SUPPLEMENTARY DATA

Supplementary Table 1. Information on DRB1*04:01 type 1 diabetic subjects used for study.

Subject ID	Age[a]	Gender[b]	Time since diagnosis[c]	Auto-antibodies[d]
T1D #1	17	M	7.8 years	GAD
T1D #2	34	F	5.0 years	GAD, IAA
T1D #3	18	M	1.6 years	GAD, IAA
T1D #4	63	F	3.3 years	IAA
T1D #5	31	M	5.6 years	GAD, IAA, IA2, ZnT8
T1D #6	22	F	3.3 years	GAD, IAA
T1D #7	26	F	6.3 years	GAD, IAA, IA2
T1D #8	25	F	8.2 years	GAD, IAA, IA2, ZnT8
T1D #9	17	M	5.4 years	IAA, IA2
T1D #10	24	M	3.2 years	GAD, IAA, IA2, ZnT8
T1D #11	27	M	4.2 years	GAD, IAA, IA2, ZnT8
T1D #12	29	M	2.1 years	GAD, IAA
T1D #13	32	M	3.2 years	GAD, IAA, IA2, ZnT8
T1D #14	26	F	2.0 years	GAD, IAA, IA2, ZnT8
T1D #15	45	M	0.7 years	GAD
T1D #16	10	M	2.6 years	GAD, IAA, IA2, ZnT8

[a] The mean age was 27.9 years.

[b] The male to female ratio of the cohort was 10:6.

[c] The average time since diagnosis was 4 years.

[d] GAD denotes glutamic acid decarboxylase 65, IAA denotes insulin, IA2 denotes tyrosine phosphatase-related islet antigen 2, ZnT8 denotes zinc transporter 8

SUPPLEMENTARY DATA

Supplementary Table 2. Information on DRB1*04:01 healthy subjects used for study.

Subject ID	Age[a]	Gender[b]	Auto-antibodies[c]
Control #1	57	F	N/A
Control #2	34	F	N/A
Control #3	20	F	N/A
Control #4	33	F	N/A
Control #5	40	M	N/A
Control #6	27	F	N/A
Control #7	33	M	N/A
Control #8	28	F	N/A
Control #9	44	M	N/A
Control #10	54	M	N/A
Control #11	23	M	N/A
Control #12	40	M	N/A
Control #13	60	F	N/A
Control #14	39	M	N/A
Control #15	61	F	N/A
autoAb+ #1	54	M	GAD
autoAb+ #2	19	F	GAD, IAA
autoAb+ #3	29	M	GAD, IAA
autoAb+ #4	43	F	GAD, IAA
autoAb+ #5	40	F	GAD, IAA
autoAb+ #6	40	M	GAD

[a] The mean age of auto-antibody negative and auto-antibody positive controls was 39.5 and 37.5 years, respectively.

[b] The male to female ratio for auto-antibody negative and auto-antibody positive controls was 7:8 and 3:3, respectively.

[c] GAD denotes glutamic acid decarboxylase 65, IAA denotes insulin

SUPPLEMENTARY DATA

Supplementary Table 3. Sequences and binding affinities for peptides that bind DR*0401.

