Cell Reports Medicine, Volume *5*

Supplemental information

Neutralization of SARS-CoV-2 BA.2.86 and JN.1 by CF501 adjuvant-enhanced immune responses targeting the conserved epitopes in ancestral RBD

Zezhong Liu, Jie Zhou, Weijie Wang, Guangxu Zhang, Lixiao Xing, Keqiang Zhang, Yuanzhou Wang, Wei Xu, Qian Wang, Qiuhong Man, Qiao Wang, Tianlei Ying, Yun Zhu, Shibo Jiang, and Lu Lu

Supplemental information

CF501 adjuvant enhances the immune response targeting the conserved epitopes in wild-type SARS-CoV-2 RBD-Fc to elicit durable broadly neutralizing antibodies against BA.2.86, JN.1 and other Omicron subvariants in non-human primates

Zezhong Liu[1,#,*], Jie Zhou[1,#], Weijie Wang[1], Guangxu Zhang[1], Lixiao Xing[1], Keqiang Zhang[1], Yuanzhou Wang[1], Wei Xu[1], Qian Wang[1], Qiuhong Man[3], Qiao Wang[1], Tianlei Ying[1], Yun Zhu[2], Shibo Jiang[1,*], Lu Lu[1,4,*]

This Word document includes: Figures S1 – S4

Supplementary Figures

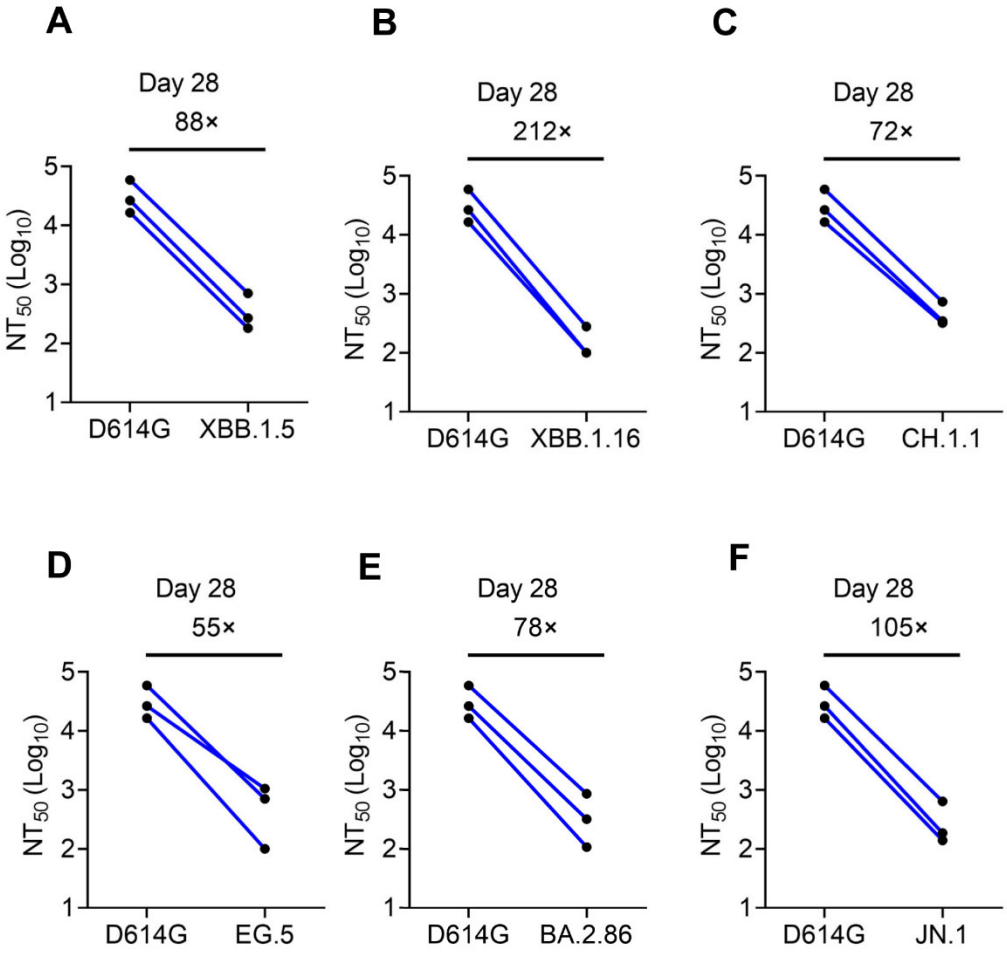

Figure S1. The fold decrease in neutralizing antibodies against the Omicron variants compared to the D614G strain. Related to Figure 3.

