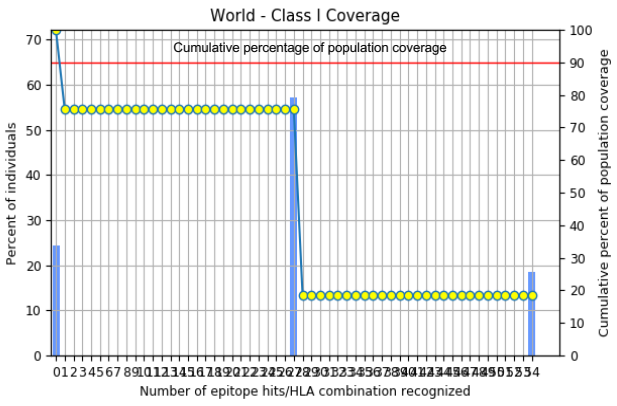
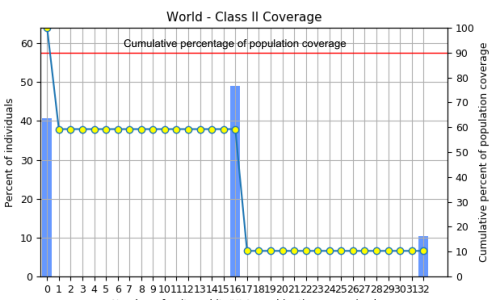
A Predicted population coverage (PPC) value of human CD8⁺ T cell epitopes



Population/Ethnicity	Class I		
	Cumulative Coverage	Average hit	pc90
World	**75.66%**	25.4	11.09

Epitope	SARS-CoV-2 derived CD8⁺ Epitopes sequence	HLA binding alleles	Cumulative PPC value (%)
ORF1ab$_{84-92}$	VMVELVAEL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{1675-1683}$	YLATALLTL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{2210-2218}$	CLEASFNYL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{2363-2371}$	WLMWLIINL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{3013-3021}$	SLPGVFCGV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{3183-3191}$	FLLNKEMYL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{3732-3740}$	SMWALIISV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{4283-4291}$	YLASGGQPI	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{5470-5478}$	KLSYGIATV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{6419-6427}$	YLDAYNMMI	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{6749-6757}$	LLLDDFVEI	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
S$_{2-10}$	FVFLVLLPL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
S$_{691-699}$	SIIAYTMSL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
S$_{958-966}$	ALNTLVKQL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
S$_{976-984}$	VLNDILSRL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
S$_{1000-1008}$	RLQSLQTYV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
S$_{1220-1228}$	FIAGLIAIV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
E$_{20-28}$	FLAFVVFLL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
E$_{26-34}$	FLLVTLAIL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
M$_{52-60}$	IFLWLLWPV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
M$_{89-97}$	GLMWLSYFI	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF6$_{3-11}$	HLVDFQVTI	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF7b$_{26-34}$	IIFWFSLEL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF8a$_{31-39}$	YVVDDPCPI	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF8a$_{73-81}$	YIDIGNYTV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF10$_{3-11}$	YINVFAFPF	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF10$_{5-13}$	NVFAFPFTI	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66

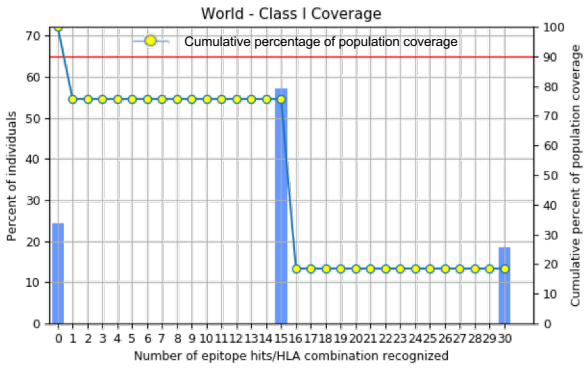
B Predicted population coverage (PPC) value of human CD4⁺ T cell epitopes



Population/ Ethnicity	Class I		
	Cumulative Coverage	Average hit	pc90
World	**59.25%**	11.13	3.96

Epitope	SARS-CoV-2 derived CD4⁺ Epitopes sequence	HLA binding alleles	Cumulative PPC value (%)
ORF1a$_{1350-1365}$	KSAFYILPSIISNEK	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF1a$_{1801-1815}$	ESPFVMMSAPPAQYE	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF1ab$_{5019-5033}$	PNMLRIMASLVLARK	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF1ab$_{6088-6102}$	RIKVQMLSDTLKNL	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF1ab$_{6420-6434}$	LDAYNMMISAGFSLW	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
S$_{1-13}$	MFVFLVLLPLVSS	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
E$_{20-34}$	FLAFVVFLLVTLAIL	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
E$_{26-40}$	FLLVTLAILTALRLC	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
M$_{176-190}$	LSYYKLGASQRVAGD	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF6$_{12-26}$	AEILLIIMRTFKVSI	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF7a$_{1-15}$	MKIILFLALITLATC	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF7a$_{3-17}$	IIFLALITLATCEL	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF7a$_{98-112}$	SPIFLIVAAIVFITL	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF7b$_{8-22}$	DFYLCFLAFLLFLVL	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF8b$_{1-15}$	MKFLVFLGIITTVAA	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
N$_{388-4031}$	KQQTVTLLPAADLDDF	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25

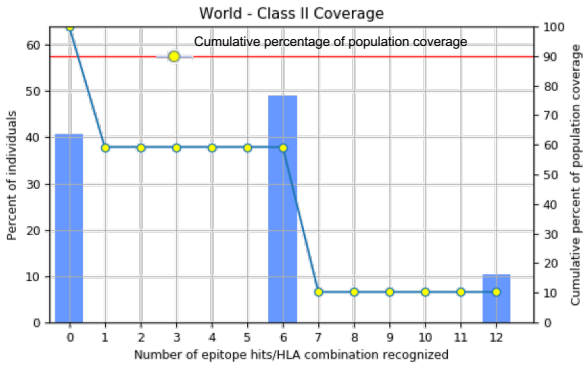
C Predicted population coverage (PPC) value of human CD8⁺ T cell epitopes in Pan-Coronavirus Vaccine candidate # 1



Population/Ethnicity	Class I		
	Cumulative Coverage	Average hit	pc90
World	**75.66%**	14.13	6.16

