Supplemental information

Glucocorticoid-mediated induction of ZBTB16

affects insulin secretion in human

islets and EndoC-βH1 β-cells

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Figure S1. **Glucocorticoid Receptor ChIP assay followed by PCR on the predicted Glucocorticoid Receptor Elements (GREs) on the _ZBTB16_ gene, related to Figure 4C.** For each GRE, the gel band intensity of the GR ChIP band in each replicate was normalized to that of the input band for each condition (Ctrl = control ChIP/control Input, Dexa = Dexa ChIP/Dexa Input) using the ImageLab software (version 6.1, Bio-Rad Laboratories) and the Fold Enrichment of the normalized signal after treatment was measured with respect to control (Dexa/Ctrl) (n=3). The red dashed line represents the baseline where no difference in GR precipitation is observed (Fold enrichment = 1).
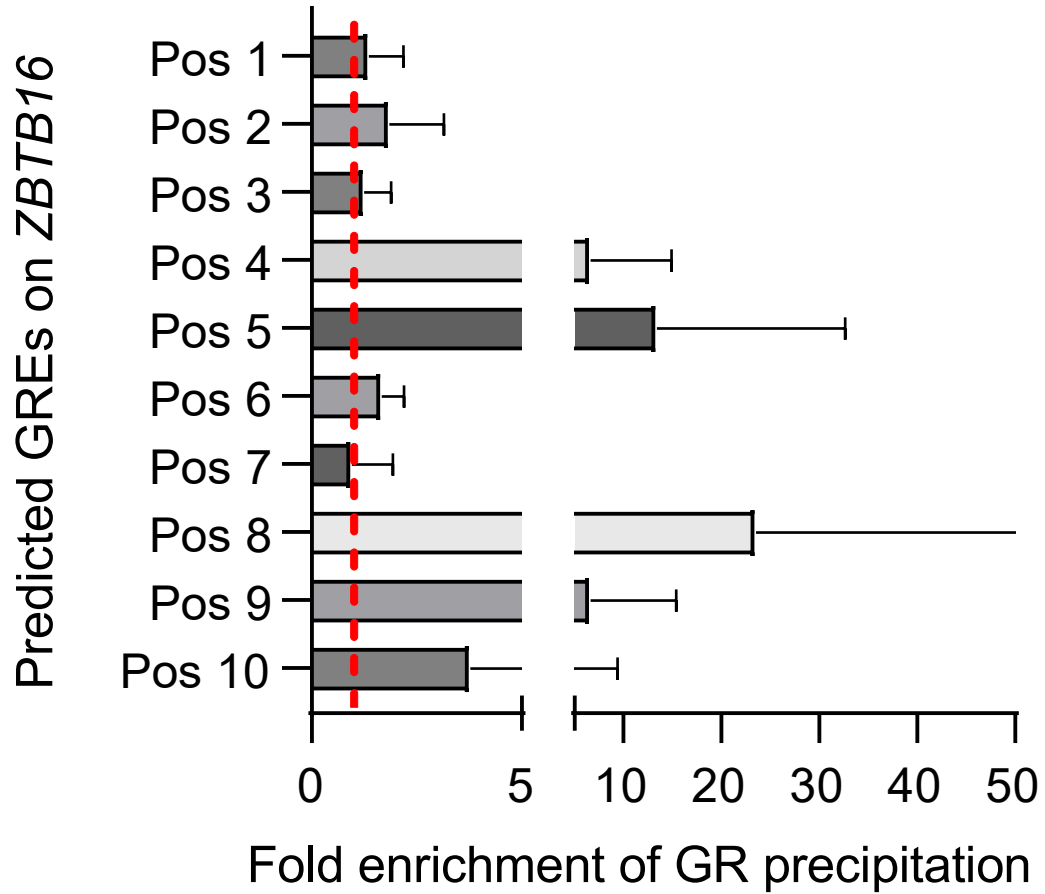
Figure S2. Insulin secretion (% insulin content) measurements, related to Figures 5D, 5E, 6C, 6J. (A) Insulin secretion of EndoC-βH1 cells upon treatment with dexamethasone at different time points (n=6 biological replicates), complementary to Figures 5D,E. (B) Insulin secretion of EndoC-βH1 cells after ZBTB16 overexpression treated with dexamethasone (n=5 biological replicates),complementary to Figure 6C. (C) Insulin secretion of EndoC-βH1 cells after ZBTB16 induction suppression and dexamethasone treatment (n=6 biological replicates), complementary to Figure 6J. Multiple Wilcoxon tests were performed to assess the significance level of all comparisons. Low glucose = 1 mM, high glucose = 20 mM, Ctrl = Control (DMSO), Dexa = 100nM Dexamethasone. Data are presented as mean ± SEM; *p < 0.05.
