SUPPLEMENTAL DATA:

MATERIALS AND METHODS:

Transgenic animals and metabolic studies. Experiments were conducted on male 6 and 9 month-old *Il1r1*-deficient mice (B6.129S7-Il1r1^{tm1Imx}/J) and their wild-type and heterozygous littermates. Strain information, genotypes, glucose tolerance, and insulin tolerance tests described in main text.

Electrophysiology. Experiments were performed on untreated dispersed mouse islets using electrophysiological solutions and protocols described in main text.

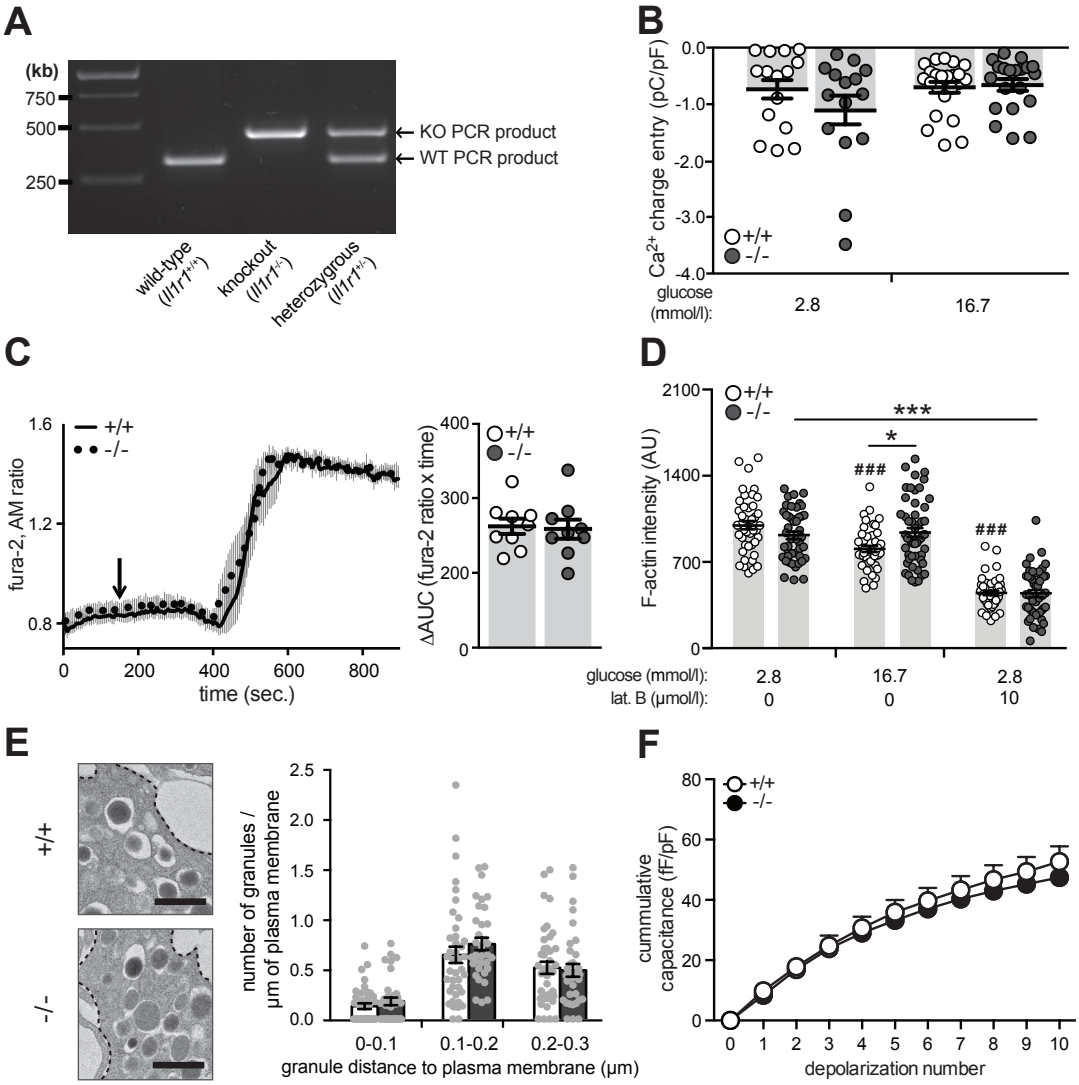
$[Ca^{2+}]_i$ measurements. Experiments were performed on untreated intact mouse islets using solutions and protocols described in main text.

