Supplemental Figures and Legends

Figure S1

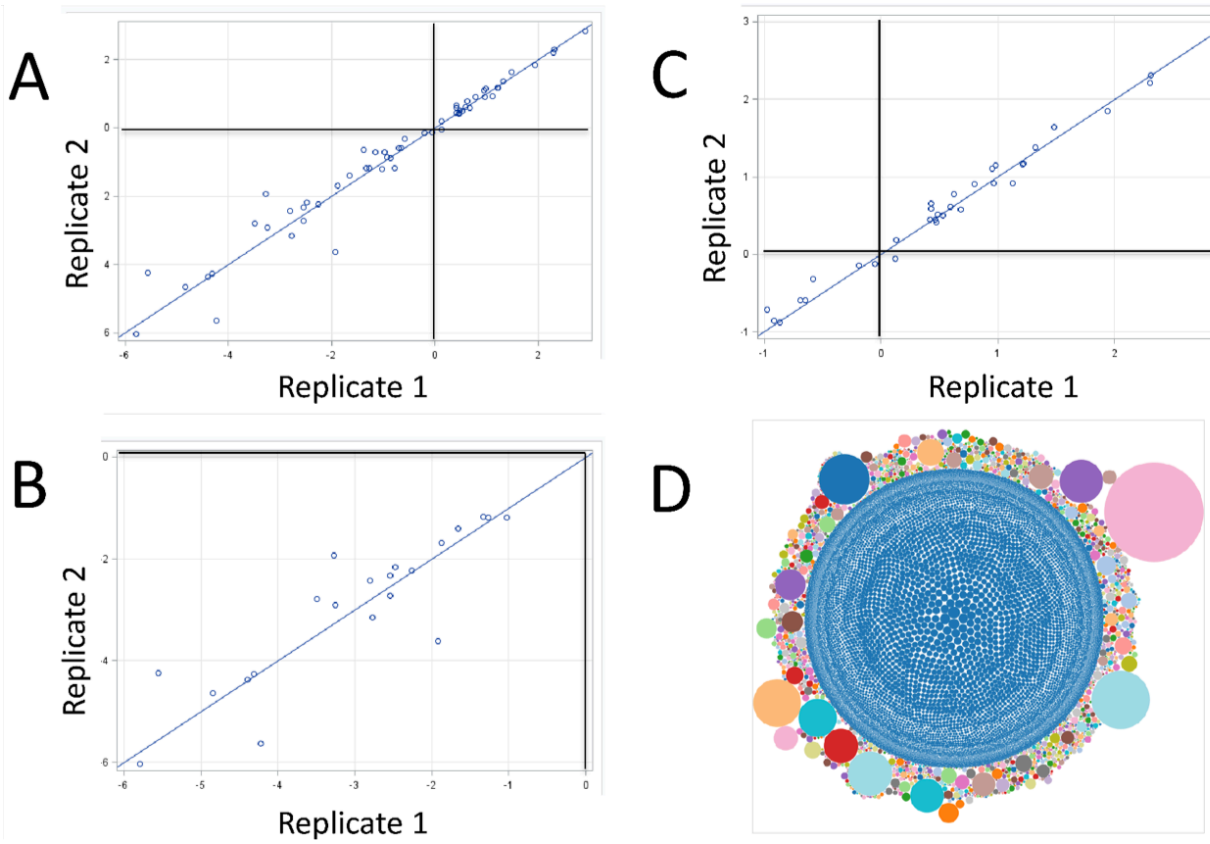


Figure S1. Determining a cut-off for reproducible analysis of common T cell receptor (TCR) gene usage. Donor 6263 spleen conventional T cell (Tconv) samples were sequenced in two separate runs as a technical replicate. (A) Log2 transformed TCR β-chain V (TCRVβ) gene frequencies were plotted as Run 1 (x-axis) versus Run 2 (y-axis) with a regression line to examine the relationship between runs. (B) Less frequent Vβ genes present at Log2(frequency) < -1 (0.5%) were determined to be correlated but inconsistently replicated across runs and likely unfit for inclusion in subsequent analysis (ρ=0.91 & $p<0.0001$, 4 genes detected in 1 run, but not the other). (C) Vβ gene sequences present at > 0.5% were correlated and consistently replicated across runs (ρ=0.99 & $p<0.0001$, 1 gene detected in 1 run, but not the other). (D) A packed bubble chart illustrating the overlap between 6263 spleen Tconv Run 1 and Run 2, wherein the size of the bubble represents the sum of the CDR3β frequency. The bubbles in the center of the figure (blue) represent sequences unique to Run 1 and the bubbles on the periphery (multi-colored) represent CDR3 AA sequences detected in both runs. Larger circles represent more frequently detected sequences. Blue circles in the center region create perceived concentric circles, which represent a step-wise increase in clone frequency going towards the most frequent in the center. The most frequently detected sequences (largest circles) are in the periphery indicating that these sequences were those detectable in both runs.

Figure S2

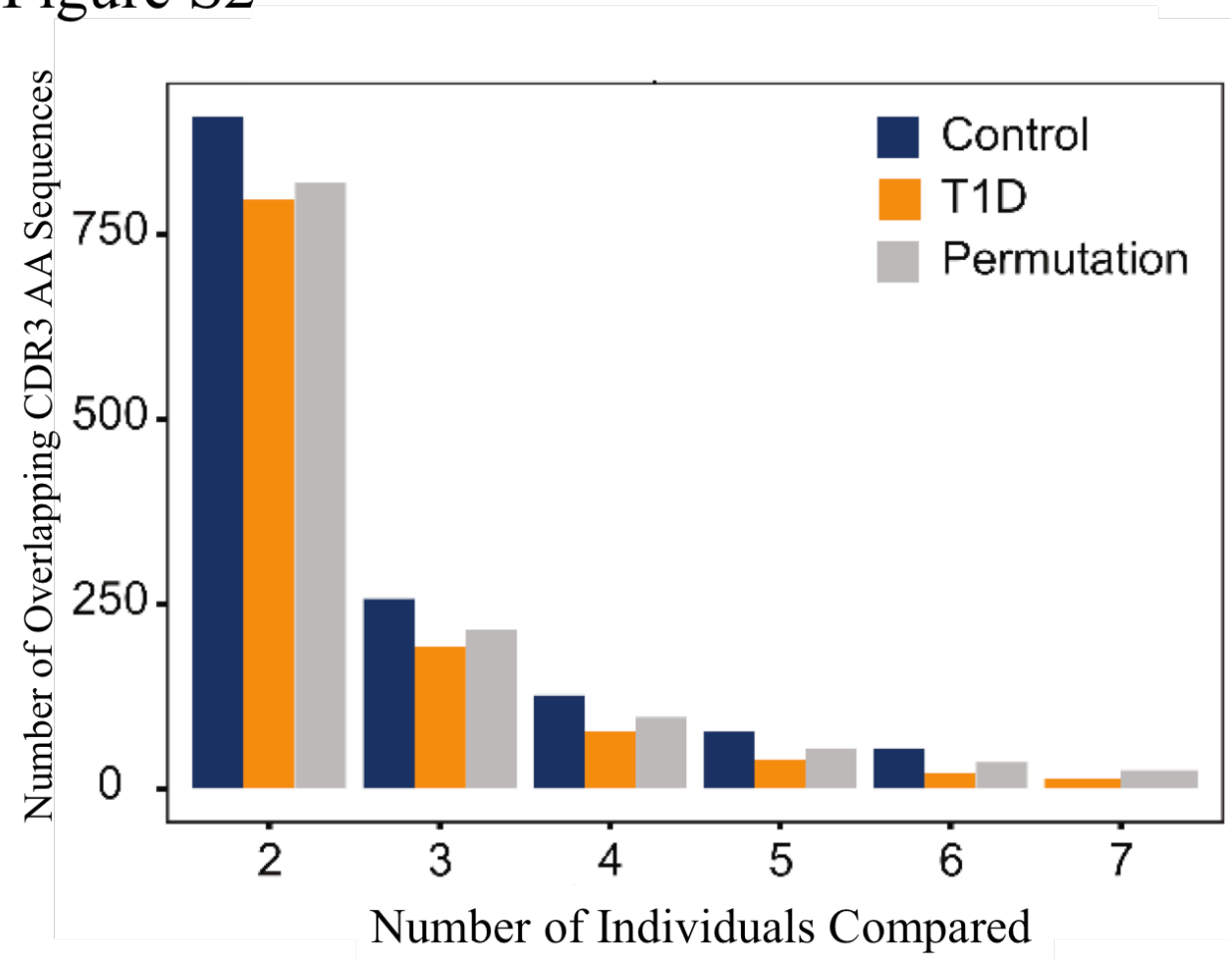

Number of Overlapping CDR3 AA Sequences
750
500
250
0
Control
T1D
Permutation
2
3
4
5
6
7
Number of Individuals Compared

Figure S2. $CD8^+$ T cell receptor (TCR) sharing among HLA-matched type 1 diabetes (T1D) and control donors. Within the pancreatic-draining lymph node (pLN), $CD8^+$ T cell clone sharing across increasing numbers of HLA-A*02 matched organ donors is compared for control (blue) and T1D (orange) subjects. Gray bars represent predicted clone sharing within the general population as determined by permutation test. As the number of subjects compared increased (x-axis), the number of shared T cell receptor β-chain (TCRβ) complementarity determining region 3 (CDR3) sequences decreased (y-axis); however, the average number of shared $CD8^+$ TCRβ CDR3 sequences was similar overall in T1D versus control donors as well as statistical control values determined by permutation test (P = NS, ANOVA). Data are presented as mean number of shared CDR3.

Figure S3

			Cell Type			
Disease Status	Tissue-1	Tissue-2	CD8+	Tconv	Treg	CD19+
Control	pLN	Spleen	47.70±19.10 (7)	11.80±6.20 (7)	12.20±13.90 (7)	5.70±3.80 (6)
		iLN	28.80±11.90 (4)	5.20±3.30 (4)	5.60±1.60 (4)	5.70±5.40 (3)
	Spleen	iLN	40.30±17.80 (4)	7.90±4.20 (4)		
	iLN	Spleen			5.20±3.40 (4)	4.00±3.50 (3)
T1D	pLN	Spleen	36.00±21.00 (12)	9.20±7.00 (14)	6.00±4.30 (12)	2.20±2.70 (6)
		iLN	36.60±0.00 (1)	10.20±0.00 (1)	8.40±6.20 (2)	
		PBMC	19.90±12.10 (4)	3.30±1.90 (4)	4.00±0.00 (1)	0.90±0.00 (1)
		Islet CD8+	10.30±0.00 (1)			
		Islet CD4+		0.20±0.00 (1)	0.30±0.00 (1)	
	Spleen	iLN		7.50±0.00 (1)	2.30±0.40 (2)	
		Islet CD8+	4.20±0.00 (1)			
		Islet CD4+		0.40±0.00 (1)	7.80±0.00 (1)	
	iLN	Spleen	40.40±0.00 (1)			
	PBMC	Spleen	25.70±18.70 (4)	4.00±2.30 (4)	4.30±0.00 (1)	1.10±0.00 (1)
		Islet CD8+	9.50±0.00 (1)			
		Islet CD4+		0.70±0.00 (1)	0.40±0.00 (1)	
T2D	pLN	Spleen	51.40±7.90 (4)	15.60±5.50 (4)	1.30±0.00 (1)	28.50±4.90 (2)
		iLN	33.40±1.80 (2)	10.10±4.70 (2)	11.50±7.10 (3)	21.40±18.30 (2)
		PBMC	28.60±0.00 (1)	14.90±0.00 (1)		
	Spleen	iLN	38.20±5.80 (2)			
	iLN	Spleen		15.50±1.20 (2)	2.10±0.00 (1)	13.00±0.00 (1)
	PBMC	Spleen	72.30±0.00 (1)	18.80±0.00 (1)		

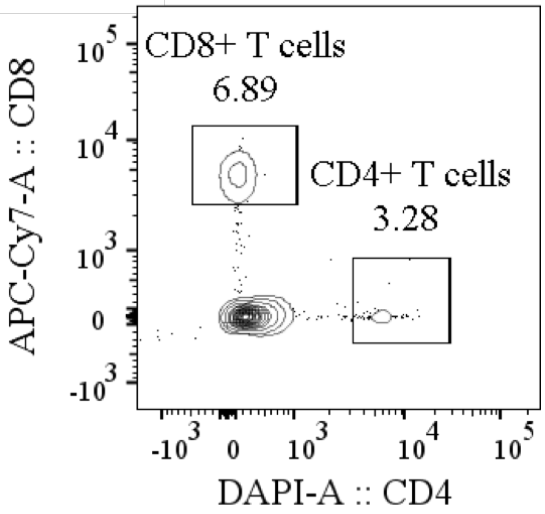
Mean percentage of shared clones

0.20 — 72.30

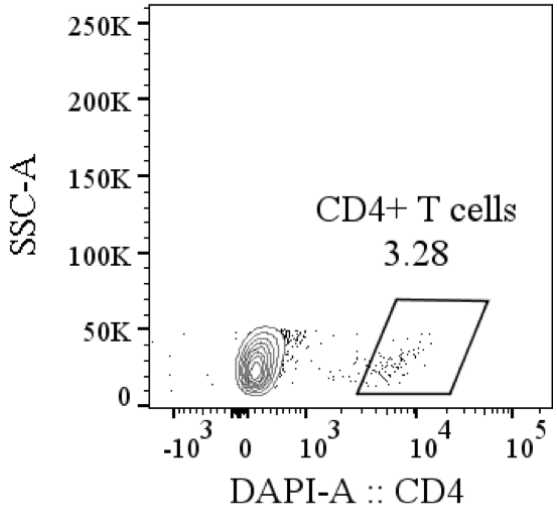
Figure S3. Immune subsets display distinct receptor distributions among various tissues. T cell receptor β-chain (TRB) and B cell receptor (BCR) immunoglobulin heavy chain (IGH) complementarity determining region 3 (CDR3) amino acid (AA) sequences overlap across the tissue [pancreatic-draining lymph node (pLN), spleen, and "irrelevant" mesenteric and/or inguinal lymph node (iLN), and peripheral blood mononuclear cells (PBMC)] is quantitated for each cell subset. Data are presented as mean percentage of shared clones ± SD (N) such that the number in parentheses indicates N of donors for whom the relevant tissues and cell subsets were available for comparison. Red indicates high mean percentage of shared clones while gray represents low clone sharing. White cells without text indicate that no samples were available for that particular comparison.

