*Review*

***Supporting Information***

**Severe Acute Respiratory Syndrome Coronavirus 2 Variants of Concern: a perspective for the emerging strains more transmissible, infectible and resistant to vaccines**

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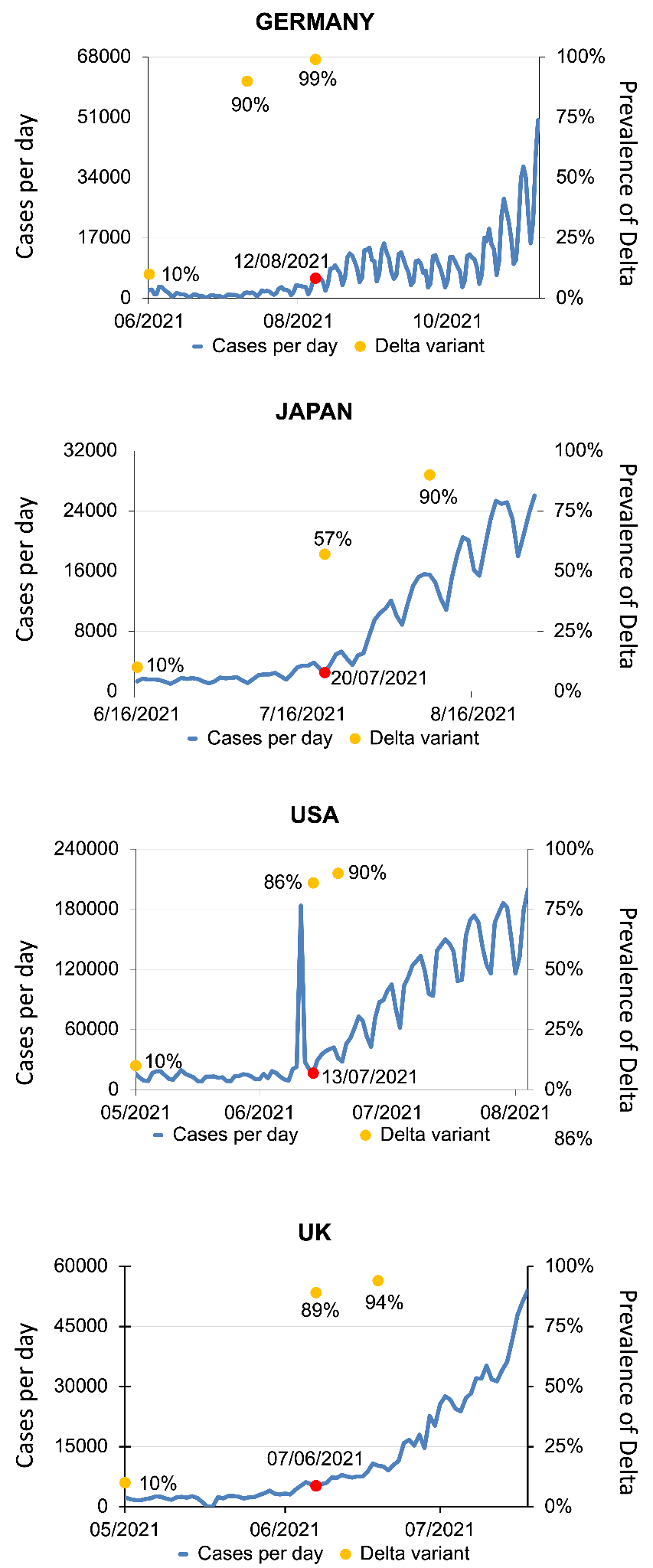
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**Running title: Impacts of SARS-CoV-2 variants of concern**

