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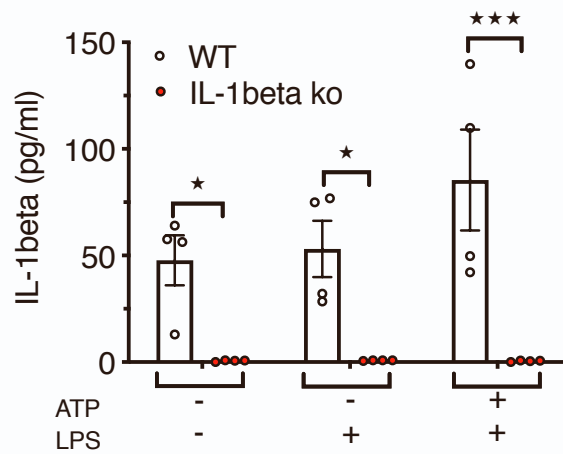
Supplemental information

**IL-1beta promotes the age-associated
decline of beta cell function**

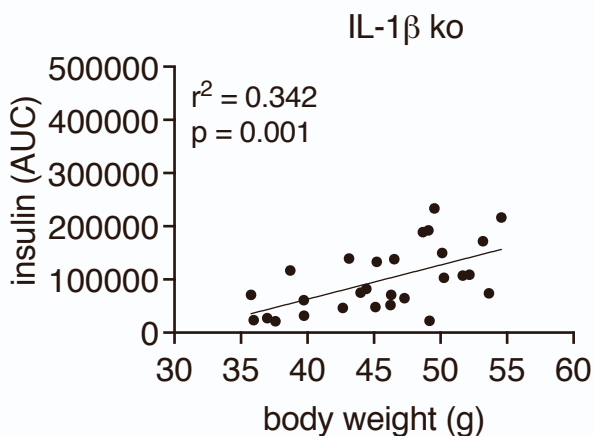
Marianne Böni-Schnetzler, Hélène Méreau, Leila Rachid, Sophia J. Wiedemann, Friederike Schulze, Kelly Trimigliozzi, Daniel T. Meier, and Marc Y. Donath

Figure S1

S1a



S1b



S1c

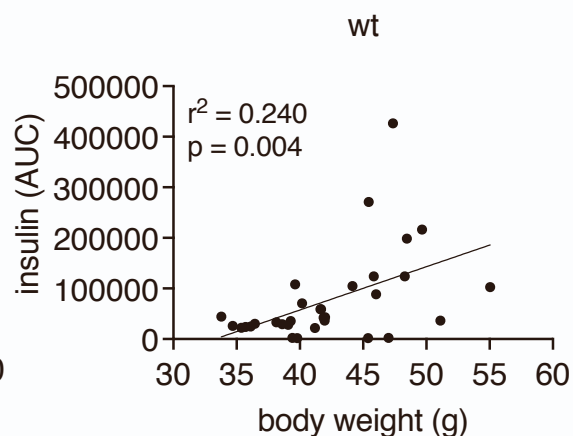


Figure S1. Related to Figure 3: IL-1beta secretion in cultured peritoneal cells from IL-1beta ko mice and correlations of insulin secretion in ipGTT with body weight in 52-week-old IL-1beta ko and control mice

(S1a) IL-1beta concentrations in culture supernatants of pools of adherent peritoneal cells from 3 wt mice and 3 IL-1beta ko mice with or without treatment with 100 ng/ml of LPS and a combination of LPS and 5 mM ATP (n=4 replicates). Statistics: two-way ANOVA and Sidak's multiple comparison test; error bars represent SEM; wt versus ko: *P < 0.05, ***P < 0.001.

(S1b,c) Positive correlations of insulin area under the curve (AUC) during 30 minutes after the glucose bolus during an ipGTT with body weight in IL-1beta ko mice (b) and littermate wt control mice (c).

