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Surveillance report

Surveillance generated by nf-ncov-voc for Delta variant

Date

This report is generated on 2022-01-18 using 162696 number of genomes collected between 2020-02-25 and 2021-12-20

Pango Lineages

Pango Lineages in this report ['AY.1', 'AY.10', 'AY.100', 'AY.101', 'AY.102', 'AY.103', 'AY.104', 'AY.105', 'AY.106', 'AY.107', 'AY.108', 'AY.108', 'AY.110', 'AY.110', 'AY.111', 'AY.113', 'AY.114', 'AY.116', 'AY.116.1', 'AY.117', 'AY.118', 'AY.119', 'AY.119.1', 'AY.120', 'AY.120.1', 'AY.121', 'AY.121.1', 'AY.122', 'AY.122.1', 'AY.124', 'AY.125', 'AY.126', 'AY.127', 'AY.13', 'AY.14', 'AY.15', 'AY.16', 'AY.16.1', 'AY.17', 'AY.18', 'AY.19', 'AY.20', 'AY.20', 'AY.21', 'AY.23', 'AY.24', 'AY.25', 'AY.25.1', 'AY.26', 'AY.27', 'AY.28', 'AY.29', 'AY.3', 'AY.3.1', 'AY.32', 'AY.33', 'AY.34', 'AY.34.1', 'AY.35', 'AY.36', 'AY.37', 'AY.38', 'AY.39', 'AY.39.1', 'AY.4', 'AY.4.2', 'AY.4.2.1', 'AY.4.2.2', 'AY.4.3', 'AY.4.4', 'AY.4.5', 'AY.4.6', 'AY.40', 'AY.41', 'AY.42', 'AY.43', 'AY.43', 'AY.43.4', 'AY.44', 'AY.45', 'AY.46', 'AY.46.2', 'AY.46.4', 'AY.46.6', 'AY.47', 'AY.48', 'AY.49', 'AY.5', 'AY.53', 'AY.54', 'AY.55', 'AY.56', 'AY.59', 'AY.66', 'AY.60', 'AY.61', 'AY.62', 'AY.62', 'AY.65', 'AY.66', 'AY.67', 'AY.68', 'AY.7.1', 'AY.70', 'AY.72', 'AY.73', 'AY.74', 'AY.75', 'AY.77', 'AY.78', 'AY.82', 'AY.83', 'AY.84', 'AY.88', 'AY.89', 'AY.89', 'AY.99.2', 'AY

Indicator

This table contains key indicators identified

| Indicator | Sub-categories from POKAY | Mutations |
|----------------------------------|-------------------------------------|-----------------------------|
| Transmissibility between hu- | transmissibility | p.D614G, p.E484Q, p.L452R, |
| mans | | p.P681R |
| Infection Severity | ACE2 receptor binding affinity, | p.D138Y, p.D614G, p.E484K, |
| | viral load, outcome hazard ratio | p.E484Q, p.H69del, p.K417N, |
| | | p.L452R, p.L5F, p.P26S, |
| | | p.P681H, p.S494P, p.T95I, |
| | | p.V70del |
| Immunity after natural infection | convalescent plasma escape, rein- | p.D614G, p.E484K, p.E484Q, |
| | fection, humoral response dura- | p.H69del, p.K417N, p.K458N, |
| | bility | p.L452R, p.P1162S, p.S494P, |
| | | p.V70del |
| Vaccines | vaccine neutralization efficacy | p.D614G, p.E484K, p.E484Q, |
| | | p.K417N, p.L452R, p.P681H |
| Monoclonal antibodies | monoclonal antibody serial pas- | p.E484K, p.E484Q, p.G142D, |
| | sage escape, pharmaceutical ef- | p.K417N, p.L452R, p.P251L, |
| | fectiveness | p.R158G, p.S255F, p.S443F, |
| | | p.S494P |
| Diagnostics | clinical indicators, antigenic test | |
| | failure, symptom prevalence | |

