

Supplemental information

CD8⁺ T cells specific for an immunodominant

SARS-CoV-2 nucleocapsid epitope display high naive

precursor frequency and TCR promiscuity

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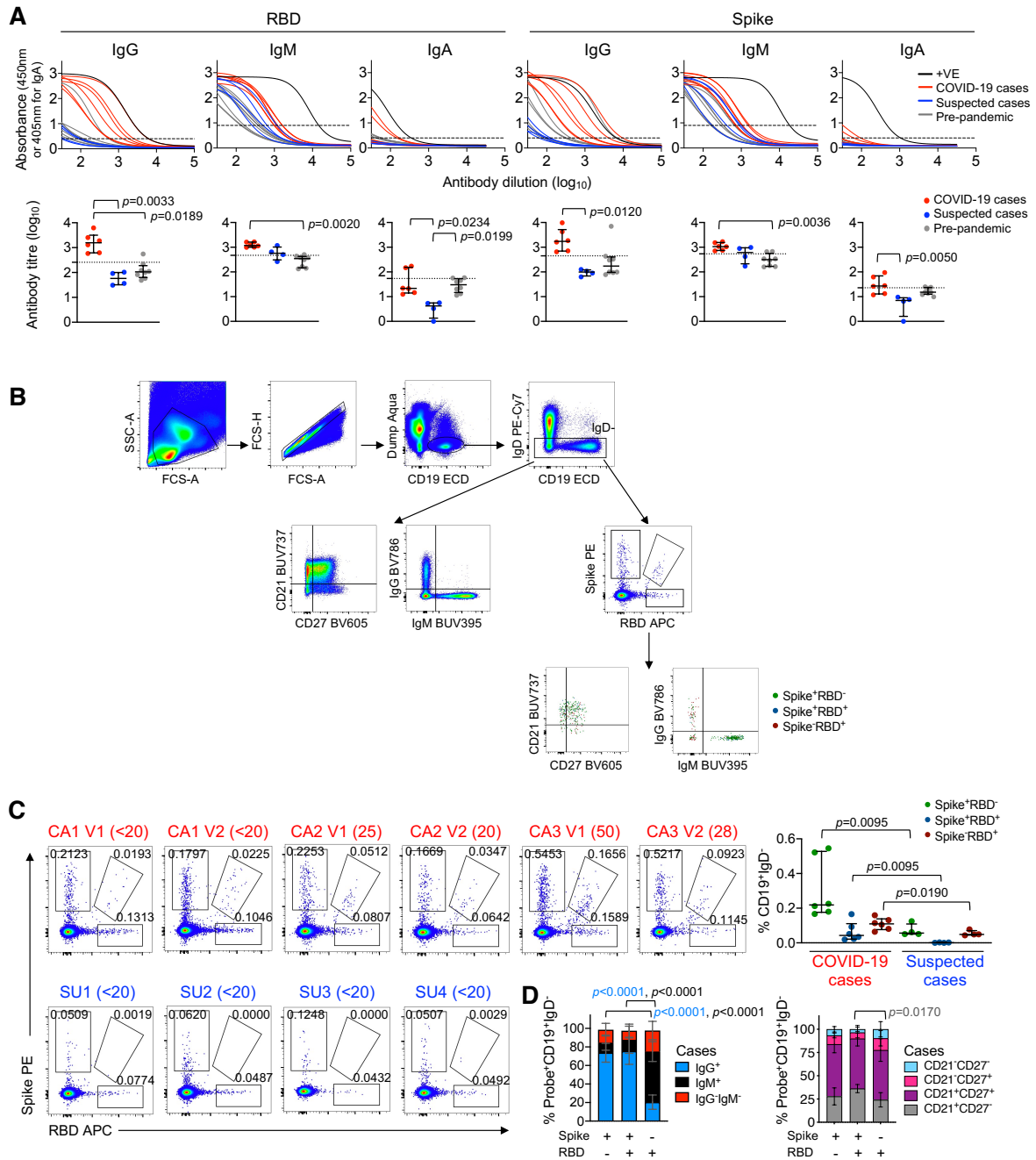


Figure S1. COVID-19 traveller cohort, SARS-CoV-2-reactive antibody and B cell signatures. (A) ELISA titration curves (top) against the SARS-CoV-2 RBD and Spike proteins for IgG, IgM and IgA in COVID-19 cases (CA, $n=3$, 2 time points each), suspected cases (SU, $n=4$) and pre-pandemic healthy donors ($n=8$). 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⁻, IgM^{+/-}, IgG^{+/-} and analysed for binding to SARS-CoV-2 probes, with expression of CD21/CD27. (C) Co-staining of class-switched B cells (CD19⁺IgD⁻) with RBD and Spike probes. Microneutralization titres are bracketed and shown alongside the donor codes. Frequencies of Spike⁺, RBD⁺ and Spike⁺RBD⁺ B cells as a proportion of CD19⁺IgD⁻ 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⁺, RBD⁺ and Spike⁺RBD⁺ CD19⁺IgD⁻ B cells; data are shown as mean with SD. Statistical significance was determined with Tukey's multiple comparisons test. Related to Figure 1.