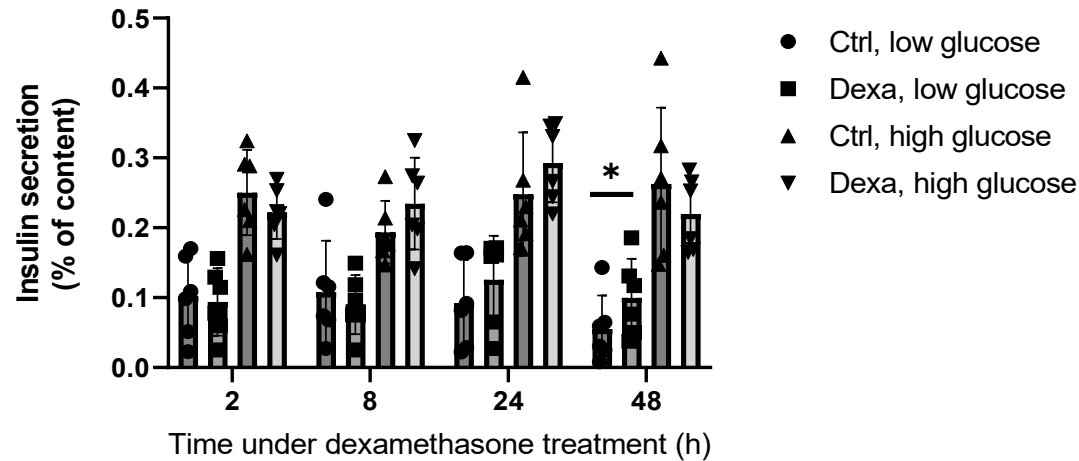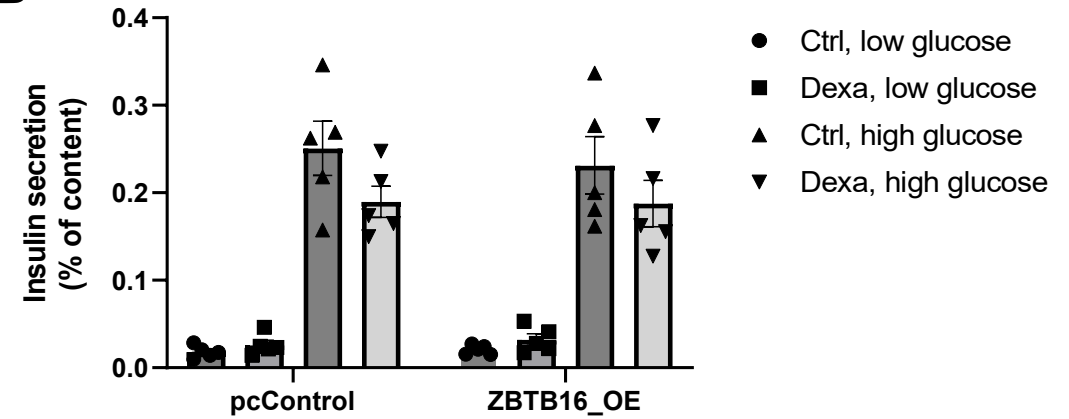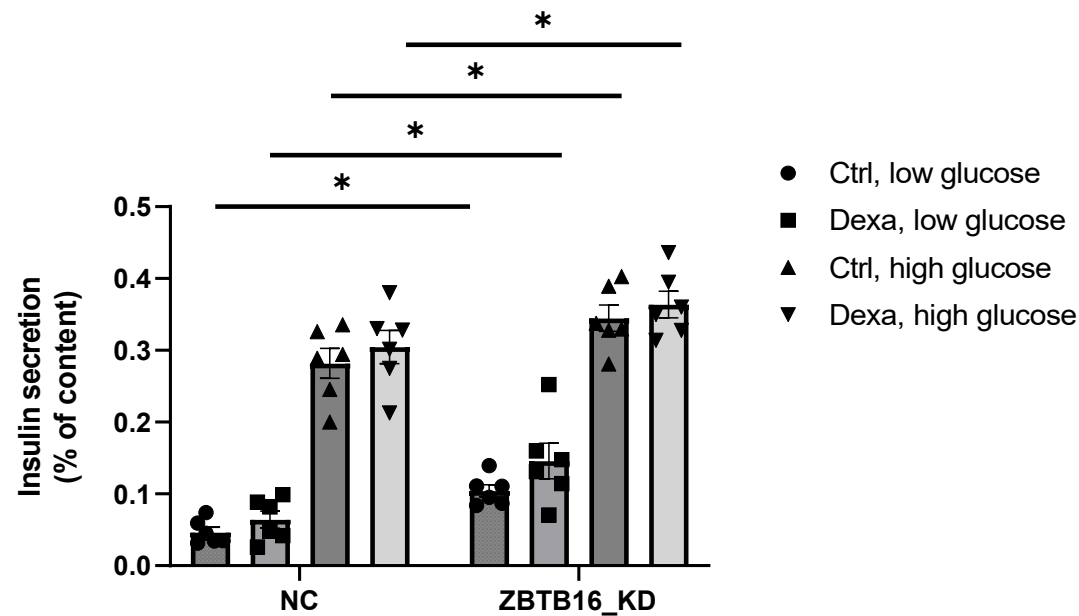
Figure S3. **Cell viability of EndoC cells after dexamethasone treatment during overexpression/induction suppression of *ZBTB16*, related to Figure 7.** Cell viability of EndoC cells, as measured with MTS assay, after treatment with 100nM dexamethasone for 48h (n=4 biological replicates) relative to the control condition. *ZBTB16* induction suppression (left) and overexpression (right) for 72h with the respective controls are shown in the barplots. Paiwise comparisons were performed with repeated measures 2-way ANOVA for each condition followed by pairwise comparisons with Tukey's multiple comparison test. Ctrl = Control (DMSO), Dexa = Dexamethasone, pcControl = Control plasmid pcDNA3.1, ZBTB16_OE = ZBTB16 overexpression, NC = Negative Control, ZBTB16_KD = ZBTB16 knockdown. Data are presented as mean ± SEM; **$p < 0.01$, ***$p < 0.001$.
