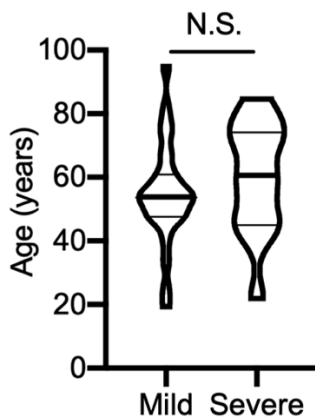


**Supplementary Fig. 1: Participant characteristics.** a) distribution of age, gender and days post symptom when sampling of the unexposed healthy controls and SSARS-CoV-2 infected patients studied. b) and c) Comparison of age ( $p=0.3465$ ) and days post symptom ( $p=0.4075$ ) when sampling between the patient groups with mild symptoms and severe symptoms. The unpaired t test with Welch's correction and Mann-Whitney test were used for data analysis of b) and c), respectively. Two tailed p value was calculated.

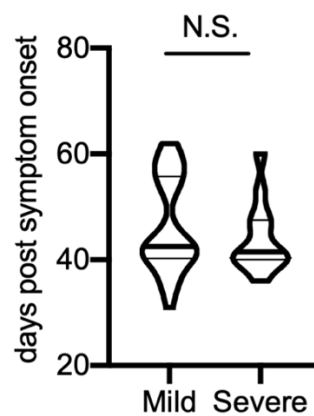
**a**

	Unexposed (N=19)	Mild Disease (n=28, 1 asymptomatic)	Severe Disease (n=14, 1 critical)
Age, y, median (IQR)	46.0(31.0-53.0)	53.8(47.6-60.9)	60.6(44.9-74.1)
Male sex	8(53.33)	17(60.71)	9(64.28)
Days post symptom, median (IQR)	NA	42.5(40.2-55.7)	41.5(40.0-47.5)

