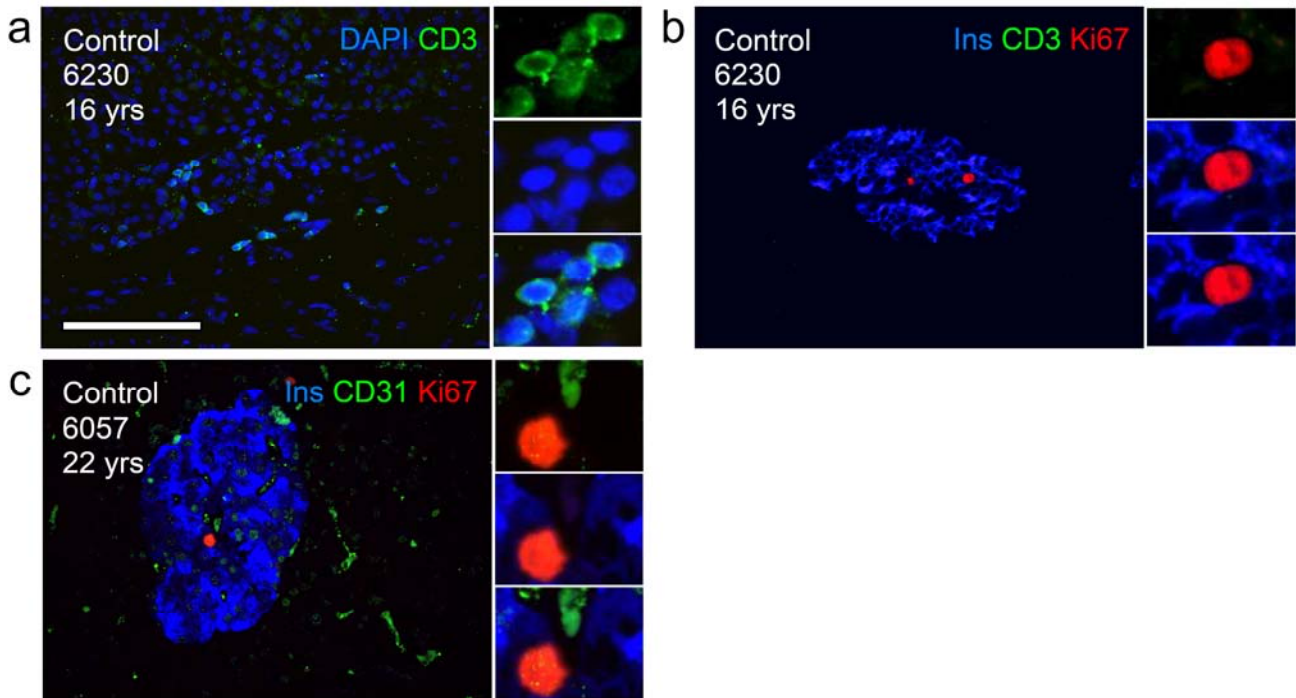


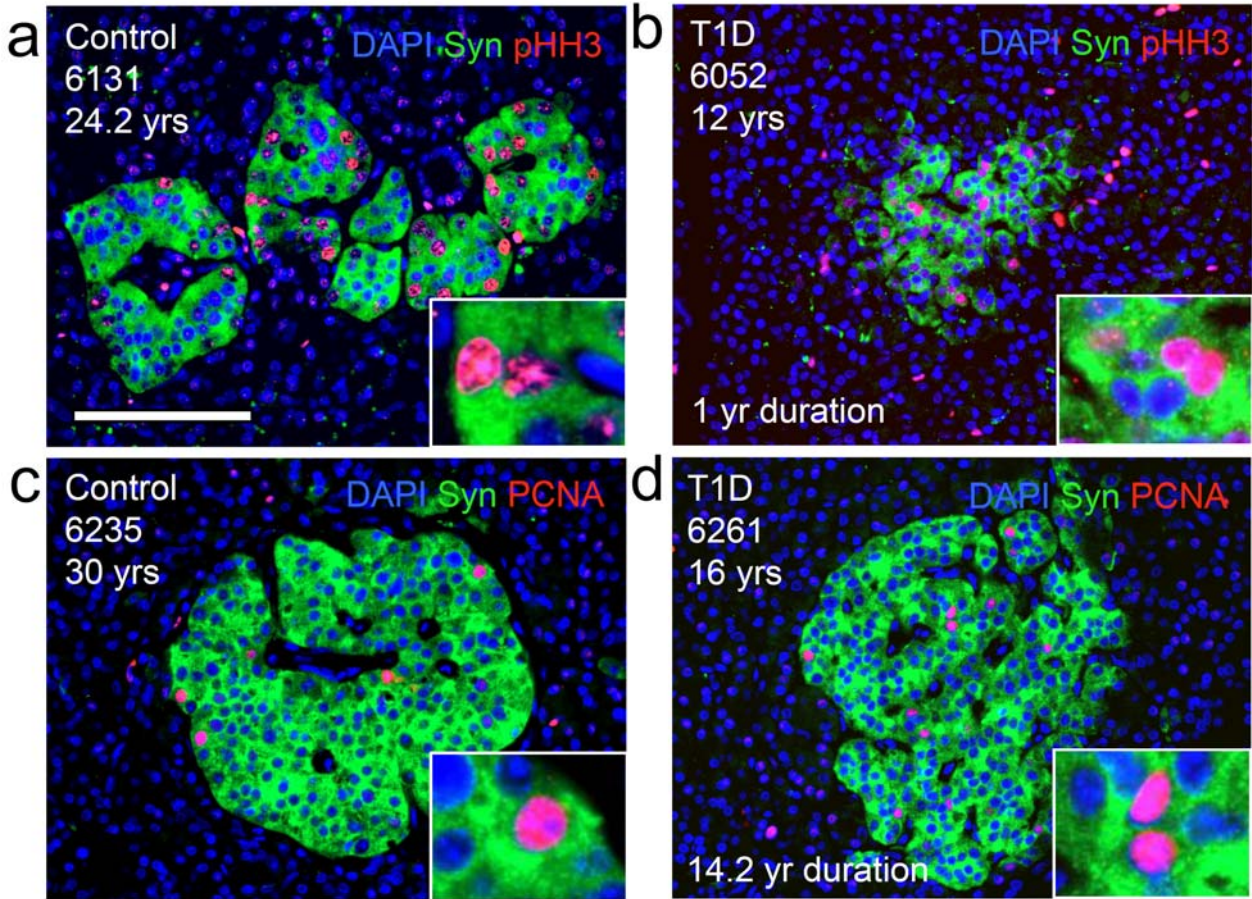
SUPPLEMENTARY DATA

Supplementary Figure. S1. T-cells or endothelial cells are not proliferating within islets. (a) Lymphocytes or **(b-c)** islet images for control pancreata stained for DAPI (blue), CD3 (green), CD31 (green) and Ki67 (red) reveal that proliferating cells are not T-cells or endothelial cells as indicated by **(a-b)** CD3 or **(c)** CD31, respectively; **(a)** CD3+ lymphocytes indicate a positive control for CD3 staining. Scale bar: 100µm.



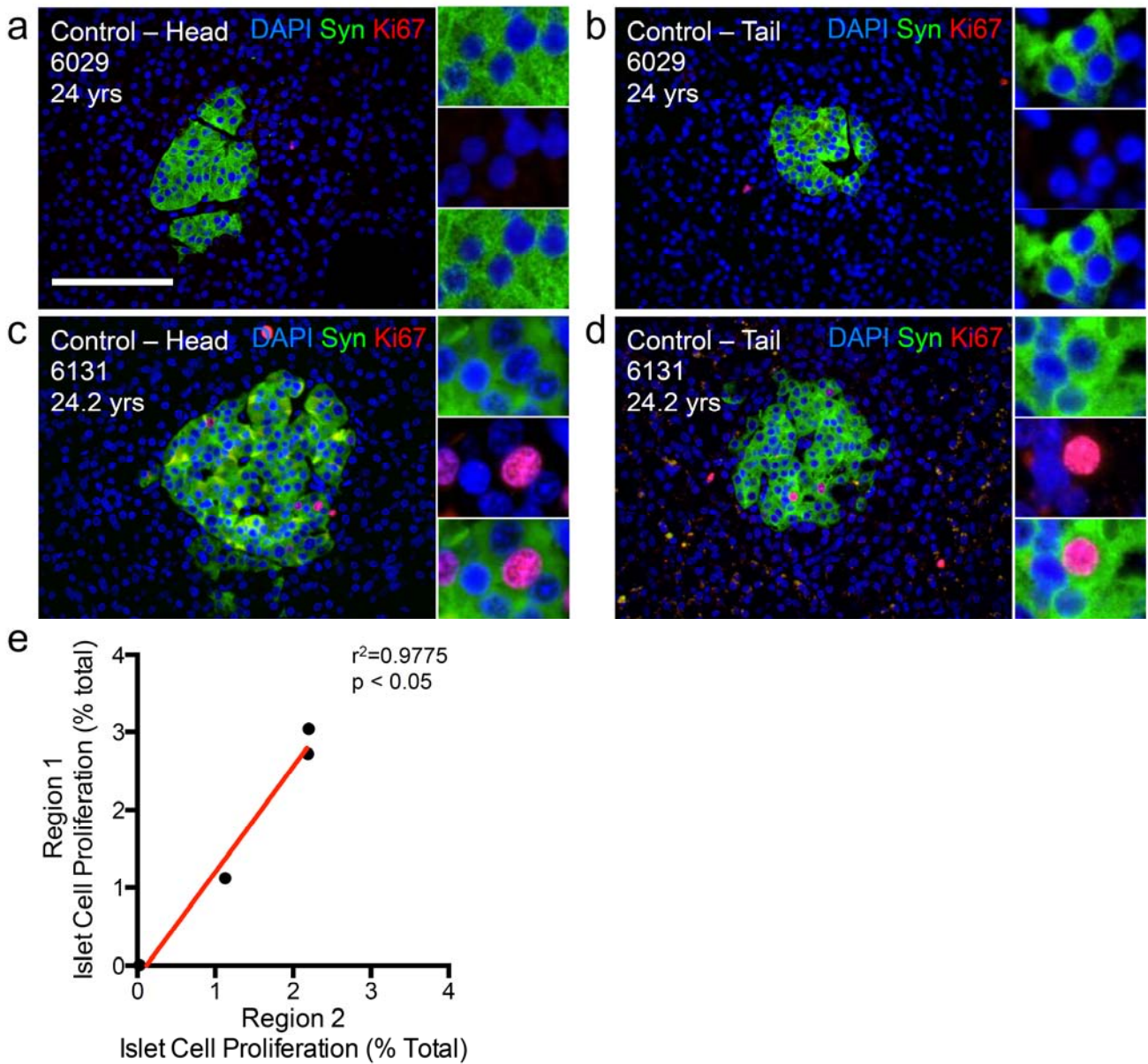
SUPPLEMENTARY DATA

Supplementary Figure. S2. Proliferating islet endocrine cells verified by multiple proliferative markers. Islet images for (a, c) control and (b, d) T1D stained for DAPI (blue), synaptophysin (Syn; green) and proliferative markers (red). Proliferating islet endocrine cells (c-d) Syn+ pHH3+ and (c-d) Syn+ PCNA+ cells found in both control and T1D islets.



SUPPLEMENTARY DATA

Supplementary Figure. S3. Islet endocrine cell proliferation is consistent across different regions of the pancreas. (a-d) Representative islet images for control pancreata stained for DAPI (blue), synaptophysin (Syn; green), and Ki67 (red) demonstrate similar proliferation rates in head and tail regions of the pancreas. (e) Correlation analysis of islet cell proliferation measured as % total confirm similar rates of islet cell proliferation in the differing regions of the pancreas.

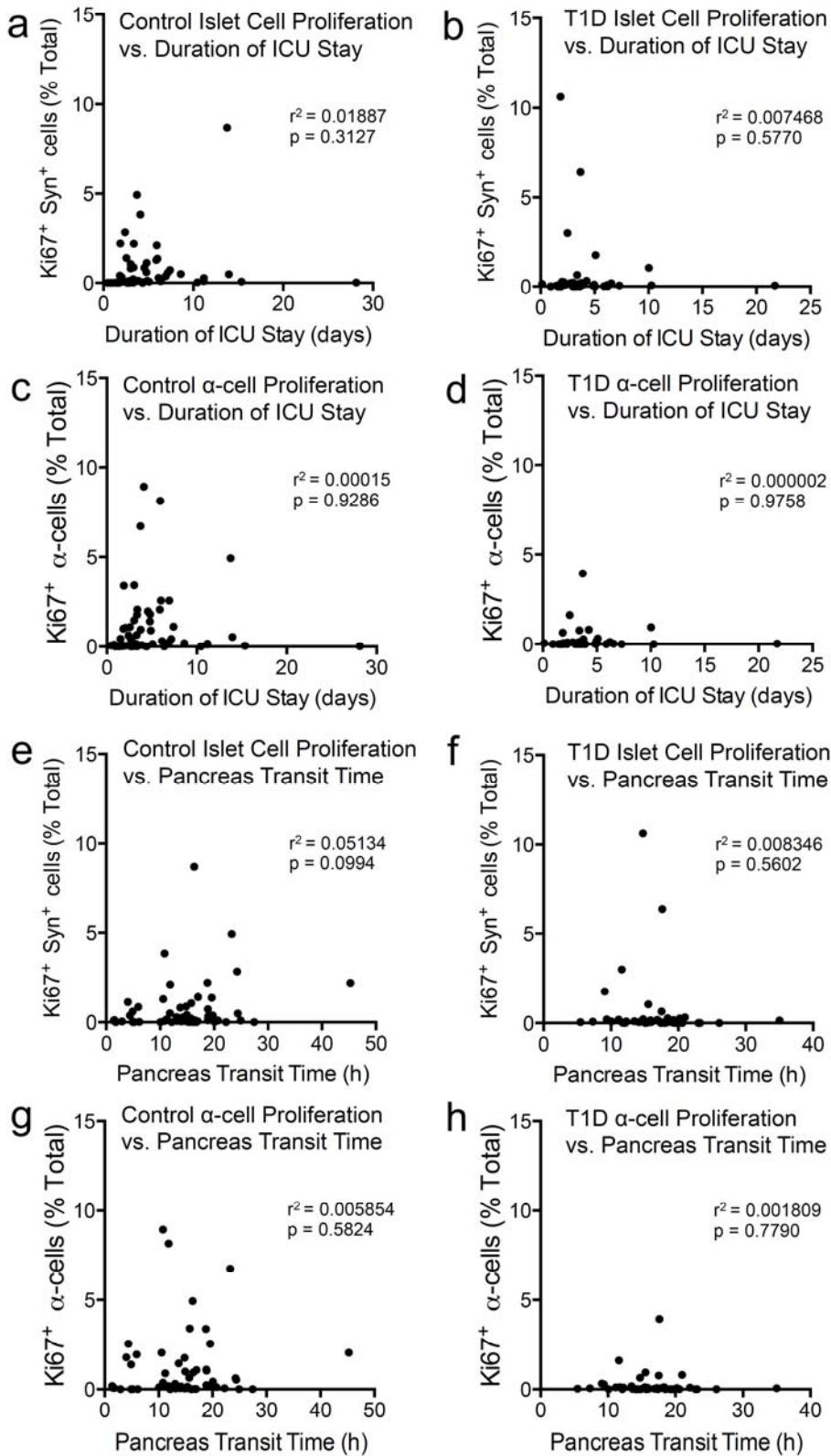


SUPPLEMENTARY DATA

Supplementary Fig. S4. Duration of ICU stay and pancreas transit time are not associated with islet endocrine cell or α -cell proliferation. (a-d) Duration of ICU stay (days) v. **(a-b)** islet cell proliferation (% total) or **(c-d)** α -cell proliferation (% total) for **(a,c)** control and **(b,d)** T1D pancreata. **(e-h)** Pancreas transit time (h) v. **(e-f)** islet cell proliferation (% total) or **(g-h)** α -cell proliferation (% total) for **(e, g)** control and **(f, h)** T1D pancreata.

