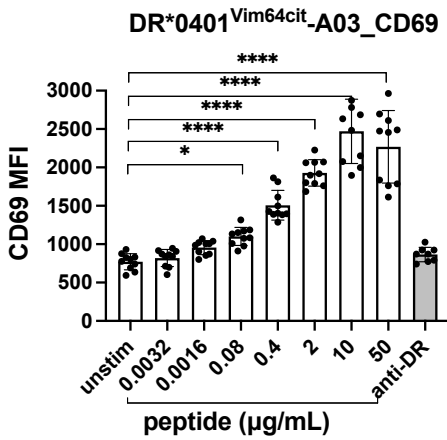
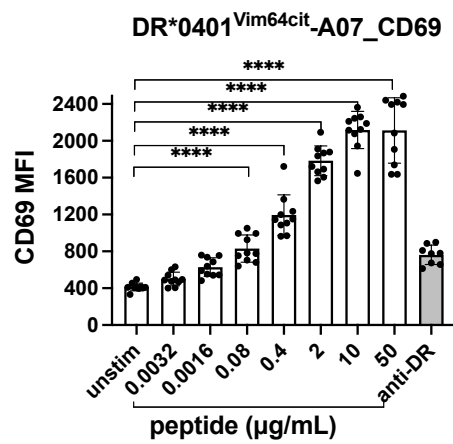
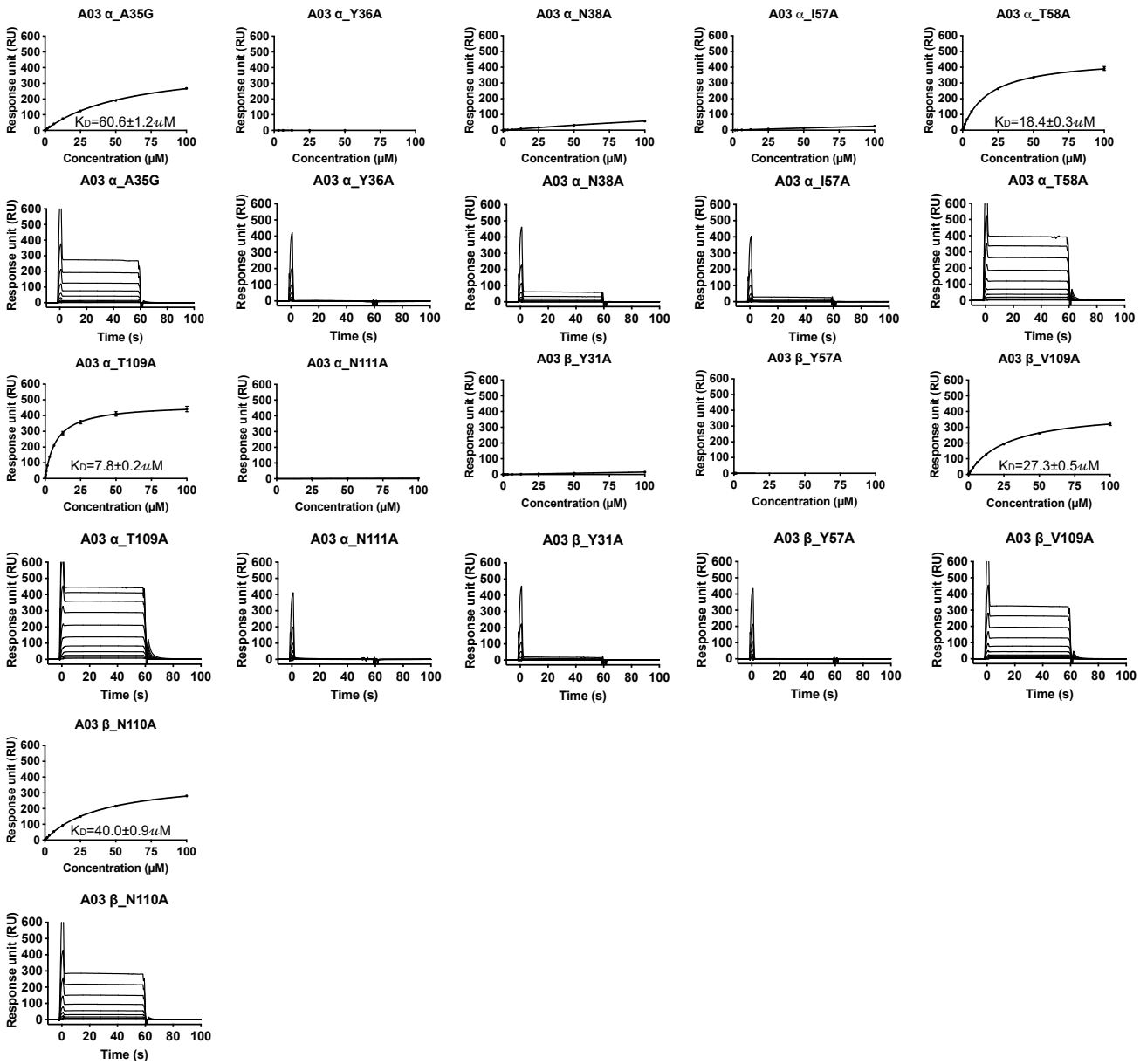


Supplementary Fig 1. Gating strategies for sorting HLA-DR4^{Vim-64cit59-71}₋ and HLA-DR4^{α-eno-15cit10-22}₋-specific CD4⁺ T cells. **a** Representative gating strategy for the detection of HLA-DR4^{Vim-64cit59-71}₋ and HLA-DR4^{α-eno-15cit10-22}₋-specific CD4⁺ T cells from the draining lymph nodes of immunized HLA-DR4 mice, which includes gating on CD62L^{lo}CD3⁺ cells prior to gating on CD4⁺ cells. Numbers in black type indicate percentage of cells within a gate. **b** Representative gating strategy for the detection of HLA-DR4^{Vim-64cit59-71}, HLA-DR4^{α-eno-15cit10-22} and HLA-DR4^{α-eno-15cit10-22V20G}₋ specific CD4⁺ T cells in PBMC isolated from HLA-DR4⁺ RA donors or healthy controls. Numbers in black type indicate percentage of cells within a gate. Shown is sample from RA donor 2.

a**b**

Supplementary Fig. 2. Antigen reactivity of A03 and A07 TCRs toward HLA-DR4^{Vim-64cit59-71}. Expression of CD69 on the surface of **a** A03 TCR transduced SKW-3 cell lines or **b** A07 TCR transduced SKW-3 cell lines stimulated overnight with serial dilution of vim64-cit 59-71 peptide-pulsed BLCL 9031. All samples were performed in duplicates and the black dots are presented as the mean fluorescence intensity (MFI) of average of duplicated values from five independent experiments (n=5). Anti-HLA-DR4 antibody used as control. P values were determined by one way ANOVA with Dunnett's multiple comparison testing, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.002$, **** $P < 0.0001$ and error bars represent \pm s.e.m.. Source data are provided as a Source Data file.

