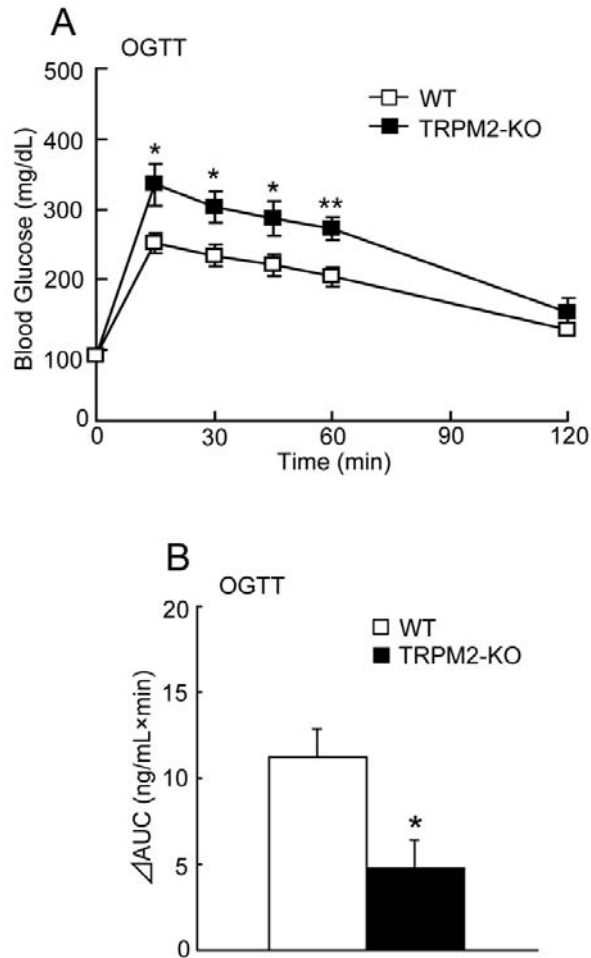
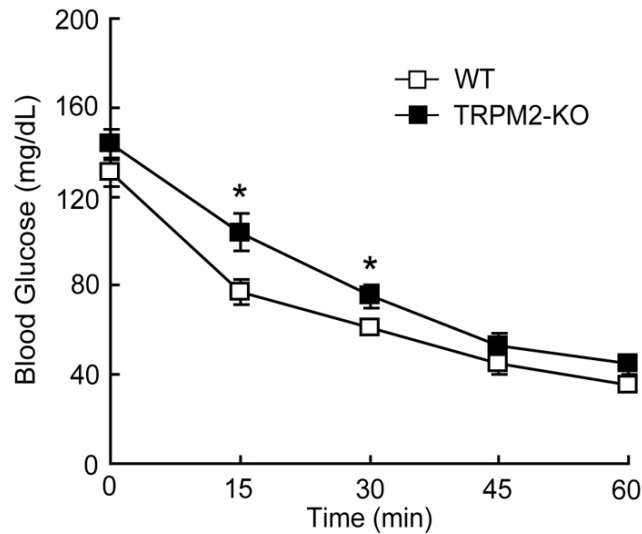


Supplementary FIG. 1 Oral glucose tolerance in female WT and TRPM2-KO mice.



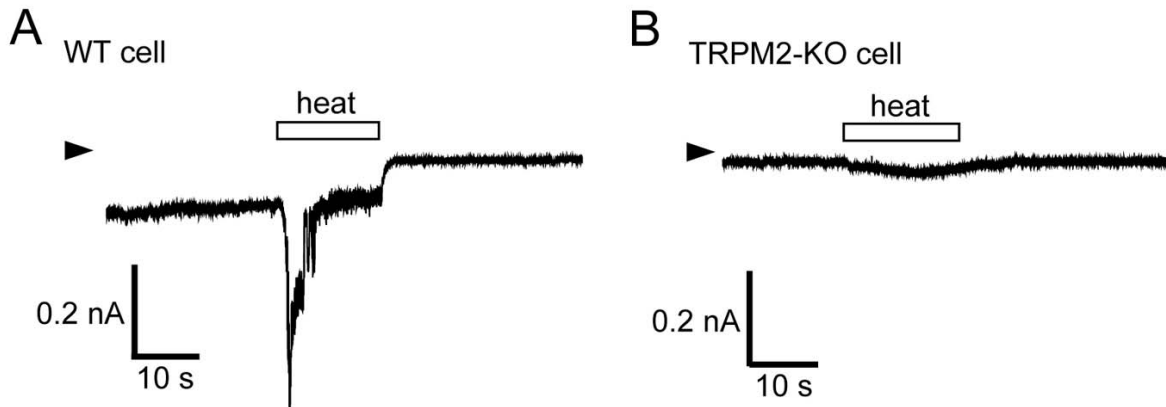
An oral glucose tolerance test (OGTT) was performed on female TRPM2-KO and WT mice fasted for 16-17 h. A 20% glucose solution (100 μ L/10 g BW) was administered at time zero. *A*, Ordinates: blood glucose concentrations. Abscissae: time after injection of glucose. Each point represents the mean \pm S.E.M. of 7-9 mice. White and black symbols indicate data from WT and TRPM2-KO mice, respectively. *B*, Ordinates: calculation of the area under the curve (AUC) for plasma insulin concentrations. Each bar represents the mean + S.E.M. of 7-9 mice. White and black bars indicate data from WT and TRPM2-KO mice, respectively. Statistical significance was assessed using Student's *t*-test, or RM ANOVA followed by Dunnett's post-hoc test. *, $P < 0.05$, **, $P < 0.01$ for WT vs. TRPM2-KO mice.