Mutation Significance

This table contains key functional impacts of mutations identified

| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|---|---|----------|-----------------------|----------|-----------|-----------|
| | | | | | Depth | Allele | Frequency |
| p.S443F | monoclonal anti- body serial passage escape | Ranked effective escape variant in the RBD for highly neutralizing COV2-2499 monoclonal antibody | AY.124 | Greaney et al. (2020) | 1 | 1 | 1.0 |
| p.D614G | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains- Fc portion IgG complex, this variant showed a 1.32x increase in binding (KD) relative to D614G. | AY.70 | Gong et al. (2021) | 8 | 1,7 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|--|-----------------------|-------------------|---------------------|------------------------|
| p.D614G | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains- Fc portion IgG complex, this variant showed a 2.66x increase in binding (KD) relative to D614G. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Gong et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant combination (representing lineage B.1.617) showed a 1.85x increase in binding (KD) relative to D614G. [exact variant list not provided in manuscript, is inferred fro common knowledge] | AY.70 | Gong et al. (2021) | 8 | 1,7 | 1.0 |
| p.D614G | ACE2 receptor binding affinity | In four cell lines (including 293T-hACE2 cells), this mutation combination increases infectivity vs D614G alone | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Li et al. (2020) | 13616 | 10759,2854 | 1.0 |
| p.D614G | convalescent plasma binding | 1.56x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.70 | Gong et al. (2021) | 8 | 1,7 | 1.0 |
| p.D614G | convalescent plasma binding | 2.15x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Gong et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | convalescent plasma binding | This variant combination (representing lineage B.1.617) showed a 1.22x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptomonset. [exact variant list not provided in manuscript, is inferred fro common knowledge] | AY.70 | Gong et al. (2021) | 8 | 1,7 | 1.0 |
| p.D614G | convalescent plasma escape | Pseudotyped viruses for B.1.617 was 2.3-fold resistant to neutralization by convalescent sera compared to wild type - a finding that was similar to that of the 3-fold resistance of the South Africa B.1.351 variant using the same assay. The resistance of B.1.617 was caused by the L452R and E484Q mutation, based on results from viruses pseudotyped for individual variants within B.1.617. [details on the convalescent patient sera collection are not abundantly clear in the preprint] | AY.70 | Tada et al. (2021) | 8 | 1,7 | 1.0 |
| p.D614G | convalescent plasma escape | Relative to B.1, Epsilon (B.1.417/429) shows 1.74x-2.35x decrease in neutralization efficiency by convalescent plasma [no cohort details provided] | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Wilhelm et al. (2021) | 13616 | 10759,2854 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--|--|--|-----------------------|-------------------|---------------------|------------------------|
| p.D614G | humoral response durability | 27yo female nurse reinfected in December 2020 (B.1.177) after initial infection in March 2020 (B.3), i.e. with a 9 month interval. Both cases were mild. No significant differences in the neutralizing capacity of the two linages were observed in 4 sera taken (1 pre-reinfection, three post-reinfection). Neutralizing antibody titres (IC50) before and immediately after re-infection were <300 against both strains, and jumped >7x upon re-infection. Viral titres were also higher in the second case also includes N:p.A220V | AY.38, AY.70, AY.57, AY.46, AY.27 | Brehm et al. (2021) | 13455 | 10624,2828 | 1.0 |
| p.D614G | immunosuppression variant emergence | Studying 94 COVID-19 extended infection cases with genomics April 1 to October 17, 2020, one case developed 23 mutations in a 19 day period, including this combination in Spike. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Landis et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | reinfection | 27yo female nurse reinfected in December 2020 (B.1.177) after initial infection in March 2020 (B.3). Both cases were mild. Second case also includes N:p.A220V | AY.38, AY.70, AY.57, AY.46, AY.27 | Brehm et al. (2021) | 13455 | 10624,2828 | 1.0 |
| p.D614G | syncytium forma- tion | Slight increase in Vero cell-cell membrane fu- sion assay under infec- tion with VSV pseudo- typed virus. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Kim et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | tissue specific neutralization | The nasal mucosa of Pfizer vaccinees with time course collection was evaluated against VSV pseudotypes: results (only one nasal swab from different previously infected vacinee neutralizing at weeks 3 and 6 against B.1.1.7 and D614G) suggest that vaccinees probably do not elicit an early humoral response detectable at mucosal surfaces even though sera neutralization was observed. They strengthen the hypothesis that some vaccines may not protect against viral acquisition and infection of the oral-nasal region, but may prevent severe disease associated with viral dissemination in the lower respiratory tract. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Planas et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | trafficking | Circulating variant shown in vitro to not have major defects or enhancement of cell sur- face protein trafficking (i.e. Spike cleavage or fusion required for cell entry) | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Barrett et al. (2021) | 13616 | 10759,2854 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|------------------|--|--|----------------------------|-------------------|---------------------|------------------------|
| p.D614G | trafficking | The increased transduction with Spike D614G ranged from 1.3- to 2.4-fold in Caco-2 and Calu-3 cells expressing endogenous ACE2 and from 1.5-to 7.7-fold in A549ACE2 and Huh7.5ACE2 over-expressing ACE2. Although there is minimal difference in ACE2 receptor binding between the D614 and G614 Spike variants, the G614 variant is more resistant to proteolytic cleavage, suggesting a possible mechanism for the increased transduction. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Daniloski et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | trafficking | No change in infectivity (24h) relative to D614G alone in Caco-2 cells, Vero or Calu-3. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Kim et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | trafficking | extasciitilde4x more efficient S2 domain cleavage compared to wild type in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3). | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Kim et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | trafficking | Among S variants tested, the D614G mutant shows the highest cell entry (extasciitide3.5x wild type), as supported by structural and binding analyses. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Ozono et al. (2020) | 13616 | 10759,2854 | 1.0 |
| p.D614G | trafficking | Quantification of the band intensities showed that the P681R mutation, which lies near the proteolytic processing site, caused a small increase in proteolytic processing as measured by a 2-fold decrease in the ratio of S/S2. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Tada et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | trafficking | We report here pseudoviruses carrying SG614 enter ACE2-expressing cells more efficiently than wild type (extasciitilde9-fold). This increased entry correlates with less S1-domain shedding and higher S-protein incorporation into the virion. D614G does not alter S-protein binding to ACE2 or neutralization sensitivity of pseudoviruses. Thus, D614G may increase infectivity by assembling more functional S protein into the virion. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Zhang et l. (2020) | 13616 | 10759,2854 | 1.0 |
| p.D614G | transmissibility | Increased infectivity of the B.1.617 spike was attributed to L452R, which itself caused a 3.5-fold increase in infec- tivity relative to D614G wild type. [In combina- tion with E484Q caused a lower 3-fold increase] | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Tada et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | transmissibility | The combination caused a 3-fold increase in infec- tivity relative to D614G wild type. [compare to 3.5x for L452R alone] | AY.70 | Tada et al. (2021) | 8 | 1,7 | 1.0 |
| p.D614G | transmissibility | Normalized for particle number, on ACE2.293T cells showed that the B.1.617 spike protein was >2-fold increase in infectivity relative to D614G wild type. | AY.70 | Tada et al. (2021) | 8 | 1,7 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------------|--|--|-------------------------------------|-------------------|---------------------|------------------------|
| p.D614G | vaccine neutraliza- tion efficacy | Pseudotyped D614G virus has reduced neutralization activity vs wild type: 1.2x (37 sera Pfizer median 9 days post 2nd dose, 37 sera Moderna median 18 days post 2nd dose). This was NOT significant by ANOVA. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Garcia- Beltran et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | vaccine neutraliza- tion efficacy | 1.4x reduction in neutralization (ID50) in sera 3 weeks after one dose of Pfizer/BioNTech BNT162b2 (up to 5 naive and post infection vaccinees) | AY.70 | Gong et al. (2021) | 8 | 1,7 | 1.0 |
| p.D614G | vaccine neutralization efficacy | Using a lentivirus virus pseudotyped with D614G Spike, sera from vaccinated individuals who received the second dose (9–11 days post-second dose of Pfizer) exhibited a robust neutralizing potential, with a mean NT50 value of 99,000. This was an average of a 2-fold increase, relative to sera drawn from the individuals who received one dose of vaccination—mean NT50 dilution of 51,300. Importantly, a 6-fold increase in mean NT50 dilution was obtained when sera from the first vaccination dose was compared to convalescent sera from cohort with severe disease (NT50 51,000 vs 8,700) 21 to 63 days post-onset. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Kuzmina et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | vaccine neutralization efficacy | Pseudotyped viruses for B.1.617 was 4-fold resistant to neutralization by 6 BNT162b2 vaccine sera 28 days post-booster compared to wild type - a finding that was similar to that of the 3.4-fold resistance of the South Africa B.1.351 variant using the same assay. Neutralization by 3 Moderna vaccine sera 28 days post-booster was 5-fold resistant (vs. 2.2-fold for B.1.351). The resistance of B.1.617 was caused by the L452R and E484Q mutation, based on results from viruses pseudotyped for individual variants within B.1.617. | AY.70 | Tada et al. (2021) | 8 | 1,7 | 1.0 |
| p.D614G | vaccine neutraliza- tion efficacy | Relative to B.1, Epsilon (B.1.417/429) shows 1.74x-2.35x decrease in neutralization efficiency by 18 vaccinee sera (BNT162b2 and mRNA1273). | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Wilhelm et al. (2021) | 13616 | 10759,2854 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|----------------------------|--|--|------------------------|-------------------|---------------------|------------------------|
| p.D614G | vaccinee plasma binding | 1.37x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.56x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.70 | Gong et al. (2021) | 8 | 1,7 | 1.0 |
| p.D614G | vaccinee plasma binding | 1.05x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.16x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Gong et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | vaccinee plasma binding | This variant combination (representing lineage B.1.617) showed a 1.30x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.18x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. [exact variant list not provided in manuscript, is inferred fro common knowledge] | AY.70 | Gong et al. (2021) | 8 | 1,7 | 1.0 |
| p.D614G | viral load | Hamsters infected with SARS-CoV-2 expressing spike(D614G) (G614 virus) produced higher infectious titres in nasal washes and the trachea, but not in the lungs, supporting clinical evidence showing that the mutation enhances viral loads in the upper respiratory tract of COVID-19 patients and may increase transmission. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Plante et al. (2020) | 13616 | 10759,2854 | 1.0 |
| p.D614G | virion structure | Estimated free energy change (ddG) for this variant is 2.5 kcal/mol (i.e. stabilizing relative to wild type) | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Spratt et al. (2021) | 13616 | 10759,2854 | 1.0 |
| p.D614G | virion structure | Negative stain EM shows increased proportion of "one-up" trimer conformation of Spike proteins on the surface of virions, where the up conformation is presumed to be more likely to bind ACE2. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Weissman et al. (2020) | 13616 | 10759,2854 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|--------------------------------|---|--|-------------------------------|----------|------------|-----------|
| Mutations | Sub-category | Function | Lineages | Citation | Depth | Allele | Frequency |
| p.D614G | virion structure | CryoEM shows increased proportion of "one-up" trimer conformation of Spike proteins on the surface of virions, where the up conformation is presumed to be more likely to bind ACE2. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Yurkovetskiy et al. (2020) | 13616 | 10759,2854 | 1.0 |
| p.D614G | virion structure | Based on pseudotyped virus experiments, D614G may increase infectivity by assembling more functional S protein into the virion. | AY.38, AY.70, AY.33, AY.57, AY.46, AY.27 | Zhang et al. (2020) | 13616 | 10759,2854 | 1.0 |
| p.D614G | ACE2 receptor binding affinity | This variant appears twice in the experiments, with slightly different affinities (both extascitildel.2x decrease in binding relative to D614G) using flow cytometry and ACE2 ectodomains-Fc portion IgG complex. | AY.77 | Gong et al. (2021) | 2 | 2 | 1.0 |
| p.D614G | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.51x increase in binding (KD) relative to D614G, mostly due to decreased in "off-rate" a.k.a. dissociation rate (Kdis). | AY.77 | Gong et al. (2021) | 2 | 2 | 1.0 |
| p.D614G | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.5x decrease in binding (KD) relative to D614G. | AY.2, AY.1 | Gong et al. (2021) | 10 | 10 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|--------------------------------|---|--|--------------------|----------------------|------------------------|-------------------------|
| p.D614G | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 2.66x increase in binding (KD) relative to D614G. | Lineages AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.44, AY.113, AY.40, AY.14, AY.65, AY.94, AY.61, AY.113, AY.98.1, AY.110, AY.31, AY.120, AY.39.1, AY.110, AY.31, AY.26, AY.55, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.28, AY.45, AY.16, B1.617.2, AY.92, AY.15, AY.61, AY.106, AY.9.2, AY.107, AY.108, AY.45, AY.40, AY.40, AY.40, AY.40, AY.41, AY.106, AY.9.2, AY.107, AY.108, AY.41, AY.106, AY.9.2, AY.118, AY.106, AY.107, AY.118, AY.107, AY.118, AY.107, AY.118, AY.108, AY.41, AY.116, AY.118, AY.41, AY. | Gong et al. (2021) | Sequence Depth 45203 | Alternate Allele 45202 | Alternate Frequency 1.0 |
| | | | AY.11, AY.34, Contact, US.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|--|--------------------|-------------------|---------------------|------------------------|
| p.D614G | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains- Fc portion IgG complex, this variant combination (representing lineage B.1.617) showed a 1.85x increase in binding (KD) relative to D614G. [exact variant list not provided in manuscript, is inferred fro common knowledge] | AY.35, AY.98 | Gong et al. (2021) | 11 | 11 | 1.0 |
| p.D614G | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains- Fc portion IgG complex, this variant showed a 1.1x decrease in binding (KD) relative to D614G. | AY.6, AY.4.4, AY.77, AY.46.4, AY.35 | Gong et al. (2021) | 31 | 31 | 1.0 |
| p.D614G | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.58x increase in binding (KD) relative to D614G. | AY.4.3 | Gong et al. (2021) | 1 | 1 | 1.0 |
| p.D614G | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.23x decrease in binding (KD) relative to D614G. | AY.5 | Gong et al. (2021) | 18 | 18 | 1.0 |
| p.D614G | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.33x decrease in binding (KD) relative to D614G. | AY.120, AY.117, AY.39.1, AY.106, AY.119, AY.124, AY.77, AY.127, AY.4.2.1, AY.110, AY.119.1, AY.102, AY.36, AY.102, AY.34.1, AY.121.1, AY.20, AY.34.1, AY.39, AY.89, AY.116.1, AY.4.3, AY.4.5, B.1.617.2, AY.92, AY.4, AY.121, AY.114, AY.121, AY.114, AY.121, AY.121, AY.121, AY.121, AY.121, AY.13, AY.14, AY.114, AY.114, AY.114, AY.114, AY.114, AY.115, AY.107, AY.108, AY.108, AY.118, AY.109, AY.113, AY.109, AY.4.4, AY.109, AY.4.5, AY.109, AY.4.6, AY.113, AY.101, AY.4.7, AY.101, AY.4.7, AY.101, AY.4.7, AY.102, AY.113, AY.101, AY.4.7, AY.103, AY.104, AY.113, AY.101, AY.4.7, AY.104, AY.113, AY.101, AY.4.7, AY.102, AY.113, AY.101, AY.4.7, AY.113, AY.101, AY.4.7, AY.102, AY.113, AY.101, AY.4.7, AY.113, AY.101, AY.4.7, AY.113, AY.101, AY.4.7, AY.102, AY.113, AY.101, AY.4.7, AY.113, AY.101, AY.4.7, AY.113, AY.101, AY.4.7, AY.113, AY.113, AY.101, AY.4.7, AY.113, AY.101, AY.4.7, AY.113, AY.101, AY.4.7, AY.113, AY.101, AY.4.7, AY.113, AY.101, AY.4.7, AY.102, AY.113, AY.101, AY.4.7, AY.113, AY.101, AY.4.7, AY.102, AY.103, AY.104, AY.104, AY.113, AY.101, AY.4.7, AY.104, AY.114, AY.115, AY.115, AY.116, AY.113, AY.101, AY.4.7, AY.102, AY.4.7, AY.103, AY.104, AY.113, AY.101, AY.4.7, AY.104, AY.125, AY.29, AY.4.4, AY.125, AY.29, AY.4.4, AY.104, AY.104, AY.104, AY.105, AY.29, AY.4.4, AY.104, AY.105, AY.29, AY.4.4, AY.104, AY.104, AY.105, AY.29, AY.4.4, AY.104, AY.104, AY.104, AY.104, AY.104, AY.104, AY.104, AY.105, AY.29, AY.404, AY.104, | Gong et al. (2021) | 4547 | 4547 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|--------------|--------------------------------|---|--|------------------|----------------------|--------------|-------------------------|
| p.D614G | ACE2 receptor binding affinity | In four cell lines (including 293T-hACE2 cells), this mutation combination increases infectivity vs D614G alone | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.511, AY.111, AY.121.1, AY.20, AY.43, AY.44, AY.121, AY.98, AY.46, AY.122, AY.35, AY.73, AY.44, AY.113, AY.98.1, AY.114, AY.115, AY.116, AY.117, AY.118, AY.119, AY.31, AY.119, AY.31, AY.44, AY.45, AY.106, AY.121, AY.107, AY.108, AY.108, AY.109, AY.109, AY.109, AY.109 | Li et al. (2020) | Sequence Depth 45203 | Allele 45202 | Alternate Frequency 1.0 |
| INFECTION OF | | | AY.11, AY.34, Contact, UY.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|------------|-----------------------|-------------------|---------------------|------------------------|
| p.D614G | convalescent plasma binding | 1.42x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.77 | Gong et al. (2021) | 2 | 2 | 1.0 |
| p.D614G | convalescent plasma binding | 1.33x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.77 | Gong et al. (2021) | 2 | 2 | 1.0 |
| p.D614G | convalescent plasma binding | 2.16x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.2, AY.1 | Gong et al. (2021) | 10 | 10 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|-----------------------------|---|--|--------------------|----------------------|--------------|---------------------|
| p.D614G | convalescent plasma binding | 2.15x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptomonset. | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.511, AY.111, AY.121.1, AY.20, AY.43, AY.44, AY.111, AY.121.1, AY.20, AY.35, AY.44, AY.113, AY.44, AY.17, AY.40, AY.44, AY.17, AY.40, AY.44, AY.113, AY.98, AY.46.6, AY.122, AY.35, AY.46, AY.113, AY.98, AY.46.1, AY.113, AY.98, AY.46.1, AY.113, AY.98, AY.46.6, AY.124, AY.43.3, AY.127, AY.40, AY.41, AY.10, AY.31, AY.26, AY.55, AY.54, AY.28, AY.45, AY.16, B.1.617.2, AY.92, AY.110, AY.31, AY.25, AY.107, AY.108, AY.42, AY.107, AY.108, AY.42, AY.107, AY.108, AY.23, AY.25, AY.104, AY.92, AY.107, AY.108, AY.23, AY.25, AY.106, AY.92, AY.107, AY.108, AY.23, AY.25, AY.106, AY.92, AY.107, AY.108, AY.92, AY.107, AY.108, AY.92, AY.53, AY.25, AY.106, AY.92, AY.53, AY.25, AY.106, AY.92, AY.118, AY.61, AY.106, AY.92, AY.53, AY.54, AY.99, AY.104, AY.92, AY.53, AY.25, AY.106, AY.92, AY.118, AY.61, AY.106, AY.92, AY.53, AY.25, AY.53, AY.25, AY.106, AY.92, AY.118, AY.106, AY.93, AY.47, AY.106, AY.93, AY.47, AY.106, AY.43, AY.40, AY.40, AY.43, AY.40, AY.43, AY.40, | Gong et al. (2021) | Sequence Depth 45203 | Allele 45202 | 1.0 |
| | | | AY.11, AY.34, C AYLA25 , US .13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|--|--------------------|-------------------|---------------------|------------------------|
| p.D614G | convalescent plasma binding | This variant combination (representing lineage B.1.617) showed a 1.22x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptomonset. [exact variant list not provided in manuscript, is inferred fro common knowledge] | AY.35, AY.98 | Gong et al. (2021) | 11 | 11 | 1.0 |
| p.D614G | convalescent plasma binding | No change in Spike binding (relative to D614G alone) by 5 plasma collected 8 months postsymptom-onset. | AY.6, AY.4.4, AY.77, AY.46.4, AY.35 | Gong et al. (2021) | 31 | 31 | 1.0 |
| p.D614G | convalescent plasma binding | 1.08x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.4.3 | Gong et al. (2021) | 1 | 1 | 1.0 |
| p.D614G | convalescent plasma binding | 1.26x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.5 | Gong et al. (2021) | 18 | 18 | 1.0 |
| p.D614G | convalescent plasma binding | No change in Spike binding (relative to D614G alone) by 5 plasma collected 8 months postsymptom-onset. | AY.120, AY.117, AY.39.1, AY.106, AY.119, AY.124, AY.77, AY.127, AY.4.2.1, AY.110, AY.119.1, AY.126, AY.102, AY.36, AY.120.1, AY.121.1, AY.20, AY.34.1, AY.39, AY.45, B.1.617.2, AY.42, AY.14, AY.114, AY.43, AY.45, B.1.617.2, AY.92, AY.14, AY.114, AY.114, AY.85, AY.4.2, AY.107, AY.118, AY.107, AY.118, AY.108, AY.108, AY.108, AY.109, AY.4.6, AY.113, AY.101, AY.4.2, AY.101, AY.4.2, AY.101, AY.4.3, AY.101, AY.4.4, AY.101, AY.4.5, AY.101, AY.4.5, AY.101, AY.4.6, AY.113, AY.101, AY.4.7, AY.101, AY.4.2, AY.101, AY.4.2, AY.103, AY.101, AY.4.2, AY.101, AY.4.2, AY.101, AY.4.2, AY.104, AY.105, AY.107, AY.107, AY.107, AY.107, AY.108, AY.109, AY.4.6, AY.113, AY.101, AY.4.2, AY.104 | Gong et al. (2021) | 4547 | 4547 | |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|-------------------------------|--|--------------|--------------------|-------------------|---------------------|------------------------|
| p.D614G | convalescent plasma escape | Pseudotyped viruses for B.1.618 was 2.5-fold resistant to neutralization by convalescent sera compared to wild type - a finding that was similar to that of the 3-fold resistance of the South Africa B.1.351 variant using the same assay. The resistance of B.1.618 was caused by the E484K mutation, based on results from viruses pseudotyped for individual variants within B.1.618. [details on the convalescent patient sera collection are not abundantly clear in the preprint] | AY.77 | Tada et al. (2021) | 2 | 2 | 1.0 |
| p.D614G | convalescent plasma escape | Pseudotyped viruses for B.1.617 was 2.3-fold resistant to neutralization by convalescent sera compared to wild type - a finding that was similar to that of the 3-fold resistance of the South Africa B.1.351 variant using the same assay. The resistance of B.1.617 was caused by the L452R and E484Q mutation, based on results from viruses pseudotyped for individual variants within B.1.617. [details on the convalescent patient sera collection are not abundantly clear in the preprint] | AY.35, AY.98 | Tada et al. (2021) | 11 | 11 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|--|--|--|-----------------------|----------------------|------------------------|-------------------------|
| p.D614G | Sub-category convalescent plasma escape | Relative to B.1, Epsilon (B.1.417/429) shows 1.74x-2.35x decrease in neutralization efficiency by convalescent plasma [no cohort details provided] | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.44, AY.113, AY.48, AY.122, AY.35, AY.48, AY.122, AY.35, AY.48, AY.111, AY.20, AY.31, AY.40, AY.113, AY.48, AY.122, AY.35, AY.44, AY.13, AY.46, AY.40, AY.14, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.60, AY.106, AY.107, AY.108, AY.40, AY.108, AY.127, AY.110, AY.31, AY.28, AY.45, AY.45, AY.46, AY.428, AY.45, AY.166, AY.121, AY.18, AY.106, AY.107, AY.108, AY.107, AY.108, AY.107, AY.108, AY.107, AY.108, AY.107, AY.108, AY.107, AY.108, AY.23, AY.25, AY.15, AY.23, AY.25, AY.15, AY.16, AY.106, AY.9.2, AY.25, AY.107, AY.108, AY.29, AY.104, AY.99, AY.104, AY.99, AY.104, AY.99, AY.104, AY.99, AY.104, AY.99, AY.104, AY.90, AY.107, AY.108, AY.20, AY.21, AY.108, AY.21, AY.22, AY.23, AY.25, AY.25, AY.25, AY.25, AY.25, AY.25, AY.25, AY.27, AY.21, AY.21, AY.21, AY.21, AY.21, AY.21, AY.21, AY.21, AY.21, AY.22, AY.22, AY.22, AY.23, AY.23, AY.24, AY.2 | Wilhelm et al. (2021) | Sequence Depth 45203 | Alternate Allele 45202 | Alternate Frequency 1.0 |
| | | | AY.11, AY.34, Contact, US.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|------------------|-----------------------------|----------------|--------------|----------|-----------|-----------|
| | _ | | | | Depth | Allele | Frequency |
| p.D614G | humoral response | 27yo female nurse rein- | AY.9.2, AY.9, | Brehm et al. | 10013 | 10012 | 1.0 |
| | durability | fected in December 2020 | AY.68, AY.61, | (2021) | | | |
| | | (B.1.177) after initial in- | AY.9.2.1, | | | | |
| | | fection in March 2020 | AY.21, | | | | |
| | | (B.3), i.e. with a 9 | AY.4.2.1, | | | | |
| | | month interval. Both | AY.67, | | | | |
| | | cases were mild. No | AY.119.1, | | | | |
| | | significant differences in | AY.26, | | | | |
| | | the neutralizing capacity | AY.10, AY.55, | | | | |
| | | of the two linages were | AY.28, AY.74, | | | | |
| | | observed in 4 sera taken | AY.24, AY.73, | | | | |
| | | (1 pre-reinfection, three | B.1.617.2, | | | | |
| | | post-reinfection). Neu- | AY.72, AY.60, | | | | |
| | | tralizing antibody titres | AY.4.2.2, | | | | |
| | | (IC50) before and imme- | AY.64, AY.14, | | | | |
| | | diately after re-infection | AY.65, AY.62, | | | | |
| | | were <300 against both | AY.59, AY.2, | | | | |
| | | strains, and jumped >7x | AY.88, AY.47, | | | | |
| | | upon re-infection. Viral | AY.75, AY.4.2, | | | | |
| | | titres were also higher in | AY.37 | | | | |
| | | the second case. Sec- | | | | | |
| | | ond case also includes | | | | | |
| | | N:p.A220V | | | | | |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | | Alternate |
|--|-------------------------------------|---|--|----------------------|-----------------------|------------------------|-------------------------|
| p.D614G | immunosuppression variant emergence | Studying 94 COVID-19 extended infection cases with genomics April 1 to October 17, 2020, one case developed 23 mutations in a 19 day period, including this combination in Spike. | Lineages AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.44, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.64, AY.42, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.42.1, AY.98, AY.46.4, AY.121, AY.98, AY.46.1, AY.121, AY.98, AY.46.1, AY.121, AY.20, AY.43, AY.44, AY.113, AY.46, AY.42, AY.43, AY.46, AY.42, AY.43, AY.46, AY.46, AY.46, AY.46, AY.46, AY.47, AY.40, AY.113, AY.46, AY.46, AY.46, AY.41, AY.41, AY.46, AY.41, AY.42, AY.43, AY.44, AY.47, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.47, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.47, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.45, AY.47, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.45, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.45, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.45, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.45, AY.45, AY.45, AY.45, AY.45, AY.45, AY.47, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.45, AY.41, AY.41 | Landis et al. (2021) | Sequence Depth 45203 | Alternate Allele 45202 | Alternate Frequency 1.0 |
| The state of the s | | | AY.11, AY.34, Contact, UY.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------|--|--|---------------------|-------------------|---------------------|------------------------|
| p.D614G | reinfection | 27yo female nurse reinfected in December 2020 (B.1.177) after initial infection in March 2020 (B.3). Both cases were mild. Second case also includes N:p.A220V | AY.9.2, AY.9, AY.68, AY.61, AY.9.2.1, AY.21, AY.4.2.1, AY.67, AY.119.1, AY.26, AY.10, AY.55, AY.28, AY.74, AY.24, AY.73, B.1.617.2, AY.72, AY.60, AY.4.2.2, AY.64, AY.14, AY.65, AY.62, AY.59, AY.2, AY.88, AY.47, AY.75, AY.4.2, AY.37 | Brehm et al. (2021) | 10013 | 10012 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | | Alternate |
|------------|--------------|---|---|-------------------|----------------------|------------------------|-------------------------|
| p.D614G | | Function Slight increase in Vero cell-cell membrane fusion assay under infection with VSV pseudotyped virus. | AY.117, AY.3, AY.9, AY.77, AY.21, | Kim et al. (2021) | Sequence Depth 45203 | Alternate Allele 45202 | Alternate Frequency 1.0 |
| INFECT, OF | | | AY.4.6, AY.43, AY.11, AY.34, CAYLAST, UY.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|--------------------------------|---|--|----------------------|-------------|--------------|---------------------|
| p.D614G | tissue specific neutralization | The nasal mucosa of Pfizer vaccinees with time course collection was evaluated against VSV pseudotypes: results (only one nasal swab from different previously infected vacinee neutralizing at weeks 3 and 6 against B.1.1.7 and D614G) suggest that vaccinees probably do not elicit an early humoral response detectable at mucosal surfaces even though sera neutralization was observed. They strengthen the hypothesis that some vaccinees may not protect against viral acquisition and infection of the oral-nasal region, but may prevent severe disease associated with viral dissemination in the lower respiratory tract. | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.20, AY.43, AY.42, AY.35, AY.44, AY.17, AY.40, AY.113, AY.46, AY.42, AY.65, AY.40, AY.113, AY.113, AY.120, AY.39.1, AY.113, AY.120, AY.39.1, AY.110, AY.39.1, AY.110, AY.39.1, AY.110, AY.31, AY.120, AY.39.1, AY.120, AY.39.1, AY.110, AY.31, AY.120, AY.31, AY.121, AY.45, AY.46, AY.42, AY.110, AY.31, AY.120, AY.110, AY.31, AY.121, AY.85, AY.46, AY.47, AY.110, AY.31, AY.110, AY.31, AY.110, AY.31, AY.120, AY.131, AY.140, AY.31, AY.15, AY.16, AY.17, AY.110, AY.31, AY.18, AY.106, AY.107, AY.108, AY.107, AY.108, AY.107, AY.108, AY.107, AY.118, AY.106, AY.107, AY.108, AY.107, AY.108, AY.109, AY.108, AY.109, AY.109, AY.109, AY.108, AY.109, AY.109, AY.109, AY.108, AY.109, AY.109, AY.109, AY.109, AY.109, AY.109, AY.109, AY.109, AY.109, AY.101, AY.110, AY.31, AY.110, AY.31, AY.110, AY.31, AY.120, AY.32, AY.13, AY.140, AY.43, AY.45, AY.40, AY.40, AY.41, AY.109, AY.43, AY.45, AY.41, AY.109, AY.43, AY.45, AY.40, AY.41, AY.109, AY.43, AY.45, AY.40, AY | Planas et al. (2021) | Depth 45203 | Allele 45202 | Frequency 1.0 |
| INTEGRAL | | | AY.11, AY.34, Centact, UY.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|--------------------------|---|--|---------------------------------|-----------------------|------------------------|-------------------------|
| p.D614G | Sub-category trafficking | Circulating variant shown in vitro to not have major defects or enhancement of cell surface protein trafficking (i.e. Spike cleavage or fusion required for cell entry) | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.166.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.44, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.55, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.99.2, AY.51, AY.111, AY.121.1, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.46, AY.40, AY.40, AY.41, AY.65, AY.40, AY.41, AY.65, AY.40, AY.40, AY.40, AY.40, AY.41, AY.62, AY.81, AY.120, AY.31, AY.120, AY.31, AY.120, AY.31, AY.121, AY.121, AY.85, AY.46.8, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.120, AY.31, AY.121, AY.85, AY.66, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.105, AY.61, AY.108, AY.45, AY.107, AY.108, AY.42, AY.92, AY.107, AY.108, AY.42, AY.92, AY.107, AY.108, AY.82, AY.15, AY.23, AY.25, AY.103, AY.105, AY.106, AY.9.2, AY.107, AY.108, AY.82, AY.107, AY.108, AY.83, AY.25, AY.103, AY.105, AY.106, AY.9.2, AY.42, AY.99, AY.43, AY.105, AY.106, AY.91, AY.116, AY.108, AY.81, AY.93, AY.47, AY.109, AY.43, AY.41, AY.116, AY. | Citation Barrett et al. (2021) | Sequence Depth 45203 | Alternate Allele 45202 | Alternate Frequency 1.0 |
| INTEGY, | | | AY.4.6, AY.43, AY.11, AY.34, CAYLAST, LAY.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|--------------|---|--|-------------------------|-------------|--------------|---------------------|
| p.D614G | trafficking | The increased transduction with Spike D614G ranged from 1.3- to 2.4-fold in Caco-2 and Calu-3 cells expressing endogenous ACE2 and from 1.5- to 7.7-fold in A549ACE2 and Huh7.5ACE2 over-expressing ACE2. Although there is minimal difference in ACE2 receptor binding between the D614 and G614 Spike variants, the G614 variant is more resistant to proteolytic cleavage, suggesting a possible mechanism for the increased transduction. | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.43, AY.48, AY.122, AY.35, AY.73, AY.44, AY.113, AY.46, AY.42, AY.40, AY.14, AY.65, AY.94, AY.62, AY.88, AY.46.1, AY.113, AY.98.1, AY.113, AY.98.1, AY.110, AY.31, AY.120, AY.39.1, AY.120, AY.39.1, AY.121, AY.121, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.26, AY.55, AY.54, AY.28, AY.45, AY.16, B.1.617.2, AY.106, AY.121, AY.185, AY.60, AY.107, AY.108, AY.127, AY.110, AY.31, AY.128, AY.127, AY.110, AY.31, AY.128, AY.45, AY.160, AY.107, AY.108, AY.45, AY.108, AY.107, AY.108, AY.107, AY.108, AY.107, AY.108, AY.121, AY.18, AY.29, AY.193, AY.194, AY.104, AY.105, AY.106, AY.9.2.1, AY.116, AY.107, AY.108, AY.25, AY.138, AY.25, AY.25, AY.139, AY.146, AY.198, AY.47, AY.109, AY.484, AY.100, AY.484, AY.100, AY.484, AY.100, AY.494, AY.100, AY.494, AY.100, AY.494, AY.100, AY.494, AY.49 | Daniloski et al. (2021) | Depth 45203 | Allele 45202 | Frequency 1.0 |
| | | | AY.11, AY.34, Contact, UY.13 | | | | CIDGOH [©] |