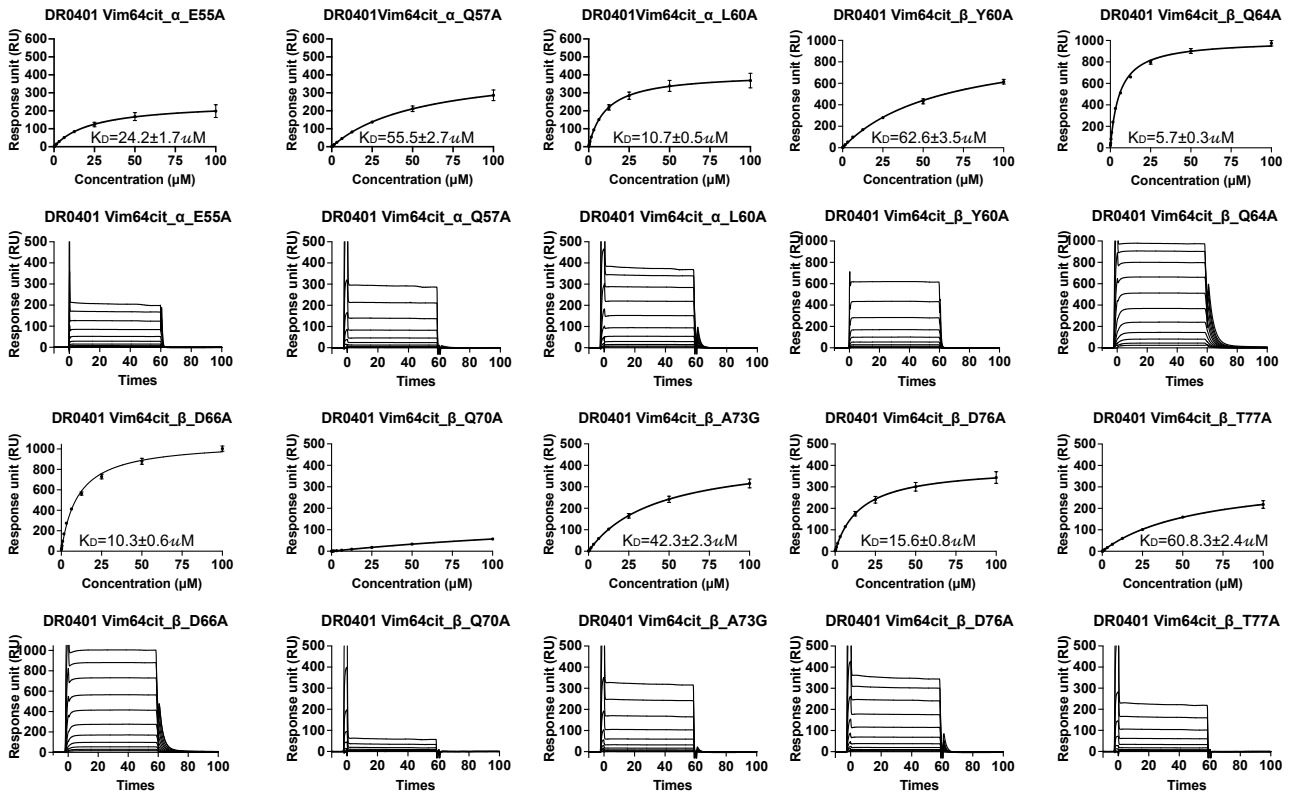
A03 TCR_HLA-DR4^{Vim-64cit59-71}



Supplementary Fig. 3. Affinity analysis of point mutations on A03 TCR toward HLA-DR4^{Vim-64cit59-71}. The equilibrium affinity constants (K_D) of A03 TCR toward HLA-DR4^{Vim-64cit59-71} for point mutations was determined by SPR. All data derived from three independent experiments ($n=3$) and a single ligand binding model was used for curve fitting. The maximal TCRs concentration used is $100 \mu\text{M}$ equal to wild type TCR concentration. HLA-DR4^{CLIP} was used as reference flow cell to control nonspecific binding. Equilibrium response curves were normalised against the calculated maximum response and the measurements then combined. Data are mean \pm standard error, s.e.m.. Source data are provided as a Source Data file.

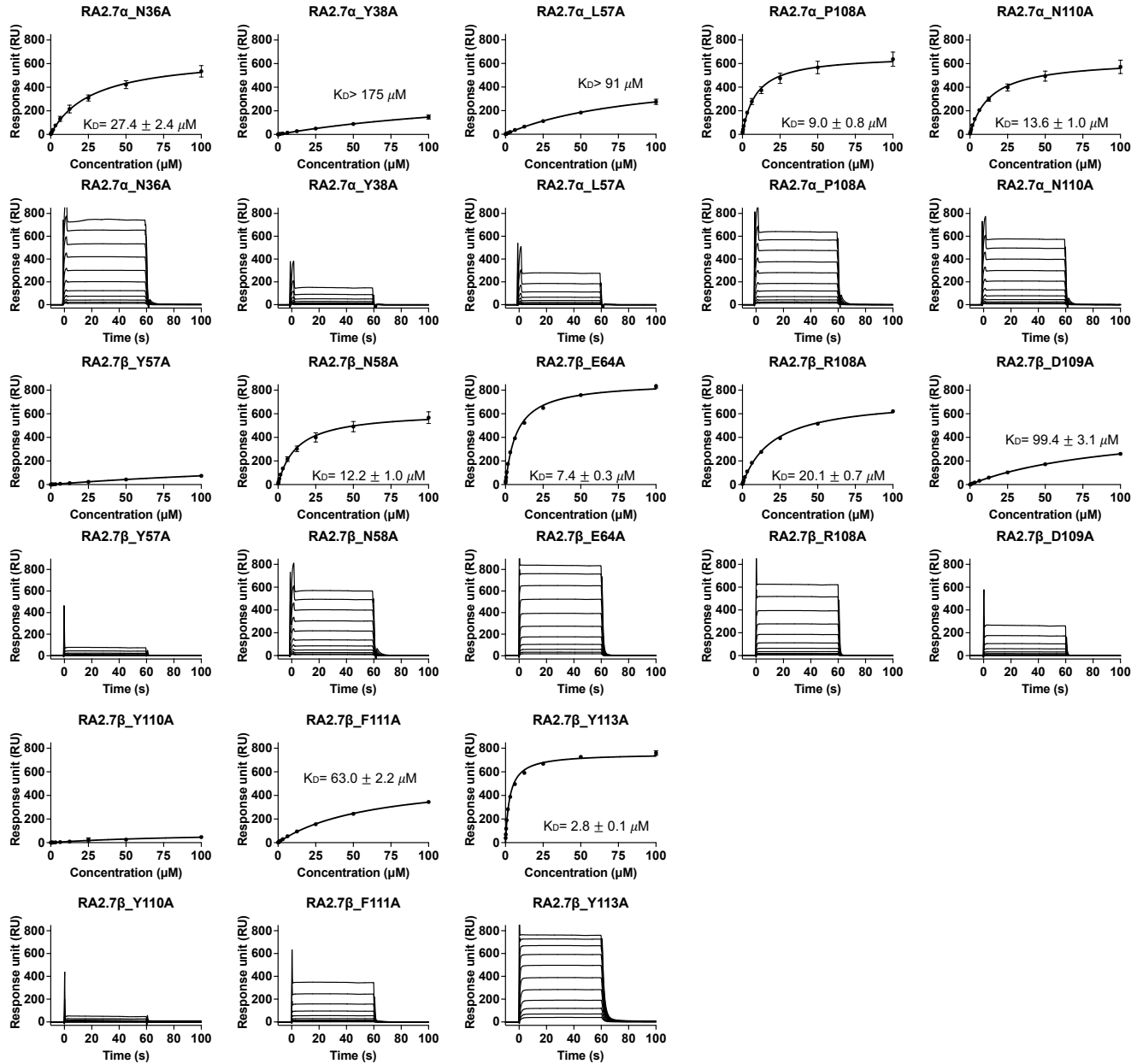
A03 TCR_HLA-DR4^{Vim-64cit59-71} mutants

