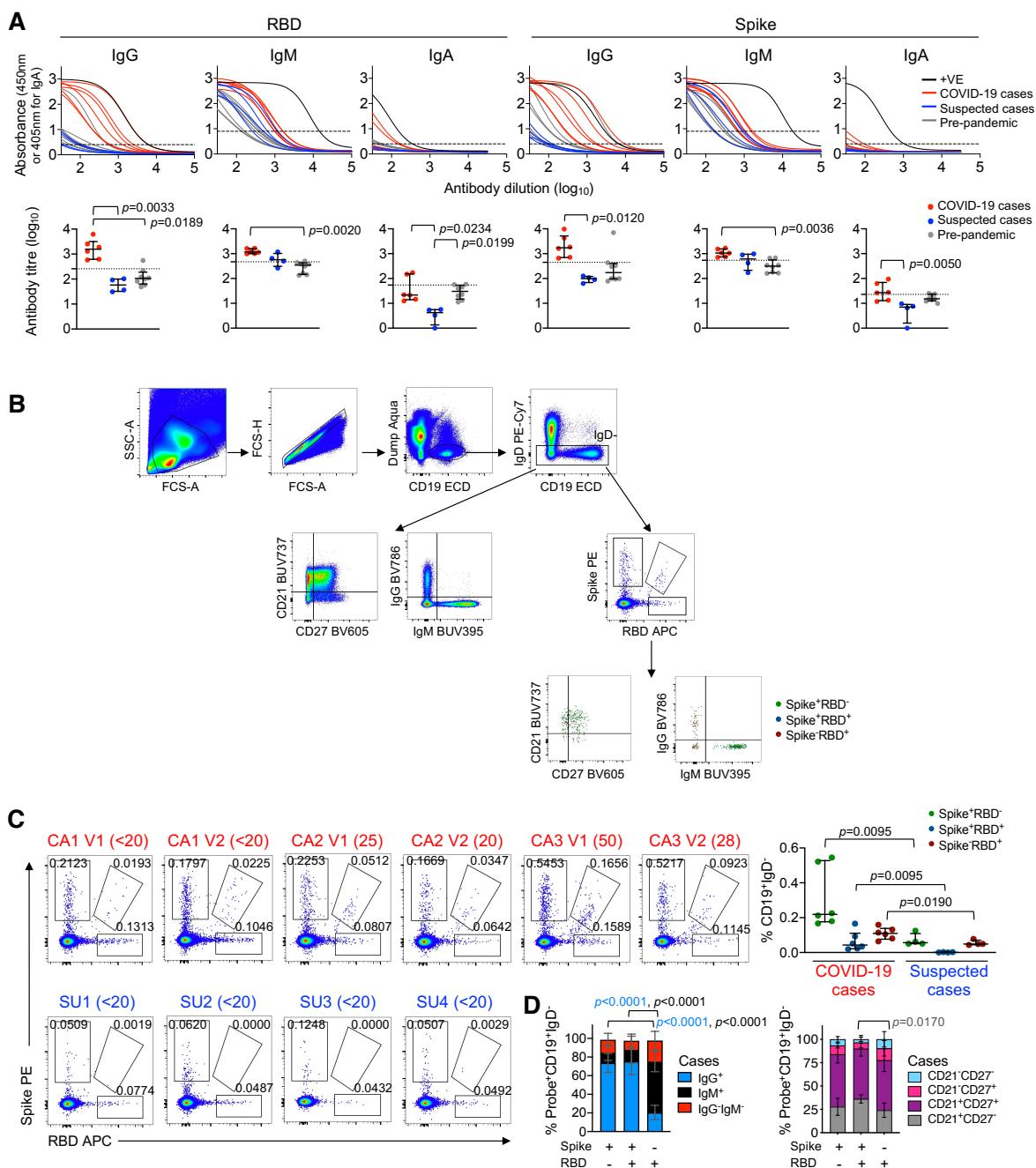


**Supplemental information**

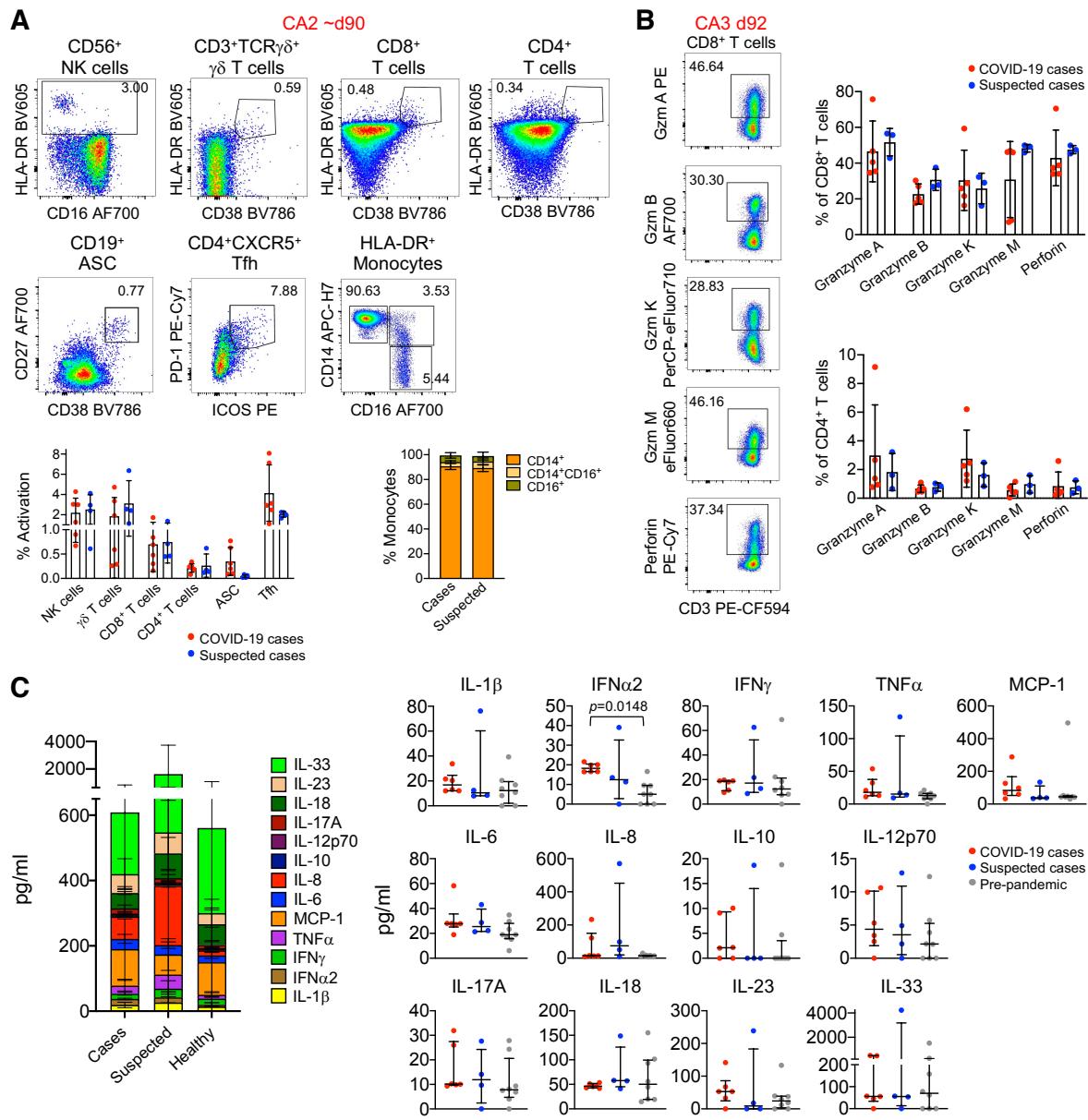
**CD8<sup>+</sup> T cells specific for an immunodominant  
SARS-CoV-2 nucleocapsid epitope display high naive  
precursor frequency and TCR promiscuity**

Thi H.O. Nguyen, Louise C. Rountree, Jan Petersen, Brendon Y. Chua, Luca Hensen, Lukasz Kedzierski, Carolien E. van de Sandt, Priyanka Chaurasia, Hyon-Xhi Tan, Jennifer R. Habel, Wuji Zhang, Lilith F. Allen, Linda Earnest, Kai Yan Mak, Jennifer A. Juno, Kathleen Wragg, Francesca L. Mordant, Fatima Amanat, Florian Krammer, Nicole A. Mifsud, Denise L. Doolan, Katie L. Flanagan, Sabrina Sonda, Jasveen Kaur, Linda M. Wakim, Glen P. Westall, Fiona James, Effie Mouhtouris, Claire L. Gordon, Natasha E. Holmes, Olivia C. Smibert, Jason A. Trubiano, Allen C. Cheng, Peter Harcourt, Patrick Clifton, Jeremy Chase Crawford, Paul G. Thomas, Adam K. Wheatley, Stephen J. Kent, Jamie Rossjohn, Joseph Torresi, and Katherine Kedzierska