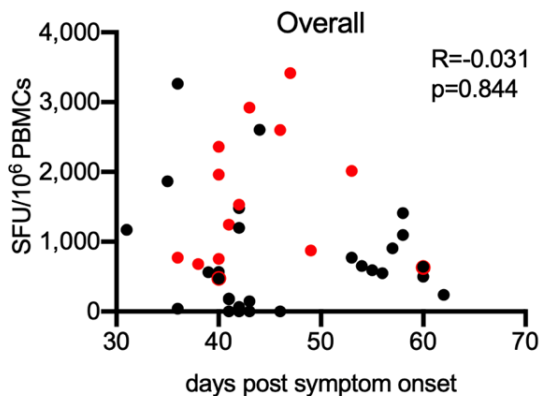
**b**



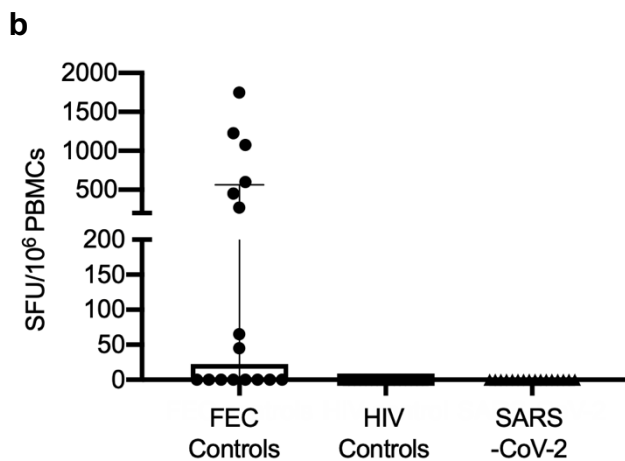
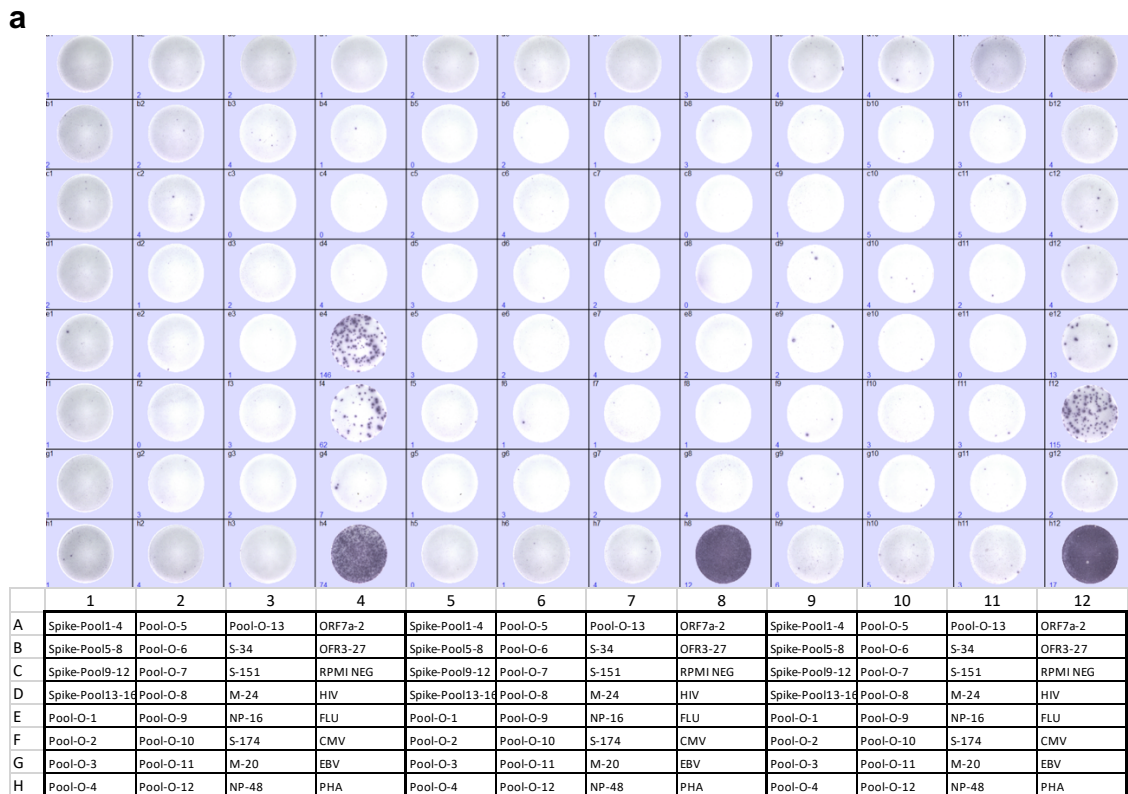
**c**



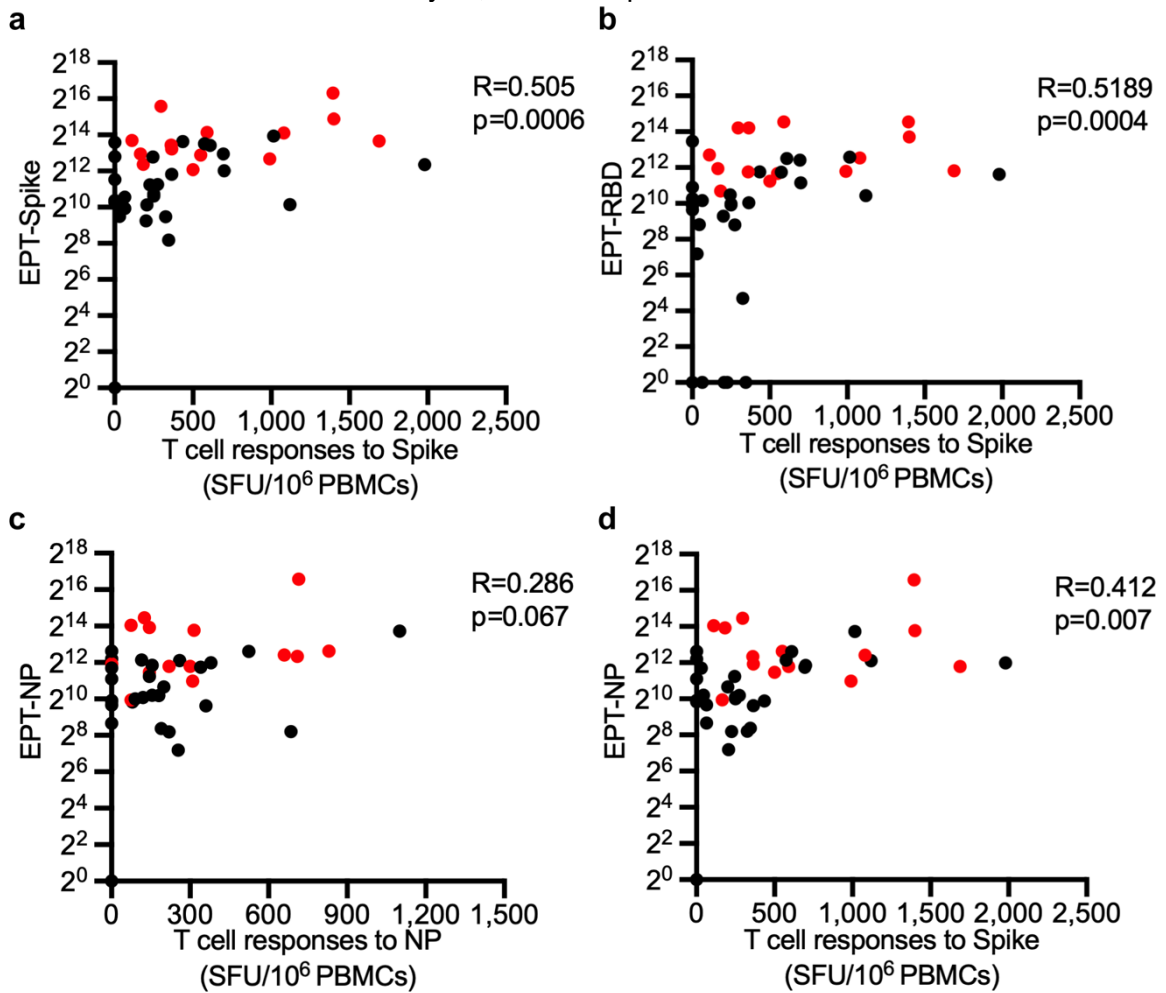
**Supplementary Fig. 2: No correlation between overall T cell response of each individual and the days post symptom when blood specimen was taken.**  $n=42$ . Black and red dots represent patients with history of mild symptoms and severe symptoms, respectively. Spearman's rank correlation coefficient was used for the correlation analysis, two tailed p value was calculated.