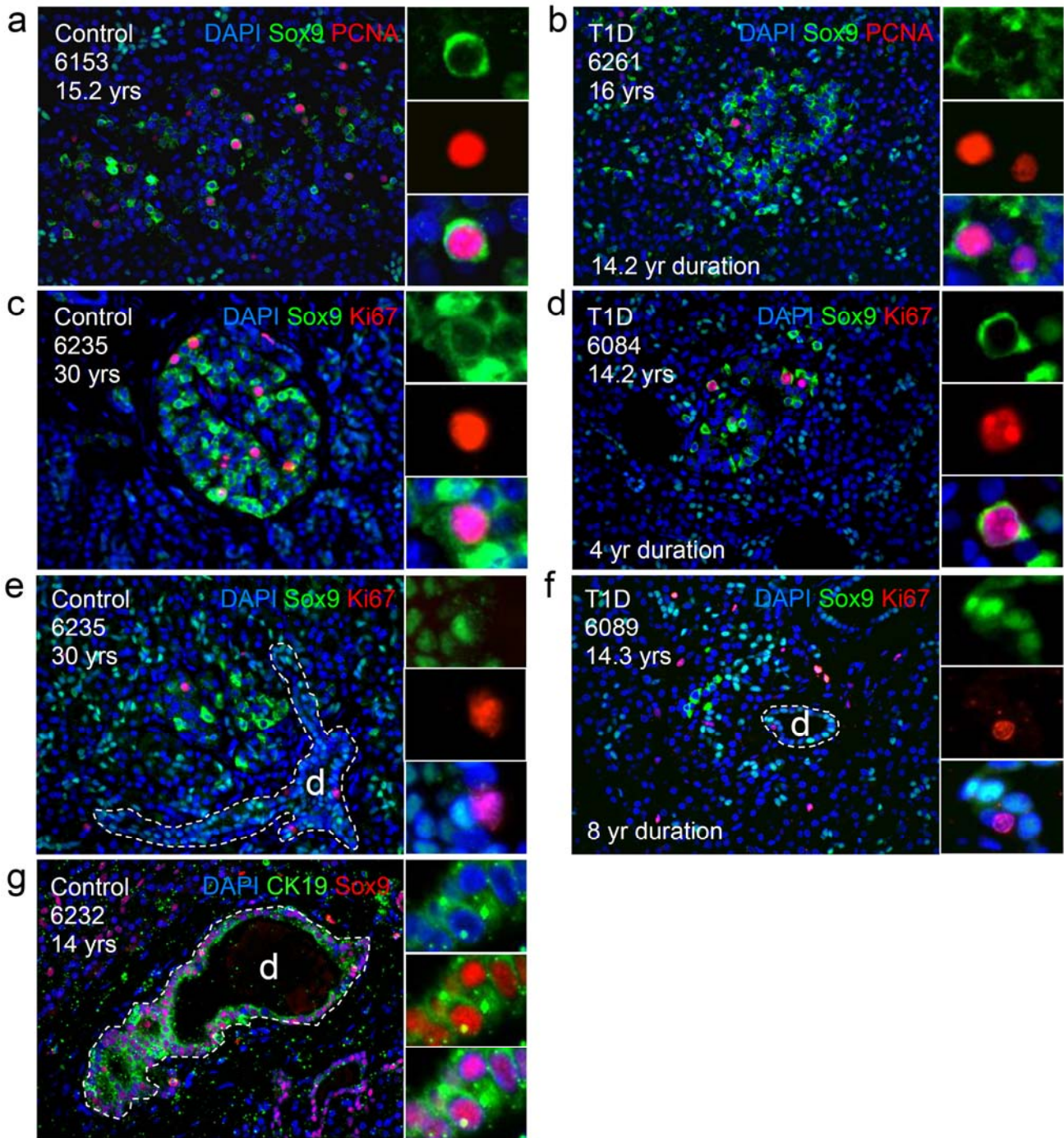
SUPPLEMENTARY DATA

Infants to Older Adults



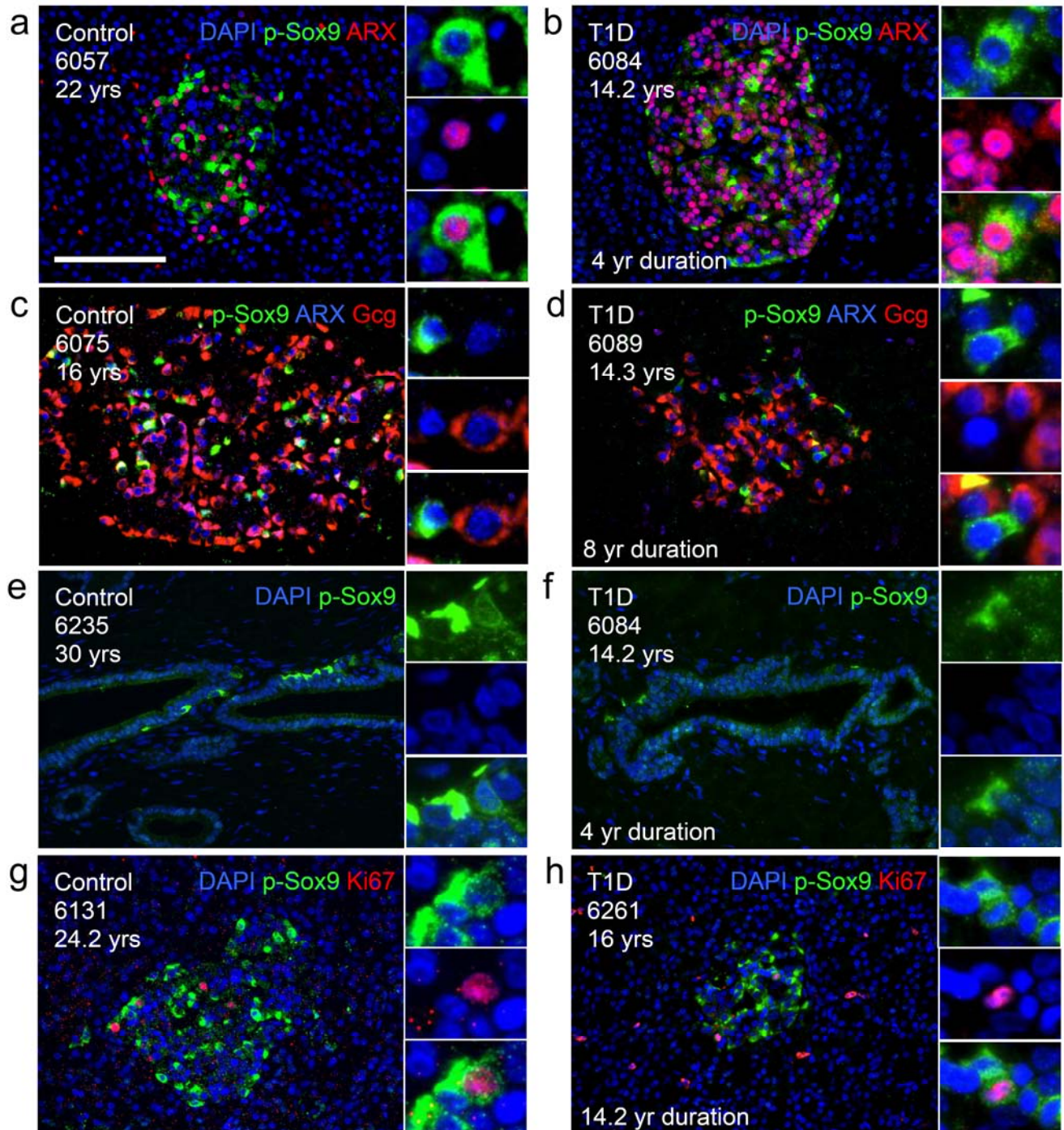
SUPPLEMENTARY DATA

Supplementary Figure. S5. Proliferating islet endocrine Sox9^{Cyt} cells verified by multiple proliferative markers. Islet images of (a, c, e, g) control and (b, d, f) T1D stained for DAPI (blue), Sox9 (green), and proliferative markers (PCNA/Ki67; red). Proliferating Sox9^{Cyt} cells are verified by (a-b) Sox9^{Cyt}+ PCNA+ and (c-f) Sox9^{Cyt}+ Ki67+ cells found in (a, c, e) control and (b, d, f) T1D islets. (e-f) Ki67+ Sox9^{Cyt}+ cells are not associated with pancreatic ducts (d, white dashed lines). (g) Nuclear Sox9 in ducts. Sox9^{Cyt}+ cells are not associated with pancreatic ducts, as detected by CK-19 (green). Scale bar: 100µm.



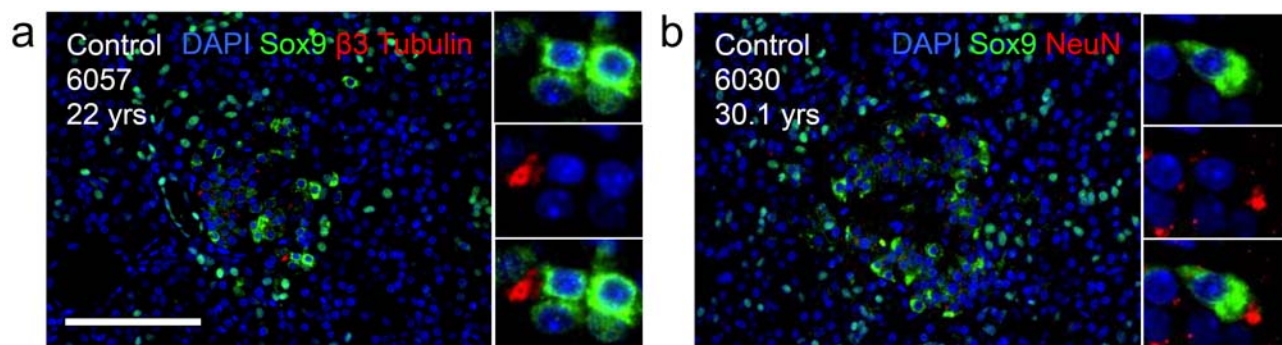
SUPPLEMENTARY DATA

Supplementary Figure. S6. Sox9^{Cyt} cells detected by Sox9 (pS181) antibody. Islet and ductal images of (a, c, e, g) control and (b, d, f, h) T1D samples – stained for DAPI (blue), Sox9 (pS181)s (green), Ki67 (red) and α -cell markers, ARX (red; blue) and glucagon (Gcg; red). (a-f) pSox9^{Cyt} intraislet cells express ARX, variable amounts of glucagon, and Ki67. (g-h) Ductal cells contain occasional pSox9^{Cyt} cells. Scale bar: 100 μ m.



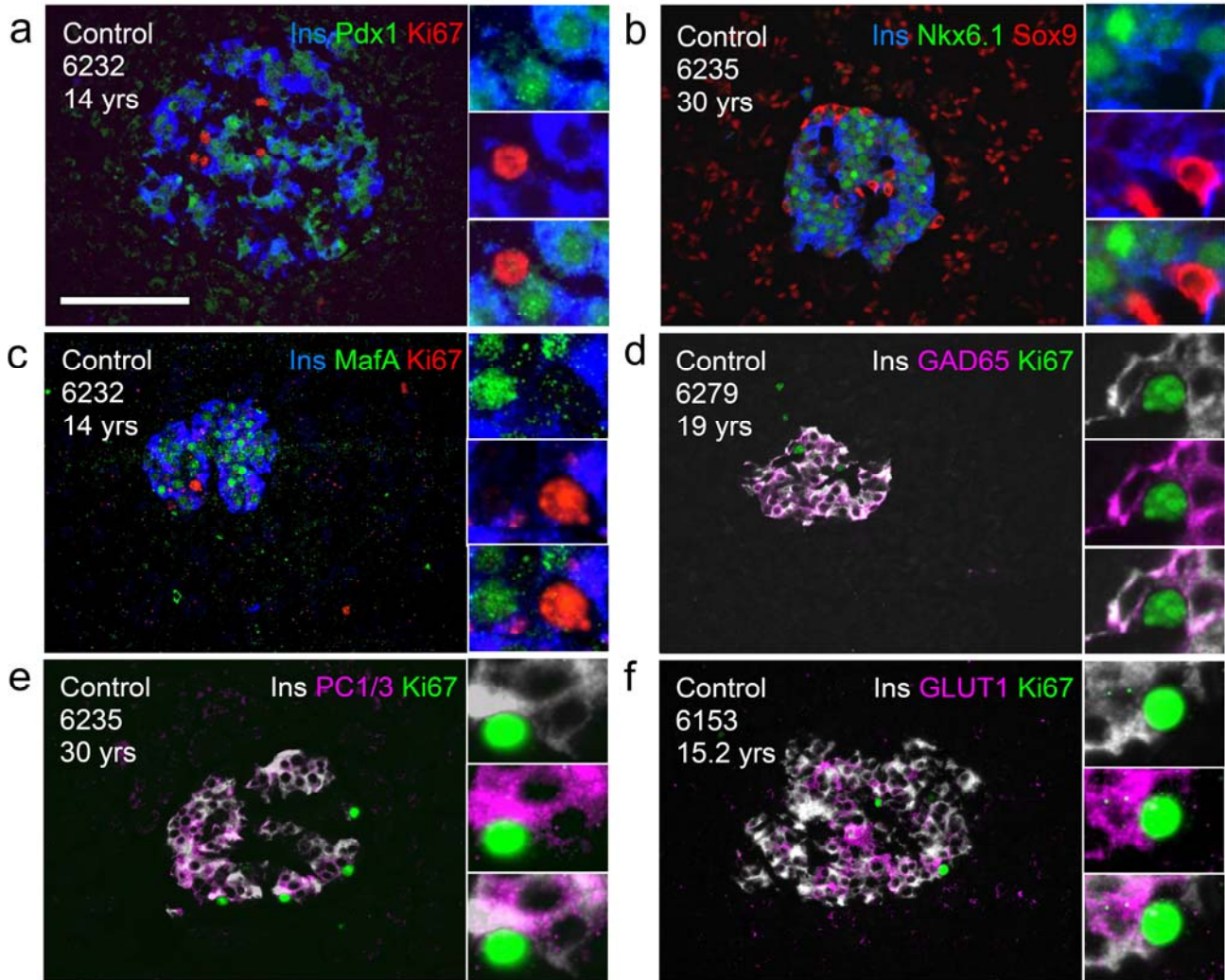
SUPPLEMENTARY DATA

Supplementary Figure. S7. Sox9^{Cyt} cells do not co-express neuronal markers. (a-b) Control young adult islets stained for DAPI (blue), Sox9 (green), and neuronal marker, **(a)** β 3 tubulin (red) or **(b)** NeuN (red). Scale bar: 100 μ m.



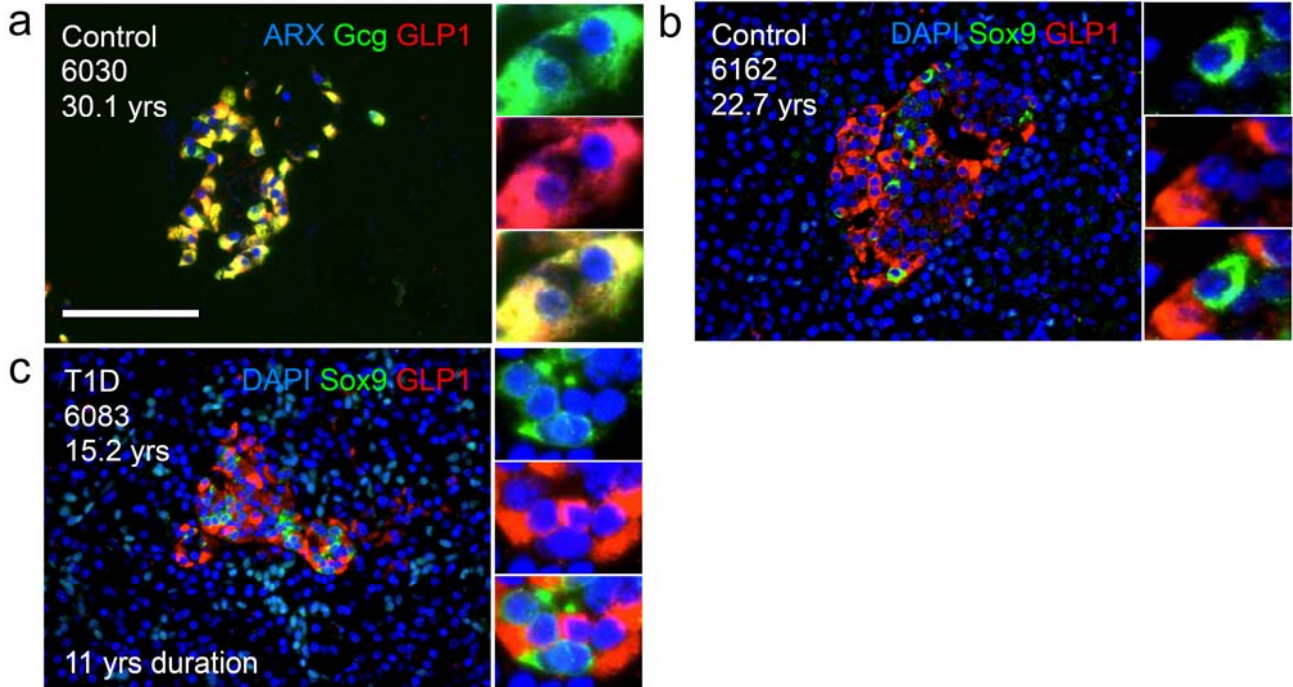
SUPPLEMENTARY DATA

Supplementary Figure. S8. Highly proliferative cells do not express β -cell specific markers. Control adolescent and young adult islets stained for Sox9, Ki67, and various β -cell markers. Most Ki67+ cells do not express β -cell markers: **(a)** Pdx1 (green), insulin (blue), Ki67 (red) **(b)** Nkx6.1 (green), insulin (blue), Sox9 (red) **(c)** MafA (green), insulin (blue), Ki67 (red) **(d)** GAD65 (magenta), insulin (white), Ki67 (green) **(e)** PC1/3 (magenta), insulin (white), Ki67 (green). **(f)** GLUT1 (magenta), insulin (white), Ki67 (green). Scale bar: 100 μ m.



