

Supplemental Information

The immunodominant and neutralization

linear epitopes for SARS-CoV-2

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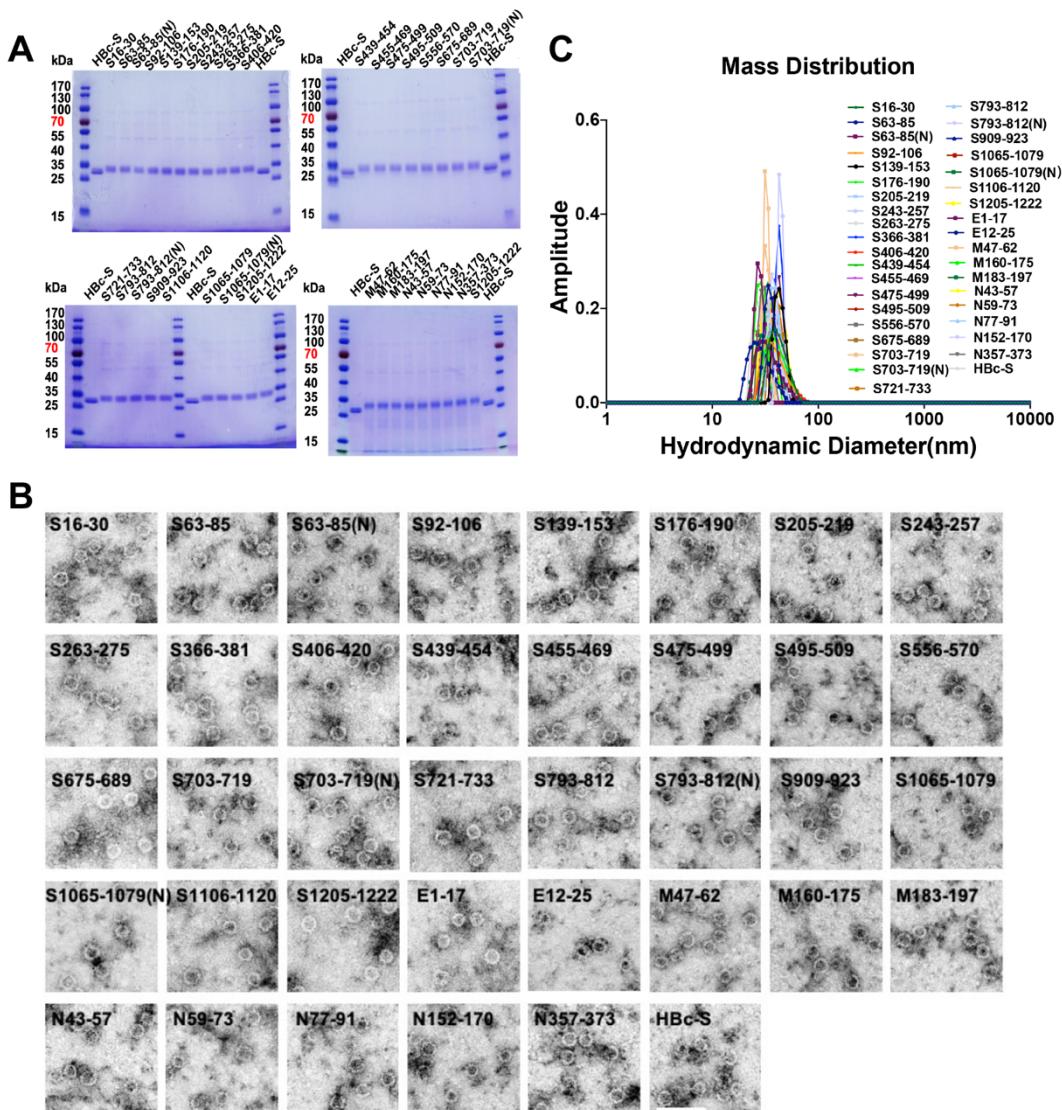


Figure S1. Preparation of HBc-S VLPs displayed with the epitopes. Related to Figure 1. (A) SDS-PAGE analysis of the conjugation of HBc-S with epitope peptides. (B) The morphology of HBc-S-P VLPs. HBc-S-P VLPs were imaged by Hitachi TEM at 80 KV at 40,000 \times magnification, the scale bar is 200 nm. (C) The representative hydrodynamic diameter of HBc-S-P VLPs.

