

Supplemental Information

The immunodominant and neutralization

linear epitopes for SARS-CoV-2

Shuai Lu, Xi-xiu Xie, Lei Zhao, Bin Wang, Jie Zhu, Ting-rui Yang, Guang-wen Yang, Mei Ji, Cui-ping Lv, Jian Xue, Er-wei Dai, Xi-ming Fu, Dong-qun Liu, Lun Zhang, Sheng-jie Hou, Xiao-lin Yu, Yu-ling Wang, Hui-xia Gao, Xue-han Shi, Chang-wen Ke, Bi-xia Ke, Chun-guo Jiang, and Rui-tian Liu

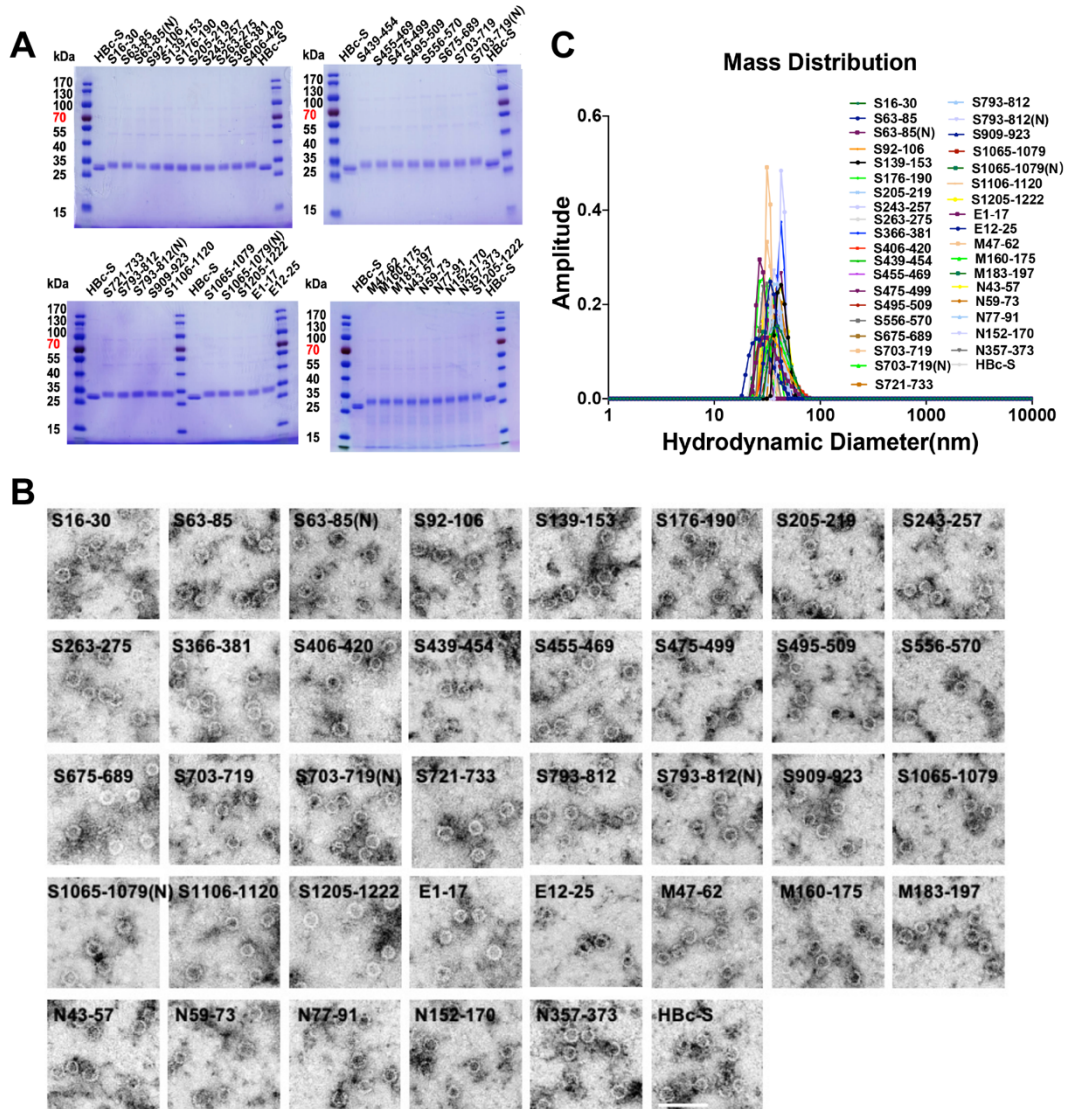


Figure S1. Preparation of HBC-S VLPs displayed with the epitopes. Related to Figure 1. (A) SDS-PAGE analysis of the conjugation of HBC-S with epitope peptides. (B) The morphology of HBC-S-P VLPs. HBC-S-P VLPs were imaged by Hitachi TEM at 80 KV at 40,000 \times magnification, the scale bar is 200 nm.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