Epitope	SARS-CoV-2 derived CD8⁺ Epitopes sequence	HLA binding alleles	Cumulative PPC (%)
ORF1ab$_{1675-1683}$	YLATALLTL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{2363-2371}$	WLMWLIINL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{3013-3021}$	SLPGVFCGV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{5470-5478}$	KLSYGIATV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF1ab$_{6749-6757}$	LLLDDFVEI	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
S$_{2-10}$	FVFLVLLPL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
S$_{958-966}$	ALNTLVKQL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
S$_{1000-1008}$	RLQSLQTYV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
S$_{1220-1228}$	FIAGLIAIV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
E$_{20-28}$	FLAFVVFLL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
E$_{26-34}$	FLLNKEMYL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF7b$_{26-34}$	IIFWFSLEL	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF8a$_{73-81}$	YIDIGNYTV	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF10$_{3-11}$	YINVFAFPF	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66
ORF10$_{5-13}$	NVFAFPFTI	HLA-A*01:01,HLA-A*02:01,HLA-A*03:01,HLA-A*11:01,HLA-A*23:01	75.66

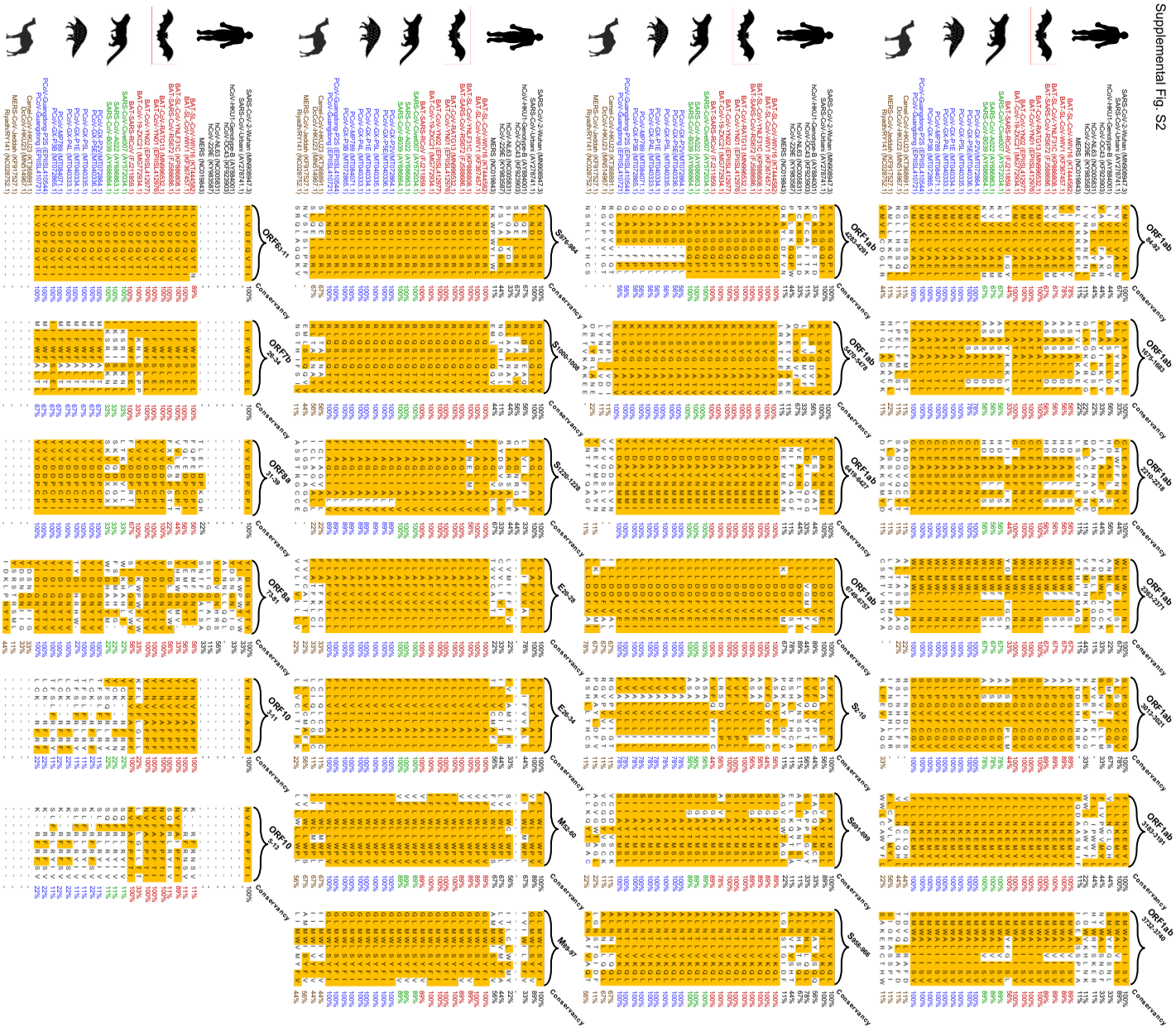
D Predicted population coverage (PPC) value of human CD4⁺ T cell epitopes in Pan-Coronavirus Vaccine candidate # 1



