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Supplemental information

Rational identification of potent and broad sarbecovirus-neutralizing antibody cocktails from SARS convalescents

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Supplemental Information

Figure S1 | FACS strategy to isolate cross-reactive memory B cells from SARS-CoV-2-vaccinated SARS convalescent plasma.

Related to Figure 1.

Target of each step and percentage of cells are labeled in each panel.

Figure S2 | Workflow for the cryo-EM 3D reconstruction.

Related to Figure 3.

(A-C) Cryo-EM data collection and processing workflow for the reconstruction of the structures of (A) BD55-3546/Delta S6P complex; (B) BD55-4637/BA.1 S6P complex; (C) SA55/SA58/BA.1 S6P complex.

Figure S3 | Structures of Group E1 and F3 bsNAbs in complex of RBD or spike.

Related to Figure 3.

(A) Interactions between BD55-3546 and SARS-CoV-2 Delta RBD. Residues on mAbs are colored and residues on RBDs are labeled with black text.

(B) Interactions between BD55-5549 and SARS-CoV-2 BA.1 RBD.

(C) Interactions between BD55-4637 and SARS-CoV-2 BA.1 RBD.

(D) Cryo-EM structure of SA55+SA58 Fab in complex of BA.1 S6P. SA55 binds "up" RBD only, while SA58 bind both "up" and "down" RBD.

(E) SPR sensorgrams for the competition assay of SA55 and SA58 on WT or BA.5 RBD. RBDs are captured on the sensor chip and the concentration of each mAb is 200 nM. Representative results of two replicates are shown.

Figure S4 | Psuedovirus neutralization of SA55 and SA58 against Omicron variants with single substitutions.

Related to Figure 4.

(A) IC50 fold changes against constructed pseudoviruses of SARS-CoV-2 Omicron variants with selected single substitutions compared to that against BA.2 were shown.

(B) Percentage of mutations (amino acids different from that in SARS-CoV-2 ancestral strain or Omicron BA.1) on sites whose mutations may affect the neutralization of SA55 or SA58 during the pandemic.

(C) Percentage of specific mutations on the selected residues with a relatively high percentage or may affect the neutralization of SA55 or SA58 during the pandemic.

Figure S5 | Detailed design and body weight changes of each group of mice

Related to Figure 5.

(A) Detailed treatment of each group of mice.

(B) Percentage of changes in body weight compared to the weight of each mouse before the experiment. Error bars indicate mean±s.d.

Table S1. Related to Figure 1. Summarized information of SARS-CoV-2-vaccinated SARS-CoV-1 convalescents.