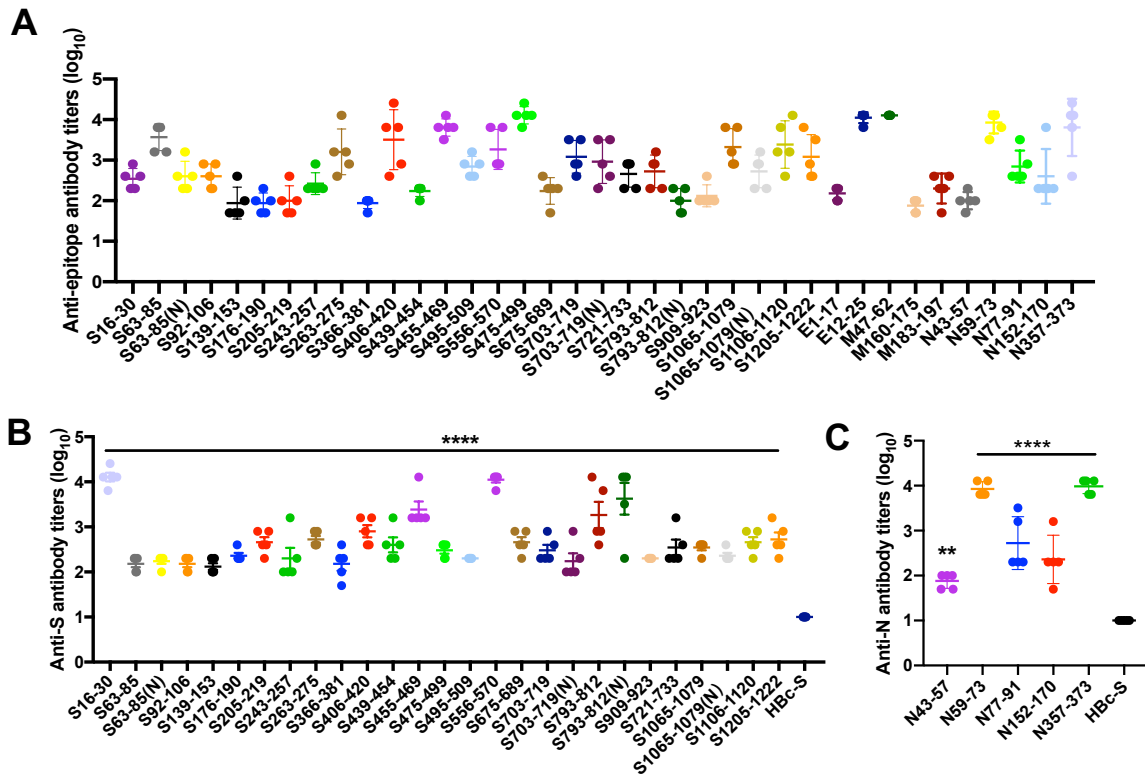


Figure S2. Epitope conjugated on HBC-S VLPs induced high antibody titers against epitope peptides and S, N proteins at 10 days after the second immunization. Related to Figure 1.