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| Debit Debi | Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|--|---------------|--------------|---|--|------------|----------|-----------|-----------|
| AY.86, AY.109, | | | No change in infectivity (24h) relative to D614G alone in Caco-2 cells, | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.44, AY.113, AY.98.1, AY.113, AY.98.1, AY.113, AY.98.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.113, AY.98.1, AY.113, AY.98.1, AY.113, AY.98.1, AY.110, AY.31, AY.127, AY.110, AY.31, AY.26, AY.46.6, AY.124, AY.127, AY.110, AY.31, AY.28, AY.45, AY.16, B.1.617.2, AY.110, AY.31, AY.28, AY.45, AY.16, BY.104, AY.105, AY.105, AY.106, AY.92, AY.104, AY.92, AY.104, AY.92, AY.105, AY.105, AY.106, AY.92.1, AY.106, AY.9.2, AY.15, AY.16, AY.106, AY.9.2, AY.25, AY.103, AY.105, AY.104, AY.99, AY.104, AY.99, AY.104, AY.99, AY.105, AY.106, AY.9.2, AY.56, AY.4.2, AY.53, AY.56, AY.4.2, AY.53, AY.56, AY.4.3, AY.66, AY.4.2, AY.53, AY.56, AY.4.4, AY.66, AY.32, AY.56, AY.4.5, AY.16, AY.106, AY.9.2, AY.53, AY.56, AY.4.4, AY.116, AY.106, AY.9.2, AY.53, AY.56, AY.4.5, AY.18, AY.93, AY.47, AY.18, AY.93, AY.47, AY.18, AY.93, AY.47, AY.116, AY.116 | Kim et al. | Depth | Allele | Frequency |
| AY.4.6, AY.43, AY.11, AY.34, | og 1NFEC7/0/- | | | AY.86, AY.109, AY.4.6, AY.43, | | | | |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|--------------|--------------|---|--|-------------------|-----------------------|------------------------|-------------------------|
| p.D614G | Sub-category | Extasciitilde4x more efficient S2 domain cleavage compared to wild type in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3). | Lineages AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.44, AY.17, AY.40, AY.14, AY.65, AY.94, AY.62, AY.88, AY.46.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.110, AY.31, AY.65, AY.94, AY.62, AY.88, AY.46.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.110, AY.31, AY.26, AY.55, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.26, AY.55, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.26, AY.55, AY.41, AY.106, AY.107, AY.108, AY.45, AY.40, AY.107, AY.108, AY.45, AY.107, AY.108, AY.45, AY.108, AY.45, AY.107, AY.108, AY.41, AY.106, AY.92, AY.107, AY.108, AY.41, AY.106, AY.92, AY.103, AY.105, AY.107, AY.108, AY.41, AY.106, AY.92, AY.103, AY.105, AY.107, AY.108, AY.41, AY.106, AY.92, AY.107, AY.108, AY.42, AY.108, AY.43, AY.40, AY.40, AY.40, AY.41, AY.106, AY.41, AY.106, AY.42, AY.43, AY.40, A | Kim et al. (2021) | Sequence Depth 45203 | Alternate Allele 45202 | Alternate Frequency 1.0 |
| INFECTION IN | | | AY.11, AY.34, Centaet, Uy.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------|--|------------|-----------------------|-------------------|---------------------|------------------------|
| p.D614G | trafficking | extasciitilde2x more infectivity than D614G alone in HEK293T- ACE2 cells 48h post- transduction. | AY.77 | Kuzmina et al. (2021) | 2 | 2 | 1.0 |
| p.D614G | trafficking | extasciitilde2x more infectivity than D614G alone in HEK293T- ACE2 cells 48h post- transduction | AY.2, AY.1 | Kuzmina et al. (2021) | 10 | 10 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|-------------------------|--|--|---------------------|----------------------|------------------------|-------------------------|
| p.D614G | Trafficking Trafficking | Among S variants tested, the D614G mutant shows the highest cell entry (extasciitilde3.5x wild type), as supported by structural and binding analyses. | Lineages AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.33, AY.72, AY.44, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.120, AY.31, AY.121.1, AY.20, AY.43, AY.44, AY.113, AY.98, AY.46.1, AY.113, AY.98, AY.46.6, AY.124, AY.43, AY.46.7, AY.40, AY.14, AY.65, AY.94, AY.65, AY.46, AY.120, AY.39.1, AY.113, AY.98.1, AY.110, AY.31, AY.120, AY.39.1, AY.110, AY.31, AY.106, AY.92, AY.15, AY.16, B.1.617.2, AY.92, AY.110, AY.31, AY.106, AY.107, AY.108, AY.42, AY.108, AY.45, AY.106, AY.107, AY.108, AY.41, AY.106, AY.92, AY.110, AY.31, AY.106, AY.92, AY.121, AY.106, AY.92, AY.121, AY.106, AY.107, AY.108, AY.42, AY.108, AY.45, AY.106, AY.42, AY.43, AY.40, AY.41, AY.106, AY.42, AY.43, AY.45, AY.106, AY.42, AY.43, AY.45, AY.106, AY.42, AY.43, AY.46, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.45, AY.45, AY.45, AY.45, AY.47, AY.41, AY.40, AY.41, AY.41, AY.41, AY.42, AY.43, AY.45, AY.47, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.45, AY.47, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.40, AY.44, AY.43, AY.44, AY.45, AY.46, AY.46, AY.47, AY.40, | Ozono et al. (2020) | Sequence Depth 45203 | Alternate Allele 45202 | Alternate Frequency 1.0 |
| | | | AY.11, AY.34, CANTACT, US.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|--------------|--|--|------------------|----------|------------------------|-------------------------|
| p.D614G | trafficking | Quantification of the band intensities showed that the P681R mutation, which lies near the proteolytic processing site, caused a small increase in proteolytic processing as measured by a 2-fold decrease in the ratio of S/S2. | Lineages AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.24, AY.116.1, AY.74, AY.84, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.511, AY.121.1, AY.20, AY.4.3, AY.44, AY.112, AY.40, AY.44, AY.122, AY.35, AY.73, AY.44, AY.17, AY.40, AY.41, AY.65, AY.94, AY.62, AY.88, AY.46.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.110, AY.31, AY.26, AY.55, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.68, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.26, AY.55, AY.48, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.26, AY.55, AY.40, AY.40, AY.41, AY.106, AY.107, AY.108, AY.45, AY.107, AY.108, AY.41, AY.106, AY.107, AY.108, AY.45, AY.107, AY.108, AY.45, AY.107, AY.108, AY.45, AY.107, AY.108, AY.47, AY.108, AY.49, AY.49, AY.40, AY.41, AY.106, AY.41, AY.106, AY.41, AY.106, AY.42, AY.43, AY.45, AY.41, AY.116, AY.78, AY.41, AY.116, AY.78, AY.41, AY.116, AY.78, AY.41, AY.106, AY.42, AY.43, AY.40, AY.40, AY.40, AY.40, AY.40, AY.41, AY.116, AY.78, AY.41, AY.116, AY.78, AY.103, AY.41, AY.104, AY.41, AY.105, AY.41, AY.106, AY.42, AY.43, AY.40, AY | Tada et a (2021) | Depth | Alternate Allele 45184 | Alternate Frequency 1.0 |
| | | | AY.11, AY.34, C entae , US.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|--|--------------|--|--|--------------------|----------------------|------------------------|-------------------------|
| p.D614G | trafficking | We report here pseudoviruses carrying SG614 enter ACE2-expressing cells more efficiently than wild type (extasciitilde9-fold). This increased entry correlates with less S1-domain shedding and higher S-protein incorporation into the virion. D614G does not alter S-protein binding to ACE2 or neutralization sensitivity of pseudoviruses. Thus, D614G may increase infectivity by assembling more functional S protein into the virion. | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.44, AY.17, AY.40, AY.14, AY.65, AY.94, AY.106, AY.107, AY.110, AY.31, AY.120, AY.39.1, AY.110, AY.31, AY.26, AY.55, AY.16, B.1.617.2, AY.92, AY.110, AY.31, AY.23, AY.29, AY.121, AY.85, AY.60, AY.107, AY.108, AY.82, AY.107, AY.108, AY.83, AY.107, AY.108, AY.92, AY.104, AY.9.2, AY.105, AY.107, AY.108, AY.109, | Zhang et 1. (2020) | Sequence Depth 45203 | Alternate Allele 45202 | Alternate Frequency 1.0 |
| INFECTION AND AND AND AND AND AND AND AND AND AN | | | AY.11, AY.34, Centar, Uy.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|------------------|--|--|------------------|----------|--------------|-------------------------|
| p.D614G | transmissibility | Increased infectivity of the B.1.617 spike was attributed to L452R, which itself caused a 3.5-fold increase in infectivity relative to D614G wild type. [In combination with E484Q caused a lower 3-fold increase] | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.46.2, AY.111, AY.121.1, AY.20, AY.43, AY.44, AY.121, AY.98, AY.46, AY.122, AY.35, AY.73, AY.44, AY.113, AY.98, AY.46.6, AY.113, AY.121, AY.65, AY.94, AY.62, AY.88, AY.46.1, AY.113, AY.98, AY.46.1, AY.113, AY.98, AY.46.1, AY.113, AY.98, AY.46.1, AY.113, AY.98, AY.46.1, AY.110, AY.31, AY.121, AY.10, AY.39, AY.45, AY.16, B.1.617.2, AY.92, AY.110, AY.31, AY.26, AY.55, AY.54, AY.28, AY.45, AY.16, B.1.617.2, AY.92, AY.104, AY.92, AY.107, AY.108, AY.23, AY.24, AY.99, AY.104, AY.92, AY.107, AY.108, AY.92, AY.108, AY.93, AY.45, AY.109, AY.40, AY.4 | Tada et a (2021) | Depth | Allele 45202 | Atternate Frequency 1.0 |
| | | | AY.11, AY.34, C AYLA25 , LAY .13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|------------------|---|--------------|--------------------|-------------------|---------------------|------------------------|
| p.D614G | transmissibility | The combination caused a 3-fold increase in infectivity relative to D614G wild type. [compare to 3.5x for L452R alone] | AY.35, AY.98 | Tada et al. (2021) | 11 | 11 | 1.0 |
| p.D614G | transmissibility | Normalized for particle number, on ACE2.293T cells showed that the B.1.617 spike protein was >2-fold increase in infectivity relative to D614G wild type. | AY.35, AY.98 | Tada et al. (2021) | 11 | 11 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|---------------------------------|---|--|------------------------------|-------------|--------------|---------------------|
| p.D614G | vaccine neutralization efficacy | Pseudotyped D614G virus has reduced neutralization activity vs wild type: 1.2x (37 sera Pfizer median 9 days post 2nd dose, 37 sera Moderna median 18 days post 2nd dose). This was NOT significant by ANOVA. | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.44, AY.17, AY.40, AY.14, AY.65, AY.94, AY.62, AY.88, AY.46.1, AY.113, AY.98.1, AY.113, AY.98.1, AY.110, AY.39.1, AY.110, AY.31, AY.26, AY.55, AY.46.6, AY.124, AY.48, AY.46.6, AY.124, AY.43.3, AY.110, AY.31, AY.92, AY.110, AY.31, AY.106, AY.92, AY.107, AY.108, AY.45, AY.106, AY.92, AY.107, AY.108, AY.107, AY.108, AY.107, AY.108, AY.28, AY.107, AY.108, AY.49, AY.107, AY.108, AY.29, AY.29, AY.107, AY.108, AY.29, AY.29, AY.25, AY.30, AY.25, AY.30, AY.30, AY.40, AY. | Garcia-Beltran et al. (2021) | Depth 45203 | Allele 45202 | Frequency 1.0 |
| | | | AY.11, AY.34, Centaet, US.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------------|---|--------------|--------------------|-------------------|---------------------|------------------------|
| p.D614G | vaccine neutraliza- tion efficacy | 1.4x reduction in neutralization (ID50) in sera 3 weeks after one dose of Pfizer/BioNTech BNT162b2 (up to 5 naive and post infection receipees) | AY.35, AY.98 | Gong et al. (2021) | 11 | 11 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|---------------------------------|--|--|-----------------------|-------------|--------------|---------------------|
| p.D614G | vaccine neutralization efficacy | Using a lentivirus virus pseudotyped with D614G Spike, sera from vaccinated individuals who received the second dose (9-11 days post-second dose of Pfizer) exhibited a robust neutralizing potential, with a mean NT50 value of 99,000. This was an average of a 2-fold increase, relative to sera drawn from the individuals who received one dose of vaccination—mean NT50 dilution of 51,300. Importantly, a 6-fold increase in mean NT50 dilution was obtained when sera from the first vaccination dose was compared to convalescent sera from cohort with severe disease (NT50 51,000 vs 8,700) 21 to 63 days post-onset. | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.43, AY.48, AY.122, AY.35, AY.73, AY.44, AY.113, AY.48, AY.122, AY.35, AY.73, AY.44, AY.113, AY.46, AY.14, AY.65, AY.94, AY.65, AY.94, AY.62, AY.88, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.120, AY.39.1, AY.120, AY.39.1, AY.120, AY.39.1, AY.110, AY.31, AY.120, AY.39.1, AY.121, AY.85, AY.46, AY.42, AY.110, AY.31, AY.127, AY.110, AY.31, AY.127, AY.110, AY.31, AY.127, AY.110, AY.31, AY.127, AY.110, AY.31, AY.128, AY.45, AY.16, B.1.617.2, AY.92, AY.110, AY.31, AY.127, AY.110, AY.31, AY.128, AY.45, AY.16, B.1.617.2, AY.110, AY.31, AY.110, AY.31, AY.127, AY.110, AY.31, AY.128, AY.129, AY.121, AY.85, AY.45, AY.16, AY.104, AY.92, AY.105, AY.106, AY.92, AY.107, AY.108, AY.107, AY.108, AY.47, AY.108, AY.49, AY.109, AY.49, AY.40, AY.41, AY.106, AY.42, AY.118, AY.106, AY.43, AY.45, AY.41, AY.118, AY.42, AY.118, AY.43, AY.44, AY.40, AY.44, AY.43, AY.45, AY.45, AY.45, AY.45, AY.45, AY.45, AY.45, AY.45, AY.45, AY.46, AY.47, AY.48, AY.49, AY.49 | Kuzmina et al. (2021) | Depth 45203 | Allele 45202 | Frequency 1.0 |
| INFECTION | | | AY.11, AY.34, Contact, U.S.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------------|---|--------------|-----------------------|-------------------|---------------------|------------------------|
| p.D614G | vaccine neutralization efficacy | This variant showed only minor in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype). | AY.77 | Kuzmina et al. (2021) | 2 | 2 | 1.0 |
| p.D614G | vaccine neutraliza- tion efficacy | This variant showed only minor in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype). | AY.2, AY.1 | Kuzmina et al. (2021) | 10 | 10 | 1.0 |
| p.D614G | vaccine neutralization efficacy | Pseudotyped viruses for B.1.618 was 2.7-fold resistant to neutralization by 6 BNT162b2 vaccine sera 28 days post-booster compared to wild type - a finding that was similar to that of the 3.4-fold resistance of the South Africa B.1.351 variant using the same assay. Neutralization by 3 Moderna vaccine sera 28 days post-booster was 3-fold resistant (vs. 2.2-fold for B.1.351). The resistance of B.1.618 was caused by the E484K mutation, based on results from viruses pseudotyped for individual variants within B.1.618. | AY.77 | Tada et al. (2021) | 2 | 2 | 1.0 |
| p.D614G | vaccine neutralization efficacy | Pseudotyped viruses for B.1.617 was 4-fold resistant to neutralization by 6 BNT162b2 vaccine sera 28 days post-booster compared to wild type - a finding that was similar to that of the 3.4-fold resistance of the South Africa B.1.351 variant using the same assay. Neutralization by 3 Moderna vaccine sera 28 days post-booster was 5-fold resistant (vs. 2.2-fold for B.1.351). The resistance of B.1.617 was caused by the L452R and E484Q mutation, based on results from viruses pseudotyped for individual variants within B.1.617. | AY.35, AY.98 | Tada et al. (2021) | 11 | 11 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|--|---|---|---------------------------------|-----------------------|------------------------|-------------------------|
| p.D614G | Sub-category vaccine neutralization efficacy | Relative to B.1, Epsilon (B.1.417/429) shows 1.74x-2.35x decrease in neutralization efficiency by 18 vaccinee sera (BNT162b2 and mRNA1273). | Lineages AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.44, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.42.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.43, AY.48, AY.121, AY.40, AY.14, AY.65, AY.94, AY.62, AY.88, AY.46.1, AY.113, AY.98.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.113, AY.98.1, AY.121, AY.85, AY.46.6, AY.124, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.39.1, AY.71, AY.68, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.39.1, AY.71, AY.68, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.39.1, AY.108, AY.45, AY.16, B.1.617.2, AY.92, AY.15, AY.16, BY.60, AY.104, AY.92, AY.15, AY.16, AY.105, AY.106, AY.92, AY.107, AY.108, AY.82, AY.15, AY.16, AY.106, AY.92, AY.17, AY.108, AY.82, AY.18, AY.99, AY.104, AY.92, AY.25, AY.105, AY.104, AY.99, AY.104, AY.92, AY.25, AY.105, AY.106, AY.92.1, AY.107, AY.108, AY.27, AY.108, AY.28, AY.15, AY.29, AY.15, AY.16, AY.106, AY.92.1, AY.18, AY.99, AY.104, AY.99, AY.104, AY.99, AY.105, AY.106, AY.92.1, AY.107, AY.108, AY.25, AY.15, AY.16, AY.106, AY.92.1, AY.18, AY.99, AY.104, AY.99, AY.104, AY.99, AY.104, AY.99, AY.104, AY.99, AY.105, AY.106, AY.92.1, AY.107, AY.108, AY.25, AY.25, AY.15, AY.16.1, AY.106, AY.92.1, AY.107, AY.108, AY.25, AY.25, AY.15, AY.17, AY.109, AY.40, | Citation Wilhelm et al. (2021) | Sequence Depth 45203 | Alternate Allele 45202 | Alternate Frequency 1.0 |
| INTEGT/O | | | AY.4.6, AY.43, AY.11, AY.34, CONTACT, US.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------------|---|------------|----------------------------|-------------------|---------------------|------------------------|
| p.D614G | vaccine neutraliza- tion efficacy | No significant change in virus neutralzation by 18 Pfizer two dose vaccinee sera compared to B.1.1.7. [results without including the used mutation A27S likely generalizable, as this is not a lineage defining mutation] | AY.5 | Zuckerman et al. (2021) | 18 | 18 | 1.0 |
| p.D614G | vaccinee plasma binding | 1.16x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.06x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.77 | Gong et al. (2021) | 2 | 2 | 1.0 |
| p.D614G | vaccinee plasma binding | 1.14x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.09x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.77 | Gong et al. (2021) | 2 | 2 | 1.0 |
| p.D614G | vaccinee plasma binding | 1.76x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.75x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.2, AY.1 | Gong et al. (2021) | 10 | 10 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Allele | Alternate |
|-----------|-------------------------|--|--|--------------------|-------------|--------------|---------------|
| p.D614G | vaccinee plasma binding | 1.05x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.16x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.20, AY.43, AY.42, AY.35, AY.44, AY.17, AY.40, AY.113, AY.46, AY.42, AY.65, AY.40, AY.113, AY.113, AY.113, AY.113, AY.113, AY.120, AY.39.1, AY.110, AY.39.1, AY.110, AY.39.1, AY.110, AY.39.1, AY.110, AY.31, AY.120, AY.31, AY.121, AY.45, AY.46, AY.45, AY.16, B1.617.2, AY.92, AY.110, AY.31, AY.106, AY.42, AY.107, AY.108, AY.45, AY.16, B1.617.2, AY.110, AY.31, AY.26, AY.45, AY.46, AY.47, AY.110, AY.31, AY.106, AY.47, AY.106, AY.49, AY.41, AY.106, AY.41, AY.106, AY.42, AY.107, AY.108, AY.45, AY.106, AY.41, AY.106, AY.42, AY.107, AY.108, AY.45, AY.41, AY.106, AY.42, AY.107, AY.108, AY.45, AY.40, AY.41, AY.106, AY.42, AY.108, AY.45, AY.41, AY.106, AY.41, AY.107, AY.108, AY.45, AY.40, AY.41, AY.108, AY.41, AY.106, AY.42, AY.108, AY.45, AY.40, AY.40, AY.41, AY.106, AY.42, AY.43, AY.40, AY.40, AY.41, AY.106, AY.42, AY.43, AY.45, AY.40, AY.41, AY.106, AY.43, AY.45, AY.40, AY.41, AY.106, AY.43, AY.40, A | Gong et al. (2021) | Depth 45203 | Allele 45202 | Frequency 1.0 |
| | | | AY.11, AY.34, Contact, UY.13 | | | | CIDGOH ® |