Figure S2

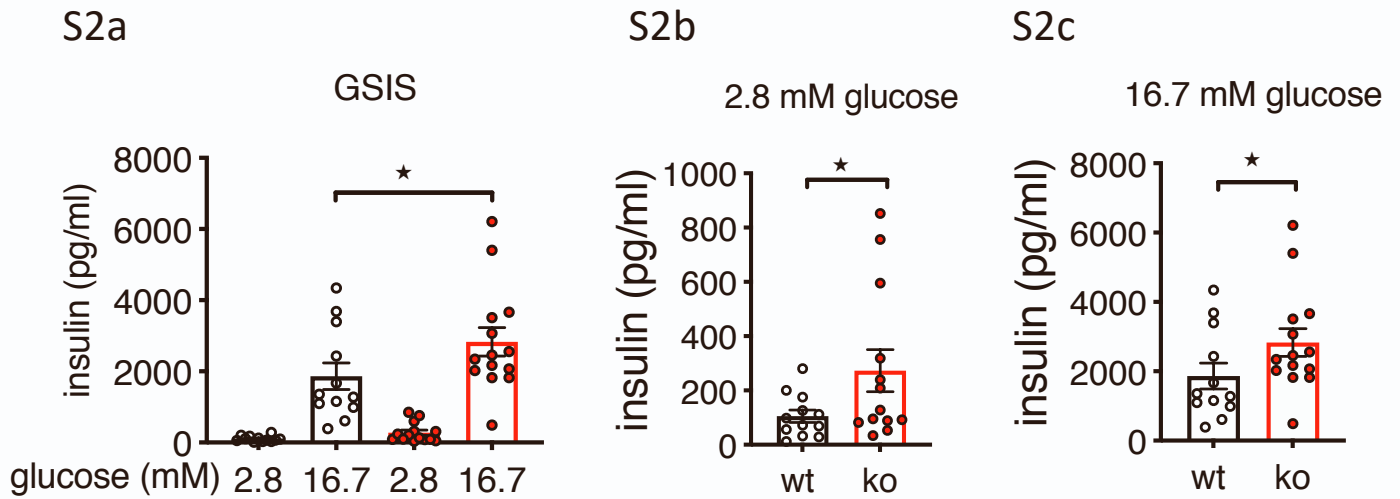


Figure S2. Related to Figure 4: Glucose-stimulated insulin secretion (GSIS) in isolated islets from IL-1beta ko and control mice (raw data)

GSIS of isolated islets of 52-weeks-old IL-1beta ko (red) and littermate wt control (black) mice, data expressed as mean per mouse:

(S2a) 1h insulin secretion of 10 islet in 1 ml (mean of 3-4 biological replicates per mouse, n=12 wt and n=13-14 ko mice).

(S2b) Comparison of 1h insulin secretion at 2.8 mM glucose in islets from ko and wt mice.

(S2c) Comparison of 1h insulin secretion at 16.7 mM glucose in islets from ko and wt mice.

Statistics: S2a; two-way ANOVA and Sidak's multiple comparison test, S2b,c; Student's t-test, error bars represent SEM, *P<0.05, **P<0.01.