SUPPLEMENTARY DATA

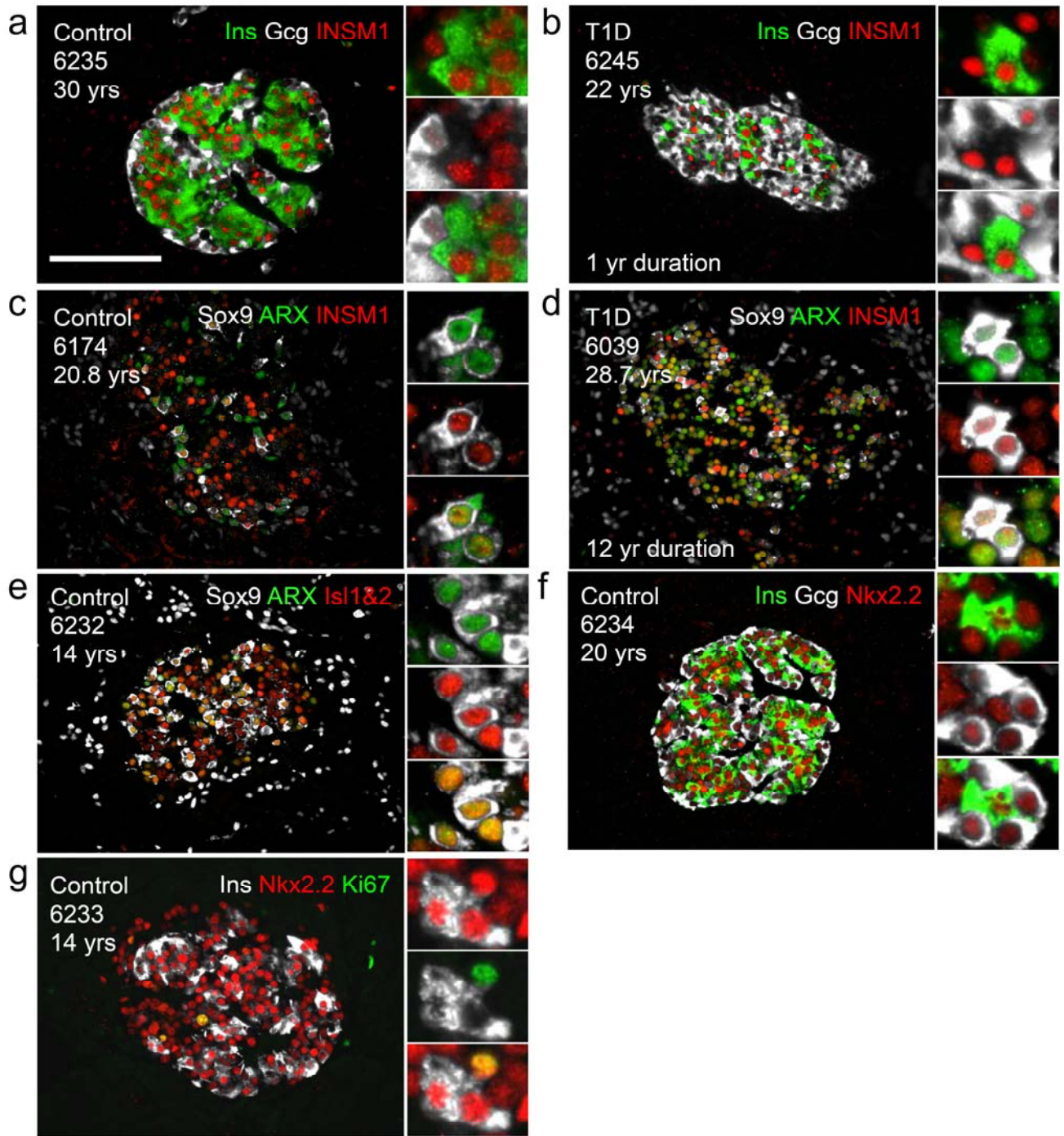
Supplementary Figure. S9. Sox9^{Cyt} cells co-express α -cell marker, GLP1. Islet images for (a-b) control and (c) T1D stained for GLP1 and various markers. (a) α -cells express ARX (blue), glucagon (green), and GLP1 (red). (b-c) Sox9^{Cyt} (green) cells express variable GLP1 (red). (c) DAPI (blue), Sox9 (green), and GLP1 (red). Scale bar: 100 μ m.



SUPPLEMENTARY DATA

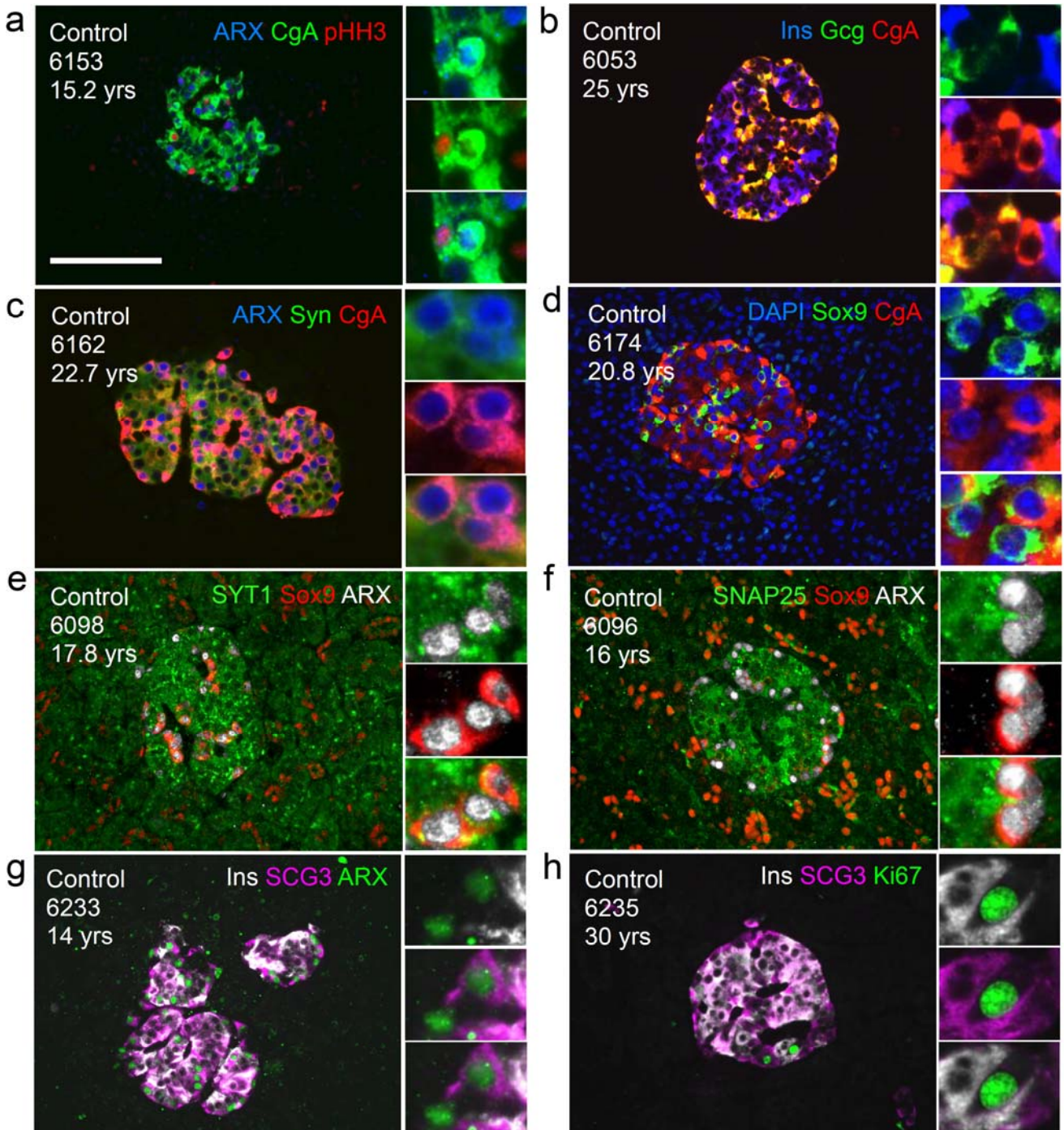
Supplementary Figure. S10. Sox9^{Cyt} cells co-express INSM1 and Isl1&2, which is common to human α - and β -cells. (a-b) Islet images for (a) control and (b) T1D stained for insulin (Ins; green), glucagon (Gcg; white), and INSM1 (red) show INSM1 expression in both human β - and α -cells. (c) Control and (d) T1D stained for Sox9 (white), ARX (green), and INSM1 (red) reveal Sox9^{Cyt} ARX+ cells expressing INSM1. (e) Control islet stained with Sox9 (white), Isl1&2 (red), and ARX (green) reveal that Sox9^{Cyt}+ cells within islets contain Isl1&2. (f) Human islets contain Nkx2.2 as shown in control islet stained with insulin (Ins; green), glucagon (Gcg, white) and Nkx2.2 (red). (g) Control islet stained with insulin (Ins; white), Nkx2.2 (red), and Ki67 (green) reveals that Ki67+ insulin negative cells within islets contain Nkx2.2. Scale bar: 100 μ m.

SUPPLEMENTARY DATA



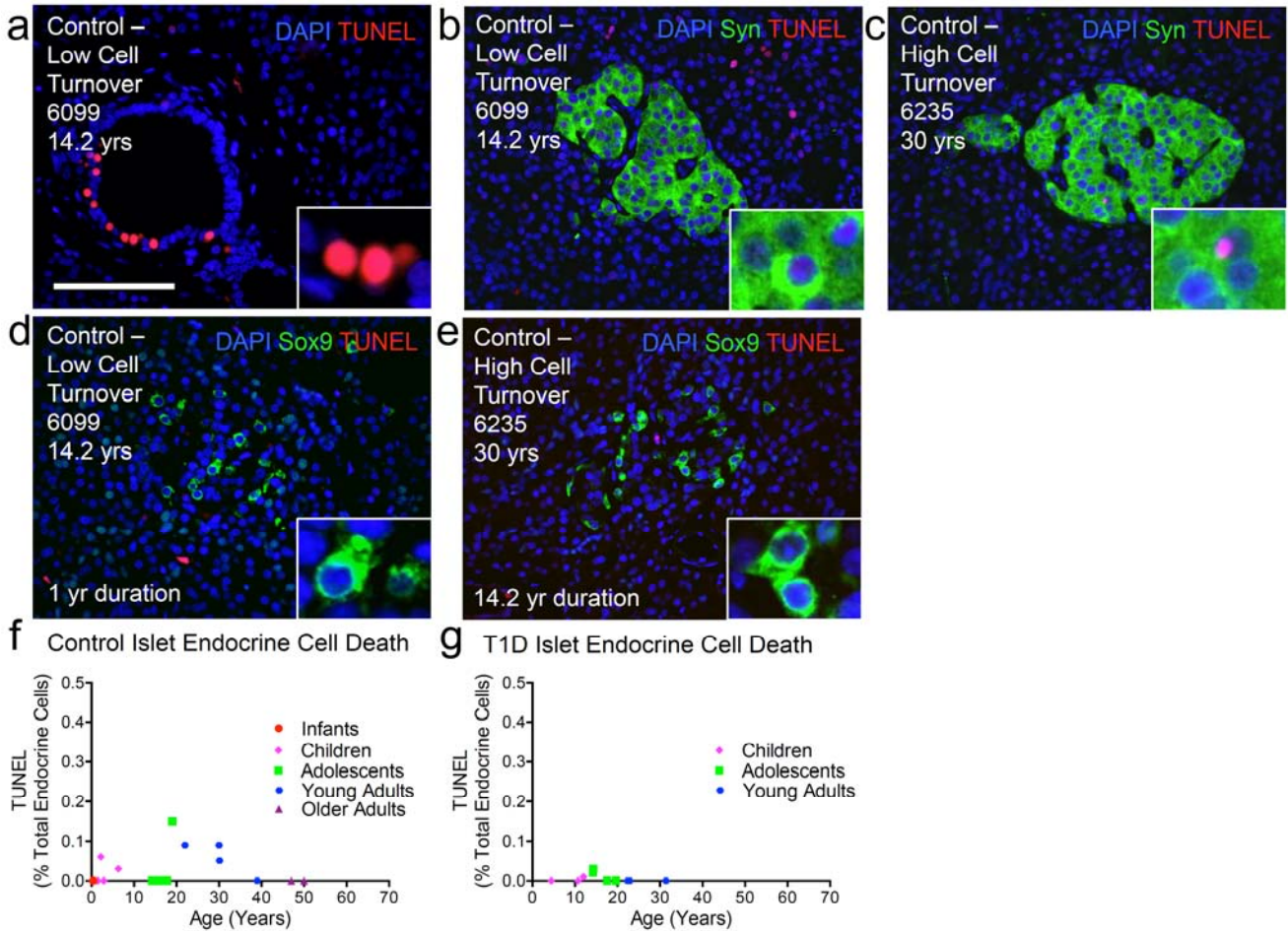
SUPPLEMENTARY DATA

Supplementary Figure. S11. Highly proliferative cells express markers of secretory vesicles and exocytotic machinery. (a-c) Control islets stained for chromagranin A (CgA; green/red), insulin (blue), glucagon (green), ARX (blue), and pHH3 reveal that pHH3+ ARX+ intra-islet cells contain CgA which is differentially expressed at higher levels in α -cells than in β -cells. (c-f) Islet images stained for DAPI (blue), synaptophysin (Syn; green), Sox9^{Cyt} (green/red), CgA (red), ARX (white), and related secretory vesicular markers (green). Sox9^{Cyt} cells are islet endocrine cells that express (c) Syn, (d) CgA, (e) synaptotagmin 1A (SYT1), and (f) SNAP25. (g-h) SCG3 is absent in (g) some ARX+ cells or in (h) Ki67+ cells. Scale bar: 100 μ m.



SUPPLEMENTARY DATA

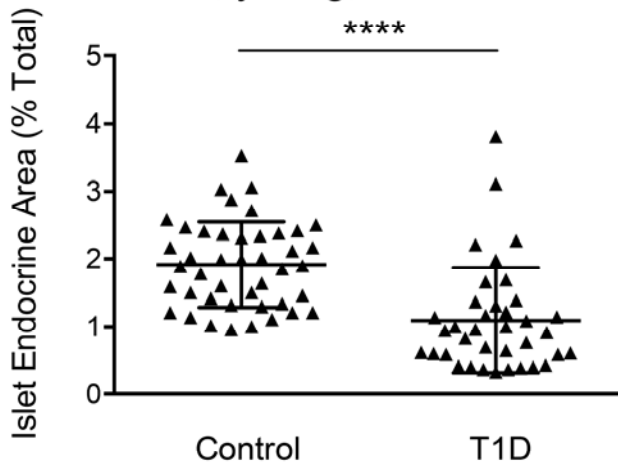
Supplementary Figure. S12. Adolescent and young adults exhibit increased islet endocrine cell death but no Sox9^{Cyt} cell death. (a-e) Images stained for DAPI (blue), synaptophysin (Syn; green), Sox9^{Cyt} (green), and TUNEL (red). (a) Positive control for TUNEL staining within ductal cells. (b-c) Control islets from (b) low and (c) high proliferating individuals reveal very low TUNEL rates in islet endocrine cells, with some TUNEL+ islet endocrine cells increased in highly proliferating adolescent and young adult islets. (d-e) Control islets images from (d) low and (e) high proliferating individuals are representative of no TUNEL+ Sox9^{Cyt} cells found in analysis. Scale bar: 100µm. (f-g) TUNEL+ islet endocrine cells (% total) v. age (years) in (f) control and (g) T1D pancreata.



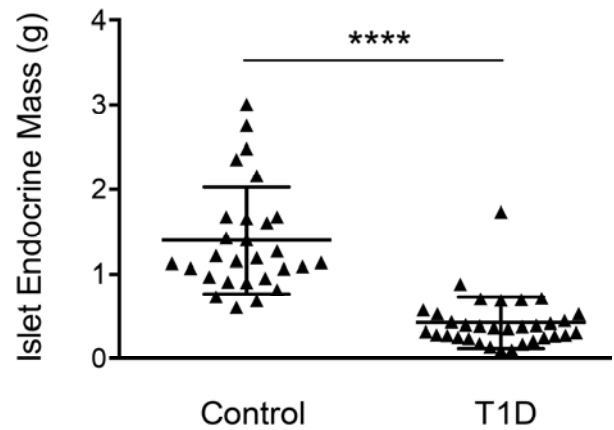
SUPPLEMENTARY DATA

Supplementary Figure. S13. Islet endocrine area and mass do not accumulate with age after adolescence or with T1D. (a-b) Islet endocrine cell area and mass are reduced in T1D pancreata. **(a)** Islet endocrine area (% total) is reduced in T1D pancreata. Results expressed as mean \pm SD for **(a)** controls (n=43) and T1D (n=37). **(b)** Islet endocrine cell mass (g) is reduced in T1D pancreata. Results expressed as mean \pm SD for controls (n=28) and T1D pancreata (n=33). **(c-d)** Correlation analysis of **(c)** islet endocrine area v. age (years) and **(d)** islet endocrine mass v. age (years). No correlation between age and islet endocrine cell **(c)** area or **(d)** mass for adolescents, young, & older adults.