Figure S4

A



B



C

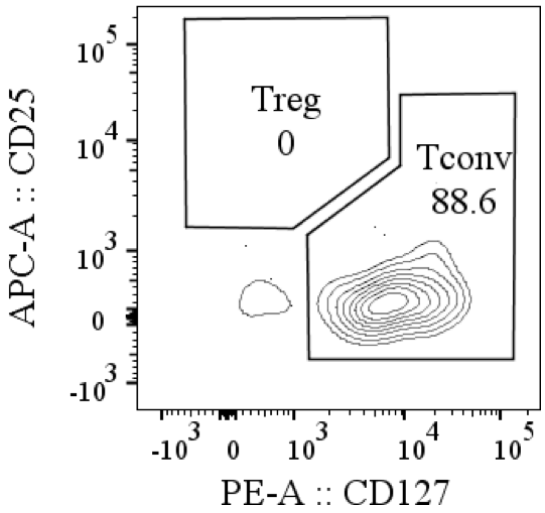
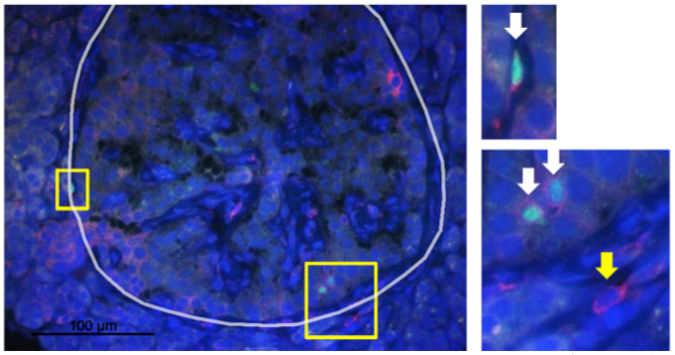
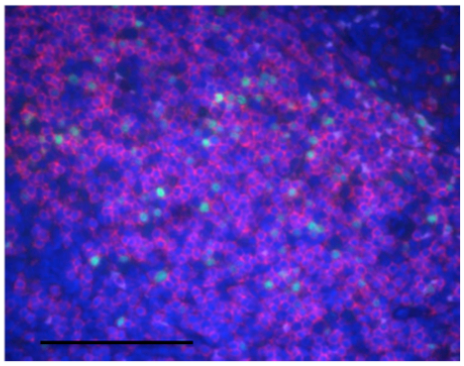


Figure S4

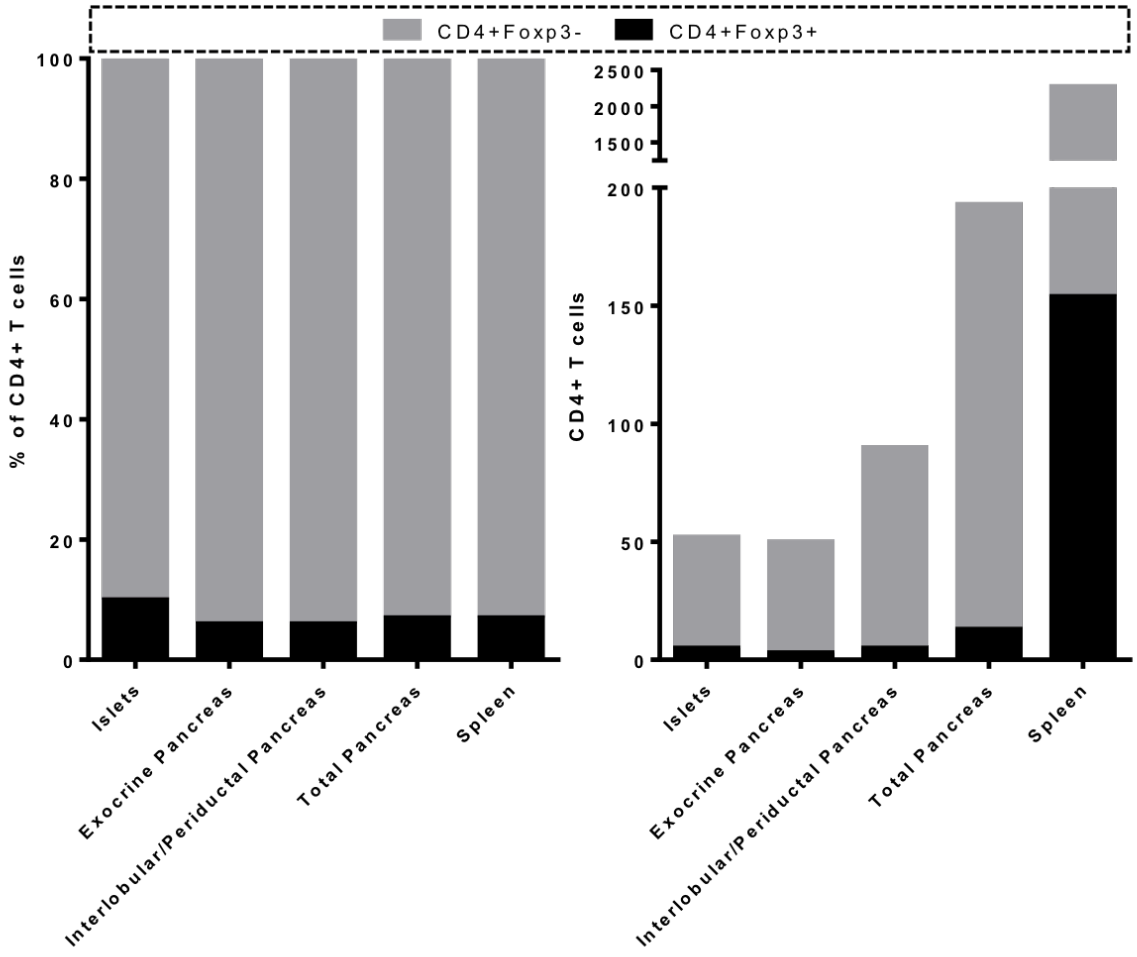
D



E



F



G

Figure S4. Isolation of intra-islet infiltrating T cells from a type 1 diabetes (T1D) donor. Fluorescence activated cell sorting (FACS) of T-cell subsets isolated from the islets of nPOD 6323. (A) Islets were isolated by hand, dissociated, and cultured with anti-CD3/anti-CD28 stimulation beads in the presence of high-dose IL-2 (1000U/mL). After 14 days of in vitro expansion, cells were FACS-purified based on extracellular markers. (A) $CD4^+$ versus $CD8^+$ T cells are shown. (B) Total $CD4^+$ T cells were gated, and (C) within the $CD4^+$ compartment, $CD25^+CD127^-$ Tregs and $CD25^-CD127^+$ conventional T cells (Tconv) were gated. FACS data demonstrate a lack of cells falling within the Treg gate. (D) Immunofluorescent staining of nPOD 6323 in pancreas tissue for nuclei (blue, DAPI), CD4 (pink, membraneous staining) and FOXP3 (green, nuclear localization) demonstrates that $CD4^+FOXP3^+$ Tregs are present within the exocrine tissue as well as the islet. (E) Immunofluorescent staining was also performed using spleen tissue (positive control). The percent $CD4^+FOXP3^+$/total $CD4^+$ cells (F) and cells counts (G) were quantified within the islets (9.6%, 5/52), exocrine tissue (6.0%, 3/50), interlobular/periductal region (5.5%, 5/90), total pancreas (6.9%, 13/193), and spleen (6.9%, 154/2273), and the proportion of $CD4^+$ T cells expressing FOXP3 was comparable across all tissues examined (P = NS, Chi-square test). Scale bars represent 100 μm.

Figure S5

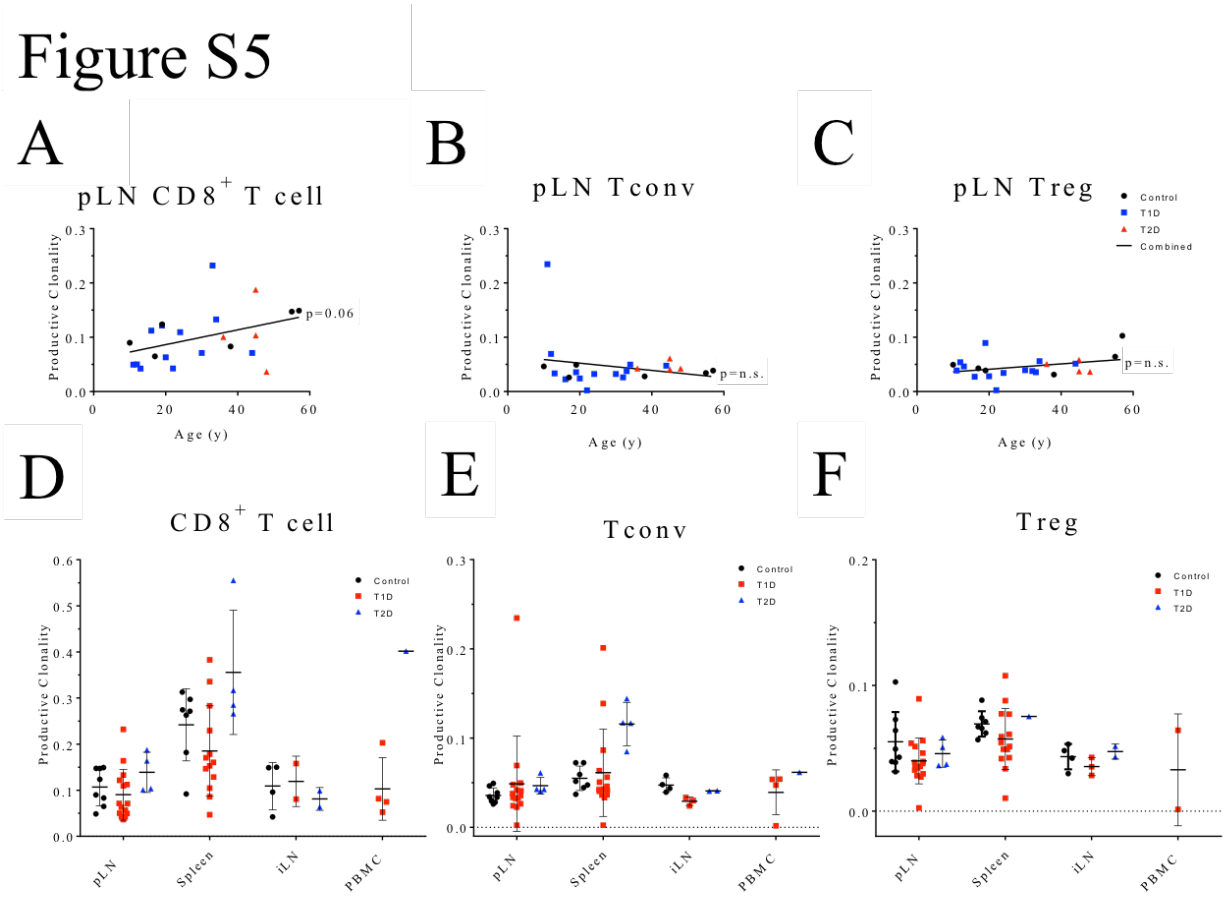
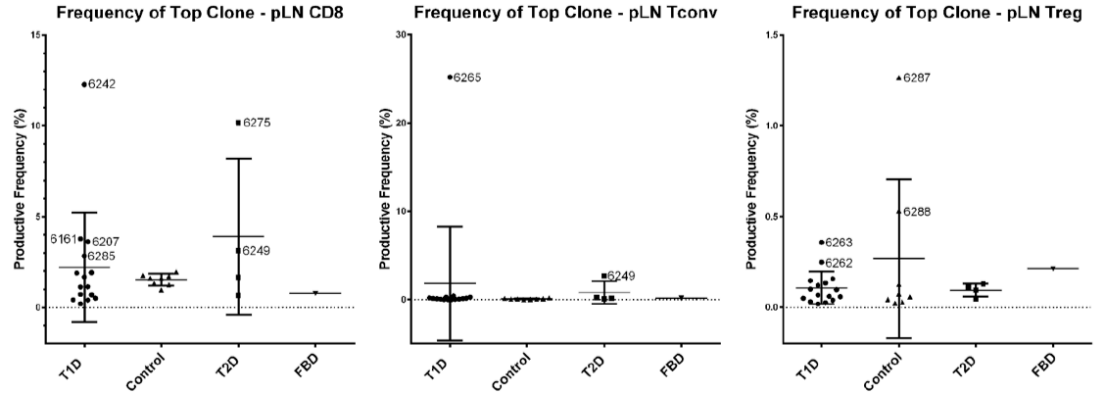

A
pLN CD8+ T cell
Productive Clonality
Age (y)
p=0.06
B
pLN Tconv
Productive Clonality
Age (y)
p=n.s.
C
pLN Treg
Control
T1D
T2D
Combined
Productive Clonality
Age (y)
p=n.s.
D
CD8+ T cell
Productive Clonality
Control
T1D
T2D
pLN
Spleen
iLN
PBMC
E
Tconv
Productive Clonality
Control
T1D
T2D
pLN
Spleen
iLN
PBMC
F
Treg
Productive Clonality
Control
T1D
T2D
pLN
Spleen
iLN
PBMC

Figure S5. Productive clonality of T cells varies based on donor age and tissue. Productive clonality indicates how much of the lymphocyte repertoire consists of *expanded* clones that are in frame and fully functional (i.e., not interrupted by a stop codon). Subjects from all donor groups [type 1 diabetes (T1D), control, type 2 diabetes (T2D), autoantibody positive, and Flatbush diabetes/other) were combined, and productive clonality was compared for pancreatic lymph node (pLN) samples. When control, T1D, and T2D groups were combined, trends were observed suggesting that productive clonality of pLN T cell subsets may increase with age for (A) $CD8^+$ T cells (r=0.39, $P = 0.07$) and (C) regulatory T cells (Treg, r=0.19, $P = 0.38$), but not (B) $CD4^+$ conventional T cells (Tconv, r=0.05, $P = 0.81$) (Spearman correlation). (D) When partitioned into experimental groups, spleen $CD8^+$ T cells from T2D displayed significantly increased clonality relative to both T1D and control donors, possibly as a function of cohort age. $CD8^+$ T cell clonality was comparable across all three groups in pLN, and "irrelevant" mesenteric/inguinal lymph node samples. Peripheral blood mononuclear cell (PBMC) samples were not available in sufficient numbers for statistical comparison. (E) Tconv and (F) Treg clonality was not significantly different within pLN, spleen, or iLN from control, T1D, or T2D donors. Again, PBMC samples were not available in sufficient numbers for statistical analysis. The dramatic outlier in the pLN Tconv from T1D results from case 6265, as a function of the highly enriched CDR3 AA (CASSLVGGPSSEAFF) discussed in **Figure 7**.

