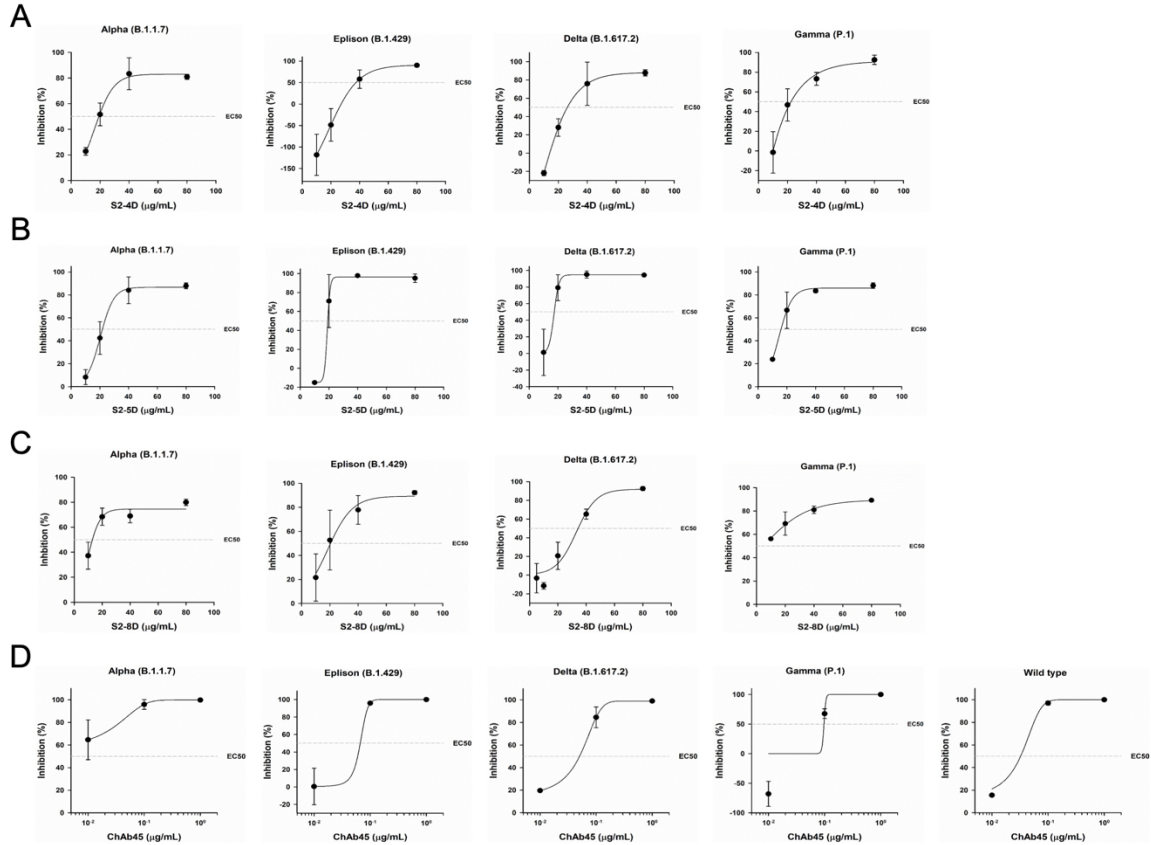
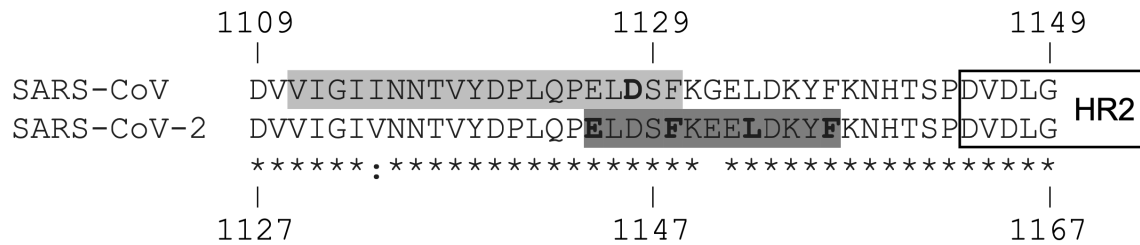


**FIG S1 Analysis of antigenic determinants of mAbs S2-4D, S2-5D, and S2-8D.** The ability of the control anti-His tag antibody (A), S2-4D (B), S2-5D (C), or S2-8D (D) to recognize sfGFP-S(1042-1167) mutants with a series of individual alanine substitution at residues 1137-1164 were determined by WB analysis using 2  $\mu$ g of bacterial cell lysates on the SDS-PAGE.



**FIG S2 Determination of the EC50 values of S2-4D, S2-5D, S2-8D, and RBD-chAb-**

**45 against different SARS-CoV-2 variants. (A-D) For determination of the EC50 values of S2-4D, S2-5D, S2-8D, and RBD-chAb-45 against SARS-CoV-2 wild type, Alpha (B.1.1.7), Epsilon (B.1.429), Delta (B.1.617.2), and Gamma (P.1) variants, a series of diluted S2-4D, S2-5D, S2-8D (80, 40, 20, and 10  $\mu\text{g/mL}$ ), and RBD-chAb-45 solutions (1, 0.1, and 0.01  $\mu\text{g/mL}$ ) were utilized in the plaque reduction assay. Data are presented as means  $\pm$  SD of three biological replicates ( $n = 3$ ), and further graphed by linear regression.**



**FIG S3** Sequence alignment of the binding epitopes of mAbs 1A9, S2-4D, S2-5D, S2-

**8D, and S2-4A in S proteins of SARS-CoV and SARS-CoV-2.** The amino acid residues

1109-1149 of SARS-CoV S protein (GenBank: AAR86775.1) and the corresponding amino

acid residues 1127-1167 of SARS-CoV-2 S protein (GenBank: BCN86353.1) were aligned.

The identical residues were marked with asterisks. The binding epitope of mAb 1A9 was

marked with a light gray background. The binding epitope of S2-4D, S2-5D, S2-8D, and

S2-4A was marked with a dark gray background. The residue D1128 in SARS-CoV S

protein and residues E1144, F1148, L1152, and F1156 in SARS-CoV-2 S protein were

noted in bold characters. The partial region of the predicted HR2 domain was labeled in a

square box.