Figure S3

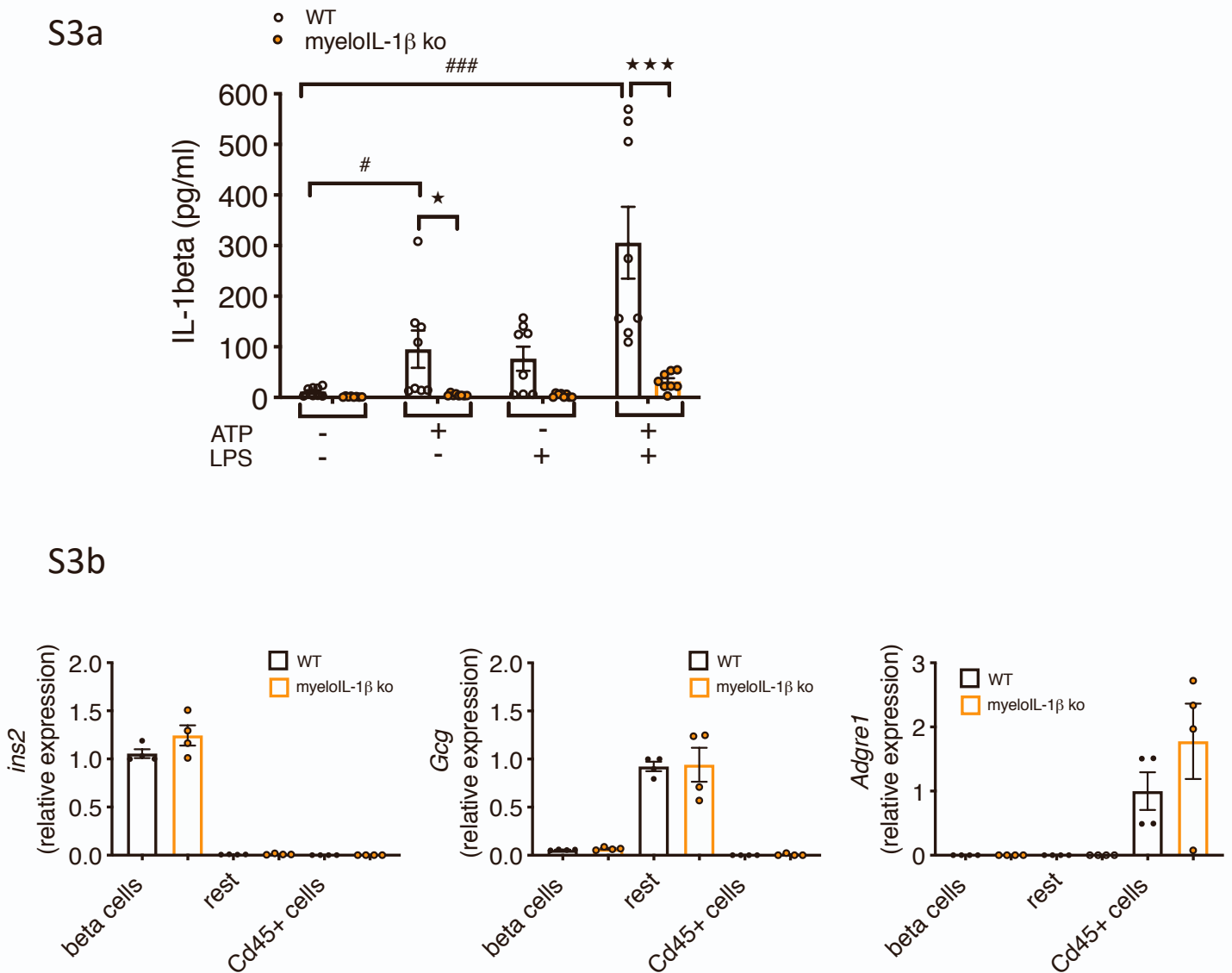


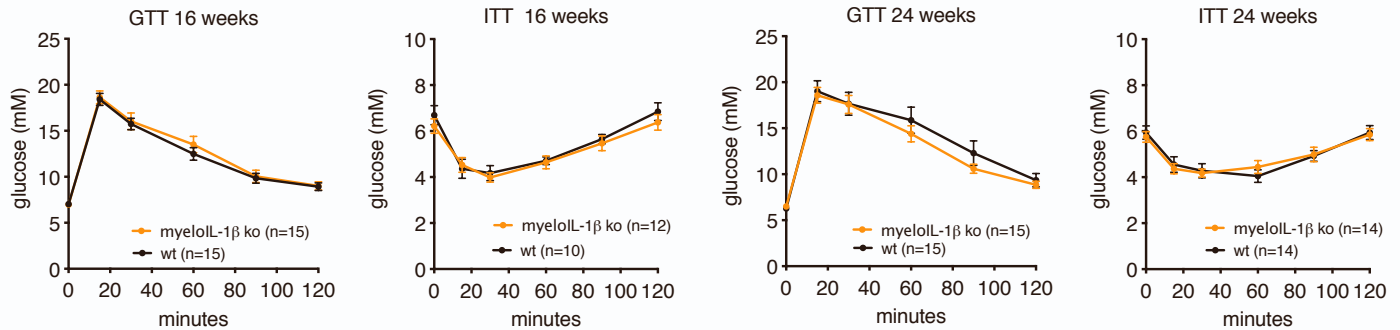
Figure S3. Related to Figure 5: IL-1beta secretion in cultured peritoneal cells from myelolL-1beta ko mice and FACS fractions controls of islet cell fractions from myelolL-1beta ko and littermate wt mice