**Figure S1. COVID-19 traveller cohort, SARS-CoV-2-reactive antibody and B cell signatures.** (A) ELISA titration curves (top) against the SARS-CoV-2 RBD and Spike proteins for IgG, IgM and IgA in COVID-19 cases (CA, n=3, 2 time points each), suspected cases (SU, n=4) and pre-pandemic healthy donors (n=8). Dotted line indicates the cut off for end-point titer determination. End-point titers (bottom) of SARS-CoV-2 RBD and Spike antibodies where the dotted line indicates the seroconversion threshold. Statistical significance was determined with Kruskal-Wallis and Dunn's multiple comparisons test. (B) Gating strategy for

SARS-CoV-2-specific B cells. B cells were gated based on FSC/SSC, singlets, live cells with exclusion for T cell/NK cell/monocyte lineage markers, then expression of CD19, and gated as IgD<sup>-</sup>, IgM<sup>+-</sup>, IgG<sup>+-</sup> and analysed for binding to SARS-CoV-2 probes, with expression of CD21/CD27. (C) Co-staining of class-switched B cells (CD19<sup>+</sup>IgD<sup>-</sup>) with RBD and Spike probes. Microneutralization titres are bracketed and shown alongside the donor codes. Frequencies of Spike<sup>+</sup>, RBD<sup>+</sup> and Spike<sup>+</sup>RBD<sup>+</sup> B cells as a proportion of CD19<sup>+</sup>IgD<sup>-</sup> B cells in PBMCs from COVID-19 cases (n=3, 2 time points each) and suspected cases (n=4); data are shown as median with IQR. Statistical significance was determined with Mann-Whitney test. (D) Isotype distribution (left) and memory B cell phenotypes (right) of Spike<sup>+</sup>, RBD<sup>+</sup> and Spike<sup>+</sup>RBD<sup>+</sup> CD19<sup>+</sup>IgD<sup>-</sup> B cells; data are shown as mean with SD. Statistical significance was determined with Tukey's multiple comparisons test. Related to Figure 1.

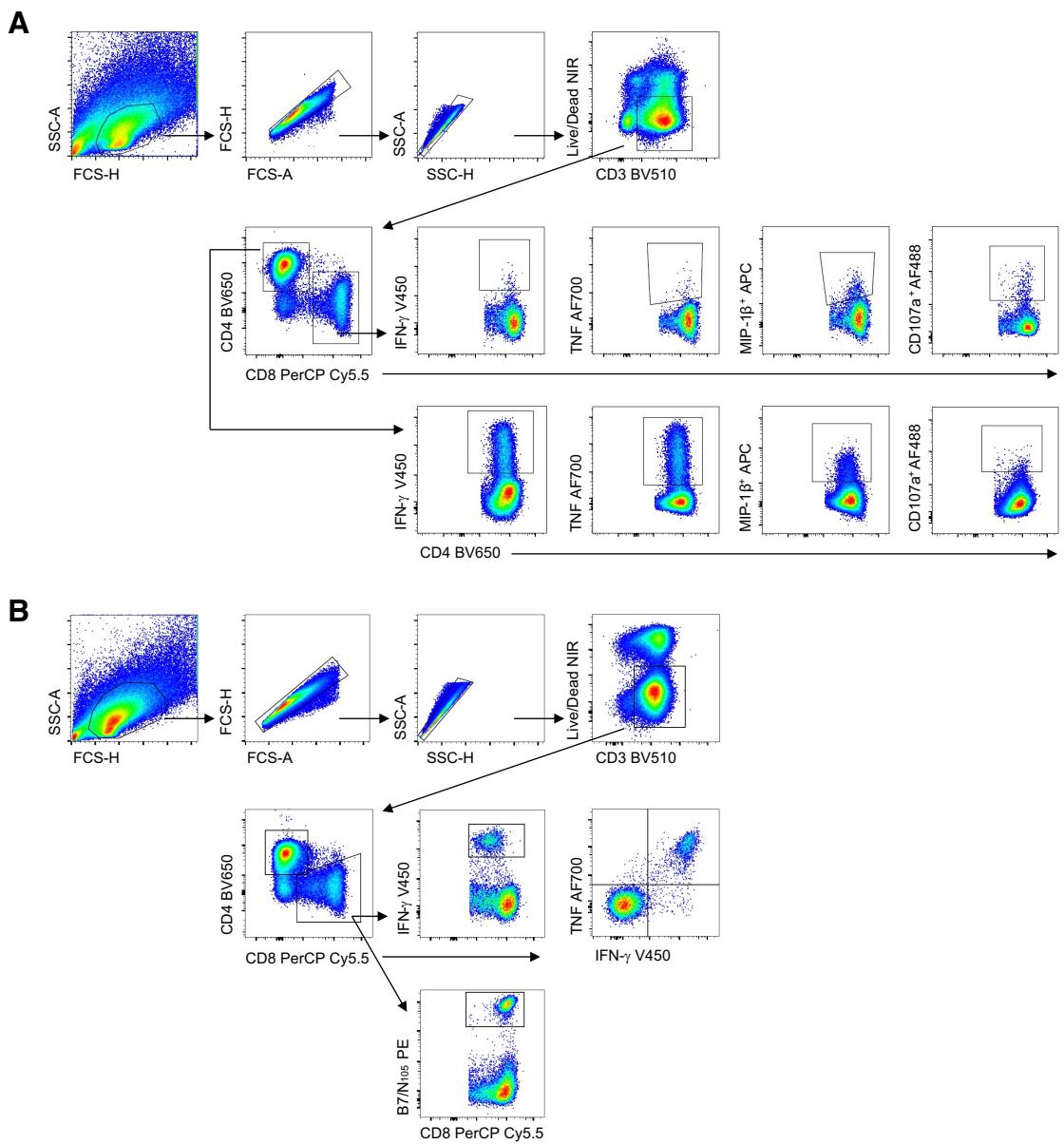


**Figure S2. Lack of immune cell activation in traveller cohort at convalescence.** (A)

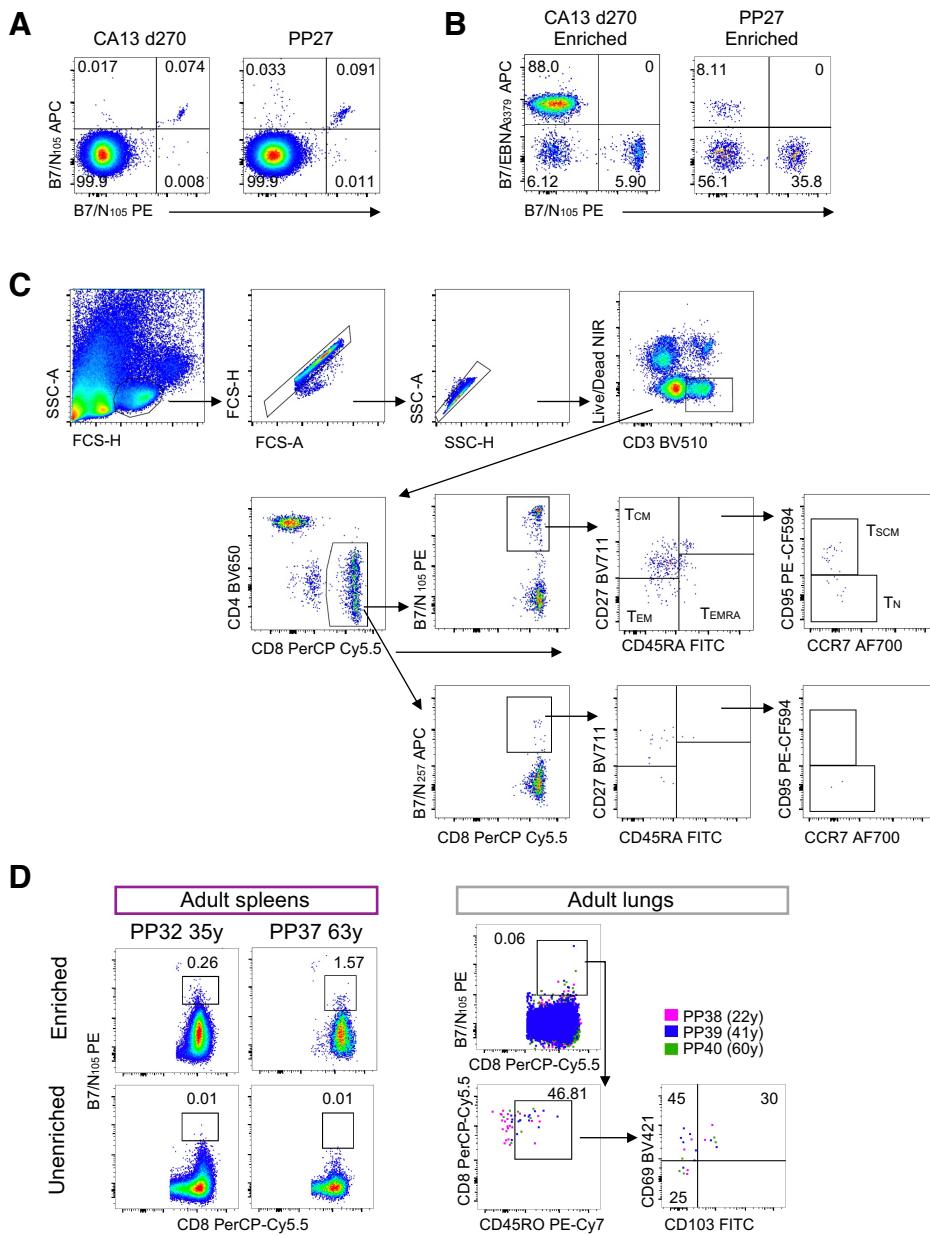
Representative FACS plots of activated CD38<sup>+</sup> NK cells, activated CD38<sup>+</sup>HLA-DR<sup>+</sup>  $\gamma\delta$ , CD8<sup>+</sup> and CD4<sup>+</sup> T cells, as well as activated CD38<sup>+</sup>CD27<sup>+</sup> ASC, ICOS<sup>+</sup>PD-1<sup>+</sup> Tfh and monocytes in a COVID-19 case. Proportion of activated immune cells (left) and monotype subsets (right) in COVID-19 cases (n=3, 2 time points each) and suspected cases (n=4); data are shown as mean with SD. (B) Representative FACS plots of CD8<sup>+</sup> T cells expressing different cytotoxic molecules (Granzyme A, B, K, and M and perforin) in a COVID-19 case. Proportion of cytotoxic CD8<sup>+</sup> and CD4<sup>+</sup> T cells in COVID-19 cases (n=3, 1 time point for CA1, 2 time points