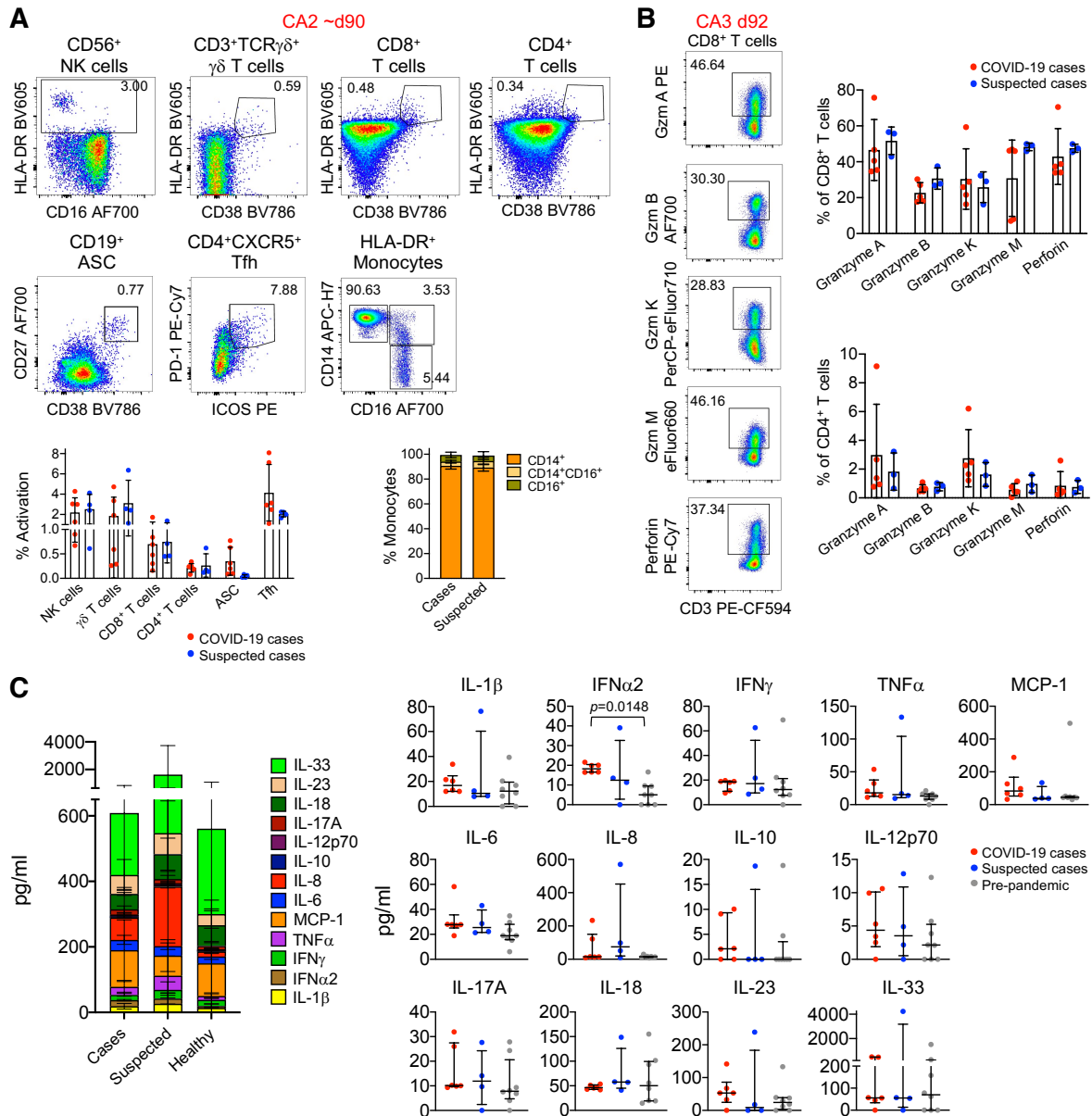


Figure S2. Lack of immune cell activation in traveller cohort at convalescence. (A) Representative FACS plots of activated CD38⁺ NK cells, activated CD38⁺HLA-DR⁺ $\gamma\delta$, CD8⁺ and CD4⁺ T cells, as well as activated CD38⁺CD27⁺ ASC, ICOS⁺PD-1⁺ Tfh and monocytes in a COVID-19 case. Proportion of activated immune cells (left) and monocyte 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⁺ T cells expressing different cytotoxic molecules (Granzyme A, B, K, and M and perforin) in a COVID-19 case. Proportion of cytotoxic CD8⁺ and CD4⁺ 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⁺ T cells with exclusion for B cell/monocyte markers, then gated as CD4⁺ or CD8⁺ 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.