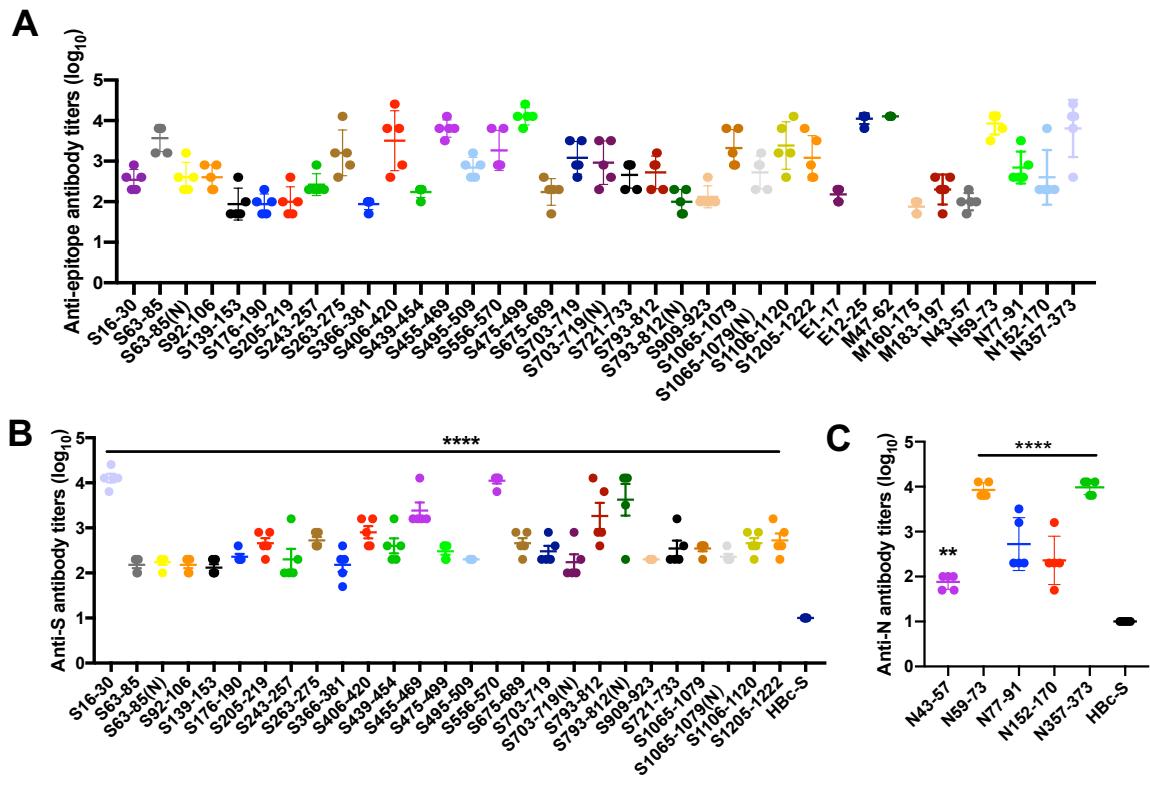


Figure S2. Epitope conjugated on HBC-S VLPs induced high antibody titers against epitope peptides and S, N proteins at 10 days after the second immunization. Related to Figure 1.

