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Supplemental Information

Vitamin-D-Binding Protein Contributes to the Maintenance of α Cell Function and Glucagon Secretion

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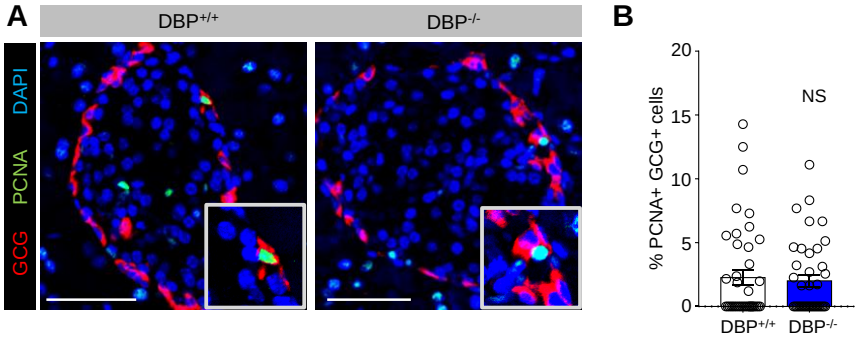

Figure S1, related to Figure 2: No changes in α-cell turnover are detected following loss of DBP

(A) Representative images showing PCNA and glucagon (GCG) staining in islets of $DBP^{+/+}$ and $DBP^{-/-}$ mice (n = 4 animals) (scale bar = 53 µm).

(B) The number of PCNA-positive α-cells is similar in islets of $DBP^{+/+}$ and $DBP^{-/-}$ mice (n = 4 animals).

Bar graph shows scatter plot with mean ± SEM. NS, non-significant. DBP, Vitamin D-binding protein; GCG, glucagon; PCNA, proliferating cell nuclear antigen.

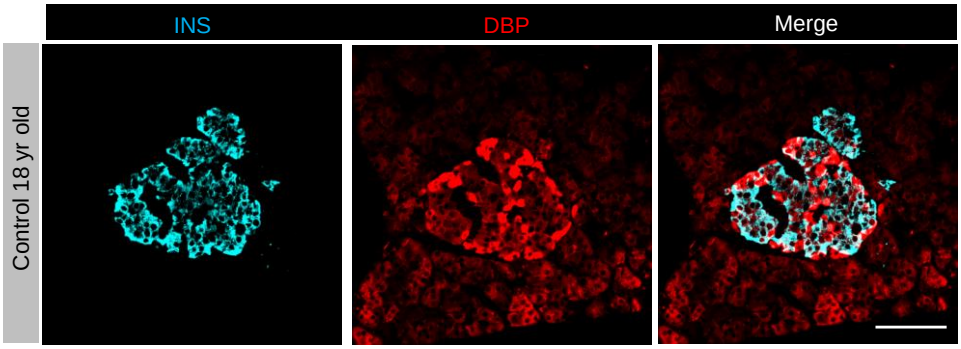

Figure S2, related to Figure 5: DBP is present at low levels in β-cells

DBP can be detected in insulin-positive cells, as well as in exocrine tissue, in control human donors. Due to the strength of DBP expression in α-cells, the image has been overexposed to allow visualization of DBP in the glucagon-negative compartment (scale bar = 42.5 µm) (representative images from n = 3 control donors). DBP, Vitamin D-binding protein; INS, insulin.

