

Supporting Information

Reversal of the unique Q493R mutation in the Omicron S1-RBD further increases its interaction with ACE2

Angelin M Philip¹, Wesam S Ahmed², Kabir H Biswas^{2,*}

Affiliation:

¹Division of Genomics and Translational Biomedicine, College of Health & Life Sciences, Hamad Bin Khalifa University, Qatar Foundation, Doha – 34110, Qatar

²Division of Biological and Biomedical Sciences, College of Health & Life Sciences, Hamad Bin Khalifa University, Qatar Foundation, Doha – 34110, Qatar

ORCID:

Angelin M Philip: 0000-0001-7222-4669

Wesam S Ahmed: 0000-0002-3441-2631

Kabir H Biswas: 0000-0001-9194-4127

*Correspondence:

Telephone number: +974 44541811

Fax: +974 44540821

Email: kbiswas@hbku.edu.qa

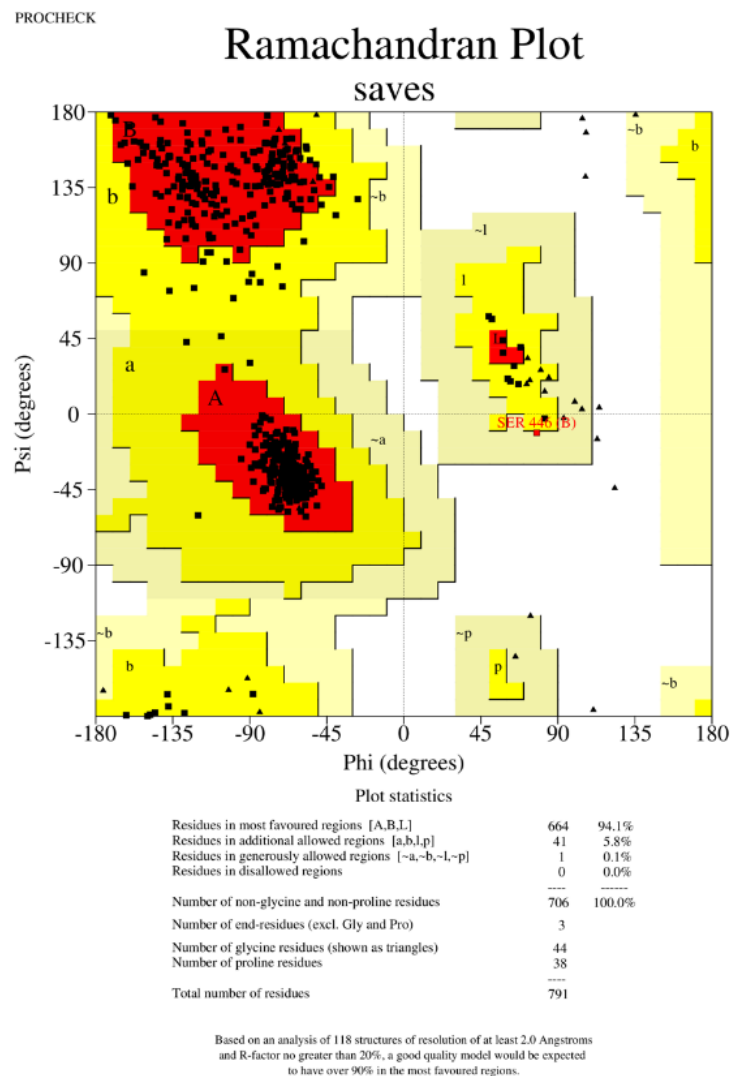
Keywords: ACE2; COVID-19; Omicron; Molecular Dynamics Simulation; Infectious Disease; SARS-CoV-2; S1 Spike Protein;