Figure S6

A


Frequency of Top Clone - pLN CD8
Frequency of Top Clone - pLN Tconv
Frequency of Top Clone - pLN Treg
Productive Frequency (%)
6242
6275
6161
6207
6285
6249
6265
6287
6288
6263
6262
T1D
Control
T2D
FBD

B

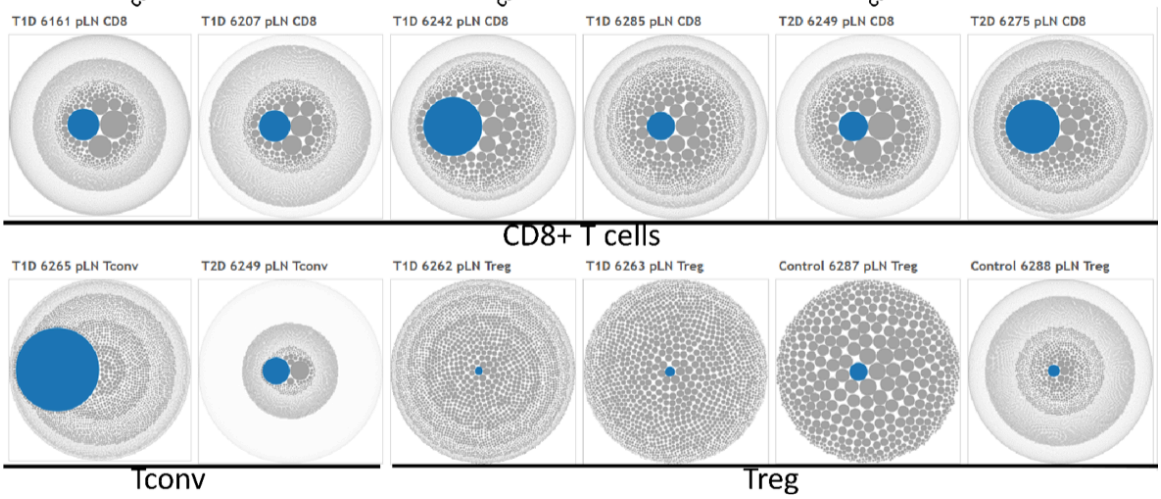

T1D 6161 pLN CD8
T1D 6207 pLN CD8
T1D 6242 pLN CD8
T1D 6285 pLN CD8
T2D 6249 pLN CD8
T2D 6275 pLN CD8
CD8+ T cells
T1D 6265 pLN Tconv
T2D 6249 pLN Tconv
T1D 6262 pLN Treg
T1D 6263 pLN Treg
Control 6287 pLN Treg
Control 6288 pLN Treg
Tconv
Treg

Figure S6. Over-represented clones in the pancreatic draining lymph node (pLN). Several type 1 diabetes (T1D) cases showed indications that there may have been an antigen-specific, clonal-dominate response occurring near or during the time of sample collection. (A) Control cases showed limited variability in the frequency of the most represented CDR3 amino acid sequence (i.e. "Top Clone") in the $CD8^+$ T cell and $CD4^+$ conventional T cell (Tconv) compartments (AVG=1.53±0.33%, SD=$3.29x10^{-1}$ and AVG=$9.43x10^{-2}$, SD=$5.67x10^{-2}$, respectively), but over-represented clones ($CD8^+$ and Tconv and clones at a frequency above 2%; Treg above 0.2%) were found within the $CD8^+$ T cell compartment of 4 T1D cases [6161 (3.77%), 6207 (3.63%), 6242 (12.3%), and 6285 (2.83%)] as well as 2 T2D cases [6275 (10.2%) and 6249 (3.15%)], and within the Tconv compartment of 1 T1D case 6265 (25.2%) as well as 1 T2D case 6249 (2.69%). Top clone frequency within the Treg compartment in control cases was more variable (AVG=$3.03x10^{-1}$, SD=$4.59x10^{-1}$), but there appeared to be over-represented clones in 2 controls [6262 (0.249%), 6263 (0.358%)] and 2 T1D donors [6287 (1.27%), and 6288 (0.531%)]. (B) For these samples noted to contain over-represented clones, packed bubble charts depict the frequency of complementarity determining region 3 (CDR3) amino acid (AA) sequences such that the size of the circle represents the frequency of the corresponding clone. The top clone is represented as a blue circle, and all other sequences as grey circles.

Figure S7

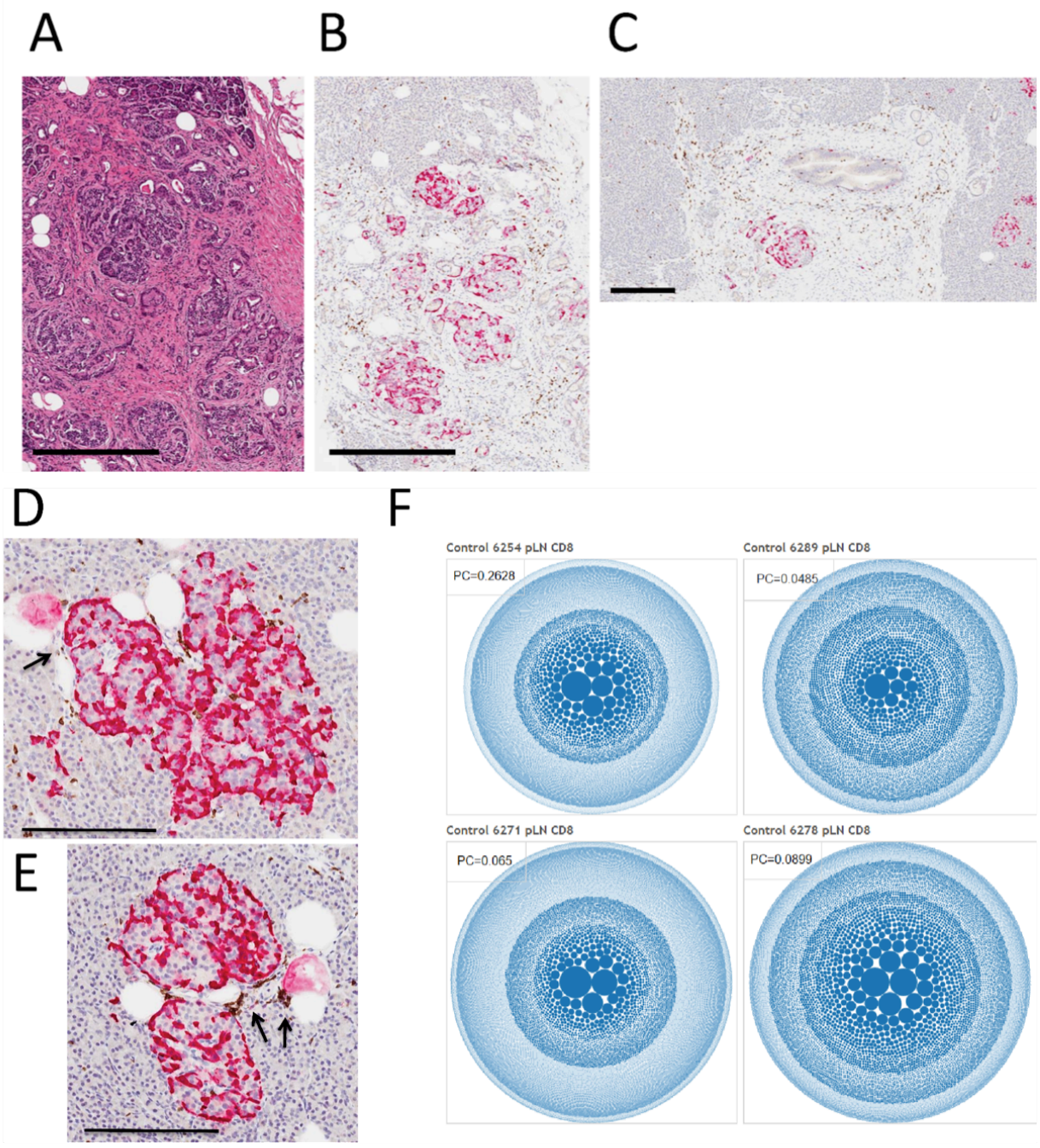

A
B
C
D
E
F
Control 6254 pLN CD8
PC=0.2628
Control 6289 pLN CD8
PC=0.0485
Control 6271 pLN CD8
PC=0.065
Control 6278 pLN CD8
PC=0.0899

Figure S7. Histopathology and diversity in Network for Pancreatic Organ Donors with Diabetes (nPOD) case 6254. Immunohistochemical analysis was performed on pancreas tissues from a 38-year old control donor (nPOD 6254). Serial sections stained (A) with hematoxylin and eosin and (B-E) for glucagon (red) and CD3 (brown) reveal pancreatic pathology consistent with chronic pancreatitis, severe loss of acinar cells with concentration of islets, fatty infiltration, interstitial fibrosis, and mononuclear lymphocytic infiltration by $CD3^+$ staining known as "isletitis". Lack of pseudoatrophic islets (none identified to date) precludes designation as having true insulitis. (C) Periductal fibrosis with mononuclear infiltrates and focal duct proliferation was also observed. (D-E) $CD3^+$ cells were adjacent and within islets or adjacent to adipocytes (black arrows). Scale bars represent (A-B) 500 μm, (C) 300 μm, and (D-E) 200 μm. (F) In these packed bubble charts, the frequency of T cell receptor (TCR) complementarity determining region 3 β-chain (CDR3β) of $CD8^+$ T cells within pancreatic draining lymph node (pLN) are represented by the size of the bubbles, and the productive clonality (PC) is noted on each chart (upper left). This comparison suggests reduced receptor diversity may be due to outgrowth of a few clones in donor 6254 relative to other control donors, supporting the notion of chronic T cell activation and inflammation.

Supplementary Tables

Table S1. Organ donor information. Demographic and health information are summarized for type 1 diabetes (T1D), type 2 diabetes (T2D), autoantibody positive without diabetes (AAb+), other/Flatbush diabetes (other/FBD), and control donors.

Characteristic	*P*-value	T1D		T2D		AAb+**		Other/FBD**		Control	
Total Subjects, n		18		4		1		1		9	
Sex											
Female, n (%)	0.172 §	9	50	3	75	0	0	1	100	2	22
Male, n (%)		9	50	1	25	1	100	0	0	7	78
Ethnicity											
Caucasian, n (%)		12	67	1	25	0	0	0	0	8	80
Black/African-American, n (%)	--	4	22	1	25	1	100	1	100	2	20
Hispanic/Latino, n (%)		2	11	1	25	0	0	0	0	0	0
Other, n (%)		0	0	1	25	0	0	0	0	0	0
Age (years), mean (± SD)	0.638 °	25	9.4	44	5.2	22	N/A	24	N/A	28	18
BMI, mean (± SD)	0.081 °	24	4.7	35	5.8	28	N/A	27	N/A	30	8.5
C-peptide (ng/mL), mean (± SD)[¥]	< 0.0001	0.3	0.7	5.9	4.5	17	N/A	1.7	N/A	7.9	3
Diabetes duration (years), mean (± SD)	0.155 ◆	12	6.2	5.5	6.4	N/A	N/A	Unknown	N/A	N/A	N/A
Autoantibody Results*											
Negative, n (%)	--	6	33	4	100	0	0	1	100	9	100
Positive for One, n (%)		5	28	0	0	0	0		0	0	0
Positive for Two or More, n (%)		7	39	0	0	1	100		0	0	0
Cause of Death^											
DKA, n (%)		1	5.6	0	0	0	0	0	0	0	0
Anoxia, n (%)		9	50	1	25	0	0	0	0	3	33
Head trauma, n (%)	--	3	17	0	0	1	100	1	100	5	56
Cerebrovascular/stroke, n (%)		5	28	1	25	0	0	0	0	1	11
Other, n (%)		0	0	1	25	0	0	0	0	0	0

**AAb+ and Other/Flatbush were not included in statistical analyses due to low sample size.

[¥]For many T1D donors, C-peptide was below detectable levels and thus, could not be accurately determined. In order to calculate mean serum C-peptide levels, these subjects were assigned C-peptide = 0.05ng/mL which is the ELISA threshold for detection.

*Autoantibody results exclude IAA for T1D and T2D subjects because exogenous insulin can induce anti-insulin antibodies, which can't be distinguished from IAA.

^For one T2D donor, cause of death was not known.

§ Chi-square test, T1D vs T2D vs Control

° Unpaired welch-corrected t-test, T1D vs Control

◆ Unpaired welch-corrected t-test, T1D vs T2D

-- Sample size too low for chi-square test

Table S2. HLA combinations previously reported to confer type 1 diabetes (T1D) susceptibility or protection in the context of race. As a key component of HLA-associated T1D risk, race has been included in this summary of the current literature linking HLA allelic combinations to increased T1D susceptibility or protection.

T1D-risk	Race	DRB1	DQA1	DQB1	Reference
Susceptible	African American	03:01	05:01	02:01	(26)
				02:02	(26)
				02:04	(26)
		04:01	03:01	03:02	(26)
		04:02	03:01	03:02	(26)
		04:04	03:01	03:02	(26)
		04:05	03:01	02:01	(26)
				02:02	(26)
				02:04	(26)
				03:02	(26)
		07:01	03:01	02:01	(26)
				02:02	(26)
				02:04	(26)
		09:01	03:01	02:01	(26)
				02:02	(26)
				02:04	(26)
		13:03	13:01	02:01	(26)
				02:02	(26)
				02:04	(26)
		16:01	01:02	05:02	(26)
	Asian	03:01	05:01	02:01	(25)
				02:02	(25)
				02:04	(25)
			05:03	02:01	(25)
				02:02	(25)
				02:04	(25)
			05:05	02:01	(25)
				02:02	(25)
				02:04	(25)
	Caucasian	03:01	05:01	02:01	(25)
				02:02	(25)
				02:04	(25)
			05:03	02:01	(25)
				02:02	(25)
				02:04	(25)
			05:05	02:01	(25)
				02:02	(25)
				02:04	(25)
		04:01	03:01	03:02	(25)
			03:02	03:02	(25)
			03:03	03:02	(25)
		04:02	03:01	03:02	(25)
			03:02	03:02	(25)
			03:03	03:02	(25)
		04:04	03:01	03:02	(25)
			03:02	03:02	(25)
			03:03	03:02	(25)
		04:05	03:01	03:02	(25)
			03:02	03:02	(25)
			03:03	03:02	(25)

T1D-risk	Race	DRB1	DQA1	DQB1	Reference
Protective	African American	03:02	04:01	04:02	(26)
		07:01	02:01	02:01	(26)
				02:02	(26)
				02:04	(26)
		08:04	04:01	03:01	(26)
		08:06	01:02	06:02	(26)