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| Mutations | Sub-catego | ry | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|---------------------|--------|--|--|--------------------|-------------------|---------------------|------------------------|
| p.D614G | vaccinee binding | plasma | This variant combination (representing lineage B.1.617) showed a 1.30x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.18x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. [exact variant list not provided in manuscript, is inferred fro common knowledge] | AY.35, AY.98 | Gong et al. (2021) | 11 | 11 | 1.0 |
| p.D614G | vaccinee binding | plasma | 1.23x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.1x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.6, AY.4.4, AY.77, AY.46.4, AY.35 | Gong et al. (2021) | 31 | 31 | 1.0 |
| p.D614G | vaccinee binding | plasma | 1.23x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.37x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.4.3 | Gong et al. (2021) | 1 | 1 | 1.0 |
| p.D614G | vaccinee binding | plasma | 1.14x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.11x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.5 | Gong et al. (2021) | 18 | 18 | 1.0 |



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| Mutations | Sub-categor | У | Function | Lineages | Citatio: | n | Sequence | Allele | Alternate |
|-----------|------------------|--------|---|---|-------------|-------|------------|-------------|---------------|
| p.D614G | vaccinee binding | plasma | 1.16x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.02x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.120, AY.117, AY.39.1, AY.106, AY.119, AY.124, AY.77, AY.127, AY.4.2.1, AY.110, AY.119.1, AY.110, AY.119.1, AY.126, AY.102, AY.36, AY.120.1, AY.111, AY.121.1, AY.20, AY.34.1, AY.39, AY.89, AY.116.1, AY.4.3, AY.4.5, B.1.617.2, AY.92, AY.121, AY.4.4, AY.114, AY.85, AY.4.2.2, AY.92, AY.116, AY.114, AY.85, AY.4.116, AY.4.116, AY.4.116, AY.4.2, AY.100, AY.4.3, AY.100, AY.4.3, AY.100, AY.4.3, AY.100, AY.4.3, AY.101, AY.101, AY.101, AY.4.4, AY.109, AY.4.5, AY.101, AY.4.5, AY.101, AY.4.6, AY.113, AY.101, AY.4.6, AY.113, AY.101, AY.34, AY.101, AY.34, AY.102, AY.4.2, AY.104, AY.105, AY.29, AY.4.2, AY.104 | Gong (2021) | et al | Depth 4547 | Allele 4547 | Frequency 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|--------------|--|--|----------------------|----------------------|--------------|---------------------|
| p.D614G | viral load | Hamsters infected with SARS-CoV-2 expressing spike(D614G) (G614 virus) produced higher infectious titres in nasal washes and the trachea, but not in the lungs, supporting clinical evidence showing that the mutation enhances viral loads in the upper respiratory tract of COVID-19 patients and may increase transmission. | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.44, AY.17, AY.40, AY.14, AY.65, AY.94, AY.65, AY.10, AY.39.1, AY.110, AY.31, AY.127, AY.110, AY.31, AY.26, AY.55, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.68, AY.45, AY.16, B.1.617.2, AY.92, AY.110, AY.31, AY.106, AY.92.1, AY.107, AY.108, AY.45, AY.106, AY.92.1, AY.107, AY.108, AY.45, AY.106, AY.107, AY.108, AY.40, AY.107, AY.108, AY.41, AY.106, AY.92.1, AY.118, AY.106, AY.92.1, AY.118, AY.106, AY.93, AY.45, AY.40, AY.41, AY.106, AY.43, AY.40, AY.41, AY.116, AY.78, AY.107, AY.118, AY.107, AY.118, AY.108, AY.41, AY.109, AY.42, AY.118, AY.43, AY.40, AY.40, AY.41, AY.116, AY.78, AY.117, AY.116, AY.78, AY.118, AY.117, AY.118, AY.11 | Plante et al. (2020) | Sequence Depth 45203 | Allele 45202 | Frequency 1.0 |
| | | | AY.11, AY.34, Contact, US.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|------------------|--|--|----------------------|----------|--------------|---------------------|
| p.D614G | virion structure | Estimated free energy change (ddG) for this variant is 2.5 kcal/mol (i.e. stabilizing relative to wild type) | AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.20, AY.43, AY.42, AY.35, AY.44, AY.17, AY.40, AY.113, AY.121.1, AY.20, AY.44, AY.17, AY.40, AY.113, AY.113, AY.121, AY.113, AY.120, AY.39.1, AY.113, AY.120, AY.39.1, AY.110, AY.39.1, AY.110, AY.31, AY.120, AY.31, AY.121, AY.45, AY.46, AY.45, AY.16, B.1.617.2, AY.92, AY.110, AY.31, AY.110, AY.31, AY.26, AY.23, AY.29, AY.110, AY.31, AY.106, AY.42, AY.106, AY.43, AY.45, AY.40, AY.40, AY.41, AY.106, AY.42, AY.107, AY.108, AY.45, AY.106, AY.41, AY.106, AY.42, AY.107, AY.108, AY.45, AY.40, AY.41, AY.106, AY.41, AY.106, AY.42, AY.107, AY.108, AY.45, AY.108, AY.45, AY.40, AY.41, AY.106, AY.41, AY.107, AY.108, AY.41, AY.108, AY.42, AY.108, AY.45, AY.40, AY.41, AY.106, AY.41, AY.107, AY.108, AY.45, AY.40, AY.40, AY.40, AY.41, AY.106, AY.42, AY.43, AY.45, AY.40, AY.40, AY.41, AY.106, AY.42, AY.43, AY.45, AY.40, AY.41, AY.106, AY.43, AY.40, AY.40, AY.41, AY.106, AY.43, AY.40, AY.41, AY.106, AY.43, AY.40, AY.40, AY.41, AY.106, AY.43, AY.40, AY.41, AY.106, AY.43, AY.40, | Spratt et al. (2021) | 45203 | Allele 45202 | Frequency 1.0 |
| | | | AY.11, AY.34, Contact, US.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|-------------------------------|---|--|----------------------------------|-----------------------|------------------------|-------------------------|
| p.D614G | Sub-category virion structure | Negative stain EM shows increased proportion of "one-up" trimer conformation of Spike proteins on the surface of virions, where the up conformation is presumed to be more likely to bind ACE2. | Lineages AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.44, AY.113, AY.40, AY.14, AY.65, AY.94, AY.61, AY.113, AY.98.1, AY.110, AY.31, AY.120, AY.39.1, AY.110, AY.31, AY.26, AY.55, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.28, AY.45, AY.16, B1.617.2, AY.92, AY.15, AY.61, AY.106, AY.9.2, AY.107, AY.108, AY.45, AY.40, AY.40, AY.40, AY.40, AY.41, AY.106, AY.9.2, AY.107, AY.108, AY.41, AY.106, AY.9.2, AY.118, AY.107, AY.118, AY.107, AY.118, AY.107, AY.118, AY.108, AY.41, AY.116, AY.78, AY.118, AY.41, AY.116, AY.78, AY.19, AY.41, AY.116, AY.78, AY.41, AY.116, AY.78, AY.19, AY.41, AY.116, AY.78, AY.41, AY.116, AY.78, AY.41, AY.118, AY.42, AY.43, AY.44, AY.43 | Citation Weissman et al. (2020) | Sequence Depth 45203 | Alternate Allele 45202 | Alternate Frequency 1.0 |
| | | | AY.11, AY.34, Contact, UY.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|------------------|--|--|----------------------------|-------------|--------------|---------------------|
| p.D614G | virion structure | CryoEM shows increased proportion of "one-up" trimer conformation of Spike proteins on the surface of virions, where the up conformation is presumed to be more likely to bind ACE2. | AY.117, AY.3, AY.9, AY.77, AY.91, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.22, AY.44, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.43, AY.48, AY.122, AY.35, AY.44, AY.113, AY.40, AY.41, AY.65, AY.94, AY.62, AY.88, AY.46.1, AY.113, AY.98.1, AY.113, AY.98.1, AY.110, AY.31, AY.120, AY.39.1, AY.113, AY.98.1, AY.110, AY.31, AY.120, AY.39.1, AY.110, AY.31, AY.100, AY.31, AY.106, AY.92, AY.107, AY.108, AY.42, AY.99, AY.104, AY.43, AY.105, AY.61, AY.106, AY.9.2.1, AY.18, AY.67, AY.108, AY.107, AY.108, AY.107, AY.108, AY.22, AY.53, AY.25, AY.103, AY.104, AY.105, AY.61, AY.106, AY.9.2.1, AY.18, AY.61, AY.106, AY.9.2.1, AY.18, AY.106, AY.9.2.1, AY.18, AY.106, AY.9.2.1, AY.18, AY.107, AY.108, AY.42, AY.193, AY.45, AY.104, AY.43, AY.40, AY.40, AY.40, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.43, AY.44, AY.43, AY.45, AY.45, AY.45, AY.47, AY.106, AY.49, AY.49, AY.40, AY.41, AY.43, AY.40, AY.43, AY.40, AY.40, AY.43, AY.40, AY.40, AY.43, AY.40, AY.43, AY.44, AY.43, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.43, AY.44, AY.43, AY.43, AY.44, AY.43, AY.44, AY.43, | Yurkovetskiy et al. (2020) | Depth 45203 | Allele 45202 | Frequency 1.0 |
| | | | AY.11, AY.34, C entals , Ley .13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|--------------|-------------------------------|---|---|---------------------|----------------------|------------------------|-------------------------|
| p.D614G | Sub-category virion structure | Based on pseudotyped virus experiments, D614G may increase infectivity by assembling more functional S protein into the virion. | Lineages AY.117, AY.3, AY.9, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.116.1, AY.84, AY.24, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.44, AY.17, AY.40, AY.113, AY.48, AY.122, AY.35, AY.73, AY.44, AY.113, AY.46, AY.113, AY.48, AY.121, AY.85, AY.46, AY.113, AY.98, AY.46, AY.113, AY.98, AY.46, AY.113, AY.98, AY.46, AY.113, AY.113, AY.98, AY.41, AY.113, AY.98, AY.45, AY.106, AY.124, AY.43, AY.107, AY.110, AY.31, AY.26, AY.55, AY.54, AY.28, AY.45, AY.16, BI.617.2, AY.92, AY.107, AY.108, AY.127, AY.110, AY.31, AY.26, AY.45, AY.16, AY.106, AY.92, AY.107, AY.108, AY.109, AY.107, AY.108, AY.107, AY.108, AY.109, AY.107, AY.108, AY.108, AY.109, | Zhang et al. (2020) | Sequence Depth 45203 | Alternate Allele 45202 | Alternate Frequency 1.0 |
| INFECTION IN | | | AY.11, AY.34, Contact, UY.13 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------|--|------------------------------------|---------------------|-------------------|---------------------|------------------------|
| p.P681R | trafficking | This mutation in the first base of the furin clevage site maintains the RXXR recognition motif, and is presumed to enhance cleavage based on the removal of a proline-directed phosphotase recognition site at \$680. In a homologuous site in Infectious Bronchitis Virus (IBV, Gammacoronaviruses), abolition of \$680 phosphorylation improves furin cleavage (and presumably cell entry). [Inference from similar positively charged substitution P681H actually described in the work] | AY.65, AY.114, AY.88, AY.127 | Maaroufi (2021) | 214 | 9,60,24,12,109 | |
| p.P681R | trafficking | Quantification of the band intensities showed that the P681R mutation, which lies near the proteolytic processing site, caused a small increase in proteolytic processing as measured by a 2-fold decrease in the ratio of S/S2. | AY.65, AY.114, AY.88, AY.127 | Tada et al. (2021) | 214 | 9,60,24,12,109 | 1.0 |
| p.P681R | virion structure | The Ratio of S2 (processed Spike) to full length Spike is higher for this mutation, due to a drop in the full length Spike measured, suggesting that this mutation compensates for decreased Spike production by improved proteolytic processing. [PG: Inferred by conservative AA substitution of described P681H] | AY.65, AY.114, AY.88, AY.127 | Tada et al. (2021) | 214 | 9,60,24,12,109 | 1.0 |
| p.P681R | symptom prevalence | Gross examination of 3+3 hamster lung specimens showed pronounced congestion and hemorrhages on days 5 and 7 post-infection in the case of the B.1.617.1 as compared with the B.1. The lung lesions with the B.1 variant were minimal to mild whereas with B.1.617.1 they were moderate. For B.1 pneumonic changes were minimal to mild (inflammatory cell infiltration, focal consolidation and mild congestion). The pronounced changes (moderate to severe) with mononuclear infiltration in the alveolar interstitial septal thickening, consolidation and pneumocyte hyperplasia were observed with B.1.617.1 variant consistently. | AY.70, AY.35, AY.98 | Yadav et al. (2021) | 19 | 19 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------|---|----------|-----------------------|-------------------|---------------------|------------------------|
| p.P681R | trafficking | This variant combination shows a extasciitilde3x decrease in cell entry efficiency (RLU measurement in 293T cells) compared to D614G, significantly less of a decrease than any B.1.617 lineage variants alone, suggesting a synergistic effect on cell entry while maintaining known immunity esacpe mutants | AY.77 | Ferriera et al (2021) | 2 | 2 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------|---|--|-----------------|-------------------|--------------------------|------------------------|
| p.P681R | trafficking | This mutation in the first base of the furin clevage site maintains the RXXR recognition motif, and is presumed to enhance cleavage based on the removal of a proline-directed phosphotase recognition site at \$680. In a homologuous site in Infectious Bronchitis Virus (IBV, Gammacoronaviruses), abolition of \$680 phosphorylation improves furin cleavage (and presumably cell entry). [Inference from similar positively charged substitution P681H actually described in the work] | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.78, AY.101, AY.79, AY.40, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.46.2, AY.119, AY.46.4, AY.42.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.38, AY.44, AY.17, AY.40, AY.14, AY.94, AY.62, AY.66, AY.46.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.104, AY.62, AY.66, AY.46.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.104, AY.62, AY.66, AY.46.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.104, AY.46.1, AY.113, AY.98, AY.46.6, AY.46.1, AY.113, AY.98, AY.46.6, AY.46.1, AY.113, AY.98, AY.46.6, AY.124, AY.43.3, AY.110, AY.39.1, AY.71, AY.85, AY.66, AY.410, AY.104, AY.92, AY.104, AY.92, AY.104, AY.92, AY.105, AY.106, AY.92, AY.107, AY.108, AY.106, AY.92, AY.107, AY.108, AY.21, AY.107, AY.108, AY.22, AY.23, AY.23, AY.25, AY.33, AY.25, AY.33, AY.25, AY.33, AY.27, AY.40, AY.41, AY.116, AY.116 | Maaroufi (2021) | 58592 | 58537,3,29 58537,3,29 | 1.0 |
| INTEGRAL | | | AY.4.6, AY.43, AY.11, AY.34, C ontact , Us AY.13, AY.46 | | | | CIDGOH ® |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------|--|--|--------------------|-------------------|---------------------|------------------------|
| p.P681R | trafficking | Quantification of the band intensities showed that the P681R mutation, which lies near the proteolytic processing site, caused a small increase in proteolytic processing as measured by a 2-fold decrease in the ratio of S/S2. | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.84, AY.16.1, AY.74, AY.84, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.46.2, AY.119, AY.46.4, AY.121.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.38, AY.44, AY.17, AY.40, AY.14, AY.94, AY.62, AY.46.1, AY.113, AY.98, AY.62, AY.46.1, AY.113, AY.94, AY.62, AY.46.1, AY.113, AY.94, AY.62, AY.46.1, AY.110, AY.31, AY.120, AY.39.1, AY.104, AY.40, AY.105, AY.406, AY.107, AY.108, AY.407, AY.108, AY.407, AY.108, AY.407, AY.108, AY.407, AY.108, AY.407, AY.108, AY.407, AY.108, AY.107, AY.108, AY.207, AY. | Tada et al. (2021) | 58590 | 58535,3,29 | 1.0 |
| | | | AY.4.6, AY.43, AY.11, AY.34, C ontact , Us AY.13, AY.46 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|------------------|---|------------------------|---------------------|-------------------|---------------------|------------------------|
| p.P681R | transmissibility | Normalized for particle number, on ACE2.293T cells showed that the B.1.617 spike protein was >2-fold increase in infectivity relative to D614G wild type. | AY.70, AY.35, AY.98 | Tada et al. (2021) | 19 | 19 | 1.0 |
| p.P681R | viral load | In 9 infected ham- sters each for B.1 and B.1.617.1, no significant change in viral load or subgenomic RNA levels were detected | AY.70, AY.35, AY.98 | Yadav et al. (2021) | 19 | 19 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | | Alternate |
|--|------------------|---|---|--------------------|-------------|-----------------------------|---------------------|
| p.P681R | virion structure | The Ratio of S2 (processed Spike) to full length Spike is higher for this mutation, due to a drop in the full length Spike measured, suggesting that this mutation compensates for decreased Spike production by improved proteolytic processing. [PG: Inferred by conservative AA substitution of described P681H] | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.46.4, AY.42.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.21.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.38, AY.44, AY.17, AY.40, AY.14, AY.94, AY.62, AY.66, AY.14, AY.113, AY.98.1, AY.110, AY.39.1, AY.113, AY.98.1, AY.110, AY.31, AY.62, AY.66, AY.46.6, AY.46.1, AY.113, AY.94, AY.65, AY.66, AY.46.1, AY.113, AY.94, AY.67, AY.106, AY.107, AY.108, AY.46, AY.107, AY.108, AY.40, AY.108, AY.107, AY.108, AY.108, AY.107, AY.108, AY.108, AY.107, AY.108, AY.108, AY.107, AY.108, AY.107, AY.108, AY.108, AY.107, AY.108, AY.108, AY.107, AY.108, AY.108, AY.109, AY.101, AY.108, AY.109, AY.101, AY.108, AY.109, AY.101, AY.108, AY.109, AY.101, AY.108, AY.109, AY.109, AY.109, AY.118, AY.27, AY.60, AY.109, AY.118, AY.21, AY.31, AY.32, AY.33, AY.34, AY.40, | Tada et al. (2021) | Depth 58592 | Alternate Allele 58537,3,29 | Frequency 1.0 |
| INFECTION OF THE PROPERTY OF T | | | AY.4.6, AY.43, AY.11, AY.34, C ontact , Us AY.13, AY.46 | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | | | |
|---------------------|--|---|---|--------------------|---------------------------|-----------------------------|--------------------------|
| Mutations p.T95I | Sub-category ACE2 receptor binding affinity | Function Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.33x decrease in binding (KD) relative to D614G. | Lineages AY.120, AY.117, AY.39.1, AY.106, AY.119, AY.124, AY.77, AY.127, AY.4.2.1, AY.110, AY.119.1, AY.126, AY.102, AY.36, AY.120.1, AY.111, AY.121.1, AY.20, AY.34.1, AY.39, AY.4.5, B.1.617.2, AY.92, AY.4.4, AY.114, AY.4.3, AY.4.5, B.1.617.2, AY.92, AY.4.4, AY.114, AY.85, AY.4.2.2, AY.5.3, AY.107, AY.1 AY.116, AY.4.3, AY.108, AY.118, AY.109, AY.4.4.6, AY.113, AY.101, AY.4.4, AY.113, AY.101, AY.34, AY.101, AY.34, AY.101, AY.34, AY.101, AY.34, AY.105, | Gong et al. (2021) | Sequence Depth 4140 | Alternate Allele 2773 | Alternate Frequency 0.67 |



