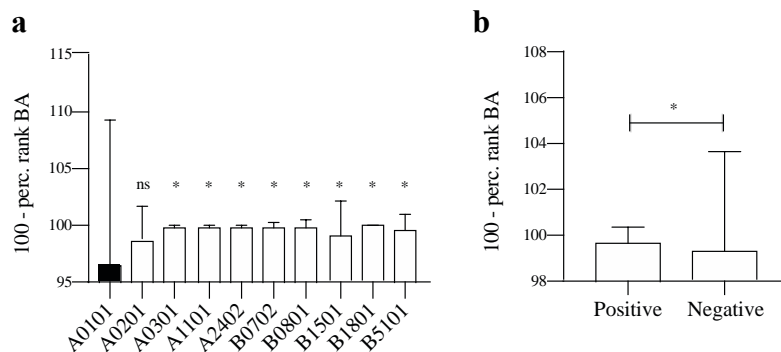


551 **Supplementary Information**



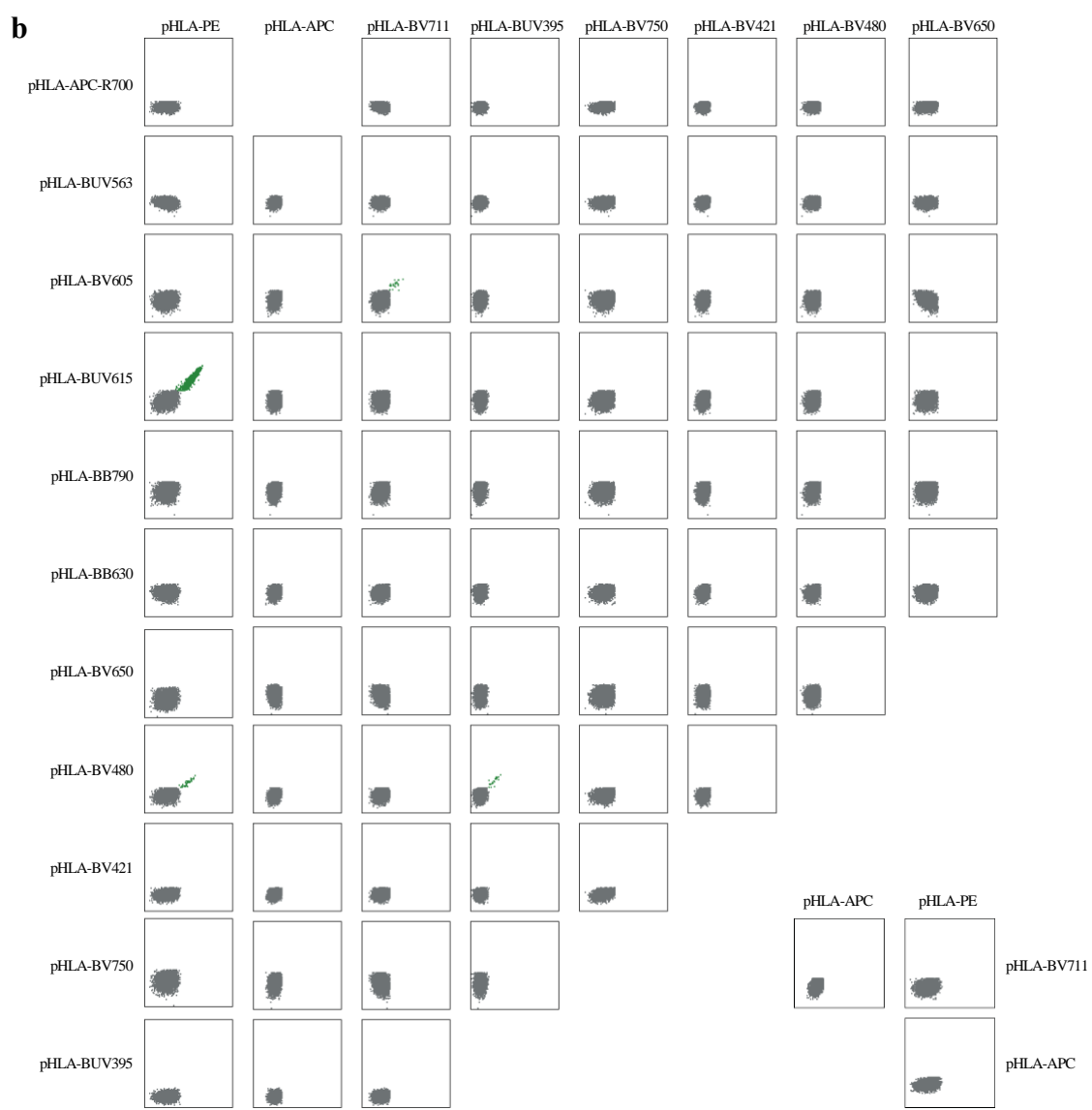
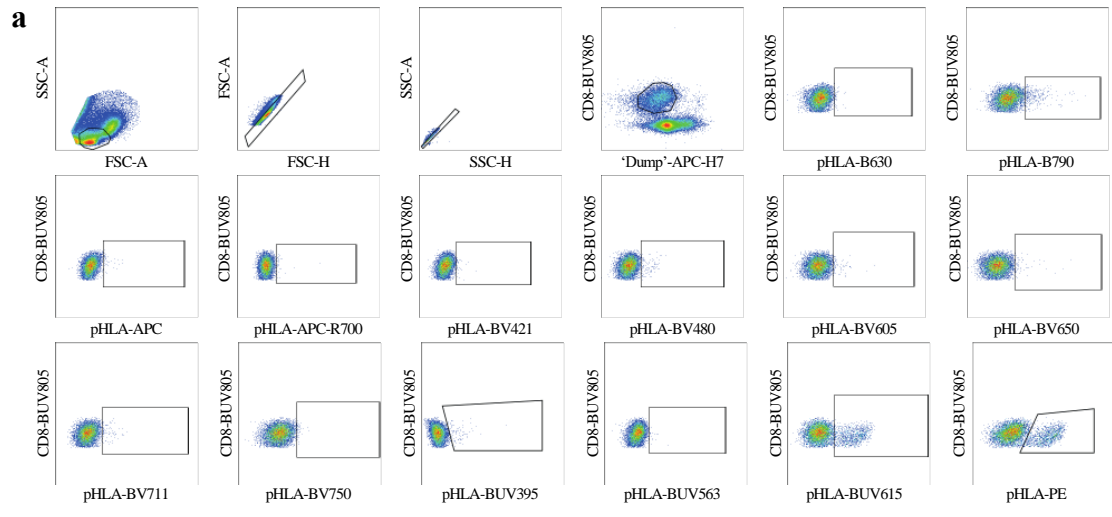
552

553 **Supplementary Figure 1:**

554 a) Overview of the inverse predicted percentile rank binding affinity of the included
555 epitopes to their HLA alleles. On average, the epitopes restricted to HLA-A*01:01 are
556 predicted to bind significantly poorer to their HLA than the other epitopes to their
557 associated HLA alleles, with the exception of epitopes restricted to HLA-A*02:01.
558 Statistical significance was tested with ordinary one-way ANOVA. ns: not significant,
559 *P < 0.05.

560 b) Comparison of the inverse predicted percentile rank binding affinity of the SARS-CoV-
561 2 epitopes to which a positive CD8 T cell response was detected and the SARS-CoV-2
562 epitopes to which no CD8 T cell response was detected. Epitopes to which a positive
563 CD8 T cell response was detected are predicted to have a significantly stronger binding
564 affinity to their HLA. Statistical significance was tested with a two-tailed Mann-
565 Whitney U test. P = 0.03. A higher percentile rank indicates stronger predicted binding.
566 Percentile rank binding affinity was determined using NetMHCpan-4.0₁₆.