A03 TCR



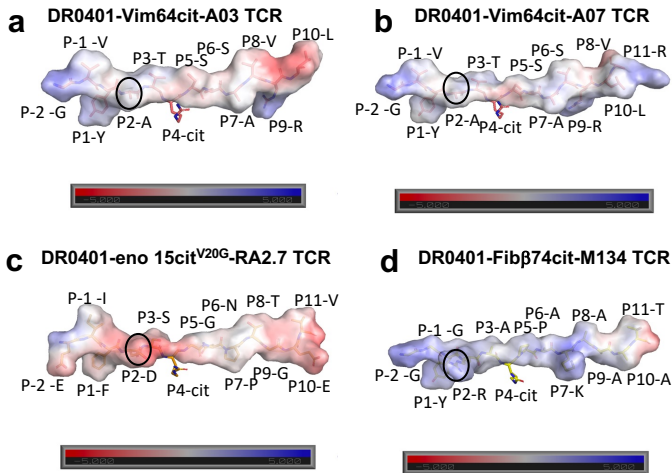
Supplementary Fig. 4. Affinity analysis of A03 TCR toward point mutation of HLA-DR4^{Vim-64cit59-71}. Binding analysis of A03 TCR toward each point mutation of HLA-DR4^{Vim-64cit59-71} was determined by SPR. All data derived from two independent experiments (n=2) and K_D determination using a single ligand binding model. To control nonspecific binding, HLA-DR4^{CLIP} was used as reference flow cell. Equilibrium response curves were normalised against the calculated maximum response and the measurements then combined. Data are mean \pm standard error, s.e.m.. Source data are provided as a Source Data file.

RA2.7 TCR_HLA-DR4 α -eno-15cit10-22V20G

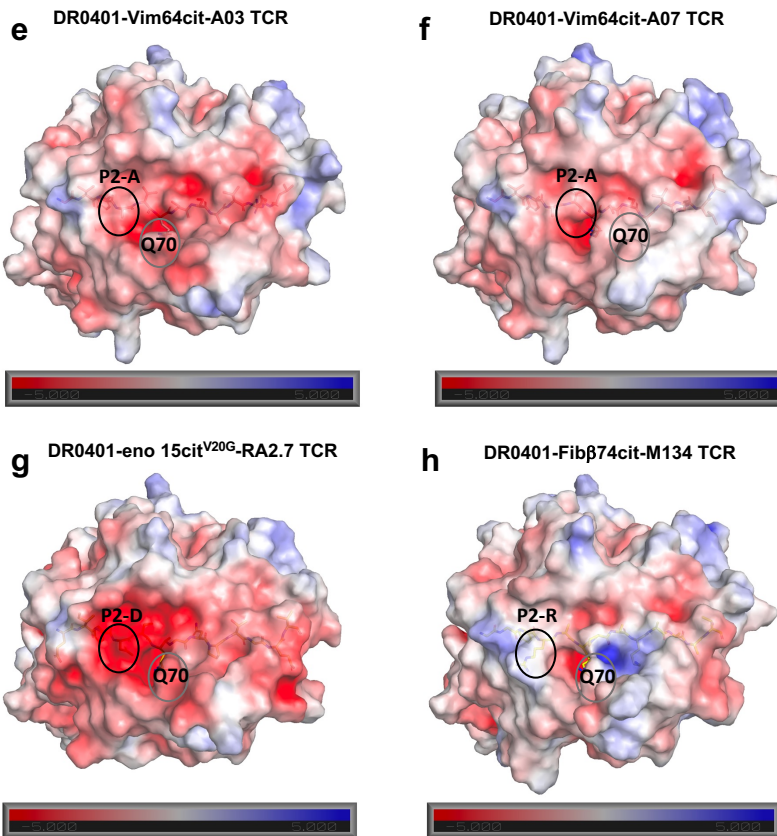


Supplementary Fig. 5. Binding affinity measurement of RA2.7 TCR point mutations towards HLA-DR4 α -eno-15cit10-22V20G. All SPR data were derived from three independent experiments ($n=3$) for K_D determination and curve fitting with a single ligand binding model. Maximal TCRs concentration used is $100 \mu\text{M}$ and HLA-DR4^{CLIP} was used as reference flow cell to control nonspecific binding. Equilibrium response curves were normalised against the calculated maximum response and the measurements then combined. Data are mean \pm standard error, s.e.m.. Source data are provided as a Source Data file.

Electro density map of peptides in ternary complex

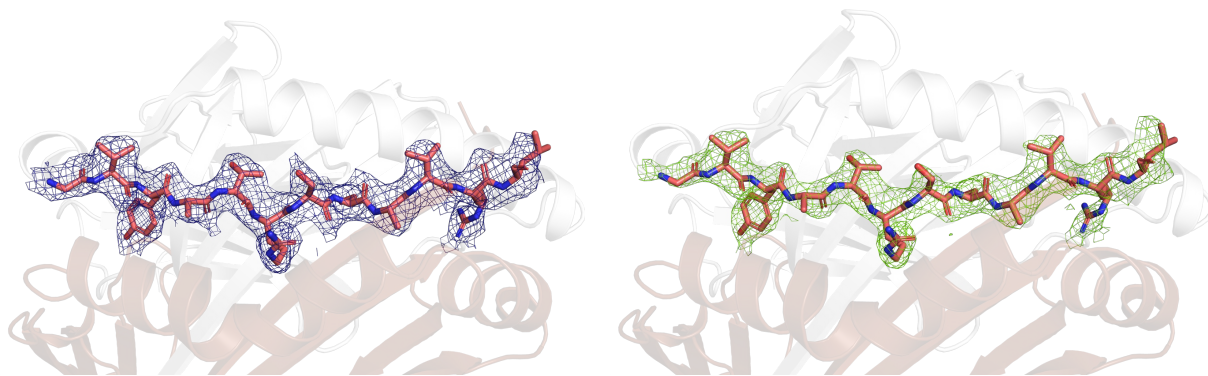


Electro density map of peptides-MHC in ternary complex

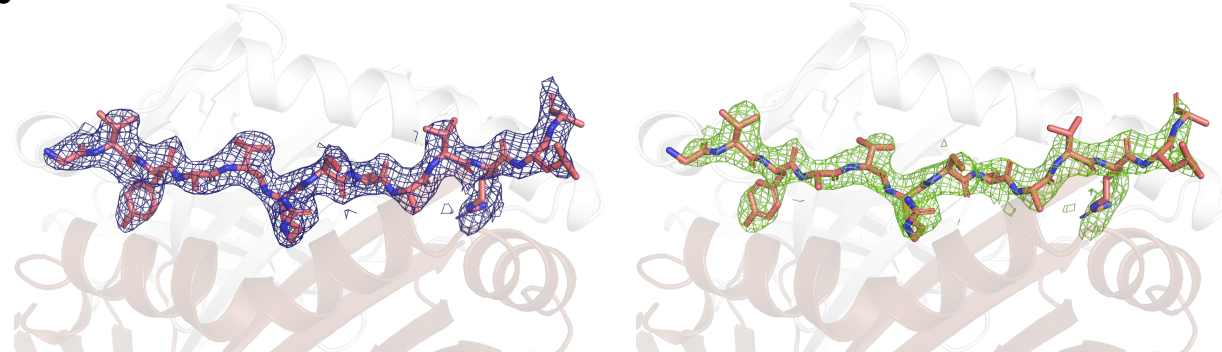


Supplementary Fig. 6. Adaptive Poisson Boltzmann Solver-generated electrostatic surface of peptide or pHLA in ternary complexes (red, negative; blue, positive; white, neutral). The view from the side, looking straight at the peptide binding groove of peptide **a** HLA-DR4^{Vim-64cit59-71}-A03 TCR complex, **b** HLA-DR4^{Vim-64cit59-71}-A07 TCR complex, **c** HLA-DR4 ^{α -eno-15cit10-22V20G}-RA2.7 TCR complex, **d** HLA-DR4^{-Fib β -74cit}-M134 TCR complex. The view from the top, looking straight into the peptide binding groove from **e** HLA-DR4^{Vim-64cit59-71}-A03 TCR complex, **f** HLA-DR4^{Vim-64cit59-71}-A07 TCR complex, **g** HLA-DR4 ^{α -eno-15cit10-22V20G}-RA2.7 TCR complex, **h** HLA-DR4^{-Fib β -74cit}-M134 TCR complex. Black circle is the position where P2 residue is located, grey circle is the position where the SE Gln⁷⁰ β is located on the HLA-DR4 β -chain.