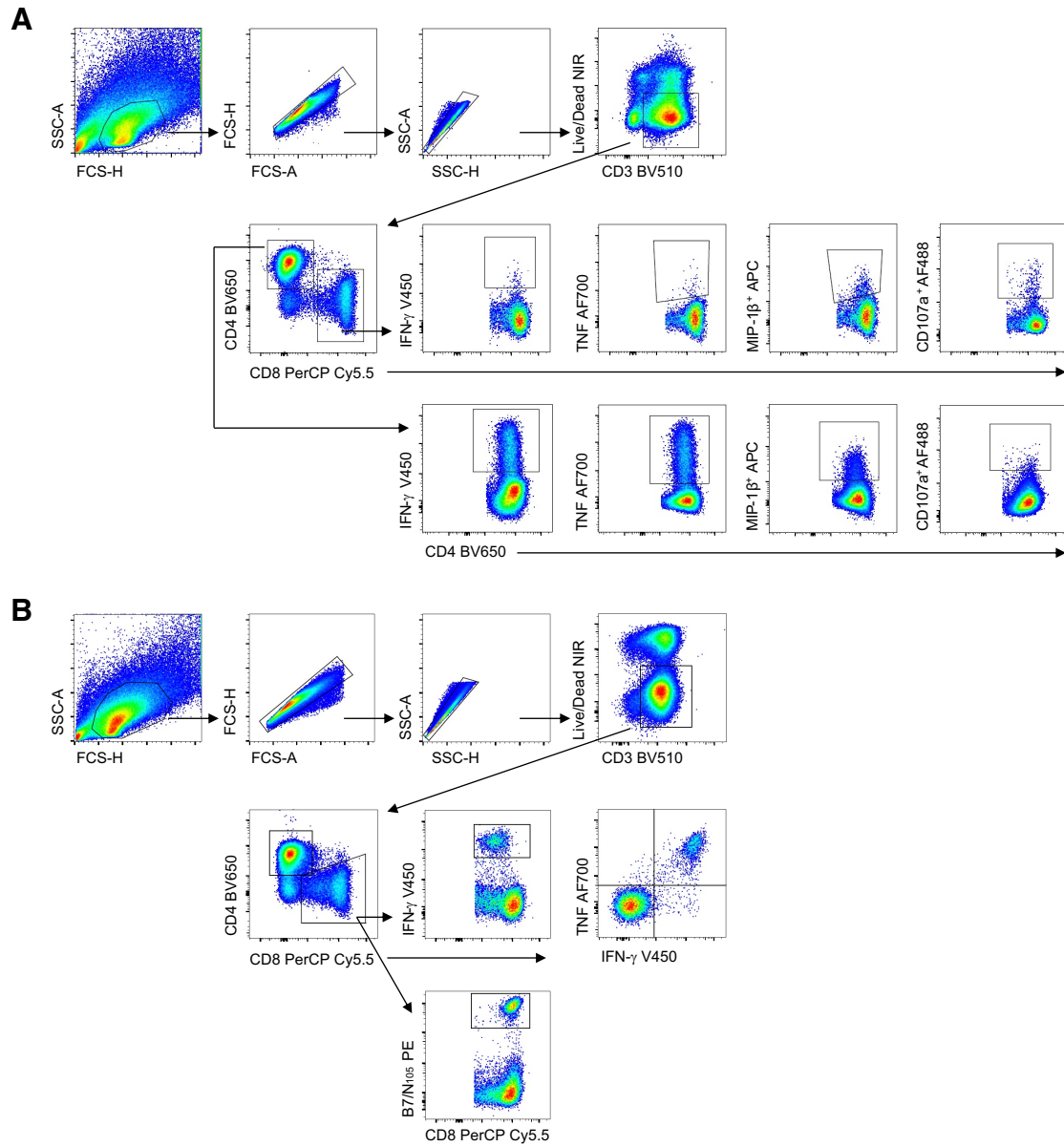


Figure S3. Gating strategies for CD4⁺ and CD8⁺ T cell responses to SARS-CoV-2 overlapping peptide pools. (A) ICS gating strategy for intracellular IFN- γ , TNF, MIP-1 β and CD107a after PBMCs were stimulated for 10 days with SARS-CoV-2 overlapping peptide pools. (B) Gating strategy after day 10-cultured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

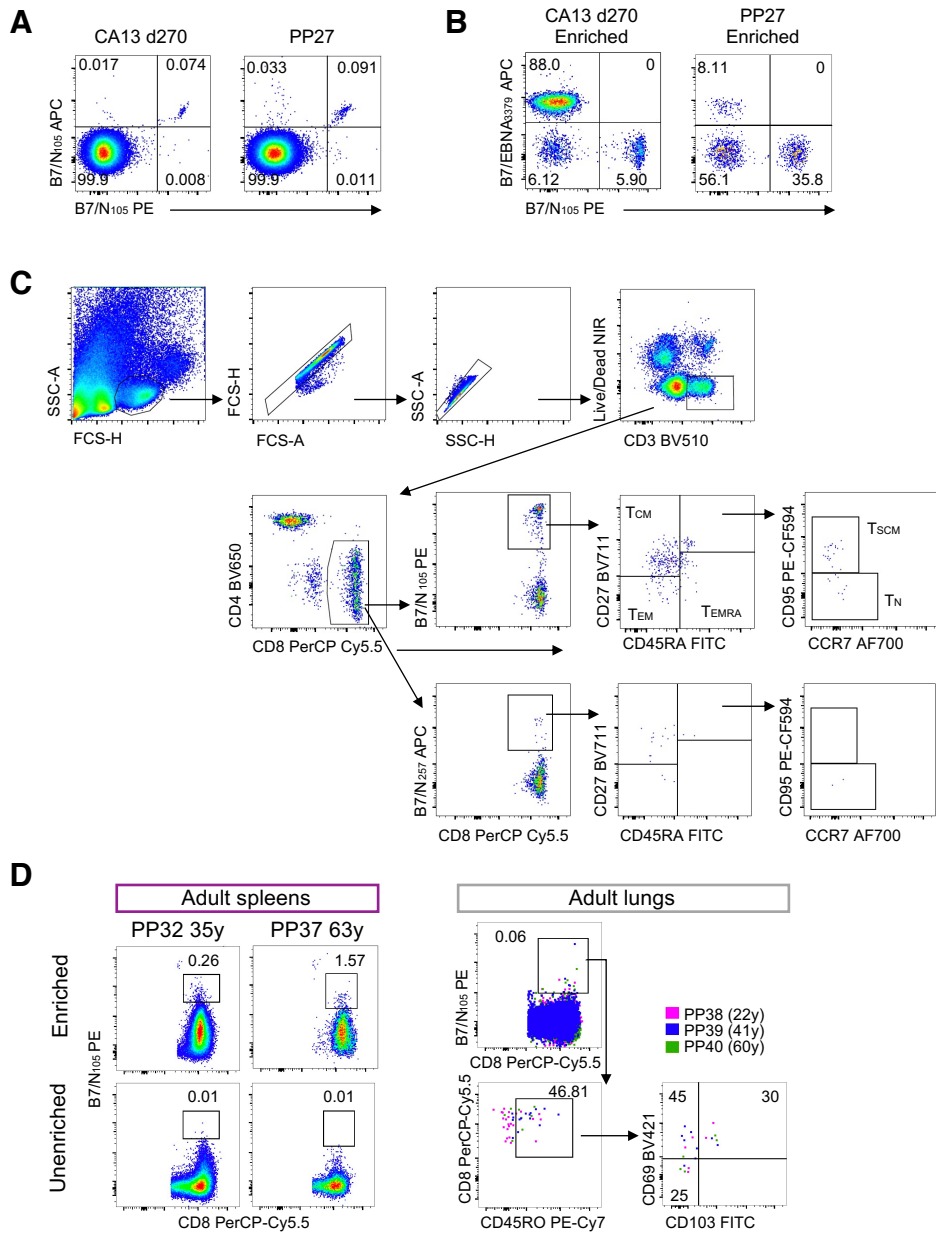
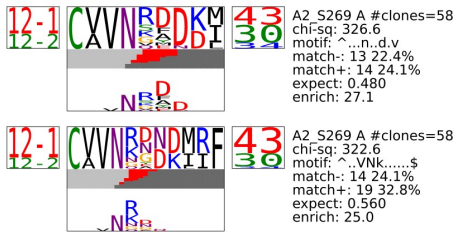