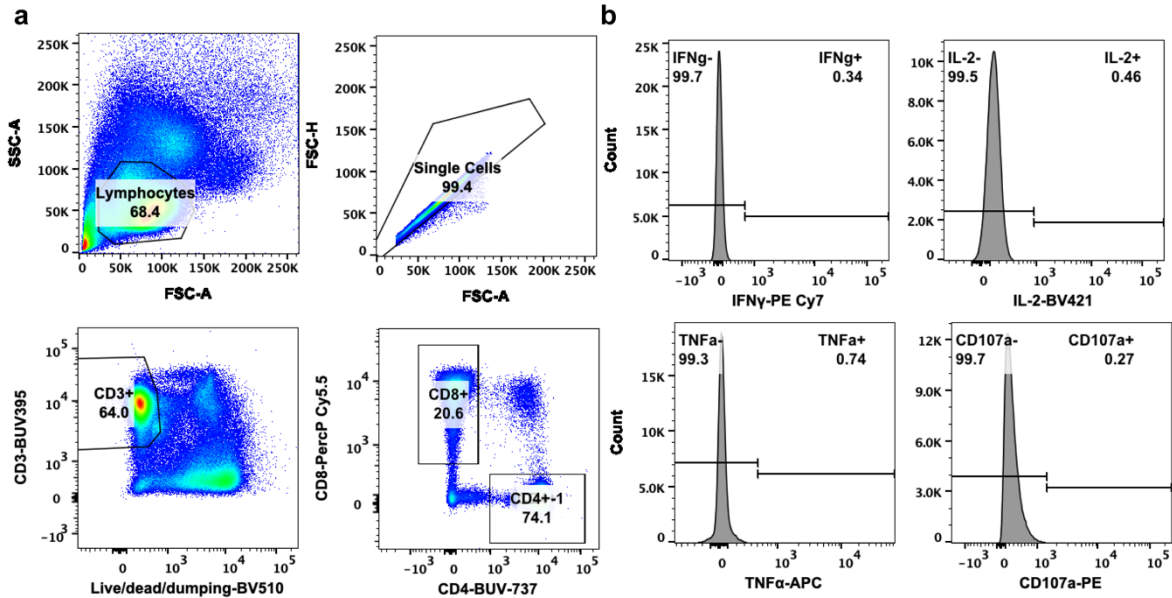
**Supplementary Fig. 3: Magnitude of T cell responses of unexposed healthy individuals against SARS-CoV-2 antigens.** a) An example of IFN- $\gamma$  ELISpot plate from three healthy individuals without SARS-CoV-2 infection. Each individual has been tested with four spike pools (Pool 1-4, Pool 5-8, Pool 9-12 and Pool-13-16), 13 first dimension of non-spike pools and nine dominant individual peptides containing epitopes, along with six control wells including: negative controls with no peptide and peptide pools of irrelevant antigens derived from HIV Gag protein; positive controls with PHA and three pools of known CD8<sup>+</sup> T cell epitopes of human influenza, CMV and EBV viruses (namely FEC controls). b) Magnitude of T cell responses of unexposed healthy individuals against SARS-CoV-2 antigens and control antigens. n=16. Data are presented as median with interquartile range.