(A-F) Fold changes in NT50 against XBB.1.5 **(A)**, XBB.1.16 **(B)**, CH.1.1 **(C)**, EG.5 **(D)**, BA.2.86 **(E)**, and JN.1 **(F)** compared with D614G for sera collected at Day 28 post-1st immunization.

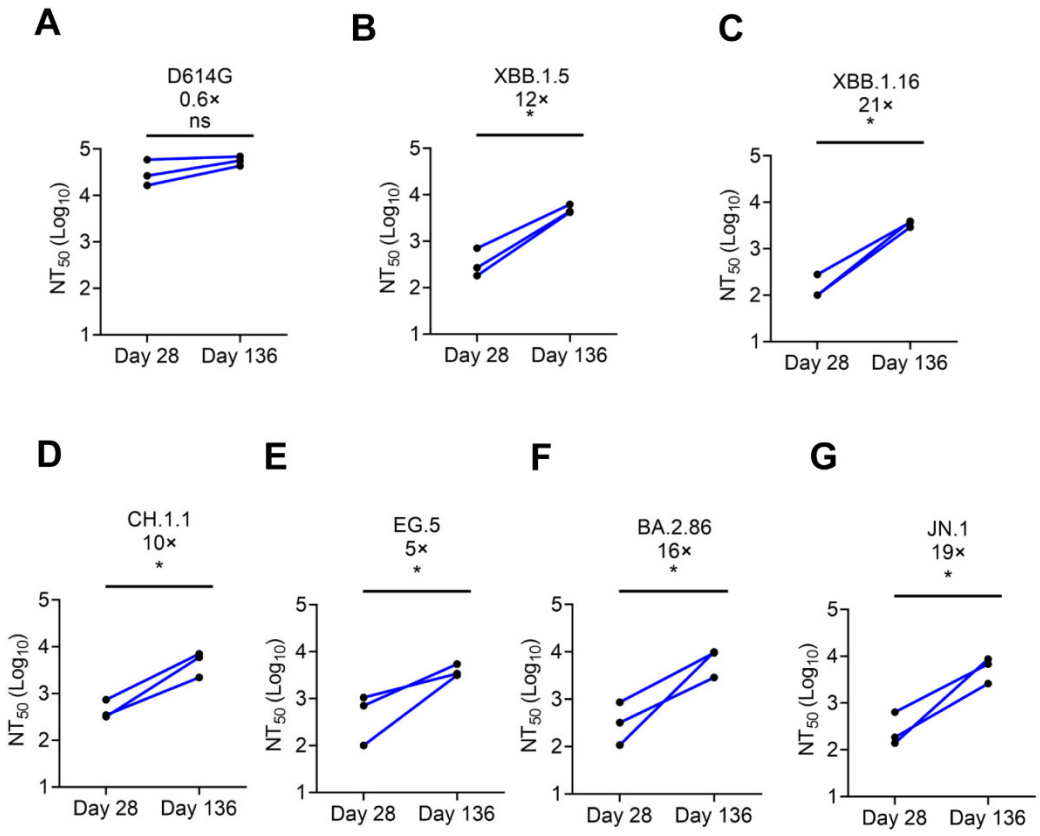

Figure S2. The fold increase in neutralizing antibodies against multiple Omicron variants at day 136 post-1st immunization compared to day 28 post-1st immunization. Related to Figure 3.

(A-G) Comparison of the neutralizing antibody titers in rhesus macaques sera against D614G **(A)**, XBB.1.5 **(B)**, XBB.1.16 **(C)**, CH.1.1 **(D)**, EG.5 **(E)**, BA.2.86 **(F)** and JN.1 **(G)** after two (Day 28) and three (Day 136) immunizations of CF501/RBD-Fc.