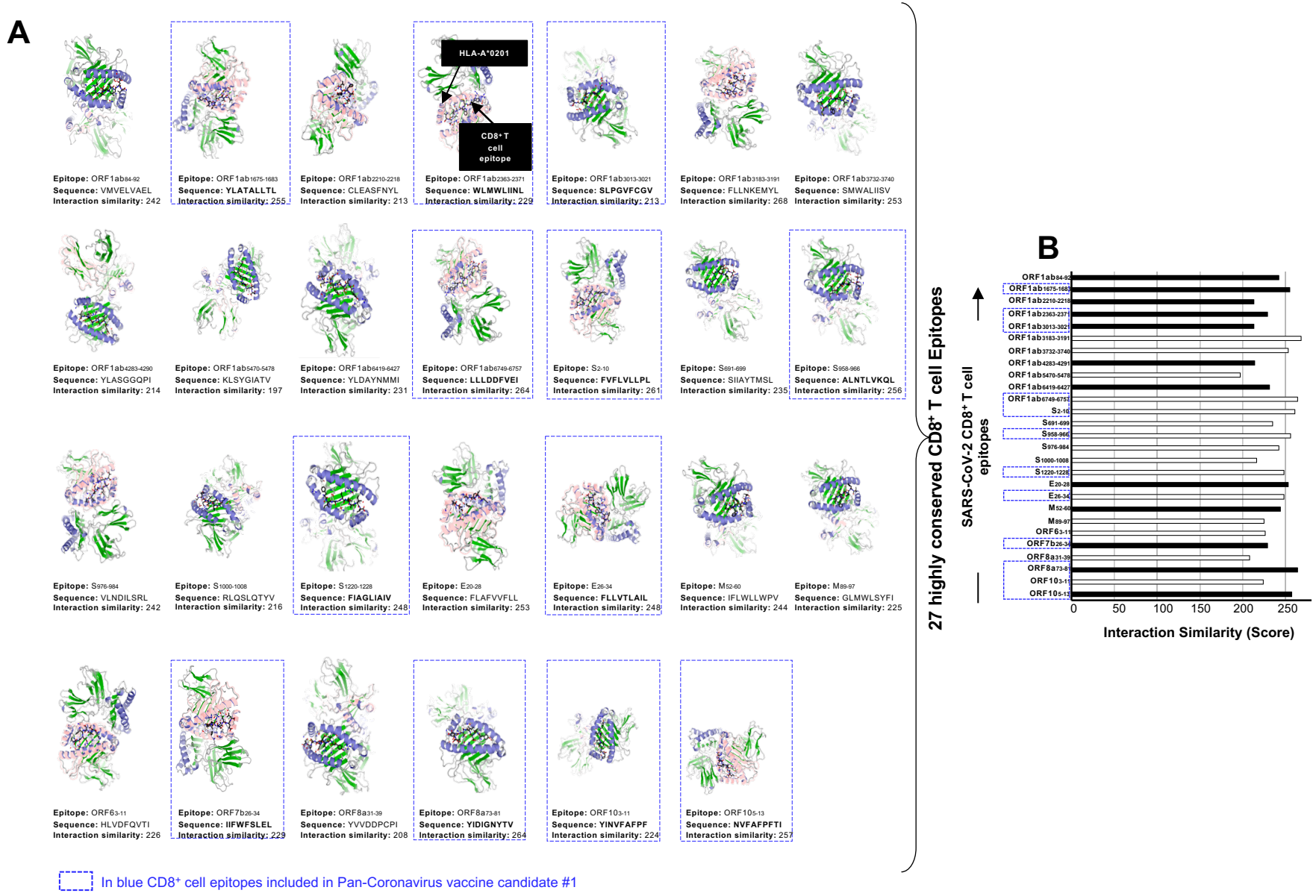
Population/Ethnicity	Class II		
	Cumulative Coverage	Average hit	pc90
World	**59.25%**	4.17	1.47

Epitope	SARS-CoV-2 derived CD4⁺ Epitopes sequence	HLA binding alleles	Cumulative PPC (%)
ORF1a$_{1350-1365}$	KSAFYILPSIISNEK	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF1ab$_{5019-5033}$	PNMLRIMASLVLARK	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
M$_{176-190}$	LSYYKLGASQRVAGD	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF6$_{12-26}$	AEILLIIMRTFKVSI	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF7b$_{8-22}$	DFYLCFLAFLLFLVL	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25
ORF8b$_{1-15}$	MKFLVFLGIITTVAA	HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01	59.25