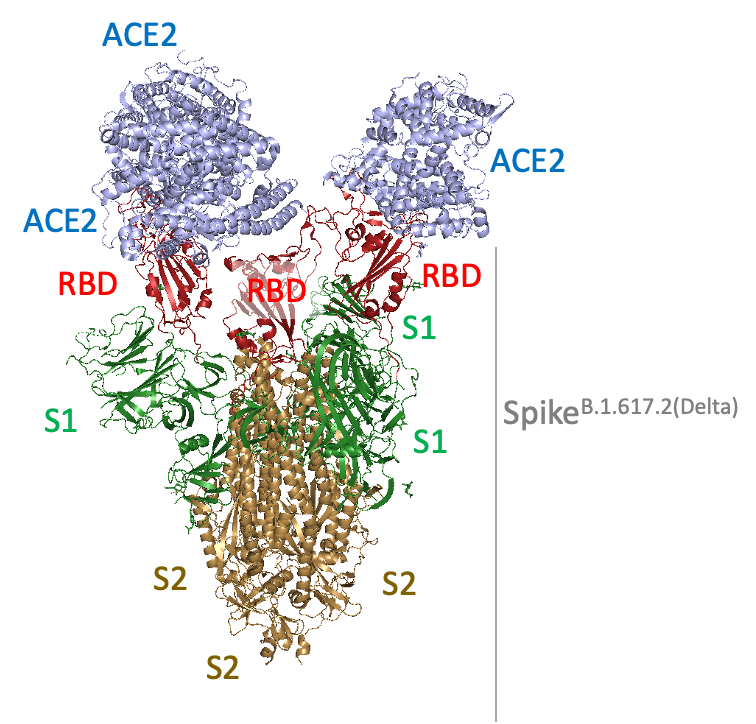
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**Keywords:** SARS-CoV-2 variants, transmissibility, viral load, sensitivity to antisera.

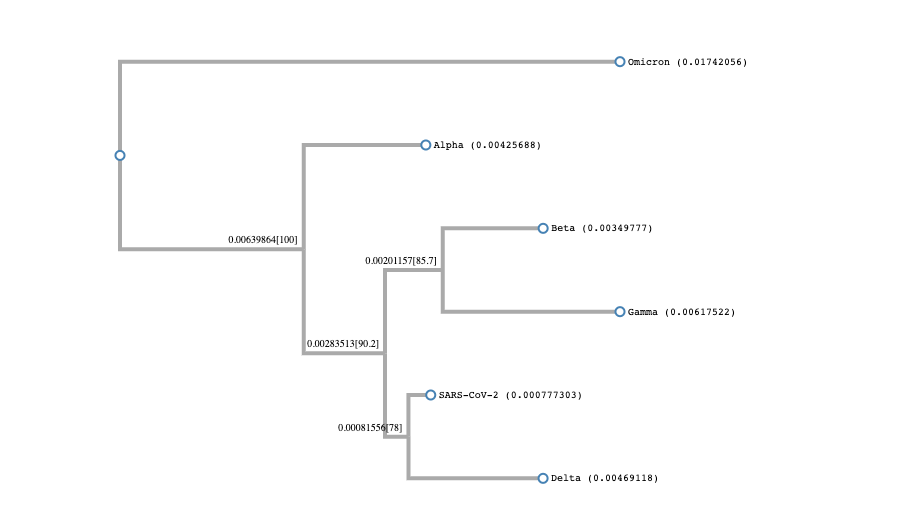
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**Figure S1. Number of COVID-19 cases and the prevalence of the SARS-CoV-2 Delta variant in the UK, Japan, USA, and Germany.** Graphs of the number of cases (blue line) and the percentage of the Delta variant (orange circles) as a function of time. Red circles show the beginning of a new COVID-19 peak case. All data were obtained from World in Data, WHO, CDC, UK Gov and Outbreak [[140–144]](https://paperpile.com/c/l3rrjp/L22Jy+RAhMH+bmR42+3MoAd+PRo6u).