	10:01	01:01	05:01	(26)
	11:01	01:02	06:02	(26)
		15:01	03:01	(26)
	11:02	15:01	03:01	(26)
	11:04	15:01	03:01	(26)
	12:01	01:01	05:01	(26)
	13:01	01:02	05:01	(26)
		01:03	06:03	(26)
	13:02	01:02	05:01	(26)
	13:03	02:01	02:01	(26)
			02:02	(26)
			02:04	(26)
		15:01	03:01	(26)
	14:01	01:01	05:03	(26)
	15:01	01:02	06:02	(26)
	15:03	01:02	06:02	(26)
Asian	15:02	01:01	05:01	(25)
		01:04	05:01	(25)
		01:05	05:01	(25)
Caucasian	07:01	02:01	03:03	(25)
	11:04	15:01	03:01	(25)
			03:09	(25)
		15:03	03:01	(25)
			03:09	(25)
		15:05	03:01	(25)
			03:09	(25)
	13:03	15:01	03:01	(25)
			03:09	(25)
		15:03	03:01	(25)
			03:09	(25)
		15:05	03:01	(25)
			03:09	(25)
	14:01	01:01	05:03	(25)
		01:04	05:03	(25)
		01:05	05:03	(25)
	15:01	01:02	06:02	(25)
			06:011	(25)

Table S3. HLA information and histopathological findings for organ donors. The HLA genotype, HLA-associated type 1 diabetes (T1D) risk, and the presence (+) or absence (-) of insulitis (na = not available) are shown for each organ donor with T1D, type 2 diabetes (T2D), no diabetes (control), diabetes-related autoantibodies (AAb+), and Flatbush/other diabetes (FBD/other). As a key component of HLA-associated type 1 diabetes (T1D) risk, race has been included. Although parental HLA types are not available for Network for Pancreatic Organ Donors with Diabetes (nPOD) donors, haplotypes were assembled based on known linkage disequilibrium within the HLA region, which is particularly strong in the class II region (www.allelefrequencies.net). Neutral indicates no reported phenotype associated with the HLA. References used to determine T1D-risk conferred by HLA are summarized in **Table S2.** Insulitis was defined by the current criteria of ≥6 $CD3^+$ cells adjacent to or within the islet for ≥3 islets per pancreas along with the presence of insulin negative (pseudoatrophic) islets (50). The presence (+) or absence (-) of histological evidence of chronic pancreatitis, determined by an expert pathologist, is indicated far right column; however, information of medical history confirming clinical diagnosis of pancreatitis is not available for nPOD donors. *nPOD 6274 classification as T2D is based on diagnosis prior to gastric surgery and weight loss. **nPOD 6254 had histological evidence of chronic pancreatitis with $CD3^+$ infiltrate of both endocrine and exocrine tissues, but insulitis has not been observed (**Figure S7**).

Disease State	T1D-risk	nPOD ID	Race	HLA-A	HLA-B	HLA-DQA1	HLA-DQB1	HLA-DRB1	Insulitis (+/-)	Chronic Pancreatitis[o]
T1D	Susceptible/Susceptible	6208	Caucasian	01:01, 68:01	08, 44	03:01, 05:01	02:01, 03:02	03:01, 04:01	-	-
		6243	Caucasian	01:01, 02:01	08, 08	05:01, 05:01	02:01, 02:01	03:01, 03:01	+	-
		6262	African American	01:02, 11:01	49, 62	03:01, 03:01	03:02, 03:02	04:01, 04:05	-	+
		6264	Caucasian	23:01, 32:01	na	03:01, 05:01	02:01, 03:02	03:01, 04:04	+	-
		6265	Caucasian	03:01, 32:01	07, 62	03:01, 05:01	02:01, 03:02	03:01, 04:01	+	-
		6266	Caucasian	01:01, 03:01	08, 61	03:01, 05:01	02:01, 03:02	03:01, 04:04	-	+
		6323	Caucasian	01:01, 25:01	08, 18	03:01, 05:01	02:01, 03:02	03:01, 04:02	+	-
	Susceptible/Neutral	6193	Caucasian	02:01, 03:01	62, 35	01:01, 03:01	03:02, 05:01	01:01, 04:01	na	-
		6207	African American	23:01, 24:02	07, 55	01:02, 03:01	02:02, 06:04	09:01, 13:02	-	-
		6211	African American	02:01, 03:01	08, 45	03:01, 05:01	03:01, 03:02	04:05, 12:01	-	+
		6242	Caucasian	02:01, 02:01	27, 44	01:01, 03:01	03:02, 05:01	01:01, 04:01	-	+
	Protective/Susceptible	6161	Caucasian	02:01, 02:05	50,62	02:01, 03:01	02:02, 03:02	04:01, 07:01	-	-
		6195	Caucasian	03:01, 03:01	07, 62	01:02, 03:01	03:02, 06:02	04:01, 15:01	+	+
		6220	Caucasian	01:01, 02:01	08, 39	02:01, 05:01	02:01, 03:03	03:01, 07:01	-	-
		6285	Hispanic/Latino	01:01, 24:02	07,45	02:01, 03:01	02:02, 03:02	04:05, 07:01	-	-
	Protective/Protective	6212	Caucasian	01:01, 02:01	44, 62	02:01, 02:01	02:02, 02:02	07:01, 07:01	+	-
	Protective/Neutral	6196	African American	03:01, 30:02	35, 58	01:01, 05:01	02:01, 05:01	12:01, 13:03	-	-
	Neutral/Neutral	6263	Hispanic/Latino	02:06, 24:02	39, 39	03:01, 05:01	03:01, 03:02	04:07, 14:06	-	+
T2D	Protective/Susceptible	6274*	Caucasian	01:01, 31:01	08, 35	05:01, 05:01	02:01, 03:01	03:01, 11:01	-	-
	Protective/Protective	6273	African American	02:02, 03:01	07, 49	01:02, 01:02	06:02, 06:02	15:01, 15:03	-	-
	Protective/Neutral	6275	Hispanic/Latino	02:01, 25:01	07, 51	01:02, 03:01	03:03, 06:02	09:01, 15:01	-	+
	Neutral/Neutral	6249	Asian	02:01, 24:02	62, 62	03:01, 03:01	04:02, 04:02	04:05, 04:05	-	+
No diabetes	Protective/Susceptible	6174	Caucasian	02:05, 26:01	08, 50	02:01, 05:01	02:01, 02:02	03:01, 07:01	-	-
		6254**	Caucasian	02:01, 29:02	07, 62	02:01, 05:01	02:01, 02:02	03:01, 07:01	-	+
	Protective/Protective	6271	Caucasian	02:01, 02:06	27, 44	01:01, 02:01	02:02, 05:01	07:01, 15:02	-	-
		6279	Caucasian	01:01, 29:01	07, 51	01:02, 02:01	02:02, 06:02	07:01, 15:01	-	-
		6282	Caucasian	03:01, 29:02	44, 51	01:02, 01:03	06:02, 06:03	13:01, 15:01	-	-
		6288	Caucasian	02:01, 24:02	39, 44	01:02, 05:01	03:01, 06:02	11:01, 15:01	-	+
	Protective/Neutral	6278	African American	23:01, 68:02	45, 71	03:01, 05:01	03:01, 05:02	11:04, 12:01	-	-
		6289	African American	02:01, 02:11	44, 52	02:01, 03:01	02:02, 03:02	04:11, 07:01	-	-
	Neutral/Neutral	6287	Caucasian	02:01, 03:01	27, 44	01:01, 03:01	03:03, 05:01	01:01, 09:01	-	-
AAb+	Protective/Protective	6197	African American	02:02, 24:02	42, 45	02:01, 04:01	02:02, 04:02	03:02, 07:01	+	+
Flatbush/other	Protective/Neutral	6284	African American	36:01, 68:02	53, 53	01:02, 03:01	02:02, 06:02	15:03, 15:03	-	-

Table S4. Shared $CD8^+$ T-cell receptor (TCR) complementarity determining region 3 (CDR3) amino acid (AA) sequences among type 1 diabetes (T1D) donors. Pancreatic-draining lymph node **(**pLN) $CD8^+$ TCR β-chain (TCRβ) CDR3 AA sequences common to all HLA-A*02 matched donors with T1D (N=7). It should be noted that each sequence was also found in HLA-A*02 control samples derived from pLN $CD8^+$ T cells.

CDR3	Average Productive Frequency	Total Templates
CASSLGTDTQYF	2.03E-05	441
CASSPGGDTQYF	2.16E-05	105
CASSLGGSYEQYF	2.65E-05	301
CASSLGQGAYEQYF	2.66E-05	294
CASSLGGNQPQHF	2.99E-05	475
CASSLGLYEQYF	3.07E-05	84
CASSLTYEQYF	3.10E-05	288
CASSPSYEQYF	3.16E-05	349
CASSLGTEAFF	3.26E-05	430
CASSLAYEQYF	3.46E-05	371
CASSSDSYEQYF	3.49E-05	171
CASSLGGTEAFF	3.53E-05	774
CASSLGGYEQYF	3.66E-05	599
CASSLGYEQYF	1.36E-04	4094

Table S5. Previously characterized autoreactive or islet-resident T cell complementarity determining region 3 (CDR3) amino acid (AA) sequences identified in our cohort. Shown are the antigen reactivities of previously reported T cell clones, the CDR3 β-chain AA sequences of those clones, the Network for Pancreatic Organ Donors with Diabetes (nPOD) identification number (case ID) for each donor where the clone was identified, the tissue sources that contained the clone [pancreatic-draining lymph node (pLN), "irrelevant" mesenteric and/or inguinal lymph node (iLN), spleen, intra-islet, and peripheral blood mononuclear cells (PBMC)], the cell subset that contained the clone [$CD4^+$ conventional T cells (Tconv), $CD4^+$ regulatory T cells (Treg), and CD8+ T cells], and the frequency of that clone within the sample. Samples were derived from the, from fluorescence activated cell sorting (FACS)-purified Tconv, Treg, and $CD8^+$ T cells from type 1 diabetes (T1D), type 2 diabetes (T2D), Flatbush/other diabetes (FBD), autoantibody positive without diabetes (AAb+), and control nPOD donors. The classification of 6274 as having T2D is based on a diagnosis made prior to gastric-bypass surgery and subsequent weight-loss.

Antigen Reactivity (Citation)	AA Sequence	Case ID	Disease Status	Tissue	Cell Subset	Productive Frequency (%)
GAD65 (37)	CASSFQGSAYEQYF	6193	T1D	pLN	Tconv	11.1E-03
		6323	T1D	pLN	Tconv	3.65E-03
	CASSLGDQPQHF	6161	T1D	pLN	CD8+	6.74E-03
		6174	Control	pLN	Treg	4.12E-03
					CD8+	3.95E-03
		6193	T1D	pLN	Tconv	8.24E-04
					Treg	1.78E-03
		6195	T1D	pLN	CD8+	1.78E-03
		6196	T1D	iLN	Tconv	1.57E-02
					Treg	1.04E-02
		6197	AAb+	pLN	Tconv	2.49E-03
		6207	T1D	pLN	Tconv	1.45E-03
					Treg	1.53E-03
					CD8+	1.12E-02
				Spleen	Tconv	4.69E-03
				iLN	Treg	1.20E-03
		6211	T1D	pLN	Tconv	2.52E-03
					CD8+	1.80E-03
				Spleen	Tconv	5.58E-03
		6212	T1D	pLN	CD8+	2.45E-03
				Spleen	CD8+	2.89E-04
		6220	T1D	pLN	Treg	4.22E-03
		6242	T1D	pLN	Tconv	4.02E-04
					Treg	8.63E-03
					CD8+	1.97E-04
				Spleen	Tconv	6.86E-03
		6243	T1D	pLN	Tconv	3.10E-03
					CD8+	1.04E-02
		6249	T2D	PBMC	Tconv	1.82E-03
				pLN	Tconv	1.61E-03
					Treg	6.66E-04
					CD8+	1.78E-03
				Spleen	CD8+	6.03E-03
		6254	Control	pLN	Treg	4.25E-03
				Spleen	Treg	3.17E-03
		6262	T1D	PBMC	Tconv	1.56E-03
		6265	T1D	pLN	Tconv	1.72E-03
					CD8+	5.84E-03
				Spleen	Tconv	4.04E-03
		6266	T1D	pLN	Tconv	5.39E-03
		6271	Control	pLN	CD8+	5.23E-03
				iLN	Tconv	1.96E-03
		6273	T2D	iLN	CD8+	9.47E-03
		6275	T2D	iLN	Treg	4.47E-03
		6278	Control	Spleen	Tconv	6.28E-04
					CD8+	1.06E-03
				iLN	Tconv	2.00E-03
					Treg	2.11E-02
		6279	Control	pLN	Treg	3.02E-03
					CD8+	1.29E-03
				iLN	CD8+	1.44E-03
		6284	FBD	pLN	Treg	7.33E-03
					CD8+	8.18E-03
		6285	T1D	pLN	Tconv	1.53E-03
				Spleen	Tconv	5.44E-04
		6288	Control	pLN	Tconv	4.73E-03

Antigen Reactivity (Citation)	AA Sequence	Case ID	Disease Status	Tissue	Cell Subset	Productive Frequency (%)
					Treg	4.56E-03
				Spleen	Tconv	4.39E-04
					Treg	5.35E-03
		6289	Control	pLN	Treg	2.28E-03
				Spleen	Tconv	4.23E-04
				iLN	Treg	4.93E-04
		6323	T1D	pLN	Treg	4.47E-03
	CASSLNAGNTIYF	6207	T1D	pLN	Treg	8.61E-04
				iLN	Tconv	8.15E-04
		6249	T2D	PBMC	Tconv	3.91E-03
		6265	T1D	pLN	CD8+	1.39E-03
		6287	Control	Spleen	Tconv	3.07E-03
		6323	T1D	pLN	Treg	4.47E-03
	CASSLTGELFF	6161	T1D	pLN	Tconv	6.64E-03
					Treg	2.44E-03
					CD8+	1.65E-03
		6174	Control	pLN	Treg	4.21E-03
					CD8+	2.24E-02
		6193	T1D	pLN	Tconv	1.24E-03
					Treg	1.51E-03
					CD8+	7.69E-03
		6195	T1D	pLN	CD8+	5.51E-03
		6196	T1D	iLN	Treg	6.41E-03
		6197	AAb+	pLN	Tconv	2.05E-03
		6207	T1D	pLN	Tconv	3.51E-03
					Treg	6.51E-03
					CD8+	2.26E-03
				Spleen	Tconv	4.19E-04
					Treg	1.21E-03
					CD8+	2.13E-03
				iLN	Tconv	4.78E-03
					Treg	5.16E-03
					CD8+	1.88E-03
		6208	T1D	pLN	Tconv	1.36E-03
					Treg	4.70E-03
				Spleen	Tconv	1.72E-03
					Treg	3.61E-03
		6211	T1D	pLN	Tconv	2.22E-03
					Treg	1.88E-03
					CD8+	5.92E-03
		6212	T1D	PBMC	CD8+	6.92E-03
				pLN	Tconv	1.06E-04
				Spleen	CD8+	1.35E-03
		6220	T1D	iLN	Treg	1.12E-02
		6242	T1D	pLN	Treg	2.82E-04
					CD8+	2.17E-03
				Spleen	Tconv	3.36E-03
					Treg	3.41E-03
		6243	T1D	pLN	Tconv	2.71E-03
					CD8+	7.19E-03
				Spleen	Tconv	1.93E-03
					CD8+	3.04E-03
		6249	T2D	PBMC	CD8+	2.33E-02
				pLN	Tconv	2.08E-03
					Treg	2.37E-03
					CD8+	1.25E-03
		6254	Control	pLN	CD8+	1.96E-03