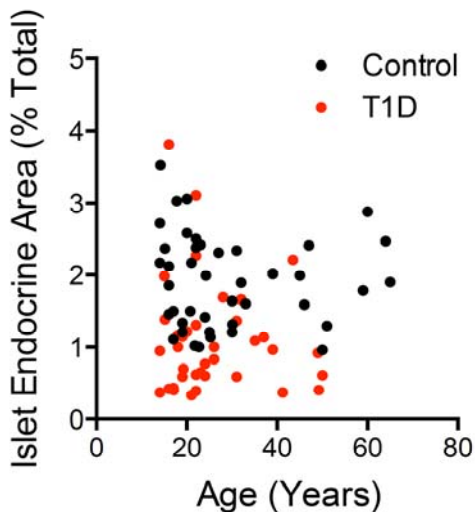
a Islet Endocrine Area – adolescent, young, & older adult



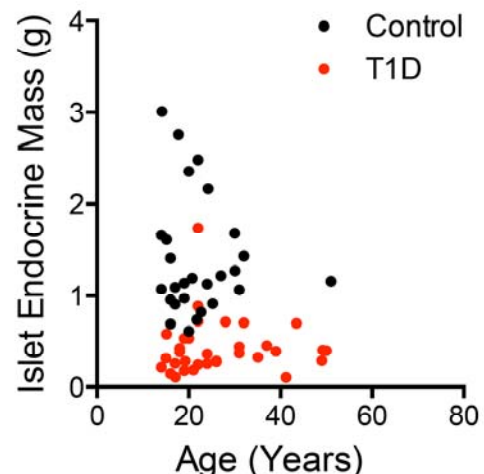
b Islet Endocrine Mass – adolescent, young, & older adult



c Islet Endocrine Area v. Age – adolescent, young, & older adult



d Islet Endocrine Mass v. Age – adolescent, young, & older adult



SUPPLEMENTARY DATA

Supplementary Table 1. Non-Diabetic Sample Population. nPOD case number, age (years), sex, ethnicity, cause of death, C-peptide (ng/ml), HbA1c (%), BMI, body weight (kg), pancreas sample region, corresponding block number, and method of tissue recovery. "n/a" indicates C-peptide measurements were not measured for that case.

Control													
nPOD Case #	Age (Years)	Sex	Ethnicity	Cause of Death	C-peptide (ng/ml)	HbA1c (%)	HbA1c (mmol/mol)	BMI	Body Weight (kg)	Pancreas Sample Region	Block #	Tissue Recovery	
Infants (0-1.4)	6200	0.005	F	Hispanic	Pulmonary Hypoplasia	0.2	n/a	n/a	14.5	2.2	PanHead	02	Autopsy
	6214	0.014	M	Caucasian	Anoxia	0.2	n/a	n/a	8	2.5	PanHead	02	Autopsy
	6164	0.030	M	Caucasian	Anoxia	n/a	5.7	39	16.5	4.7	PanOther	02	Organ Donor
	6218	0.080	F	African American	Anoxia	1.5	n/a	n/a	17.2	5.2	PanOther	02	Organ Donor
	6222	0.170	M	Caucasian	Anoxia	n/a	n/a	n/a	16.4	6.3	PanHead	02	Organ Donor
	6117	0.330	M	Caucasian	Head Trauma	3.27	n/a	n/a	18.4	8.5	PanTail	02	Organ Donor
	6115	0.420	M	Caucasian	Anoxia	4.59	n/a	n/a	17.1	7.0	PanTail	02	Organ Donor
	6092	0.500	F	African American	Anoxia	0.35	n/a	n/a	13.8	9.0	PanTail	02	Organ Donor
	6103	1.5	M	Caucasian	Anoxia	0.98	6.1	43	16.8	8.0	PanTail	04	Organ Donor
	6107	2.2	M	African American	Anoxia	5.9	5.2	33	15.9	15.0	PanTail	04	Organ Donor
Children (1.5-13.9)	6094	2.9	M	African American	Anoxia	3.55	n/a	n/a	15.8	14.0	PanTail	06	Organ Donor
	6106	2.9	M	Caucasian	Anoxia	7.36	n/a	n/a	18.1	16.0	PanTail	04	Organ Donor
	6005	5.0	F	Caucasian	Cerebrovascular/Stroke	n/a	n/a	n/a	15.7	16.8	PanTail	04	Organ Donor
	6112	6.3	F	Hispanic	Head Trauma	5.11	5.6	38	18.4	26.0	PanTail	04	Organ Donor
	6007	9.0	M	African American	Anoxia	n/a	n/a	n/a	20	41.0	PanTail	02	Organ Donor
	6278	10.0	F	African American	Anoxia	4.54	6.3	45	21.3	52.4	PanBody	02	Organ Donor
	6232	14.0	F	Caucasian	Head Trauma	19.5	n/a	n/a	20.8	50.0	PanTail	04	Organ Donor
	6233	14.0	M	Caucasian	Anoxia	7.26	n/a	n/a	21.9	67.0	PanTail	02	Organ Donor
	6099	14.2	M	Caucasian	Head Trauma	5.37	n/a	n/a	30	92.0	PanTail	06	Organ Donor
	6153	15.2	M	Hispanic	Head Trauma	8.38	5.5	37	20.5	58.0	PanHead	04	Organ Donor
Adolescents (14-20.9)	6075	16.0	M	African American	Anoxia	2.94	n/a	b.a	14.9	30.0	PanTail	01/02	Organ Donor
	6096	16.0	F	African American	Head Trauma	2.97	n/a	n/a	18.8	50.0	PanTail	03	Organ Donor
	6230	16.0	M	Caucasian	Head Trauma	5.22	5.3	34	18.9	56.7	PanTail	04	Organ Donor
	6227	17.0	F	Caucasian	Cerebrovascular/Stroke	2.75	n/a	n/a	26.4	74.6	PanBody	04	Organ Donor
	6271	17.0	M	Caucasian	Head Trauma	11.47	n/a	n/a	24.4	77.1	PanBody	04	Organ Donor
	6098	17.8	M	Caucasian	Head Trauma	1.41	4.9	30	22.8	74.0	PanTail	06	Organ Donor
	6253	19.0	F	African American	Head Trauma	7.22	n/a	n/a	34.3	85.0	PanBody	02	Organ Donor
	6279	19.0	M	Caucasian	Head Trauma	8.01	n/a	n/a	34	110.2	PanBody	02	Organ Donor
	6234	20.0	F	Caucasian	Head Trauma	6.89	5.8	40	25.6	67.6	PanTail	04	Organ Donor
	6238	20.0	M	African American	Head Trauma	1.17	n/a	n/a	21.7	74.3	PanTail	04	Organ Donor
Young Adults (21-39)	6174	20.8	M	Caucasian	Cerebrovascular/Stroke	3	n/a	n/a	19.5	75.0	PanBody	06	Organ Donor
	6024	21.0	M	Caucasian	Head Trauma	3.52	n/a	n/a	27.8	95.0	PanHead	10	Organ Donor
	6179	21.8	F	Caucasian	Head Trauma	2.74	n/a	n/a	20.7	51.0	PanBody	01A	Organ Donor
	6001	22.0	M	Caucasian	Head Trauma	1.58	n/a	n/a	21.9	75.0	PanTail	06	Organ Donor
	6057	22.0	M	Caucasian	Head Trauma	16.23	n/a	n/a	26	92.0	PanTail	06	Organ Donor
	6162	22.7	M	African American	Head Trauma	7.61	n/a	n/a	28.9	102.0	PanBody	02	Organ Donor
	6003	23.0	F	Caucasian	Head Trauma	n/a	n/a	n/a	29.3	75.0	PanTail	11	Organ Donor
	6029	24.0	F	Hispanic	Cerebrovascular/Stroke	n/a	n/a	n/a	22.6	60.0	PanTail	02	Organ Donor
	6131	24.2	M	Caucasian	Anoxia	1.01	n/a	n/a	24.8	83.0	PanHead	05	Organ Donor
	6053	25.0	M	Caucasian	Head Trauma	1.77	n/a	n/a	21.2	59.0	PanOther	01	Organ Donor
Older Adults (≥40)	6126	25.2	M	Caucasian	Head Trauma	0.88	n/a	n/a	25.1	77.0	PanBody	04	Organ Donor
	6058	27.0	M	Hispanic	Head Trauma	9.09	n/a	n/a	19.1	52.0	PanTail	05	Organ Donor
	6048	30.0	M	Caucasian	Cerebrovascular/Stroke	17.91	n/a	n/a	20.6	56.0	PanTail	04	Organ Donor
	6235	30.0	M	Caucasian	Head Trauma	8.1	n/a	n/a	25.4	76.0	PanTail	04	Organ Donor
	6030	30.1	M	Caucasian	Head Trauma	2.54	n/a	n/a	27.1	86.0	PanBody	04	Organ Donor
	6229	31.0	F	Caucasian	Head Trauma	6.23	5.5	37	26.9	65.5	PanTail	02	Organ Donor
	6034	32.0	F	Caucasian	Head Trauma	3.15	n/a	n/a	25.2	62.0	PanBody	02	Organ Donor
	6004	33.0	M	Caucasian	Head Trauma	n/a	n/a	n/a	n/a	n/a	PanHead	02	Organ Donor
	6002	39.0	M	Caucasian	Head Trauma	n/a	n/a	n/a	23.7	75.0	PanHead	04	Organ Donor
	6015	39.0	F	Caucasian	Anoxia	1.99	n/a	n/a	n/a	102.0	PanTail	09	Organ Donor
Older Adults (≥40)	6009	45.0	M	Caucasian	Anoxia	11.32	n/a	n/a	30.6	97.0	PanHead	04	Organ Donor
	6011	46.0	F	African American	Cerebrovascular/Stroke	n/a	n/a	n/a	26.3	70.0	PanHead	02	Organ Donor
	6010	47.0	F	Caucasian	Cerebrovascular/Stroke	n/a	n/a	n/a	19.7	56.8	PanTail	09	Organ Donor
	6008	50.0	F	Caucasian	Head Trauma	n/a	n/a	n/a	24.2	62.0	PanHead	08	Organ Donor
	6168	51.0	M	Hispanic	Cerebrovascular/Stroke	n/a	6.2	44	25.2	73.0	PanHead	02	Organ Donor
	6017	59.0	F	Caucasian	Cerebrovascular/Stroke	9.89	n/a	n/a	24.8	68.0	PanHead	08	Organ Donor
	6020	60.0	M	Caucasian	Cerebrovascular/Stroke	2.82	n/a	n/a	29.8	102.0	PanHead	08	Organ Donor
	6016	64.0	F	Caucasian	Cerebrovascular/Stroke	n/a	n/a	n/a	31.2	88.0	PanHead	08	Organ Donor
6013	65.0	M	Caucasian	Cerebrovascular/Stroke	2.8	n/a	n/a	24.2	90.0	PanHead	06	Organ Donor	

SUPPLEMENTARY DATA

Supplementary Table 2. T1D Sample Population. nPOD case number, age (years), duration of diabetes (years), sex, ethnicity, cause of death, C-peptide (ng/ml), HbA1c (%), positive autoantibodies and total autoantibody count (out of the 4 autoantibodies tested), BMI, body weight (kg), pancreas sample region, corresponding block number, method of tissue recovery. T1D diagnosis for nPOD cases was based on review of terminal charts, clinical and biochemical testing, and histopathology. Consideration from medical records includes the donor's admission course, age, BMI, body weight, laboratory profiles (chemistry, urinalysis, toxicology), diagnoses, and medications. nPOD expert clinicians and pathologists assessed medical records in conjunction with the results of biochemical tests and histopathological analysis. These include autoantibody and C-peptide testing in addition to high-resolution HLA typing. Tissue sections were screened for histological features such as presence of amyloid, islet hormones, inflammation, and fibrosis. Pancreatic tissue diagnosed (Dx'd) by nPOD for fibrosis and acinar atrophy are marked by "X." "<0.05 ng/ml" C-peptide infers that C-peptide levels were not measured using an ultra-sensitive C-peptide kit; "n/a" indicates C-peptide measurements were not measured for that case. GADA - Glutamic acid decarboxylase autoantibodies; IA 2A - Insulinoma-2-associated autoantibodies; M IAA - insulin autoantibodies; ZnT8A - Zinc transporter 8 autoantibodies.

T1D																					
nPOD Case #	Age (Years)	Years with Diabetes	Sex	Ethnicity	Cause of Death	C-peptide (ng/ml)	HbA1c (%)	HbA1c (mmol/mol)	GADA	IA 2A	M IAA	ZnT8A	Total Auto Ab Count (out of 4)	BMI	Body Weight (kg)	Pancreas Sample Region	Block #	Tissue Recovery	Fibrosis Dx'd by nPOD	Acinar Atrophy Dx'd by nPOD	
Children (1.5-13.9)	6063	4.4	3.0	M	Caucasian	Anoxia	<0.05	n/a	n/a	-	-	+	-	1	23.8	16.0	PanTail	02	Organ Donor		
	6209	5.0	0.3	F	Caucasian	DKA, Cerebral Edema	0.1	n/a	n/a	-	+	+	+	3	12	15.0	PanBody	04	Autopsy		
	6062	10.7	6.0	M	African American	DKA, Cerebral Edema	n/a	12.4	112	n/a	n/a	n/a	n/a	n/a	21.9	48.0	PanTail	03	Organ Donor		
	6265	11.0	8.0	M	Caucasian	Cerebrovascular/Stroke	0.06	n/a	n/a	+	-	+	-	2	12.9	26.0	PanBody	02	Organ Donor	X	X
	6052	12.0	1.0	M	African American	Cerebral Edema	0.18	n/a	n/a	-	+	+	-	2	20.3	56.0	PanTail	02	Organ Donor		
	6268	12.0	3.0	F	Caucasian	Anoxia	0.05	9.8	84	-	-	+	-	1	23.5	68.0	PanTail	01	Organ Donor		X
	6264	12.0	9.0	F	Caucasian	DKA	0.001	8.9	74	-	-	-	-	0	22	34.0	PanBody	02	Organ Donor	X	X
	6228	13.0	0.0	M	Caucasian	Anoxia	0.1	13.3	122	+	+	-	+	3	17.4	45.0	PanBody	04	Organ Donor		X
	6243	13.0	5.0	M	Caucasian	Cerebrovascular/Stroke	0.42	13.1	120	-	-	+	-	1	21.3	58.1	PanHead	01	Organ Donor		
	6113	13.1	1.6	F	Caucasian	Head Trauma	<0.05	n/a	n/a	-	-	+	-	1	24.5	48.0	PanBody	04	Organ Donor		X
Adolescents (14-20.9)	6084	14.2	4.0	M	Caucasian	Anoxia	<0.05	n/a	n/a	-	-	+	-	1	26.3	60.0	PanBody	02	Organ Donor		
	6089	14.3	8.0	M	Caucasian	Anoxia	<0.05	10.4	90	-	-	+	-	1	26	69.0	PanTail	02	Organ Donor		
	6049	15.0	10.0	F	African American	Anoxia	<0.05	n/a	n/a	+	-	+	-	2	20.8	52.0	PanTail	04	Organ Donor		
	6083	15.2	11.0	F	Caucasian	DKA, Cerebral Edema	<0.05	n/a	n/a	-	-	+	-	1	18.4	50.0	PanTail	04	Organ Donor		
	6207	16.0	10.0	F	African American	Cerebrovascular/Stroke	0.001	n/a	n/a	-	+	+	+	3	24.4	66.2	PanHead	02	Organ Donor		
	6261	16.0	14.2	M	Caucasian	Anoxia	0.001	7.2	55	+	-	+	-	2	20.7	63.5	PanOther	08	Organ Donor	X	X
	6148	17.1	7.0	M	Caucasian	Anoxia	0.001	n/a	n/a	+	-	+	-	2	23.9	65.0	PanBody	02	Organ Donor		
	6087	17.5	4.0	M	Caucasian	Head Trauma	<0.05	n/a	n/a	-	-	+	+	3	21.9	71.0	PanBody	01	Organ Donor		
	6145	18.0	11.0	M	Caucasian	Head Trauma	0.06	n/a	n/a	+	-	+	+	2	23.1	67.0	PanBody	04	Organ Donor		
	6237	18.0	12.0	F	Caucasian	Head Trauma	0.001	n/a	n/a	+	-	+	-	2	26	75.0	PanHead	02	Organ Donor		X
Young Adults (21-39)	6195	19.2	5.0	M	Caucasian	Head Trauma	<0.05	n/a	n/a	+	+	+	+	4	23.7	75.0	PanBody	04	Organ Donor		X
	6161	19.2	7.0	F	Caucasian	Cerebrovascular/Stroke	0.001	11.1	98	-	+	+	-	2	36.1	102.0	PanHead	02	Organ Donor		
	6064	19.6	9.0	F	Caucasian	Anoxia	<0.05	n/a	n/a	+	+	+	-	3	22.6	59.0	PanTail	02	Organ Donor		
	6212	20.0	5.0	M	Caucasian	Anoxia	0.001	6.4	46	-	-	+	-	1	29.1	80.2	PanTail	02	Organ Donor		
	6224	21.0	1.5	F	Caucasian	Anoxia	0.001	n/a	n/a	-	-	-	-	0	22.8	60.2	PanHead	04	Organ Donor		
	6198	22.0	3.0	F	Hispanic/Latino	Cerebrovascular/Stroke	0.001	n/a	n/a	+	+	+	+	4	23.1	63.0	PanTail	04	Organ Donor		X
	6245	22.0	7.0	M	Caucasian	Head Trauma	0.001	n/a	n/a	+	+	-	-	2	23.2	77.7	PanBody	02	Organ Donor		X
	6026	22.4	14.0	M	Caucasian	Head Trauma	<0.05	n/a	n/a	-	-	+	-	1	24.1	68.0	PanHead	01	Organ Donor		
	6070	22.6	7.0	F	Caucasian	Anoxia	<0.05	n/a	n/a	-	+	+	-	2	21.6	61.0	PanBody	04	Organ Donor		
	6069	22.9	7.0	M	African American	Head Trauma	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	28.8	104.0	PanTail	02	Organ Donor	X	X
Older Adults	6025	23.8	19.0	M	Caucasian	Anoxia	<0.05	n/a	n/a	-	-	+	-	1	26.6	79.0	PanOther	04	Organ Donor		
	6247	24.0	0.6	M	Caucasian	Head Trauma	0.47	n/a	n/a	-	-	+	-	1	24.3	81.2	PanTail	02	Organ Donor		X
	6211	24.0	4.0	F	African American	Anoxia	0.001	10.5	91	+	+	+	+	4	24.4	74.8	PanHead	02	Organ Donor		
	6196	28.0	15.0	F	African American	Anoxia	0.48	n/a	n/a	+	-	+	-	2	28.6	65.7	PanHead	02	Organ Donor		X
	6041	28.3	23.0	M	Caucasian	Cerebrovascular/Stroke	<0.05	n/a	n/a	+	-	-	-	0	28.4	87.0	PanHead	02	Organ Donor		
	6039	28.7	12.0	F	Caucasian	Head Trauma	<0.05	n/a	n/a	+	+	+	+	4	23.4	74.0	PanHead	01	Organ Donor		
	6088	31.2	5.0	M	Caucasian	Head Trauma	<0.05	n/a	n/a	+	+	+	+	4	27	78.0	PanTail	04	Organ Donor	X	X
	6081	31.4	15.0	M	Hispanic	Cerebrovascular/Stroke	0.24	n/a	n/a	-	-	-	-	0	28	78.0	PanHead	02	Organ Donor		
	6035	32.1	28.0	M	Caucasian	Cerebrovascular/Stroke	<0.05	n/a	n/a	-	-	+	-	1	27.1	86.0	PanHead	05	Organ Donor		
	6054	35.1	30.0	F	Caucasian	Cerebrovascular/Stroke	<0.05	n/a	n/a	-	-	+	-	1	30.4	75.0	PanBody	04	Organ Donor	X	X
6038	37.2	20.0	F	Caucasian	Anoxia	0.2	n/a	n/a	-	-	-	-	0	30.9	83.9	PanHead	01	Organ Donor	X	X	
6031	39.0	35.0	M	Caucasian	Cerebrovascular/Stroke	<0.05	n/a	n/a	-	-	+	-	1	24.5	82.0	PanOther	02	Organ Donor	X	X	
6150	41.2	35.0	M	Caucasian	Anoxia	<0.05	n/a	n/a	-	-	+	-	1	25.5	72.0	PanBody	04	Organ Donor	X	X	
6135	43.5	21.0	M	Caucasian	Anoxia	<0.05	n/a	n/a	+	-	+	-	2	28.7	81.0	PanHead	02	Organ Donor	X	X	
6036	49.2	34.0	F	African American	Anoxia	<0.05	n/a	n/a	-	-	+	-	1	25.5	59.0	PanHead	04	Organ Donor		X	
6138	49.2	41.0	F	Caucasian	Anoxia	<0.05	n/a	n/a	-	-	+	-	1	33.7	95.0	PanBody	04	Organ Donor			
6040	50.0	20.0	F	Caucasian	Cerebrovascular/Stroke	<0.05	7.3	56	-	-	+	-	1	31.6	85.0	PanHead	04	Organ Donor		X	