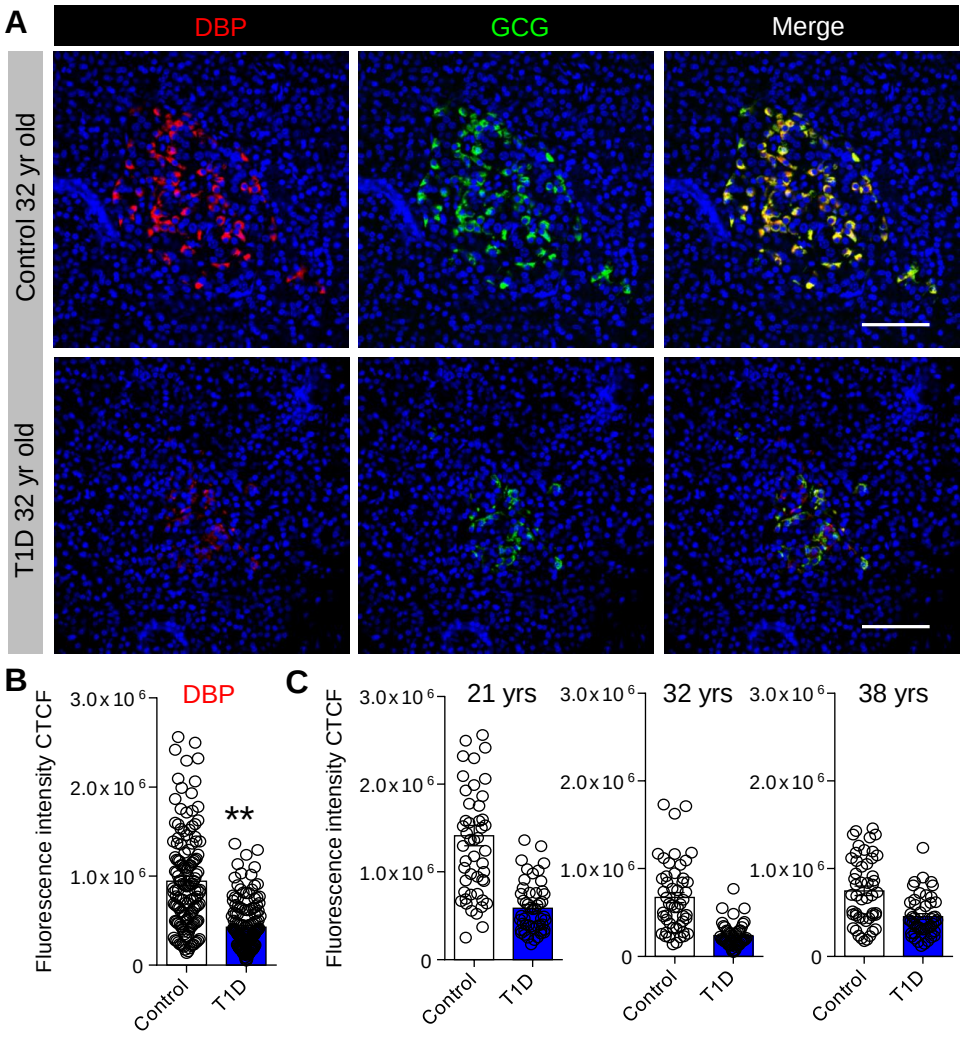

Figure S3, related to Figure 5: DBP is decreases in islets of donors with morelongstanding T1D.

(A) Representative images showing DBP expression in islets of donors with more longstanding T1D, together with their age-matched controls, both obtained from the IsletCore (Alberta) biobank (3 T1D donors and 3 age-matched controls).

(B and C) DBP levels are decreased in adult donors with longstanding T1D, as shown by mean (B) and individual donor (C) data (n = 150 cells, 30 islets, 3 T1D donors and 3 age-matched controls) (unpaired t-test). Scale bar = 42.5 µm.

Bar graphs show scatter plot with mean ± SEM. **P<0.01 and NS, non-significant. DBP, Vitamin D-binding protein; GCG, glucagon.