Actin Staining. Dispersed mouse islets were plated onto untreated coverslips. Cells were pre-incubated with 2.8 mmol/L Krebs-Ringer Bicarbonate (KRB) solution for 2 hours prior to a 2-minute treatment with latrunculin B (Sigma-Aldrich, Oakville, ON; 10 μmol/l) or a 15-minute treatment with 2.8 or 16.7 mmol/l glucose-KRB, as indicated. Solution components, sample preparation, imaging, and analysis as described in main text.

Electron Microscopy. Experiments were performed on untreated intact mouse islets using solutions, protocols, and analysis software described in main text.

Insulin secretion assay. Measurements were performed at 37°C in KRB. Islet perifusion was performed at a flow rate of 100 μl/min. Islets were perfused with 2.8 mmol/l glucose for 30 minutes (as a pre-incubation step) and then with glucose and/or recombinant human IL-1β (Sigma-Aldrich, Oakville, ON; 10 ng/ml), as indicated. Solution components, sample storage, and insulin measurements described in main text.

Supplemental Figure 1:



***Il1r1*-deficiency impairs filamentous-actin dynamics in pancreatic β-cells.**

A: Representative PCR-based genotyping using genomic DNA (from eat notches) of mice with indicated genotypes.

B: Quantification of responses following a single depolarization from -70 to 0 mV in dispersed mouse β-cells from wild-type (+/+) or *Il1r1*-knockout (-/-) mice in the presence of either 2.8 or 16.7 mmol/l glucose (*n*=16, 15, 23, 20; 3 experiments).

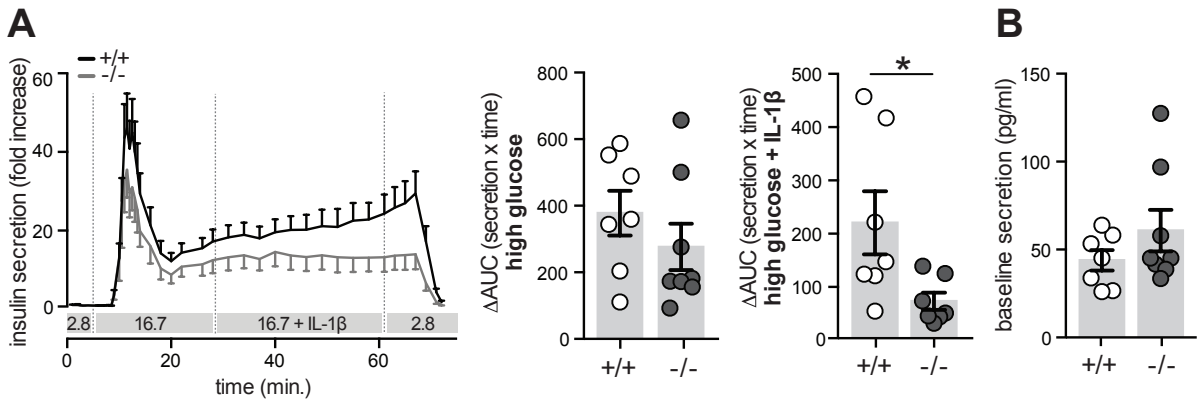
C: Responses in intracellular Ca^{2+} concentrations ($[Ca^{2+}]_i$) from wild-type (+/+) or *Il1r1*-knockout (-/-) islets following glucose-stimulation (arrow; *left*) and change in area under the curve (ΔAUC) of $[Ca^{2+}]_i$ responses (*right*) (*n*=9, 9; 3 experiments).

