



Supplemental Figure 1: T cell IFN- γ responses to SARS-CoV-2 and CCCs. A representative IFN- γ ELISpot from one donor (VR2) obtained pre- and post-vaccination (A-D). The spot forming units (SFU) and stimulation indices of PBMCs (A, B) and CD8+ T cell depleted PBMCs (C, D) in response to HCoV-NL63, HCoV-229E, HCoV-OC43 and SARS-CoV-2 peptide pools are shown. IFN- γ ELISpot in PBMCs (E) and CD8 depleted PBMCs (F) in 15 donors obtained pre- and post-vaccination (replicate of Figure 1 to indicate change in T cell responses for each donor). Each data point represents the mean of 3 replicate values. Horizontal bars represent the median. * $p = 0.0332$ and ** $P = 0.0021$, by 2-tailed, paired Student's t test. Horizontal bars represent the median. (E-G) Correlation between post-vaccination SARS-CoV-2 PBMC ELISpot responses and pre-vaccination responses to HCoV-OC43, HCoV-229E and HCoV-NL63 respectively. Pearson correlation test, $r=0.065$, 0.36 and 0.12 respectively ($n=15$).

Supplementary Table 1: Peptides targeted by vaccine recipients' CD4+ T cells

VR	#	Amino acid #	Targeted peptide	Predicted HLA-restricting alleles	SI
VR14 DRB1*11:01 DRB3* 02:02 DQA1*05:05/DQB1*03:01 DPA1*01:03/DPB1*02:01 DPA1*01:03/DPB1*04:01					
	64	442-458	<u>DSKVGGNYNLYRLFRK</u>	DRB1*11:01	3.7
	117	813-829	<u>SKRSFIEDLLFNKVTLA</u>	DPA1*01:03/DPB1*04:01	5.1
VR20 DRB1*07:01, 15:02 DRB4* 01:01 DRB5*01:02 DQA1*02:01/DQB1*02:02 DQA1*01:03/DQB1*06:01 DPA1*01:03/DPB1*04:01					
	54	372-388	ASFSTFKCYGVSP TKLN	DRB1*15:02	
	105	729-745	<u>VSMTKTSVDCTMYICGD</u>	DQA1*02:01/DQB1*02:02	
	117	813-829	<u>SKRSFIEDLLFNKVTLA</u>	DPA1*01:03/DPB1*04:01	3.7
VR21 DRB1*03:01, 15:01 DRB3* 01:01 DRB5*01:01 DQA1*05:01/DQB1*02:01 DQA1*01:02/DQB1*06:02 DPA1*02:01/DPB1*01:01 DPA1*02:06/DPB1*05:01					
	28	190-206	REFVFNKIDGYFKIYSK	DRB5*01:01	4
	108	750-766	<u>SNLLQYGSFCTQLNRA</u>	DRB1*15:01	8.9
	117	813-829	<u>SKRSFIEDLLFNKVTLA</u>	DPA1*02:01/DPB1*01:01	8.0
VR25 DRB1*07:01, 13:01 DRB3* 02:02 DRB5*01:02 DQA1*02:01/DQB1*02:02 DQA1*01:03/DQB1*06:03 DPA1*01:03/DPB1*01:01 DPA1*02:02/DPB1*02:01					
	51	351-367	<u>YAWNRRKISNCVADYSV</u>	DRB3*02:02	4.1
	88	610-626	<u>VLYQDVNCTEVPVAIHA</u>	DRB1*13:01	3.0
	94	652-668	<u>GAEHVNNSYECDIPIGA</u>	DQA1*02:01/DQB1*02:02	3.2
	98	680-696	<u>SPRRARSVASQSIIAYT</u>	DQA1*01:03/DQB1*06:03	4.1