Antigen Reactivity (Citation)	AA Sequence	Case ID	Disease Status	Tissue	Cell Subset	Productive Frequency (%)
		6262	T1D	PBMC	Tconv	8.83E-03
					CD8+	2.78E-03
				pLN	CD8+	5.21E-03
				Spleen	Treg	4.80E-04
		6263	T1D	Spleen	CD8+	1.45E-03
		6264	T1D	pLN	CD8+	8.68E-04
		6265	T1D	pLN	Tconv	1.72E-03
					CD8+	2.78E-04
				Spleen	Tconv	1.01E-03
		6266	T1D	PBMC	CD8+	3.46E-03
				pLN	Tconv	1.20E-03
					Treg	9.85E-04
		6271	Control	pLN	Treg	3.05E-03
					CD8+	2.57E-03
				Spleen	Treg	1.56E-03
				iLN	Tconv	1.96E-04
					Treg	1.64E-03
		6273	T2D	pLN	Treg	2.16E-03
					CD8+	1.01E-04
				iLN	Tconv	3.99E-04
					Treg	1.34E-03
					CD8+	5.03E-03
		6275	T2D	pLN	Treg	8.52E-03
					CD8+	6.21E-03
				iLN	Tconv	2.41E-03
					Treg	4.31E-03
		6278	Control	Spleen	Tconv	1.70E-03
					CD8+	8.38E-03
				iLN	Tconv	2.63E-03
					Treg	1.95E-03
		6279	Control	pLN	Treg	9.05E-04
					CD8+	1.19E-2
				Spleen	Tconv	7.46E-04
					Treg	8.63E-03
				iLN	Tconv	1.47E-03
					Treg	1.26E-03
		6284	FBD	pLN	Treg	2.75E-03
					CD8+	4.09E-03
				Spleen	Tconv	3.04E-02
		6285	T1D	pLN	Tconv	3.40E-04
		6287	Control	pLN	CD8+	3.32E-03
				Spleen	Tconv	5.26E-03
		6288	Control	pLN	CD8+	1.53E-03
				Spleen	Tconv	3.95E-03
		6289	Control	pLN	Tconv	1.35E-03
					Treg	3.04E-04
				Spleen	Tconv	1.91E-03
					Treg	4.90E-03
		6323	T1D	PBMC	Treg	1.35E-02
					CD8+	2.52E-03
				pLN	Treg	4.47E-03
				Spleen	Treg	1.84E-02
	CASSLVGGNEQFF	6161	T1D	pLN	Tconv	3.02E-03
		6193	T1D	pLN	Tconv	3.49E-04
					Treg	9.77E-04
		6207	T1D	pLN	Tconv	1.27E-03
					Treg	2.25E-03

Antigen Reactivity (Citation)	AA Sequence	Case ID	Disease Status	Tissue	Cell Subset	Productive Frequency (%)
				Spleen	CD8+	3.14E-03
		6212	T1D	pLN	Tconv	7.04E-04
					CD8+	2.36E-03
		6243	T1D	pLN	Tconv	7.17E-03
				Spleen	Tconv	1.46E-03
					CD8+	1.65E-04
		6249	T2D	PBMC	Tconv	8.08E-04
				pLN	Tconv	2.83E-04
					CD8+	1.32E-04
		6254	Control	pLN	Tconv	4.68E-04
		6262	T1D	PBMC	Tconv	3.12E-03
				pLN	Tconv	3.95E-03
		6264	T1D	pLN	CD8+	9.92E-04
		6271	Control	Spleen	Tconv	6.37E-03
				iLN	Treg	1.23E-03
		6273	T2D	pLN	Tconv	3.18E-04
				iLN	CD8+	8.88E-04
		6275	T2D	iLN	Tconv	1.69E-03
					Treg	9.08E-04
		6279	Control	Spleen	Tconv	2.77E-03
		6285	T1D	Spleen	CD8+	6.38E-04
		6288	Control	pLN	CD8+	2.14E-03
		6289	Control	pLN	CD8+	9.06E-04
				Spleen	Tconv	2.33E-03
		6323	T1D	pLN	Treg	4.47E-03
	CASSPTGYEQYF	6161	T1D	pLN	CD8+	2.85E-03
		6174	Control	pLN	Treg	1.32E-03
					CD8+	3.07E-03
		6193	T1D	pLN	Tconv	1.17E-03
					Treg	3.02E-03
					CD8+	1.15E-02
		6195	T1D	pLN	CD8+	7.54E-03
		6208	T1D	pLN	Tconv	1.05E-03
				Spleen	Tconv	3.14E-03
					Treg	1.84E-02
		6212	T1D	pLN	Tconv	1.45E-03
					Treg	1.76E-03
				Spleen	CD8+	8.76E-03
		6220	T1D	pLN	Treg	1.26E-02
		6242	T1D	pLN	Tconv	4.77E-03
				Spleen	Tconv	2.29E-03
					Treg	1.52E-03
		6243	T1D	pLN	Treg	5.52E-03
				Spleen	Tconv	4.69E-04
					CD8+	1.65E-03
		6249	T2D	pLN	Tconv	1.37E-03
					Treg	7.11E-03
					CD8+	4.93E-03
				Spleen	Tconv	5.28E-03
		6254	Control	pLN	Treg	1.25E-03
					CD8+	4.70E-04
		6262	T1D	PBMC	CD8+	2.16E-03
				Spleen	CD8+	6.03E-03
		6263	T1D	Spleen	Tconv	2.22E-03
		6264	T1D	pLN	Tconv	2.00E-03
					CD8+	2.11E-03
		6265	T1D	Spleen	Tconv	8.41E-03

Antigen Reactivity (Citation)	AA Sequence	Case ID	Disease Status	Tissue	Cell Subset	Productive Frequency (%)
		6266	T1D	PBMC	CD8+	4.73E-03
				pLN	Treg	1.14E-02
				Spleen	Tconv	5.74E-03
		6271	Control	pLN	Tconv	2.00E-03
					Treg	4.52E-03
					CD8+	9.13E-03
				Spleen	Tconv	5.46E-03
					Treg	4.43E-03
				iLN	Treg	2.25E-03
					CD8+	5.86E-03
		6273	T2D	pLN	Treg	2.66E-03
				iLN	CD8+	2.96E-03
		6274	T2D	pLN	Tconv	3.17E-02
		6275	T2D	pLN	Tconv	5.16E-03
					Treg	4.72E-03
					CD8+	9.68E-03
				iLN	Tconv	2.05E-03
					Treg	8.70E-03
		6279	Control	pLN	Treg	2.41E-03
					CD8+	3.55E-03
				Spleen	Tconv	4.26E-04
					Treg	3.85E-03
				iLN	Tconv	2.41E-03
					Treg	3.93E-03
					CD8+	1.77E-02
		6284	FBD	pLN	CD8+	1.72E-02
		6285	T1D	pLN	Tconv	1.36E-03
					Treg	1.96E-03
					CD8+	5.53E-03
				Spleen	CD8+	5.74E-03
		6287	Control	pLN	CD8+	3.56E-02
				Spleen	Treg	2.35E-03
					CD8+	2.75E-02
		6288	Control	pLN	Tconv	3.16E-04
					Treg	7.20E-04
				Spleen	Tconv	3.40E-03
					Treg	1.96E-03
					CD8+	4.18E-03
		6323	T1D	PBMC	CD8+	2.52E-03
				pLN	Treg	4.47E-03
	CASSPWDGSYEQYF	6212	T1D	pLN	Tconv	9.68E-04
		6266	T1D	pLN	Treg	6.11E-03
		6273	T2D	iLN	CD8+	1.97E-03
		6279	Control	iLN	CD8+	8.25E-04
		6323	T1D	pLN	Tconv	3.65E-03
	CASSRGTEAFF	6161	T1D	pLN	CD8+	1.20E-03
				Spleen	CD8+	1.37E-02
		6174	T2D	pLN	Treg	3.86E-03
		6193	T1D	pLN	Treg	3.01E-03
		6195	T1D	pLN	CD8+	4.24E-03
		6196	T1D	iLN	Treg	1.45E-02
		6197	AAb+	pLN	Tconv	6.00E-03
		6207	T1D	pLN	Tconv	3.15E-03
					CD8+	2.11E-03
				Spleen	Tconv	1.67E-04
					CD8+	4.14E-03
				iLN	Tconv	3.75E-03

Antigen Reactivity (Citation)	AA Sequence	Case ID	Disease Status	Tissue	Cell Subset	Productive Frequency (%)
					Treg	9.52E-03
					CD8+	2.37E-03
		6208	T1D	pLN	Tconv	3.01E-03
					Treg	7.36E-03
				Spleen	Treg	7.60E-04
		6211	T1D	pLN	Tconv	1.21E-02
					Treg	9.32E-03
					CD8+	1.05E-04
				Spleen	Tconv	7.35E-03
		6212	T1D	pLN	Tconv	3.96E-04
					Treg	8.67E-03
					CD8+	1.54E-03
				Spleen	CD8+	4.72E-03
		6220	T1D	pLN	Treg	7.03E-04
				iLN	Treg	3.78E-02
		6242	T1D	pLN	Tconv	9.76E-04
					Treg	8.176E-03
				Spleen	Tconv	1.75E-03
					Treg	1.70E-03
					CD8+	2.43E-03
		6243	T1D	pLN	Tconv	1.36E-03
					CD8+	8.46E-04
				Spleen	CD8+	3.54E-03
		6249	T2D	pLN	Tconv	2.98E-03
					Treg	5.18E-04
		6254	Control	pLN	Tconv	1.40E-02
					Treg	1.95E-02
					CD8+	2.82E-03
				Spleen	Tconv	7.85E-03
					Treg	3.35E-02
		6263	T1D	Spleen	Tconv	8.13E-04
		6264	T1D	Spleen	CD8+	6.84E-03
		6265	T1D	Spleen	Tconv	2.36E-03
		6266	T1D	pLN	Tconv	4.99E-03
		6271	Control	pLN	Tconv	3.07E-03
					Treg	2.42E-03
					CD8+	2.26E-03
		6273	T2D	pLN	Tconv	4.70E-03
					Treg	2.35E-03
				iLN	Tconv	1.20E-03
		6274	T2D	pLN	CD8+	2.56E-02
				Spleen	CD8+	2.15E-02
		6275	T2D	pLN	CD8+	6.21E-03
				iLN	Treg	1.82E-03
		6278	Control	Spleen	Tconv	1.15E-03
				iLN	Tconv	2.17E-03
					Treg	6.39E-03
					CD8+	1.38E-03
		6279	Control	pLN	Tconv	1.22E-03
					Treg	2.71E-03
				Spleen	Tconv	8.52E-04
				iLN	Treg	2.36E-03
		6285	T1D	Spleen	Tconv	1.36E-03
					CD8+	3.51E-03
		6288	Control	Spleen	Tconv	4.61E-03
		6289	Control	pLN	Treg	1.37E-03
				Spleen	Tconv	1.48E-03

Antigen Reactivity (Citation)	AA Sequence	Case ID	Disease Status	Tissue	Cell Subset	Productive Frequency (%)
		6323	T1D	PBMC	CD8+	5.04E-03
				pLN	Treg	4.47E-03
				Spleen	Tconv	2.45E-02
					Treg	4.60E-03
	CASSRQGTGELFF	6193	T1D	pLN	Treg	1.07E-04
		6195	T1D	pLN	CD8+	2.54E-04
		6197	AAb+	pLN	Tconv	7.57E-04
		6207	T1D	pLN	Tconv	7.26E-04
					Treg	1.82E-03
				iLN	Tconv	5.98E-04
					Treg	1.51E-03
		6208	T1D	pLN	Tconv	3.39E-04
		6211	T1D	pLN	Tconv	1.46E-03
				Spleen	Treg	2.97E-02
		6212	T1D	pLN	Tconv	3.52E-04
					Treg	7.38E-03
		6220	T1D	pLN	Treg	3.43E-03
		6242	T1D	pLN	Treg	1.50E-03
				Spleen	Tconv	6.06E-04
		6243	T1D	Spleen	Tconv	7.03E-04
		6249	T2D	pLN	Tconv	9.68E-04
		6265	T1D	Spleen	Tconv	1.18E-03
		6271	Control	pLN	Tconv	2.24E-03
		6273	T2D	pLN	Tconv	5.17E-03
					Treg	2.98E-03
				Spleen	Tconv	3.20E-03
				iLN	Tconv	3.59E-03
		6275	T2D	pLN	Tconv	5.70E-03
		6279	Control	pLN	Treg	2.72E-03
				Spleen	Tconv	6.39E-04
				iLN	Treg	9.43E-04
		6287	Control	Spleen	Tconv	1.10E-03
					CD8+	7.30E-04
		6288	Control	pLN	Treg	9.60E-04
		6289	Control	pLN	Treg	2.28E-04
				Spleen	Tconv	4.23E-04
		6323	T1D	pLN	Treg	4.47E-03
	CASSRTGYGYTF	6161	T1D	pLN	Tconv	1.06E-03
		6174	Control	pLN	Treg	8.78E-04
					CD8+	2.05E-03
		6193	T1D	pLN	Treg	1.96E-03
					CD8+	3.85E-03
		6197	AAb+	pLN	Tconv	1.89E-03
		6207	T1D	pLN	Tconv	2.72E-03
					CD8+	1.51E-04
				iLN	Tconv	3.37E-03
		6208	T1D	pLN	Tconv	2.64E-03
		6211	T1D	pLN	Tconv	1.51E-04
					Treg	5.9E-03
		6220	T1D	pLN	Treg	1.23E-03
				iLN	Treg	2.38E-02
		6249	T2D	pLN	Tconv	1.32E-03
					Treg	4.44E-04
		6254	Control	pLN	Tconv	1.87E-03
				Spleen	Treg	2.31E-03
		6262	T1D	pLN	Tconv	8.65E-04
		6263	T1D	Spleen	Tconv	9.53E-03

