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Supporting information for article:

The structure of the RBD–E77 Fab complex reveals neutralization and immune escape of SARS-CoV-2

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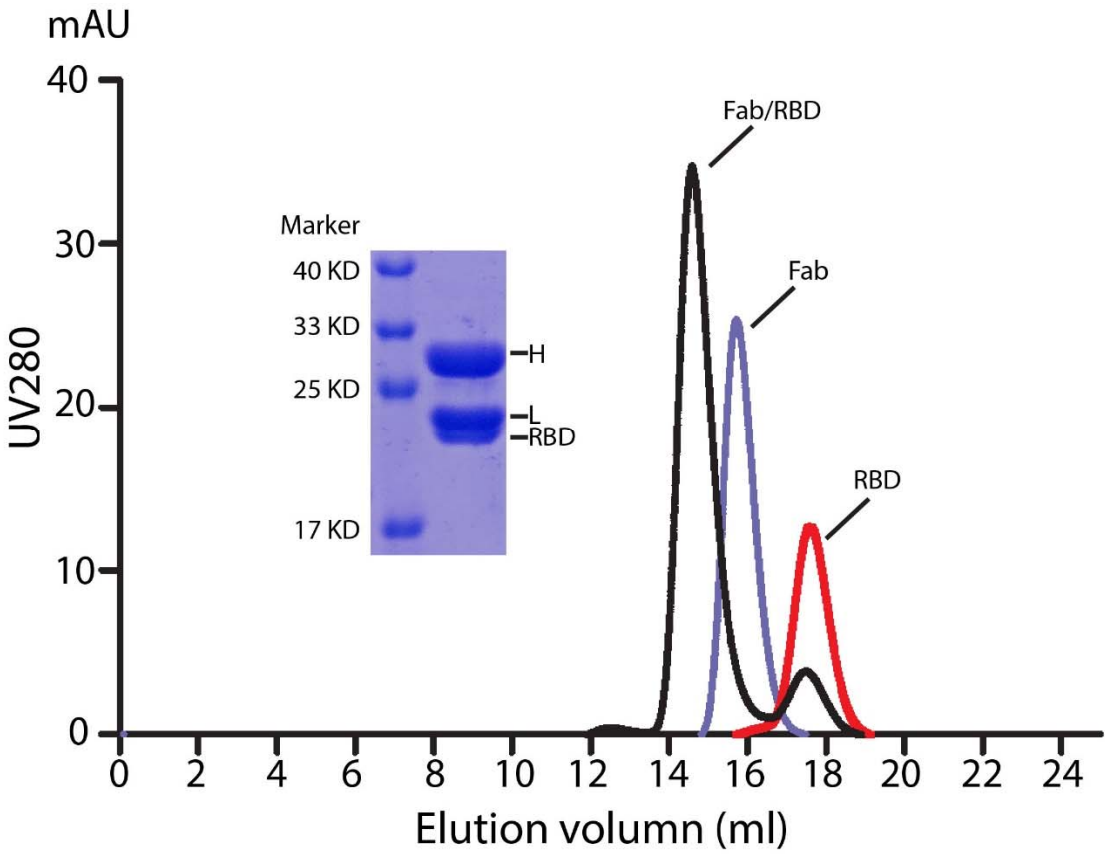

Figure S1 Size exclusion chromatography analysis of E77-Fab/RBD complex. Protein complex was resolved by SDS-PAGE and stained with Coomassie Blue R250. H and L denote Heavy chain (residues 1-239) and light chain respectively. Data are representative of three independent experiments.