567



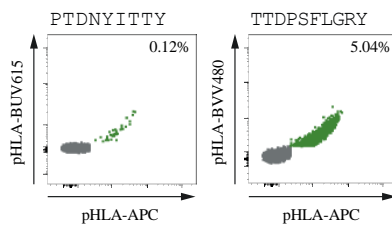
568
569
570
571

572 **Supplementary Figure 2:**

573 a) Representative gating strategy used for the identification of antigen-specific CD8 T cell
574 responses. Single mononuclear cells were selected by FSC and SSC. Within the single
575 cells, live CD8 T cells were selected based on gating on single live mononuclear cells
576 positive for anti-CD8-BUV805, dim of live/dead and negative for anti-CD4/-CD14/-
577 CD16/-CD19-APC-H7. Antigen-specific CD8 T cells were identified based on
578 selection of CD8 T cells positive for only two of the 14 fluorescent pHLA multimers
579 using Boolean gating. pHLA, peptide-major histocompatibility complex.

580 a) Representative overview of all 75 dual colour combinations used to identify the
581 antigen-specific CD8 T cell responses (green) in patient COVID-143.

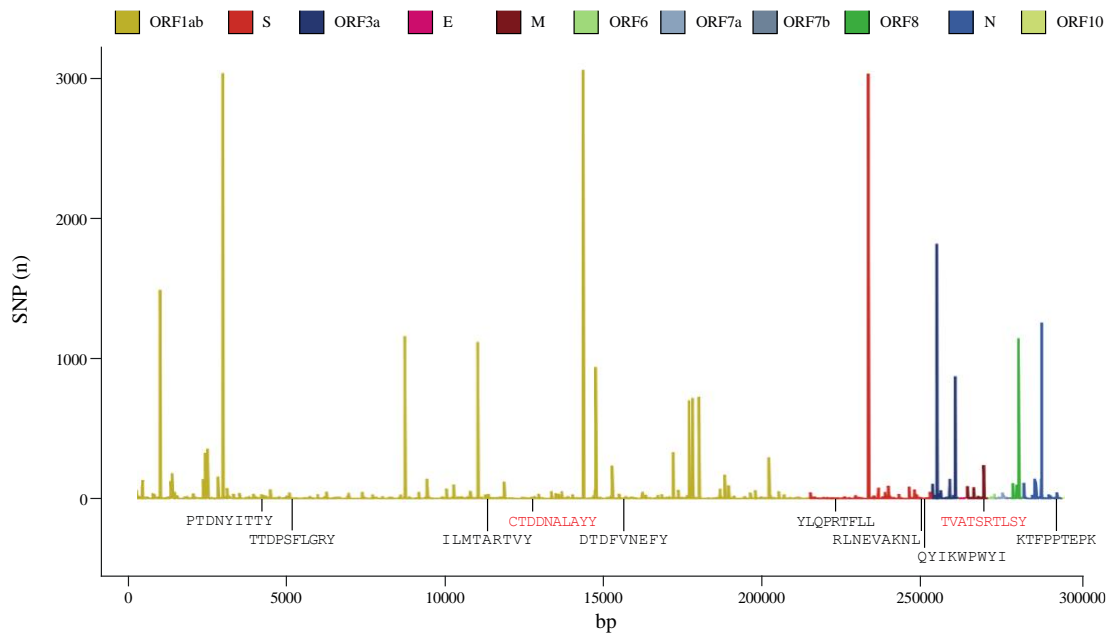
582



585 **Supplementary Figure 3:**

586 Representative flow cytometry plots for confirmed responses in patient COVID-096.

587

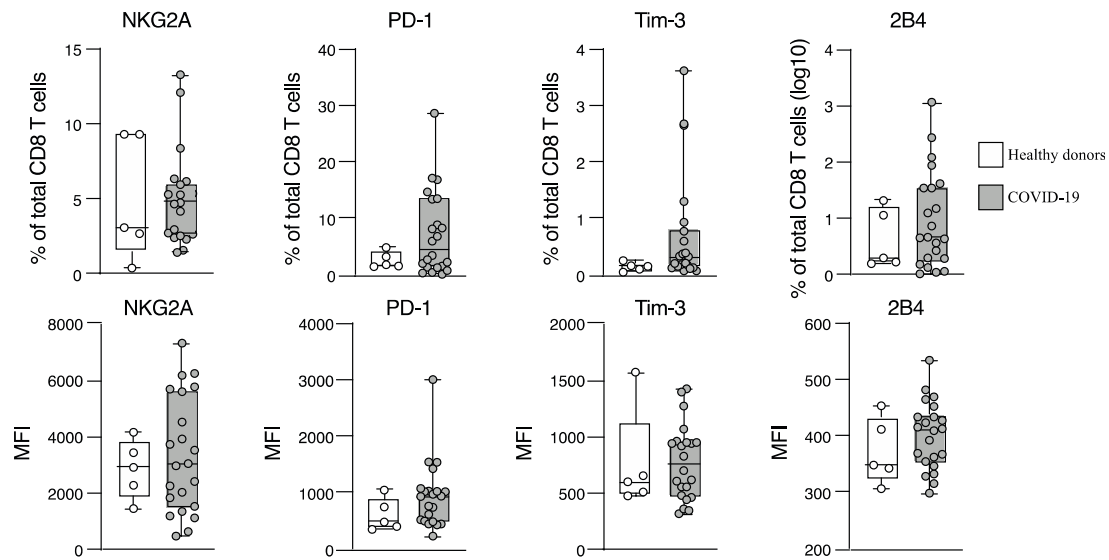


588

589 **Supplementary Figure 4:**

590 Bar graph indicating the number of SNPs reported across the SARS-CoV-2 genome. The
591 location of the CD8 T cell recognized SARS-CoV-2 epitopes are indicated. The peptides in red
592 are peptides that contain sites of significant homoplasy according to the SARS-CoV-2
593 Alignment Screen tool. The exact coding nucleotide ranges of the epitopes on the SARS-CoV-
594 2 genome are: PTDNYITTY (4226-4252), TTDP SFLGRY (5174-5203), ILMTARTVY
595 (11342-11368), CTDDNALAYY (12752-12781), DTDFVNEFY (15652-15678),
596 YLQPRTFLL (22367-22393), RLNEVAKNL (25115-25141), QYIKWPWYI (25184-25210),
597 TVATSRTL SY (27027-27056) and KTFPPTEPK (29354-29380). More information about the
598 SNPs can be found in Table S. 2. Adapted from van Dorp et al. 21.

599



600

601 **Supplementary Figure 5:**

602 Fraction (% of total CD8 T cells) and expression levels (MFI) of total CD8 T cells expressing
 603 PD-1, NKG2A, 2B4 and Tim-3 in COVID-19 patients compared to healthy donors. Statistical
 604 significance was tested with a two-tailed Mann-Whitney U-test. No significance was found.