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**Figure S2. Cryo-EM structure of SARS-CoV-2 SpikeB.1.617.2(Delta) in complex with Angiotensin-converting enzyme 2 (ACE2) ectodomain.** ACE2 is colored in blue, Spike protein structure in red (RBD domain), green (S1 subunit not considering the RBD domain) and brown (S2 domain) (protein data bank, PDB, 7V8A, not published).

**A**



**B**

SARS-CoV-2 MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60

Delta/B.1.617.2 MFVFLVLLPLVSSQCVNLRTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60

Omicron/B.1.1.529 MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60

Alpha/B.1.1.7 MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60

P.1/Gamma MFVFLVLLPLVSSQCVNFTNRTQLPSAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60

Beta/B.1.351 MFVFLVLLPLVSSQCVNFTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFS 60

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SARS-CoV-2 NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120

Delta/B.1.617.2 NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120

Omicron/B.1.1.529 NVTWFHVI--SGTNGTKRFDNPVLPFNDGVYFASIEKSNIIRGWIFGTTLDSKTQSLLIV 118

Alpha/B.1.1.7 NVTWFHAI--SGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 118

P.1/Gamma NVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120

Beta/B.1.351 NVTWFHAIHVSGTNGTKRFANPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIV 120

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SARS-CoV-2 NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180

Delta/B.1.617.2 NNATNVVIKVCEFQFCNDPFLDVYYHKNNKSWMESG--VYSSANNCTFEYVSQPFLMDLE 180

Omicron/B.1.1.529 NNATNVVIKVCEFQFCNDPFLD---HKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 175

Alpha/B.1.1.7 NNATNVVIKVCEFQFCNDPFLGVY-HKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 177

P.1/Gamma NNATNVVIKVCEFQFCNYPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180

Beta/B.1.351 NNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLE 180

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SARS-CoV-2 GKQGNFKNLREFVFKNIDGYFKIYSKHTPINL--VRDLPQGFSALEPLVDLPIGINITRF 238

Delta/B.1.617.2 GKQGNFKNLREFVFKNIDGYFKIYSKHTPINL--VRDLPQGFSALEPLVDLPIGINITRF 238

Omicron/B.1.1.529 GKQGNFKNLREFVFKNIDGYFKIYSKHTPIIVREPEDLPQGFSALEPLVDLPIGINITRF 235

Alpha/B.1.1.7 GKQGNFKNLREFVFKNIDGYFKIYSKHTPINL--VRDLPQGFSALEPLVDLPIGINITRF 235

P.1/Gamma GKQGNFKNLSEFVFKNIDGYFKIYSKHTPINL--VRDLPQGFSALEPLVDLPIGINITRF 238

Beta/B.1.351 GKQGNFKNLREFVFKNIDGYFKIYSKHTPINL--VRGLPQGFSALEPLVDLPIGINITRF 238

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SARS-CoV-2 QTLLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSE 298

Delta/B.1.617.2 QTLLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSE 298

Omicron/B.1.1.529 QTLLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSE 295

Alpha/B.1.1.7 QTLLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSE 295

P.1/Gamma QTLLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSE 298

Beta/B.1.351 QT---LHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSE 295

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SARS-CoV-2 TKCTLKSFTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRI 358

Delta/B.1.617.2 TKCTLKSFTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRI 358

Omicron/B.1.1.529 TKCTLKSFTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFDEVFNATRFASVYAWNRKRI 355

Alpha/B.1.1.7 TKCTLKSFTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRI 355

P.1/Gamma TKCTLKSFTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRI 358

Beta/B.1.351 TKCTLKSFTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRI 355

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SARS-CoV-2 SNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKI 418

Delta/B.1.617.2 SNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKI 418

Omicron/B.1.1.529 SNCVADYSVLYNLAPFFTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTG**N**I 415

Alpha/B.1.1.7 SNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKI 415

P.1/Gamma SNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTG**T**I 418

Beta/B.1.351 SNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTG**N**I 415

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SARS-CoV-2 ADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGST 478