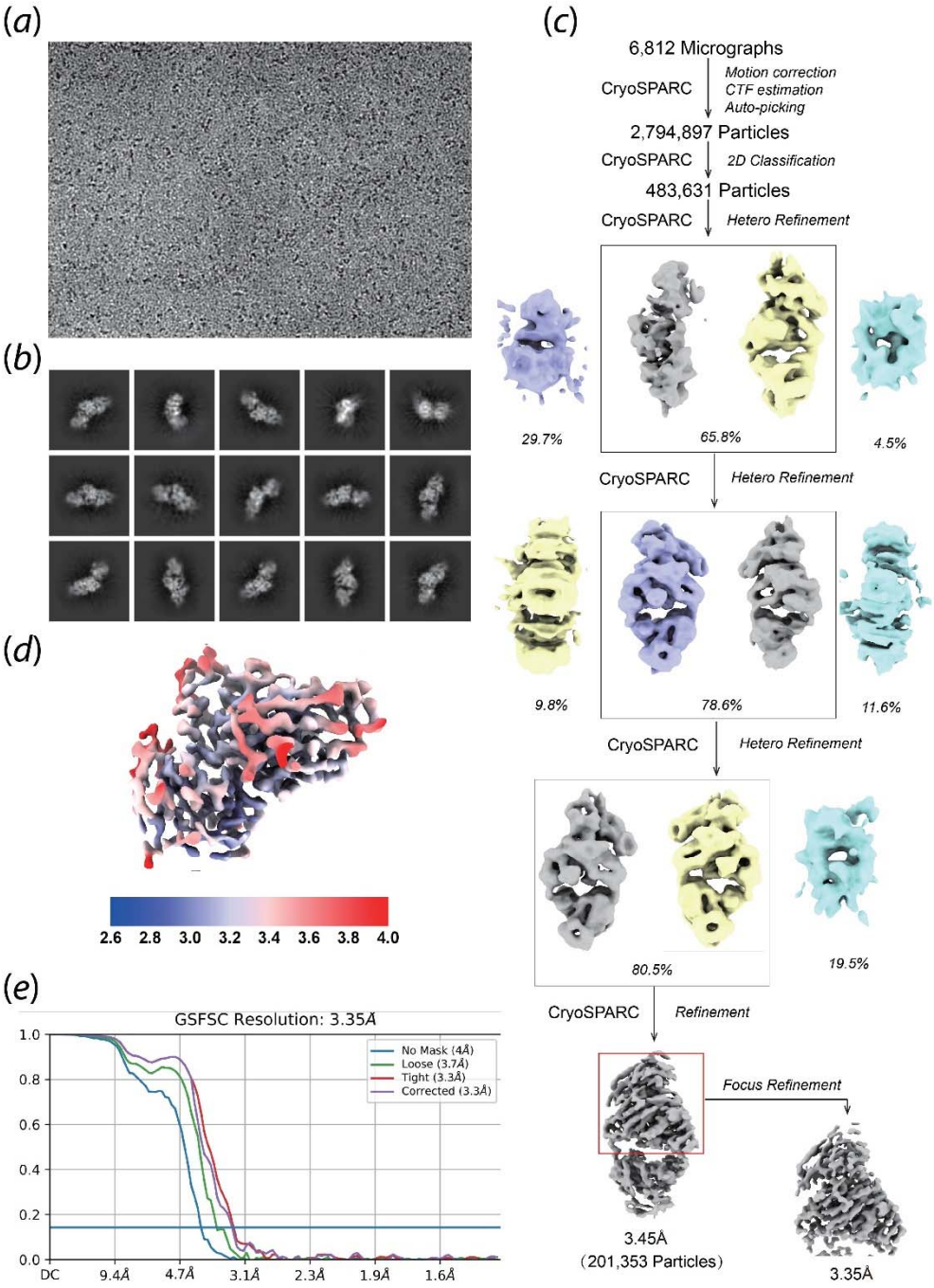

Figure S2 Cryo-EM analysis of RBD/E77-Fab complex. (*a*) A representative Cryo-EM micrograph of RBD/E77-Fab complex. Scale bar, 100 nm. (*b*) Gallery of 2D class average images of RBD/E77-Fab complex. (*c*) Flow chart of Cryo-EM data processing. (*d*) Local resolution distribution for the density map of RBD/E77-Fab complex. (*e*) The FSC curve for the reconstruction. The FSC 0.143 cut-off value is indicated by blue line.

