

ESM Table 1

Donor demographic information including age, percentage of males and females, ethnicity, BMI, disease duration, and C-peptide levels.

	Non-diabetic (n=51)	AAb+ (n= 30)	Type 1 diabetes (n=48)	Total (N=129)
Age, mean \pm SD (years)	23.4 \pm 15.4	25.4 \pm 12.5	26.7 \pm 11.9	22.5 \pm 6.8
Sex, <i>n</i> (%)				
Female	22 (43.1)	13 (43.3)	18 (37.5)	53 (41)
Male	29 (56.9)	17 (56.7)	30 (62.5)	76 (58.9)
Ethnicity, <i>n</i> (%)				
African American	7 (13.7)	5 (16.7)	7 (14.6)	19 (14.7)
Caucasian	40 (78.4)	15 (50)	36 (75)	91 (70.5)
Hispanic	4 (7.8)	10 (33.3)	5 (10.4)	19 (14.7)
BMI, mean \pm SD (kg/m ²)	23 \pm 5.1	27 \pm 8	24.5 \pm 4.9	24.6 \pm 6.1
Disease duration, mean \pm SD (years)	-	-	12 \pm 11.7	-
C-peptide, mean \pm SD (nmol/L)	1.9 \pm 1.5	2.1 \pm 1.5	0.05 \pm 0.1	-

ESM Table 2

Donor characteristics information including Case identification (CaseID), type of donor (TypeID), donor sample method used (RT= real time PCR; IF= immunofluorescence; WB= western blot), autoantibody results (AAb results), donor age in years, diabetes duration (Dur.), gender, race, BMI, HbA1c and C-peptide results.

CaseID	TypeID	Method			AAb Results	Age (yr)	Dur.	Gender	Race	BMI kg/m ²	HbA1c mmol/mol (%)	Cpeptide nmol/L
5000	T1D	-	IF	-	GADA+ mIAA*+	18.76	2	Female	Caucasian	25.03	89 (10.30)	0.0198
6025	T1D	RT	-	-	mIAA*+	23.8	19	Male	Caucasian	26.6	-	<0.016
6026	T1D	RT	-	-	mIAA*+	22.4	9	Male	Caucasian	24.1	-	<0.016
6032	T1D	RT	-	-	mIAA*+	33.8	n/a	Male	Caucasian	29.4	-	<0.016
6039	T1D	RT	-	-	GADA+ IA-2A+ ZnT8A+ mIAA*+	28.7	12	Female	Caucasian	23.4	-	<0.016
6041	T1D	RT	-	-	Negative	26.3	23	Male	Caucasian	28.4	-	<0.016
6049	T1D	RT	-	-	GADA+ mIAA*+	15	10	Female	African Am	20.8	-	<0.016
6063	T1D	RT	-	-	mIAA*+	4.4	3	Male	Caucasian	23.8	-	<0.016
6070	T1D	RT	-	-	IA-2A+ mIAA*+	22.6	7	Female	Caucasian	21.6	-	<0.016
6076	T1D	RT	-	-	GADA+ mIAA*+	25.8	14	Male	Caucasian	18.8	66 (8.2)	<0.016
6084	T1D	-	IF	-	mIAA*+	14.20	4	Male	Caucasian	26.30	-	0.0082
6141	T1D	RT	-	-	GADA+ IA-2A+ ZnT8A+ mIAA*+	36.7	28	Male	Caucasian	26	-	<0.016
6198	T1D	-	IF	-	GADA+ IA-2A+ ZnT8A+ mIAA*+	22.00	3	Female	Hispanic	23.10	-	0.0082
6242	T1D	RT	-	-	IA-2A+ mIAA*+	39	19	Male	Caucasian	19.5	-	<0.016
6244	T1D	RT	-	WB	mIAA*+	34	28	Male	Caucasian	23.8	41 (5.9)	0.016
6247	T1D	RT	-	-	mIAA*+	24	0.6	Male	Caucasian	24.3	-	0.15
6258	T1D	RT	-	WB	mIAA*+	39	37	Female	Caucasian	28.7	64 (8)	<0.016
6261	T1D	RT	-	-	GADA+ mIAA*+	16	14.1 6	Male	Caucasian	20.7	55 (7.2)	<0.016