Figure S4. B7/N₁₀₅⁺CD8⁺ tetramer validation and staining in spleen and lungs. (A) FACS plots showing direct *ex vivo* dual-tetramer staining of the immunodominant B7/N₁₀₅ tetramer conjugated to PE and APC fluorophores in a COVID-19 and pre-pandemic donor. (B) TAME-enriched tetramer populations using B7/N₁₀₅ tetramer-PE and an irrelevant B7/EBV-tetramer (EBNA-3₃₇₉₋₃₈₇, RPPIFIRRL) conjugated to APC, representing 2 out of 4 experiments. Cells were gated on the total CD8⁺ T cell population. (C) Gating strategy of enriched tetramer⁺ cells and phenotype populations. (D) B7/N₁₀₅ 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⁺ T cells. Related to Figure 2 and Figure 3.

TCR-α



TCR-β

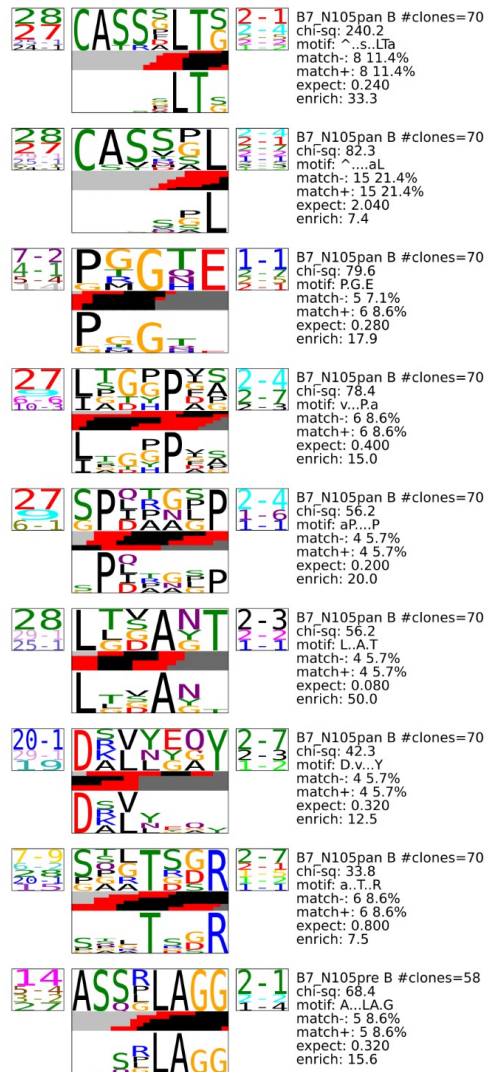
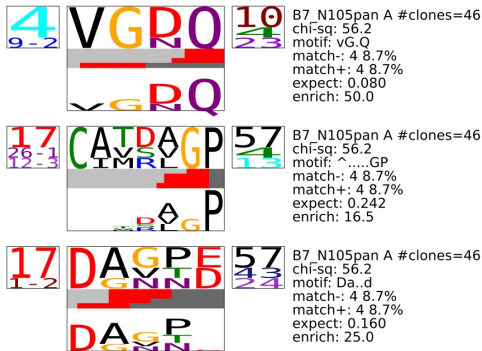
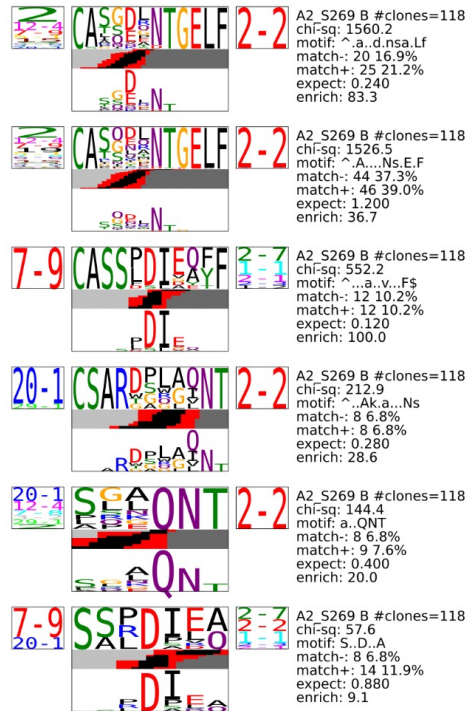


Figure S5. TCRdist analysis of alpha and beta motifs for COVID-19 epitopes. Enriched alpha and beta amino acid motifs in the CDR3 region were generated by TCRdist for all TCR pairs. Each TCR chain motif depicts the variable (left side) and joining (right side) gene frequencies, CDR3 amino acid sequences (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.