**Supplementary Fig. 4: Correlation between SARS-CoV-2 antigen-specific T cell responses and SARS-CoV-2 antigen-specific antibody responses.** a), b) and c) Correlation of Spike-, RBD-, and NP-specific antibody responses to corresponding antigen-specific T cell responses. d) Correlation between NP-specific antibody response and Spike-specific T cell response. n=42. Black and red dots represent patients with history of mild symptoms and severe symptoms, respectively. Spearman's rank correlation coefficient was used for the correlation analysis, two tailed p value was calculated.

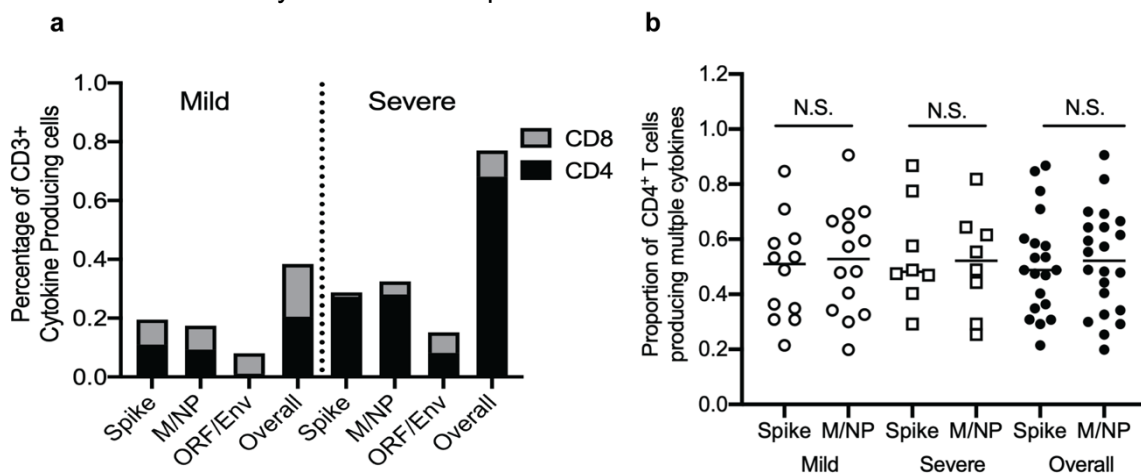


**Supplementary Fig. 5: Gating strategy of flow cytometry analysis.** a) Gating for CD4<sup>+</sup>/CD8<sup>+</sup> T cells. Cells were gated on single cell by a forward side scatter gate, followed by CD3/ CD4/CD8 gating excluding dead cells, CD14<sup>+</sup>, CD19<sup>+</sup>, and CD16<sup>+</sup> cells. This gating strategy was used for Fig. 4-7 and Supplementary Fig. 6. b) Gating for IFN $\gamma$ <sup>+/−</sup>, TNF $\alpha$ <sup>+/−</sup>, IL-2<sup>+/−</sup>, and CD107a<sup>+/−</sup> population were based on corresponding negative controls. This gating strategy was used for Fig. 4-5.