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| onvalescent plasma inding | No change in Spike bind- | AY.120, | Gong | et al. | Depth 4140 | Allele 2773 | Frequency 0.67 |
|------------------------------|---|--|--------|--------|---------------|----------------|----------------|
| | ing (relative to D614G alone) by 5 plasma collected 8 months postsymptom-onset. | AY.117, AY.39.1, AY.106, AY.119, AY.124, AY.77, AY.127, AY.4.2.1, AY.110, AY.119.1, AY.126, AY.1102, AY.36, AY.120.1, AY.111, AY.20, AY.34.1, AY.39, AY.34.1, AY.39, AY.4.5, B.1.617.2, AY.92, AY.4.4, AY.121, AY.4.4, AY.114, AY.85, AY.4.5, B.1.617.2, AY.92, AY.4.7, AY.114, AY.114, AY.85, AY.4.7, AY.114, AY.114, AY.114, AY.114, AY.116, AY.4.2, AY.107, AY.1, AY.108, AY.108, AY.108, AY.109, AY.4.3, AY.109, AY.4.3, AY.109, AY.4.6, AY.113, AY.101, | (2021) | | | | |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|-------------------------------|--|--|--------------------|-------------------|---------------------|------------------------|
| p.T95I | vaccinee plasma binding | 1.16x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.02x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.120, AY.117, AY.39.1, AY.106, AY.119, AY.124, AY.77, AY.127, AY.4.2.1, AY.110, AY.119.1, AY.126, AY.102, AY.36, AY.120.1, AY.111, AY.211.1, AY.20, AY.34.1, AY.39, AY.89, AY.116.1, AY.4.3, B.1.617.2, AY.92, AY.4, AY.121, AY.4.3, AY.4.5, B.1.617.2, AY.93, AY.114, AY.121, AY.121, AY.121, AY.121, AY.121, AY.13, AY.4.5, B.1.617.2, AY.92, AY.4.4, AY.114, AY.114, AY.116, AY.4.2, AY.108, AY.4.3, AY.4.3, AY.4.3, AY.4.3, AY.4.3, AY.4.3, AY.4.3, AY.101, AY.4.3, AY.100, AY.4.3, AY.101, AY.4.3, AY.101, AY.4.3, AY.101, AY.4.4, AY.101, AY.4.5, AY.102, AY.4.6, AY.103, AY.4.6, AY.104, AY.104, AY.105, AY.4.6, AY.106, AY.107, AY.108, AY.108, AY.109, AY.4.6, AY.101, AY.4.6, AY.101, AY.4.7, AY.101, AY.4.7, AY.101, AY.4.8, AY.101, AY.4.9, AY.101, AY.4.9, AY.101, AY.4.9, AY.102, AY.103, AY.101, AY.4.9, AY.104, AY.104, AY.104, AY.104, AY.104, AY.105, AY.106, AY.107, AY.107, AY.108, AY.108, AY.108, AY.109, AY.4.6, AY.101, AY.4.6, AY.101, AY.4.7, AY.104, AY.1 | Gong et al. (2021) | 4140 | 2773 | 0.67 |
| p.K458N | convalescent plasma escape | Resistant to a pool of 10 convalescent sera (but less than 4x, a typical threshold for definition of escape) | AY.46.1 | Li et al. (2020) | 4 | 4 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|--|---|---|---|------------------------|----------------------|------------------------|-------------------------|
| Mutations p.R158G | monoclonal antibody serial passage escape | Escape mutation against Spike N terminal domain antigenic supersite i mAb S2X28 | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.24, AY.116.1, AY.74, AY.84, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.111, AY.20, AY.41, AY.121.1, AY.20, AY.41, AY.121.1, AY.20, AY.41, AY.121, AY.20, AY.43, AY.121, AY.111, AY.121.1, AY.20, AY.48, AY.122, AY.35, AY.38, AY.48, AY.120, AY.35, AY.38, AY.44, AY.17, AY.40, AY.14, AY.65, AY.94, AY.66, AY.124, AY.43, AY.120, AY.39.1, AY.120, AY.31, AY.26, AY.45, AY.16, B1.617.2, AY.92, AY.104, AY.92, AY.105, AY.105, AY.105, AY.61, | McCallum et al. (2021) | Sequence Depth 58019 | Alternate Allele 58010 | Alternate Frequency 1.0 |
| | | | AY.92, AY.121, AY.85, AY.60, AY.107, AY.108, AY.82, AY.15, AY.75, AY.33, AY.23, AY.29, AY.4.2, AY.99, AY.104, AY.9.2, AY.25, AY.103, AY.105, AY.61, AY.9.2.1, | | | | |
| | | | AY.18, AY.27, AY.67, AY.41, AY.10, AY.39, AY.45, AY.4, AY.6, AY.32, AY.56, AY.4.2.2, AY.5.3, AY.53, AY.25.1, AY.1, AY.116, AY.78, AY.2, AY.118, AY.93, AY.47, AY.100, AY.43.4, | | | | |
| NITECTYON OF THE PROPERTY OF T | | | AY.43.4, AY.86, CAMAOO, Us AY.4.6, AY.43, AY.11, AY.34, | | | | CIDGOH |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--|---|--|--------------------------|-------------------|---------------------|------------------------|
| p.L5F | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.1x decrease in binding (KD) relative to D614G. | AY.6, AY.4.4, AY.77, AY.46.4, AY.35 | Gong et al. (2021) | 31 | 8 | 0.26 |
| p.L5F | convalescent plasma binding | No change in Spike binding (relative to D614G alone) by 5 plasma collected 8 months postsymptom-onset. | AY.6, AY.4.4, AY.77, AY.46.4, AY.35 | Gong et al. (2021) | 31 | 8 | 0.26 |
| p.L5F | vaccinee plasma binding | 1.23x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.1x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.6, AY.4.4, AY.77, AY.46.4, AY.35 | Gong et al. (2021) | 31 | 8 | 0.26 |
| p.V70del | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.51x increase in binding (KD) relative to D614G, mostly due to decreased in "off-rate" a.k.a. dissociation rate (Kdis). | AY.77 | Gong et al. (2021) | 2 | 1 | 0.5 |
| p.V70del | antibody epitope effects | Reduces neutralization by structurally un- mapped mAb COVA1-21 (cluster XI). | AY.77 | Rees-Spear et al. (2021) | 2 | 1 | 0.5 |
| p.V70del | convalescent plasma binding | 1.33x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.77 | Gong et al. (2021) | 2 | 1 | 0.5 |
| p.V70del | convalescent plasma escape | Fatal COVID-19 compli- cations in immunocom- primised patient after immune escape from con- valescent plasma | AY.77 | Kemp et al. (2020) | 2 | 1 | 0.5 |
| p.V70del | convalescent plasma escape | Neutralization activity of almost all Moderna Phase 1 sera tested actually *increased*. | AY.77 | Shen et al. (2021) | 2 | 1 | 0.5 |
| p.V70del | convalescent plasma escape | Viruses containing the point mutations of B.1.1.7 showed that the single point mutations $(\Delta 69\text{-}70 \text{ and } \text{N501Y})$ were neutralized as efficiently as D614G across 10 convalescent sera from April 2020 infectees. | AY.77 | Tada et al. (2021) | 2 | 1 | 0.5 |
| p.V70del | immunosuppression variant emergence | The delH69/V70 enhances viral infectivity, indicating its effect on virus fitness is independent to the N501Y RBM change [with which it is found in lineage B.1.1.7] Possibly arisen as a result of the virus evolving from immune selection pressure in infected individuals and possibly only one chronic infection in the case of lineage B.1.1.7. | AY.77 | Kemp et al. (2020) | 2 | 1 | 0.5 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|---|------------|-----------------------------|-------------------|---------------------|------------------------|
| p.V70del | vaccinee plasma binding | 1.14x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.09x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.77 | Gong et al. (2021) | 2 | 1 | 0.5 |
| p.K417N | ACE2 receptor binding affinity | The K417N mutation decreased the affinity extasciitilde4 fold, mainly by decreasing the k(on) but also by increasing the k(off) as measured by surface plasmon resonance. | AY.2, AY.1 | Barton et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | ACE2 receptor binding affinity | This combination showed extasciitilde3x increase binding to ACE2 vs wild type, about half that of the B.1.1.7 lineage, suggesting that the K417N mutation is slightly detrimental to ACE2 binding, probably as a result of disrupting the salt bridge formed with ACE2 residue D30 | AY.2, AY.1 | Collier et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains- Fc portion IgG complex, this variant showed a 1.5x decrease in binding (KD) relative to D614G. | AY.2, AY.1 | Gong et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | ACE2 receptor binding affinity | RBD containing the N501Y mutation results in 9-fold stronger binding to the hACE2 receptor than wild type RBD. The E484K mutation does not significantly influence the affinity for the receptor, while K417N attenuates affinity. As a result, RBD from B.1.351 containing all three mutations binds 3-fold stronger to hACE2 than wild type RBD but 3-fold weaker than N501Y. | AY.2, AY.1 | Laffeber et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | ACE2 receptor binding affinity | Studying the key covariants in lineage of concern 501Y.V2, observed about 2-fold increase in ACE2 binding vs wildtype, but greatly decreased mAb binding, suggesting evolutionary optimum tension between immune evasion and ACE2 binding affinity as the N501Y variant alone has 10x increase in affinity but no effect on tested mAb binding. | AY.2, AY.1 | Liu et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | ACE2 receptor binding affinity | Using Mircoscale Thermopheresis, the B.1.351 variant harboring three mutations, binds ACE2 at nearly five-fold greater affinity than the original SARS-COV-2 RBD (Kd 87.6, vs 402.5 nM). | AY.2, AY.1 | Ramanathan et al. (2021) | 10 | 10 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|------------|----------------------|-------------------|---------------------|------------------------|
| p.K417N | ACE2 receptor binding affinity | Reported 3-fold decrease in affinity compared to wild-type RBD on the cell surface (Kd | AY.2, AY.1 | Tian et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | ACE2 receptor binding affinity | Reported slight increase in affinity compared to wild-type RBD on the cell surface (Kd | AY.2, AY.1 | Tian et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | ACE2 receptor binding affinity | The affinity of ACE2 for this mutation combination was twice as high as for wild type. Having in mind that the affinity of SARS-CoV-2 for ACE2 is only 4-fold higher compared to SARS-CoV-1, this factor of 2 is expected to be biologically significant. | AY.2, AY.1 | Vogel et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | antibody epitope effects | >20% (ELISA significance threshold) drop in antibody binding (ELISA) by this variant against IgG1 monoclonal antibody ab1. | AY.2, AY.1 | Sun et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | antibody epitope effects | 5 antibodies tested were less potent against K417N by ten-fold or more (class 1 mAbs) | AY.2, AY.1 | Wang et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | antibody epitope effects | Pseudotyped virus model ablates binding by RBD-directed mAbs CB6 and 910-30 (targeting the inner side of the RBD). Pseudotyped virus model impairs binding by RBD-directed mAbs 4-20 and REGN10933. | AY.2, AY.1 | Wang et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | convalescent plasma binding | 2.16x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.2, AY.1 | Gong et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | convalescent plasma escape | The 501Y.V2 to first wave IC50 ratio ranged from 6 to 200-fold. Averaging across all 7 participant convalescent sera highlighted the dramatic decrease in sensitivity to neutralization of authentic 501Y.V2 variants. PG: I'm purposefully ignoring D614G and A701V as contributors | AY.2, AY.1 | Cele et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | convalescent plasma escape | In 19 convalescent human sera extasci- itilde1mo post infection, Two-tailed Wilcoxon matched-pairs signed- rank test shows mild resistence P | AY.2, AY.1 | Chen et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | convalescent plasma escape | 27% of 44 early pandemic exposure convalescent plasma/sera lose all activity against a RBD triple mutant pseudovirus (RBD mutatants of the 501Y.V2 "South African" lineage), while only 23% retained high titres | AY.2, AY.1 | Wibmer et al. (2021) | 10 | 10 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|---|---|------------|-------------------------|-------------------|---------------------|------------------------|
| p.K417N | convalescent plasma escape | Nearly half (21 of 44, 48%) of early pandemic exposure convalescent plasma/sera failed to neutralize the 501Y.V2 ("South African") lineage pseudovirus construct Only 3 of 44 convascent sera (those with the highest titer, which correlated directly with initial infection severity) had high neutralization against this 501Y.V2 PG: note that lineage variant R246I was excluded from the text in reference to these sera assays, not sure if that was an oversight. | AY.2, AY.1 | Wibmer et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | gene expression increase | Experimentally, Spike gene expression increased 0.1 fold | AY.2, AY.1 | Starr et al. (2020) | 10 | 10 | 1.0 |
| p.K417N | monoclonal anti- body serial passage escape | Escape mutation against monoclonal antibody LY-CoV016 | AY.2, AY.1 | Starr et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | monoclonal anti- body serial passage escape | In vitro selection against class 1 (Spike 'up' conformation) monoclonal antibody C682, and to a lesser extent C614 and C660 | AY.2, AY.1 | Wang et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | pharmaceutical effectiveness | COR-101 lost extasci- itilde6x binding against this isolated mutation. Estesevimab lost ex- tasciitilde100x binding against this isolated mutation. | AY.2, AY.1 | Engelhart et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | pharmaceutical effectiveness | Tixagevimab, Regdan- vimab and COR-101 display reduced binding affinity to virus pseu- dotyped as RBD from B.1.351. | AY.2, AY.1 | Engelhart et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | pharmaceutical effectiveness | This mutated version of RBD completely abol- ishes the binding to a therapeutic antibody, Bamlanivimab, in vitro. | AY.2, AY.1 | Liu et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | trafficking | extasciitilde2x more infectivity than D614G alone in HEK293T- ACE2 cells 48h post- transduction. | AY.2, AY.1 | Kuzmina et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | trafficking | Lentiviral pseudotyped with this individual mutation from B.1.351 was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing mild decrease in infection rate amongst the cells, suggesting that this mutation does not contributing to cell entry fitness. | AY.2, AY.1 | Tada et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | vaccine neutraliza- tion efficacy | This variant showed only minor in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype). | AY.2, AY.1 | Kuzmina et al. (2021) | 10 | 10 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--|--|------------|--------------------------|-------------------|---------------------|------------------------|
| p.K417N | vaccinee plasma binding | 1.76x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.75x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.2, AY.1 | Gong et al. (2021) | 10 | 10 | 1.0 |
| p.K417N | virion structure | Estimated free energy change (ddG) for this variant is -0.86 kcal/mol (i.e. destabilizing relative to wild type) | AY.2, AY.1 | Spratt et al. (2021) | 10 | 10 | 1.0 |
| p.H69del | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.51x increase in binding (KD) relative to D614G, mostly due to decreased in "off-rate" a.k.a. dissociation rate (Kdis). | AY.77 | Gong et al. (2021) | 2 | 1 | 0.5 |
| p.H69del | antibody epitope effects | Reduces neutralization by structurally un- mapped mAb COVA1-21 (cluster XI). | AY.77 | Rees-Spear et al. (2021) | 2 | 1 | 0.5 |
| p.H69del | convalescent plasma binding | 1.33x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.77 | Gong et al. (2021) | 2 | 1 | 0.5 |
| p.H69del | convalescent plasma escape | Fatal COVID-19 complications in immunocomprimised patient after immune escape from convalescent plasma | AY.77 | Kemp et al. (2020) | 2 | 1 | 0.5 |
| p.H69del | convalescent plasma escape | Neutralization activity of almost all Moderna Phase 1 sera tested actually *increased*. | AY.77 | Shen et al. (2021) | 2 | 1 | 0.5 |
| p.H69del | convalescent plasma escape | Viruses containing the point mutations of B.1.1.7 showed that the single point mutations $(\Delta 69-70 \text{ and } N501Y)$ were neutralized as efficiently as D614G across 10 convalescent sera from April 2020 infectees. | AY.77 | Tada et al. (2021) | 2 | 1 | 0.5 |
| p.H69del | immunosuppression variant emergence | The delH69/V70 enhances viral infectivity, indicating its effect on virus fitness is independent to the N501Y RBM change [with which it is found in lineage B.1.1.7] Possibly arisen as a result of the virus evolving from immune selection pressure in infected individuals and possibly only one chronic infection in the case of lineage B.1.1.7. | AY.77 | Kemp et al. (2020) | 2 | 1 | 0.5 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|---|----------|-----------------------------|-------------------|---------------------|------------------------|
| p.H69del | vaccinee plasma binding | 1.14x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.09x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.77 | Gong et al. (2021) | 2 | 1 | 0.5 |
| p.E484K | ACE2 receptor binding affinity | This combination showed extasciitilde3x increase binding to ACE2 vs wild type, about half that of the B.1.1.7 lineage, suggesting that the K417N mutation is slightly detrimental to ACE2 binding, probably as a result of disrupting the salt bridge formed with ACE2 residue D30 | AY.77 | Collier et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | ACE2 receptor binding affinity | This variant appears twice in the experiments, with slightly different affinities (both extascitidel.2x decrease in binding relative to D614G) using flow cytometry and ACE2 ectodomains-Fc portion IgG complex. | AY.77 | Gong et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | ACE2 receptor binding affinity | RBD containing the N501Y mutation results in 9-fold stronger binding to the hACE2 receptor than wild type RBD. The E484K mutation does not significantly influence the affinity for the receptor, while K417N attenuates affinity. As a result, RBD from B.1.351 containing all three mutations binds 3-fold stronger to hACE2 than wild type RBD but 3-fold weaker than N501Y. | AY.77 | Laffeber et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | ACE2 receptor binding affinity | Studying the key covariants in lineage of concern 501Y.V2, observed about 2-fold increase in ACE2 binding vs wildtype, but greatly decreased mAb binding, suggesting evolutionary optimum tension between immune evasion and ACE2 binding affinity as the N501Y variant alone has 10x increase in affinity but no effect on tested mAb binding. | AY.77 | Liu et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | ACE2 receptor binding affinity | Using Mircoscale Thermopheresis, the B.1.351 variant harboring three mutations, binds ACE2 at nearly five-fold greater affinity than the original SARS-COV-2 RBD (Kd 87.6, vs 402.5 nM). | AY.77 | Ramanathan et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | ACE2 receptor binding affinity | Experimentally, ACE2 binding affinity in- creased 0.06 fold | AY.77 | Starr et al. (2020) | 2 | 1,1 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|---|----------|----------------------------|-------------------|---------------------|------------------------|
| p.E484K | ACE2 receptor binding affinity | Reported moderate increase in affinity compared to wild-type RBD on the cell surface (Kd | AY.77 | Tian et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | ACE2 receptor binding affinity | Reported slight increase in affinity compared to wild-type RBD on the cell surface (Kd | AY.77 | Tian et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | ACE2 receptor binding affinity | The affinity of ACE2 for this mutation combination was twice as high as for wild type. Having in mind that the affinity of SARS-CoV-2 for ACE2 is only 4-fold higher compared to SARS-CoV-1, this factor of 2 is expected to be biologically significant. | AY.77 | Vogel et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | ACE2 receptor binding affinity | Among the first selected variants in an in vitro evolution experiment for ACE2 binding. | AY.77 | Zahradnik et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | T cell evasion | Analyzing responses to the E484K mutation seen in B.1.351 and P.1 variants, we noted that it did not fall in a region predicted to bind the HLAII alleles tested (table S4). The mutation appeared to have no substantial or differential impact on T cell responses. | AY.77 | Reynolds et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | antibody epitope effects | Ablates Class 1 receptor- binding-motif targeting antibodies COV2-2050, 1B07, COVOX-384 and | AY.77 | Chen et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | antibody epitope effects | S2H58. Of 50 mAbs tested, major loss of neutralization observed for S2N28, S2X615, S2N12, S2X192, S2H7, S2X16, S2X58, S2H70, S2X613, S2D19, S2N22, S2D32, S2H58, S2M11, S2D106, S2X30. | AY.77 | Collier et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | antibody epitope effects | Ablates binding by class 2 mAbs such as C144 that directly interfere with ACE2 binding, but clonal somatic mutations of memory B cells at 6.2 months (evolving humoral immune response) show pronounced increase in binding to the variant. | AY.77 | Gaebler et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | antibody epitope effects | Monoclonal antibodies 13G9 and 58G6 maintain fairly high neutraliza- tion potency, compared to others interfacing with E484K. | AY.77 | Li et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | antibody epitope effects | Mutant screen in neutralization assay with a broad range of monoclonal antibodies shows high resistence to 4 antibodies, and broad low level resistence against much of the rest of the panel. | AY.77 | Liu et al. (2020) | 2 | 1,1 | 1.0 |
| p.E484K | antibody epitope effects | Massive reduction in binding efficiency vs wild type for mAb LY-CoV555. | AY.77 | Rappazzo et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | antibody epitope effects | Complete loss of binding in ELISA by the variant against monoclonal antibody VH-Fc ab8 | AY.77 | Sun et al. (2021) | 2 | 1,1 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|----------|------------------------|-------------------|---------------------|------------------------|
| p.E484K | antibody epitope effects | Pseudotyped virus model ablates neutralization by RBD-directed mAbs 4-20, 2-4, 2-43, 2-30, 2-15, LY-Cov555, C121. Pseudotyped virus model impairs neutralization by RBD-directed mAb COV2-2196 (somewhat more than fully pseudotyped B.1.351 or live virus) | AY.77 | Wang et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | antibody epitope effects | Resistent to all seven class 2 (Spike 'up' or 'down' conformation, RBD targeting) antibodies tested, with 10-fold or greater reduction in neutralization (plus notable reudction in two unclassfied mAbs). | AY.77 | Wang et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma binding | 1.42x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.77 | Gong et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma escape | Average extasciitilde5- fold reduction in neu- tralization efficacy in convalescent sera of 16 health workers infected in Spring 2020. | AY.77 | Alenquer et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma escape | This mutation occurred in 100% of sequenced virions after 12 passages and led to a 4-fold de- crease in convalescent plasma neutralization ac- tivity | AY.77 | Andreano et al. (2020) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma escape | The 501Y.V2 to first wave IC50 ratio ranged from 6 to 200-fold. Averaging across all 7 participant convalescent sera highlighted the dramatic decrease in sensitivity to neutralization of authentic 501Y.V2 variants. PG: I'm purposefully ignoring D614G and A701V as contributors | AY.77 | Cele et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma escape | Remarkably, several of the E484 escape mutants were resistant to neutralization at the highest concentration (1:80 initial dilution) of all 4 convalescent sera tested (triplicate experiments). Against a wider panel of 16 convalescent plasma (no replicates), all but one show major resistance. | AY.77 | Liu et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma escape | Escape mutant found after in passage in plasma pool of 26 convalescents mean 1.5 post symptom onset. | AY.77 | Schmidt et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma escape | The only mutation in the B.1.351 lineage that appears to contribute to neutralization reduction (extasciitide1.7x across 10 convalescent sera from April 2020 infectees) | AY.77 | Tada et al. (2021) | 2 | 1,1 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|---|--|----------|----------------------|-------------------|---------------------|------------------------|
| p.E484K | convalescent plasma escape | Pseudotyped viruses for B.1.618 was 2.5-fold resistant to neutralization by convalescent sera compared to wild type - a finding that was similar to that of the 3-fold resistance of the South Africa B.1.351 variant using the same assay. The resistance of B.1.618 was caused by the E484K mutation, based on results from viruses pseudotyped for individual variants within B.1.618. [details on the convalescent patient sera collection are not abundantly clear in the preprint] | AY.77 | Tada et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma escape | As measured by surface plasmon resonance, RBD with the E484K mutation alone showed a mean 19.1x decrease in binding affinity for six batches of hyperimmune immunoglobulin (hCoV-2IG) preparations generated from SARS-CoV-2 convalescent plasma. | AY.77 | Tang et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma escape | The neutralizing activity of 15/20 convalescent sera was significantly lower against this pseudotyped virus model | AY.77 | Wang et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma escape | 27% of 44 early pandemic exposure convalescent plasma/sera lose all activity against a RBD triple mutant pseudovirus (RBD mutatants of the 501Y.V2 "South African" lineage), while only 23% retained high titres | AY.77 | Wibmer et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma escape | Nearly half (21 of 44, 48%) of early pandemic exposure convalescent plasma/sera failed to neutralize the 501Y.V2 ("South African") lineage pseudovirus construct Only 3 of 44 convascent sera (those with the highest titer, which correlated directly with initial infection severity) had high neutralization against this 501Y.V2 PG: note that lineage variant R246I was excluded from the text in reference to these sera assays, not sure if that was an oversight. | AY.77 | Wibmer et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | convalescent plasma escape | Subtype of the B.1.526 "New York" lineage, lentivirus pseudotyped with this mutation com- bination in showed 3.3x reduction in IC50 serum dilution concentration for 6 convalescent sera. | AY.77 | Zhou et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | monoclonal anti- body serial passage escape | The engineered mutation cause 10-fold or more increase in the disassociation constant with many monoclonal antibodies (C144/C002/C121/C104/C | AY.77 | Barnes et al. (2020) | 2 | 1,1 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|---|---|----------|-------------------------|-------------------|---------------------|------------------------|
| p.E484K | monoclonal anti- body serial passage escape | Escape variant 100% appearance in 2 pas- sages against Regeneron monoclonal antibody REGN10989 @ 50ug/mL (99% after one passage) | AY.77 | Baum et al. (2020) | 2 | 1,1 | 1.0 |
| p.E484K | monoclonal anti- body serial passage escape | Mildly effective mutant against this position in the RBD for highly neutralizing COV2-2479 monoclonal antibody Effective mutant against this position in the RBD for highly neutralizing COV2-2050 monoclonal antibody | AY.77 | Greaney et al. (2020) | 2 | 1,1 | 1.0 |
| p.E484K | monoclonal anti- body serial passage escape | Escape mutation against monoclonal antibody LY-CoV555 (antibody that forms the basis for Eli Lilly's bam- lanivimab) | AY.77 | Starr et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | monoclonal anti- body serial passage escape | Class 2 antibodies C627, C602, C671, C643, and class 2/3 antibody C603 selected for the emer- gence of the E484K mu- tation in vitro. | AY.77 | Wang et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | monoclonal anti- body serial passage escape | Strong positive selection (up to 50% of supernatant sequences) after C121 monoclonal antibody assay, decreasing in subsequent passages Strong positive selection (up to 44% of supernatant sequences) after after one round of C144 monoclonal antibody passage, then waning on subsequent passages | AY.77 | Weisblum et al. (2020) | 2 | 1,1 | 1.0 |
| p.E484K | pharmaceutical effectiveness | Bamlanivimab (LY-CoV555) lost extasci- itilde16x binding against this isolated mutation. Casirivimab lost extasci- itilde16x binding against this isolated mutation. | AY.77 | Engelhart et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | pharmaceutical effectiveness | Tixagevimab, Regdan- vimab and COR-101 display reduced binding affinity to virus pseu- dotyped as RBD from B.1.351. | AY.77 | Engelhart et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | pharmaceutical effectiveness | This mutated version of RBD completely abolishes the binding to a therapeutic antibody, Bamlanivimab, in vitro. | AY.77 | Liu et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | trafficking | This variant alone shows a extasciitilde5x decrease in cell entry efficiency (RLU measurement in 293T cells) compared to D614G. | AY.77 | Ferriera et al (2021) | 2 | 1,1 | 1.0 |
| p.E484K | trafficking | This variant combination shows a extasciitilde4-5x decrease in cell entry efficiency (RLU measurement in 293T cells) compared to D614G, same as L452R alone. | AY.77 | Ferriera et al (2021) | 2 | 1,1 | 1.0 |
| p.E484K | trafficking | This variant combination shows a extasciitide3x decrease in cell entry efficiency (RLU measurement in 293T cells) compared to D614G, significantly less of a decrease than any B.1.617 lineage variants alone, suggesting a synergistic effect on cell entry while maintaining known immunity esacpe mutants. | AY.77 | Ferriera et al (2021) | 2 | 1,1 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------------|--|----------|--------------------------|-------------------|---------------------|------------------------|
| p.E484K | trafficking | extasciitilde2x more infectivity than D614G alone in HEK293T- ACE2 cells 48h post- transduction. | AY.77 | Kuzmina et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | trafficking | Lentiviral pseudotyped with this individual mutation from B.1.351 was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing no change in infection rate amongst the cells. | AY.77 | Tada et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | vaccine neutraliza- tion efficacy | Nine stored sera from Pfizer BNT162b2 vacci- nees were tested against a range of spike muta- tion bearing PV. E484K conferred a ten-fold re- duction in neutralisation by vaccine sera. | AY.77 | Ferreira et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | vaccine neutralization efficacy | E484K pseudotyped VSV was tested for neutralization in a clonal HEK-293T ACE2 TMPRSS2 cell line optimized for highly efficient S-mediated infection. A cohort of 12 Argentinian recipients of the Gamaleya Sputnik V Ad26 / Ad5 vaccine showed a mean 2.8x decrease in neutralization effiacacy. | AY.77 | Ikegame et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | vaccine neutralization efficacy | Human sera from 5 two-dose Pfizer vaccinated individuals (47-68 days post 1st-dose) neutralized this variant 3.4x less relative to reference USA-WA1/2020 strain. 8 convalescent plasma with weak IgG ELISA titre neutralized this variant 2.4x less relative to reference USA-WA1/2020 strain. One plasma failed to neutralize at all. 11 convalescent plasma with moderate IgG ELISA titre neutralized this variant 4.2x less relative to reference USA-WA1/2020 strain. 11 convalescent plasma with moderate IgG ELISA titre neutralized this variant 4.2x less relative to reference USA-WA1/2020 strain. 11 convalescent plasma with high IgG ELISA titre neutralized this variant 2.6x less relative to reference USA-WA1/2020 strain. | AY.77 | Jangra et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | vaccine neutraliza- tion efficacy | This variant showed only minor in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype). | AY.77 | Kuzmina et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | vaccine neutraliza- tion efficacy | Neutralizing antibody titers of non-human primate sera after one or two doses of Ad26.COV2.S (Jannsen vaccine) against the variants containing the E484K substitution in the RBD were present but reduced (fold reduction between 3.35–7.78, 95% confidence interval all above twofold difference, one-sample t test). | AY.77 | Solfrosi et al. (2021) | 2 | 1,1 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------------|---|----------|----------------------|-------------------|---------------------|------------------------|
| p.E484K | vaccine neutralization efficacy | Pseudotyped viruses for B.1.618 was 2.7-fold resistant to neutralization by 6 BNT162b2 vaccine sera 28 days post-booster compared to wild type - a finding that was similar to that of the 3.4-fold resistance of the South Africa B.1.351 variant using the same assay. Neutralization by 3 Moderna vaccine sera 28 days post-booster was 3-fold resistant (vs. 2.2-fold for B.1.351). The resistance of B.1.618 was caused by the E484K mutation, based on results from viruses pseudotyped for individual variants within B.1.618. | AY.77 | Tada et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | vaccine neutraliza- tion efficacy | In a cohort of 20 patients 8+ weeks after second vaccine dose of Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) vaccines, ELISA tests show 10x reduced efficacy of a majority of isolated antibodies, but only a modest decrease for vaccine plasma overall. | AY.77 | Wang et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | vaccinee plasma binding | 1.16x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.06x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.77 | Gong et al. (2021) | 2 | 1,1 | 1.0 |
| p.E484K | virion structure | Estimated free energy change (ddG) for this variant is -0.6 kcal/mol (i.e. destabilizing relative to wild type) | AY.77 | Spratt et al. (2021) | 2 | 1,1 | 1.0 |
| p.D138Y | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains- Fc portion IgG complex, this variant showed a 1.32x increase in binding (KD) relative to D614G. | AY.70 | Gong et al. (2021) | 3 | 1 | 0.33 |
| p.D138Y | convalescent plasma binding | 1.56x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.70 | Gong et al. (2021) | 3 | 1 | 0.33 |
| p.D138Y | vaccinee plasma binding | 1.37x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.56x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.70 | Gong et al. (2021) | 3 | 1 | 0.33 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|---|---|-------------------|------------------------|-------------------|---------------------|------------------------|
| p.D138Y | virion structure | Estimated free energy change (ddG) for this variant is 0.43 kcal/mol (i.e. stabilizing relative to wild type) | AY.70 | Spratt et al. (2021) | 3 | 1 | 0.33 |
| p.P251L | monoclonal anti- body serial passage escape | Escape mutation against Spike N terminal do- main antigenic supersite i mAb S2X28 | AY.86, AY.98.1 | McCallum et al. (2021) | 403 | 161 | 0.4 |
| p.P681H | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains- Fc portion IgG complex, this variant showed a 1.23x decrease in binding (KD) relative to D614G. | AY.5 | Gong et al. (2021) | 18 | 1,1,16 | 1.0 |
| р.Р681Н | antibody epitope effects | Ablates Class 3 N- terminal domain tar- geting antibody COV2- 2489, diminishes COV2- 2676. | AY.5 | Chen et al. (2021) | 18 | 1,1,16 | 1.0 |
| p.P681H | antibody epitope effects | Wildtype elicits immune response, COVID-19 cohort epitope score > 99th percentile of the 497 pre-pandemic controls, mutant drops PIWAS epitope score from 7.8% to 1.2% (significantly poorer immune recognition) Together with other B1.1.7 lineage mutational changes (Spike: Y144del,N501Y, A570D Nucleoprotein: D3L, S235F) resulted in only 2 of 579 individuals (0.3% of the population) having a dramatic reduction in PIWAS antigen scores, which reflects the peak epitope signal along the entire antigen. | AY.5 | Haynes et al. (2021) | 18 | 1,1,16 | 1.0 |
| p.P681H | antibody epitope effects | This variant is adjacent to the Spike protein furin cleavage site (cleavage of S into S1 and S2 subunits is required for viral membrane fusion and subsequent entry into host cells), a site shown to be highly immunogenic. | AY.5 | Johnson et al. (2020) | 18 | 1,1,16 | 1.0 |
| p.P681H | convalescent plasma binding | 1.26x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.5 | Gong et al. (2021) | 18 | 1,1,16 | 1.0 |
| p.P681H | trafficking | While the introduction of P681H in the SARS-CoV-2 B.1.1.7 variant may increase spike cleavage by furin-like proteases, this does not significantly impact viral entry or cell-cell spread. We consider that other factors are at play to account for the increased in transmission and disease severity attributed to this variant of concern (VOC). | AY.5 | Lubinski et al. (2021) | 18 | 1,1,16 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|---|---|----------|----------------------------|-------------------|---------------------|------------------------|
| p.P681H | trafficking | This mutation in the first base of the furin clevage site maintains the RXXR recognition motif, and is presumed | AY.5 | Maaroufi (2021) | 18 | 1,1,16 | 1.0 |
| | | to enhance cleavage based on the removal of a proline-directed phosphotase recogni- | | | | | |
| | | tion site at S680. In a homologuous site in Infectious Bronchitis Virus (IBV, Gamma- coronaviruses), abolition | | | | | |
| | | of S680 phosphorylation improves furin cleavage (and presumably cell entry). | | | | | |
| р.Р681Н | trafficking | Lentiviral pseudotyped with this individual mu- tation from B.1.1.7 was tested on ACE2.293T cells. Luciferase activity | AY.5 | Tada et al. (2021) | 18 | 1,1,16 | 1.0 |
| | | was measured two days postinfection, showing NO statistically sig- nificant infection rate change amongst the cells, suggesting that furin cleavage typically | | | | | |
| | | used for cell entry is not affected by this change one amino acid upstream of the RXXR recognition pattern. | | | | | |
| р.Р681Н | vaccine neutraliza- tion efficacy | No significant change in virus neutralzation by 18 Pfizer two dose vacci- nee sera compared to | AY.5 | Zuckerman et al. (2021) | 18 | 1,1,16 | 1.0 |
| | | B.1.1.7. [results without including the used mutation A27S likely generalizable, as this is not a lineage defining mutation] | | | | | |
| р.Р681Н | vaccinee plasma | 1.14x decrease in Spike | AY.5 | Gong et al. | 18 | 1,1,16 | 1.0 |
| | binding | binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non- | | (2021) | | | |
| | | seroconverted subjects. 1.11x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech | | | | | |
| | | BNT162b2 vaccine in post-infection vaccinees. | | | | | |
| р.Р681Н | virion structure | The Ratio of S2 (processed Spike) to full length Spike is higher for this mutation, due to a drop in the full | AY.5 | Tada et al. (2021) | 18 | 1,1,16 | 1.0 |
| | | length Spike measured, suggesting that this mu- tation compensates for decreased Spike produc- tion by improved prote- | | | | | |
| n Coren | monoglamal | olytic processing. | AV 100 | MaCaller | 114 | 70 | 0.60 |
| p.S255F | monoclonal anti- body serial passage escape | Escape mutation against Spike N terminal do- main antigenic supersite i mAb S2L28 | AY.106 | McCallum et al. (2021) | 114 | 78 | 0.68 |
| p.L452R | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains- Fc portion IgG complex, this variant showed a 2.66x increase in binding | AY.3.1 | Gong et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | ACE2 receptor binding affinity | (KD) relative to D614G. extasciitilde1.7-fold increase in binding affinity vs wild type. | AY.3.1 | Motozono et al. (2021) | 9 | 1,8 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|---|--|----------|---------------------------|-------------------|---------------------|------------------------|
| p.L452R | T cell evasion | L452R derivative virus did not induce IFN-gamma expression even at the highest concentration tested (10 nM) in two different A*24:02 convalescent sera donor plasma (linear epitope NYNYLYRLF 448,456). | AY.3.1 | Motozono et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | antibody epitope effects | Resistent to some neutralizing antibodies: mAbs X593 and P2B- 2F6 | AY.3.1 | Li et al. (2020) | 9 | 1,8 | 1.0 |
| p.L452R | antibody epitope effects | Mutant screen in neutralization assay with a broad range of monoclonal antibodies shows resistence to more than one antibody. | AY.3.1 | Liu et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | antibody epitope effects | 10 of 14 RBD-specific mAbs that showed at least 10-fold reduced neutralization of B.1.427/B.1.429 variant pseudotype (S13I, W152C, and L452R) were also found to poorly bind to just a L452R RBD mutant, demonstrating a role for this mutation as an escape mechanism for certain RBD-targeting mAbs. | AY.3.1 | McCallum et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | antibody epitope effects | extasciitilde20% (ELISA significance threshold) drop in antibody binding (ELISA) by this variant against monoclonal antibody VH ab6. | AY.3.1 | Sun et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | convalescent plasma binding | 2.15x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.3.1 | Gong et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | convalescent plasma escape | Observed extasciitilde2x decrease on average in 16 health workers' convales- cent sera. | AY.3.1 | Alenquer et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | convalescent plasma escape | Ablation of neutralization capability of 3 of 4 convalescent sera tested, the other is significantly hindered. | AY.3.1 | Liu et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | convalescent plasma escape | Relative to B.1, Epsilon (B.1.417/429) shows 1.74x-2.35x decrease in neutralization efficiency by convalescent plasma [no cohort details provided] | AY.3.1 | Wilhelm et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | gene expression increase | Experimentally, Spike gene expression in- creased 0.32 fold | AY.3.1 | Starr et al. (2020) | 9 | 1,8 | 1.0 |
| p.L452R | monoclonal anti- body serial passage escape | Ranked effective mutant against this position in the RBD for highly neu- tralizing COV2-2096 | AY.3.1 | Greaney et al. (2020) | 9 | 1,8 | 1.0 |
| p.L452R | monoclonal anti- body serial passage escape | Escape mutation against monoclonal antibody LY-CoV555 (antibody that forms the basis for Eli Lilly's bamlanivimab) | AY.3.1 | Starr et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | monoclonal anti- body serial passage escape | Class 2/3 antibody C628 and class 2 antibody C643 selected for the emergence of the L452R mutation in vitro. | AY.3.1 | Wang et al. (2021) | 9 | 1,8 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|---------------------------------|---|----------|---------------------------|-------------------|---------------------|------------------------|
| p.L452R | pharmaceutical effectiveness | Bamlanivimab (LY-CoV555) lost extasci- itilde5x binding against this isolated mutation. Cligavimab lost extasci- itilde4x binding against this isolated mutation. Regdanvimab lost ex- tasciitilde4x binding against this isolated mutation. | AY.3.1 | Engelhart et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | pharmaceutical effectiveness | Bamlanivimab (LY-CoV555) entirely lost its neutralizing activity due to the central location of L452R in the epitopes recognized by this mAb. Regdanvimab (CT-P59), and to a smaller extent etesevimab, showed a reduction in neutralization potency. | AY.3.1 | McCallum et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | trafficking | We observed increased entry by pseudoviruses carrying the L452R mutation compared to D614G alone, with a 6.7 to 22.5-fold increase in 293T cells and a 5.8 to 14.7-fold increase in human airway organoids. | AY.3.1 | Deng et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | trafficking | This variant alone shows a extasciitilde5x decrease in cell entry efficiency (RLU measurement in 293T cells) compared to D614G. [listed as L454R in Figure, but L452R in text, also text suggests not statistucally significant, but error bars say otherwise in Figure 4 | AY.3.1 | Ferriera et al (2021) | 9 | 1,8 | 1.0 |
| p.L452R | trafficking | Increased stability of RBD expression in yeast, suggesting in- creased Spike protein | AY.3.1 | Motozono et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | transmissibility | stability. Increased infectivity of the B.1.617 spike was attributed to L452R, which itself caused a 3.5-fold increase in infectivity relative to D614G wild type. [In combination with E484Q caused a lower 3-fold increase] | AY.3.1 | Tada et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | vaccine neutralization efficacy | Nine stored sera from Pfizer BNT162b2 vaccinees were tested against a range of spike mutation bearing PV. L452R conferred about a two-fold reduction in neutralisation by vaccine sera, but was not statistically significant with this sample size. | AY.3.1 | Ferreira et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | vaccine neutralization efficacy | The presence of this variant in 189 post-mRNA-vaccination COVID-19 cases was proportionally in line with lineage prevalence in Northen California during the study period, suggesting no effect of these variants on immune escape. | AY.3.1 | Jacobson et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | vaccine neutralization efficacy | Relative to B.1, Epsilon (B.1.417/429) shows 1.74x-2.35x decrease in neutralization efficiency by 18 vaccinee sera (BNT162b2 and mRNA1273). | AY.3.1 | Wilhelm et al. (2021) | 9 | 1,8 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|----------------------------|---|----------|-----------------------|-------------------|---------------------|------------------------|
| p.L452R | vaccinee plasma binding | 1.05x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.16x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.3.1 | Gong et al. (2021) | 9 | 1,8 | 1.0 |
| p.L452R | virion structure | Estimated free energy change (ddG) for this variant is -0.67 kcal/mol (i.e. destabilizing relative to wild type) | AY.3.1 | Spratt et al. (2021) | 9 | 1,8 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|---------------|--------------------------------|---|--|--------------------|-------------------|---------------------|------------------------|
| p.L452R | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 2.66x increase in binding (KD) relative to D614G. | AY.117, AY.3, AY.9, AY.57, AY.77, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.43, AY.44, AY.122, AY.35, AY.73, AY.38, AY.44, AY.121, AY.65, AY.94, AY.62, AY.88, AY.410, AY.113, AY.98.1, AY.113, AY.98.1, AY.110, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.107, AY.110, AY.206, AY.107, AY.110, AY.211, AY.121, AY.121, AY.120, AY.39.1, AY.120, AY.39.1, AY.110, AY.39.1, AY.127, AY.110, AY.28, AY.46, AY.124, AY.43.3, AY.127, AY.110, AY.28, AY.45, AY.46, AY.127, AY.110, AY.28, AY.45, AY.16, AY.105, AY.107, AY.108, AY.29, AY.104, AY.92, AY.107, AY.108, AY.23, AY.29, AY.104, AY.92, AY.105, AY.106, AY.92, AY.107, AY.108, AY.106, AY.92, AY.107, AY.108, AY.109, AY.107, AY.108, AY.109, AY.107, AY.108, AY.23, AY.23, AY.29, AY.101, AY.118, AY.119, AY.118, AY.1 | Gong et al. (2021) | | | |
| os infections | | | AY.43.4, AY.86, AY.109, | | | | |
| | | | Contact, Wy.43, AY.11, AY.34, AY.125, | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|---------------------|---------------------------|---------------|-------------|----------|-----------|-----------|
| | | | | | Depth | Allele | Frequency |
| p.L452R | ACE2 receptor bind- | Using flow cytometry | AY.70, AY.35, | Gong et al. | 23 | 23 | 1.0 |
| _ | ing affinity | and ACE2 ectodomains- | AY.98 | (2021) | | | |
| | | Fc portion IgG com- | | , , | | | |
| | | plex, this variant combi- | | | | | |
| | | nation (representing lin- | | | | | |
| | | eage B.1.617) showed a | | | | | |
| | | 1.85x increase in binding | | | | | |
| | | (KD) relative to D614G. | | | | | |
| | | exact variant list not | | | | | |
| | | provided in manuscript, | | | | | |
| | | is inferred fro common | | | | | |
| | | knowledgel | | | | | |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-------------------|--------------------------------|--|--|------------------------|----------------------|------------------------|-------------------------|
| Mutations p.L452R | ACE2 receptor binding affinity | extasciitilde1.7-fold increase in binding affinity vs wild type. | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.38, AY.44, AY.17, AY.40, AY.14, AY.65, AY.94, AY.17, AY.40, AY.14, AY.65, AY.94, AY.17, AY.100, AY.39.1, AY.110, AY.111, AY.20, AY.39.1, AY.110, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.26, AY.46.6, AY.124, AY.48, AY.46.7, AY.110, AY.27, AY.110, AY.28, AY.48, AY.46.8, AY.46.9, AY.107, AY.108, AY.48, AY.45, AY.107, AY.108, AY.23, AY.29, AY.101, AY.108, AY.23, AY.29, AY.104, AY.92, AY.105, AY.105, AY.106, AY.92.1, AY.18, AY.27, AY.67, AY.106, AY.106, AY.9.2.1, AY.18, AY.27, AY.67, AY.107, AY.108, AY.92, AY.104, AY.92, AY.21, AY.18, AY.27, AY.67, AY.41, AY.18, AY.27, AY.67, AY.41, | Motozono et al. (2021) | Sequence Depth 58814 | Alternate Allele 58807 | Alternate Frequency 1.0 |
| | | | AY.9.2.1, AY.18, AY.27, | | | | CIDGOH [©] |