Delta/B.1.617.2 ADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNY**R**YRLFRKSNLKPFERDISTEIYQAGS**K** 478

Omicron/B.1.1.529 ADYNYKLPDDFTGCVIAWNSNKLDSKV**S**GNYNYLYRLFRKSNLKPFERDISTEIYQAG**NK** 475

Alpha/B.1.1.7 ADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGST 475

P.1/Gamma ADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGST 478

Beta/B.1.351 ADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGST 475

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SARS-CoV-2 PCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKC 538

Delta/B.1.617.2 PCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKC 538

Omicron/B.1.1.529 PCNGV**A**GFNCYFPL**R**SY**S**F**R**PT**Y**GVG**H**QPYRVVVLSFELLHAPATVCGPKKSTNLVKNKC 535

Alpha/B.1.1.7 PCNGVEGFNCYFPLQSYGFQPT**Y**GVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKC 535

P.1/Gamma PCNGVKGFNCYFPLQSYGFQPT**Y**GVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKC 538

Beta/B.1.351 PCNGVKGFNCYFPLQSYGFQPT**Y**GVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKC 535

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SARS-CoV-2 VNFNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVI 598

Delta/B.1.617.2 VNFNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVI 598

Omicron/B.1.1.529 VNFNFNGLKGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVI 595

Alpha/B.1.1.7 VNFNFNGLTGTGVLTESNKKFLPFQQFGRDIDDTTDAVRDPQTLEILDITPCSFGGVSVI 595

P.1/Gamma VNFNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVI 598

Beta/B.1.351 VNFNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVI 595

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SARS-CoV-2 TPGTNTSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNN 658

Delta/B.1.617.2 TPGTNTSNQVAVLYQ**G**VNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNN 658

Omicron/B.1.1.529 TPGTNTSNQVAVLYQ**G**VNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEYVNN 655

Alpha/B.1.1.7 TPGTNTSNQVAVLYQ**G**VNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNN 655

P.1/Gamma TPGTNTSNQVAVLYQ**G**VNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEYVNN 658

Beta/B.1.351 TPGTNTSNQVAVLYQ**G**VNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNN 655

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**S1/S2**

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SARS-CoV-2 SYECDIPIGAGICASYQTQTNSPRRARSVASQSIIAYTMSLGAENSVAYSNNSIAIPTNF 718

Delta/B.1.617.2 SYECDIPIGAGICASYQTQTNS**R**RRARSVASQSIIAYTMSLGAENSVAYSNNSIAIPTNF 718

Omicron/B.1.1.529 SYECDIPIGAGICASYQTQTKS**H**RRARSVASQSIIAYTMSLGAENSVAYSNNSIAIPTNF 715

Alpha/B.1.1.7 SYECDIPIGAGICASYQTQTNS**H**RRARSVASQSIIAYTMSLGAENSVAYSNNSIAIPINF 715

P.1/Gamma SYECDIPIGAGICASYQTQTNSPRRARSVASQSIIAYTMSLGAENSVAYSNNSIAIPTNF 718

Beta/B.1.351 SYECDIPIGAGICASYQTQTNSPRRARSVASQSIIAYTMSLGVENSVAYSNNSIAIPTNF 715

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SARS-CoV-2 TISVTTEILPVSMTKTSVDCTMYICGDSTECSNLLLQYGSFCTQLNRALTGIAVEQDKNT 778

Delta/B.1.617.2 TISVTTEILPVSMTKTSVDCTMYICGDSTECSNLLLQYGSFCTQLNRALTGIAVEQDKNT 778

Omicron/B.1.1.529 TISVTTEILPVSMTKTSVDCTMYICGDSTECSNLLLQYGSFCTQLKRALTGIAVEQDKNT 775

Alpha/B.1.1.7 TISVTTEILPVSMTKTSVDCTMYICGDSTECSNLLLQYGSFCTQLNRALTGIAVEQDKNT 775

P.1/Gamma TISVTTEILPVSMTKTSVDCTMYICGDSTECSNLLLQYGSFCTQLNRALTGIAVEQDKNT 778

Beta/B.1.351 TISVTTEILPVSMTKTSVDCTMYICGDSTECSNLLLQYGSFCTQLNRALTGIAVEQDKNT 775

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**S2,**

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SARS-CoV-2 QEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYG 838