6262	T1D	RT	-	-	GADA+ IA-2A+ mIAA*+	44	8	Male	African Am	21.5	-	<0.016
6264	T1D	RT	-	-	Negative	12	9	Female	Caucasian	22	74 (8.9)	<0.016
6298	T1D	RT	-	-	mIAA*+	29	26	Male	African Am	24.3	122 (13.3)	<0.016
6299	T1D	RT	-	WB	mIAA*+	32	23	Male	Caucasian	31.8	-	<0.016
6302	T1D	RT	-	WB	Negative	38.5	32.5	Male	African Am	20.5	66 (8.2)	0.056
6307	T1D	RT	-	WB	GADA+ mIAA*+	45	10	Female	Caucasian	19.5	-	<0.016
6319	T1D	RT	-	WB	GADA+ mIAA*+	52	25	Male	Caucasian	25.5	70 (8.6)	<0.006
6321	T1D	RT	-	-	IA-2A+ mIAA*+ ZnT8A+	27	16	Female	Caucasian	20.3	65 (8.1)	<0.006
6322	T1D	RT	-	WB	mIAA*+	22	17	Male	Caucasian	23.6	-	<0.006
6324	T1D	RT	-	WB	GADA+ mIAA*+	29	2	Male	Hispanic	26.2	88 (10.2)	<0.006
6325	T1D	RT	IF	-	GADA+ IA-2A+ mIAA*+	20.00	6	Female	African Am	31.20	-	0.046
6327	T1D	RT	-	-	mIAA*+	71.2	57	Male	Hispanic	23.2	-	<0.006
6328	T1D	RT	-	-	GADA+ mIAA*+	39	20	Male	Hispanic	24	72 (8.7)	<0.006
6330	T1D	RT	-	-	IA-2A+ mIAA*+	22	18	Male	Caucasian	22.6	-	<0.006
6337	T1D	RT	-	WB	mIAA*+	20.6	5	Female	Caucasian	17.9	113 (12.5)	<0.006
6341	T1D	RT	-	-	mIAA*+	26	15	Male	Caucasian	21.8	125 (13.6)	<0.006
6360	T1D	RT	-	-	mIAA*+	4.8	2.5	Female	Caucasian	26.1	88 (10.2)	<0.006
6362	T1D	RT	-	WB	GADA+	24.9	0	Male	Caucasian	28.5	86 (10)	0.125
6371	T1D	RT	IF	-	GADA+ IA-2A+ mIAA*+ ZnT8A+	12.50	2	Female	Caucasian	16.60	80 (9.50)	0.036
6380	T1D	RT	-	-	Negative	11.6	0	Female	African Am	14.6	124 (13.5)	0.072
6396	T1D	RT	-	-	Negative	17.1	2	Female	Caucasian	22.6	123 (13.4)	0.019

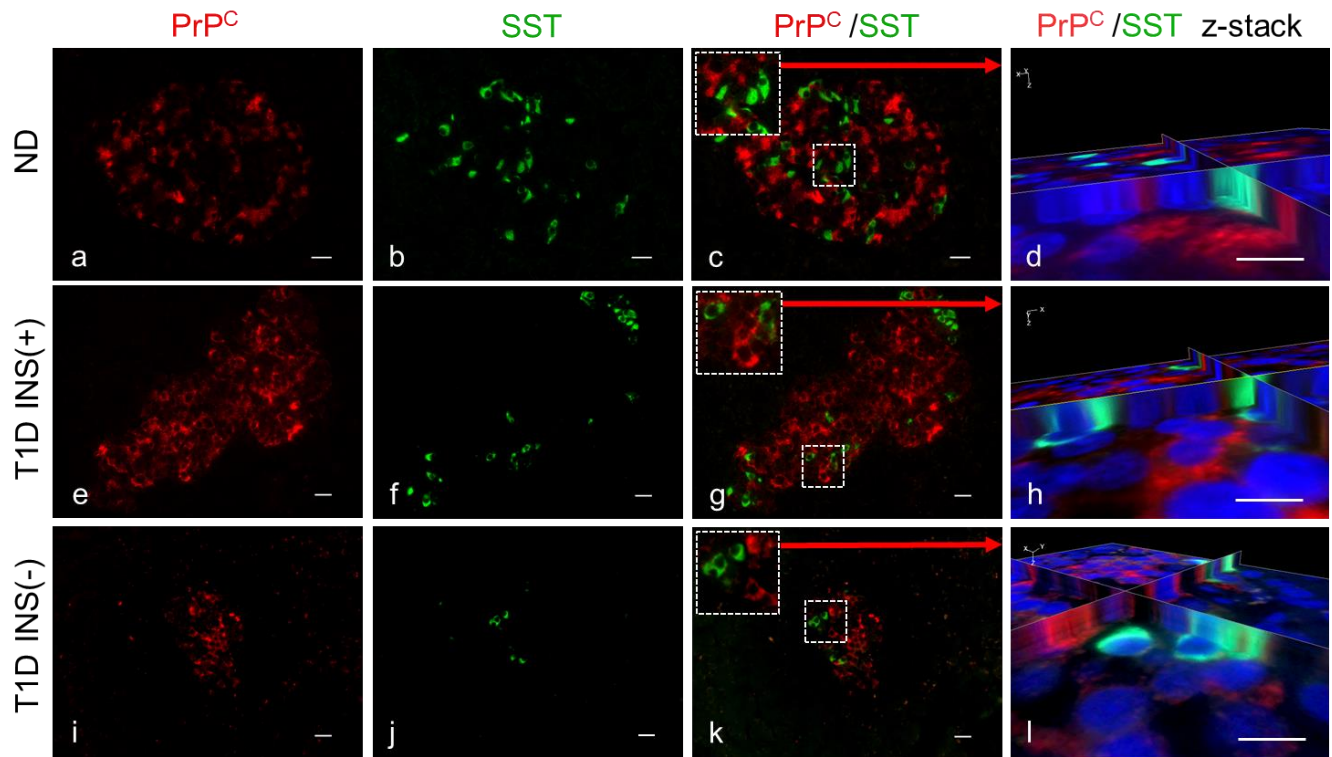
6399	T1D	RT	-	-	GADA+ IA-2A+ ZnT8A+	17.42	0	Male	Caucasian	32	90 (10.4)	0.465
6405	T1D	RT	-	-	GADA+ IA-2A+ ZnT8A+	29.1	0.6	Female	Hispanic	42.5	53 (7)	0.60
6436	T1D	-	IF	-	IA-2A+ mIAA**	26.33	3	Male	Caucasian	30.30	75 (9.00)	<0.016
6438	T1D	-	IF	-	GADA+	39.01	10	Female	Caucasian	35.00	97 (11.00)	<0.016
6441	T1D	-	IF	-	GADA+ IA-2A+	29.17	5	Male	Caucasian	16.50	130 (14.00)	<0.016
6449	T1D	-	IF	-	IA-2A+ mIAA** ZnT8A+	24.00	2	Male	Caucasian	23.02	88 (10.20)	<0.016
6469	T1D	-	IF	-	GADA+	27.06	1.5	Female	Caucasian	26.90	57 (7.40)	0.217
6480	T1D	-	IF	-	IA-2A+ mIAA**	17.18	2.5	Male	Caucasian	27.10	88 (10.20)	0.042
6484	T1D	-	IF	-	GADA+ IA-2A+	28.00	10	Male	African Am	24.90	92 (10.60)	<0.016
6007	No diabetes	RT	-	-	No serum available	9	n/a	Male	African Am	20	-	no serum
6008	No diabetes	RT	-	WB	No serum available	50	n/a	Female	Caucasian	24.2	-	no serum
6012	No diabetes	RT	-	-	Negative	68	n/a	Female	Caucasian	23.7	-	0.9801
6013	No diabetes	RT	-	-	Negative	65	n/a	Male	Caucasian	24.2	-	0.924
6017	No diabetes	RT	-	-	Negative	59	n/a	Female	Caucasian	24.8	-	3.2637
6024	No diabetes	RT	-	-	Negative	21	n/a	Male	Caucasian	27.8	-	1.1616
6030	No diabetes	RT	-	-	Negative	30.1	n/a	Male	Caucasian	27.1	-	0.8382
6047	No diabetes	RT	-	-	Negative	7.8	n/a	Male	Caucasian	23.9	37 (5.5)	0.2145
6048	No diabetes	RT	-	-	Negative	30	n/a	Male	Caucasian	20.6	-	5.9103
6055	No diabetes	RT	-	-	Negative	27	n/a	Male	Caucasian	22.7	-	0.1947
6058	No diabetes	RT	-	WB	Negative	27	n/a	Male	Hispanic	19.1	-	2.9997
6073	No diabetes	RT	-	-	Negative	19.2	n/a	Male	Caucasian	36	-	0.2277