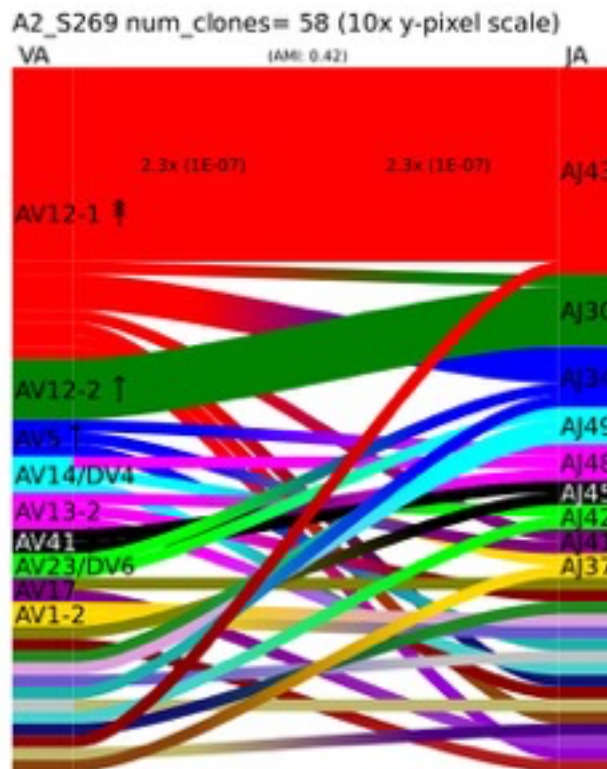


Figure S6. Significant TRAV12-1 to AJ43 gene pairing for the A2/S269 epitope. Gene segment usage and pairing landscapes are shown for the dominant A2/S269 TCR motif. Each clonotype is assigned the same vertical length irrespective of clonotype size. Each vertical stack reflects the V (left) and J (right) 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, 24:02	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	07:02
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, 24:02	07:02
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	02:01	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	02:01 , 03:01	07:02, 39:10
CA17	52	F	Heparinized blood	COVID-19 Case	5	-	-	-	ICU	High flow nasal prong	02:01 , 68:01	08:01, 44:02
CA18	54	M	Heparinized blood	COVID-19 Case	-	46	-	-	Ward	No	02:01 , 31:01	38:01, 44:03
CA19	56	M	Heparinized blood	COVID-19 Case	-	145	-	-	Home	No	02:01 , 26:01	44:02
CA20	58	M	Heparinized blood	COVID-19 Case	-	71	-	-	Home	No	24:02	35:01, 55:01
CA21	75	M	Heparinized blood	COVID-19 Case	-	121	-	-	Home	No	01:01, 24:02	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	07:02
PP10	5	M	Tonsil/ Heparinized blood	Pre-pandemic Child	-	-	-	-	-	-	03:01	07:02 , 57:01
PP11	7	F	Tonsil/ Heparinized blood	Pre-pandemic Child	-	-	-	-	-	-	01:01, 03:01	07:02 , 08:01
PP12	15	M	Tonsil/ Heparinized blood	Pre-pandemic Child	-	-	-	-	-	-	03:01	07:02 , 14:01
PP13	30	M	Buffy pack	Pre-pandemic Adult	-	-	-	-	-	-	01:01, 24:02	07:02 , 57:01
PP14	35	F	Buffy pack	Pre-pandemic Adult	-	-	-	-	-	-	01:01, 03:01	07:02 , 08:01
PP15	36	F	Buffy pack	Pre-pandemic Adult	-	-	-	-	-	-	02:01, 02:05	07:02 , 41:01

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

*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⁺CD8⁺ TCRab repertoires. Related to Figure 5.