Supporting Table

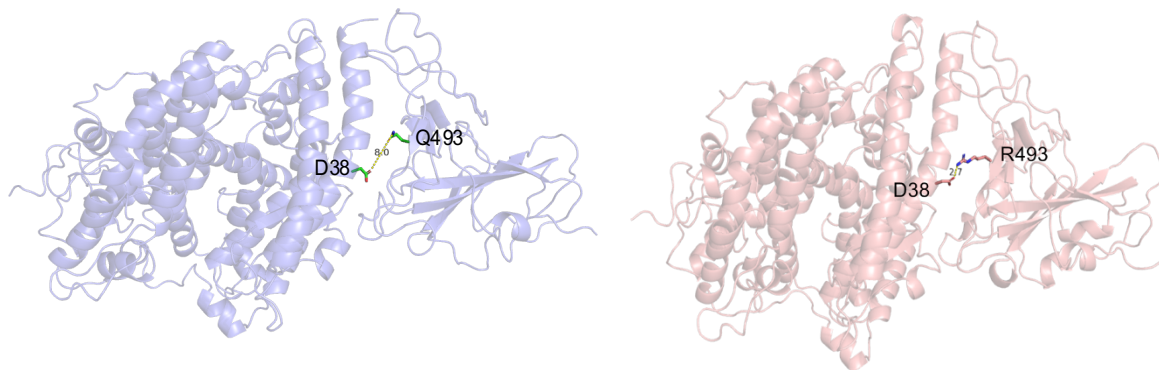
#		ACE2 RBD	Omicron			Omicron+Q493			Difference mean \pm S.D (p value)
			Run 01	Run 02	Run 03	Run 01	Run 02	Run 03	
1	Residues mutated in Omicron	D38-Side Q493(R)-Side*	138.6	74.0	131.8	0.0	0.0	0.0	-114.8 \pm 13.1 (0.005)
2		K353-Main Y505(H)-Side	31.9	16.0	15.7	1.5	6.1	1.3	-18.3 \pm 5.2 (0.0306)
3		S19-Main S477(N)-Side*	29.9	22.2	49.2	25.3	22.8	25.6	-9.2 \pm 3.7 (0.3179)
4		K31-Side Q493(R)-Side	0.0	0.0	0.0	6.1	9.6	9.0	8.3 \pm 3.5 (0.0015)
5		Y41-Side Q498(R)-Side	0.0	0.0	0.0	51.0	52.1	43.0	48.7 \pm 8.5 (0.0001)
6		Q42-Side Q498(R)-Side	4.2	6.4	0.0	6.5	8.8	9.5	4.7 \pm 2.7 (0.086)
7		K353-Side Q498(R)-Side	0.0	0.0	0.0	0.0	0.0	0.0	0 \pm 0 (NA)
8		E37-Side Y505(H)-Side	0.0	1.6	0.0	0.0	1.9	1.3	0.5 \pm 0.9 (0.5142)
9		E35-Side Q493(R)-Side	6.8	0.0	0.0	0.0	0.0	36.0	9.7 \pm 3.8 (0.4697)
10		D30-Side K417(N)-Side	0.0	0.0	0.0	0.0	0.0	0.0	0 \pm 0 (NA)
11	Residues not mutated in Omicron	D355-Side T500-Side	49.2	50.9	50.5	61.0	55.0	65.3	10.2 \pm 3.9 (0.0279)
12		K353-Main G502-Main	44.1	50.2	23.8	51.0	52.0	56.4	13.8 \pm 4.5 (0.1659)
13		Q24-Side A475-Main	12.7	15.9	13.4	0.0	0.0	0.0	-14 \pm 4.6 (0.0001)
14		S19-Side A475-Main	32.1	22.7	23.7	29.6	21.4	34.0	2.2 \pm 1.8 (0.6734)
15		D38-Side Y449-Side	0.0	0.0	0.0	2.1	5.1	23.0	10.1 \pm 3.9 (0.1983)

Supp. Table 1. Altered H-bond interaction between interfacial residues in the Omicron variant and Revertant (Omicron+Q493) ACE2-S1-RBD complex. This is in line to the observations made earlier that R493 plays a major role in the increased H-bond formation in the omicron variant in comparison with the WT. The Revertant do not possess the R493 mutation and is seen that most of the H-bonds formed in the Omicron variant are lost in this. However, the increase in D355-T500 H-bond which was earlier thought to be because of R493 residue was later found to be because of other mutation in the S1-RBD from the results obtained from the Revertant complex. Another interesting observation made was decreased H bond occupancy K353-Y505(H) and a complete loss of H-bond between Q24-A475 in the Revertant (Omicron+Q493), implying a higher chance of structural variation that impeded the bond formation. However, few H-bond completely lost in omicron were re-observed in Revertant highlighted in blue.