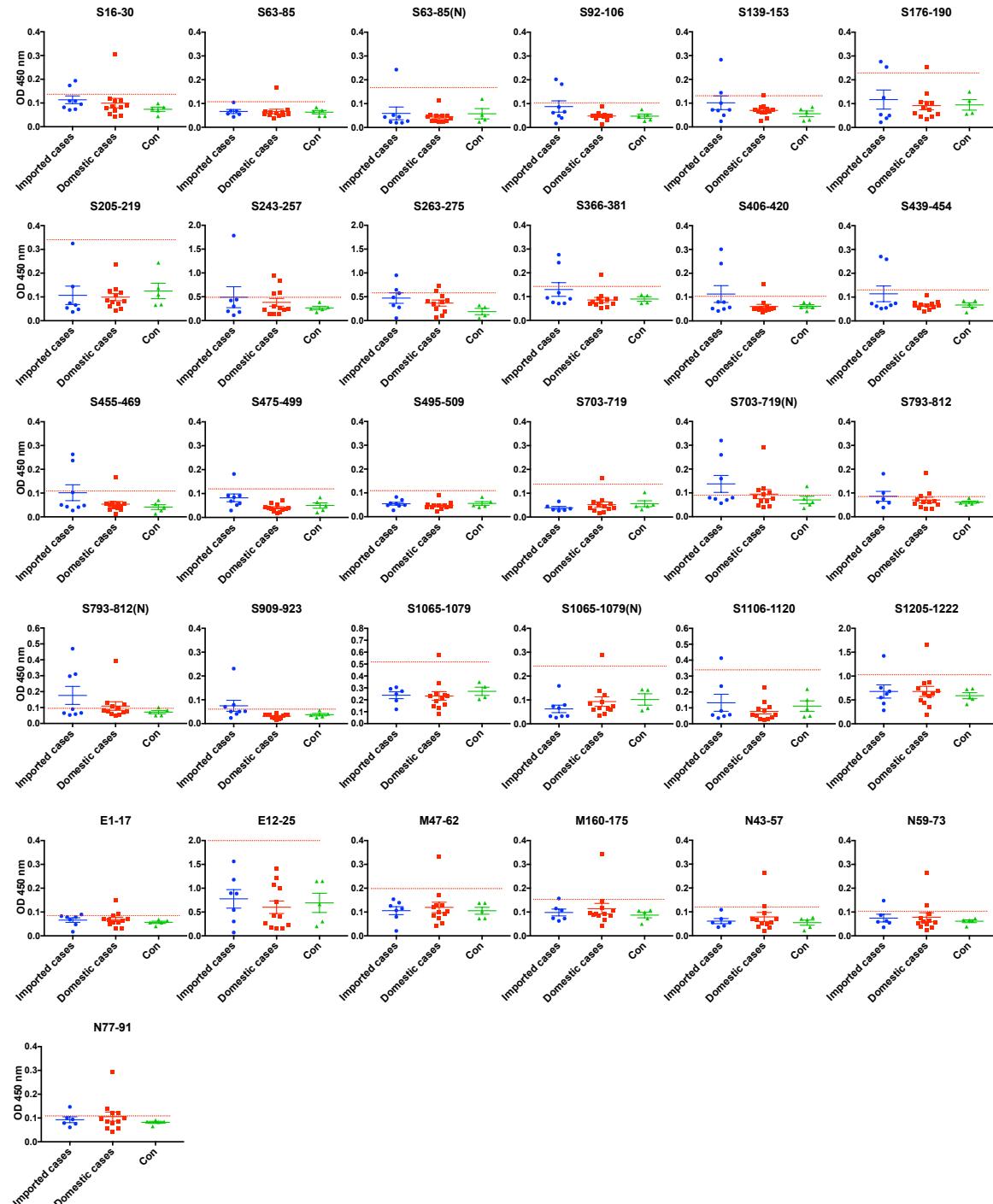


Figure S3. The non-immunodominant epitopes against S, E, M, N in early convalescent sera from COVID-19 patients. Related to Figure 2.

Table S1. Predicted epitope peptides. Related to Figure 1.