6075	No diabetes	RT	-	WB	Negative	16	n/a	Male	African Am	14.9	-	0.9702
6096	No diabetes	RT	-	-	Negative	16	n/a	Female	African Am	18.8	-	0.9801
6098	No diabetes	RT	-	-	Negative	17.8	n/a	Male	Caucasian	22.8	30 (4.9)	0.4653
6102	No diabetes	RT	-	-	Negative	45.1	n/a	Female	Caucasian	35.1	43 (6.1)	0.1815
6103	No diabetes	RT	-	-	Negative	1.5	n/a	Male	Caucasian	16.8	43 (6.1)	0.3234
6117	No diabetes	RT	-	-	Negative	0.33	n/a	Male	Caucasian	18.4	-	1.0791
6129	No diabetes	RT	-	-	Negative	42.9	n/a	Female	Caucasian	23.4	33 (5.2)	0.1683
6131	No diabetes	RT	-	-	Negative	24.2	n/a	Male	Caucasian	24.8	-	0.3333
6137	No diabetes	RT	-	-	Negative	8.9	n/a	Female	Hispanic	24.2	44 (6.2)	4.0029
6140	No diabetes	RT	-	-	Negative	38	n/a	Male	Caucasian	21.7	42 (6)	3.663
6144	No diabetes	RT	-	-	Negative	7.5	n/a	Female	Hispanic	16.3	-	0.4191
6160	No diabetes	RT	-	-	Negative	22.1	n/a	Male	Caucasian	23.9	33 (5.2)	0.132
6165	No diabetes	RT	-	-	Negative	45.8	n/a	Female	Caucasian	25	38 (5.6)	1.4685
6172	No diabetes	RT	-	-	Negative	19.2	n/a	Female	Caucasian	32.4	36 (5.4)	2.6466
6174	No diabetes	RT	-	-	Negative	20.9	n/a	Male	Caucasian	19.5	-	0.99
6178	No diabetes	RT	IF	-	Negative	24.50	n/a	Female	Caucasian	27.50	31 (5.00)	1.5015
6183	No diabetes	RT	-	-	No serum available	0.3	n/a	Male	African Am	15.4	-	No serum
6217	No diabetes	RT	-	-	Negative	0.58	n/a	Male	Caucasian	17.6	-	0.4323
6229	No diabetes	RT	-	-	Negative	31	n/a	Female	Caucasian	26.9	37 (5.5)	2.0559
6232	No diabetes	RT	-	WB	Negative	14	n/a	Female	Caucasian	20.8	-	6.435
6233	No diabetes	RT	-	-	Negative	14	n/a	Male	Caucasian	21.9	37 (5.5)	2.3958
6251	No diabetes	-	-	WB	Negative	33.00	n/a	Female	Caucasian	29.50	34 (5.30)	0.6336