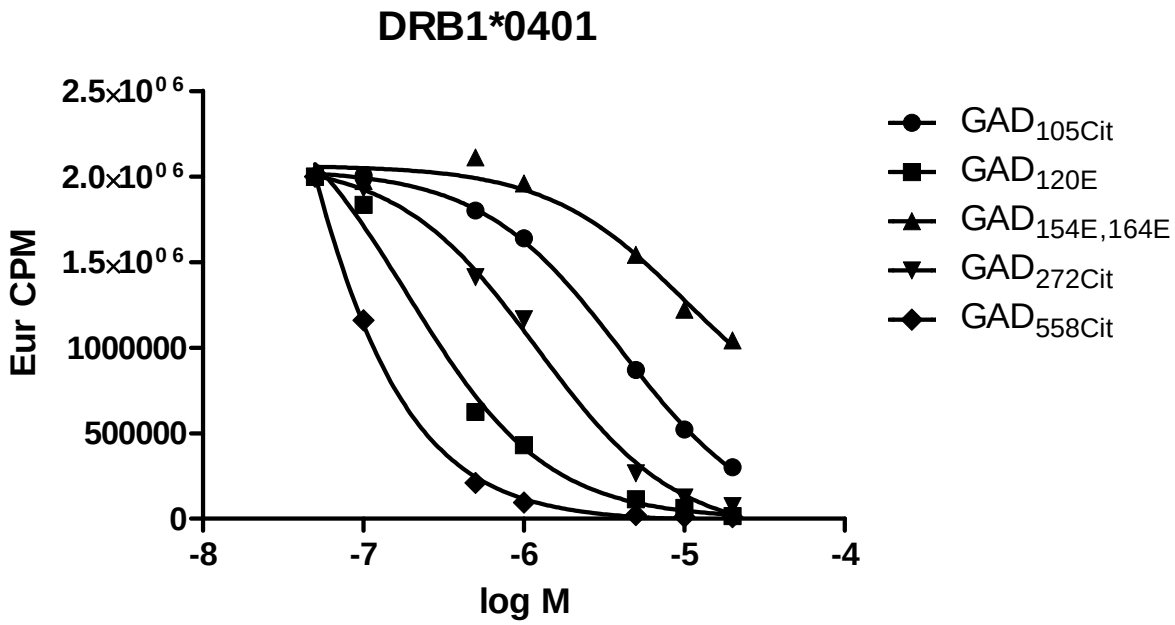
Peptide [a]	Modification [b]	Sequence	Modified IC_{50} (μM)
GAD 73-92	77E	CACDEKPCSCSKVDVNYAFL	5.02
GAD115-127 [a]	120E	MNILLEYVVKSFD	0.20
GAD 153-172 [a]	154E, 164E	PENLEEILMHCETTLKYAIK	12.79
GAD 177-196	181E	RYFNELSTGLDMVGLAADWL	2.70
GAD 321-340	324E	EAKEKGFVPFLVSATAGTTV	5.09
GAD 89-108 [a]	105X	YAFLHATDLLPACDGEXPTL	2.88
GAD 265-284 [a]	272X	KGMAALPXLIAFTSEHSHFS	0.81
GAD 377-396	386X	HKWKLSGVEXANSVTWNPHK	7.94
GAD 441-456	448X	DKALQCGXHVDVFKLWLMW	20.55
GAD 473-492	488X	KCLELAEYLYNIIKNXEGYE	0.89
GAD 481-500	488X	LYNIIKNXEGYEMVFDGKPQ	3.81
GAD 505-524	514X, 522X	CFWYIPPSLXTLEDNEEXMS	3.30
GAD 529-548	536X	VAPVIKAXMMEYGTTMVSYQ	5.23
GAD 545-564	558X	VSYQPLGDKVNFFXMVISNP	8.07
GAD 553-572 [a]	558X	KVNFFXMVISNPAATHQDID	0.04

[a] indicates peptides that were shown to be immunogenic

[b] X denotes a citrullination, E denotes a transglutamination.