for CA2, CA3) and suspected cases (n=3); data are shown as mean with SD. T cells were gated based on FSC/SSC, singlets, CD3<sup>+</sup> T cells with exclusion for B cell/monocyte markers, then gated as CD4<sup>+</sup> or CD8<sup>+</sup> and analyzed for expression of granzyme A, B, K and M and perforin.

(C) Total (left) and individual (right) levels across 13 cytokines in COVID-19 cases (n=3, 2 time points each), suspected cases (n=4) and healthy donors (n=8); data are shown as mean with SD and median with IQR, respectively. Statistical significance was determined with Kruskal-Wallis and Dunn's multiple comparisons test. Related to Figure 1.

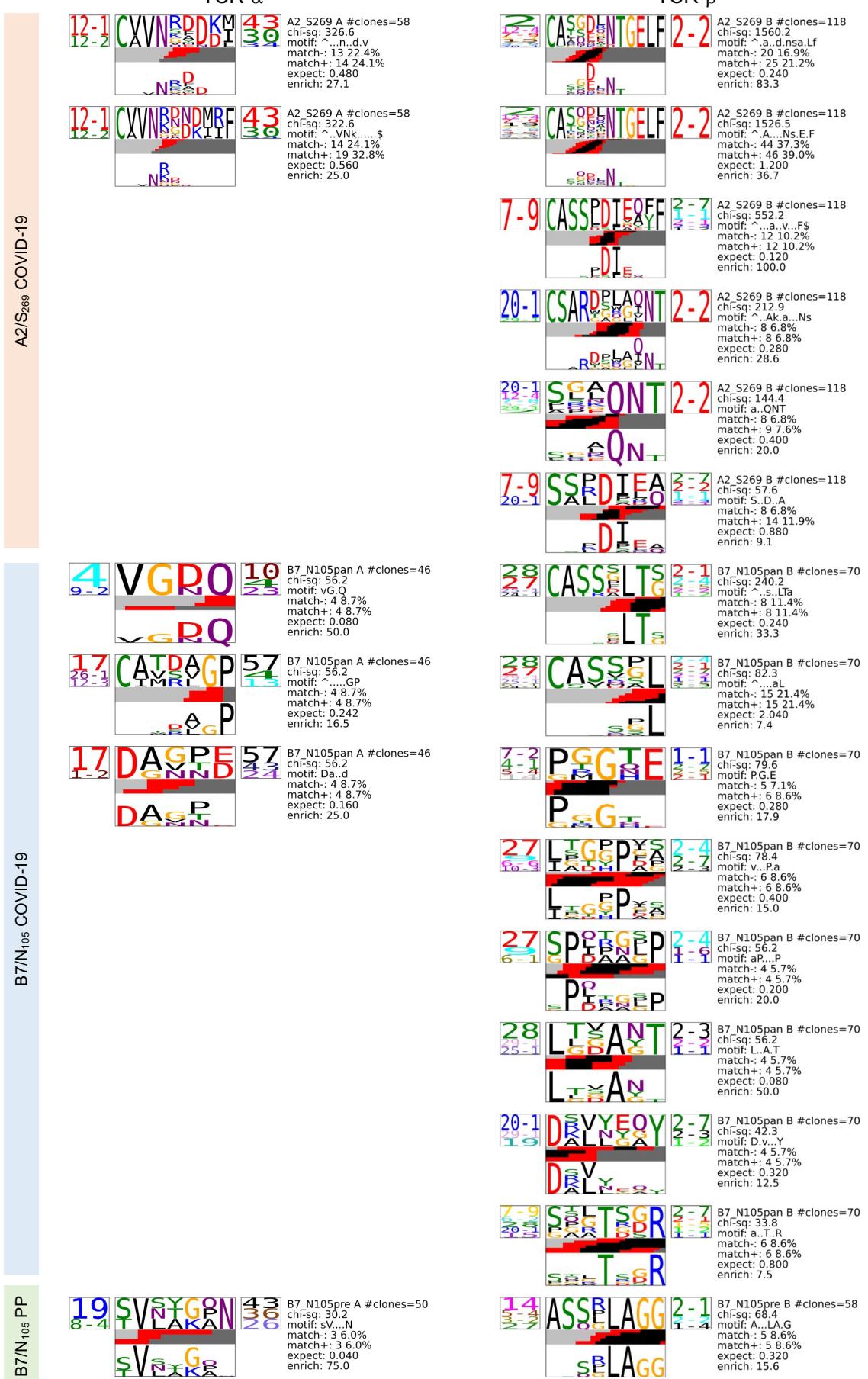


**Figure S3. Gating strategies for CD4<sup>+</sup> and CD8<sup>+</sup> T cell responses to SARS-CoV-2 overlapping peptide pools.** (A) ICS gating strategy for intracellular IFN- $\gamma$ , TNF, MIP-1 $\beta$  and CD107a after PBMCs were stimulated for 10 days with SARS-CoV-2 overlapping peptide pools. (B) Gating strategy after day 10-cultured CD8<sup>+</sup> T cells were dissected with individual peptides and assessed by ICS or by tetramer staining. Related to Figure 1.

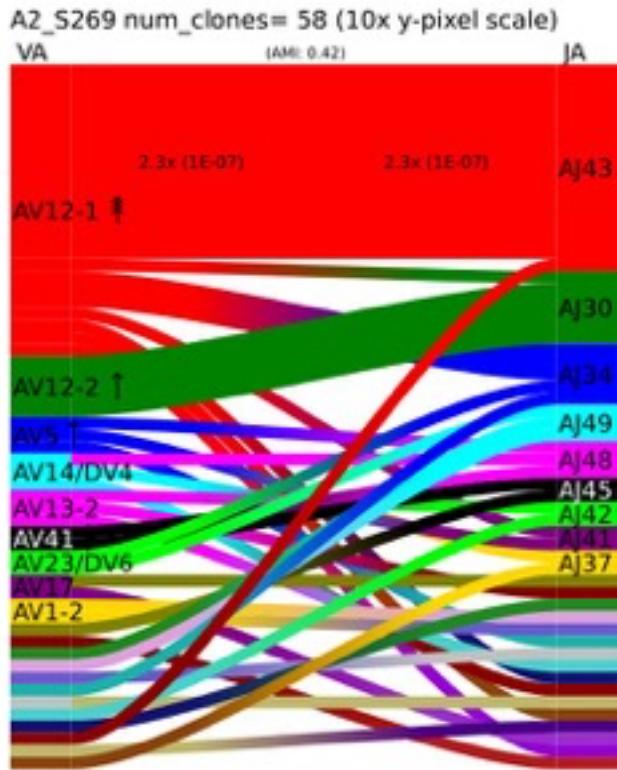


**Figure S4. B7/N<sub>105</sub><sup>+</sup>CD8<sup>+</sup> tetramer validation and staining in spleen and lungs.** (A) FACS plots showing direct *ex vivo* dual-tetramer staining of the immunodominant B7/N<sub>105</sub> tetramer conjugated to PE and APC fluorophores in a COVID-19 and pre-pandemic donor. (B) TAME-enriched tetramer populations using B7/N<sub>105</sub> tetramer-PE and an irrelevant B7/EBV-tetramer (EBNA-3<sub>379-387</sub>, RPPIFIRRL) conjugated to APC, representing 2 out of 4 experiments. Cells were gated on the total CD8<sup>+</sup> T cell population. (C) Gating strategy of enriched tetramer<sup>+</sup> cells and phenotype populations. (D) B7/N<sub>105</sub> tetramer staining of adult spleens following TAME enrichment (showing 2 out of 6 experiments) and direct tetramer staining of lung cells (non-