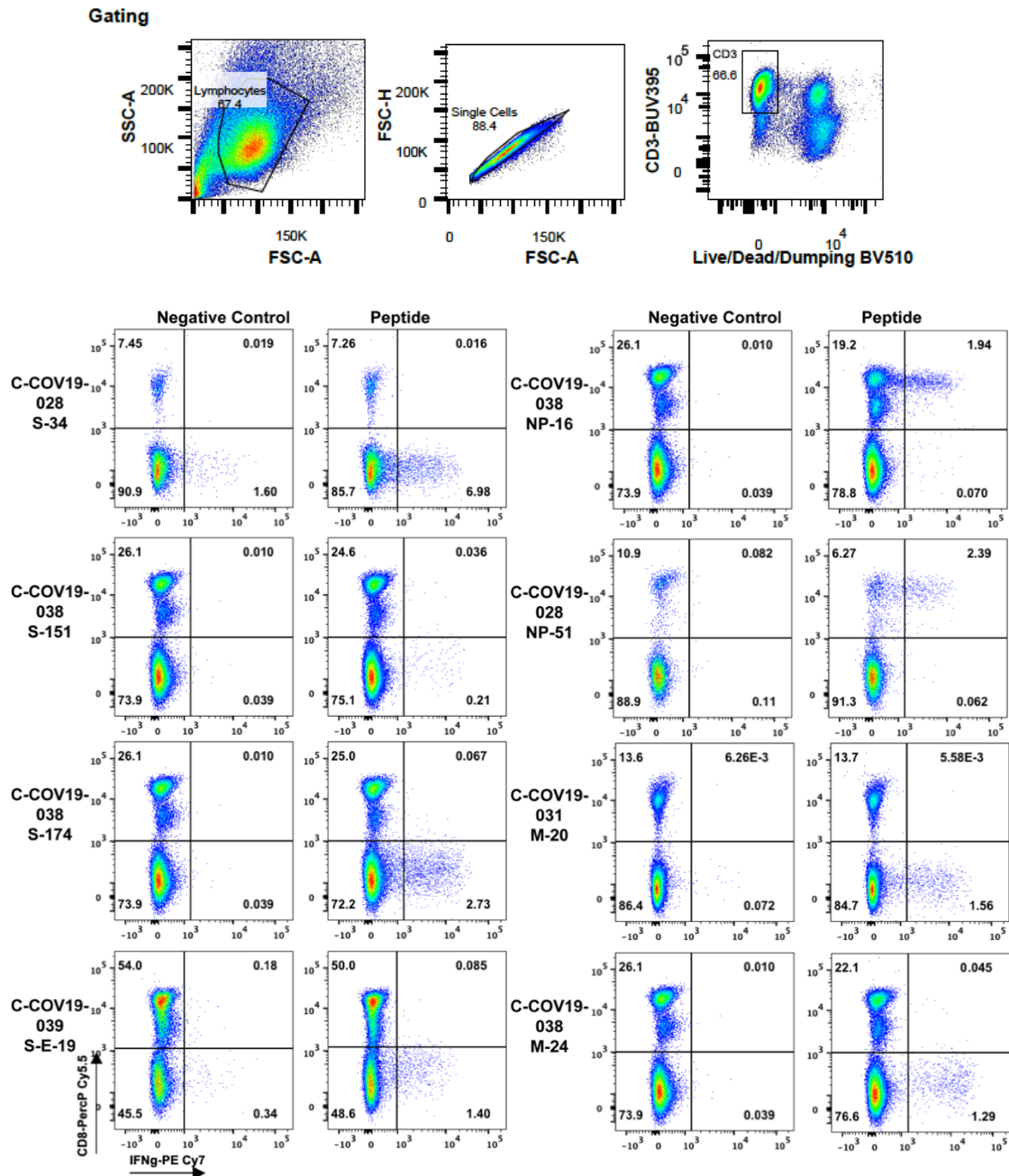


**Supplementary Fig. 6: Comparison of Cytokine production of T cells between the patients with different disease severity and T cells targeting different viral proteins.**

a) No significant difference in the percentage of CD4<sup>+</sup> and CD8<sup>+</sup> T cells producing IFN- $\gamma$  and/or TNF $\alpha$ , and/or IL-2 targeting each viral antigen between mild cases (n=14) and severe cases (n=8). Data are shown in value of median. b) No significant difference in proportion of multifunctional CD4<sup>+</sup> T cells targeting spike protein (Mild group, n=12; Severe group, n=8) and M/NP protein (Mild group, n=14; Severe group, n=8). Mann-Whitney test was used for the analysis. Two-tailed p value was calculated. N.S. P>0.05



**Supplementary Fig. 7: Confirmation of dominant T cell responses with cultured short-term T cell lines.** Patient C-COV19-028 showed a CD4 T cell response to peptide S-34 and CD8 T cell response to peptide NP-51. Patient C-COV-19-038 showed CD4 T cell response to three dominant peptides: S-151 (weak), S-174, M24 and a CD8 T cell response to NP-16. Patient C-COV-19-039 showed CD4 T cell response to peptide S-E-19, whereas donor C-COV19-031 had a CD4 T cell response targeting peptide M-20. PBMCs were stimulated with corresponding peptide pools corresponding to the ex vivo ELISpot results and then cultured for 10 days. Cytokine production of the cell lines was then examined by ICS upon the stimulation with single peptides. Cells were gated on the live/singlet/ CD3+ Lymphocyte population.