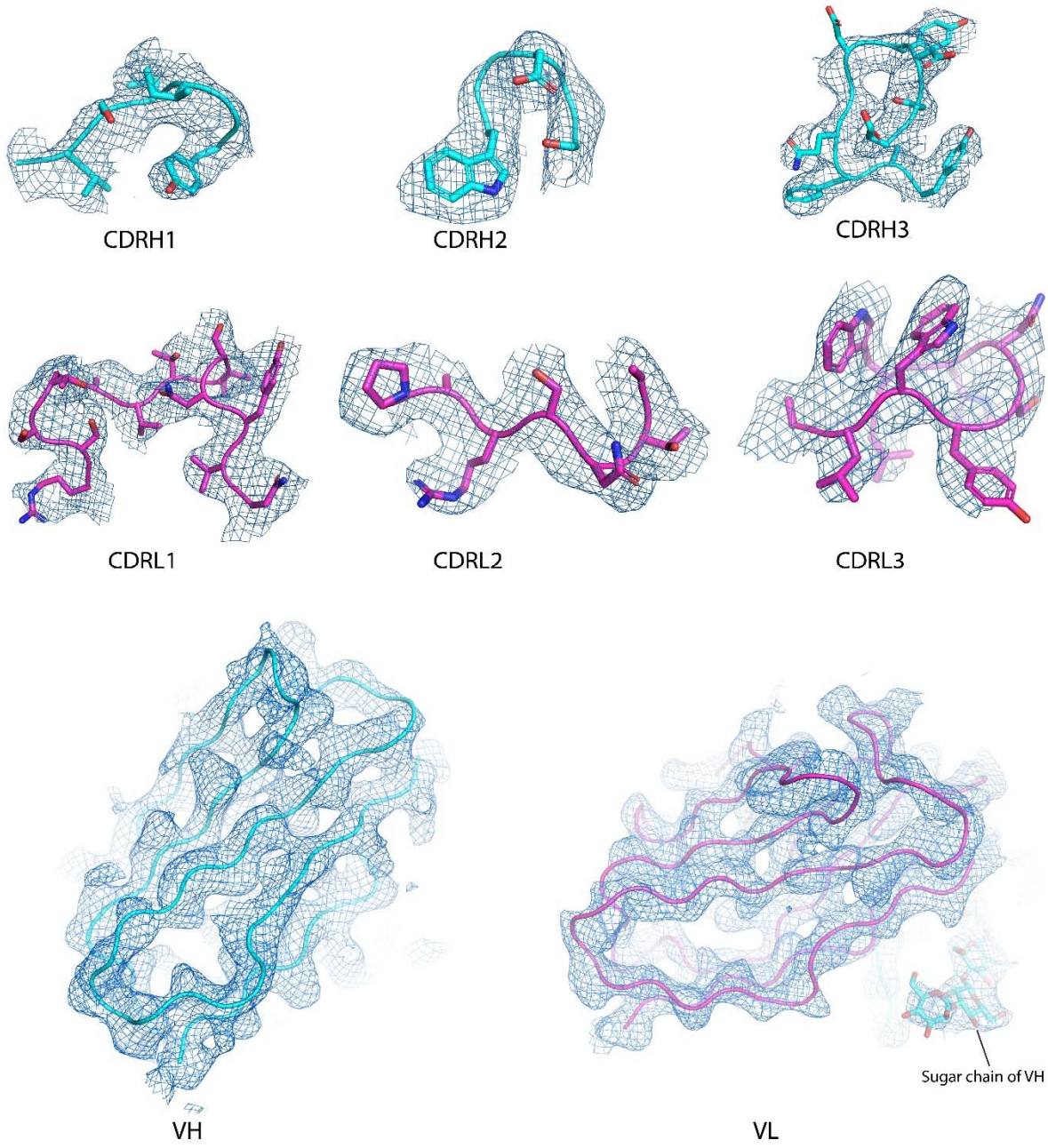

Figure S3 Sample density maps. Sample density maps from CDRs of RBD/E77-Fab complex.