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| ## Cell consistent wires and the content of the con | Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|--|--------------|--------------|---|--|-------------|-------------------|---------------------|------------------------|
| AY.43.4, AY.86, | | | L452R derivative virus did not induce IFN-gamma expression even at the highest concentration tested (10 nM) in two different A*24:02 convalescent sera donor plasma (linear epitope | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.121.1, AY.98, AY.121, AY.121.1, AY.121.1, AY.20, AY.43, AY.42, AY.111, AY.121.1, AY.121, AY.13, AY.46, AY.46.6, AY.46.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.120, AY.39.1, AY.120, AY.39.1, AY.121, AY.88, AY.66, AY.46.6, AY.124, AY.43.3, AY.127, AY.106, AY.121, AY.106, AY.121, AY.106, AY.121, AY.106, AY.107, AY.108, AY.28, AY.45, AY.16, B.1.617.2, AY.10, AY.106, AY.107, AY.108, AY.28, AY.45, AY.106, AY.107, AY.108, AY.29, AY.104, AY.90, AY.104, AY.90, AY.105, AY.106, AY.107, AY.108, AY.21, AY.108, AY.22, AY.23, AY.29, AY.42, AY.33, AY.29, AY.43, AY.45, AY.41, AY.106, AY.90, AY.107, AY.108, AY.27, AY.107, AY.108, AY.28, AY.45, AY.41, AY.106, AY.90, AY.107, AY.108, AY.27, AY.107, AY.108, AY.28, AY.45, AY.41, AY.107, AY.108, AY.29, AY.41, AY.107, AY.108, AY.29, AY.41, AY.107, AY.108, AY.29, AY.42, AY.43, AY.45, AY.41, AY.45, AY.41, AY.45, AY.41, AY.45, AY.41, | Motozono et | Depth | Allele | Frequency |
| CIDGOH® | INTECOTOR OF | | | AY.86, AY.109, | | | | CIDGOH ® |