(S3a) IL-1beta concentrations in culture supernatants of pools of adherent peritoneal cell from 4 wt mice and 5 myelolL-1beta ko mice with or without treatment with 100 ng/ml LPS and a with and without 5 mM ATP (n=8 replicates). Statistics: two-way ANOVA and Sidak's multiple comparison test; error bars represent SEM; wt versus ko: *P<0.05, **P<0.01, ***P<0.001; comparison between treatments: #P<0.05, ###P<0.001

(S3b) Relative gene expression in FACS-isolated beta cell fractions, rest cell fractions and CD45+ pan-immune cell fractions (n=4, cells from 2 mice were pooled per data point). Statistics: Error bars represent SEM.

Figure S4

S4a



S4b

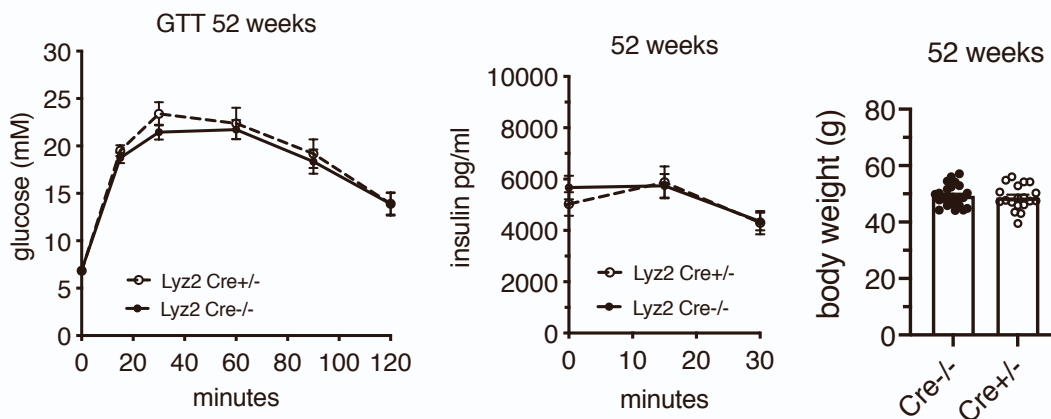


Figure S4. Related to Figure 5: ipGTT and ipITT of a trajectory of myelolL-1beta ko and wt littermate control mice and ipGTT and insulin secretion in 52-week-old Lyz2 Cre^{+/-} and littermate controls (Lyz2 Cre^{-/-})

(S4a) IpGTT and ipITT of the same mice from 2 separate cohorts followed over time; myelolL-1beta ko mice (orange) and littermate controls (black), 52-weeks time points and corresponding insulin values see Fig. 3C-G. Statistics: error bars represent SEM.

(S4b) Blood glucose concentrations during ipGTT (A) and plasma insulin concentration (B) of Lyz2 Cre^{+/-} only mice (n=23) and littermate Lyz2 Cre^{-/-} mice (n=27). C: body weight at 52 weeks of age. Statistics: error bars represent SEM.