SUPPLEMENTARY DATA

Supplementary Table 3. Immunohistochemistry Antibodies. Antibody antigen, host, dilution, manufacturer, and catalog number.

SUPPLEMENTARY DATA

PRIMARY ANTIBODIES				
Antigen	Host	Dilution	Manufacturer	Catalog #
ARX	Sheep	1:100	R&D Systems	AF7068
β3 Tubulin	Chicken	1:100	Novus Biologicals	NB100-1612
CD3	Rabbit	1:100	Thermo Fisher	PA1-37282
CD31	Rabbit	1:100	Abcam	ab28364
Chromagranin A	Mouse	1:100	Abcam	ab8204
Ghrelin	Rabbit	1:100	Phoenix Pharmaceuticals	H-031-77
Glucagon	Rabbit	1:250	Abcam	ab8055
Glucagon	Mouse	1:250	Abcam	ab10988
GLUT1	Mouse	1:100	Millipore	07-1401
ISL1 & 2	Mouse	1:100	DSHB	39.4D5
INSM1	Mouse	1:100	Santa Cruz	sc-271408
Insulin	Guinea Pig	1:1500	Dako	A0564
Ki67	Mouse	1:250	BD Biosciences	#550609
NeuN	Mouse	1:100	Millipore	MAB377
Nkx2.2	Rabbit	1:100	Abcam	ab191077
Nkx6.1	Mouse	1:100	DSHB	F55A12
Pancreatic Polypeptide	Rabbit	1:100	Invitrogen	18-0043
PCNA	Mouse	1:100	Cell Signaling	2586S
PC1/3	Rabbit	1:100	Millipore	AB10553
Pdx1	Rabbit	1:100	Novus Biologicals	NBP2-38865
Phospho-Histone H3	Rabbit	1:100	Cell Signaling	9701S
Proinsulin	Rat	1:100	DSHB	GN-ID4
SNAP25	Mouse	1:100	Millipore	MAB331
Somatostatin	Rabbit	1:100	Invitrogen	18-0078
Synaptotagmin 1A	Chicken	1:100	Abcam	ab133856
Sox9	Rabbit	1:100	Millipore	AB5535
Sox9 (pS181)	Rabbit	1:100	Abcam	ab59252
Synaptophysin	Rabbit	1:100	Thermo Fisher	18-0130
Synaptophysin	Mouse	1:100	Abcam	AB6245
SECONDARY ANTIBODIES				
Secondary Antibody		Dilution	Manufacturer	Catalog Number
Alexa Fluor	Donkey α-Guinea Pig	1:3000	Jackson ImmunoResearch	706-155-148 706-545-148 706-165-148 706-605-148
Alexa Fluor	Donkey α-Chicken	1:250	Jackson ImmunoResearch	703-155-155 703-545-155 703-165-155 703-605-155
Alexa Fluor	Donkey α-Mouse	1:250	Jackson ImmunoResearch	715-155-150 715-545-150 715-165-150 715-605-150
Alexa Fluor	Donkey α-Rabbit	1:250	Jackson ImmunoResearch	711-155-152 711-545-152 711-165-152 711-605-152
Alexa Fluor	Donkey α-Rat	1:250	Jackson ImmunoResearch	712-155-153 712-545-153 712-165-153 712-605-153
Alexa Fluor	Donkey α-Sheep	1:250	Jackson ImmunoResearch	713-155-147 713-545-147 713-165-147 713-605-147

SUPPLEMENTARY DATA

Supplementary Table 4. Summary of experimental details. The number of pancreas donors, pancreas sections, and cells counted for each analysis performed. "n/a" indicates that data analysis is not available or not performed for the indicated cohort.

	Islet Endocrine Cell Proliferation	α-cell Proliferation	β-cell/Islet cross section	PP Proliferation	SS Proliferation	Ghrelin Proliferation	Sox9 Proliferation	Islet Endocrine Proliferation (% Intraislet Ki67)	α-cell Proliferation (% Intraislet Ki67)	β-cell Proliferation (% Intraislet Ki67)	PP Proliferation (% Intraislet Ki67)	SS Proliferation (% Intraislet Ki67)	Ghrelin Proliferation (% Intraislet Ki67)	Sox9 ^{hi} Proliferation (% Intraislet Ki67)	Sox9 ^{int} Ductal Proliferation (% Intraislet Ki67)	Syn+ Sox9 ^{hi} Proliferation (% Sox9 ^{hi})	Sox9 ^{hi} ARX+ Proliferation (% Intraislet Ki67)	Ki67+ ARX+ Dcp Proliferation (% Intraislet Ki67)	Islet Endocrine Cell TUNEL	Sox9 TUNEL	
Control	Pancreas Donors	59	59	59	5	6	5	6	12	12	12	3	3	3	6	6	3	3	3	18	6
	Pancreas Sections	59	59	59	5	6	5	6	12	12	12	3	3	3	6	6	3	3	3	18	6
	Cells	624233	184431	184431	2321	8968	872	5820	133060	36825	85055	1375	6533	604	5820	6258	21545	12889	5364	154874	893 cells
T1D	Pancreas Donors	48	48	48	9	9	9	6	6	6	8	7	9	6	6	3	3	3	12	n/a	
	Pancreas Sections	48	48	48	9	9	9	6	6	6	8	7	9	6	6	3	3	3	12	n/a	
	Cells	458626	259175	259175	1088	8941	795	3230	70297	46403	6089	690	4008	261	3230	1478	18077	10156	1167	85768	n/a

SUPPLEMENTARY DATA

Supplementary Table 5. Individual intraislet proliferation from non-diabetic and T1D pancreata.
 Intraislet Ki67+ cells (number and % total), total intraislet cells (number).

nPOD Case #	Age (Years)	Control		
		Intraislet Ki67+ cells	Total Intraislet cells	Ki67+ Intraislet (% Total)
6200	0.005	403	12073	3.34
6214	0.014	169	6268	2.70
6164	0.030	659	8073	8.16
6218	0.080	115	8764	1.31
6222	0.170	49	5815	0.84
Average	0.1	279	8199	3.27
SD	0.1	251	2488	2.92
SEM	0.0	112	1113	1.30
6278	10.0	77	17078	0.45
6232	14.0	80	8218	0.97
6233	14.0	183	23368	0.78
6230	16.0	182	17406	1.05
6227	17.0	11	9061	0.12
6271	17.0	5	14686	0.03
6253	19.0	63	14768	0.43
6279	19.0	289	12798	2.26
6234	20.0	110	16636	0.66
6238	20.0	7	9126	0.08
6174	20.8	9	14792	0.06
Average	17.0	92	14358	0.63
SD	3.3	92	4462	0.65
SEM	1.0	28	1345	0.20
6024	21.0	6	14876	0.04
6179	21.8	72	13048	0.55
6162	22.7	2	7025	0.03
6003	23.0	20	13054	0.15
6029	24.0	6	15409	0.04
6131	24.2	412	17817	2.31
6048	30.0	8	10365	0.08
6235	30.0	197	12293	1.60
6030	30.1	60	8558	0.70
6229	31.0	20	29318	0.07
6011	46.0	5	3366	0.15
6008	50.0	11	5868	0.19
6168	51.0	38	11142	0.34
6017	59.0	1	11146	0.01
6020	60.0	17	9995	0.17
6016	64.0	0	3577	0.00
6013	65.0	0	9939	0.00
Average	38.4	51	11576	0.38
SD	16.5	105	6047	0.64
SEM	4.0	25	1467	0.15

nPOD Case #	Age (Years)	Years with Diabetes	T1D		
			Intraislet Ki67+ cells	Total Intraislet cells	Ki67+ Intraislet (% Total)
6209	5.0	0.3	49	17078	0.29
6265	11.0	8.0	7	1834	0.38
6268	12.0	3.0	89	12584	0.71
6264	12.0	9.0	44	14595	0.30
6228	13.0	0.0	266	19965	1.33
6243	13.0	5.0	13	4364	0.30
6243	13.0	5.0	13	4364	0.30
6207	16.0	10.0	28	10811	0.26
6261	16.0	14.2	1104	18482	5.97
6148	17.1	7.0	6	7928	0.08
6237	18.0	12.0	83	45235	0.18
6161	19.2	7.0	21	10334	0.20
6212	20.0	5.0	75	33015	0.23
Average	14.3	6.6	138	15430	0.81
SD	4.0	4.2	298	12153	1.58
SEM	1.1	1.2	83	3371	0.44
p-value (v. control)	0.1	///	1	1	0.72
6224	21.0	1.5	41	18468	0.22
6198	22.0	3.0	12	6939	0.17
6245	22.0	7.0	64	36377	0.18
6247	24.0	0.6	12	14780	0.08
6211	24.0	4.0	61	17658	0.35
6196	26.0	15.0	142	33498	0.42
Average	23.2	5.2	55	21287	0.24
SD	1.83	5.3	48	11368	0.13
SEM	0.75	2.2	20	4641	0.05
p-value (v. control)	0.04	///	1	0	0.60

SUPPLEMENTARY DATA

Supplementary Table 6. Individual β -cell proliferation expressed as % of inтраislet Ki67+ cells in non-diabetic and T1D pancreata. Ki67+ β -cell (number; % total inтраislet Ki67+ cells), total inтраislet Ki67+ cells (number) from highly proliferative samples.

Control				
nPOD Case #	Age (Years)	Ki67+ β -cells	Total Inтраislet Ki67+ cells	Ki67+ β -cells (% Total)
6232	14.0	11	69	15.94
6233	14.0	16	168	9.52
6153	15.2	5	32	15.63
6075	16.0	6	104	5.77
6230	16.0	29	172	16.86
6279	19.0	18	270	6.67
6179	21.8	3	59	5.08
6057	22.0	9	22	40.91
6131	24.2	5	377	1.33
6235	30.0	8	169	4.73
6030	30.1	0	49	0.00
6004	33.0	0	51	0.00
Average	21.3	9	129	10.20
SD	6.8	8	108	11.38
SEM	2.0	2	31	3.29

T1D					
nPOD Case #	Age (Years)	Years with Diabetes	Ki67+ β -cells	Total Inтраislet Ki67+ cells	Ki67+ β -cells (% Total)
6052	12.0	1.0	10	849	1.18
6268	12.0	3.0	0	89	0.00
6228	13.0	0.0	10	375	2.67
6113	13.1	1.6	1	72	1.39
6084	14.2	4.0	5	317	1.58
6261	16.0	14.2	0	1516	0.00
Average	13.4	4.0	4	536	1.14
SD	1.52	5.2	5	556	1.02
SEM	0.62	2.1	2	227	0.42
p-value (v. control)	0.01		0.21	0.02	0.07

SUPPLEMENTARY DATA

Supplementary Table 7. Individual islet endocrine and α -cell proliferation from non-diabetic pancreata. Total synaptophysin+ (Syn) islet endocrine cells (number), Ki67+ Syn+ cells (number and % total), α -cells (number), Ki67+ α -cells (number and % Total).