enriched) from 3 donors as concatenated FACS plots. Spleen and lungs were gated on CD8<sup>+</sup> T cells. Related to Figure 2 and Figure 3.



**Figure S5. TCRdist analysis of alpha and beta motifs for COVID-19 epitopes.** Enriched alpha and beta amino acid motifs in the CDR3 region were generated by TCRdist for all TCR pairs. Each TCR chain motif depicts the variable (left side) and joining (right side) gene frequencies, CDR3 amino acid sequences (middle), and inferred rearrangement structure (bottom bars coloured by source region: light grey = V-region, dark grey = J-region, black = diversity (D)-region, red = insertions). Chi-squared values greater than 50 were considered highly significant, values below 50 were borderline significant. Related to Figure 7.



**Figure S6. Significant TRAV12-1 to AJ43 gene pairing for the A2/S269 epitope.** Gene segment usage and pairing landscapes are shown for the dominant A2/S269 TCR motif. Each clonotype is assigned the same vertical length irrespective of clonotype size. Each vertical stack reflects the V (left) and J (right) gene segment usage and pairing is shown by curved connecting lines. Genes are ranked in colour by the frequency distribution with red being the highest frequency, followed by green, dark blue, aqua, magenta, black and thereafter. Enrichment or depletion of gene usage is indicated by up or down arrows respectively where 1 arrowhead correlates to a 2-fold increase or decrease. Related to Figure 7.

## Supplementary Tables

**Table S1.** Donor demographics and clinical data. Related to Figure 1.

Donor	Age	Sex	Specimen	Cohort	Days post disease onset				Location during disease	Oxygen	HLA-A	HLA-B
					Acute	Visit 1	Visit 2	Visit 3				
CA1	24	M	Heparinized blood	COVID-19 Case	-	5*	9*	-	Asymptomatic/home	No	01:01, 32:01	08:01, 14:01
CA2	21	M	Heparinized blood	COVID-19 Case	-	~90#	~160#	-	Overseas	No	02:01, 11:01	07:02, 55:01
CA3	19	M	Heparinized blood	COVID-19 Case	-	92	162	-	Overseas	No	1:01	08:01, 52:01
CA4	32	F	Heparinized blood	COVID-19 Case	-	45	-	-	Home	No	03:01, 11:01	07:02, 50:01
CA5	49	F	Heparinized blood	COVID-19 Case	-	47	208	-	Home	No	02:01, 03:01	07:02, 55:01
CA6	52	M	Heparinized blood	COVID-19 Case	-	41	81	142	Home	No	02:01, <b>24:02</b>	07:02, 40:01
CA7	57	F	Heparinized blood	COVID-19 Case	16	108	-	-	Ward	No	01:01, 02:01	07:02, 38:01
CA8	58	F	Heparinized blood	COVID-19 Case	7	74	-	-	Ward	Nasal prong	02:01, 24:02	<b>07:02</b>
CA9	59	M	Heparinized blood	COVID-19 Case	-	69	216	-	Home	No	01:01, 02:01	07:02, 08:01
CA10	65	M	Heparinized blood	COVID-19 Case	-	46	135	217	Home	No	02:01, <b>24:02</b>	<b>07:02</b>
CA11	69	M	Heparinized blood	COVID-19 Case	-	66	128	233	Home	No	02:01, 03:01	07:02, 27:05
CA12	72	F	Heparinized blood	COVID-19 Case	11	38	-	-	Ward	Supplemental	02:01	07:02, 15:18
CA13	74	M	Heparinized blood	COVID-19 Case	-	90	178	270	Home	No	03:01, 26:01	07:02, 40:01
CA14	38	M	Heparinized blood	COVID-19 Case	6	41	-	-	Ward	No	<b>02:01</b>	15:01, 37:01
CA15	50	F	Heparinized blood	COVID-19 Case	8	-	-	-	Ward	Nasal prong	02:01, 68:01	15:01, 40:01
CA16	51	M	Heparinized blood	COVID-19 Case	11	-	-	-	Ward	No	<b>02:01</b> , 03:01	07:02, 39:10
CA17	52	F	Heparinized blood	COVID-19 Case	5	-	-	-	ICU	High flow nasal prong	<b>02:01</b> , 68:01	08:01, 44:02
CA18	54	M	Heparinized blood	COVID-19 Case	-	46	-	-	Ward	No	<b>02:01</b> , 31:01	38:01; 44:03
CA19	56	M	Heparinized blood	COVID-19 Case	-	145	-	-	Home	No	<b>02:01</b> , 26:01	44:02
CA20	58	M	Heparinized blood	COVID-19 Case	-	71	-	-	Home	No	<b>24:02</b>	35:01, 55:01
CA21	75	M	Heparinized blood	COVID-19 Case	-	121	-	-	Home	No	01:01, <b>24:02</b>	08:01, 14:02
SU1	20	M	Heparinized blood	Suspected case	-	~160^	-	-	Asymptomatic/ overseas	-	-	-
SU2	20	M	Heparinized blood	Suspected case	-	~160^	-	-	Asymptomatic/ overseas	-	-	-
SU3	20	M	Heparinized blood	Suspected case	-	~160^	-	-	Asymptomatic/ overseas	-	-	-
SU4	20	M	Heparinized blood	Suspected case	-	~160^	-	-	Asymptomatic/ overseas	-	-	-
PP1	21	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	-	-
PP2	23	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	-	-
PP3	24	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	-	-
PP4	26	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	-	-
PP5	27	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	-	-
PP6	28	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	-	-
PP7	31	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	-	-
PP8	31	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	-	-
PP9	3	F	Tonsil/ Heparinized blood	Pre-pandemic Child	-	-	-	-	-	-	03:01	<b>07:02</b>
PP10	5	M	Tonsil/ Heparinized blood	Pre-pandemic Child	-	-	-	-	-	-	03:01	<b>07:02</b> , 57:01
PP11	7	F	Tonsil/ Heparinized blood	Pre-pandemic Child	-	-	-	-	-	-	01:01, 03:01	<b>07:02</b> , 08:01
PP12	15	M	Tonsil/ Heparinized blood	Pre-pandemic Child	-	-	-	-	-	-	03:01	<b>07:02</b> , 14:01
PP13	30	M	Buffy pack	Pre-pandemic Adult	-	-	-	-	-	-	01:01, <b>24:02</b>	<b>07:02</b> , 57:01
PP14	35	F	Buffy pack	Pre-pandemic Adult	-	-	-	-	-	-	01:01, 03:01	<b>07:02</b> , 08:01
PP15	36	F	Buffy pack	Pre-pandemic Adult	-	-	-	-	-	-	02:01, 02:05	<b>07:02</b> , 41:01