605

Proj. ID	Proj. Name	Activity	Priority	Phase	Responsibility	Start Date	End Date	Status	Progress %	Cost (k\$)	Revenue (k\$)	Profit (k\$)	ROI %	Risk	Notes
PT01-01	Project Alpha	Phase 1	High	Initiation	John Doe	2023-01-01	2023-03-31	Completed	100	500	1000	500	100	Low	Successful launch.
PT02-01	Project Beta	Phase 1	Medium	Planning	Jane Smith	2023-02-15	2023-04-15	On Track	75	800	1600	800	100	Low	Minor delays, on budget.
PT03-01	Project Gamma	Phase 1	Low	Execution	Mike Johnson	2023-03-01	2023-05-31	Delayed	40	1200	2400	1200	100	High	Significant budget overruns.
PT04-01	Project Delta	Phase 1	High	Monitoring	Sarah Lee	2023-04-01	2023-06-30	On Track	90	600	1200	600	100	Medium	Good communication throughout.
PT05-01	Project Epsilon	Phase 1	Medium	Closing	David King	2023-05-01	2023-07-31	Completed	100	400	800	400	100	Low	Smooth transition to maintenance.
PT06-01	Project Zeta	Phase 1	High	Initiation	Emily White	2023-06-01	2023-08-31	On Track	85	900	1800	900	100	Medium	Scope creep managed well.
PT07-01	Project Eta	Phase 1	Low	Planning	Chris Brown	2023-07-01	2023-09-30	Delayed	30	1100	2200	1100	100	High	Resource allocation issues.
PT08-01	Project Theta	Phase 1	Medium	Execution	Alex Green	2023-08-01	2023-10-31	On Track	70	700	1400	700	100	Medium	Regular reporting and updates.
PT09-01	Project Iota	Phase 1	High	Monitoring	Mia Black	2023-09-01	2023-11-30	On Track	95	500	1000	500	100	Low	Excellent stakeholder engagement.
PT10-01	Project Kappa	Phase 1	Medium	Closing	Noah Grey	2023-10-01	2024-01-31	Completed	100	300	600	300	100	Low	Final review completed.
PT11-01	Project Lambda	Phase 1	High	Initiation	Olivia Blue	2023-11-01	2024-03-31	On Track	80	1000	2000	1000	100	Medium	Clear objectives and milestones.
PT12-01	Project Mu	Phase 1	Low	Planning	Liam Purple	2023-12-01	2024-04-30	Delayed	20	1300	2600	1300	100	High	Complex dependencies.
PT13-01	Project Nu	Phase 1	Medium	Execution	Ava Yellow	2024-01-01	2024-05-31	On Track	65	850	1700	850	100	Medium	Proactive risk management.
PT14-01	Project Xi	Phase 1	High	Monitoring	Ethan Orange	2024-02-01	2024-06-30	On Track	92	650	1300	650	100	Low	Strong team collaboration.
PT15-01	Project Omicron	Phase 1	Medium	Closing	Sophia Pink	2024-03-01	2024-07-31	Completed	100	450	900	450	100	Low	Final handover successful.

606 **Supplementary Table 1: List of selected epitopes.**

607 List including the literature source of included peptides (columns ‘ViPR T cell response’ to
608 ‘NetMHCpan4.0’)16, reported scores (percentile rank binding affinity according to
609 NetMHCpan-4.016, percentage pMHC stability as determined by NeoScreen MHC binding
610 assays37, average binding energy of the peptide to the MHC as predicted by RosettaMHC (dG
611 kcal/mol; Nerli and Sgourakis, 2020) and annotation in the Virus Pathogen Database and
612 Analysis Resource (ViPR)) columns ‘NetMHCpan-4.016 perc.rank binding affinity’ to ‘ViPR
613 measurement’), and overlap of included peptide with the the SARS-CoV proteome (UniProt:
614 UP000160648) and known ‘common cold’ coronaviruses (HCoV-NL63, UniProt:
615 UP000145724; HCoV-299E, UniProt: UP000006716; HCoV-OC43, UniProt: UP000007552;
616 HCoV-HKU1, UniProt: UP000006551). The overlap between viruses was determined by
617 comparing the peptides in this study with all 9-11mer peptide sequences encompassing each
618 compared viral proteome.