Delta/B.1.617.2 QEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYG 838

Omicron/B.1.1.529 QEVFAQVKQIYKTPPIKYFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYG 835

Alpha/B.1.1.7 QEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYG 835

P.1/Gamma QEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYG 838

Beta/B.1.351 QEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQYG 835

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SARS-CoV-2 DCLGDIAARDLICAQKFNGLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAALQIPF 898

Delta/B.1.617.2 DCLGDIAARDLICAQKFNGLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAALQIPF 898

Omicron/B.1.1.529 DCLGDIAARDLICAQKFKGLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAALQIPF 895

Alpha/B.1.1.7 DCLGDIAARDLICAQKFNGLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAALQIPF 895

P.1/Gamma DCLGDIAARDLICAQKFNGLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAALQIPF 898

Beta/B.1.351 DCLGDIAARDLICAQKFNGLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAALQIPF 895

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SARS-CoV-2 AMQMAYRFNGIGVTQNVLYENQKLIANQFNSAIGKIQDSLSSTASALGKLQDVVNQNAQA 958

Delta/B.1.617.2 AMQMAYRFNGIGVTQNVLYENQKLIANQFNSAIGKIQDSLSSTASALGKLQNVVNQNAQA 958

Omicron/B.1.1.529 AMQMAYRFNGIGVTQNVLYENQKLIANQFNSAIGKIQDSLSSTASALGKLQDVVNHNAQA 955

Alpha/B.1.1.7 AMQMAYRFNGIGVTQNVLYENQKLIANQFNSAIGKIQDSLSSTASALGKLQDVVNQNAQA 955

P.1/Gamma AMQMAYRFNGIGVTQNVLYENQKLIANQFNSAIGKIQDSLSSTASALGKLQDVVNQNAQA 958

Beta/B.1.351 AMQMAYRFNGIGVTQNVLYENQKLIANQFNSAIGKIQDSLSSTASALGKLQDVVNQNAQA 955

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SARS-CoV-2 LNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEI 1018

Delta/B.1.617.2 LNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEI 1018

Omicron/B.1.1.529 LNTLVKQLSSKFGAISSVLNDIFSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEI 1015

Alpha/B.1.1.7 LNTLVKQLSSNFGAISSVLNDILARLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEI 1015

P.1/Gamma LNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEI 1018

Beta/B.1.351 LNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEI 1015

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SARS-CoV-2 RASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNFTTA 1078

Delta/B.1.617.2 RASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNFTTA 1078

Omicron/B.1.1.529 RASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNFTTA 1075

Alpha/B.1.1.7 RASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNFTTA 1075

P.1/Gamma RASANLAAIKMSECVLGQSKRVDFCGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNFTTA 1078

Beta/B.1.351 RASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNFTTA 1075

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SARS-CoV-2 PAICHDGKAHFPREGVFVSNGTHWFVTQRNFYEPQIITTDNTFVSGNCDVVIGIVNNTVY 1138

Delta/B.1.617.2 PAICHDGKAHFPREGVFVSNGTHWFVTQRNFYEPQIITTDNTFVSGNCDVVIGIVNNTVY 1138

Omicron/B.1.1.529 PAICHDGKAHFPREGVFVSNGTHWFVTQRNFYEPQIITTDNTFVSGNCDVVIGIVNNTVY 1135

Alpha/B.1.1.7 PAICHDGKAHFPREGVFVSNGTHWFVTQRNFYEPQIITTHNTFVSGNCDVVIGIVNNTVY 1135

P.1/Gamma PAICHDGKAHFPREGVFVSNGTHWFVTQRNFYEPQIITTDNTFVSGNCDVVIGIVNNTVY 1138

Beta/B.1.351 PAICHDGKAHFPREGVFVSNGTHWFVTQRNFYEPQIITTDNTFVSGNCDVVIGIVNNTVY 1135

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SARS-CoV-2 DPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLNESLI 1198