TRB V	TRB J	CDR3β	TRAV	TRA J	CDR3α	#0	CA 5	CA 2	CA 4	BP12 4	BP15 5	BP16 1	BP16 0
20-1	2-1	CSARDTAGATYNEQFF	ND	ND	ND								
20-1	2-1	CSAWRGRGADNEQFF	ND	ND	ND					1			
28	2-3	CASMPGLEVLDTQYF	ND	ND	ND							1	
28	2-5	CASSDRGMGETQYF	ND	ND	ND							1	
29-1	2-5	CSVVGTGGPETQYF	ND	ND	ND							1	
29-1	2-7	CSVVPLAGPYEQYF	ND	ND	ND							1	
7-2	1-1	CASRGGGTEAFF	ND	ND	ND			4				2	
28	2-1	CASSSLASSSYNEQFF	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							1	
27	1-4	CASSLLAGGRAADKEKLF	1-2	18	CAA#DRGSTLGRLYF						1		
2	2-4	CASSEEIAKNIQYF	1-2	31	CAVRVFNARLMF			1					
5-4	2-4	CASSLETGRNIQYF	1-2	35	WAIGFGNVLHC				2				
20-1	1-6	CSARDRTDSYNSPLHF	1-2	43	CADANNDMRF				1				
ND	ND	ND	1-2	6	CAVRDRGLTGGSYIPTF					1			
2	2-1	CASSELDGRL	10	18	CVVSTLGRLYF							1	
27	2-4	CASSPLTGGPPVAKNIQYF	10	20	CVPRA#KLSF		1						
27	2-4	CASNPLAGEFTAKNIQYF	10	31	CVVNGRDARLMF				9				
4-1	2-7	CASSPGTSEYQYF	10	42	CVVSAH#YGGSQGNLIF					1			
2	2-1	CASSEAELAGGQL#SYNEQF	12-1	12	CVVNVVDSSYKLI			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	CAMSLPGGYQKVTF			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	CSAATRDVYEQYF	13-1	21	NFNKIFY				1				
28	1-2	CASSGLTSDRAKYGYTF	13-1	3	CAASXXQTVXQXXX				1				
6-5	1-1	CASSYSNPGQGAEEFF	13-1	4	#				1				
29-1	2-7	CSVVPLAGPYEQYF	13-1	44	LCXXPXXXXXQ'XX#F				1				
29-1	2-7	CSVVPLMGGEYQYF	13-1	44	CAALAGTASKLTF							8	
10-3	2-3	CAISDYPGPKTQDTQYF	13-1	9	CACLTGTASKLTF				2				
12-3	2-2	CASSAGLAGANTGELFF	13-2	16	ND	1							
5-5	2-2	CASIPTRDTGELFF	13-2	17	CAENQRFSDGQKLLF				1		1		
ND	ND	ND	13-2	28	CAENLL#AAGNKLTF				1		1		
ND	ND	ND	13-2	49	CAEIKRSGAGSYQLTF								
14	2-7	CASSRVPQGTGSYEQYF	13-2	49	CADPNTGNQFYF							1	26
7-6	2-7	CASSRRWGSSEYQYF	13-2	49	XAXXNTXXXFYF								1
9	2-3	CASSPTDNF	13-2	49	CADPNTGNQFYF								3
25-1	2-3	CASSPGDTQYF	13-2	50	CADPNTGNQFYF							1	
11-2	2-7	CASSHLMAGGRYEQYF	14/DV	13	CAEKTSYDKVIF								
20-1	2-1	CSARRGLNEQFF	14/DV	20	XXXXXXSGXDHKXXX					1			
2	1-3	CAAVRPSTIYF	14/DV	29	F								
20-1	2-1	CSARGGFRSGGGTDEQFF	14/DV	31	CAMREGYSNDYKLSF						1		
9	2-7	CASSLGTGPFSEYQYF	14/DV	37	CAMRGSNTXXXF				1				
9	2-1	CASSSKPGGDYNEQFF	14/DV	9	CAMRGSARLMF		3						
ND	ND	ND	16	12	CXMRGXXSNTGKLIF	1							
4-1	2-7	CASSQWSGSPSYEQYF	16	12	CAITGGFKTIF				2				
7-9	1-5	CASSLTGSRNQPQHF	16	39	CAEGDSSYKLI					1			
5-6	1-5	CASSRRATGNYQPQHF	16	8	CALP#SSNTGKLIF					1			
24-1	2-3	CATSDLVSDTQYF	17	13	CXIRNFWQATXS#F		1					1	
7-9	2-1	ND	17	21	XAXL#VF								
4-1	2-5	CASSQDGPGRQETQYF	17	22	CDTAPERGGYQKVTF				1				
27	1-1	CASWTGAAEAF	17	24	CVGADNFNKIFY				2				
29-1	2-2	CSVQGRGELFF	17	34	CATDLIVSARQLTF		1						
28	2-1	CASNLRVDEQFF	17	47	CATDGVTDSWGKLF				1				
4-1	1-1	CASSQSPGGTEAFF	17	48	CATAGSYNTDKLIF					1			
6-6	2-7	CASRQLAGFYEQYF	17	57	XXEWDGNKLVF				1				
25-1	1-1	CASSGLTDANTEAFF	19	11	CATDD#GNEKLT	1							
4-2	2-1	CASSQTYPGAYNEQFF	19	11	CATDAGPEKLVF	1	21						
19	2-1	CASSISGGYNEQFF	19	17	CALTRSGYSTLTF		1						
29-1	2-7	CSVETPGVYEQYF	19	20	CALSEAGSGYSTLTF							1	
2	1-4	CARRQGNELFF	19	26	CALITIKAAAGNKLTF							1	
14	2-2	CASSQVLGPGLFF	19	30	XAVXFRAXKDYKLSF								1
9	2-3	CASSPTDNF	19	36	CALSVNYGQNFV								
9	2-1	CASSARDF	19	54	YFCXXSRSRDXKIIF					1			
9	2-7	CASGSGGEHF	19	56	CALSVLTGANLFF							1	
20-1	1-6	CSATDRAASYNPLHF	20	13	CALSEIQGAQKLVF								1
5-5	2-5	CASSFTIAA#QETQYF	21	13	CALSRVGANSKLT							1	
20-1	2-1	CSARAGIREGFYNEQFF	21	21	CAVQGGNSGGYQKVTF			2					
27	2-4	CASSTIAGETKNIQYF	21	30	CAVLNSGGYQKVTF					1			
20-1	1-5	CSATDRANVNQPQHF	23/DV	40	CGLRDNFNKIFY		1		1				
24-1	1-2	CATSDPTDRVDGYTF	24	40	CAVPIMNRDDKIIF			1					
28	2-2	CASSFLTSANTGELFF	26-1	4	CAASITPGTYKYIF				1				
2	1-1	CASRLANTEAFF	26-1	53	CAFISTSGTYKYIF					1			
9	1-6	CASSVEGTVNSPLHF	26-2	12	CIVRVGPGGYNKLIF			1					
6-1	2-4	CASSDIFLAKNIQYF	3	29	CIVRLGGLGGGSNKLTF		1						
2	1-5	CASSEAISTRAQHF	3	3	CILRTPLDSSYKLI	1							
29-1	1-1	ND	3	30	CAVRVLTPLVF					1			
9	2-1	CASSVSGGAYNEQFF	3	31	CXLRQEWX#KIIF				1				
5-6	1-2	CASSLGRAVIWGYTF	3	37	ND								
24-1	2-1	CATSDLTGANEQFF	36/DV	13	CAVRDYNARLMF	26							
3-1	2-3	CASSQDLASSTDTQYF	38-1	4	CAPPRGSSNTGKLIF	1							
ND	ND	ND	38-1	44	CAGDSGGYQKVTF				1				
4-1	1-6	CASSQDQAGSPLHF	4	10	CAFLSGGYKLI				1				
5-4	2-1	CASSPPTGNEQFF	4	10	CAFMKHRTGTASKLTF							1	
6-1	2-7	CASSDRTGRRNEQYF	4	10	VLXGGXXXXF								1
7-2	1-5	CASSLATGSGNQPQHF	4	10	CLVGDQAGGGNKLTF			1					
7-3	2-5	CASSLGTGAQETQYF	4	10	CLVAAPGNKLT					1			
30	2-2	CAWDYLTNTGELFF	4	13	CLVGDQILTGGGNKLT				1				
2	2-1	SPAVHRVANNEQLF	4	16	F							1	
4-2	2-7	CASSQSGTGPYEQYF	4	18	CLVGDGSHCGGYQKVTF				1				
					F								