6253	No diabetes	-	IF	-	Negative	19.00	n/a	Female	African Am	34.30	-	2.3826
6271	No diabetes	RT	-	-	Negative	17	n/a	Male	Caucasian	24.4	-	3.7851
6278	No diabetes	RT	-	WB	Negative	12	n/a	Female	African Am	21.3	45 (6.3)	1.4982
6318	No diabetes	RT	-	WB	Negative	10	n/a	Female	Caucasian	17.6	33 (5.2)	1.2837
6333	No diabetes	-	IF	-	Negative	27.10	n/a	Female	Caucasian	24.90	28 (4.70)	3.0921
6336	No diabetes	-	IF	-	Negative	14.30	n/a	Female	Caucasian	28.90	33 (5.20)	2.5971
6366	No diabetes	-	IF	-	Negative	21.00	n/a	Female	Hispanic	20.50	45 (6.3)	0.1353
6373	No diabetes	-	-	WB	Negative	15.70	n/a	Male	Caucasian	25.00	51 (6.8)	4.3296
6425	No diabetes	-	IF	-	Negative	38.66	n/a	Female	Caucasian	28.28	42 (6.0)	2.6598
6430	No diabetes	-	IF	-	Negative	27.10	n/a	Male	Caucasian	21.60	40 (5.8)	3.6696
6439	No diabetes	-	IF	-	Negative	26.96	n/a	Male	African Am	29.10	28 (4.7)	1.7589
6445	No diabetes	-	IF	-	Negative	17.25	n/a	Male	Caucasian	20.60	35 (5.6)	3.9963
6461	No diabetes	-	IF	-	Negative	14.29	n/a	Male	Caucasian	18.50	37 (5.5)	1.7358
6470	No diabetes	-	IF	-	Negative	30.10	n/a	Male	Caucasian	22.50	37 (5.5)	1.9899
6482	No diabetes	-	IF	-	Negative	18.69	n/a	Female	Caucasian	20.00	34 (5.30)	2.4651
6493	No diabetes	-	-	WB	Negative	18.84	n/a	Male	Caucasian	17.70	33 (5.2)	2.3364
6495	No diabetes	-	-	WB	Negative	9.60	n/a	Male	Caucasian	10.70	41 (5.9)	2.6202
6090	Autoab Pos	RT	-	-	GADA+	2.2	n/a	Male	Hispanic	18.8	-	1.7622
6101	Autoab Pos	RT	-	-	GADA+	64.8	n/a	Male	Caucasian	34.3	-	8.6394
6123	Autoab Pos	RT	-	-	GADA+	23.2	n/a	Female	Caucasian	17.6	36 (5.4)	0.6633
6147	Autoab Pos		IF	-	GADA+	23.8	n/a	Female	Caucasian	32.9	33 (5.2)	1.0527
6151	Autoab Pos	RT	-	-	GADA+	30	n/a	Male	Caucasian	24.2	-	1.8117