SUPPLEMENTARY DATA

		Control						
		Islet Endocrine Cells			α-cells			
nPOD Case #	Age (Years)	Syn+ cells	Ki67+ Syn+ cells	Ki67+ Syn+ cells (% Total)	α-cells	Ki67+ α-cells	Ki67+ α-cells (% Total)	
Infants (0-1.4)	6200	0.005	11573	328	2.83	809	5	0.62
	6214	0.014	5630	119	2.11	908	74	8.15
	6164	0.030	7535	654	8.68	1157	57	4.93
	6218	0.080	8010	109	1.36	1561	40	2.56
	6222	0.170	5511	48	0.87	1469	26	1.77
	6117	0.330	8651	17	0.20	3074	20	0.65
	6115	0.420	7130	19	0.27	1934	3	0.16
	6092	0.500	3333	128	3.84	1198	107	8.93
	Average	0.2	7172	178	2.52	1514	42	3.47
	SD	0.2	2457	216	2.79	728	36	3.48
SEM	0.1	869	77	0.99	257	13	1.23	
Children (1.5-13.9)	6103	1.5	5839	75	1.28	2133	44	2.06
	6107	2.2	14578	718	4.93	3239	218	6.73
	6094	2.9	4450	3	0.07	2217	3	0.14
	6106	2.9	10907	11	0.10	8106	19	0.23
	6005	5.0	19916	18	0.09	992	0	0.00
	6112	6.3	12523	40	0.32	3722	39	1.05
	6007	9.0	26002	95	0.37	2971	76	2.56
	6278	10.0	16328	65	0.40	3325	33	0.99
	Average	5.0	13818	128	0.94	3338	54	1.72
	SD	3.2	7112	241	1.66	2112	71	2.22
SEM	1.1	2515	85	0.59	747	25	0.79	
Adolescents (14-20.9)	6232	14.0	8636	69	0.80	2882	42	1.46
	6233	14.0	22593	163	0.72	1908	21	1.10
	6099	14.2	11656	7	0.06	4595	2	0.04
	6153	15.2	3512	32	0.91	1511	36	2.38
	6075	16.0	9300	104	1.12	3740	67	1.79
	6096	16.0	7112	11	0.15	2176	3	0.14
	6230	16.0	16285	172	1.06	2002	68	3.40
	6227	17.0	8787	8	0.09	824	1	0.12
	6271	17.0	14945	2	0.01	2185	1	0.05
	6098	17.8	6360	3	0.05	4366	1	0.02
	6253	19.0	15244	43	0.28	1691	5	0.30
	6279	19.0	12342	270	2.19	1067	22	2.06
	6234	20.0	13626	13	0.10	4135	39	0.94
	6238	20.0	9368	1	0.01	4261	2	0.05
	6174	20.8	14425	1	0.01	1918	2	0.10
	Average	17.1	11613	60	0.50	2617	21	0.93
SD	2.3	4780	82	0.62	1275	24	1.07	
SEM	0.59	1234	21	0.16	329	6	0.28	
Young Adults (21-39)	6024	21.0	14111	3	0.02	585	0	0.00
	6179	21.8	12370	59	0.48	2848	15	0.53
	6001	22.0	4824	0	0.00	11414	8	0.07
	6057	22.0	4492	22	0.49	2236	4	0.18
	6162	22.7	6507	1	0.02	1637	7	0.43
	6003	23.0	13816	13	0.09	5126	9	0.18
	6029	24.0	15098	2	0.01	5352	1	0.02
	6131	24.2	17130	377	2.20	2334	79	3.38
	6053	25.0	12280	8	0.07	3509	13	0.37
	6126	25.2	5688	7	0.12	1014	9	0.89
	6058	27.0	4070	3	0.07	2240	1	0.04
	6048	30.0	10157	2	0.02	3213	0	0.00
	6235	30.0	12107	169	1.40	10694	115	1.08
	6030	30.1	8254	49	0.59	2088	29	1.39
	6229	31.0	28550	10	0.04	14655	9	0.06
	6035	32.0	7350	1	0.01	2594	0	0.00
	6004	33.0	6039	51	0.84	3515	69	1.96
	6002	39.0	14758	17	0.12	4967	4	0.08
6015	39.0	8380	2	0.02	5127	0	0.00	
Average	27.5	10841	42	0.35	4481	20	0.56	
SD	5.6	5908	90	0.58	3782	32	0.88	
SEM	1.3	1355	21	0.13	868	7	0.20	
Older Adults (≥40)	6009	45.0	7745	44	0.57	2134	9	0.42
	6011	46.0	4025	1	0.02	4831	1	0.02
	6010	47.0	5744	0	0.00	2223	0	0.00
	6008	50.0	5747	2	0.03	1681	0	0.00
	6168	51.0	9884	37	0.37	1728	4	0.23
	6017	59.0	10489	0	0.00	3015	0	0.00
	6020	60.0	9427	4	0.04	2214	0	0.00
	6016	64.0	11354	0	0.00	8716	1	0.01
	6013	65.0	11730	0	0.00	4665	0	0.00
	Average	54.1	8461	10	0.12	3467	2	0.08
SD	7.9	2763	18	0.21	2296	3	0.15	
SEM	2.6	921	6	0.07	765	1	0.05	

SUPPLEMENTARY DATA

Supplementary Table 8. Individual islet endocrine and α -cell proliferation from T1D pancreata.

Total synaptophysin+ (Syn) islet endocrine cells (number), Ki67+ Syn+ cells (number and % total), α -cells (number), Ki67+ α -cells (number and % total). "n/a" indicates that the case sample was not available for this analysis.

SUPPLEMENTARY DATA

				T1D					
				Islet Endocrine Cells			α-cells		
nPOD Case #	Age (Years)	Years with Diabetes	Syn+ cells	Ki67+ Syn+ cells	Ki67+ Syn+ cells (% Total)	α-cells	Ki67+ α-cells	Ki67+ α-cells (% Total)	
Children (1.5-13.9)	6063	4.4	3.0	10634	0	0.00	7892	3	0.04
	6209	5.0	0.3	5542	8	0.14	5355	3	0.06
	6062	10.7	6.0	5594	18	0.32	3831	31	0.81
	6265	11.0	8.0	878	1	0.11	1157	0	0.00
	6052	12.0	1.0	7993	849	10.62	3767	24	0.64
	6268	12.0	3.0	8560	56	0.65	4527	35	0.77
	6264	12.0	9.0	10084	26	0.26	5629	4	0.07
	6228	13.0	0.0	20857	216	1.04	11597	110	0.95
	6243	13.0	5.0	3609	4	0.11	1199	2	0.17
	6113	13.1	1.6	4109	72	1.75	4060	13	0.32
	Average	10.6	3.7	7786	125.0	1.50	4901	22.5	0.38
	SD	3.2	3.2	5512	262.6	3.25	3083	33.3	0.37
	SEM	1.0	1.0	1743	83.0	1.03	975	10.5	0.12
p-value (v. control)	0.002	////	0.06	0.98	0.67	0.24	0.23	0.08	
Adolescents (14-20.9)	6084	14.2	4.0	10617	317	2.99	862	14	1.62
	6089	14.3	8.0	2608	5	0.19	1925	2	0.10
	6049	15.0	10.0	7337	16	0.22	3985	0	0.00
	6083	15.2	11.0	4228	7	0.17	3342	0	0.00
	6207	16.0	10.0	9625	8	0.08	4959	5	0.10
	6261	16.0	14.2	18161	1160	6.39	21590	848	3.93
	6148	17.1	7.0	5275	0	0.00	3078	2	0.06
	6087	17.5	4.0	3005	8	0.27	14064	6	0.04
	6145	18.0	11.0	5697	3	0.05	3250	0	0.00
	6237	18.0	12.0	36085	32	0.09	7412	7	0.09
	6195	19.2	5.0	n/a	n/a	n/a	5724	1	0.02
	6161	19.2	7.0	6486	9	0.14	5148	6	0.12
	6064	19.6	9.0	12291	1	0.01	1225	0	0.00
	6212	20.0	5.0	25146	38	0.15	14384	11	0.08
	Average	17.1	8.4	11274	123.4	0.83	6496	64.4	0.44
SD	2.0	3.2	9825	322.9	1.85	6025	225.6	1.09	
SEM	0.53	0.85	2626	86.3	0.49	1610	60.3	0.29	
p-value (v. control)	0.97	////	0.91	0.47	0.53	0.02	0.46	0.23	
Young Adults (21-39)	6224	21.0	1.5	13646	11	0.08	4825	3	0.06
	6198	22.0	3.0	5197	3	0.06	3153	1	0.03
	6245	22.0	7.0	24760	16	0.06	21661	9	0.04
	6026	22.4	14.0	2021	1	0.05	1793	0	0.00
	6070	22.6	7.0	20830	11	0.05	17807	3	0.02
	6069	22.9	7.0	9097	6	0.07	312	0	0.00
	6025	23.8	19.0	7190	1	0.01	1551	1	0.06
	6247	24.0	0.6	10464	0	0.00	8170	1	0.01
	6211	24.0	4.0	15774	29	0.18	5967	2	0.03
	6196	26.0	15.0	26754	54	0.20	3620	10	0.28
	6041	26.3	23.0	14822	5	0.03	2502	3	0.12
	6039	28.7	12.0	14701	3	0.02	1107	1	0.09
	6088	31.2	5.0	1837	0	0.00	4384	0	0.00
	6081	31.4	15.0	1819	1	0.05	833	0	0.00
	6035	32.1	28.0	16889	4	0.02	846	1	0.12
	6054	35.1	30.0	5716	0	0.00	6999	1	0.01
	6038	37.2	20.0	10766	2	0.02	8937	0	0.00
	6031	39.0	35.0	2614	0	0.00	5353	0	0.00
Average	27.3	13.7	11383	8.2	0.05	5546	2.0	0.05	
SD	5.7	10.4	7759	13.6	0.06	5804	2.9	0.07	
SEM	1.3	2.4	1829	3.2	0.01	1368	0.7	0.02	
p-value (v. control)	0.93	////	0.81	0.13	0.04	0.51	0.03	0.02	
Older Adults (≥40)	6150	41.2	35.0	1174	1	0.09	1355	0	0.00
	6135	43.5	21.0	6832	6	0.09	9493	7	0.07
	6036	49.2	34.0	9223	1	0.01	1639	0	0.00
	6138	49.2	41.0	1824	0	0.00	1426	1	0.07
	6040	50.0	20.0	1608	0	0.00	1918	0	0.00
	Average	46.6	30.2	4132	2	0.04	3166	1.6	0.03
SD	4.0	9.3	3662	3	0.05	3544	3.0	0.04	
SEM	1.8	4.1	1638	1	0.02	1585	1.4	0.02	
p-value (v. control)	0.07	////	0.03	0.33	0.42	0.85	0.97	0.51	

SUPPLEMENTARY DATA

Supplementary Table 9. Individual synaptophysin cell proliferation expressed as % of intraislet Ki67+ cells in nondiabetic and T1D pancreata. Ki67+ Syn+ cells (number; % total intraislet Ki67+ cells), total intraislet Ki67+ cells (number) from highly proliferative samples.

Control				
nPOD Case #	Age (Years)	Ki67+ Syn+ cells	Total Intraislet Ki67+ cells	Ki67+ Syn+ (% Total)
6232	14.0	69	79	87.34
6233	14.0	163	183	89.07
6153	15.2	44	65	67.69
6075	16.0	120	159	75.47
6230	16.0	172	181	95.03
6279	19.0	270	289	93.43
6179	21.8	62	72	86.11
6057	22.0	35	41	85.37
6131	24.2	382	412	92.72
6235	30.0	177	197	89.85
6030	30.1	49	60	81.67
6004	33.0	178	185	96.22
Average	21.3	143	160	86.66
SD	6.8	104	109	8.38
SEM	2.0	30	31	2.42

T1D					
nPOD Case #	Age (Years)	Years with Diabetes	Ki67+ Syn+ cells	Total Intraislet Ki67+ cells	Ki67+ Syn+ (% Total)
6052	12.0	1.0	510	542	94.10
6268	12.0	3.0	56	89	62.92
6228	13.0	0.0	226	375	60.27
6113	13.1	1.6	60	73	82.19
6084	14.2	4.0	284	311	91.32
6261	16.0	14.2	1160	1516	76.52
Average	13.4	4.0	383	484	77.89
SD	1.52	5.2	416	536	14.13
SEM	0.62	2.1	170	219	5.77
p-value (v. control)	0.01		0.07	0.05	0.11

SUPPLEMENTARY DATA

Supplementary Table 10. Regional islet endocrine cell proliferation. Pancreas region, Syn+ cells (number), total Ki67+ Syn+ cells (number; % total).

nPOD Case #	Age (Years)	Pancreas Sample Region 1	Syn+ cells	Ki67+ Syn+ cells	Ki67+ Syn+ (% Total)	Pancreas Sample Region 2	Syn+ cells	Ki67+ Syn+ cells	Ki67+ Syn+ (% Total)
6075	16	Head	10664	120	1.13	Tail	9300	104	1.12
6279	19	Body	12342	270	2.19	Tail	19869	540	2.72
6029	24	Head	8614	3	0.03	Tail	15098	2	0.01
6131	24.2	Head	17130	377	2.20	Tail	24758	752	3.04
Average	20.8	n/a	12188	193	1.39	n/a	17256	350	1.72
SD	4.0	n/a	3631	165	1.03	n/a	6610	356	1.41
SEM	2.0	n/a	1815	82	0.52	n/a	3305	178	0.71

SUPPLEMENTARY DATA

Supplementary Table 11. Average α -cell number per islet cross section of non-diabetic and T1D samples. α -cells (number; per islet), Ki67+ α -cells (number; per islet), and islets (number).

	Control							T1D							
	nPOD Case #	Age (Years)	α -cells	Ki67+ α -cells	Islets	α -cells (per islet)	Ki67+ α -cells (per islet)	nPOD Case #	Age (Years)	Years with Diabetes	α -cells	Ki67+ α -cells	Islets	α -cells (per islet)	Ki67+ α -cells (per islet)
Children (1.5-13.9)	6103	1.5	2133	44	101	21	2.1	6063	4.4	3.0	7892	3	167	47	0.02
	6107	2.2	3239	218	110	29	6.7	6209	5.0	0.3	5355	3	151	35	0.02
	6094	2.9	2217	3	73	30	0.1	6062	10.7	6.0	3831	31	116	33	0.27
	6106	2.9	8106	19	276	29	0.2	6265	11.0	8.0	1157	0	59	20	0.00
	6005	5.0	992	0	107	9	0.0	6052	12.0	1.0	3767	24	52	72	0.46
	6112	6.3	3722	39	105	35	1.0	6268	12.0	3.0	4527	35	142	32	0.25
	8007	9.0	2971	76	113	26	2.6	6264	12.0	9.0	5629	4	267	21	0.01
	6276	10.0	3325	33	66	50	1.0	6228	13.0	0.0	11597	110	301	39	0.37
	Average	5.0	3338	54	119	29	1.7	6243	13.0	5.0	1199	2	45	27	0.04
	SD	3.2	2112	71	66	12	2.2	6113	13.1	1.6	4060	13	56	73	0.23
SEM	1.1	747	25	23	4	0.8	Average	10.6	3.7	4901	23	136	40	0.17	
Adolescents (14-20.9)	6232	14.0	2882	42	198	15	1.5	SD	3.2	3.2	3083	33	90	19	0.17
	6233	14.0	1908	21	135	14	1.1	SEM	0.9	0.9	882	10	26	5	0.05
	6099	14.2	4595	2	61	75	0.0	p-value (v. control)	0.002	///	0.24	0.23	0.67	0.18	0.04
	6153	15.2	1511	36	59	26	2.4	6084	14.2	4.0	862	14	29	30	0.48
	6075	16.0	3740	67	55	68	1.8	6089	14.3	8.0	1925	2	24	80	0.08
	6096	16.0	2176	3	42	52	0.1	6049	15.0	10.0	3985	0	46	87	0.00
	6230	16.0	2002	68	151	13	3.4	6083	15.2	11.0	3342	0	56	60	0.00
	6227	17.0	824	1	54	15	0.1	6207	16.0	10.0	4959	5	152	33	0.03
	6271	17.0	2185	1	204	11	0.0	6261	16.0	14.2	21590	848	303	71	2.80
	6098	17.8	4366	1	78	56	0.0	6148	17.1	7.0	3078	2	211	15	0.01
	6253	19.0	1691	5	180	9	0.3	6087	17.5	4.0	14064	6	193	73	0.03
	6279	19.0	1067	22	133	8	2.1	6145	18.0	11.0	3250	0	36	90	0.00
	6234	20.0	4135	39	182	23	0.9	6237	18.0	12.0	7412	7	287	26	0.02
	6238	20.0	4261	2	256	17	0.0	6195	19.2	5.0	5724	1	138	41	0.01
	6174	20.8	1918	2	91	21	0.1	6161	19.2	7.0	5148	6	171	30	0.04
	Average	17.1	2617	21	125	28	0.9	6064	19.6	9.0	1225	0	36	34	0.00
SD	2.3	1275	24	68	23	1.1	6212	20.0	5.0	14384	11	521	28	0.02	
SEM	0.59	329	6	18	6	0.3	Average	17.1	8.4	6496	64	157	50	0.25	
Young Adults (21-39)	6024	21.0	585	0	32	18	0.0	SD	2.00	3.18	6025	226	142	26	0.74
	6179	21.8	2848	15	110	26	0.5	SEM	0.53	0.85	1610	60	38	7	0.20
	6001	22.0	11414	8	291	39	0.1	p-value (v. control)	4.28	///	0.02	0.46	0.44	0.02	0.06
	6057	22.0	2236	4	74	30	0.2	6224	21.0	1.5	4825	3	210	23	0.01
	6162	22.7	1637	7	53	31	0.4	6198	22.0	3.0	3153	1	185	17	0.01
	6003	23.0	5126	9	131	39	0.2	6245	22.0	7.0	21661	9	398	54	0.02
	6029	24.0	5352	1	186	29	0.0	6026	22.4	14.0	1793	0	35	51	0.00
	6131	24.2	2334	79	36	65	3.4	6070	22.6	7.0	17807	3	145	123	0.02
	6053	25.0	3509	13	74	47	0.4	6069	22.9	7.0	312	0	16	20	0.00
	6126	25.2	1014	9	62	16	0.9	6025	23.8	19.0	1551	1	95	16	0.01
	6058	27.0	2240	1	59	38	0.0	6247	24.0	0.6	8170	1	263	31	0.00
	6048	30.0	3213	0	99	32	0.0	6211	24.0	4.0	5967	2	181	33	0.01
	6235	30.0	10694	115	177	60	1.1	6196	26.0	15.0	3620	10	234	15	0.04
	6030	30.1	2088	29	88	24	1.4	6041	26.3	23.0	2502	3	54	46	0.06
	6229	31.0	14655	9	323	45	0.1	6039	28.7	12.0	1107	1	39	28	0.03
	6035	32.0	2594	0	323	8	0.0	6088	31.2	5.0	4384	0	145	30	0.00
6004	33.0	3515	69	111	32	2.0	6081	31.4	15.0	833	0	66	13	0.00	
6002	39.0	4967	4	142	35	0.1	6035	32.1	28.0	846	1	32	26	0.03	
6015	39.0	5127	0	115	45	0.0	6054	35.1	30.0	6999	1	67	104	0.01	
Average	27.5	4481	20	131	35	0.6	6038	37.2	20.0	8937	0	172	52	0.00	
SD	5.6	3782	32	91	14	0.9	6031	39.0	35.0	5353	0	101	53	0.00	
SEM	1.3	868	7	21	3	0.2	Average	27.3	13.7	5546	2.0	135.4	41	0.01	
Older Adults (≥ 40)	6009	45.0	2134	9	53	40	0.4	SD	5.7	10.4	5804	2.9	100.0	30	0.02
	6011	46.0	4831	1	154	31	0.0	SEM	1.3	2.4	1368	0.7	23.6	7	0.00
	6010	47.0	2223	0	109	20	0.0	p-value (v. control)	0.93	///	0.51	0.03	0.88	0.42	0.01
	6008	50.0	1681	0	52	32	0.0	6150	41.2	35.0	1355	0	35	39	0.00
	6168	51.0	1728	4	101	17	0.2	6135	43.5	21.0	9493	7	133	71	0.05
	6017	59.0	3015	0	128	24	0.0	6036	49.2	34.0	1639	0	32	51	0.00
	6020	60.0	2214	0	71	31	0.0	6138	49.2	41.0	1426	1	72	20	0.01
	6016	64.0	8716	1	343	25	0.0	6040	50.0	20.0	1918	0	35	55	0.00
	6013	65.0	4665	0	187	25	0.0	Average	46.6	30.2	3166	2	61	47	0.01
	Average	54.1	3467	2	133	27	0.1	SD	4.0	9.3	3544	3.0	43.3	19	0.02
SD	7.9	2296	3	91	7	0.1	SEM	1.8	4.1	1585	1.4	19.4	9	0.01	
SEM	2.6	765	1	30	2	0.0	p-value (v. control)	0.07	///	0.85	0.97	0.13	0.02	0.38	

SUPPLEMENTARY DATA

Supplementary Table 12. Individual α -cell proliferation expressed as % of intraislet Ki67+ cells in non-diabetic and T1D pancreata. Ki67+ α -cells (number; % total intraislet Ki67+ cells), total intraislet Ki67+ cells (number) from highly proliferative samples.