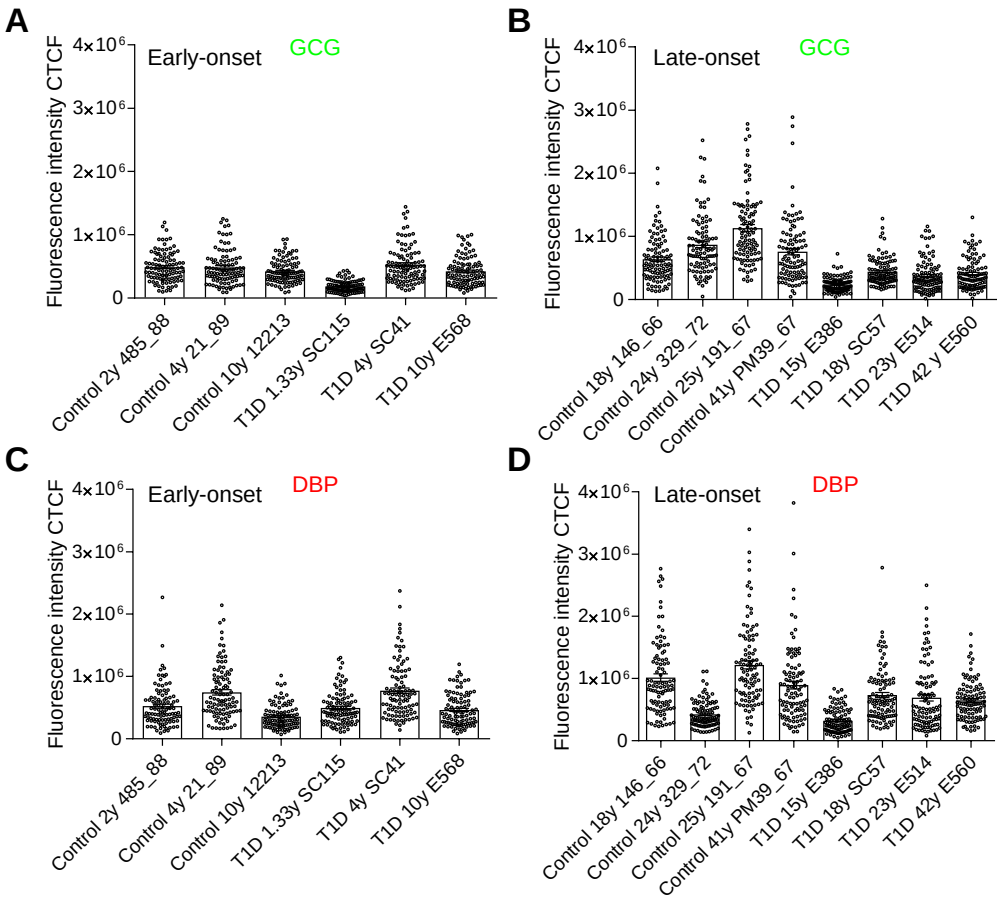

Figure S4, related to Figure 5: Individual donor glucagon and DBP expression levels

(A and B) Expression levels of glucagon in individual early-onset (≤ 10 yrs old) (A) and late-onset (≥ 15 yrs old) (B) T1D donors together with their age-matched controls (n = 100 cells, 10 islets from each donor).

(C and D) Expression levels of DBP in individual early-onset (C) and late-onset (D) T1D donors together with their age-matched controls (n = 100 cells, 10 islets from each donor).

Bar graphs show scatter plot with mean ± SEM. DBP, Vitamin D-binding protein; GCG, glucagon.

Tissue	Donor case ID	Age (years)	Sex	Cohort	Duration
Control	485/88	2	F	Exeter	
Control	21/89	4	F	Exeter	
Control	12213	10	unknown	Exeter	
Control	146/66	18	unknown	Exeter	
Control	329/72	24	unknown	Exeter	
Control	191_67	25	M	Exeter	
Control	447/71	32	F	Exeter	
Control	PM39/67	41	unknown	Exeter	
Control	330_71	47	M	Exeter	
Control	3730A/88	53	F	Exeter	
Control	9310/08	58	F	Exeter	
Control	224/66	67	M	Exeter	
Control	36/66	70	F	Exeter	
Control	424/67	70	M	Exeter	
Control	R187	21	M	Alberta	
Control	R294	32	M	Alberta	
Control	R044	38	M	Alberta	
T1D	SC115	1.33	F	Exeter	3 days
T1D	SC41	4	F	Exeter	3 wks
T1D	E568	10	M	Exeter	2 days
T1D	E386	15	M	Exeter	6 mths
T1D	SC57	18	F	Exeter	< 1 wk
T1D	E514	23	M	Exeter	2 wks
T1D	E560	42	n/a	Exeter	n/a
T1D	R015	21	M	Alberta	n/a
T1D	R079	32	M	Alberta	17 yrs
T1D	R035	38	F	Alberta	15 yrs

Table S1, related to Figure 5 and Figure 6: List of control and T1D donors used for immunohistochemical analyses in Figure 5 & 6. M, male; F, female; n/a, not available.