PP16	45	N/A	Buffy pack	Pre-pandemic Adult	-	-	-	-	-	-	03:01, 11:01	<b>07:02,</b> 15:01
PP17	47	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	03:01, 26:01	<b>07:02,</b> 15:01
PP18	49	M	Buffy pack	Pre-pandemic Adult	-	-	-	-	-	-	01:01, 31:01	<b>07:02,</b> 08:01
PP19	55	M	Buffy pack	Pre-pandemic Adult	-	-	-	-	-	-	02:01; 03:01	<b>07:02;</b> 57:01
PP20	60	N/A	Buffy pack	Pre-pandemic Adult	-	-	-	-	-	-	24:02, 25:01	<b>07:02,</b> 18:01
PP21	63	N/A	Buffy pack	Pre-pandemic Adult	-	-	-	-	-	-	03:01, 26:01	<b>07:02,</b> 44:02
PP22	65	F	Buffy pack	Pre-pandemic Elderly	-	-	-	-	-	-	02:01,03:01	<b>07:02,</b> 44:03
PP23	69	N/A	Buffy pack	Pre-pandemic Elderly	-	-	-	-	-	-	02:01, 32:01	<b>07:02,</b> 44:03
PP24	69	N/A	Buffy pack	Pre-pandemic Elderly	-	-	-	-	-	-	11:01	<b>07:02</b>
PP25	72	N/A	Buffy pack	Pre-pandemic Elderly	-	-	-	-	-	-	02:01,11:01	<b>07:02,</b> 44:02
PP26	73	N/A	Buffy pack	Pre-pandemic Elderly	-	-	-	-	-	-	01:01, 03:01	<b>07:02,</b> 08:01
PP27	76	M	Buffy pack	Pre-pandemic Elderly	-	-	-	-	-	-	01:01	<b>07:02,</b> 08:01
PP28	76	F	Heparinized blood	Pre-pandemic Elderly	-	-	-	-	-	-	01:01, 31:01	<b>07:02,</b> 44:03
PP29	24	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	02:03, <b>24:02</b>	27:06, 40:01
PP30	59	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	<b>24:02</b>	07:02
PP31	32	M	Heparinized blood	Pre-pandemic Adult	-	-	-	-	-	-	01:01, <b>24:02</b>	07:06, 15:02
PP32	35	M	Spleen	Pre-pandemic Adult	-	-	-	-	-	-	1, 68	<b>7, 18</b>
PP33	41	F	Spleen	Pre-pandemic Adult	-	-	-	-	-	-	2, 25	<b>7, 8</b>
PP34	46	M	Spleen	Pre-pandemic Adult	-	-	-	-	-	-	02:01, 03:01	<b>07:02,</b> 57:01
PP35	49	M	Spleen	Pre-pandemic Adult	-	-	-	-	-	-	2, 3	<b>7, 57</b>
PP36	59	M	Spleen	Pre-pandemic Adult	-	-	-	-	-	-	2	<b>7</b>
PP37	63	F	Spleen	Pre-pandemic Adult	-	-	-	-	-	-	02:01, 24:02	<b>07:02,</b> 15:01
PP38	22	M	Lung	Pre-pandemic Adult	-	-	-	-	-	-	2, 32	<b>7, 8</b>
PP39	41	F	Lung	Pre-pandemic Adult	-	-	-	-	-	-	2, 25	<b>7, 8</b>
PP40	60	F	Lung	Pre-pandemic Adult	-	-	-	-	-	-	3	<b>7, w6</b>

\*Days are calculated from first positive PCR result for CA1 after returning home from overseas for ~3 months.

#Days are approximate after they experienced mild symptoms while travelling overseas with CA1 and CA3.

^Days are approximate from the time they travelled overseas with suspected COVID-19, but PCR-negative on return.

HLA in bold were analysed for COVID-19-specific T cell responses or TCRs.

**Table S2.** B7/N105<sup>+</sup>CD8<sup>+</sup> TCRab repertoires. Related to Figure 5.

TRBV	TRBJ	CDR3β	TRAV	TRAJ	CDR3α	#80	C5	C2	C4	BP124	BP155	BP161	BP160
20-1	2-1	CSARDTAGATYNEQFF	ND	ND	ND						1		
20-1	2-1	CSAWRGRGADNEQFF	ND	ND	ND							1	
28	2-3	CASTPMGLEVLDTQYF	ND	ND	ND							1	
28	2-5	CASSDRGMGETQYF	ND	ND	ND							1	
29-1	2-5	CSVVTGGPETQYF	ND	ND	ND							1	
29-1	2-7	CSVVPLAGPYEQYF	ND	ND	ND							2	
7-2	1-1	CASRGGGTEAFF	ND	ND	ND					4			
28	2-1	CASSLASSSSYNEQFF	1-1	16	CAVRG#FSDGQKLLF					1			
6-5	2-1	CASSYYGVNEQFF	1-1	39	CAVT#NAGNMLTF						1		
18	1-3	CASSQGPYSGNTIYF	1-1	40	CAVRTP#TSGTYKYI	F						1	
27	1-4	CASSLLAGGRAADKEKLFF	1-2	18	CAA#DRGSTLGRLYF							1	
2	2-4	CASSEEIAKNIQYF	1-2	31	CAVRVFNARLMF		1						
5-4	2-4	CASSLETGRNIQYF	1-2	35	WAIFGNVLHC						2		
20-1	1-6	CSARDRTDSYNSPLFH	1-2	43	CADANNDMRF					1			
ND	ND	ND	1-2	6	CAVRDRLGTLGSYIPTF						1		
2	2-1	CASSELGRL	10	18	CVVSTSLGRLYF							1	
27	2-4	CASSPLTGPVAKNIQYF	10	20	CVPRA#KLSF		1						
27	2-4	CASNPLAGEFTAKNIQYF	10	31	CVVNGRDARLMF					9			
4-1	2-7	CASSPGTSYEOYF	10	42	CVVSAH#YGGSQGNLIF						1		
2	2-1	CASSEALLAGGQL#SYNEQF	12-1	12	CVVNVRVDSSYKLIF					1			
20-1	2-7	CSASGRDSVYEQYF	12-1	8	ND					1			
9	2-2	CASSVTANTGELFF	12-2	16	CAVTRFSDGQKLLF		1						
28	1-6	ND	12-3	13	CAMSLGPFGYQKVTF					1			
25-1	2-1	CASSGLTSAKNEQFF	13-1	11	CAASPLGGYSTLTF					1			
29-1	2-3	CSVDALLGAYTQYF	13-1	20	CAALPSADYKLSF					2			
20-1	2-7	CSAATRDRVYEQYF	13-1	21	NFNKFYF					1			
28	1-2	CASSGLTSRADKYGYT	13-1	3	CAASXXQTVXQXXX					1			
6-5	1-1	CASSYNSPGQGAEAFF	13-1	4	#	LCPXPXXXXXQ*XX#F					1		
29-1	2-7	CSVVPLAGPYEQYF	13-1	44	CAALAGTASLTF							8	
29-1	2-7	CSVVPLMGGYEQYF	13-1	44	CACLTGTASKLTF					2			
10-3	2-3	CAISDYPGPKTQDTQYF	13-1	9	ND		1						
12-3	2-2	CASSAGLAGANTGELFF	13-2	16	CAENORFSDGQKLLF						1		
5-5	2-2	CASIPTRDGTGELFF	13-2	17	CAENLL#AGNKLT	F				1			
ND	ND	ND	13-2	28	CAEIKRSGAGSYQLTF								26
ND	ND	ND	13-2	49	CADPNITGNQFYF								
14	2-7	CASSRVPQGTGSYEQYF	13-2	49	XAXNTXXXFYF						1		
7-6	2-7	CASSRRWGSSEYEQYF	13-2	49	CADPNITGNOFYF						1		
9	2-3	CASSPTDNF	13-2	49	CADPNITGNQFYF						3		
25-1	2-3	CASSPGDGTQYF	13-2	50	CAEKTSYDKVIF						1		
11-2	2-7	CASHLMLAGGRYEQYF	14/DV4	13	XXXXXXXXSGDXDHKXX	F				1			
20-1	2-1	CSARRGLNEQFF	14/DV4	20	CAMREGYSNDYKLSF						1		
2	1-3	CAAVRPSTIYF	14/DV4	29	CAMRGSGNTXXXF					1			
20-1	2-1	CSARGGFRSQQGTDEQFF	14/DV4	31	CAMREGRSARLMF		3						
9	2-7	CASSLGTGPFSSEQYF	14/DV4	37	CXMRGXXSNTGKLIF		1						
9	2-1	CASSSKPGGDYNEQFF	14/DV4	9	CAITGGFKTIF					2			
ND	ND	ND	16	12	CAEGGDSSYKLF						1		
4-1	2-7	CASSQWGPSYEQYF	16	37	CALP#SSNTGKLIF						1		
7-9	1-5	CASSLTGSRNQPQHF	16	39	CXIRNFWQATXSHF		1						
5-6	1-5	CASSRRTATGNYQPOHF	16	8	XAXLI#VF								1
24-1	2-3	CATSDLVSQDTQYF	17	13	CDTAPERGGYQKVTF								
7-9	2-1	ND	17	21	CVGADNFNKFYF					2	1		
4-1	2-5	CASSQDGPRQQETQYF	17	22	CATDLIVSARQLTF		1				1		
27	1-1	CASWTGAEEAFF	17	24	CATDGVTDSWGKLQF						1		
29-1	2-2	CSVQRGRGELFF	17	34	CATAGSYNTDKLIF								
28	2-1	CASNLRVDEQFF	17	47	XXXEWWDGKNLVF					1			
4-1	1-1	CASSQSPGGTEAFF	17	48	CATDD#GNEKLT		1						
6-6	2-7	CASRQLAGFYEQYF	17	57	CATDAGPEKLVF		1	21					
25-1	1-1	CASSGLTDANTEAFF	19	11	CALTRSGYSTLTF		1						
4-2	2-1	CASSQTPGAYNEQFF	19	11	CALSEAGSGYSTLTF					1			
19	2-1	CASSISGGYNEQFF	19	17	CALITIKAAGNKLIF		1						
29-1	2-7	CSVETPGVYEQYF	19	20	XAVXFRAKXDKYKLSF						1		
2	1-4	CARRQGNEKLF	19	26	CALSVNQGQNFVF						1		
14	2-2	CASSQVLGPGELEFF	19	30	YFCXXSERSRDXKII	F				1			1
9	2-3	CASSPTDNF	19	36	CALSVLTGANNLFF								
9	2-1	CASSARDF	19	54	CALSEIQQAQKLF						1		
9	2-7	CASGSQGEHF	19	56	CALSRVGANSKLT						1		
20-1	1-6	CSATDRAAISNSPLHF	20	13	CAVQQQNNSGGYQKVTF					2		1	
5-5	2-5	CASSFTIAA#QETQYF	21	13	CAVLNNSGGYQKVTF								
20-1	2-1	CSARAGIREGYNEQFF	21	21	CGLRDNFNKFYF								
27	2-4	CASSTIAGETKNIQYF	21	30	CAVPIMRNDDKIIF		1						
20-1	1-5	CSATDRAVNQPOHF	23/DV6	40	CAASITPGTYKYIF					1			
24-1	1-2	CATSDPTDRVGDGYTF	24	40	CAFISTSGTYKYIF					1			
28	2-2	CASSFLTSANTGELFF	26-1	4	CIVRVPGPFGYKLF					1			
2	1-1	CASRLANTEAFF	26-1	53	CIVRLGGGGSNYKLT		1						
9	1-6	CASSVEGTVNPLHF	26-2	12	CILRTPLDSSYKLF		1						
6-1	2-4	CASSDIFLAKNIQYF	3	29	CAVRVLNTPLVF								
2	1-5	CASSEIASTRAOHF	3	3	CXLREQWXKII					1			
29-1	1-1	ND	3	30	ND					1			
9	2-1	CASSVSGGAYNEQFF	3	31	CAVRDYNARNALMF		26						
5-6	1-2	CASSLGRAVIWGYTF	3	37	CAPPRGSSNTGKLIF		1						
24-1	2-1	CATSDLTGANEQFF	36/DV7	13	CAGDGGYQKVTF					1			
3-1	2-3	CASSQDLASSTDQYF	38-1	4	CAFLFSGGYKLF					1			
ND	ND	ND	38-1	44	CAFMKHRTGTASKLTF								
4-1	1-6	CASSQDQAGASPLHF	4	10	VLXGGXXXXF								
5-4	2-1	CASSPPTGNEQFF	4	10	CLVGDDQAGGGGNKLTF					1			
6-1	2-7	CASSDRTGRNREQYF	4	10	CLVAAPGNKLTF						1		
7-2	1-5	CASSLATGSGNQPOHF	4	10	CLVGDDQILTGGGNKLTF					1			
7-3	2-5	CASSLGTGAQETQYF	4	10	CLVATILTGGGNKLTF						1		
30	2-2	CAWDYLTNTGELFF	4	13	CXVGDSHCGGYQKVTF					1			
2	2-1	SPAVERVANNEQLF	4	16	CLVGAYGQRLLF						1		
4-2	2-7	CASSQSGTGPYEQYF	4	18	CLVGDRGSTLGRLY	F					1		