Control				
nPOD Case #	Age (Years)	Ki67+ α -cells	Total Intraislet Ki67+ cells	Ki67+ α -cells (% Total)
6232	14.0	42	189	22.22
6233	14.0	21	102	20.59
6153	15.2	24	136	17.65
6075	16.0	13	92	14.13
6230	16.0	68	139	48.92
6279	19.0	22	126	17.46
6179	21.8	15	86	17.44
6057	22.0	4	23	17.39
6131	24.2	79	223	35.43
6235	30.0	115	378	30.42
6030	30.1	29	102	28.43
6004	33.0	69	392	17.60
Average	21.3	42	166	23.97
SD	6.8	34	114	10.16
SEM	2.0	10	33	2.93

T1D					
nPOD Case #	Age (Years)	Years with Diabetes	Ki67+ α -cells	Total Intraislet Ki67+ cells	Ki67+ α -cells (% Total)
6052	12.0	1.0	24	699	3.43
6268	12.0	3.0	35	119	29.41
6228	13.0	0.0	110	423	26.00
6113	13.1	1.6	3	8	37.50
6084	14.2	4.0	68	163	41.72
6261	16.0	14.2	848	1988	42.66
Average	13.4	4.0	181	567	30.12
SD	1.52	5.2	329	739	14.67
SEM	0.62	2.1	134	302	5.99
p-value (v. control)	0.01		0.15	0.08	0.31

SUPPLEMENTARY DATA

Supplementary Table 13. Individual PP, somatostatin, and ghrelin cell proliferation from non-diabetic and T1D pancreata. Ki67+ PP+ cells (number; % total PP cells), total PP+ cells (number), Ki67+ somatostatin+ cells (number: % total somatostatin cells), total somatostatin+ cells (number), Ki67+ ghrelin+ cells (numbers; % total ghrelin cells), total ghrelin+ cells (number) counted. "n/a" indicates the measurement is not applicable for the case or the case sample was not available for this analysis.

	nPOD Case #	Age (Years)	Years with Diabetes	PP Cells			SS Cells			Ghrelin Cells		
				Ki67+ PP+ Cells	Total PP+ Cells	Ki67+ PP+ Cells (% total)	Ki67+ Somatostatin+ Cells	Total Somatostatin+ Cells	Ki67+ Somatostatin+ Cells (% total)	Ki67+ Ghrelin+ Cells	Total Ghrelin+ Cells	Ki67+ Ghrelin+ Cells (% total)
Control	6233	14.0	n/a	0	174	0.00	13	4378	0.30	0	267	0.00
	6099	14.2	n/a	n/a	n/a	n/a	0	546	0.00	n/a	n/a	n/a
	6153	15.2	n/a	7	1011	0.69	2	1023	0.20	0	217	0.00
	6075	16.0	n/a	1	190	0.53	2	1132	0.18	0	120	0.00
	6096	16.0	n/a	0	259	0.00	1	1360	0.07	0	208	0.00
	6098	17.8	n/a	0	687	0.00	0	1528	0.00	0	60	0.00
	Average	15.5		2	537	0.30	3	1661	0.12	0	151	0.00
	SD	1.4		3	371	0.34	5	1373	0.12	0	83	0.00
SEM	0.57		1	151	0.14	2	560	0.05	0	34	0.00	
T1D	6052	12.0	1	0	296	0.00	4	905	0.44	0	64	0.00
	6113	13.1	1.6	0	176	0.00	0	1167	0.00	0	129	0.00
	6084	14.2	4	0	218	0.00	3	1936	0.15	0	68	0.00
	6089	14.3	8	0	52	0.00	0	676	0.00	0	43	0.00
	6049	15.0	10	0	0	0.00	1	1284	0.08	0	202	0.00
	6083	15.2	11	0	71	0.00	1	1975	0.05	0	145	0.00
	6087	17.5	4	0	135	0.00	0	0	0.00	0	85	0.00
	6145	18.0	11	0	104	0.00	1	998	0.10	0	27	0.00
	6064	19.6	9	0	36	0.00	0	0	0.00	1	35	2.86
	Average	15.4	6.6	0	121	0.00	1	993	0.09	0	89	0.32
	SD	2.5	4.0	0	95	0.00	1	711	0.14	0	59	0.95
SEM	0.82	1.3	0	32	0.00	0	237	0.05	0	20	0.32	
p-value (v. control)	0.93			0.13	0.02	0.05	0.30	0.24	0.66	0.48	0.04	0.48

SUPPLEMENTARY DATA

Supplementary Table 14. Individual PP, somatostatin, and ghrelin cell proliferation as a percentage of intraislet proliferation from non-diabetic and T1D pancreata. Ki67+ PP cells (number; % Total), total Intraislet Ki67+ cells per sample analysis (number), Ki67+ somatostatin+ cells (number; % Total), Ki67+ ghrelin+ cells (numbers; % Total) from highly proliferative samples. "n/a" indicates the measurement is not applicable for the case or the case sample was not available for this analysis. Cross-hatched boxes indicates that the measurement could not be calculated.

	nPOD Case #	Age (Years)	Years with Diabetes	PP Cells			SS Cells			Ghrelin Cells		
				Ki67+ PP+ Cells	Intraislet Ki67+ Cells	Ki67+ PP+ Cells (% Total)	Ki67+ Somatostatin+ Cells	Intraislet Ki67+ Cells	Ki67+ Somatostatin+ Cells (% Total)	Ki67+ Ghrelin+ Cells	Intraislet Ki67+ Cells	Ki67+ Ghrelin+ Cells (% Total)
Control	6233	14.0	n/a	0	41	0.00	13	272	4.78	0	45	0.00
	6153	15.2	n/a	16	130	12.31	2	80	2.50	0	61	0.00
	6075	16.0	n/a	1	20	5.00	2	12	16.67	0	38	0.00
	Average	15.1		6	64	6	6	121	8	0	48	0.00
	SD	1.0		9	58	6	6	135	8	0	12	0
	SEM	0.58		5	34	4	4	78	4	0	7	0
T1D	6052	12.0	1	0	99	0.00	4	429	0.93	0	144	0.00
	6113	13.1	1.6	0	1	0.00	0	18	0.00	0	19	0.00
	6084	14.2	4	0	21	0.00	3	41	7.32	0	32	0.00
	Average	13.1	2.2	0	40	0.00	2	163	2.75	0	65	0.00
	SD	1.1	1.6	0	52	0	2	231	3.98	0	69	0.00
	SEM	0.64	0.92	0	30	0.00	1	133	2.30	0	40	0.00
	p-value (v. control)	0.0844		0.33	0.63	0.18	0.44	0.80	0.35		0.69	

SUPPLEMENTARY DATA

Supplementary Table 15. Individual pancreas weights, pancreas transit times, and duration of ICU stay for non-diabetic and T1D individuals. Case number, age (years), pancreas weight (g), pancreas transit time (h), and duration of ICU stay (days). "n/a" indicates measurements were not available for that case. Cross-hatched boxes indicates that the measurement could not be calculated.

SUPPLEMENTARY DATA

		Control				
		nPOD Case #	Age (Years)	Pancreas Weight	Pancreas Transit Time (h)	Duration of ICU Stay (Days)
Infants (0-1.4)	6200	0.005	4.290	24.27	2.4	
	6214	0.014	1.000	11.85	5.95	
	6164	0.030	2.980	16.33	13.75	
	6218	0.080	0.730	19.55	6.01	
	6222	0.170	5.770	14.80	3.37	
	6117	0.330	5.400	15.67	3.32	
	6115	0.420	3.900	14.13	11.19	
	6092	0.500	5.300	10.83	4.11	
	Average	0.194	3.67	15.93	6.26	
	SD	0.197	1.95	4.31	4.09	
SEM	0.070	0.69	1.52	1.45		
Children (1.5-13.9)	6103	1.5	10.4	10.55	5.89	
	6107	2.2	15.9	23.25	3.74	
	6094	2.9	21.2	15.37	5.08	
	6106	2.9	16.3	18.85	2.89	
	6005	5.0	n/a	24.93	6.38	
	6112	6.3	30.0	18.90	2.05	
	6007	9.0	n/a	4.40	6.93	
	6278	10.0	33.6	14.92	1.84	
	Average	5.0	21.22	16.40	4.35	
	SD	3.2	8.95	6.69	1.99	
SEM	1.1	3.16	2.37	0.70		
Adolescents (14-20.9)	6232	14.0	49.4	13.72	3.03	
	6233	14.0	60.9	18.87	7.42	
	6099	14.2	85.6	14.83	2.05	
	6153	15.2	67.8	n/a	n/a	
	6075	16.0	47.3	4.03	4.82	
	6096	16.0	51.5	11.17	3.28	
	6230	16.0	66.3	15.78	3.03	
	6227	17.0	60.4	20.73	11.17	
	6271	17.0	98.0	15.32	0.48	
	6098	17.8	91.1	16.92	1.74	
6253	19.0	85.3	13.05	6.14		
6279	19.0	80.2	45.25	3.38		
6234	20.0	49.9	16.45	3.77		
6238	20.0	91.5	22.22	1.66		
6174	20.8	79.3	10.07	0.82		
Average	17.1	70.95	17.03	3.77		
SD	2.28	17.37	9.32	2.87		
SEM	0.59	4.49	2.41	0.74		
Young Adults (21-39)	6024	21.0	n/a	n/a	n/a	
	6179	21.8	72.4	24.40	13.96	
	6001	22.0	n/a	1.75	1.7	
	6057	22.0	104.4	11.82	8.62	
	6162	22.7	81.5	20.05	1.52	
	6003	23.0	n/a	1.40	2.77	
	6029	24.0	79.3	16.67	n/a	
	6131	24.2	108.9	18.78	1.9	
	6053	25.0	19.4	10.80	2.68	
	6126	25.2	80.2	11.22	4.88	
6058	27.0	52.7	13.15	15.36		
6048	30.0	139.0	6.13	1.34		
6235	30.0	102.3	17.00	2.56		
6030	30.1	96.3	4.90	4.78		
6229	31.0	45.6	13.92	3.12		
6034	32.0	75.4	27.42	2.88		
6004	33.0	n/a	5.92	4.55		
6002	39.0	n/a	1.50	3.88		
6015	39.0	n/a	4.95	3.33		
Average	27.5	81.34	11.76	4.70		
SD	5.58	30.73	7.88	4.14		
SEM	1.28	7.05	1.81	0.95		
Older Adults (≥40)	6009	45.0	n/a	n/a	7.17	
	6011	46.0	n/a	n/a	28.15	
	6010	47.0	n/a	16.08	0.95	
	6008	50.0	n/a	n/a	10.46	
	6168	51.0	88.8	19.75	6.91	
	6017	59.0	n/a	4.92	1.36	
	6020	60.0	n/a	2.95	4.43	
	6016	64.0	n/a	12.13	2.67	
	6013	65.0	n/a	5.20	4.36	
	Average	54.1	88.76	10.17	7.38	
SD	7.9		6.86	8.36		
SEM	2.6		2.29	2.79		

		T1D					
		nPOD Case #	Age (Years)	Years with Diabetes	Pancreas Weight (g)	Pancreas Transit Time (h)	Duration of ICU Stay (Days)
Children (1.5-13.9)	6063	4.4	3.0	11.20	15.13	3.27	
	6209	5.0	0.3	12.50	35.00	0.14	
	6062	10.7	6.0	18.20	20.97	4.26	
	6265	11.0	8.0	18.48	19.98	3.51	
	6052	12.0	1.0	22.10	14.75	1.84	
	6268	12.0	3.0	41.1	17.50	3.38	
	6264	12.0	9.0	20.35	20.20	2.13	
	6228	13.0	0.0	30.35	15.55	10.04	
	6243	13.0	5.0	29.35	13.48	4.96	
	6113	13.1	1.6	33.50	9.08	5.10	
Average	10.6	3.7	23.71	18.16	3.86		
SD	3.2	3.2	9.59	6.92	2.64		
SEM	1.0	1.0	3.03	2.19	0.83		
p-value (v. control)	0.002			0.61	0.59	0.67	
Adolescents (14-20.9)	6084	14.2	4.0	n/a	11.60	2.48	
	6089	14.3	8.0	56.80	11.15	2.79	
	6049	15.0	10.0	15.80	14.78	3.00	
	6083	15.2	11.0	41.75	19.27	2.23	
	6207	16.0	10.0	33.2	18.38	6.18	
	6261	16.0	14.2	n/a	17.60	3.69	
	6148	17.1	7.0	26.36	17.45	1.86	
	6087	17.5	4.0	58.40	18.43	1.96	
	6145	18.0	11.0	42.19	14.15	1.46	
	6237	18.0	12.0	32.51	12.27	2.28	
6195	19.2	5.0	29.80	13.65	1.84		
6161	19.2	7.0	39.8	18.28	3.43		
6064	19.6	9.0	46.15	12.13	3.27		
6212	20.0	5.0	43.5	15.88	3.77		
Average	17.1	8.4	38.86	15.36	2.87		
SD	2.00	3.2	12.21	2.89	1.20		
SEM	0.53	0.85	3.26	0.77	0.32		
p-value (v. control)	0.97			1.29E-05	0.53	0.29	
Young Adults (21-39)	6224	21.0	1.5	56.09	7.33	3.34	
	6198	22.0	3.0	n/a	5.48	21.71	
	6245	22.0	7.0	31.58	15.52	3.07	
	6026	22.4	14.0	67.30	15.67	n/a	
	6070	22.6	7.0	39.10	15.97	4.85	
	6069	22.9	7.0	55.70	14.33	10.28	
	6025	23.8	19.0	n/a	n/a	2.99	
	6247	24.0	0.6	59.77	22.98	1.71	
	6211	24.0	4.0	33.00	16.87	6.55	
	6196	26.0	15.0	28.19	9.38	3.77	
6041	26.3	23.0	32.50	15.48	3.34		
6039	28.7	12.0	42.20	22.15	n/a		
6088	31.2	5.0	32.00	17.42	0.93		
6081	31.4	15.0	62.43	18.50	7.30		
6035	32.1	28.0	42.10	11.75	6.22		
6054	35.1	30.0	29.45	26.08	1.89		
6038	37.2	20.0	39.50	19.25	5.88		
6031	39.0	35.0	40.20	20.58	0.95		
Average	27.3	13.7	43.19	16.16	5.30		
SD	5.7	10.4	12.87	5.47	5.06		
SEM	1.3	2.4	3.03	1.29	1.19		
p-value (v. control)	0.93			0.0001	0.07	0.71	
Older Adults (≥40)	6150	41.2	35.0	27.14	10.07	3.92	
	6135	43.5	21.0	31.39	17.22	3.25	
	6036	49.2	34.0	31.13	23.23	3.63	
	6138	49.2	41.0	99.60	18.00	5.03	
	6040	50.0	20.0	64.90	19.65	1.62	
	Average	46.6	30.2	50.83	17.63	3.49	
	SD	4.0	9.3	31.24	4.82	1.24	
	SEM	1.8	4.1	13.97	2.16	0.55	
	p-value (v. control)	0.07				0.07	0.33

SUPPLEMENTARY DATA

Supplementary Table 16. Individual cytoplasmic Sox9 cell proliferation from non-diabetic and T1D samples. Ki67+ cytoplasmic Sox9+ cells (number; % total cytoplasmic Sox9; % total Intraislet Ki67+), total cytoplasmic Sox9+ cells (number), total intraislet Ki67+ cells (number).