Table S3. A2/S269⁺CD8⁺ TCRαβ repertoires. Related to Figure 6.

TRBV	TRBJ	CDR3β	TRAV	TRAJ	CDR3α	#02 0 Ac	#89 Ac	#8 9 F _{up}	CA 6	CA 7	CA 2
19	2-2	CATQNMNTGELFF	ND	ND	ND						1
2	2-2	CASSEIDTGELFF	ND	ND	ND		1				
7-9	2-7	CASSPDIEQYF	ND	ND	ND					1	
4-2	2-3	CASSQTESTDTQYF	1-1	37	CAHWGSSNTGKLI						1
3-1	2-2	CASQLQNTGELFF	1-2	38	XAVRDNAGXXXKI						1
20-1	2-2	CSARDPRAQNTGELFF	1-2	4	CAGPPNKLIF						1
20-1	1-2	CSAQTDRLGGYTF	10	39	CVVSAR#AGNMLTF		2				
3-1	2-2	CAVQGMNTGELFF	10	55	ND		1				
28	2-2	CASSPTGGGNTGELFF	12-1	11	CVVNEPLSGYSTLTF		1				
29-1	2-2	CSARGLAELANTGELFF	12-1	15	CVVNIPQAGTALIF		1	2			
13	2-2	CASSFPGGGNTGELFF	12-1	24	CVVNAADSWGKLFQ						1
20-1	2-2	CSARGGQGLNTGELFF	12-1	29	CVVNLPEGNTPLVF						1
7-9	2-7	CASSLDIEQYF	12-1	30	CVVNKYDKIIF						1
7-9	2-7	CASSLDIEQYF	12-1	31	XVVNXXDRLMX			1			
12-3	2-2	CALGEQNTGELFF	12-1	34	CVVNKDDKLI		1				
2	2-2	CASPNQNTGELFF	12-1	34	CVVNGTNDKLI		1				
7-9	2-2	CARGLANTGELFF	12-1	34	CVVNGADKLI		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	CVVNNNDMRF			1			
12-3	2-2	CALGDLNTGELFF	12-1	43	CVVNRNDMRF						1
12-3	2-2	CASGKQNTGELFF	12-1	43	CVVNEKDDMRF						1
12-3	2-2	CAAGQGNTGELFF	12-1	43	CVVNRADDMRF						1
12-3	2-2	CASINLNTGELFF	12-1	43	CVVNNNDMRF						1
12-3	2-2	CARGDANTGELFF	12-1	43	CVVNNNDMRF						2
19	2-2	CAGQVTNTGELFF	12-1	43	CVVNRNDMRF				1		
2	2-2	CASSDLNTGELFF	12-1	43	CVVNGGNDMRF		1				
2	2-2	CASSDLNTGELFF	12-1	43	CVVNGNNDMRF		1				
2	2-2	CASSEIDTGELFF	12-1	43	CVVNRNDMRF		1				
2	2-2	CASGQLNTGELFF	12-1	43	CVVNRGNDMRF						1
2	2-2	CASNDLNTGELFF	12-1	43	CVVNKGNMRF						1
2	2-2	CASQDTNTGELFF	12-1	43	CVVNKGNMRF				1		
2	2-2	CAVEGNLNTGELFF	12-1	43	CVVNNNDMRF						1
20-1	2-2	CSARDRQGQNTGELFF	12-1	43	CVVXSFDMMRF						1
24-1	2-2	CATQRANTGELFF	12-1	43	GVVNMGDDMRF		1				
3-1	2-2	CAVQGMNTGELFF	12-1	43	CVVNNNDMRF		1				
5-1	2-2	CASGEENT#GELFF	12-1	43	CVVNKNDMRF			1			
5-4	2-2	CASSPDRNTGELFF	12-1	43	CVVNVMDMMRF		1				
5-8	2-2	CAIIDRNTGELFF	12-1	43	CVVNRDDMRF						1
6-5	2-2	CATTSLNTGELFF	12-1	43	CVVNRDNDMRF			1			
7-8	2-2	CASGQLNTGELFF	12-1	43	CVVNNNDMRF			1			
7-8	2-2	CASYFQDTGELFF	12-1	43	XVVNGXXDMXF		1				
7-8	2-7	CASSAGVSGEQYF	12-1	43	CVVNVVDDMRF			2			
7-9	2-3	CASSLDIEQYF	12-1	43	CVVNSFDDMRF					1	
29-1	2-2	CSARTSGGQNTGELFF	12-1	47	XVXNREDKLVF		1				
7-9	1-1	CASSPDIVAFF	12-2	30	CAVNRDDKIIF						1
7-9	1-1	CASSDIEAFF	12-2	30	CAVNGDDKIIF		1	1			