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| p.L452R antibody epitope effects | Resistent to some neutralizing antibodies: mAbs X593 and P2B- 2F6 | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, | Li et (2020) | al. 58814 | Allele 58807 | Frequency 1.0 |
|----------------------------------|---|--|--------------|-----------|-----------------|---------------------|
| | | AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.4, AY.4.2.1, AY.98, AY.46.4, AY.4.2.1, AY.98, AY.40, AY.111, AY.121.1, AY.20, AY.43, AY.42, AY.35, AY.44, AY.112, AY.35, AY.46, AY.42, AY.38, AY.44, AY.17, AY.40, AY.14, AY.65, AY.94, AY.62, AY.88, AY.66, AY.46.1, AY.113, AY.98.1, AY.113, AY.98.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.110, AY.46.6, AY.46.6, AY.46.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.110, AY.26, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.26, AY.45, AY.16, B.1.617.2, AY.92, AY.111, AY.85, AY.66, AY.124, AY.43.3, AY.127, AY.110, AY.26, AY.53, AY.16, B.1.617.2, AY.92, AY.110, AY.26, AY.45, AY.16, B.1.617.2, AY.92, AY.111, AY.108, AY.45, AY.16, B.1.617.2, AY.92, AY.110, AY.26, AY.53, AY.23, AY.29, AY.41, AY.106, AY.92.1, AY.108, AY.42, AY.99, AY.104, AY.99, AY.41, AY.10, AY.99, AY.42, AY.99, AY.104, AY.99, AY.104, AY.99, AY.105, AY.67, AY.116, AY.106, AY.92.1, AY.116, AY.78, AY.22, AY.53, AY.25, AY.45, AY.41, AY.10, AY.39, AY.45, AY.41, AY.116, AY.78, AY.22, AY.23, AY.23, AY.24, AY.24, AY.24, AY.24, AY.24, AY.24, AY.25, AY.25, AY.25, AY.25, AY.25, AY.25, AY.25, AY.27, AY.67, AY.41, AY.116, AY.78, AY.27, AY | | | | |
| | | AY.118, AY.93, AY.47, AY.100, AY.43.4, AY.86, | | | | |
| | | AY.109, CANTACT WY.43, | | | | CIDGOH [©] |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|---------------|--------------------------|---|---|-------------------|-------------------|---------------------|------------------------|
| p.L452R | antibody epitope effects | Mutant screen in neutralization assay with a broad range of monoclonal antibodies shows resistence to more than one antibody. | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.5, AY.46.2, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.121.1, AY.20, AY.51, AY.111, AY.121.1, AY.20, AY.48, AY.122, AY.35, AY.44, AY.113, AY.48, AY.122, AY.38, AY.44, AY.17, AY.40, AY.14, AY.65, AY.94, AY.62, AY.88, AY.62, AY.88, AY.62, AY.88, AY.66, AY.46.1, AY.113, AY.98.1, AY.110, AY.61, AY.110, AY.62, AY.84, AY.127, AY.110, AY.63, AY.127, AY.110, AY.64, AY.127, AY.110, AY.65, AY.46, AY.124, AY.43.3, AY.127, AY.110, AY.26, AY.46, AY.124, AY.43.3, AY.127, AY.110, AY.27, AY.110, AY.28, AY.49, AY.105, AY.107, AY.108, AY.40, AY.107, AY.108, AY.23, AY.21, AY.104, AY.92, AY.105, AY.107, AY.108, AY.107, AY.108, AY.23, AY.29, AY.104, AY.92, AY.104, AY.92, AY.105, AY.105, AY.106, AY.92.1, AY.107, AY.108, AY.107, AY.108, AY.107, AY.108, AY.107, AY.108, AY.109, AY.107, AY.108, AY.107, AY.108, AY.109, AY.107, AY.108, AY.107, AY.108, AY.109, AY.109, AY.101, AY.108, AY.109, AY.109, AY.109, AY.101, AY.108, AY.109, | Liu et al. (2021) | | | |
| SS_INFECTIONS | | | AY.43.4, AY.86, AY.109, | | | | |
| AND ONLY | | | Contact Wy.43, AY.11, AY.34, AY.125, | | | | CIDGOH [©] |