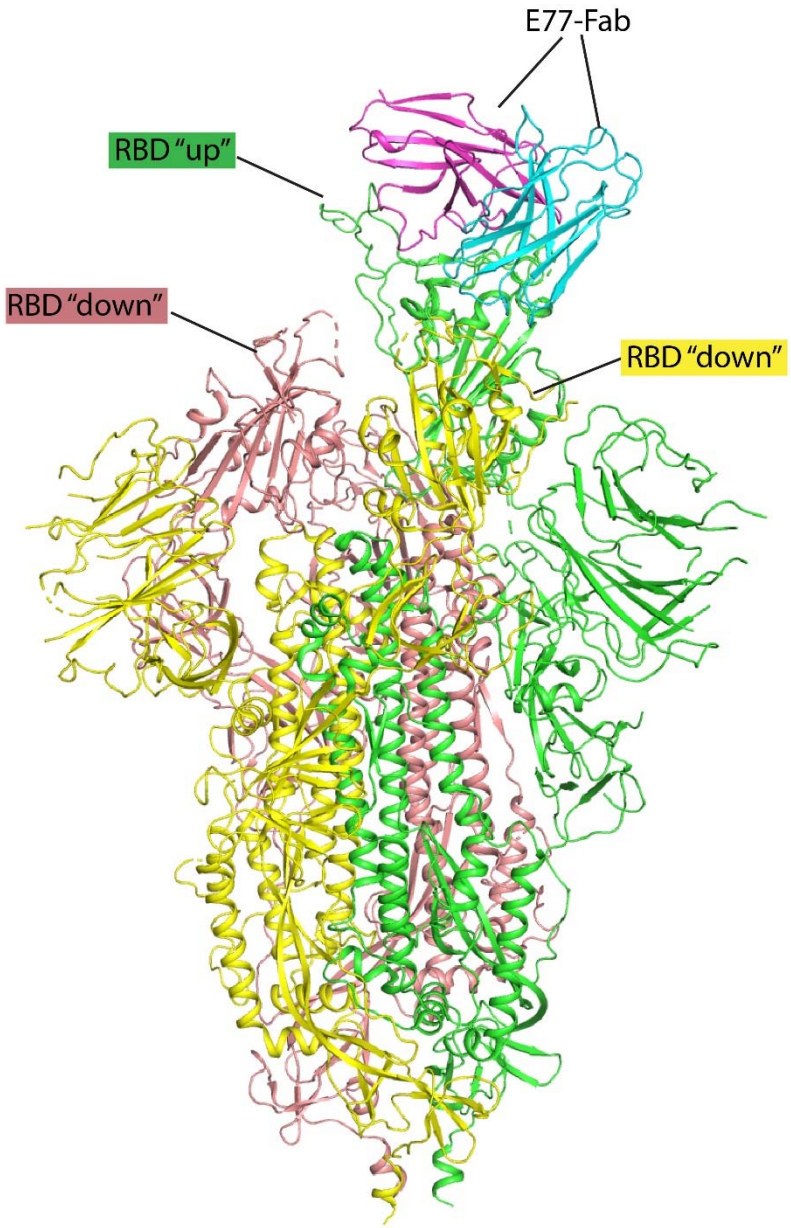

Figure S4 Modeling of interactions between E77-Fab and RBD with an "up" conformation in S trimer (PDB: 6VSB). The protomers of S trimer are shown in cartoon with green, yellow and brown colors, respectively. Heavy chain and light chain are shown in cartoon with cyan and purple colors, respectively. It clearly shows that only RBD with "up" conformation exposing the RBM region could engage E77 while RBD in "down" conformation burying its RBM is inaccessible for E77.