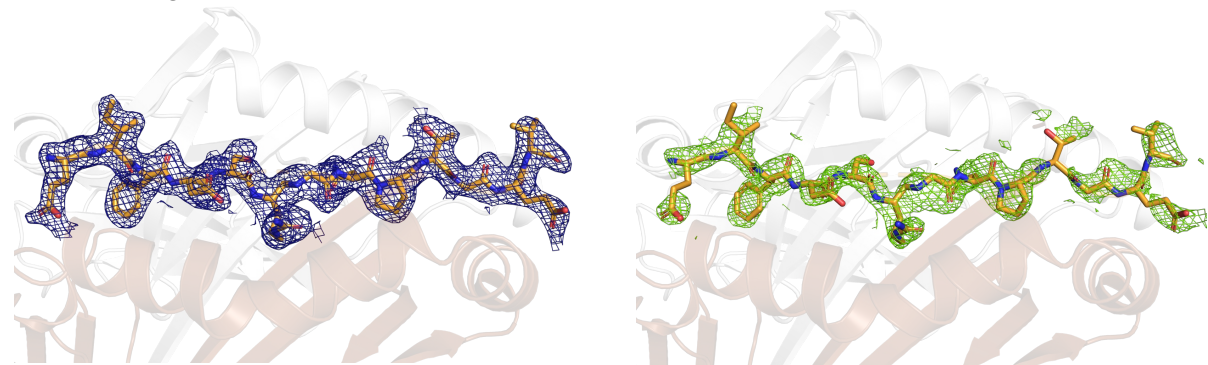
a A03 TCR-HLA-DR4^{Vim-64cit59-71}



b A07 TCR-HLA-DR4^{Vim-64cit59-71}



c RA2.7 TCR-HLA-DR4^{α-eno15cit10-22V20G}



Supplementary Fig. 7. Peptide antigen electron density map. Electron density map of the peptide antigen for **a** A03 TCR-HLA-DR4^{Vim-64cit59-71}, **b** A07 TCR-HLA-DR4^{Vim-64cit59-71}, and **c** RA2.7 TCR-HLA-DR4^{α-eno15cit10-22V20G} complexes are presented in refined 2mF_o-DF_c map (left; blue mesh) and SA Omit map (right; green mesh), respectively, contoured at 1σ. The HLA-DR4 α and β chains are coloured in white and brown, respectively. Vim-64cit₅₉₋₇₁ and α-eno15cit₁₀₋₂₂ peptides are coloured in pink and orange, respectively.

Supplementary Table 1. Paired TCR $\alpha\beta$ sequences of confirmed HLA-DR4 α -eno-15cit10-22V20G-specific CD4⁺ cells isolated from peripheral blood of ACPA⁺ RA donor and HLA-DR4⁺ healthy control donors. Epitope specificity was verified by tetramer staining of TCR transfectants.

Subject	TRAV	TRAJ	CDR1 α	CDR2 α	CDR3 α	TRBV	TBRD	TRBJ	CDR1 β	CDR2 β	CDR3 β
RA donor 2	26-1	49	TISGNEY	GLKNN	CIVRASNTGNQFYF	20-1	2	2-7	DFQATT	SNEGSKA	CSAATGTSGYEQYF
RA donor 2	27	26	SVFSS	VVTGGEV	CAGKAGNYGQNFVF	19	1	2-2	LNHDA	SQIVND	CASSTGGQNTGELFF
HC 10195	26-1	53	TISGNEY	GLKNN	CIVRTSGGSNYKLTF	2	1	2-1	SNHLY	FYNNEI	CAGTYWNEQFF
HC 4737	26-1*	56	TISGNEY	GLKNN	CIVRVAGANSKLTF	5-4	1	2-7	SGHNT	YYREEE	CASSYDLAGPYEQYF
HC 4737	35	39	SIFNT	LYKAGEL	CAGRNNAGNMLTF	2	2	1-2	SNHLY	FYNNEI	CASNVIINYGTYF

RA = rheumatoid arthritis, HC = healthy control.

* Two cells isolated for this clone

CDR3 nucleotide sequences are listed in Supplementary Table 10.

Supplementary Table 2. Data collection and refinement statistics

	A03 TCR-HLA- DR4 ^{Vim-64cit59-71}	A07 TCR-HLA- DR4 ^{Vim-64cit59-71}	RA2.7 TCR-HLA- DR4 ^{α-enolase-15cit10-22V20G}
Data collection			
Space group	I121	P 2 21 21	C121
Cell dimensions			
a, b, c (Å)	98.93, 59.97, 379.16	58.60, 76.62, 224.18	185.86, 58.55, 216.48
a, b, g (°)	90, 90.16, 90	90, 90, 90	90, 113.60, 90
Resolution (Å)	49.52-2.65 (2.72-2.65)	46.55-2.75 (2.90-2.75)	45.87-2.40 (2.44-2.40)
R _{sym} or R _{merge}	0.102 (1.135)	0.161 (1.825)	0.07 (0.88)
I / σ I	11.9 (1.9)	12.4 (1.7)	12.5 (2.1)
Completeness (%)	100 (100)	100 (100)	100.0 (100.0)
Redundancy	7.0 (7.2)	13.4 (13.8)	6.2 (6.1)
Refinement			
Resolution (Å)	49.486-2.65	46.548-2.75	45.87-2.40
No. reflections	65333	27098	84262
R _{work} / R _{free}	0.2086/0.2441	0.2160/0.2635	0.2053/0.2322
No. atoms	13047	6638	12917
Protein	12704	6513	12325
Ligand/ion	252	88	249
Water	91	37	343
B-factors	79.48	71.21	62.89
Protein	79.47	71.17	63.34
Ligand/ion	103.80	89.38	70.82
Water	67.79	66.51	52.44
R.m.s. deviations			
Bond lengths (Å)	0.002	0.003	0.003
Bond angles (°)	0.539	0.521	0.606
Rama allowed (%)	99.81	99.88	99.94
Rama favoured (%)	96.89	95.22	96.5
Rama Outlier (%)	0.19	0.12	0.06

Supplementary Table 3. TCR-pHLA complex statistics.

