

SUPPLEMENTARY ONLINE DATA

Loss of AMP-activated protein kinase  $\alpha 2$  subunit in mouse  $\beta$ -cells impairs glucose-stimulated insulin secretion and inhibits their sensitivity to hypoglycaemia

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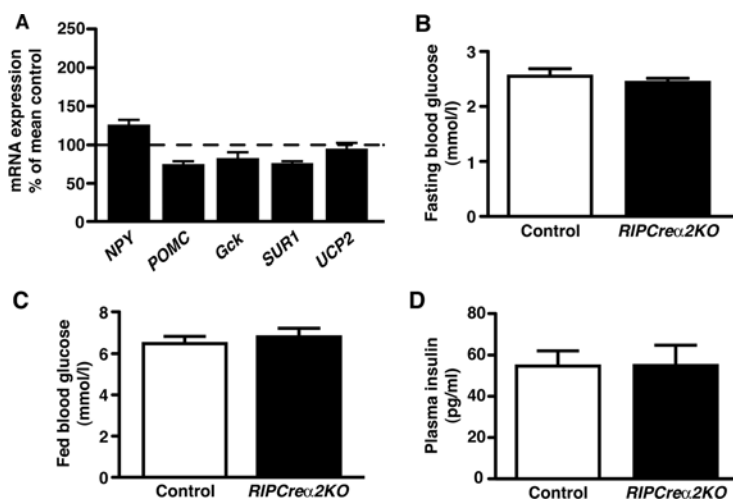


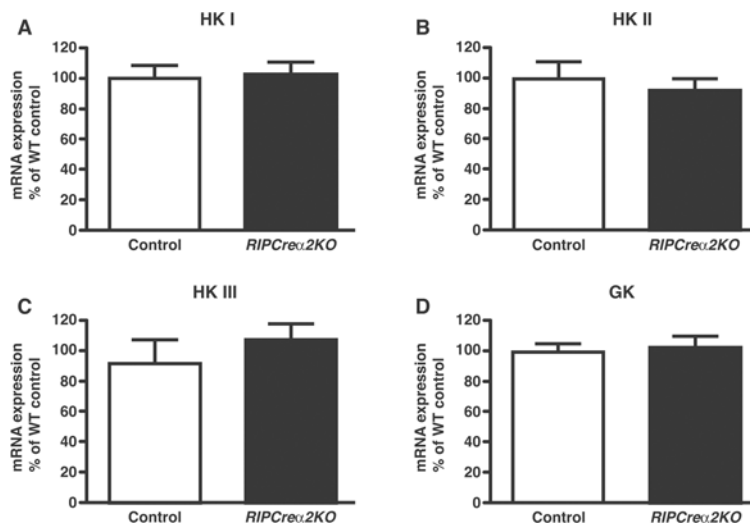
Figure S1 Hypothalamic mRNA expression profile and glucose homeostasis parameters in *RIPCre $\alpha 2$ KO* mice

(A) Expression of mRNA in the hypothalamus of *RIPCre $\alpha 2$ KO* mice, relative to control WT mice ( $n = 5$ ). Fasting (B) and fed (C) blood glucose levels in control ( $n = 8$ ) and *RIPCre $\alpha 2$ KO* 16- and 20-week-old male mice respectively ( $n = 8$ ). (D) Fasted plasma insulin levels in control ( $n = 9$ ) and *RIPCre $\alpha 2$ KO* 10-week-old male mice ( $n = 7$ ).

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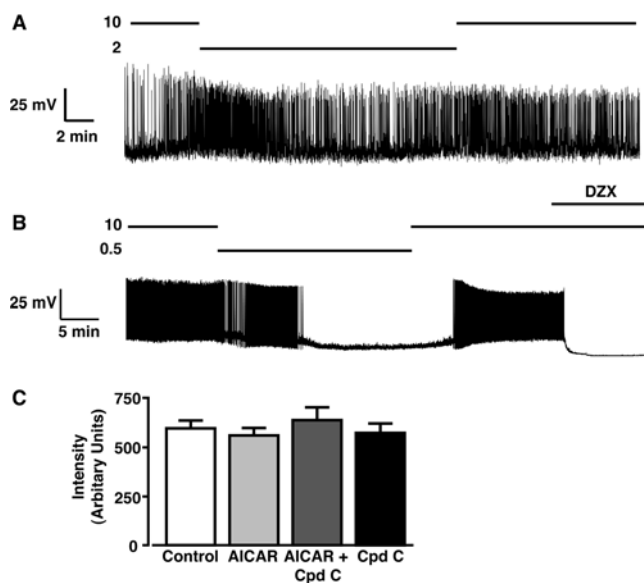
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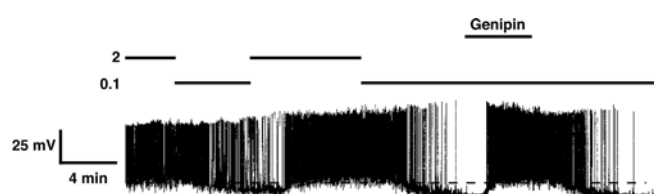
**Figure S2** Expression of mRNA in islets of *RIPCre;2KO* mice, relative to control (*RIPCre*) islets for (A) HK I, (B) HK II, (C) HK III, and (D) GK

Values are means  $\pm$  S.E.M. for  $n = 7-9$  determinations for each. The probes used were: Hexokinase I, Mm01145241\_m1; Hexokinase II, Mm00443395\_m1; and Hexokinase III, Mm01341937\_m1.



**Figure S3** CRI-G1  $\beta$ -cells exhibit glucose-sensing behaviour, and AMPK manipulation does not influence glucose uptake

Representative perforated patch recordings from CRI-G1  $\beta$ -cells, showing (A) the lack of electrical response to reduction of glucose from 10 mmol/l to 2 mmol/l and (B) the hyperpolarization and inhibition of firing on reduction of glucose from 10 mmol/l to 0.1 mmol/l. Note that the application of 250  $\mu$ mol/l diazoxide (DZX) hyperpolarizes the  $\beta$ -cell in the presence of 10 mmol/l glucose. (C) Glucose uptake, as measured by 2-NBDG uptake, in CRI-G1  $\beta$ -cells is unaltered by treatment of cells (1 h) with 1 mmol/l AICAR  $\pm$  40  $\mu$ mol/l compound C (CpdC) ( $n = 44$ , from six separate experiments).



**Figure S4** Representative perforated patch recording from a POMC arcuate nucleus neuron

Reducing glucose from 2 mM to 0.1 mM reversibly hyperpolarizes and reduces firing frequency, but this effect is reversibly occluded by the presence of 20  $\mu$ M genipin. The broken line in the trace represents 0 mV.