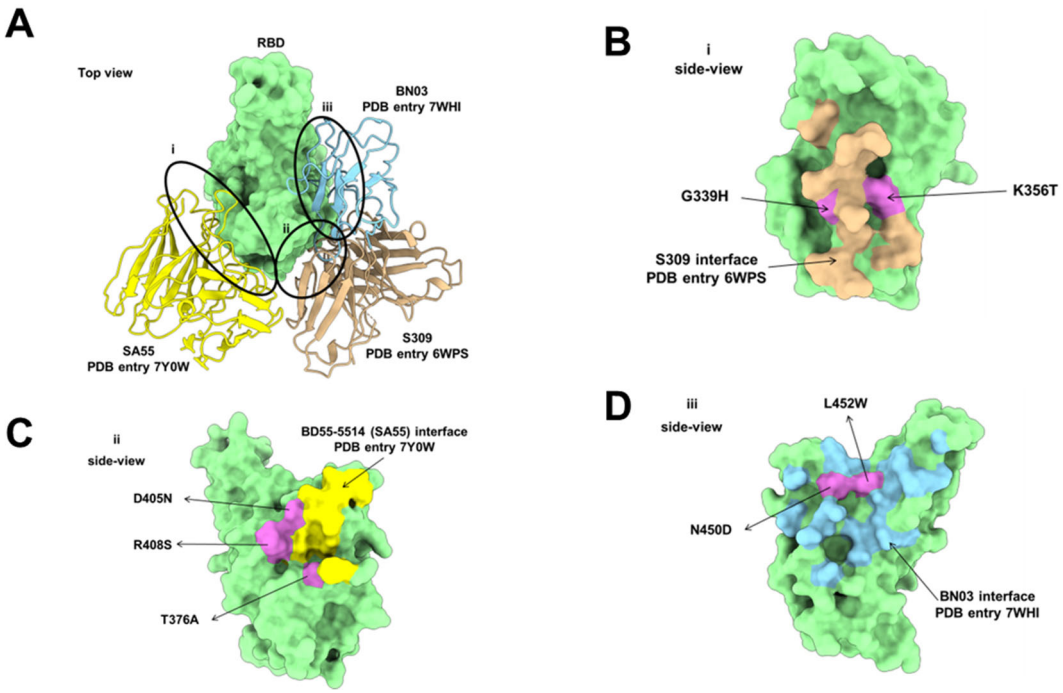

Figure S3. Analysis of the specific epitope locations on the RBD for broad-spectrum neutralizing antibodies SA55, BN03, and S309. **Related to Figure 4.**

(A) The complex structure of RBD (surface representation, colored in pale green) bound with S309 (PDB entry 6WPS, cartoon representation, colored in burly wood), BN03 (PDB entry 7WHI, cartoon representation, colored in sky blue) and SA55 (PDB entry 7Y0W, cartoon representation, colored yellow). The antibody epitopes are indicated by black circles and represented by the buried interface residues on RBD that interact with the antibodies. These residues were determined using the default parameters of the interface command in ChimeraX.

(B) BA.2.86 unique mutation sites (G339H and K356T, colored in orchid) within the S309 epitope (colored in burly wood, including residue numbers 334, 335, 337, 339, 340, 343, 344, 345, 346, 356, 357, 359, and 441).

(C) BA.2.86 unique mutation sites (D405, R408S and T376A, colored in orchid) within the SA55 epitope (colored in yellow, including residue numbers 374, 376, 404, 405, 407, 408, 499, 500, 501, 502, 503, 504, 505, and 508).

(D) BA.2.86 unique mutation sites (L452W and N450D, colored in orchid) within the BN03 epitope (colored in sky blue, including residue numbers 340, 345, 346, 348, 351, 352, 354, 441, 444, 449, 450, 452, 466, 470, 471, 490, 492 and 494).