Location	Sequence	Homology
S16-30	VNLTTRTQLPPAYTN	33.30%
S63-85	TWFHAIHVGSGTNGTKRFDNPVLP	60.90%
S63-85(N)	TWFHAIHVGSGTNGTKRFDN(GlcNAc)PVLP	60.90%
S92-106	FASTEKSNIIRGWIF	100%
S139-153	PFLGVYYHKNNKSWM	26.70%
S176-190	LMDLEGKQGNFKNLR	73.30%
S205-219	SKHTPINLVRDLPQG	73.30%
S243-257	ALHRSYLTGPGDSSSG	13.30%
S263-275	AAYYVGYLQPRTF	92.30%
S366-381	SVLYNSASFSTFKCYG	93.70%
S406-420	EVRQIAPGQTGKIAD	93.30%
S439-454	NNLDSKVGGNNYNYLYR	62.50%
S455-469	LFRKSNLKPFERDIS	86.70%
S475-499	AGSTPCNGVEGFNCYFPLQSYGFQP	48%
S495-509	YGFQPTNGVGYQPYR	80%
S556-570	NKKFLPFQQFGRDIA	86.70%
S675-689	QTQTNSPERRARSVAS	40%
S703-719	NSVAYSNNNSIAIPTNFT	94.10%
S703-719(N)	NSVAYSNNNSIAIPTN(GlcNAc)FT	94.10%
S721-733	SVTTEILPVSMNK	100%
S793-812	PIKDFGGFNFSQILPDPSKP	85%
S793-812(N)	PIKDFGGFN(GlcNAc)FSQILPDPSKP	85%
S909-923	IGVTQNVLYENQKLI	93.30%
S1065-1079	VTYVPAQEKNFTTAP	100%
S1065-1079(N)	VTYVPAQEKN(GlcNAc)FTTAP	100%
S1106-1120	QRNFYEPQIITTDNT	93.30%
S1205-1222	KYEQYIKWPWYIWLGFI	100%
E1-17	MYSFVSEETGTLIVNSV	100%
E12-25	LIVNSVLLFLAFVV	100%
M47-62	YIIKLIFLWLLWPVTL	100%
M160-175	DIKDLPKETVATSR	100%
M183-197	ASQRVAGDSGFAAYS	86.70%
N43-57	QGLPNNTASWFTALT	100%
N59-73	HGKEDLKFPRGQQGVP	100%
N77-91	NSSPDDQIGYYRRAT	93.30%
N152-170	ANNAAIVLQLPQGTTLPKG	89.40%
N357-373	IDAYKTFPPTEPKDKK	100%

Table S2. The Hydrodynamic Diameter and PDI of HBc-S-P VLPs. Related to Figure 1.

Sample	S16-30	S63-85	S63-85(N)	S92-106	S139-153	S176-190	S205-219	S243-257	S263-275	S366-381	S406-420	S439-454	S455-469
PDI	0.08	0.07	0.18	0.19	0.04	0.06	0.05	0.01	0.04	0.01	0.01	0.01	0.06
Hydrodynamic Diameter(nm)	48.0±13.0	37.3±10.0	39.8±13.0	45.5±14.5	45.0±8.5	45.1±10.7	44.7±10.2	46.7±4.7	44.2±8.7	45.9±12.2	45.7±3.4	44.8±10.8	45.4±3.8
Sample	S475-499	S495-509	S556-570	S675-689	S703-719	S703-719(N)	S721-733	S793-812	S793-812(N)	S909-923	S1065-1079	S1065-1079(N)	S1106-1120
PDI	0.02	0.21	0.04	0.03	0.10	0.09	0.03	0.06	0.14	0.04	0.06	0.04	0.06
Hydrodynamic Diameter(nm)	44.8±9.1	45.5±10.8	46.6±8.8	45.6±8.3	34.9±11.2	35.4±11.0	45.2±7.9	37.9±9.5	41.6±15.3	44.8±9.0	37.2±8.8	37.9±9.5	48.0±12.1
Sample	S1205-1222	E1-17	E12-25	M47-62	M160-175	M183-197	N43-57	N59-73	N77-91	N152-170	N357-373	HBc-S	
PDI	0.06	0.12	0.08	0.15	0.01	0.02	0.10	0.14	0.01	0.04	0.04	0.06	
Hydrodynamic Diameter(nm)	45.1±11.4	35.4±13.1	34.1±9.3	48.0±10.5	37.1±3.7	44.3±6.1	39.4±12.6	39.3±7.4	44.7±4.7	43.8±6.0	36.7±7.4	36.7±5.2	

Table S3. Characteristics of epitopes. Related to Figure 1-3.