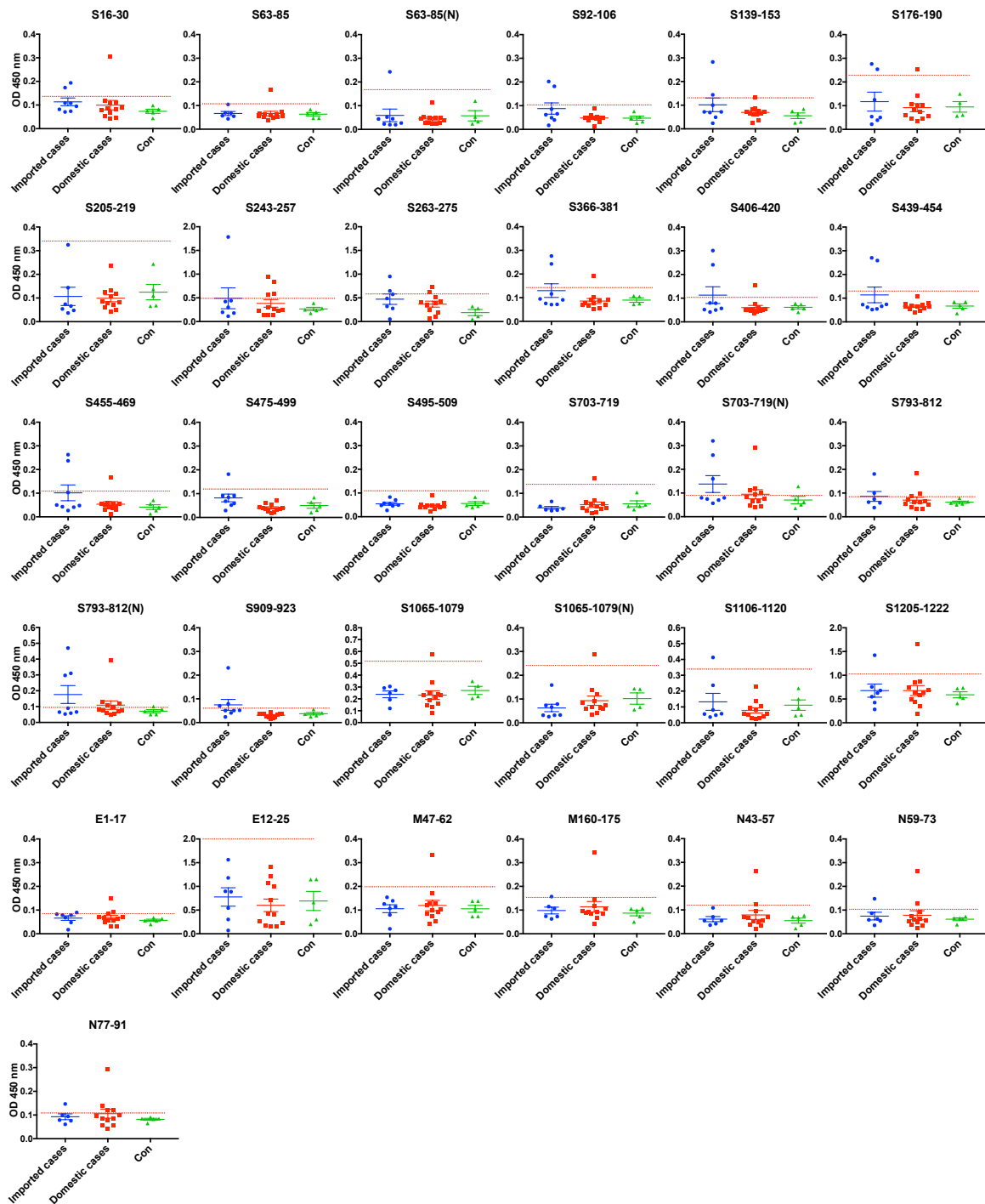


Figure S3. The non-immunodominant epitopes against S, E, M, N in early convalescent sera from COVID-19 patients. Related to Figure 2.

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

Location	Sequence	Homology
S16-30	VNLTTTRTQLPPAYTN	33.30%
S63-85	TWFHAIHVSGTNGTKRFDNPVLP	60.90%
S63-85(N)	TWFHAIHVSGTNGTKRFDN(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	ALHRSYLTPGDSSSG	13.30%
S263-275	AAYYVGYLQPRTF	92.30%
S366-381	SVLYNSASFSTFKCYG	93.70%
S406-420	EVRQIAPGQTGKIAD	93.30%
S439-454	NNLDSKVGGNYNLYR	62.50%
S455-469	LFRKSNLKPFERDIS	86.70%
S475-499	AGSTPCNGVEGFNCYFPLQSYGFQP	48%
S495-509	YGFQPTNGVGYQPYPYR	80%
S556-570	NKKFLPFQQFGRDIA	86.70%
S675-689	QTQTNSPRRARSVAS	40%
S703-719	NSVAYSNNIAIPTNFT	94.10%
S703-719(N)	NSVAYSNNIAIPTN(GlcNAc)FT	94.10%
S721-733	SVTTEILPVSMTK	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	QRNFYEPQIITDNT	93.30%
S1205-1222	KYEQYIKWPWYIWLGFIA	100%
E1-17	MYSFVSEETGTLIVNSV	100%
E12-25	LIVNSVLLFLAFVV	100%
M47-62	YIIKLIFLWLLWPVTL	100%
M160-175	DIKDLPKEITVATSRT	100%
M183-197	ASQRVAGDSGFAAYS	86.70%
N43-57	QGLPNNTASWFTALT	100%
N59-73	HGKEDLKFPRGQGV	100%
N77-91	NSSPDDQIGYRRAT	93.30%
N152-170	ANNAIVLQLPQGTTLPKG	89.40%
N357-373	IDAYKTFPPTPEPKDKK	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