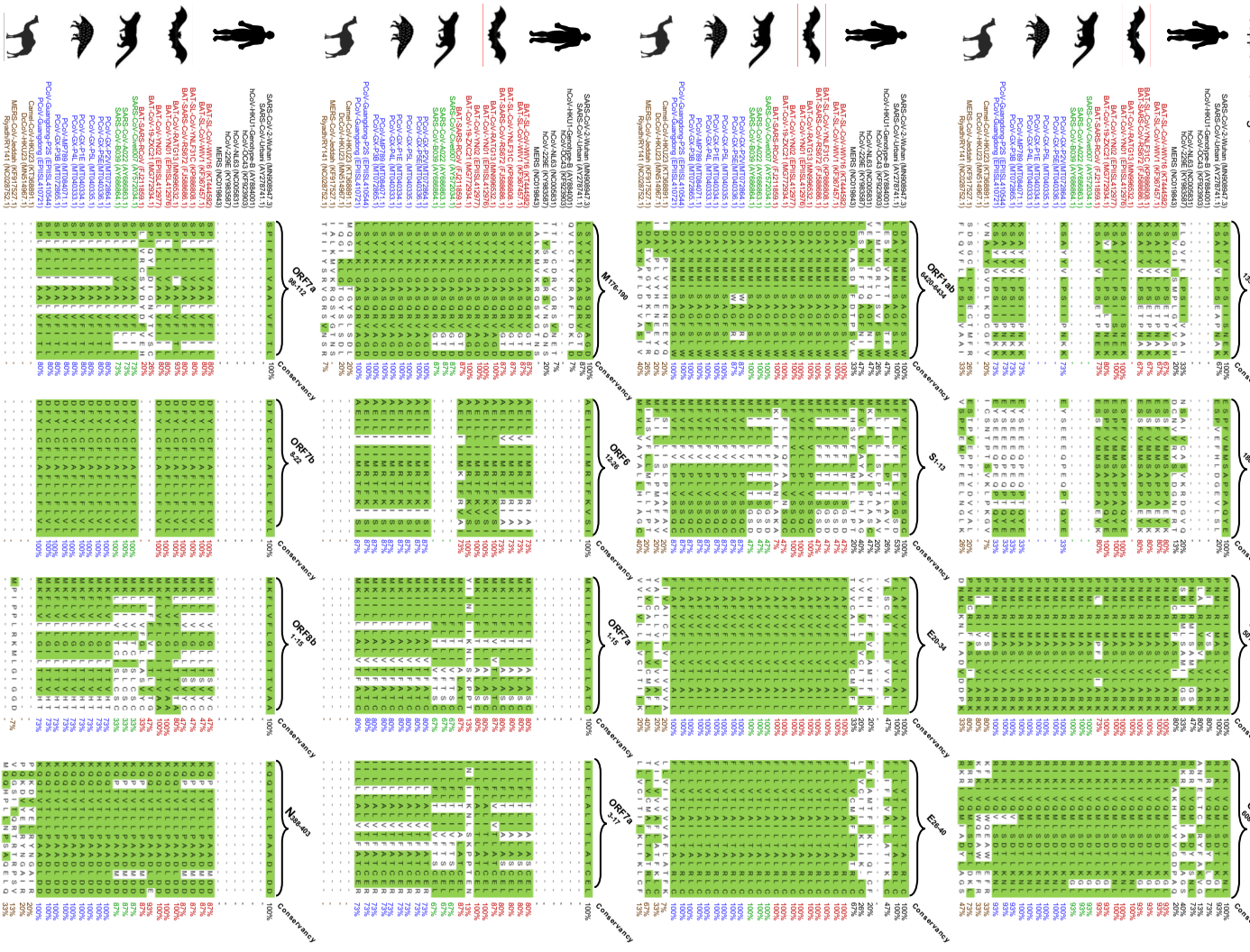
<u>Supplemental Figure S1</u>: Population coverage calculation for all the high binding CD8⁺ and CD4⁺ T cell epitopes screened in the current study: (**A**) The SARS-CoV-2-derived CD8⁺ T cell epitopes are screened based on their presence among most frequently observed HLA-A alleles in global population (HLA-A*01:01, HLA-A*02:01, HLA-A*03:01, HLA-A*11:01, HLA-A*23:01). MHC-I binding affinity and high degree of immunogenicity showed high PPC value of 75.66%, average number of epitope hits / HLA combinations recognized by the population is 25.4, and minimum number of epitope hits / HLA combinations recognized by 90% of the population (pc90) is 11.09 (**B**) The SARS-CoV-2-derived CD4⁺ T cell epitopes are screened based on their presence among most frequently observed HLA-DRB1 alleles in global population (HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01). MHC-II binding affinity and high degree of immunogenicity showed high PPC values at 59.25%, average number of epitope hits / HLA combinations recognized by the population is 11.13, and minimum number of epitope hits / HLA combinations recognized by 90% of the population (pc90) is 3.96. The PPC plot shows percentage of individuals possessing combination of a number of epitopes/HLA alleles of interest and represents the cumulative percentage of population coverage. The line (-o-) shows the cumulative percentage of population coverage of epitope/HLA combination while the bars depict the population coverage for individual epitope. The analysis also generates the average number of epitope hits / HLA combinations recognized by the world population, and minimum number of epitope hits / HLA combinations recognized by 90% of the world population (pc90) as shown below the PPC plot. (**C**) The SARS-CoV-2-derived CD8⁺ T cell epitopes are screened based on their presence among most frequently observed HLA-A alleles in global population (HLA-A*01:01, HLA-A*02:01, HLA-A*03:01, HLA-A*11:01, HLA-A*23:01). MHC-I binding affinity and high degree of immunogenicity showed high PPC value of 75.66%, average number of epitope hits / HLA combinations recognized by the population is 14.13, and minimum number of epitope hits / HLA combinations recognized by 90% of the population (pc90) is 6.16. (**D**) The SARS-CoV-2-derived CD4⁺ T cell epitopes are screened based on their presence among most frequently observed HLA-DRB1 alleles in global population (HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01, HLA-DRB1*04:01). MHC-II binding affinity and high degree of immunogenicity showed high PPC value at 59.25%, average number of epitope hits / HLA combinations recognized by the population is 4.17, and minimum number of epitope hits / HLA combinations recognized by 90% of the population (pc90) is 1.47. The PPC plot shows percentage of individuals possessing combination of a number of epitopes/HLA alleles of interest and represents the cumulative percentage of population coverage. The line (-o-) shows the cumulative percentage of population coverage of epitope/HLA combination while the bars depict the population coverage for individual epitope. The analysis also generates the average number of epitope hits / HLA combinations recognized by the world population, and minimum number of epitope hits / HLA combinations recognized by 90% of the world population (pc90) as shown below the PPC plot.



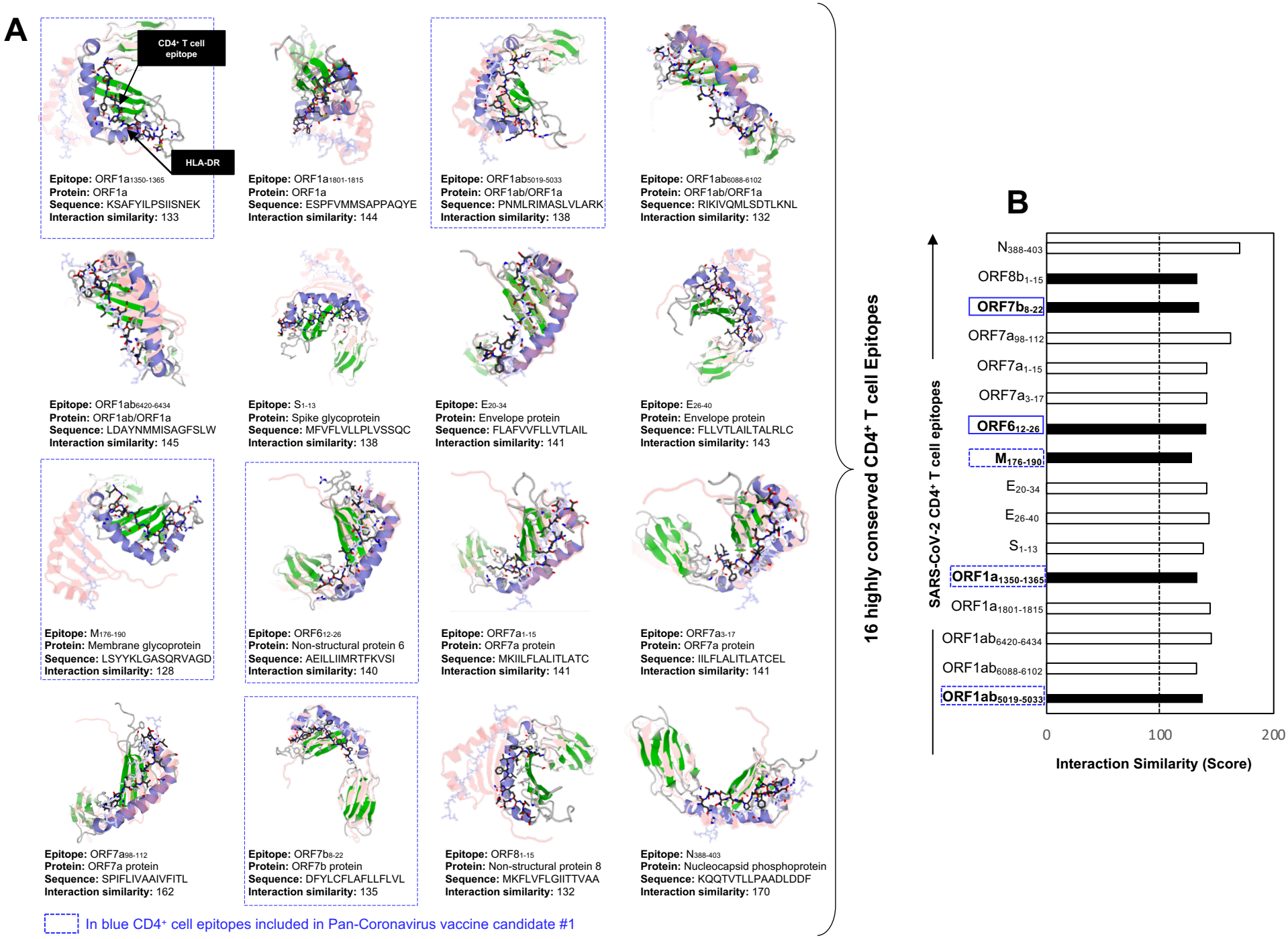
Supplemental Figure S2: Sequence homology analysis to screen conservancy of potential SARS-CoV-2-derived human CD8⁺ T cell epitopes: Shown are the comparison of sequence homology for the potential CD8⁺ T cell epitopes among 81,963 SARS-CoV-2 strains (that currently circulate in 190 countries on 6 continents), the 4 major "common cold" Coronaviruses that cased previous outbreaks (i.e. hCoV-OC43, hCoV-229E, hCoV-HKU1-Genotype B, and hCoV-NL63), and the SL-CoVs that were isolated from bats, civet cats, pangolins and camels. Epitope sequences highlighted in yellow present a high degree of homology among the currently circulating 81,963 SARS-CoV-2 strains and at least a 50% conservancy among two or more humans SARS-CoV strains from previous outbreaks, and the SL-CoV strains isolated from bats, civet cats, pangolins and camels, as described in *Materials* and *Methods*. *Homo Sapiens- black*, bats (*Rhinolophus affinis*, *Rhinolophus malayanus -red*), pangolins (*Manis javanica-blue*), civet cats (*Paguma larvata-green*), and camels (*Camelus dromedaries-brown*).