Delta/B.1.617.2 DPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLNESLI 1198

Omicron/B.1.1.529 DPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLNESLI 1195

Alpha/B.1.1.7 DPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLNESLI 1195

P.1/Gamma DPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASFVNIQKEIDRLNEVAKNLNESLI 1198

Beta/B.1.351 DPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLNESLI 1195

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SARS-CoV-2 DLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDE 1258

Delta/B.1.617.2 DLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDE 1258

Omicron/B.1.1.529 DLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDE 1255

Alpha/B.1.1.7 DLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDE 1255

P.1/Gamma DLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDE 1258

Beta/B.1.351 DLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDE 1255

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SARS-CoV-2 DDSEPVLKGVKLHYT 1273

Delta/B.1.617.2 DDSEPVLKGVKLHYT 1273

Omicron/B.1.1.529 DDSEPVLKGVKLHYT 1270

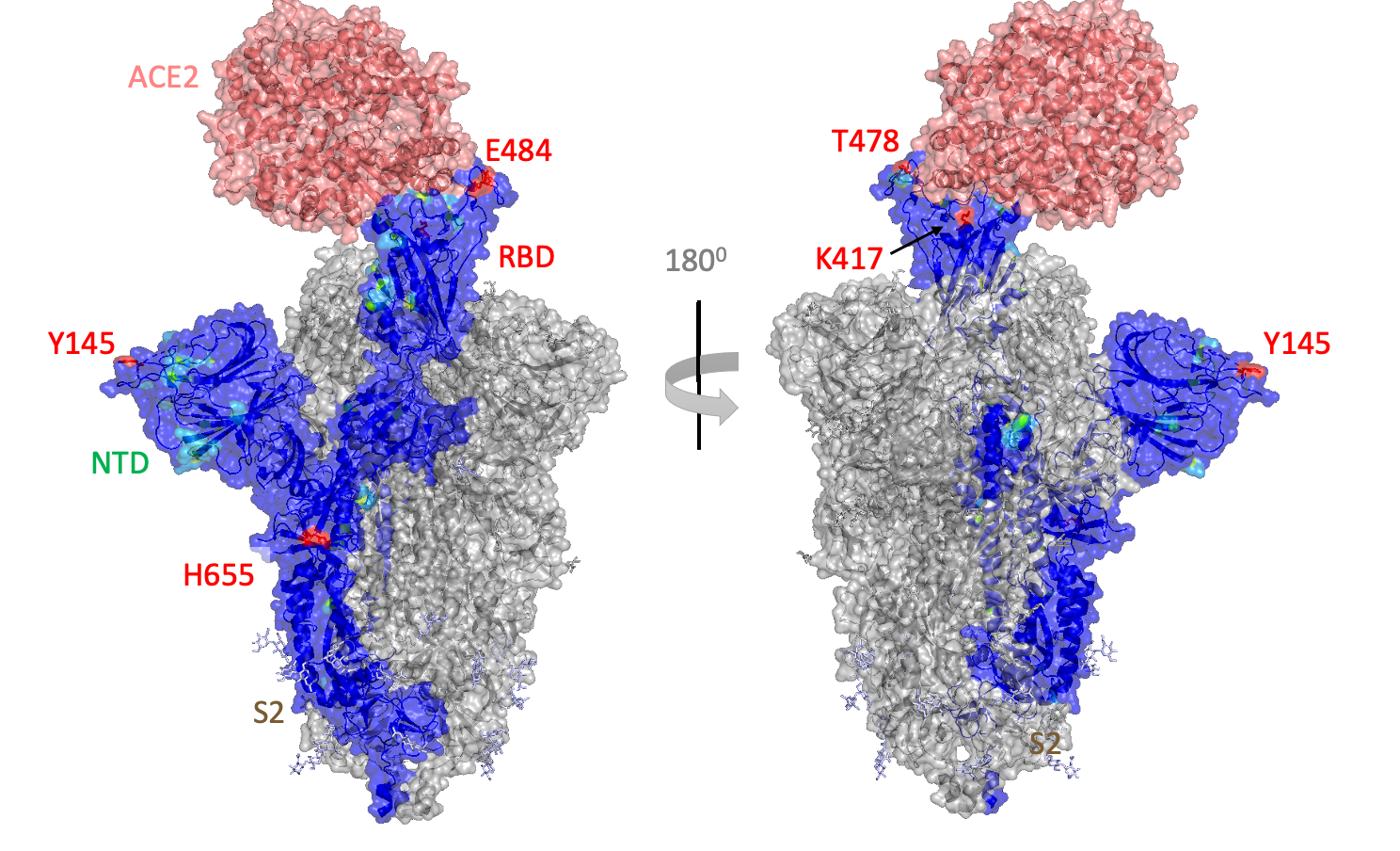
Alpha/B.1.1.7 DDSEPVLKGVKLHYT 1270

P.1/Gamma DDSEPVLKGVKLHYT 1273

Beta/B.1.351 DDSEPVLKGVKLHYT 1270

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**Figure S3. Multiple sequence alignment and construction of the phylogenetic tree of SARS-CoV-2 VOCs.