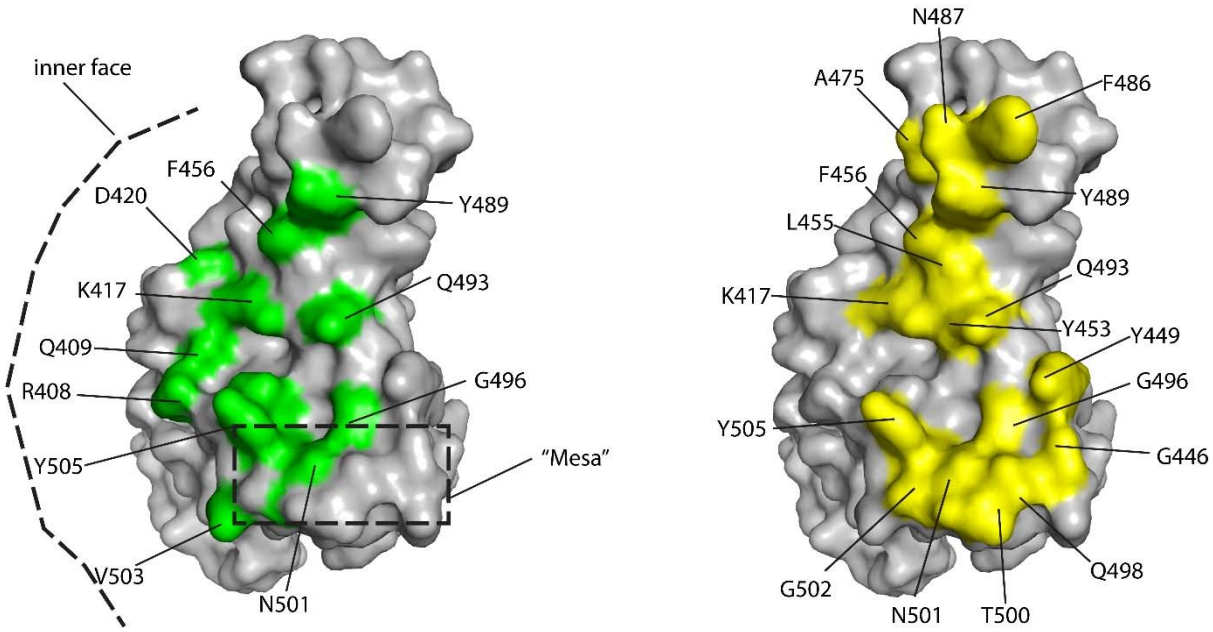

Figure S5 Footprint of E77 and hACE2 on the RBD. Left panel: the epitope of RBD for E77 is shown in green and related residues is labelled. Right panel: the epitope of RBD for hACE2 is shown in yellow and related residues is labelled.