7-9	2-1	CASSFDIAEFF	12-2	30	CAVNQDDKIIF		1				
7-9	2-7	CASSPDIEQYF	12-2	30	CAVNRDDKIIF	1				1	
9	2-5	XPXXGXXX	13-1	21	CAVGNFNKYF					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	CASSPDDGQPQHF	13-1	39	XPXXRXXXQX##TF						1
7-8	2-2	CGELAQNTGELFF	13-1	47	CAAFGXKXQ##VF				1		
2	1-1	CASPRTGLSNTAEFF	13-1	48	XXXXXXXXX##F						1
9	2-2	CASSEENTGELFF	13-2	3	CAEPSASKIIF		1				
2	2-2	CASQNRDTGELFF	13-2	35	CAES#IGFGNVLHC						2
20-1	2-2	CSARGKREHNTGELFF	13-2	42	CAENSHPRGGGSGGNLIF		1				
7-9	2-2	CAPGVNTGELFF	13-2	49	CADT##NTGNQFYF		1				
25-1	2-2	CALQDXTGEXFF	14/DV4	20	CAMRE#SNDYKLSF		1				
24-1	2-1	CATSGPLPR*#SYNEQF	14/DV4	21			1				
		F									
15	2-2	CATTEGVAGELFF	14/DV4	27	ND						1
27	2-7	CASSDRGRSYEQYF	14/DV4	28	CAMREAPFAYSGAGSYQ				1		
					LTF						
ND	ND	ND	14/DV4	41	CAMREGSGYALNF						1
15	2-2	CATTEGVAGELFF	14/DV4	42	CATR##GSQGNLIF						3
9	2-7	CASSVEPGWDEQYF	14/DV4	48	CAMRGAGNEKLT					1	
19	2-7	CASSIGDEQYF	14/DV4	5	LLLCRDC#DTGRRALTF				1		
19	2-3	CASSIDLADTQYF	16	15	CAXPXACXXC##IF						1
6-1	2-2	CASQRMNTGELFF	16	37	CALQ#GSSNTGKLI						1
24-1	2-1	CATSGPLPR*#SYNEQF	16	42	CALSD#YGGGSGGNLIF		1				
		F									
7-8	1-2	CASSDSYGYTF	16	42	CALSD#YGGGSGGNLIF			1			
2	2-2	CASTRDLNTGELFF	16	43	CALGGRVDNDMRF			1			
ND	ND	ND	17	16	CGGGGQKLLF		1				
20-1	2-2	CSARDPWGINTGELFF	17	29	VXXVSSGNTHLXF			1			
7-8	2-2	CASSFQDTGELFF	17	52	CVXXIXXWXXXKX##TF						1
6-6	2-2	CASENRNTGELFF	17	54	CAPEIQGAQKLVF			1			
19	2-2	CASQTLNTGELFF	19	47	CALTPLRPKLVF			1			
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	CAGGEPNTGELFF	23/DV6	34	CAASRADKLI		1				
2	2-2	CAINEQNTGELFF	23/DV6	35	CAASXXXAXGMX#HC						1
7-9	1-1	CASSPDIEAFF	23/DV6	4	XAASRNLWXXQ##IF						1
15	2-2	CATQEGNTGELFF	23/DV6	44	CAV*GTASKXTF						1
10-2	2-2	CASLVQENTGELFF	23/DV6	45	ND		1				
20-1	2-2	CSAPSYGELFF	23/DV6	49	CAADYTGNTQFYF						1
4-2	2-3	CASSQVESADTQYF	23/DV6	49	CAAXYXXQXYX				1		
27	1-5	CASSYSSYGSNQPQHF	24	28	XXXXWGXSQQLTX						1
4-2	2-2	CATQDANTGELFF	25	42	CAGLGDGGSQGNLIF		1				

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- α	TCRdiv- β	TCRdiv- $\alpha\beta$
A2/S ₂₆₉ *	COVID-19	4	43	35	34.8	101.0	147.9
A2/S ₂₆₉	COVID-19	5	75	57	29.8	76.9	100.1
B7/N ₁₀₅	Pre-pandemic	4	43	37	935.7	322.9	730.4
B7/N ₁₀₅ *	COVID-19	4	42	25	282.3	291	299.9
B7/N ₁₀₅	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/N₁₀₅ pre-pandemic and A2/S₂₆₉ COVID-19 TCR datasets.