Epitopes	S protein		N protein	M protein	E protein
	non-glycosylation	Glycosylation			
Number	23	4	5	3	2
Conserved (>80% homology)	S92-106, S263-275, S366-381, S406-420, S455-469, S495-509, S556-570, S703-719, S721-733, S793-812, S909-923, S1065-1079, S1106-1120, S1205-1222	S703-719(N), S793-812(N), S1065-1079(N)	N43-57, N59-73, N77-91, N152-170, N357-373	M47-62, M160-175, M183-197	E12-25, E55-69
High immunogenicity (antibody titer>10 ⁴)	S16-30, S205-219, S455-469, S475-499, S556-570, S721-733, S793-812, S1106-1120, S1205-1222	S793-812(N)	N59-73, N353-373	M47-62	E12-25
Immunodominant					
Imported cases*	S675-689, S721-733	None	N152-170	None	None
Domestic cases*	S556-570	None	N357-373, N152-170	M183-197	None
Neutralizing					
D614 SARS-CoV-2	S16-30, S92-106, S139-153, S243-275, S406-420, S439-454, S455-469, S475-499, S556-570, S909-923	S793-812(N)	NT ^a	NT	NT
G614 SARS-CoV-2	S63-85, S92-106, S139-153, S406-420, S439-454, S455-469, S475-499, S495-509, S675-689, S703-719, S793-812, S909-923, S1065-1079, S1106-1120	S703-719(N), S793-812(N), S1065-1079(N)	NT	NT	NT

*Imported (Europe) cases infected SARS-CoV-2 in early April, 2020 and domestic (China) cases in early February, 2020

^aNT represents not tested

S Protein

SARS-CoV	YGECLGDINARDLICAQKFNGTHLPLTDDMIAAYTAALVSGTATAAGWTFGAGAALQI
SARS-CoV-2	YGDCCLGDIARADLICAQKFNGTHLPLTDEMIAQYTSALLAGTITSGWTFGAGAALQI
RaTG13	YGDCCLGDIARADLICAQKFNGTHLPLTDEMIQYTSALLAGTITSGWTFGAGAALQI *****:*****:*****:*****:*****:*****:*****:*****:*****:*****
SARS-CoV	PFAMQMAYRFNGIGVTQNVLVYENQKQIANQFNKAISQIQCESLTSTALGKLQDVVNQNA
SARS-CoV-2	PFAMQMAYRFNGIGVTQNVLVYENQKLIANQFNSAIGKIQDSSLSTASALGKLQDVVNQNA
RaTG13	PFAMQMAYRFNGIGVTQNVLVYENQKLIANQFNSAIGKIQDSSLSTASALGKLQDVVNQNA *****:*****:*****:*****:*****:*****:*****:*****:*****:*****
SARS-CoV	QALNTLVKQLSSNFGAISSVNLNDILSLRDLKVEAEVQIDRLITGRLQSLQTYVTQQLIRAA
SARS-CoV-2	QALNTLVKQLSSNFGAISSVNLNDILSLRDLKVEAEVQIDRLITGRLQSLQTYVTQQLIRAA
RaTG13	QALNTLVKQLSSNFGAISSVNLNDILSLRDLKVEAEVQIDRLITGRLQSLQTYVTQQLIRAA *****:*****:*****:*****:*****:*****:*****:*****:*****:*****
SARS-CoV	EIRASANLAATKMSCEVLGQSKRVDFCGKGYHLMSPQAHPGVFLHVTYVPSQERNFT
SARS-CoV-2	EIRASANLAATKMSCEVLGQSKRVDFCGKGYHLMSPQSAPHGTVFLHVTYVPAQEKNFT
RaTG13	EIRASANLAATKMSCEVLGQSKRVDFCGKGYHLMSPQSAPHGTVFLHVTYVPAQEKNFT *****:*****:*****:*****:*****:*****:*****:*****:*****:*****
SARS-CoV	TAPAICHEGKAYFPREGVFVFNGTSWIFQRNFFSPQIITTDNTFVSGNCDVVIGIINNT
SARS-CoV-2	TAPAICHDGKAHPREGVFVFNSNGTHWFVTQRNFYEPQIITTDNTFVSGNCDVVIGIVNNNT
RaTG13	TAPAICHDGKAHPREGVFVFNSNGTHWFVTQRNFYEPQIITTDNTFVSGSCDVVIGIVNNNT *****:*****:*****:*****:*****:*****:*****:*****:*****:*****
SARS-CoV	VYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASAVNVIQKEIDRNEVAKNLNES
SARS-CoV-2	VYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASAVNVIQKEIDRNEVAKNLNES
RaTG13	VYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASAVNVIQKEIDRNEVAKNLNES *****:*****:*****:*****:*****:*****:*****:*****:*****:*****
SARS-CoV	LIDLQELGKYEQYIKWPWVWLGFIAGLIAIVMVTILLCCMTSCSCLKGACSCGSCCKF
SARS-CoV-2	LIDLQELGKYEQYIKWPWVWLGFIAGLIAIVMVTIMLCMTSCSCLKGCCSCGSCCKF
RaTG13	LIDLQELGKYEQYIKWPWVWLGFIAGLIAIIIMVTIMLCMTSCSCLKGCCSCGSCCKF *****:*****:*****:*****:*****:*****:*****:*****:*****:*****
SARS-CoV	DEDDSEPVLKGVKLHYT
SARS-CoV-2	1255
RaTG13	DEDDSEPVLKGVKLHYT
	1273
	DEDDSEPVLKGVKLHYT
	1269
	*****:*****:*****