TCR-pHLA	BSA (Å²)	Vα (%)	Vβ (%)	Peptide (%)	1α (%)	2α (%)	3α (%)	Fα (%)	1β (%)	2β (%)	3β (%)	Fβ (%)	K_D (μM)	Angle (°)
A03-HLA-DR4 ^{Vim6-4cit59-71}	2010	54.5	45.5	27.1	20.7	9.6	20.8	3.4	6.3	10.7	27.5	1	6.2± 0.3μM	67
A07-HLA-DR4 ^{Vim-64cit59-71}	1665	63.7	36.3	28.7	23.1	8.7	29.6	2.3	0	0	36.3	0	31.9± 1.5μM	61
RA2.7-HLA-DR4 ^{Vim-64cit59-71v20G}	1940	38	62	20.95	17	3	17	1	7	17	33	5	7.1± 0.5μM	60

Supplementary Table 4. Contact table of A03 TCR- HLA-DR4^{Vim-64cit59-71}

TCR segment	TCR residues	HLA-DR4	Type of bond
CDR1α	A35	H81 β	HB, VDW
	Y36	D76 β , T77 β	VDW
	N38	Q70 β	HB, VDW
FWα	K55	D66 β	SB
CDR2α	I57	Q70 β	VDW
	T58	A73 β , T77 β	VDW
CDR3α	T109	Q70 β	HB, VDW
	G110	G58 α	VDW
	N111	Q57 α , G58 α	VDW
	Y112	Q57 α	HB, VDW
	K113	E55 α	HB, VDW
CDR1β	Y31	Q57 α , A61 α	HB, VDW
FWβ	Y55	Q57 α	VDW
CDR2β	Y57	Q57 α , L60 α	VDW
CDR3β	N110	Y60 β , Q64 β , L67 β	HB, VDW
	S111	D66 β	VDW
TCR segment	TCR residues	Vim-64cit ₅₉₋₇₁ peptide	Type of bond
CDR1α	T28	P-1-V	VDW
	S29	P-1-V	VDW
	I30	P-1-V	VDW
	A31	P-1-V, P1-Y, P2-A	VDW
CDR3α	T109	P4-Cit, P5-S	VDW, HB
	G110	P3-T, P5-S	VDW
CDR1β	D30	P8-V	VDW
CDR3β	V109	P5-S, P6-S	VDW
	N110	P8-V	HB, VDW

VDW: Van der Waals interaction (cut-off at 4Å)

HB: hydrogen bond (cut-off at 3.5 Å)

SB: salt bridge (cut-off at 4.5 Å)

Supplementary Table 5. Contact table of A07 TCR- HLA-DR4^{Vim-64cit59-71}

TCR segment	TCR residues	HLA-DR4	Type of bond
CDR1α	S29	E55 α	VDW
	A35	H81 β	VDW
	Y36	T77 β , H81 β	VDW
FWα	K55	D66 β	SB
CDR2α	I57	E69 β , T77 β	VDW
	T58	A73 β	VDW
CDR3α	H109	Q70 β , A73 β , T77 β	HB, VDW
	S110	Q70 β	HB, VDW
	S112	A61 α	VDW
	W113	E55 α	VDW
CDR3β	R109	V65 α	VDW
	T110	Q64 β , L67 β	VDW
	G111	Q70 β	HB, VDW
	A112	D66 β , L67 β , Q70 β	VDW
	D115	D66 β	VDW
TCR segment	TCR residues	Vim-64cit₅₉₋₇₁ peptide	Type of bond
CDR1α	A31	P-1V, P1-Y, P2-A	VDW
CDR3α	H109	P4-Cit	HB, VDW
	S110	P3-T, P4-Cit, P5-S	VDW
CDR3β	R109	P8-V	VDW
	T110	P7-A, P8-V	VDW
	G111	P5-S, P8-V	HB, VDW

VDW: Van der Waals interaction (cut-off at 4Å)

HB: hydrogen bond (cut-off at 3.5 Å)

SB: salt bridge (cut-off at 4.5 Å)

Supplementary Table 6. Contact table of RA2.7 TCR- HLA-DR4 α -enolase-15cit10-22V20G

TCR segment	TCR residues	HLA-DR4	Type of bond
CDR1α	G30	T77 β , H81 β	VDW
	N36	T77 β , H81 β	VDW, HB
	Y38	Q70 β , A73 β	VDW
CDR2α	L57	T77 β	VDW
CDR3α	A109	Q70 β	VDW
	N110	G58a, N62a	VDW, HB
CDR1β	Y38	V65a	VDW
CDR2β	Y57	A64a, V65a, A68a	VDW
	N58	A68a	VDW
	E64	K67a	SB
FWβ	S66	Q57a	HB, VDW
	E67	Q57a	VDW
CDR3β	R108	Y60 β , Q64 β	HB
	Y110	Q70 β , K71 β	HB, VDW
	F111	Q64 β , L67 β , Q70 β	VDW
	Y113	D66 β	VDW, HB
TCR segment	TCR residues	α-enolase-15cit₁₀₋₂₂V20G peptide	Type of bond
CDR1α	N36	P2-D	HB, VDW
CDR3α	P108	P2-D	VDW
	N110	P3-S, P4-Cit, P5-G	HB, VDW
CDR1β	L37	P8-T	VDW
CDR2β	Y57	P8-T	HB, VDW
CDR3β	D109	P7-P, P8-T	HB, VDW
	Y110	P4-cit, P5-G, P6-N, P7-P	HB, VDW
	F111	P7-P	VDW

VDW: Van der Waals interaction (cut-off at 4 Å)

HB: hydrogen bond (cut-off at 3.5 Å)

SB: salt bridge (cut-off at 4.5 Å)

Supplementary Table 7. Antibody list

Antibody name	Clone	Company	Dilution used	Catalog number
BUV395 mouse anti-human CD3	UCHT1	BD Biosciences	1:100	563546
APC Mouse Anti-Human CD69	FN50	BD Biosciences	1:100	555533
anti-HLA-DR4	LB3.1			
APC-Cy TM 7 Hamster Anti-Mouse TCR β Chain	H57-597	BD Biosciences	1:200	560656
FITC Rat Anti-Mouse CD45R/B220	RA3-6B2	BD Biosciences	1:400	553088
FITC Mouse Anti-Mouse NK-1.1	PK136	BD Biosciences	1:400	553164
FITC Rat anti-Mouse F4/80	BM8	eBioscience, ThermoFisher Scientific	1:400	11-4801-82
BV711 Hamster Anti-Mouse CD3e	145-2C11	BD Biosciences	1:200	563123
BV605 Rat Anti-Mouse CD62L	MEL-14	BD Biosciences	1:400	563252
BUV395 Rat Anti-Mouse CD4	GK1.5	BD Biosciences	1:200	563790
Pacific Blue TM Rat Anti-Mouse CD8a	53-6.7	BD Biosciences	1:200	558106
Alexa Fluor 700 Mouse anti-human CD14	M5E2	BD Biosciences	1:100	557923
Alexa Fluor 700 Mouse anti-human CD19	HIB19	BD Biosciences	1:200	557921
BV480 Mouse anti-human CD3	UCHT1	BD Biosciences	1:200	566105
BUV395 mouse anti-human CD4	SK3	BD Biosciences	1:400	563550
APC hamster anti-mouse TCR β chain	H57-597	Biologend	1:400	109212
APC mouse anti-human CD3	UCHT1	Biologend	1:200	300412
LIVE/DEAD TM Fixable Aqua Dead Cell Stain Kit, for 405 nm excitation		ThermoFisher Scientific	1:800	L34966
LIVE/DEAD Fixable Near-IR Dead Cell Stain Kit, for 633 or 635 nm excitation		ThermoFisher Scientific	1:1000	L10119
Zombie NIR TM Fixable Viability Kit		Biologend	1:1000	423106
BD Horizon TM Fixable Viability Stain 700 (FVS700)		BD Biosciences	1:1000	564997

Supplementary Table 8. Primers targeting mouse T cell receptor α (TRA) and β (TRB) genes

