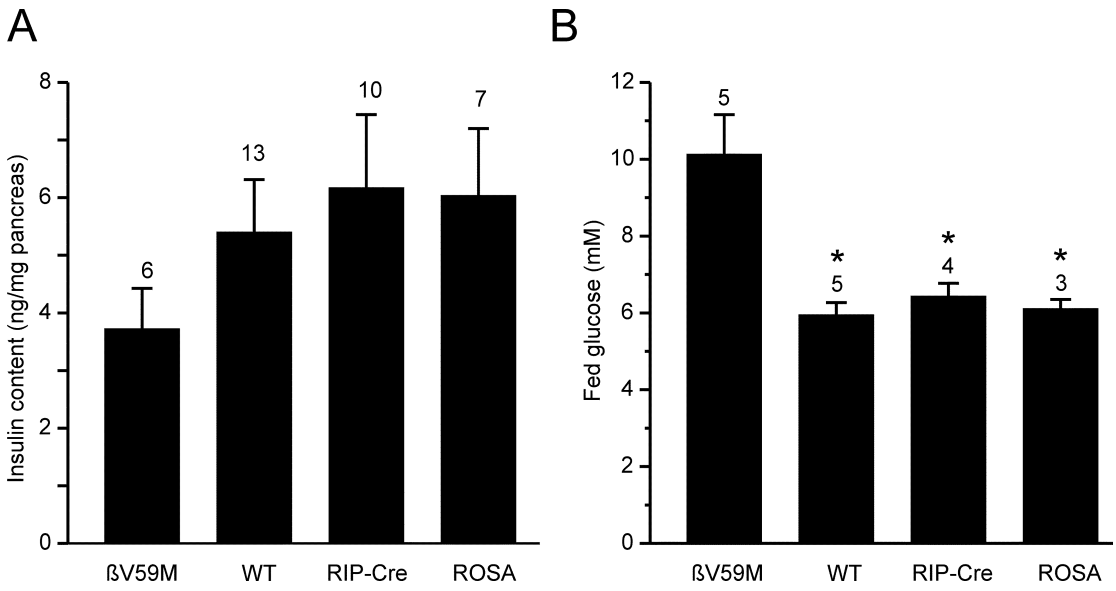
A mouse model of neonatal diabetes caused by the V59M mutation in the Kir6.2 K_{ATP} channel subunit by Girard et al.



Supplementary Figure 1.

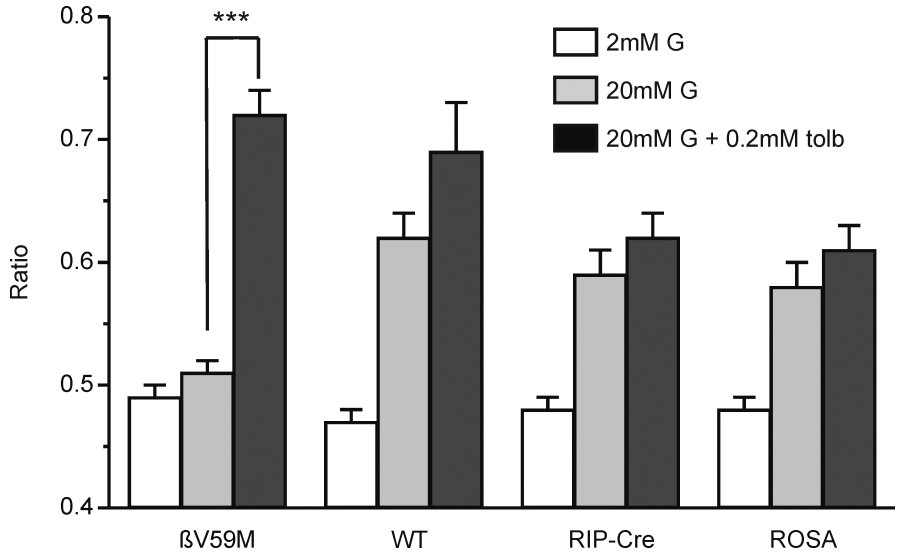
A. Representative sections of β-V59M, WT, RIP-Cre and ROSA mouse pancreas, to illustrate the differences in islet morphology. Sections were stained for insulin using DAB (thus beta-cells appear brown) and counterstained with haematoxylin. Scale bar = 100μm.
B.**C** Relative expression levels of unspliced (Xbp1-uns) and spliced (Xbp1-spl) forms of Xbp1 (**B**), and of Chop (**C**), in islets isolated from 5-week old WT, β-V59M, RIP-Cre and ROSA mice measured by quantitative PCR. Results are normalized to Gapdh levels and expressed relative to WT mice of the same litter. Results are the mean±SEM. The number of mice is given above each bar.