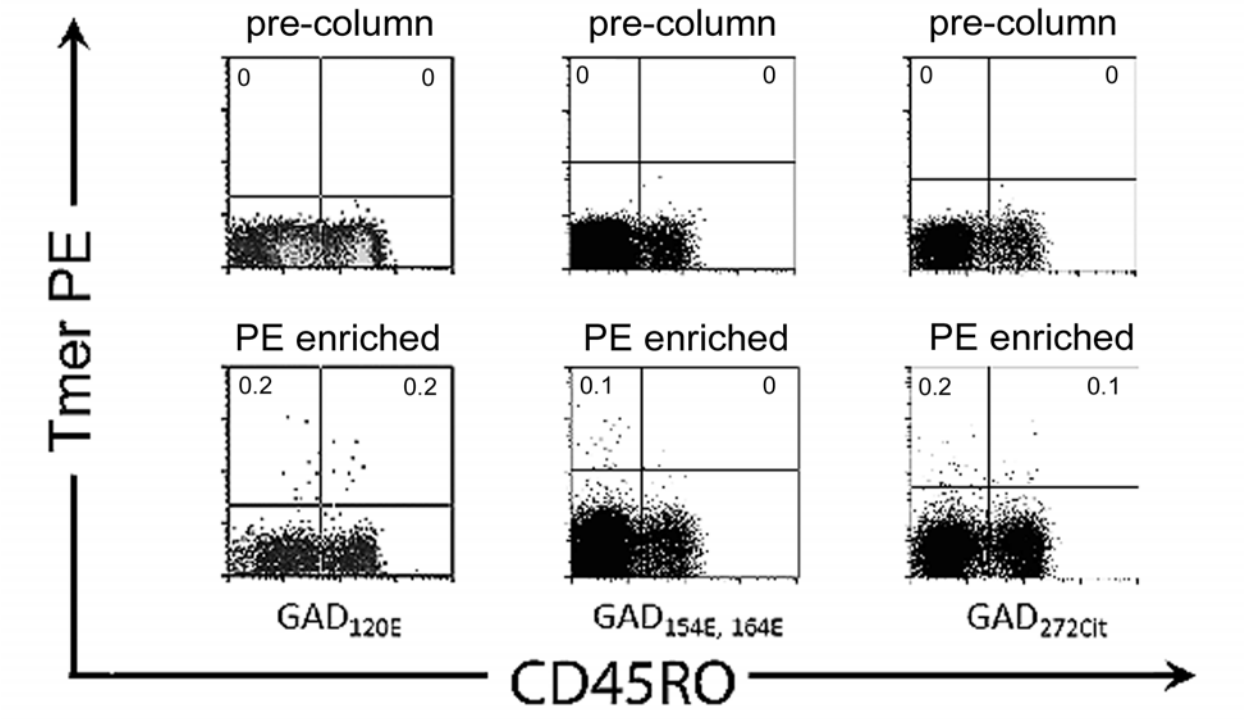
SUPPLEMENTARY DATA

Supplementary Figure 1. Binding affinity curves of modified GAD65 epitopes found to elicit *in vitro* T cell responses. Increasing concentrations of each modified GAD peptide were bound to DR0401 protein in competition with a biotinylated reference peptide. IC_{50} values were determined as the concentration of peptide needed to displace 50% of the reference peptide. A lower IC_{50} value indicates stronger binding.



SUPPLEMENTARY DATA

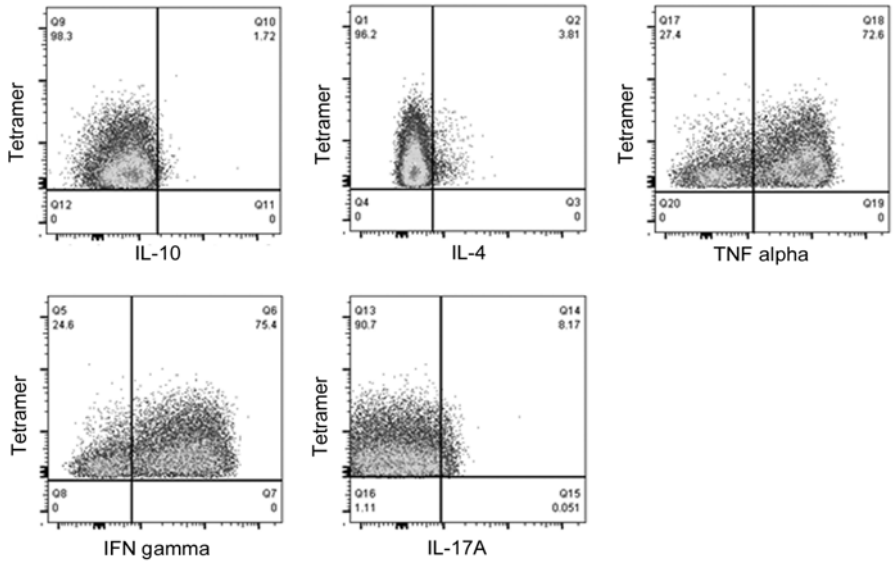
Supplementary Figure 2. Direct ex vivo analysis of T cells specific for modified GAD65 epitopes. A magnetic enrichment procedure was used to visualize T cells specific for modified GAD65 epitopes directly ex vivo. PBMCs were isolated and co-stained *ex vivo* with tetramer and surface antibodies. Each upper panel shows a pre-column fraction, which is used to determine the total number of CD4+ T cells in the unmanipulated sample. Each lower panel shows the corresponding PE enriched fraction, which is used to determine the total number of epitope specific CD4+ T cells in the sample. Cells were gated based on size, viability and lack of CD14/CD19 expression, CD4 expression, and then displayed on a CD45RO versus tetramer plot as shown.



SUPPLEMENTARY DATA

Supplementary Figure 3. Intra-cellular cytokine profiling of PTM specific T cell clones. T cell clones that recognize modified GAD65 epitopes were activated using PMA/ionomycin, and analyzed for intracellular cytokine content by flow cytometry in the presence Brefeldin A. (A) Intracellular cytokine staining results for a representative T cell clone (specific for GAD_{120E}) gated based on size and positive tetramer staining. (B) Cumulative cytokine profiling data for six T cell clones: 3 pairs of clones specific for $GAD_{154E,164E}$ (clones 1 and 2), GAD_{272Cit} (clones 3 and 4), and GAD_{120E} (clones 5 and 6).

A



B