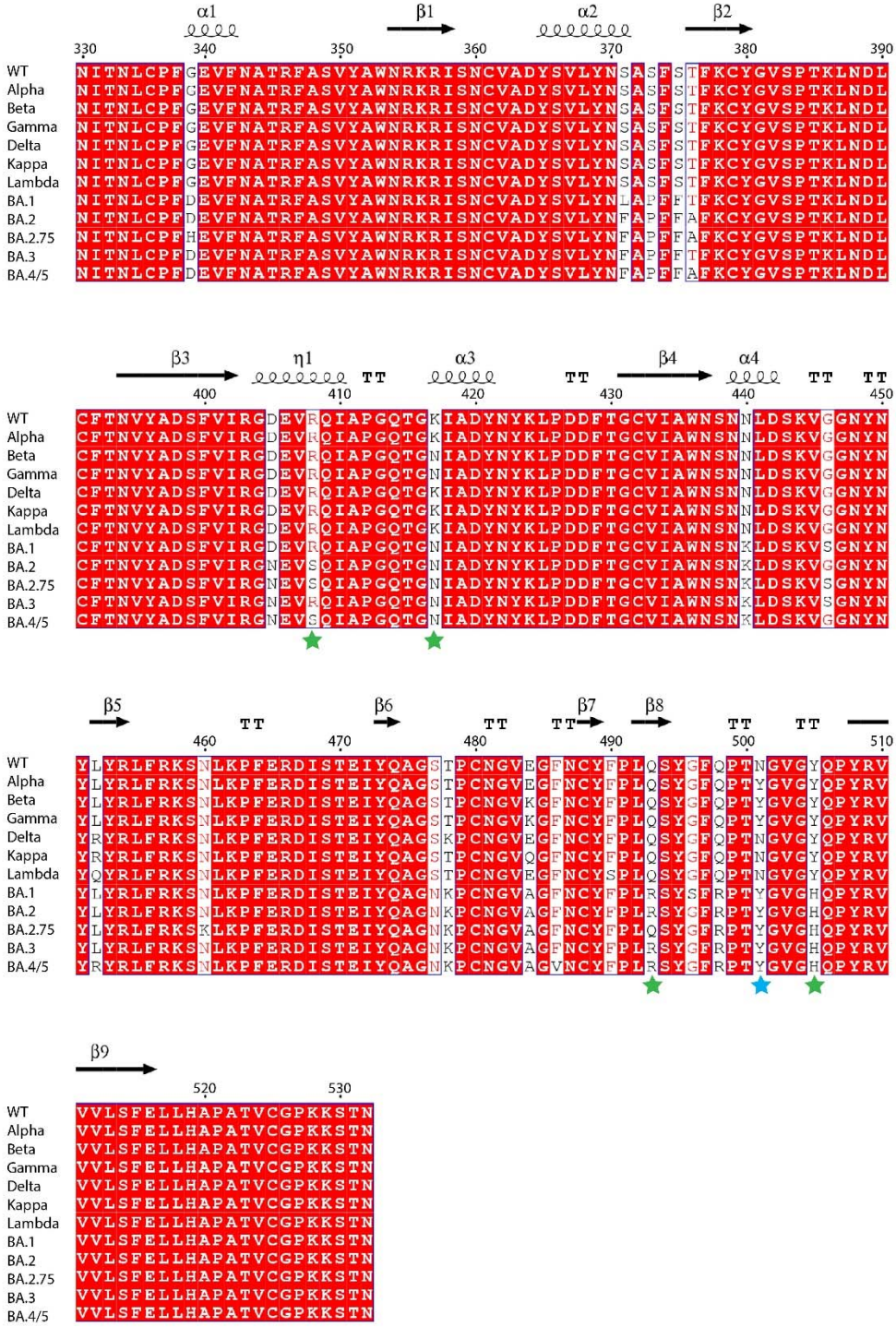

Figure S6 Sequence alignment of RBD from various SARS-CoV-2 variants. Secondary structure assignments based on the RBD structure are shown. The residues affecting the binding of E77 to RBD was denoted as green star and the residue 501 was denoted as cyan star.

Table S1 Mutations occurring in the RBD of SARS-CoV-2 variants

Mutations affecting the binding affinity are colored orange and N501Y is colored red.

Variants	Mutation sites
Alpha	N501Y
Beta	K417N/E484K/N501Y
Gamma	K417T/E484K/N501Y
Delta	L452R/T478K
Kappa	L452R/E483Q
Lambda	L452Q/F490S
Omicron BA.1	G339D/S371L/S373P/S375F/K417N/N440K/G446S/S477N/T478K/E484A/Q493R/G496S/Q498R/N501Y/Y505H
Omicron BA.2	G339D/S371F/S373P/S375F/T376A/D405N/R408S/K417N/N440K/S477N/T478K/E484A/Q493R/Q498R/N501Y/Y505H
Omicron BA.2.75	G339H/S371F/S373P/S375F/T376A/D405N/R408S/K417N/N440K/G446S/S477N/T478K/E484A /Q498R/N501Y/Y505H
Omicron BA.3	G339D/S371F/S373P/S375F/ D405N/K417N/N440K/G446S/S477N/T478K/E484A/Q493R/Q498R/N501Y/Y505H
Omicron BA.4/5	G339D/S371F/S373P/S375F/T376A/D405N/R408S/K417N/N440K/L452R/F486V/S477N/T478K/E484A/Q493R/Q498R/N501Y/Y505H