

Sequence variation in COVID-19 is predicted to facilitate stronger interaction with ACE2 promoting high infectivity

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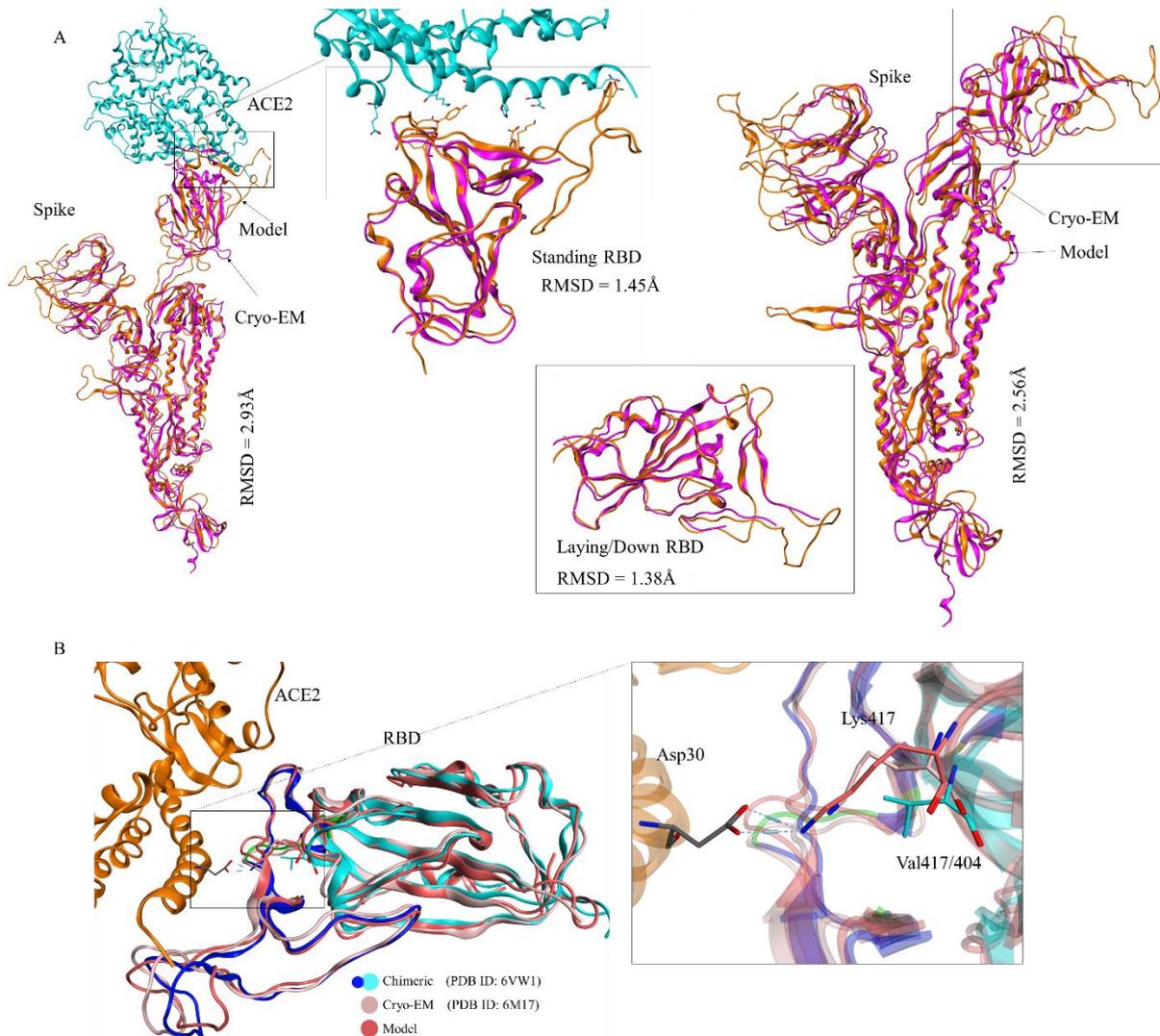
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Supplementary Data.