E protein

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SARS-CoV-2 MYSFVSEETGTLIVNSVLLFLAFVVFLLVTLAILTALRLCAYCCNIVNVSLVKPSFYVYS
RaTG13 MYSFVSEETGTLIVNSVLLFLAFVVFLLVTLAILTALRLCAYCCNIVNVSLVKPSFYVYS
SARS-CoV MYSFVSEETGTLIVNSVLLFLAFVVFLLVTLAILTALRLCAYCCNIVNVSLVKPTVYVYS
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SARS-CoV-2 RVKNLNSSR-VPDLLV
RaTG13 RVKNLNSSR-VPDLLV
SARS-CoV RVKNLNSESEGVDPDLLV
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N Protein

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SARS-CoV-2 MSDNGPQ-NQRNAPRITFGGPSDSTGSNQNNGERSGARSKQRRPQGLPNNTASWFTALTQH
RaTG13 MSDNGPQ-NQRNAPRITFGGPSDSTGSNQNNGERSGARPKQRRPQGLPNNTASWFTALTQH
SARS-CoV MSDNGPQSNQRSAPRITFGGPTDSTDNNQNGGRNGARPKQRRPQGLPNNTASWFTALTQH
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SARS-CoV-2 GKEDLKFRPGQGVFINTNSSPDDQIGYRRATRRIRGGDGKMKDLSRWYFYLLGTGPEA
RaTG13 GKEDLKFRPGQGVFINTNSSPDDQIGYRRATRRIRGGDGKMKDLSRWYFYLLGTGPEA
SARS-CoV GKELRFRPGQGVFINTNSGPDDQIGYRRATRRVIRGGDGKMKELSPRWYFYLLGTGPEA
**.*:*****.*****:*****:*****:*****

SARS-CoV-2 GLPYGANKDGIWVATEGALNTPKDHIIGTRNPANNAIVLQLPQGTTLPKGFYAEGSRGG
RaTG13 GLPYGANKDGIWVATEGALNTPKDHIIGTRNPANNAIVLQLPQGTTLPKGFYAEGSRGG
SARS-CoV SLPYGANKGIVVWVATEGALNTPKDHIIGTRNPANNAATVQLPQGTTLPKGFYAEGSRGG
.*****:*.***** **.* *****

SARS-CoV-2 SQASSRSSRSRNSRNSTPGSSRGTS PARMAGNGGDAALALLLDRLNQLESKMSGKGQ
RaTG13 SQASSRSSRSRNSRNSTPGSSRGTS PARMAGNGS DAALALLLDRLNQLESKMSGKGQ
SARS-CoV SQASSRSSRSRNSRNSTPGSSRGNS PARMASGGGTALALLLDRLNQLESKMSGKGQ
*****.*****.*****.***:*****:*****

SARS-CoV-2 QQQGQTVTKKSAEASKKPRQKRTATKAYNVTQAFGRRGPEQTQGNFGDQELIRQGTDYK
RaTG13 QQQSQTVTKKSAEASKKPRQKRTATKQYNVTQAFGRRGPEQTQGNFGDQELIRQGTDYK
SARS-CoV QQQGQTVTKKSAEASKKPRQKRTATKQYNVTQAFGRRGPEQTQGNFGDQDLIRQGTDYK
**.* *****

SARS-CoV-2 HWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKHIDA
RaTG13 HWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKHIDA
SARS-CoV HWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYHGAIKLDDKDPQFKDNVILLNKHIDA
*****:*****:*****

SARS-CoV-2 YKTFPPTPEPKKDKKKADETTQALPQRQKQQTVTLLPAADLDFSKQLQQSMSSADSTQA
RaTG13 YKTFPPTPEPKKDKKKADETTQALPQRQKQQTVTLLPAADLDFSKQLQQSMSSADSTQA
SARS-CoV YKTFPPTPEPKKDKKKTDEAQPLPQRQKQPTVTLLPAADMDDFSRQLQNSMSGASADST
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SARS-CoV-2 --
RaTG13 --
SARS-CoV QA
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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.