M Protein

SARS-CoV	-MADNGTITVEELKQLLEQWNLVLIGFLFLAWIMLLQFAYSNRNRFLYI ₁ IKLVFLWLLWPV
SARS-CoV-2	MADNGTITVEELKKLLEQWNLVLIGFLFLTWICLLQFAYANRNRFLYI ₁ IKLFLWLLWPV
RaTG13	-MADNGTITVEELKKLLEQWNLVLIGFLFLTWICLLQFAYANRNRFLYI ₁ IKLFLWLLWPV .*****:*****:*****:*****:*****:*****:*****:*****:*****:*****
SARS-CoV	TLACFVLAAVYRINWVTGGIAIAMACIVGLMWLSYFVASFRLFARTRSMSFNPETNILL
SARS-CoV-2	TLACFVLAAVYRINWITGGIAIAMACIVGLMWLSYFIASFRLFARTRSMSFNPETNILL
RaTG13	TLACFVLAAVYRINWITGGIAIAMACIVGLMWLSYFIASFRLFARTRSMSFNPETNILL .*****:*****:*****:*****:*****:*****:*****:*****:*****:*****
SARS-CoV	NVPLRGTIVTRPLMESELVIGAVIIRGHGLMAGHSILGRCDIKDLPKEITVATSRTLSYYK
SARS-CoV-2	NVPLHGTILTRPLLESELVIGAVILRGHLRIAGHHLGRCDIKDLPKEITVATSRTLSYYK
RaTG13	NVPLHGTILTRPLLESELVIGAVILRGHLRIAGHHLGRCDIKDLPKEITVATSRTLSYYK ****:****:****:*****:*****:*****:*****:*****:*****:*****:*****
SARS-CoV	LGASQRVGTDGSFAYNRYRIGNYKLNTDHAGSNDNIALLVQ
SARS-CoV-2	LGASQRVGDSGFAYNRYRIGNYKLNTDHSSSDNIALLVQ
RaTG13	LGASQRVGDSGFAYNRYRIGNYKLNTDHSSSDNIALLVQ *****:*****:*****:*****:*****:*****:*****:*****