Antigen Reactivity (Citation)	AA Sequence	Case ID	Disease Status	Tissue	Cell Subset	Productive Frequency (%)
		6264	T1D	pLN	Tconv	2.94E-03
		6265	T1D	pLN	Treg	1.05E-02
		6271	Control	pLN	Tconv	3.30E-03
				iLN	Treg	4.92E-03
		6273	T2D	pLN	Treg	1.27E-03
		6278	Control	Spleen	CD8+	1.63E-03
				iLN	Tconv	3.72E-03
		6279	Control	pLN	Treg	1.75E-02
				Spleen	Treg	2.33E-03
		6284	FBD	Spleen	Treg	5.26E-03
		6287	Control	Spleen	Tconv	1.53E-03
		6288	Control	pLN	Treg	8.40E-04
				Spleen	Tconv	1.21E-03
		6289	Control	pLN	CD8+	8.88E-03
		6323	T1D	PBMC	CD8+	2.52E-03
				pLN	Tconv	7.30E-03
					Treg	4.47E-03
	CATSDQETQYF	6161	T1D	pLN	CD8+	3.00E-04
		6207	T1D	pLN	Tconv	1.63E-03
		6208	T1D	pLN	Tconv	7.91E-04
		6242	T1D	pLN	Tconv	6.90E-04
		6249	T2D	pLN	Treg	1.48E-04
		6278	Control	iLN	Tconv	1.32E-03
		6323	T1D	pLN	Tconv	3.65E-03
	CSAKDRGNYGYTF	6197	AAb+	pLN	Tconv	1.08E-04
		6243	T1D	Spleen	Tconv	4.10E-04
		6323	T1D	pLN	Tconv	3.65E-03
GAD65 clone 4.13 (32)	CASSLVGGPSSEAFF	6193	T1D	pLN	Treg	3.55E-04
		6207	T1D	iLN	CD8+	3.92E-03
		6220	T1D	iLN	Treg	2.80E-03
		6254	Control	pLN	Treg	6.74E-03
					CD8+	1.07E-02
				Spleen	Tconv	1.96E-03
		6262	T1D	pLN	Tconv	1.11E-04
		6263	T1D	Spleen	CD8+	1.14E-02
		6265	T1D	pLN	Tconv	2.52E+01
					Treg	1.57E-01
					CD8+	5.10E-01
		6323	T1D	intra-	CD4+	1.01E-02
GAD65 clone PM1#11 (42)	CASGRSSYNEQFF	6161	T1D	Spleen	Treg	4.19E-03
		6207	T1D	iLN	Tconv	5.44E-04
					CD8+	3.26E-04
		6212	T1D	Spleen	CD8+	5.97E-03
		6249	T2D	PBMC	Tconv	2.40E-02
				pLN	Tconv	4.60E-03
					CD8+	2.63E-03
				Spleen	Tconv	4.54E-03
					CD8+	7.20E-03
		6262	T1D	PBMC	Tconv	1.04E-04
				pLN	Tconv	1.73E-03
					CD8+	1.01E-02
		6265	T1D	pLN	Treg	4.39E-03
					CD8+	9.73E-04
		6266	T1D	Spleen	CD8+	3.52E-03
		6271	Control	iLN	CD8+	3.59E-04
		6274	T2D	pLN	CD8+	8.54E-03

Antigen Reactivity (Citation)	AA Sequence	Case ID	Disease Status	Tissue	Cell Subset	Productive Frequency (%)
		6275	T2D	pLN	CD8+	1.10E-02
				iLN	Treg	4.01E-03
		6279	Control	iLN	CD8+	4.12E-04
GAD65 clone R164 (41)	CASSLAGGANSPLHF	6273	T2D	pLN	Tconv	7.96E-04
					CD8+	4.05E-04
		6278	Control	pLN	Tconv	2.73E-04
		6289	Control	Spleen	Treg	4.08E-04
IGRP clone 32 (38)	CSASRQGWVNEQFF	6197	AAb+	pLN	Tconv	1.62E-04
Insulin-A clone SD32.5 (39)	CASSPRANTDTQYF	6208	T1D	pLN	Treg	1.41E-03
Insulin-B (40)	CSVEDRNTGELFF	6161	T1D	pLN	CD8+	3.00E-04
		6212	T1D	Spleen	CD8+	6.74E-04
		6289	Control	pLN	Tconv	2.71E-04
Proinsulin (36)	CASSLEASSYNSPLHF	6207	T1D	pLN	Tconv	7.26E-04
					Treg	4.31E-04
		6208	T1D	pLN	Tconv	5.65E-04
		6266	T1D	Spleen	Tconv	4.02E-02
	CASSLERDGYTF	6196	T1D	iLN	Tconv	4.36E-04
		6208	T1D	pLN	Tconv	3.39E-04
		6278	Control	Spleen	Tconv	3.59E-04
		6288	Control	Spleen	Tconv	2.19E-04
		6289	Control	Spleen	Tconv	3.74E-03
	CASSLERETQYF	6193	T1D	pLN	Tconv	3.17E-03
					Treg	1.78E-04
		6207	T1D	pLN	Tconv	9.08E-04
					Treg	5.26E-04
					CD8+	3.77E-04
				iLN	Tconv	1.63E-04
		6212	T1D	pLN	Tconv	9.24E-04
					Treg	3.52E-03
		6242	T1D	pLN	Tconv	5.17E-04
					Treg	1.22E-03
				Spleen	Treg	1.79E-04
		6243	T1D	Spleen	Tconv	5.86E-04
		6249	T2D	pLN	Treg	1.55E-03
		6263	T1D	Spleen	Tconv	4.93E-04
		6265	T1D	pLN	Treg	4.58E-03
				Spleen	Tconv	3.70E-03
		6271	Control	pLN	Tconv	2.36E-04
		6273	T2D	iLN	Treg	5.95E-04
					CD8+	1.97E-04
		6275	T2D	iLN	Tconv	5.41E-03
		6288	Control	Spleen	Treg	1.78E-04
	CASSLGPGQRETQYF	6266	T1D	pLN	Tconv	1.60E-03
		6273	T2D	iLN	CD8+	3.95E-04
	CASSPTTGGDEAFF	6279	Control	iLN	Tconv	2.41E-03
Unknown (36)	CASGTGDSPLHF	6195	T1D	pLN	CD8+	5.09E-04
		6207	T1D	iLN	Tconv	1.25E-03
		6212	T1D	pLN	Tconv	8.80E-05
		6273	T2D	pLN	Treg	2.79E-03
		6278	Control	pLN	CD8+	1.03E-02
				Spleen	Tconv	4.93E-03
	CASRSGQVNTEAFF	6285	T1D	Spleen	Tconv	5.44E-04
	CASSADRVTDTQYF	6207	T1D	iLN	Tconv	1.63E-04
		6211	T1D	Spleen	Tconv	3.07E-03
		6279	Control	Spleen	Tconv	4.26E-04
		6284	FBD	pLN	Treg	2.75E-03
		6323	T1D	PBMC	Tconv	8.45E-03

Antigen Reactivity (Citation)	AA Sequence	Case ID	Disease Status	Tissue	Cell Subset	Productive Frequency (%)
	CASSLGLAGSTDTQYF	6161	T1D	pLN	Tconv	4.53E-04
		6174	Control	pLN	Treg	5.27E-04
		6193	T1D	pLN	Treg	5.33E-04
		6197	AAb+	pLN	Tconv	1.24E-03
		6207	T1D	pLN	Tconv	3.63E-04
					Treg	4.31E-04
				Spleen	Tconv	7.54E-04
				iLN	Treg	5.65E-03
					CD8+	1.06E-03
		6208	T1D	pLN	Tconv	8.29E-04
		6211	T1D	pLN	Tconv	3.53E-04
					Treg	3.35E-04
		6212	T1D	PBMC	CD8+	1.15E-04
				pLN	Tconv	1.23E-03
					Treg	2.57E-03
				Spleen	Tconv	2.86E-03
					CD8+	6.74E-04
		6220	T1D	pLN	Treg	7.03E-04
		6242	T1D	pLN	CD8+	1.18E-03
				Spleen	Tconv	3.36E-04
		6243	T1D	pLN	Tconv	3.88E-04
				Spleen	Tconv	4.57E-03
		6249	T2D	PBMC	Tconv	2.02E-04
				pLN	Tconv	5.67E-04
					Treg	2.96E-04
		6254	Control	Spleen	Treg	1.15E-04
		6262	T1D	Spleen	Tconv	1.03E-02
					Treg	3.24E-03
					CD8+	5.48E-04
		6264	T1D	pLN	Tconv	5.21E-03
					Treg	1.39E-03
		6271	Control	iLN	Tconv	1.96E-04
		6273	T2D	pLN	Treg	2.54E-04
				iLN	Tconv	1.99E-03
		6279	Control	pLN	Tconv	2.64E-03
					Treg	9.05E-04
				Spleen	Tconv	8.52E-04
					Treg	4.66E-04
		6284	FBD	Spleen	Treg	1.81E-03
		6285	T1D	Spleen	Tconv	5.44E-04
		6287	Control	Spleen	CD8+	1.28E-03
		6288	Control	pLN	Tconv	4.73E-04
					Treg	7.20E-04
					CD8+	6.24E-04
				Spleen	Tconv	6.58E-04
					Treg	6.24E-04
		6289	Control	Spleen	Tconv	1.41E-04
					Treg	1.02E-04
		6323	T1D	pLN	Tconv	3.65E-03
	CASSLRDRGNYGYTF	6174	Control	pLN	Treg	6.14E-04
		6207	T1D	pLN	Tconv	1.21E-04
		6208	T1D	pLN	Tconv	1.13E-03
		6212	T1D	PBMC	Tconv	5.84E-04
		6243	T1D	Spleen	Tconv	4.69E-04
		6249	T2D	pLN	Treg	6.66E-04
		6262	T1D	Spleen	CD8+	4.39E-03
		6265	T1D	pLN	Tconv	5.72E-04

Antigen Reactivity (Citation)	AA Sequence	Case ID	Disease Status	Tissue	Cell Subset	Productive Frequency (%)
		6273	T2D	iLN	Treg	7.43E-04
		6278	Control	iLN	Tconv	1.37E-03
	CSAPLSGGSTDTQYF	6207	T1D	iLN	Treg	6.68E-04
	CSARDAGASTDTQYF	6174	Control	pLN	Treg	1.76E-04
		6207	T1D	pLN	Treg	6.70E-04
	CSASGNEQFF	6174	Control	pLN	Treg	1.05E-03
		6193	T1D	pLN	Tconv	6.34E-05
					Treg	1.78E-04
		6196	T1D	iLN	Treg	4.07E-04
		6197	AAb+	pLN	Tconv	1.08E-04
		6207	T1D	pLN	Tconv	1.21E-04
		6266	T1D	pLN	Tconv	3.99E-04
		6271	Control	pLN	Tconv	9.43E-04
				Spleen	Treg	2.40E-04
				iLN	Treg	1.43E-03
		6278	Control	iLN	Tconv	4.01E-04
		6279	Control	Spleen	Treg	2.33E-04
		6285	T1D	pLN	Tconv	3.39E-04

Table S6. Previously characterized glutamic acid decarboxylase 65 (GAD65)-reactive T cell receptor β-chain (TCRβ) complementarity determining region 3 (CDR3) amino acid (AA) sequences identified in Network for Pancreatic Organ Donors with Diabetes (nPOD) donor 6323. TCRβ CDR3 AA sequences identical to those of previously characterized GAD65-reactive T cell clones (32, 37) were identified within our dataset in the pancreatic-draining lymph node (pLN), peripheral blood mononuclear cells (PBMC), $CD4^+$ conventional T cells (Tconv), regulatory T cells (Treg), and $CD8^+$ T cells ($CD8^+$) of a donor with type 1 diabetes (T1D, nPOD 6323). No clones identified by Eugster et al. were found in the intra-islet region.

CDR3 Sequence	Tissue	Subset	Receptor (TCRBV|CDR3 AA|TCRBJ)	Frequency	Rank
CASSFQGSAYEQYF	pLN	Tconv	TCRBV12|CASSFQGSAYEQYF|TCRBJ02-07*01	0.00295954	1583
CASSLGDQPQHF	pLN	Treg	TCRBV12|CASSLGDQPQHF|TCRBJ01-05*01	0.00359079	974
CASSLNAGNTIYF	pLN	Treg	TCRBV07-02*01|CASSLNAGNTIYF|TCRBJ01-03*01	0.00359079	974
CASSLTGELFF	PBMC	CD8+	TCRBV12|CASSLTGELFF|TCRBJ02-02*01	0.00207082	2455
		Treg	TCRBV07-09|CASSLTGELFF|TCRBJ02-02*01	0.01092538	232
	pLN	Treg	TCRBV12|CASSLTGELFF|TCRBJ02-02*01	0.00359079	974
	Spleen	Treg	TCRBV05-01*01|CASSLTGELFF|TCRBJ02-02*01	0.01474818	113
CASSLVGGNEQFF	pLN	Treg	TCRBV11-03*01|CASSLVGGNEQFF|TCRBJ02-01*01	0.00359079	974
CASSPTGYEQYF	PBMC	CD8+	TCRBV27-01*01|CASSPTGYEQYF|TCRBJ02-07*01	0.00207082	2455
	pLN	Treg	TCRBV03|CASSPTGYEQYF|TCRBJ02-07*01	0.00359079	974
CASSPWDGSYEQYF	pLN	Tconv	TCRBV18-01*01|CASSPWDGSYEQYF|TCRBJ02-07*01	0.00295954	1583
CASSRGTEAFF	PBMC	CD8+	TCRBV19-01|CASSRGTEAFF|TCRBJ01-01*01	0.00414164	1059
	pLN	Treg	TCRBV04-01*01|CASSRGTEAFF|TCRBJ01-01*01	0.00359079	974
	Spleen	Tconv	TCRBV06|CASSRGTEAFF|TCRBJ01-01*01	0.01923817	86
		Treg	TCRBV14-01*01|CASSRGTEAFF|TCRBJ01-01*01	0.00368704	3146
CASSRQGTGELFF	pLN	Treg	TCRBV06-06|CASSRQGTGELFF|TCRBJ02-02*01	0.00359079	974
CASSRTGYGYTF	PBMC	CD8+	TCRBV07-09|CASSRTGYGYTF|TCRBJ01-02*01	0.00207082	2455
	pLN	Tconv	TCRBV12|CASSRTGYGYTF|TCRBJ01-02*01	0.00591909	71
		Treg	TCRBV12|CASSRTGYGYTF|TCRBJ01-02*01	0.00359079	974
CATSDQETQYF	pLN	Tconv	TCRBV24|CATSDQETQYF|TCRBJ02-05*01	0.00295954	1583
CSAKDRGNYGYTF	pLN	Tconv	TCRBV20|CSAKDRGNYGYTF|TCRBJ01-02*01	0.00295954	1583

Table S7. Frequency of shared glutamic acid decarboxylase (GAD)-reactive clones found in Network for Pancreatic Organ Donors with Diabetes (nPOD) donor tissue and previously reported simultaneous pancreas-kidney (SPK) transplant patient with recurrent type 1 diabetes (T1D). T cell receptor β-chain (TCRβ) amino acid (AA) sequences corresponding to $GAD_{(555-567)}$-reactive TCRβ were previously identified by Vendrame et al. via MHC-tetramer staining of lymphocytes. These cells were derived from the first peripheral blood sample tested following hyperglycemia of SPK transplant patients with recurrent T1D (44). Clonotypes with identical TCRβ Complementarity Determining Region 3 (CDR3β) were identified in $CD4^+$ conventional T cell (Tconv), $CD4^+$ regulatory T cell (Tregs), and $CD8^+$ T cell ($CD8^+$) subsets isolated from pancreatic-draining lymph node (pLN), "irrelevant" mesenteric and/or inguinal lymph node (iLN), and spleen samples obtained from nPOD donors with T1D, without T1D (control), without T1D but with autoantibodies (AAb+), or with type 2 diabetes (T2D) using the Adaptive immunosequencing platform. Here are listed, the tetramers previously used by Vendrame et al.; the corresponding CDR3β AA sequence; the nPOD donor, tissue, and cell subset from which the CDR3 AA was identified; the nPOD donor disease state and HLA-DR haplotype; the number of reads and read frequency corresponding to the CDR3β AA sequence; and the V, D, and J gene families that make up the CDR3β (Max V Resolved, Max D Resolved, Max J Resolved, respectively).