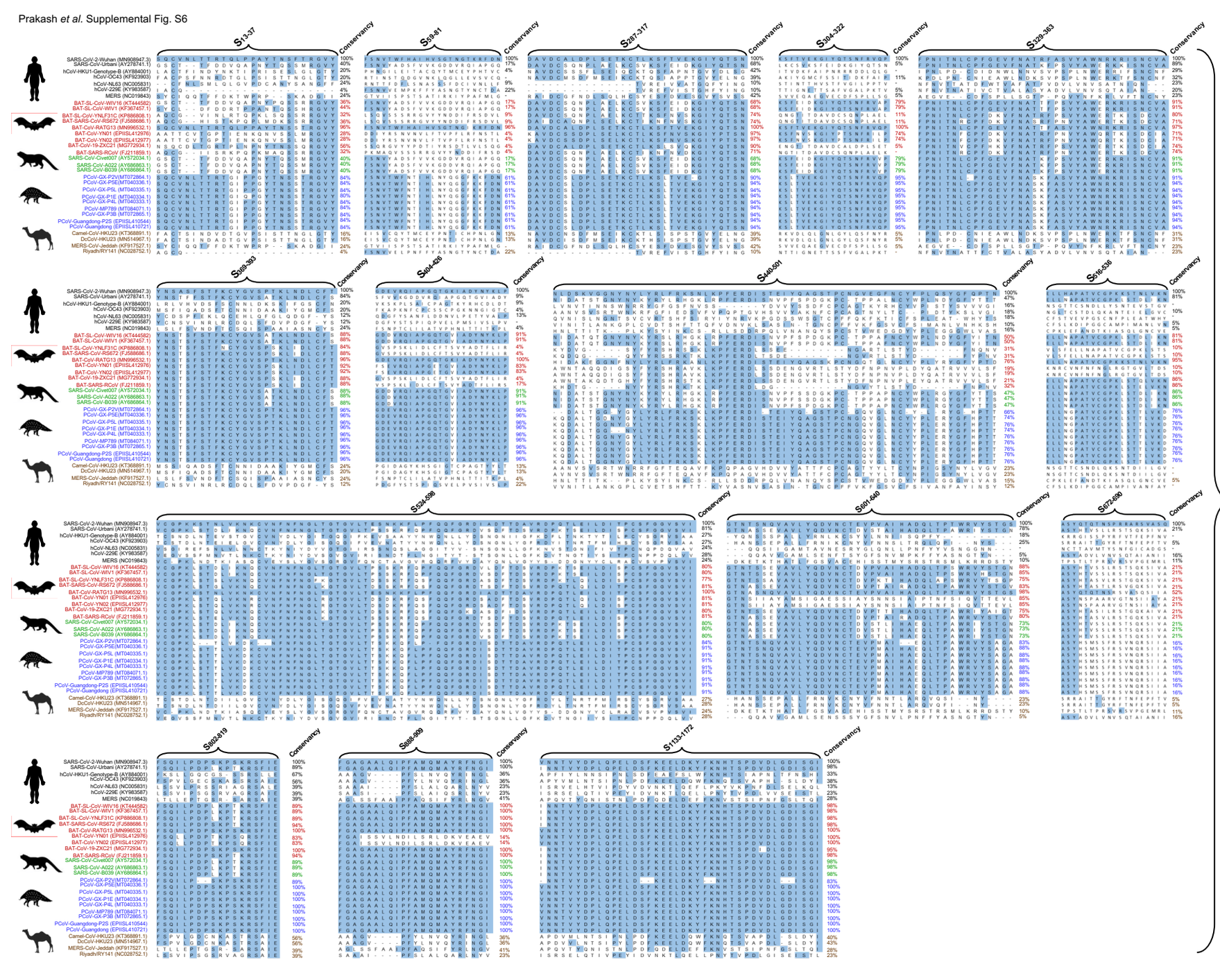
<u>Supplemental Figure S3</u>: Docking of highly conserved SARS-CoV-2-derived human CD8⁺ T cell epitopes to HLA-A*02:01 molecules: (**A**) Docking of the 27 high-affinity CD8⁺ T cell binder peptides to the groove of HLA-A*02:01 molecules. (**B**) Summary of the interaction similarity scores of the 27 high-affinity CD8⁺ T cell epitope peptides to HLA-A*02:01 molecules determined by protein-peptide molecular docking analysis. Black columns depict CD8⁺ T cell epitope peptides with high interaction similarity scores.