**  **A)** Phylogenetic tree of SARS-CoV-2 Spike protein VOCs. **B)** Multiple sequence alignment of the Spike protein VOCs. The domains are colored as: signal peptide (orange); N-terminal domain (green), RBD (red), SD1 (pink) and SD2 (purple), cleavage sites (S1/S2 and S2' are colored in black) the fusion peptide (brown), HR1 (cyan and blue), HR2 (dark green), a transmembrane domain (grey), and cytoplasm domain (not colored)[5,6](https://paperpile.com/c/5ZOiJk/rF3pf+TThvd). The predominant residues D614G and N501Y are pointed using arrows. The residues of the Spike protein involved in hACE2 interaction are highlighted: E1 region in yellow (corresponds to residues 417, 455-456, 470-490) and E2 region in light blue (made up of residues 444-454 and 493-505)[7](https://paperpile.com/c/5ZOiJk/VUyf). Multiple sequence alignment and the phylogenetic tree were performed using the ClustalW server [8](https://paperpile.com/c/5ZOiJk/Soir).



**Figure S4.** **Conservation profile of the Spike protein among VOCs.** The surface of the structure of the SpikeWT protein in complex with ACE2 (PDB ID: 7DF4[11](https://paperpile.com/c/5ZOiJk/yYvC)) is colored based on the conservation profile. The ACE2 structure is colored in salmon, and the chains A and C in the trimeric form of Spike protein are colored in grey. The residues Y145, K417, T478, E484 and H655 are colored in red and correspond to the residues in the SARS-CoV-2 VOCs with more variability.

**Table S1.** Conservation score in the Consurf Server analysis[9,10](https://paperpile.com/c/5ZOiJk/ImkN+bxxp). The Spike protein residues with the highest values are listed. High values meaning not conserved residues in the Spike protein among SARS-CoV-2 VOCs.