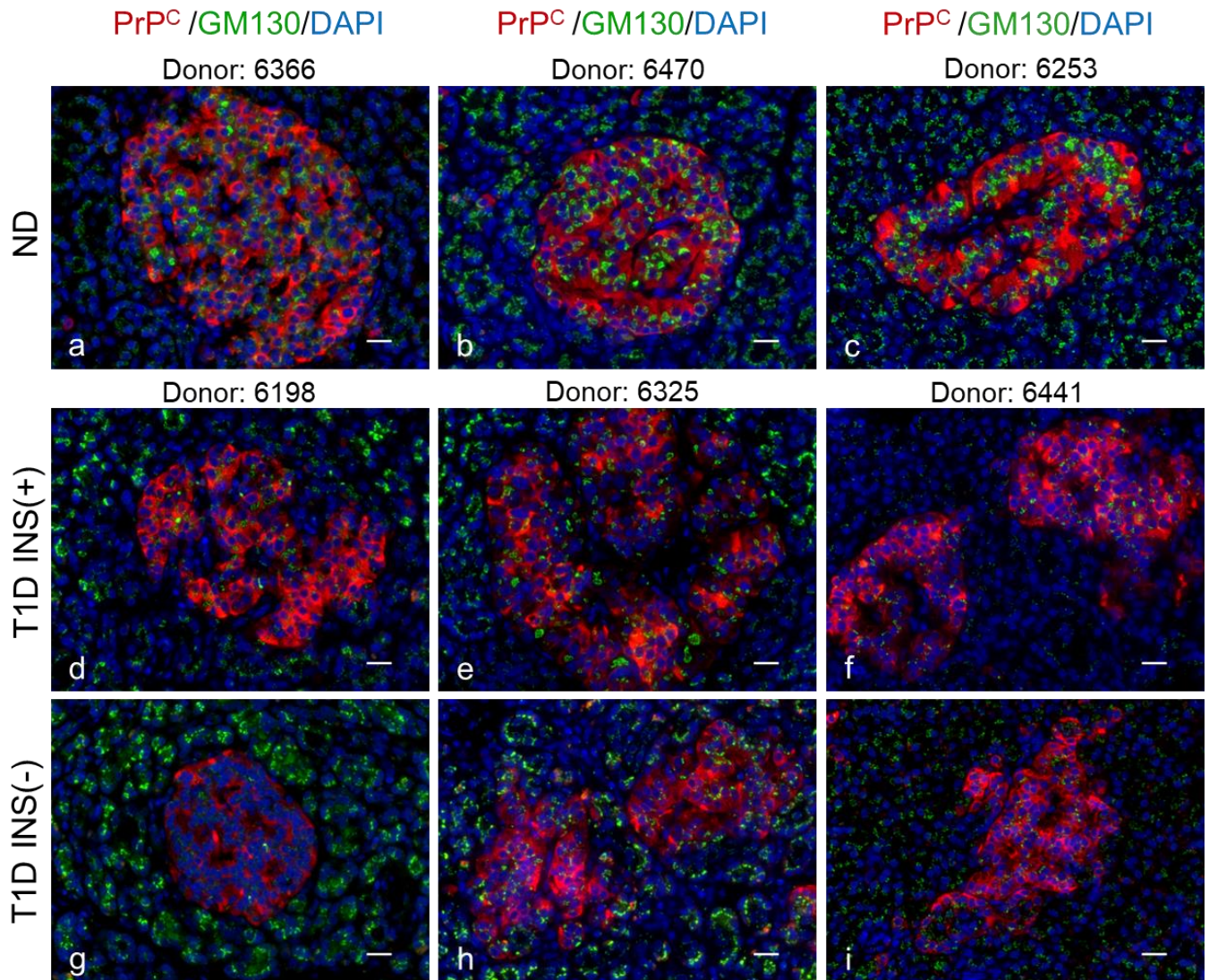
6154	Autoab Pos	RT	-	-	GADA+	48.5	n/a	Female	Caucasian	24.5	-	<0.016
6170	Autoab Pos	RT	-	-	GADA+	34.5	n/a	Female	African Am	36.9	52 (6.9)	1.4157
6171	Autoab Pos		IF	-	GADA+	4.4	n/a	Female	Caucasian	14.8	-	2.9535
6181	Autoab Pos	RT	-	-	GADA+	31.9	n/a	Male	Caucasian	21.9	-	0.198
6184	Autoab Pos	RT	-	-	GADA+	47.6	n/a	Female	Hispanic	27	-	1.1286
6197	Autoab Pos	RT	-	-	GADA+ IA-2A+	22	n/a	Male	African Am	28.2	37 (5.5)	5.7684
6267	Autoab Pos	RT	-	-	GADA+ IA-2A+	23	n/a	Female	Caucasian	23.5	31 (5)	5.4747
6301	Autoab Pos	RT	-	-	GADA+	26	n/a	Male	African Am	32.1	37 (5.5)	1.2936
6303	Autoab Pos	RT	-	-	GADA+	22	n/a	Male	Caucasian	31.9	36 (5.4)	0.9999
6310	Autoab Pos	RT	IF	-	GADA+	28	n/a	Female	Hispanic	22.4	-	3.4782
6314	Autoab Pos	RT	-	-	GADA+	21	n/a	Male	Caucasian	23.8	-	0.4917
6347	Autoab Pos	RT	-	-	mIAA+	8.5	n/a	Male	Caucasian	19.5	-	1.0758
6388	Autoab Pos	RT	-	-	GADA+ mIAA+	25.2	n/a	Female	Hispanic	26	39 (5.7)	0.4554
6397	Autoab Pos	RT	-	-	GADA+	21.16	n/a	Female	Caucasian	29.6	42 (6)	4.2141
6400	Autoab Pos	RT	-	-	GADA+	25.15	n/a	Male	Hispanic	22.2	37 (5.5)	1.3761
6421	Autoab Pos	RT	-	-	GADA+	6.73	n/a	Male	Hispanic	17.9	38 (5.6)	0.6072
6424	Autoab Pos	RT	IF	-	GADA+ mIAA+*	17.65	n/a	Male	Caucasian	51.40	40 (5.8)	2.3001
6429	Autoab Pos	RT	IF	-	GADA+ mIAA+*	22.1	n/a	Male	African Am	19.6	37 (5.5)	0.7425
6433	Autoab Pos	RT	IF	-	GADA+	23.96	n/a	Male	Hispanic	30.8	34 (5.3)	1.4652
6437	Autoab Pos	RT	IF	-	GADA+	24.73	n/a	Male	Caucasian	24.17	39 (5.7)	2.0559
6450	Autoab Pos	-	IF	-	GADA+ ZnT8A+	22.00	n/a	Female	Caucasian	24.40	39 (5.7)	1.8051
6496	Autoab Pos	-	IF	-	GADA+	26.11	n/a	Male	African Am	46.1	39 (5.7)	0.4884

6505	Autoab Pos	-	IF	-	GADA+ mIAA+*	20.59	n/a	Female	Hispanic	22.4	32 (5.1)	6.864
6512	Autoab Pos	-	IF	-	IA2A+ mIAA+* ZnT8A+	30.59	n/a	Female	Caucasian	38.8	33 (5.2)	1.056
6521	Autoab Pos	-	IF	-	GADA+ IA2A+ ZnT8A+	19.77	n/a	Male	Hispanic	24.1	40 (5.8)	2.4552
6108	T2D	-	IF	-	Negative	57.9	n/a	Male	Asian	30.4	-	1.250