Supplementary FIG. 2 Insulin tolerance in WT and TRPM2-KO mice.



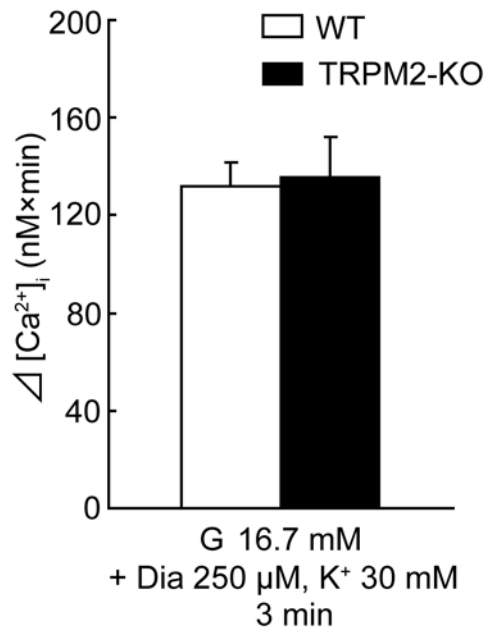
An intraperitoneal insulin tolerance test was performed in TRPM2-KO and WT mice fasted for 4 h. Porcine insulin (1 unit/kg BW) was injected at time zero. Ordinates: blood glucose concentrations. Abscissae: time after injection of insulin. Each point represents the mean \pm S.E.M. of 7-8 mice. White and black symbols indicate data from WT and TRPM2-KO, respectively. Statistical significance was assessed by RM ANOVA followed by Dunnett's post-hoc test. *, $P < 0.05$ for WT vs. TRPM2-KO mice.

Supplementary FIG. 3 Heat-evoked currents in isolated pancreatic cells.



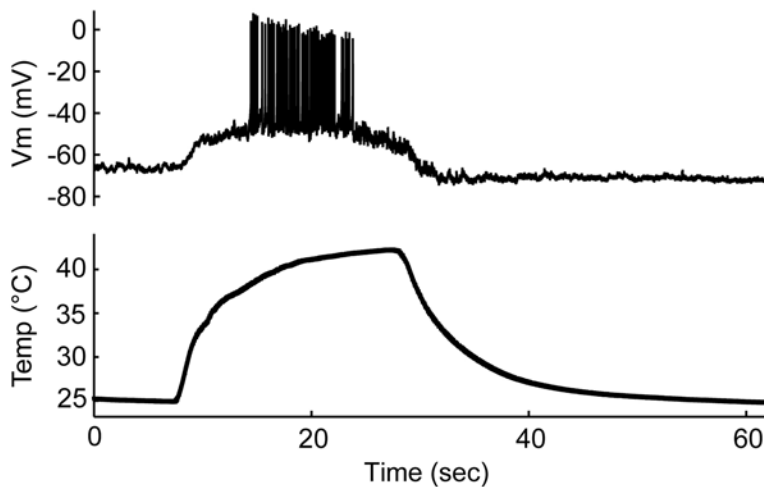
Representative heat-evoked inward currents at -60 mV with pipette solution containing 100 μ M cADPR in isolated pancreatic cells from WT (A) and TRPM2-KO (B) mice. Black arrow heads indicate 0 current levels. The initial apparent inward current prior to heat stimulation may indicate a cADPR-evoked current at room temperature. Three of the eight WT pancreatic cells showed similar inward currents. Those three cells are presumed to be β -cells. None of the TRPM2-KO pancreatic cells (0/6) responded to heat stimulation.

Supplementary FIG. 4 Measurement of $[Ca^{2+}]_i$ in β -cells isolated from WT and TRPM2-KO mice.



Quantification of $[Ca^{2+}]_i$ changes in response to 16.7 mM glucose (G), 250 μ M dizoxide (Dia) and 30 mM K⁺ for 3 min. Each bar represents the mean + S.E.M. White and black bars indicate data from WT and TRPM2-KO, respectively.

Supplementary FIG. 5 Heat-evoked action potentials in isolated pancreatic cell from WT mice.



A representative heat-evoked depolarization of the membrane potential in a pancreatic cell. A lower panel indicates the bath temperature.