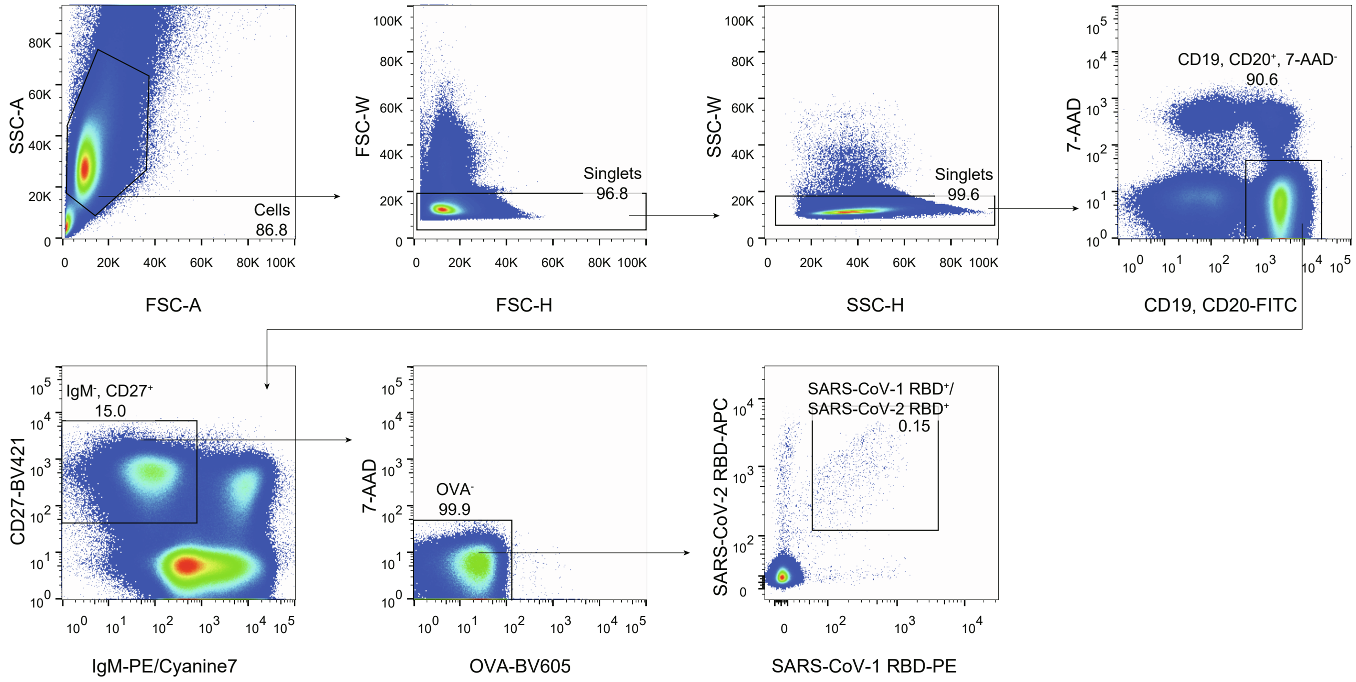
Table S2. Related to Figure 1. Neutralizing activities and binding capabilities against sarbecoviruses of 314 broad sarbecovirus neutralizing antibodies.

Table S3. Related to Figure 1. SHM counts and rates in nucleotides and amino acids, in addition to the germline V-J gene combinition of the 12 candidates from 3 epitope groups.

Table S4. Related to Figure 3. Crystal data collection, refinement and validation statistics.

Table S5. Related to Figure 3. Cryo-EM data collection, refinement and validation statistics.