7-2	2-7	CASSPSSREQYF	4	21	CLVVGFKFYF	1
2	2-7	CASSLNLDRYEQYF	4	22	CLVGFPSGSARQLTF	1
12-3	1-1	CASRQRGGRVNXEAFF	4	23	CLVGDPFWNQQGKLIF	1
4-1	2-1	CASSQVRGPQFF	4	23	CLVGDQGGKLIF	1
ND	ND	ND	4	27	CLVGDMNTNAGKSTF	2
20-1	1-5	ND	4	29	CXXQGGNTHLWI	1
ND	ND	ND	4	3	CXXGDSXXSKII	1
11-2	1-4	CASSLFRGGEKLF	4	30	CLLYRDDKII	1
2	2-7	CASRTPTGSGSYEQYF	4	30	CLVGDPSPRRDKII	1
ND	ND	ND	4	32	CLVGDKTPGATNKXF	1
4-1	2-2	CASSHNGELFF	4	32	CLVDGGATKNLIF	1
2	2-2	CASSLNRELF	4	39	CLVGVRYAGNMMLTF	1
5-6	1-1	CASSLLRDGGRGAFF	4	39	CLVGGWDAGNMMLTF	1
6-5	1-3	CASRGQRNTIYF	4	39	CLVGDPLNNAGNMMLTF	1
14	2-7	CASSPMGHEQYF	4	4	CLVGDQGGGYNKLIF	1
29-1	2-3	CVERGDTQYF	4	4	CLVGVFXGGXNKLIF	1
29-1	1-1	CSVPGTGNEAFF	4	40	ND	1
10-3	2-7	CAIRIKGHAXATSSHF	4	41	CLVSSGYALNF	1
20-1	2-2	CSAGGLAAGPELFF	4	42	XXVGXXKXGGSQGNLIF	1
5-4	2-1	CASSRLLAGGRNEQFF	4	45	CLMYSSGGADGLTF	1
11-3	1-2	CASSSPGREMTF	4	5	CLVGDPMDTGRRALTF	1
3-1	2-6	ND	4	6	CLVGDVGGSYIPTF	1
7-9	ND	ND	41	50	CAVRSR#TSYDKVIF	1
28	2-3	CASSLVAGTDTQYF	41	58	CAREIGSRLTF	1
29-1	2-7	CSVVPLAGPYEQYF	6	3	CAG#GYSSASKII	1
24-1	2-2	CATSPLAGEYSGELFF	6	35	CALVVGFGNVLHC	1
25-1	2-7	CASSPLLGFFAEQYF	6	35	CAP#FGNVLHC	1
20-1	1-6	CSAKPRENWNSPLFH	6	38	CALDPOXGNRNRKLW	1
29-1	2-7	CSVVPLAGPYEQYF	6	38	XGFEVRAGNNTKLFW	1
15	2-5	CATSRRTVLRETQYF	6	43	CALGVNNNDMRF	1
28	2-7	CASMGLAGGQEQQYF	6	6	CALDPR#SSGGSYIPTF	1
6-5	2-1	CASSYMMGRASQEYNEQFF	6	8	CALE#NTFGOKLIF	1
29-1	2-5	CSVSGQKEETQYF	8-1	12	CAPPDDSSYKLIF	1
9	1-6	CASSSPGPQPNNSPLHF	8-1	16	CAVITSDGQKXXF	1
6-2	2-1	CASAALAAAYNEQFF	8-2	13	CAGGYQKVTF	1
6-1	2-2	CASVGLAVGELFF	8-2	16	CAVAFADGQKLLF	1
5-6	2-6	CASTPKPFSGANVLTF	8-2	28	CVVSR#HR#GAGSYQLTF	1
15	2-1	CATSGTGTSGRNEQFF	8-2	3	CAPVSYSSASKII	1
28	1-1	CASTPLGTSSFLNTEAFF	8-2	4	CVVSEAGGYNKLIF	1
6-5	1-1	ND	8-2	41	CAVSYSNSGYALN	1
27	2-4	CASSPIAGGPISKNIQYF	8-2	44	CAVSATGTASKLTF	1
6-2	1-6	ND	8-2	48	CAVPNFGNEKLTF	1
14	2-2	CASSRLAGGNTGELFF	8-2	9	CVVANGFKTF	1
3-1	1-2	CASSQPAGYGGYTF	8-3	16	CAVVFGSDGQKLLF	1
27	2-4	CASRALTGHDPAKNIQYF	8-3	34	CAVGARNTDKLIF	1
29-1	2-5	CSVVGTGPPETQYF	8-4	15	CAVMRGTLIF	1
6-6	2-7	CASSYLPGPAGEQYF	8-4	27	CAVTPP#NAGKSTF	1
18	2-5	CASSPADRTSLEGETQYF	8-4	29	CAVSA#SGNTPLVF	1
7-2	2-7	CASSGGYEQYF	8-4	3	CAPVYSSASKII	1
3-1	2-1	CASQPLAGGPNEQFF	8-4	39	CAVITSNNAGNMMLTF	1
ND	ND	ND	8-4	43	CTVSAKPNDMRF	1
6-1	1-1	CASSPDRALPEAFF	8-4	48	CAVPNFGNEKLTF	1
28	2-5	CASSSLTQGSQETQYF	8-4	5	CVGRDTGRRALTF	5
7-9	2-7	CASSPQTGSRPYEQYF	8-6	31	CASETGPARLMF	1
14	1-3	CASTPGGRRSQNTIYF	8-6	36	CAVTG#QTGANLFF	1
9	1-2	ASKLWASGSGYGYTF	8-6	5	CAVRL#DTGRRALTF	1
27	1-2	CASRGGGQQGGSYGYTF	8-6	F	1	
27	2-3	CASSTRTGFSDTQYF	8-6	52	CAGGGYQKLIF	1
14	2-1	CASSGLAGGYNEQFF	8-6	6	CAVSVLY#SSGGSYIPTF	1
19	1-2	CASSTLTGADKLNYGTYF	9-2	9	CAARLSFKTF	1
27	2-1	CASSSLTSGAHNEQFF	9-2	23	CALSVQNGGKLIF	1
11-3	2-1	ND	9-2	39	CALTRRNAGNMMLTF	4
14	1-3	CAXTPGGRRSKNTHIF	9-2	40	CALSSTS GTYKYIF	1
27	2-5	CASSPLSGTSATKETQYF	9-2	40	CALSATS GTYKYIF	1
10-3	2-3	CAISDYPGPKTQDQYF	9-2	9	CAXSDRGGFKTIF	1
				Total	36	32
					40	39
					24	31
					31	31
					31	31