	117	813-829	<u>SKRSFIEDLLFNKVTLA</u>	DPA1*02:02/DPB1*02:01	4.8
VR	Peptide	Amino acid	Targeted peptide	HLA alleles	SI
VR28 DRB1*04:04,11:01, DRB3*0202, DRB4*0103, DQA1*03:01/DQB1*03:02, DQA1*05:05/DQB1*03:01, DPA1*01:03/DPB1*06:01, DPA1*02:01/DPB1*14:01					
	13	85-101	<u>PFNDGVYFASTEKSNII</u>	DRB3*02:02	7.5
	15	99-115	<u>NIIRGWIFGTTLDSKTQ</u>	DPA1*01:03/ DPB1*06:01	14.5
	18	120-136	<u>VNNATNVVIKVFCEQFC</u>	DRB3*02:02	7.5
	20	134-150	<u>QFCNDPFLGVYHKNNK</u>	DRB1*11:01	10.5
	51	351-367	<u>YAWNRRKRISNCVADYSV</u>	DRB3*02:02, DRB4*01:03	18.5
	54	372-388	<u>ASFSTFKCYGVSPTKLN</u>	DPA1*01:03/DPB1*06:01	14.5
	56	386-402	<u>KLNDLCFTNVYADSFVI</u>	DPA1*02:01/DPB1*14:01	17.5
	58	400-416	<u>FVIRGDEVQRQIAPGQTG</u>	DQA1*05:05/DQB1*03:01	14.5
	132	918-934	<u>ENQKLIANQFNSAIGKI</u>	DRB3*02:02	16
	138	960-976	<u>NTLVKQLSSNFGAISSV</u>	DRB3*02:02	22
VR32 DRB1*01:01, 07:01, DRB4* 01:01, DQA1*02:01/DQB1*02:02 DQA1*01:01/DQB1*05:01 DPA1*01:03/DPB1*04:01					
	2	8-24	<u>LPLVSSQCVNLTTRTQL</u>	DRB4*01:01	4.8
	6	36-52	<u>VYYPDKVFRSSVLHSTQ</u>	DPA1*01:03/DPB1*04:01	8.4
	24	162-178	<u>SANNCTFEYVSQPFLMD</u>	DPA1*01:03/DPB1*04:01	10.2
	28	190-206	<u>REFVFKNIDGYFKIYSK</u>	DQA1*01:01/DQB1*05:01 DRB5*01:01	8.8
	103	715-731	<u>PTNFTISVTTEILPVSM</u>	DRB1*07:01	8
	105	729-745	<u>VSMTKTSVDCTMYICGD</u>	DQA1*02:01/DQB1*02:02	13

VR36 DRB1*01:01, 15:01 DRB5*01:01 DQA1*01:01/DQB1*05:01 DQA1*01:03/DQB1*06:01 DPA1*01:03/DPB1*04:01					
	108	750-766	<u>SNLLQYGSFCTQLNRA</u>	DRB1*15:01	3.2
	117	813-829	<u>SKRSFIEDLLFNKVTLA</u>	DPA1*01:03/DPB1*04:01	4.9
VR40 DRB1*03:01, 15:01 DRB3* 01:01 DRB5*01:01 DQA1*05:01/DQB1*02:01 DQA1*01:02/DQB1*06:02 DPA1*01:03/DPB1*04:01 DPA1*01:03/DPB1*06:01					
	108	750-766	<u>SNLLQYGSFCTQLNRA</u>	HLA-DRB1*15:01	6.8
	117	813-829	<u>SKRSFIEDLLFNKVTLA</u>	DPA1*01:03/DPB1*04:01	4.7
VR41 DRB1*07:01,11:01 DRB3*0202 DQA1*02:01/DQB1*03:03 DQA1*05:05/DQB1*03:01 DPA1*01:03/DPB1*04:01 DPA1*02:01/DPB1*13:01					
	21	141-157	<u>LGVYHKNKSWMESEF</u>	DRB3*02:02	4.8
	98	680-696	<u>SPRRARSVASQSIIAYT</u>	DQA1*02:01/DQB1*03:03	3.6
	105	729-745	<u>VSMTKTSVDCTMYICGD</u>	DQA1*02:01/DQB1*03:03	5.0

*Predicted optimal epitopes are underlined

SI= stimulation index

Amino acids in red font are present in B.1.1.7 and B.1.351 variants