Figure S1



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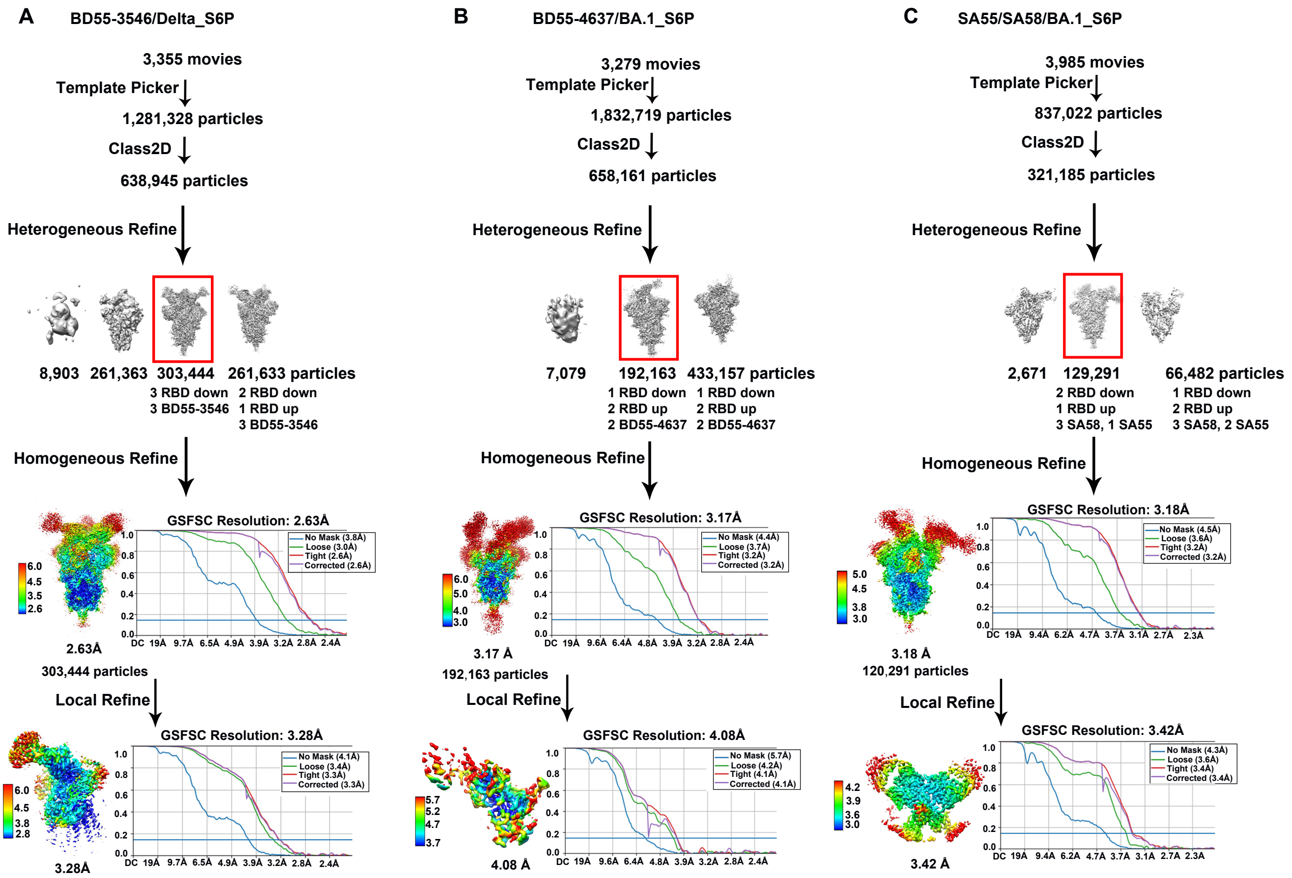