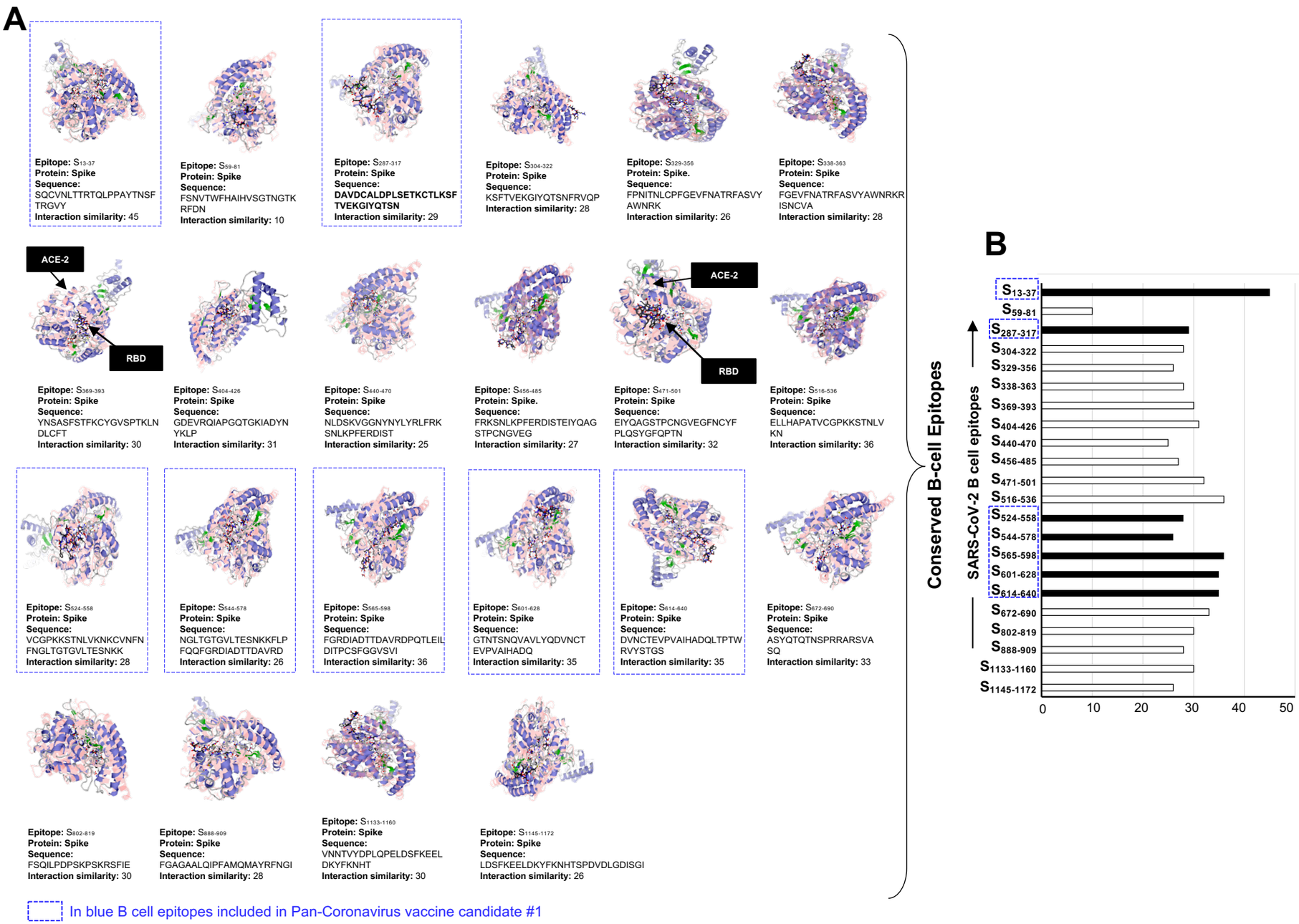
<u>Supplemental Figure S4</u>: Identification of highly conserved potential SARS-CoV-2-derived human CD4⁺ T cell epitopes that bind with high affinity to HLA-DR molecules: Out of a total of 9,594 potential HLA-DR-restricted CD4⁺ T cell epitopes from the whole genome sequence of SARS-CoV-2-Wuhan-Hu-1 strain (MN908947.3), 16 epitopes that bind with high affinity to HLA-DRB1 molecules were selected. The conservancy of the 16 CD4⁺ T cell epitopes was analyzed among human and animal Coronaviruses. Shown are the comparison of sequence homology for the 16 CD4⁺ T cell epitopes among 81,963 SARS-CoV-2 strains (that currently circulate in 6 continents), the 4 major ''common cold'' Coronaviruses that cased previous outbreaks (i.e. hCoV-OC43, hCoV-229E, hCoV-HKU1, and hCoV-NL63), and the SL-CoVs that were isolated from bats, civet cats, pangolins and camels. Epitope sequences highlighted in green present high degree of homology among the currently circulating 81,963 SARS-CoV-2 strains and at least a 50% conservancy among two or more humans SARS-CoV strains from previous outbreaks, and the SL-CoV strains isolated from bats, civet cats, pangolins and camels, as described in *Materials* and *Methods*. *Homo Sapiens-black*, bats (*Rhinolophus affinis*, *Rhinolophus malayanus -red*), pangolins (*Manis javanica-blue*), civet cats (*Paguma larvata-green*), and camels (*Camelus dromedaries-brown*).



