Supporting Information for: Molecular Mechanism of the N501Y Mutation for Enhanced Binding between SARS-CoV-2's Spike Protein and Human ACE2 Receptor

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MD simulation of the sRBD-hACE2 complex with the N501Y mutation

To verify the binding mode (Fig. 3 in the paper) revealed from the alchemy FEP simulation for the N501Y mutation, we carried out all-atom MD simulation using the same protocol described in the Method section. As shown in Fig. S1a, the sRBD-hACE2 complex (including all glycosylations resolved in the crystal structure) was solvated in water that measures about 132×132×132 Å^3. Na^+ and Cl^- were added to neutralize the whole system and set the ion concentration to be 0.15 M. The final simulation system contains 232,377 atoms. Fig. S1b shows an enlarged view of the complex with the N510Y mutation.

During the entire 230 ns MD simulation, Y510 was always around and interacted with

residues Y41 and K353 in the hACE2. FigS1 (a-f) show the instantaneous binding conformations at 0, 75, 150 and 230 ns, respectively. As also illustrated in the Movie (N501Y-MD.mpg), we conclude that the N501Y-mutation-induced new binding mode was stable during the MD simulation.

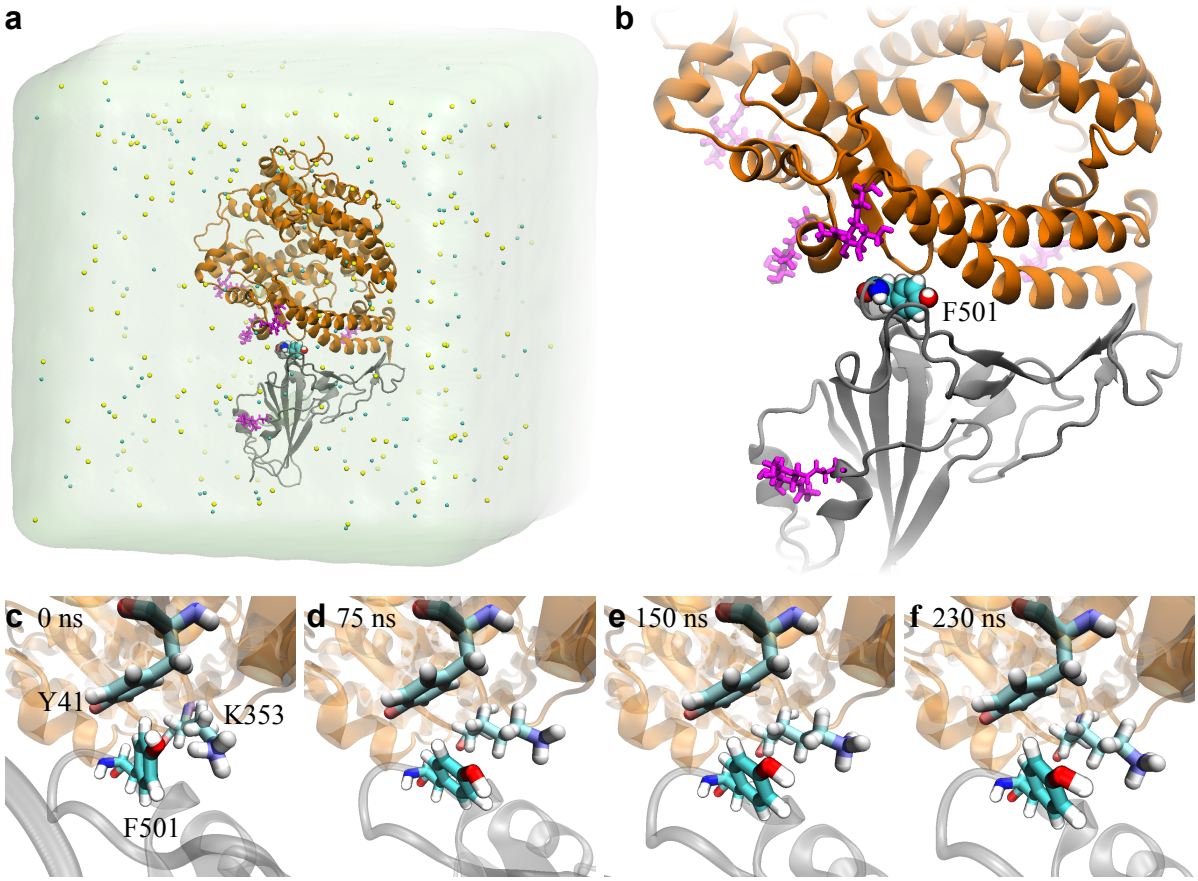

Figure S1: MD simulation of the sRBD-hACE2 complex with the N501Y mutation. a) Simulation system. hACE2 (orange) and sRBD (gray) are in the cartoon representation. The glycosylated residues are highlighted in purple. The Y501 residue on sRBD is in the van der Waals sphere representation. Na^+ and Cl^- ions are shown as yellow and cyan balls. Water is shown transparently. b) Enlarged view of the sRBD-hACE2 complex. c-f) Snapshots of F501's interfacial binding with Y41 and K353 in hACE2 when t=0, 75, 150 and 230 ns.

Supplementary Movies

Supplementary Movie 1 (N501Y-FEP.mpg): showing the trajectory of the free energy perturbation simulation for the N501Y mutation in the sRBD-ACE2 complex.

Supplementary Movie 2 (N501Y-MD.mpg): showing the trajectory of the MD simulation for the sRBD-ACE2 complex, with the N501Y mutation on sRBD.