Tetramer	Amino Acid	Disease State	nPOD ID	HLA-DR	Tissue	Cell Type	Reads	Frequency	Max V Resolved	Max D Resolved	Max J Resolved
DRB1*0402	CASSLRGGPDTQYF	AAB+	6197	03:02, 07:01	pLN	Tconv	3	0.00014033	TCRBV07-03*01	TCRBD01-01*01	TCRBJ02-03*01
		Control	6254	03:01, 07:01	Spleen	Tconv	10	0.0016535	TCRBV05-01*01	unresolved	TCRBJ02-03*01
			6271	07:01, 15:02	iLN	Tconv	4	0.00016268	TCRBV05-08*01	TCRBD02-01*01	TCRBJ02-03*01
			6289	04:11, 07:01	Spleen	Treg	129	0.02134115	TCRBV27-01*01	TCRBD02-01*01	TCRBJ02-03*01
					pLN	Treg	144	0.00892451	TCRBV27-01*01	TCRBD02-01*01	TCRBJ02-03*01
		T1D	6161	04:01, 07:01	Spleen	CD8+	6	0.00272013	TCRBV07-03*01	TCRBD02-01*01	TCRBJ02-03*01
					pLN	Treg	2	0.00128932	TCRBV03	TCRBD02-01*01	TCRBJ02-03*01
			6193	01:01, 04:01	pLN	Treg	4	0.00028447	TCRBV05-06*01	TCRBD02-01*01	TCRBJ02-03*01
			6195	01:01, 04:01	pLN	CD8+	10	0.00069347	TCRBV05-06*01	TCRBD01-01*01	TCRBJ02-03*01
			6208	03:01, 04:01	pLN	Tconv	16	0.00050486	TCRBV05-01*01	TCRBD02-01*01	TCRBJ02-03*01
			6265	03:01, 04:01	pLN	Treg	42	0.0032526	TCRBV07-09	TCRBD02-01*01	TCRBJ02-03*01
						CD8+	12	0.00139958	TCRBV13-01*01	TCRBD02-01*01	TCRBJ02-03*01
							9	0.00104969	TCRBV07-09	TCRBD02-01*02	TCRBJ02-03*01
							2	0.00023326	TCRBV07-06*01	TCRBD02-01*02	TCRBJ02-03*01
		T2D	6273	15:01, 15:03	iLN	CD8+	21	0.0016722	TCRBV12	TCRBD02-01*01	TCRBJ02-03*01
							5	0.00039814	TCRBV07-06*01	TCRBD02-01*01	TCRBJ02-03*01
			6275	09:01, 15:01	iLN	Treg	8	0.00048195	TCRBV07-03*01	TCRBD02-01*01	TCRBJ02-03*01
DRB1*0405	CASSFTGDTGELFF	AAb+	6197	03:02, 07:01	pLN	Tconv	3	0.00014033	TCRBV05-04*01	TCRBD01-01*01	TCRBJ02-02*01
		Control	6271	07:01, 15:02	Spleen	CD8+	3	0.00051596	TCRBV07-09	TCRBD01-01*01	TCRBJ02-02*01
			6278	11:04, 12:01	iLN	CD8+	12	0.00107811	TCRBV05-01*01	TCRBD02-01*01	TCRBJ02-02*01
						Tconv	9	0.00043688	TCRBV05-06*01	TCRBD01-01*01	TCRBJ02-02*01
							2	0.00009708	TCRBV05-01*01	TCRBD02-01*01	TCRBJ02-02*01
			6288	11:01, 15:01	pLN	CD8+	27	0.00237809	TCRBV27-01*01	TCRBD01-01*01	TCRBJ02-02*01
		T1D	6161	04:01, 07:01	pLN	Tconv	14	0.00174484	TCRBV05-01*01	TCRBD01-01*01	TCRBJ02-02*01
			6212	07:01, 07:01	pLN	CD8+	10	0.00073189	TCRBV27-01*01	TCRBD01-01*01	TCRBJ02-02*01
			6242	01:01, 04:01	pLN	Treg	21	0.00161622	TCRBV07-09	TCRBD01-01*01	TCRBJ02-02*01
			6243	03:01, 03:01	Spleen	CD8+	18	0.00116804	TCRBV28-01*01	TCRBD02-01*01	TCRBJ02-02*01
		T2D	6249	04:05, 04:05	pLN	Treg	21	0.00127803	TCRBV05-01*01	TCRBD02-01*01	TCRBJ02-02*01
			6273	15:01, 15:03	pLN	CD8+	8	0.00064911	TCRBV06-04	TCRBD01-01*01	TCRBJ02-02*01
					Spleen	Tconv	4	0.00047039	TCRBV06-04	TCRBD01-01*01	TCRBJ02-02*01
			6275	09:01, 15:01	iLN	Treg	14	0.00084342	TCRBV05-01*01	TCRBD01-01*01	TCRBJ02-02*01
							6	0.00036146	TCRBV05-01*01	TCRBD01-01*01	TCRBJ02-02*01
DRB4*0101	CASSQVTAETQYF	Control	6279	07:01, 15:01	iLN	CD8+	4	0.00065988	TCRBV03	TCRBD02-01	TCRBJ02-05*01

Table S8. T cell receptor (TCR) α-chain (TCRα) and β-chain (TCRβ) pairing from intra-islet T cells. Intra-islet T cells were isolated and expanded, as described in the methods section, from type 1 diabetes (T1D) Network for Pancreatic Organ Donors with Diabetes (nPOD) donor 6323 followed by single-cell RNAseq analysis using the Fluidigm C1 platform. High frequency TCRα and TCRβ data were extracted using TraCeR for reconstruction of TCRα/β pairs (69). TCRβ complementarity determining region 3 (CDR3) amino acid (AA) sequences are shown. After isolation, individual cells were each given a sample ID. ------ indicates TCRα could not be determined. ◆ indicates the RNAseq expression data showed that these CD8 expressed CD4 transcripts, but no CD8.

TCRα		TCRβ					CDR3β Frequency in Islet
V-gene	**J-gene**	**CDR3 AA**	**V-gene**	**D-gene**	**J-gene**	**Sample ID**	
08-04	10	CASSLVGQNYGYTF	11-02*02	01-01*01	01-02*01	CD4_04	24.8%
						CD4_24	
						CD4_45	
						CD8_42♦	
26-02	32	CASYGSRQGVGSNQPQHF	06	01-01*01	01-05*01	CD4_43	3.1%
						CD8_37	
------	------	CASYGSRQGVGSNQPQHF	06	01-01*01	01-05*01	CD8_32	
23	7	CASSAGGSYEQYF	28-01*01	01-01*01	02-07*01	CD4_29	12.2%
						CD8_21♦	

Table S9. Single cell T cell receptor (TCR) α-/β-chain sequencing and pairing data from Network for Pancreatic Organ Donors with Diabetes (nPOD) donor 6265. Individual $CD4^+$ and $CD8^+$ T cells were purified by fluorescence activated cell sorting (FACS) from a pancreatic-draining lymph node (pLN) sample from a donor with type 1 diabetes (T1D, nPOD 6265). Full TCR α-chain V gene (TRAV) and TCR β-chain V gene (TRBV) data were obtained by directed sequencing. The resolved gene usage for each individual cell is shown along with the respective overlap with prior sequencing of nPOD 6265 pLN and spleen using the Adaptive immunosequencing platform (Far right two columns: Frequency of complementarity determining region 3 β-chain [CDR3β]). Note, through Adaptive immunosequencing of nPOD 6265 pLN samples, we identified a highly enriched clone carrying a TCR CDR3β amino acid (AA) sequence identical to a previously identified glutamic acid decarboxylase (GAD)-reactive T cell clone (clone 4.13; **Figure 7**). With single cell sequencing, no CDR3β AA sequences corresponding to that of clone 4.13 were identified from this pLN sample.

Cell Type	Max Vα resolved	Max Jα Resolved	CDR3α	Max Vβ Resolved	Max Jβ Resolved	CDR3β	Frequency of CDR3β in 6265 pLN	Frequency of CDR3β in 6265 Spleen
CD4	TRAV19*01	TRAJ58*01	CALSGETSGSRLTF	TRBV11-2*01	TRBJ2-2*01	CAGRGGNTGELFF	0%	0%
CD8	TRAV27	TRAJ22*01	CAGPGSARQLTF	TRBV10-3	TRBJ1-1*01	CAISEGGANTEAFF	0%	0%
CD4	TRAV40*01	TRAJ40*01	CLLLTSGTYKYIF	TRBV10-3	TRBJ2-6*01	CAISESWDRAYSGANVLTF	0%	0%
CD4	TRAV17*01	TRAJ56*01	CATGFSYTGANSKLTF	TRBV2	TRBJ2-7*01	CAIVDGQGPSYEQYF	0%	0%
CD4	TRAV26-1	TRAJ52*01	CIVRGSNAGGTSYGKLTF	TRBV2	TRBJ2-5*01	CASKDRESQETQYF	0%	0%
CD4				TRBV5-1*01	TRBJ1-1*01	CASLDRFGTEAFF	0%	0%
CD4	TRAV30*01	TRAJ18*01	CGTEVDRGSTLGRLYF	TRBV19*01	TRBJ1-1*01	CASMGGGRYKGNTEAFF	0%	0%
CD8	TRAV38-1	TRAJ39*01	CAFQGNMLTF	TRBV7	TRBJ1-2*01	CASRGLNYGYTF	0%	0%
CD8	TRAV12-3*02	TRAJ27*01	CATEGTNAGKSTF	TRBV2	TRBJ2-2*01	CASRPLGTTNTGELFF	0%	0%
CD8	TRAV26-1	TRAJ57*01	CIVRVQGGSEKLVF	TRBV19*01	TRBJ2-7*01	CASSAGQGAYEQYF	0.42%	0%
CD8	TRAV14	TRAJ22*01	CAMRERSGSARQLTF	TRBV28*01	TRBJ2-2*01	CASSDHPGESNTGELFF	0%	0%
CD4	TRAV26-1	TRAJ44*01	CIVINTGTASKLTF	TRBV3-1*01	TRBJ1-1*01	CASSEEGVGNTEAFF	0%	0%
CD4	TRAV14	TRAJ28*01	CAMREVYSGAGSYQLTF	TRBV9*01	TRBJ1-3*01	CASSERDRQSSGNTIYF	0%	0%
CD4	TRAV13-1	TRAJ44*01	CAAQEGGTASKLTF	TRBV7-2	TRBJ2-7*01	CASSFRLGSEQYF	0%	0%
CD8	TRAV19*01	TRAJ34*01	CALSEPYNTDKLIF	TRBV25-1*01	TRBJ1-2*01	CASSGGRGILYGYTF	0%	0%
CD4				TRBV3-1*01	TRBJ2-5*01	CASSHWQTQETQYF	0%	0%
CD4				TRBV6-1*01	TRBJ1-1*01	CASSISAPQIVAFF	0%	0%
CD4				TRBV19*01	TRBJ2-5*01	CASSISSLKTQYF	0%	0%
CD4				TRBV6-5*01	TRBJ2-7*01	CASSITPGQGAYEQYF	0%	0%
CD4	TRAV13-2*01	TRAJ39*01	AGNMLTF	TRBV7-9	TRBJ1-3*01	CASSLAAGGSGNTIYF	0%	0%
CD4				TRBV5-1*01	TRBJ2-3*01	CASSLAGQPTDTQYF	0%	0%
CD4	TRAV35	TRAJ44*01	CAGRTTGTASKLTF	TRBV7-2	TRBJ2-3*01	CASSLAIGRGSTDTQYF	0%	0%
CD8	TRAV26-2*01	TRAJ39*01	CILYNNAGNMLTF	TRBV7-6	TRBJ1-6*02	CASSLDPKDPPLHF	0%	0%
CD8	TRAV38-2	TRAJ43*01	CAYRSSYNNNDMRF	TRBV13*01	TRBJ1-3*01	CASSLENSGNTIYF	0%	0%
CD8				TRBV7-3	TRBJ1-2*01	CASSLESTYGYTF	1.28%	2.77%
CD4				TRBV5-5	TRBJ1-1*01	CASSLEWGPKNTEAFF	0%	0%
CD4	TRAV10*01	TRAJ42*01	CVVSA*SYGGSQGNLIF	TRBV5-1*01	TRBJ2-5*01	CASSLFMEETQYF	0%	0%
CD4	TRAV23	TRAJ22*01	CATRGSARQLTF	TRBV7-9	TRBJ1-4*01	CASSLGQGNEKLFF	0.12%	0.18%
CD4				TRBV4-2*01	TRBJ2-5*01	CASSLGTVQETQYF	0%	0.03%
CD8				TRBV5-1*01	TRBJ2-3*01	CASSLKTLRGADTQYF	0%	0%
CD4				TRBV7-9	TRBJ2-7*01	CASSLLGGGSYEQYF	0%	0.07%
CD8	TRAV13-1	TRAJ10*01	CAASLTGGGNKLTF	TRBV12	TRBJ1-5*01	CASSLMWSNQPQHF	0%	0%
CD4	TRAV8-3*01	TRAJ30*01	CAVGAPGDDKIIF	TRBV7-2	TRBJ2-7*01	CASSLNRGGEQYF	0%	0%
CD4	TRAV8-4*03	TRAJ52*01	GGTSYGKLTF	TRBV11-2*01	TRBJ2-1*01	CASSLNWGYNEQFF	0%	0%
CD4				TRBV7-8	TRBJ2-1*01	CASSLPTLGTGSTEQFF	0%	0%
CD8	TRAV26-1	TRAJ37*02	CIVRTSNTGKLIF	TRBV5-1*01	TRBJ1-1*01	CASSLRGGEKTEAFF	0%	0%
CD8				TRBV7-9	TRBJ2-1*01	CASSLSGGGSHEQFF	0%	0%
CD8	TRAV19*01	TRAJ18*01	CALKGTRGSTLGRLYF	TRBV27*01	TRBJ1-5*01	CASSLSSGGDNQPQHF	1.67%	3.92%
CD4				TRBV5-1*01	TRBJ1-1*01	CASSLVGMDTEAFF	0%	0%
CD4	TRAV9-2	TRAJ53*01	CALTGGSNYKLTF	TRBV5-1*01	TRBJ2-5*01	CASSPEEETQYF	0%	0%