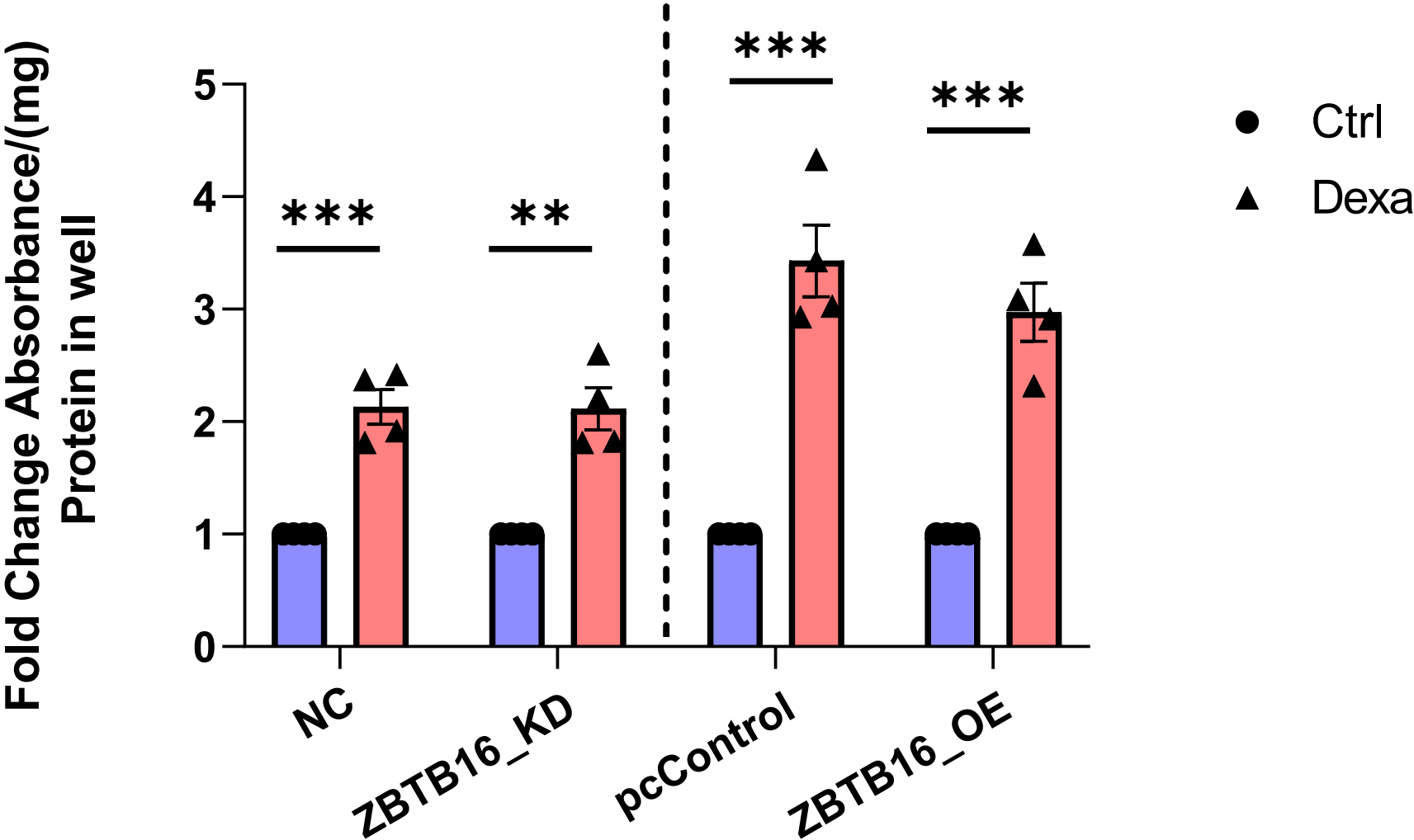
Figure S4. Full-length Western blot images, related to Figure 3D. EndoC-βH1 cells (n=6 biological eplicates) treated with DMSO (Ctrl) or 2μM dexamethasone (Dexa).