D: Quantification of average peak filamentous-actin (F-actin) intensities of dispersed β-cells from wild-type (+/+) or *Il1r1*-knockout (-/-) mice treated with 2.8 or 16.7 mmol/l (10 minutes) glucose or latrunculin B (lat. B; 10 μmol/l; 2 minutes) (*n*=45, 45, 46, 53, 45, 47; 3 experiments). Data were compared using 2-way ANOVA with Tukey post-test. $^{\#}P<0.05$, $^{\#\#}P<0.005$ versus 2.8 mmol/l wild-type control; $^{*}P<0.05$, $^{***}P<0.005$ as indicated.

E: Representative electron micrographs of mouse β-cells from wild-type (+/+) or *Il1r1*-knockout (-/-) mice (*left*), and quantification of the number of granules per micron of plasma membrane (*right*). Experiments were performed in 2.8 mmol/l glucose. Black dashed line indicates plasma membrane. (*n*=40, 35, 40, 35, 41, 35; 3 experiments). Scale bar represents 500 nm.

F: Exocytotic responses from single wild-type (+/+) or *Il1r1*-knockout (-/-) mouse β-cells measured as an increase in cell membrane capacitance, during a train of membrane depolarizations from -70 to 0 mV in 16.7 mmol/l glucose (*n*=32, 35; 3 experiments).

Supplemental Figure 2:



***Il1r1*-deficiency has a minor effect on glucose-stimulated insulin secretion.**

A: Insulin secretion normalized to fold increase over baseline at low glucose from wild-type (+/+) or *Il1r1*-knockout (-/-) islets exposed to 2.8 or 16.7 mmol/l glucose and treated with IL-1β (10 ng/ml), as indicated (*left*) (*n*=7, 8 mice). Change in area under the curve (ΔAUC) of the response to high glucose (*middle*) (*n*=7, 7 mice) and to high glucose and IL-1β (*right*) (*n*=7, 8 mice) are shown. Data were compared using a two-tailed Student's *t*-test. **P*<0.05 as indicated.

B: Average insulin secretion during 2.8 mmol/l glucose baseline from wild-type (+/+) or *Il1r1*-knockout (-/-) islets (*n*=7, 8 mice).

Supplemental Table 1:

Donor	Age (years)	Sex	BMI (kg/m^2)	HbA_{1c} (%)	IL-1β Index	Type 2 Diabetic
H1744	56	n/a	16.7	5.9	1.27	-
H1732	61	male	27.5	5.5	1.47	-
H1919	n/a	n/a	26.7	5.9	1.73	-
R066	44	male	32.2	n/a	2.33	-
R067	60	male	26.0	5.5	1.09	-
R072	54	female	30.8	6.2	1.95	-
R073	74	female	28.3	5.4	1.81	-
R140	49	female	22.0	5.6	1.03	-
R141	56	female	33.2	5.5	0.99	yes
R142	63	female	25.3	4.9	1.80	-
R150	42	male	31.7	5.9	1.49	-
R151	46	female	26.7	5.4	1.51	-
R152	54	female	42.6	8.3	1.19	yes
R154	57	female	40.9	7.2	1.10	yes
R157	60	female	23.3	6.0	0.85	-
R159	60	male	30.4	5.5	1.68	-
R160	27	male	25.4	5.7	0.83	-

Human islet donor information.

Individual characteristics of human donors assessed in Figure 1C-E. HbA_{1c}: glycated hemoglobin. IL-1β Index: IL-1β potentiation index, defined as the ratio of insulin secretion induced by 16.7 mmol/l glucose in the presence of IL-1β to the insulin secretion induced by 16.7 mmol/l glucose alone.