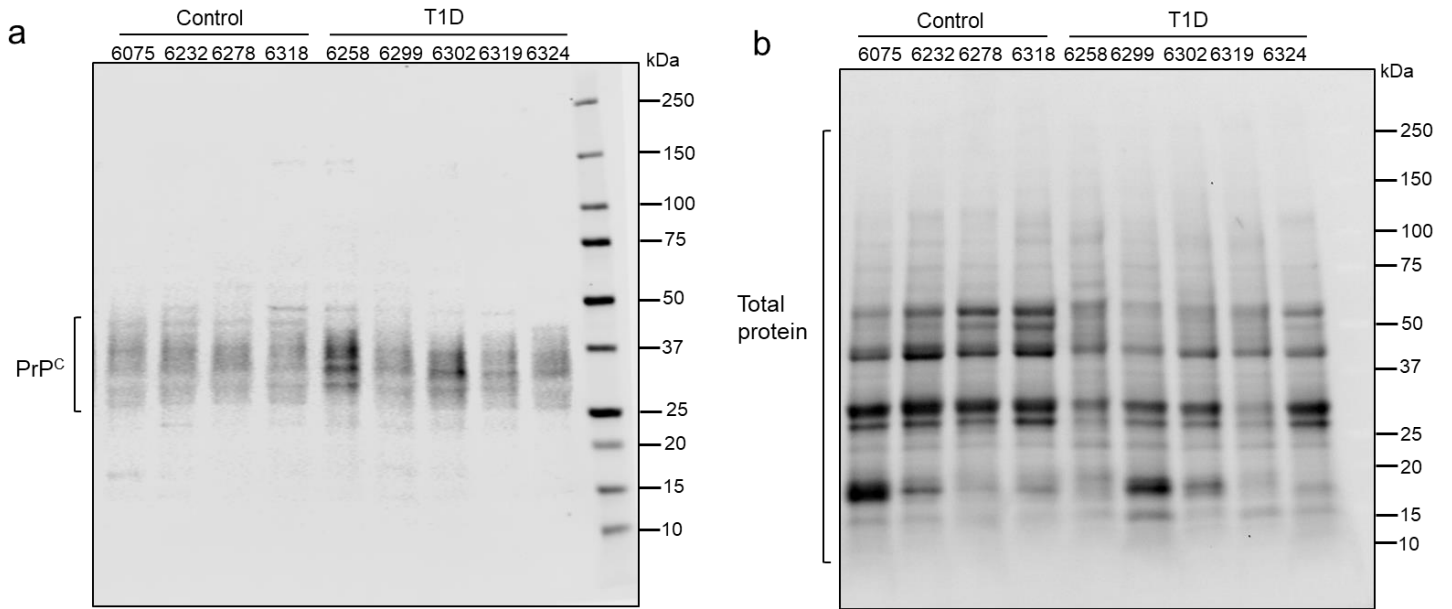


ESM Figure 1. Immunofluorescence analysis of PrP^C expression in relation to δ -cells of

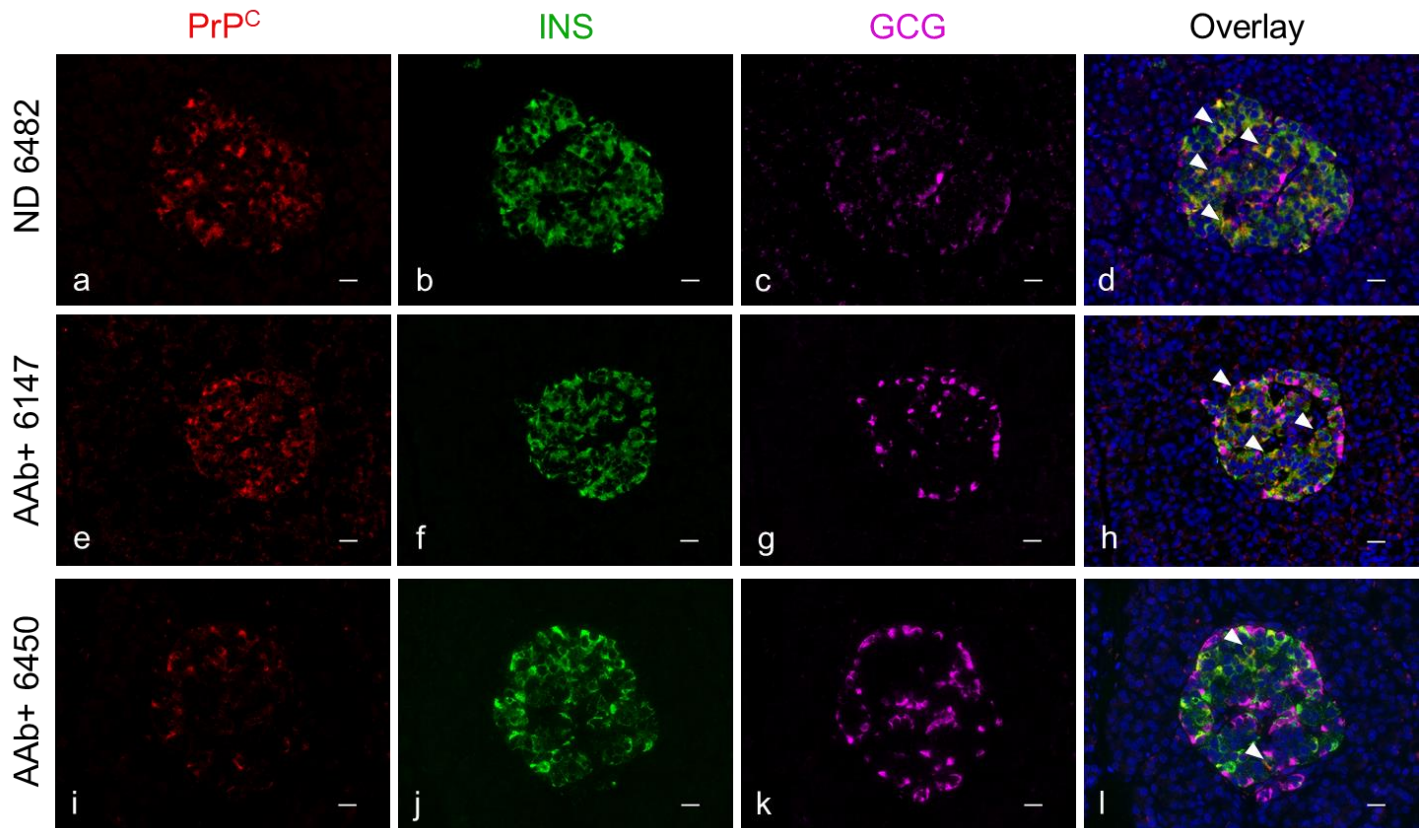
human pancreata. a-d: As previously shown in Figure 1, PrP^C expression in ND donors localizes in the pancreatic islet. No co-registration was observed between PrP^C/SST cells, confirmed using z-stack 3D image reconstruction (d). e-h: Similar to ND donors, type 1 diabetes donors with INS(+) islets show no co-registration between PrP^C/SST cells (g, h). i-l: PrP^C expression in type 1 diabetes donors with INS(-) islets does not present co-registration of PrP^C/SST cells (k, l). Scale: 20 μ m.