Figure S5

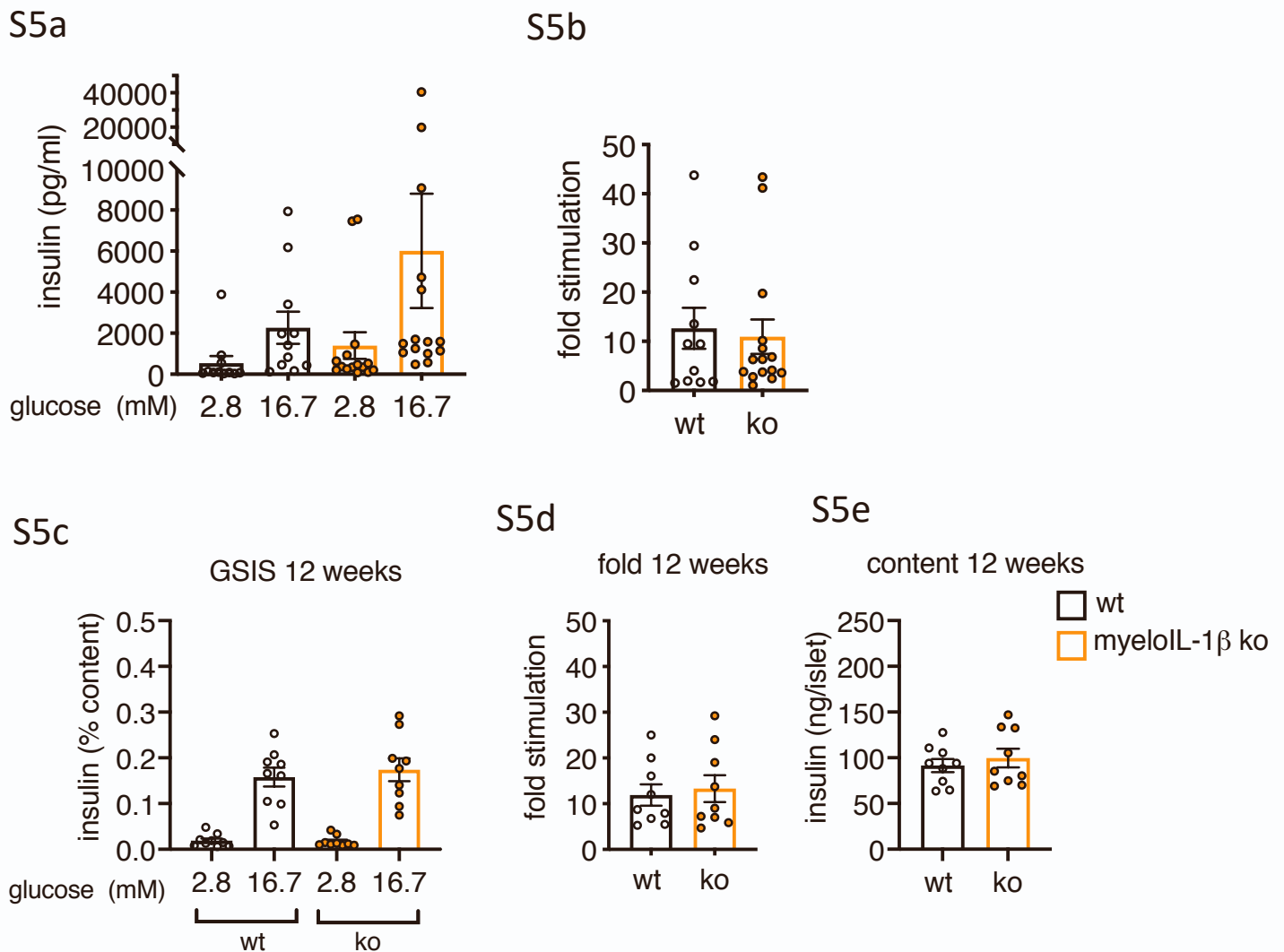


Figure S5. Related to Figure 6: GSIS of islets from 12- and 52-week-old myelolL-1 β ko and wt littermates

(S5a,b) GSIS (a) of isolated islets of 52-weeks-old IL-1 β ko (orange) and littermate wt control (black) mice, raw data expressed as mean per mouse (3-4 replicates per mouse) and (b) fold stimulation of mean insulin at 2.8 and 17.6 mM glucose expressed per mouse.

(S5c-e) GSIS (c) of isolated islets of 12-weeks-old IL-1 β ko (orange) and littermate wt control (black) mice, data expressed as mean % of the content per mouse (3-4 replicates per mouse, n=9 myelolL-1 β ko mice, n=9 control mice); (d) fold stimulation (ratio of insulin secretion at 16.7 to 2.8 mM glucose); (e) mean islet insulin content per mouse.