Ac = acute; F<sub>up</sub> = follow-up convalescent sample; ND, not determined; X = any amino acid; # indicates an out-of-frame shift; \* = stop codon.

**Table S3.** A2/S269<sup>+</sup>CD8<sup>+</sup> TCR $\alpha\beta$  repertoires. Related to Figure 6.

TRBV	TRBJ	CDR3 $\beta$	TRAV	TRAJ	CDR3 $\alpha$	#02 0 Ac	#89 Ac	#86 F <sub>up</sub>	CA7	CA2
19	2-2	CATQNMMNTGELFF	ND	ND	ND					1
2	2-2	CASSEIDTGEFFF	ND	ND	ND		1			
7-9	2-7	CASSPDIEQYF	ND	ND	ND					1
4-2	2-3	CASSQTESTDTQYF	1-1	37	CAHWGSSNTGKLIF					1
3-1	2-2	CASQLQNTGELFF	1-2	38	XAVRDNAGXXXKXW					1
20-1	2-2	CSARDPRAQNTGELFF	1-2	4	CAGPPNKLIF					1
20-1	1-2	CSAQTDRLNLGGYTF	10	39	CVVSAR#AGNMLT	2				
3-1	2-2	CAVQGMNTGELFF	10	55	ND	1				
28	2-2	CASSPTGGGNTGELFF	12-1	11	CVVNEPLSGYSTLTF	1				
29-1	2-2	CSARGLAEANTGELFF	12-1	15	CVVNIPQAGTALIF	1	2			
13	2-2	CASSFPGGGNTGELFF	12-1	24	CVVNAADSWGKLQF					1
20-1	2-2	CSARGQQGLNTGELFF	12-1	29	CVVNLPENGTPLVF					1
7-9	2-7	CASSLDIEQYF	12-1	30	CVVNKYDKIIF					1
7-9	2-7	CASSLDIEQYF	12-1	31	XVNNXXDRMLX		1			
12-3	2-2	CALGEQNTGELFF	12-1	34	CVVNKKDKLIF	1				
2	2-2	CASPQNQTGELFF	12-1	34	CVVNGNTDKLIF	1				
7-9	2-2	CARGLANTGELFF	12-1	34	CVVNGADKLIF	1				
12-3	2-2	CASINLNTGELFF	12-1	39	CVVNSHAGNMLTF					1
29-1	2-2	CSVEADRNTGELFF	12-1	41	CVVNKDSGYALNF					1
11-2	2-2	ND	12-1	43	CVVNNNNNDMRF		1			
12-3	2-2	CALGDLNTGELFF	12-1	43	CVVNRNNNDMRF					1
12-3	2-2	CASGKQNTGELFF	12-1	43	CVVNEKDDMRF					1
12-3	2-2	CAAGQGNTGELFF	12-1	43	CVVNRAADDMRF					1
12-3	2-2	CASINLNTGELFF	12-1	43	CVVNNNNNDMRF					1
12-3	2-2	CARGDANTGELFF	12-1	43	CVVNNNNNDMRF		2			
19	2-2	CAGQVTNTGELFF	12-1	43	CVVNRNNNDMRF		1			
2	2-2	CASSDLNTGELFF	12-1	43	CVVNGGNDMRF	1				
2	2-2	CASSDLNTGELFF	12-1	43	CVVGNNNNDMRF	1				
2	2-2	CASSEIDTGEFFF	12-1	43	CVVNRRNNNDMRF	1				
2	2-2	CASGQLNTGELFF	12-1	43	CVVNRGNDMRF					1
2	2-2	CASNDLNTGELFF	12-1	43	CVVNKGNDMRF					1
2	2-2	CASQDTNTGELFF	12-1	43	CVVNKGNDMRF		1			
2	2-2	CAVEGNLNTGELFF	12-1	43	CVVNNNNNDMRF					1
20-1	2-2	CSARDRQQGNTGELFF	12-1	43	CVVXSFDMMRF					1
24-1	2-2	CATQRANTGELFF	12-1	43	GVVNMGDDMMRF	1				
3-1	2-2	CAVQGMNTGELFF	12-1	43	CVVNNNNXDMRF	1				
5-1	2-2	CASGEENT#GELFF	12-1	43	CVVNKNNDMRF		1			
5-4	2-2	CASSPDRTNGELFF	12-1	43	CVVNVMDMMRF	1				
5-8	2-2	CAIIDRNTGELFF	12-1	43	CVVNREDDMRF	1				1
6-5	2-2	CATTSLNTGELFF	12-1	43	CVVNRDNDMRF		1			
7-8	2-2	CASGQLNTGELFF	12-1	43	CVVNNNNNDMRF		1			
7-8	2-2	CASYFQDTGELFF	12-1	43	XVNGXXDMXF	1				
7-8	2-7	CASSAGVSGEQYF	12-1	43	CVVNVVDDMMRF	2				
7-9	2-3	CASSLDIEQYF	12-1	43	CVVNSFDDMMRF					1
29-1	2-2	CSARTSGQNTGELFF	12-1	47	XVXNREDKLVF	1				
7-9	1-1	CASSPDIVAFF	12-2	30	CAVNRRDDKIIF					1
7-9	1-1	CASSLDIEAFF	12-2	30	CAVNQDDKIIF	1	1			
7-9	2-1	CASSFDIAEFF	12-2	30	CAVNQDDKIIF	1				
7-9	2-7	CASSPDIEQYF	12-2	30	CAVNRRDDKIIF	1			1	
9	2-5	XPXGXXXX	13-1	21	CAVQNFNKFY				1	
20-1	2-2	CSARDPLAINTGELFF	13-1	28	CAAS#YSGAGSYQLTF	1				
20-1	2-2	CSARDPLAINTGELFF	13-1	29	ND	1				
7-9	2-1	CASSPDIDQFF	13-1	3	CAATPE##SSASKIIF					1
7-3	1-5	CASSPDDGQPQHWF	13-1	39	XPXXRXXXXQ##TF					1
7-8	2-2	CGELAQNTGELFF	13-1	47	CAAFGXXXQ##VF		1			
2	1-1	CASPKRTGLSNTAEFF	13-1	48	XXXXXXXXX##F					1
9	2-2	CASSEENTGELFF	13-2	3	CAEPSSASKIIF	1				
2	2-2	CASQNRDTGELFF	13-2	35	CAES#IGFNVHLHC					2
20-1	2-2	CSARGKREHNTGELFF	13-2	42	CAENSHPRGGGSQGNLIF	1				
7-9	2-2	CAPGVPTNGELFF	13-2	49	CADT##NTGNQFYF	1				
25-1	2-2	CALQDXNTGEXXF	14/DV4	20	CAMRE#SNDYKLSF	1				
24-1	2-1	CATSGPLPR#SYNEQF	14/DV4	21		1				
15	2-2	CATTEGVAGELF	14/DV4	27	ND					1
27	2-7	CASSDRGRSYEQYF	14/DV4	28	CAMREAPFAYSGAGSYQ		1			
ND	ND	ND	14/DV4	41	LTF					
15	2-2	CATTEGVAGELF	14/DV4	42	CAMREGSGYALNF					1
9	2-7	CASSVEPGWDQEYF	14/DV4	48	CATR##GSQGNLIF					3
19	2-7	CASSIGDEQYF	14/DV4	5	CAMRGAGNEKLTF					
19	2-3	CASSIDLADTQYF	16	15	LLLCRDC#DTGRRALTF		1			
6-1	2-2	CASQRMMNTGELFF	16	37	CAXPXACXXC##IF					1
24-1	2-1	CATSGPLPR#SYNEQF	16	42	CALQ#GSSNTGKLIF					1
7-8	1-2	CASSSDSYGYTF	16	42	CALSD#YGGSGQGNLIF		1			
2	2-2	CASTRDLNTGELFF	16	43	CALGGRVDNDMRF		1			
ND	ND	ND	17	16	CGGGGQKLLF	1				
20-1	2-2	CSARDPWGINTGELFF	17	29	VXXVSSGNTLHF		1			
7-8	2-2	CASSFQDTGELFF	17	52	CVXXIXXXXXXXXK##TF					1
6-6	2-2	CASENRNTGELFF	17	54	CAPEIQGAQKLVF					
19	2-2	CASQTLNTGELFF	19	47	CALTPLRPKLVF					
13	2-2	CASSPLQGGNTGELFF	21	28	ND	2				
7-8	2-2	CASSLQNTGELFF	21	30	ATYLCAAGDDKIIF	1				
5-1	2-2	CASGDENTGELFF	23/DV6	34						1
7-9	2-2	CAGGEPTNGELFF	23/DV6	34	CAASRADKLIF	1				
2	2-2	CAINEQNTGELFF	23/DV6	35	CAASXXXXAXGMX#HC					1
7-9	1-1	CASSPDIEAFF	23/DV6	4	XAASRNLLWXOX###IF					1
15	2-2	CATQEGNTGELFF	23/DV6	44	CAV*TGTASKXTF					1
10-2	2-2	CASLVQENTGELFF	23/DV6	45	ND	1				
20-1	2-2	CSAPSYGELEFF	23/DV6	49	CAADYTGNQFYF					1
4-2	2-3	CASSQVESADTQYF	23/DV6	49	CAAXYXXXQXYX					
27	1-5	CASSYSSYGSNQPHF	24	28	XXXXWGXGSXQLTX		1			1
4-2	2-2	CATQDANTGELFF	25	42	CAGLGDGGSQGNLIF		1			