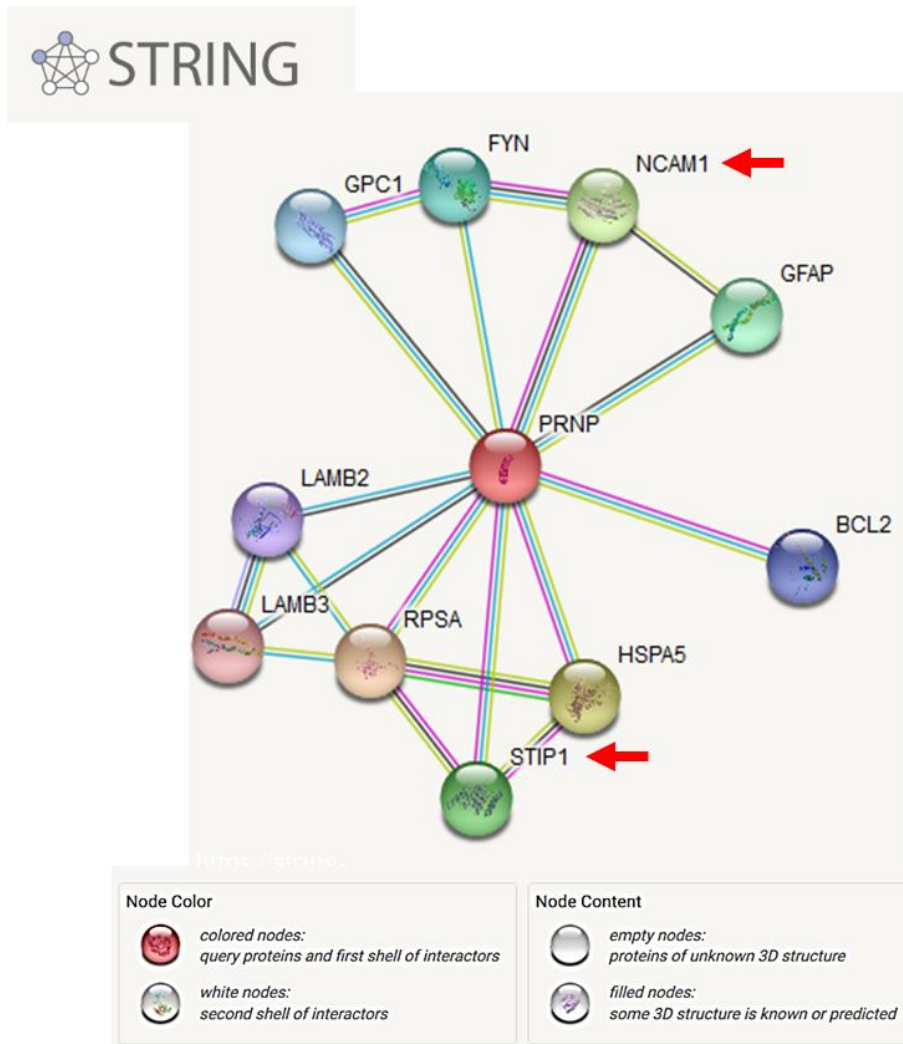
ESM Figure 2. Golgi intracellular localization of PrP^C in 3 ND, 3 type 1 INS(+) and 3 type 1 INS(-) diabetes donors. Specific co-staining of PrP^C and cellular marker Golgi (GM130) to assess PrP^C Golgi intracellular localization within endocrine cells. a-c: Three different ND donors show no colocalization between PrP^C and GM130. d-f: No colocalization was observed in 3 T1D INS(+) donors. g-i: In T1D INS(-) donors, we didn't find any evidence of colocalization between PrP^C and GM130 cells. Scale 20 μ m.



ESM Figure 3. Immunoblotting analysis of PrP^C using total protein lysates from non-diabetic controls and T1D donors. a: Full-length blot of data presented in Figure 4b. PrP^C bands run at the expected molecular weight. b: Total protein stain from blot shown in panel a.