TRA gene(s) targeted by primer	External primer sequence	Internal primer sequence	Reference
TRAV1	5' GCACATACAGCACCTCAG 3'	5' AACGTGAAGGCCAAGC 3'	
TRAV2	5' CCACCAGGGACCACAG 3'	5' ACTCTGAGCCTGCCCT 3'	50 (Internal only)
TRAV3	5' GGCGAGCAGGTGGAG 3'	5' GCCCTCCTCACCTGAG 3'	50
TRAV4	5' TCTGSTCTGAGATGCAATTTT 3'	5' GGITIMAGGAACAAAGGAGAAT 3'	50
TRAV5-1/5-4(D)	5' CTTCCYTTGGTATAAGCAAGA 3'	5' ATYCGTTCAAATATGGAAAGAAA 3'	50 (Internal only)
TRAV6-1/6-2	5' CAGATGCAAGGTCAAGTGAC 3'	5' GGAGAAGGTCCACAGCTC 3'	50
TRAV6-3/6-4(D)	5' AAGGTCCACAGCTCCTTC 3'	5' CAACTGCCAACACAAGG 3'	50
TRAV6(D)-5	5' CTTCTCTGACTGTGAACTGTTC 3'	5' CAGTACCCAACCCTGTTCTG 3'	
TRAV6-6	5' AGATTCCGTGACTCAAACAG 3'	5' ACGGCTGGCCAGAAG 3'	50
TRAV6(D/N)-7	5' GCCTCAAGGGACAAAGAG 3'	5' AAAGGAAGCAGCAGAGG 3'	
TRAV7	5' AGAAGGTRCAGCAGAGCCCAGAATC 3'	5' CAKGRCYTCYYTCAACTGCAC 3'	50
TRAV8	5' TGAAYTGYAGTTACAAGAC 3'	5' TAATCTTAATACGTTCAAATGAG 3'	
TRAV9	5' CTCKSTGSAGCTGAGATGCAA 3'	5' CAGYTKCTCCTCAAGTACTAT 3'	
TRAV10	5' GGAGAGAAGGTTCGAGCAAC 3'	5' GAGGGAGACAGCGCTG 3'	
TRAV11	5' AAGACCCAAGTGGAGCAG 3'	5' AACAGGACACAGGCCAAAG 3'	50
TRAV12	5' GACCCAGAMRGAAGGCCTG 3'	5' GCTGAACWGCACCTATCAG 3'	
TRAV12-4	5' GGGAGGAGCAATGGAGATGG 3'	5' CAGTGACCCAGAAGGAAGG 3'	
TRAV13	5' TCCTTGTTCTGCAGG 3'	5' TGCAGTGGTTTTACCAA 3'	50 (External only)
TRAV14	5' GCAGCAGGTGAGACAAAG 3'	5' CTCTGACAGTCTGGGAAGG 3'	50
TRAV15	5' CTGSAYTGTTTCATATRAGACAAGT 3'	5' TTAGTGGAGAGATGGTTTT 3'	
TRAV16	5' GTACAAGCAAACAGCAAGTG 3'	5' ATTATTCTCTGAACTTTCAGAAGC 3'	50
TRAV17	5' CAGTCCGTGGACCAGC 3'	5' TATGAAGGAGCCTCCCTG 3'	50
TRAV18	5' CAAGATTTCACTGCACG 3'	5' TACTGGTACCGACAGGTC 3'	
TRAV19	5' CAAGTTAAACAAAGCTCTCCATC 3'	5' GCTGACTGTTCAAGAGGGA 3'	50 (Internal only)
TRAV21	5' GTGCACTTGCTTGTAGC 3'	5' AATAGTATGGCTTTCCTGGC 3'	50
TRAC	5' GGCATCACAGGGAACG 3'	5' GCACATTGATTTGGGAGTC 3'	50

TRB gene(s) targeted by primer	External primer sequence	Internal primer sequence	Reference
TRBV1	5' TACCACGTGGTCAAGCTG 3'	5' GTATCCCTGGATGAGCTG 3'	50
TRBV2	5' CAGTATCTAGGCCACAATGC 3'	5' GGACAATCAGACTGCCTC 3'	50
TRBV3	5' CCCAAAGTCTTACAGATCCC 3'	5' GATATGGGGCAGATGGTG 3'	50
TRBV4	5' GACGGCTGTTTTCCAGAC 3'	5' CAGGTGGGAAATGAAGTG 3'	50
TRBV5	5' GGTATAAACAGAGCGCTGAG 3'	5' GCCAGAGCTCATGTTTCTC 3'	50
TRBV12	5' GGGGTTGTCCAGTCTCC 3'	5' CCAGCAGATTCTCAGTCC 3'	50
TRBV13	5' GCTGCAGTCACCCAAAG 3'	5' GTACTGGTATCGGCAGGAC 3'	50
TRBV14	5' GCAGTCCACAGGAAGGG 3'	5' GGTATCAGCAGCCCAGAG 3'	50
TRBV15	5' GAGTTACCCAGACACCCAG 3'	5' GTGTGAGCCAGTTTCAGG 3'	50
TRBV16	5' CCTAGGCACAAGGTGACAG 3'	5' GAAGCAACTCTGTGGTGTG 3'	50
TRBV17	5' GAAGCCAAACCAAGCAC 3'	5' GAACAGGGAAGCTGACAC 3'	50
TRBV19	5' GATTGGTCAGGAAGGGC 3'	5' GGTACCGACAGGATTCAG 3'	50
TRBV20	5' GGATGGAGTGTCAAGCTG 3'	5' GCTTGGTATCGTCAATCG 3'	50
TRBV23	5' CTGCAGTTACACAGAAGCC 3'	5' GCCAGGAAGCAGAGATG 3'	50
TRBV24	5' CAGACTCCACGATACCTGG 3'	5' GCACACTGCCTTTTACTGG 3'	50
TRBV26	5' GGTGAAAGGGCAAGGAC 3'	5' GAGGTGTATCCCTGAAAAGG 3'	50
TRBV29	5' GCTGGAATGTGGACAGG 3'	5' GTACTGGTATCGACAAGACCC 3'	50
TRBV30	5' CCTCCTCTACCAAAGCC 3'	5' GGACATCTGTCAAAGTGGC 3'	50
TRBV31	5' CTAACCTCTACTGGTACTGGCAG 3'	5' CTGTTGGCCAGGTAGAGTC 3'	50
TRBC	5' CCAGAAGGTAGCAGAGACCC 3'	5' CCTCCTTGCCATTCACCCAC 3'	50 (External only)

Primers targeting TRAV and TRBV genes are sense. Primers targeting TRAC and TRBC genes are antisense. TRAV, T cell receptor V α , TRAC, T cell receptor C α ; TRBV, T cell receptor V β , TRBC, T cell receptor C β .

Supplementary Table 9. Primers targeting human T cell receptor α (TRA) and β (TRB) genes