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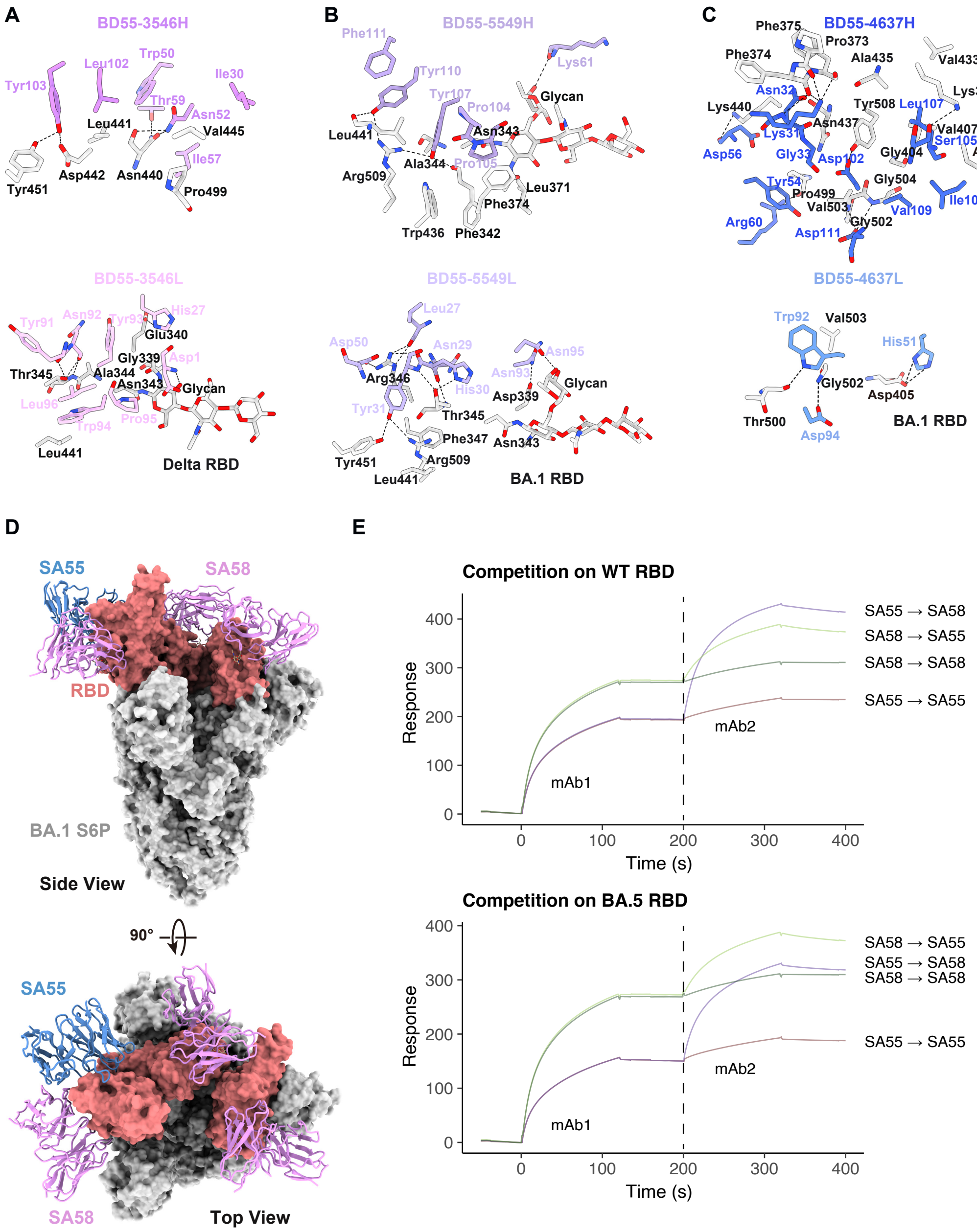

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Figure S4

A **Pseudovirus neutralizing IC50 Fold Change (Compared to IC50 against BA.2)** <10 >10 >100

	BA.2+ D339Y	BA.2+ E340K	BA.2+ E340D	BA.2+ T345N	BA.2+ R346Q	BA.2+ R346T	BA.2+ K356R	BA.2+ K356T	BA.2+ K440E	BA.2+ K444N	BA.2.12.1 +K444N	BA.4+ K444N	BA.2+ K444R	BA.2+ K444E	BA.4+ K444E	BA.4+ K444T	BA.4+ V445E	BA.4+ V445S	BA.2+ V503E	BA.2+ G504D	BA.2+ G504S	BA.2+ Y508H
SA55	0.5	0.6	0.3	0.4	0.6	0.7	0.4	0.6	313	1.6	1.1	0.6	0.3	1.3	1.5	0.4	0.7	0.5	>500	>500	16.2	3.7
SA58	5.9	>500	183	10.4	22.7	38.9	0.1	2.3	0.3	5.3	4.2	3.3	0.6	>500	>500	1.0	1.1	0.2	0.4	0.5	0.5	0.3
SA55+SA58	0.7	1.2	0.6	0.9	0.9	0.9	0.3	0.5	0.5	0.8	1.1	0.7	0.3	2.6	3.3	0.5	0.5	0.3	1.0	1.6	1.1	0.7