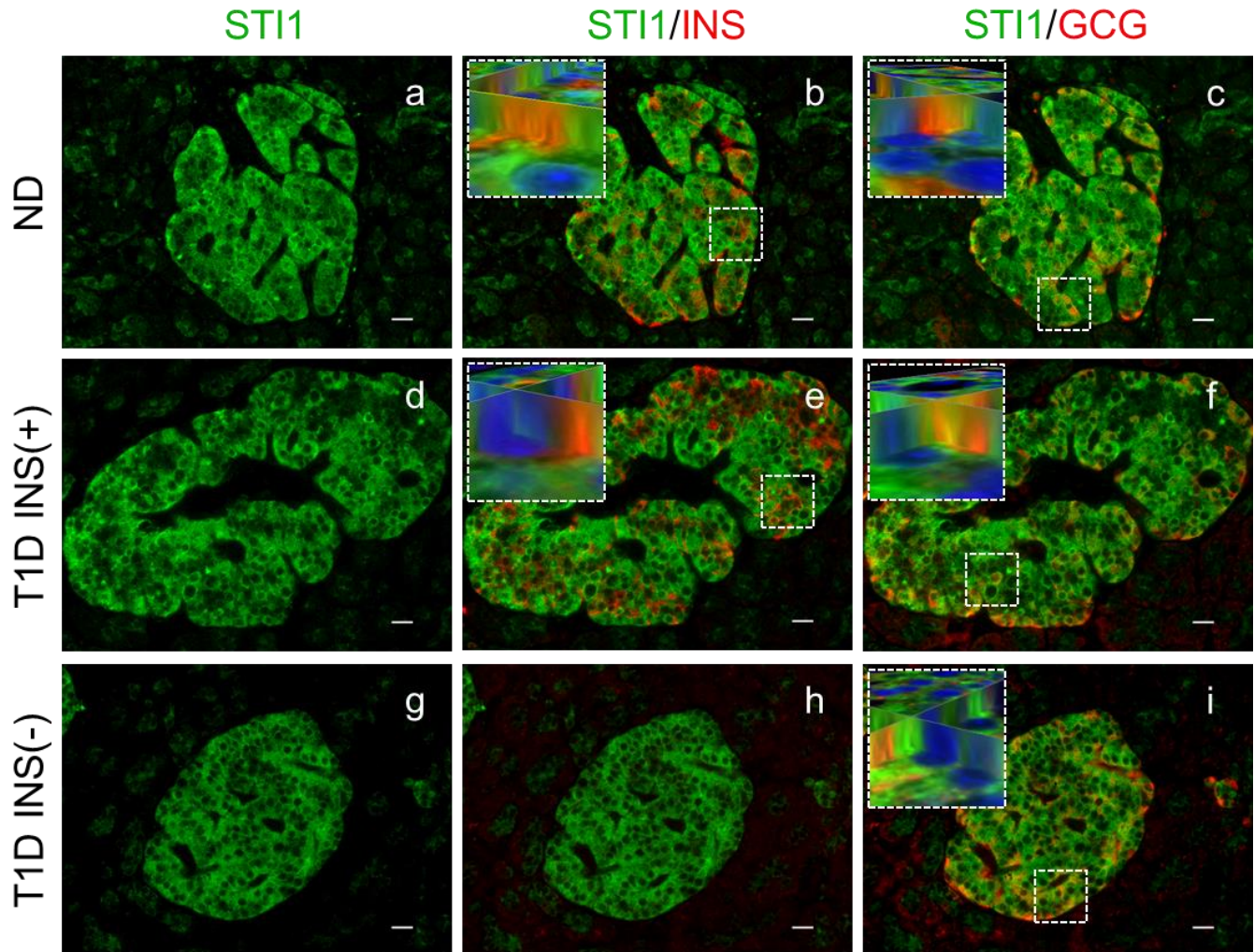


ESM Figure 4. Expression of PrP^C in AAb+ donors in human pancreata. a-d: As previously shown in Figure 1, PrP^C expression in ND donors localizes in the pancreatic islet and co-registers with beta-cells (d; white arrows). e-l: Similar to ND and type 1 diabetes INS(+) donors, PrP^C in AAb+ donors is expressed primarily in islets and specifically in beta-cells based on co-localization with INS and not GCG (d, h, l). We found that in a majority of the 12 studied AAb+ donors, PrP^C expression in pancreatic islets appeared consistently lower than ND, as seen for case 6450 using identical microscope parameters (i). No co-registration was observed between PrP^C and alpha-cells in any of the AAb+ cases. Scale 20 μ m.



ESM Figure 5. Protein-Protein interaction network analysis between cellular prion protein and interacting proteins using STRING (version 11.0) database. STRING analysis presenting PrP^C predicted protein-protein interaction model. Based on this model, STI1 (stress-inducible protein phosphoprotein 1) and NCAM1 (neural cell adhesion molecule) were selected for further immunofluorescence analysis. STI1 is an adaptor protein that coordinates chaperon functions of heat-shock protein 70 (HSP70) and 90 (HSP90) in protein folding. It is know, that STIP1 has a close partnership with PrP^C, especially in the brain, where it triggers neuroprotection and

neurogenesis. NCAM1 encodes a cell adhesion protein and member of the immunoglobulin superfamily coordinating cell-cell and cell-matrix interactions.



ESM Figure 6. Stress-inducible protein 1 (STI1) expression in relation to alpha and beta-cells. a, d, g: STI1 is highly expressed in the pancreatic islets of ND, type 1 with INS(+) and type 1 with INS(-) islets. b-c: In ND donors, STI1 co-registers with beta-cells and alpha-cells, as shown in the z-stack 3D reconstruction insert. e-f: In type 1 diabetes donors with residual INS(+) islets, STI1 also co-registers with beta-cells and alpha-cells, as shown in the inserts. i: In type 1 diabetes donors with INS(-) islets, STI1 co-registers with alpha-cells. Scale 20 μ m.