TRA gene(s) targeted by primer	External primer sequence	Internal primer sequence	Reference
TRAV1	5' AACTGCACGTACCAGACATC 3'	5' GCACCCACATTTCTKTCTTAC 3'	51
TRAV2	5' GATGTGCACCAAGACTCC 3'	5' CACTCTGTGTCCAATGCTTAC 3'	51
TRAV3	5' AAGATCAGGTCAACGTTGC 3'	5' ATGCACCTATTCAGTCTCTGG 3'	51
TRAV4	5' CTCATGGACTCATATGAAGG 3'	5' ATTATATCACGTGGTACCAACAG 3'	51
TRAV5	5' CTTTTCTGAGTGTCCGAG 3'	5' TACACAGACAGCTCCTCCAC 3'	51
TRAV6	5' CACCCTGACCTGCAACTATAC 3'	5' TGGTACCGACAAGATCCAG 3'	51
TRAV7	5' GCAAATAACAGGGATGGG 3'	5' TATGAGAAGCAGAAAGGAAGAC 3'	
TRAV8-1	5' CTCACTGGAGTTGGGATG 3'	5' GTCAACACCTTCAGCTTCTC 3'	51
TRAV8-2, 8-4	5' GCCACCCTGGTTAAAGG 3'	5' AGAGTGAAACCTCCTTCCAC 3'	51
TRAV8-3	5' CACTGTCTCTGAAGGAGCC 3'	5' TTTGAGGCTGAATTTAAGAGG 3'	51
TRAV8-6	5' GAGCTGAGGTGCAACTACTC 3'	5' AACCAAGGACTCCAGCTTC 3'	51
TRAV8-7	5' CTAACAGAGGCCACCCAG 3'	5' ATCAGAGGTTTTGAGGCTG 3'	51
TRAV9-1, 9-2	5' TGGTATGTCCAATATCCTGG 3'	5' GAAACCACTTCTTTCCACTTG 3'	51
TRAV10	5' CAAGTGGAGCAGAGTCCTC 3'	5' GAAAGAAGTGCCTCTTCAATG 3'	51
TRAV12-1, 12-2, 12-3	5' CARTGTTCCAGAGGGAGC 3'	5' AAGATGGAAGGTTTACAGCAC 3'	51
TRAV13-1	5' CATCCTTCAACCCTGAGTG 3'	5' TCAGACAGTGCCTCAAACACTAC 3'	51
TRAV13-2	5' CAGCGCCTCAGACTACTTC 3'	5' CAGTGAACATCTCTCTCTGC 3'	51
TRAV14	5' AAGATAACTCAAACCAACCAG 3'	5' AGGCTGTGACTCTGGACTG 3'	51
TRAV16	5' AGTGGAGCTGAAGTGCAAC 3'	5' GTCCAGTACTCCAGACAACG 3'	51
TRAV17	5' GGAGAAGAGGATCCTCAGG 3'	5' CCACCATGAACTGCAGTTAC 3'	51
TRAV18	5' TCCAGTATCTAAACAAAGAGCC 3'	5' TGACAGTTCCTTCCACCTG 3'	51
TRAV19	5' AGGTAACTCAAGCGCAGAC 3'	5' TGTGACCTTGGACTGTGTG 3'	51
TRAV20	5' CACAGTCAGCGTTTAAGAG 3'	5' TCTGGTATAGGCAAGATCCTG 3'	51
TRAV21	5' TTCCTGCAGCTCTGAGTG 3'	5' AACTTGGTTCTCAACTGCAG 3'	51
TRAV22	5' GTCCTCCAGACCTGATTCTC 3'	5' CTGACTCTGTGAACAATTTGC 3'	51
TRAV23	5' TGCTTATGAGAACACTGCG 3'	5' TGCATTATTGATAGCCATACG 3'	51
TRAV24	5' CTCAGTCACTGCATGTTCAG 3'	5' TGCCTTACTGGTACAGATG 3'	51

TRAV25	5' GGA CTT CACCACGTACTGC 3'	5' TATAAGCAAAGGCCTGGTG 3'	51
TRAV26-1	5' GCAAACCTGCCTTGTAATC 3'	5' CGACAGATTCCTCCAG 3'	51
TRAV26-2	5' AGCCAAATTCAATGGAGAG 3'	5' TTCCTTGCCCTTGTAACCAC 3'	51
TRAV27	5' TCAGTTTCTAAGCATCCAAGAG 3'	5' CTCCTGTGTACTGCAACTCC 3'	51
TRAV29	5' GCAAGTTAAGCAAATTCACC 3'	5' CTGCTGAAGGTCCTACATTC 3'	51
TRAV30	5' CAACAACCAGTGCAGAGTC 3'	5' AGAAGCATGGTGAAGCAC 3'	51
TRAV34	5' AGAACTGGAGCAGAGTCCTC 3'	5' ATCTCACCATAAACTGCACG 3'	51
TRAV35	5' GGTCAACAGCTGAATCAGAG 3'	5' ACCTGGCTATGGTACAAGC 3'	51
TRAV36	5' GAAGACAAGGTGGTACAAAGC 3'	5' ATCTCTGGTTGTCCACGAG 3'	51
TRAV38-1, 38-2	5' GCACATATGACACCAGTGAG 3'	5' CAGCAGGCAGATGATTCTC 3'	51
TRAV39	5' CTGTTCTGAGCATGCAG 3'	5' TCAACCACTTCAGACAGACTG 3'	51
TRAV40	5' GCATCTGTGACTATGAACTGC 3'	5' GGAGGCGGAAATATTAAGAC 3'	51
TRAV41	5' AATGAAGTGGAGCAGAGTCC 3'	5' TTGTTTATGCTGAGCTCAGG 3'	51
TRAC	5' GACCAGCTTGACATCACAG 3'	5' TGTTGCTCTTGAAGTCCATAG 3'	51

TRB gene(s) targeted by primer	External primer sequence	Internal primer sequence	Reference
TRBV2	5' TCGATGATCAATTCTCAGTTG 3'	5' TTCCTCTGAAGATCCGGTC 3'	51
TRBV3-1	5' CAAAATACCTGGTCACACAG 3'	5' AATCTTCACATCAATTCCTG 3'	51
TRBV4-1, 4-2, 4-3	5' TCGCTTCTCACCTGAATG 3'	5' CCTGCAGCCAGAAGACTC 3'	51
TRBV5-1, 5-3, 5-4	5' GATTCTCAGGKCKCCAGTTC 3'	5' CTTGGAGCTGGRSGACTC 3'	51
TRBV5-5, 5-6, 5-7, 5-8	5' GTACCAACAGGYCCTGGGT 3'	5' TCTGAGCTGAATGTGAACG 3'	51
TRBV6-1, 6-2, 6-3, 6-5, 6-6, 6-7, 6-8, 6-9	5' ACTCAGACCCCAAATTC 3'	5' GTGTRCCCAGGATATGAACC 3'	51
TRBV6-4	5' ACTGGCAAAGGAGAAGTCC 3'	5' TGGTTATAGTGTCTCCAGAGC 3'	51
TRBV7-1, 7-2, 7-3	5' TRTGATCCAATTTTCAGGTCA 3'	5' TCYACTCTGAMGWTCCAGCG 3'	51
TRBV7-4, 7-6, 7-7, 7-8, 7-9	5' CGSWTCTYTG CAGARAGGC 3'	5' TGRMGATYCAGCGCACA 3'	51
TRBV9	5' GATCACAGCAACTGGACAG 3'	5' GTACCAACAGAGCCTGGAC 3'	51
TRBV10-1	5' CAGAGCCCAAGACACAAG 3'	5' TGGTATCGACAAGACCTGG 3'	
TRBV10-2	5' ACCTTGATGTGTCACCAGAC 3'	5' GGAACACCAGTGA CTCTGAG 3'	

TRBV11-1, 11-2, 11-3	5' CGATTTTCTGCAGAGACGC 3'	5' GACTCCACTCTCAAGATCCA 3'	51
TRBV12-3, 12-4, 12-5	5' ARGTGACAGARATGGGACAA 3'	5' CYACTCTGARGATCCAGCC 3'	51
TRBV13	5' AGCGATAAAGGAAGCATCC 3'	5' CATTCTGAACTGAACATGAGC 3'	51
TRBV14	5' CCAACAATCGATTCTTAGCTG 3'	5' ATTCTACTCTGAAGGTGCAGC 3'	51
TRBV15	5' AGTGACCCTGAGTTGTTCTC 3'	5' ATAACTTCCAATCCAGGAGG 3'	51
TRBV16	5' GTCTTTGATGAAACAGGTATGC 3'	5' CTGTAGCCTTGAGATCCAGG 3'	51 (External only)
TRBV17	5' CAGACCCCCAGACACAAG 3'	5' TGTTCACTGGTACCGACAG 3'	51
TRBV18	5' CATAGATGAGTCAGGAATGCC 3'	5' CGATTTTCTGCTGAATTTCC 3'	51
TRBV19	5' AGTTGTGAACAGAATTTGAACC 3'	5' TTCCTCTCACTGTGACATCG 3'	51
TRBV20-1	5' AAGTTTCTCATCAACCATGC 3'	5' ACTCTGACAGTGACCAGTGC 3'	51
TRBV23-1	5' GCGATTCTCATCTCAATGC 3'	5' GCAATCCTGTCCTCAGAAC 3'	51
TRBV24-1	5' CCTACGGTTGATCTATTACTCC 3'	5' GATGGATACAGTGTCTCTCGA 3'	51
TRBV25-1	5' ACTACACCTCATCCACTATTCC 3'	5' CAGAGAAGGGAGATCTTTCC 3'	51
TRBV27, 28	5' TGGTATCGACAAGACCCAG 3'	5' TTCYCCCTGATYCTGGAGTC 3'	51
TRBV29-1	5' TTCTGGTACCGTCAGCAAC 3'	5' TCTGACTGTGAGCAACATGAG 3'	51
TRBV30	5' TCCAGCTGCTCTTCTACTCC 3'	5' AGAATCTCTCAGCCTCCAGAC 3'	51
TRBC	5' TAGAACTGGACTTGACAGCG 3'	5' TTCTGATGGCTCAAACACAG 3'	51