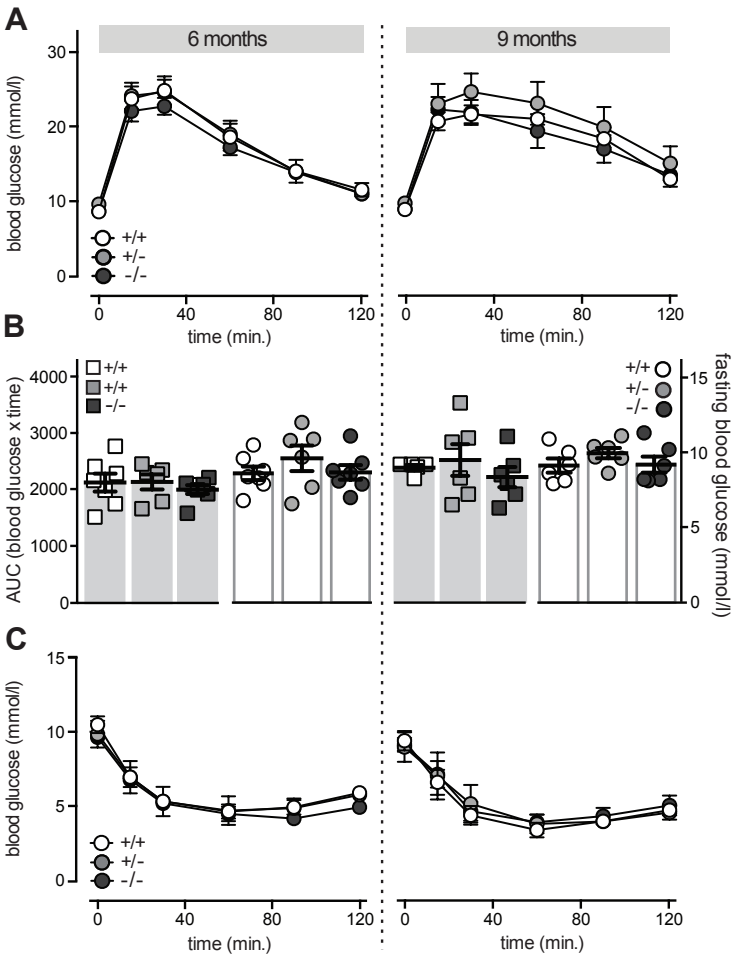
Supplemental Table 2:

	Age (years)	**BMI (kg/m^2)**	**HbA_{1c} (%)**	**IL-1β Index**
lean [<25 kg/m^2]:				
average	55.0	20.7	5.8	1.05
SEM	± 3.21	± 2.02	± 0.12	± 0.122
overweight [25 – 30 kg/m^2]:				
average	55.2	26.6	5.5	1.46
SEM	± 6.71	± 0.414	± 0.12	± 0.142
obese [>30 kg/m^2]:				
average	50.0	31.3	5.9	1.86
SEM	± 4.24	±0.411	± 0.20	± 0.182
obese, T2D [>30 kg/m^2]:				
average	55.7	38.9	7.0	1.09
SEM	± 0.882	± 2.89	± 0.81	± 0.058

Summary characteristics of human islet donors.

Mean characteristics of human donors studied in Figure 1C-E, according to BMI tertiles as indicated. HbA_{1c}: glycated hemoglobin. T2D: type 2 diabetic. IL-1β Index: IL-1β potentiation index, defined as the ratio of insulin secretion induced by 16.7 mmol/l glucose in the presence of IL-1β to the insulin secretion induced by 16.7 mmol/l glucose alone.

Supplemental Figure 3:



***Il1r1*-deficient mice have normal glucose tolerance.**

A: Blood glucose measurements following intraperitoneal glucose injection of 6 and 9 month wild-type (+/+), heterozygous (+/-), and *Il1r1*-knockout (-/-) mice (*n*=7, 6, 7; *n*=6, 6, 6 mice) following a 3-hour fast.

B: Area under the curve (AUC) for glucose tolerance tests in (**A**), indicated by squares (*n*=7, 6, 7; *n*=5, 6, 6) and fasting blood glucose concentrations following a 3-hour fast, indicated by circles (*n*=7, 6, 7; *n*=6, 6, 6 mice).

C: Blood glucose measurements following intraperitoneal insulin injections from wild-type (+/+), heterozygous (+/-), and *Il1r1*-knockout mice (-/-) (*n*=6, 5, 6; *n*=7, 7, 8 mice) following a 3-hour fast.