E protein

SARS-CoV-2	MYSFVSEETGTLLIVNSVLLFLAFVV FLVTLAILTALRLCAYCCNIVNVSLVKPSFYVYS
RaTG13	MYSFVSEETGTLLIVNSVLLFLAFVV FLVTLAILTALRLCAYCCNIVNVSLVKPSFYVYS
SARS-CoV	MYSFVSEETGTLLIVNSVLLFLAFVV FLVTLAILTALRLCAYCCNIVNVSLVKPTVYVYS *****:****
SARS-CoV-2	RVKNLNSSR-VPDLLV
RaTG13	RVKNLNSSR-VPDLLV
SARS-CoV	RVKNLNSSEGVPDLLV *****

N Protein

SARS-CoV-2	MSDNGPQ-NQRNAPRITFGGPDSTGSQNNGERSGARSKQRRP QGLPNNTASWFTALTQH
RaTG13	MSDNGPQ-NQRNAPRITFGGPDSTGSQNNGERSGARPKQRRP QGLPNNTASWFTALTQH
SARS-CoV	MSDNGPQSNQRSAPRITFGGPTDSTDNNQNNGGRNGARPQKRRP QGLPNNTASWFTALTQH *****:*****
SARS-CoV-2	GKEDLKFRPGQGVPI NTNSPDDQIGYYRRAT RRIRGGDGKMKDLSPRWFYYLGTGPEA
RaTG13	GKEDLKFRPGQGVPI NTNSPDDQIGYYRRAT RRIRGGDGKMKDLSPRWFYYLGTGPEA
SARS-CoV	GKEELRFPRGQGVPI NTNSPDDQIGYYRRAT RRVRGGDGKMKELSPrWFYYLGTGPEA *****:*****
SARS-CoV-2	GLPYGANKDGIIWVATEGALNTPKDHIGHTRNP ANNAAIVLQLPQGTTLPKGFYAEGRGG
RaTG13	GLPYGANKDGIIWVATEGALNTPKDHIGHTRNP ANNAAIVLQLPQGTTLPKGFYAEGRGG
SARS-CoV	SLPYGANKEGIVWVATEGALNTPKDHIGHTRNP NNNAATVLQLPQGTTLPKGFYAEGRGG *****:*****
SARS-CoV-2	SQASSRSSSSRSRNSSRNSTPGSSRGTS <i>PARMAGNGDAALALLLDRLNQLESKMSGKGQ</i>
RaTG13	SQASSRSSSSRSRNSSRNSTPGSSRGTS <i>PARMAGNGDSAALALLLDRLNQLESKMSGKGQ</i>
SARS-CoV	SQASSRSSSSRSRGNSRNSTPGSSRGNS <i>PARMASGGGETALALLLDRLNQLESKVSGKGQ</i> *****:*****
SARS-CoV-2	QQQGQTVTKSAAEASKPRQKRTATKAYNVTQAFGRGGPEQTQGNFGDQELIRQGTDYK
RaTG13	QQQGQTVTKSAAEASKPRQKRTATQYNVTQAFGRGGPEQTQGNFGDQELIRQGTDYK
SARS-CoV	QQQGQTVTKSAAEASKPRQKRTATQYNVTQAFGRGGPEQTQGNFGDQDLIRQGTDYK *****:*****
SARS-CoV-2	HWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGAIKLDKDPNFKDQVILLNKH IDA
RaTG13	HWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGAIKLDKDPNFKDQVILLNKH IDA
SARS-CoV	HWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYHGAIKLDKDPQFKDNVILLNKH IDA *****:*****
SARS-CoV-2	YKTFFPTEPKKD KKKADETQALPQRQKKQQTVTLPAADLDDFSKQLQQSMSADSTQA
RaTG13	YKTFFPTEPKKD KKKADETQALPQRQKKQQTVTLPAADLDDFSKQLQQSMSADSTQA
SARS-CoV	YKTFFPTEPKKD KKKDEAQPLPQRQKKOPTVTLPAADMDDFSRQLQNSMSGASADST *****:*****
SARS-CoV-2	--
RaTG13	--
SARS-CoV	QA

Data S1. Homology of the predicted epitopes of S, M, E, N proteins among SARS-CoV-2, SARS-CoV and bat coronavirus RaTG13. Related to Figure 1.