| **Spike Residue** | **Conservation Score** |
| --- | --- |
| **L18** | **4.5** |
| **T19** | **4.0** |
| **P26** | **4.4** |
| **H69** | **4.1** |
| **D80** | **4.2** |
| **T95** | **4.0** |
| **D138** | **4.2** |
| **Y145** | **7.5** |
| **H146** | **4.3** |
| **E156** | **4.3** |
| **R190** | **4.2** |
| **N211** | **4.3** |
| **L212** | **4.5** |
| **V213** | **4.7** |
| **R214** | **5.0** |
| **D215** | **4.2** |
| **G339** | **4.6** |
| **S371** | **4.2** |
| **G339** | **4.6** |
| **S371** | **4.2** |
| **S373** | **4.0** |
| **S375** | **4.1** |
| **K417** | **8.6** |
| **N440** | **4.1** |
| **G446** | **4.4** |
| **L452** | **4.5** |
| **S477** | **3.9** |
| **T478** | **7.2** |
| **E484** | **7.3** |
| **Q493** | **4.3** |
| **G496** | **4.4** |
| **Q498** | **4.3** |
| **N501** | **4.5** |
| **Y505** | **4.4** |
| **T547** | **4.2** |
| **D614** | **4.5** |
| **H655** | **7.2** |
| **A701** | **4.0** |
| **T716** | **4.0** |
| **N764** | **4.1** |
| **D796** | **4.4** |
| **N856** | **4.1** |
| **D950** | **4.1** |
| **Q954** | **4.2** |
| **N969** | **4.1** |
| **L981** | **4.5** |
| **S982** | **3.9** |
| **T1027** | **4.0** |
| **D1118** | **4.2** |

**REFERENCES**

1. [Matsuyama, S. *et al.* Efficient activation of the severe acute respiratory syndrome coronavirus spike protein by the transmembrane protease TMPRSS2. *J. Virol.* **84**, 12658–12664 (2010).](http://paperpile.com/b/5ZOiJk/e57eq)

2. [Shulla, A. *et al.* A transmembrane serine protease is linked to the severe acute respiratory syndrome coronavirus receptor and activates virus entry. *J. Virol.* **85**, 873–882 (2011).](http://paperpile.com/b/5ZOiJk/9x4dJ)

3. [Djomkam, A. L. Z., Olwal, C. O., Sala, T. B. & Paemka, L. Commentary: SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Frontiers in oncology* vol. 10 1448 (2020).](http://paperpile.com/b/5ZOiJk/NxC2I)

4. [Hoffmann, M. *et al.* SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell* **181**, 271–280.e8 (2020).](http://paperpile.com/b/5ZOiJk/KZZxP)

5. [Wrapp, D. *et al.* Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science* **367**, 1260–1263 (2020).](http://paperpile.com/b/5ZOiJk/rF3pf)

6. [Walls, A. C. *et al.* Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. *Cell* **183**, 1735 (2020).](http://paperpile.com/b/5ZOiJk/TThvd)

7. [Silva de Souza, A. *et al.* Molecular Dynamics Reveals Complex Compensatory Effects of Ionic Strength on the Severe Acute Respiratory Syndrome Coronavirus 2 Spike/Human Angiotensin-Converting Enzyme 2 Interaction. *J. Phys. Chem. Lett.* **11**, 10446–10453 (2020).](http://paperpile.com/b/5ZOiJk/VUyf)

8. [Madeira, F. *et al.* The EMBL-EBI search and sequence analysis tools APIs in 2019. *Nucleic Acids Res.* **47**, W636–W641 (2019).](http://paperpile.com/b/5ZOiJk/Soir)

9. [Landau, M. *et al.* ConSurf 2005: the projection of evolutionary conservation scores of residues on protein structures. *Nucleic Acids Res.* **33**, W299–302 (2005).](http://paperpile.com/b/5ZOiJk/ImkN)

10. [Glaser, F. *et al.* ConSurf: identification of functional regions in proteins by surface-mapping of phylogenetic information. *Bioinformatics* **19**, 163–164 (2003).](http://paperpile.com/b/5ZOiJk/bxxp)

11. [Xu, C. *et al.* Conformational dynamics of SARS-CoV-2 trimeric spike glycoprotein in complex with receptor ACE2 revealed by cryo-EM. *Sci Adv* **7**, (2021).](http://paperpile.com/b/5ZOiJk/yYvC)