	nPOD Case #	Age	Years with Diabetes	Ki67+ Sox9 ^{Cyt} + Cells	Total Sox9 ^{Cyt} + Cells	Total Intraislet Ki67+ Cells	Ki67+ Sox9 ^{Cyt} + Cells (% Total Sox9 ^{Cyt})	Ki67+ Sox9 ^{Cyt} + (% Total Intraislet Ki67+)
Control	6099	14.20	n/a	2	1300	6	0.15	33.33
	6153	15.20	n/a	22	554	28	3.97	78.57
	6075	16.00	n/a	25	780	45	3.21	55.56
	6096	16.00	n/a	1	547	1	0.18	100.00
	6098	17.80	n/a	1	592	1	0.17	100.00
	6279	19.00	n/a	212	2047	259	10.36	81.85
	Average	16.4		44	970	57	3.01	74.89
	SD	1.75		83	600	101	3.98	26.17
	SEM	0.71		34	245	41	1.62	10.68
	T1D	6052	12.0	1.0	100	777	122	12.87
6113		13.1	1.6	17	454	28	3.74	60.71
6084		14.2	4.0	67	546	90	12.27	74.44
6089		14.3	8.0	2	853	13	0.23	15.38
6049		15.0	10.0	2	345	4	0.58	50.00
6145		18.0	11.0	0	255	2	0.00	0.00
Average		14.4	5.9	31	538	43	4.95	47.09
SD		2.04	4.3	42	237	51	6.06	32.81
SEM		0.83	1.8	17	97	21	2.47	13.39
p-value (v. control)		0.11		0.75	0.13	0.78	0.53	0.14

SUPPLEMENTARY DATA

Supplementary Table 17. Nuclear Sox9 ductal cell proliferation from non-diabetic and T1D samples. Total ductal cells (number), Ki67+ nuclear Sox9+ ductal cells (number; % total).

	nPOD Case #	Age	Years with Diabetes	Ductal Cells	Ki67+ Sox9 ^{Nuc+} Ductal Cells	Ki67+ Sox9 ^{Nuc+} Ductal Cells (% Total Duct Cells)
Control	6099	14.2	n/a	315	0	0.00
	6153	15.2	n/a	282	0	0.00
	6075	16.0	n/a	331	0	0.00
	6096	16.0	n/a	761	0	0.00
	6098	17.8	n/a	2977	5	0.17
	6279	19.0	n/a	592	1	0.17
	Average	16.4		876	1	0.06
	SD	1.75		1046	2	0.09
	SEM	0.71		427	1	0.04
T1D	6052	12.0	1.0	178	0	0.00
	6113	13.1	1.6	83	0	0.00
	6084	14.2	4.0	559	0	0.00
	6049	15.0	10.0	280	0	0.00
	6145	18.0	11.0	197	0	0.00
	6195	19.2	5.0	179	0	0.00
	Average	15.3	5.4	246	0	0.00
	SD	2.8	4.2	166	0	0.00
	SEM	1.1	1.7	68	0	0.00
p-value (v. control)	0.43		0.18	0.25	0.14	

SUPPLEMENTARY DATA

Supplementary Table 18. Sox9^{Cyt+} islet endocrine cells from non-diabetic and T1D samples.
 Total Syn⁺ cells (number), Sox9^{Cyt+} cells (number; % of syn+ cells), and Syn⁺ Sox9^{Cyt+} cells (number; % of Sox9^{Cyt+} cells). "n/a" indicates the measurement is not applicable for the case. Cross-hatched boxes indicates that the measurement could not be calculated.

	nPOD Case #	Age (Years)	Years with Diabetes	Syn+ Cells	Sox9 ^{Cyt+} Cells	Syn+ Sox9 ^{Cyt+} Cells	Syn+ Sox9 ^{Cyt+} Cells (% Sox9 ^{Cyt+} Cells)	Sox9 ^{Cyt+} Cells (% Syn+ Cells)
Control	6048	30.0	n/a	8707	671	669	99.70	7.71
	6030	30.1	n/a	8033	402	402	100.00	5.00
	6002	39.0	n/a	4805	358	358	100.00	7.45
	Average	33.0		7182	477	476	99.90	6.72
	SD	5.2		2086	169	168	0.17	1.49
	SEM	3.0		1204	98	97	0.10	0.86
T1D	6212	20.0	5.0	6873	1106	1100	99.46	16.09
	6025	23.8	19.0	2689	299	298	99.67	11.12
	6211	24.0	4.0	6515	987	984	99.70	15.15
	Average	22.6	9.3	5359	797	794	99.61	14.12
	SD	2.3	8.4	2319	436	433	0.13	2.64
	SEM	1.3	4.8	1339	252	250	0.07	1.52
	p-value (v. control)	0.03		0.37	0.30	0.30	0.08	0.013

SUPPLEMENTARY DATA

Supplementary Table 19. Sox9^{Cyt} ARX co-positive cells from non-diabetic and T1D samples. Total ARX+ cells, Sox9^{Cyt}+ cells (number; % of ARX+ cells), Sox9^{Cyt}+ ARX+ cells (number; % of Sox9^{Cyt}+ cells). "n/a" indicates the measurement is not applicable for the case. Cross-hatched boxes indicates that the measurement could not be calculated.

	nPOD Case #	Age (Years)	Years with Diabetes	ARX+ Cells	Sox9 ^{Cyt} + Cells	Sox9 ^{Cyt} + ARX+ Cells	Sox9 ^{Cyt} +ARX+ Cells (% of Sox9 ^{Cyt} + Cells)	Sox9 ^{Cyt} + Cells (% of ARX+ Cells)
Control	6238	20	n/a	4250	899	884	98.33	21.15
	6029	24	n/a	1985	736	735	99.86	37.08
	6229	31	n/a	6434	1775	1772	99.83	27.59
	Average	25		4223	1137	1130	99.34	28.61
	SD	5.6		2225	559	561	0.88	8.01
	SEM	3.2		1284	323	324	0.51	4.63
T1D	6212	20.0	5.0	4045	1106	1089	98.46	27.34
	6025	23.8	19.0	1567	299	296	99.00	19.08
	6211	24.0	4.0	4544	987	966	97.87	21.72
	Average	22.6	9.3	3385	797	784	98.44	22.71
	SD	2.3	8.4	1594	436	427	0.56	4.22
	SEM	1.3	4.8	921	252	246	0.32	2.44
	p-value (v. control)	0.53		0.62	0.45	0.44	0.21	0.32

SUPPLEMENTARY DATA

Supplementary Table 20. Proliferating ARX+ glucagon negative cells from non-diabetic and T1D samples. Total ARX+ Gcg- (number), Ki67+ ARX+ Gcg- Cells (number; % of ARX+ Gcg- cells). "n/a" indicates the measurement is not applicable for the case. Cross-hatched boxes indicates that the measurement could not be calculated.

	nPOD Case #	Age (Years)	Years with Diabetes	ARX+ Gcg- Cells	Ki67+ ARX+ Gcg- Cells	Ki67+ ARX+ Gcg- Cells (% of ARX+ Gcg- Cells)
Control	6075	16.0	n/a	419	7	1.67
	6131	24.2	n/a	4255	23	0.54
	6235	30.0	n/a	690	96	13.91
	Average	23.4		1788	42	5.37
	SD	7.0		2141	47	7.42
	SEM	4.1		1236	27	4.28
T1D	6113	13.1	1.6	373	18	4.83
	6084	14.2	4.0	350	37	10.57
	6261	16.0	14.2	444	159	35.81
	Average	14.4	6.6	389	71	17.07
	SD	1.5	6.7	49	77	16.48
	SEM	0.8	3.9	28	44	9.52
	p-value (v. control)	0.10		0.32	0.60	0.33

SUPPLEMENTARY DATA

Supplementary Table 21. Adolescent synaptophysin cell death. TUNEL+ synaptophysin (Syn+) cell proliferation (number; % total), total islet endocrine cell (number).

	nPOD Case #	Age (Years)	Years with Diabetes	TUNEL+ Syn+ Cells	Total Syn+ Cells	TUNEL+ Syn+ Cell Death (% Total)	
Control	6117	0.33	n/a	0	6264	0.00	
	6115	0.42	n/a	0	5797	0.00	
	6092	0.50	n/a	0	3262	0.00	
	6103	1.5	n/a	0	4985	0.00	
	6107	2.2	n/a	9	14539	0.06	
	6094	2.9	n/a	0	4968	0.00	
	6106	2.9	n/a	0	10431	0.00	
	6112	6.3	n/a	2	7905	0.03	
	6099	14.2	n/a	0	15220	0.00	
	6096	16.0	n/a	0	4509	0.00	
	6098	17.8	n/a	0	10413	0.00	
	6253	19.0	n/a	19	12328	0.15	
	6057	22.0	n/a	6	6706	0.09	
	6235	30.0	n/a	18	19782	0.09	
	6030	30.1	n/a	4	8441	0.05	
	6015	39.0	n/a	0	7650	0.00	
	6010	47.0	n/a	0	5815	0.00	
	6008	50.0	n/a	0	5959	0.00	
	Average	16.8		3	8610	0.03	
	SD	16.5		6	4401	0.05	
	SEM	3.9		1	1037	0.01	
T1D	6063	4.4	3.0	0	9560	0.00	
	6062	10.7	6.0	0	3880	0.00	
	6052	12.0	1.0	1	9380	0.01	
	6084	14.2	4.0	2	9236	0.02	
	6089	14.3	8.0	1	3105	0.03	
	6087	17.5	4.0	0	2590	0.00	
	6064	19.6	9.0	0	11240	0.00	
	6026	22.4	14.0	0	1907	0.00	
	6070	22.6	7.0	0	21220	0.00	
	6069	22.9	7.0	0	11390	0.00	
	6081	31.4	15.0	0	2258	0.00	
		Average	17.5	7.1	0	7797	0.01
		SD	7.4	4.3	1	5852	0.01
	SEM	2.2	1.3	0	1764	0.00	
	p-value (v. control)	0.90		0.14	0.67	0.16	

SUPPLEMENTARY DATA

Supplementary Table 22. TUNEL+ Sox9^{Cyt+} Analysis. Total Sox9^{Cyt+} cells (number), islets (number), TUNEL+ Sox9^{Cyt+} cells (number per islet), and islet endocrine proliferation as measured by Ki67+ Syn+ cells (% total).

nPOD Case #	Age (Years)	TUNEL+ Sox9+ cells	Islets (#)	TUNEL+ Sox9 ^{Cyt+} cells (# per Islet)	Ki67+ Syn+ (% Total Syn+)
6099	14.2	0	199	0.000	0.060
6096	16.0	0	134	0.000	0.150
6098	17.8	0	267	0.000	0.050
6253	19.0	0	126	0.000	0.280
6235	30.0	0	185	0.000	1.400
6030	30.1	0	82	0.000	0.590
Average	21.2	0	166	0.000	0.422
SD	7.1	0	65	0.000	0.519
SEM	2.9	0	26.7	0.000	0.212

SUPPLEMENTARY DATA

Supplementary Table 23 Control and T1D Islet Cell Area & Mass. Pancreas weight (g), islet endocrine cell area (% total), and islet endocrine cell mass (g). "n/a" indicates pancreas weight was not measured for that case. Cross-hatched boxes indicates that the measurement could not be calculated.

		Control					T1D						
		nPOD Case #	Age (Years)	Pancreas Weight (g)	Islet Endocrine Area (% Total)	Islet Endocrine Mass (g)	nPOD Case #	Age (Years)	Years with Diabetes	Pancreas Weight (g)	Islet Endocrine Area (% Total)	Islet Endocrine Mass (g)	
Adolescents (14-20.9)		6232	14.0	49.40	2.17	1.070							
		6233	14.0	60.93	2.72	1.658							
		6099	14.2	85.56	3.52	3.009							
		6153	15.2	67.75	2.37	1.607							
		6075	16.0	47.29	1.46	0.690							
		6096	16.0	51.50	1.85	0.955							
		6230	16.0	66.27	2.12	1.404							
		6227	17.0	60.40	1.50	0.906							
		6271	17.0	97.99	1.11	1.090							
		6098	17.8	91.10	3.03	2.756							
		6253	19.0	85.29	1.34	1.139							
		6279	19.0	80.17	1.21	0.970							
		6234	20.0	19.66	3.06	0.607							
		6238	20.0	91.50	2.58	2.357							
		6174	20.8	79.30	1.50	1.192							
		Average	17.1	68.95	2.10	1.427							
		SD	2.28	21.26	0.76	0.733							
	SEM	0.59	5.49	0.20	0.189								
Young Adults (21-39)		6024	21.0	n/a	2.17								
		6179	21.8	72.40	1.02	0.736							
		6001	22.0	n/a	2.50								
		6057	22.0	104.36	2.38	2.485							
		6162	22.7	81.50	1.00	0.818							
		6003	23.0	n/a	2.42								
		6029	24.0	79.30	1.42	1.127							
		6131	24.2	108.92	1.99	2.166							
		6053	25.0	n/a	1.21								
		6126	25.2	80.20	1.14	0.911							
		6058	27.0	52.68	2.31	1.219							
		6048	30.0	139.00	1.21	1.680							
		6235	30.0	102.31	1.64	1.677							
		6030	30.1	96.30	1.32	1.271							
		6229	31.0	45.60	2.34	1.065							
		6034	32.0	75.40	1.89	1.428							
		6004	33.0	n/a	1.60								
	6002	39.0	n/a	2.01									
	6015	39.0	n/a	2.02									
	Average	27.5	66.50	1.77	1.36								
	SD	5.6	25.55	0.52	0.537								
	SEM	1.3	5.86	0.12	0.15								
Older Adults (≥40)		6009	45.0	n/a	1.99								
		6011	46.0	n/a	1.59								
		6010	47.0	n/a	2.41								
		6008	50.0	n/a	0.96								
		6168	51.0	88.76	1.30	1.158							
		6017	59.0	n/a	1.78								
		6020	60.0	n/a	2.88								
		6016	64.0	n/a	2.47								
		6013	65.0	n/a	1.90								
		Average	54.1	88.76	1.92	1.158							
		SD	7.9		0.60								
		SEM	2.6										
	Adolescents (14-20.9)		6084	14.2						n/a	0.95		
			6089	14.3	8.0	56.80	0.37	0.211					
			6049	15.0	10.0	15.80	1.98	0.312					
			6083	15.2	11.0	41.78	1.39	0.580					
			6207	16.0	10.0	33.20	0.42	0.141					
		6261	16.0	14.2	n/a	3.81							
		6148	17.1	7.0	26.36	0.40	0.104						
		6087	17.5	4.0	58.40	0.43	0.254						
		6145	18.0	11.0	42.19	1.00	0.422						
		6237	18.0	12.0	32.51	1.17	0.381						
		6195	19.2	5.0	29.80	0.59	0.175						
		6161	19.2	7.0	39.80	0.70	0.277						
		6064	19.6	9.0	46.15	1.15	0.532						
		6212	20.0	5.0	43.50	1.22	0.533						
		Average	17.1	8.4	38.86	1.11	0.327						
		SD	2.00	3.18	12.22	0.90	0.162						
		SEM	0.53	0.85	3.26	0.24	0.047						
	p-value (v. control)	0.9741		0.0000	0.3119	0.0000							
Young Adults (21-39)		6224	21.0	1.5	56.09	0.33	0.182						
		6198	22.0	3.0	n/a	0.39							
		6245	22.0	7.0	31.58	2.27	0.718						
		6026	22.4	14.0	67.30	1.31	0.885						
		6070	22.6	7.0	39.10	0.62	0.243						
		6069	22.9	7.0	55.70	3.11	1.734						
		6025	23.8	19.0	n/a	0.65							
		6247	24.0	0.6	59.77	0.60	0.357						
		6211	24.0	4.0	33.00	0.77	0.253						
		6196	26.0	15.0	28.19	1.00	0.282						
		6041	26.3	23.0	32.50	0.83	0.270						
		6039	28.7	12.0	42.20	1.69	0.713						
		6088	31.2	5.0	32.00	1.37	0.439						
		6081	31.4	15.0	62.43	0.59	0.369						
		6035	32.1	28.0	42.10	1.66	0.701						
		6054	35.1	30.0	29.45	1.09	0.321						
		6038	37.2	20.0	39.50	1.14	0.451						
	6031	39.0	35.0	40.20	0.966	0.388							
	Average	27.3	13.7	43.19	1.13	0.519							
	SD	5.7	10.4	12.87	0.71	0.384							
	SEM	1.3	2.4	3.03	0.17	0.096							
	p-value (v. control)	0.9330		0.0000	0.3083	0.0000							
Older Adults (≥40)		6036	19.2	34.0	31.13	0.92	0.285						
		6150	41.2	35.0	27.14	0.37	0.100						
		6135	43.5	21.0	31.39	2.21	0.695						
		6138	49.2	41.0	99.66	0.40	0.403						
		6040	50.0	20.0	64.90	0.61	0.396						
		Average	40.6	30.2	50.84	0.90	0.376						
		SD	12.5	9.3	31.26	0.76	0.216						
		SEM	5.6	4.1	13.98	0.34	0.097						
		p-value (v. control)	0.0283										