

Supplementary Information

Omicron SARS-CoV-2 variant spike protein shows an increased affinity to the human ACE2 receptor, an in silico analysis

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B.1	319	RVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRRKRISNCVADYSVLVNSASFSTFK
B.1.617.2	319	RVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRRKRISNCVADYSVLVNSASFSTFK
B.1.1.529	319	RVQPTESIVRFPNITNLCPFDEVFNATRFASVYAWNRRKRISNCVADYSVLVNLAPFFTFK
B.1	379	CYGVSP TKLNDLCFTN VYADSFVIRGDEV RQIAPGQTGKIADYNYKLPDDFTGCVIAWNS
B.1.617.2	379	CYGVSP TKLNDLCFTN VYADSFVIRGDEV RQIAPGQTGKIADYNYKLPDDFTGCVIAWNS
B.1.1.529	379	CYGVSP TKLNDLCFTN VYADSFVIRGDEV RQIAPGQTGN IADYNYKLPDDFTGCVIAWNS
B.1	439	NNLDSKVGGN YNYL RLF RKS NLK PFER DISTE IYQAG STPCNG VEGFN CYFP LQSYGFQ
B.1.617.2	439	NNLDSKVGGN YNYL RLF RKS NLK PFER DISTE IYQAG SKPCNG VEGFN CYFP LQSYGFQ
B.1.1.529	439	NK LDSKV SGN YNYL RLF RKS NLK PFER DISTE IYQAG NKPCNG VAGFN CYFP LRSY SFR
B.1	499	PTNGVGYQ PYRVVLSFELLHAPATVCGPKK
B.1.617.2	499	PTNGVGYQ PYRVVLSFELLHAPATVCGPKK
B.1.1.529	499	PT YGVGHQ PYRVVLSFELLHAPATVCGPKK

Figure S1. Alignment of a portion of the SARS-CoV-2 spike sequence that includes the receptor-binding domain (RBD) shown in bold. B.1 (Wild Type), B.1.617.2 (Delta), B.1.1.529 (Omicron). Mutations in Delta and Omicron are labeled in blue and red, respectively.

Supplementary Methods.

Protein modeling and computational analysis

The Omicron variant data was retrieved from GISAID [17] and covariants.org webserver (GISAID code WT EPI_ISL_759860, Delta EPI_ISL_3298770, and Omicron EPI_ISL_6699728) on November 26, 2021. Sequence alignment was performed using DNAMAN (Lynnon Biosoft). The FASTA sequence of the WT SARS-CoV-2 viral spike protein was retrieved from the Uniprot server (sequence number P0DTC2). The Omicron mutated residues were included manually in the FASTA file, and a homology structural model was built using the tools of the SWISS-MODEL modeling server and the DeepView/Swiss-PdbViewer 4.01 software [20]. Then, the model quality was validated via ProSA-web and PROCHECK programs [21,22]. The model was optimized by adding hydrogen atoms and assigning partial charges energy refinement. Followed by molecular dynamic (MD) simulations with NAMD 2.12, as described in Ortega et al. [15] using the CHARMM force field and Gasteiger charges [23,24]. The obtained structure represents the lowest energy frame of the MD simulation. To develop molecular docking the crystal structure of the SARS-CoV-2 spike protein bound to the human ACE2 receptor (PDB code: 6M0J) and the structure of the human ACE2 receptor (PDB code: 1R42) were retrieved from the Protein Data Bank. Then, the binding patterns and affinity estimations for the interaction between the viral spike protein (WT and Omicron variant) and the ACE2 receptor were calculated using two molecular docking approaches. First, protein docking was carried out with Z-Dock [25]. The resulting complexes were analyzed using PRODIGY [26]. Next, the Haddock server was used as a second approach to evaluate the protein docking [27]. Finally, the resulting complexes were evaluated by molecular dynamic simulations. The PDB files were submitted to the CABS-flex server to assess the stability of the spike protein-ACE2 complex, and the parameters were adjusted as a default [28]. The MD simulation data were analyzed according to root-mean-square deviation (RMSF).