Cell Type	Max Vα resolved	Max Jα Resolved	CDR3α	Max Vβ Resolved	Max Jβ Resolved	CDR3β	Frequency of CDR3β in 6265 pLN	Frequency of CDR3β in 6265 Spleen
CD8	TRAV29	TRAJ39*01	CAASGGNNAGNMLTF	TRBV13*01	TRBJ2-1*01	CASSPGGPRAFF	0%	0%
CD4	TRAV12-3*02	TRAJ6*01	CAMRSGGSYIPTF	TRBV4-2*01	TRBJ2-1*01	CASSPGLAGDNEQFF	0%	0%
CD4				TRBV5-1*01	TRBJ1-2*01	CASSPGLGGYGYTF	0%	0%
CD4	TRAV38-2	TRAJ40*01	CAYRKTLAGTYKYIF	TRBV9*01	TRBJ2-1*01	CASSPGTSGGNEQFF	0%	0%
CD4	TRAV13-2	TRAJ11*01	CAEIGAKDSGYSTLTF	TRBV3-1*01	TRBJ2-3*01	CASSPGYPQGAVTDTQYF	0%	0%
CD8				TRBV6-1*01	TRBJ1-5*01	CASSPNRGNNQPQHF	0%	0%
CD4	TRAV23	TRAJ35*01	CAPRIGFGNVLHC	TRBV4-2*01	TRBJ2-1*01	CASSPPTDNEQFF	0%	0%
CD8	TRAV29	TRAJ30*01	CAASDRDDKIIF	TRBV12	TRBJ1-5*01	CASSPRDGNQPQHF	0%	0%
CD8	TRAV26-1	TRAJ11*01	CIVRDSRPKSGYSTLTF	TRBV6-5*01	TRBJ1-2*01	CASSPTGRANYGYTF	0%	0%
CD8	TRAV22*01	TRAJ45*01	CAGRGLYSGGGADGLTF	TRBV4-3	TRBJ2-2*01	CASSQDPRAVDTGELFF	0%	0%
CD4				TRBV3-1*01	TRBJ1-1*01	CASSQDSGTEAFF	0%	0%
CD8	TRAV26-1	TRAJ28*01	CIVRNGAGSYQLTF	TRBV3-1*01	TRBJ2-7*01	CASSQDTSMSYEQYF	0%	0%
CD8	TRAV21	TRAJ42*01	CAVGSQGNLIF	TRBV3-1*01	TRBJ1-1*01	CASSQDWRGSNTEAFF	2.55%	0%
CD8				TRBV4-3	TRBJ1-1*01	CASSQEIGRQNTEAFF	0%	0%
CD4	TRAV9-2	TRAJ20*01	CALGSYKLSF	TRBV14*01	TRBJ2-5*01	CASSQGISGAQETQYF	0%	0%
CD8	TRAV25*01	TRAJ41*01	CAGLGLSSGYALNF	TRBV4-3	TRBJ2-7*01	CASSQMIAYEQYF	0%	0%
CD8				TRBV5-1*01	TRBJ1-2*01	CASSQRGSDREHGYTF	0%	0%
CD4	TRAV27	TRAJ41*01	CAGAQSGYALNF	TRBV6-5*01	TRBJ2-7*01	CASSQRGTSGGRTYEQYF	0%	0%
CD4	TRAV19*01	TRAJ37*02	CALGSSNTGKLIF	TRBV3-1*01	TRBJ2-5*01	CASSQRKLTGTAYQETQYF	0%	0%
CD4				TRBV7-9	TRBJ1-6*02	CASSRGGQRNSPLHF	0%	0%
CD8	TRAV29	TRAJ49*01	CAASGGNQFYF	TRBV7-9	TRBJ1-2*01	CASSRPPTRTDYGYTF	0%	0%
CD4	TRAV14	TRAJ56*01	CAMRRPFTGANSKLTF	TRBV11-2*01	TRBJ2-1*01	CASSRWTSVKNEQFF	0%	0%
CD4	TRAV17*01	TRAJ22*01	CASSLASGSARQLTF	TRBV5-4	TRBJ2-2*01	CASSSDVGAGELFF	0%	0%
CD4	TRAV8-4*03	TRAJ5*01	CAVTPMDTGRRALTF	TRBV11-2*01	TRBJ1-2*01	CASSSGGTASGYTF	0%	0%
CD8	TRAV27*01	TRAJ31*01	CAGERNNARLMF	TRBV5-1*01	TRBJ1-4*01	CASSSHRDGPTNEKLFF	0%	0%
CD4				TRBV7-6	TRBJ2-3*01	CASSSSLAGGADTQYF	0%	0%
CD4				TRBV7-9*01	TRBJ2-7*01	CASSSVSDYEQYF	0%	0%
CD4				TRBV12	TRBJ1-5*01	CASSTGWDQPQHF	0%	0%
CD8	TRAV8-1*01	TRAJ39*01	CAVNANNAGNMLTF	TRBV12	TRBJ2-2*01	CASSTPTSDTGELFF	0%	0%
CD8	TRAV14	TRAJ48*01	CAMRENFGNEKLTF	TRBV6-5*01	TRBJ1-1*01	CASSTQGNTEAFF	0%	0%
CD4	TRAV12-3	TRAJ42*01	CAMSAIGGSQGNLIF	TRBV5-5	TRBJ1-5*01	CASSVNGVRDQPQHF	0%	0%
CD8				TRBV9*01	TRBJ2-1*01	CASSVPRTGPPIF	0%	0%
-----				TRBV13	TRBJ1-1*01	CASSVTGVGWKNTEAFF	0%	0%
CD8	TRAV14	TRAJ57*01	CAMREGVEGGSEKLVF	TRBV9	TRBJ2-6*01	CASSVVGGRSHSGANVLTF	0%	0%
CD8				TRBV6-2	TRBJ2-3*01	CASSWTVGNTDTQYF	0%	0%
CD8	TRAV8-4*03	TRAJ10*01	CAVSESLTGGGNKLTF	TRBV6-5*01	TRBJ1-4*01	CASSYDRAEKLFF	0%	0%
CD4				TRBV6-5*01	TRBJ2-4*01	CASSYQGGAGKNIQYF	0%	0%
CD4	TRAV30*01	TRAJ58*01	CGARETSGSRLTF	TRBV6-5*01	TRBJ2-7*01	CASSYSGTGYYEQYF	0%	0.03%
CD4				TRBV6-5*01	TRBJ1-2*01	CASSYSPQGHTYGYTF	0%	0%
-----				TRBV27*01	TRBJ2-2*01	CASTLLVGSNTGELFF	0%	0%

Cell Type	Max Vα resolved	Max Jα Resolved	CDR3α	Max Vβ Resolved	Max Jβ Resolved	CDR3β	Frequency of CDR3β in 6265 pLN	Frequency of CDR3β in 6265 Spleen
CD8				TRBV6-5*01	TRBJ1-2*01	CASTQTGSNYGYTF	0%	0%
CD8				TRBV4-1	TRBJ2-3*01	CASTRAGPKDTQYF	0%	0%
-----				TRBV12-5*01	TRBJ1-1*01	CASVKGTELGTEAFF	0%	0%
CD4				TRBV15*02	TRBJ1-2*01	CATSTRDRVRYGYTF	0%	0%
CD4				TRBV20-1	TRBJ1-1*01	CRAYRGTNTEAFF	0%	0%
CD4				TRBV20-1	TRBJ2-7*01	CSAKASAYEQYF	0%	0%
CD4	TRAV26-1	TRAJ32*01	CIVRARTMNYGGATNKLIF	TRBV20-1	TRBJ1-1*01	CSAKNPNTEAFF	0%	0%
CD4	TRAV8-1*01	TRAJ43*01	CAVRQGSNDMRF	TRBV20-1	TRBJ2-7*01	CSANPGRPGEQYF	0%	0%
CD4				TRBV20-1	TRBJ1-1*01	CSAPAELIEAFF	0%	0%
CD4	TRAV9-2	TRAJ12*01	CALMDSSYKLIF	TRBV20-1	TRBJ2-2*01	CSARDTGTAGTGELFF	0%	0%
CD8	TRAV29	TRAJ34*01	CAASSNTDKLIF	TRBV20-1	TRBJ2-7*01	CSARGTSAYEQYF	0%	0%
CD4				TRBV20-1	TRBJ2-3*01	CSARTRGTDTQYF	0%	0%
CD8				TRBV20-1	TRBJ2-7*01	CSASIAGGAYEQYF	0%	0%
CD4	TRAV12-3*02	TRAJ42*01	CAMSAGSQGNLIF	TRBV20-1	TRBJ2-3*01	CSASRSGGKYPGSQYF	0%	0%
CD8	TRAV3*01	TRAJ13*02	CAVSRAGGYQKVTF				0%	0%
CD8	TRAV13-1	TRAJ49*01	CAATGNQFYF				0%	0%
CD4	TRAV29	TRAJ28*01	CGGAGSYQLTF				0%	0%
CD8	TRAV30*01	TRAJ52*01	CGTERGGMNAGGTSYGKLTF				0%	0%
CD8	TRAV12-1*01	TRAJ10*01	CVVNGGGNKLTF				0%	0%
CD8	TRAV14	TRAJ11*01	CAMRDSGYSTLTF				0%	0%
CD4	TRAV38-2	TRAJ57*01	CAYRSARRRASGSEKLVF				0%	0%
CD8	TRAV12-2	TRAJ16*01	CALRFSDGQKLLF				0%	0%
CD8	TRAV29	TRAJ29*01	CAASPNSGNTPLVF				0%	0%
CD4	TRAV22*01	TRAJ3*01	CAVSLYSSASKIIF				0%	0%
CD4	TRAV13-1*01	TRAJ7*01	CAASMGGNNRLAF				0%	0%
CD4	TRAV30*01	TRAJ52*01	CGTEPSNAGGTSYGKLTF				0%	0%
CD4	TRAV14	TRAJ9*01	CAMRDPTGGFKTIF				0%	0%
CD4	TRAV13-1*01	TRAJ8*01	CAATVTGFQKLVF				0%	0%
CD8	TRAV12-3*02	TRAJ31*01	CAMRGNNNARLMF				0%	0%
CD4	TRAV8-1*01	TRAJ42*01	CAVNAGGSQGNLIF				0%	0%
CD8	TRAV4*01	TRAJ4*01	CLVGDGFSGGYNKLIF				0%	0%
CD8	TRAV12-3	TRAJ53*01	CAMSERGGSNYKLTF				0%	0%
CD8	TRAV3*01	TRAJ18*01	CAVRRSTLGRLYF				0%	0%

Table S10. Frequency of complementarity determining region 3 heavy chain (CDR3H) sequences from B cells reactive to insulin. B cell receptor (BCR) CDR3H amino acid (AA) sequences corresponding to newly (first two sequences) and previously (last two sequences) (46) identified insulin-reactive B cells derived from peripheral blood were identified in $CD19^+$ B cells isolated from pancreatic-draining lymph node (pLN), "irrelevant" mesenteric and/or inguinal lymph node (iLN), and spleen samples obtained from Network for Pancreatic Organ Donors with Diabetes (nPOD) donors with T1D, without T1D (control), and with Flatbush/other diabetes (FBD) using the Adaptive immunosequencing platform. Here are listed, the BCR CDR3 AA sequence previously reported by Wardemann et al. (46); the V, D, and J gene families that made up the reported BCRs (HV, J, and JH, respectively, on the left side of the table); the nPOD donor and tissue from which the BCR CDR3 AA sequence was identified; the nPOD donor disease state; the number of reads and read frequency corresponding to the BCR CDR3 AA sequence; and the V, D, and J gene families that were determined to make up the BCRs identified from nPOD donors (HV, J, and JH, respectively, on the right side of the table).

Amino Acid Sequence (citation)	IgHV	IgHD	IgHJ	Disease Status	nPOD ID	Tissue	Matching Amino Acid	Reads	Frequency	HV	D	JH
DDYYDSSGYYP (John Cambier, Previously Unreported Data)	03-30		05*02	T1D	6161	pLN	CTSVE**DDYYDSSGYYP**DW	107	0.64%	03-49	03-22*01	04-01*02
				Control	6271	pLN	CAMR**DDYYDSSGYYP**RFDYW	75	0.36%	07-04_1*02	03-22*01	04-01*02
						Spleen	CAKG**DDYYDSSGYYP**W	22	0.10%	03-43	03-22*01	05-01*02
				FBD	6284	pLN	CAKA**DDYYDSSGYYP**SLYYFDYW	4	0.02%	03-23	03-22*01	04-01*02
RRRMDV (John Cambier, Previously Unreported Data)	03-48		06*02	T1D	6161	Spleen	CAGGGGYCSGGSC**RRRMDV**W	282	1.22%	04	02-15*01	06-01*02
				Control	6289	pLN	CARDRITG**RRRMDV**W	20	0.08%	04-34	01	06-01*03
						pLN	CARDRITG**RRRMDV**W	9	0.03%	04-34	01	06-01*03
				T2D	6274	Spleen	CARG**RRRMDV**W	7	0.03%	04	01-14*01	06-01*02
LWFGSYYYYGMDV (46)	03-7	03-10	6	T1D	6243	Spleen	CARIGGL**LWFGSYYYYGMDV**W	15	0.07%	02-26*01	03-10*01	06-01*02
DRSYYYYGMDV (46)	03-30	unresolved	6	Control	6279	iLN	CVRDLSGHCGG**DRSYYYYGMDV**W	31	0.15%	01-17*02	02-21*02	06-01*02
				FBD	6284	pLN	CARDDYG**DRSYYYYGMDV**W	21	0.08%	04-34	04-17*01	06-01*02
				T1D	6263	Spleen	CARDHVPAA**DRSYYYYGMDV**W	10	0.03%	04	02-02	06-01*02
				T1D	6243	Spleen	CAR**DRSYYYYGMDV**W	5	0.02%	**03**	unresolved	06-01*02
				T1D	6266	Spleen	CAKGVVDTAEIAG**DRSYYYYGMDV**W	2	0.01%	03-23	05	06-01*02