619

620 **Supplementary Table 2:**

621 Overview of the CD8 T cell recognized epitopes and associated SNPs as reported by van Dorp
 622 et al.²¹. NCBI reference sequence NC_045512.2 was used to indicate the location of the SNPs.
 623 Empty cells are ‘unknown’. *Due to lack of annotation of SNPs, the estimated minimum
 624 frequency of isolates was obtained by dividing the reported number of SNPs by the total
 625 number of samples in the database (7667 per May 14th, 2020) multiplied by a 100. SNP: Single
 626 Nucleotide Polymorphism, AA: Amino acid, nt: nucleotide.

627

Viral gene	T cell recognized epitope	SNP location (nt)	Ratio (A:C:G:T)	Total reported SNPs	Ref. codon	Ref. AA	SNP codon	AA change	Alt. epitope	Isolates with alt. epitope (%)
ORF1ab	PTDNYITTY	4236		6	AAT	N		yes	yes	0.0783*
		4246		1	ACC	T		no	no	
		4252		1	TAC	Y				
	TTDPSFLGRY	5183	0:6994:0:7	7	CCT	P	TCT	P > S	TTDSSFLGRY	0.100
		5184		1	CCT	P		yes	yes	0.0130*
		5192		1	CTG	L				
		5194		1	CTG	L		no	no	
	ILMTARTVY	11355	0:7002:0:3	3	GCA	A	GTA	A > V	ILMTYRTVY	0.0428
		11356		1	GCA	A		no	no	
	CTDDNALAYY	12754		1	TGC	C				
		12756	0:7002:0:3	3	ACT	T	ATT	T > I	CIDDNALAYY	0.0428
		12769		1	GCG	A		no	no	
		12778	2:7000:0:3	5	TAC	Y	TAA, TAT	Y > stop, no	CTDDNALA	0.0285
		12781	0:6994:0:11	11	TAC	Y	TAT	no	no	
	DTDFVNEFY	15654	0:7003:0:2	2	GAC	D	GAT	no	no	
15672			1	GAG	E					
S	YLQPRTFLL	22374		2	CAA	Q				
		22381		1	AGG	R				
		22384		1	ACT	T		no	no	
		22388		1	CTA	L				
		22391		1	TTA	L				
		22393		1	TTA	L				
	RLNEVAKNL	25116		1	CGC	R		yes	yes	0.0130*
		25135	0:0:7001:3	3	AAG	K	AAT	K > N	RLNEVANL	0.0428
	QYIKWPWYI	25187		1	TAT	Y		yes	yes	0.0130*
		25191		1	ATA	I		yes	yes	0.0130*
		25207	0:6997:0:6	6	TAC	Y	TAT	no	no	
25209			2	AIT	I		yes	yes	0.0130*	
25210			1	ATT	I					
N	KTFPPEPK	29360		1	TTC	F		yes	yes	0.0130*
		29361		1	TTC	F		yes	yes	0.0130*
		29362		1	TTC	F				
		29366		1	CCA	P		yes	yes	0.0130*
		29370	0:6994:0:2	2	ACA	T	ATA	T > I	KTFPIEPK	0.0286
		29374		18	GAG	E				
M	TVATSRILSY	27046	0:6796:0:201	238	ACG	T	AIG	T > M	TVATSRMLSY	2.87
		27056	0:2:0:7002	2	TAT	Y	TAC	no	no	

628 **Supplementary Table 3:**

629 Overview of UV-sensitive peptides used for generating the corresponding UV-sensitive pHLA
630 monomers. 'J' indicates the UV-sensitive amino acid.

631

Allele	Conditional ligand
A*01:01	STAPG-J-LEY ₃₆
A*02:01	KILGFVF-J-V ₃₁
A*03:01	RIYR-J-GATR ₃₆
A*11:01	AIFQSS-J-TK ₃₆
A*24:01	VYG-J-VRACL ₃₅
B*07:02	AARG-J-TLAM ₃₆
B*08:01	FLRGRA-J-GL ₃₄
B*15:01	ILGP-J-GSVY ₃₄
B*18:01	SELE-J-KRY
B*51:01	IPT-J-FSISI

632