### Supplementary Table 1: Two-dimensional peptide Matrix pools.

a: Spike protein: 253 peptides in total 32 pools including 16 pools in 1<sup>st</sup> dimension and 16 pools in 2<sup>nd</sup> dimension

	Pool-17	Pool-18	Pool-19	Pool-20	Pool-21	Pool-22	Pool-23	Pool-24	Pool-25	Pool-26	Pool-27	Pool-28	Pool-29	Pool-30	Pool-31	Pool-32
Pool 1	S-1	S-2	S-3	S-4	S-5	S-6	S-7	S-8	S-9	S-10	S-11	S-12	S-13	S-14	S-15	S-16
Pool 2	S-17	S-18	S-19	S-20	S-21	S-22	S-23	S-24	S-25	S-26	S-27	S-28	S-29	S-30	S-31	S-32
Pool 3	S-33	S-34	S-35	S-36	S-37	S-38	S-39	S-40	S-41	S-42	S-43	S-44	S-45	S-46	S-47	S-48
Pool 4	S-49	S-50	S-51	S-52	S-53	S-54	S-55	S-56	S-57	S-58	S-59	S-60	S-61	S-62	S-63	S-64
Pool 5	S-65	S-66	S-67	S-68	S-69	S-70	S-71	S-72	S-73	S-74	S-75	S-76	S-77	S-78	S-79	S-80
Pool 6	S-81	S-82	S-83	S-84	S-85	S-86	S-87	S-88	S-89	S-90	S-91	S-92	S-93	S-94	S-95	S-96
Pool 7	S-97	S-98	S-99	S-100	S-101	S-102	S-103	S-104	S-105	S-106	S-107	S-108	S-109	S-110	S-111	S-112
Pool 8	S-113	S-114	S-115	S-116	S-117	S-118	S-119	S-120	S-121	S-122	S-123	S-124	S-125	S-126	S-127	S-128
Pool 9	S-129	S-130	S-131	S-132	S-133	S-134	S-135	S-136	S-137	S-138	S-139	S-140	S-141	S-142	S-143	S-144
Pool 10	S-145	S-146	S-147	S-148	S-149	S-150	S-151	S-152	S-153	S-154	S-155	S-156	S-157	S-158	S-159	S-160
Pool 11	S-161	S-162	S-163	S-164	S-165	S-166	S-167	S-168	S-169	S-170	S-171	S-172	S-173	S-174	S-175	S-176
Pool 12	S-177	S-178	S-179	S-180	S-181	S-182	S-183	S-184	S-185	S-186	S-187	S-188	S-189	S-190	S-191	S-192
Pool 13	S-193	S-194	S-195	S-196	S-197	S-198	S-199	S-200	S-201	S-202	S-203	S-204	S-205	S-206	S-207	S-208
Pool 14	S-209	S-210	S-211	S-212	S-213	S-214	S-215	S-216	S-217	S-218	S-219	S-220	S-221	S-222	S-223	S-224
Pool 15	S-225	S-226	S-227	S-228	S-229	S-230	S-231	S-232	S-233	S-234	S-235	S-236	S-237	S-238	S-239	S-240
Pool 16	S-241	S-242	S-243	S-244	S-245	S-246	S-247	S-248	S-249	S-250	S-251	S-252	S-253			

b: Non-spike proteins: total 29 pools, 13 pools in 1<sup>st</sup> dimension including ORF3a (35 peptides in 3 pools), ORF6 (7 peptides in 1 pool), ORF7a(15 peptides in 1 pool), ORF8(16 peptides in 1 pool), Envelope(9 peptides in 1 pool), Membrane Protein(29 peptides in 2 pools) and Nucleoprotein( 59 peptides in 4 pools).

