**Virologica Sinica**

**Supplementary Data**

**Mutational escape prevention by combination of four neutralizing antibodies that target RBD conserved regions and stem helix**

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**Supplementary Fig. S1**. The combinations of two/three/four antibodies did not show significantly enhanced neutralization IC50 values as compared to the individual antibodies in Fig. 2A. Neutralization ratios were calculated as described in Fig. 2A (mean ± standard deviation, n = 2). IC50 values were calculated by four parameter nonlinear regression fitting.



**Supplementary Fig. S2.** Projection of mutated residues in the escaped viral populations of single or paired antibodies. **A–D** Mutated residues on RBD or stem helix that occurred in the escaped viral populations of 2G1, REGN-10987, S2X259, or CV3-25, respectively. **E–H** Mutated residues on RBD or entire spike protein that occurred in the escaped viral populations of 2G1+CV3-25, REGN-10987+S2X259, REGN-10987+CV3-25, or S2X259+CV3-25, respectively. All the above mutated residues are colored in red. The PDB ID of mAbs 2G1, REGN-10987, S2X259, and CV3-25 were referred as indicated in the legend of Fig. 1. The mAbs and proteins were colored as the same as those in Fig. 1.



**Supplementary Fig. S3.** The stem helix region is highly conserved among currently circulating Omicron sublineages. Mutations carried by Omicron sublineages are indicated by red boxes. These mutations all occurred within residues 19–981 aa, with no mutation presented in stem helix region (residues 1140–1165 aa).