Figure S6

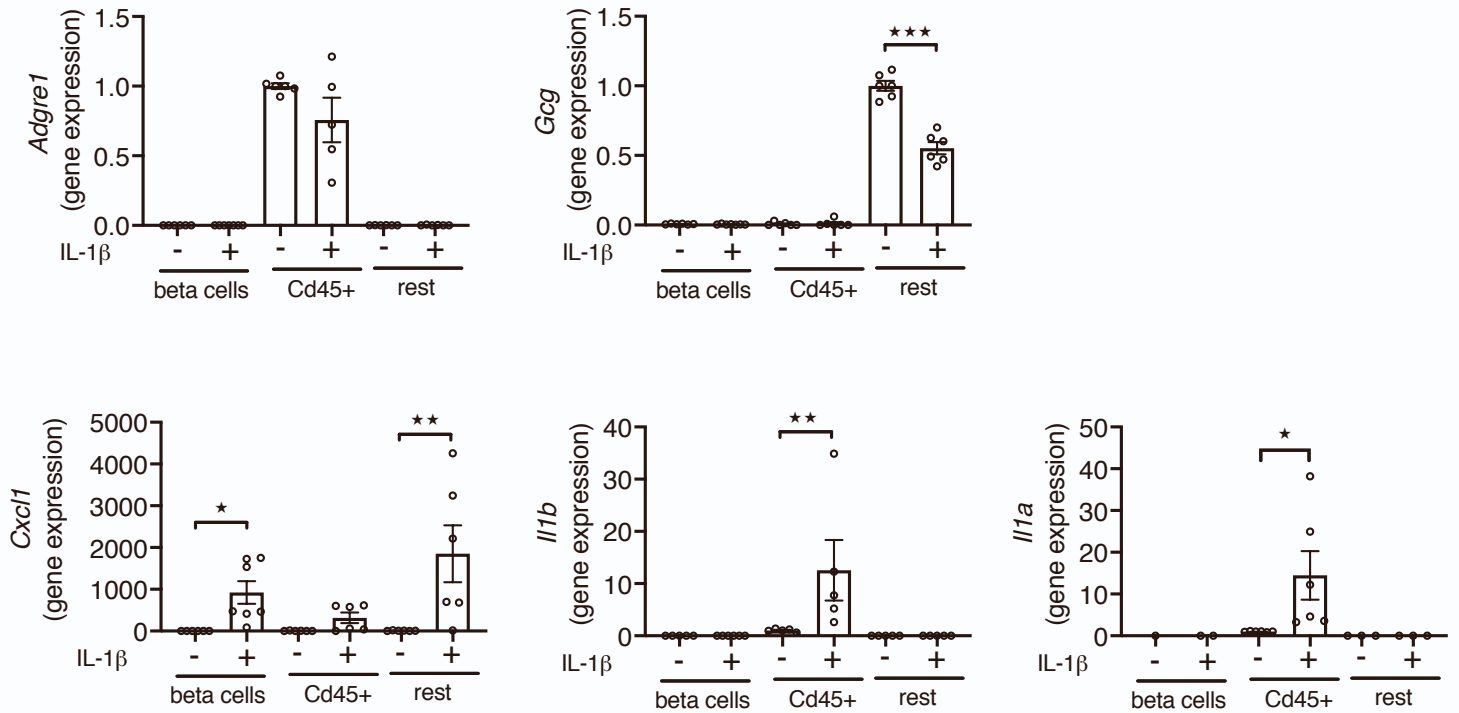


Figure S6. Related to Figure 6: Gene expression in FACS-isolated islet cell fractions from islets treated with or without IL-1beta *in vitro*

Gene expression in FACS-isolated islet cell fractions from islets isolated from EYFP beta cell reporter mice and treated with or without 1ng/ml IL-1beta for 16 hours (n=4-7 FACS isolations, islet pools of 2 mice per FACS isolation). Statistics: one-way ANOVA and Sidak's multiple comparison test; error bars represent SEM, *P<0.05, **P<0.01, ***P<0.001.