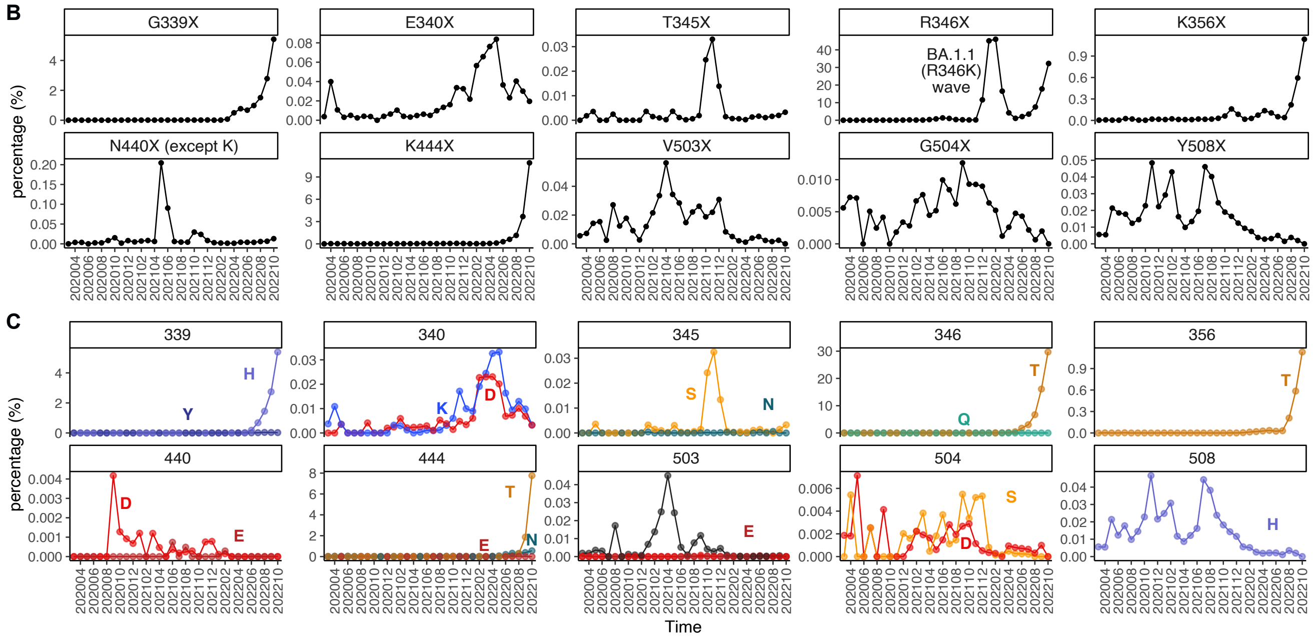

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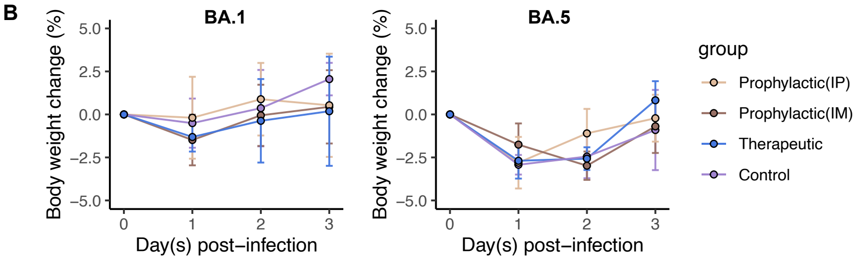
Figure S5

A

Group	Design	Drug	Drug Delivery	Dosage	Number of mice	Strain
1	Therapeutic	SA55+SA58	IP	20mg/kg	5	BA.1
2	Prophylactic	SA55+SA58	IP		5	BA.1
3	Prophylactic	SA55+SA58	IM		5	BA.1
4	Control	PBS	IP	/	5	BA.1
5	Therapeutic	SA55+SA58	IP	20mg/kg	5	BA.5
6	Prophylactic	SA55+SA58	IP		5	BA.5
7	Prophylactic	SA55+SA58	IM		5	BA.5
8	Control	PBS	IP	/	5	BA.5



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