Non-conventional splicing of the X-box binding protein (Xbp-1) is stimulated by ER stress as part of the unfolded protein response (UPR), and converts mRNA for 'unspliced' Xbp-1 to the 'spliced' form. The fact that we observe (if anything) an increase in the relative level of 'unspliced' Xbp-1 mRNA in β-V59M islets is not consistent with the idea that the UPR is triggered.



Supplementary Figure 2.

A. Insulin content of whole pancreas isolated from 5-day old mutant and control mice, as indicated. The number of mice is given above each bar.
B. Mean plasma glucose concentrations from 5-day old fed mice. The number of mice is given above each bar. *p<0.05 versus β−V59M.



Supplementary Figure 3.

Intracellular calcium (expressed as the F340/F380 ratio) in 2mM or 20mM glucose (G) or 20mM glucose plus 0.2 mM tolbutamide (tolb) in β-V59M and control islets, as indicated. The steady state (basal) level is measured in 2mM glucose, and the peak response is measured for 20mM glucose plus 0.2 mM tolbutamide. The peak response to 20mM glucose is given for control islets. For β-V59M islets (where no peak response was evident), we measured the fluorescence ratio at 250ms after the start of glucose perfusion, which corresponds to the mean time at which the peak response occurs in control islets. We define this as the initial $[Ca^{2+}]_i$ response. Data are mean ± SEM of 7-9 islets from two different animals in each group. ***, $p<0.001$.

Supplementary Table 1. *Mean fasting plasma insulin levels for 5-week old mice.*

	Plasma Insulin (pg/ml)	n
β-V59M	19 ± 8	20
WT	148 ± 37**	24
RIP-Cre	91 ± 19**	19
ROSA	123 ± 25**	25

Data are mean ± SEM (n=number of mice). Data from male and female mice have been pooled. ** $p<0.01$ vs. β-V59M.

Supplementary Table 2. *Mean fasting plasma glucagon levels for 5-week old mice*

	Plasma Glucagon (pg/ml)	n
β-V59M	96 ± 6	10
WT	73 ± 4**	13
RIP-Cre	78 ± 12	8
ROSA	78 ± 5*	13

Data are mean ± SEM. * $p<0.05$, ** $p<0.01$ vs β-V59M mice. Data from male and female mice have been pooled.

Supplementary Table 3. *Values of IC_{50} for MgATP inhibition of wild-type and V59M mutant K_{ATP} channels recorded from beta-cells and oocytes.*

	mean of fits (μM)	fit of mean data (μM)
WT (beta-cell)	36 ± 8 (n=7)	25
β-V59M (beta-cell)	385 ± 184 (n=5) *	265
WT (oocyte)	20 ± 6 (n=9)	16
hetV59M (oocyte)	64 ± 13 (n=5) **	60
homV59M (oocyte)	835 ± 322 (n=9) *	440

The "mean of fits" ± SEM was obtained by fitting each concentration-response curve individually and then averaging the value of the IC_{50} obtained. The 'fit of the mean data' is the best fit to the mean concentration-response curve (as in Fig. 5A). Oocyte data are taken from reference 9. * $p<0.05$, ** $p<0.01$ vs. WT. n values refer to the number of beta-cells or oocytes.

Supplementary Table 4. *Percentage of beta-cells stimulated by 20mM glucose in calcium imaging experiments.*

	Mean percentage of cells responding to 20mM Glucose
β-V59M	42 ± 4 (n=5)
WT	89 ± 7 (n=7)***
RIP-Cre	67 ± 7 (n=5)*
ROSA	89 ± 3 (n=7)***

Data are mean ± SEM * $p<0.05$, *** $p<0.001$ vs β-V59M mice. n values refer to the number of islets.