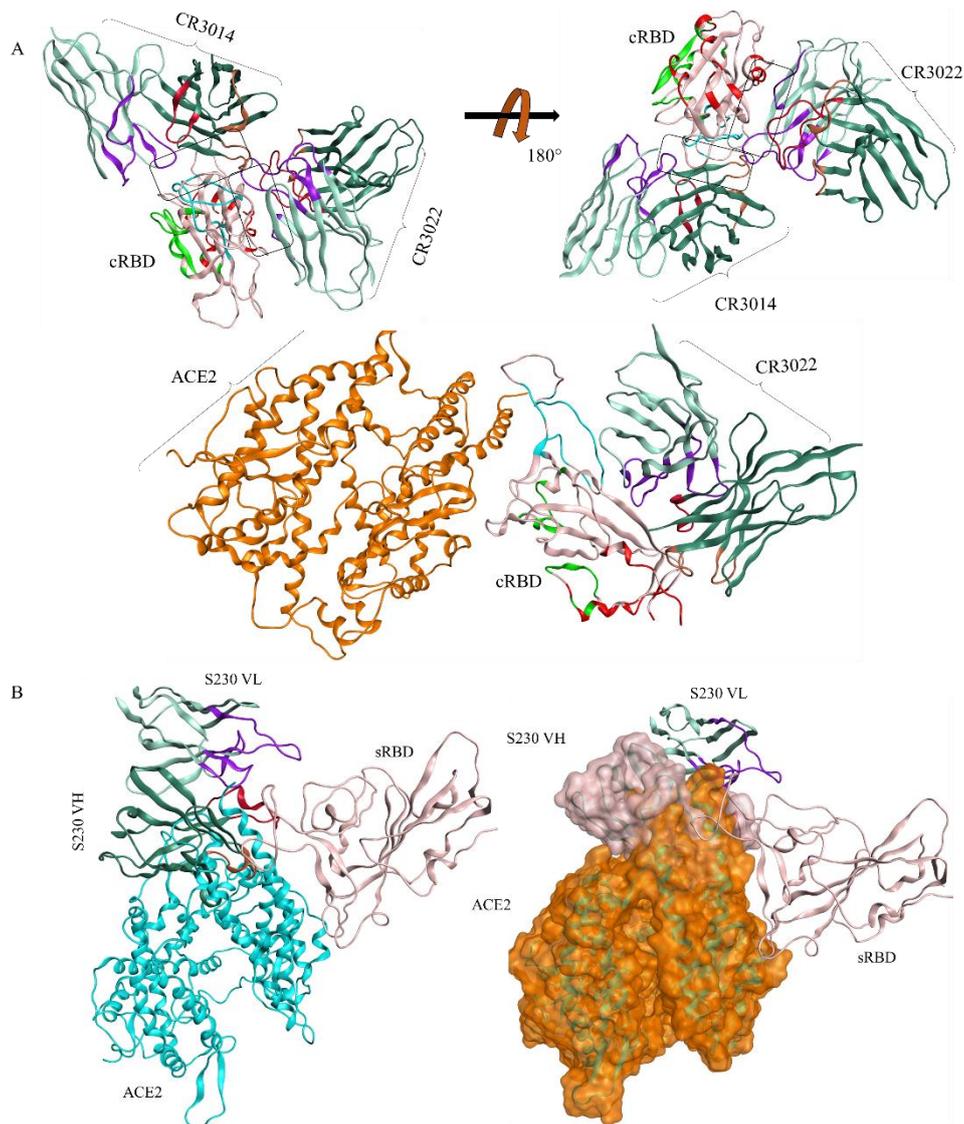
Supplementary Figure 1.

A) The homology model and recently reported cryo-EM structures of full-length Spike (PDB ID: 6VSB) and RBD in standing and laying poses are superimposed. The missing regions (ACE2 binding loops) in cryo-EM are shown. **B)** The chimeric crystal structure of the SARS-CoV-2 RBD in complex with ACE2 (PDB ID: 6VW1) is superimposed on the recently reported Cryo-EM (PDB ID: 6M17) and our modeled cRBD-ACE2 complexes. The cyan color in the chimeric crystal structure corresponds to the SARS-CoV RBD scaffold and the blue part belongs to SARS-CoV-2 RBD. The Lys-to-Val substitution in cRBD with respect to its interaction with Asp30 of ACE2 is highlighted in the enhanced box.



Supplementary Figure 2.

A) CR3022 does not overlap with the ACE2 and CR3014 binding interface of cRBD. **B)** The overlapping interface of the anti-sRBD mAB, S230, with ACE2 is shown. This superimposed model suggests that the variable heavy (VH) chain of S230 completely overlap with the ACE2 binding interface of sRBD. This model was generated by superimposing the 6NB7 and 6ACG structures retrieved from the protein data bank (PDB).



Supplementary movie 1. This animation is based on the structural coordinates extracted from the molecular dynamic trajectory. The cyan colored cartoon represents ACE2 and the brown colored cartoon represents SARS-CoV-2 cRBD. The interacting residues are depicted and labelled accordingly. The electrostatic contact between Lys417 and Asp30 can be seen.

Supplementary movie 2. This animation is based on the structural coordinates extracted from the molecular dynamic trajectory. The purple colored cartoon represents ACE2 and the brown colored cartoon represents SARS-CoV sRBD. The interacting residues are depicted and labelled accordingly. The electrostatic contact between Arg426 and Glu329 can be seen.

Supplementary Structures

1. The 3D coordinates of the modeled CR3022 mAb.
2. The 3D coordinates of the modeled CR3014 mAb.
3. The 3D coordinates of the modeled SARS-CoV-2 Spike trimer ion prefusion form in the absence of ACE2.
4. The 3D coordinates of the modeled SARS-CoV-2 Spike trimer ion prefusion form in the presence of ACE2.
5. The 3D coordinates of the modeled SARS-CoV-2 Spike cRBD in complex with ACE2.