	Pool-O-14	Pool-O-15	Pool-O-16	Pool-O-17	Pool-O-18	Pool-O-19	Pool-O-20	Pool-O-21	Pool-O-22	Pool-O-23	Pool-O-24	Pool-O-25	Pool-O-26	Pool-O-27	Pool-O-28	Pool-O-29
Pool-O-1	ORF3a-1	ORF3a-2	ORF3a-3	ORF3a-4	ORF3a-5	ORF3a-6	ORF3a-7	ORF3a-8	ORF3a-9	ORF3a-10	ORF3a-11	ORF3a-12	ORF3a-13	ORF3a-14	ORF3a-15	ORF3a-16
Pool-O-2	ORF3a-17	ORF3a-18	ORF3a-19	ORF3a-20	ORF3a-21	ORF3a-22	ORF3a-23	ORF3a-24	ORF3a-25	ORF3a-26	ORF3a-27	ORF3a-28	ORF3a-29	ORF3a-30	ORF3a-31	ORF3a-32
Pool-O-3	ORF3a-33	ORF3a-34	ORF3a-35													
Pool-O-4	ORF6-1	ORF6-2	ORF6-3	ORF6-4	ORF6-5	ORF6-6	ORF6-7									
Pool-O-5	ORF7a-1	ORF7a-2	ORF7a-3	ORF7a-4	ORF7a-5	ORF7a-6	ORF7a-7	ORF7a-8	ORF7a-9	ORF7a-10	ORF7a-11	ORF7a-12	ORF7a-13	ORF7a-14	ORF7a-15	
Pool-O-6	ORF8-1	ORF8-2	ORF8-3	ORF8-4	ORF8-5	ORF8-6	ORF8-7	ORF8-8	ORF8-9	ORF8-10	ORF8-11	ORF8-12	ORF8-13	ORF8-14	ORF8-15	ORF8-16
Pool-O-7	Env-1	Env-2	Env-3	Env-4	Env-5	Env-6	Env-7	Env-8	Env-9							
Pool-O-8	M-1	M-2	M-3	M-4	M-5	M-6	M-7	M-8	M-9	M-10	M-11	M-12	M-13	M-14	M-15	M-16
Pool-O-9	M-17	M-18	M-19	M-20	M-21	M-22	M-23	M-24	M-25	M-26	M-27	M-28				
Pool-O-10	NP-1	NP-2	NP-3	NP-4	NP-5	NP-6	NP-7	NP-8	NP-9	NP-10	NP-11	NP-12	NP-13	NP-14	NP-15	NP-16
Pool-O-11	NP-17	NP-18	NP-19	NP-20	NP-21	NP-22	NP-23	NP-24	NP-25	NP-26	NP-27	NP-28	NP-29	NP-30	NP-31	NP-32
Pool-O-12	NP-33	NP-34	NP-35	NP-36	NP-37	NP-38	NP-39	NP-40	NP-41	NP-42	NP-43	NP-44	NP-45	NP-46	NP-47	NP-48
Pool-O-13	NP-49	NP-50	NP-51	NP-52	NP-53	NP-54	NP-55	NP-56	NP-57	NP-58						

**Supplementary Table 2: HLA class I typing of CD8<sup>+</sup> epitope peptides in subjects with confirmed responses.** Each patient listed made a CD8 T cell response to the peptides shown. Optimal epitopes and the corresponding HLA-restriction were predicted by IEDB analysis tool (<http://tools.iedb.org/mhci>). Red highlights are the predicted optimal epitope sequences.

Protein	Peptide ID	Peptide sequence	Predicted HLA Restriction	Patients	HLA					
					A1	A2	B1	B2	Cw1	Cw2
NP	NP-1	MSDNGPQN <b>QRNAPRITF</b>	B*2705/06	C-COV19-044	02:07	11:01	27:06	40:01	03:04	07:02
	NP-2	<b>NQRNAPRITF</b> GGPSDSTG		C-COV19-047	24:02	24:02	27:05	27:05	01:02	02:02
				C-COV19-025	02:01	24:02	27:05	44:02	02:02	05:01/03
	NP-16	<b>LSPRWYFY</b> YLTGTGPEAGL		C-COV19-001	02:01	23:01	07:02	49:01	07:01	07:02
				C-COV19-002	03:01	68:02	07:02	49:01	06:02	07:02
				C-COV19-003	02:01	32:01	07:02	44:02	05:01/03	07:02
				C-COV19-004	02:01	02:01	07:02	40:01	03:04	07:02
				C-COV19-005	01:01/04N	02:01	07:02	40:01	01:02	07:02
				C-COV19-006	01:01/04N	29:02	07:02	45:01	07:01	07:02
				C-COV19-007	01:01/04N	01:01/04N	07:02	07:02	07:02	07:02
				C-COV19-035	11:01	11:01	07:02	07:05/06	03:04	07:02
				C-COV19-036	01:01/04N	03:01	07:02	52:01	07:02	12:02
				C-COV19-038	02:01	24:02	07:02	51:01	04:01	07:02
	C-COV19-045	01:01/04N	02:01	07:02	45:01	06:02	07:02			
	C-COV19-046	02:01	03:01	07:02	44:02	05:01/03	07:02			
NP-E-3	MEVTPSGT <b>WL</b>	B*4001	C-COV19-021	02:01	31:01	40:01	40:01	03:04	03:04	
NP-51	LLNKHIDAY <b>KTFPPTEPK</b>	A*0301	C-COV19-028	02:01	03:01	15:01	44:02	03:03	07:04/11	
			C-COV19-036	01:01/04N	03:01	07:02	52:01	07:02	12:02	
NP-51	LLNKHIDAY <b>KTFPPTEPK</b>	A*1101	C-COV19-035	11:01	11:01	07:02	07:05/06	03:04	07:02	
ORF	ORF3a-27	KDCVVLHSY <b>FTSDYYQLY</b>	A*0101	C-COV19-022	01:01/04N	01:01/04N	08:01	08:01	07:01	07:02
	ORF3a-28	<b>YFTSDYYQLY</b> STQLSTDTGV		C-COV19-036	01:01/04N	03:01	07:02	52:01	07:02	12:02
				C-COV19-037	01:01/04N	26:01	08:01	38:01	07:01	12:03
				C-COV19-040	01:04N	03:01	27:05	57:01	01:02	06:02
Spike	S-34	CTF <b>EYVSQPFL</b> MDLE	Cw*0702	C-COV19-035	11:01	11:01	07:02	07:05/06	03:04	07:02
	S-106	GPK <b>KSTNLVKNK</b> CVN	A*3101	C-COV19-021	02:01	31:01	40:01	40:01	03:04	03:04

