| | A | Duration of | C-peptide* | |
|-------------|----------|----------------|------------|--|
| TID Subject | Age | disease (days) | 1 1 | |
| K743T1D | 33 | 387 | D | |
| K685T1D | 18 | 713 | NA | |
| K276T1D | 10 | 883 | NA | |
| K787T1D | 41 | 140 | D | |
| K807T1D | 19 | 468 | NA | |
| K814T1D | 47 | 541 | D | |
| K843T1D | 12 | 383 | D | |
| K847T1D | 26 | 161 | D | |
| K151T1D | 16 | 1653 | NA | |
| K180T1D | 15 | 2482 | NA | |
| K877T1D | 27 | 270 | D | |
| K878T1D | 12 | 240 | D | |
| K899T1D | 25 | 70 | D | |
| K278T1D | 59 | 8472 | ND | |
| K454T1D | 27 | 5110 | NA | |

Supplemental Table 1: T1D Patient Information.

*random serum C-peptide was obtained within 6 months of the cellular assay.

D: detectable at >0.05 ng/mL; ND: not detectable at limit of detection = 0.05 ng/mL; NA: not

measured

Supplemental Table 2: Frequency of epitopes identified from oligoclones

| Ĩ | | | | |
|-------------|---|-------------------------------|-----------------------|--|
| T1D Subject | # of oligo- | Name of | # of oligo- clones | |
| 5 | clones generated | Peptide | positive | |
| | 4 oligo-clones generated from 41 CD38+ cells | PPI78-90 ^{K88S} | 4 | |
| | | GADp15 | 3 | |
| | | GADp45 | 1 | |
| | | GADp47 | 1 | |
| K787T1D | | GADp48 | 1 | |
| | | GADp55 | 1 | |
| | | Zn8Tp28 | 1 | |
| | | ZnT8p36 | 1 | |
| | | IGp39 | 1 | |
| | | ChgA: NEI | | |
| | | PPI78-90 ^{K88S} | 5 | |
| | 5 oligo-clones | GADp23 | 1 | |
| K276T1D | from 53 CD38+ | ZnT8p28 | 2 | |
| | cells | Igp31 | 1 | |
| | | ChgA: NEI | | |
| | | PPI78-90 ^{K88S} | 6 | |
| | ChgA: NEI5 oligo-clonesPPI78-90K88Sfrom 53 CD38+GADp23cellsIgp31ChgA: NEIChgA: NEIPPI78-90K88SGADp28GADp29GADp326 oligo-clonesGADp3462 CD38+ cellsGADp35ZnT8p28Igp23ChgA: NEIIgp231 oligo-cloneGADp70 | GADp28 | 1 | |
| K743T1D | | GADp29 | 1 | |
| | | GADp32 | 1 | |
| | | GADp34 | 1 | |
| | | 1 | | |
| | | ZnT8p28 | 4 | |
| | | Igp23 | 1 | |
| | | ChgA: NEI | | |
| K877T1D | 1 oligo-clone | | 1 | |
| | from 4 CD38+ | GADp70 | | |
| | cells | DD170 00K885 | 2 | |
| K877T1D | | $\frac{PPI/8-90^{1000}}{CAD}$ | <u> </u> | |
| | 4 oligo-clones from 40 resting memory cells | GADP10 | | |
| | | | 1 | |
| | | Zn18p28 | 1 | |
| | | IGRP: NEI | | |
| | | ChgA: NEI | | |

NEI: no epitope identified

Supplemental Table 3: Top 10 TCR Vbeta VDJ sequences of PPI₇₈₋₉₀^{K88S} specific T cells

isolated from CD45RO+CD38+ oligoclones.

| Nucleotide | Amino Acid | TCRB V | TCRB D | TCRB J | Freque |
|----------------------|------------|--------|-----------|--------|--------|
| | | region | region | region | ncy |
| TGTGCCAGCAGCCCCCAGG | CASSPQGTT | V07-09 | D01- | J01- | 26.9% |
| GTACTACGGGAAACACCAT | GNTIYF | | 01*01 | 03*01 | |
| ATATTTT | | | | | |
| TGTGCCAGCTCACCTAAAA | CASSPKMY | V18- | D02-01 | J02- | 15.4% |
| TGTATGAGCAGTTCTTC | EQFF | 01*01 | | 01*01 | |
| TGTGCCAGCAGCTTGGGCC | CASSLGRA | V07- | D02- | J01- | 12.2% |
| GGGCCGGGGGGGGGAATCA | GAGNQPQH | 08*01 | 01*01 | 05*01 | |
| GCCCCAGCATTTT | F | | | | |
| TGTGCCAGCAGCTCCCCGA | CASSSPRSP | V09-01 | D02- | J02- | 6.5% |
| GGTCTCCAGCGGGGGGGGGG | AGGRYNEQ | | 01*01 | 01*01 | |
| GTACAATGAGCAGTTCTTC | FF | | | | |
| TGTGCCAGCAGCGCGGCTG | CASSAAAS | V05- | D02- | J02- | 6.5% |
| CTAGCGGGGGGGCCAGTCAG | GGPVRVTD | 04*01 | 01*01 | 03*01 | |
| GGTCACAGATACGCAGTAT | TQYF | | | | |
| TTT | | | | | |
| TGTGCCAGCAGCTTTTGGA | CASSFWTG | V07-09 | D02- | J01- | 5.9% |
| CGGGGGGGGAATCAGCCCCA | GNQPQHF | | 01*01 | 05*01 | |
| GCATTTT | | | | | |
| TGTGCCAGCAGCCTAGACA | CASSLDRIN | V11- | D01- | J01- | 3.2% |
| GAATTAATGAAAAACTGTT | EKLFF | 02*02 | 01*01 | 04*01 | |
| TTTT | | | | | |
| TGTGCCAGCAGTTACGGAAT | CASSYGIGRA | V06-06 | D02- | J02- | 2.3% |
| AGGGAGGGCAGATACGCAGT | DTQYF | | 01*02 | 03*01 | |
| ATTTT | | | | | |
| TGTGCCAGCAGCTTCGGGA | CASSFGTGR | V07-09 | unresolve | J01- | 1.7% |
| CGGGGAGAAGGGATGGCTA | RDGYTF | | d | 02*01 | |
| CACCTTC | | | | | |
| TGTGCCAGCAGCTTGCAGG | CASSLQGT | V07-09 | D01- | J01- | 0.4% |
| GAACGGCTGGAAACACCAT | AGNTIYF | | 01*01 | 03*01 | |
| ATATTT | | | | | |

Italic indicates this sequence is also detected in the memory population of T cells with a

frequency of $3.7/10^6$.



Supplemental Figure 1. Determining *in vivo* proliferation and persistence of PPI₇₈₋₉₀^{K88S} specific T cells.

PPI₇₈₋₉₀^{K88S}-specific T cells identified by CD154 epitope mapping from subject K276T1D were enriched and selected and TCR Vbeta chains sequenced. Plot includes top 10 T cells with unique rearranged CDR3 region according to the frequency of their sequence reads. X-axis: T Cell frequency in resting memory. Y-axis: Frequency from TCR Vbeta sequencing of memory (CD45RO+) T cells obtained 4 months after CD154 epitope mapping assay. One identical rearranged CDR3 region with high counts was identified in the memory fraction of PBMC.