11-2	2-3	CASSLGWDGNTDTQY F	25	43	GLNDMRF		1
20-1	2-2	CSARDALAQNTGELFF	26-1	43	XSQLHPRGEQXQXHX#F	1	
19	2-2	CATQITNTGELFF	27	30	CAGP#MRDDKIF		1
7-9	1-2	CASSDSLGYTF	27	42	XXXXXXXXXXXX#	1	
27	2-3	CAKTGIA#QYF	29/DV5	17	CAASALWA#AGNKLTF	1	
4-1	2-3	CASQLVNTGELFF	29/DV5	21	CAAS'RNFNKFYF		1
20-1	2-2	CSAGDLNTGELFF	29/DV5	26	CAATNGSNYGQNFFF	2	1
7-9	2-2	CASSNDPNTGELFF	29/DV5	31	#RLMF		1
29-1	2-2	CSARGLAEANTGELFF	3	17	CAVS#KAAGNKLTF	6	
29-1	2-2	CSVTDNRNTGELFF	3	34		1	
6-5	2-5	CASSYPTGEGQETQYF	3	34	CAVRDKNTDKLIF	2	2
15	2-2	CATGELNTGELFF	35	42	CAGPPR#GSQGNLIF	2	
20-1	2-2	CSAQGDLNNTGELFF	35	42	CAGQC#GSQGNLIF	1	
7-9	2-2	CASGEGNNTGELFF	35	49	CAGQGGET#FYF		1
28	2-2	CASSYKNTGELFF	35	52	CAGPT#GGTSYGKLTF		1
12-3	2-3	CASSFARAQADTQYF	38-2/DV8	31	CALMSARLMF		1
28	2-7	CASSLETAGEQYF	39	49	CAVDMDTNQFYF	1	
29-1	2-7	CSVDRGSPSYEQYF	41	45	CAVREGADGLTF		1
18	2-7	CASRDGRESYEQYF	41	48	CAVIPDFGNEKLTF		1
2	1-1	CASSPRNNSLEAFF	41	57	CAVQP#QGGSEKLVF		1
2	2-2	CASQDRNTGELFF	5	14		1	
2	2-2	CASSGGQGANTGELFF	5	23	CAEKAY##NQGGKLIF	1	
7-9	1-1	CASSPDIEAFF	5	30	PPTXVP#NRDDKIF		1
7-9	2-1	CASSLAGPNEQFFF	5	36	XAEEDQXGANNNXF		1
7-3	2-1	CASSTPLENEQFFF	5	37	CAEENGTGKLIF		1
20-1	1-4	CSARDPSGVKLFF	5	48	CAEILDFTGNEKLTF	2	13
10-3	2-5	CAISDGDWETQYF	6	23	ND		1
2	2-2	CASSDLDTGELFF	6	43	CALDVAL#NDMRF		1
7-9	2-2	CASNANTGELFF	6	49	CALVGNQFYF		2
19	2-2	CASQILNTGELFF	8-1	50	XXVNVSPIKEXXXRQXXX#		1
20-1	1-2	CSARDFLGGYTF	8-2	8	XXXSDXXEXRXSXXX#		1
20-1	1-4	CSARDPSGVKLFF	8-2	8	XXXIXXXXXXKKFFF		1
2	2-2	CASSELNGGNTGELFF	8-3	22	S#SGSARQLTF		1
2	2-2	CASSELDGELFF	8-4	27	CAVLpq#AGKSTF	1	
5-4	2-2	CASSPDRTGELFF	8-4	34	CAVT'SYNTDKLIF	1	
5-1	2-2	CATSDSNTGELFF	8-4	52	CAVSRA#AGGTSYGKLTF	1	
12-3	1-4	CASTLAGTGEEKLFF	8-6	11	CAYSGYSTLTTF		1
7-8	2-2	CASSLGISGELFF	8-6	13	SA#QKVTF	1	
20-1	2-7	CSAEGDRNSLRTYF	8-6	41	CAHVA#NSNSGYALNF		2
20-1	2-2	CSARWGLLVNTGELFF	8-6	6	S*GAGGSYIPTF		
28	2-2	CASSPTGGGNTGELFF	9-2	3	CAVRTY#SSASKIIF	3	
7-8	2-2	CAKQGLDTGELFF	9-2	37	CGGREL*QHRO##IF	1	
5-1	2-2	CASSGLNTGELFF	9-2	43	CAXSDKXX#DMRF		1
2	2-2	CASSDLNTGELFF	9-2	45	CALSAPYSGGGADGLTF	1	
20-1	2-2	CSARDLSAQNTGELFF	9-2	5	CXSSSRAGEHL#F		
		Total		3	60	37	12
						6	57

Ac = acute; F<sub>up</sub> = follow-up convalescent sample; ND, not determined; X = any amino acid; # indicates an out-of-frame shift; \* = stop codon.

**Table S4.** TCR diversity scores of pre-pandemic and COVID-19 TCR $\alpha\beta$  repertoires. Related to Figure 7.

Epitope	Group	#Donors	#TCR $\alpha\beta$ pairs	#TCR $\alpha\beta$ clones	TCRdiv- $\alpha$	TCRdiv- $\beta$	TCRdiv- $\alpha\beta$
A2/S <sub>269</sub> *	COVID-19	4	43	35	34.8	101.0	147.9
A2/S <sub>269</sub>	COVID-19	5	75	57	29.8	76.9	100.1
B7/N <sub>105</sub>	Pre-pandemic	4	43	37	935.7	322.9	730.4
B7/N <sub>105</sub> *	COVID-19	4	42	25	282.3	291	299.9
B7/N <sub>105</sub>	COVID-19	4	82	42	809.8	831.9	860.6
A2/EBV*	Dash et al., 2017	4	46	17	5	9.2	6.6
A2/EBV	Dash et al., 2017	6	470	76	9.5	15.3	14.9
A2/M1*	Dash et al., 2017	4	43	19	15.4	8	16.9
A2/M1	Dash et al., 2017	15	453	275	21.3	5.8	21.4
A2/CMV*	Dash et al., 2017	4	48	9	36	35.4	36
A2/CMV	Dash et al., 2017	10	307	61	61.3	134	421.5

\*TCRs were randomly subsampled from the full dataset for ease of comparisons to the smaller B7/N<sub>105</sub> pre-pandemic and A2/S<sub>269</sub> COVID-19 TCR datasets.