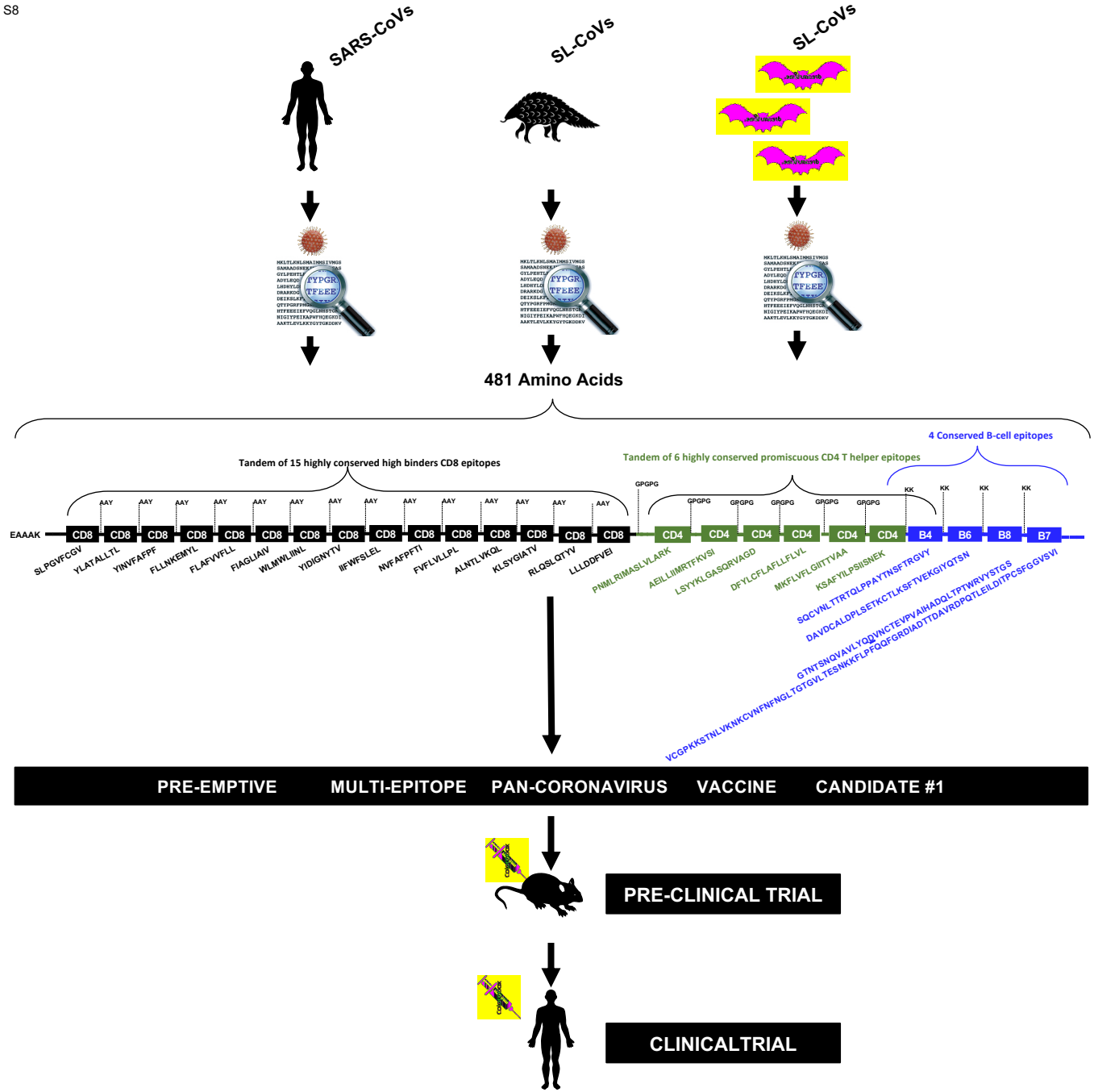
<u>Supplemental Figure S5</u>: Molecular docking of highly conserved SARS-CoV-2 CD4⁺ T cell epitopes to HLA-DRB1 molecules: (**A**) Molecular docking of 16 CD4⁺ T cell epitopes, conserved among human SARS-CoV-2 strains, previous humans SARS/MERS-CoV and bat SL-CoVs into the groove of the HLA-DRB1 protein crystal structure (PDB accession no: 4UQ3) was determined using the GalaxyPepDock server. The 16 CD4⁺ T cell epitopes are promiscuous restricted to HLA-DRB1*01:01, HLA-DRB1*11:01, HLA-DRB1*15:01, HLA-DRB1*03:01 and HLA-DRB1*04:01 alleles. The CD4⁺ T cell peptides are shown in ball and stick structures, and the HLA-DRB1 protein crystal structure is shown as a template. The prediction accuracy is estimated from a linear model as the relationship between the fraction of correctly predicted binding site residues and the template-target similarity measured by the protein structure similarity score (TM score) and interaction similarity score (S_{Inter}) obtained by linear regression. SInter shows the similarity of the amino acids of the CD8⁺ T cell peptides aligned to the contacting residues in the amino acids of the HLA-DRB1 template structure. (**B**) Histograms representing interaction similarity score of CD4⁺ T cells specific epitopes observed from the protein-peptide molecular docking analysis.



