Supplemental figure legends

Figure S1. Immunoblots of CIC wild type and KO islets. Companion images from Figures 1A and 4A showing the complete immunoblot along with molecular weight markers. CIC$^{fl/fl}$; Ins1-Cre vs. CIC$^{fl/fl}$ (**A**, **B**) and CIC$^{fl/fl}$; MIP-CreERT vs. CIC$^{fl/fl}$ (**C**, **D**) with anti-CIC (**A**, **C**) and anti-gamma-tubulin (**B**, **D**) antibodies.

Figure S2. Glucose tolerance in MIP-CreERT compared to wild type control mice. 4-6 h fasted wild type (C57BL6/J) and MIP-CreERT male mice were injected i.p. with 1.5 mg/g bw glucose. Blood glucose (**A**) and plasma insulin (**B**) were recorded at the indicated times. Data represent the mean ± S.E.M. (n=9-10 mice per genotype).

Figure S3. BTC-mediated inhibition of GSIS in β-cell CIC KO islets. (**A**-**D**) Islets were isolated from CIC$^{fl/fl}$; MIP-CreERT vs. CIC$^{fl/fl}$ mice 4-6 weeks post-tamoxifen (14-20 weeks of age) and analyzed by perifusion. Following stabilization at basal (2.5 mM) glucose, islets were stimulated with 11.2 mM Glc with or without BTC (2 mM) as indicated. Comparisons of insulin secretion profiles are shown of CIC$^{fl/fl}$ mice (**A**), CIC$^{fl/fl}$; MIP-CreERT (**B**), or CIC$^{fl/fl}$; MIP-CreERT vs. CIC$^{fl/fl}$ mice (**C**). (**D**) Area under the curve (AUC) of the perifusion profiles is shown. Data represent the mean ± S.E.M. (n=8-9 mice per group). (**E**) Islets from wild type mice were perifused at basal (2.5 mM) glucose for 32 min followed by with 11.2 mM Glc with or without BTC as indicated. Data represent the mean ± S.E.M. (**A**-**D**, n=8-9 mice per group; **E**, n=3 per treatment group). * p < 0.05 by 2-way ANOVA.

Supplementary Table 1: Donor characteristics of human islets used for Figure 3F

	ID	Age (years)	Sex (M/F)	BMI (kg/m^2)	HbA1c
Non-diabetic	SAMN11155033	51	M	24.0	4.7
	SAMN12129273	30	F	35.7	4.5
	SAMN15894111	58	F	26.8	n.r.
	SAMN15944113	42	F	23.5	n.r
	SAMN16452455	39	M	31.1	5.6
	SAMN18200483	48	F	47.6	5.4
	SAMN18207297	47	M	40.3	5.5
	Mean ± s.e.m.	45.0±3.4	3/4	32.7±3.2	5.1±0.2
T2D	SAMN10372788	50	F	35.4	9.9
	SAMN12123358	66	F	29.1	7.2
	SAMN12597653	42	F	40.3	9.5
	SAMN12634037	63	M	31.7	5.9
	SAMN16365027	62	F	28.5	7.6
	SAMN17831932	60	M	41.3	7.5
	R276	54	F	24.4	7.2
	Mean ± s.e.m.	56.7±3.2*	1/6	33.0±2.4	7.8±0.5*

Refer to human islet check list for islet parameters and additional donor information
n.r.:not reported
*p<0.05 by two tailed Student's t test versus non-diabetic