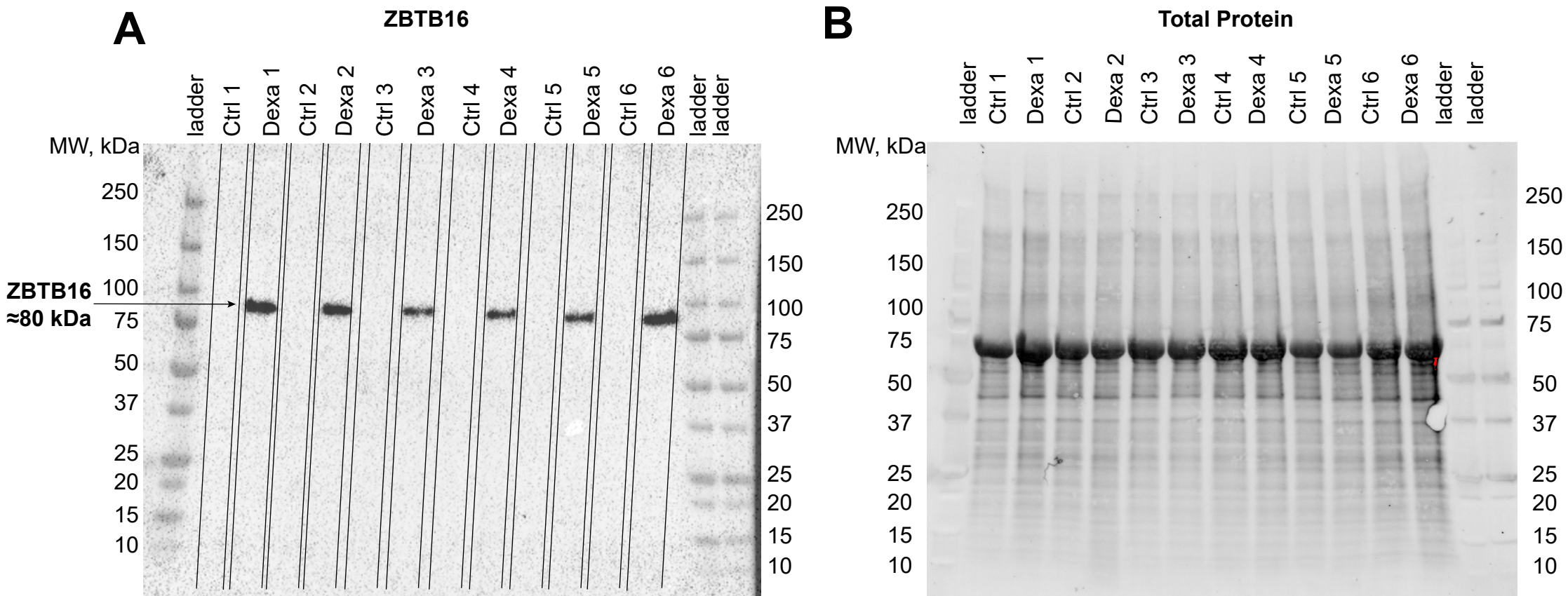
Table S1. Human Islet Donor Characteristics, related to Figure 1

Donor ID	Gender	Age, yr	BMI	HbA1c, %	HbA1c (mmol/mol)
1	Male	66	24.3	5.7	39
2	Male	67	26.1	5.6	38
3	Female	81	22.8	5.7	39
4	Male	43	30.9	5.8	40

Table S7. Primers for Glucocortcoid Receptor (GR) binding sites on *ZBTB16* gene, related to Figure 4

Position number	Position ID/Coords (hg38)	Forward (5'->3')	Reverse (5'->3')	Size (bp)
1	*chr11_114159912_114160415*	GAGCATTGCCTGTGTTTGTTAT	GGAATTCAATGCGGCCTATTC	211
2	*chr11_114162764_114163180*	GTGATGCGGATGCAGAGAGT	CAGTGACGACACCACTCTGG	143
3	*chr11_114179131_114179656*	AGTGTGCTGTTCTCCGTCTG	ATCTGCACGCCTGCTTACAT	166
4	*chr11_114098946_114099330*	CTCAGCCCTGTTCTCCTTTC	CCCAGTAAGATCACGGTTGTT	218
5	*chr11_114080268_114080696*	CATCCACTGAGCCCAAGATT	TAGCACAACCTGGCCTTAAATA	277
6	*chr11_114197742_114198458*	GTATCGGGGAGGACAGGACA	AAGTGCCTATGACGTTCCGC	204
7	*chr11_114173033_114173448*	AAACACCAAAGGCAAGCCAAT	TACTCCCCAACACCCATTCAG	141
8	*chr11_114124563_114124916*	GCATCTCTTGGCCATATCCCT	TGCGTCCAACTGACAATGAGA	153
9	*chr11_114139420_114140069*	CCTCCTGGCAAGTGACCAAA	TGCCGTCCTTCCTATCCTGA	180
10	*chr11_114180474_114180830*	CCTAGGGGACAGACAGCTTG	AGTCTGTGCCCACTAAATGCT	122