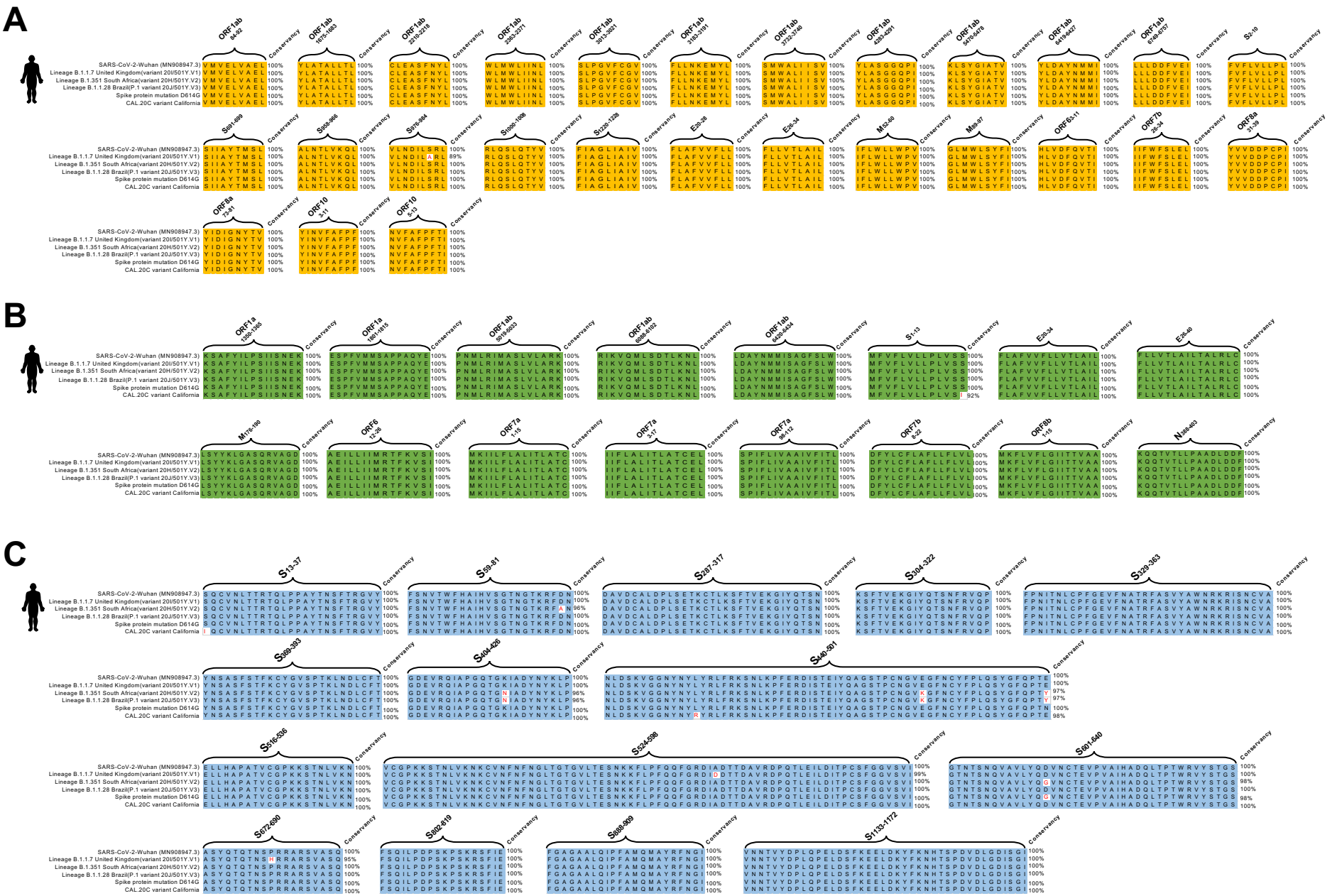
<u>Supplemental Figure S6:</u> Conservation of Spike-derived B cell epitopes among human, bat, civet cat, pangolin, and camel coronavirus strains: Multiple sequence alignment performed using ClustalW among 29 strains of SARS coronavirus (SARS-CoV) obtained from human, bat, civet, pangolin, and camel. This includes 7 human SARS/MERS-CoV strains (SARS-CoV-2-Wuhan (MN908947.3), SARS-HCoV-Urbani (AY278741.1), CoV-HKU1-Genotype-B (AY884001), CoV-OC43 (KF923903), CoV-NL63 (NC005831), CoV-229E (KY983587), MERS (NC019843)); 8 bat SARS-CoV strains (BAT-SL-CoV-WIV16 (KT444582), BAT-SL-CoV-WIV1 (KF367457.1), BAT-SL-CoV-YNLF31C (KP886808.1), BAT-SARS-CoV-RS672 (FJ588686.1), BAT-CoV-RATG13 (MN996532.1), BAT-CoV-YN01 (EPIISL412976), BAT-CoV-YN02 (EPIISL412977), BAT-CoV-19-ZXC21 (MG772934.1)); 3 Civet SARS-CoV strains (SARS-CoV-Civet007 (AY572034.1), SARS-CoV-A022 (AY686863.1), SARS-CoV-B039 (AY686864.1)); 9 pangolin SARS-CoV strains (PCoV-GX-P2V(MT072864.1), PCoV-GX-P5E(MT040336.1), PCoV-GX-P5L (MT040335.1), PCoV-GX-P1E (MT040334.1), PCoV-GX-P4L (MT040333.1), PCoV-MP789 (MT084071.1), PCoV-GX-P3B (MT072865.1), PCoV-Guangdong-P2S (EPIISL410544), PCoV-Guangdong (EPIISL410721)); 4 camel SARS-CoV strains (Camel-CoV-HKU23 (KT368891.1), DcCoV-HKU23 (MN514967.1), MERS-CoV-Jeddah (KF917527.1), Riyadh/RY141 (NC028752.1)) and 1 recombinant strain (FJ211859.1)). Regions highlighted with blue color represent the sequence homology. The B cell epitopes, which showed at least 50% conservancy among two or more strains of the SARS Coronavirus or possess receptor-binding domain (RBD) specific amino acids were selected as candidate epitopes.



<u>Supplemental Figure S7</u>: Docking of SARS-CoV-2 Spike glycoprotein-derived B cell epitopes to human ACE2 receptor: (**A**) Molecular docking of 22 B-cell epitopes, identified from the SARS-CoV-2 Spike glycoprotein, with ACE2 receptors. B cell epitope peptides are shown in ball and stick structures whereas the ACE2 receptor protein is shown as a template. $S_{471\text{-}501}$ and $S_{369\text{-}393}$ peptide epitopes possess receptor binding domain region specific amino acid residues. The prediction accuracy is estimated from a linear model as the relationship between the fraction of correctly predicted binding site residues and the template-target similarity measured by the protein structure similarity score and interaction similarity score (S_{Inter}) obtained by linear regression. S_{Inter} shows the similarity of amino acids of the B-cell peptides aligned to the contacting residues in the amino acids of the ACE2 template structure. Higher S_{Inter} score represents a more significant binding affinity among the ACE2 molecule and B-cell peptides. (**B**) Summary of the interaction similarity score of 22 B cells specific epitopes observed from the protein-peptide molecular docking analysis. B cell epitopes with high interaction similarity scores are indicated in black.



<u>Supplemental Figure S8</u>: A prototype multi-epitope Pan-Coronavirus vaccine.



Supplemental Figure S9: Screening for the CD8⁺ T cell, CD4⁺ T cell, and B-cell epitopes against highly transmissible variants of SARS-CoV-2: Keeping in mind the high degree of transmissibility of SARS-CoV-2 variants namely, Lineage B.1.1.7 from United Kingdom(variant 20I/501Y.V1), Lineage B.1.351 from South Africa(variant 20H/501Y.V2), Lineage B.1.1.28 from Brazil(P.1 variant 20J/501Y.V3), CAL.20C variant from California, and Spike protein mutation D614G; it is of importance to evaluate whether our screened epitopes are conserved for these variants or not, which in turn will ascertain the immunogenicity/antigenicity of our candidate epitopes. Results show (**A**) 26 out of 27 CD8⁺ T cell epitopes, and (**B**) 15 out of 16 CD4⁺ T cell epitopes are 100% conserved against all the higher transmissible variants. (**C**) Similarly, 8 B-cell epitopes showed 100% conservancy against all the highly pathogenic SARS-CoV-2 variants.