Primers targeting TRAV and TRBV genes are sense. Primers targeting TRAC and TRBC genes are antisense. TRAV, T cell receptor V α , TRAC, T cell receptor C α ; TRBV, T cell receptor V β , TRBC, T cell receptor C β .

Supplementary Table 10. CDR3 α and CDR3 β nucleotide sequences for TCRs listed in Figure 1c, Figure 2c and Supp Table 1.

Figure	CDR3 α amino acid sequence	CDR3 β amino acid sequence	CDR3 α nucleotide sequence	CDR3 β nucleotide sequence
Fig. 1c	CALGDSNYQLIW	CAACGAGGAGQNTLYF	tgtgctctgggtgatagcaactatcagttgatctgg	tgtgcccgctgctggggctggggggctggtcaaaacaccttgtacttt
	CALGDHSGSWQLIF	CASSLRTGANSDYTF	tgtgctctgggtgatcattctggcagctggcaactcatcttt	tgtgccagcagctctacggacaggggcaactccgactacaccttc
	CALGDTGNYKYVF	CASSGHNSGNTLYF	tgtgctctgggtgatacaggaactacaaatacgtcttt	tgtgccagcagtggaacataaattctgaaatacgtctatcttt
	CALGDTGNYKYVF	CASSAVNSGNTLYF	tgtgctctgggtgatacaggaactacaaatacgtcttt	tgtgccagcagtgagtggaattctgaaatacgtctatcttt
	CAAGITGNTGKLI	CASSQFRDRGAEQFF	tgtgctctgggtataacaggcaataaccggaaaactcatcttt	tgtgccagcagccaattccgggacaggggtgctgagcagttcttc
	CALGPSGGNYKPTF	CASSPTSSNERLFF	tgcgctctggggccctcaggaggaaactacaaactacgttt	tgtgccagcagcccacatcttccaacgaaagattatctttc
	CALNQGGSAKLIF	CASSQDPSNTGQLYF	tgcgctcttaatacaaggagggtctgcaagctcatcttt	tgtgccagcagccaagaccatcaaacaccgggagctctacttt
	CALSGANTGKLTF	CASSQDRSNTVEFF	tgcgctctgagtgaggtaaacactggaagctcacgttt	tgtgccagcagccaagacaggtcaaacacagaagtctcttt
	CALRTGGYKVVVF	CASSQDSANTEVFF	tgcgctctgcgactggaggctataaagtggctcttt	tgtgccagcagccaagattcagcaaacacagaagtctcttt
	CALGTGGYKVVVF	CASSRDNSNSDYTF	tgcgctctggggactggaggctataaagtggctcttt	tgtgccagcagccgcaactcaactccgactacaccttc
	CASGTGGYKVVVF	CASSLEQNSDYTF	tgcgctctcgggactggaggctataaagtggctcttt	tgtgccagcagcttagaacagtcaactccgactacaccttc
	CALRNTNTGKLT	CASSPRHSGNTLYF	tgcgctctgagaaacaccaatacaggcaaatcaactcttt	tgtgccagcagccccgacattctgaaatacgtctatcttt
	CALNNGGSNAKLT	CASSPQTGGYEQYF	tgcgctctgaatggaggaagcaatgcaagctaaccttc	tgtgccagcagccccagactgggggtatgaacagacttc
	CALTGGSNAKLT	CASSQGHERLFF	tgcgctctgactggaggaagcaatgcaagctaaccttc	tgtgccagcagccaagggcacgaaagattatctttc
	CALGSGGNYKPTF	CASSQNSGNTLYF	tgcgctctgggctcaggaggaaactacaaactacgttt	tgtgccagcagcagcaaaattctgaaatacgtctatcttt
	CALGTGGYKVVVF	CASSDFSVEQYF	tgcgctctggggactggaggctataaagtggctcttt	tgtgccagcagtgatcttccggtgaaacagacttc
	CAYYGSSGNKLI	CASSFRGDNSTLYF	tgcgcttattatgggagcagtggaacaagctcatcttt	tgtgccagcagtttcaggggtgataattcgcccctacttt
	CALSDGGQKLVF	CASGDFRAEQFF	tgcgctctgagtgatgggtggccagaagctgggtttt	tgtgccagcagtgatcttccgggtgagcagttcttc
	CALGGGSALGRLHF	CASSRGGTANTGQLYF	tgtgctctgggtggaggttcagccttagggaggctgcatcttt	tgtgctagcagtagaggcggaacagcaaacaccgggagctctacttt
	CALSVPNNAKLT	CASSLGQSSYEQYF	tgtgctctgagtgctccgaataatgcaggtgccaagctcacattc	tgtgccagcagctctcgggaggggagctcctatgaacagacttc
	CALRGSGGNYKPTF	CAWSLGTGQDTQYF	tgcgctctgaggggtcaggaggaaactacaaactacgttt	tgtgctcggagcttagggacagggcaagacaccagactcttt
	CALSGGNYKPTF	CAWSLGQGGNERLFF	tgcgctctgtcaggaggaaactacaaactacgttt	tgtgctcggagcttaggtcaggggggaaacgaaagattatctttc
Fig. 2c	CIVRVNYGQNFVF	CASSQAGPLHF	tgcacgtcagagttaactatggtcagaattttgtcttt	tgtgccagcagccaagcgggaccctccacttt
	CIVNPANTGNQFYF	CASRRDYFSYEQYF	tgcacgtcaatcctggaacaccggtaaccagttctatcttt	tgtgccagcagaaggactatctctcactagcagacttc
Supp Table 1	CIVRASNTGNQFYF	CSAATGTSGYEQYF	tgcacgtcagagcttgaacaccggtaaccagttctatcttt	tgcagtgctgctaccgggactagcggctacgagcagacttc
	CAGKAGNYGQNFVF	CASSTGGQNTGELFF	tgtgcagggaaagctgggaactatggtcagaattttgtcttt	tgtgccagtagtaccggggacagaaacaccggggagctgttttt
	CIVRTSGGSNYKLT	CAGTYWNEQFF	tgcacgtcagaacaagtggaggtagcaactataaactgacattt	tgtgccgggactactggaatgagcagttcttc
	CIVRVAGANSKLT	CASSYDLAGPYEQYF	tgcacgtcagagtcgctggagccaatagtaagctgacattt	tgtgccagcagttatgatctagcggggccctacgagcagacttc
	CAGRNNAGNMLTF	CASNVIINYGYTF	tgtgctggccgaaataatgcaggcaacatgctcaccttt	tgtgccagcaatgctgggattattaactatggctacaccttc