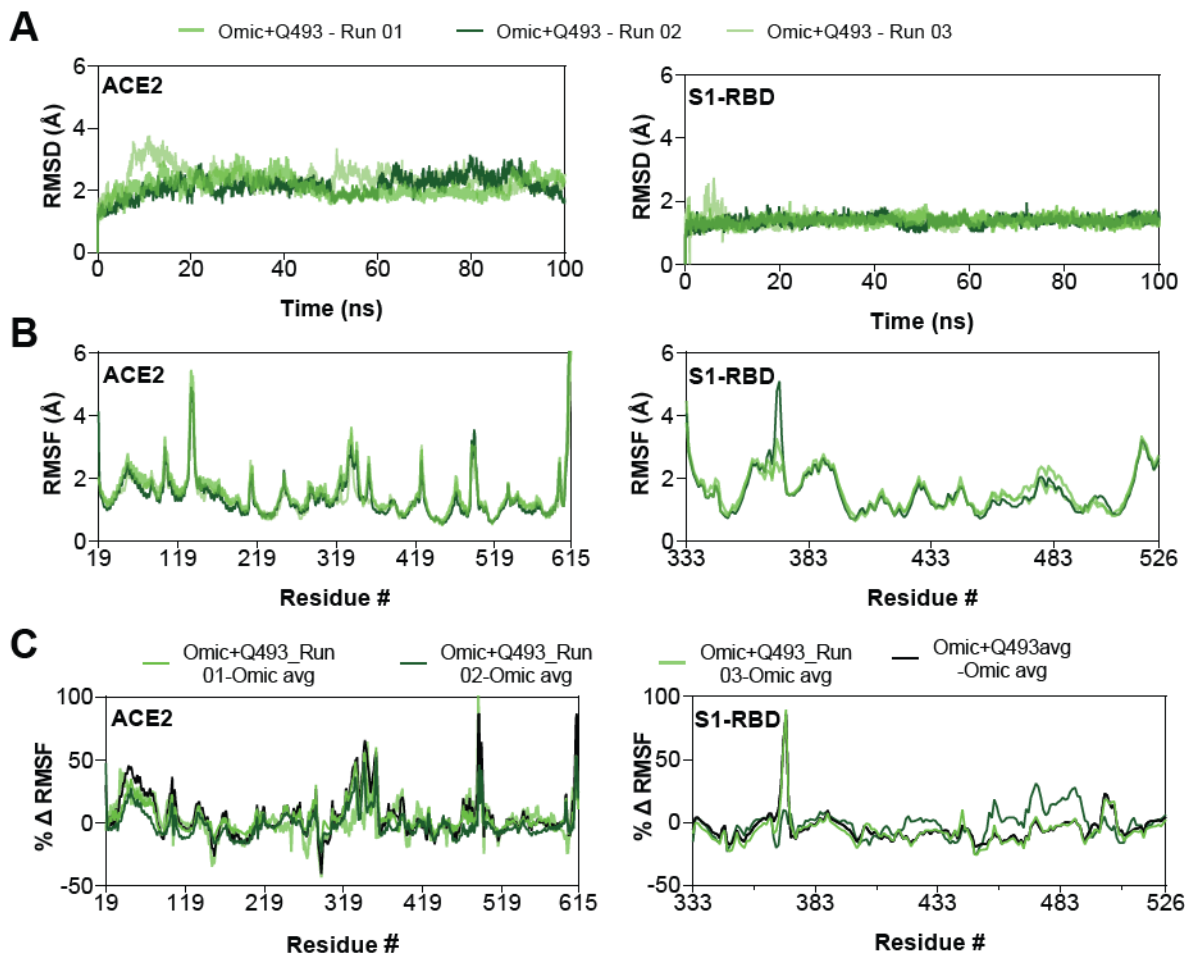
Supporting Figures



Supp. Fig. 1. Ramachandran plot of the Omicron variant S1-RBD modelled protein. The structural model of the Omicron variant S1-RBD spanning residues from T333 to G526 of the SARS-CoV-2 spike (S) protein and containing all mutations in complex with ACE2 spanning residues from S19 to D615 of human ACE2 was generated. The core regions (red) representing the most favorable combination of phi-psi values. The percentage of residue in the core is 94.1% depicting a better stereochemical quality of the protein.