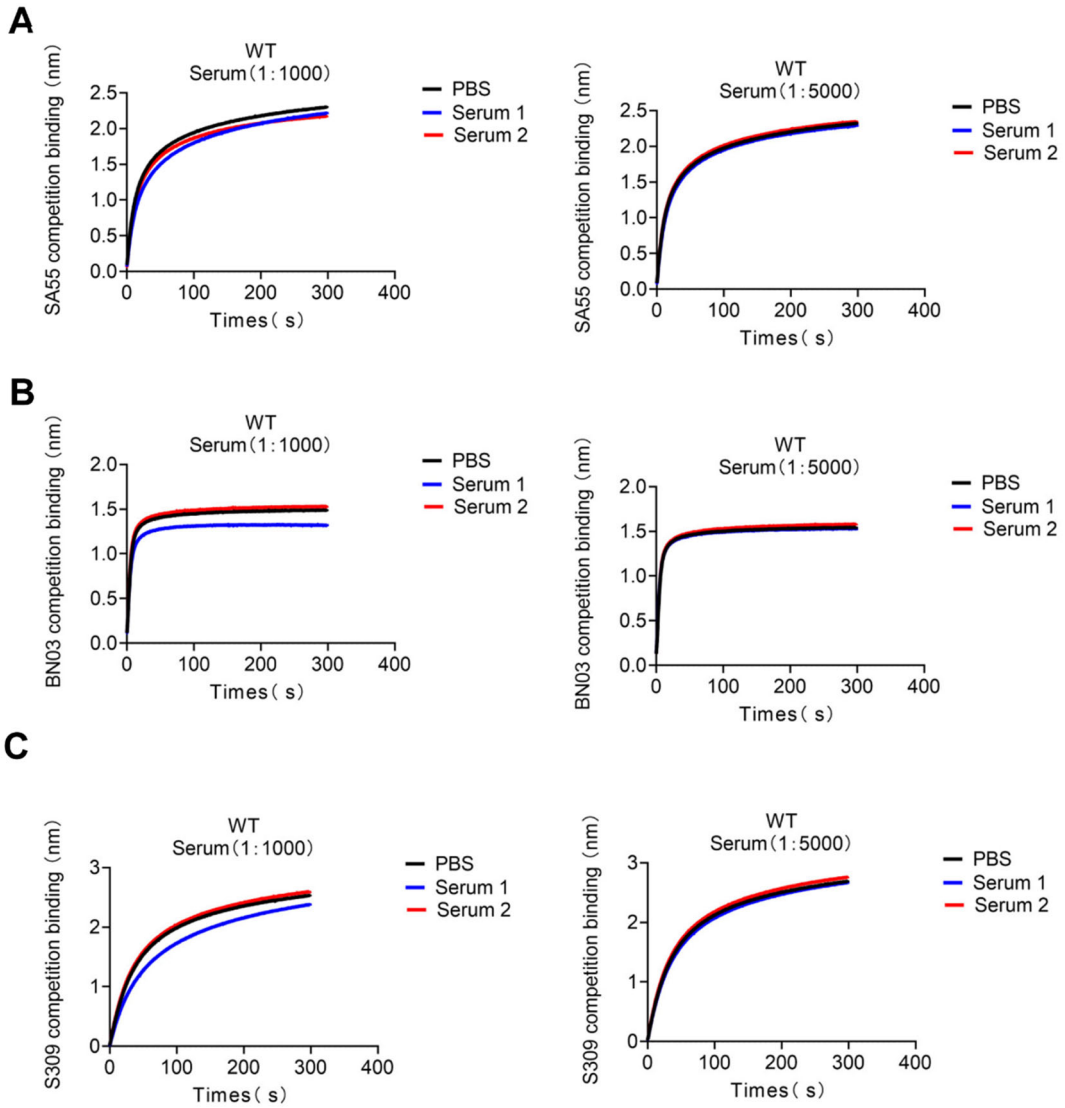

Figure S4. Detection of serum from individuals infected with SARS-CoV-2 for their ability to inhibit the binding of SA55, BN03, and S309 to the RBD. Related to Figure 4.

(A-C) Sera from individuals infected with BA.5/BF.7 to block binding of S309 **(A)**, BN03 **(B)** and SA55 **(C)** with RBD. Sera 1 and 2 represent the serum of individuals who were previously infected with BA.5/BF.7. PBS represents the control serum of rhesus macaques treated with PBS.