**Supplementary Table 3: Known SARS epitopes with identical sequences to SARS-CoV-2 , and Tetramers/Pentamers.** Red highlights the epitope responses detected in the patients who had recovered from COVID-19, whether by tetramer/pentamer staining or ELISpot assay.

Peptide ID	Epitope	Protein	MHC allele	Tetramer/Pentamer
N-E-01	ILLNKHID	NP	HLA-A*02:01	Y
N-E-02	AFFGMSRIGMEVTPSGTW	NP	NA	
<b>N-E-03</b>	<b>MEVTPSGTWL</b>	<b>NP</b>	<b>HLA-B*40:01 I</b>	<b>Y</b>
N-E-04	GMSRIGMEV	NP	HLA-A*02:01 I	Y
N-E-05	ILLNKHIDA	NP	HLA-A*02:01 I	Y
N-E-06	ALNTPKDHI	NP	HLA-A*02:01 I	Y
N-E-07	IRQGTDYKHWPQIAQFA	NP	NA	
N-E-08	KHWPQIAQFAPSASAFF	NP	NA	
N-E-09	LALLLDRL	NP	HLA-A*02:01 I	Y
N-E-10	LLDRLNQL	NP	HLA-A*02:01 I	Y
<b>N-E-11</b>	<b>LLNKHIDAYKTFPPTPEPK</b>	<b>NP</b>	<b>NA</b>	
N-E-12	LQLPQGTTL	NP	HLA-A*02:01 I	Y
N-E-13	AQFAPSASAFFGMSR	NP	NA	
N-E-14	AQFAPSASAFFGMSRIGM	NP	NA	
N-E-15	RRPQGLPNNTASWFT	NP	NA I	
N-E-16	YKTFPPTPEPKDKKKK	NP	NA	
S-E-17	GAALQIPFAMQMAYRF	Spike	HLA-DRA*01:01,HLA-DRB1*07:01	Y
S-E-18	MAYRFNGIGVTQNVLY	Spike	HLA-DRB1*04:01	Y
<b>S-E-19</b>	<b>QLIRAAEIRASANLAATK</b>	<b>Spike</b>	<b>HLA-DRB1*04:01</b>	<b>Y</b>
S-E-20	FIAGLIAIV	Spike	HLA-A*02:01	Y
S-E-21	ALNTLVKQL	Spike	HLA-A*02:01 I	Y
S-E-22	LITGRLQSL	Spike	HLA-A2 I	Y
S-E-23	NLNESLIDL	Spike	HLA-A*02:01 I	Y
S-E-24	QALNTLVKQLSSNFGAI	Spike	HLA-DRB1*04:01	Y
S-E-25	RLNEVAKNL	Spike	HLA-A*02:01 I	Y
S-E-26	VLNDILSRL	Spike	HLA-A*02:01 I	Y
S-E-27	VVFLHVTYV	Spike	HLA-A*02:01 I	Y



#### **Supplementary Table 4:**

##### **Oxford Immunology Network Covid-19 response: T cell Immunity Team – additional contributors**

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