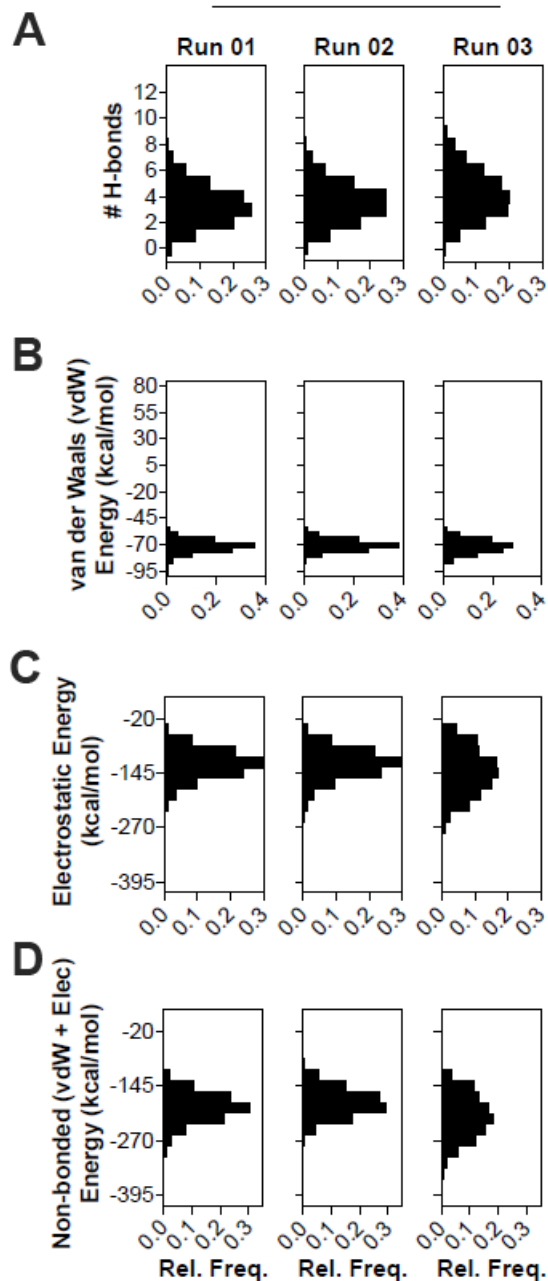


Supp. Fig. 2. Decrease in the interfacial residue distance between D38-R493 in the Omicron variant (pink). The omicron variant possesses the key mutation Q493R that resulted in a prominent salt bridge formation between D38-R493 in the Omicron variant as the distance between the residues decreased from 8Å (WT) to 2.7Å (Omicron). The WT (WT) showed in Blue and Omicron in Pink.



Supp. Fig. 3. Structural dynamics in the Revertant (Omicron+Q493) S1-RBD in complex with ACE2. (A) Graph showing backbone (C α) root-mean-square deviation (RMSD) values of ACE2 and S1-RBD obtained from the simulation of the Revertant ACE2-S1-RBD complexes. (B) Graph showing backbone (C α) root-mean-square fluctuation (RMSF) values of ACE2 and S1-RBD obtained from three individual 100 ns MD simulations of Revertant ACE2-S1-RBD complexes. (C) Graph showing mean RMSF difference between Omicron and Revertant (Omicron+Q493) complexes.

Omicron+Q493



Supp. Fig. 4. Interaction of the Revertant (Omicron+Q493) S1-RBD with ACE2. (A) Histogram showing the distribution of the number of H-bonds formed by Revertant (Omicron+Q493) S1-RBD in complex with ACE2 over three individual 100 ns of MD simulation. (B,C,D) Histograms showing the distribution of van der Waals (vdW) energy (B) electrostatic energy (Ele) (C) and total interaction energy (D) of Revertant (Omicron+Q493) in complex with ACE2 obtained from three independent 100 ns MD simulations.