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| Mutations Sub-category | Function | Lineages | Citation | Sequence Depth | | Alternate Frequency |
|-----------------------------------|----------|--|--------------------|----------------------|------------------------|-------------------------|
| p.L452R convalescent plas binding | | Lineages AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.38, AY.44, AY.113, AY.121, AY.65, AY.94, AY.62, AY.88, AY.46.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.65, AY.94, AY.62, AY.88, AY.46.6, AY.121, AY.85, AY.61, AY.106, AY.107, AY.108, AY.107, AY.108, AY.108, AY.109, AY.109, AY.101, AY.108, AY.109, AY.101, AY.108, AY.108, AY.109, AY.109, AY.101, AY.108, AY.108, AY.109, AY.109, AY.109, AY.101, AY.108, AY.109, AY.109, AY.109, AY.101, AY.108, AY.109, AY.109, AY.109, AY.101, AY.108, AY.109, AY.109, AY.101, AY.108, AY.109, AY.109, AY.109, AY.109, AY.101, AY.108, AY.109, AY.109, AY.109, AY.109, AY.101, AY.109, AY.101, AY.109, AY.101, A | Gong et al. (2021) | Sequence Depth 58812 | Alternate Allele 58805 | Alternate Frequency 1.0 |
| | | AY.118, AY.93, AY.47, AY.100, AY.43.4, | | | | |
| | | AY.86, | | | | |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|------------------------|-----------------------|-------------------|---------------------|------------------------|
| p.L452R | convalescent plasma binding | This variant combination (representing lineage B.1.617) showed a 1.22x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptomonset. [exact variant list not provided in manuscript, is inferred fro common knowledge] | AY.70, AY.35, AY.98 | Gong et al. (2021) | 23 | 23 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-------------------|---|--|--|-------------------|----------------------|------------------------|-------------------------|
| Mutations p.L452R | Sub-category convalescent plasma escape | Ablation of neutralization capability of 3 of 4 convalescent sera tested, the other is significantly hindered. | Lineages AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.38, AY.48, AY.122, AY.35, AY.46.6, AY.14, AY.17, AY.40, AY.14, AY.65, AY.94, AY.62, AY.88, AY.66, AY.46.1, AY.113, AY.120, AY.39.1, AY.71, AY.106, AY.124, AY.43.3, AY.127, AY.110, AY.26, AY.85, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.26, AY.85, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.28, AY.45, AY.16, B.1.617.2, AY.108, AY.45, AY.108, AY.45, AY.108, AY.45, AY.108, AY.40, AY.108, AY.41, AY.108, AY.42, AY.43, AY.45, AY.106, AY.107, AY.108, AY.40, AY.108, AY.410, AY.108, AY.42, AY.43, AY.44, AY.45, AY.41, AY.106, AY.92, AY.42, AY.99, AY.104, AY.92, AY.25, AY.105, AY.107, AY.108, AY.27, AY.108, AY.27, AY.108, AY.27, AY.109, AY.410, AY.39, AY.42, AY.43, AY.45, AY.41, AY.40, AY.41, AY.40, AY.41, AY.40, AY.41, AY.40, AY.41, AY.40, AY.41, AY.41, AY.41, AY.42, AY.43, AY.45, AY.45, AY.41, AY.40, AY.41, AY.41, AY.41, AY.42, AY.43, AY.43, AY.44, AY.43, AY.45, AY.45, AY.45, AY.47, AY.47, AY.48, AY.49, AY.49, AY.40, AY.41, AY.41, AY.41, AY.42, AY.43, AY.45, AY.43, AY.45, AY.41, AY.40, AY.41, AY.41, AY.42, AY.43, AY.45, AY.41, AY.41, AY.41, AY.42, AY.43, AY.45, AY.45, AY.45, AY.41, AY.40, AY.41, AY.41, AY.42, AY.43, AY.43, AY.45, A | Liu et al. (2021) | Sequence Depth 58814 | Alternate Allele 58807 | Alternate Frequency 1.0 |
| | | | AY.25.1, AY.1, AY.116, AY.78, AY.2, AY.118, AY.93, AY.47, AY.100, AY.43.4, AY.86, AY.109, Contact Wy.43, AY.11, AY.34, | | | | CIDGOH |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|-------------------------------|--|------------------------|--------------------|-------------------|---------------------|------------------------|
| p.L452R | convalescent plasma escape | Pseudotyped viruses for B.1.617 was 2.3-fold resistant to neutralization by convalescent sera compared to wild type - a finding that was similar to that of the 3-fold resistance of the South Africa B.1.351 variant using the same assay. The resistance of B.1.617 was caused by the L452R and E484Q mutation, based on results from viruses pseudotyped for individual variants within B.1.617. [details on the convalescent patient sera collection are not abundantly clear in the preprint] | AY.70, AY.35, AY.98 | Tada et al. (2021) | 23 | 23 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-------------------|---|--|--|---------------------------------|----------------------|------------------------|-------------------------|
| Mutations p.L452R | Sub-category convalescent plasma escape | Relative to B.1, Epsilon (B.1.417/429) shows 1.74x-2.35x decrease in neutralization efficiency by convalescent plasma [no cohort details provided] | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.38, AY.44, AY.17, AY.40, AY.14, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.61, AY.110, AY.20, AY.39.1, AY.110, AY.20, AY.39.1, AY.110, AY.21, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.26, AY.39.1, AY.120, AY.39.1, AY.121, AY.85, AY.65, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.28, AY.45, AY.46, AY.29, AY.104, AY.92, AY.105, AY.105, AY.106, AY.92.1, AY.108, AY.92, AY.104, AY.92, AY.105, AY.105, AY.106, AY.92.1, AY.18, AY.27, AY.106, AY.106, AY.92.1, AY.18, AY.29, AY.107, AY.108, AY.99, AY.104, AY.92, AY.21, AY.18, AY.27, AY.67, AY.104, AY.92, AY.105, AY.67, AY.105, AY.67, AY.41, AY.106, AY.92.1, AY.18, AY.27, AY.67, AY.41, AY.10, AY.39, AY.45, AY.41, AY.10, AY.39, AY.45, AY.46, AY.32, AY.56, AY.56, AY.32, AY.56, AY.56, AY.32, AY.56, AY.32, AY.56, AY.32, AY.57, AY.67, AY.67, AY.67, AY.67 | Citation Wilhelm et al. (2021) | Sequence Depth 58812 | Alternate Allele 58805 | Alternate Frequency 1.0 |
| | | | AY.56, AY.4.2.2, AY.5.3, AY.53, AY.25.1, AY.1, AY.116, AY.78, AY.2, AY.118, AY.93, AY.47, AY.100, AY.43.4, AY.86, AY.109, Contact Wy.43, AY.11, AY.34, | | | | CIDGOH [©] |

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| pn.1466ff generation in ferromanically, Spillor generation of the constitution of the | Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|---|-----------|---------------------|---|---|--------------|-------------------|---------------------|------------------------|
| AY.43.4, AY.86, | | gene expression in- | Experimentally, Spike gene expression in- | AY.117, AY.3, AY.9, AY.57, AY.17, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.44, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.51, AY.111, AY.121.1, AY.64, AY.122, AY.35, AY.121, AY.64, AY.122, AY.35, AY.111, AY.121.1, AY.121.1, AY.121.1, AY.121.1, AY.121.1, AY.121, AY.46, AY.122, AY.35, AY.46, AY.124, AY.46, AY.14, AY.65, AY.94, AY.66, AY.124, AY.67, AY.106, AY.121, AY.107, AY.108, AY.46.6, AY.121, AY.108, AY.46.7, AY.108, AY.46.8, AY.46.9, AY.107, AY.108, AY.46.9, AY.107, AY.108, AY.107, AY.108, AY.107, AY.108, AY.40, AY.107, AY.108, AY.107, AY.108, AY.40, AY.107, AY.108, AY.40, AY.107, AY.108, AY.40, AY.107, AY.108, AY.40, AY.107, AY.108, AY.21, AY.108, AY.42, AY.43, AY.107, AY.108, AY.45, AY.107, AY.108, AY.21, AY.108, AY.22, AY.23, AY.25, AY.103, AY.105, AY.61, AY.106, AY.9.2.1, AY.106, AY.9.2.1, AY.107, AY.108, AY.23, AY.25, AY.25, AY.25, AY.33, AY.25, AY.25, AY.103, AY.104, AY.105, AY.107, AY.108, AY.21, AY.108, AY.22, AY.33, AY.23, AY.25, AY.104, AY.105, AY.107, AY.108, AY.21, AY.108, AY.22, AY.33, AY.25, AY.103, AY.104, AY.105, AY.107, AY.108, AY.27, AY.108, AY.29, AY.40, AY.41, AY.108, AY.21, AY.108, AY.22, AY.33, AY.25, AY.25, AY.33, AY.25, AY.25, AY.34, AY.47, AY.48, AY.49, AY.49, AY.49, AY.41, | Starr et al. | Depth | Allele | Frequency |
| CANTACT BY .43, CIDGOH | INTECT/O | | | AY.86, AY.109, | | | | CIDGOH ® |

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| p.144-0ff boots and arti- monoclousal amonoclousal monoclousal mon | Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|--|--------------|---|---|--|--------------|-------------------|---------------------|------------------------|
| AY.43.4, AY.86, AY.109, | | monoclonal anti- body serial passage | Escape mutation against monoclonal antibody LY-CoV555 (antibody that forms the basis for Eli Lilly's bam- | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.121.1, AY.98, AY.121, AY.121.1, AY.121.1, AY.20, AY.43, AY.42, AY.111, AY.121.1, AY.121, AY.13, AY.46, AY.46.6, AY.46.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.120, AY.39.1, AY.120, AY.39.1, AY.121, AY.88, AY.66, AY.46.6, AY.124, AY.43.3, AY.127, AY.106, AY.121, AY.106, AY.121, AY.106, AY.121, AY.106, AY.107, AY.108, AY.28, AY.45, AY.16, B.1.617.2, AY.10, AY.106, AY.107, AY.108, AY.28, AY.45, AY.106, AY.107, AY.108, AY.29, AY.104, AY.90, AY.104, AY.90, AY.105, AY.106, AY.107, AY.108, AY.21, AY.108, AY.22, AY.23, AY.29, AY.42, AY.33, AY.29, AY.43, AY.45, AY.41, AY.106, AY.90, AY.107, AY.108, AY.27, AY.107, AY.108, AY.28, AY.45, AY.41, AY.106, AY.90, AY.107, AY.108, AY.27, AY.107, AY.108, AY.28, AY.45, AY.41, AY.107, AY.108, AY.29, AY.41, AY.107, AY.108, AY.29, AY.41, AY.107, AY.108, AY.29, AY.42, AY.43, AY.45, AY.41, AY.45, AY.41, AY.45, AY.41, AY.45, AY.41, | Starr et al. | Depth | Allele | Frequency |
| Contact WY.43, CIDGOH | SON INTEGRAL | | | AY.86, AY.109, | | | | CIDGOH ® |

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| District passage ecopie and passage ecopie and passage pas | Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|--|-----------|---|--|--|-------------|-------------------|---------------------|------------------------|
| AY.43.4, AY.86, | | monoclonal anti- body serial passage | Class 2/3 antibody C628 and class 2 antibody C643 selected for the emergence of the L452R | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.121.1, AY.98, AY.121, AY.121.1, AY.121.1, AY.20, AY.43, AY.42, AY.111, AY.121.1, AY.121, AY.13, AY.46, AY.46.6, AY.46.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.120, AY.39.1, AY.120, AY.39.1, AY.121, AY.88, AY.66, AY.46.6, AY.124, AY.43.3, AY.127, AY.106, AY.121, AY.106, AY.121, AY.106, AY.121, AY.106, AY.107, AY.108, AY.28, AY.45, AY.16, B.1.617.2, AY.10, AY.106, AY.107, AY.108, AY.28, AY.45, AY.106, AY.107, AY.108, AY.29, AY.104, AY.90, AY.104, AY.90, AY.105, AY.106, AY.107, AY.108, AY.21, AY.108, AY.22, AY.23, AY.29, AY.42, AY.33, AY.29, AY.43, AY.45, AY.41, AY.106, AY.90, AY.107, AY.108, AY.27, AY.107, AY.108, AY.28, AY.45, AY.41, AY.106, AY.90, AY.107, AY.108, AY.27, AY.107, AY.108, AY.28, AY.45, AY.41, AY.107, AY.108, AY.29, AY.41, AY.107, AY.108, AY.29, AY.41, AY.107, AY.108, AY.29, AY.42, AY.43, AY.45, AY.41, AY.45, AY.41, AY.45, AY.41, AY.45, AY.41, | Wang et al. | Depth | Allele | Frequency |
| CATATOS, CANTACT WY.43, CIDGOH | | | | AY.86, AY.109, | | | | CIDGOH ® |

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| | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|---------|------------------------------|---|--|------------------------|-------------------|---------------------|------------------------|
| p.L452R | pharmaceutical effectiveness | Bamlanivimab (LY-CoV555) entirely lost its neutralizing activity due to the central location of L452R in the epitopes recognized by this mAb. Regdanvimab (CT-P59), and to a smaller extent etesevimab, showed a reduction in neutralization potency. | AY.117, AY.3, AY.9, AY.57, AY.77, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.99, AY.16.1, AY.89, AY.16.1, AY.84, AY.116.1, AY.83, AY.72, AY.44, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.121.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.20, AY.43, AY.48, AY.122, AY.35, AY.44, AY.121, AY.65, AY.46, AY.113, AY.88, AY.44, AY.17, AY.65, AY.94, AY.18, AY.120, AY.113, AY.98.1, AY.113, AY.98.1, AY.110, AY.26, AY.46.1, AY.113, AY.98.1, AY.110, AY.27, AY.100, AY.39.1, AY.100, AY.39.1, AY.107, AY.108, AY.46, AY.46.1, AY.110, AY.26, AY.46, AY.41, AY.10, AY.28, AY.45, AY.16, AY.107, AY.108, AY.108, AY.109, AY.109, AY.109, AY.104, AY.92, AY.118, AY.106, AY.107, AY.108, AY.108, AY.109, AY. | McCallum et al. (2021) | | | |
| | | | AY.43.4, -AY.86, | | | | + |
| NECTION | | | AY.109, | | | | |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------|--|------------------------|---------------------|-------------------|---------------------|------------------------|
| p.L452R | symptom prevalence | Gross examination of 3+3 hamster lung specimens showed pronounced congestion and hemorrhages on days 5 and 7 post-infection in the case of the B.1.617.1 as compared with the B.1. The lung lesions with the B.1 variant were minimal to mild whereas with B.1.617.1 they were moderate. For B.1 pneumonic changes were minimal to mild (inflammatory cell infiltration, focal consolidation and mild congestion). The pronounced changes (moderate to severe) with mononuclear infiltration in the alveolar interstitial space, interstitial space, interstitial spatal thickening, consolidation and pneumocyte hyperplasia were observed with B.1.617.1 variant consistently. | AY.70, AY.35, AY.98 | Yadav et al. (2021) | 23 | 23 | 1.0 |



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| D. 1.4667R We observed increased on Design We observed increased We observed We observed increased We observed We observed We observed increased We observed We obse | Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|--|-----------|--------------|---|--|-------------|-------------------|---------------------|------------------------|
| AY.43.4, | | | We observed increased entry by pseudoviruses carrying the L452R mutation compared to D614G alone, with a 6.7 to 22.5-fold increase in 293T cells and a 5.8 to 14.7-fold increase in hu- | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.44, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.51, AY.111, AY.46.4, AY.42.1, AY.98, AY.122, AY.35, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.46, AY.124, AY.46, AY.42, AY.48, AY.120, AY.38, AY.46, AY.46, AY.14, AY.65, AY.94, AY.66, AY.124, AY.67, AY.68, AY.66, AY.124, AY.46, AY.120, AY.39.1, AY.71, AY.68, AY.46.6, AY.124, AY.46, AY.120, AY.39.1, AY.71, AY.68, AY.46.6, AY.124, AY.48, AY.49, AY.40, AY.106, AY.107, AY.108, AY.40, AY.107, AY.108, AY.40, AY.108, AY.40, AY.107, AY.108, AY.42, AY.43, AY.107, AY.108, AY.42, AY.43, AY.21, AY.104, AY.40, A | Deng et al. | Depth | Allele | Frequency |
| AY.109, | | | | AY.86, AY.109, | | | | CIDGOH ® |

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| Tris Walter abose act Act | Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|---|--------------|--------------|---|--|----------------|-------------------|---------------------|------------------------|
| AY.93, AY.47, AY.100, | | | This variant alone shows a extasciitilde5x decrease in cell entry efficiency (RLU measurement in 293T cells) compared to D614G. [listed as L454R in Figure, but L452R in text, also text suggests not statistucally significant, but error bars say | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.121.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.38, AY.44, AY.17, AY.40, AY.14, AY.65, AY.94, AY.65, AY.94, AY.66, AY.124, AY.13, AY.120, AY.39.1, AY.113, AY.98.1, AY.120, AY.39.1, AY.110, AY.65, AY.94, AY.66, AY.124, AY.43.3, AY.127, AY.110, AY.26, AY.55, AY.54, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.26, AY.55, AY.54, AY.46, AY.124, AY.43.3, AY.127, AY.110, AY.26, AY.410, AY.128, AY.45, AY.16, B.1.617.2, AY.19, AY.108, AY.45, AY.107, AY.108, AY.28, AY.45, AY.107, AY.108, AY.29, AY.104, AY.9.2, AY.28, AY.45, AY.16, AY.105, AY.106, AY.9.2, AY.25, AY.103, AY.105, AY.104, AY.9.2, AY.25, AY.104, AY.9.2, AY.25, AY.104, AY.9.2, AY.25, AY.104, AY.9.2, AY.25, AY.104, AY.9.2, AY.27, AY.106, AY.9.2.1, AY.116, AY.106, AY.9.2.1, AY.116, AY.106, AY.9.2.1, AY.116, AY.106, AY.9.2.1, AY.116, AY.107, AY.108, AY.27, AY.108, AY.27, AY.107, AY.108, AY.28, AY.29, AY.4104, AY.92, AY.29, AY.104, AY.92, AY.29, AY.104, AY.92, AY.21, AY.106, AY.92.1, AY.116, AY.106, AY.9.2.1, AY.116, AY.106, AY.9.2.1, AY.116, AY.106, AY.9.2.1, AY.116, A | Ferriera et al | Depth | Allele | Frequency |
| AY.86, AY.109. | INFECTION S. | | | AY.43.4, AY.86, AY.109, | | | | CIDGOH © |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------|---|----------|-----------------------|-------------------|---------------------|------------------------|
| p.L452R | trafficking | This variant combination shows a extasciitilde4-5x decrease in cell entry efficiency (RLU measurement in 293T cells) compared to D614G, same as L452R alone. | AY.77 | Ferriera et al (2021) | 4 | 4 | 1.0 |
| p.L452R | trafficking | This variant combination shows a extasciitide3x decrease in cell entry efficiency (RLU measurement in 293T cells) compared to D614G, significantly less of a decrease than any B.1.617 lineage variants alone, suggesting a synergistic effect on cell entry while maintaining known immunity esacpe mutants. | AY.77 | Ferriera et al (2021) | 4 | 4 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|------------------|---|------------------------|--------------------|-------------------|---------------------|------------------------|
| p.L452R | transmissibility | The combination caused a 3-fold increase in infec- tivity relative to D614G wild type. [compare to 3.5x for L452R alone] | AY.70, AY.35, AY.98 | Tada et al. (2021) | 23 | 23 | 1.0 |
| p.L452R | transmissibility | Normalized for particle number, on ACE2.293T cells showed that the B.1.617 spike protein was >2-fold increase in infectivity relative to D614G wild type. | AY.70, AY.35, AY.98 | Tada et al. (2021) | 23 | 23 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------------|--|------------------------|------------------------|-------------------|---------------------|------------------------|
| p.L452R | vaccine neutralization efficacy | Nine stored sera from Pfizer BNT162b2 vaccinees were tested against a range of spike mutation bearing PV. E484Q had a extasciitilde5x drop in neutralization (vs extasciitilde10x for E484K). When E484Q and L452R were combined, the fold change was significant, but similar to that of L452R alone (extasciitilde2x), suggesting no evidence for an additive effect [perhaps even E484Q effect dilution]. | AY.70, AY.35, AY.98 | Ferreira et al. (2021) | 23 | 23 | 1.0 |
| p.L452R | vaccine neutraliza- tion efficacy | 1.4x reduction in neutralization (ID50) in sera 3 weeks after one dose of Pfizer/BioNTech BNT162b2 (up to 5 naive and post infection vaccinees) | AY.70, AY.35, AY.98 | Gong et al. (2021) | 23 | 23 | 1.0 |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence | Alternate | Alternate |
|-----------|---------------------|----------------------------|---------------|-------------|----------|-----------|-----------|
| | | | | | Depth | Allele | Frequency |
| p.L452R | vaccine neutraliza- | Pseudotyped viruses | AY.70, AY.35, | Tada et al. | 23 | 23 | 1.0 |
| | tion efficacy | for B.1.617 was 4-fold | AY.98 | (2021) | | | |
| | | resistant to neutraliza- | | | | | |
| | | tion by 6 BNT162b2 | | | | | |
| | | vaccine sera 28 days | | | | | |
| | | post-booster compared | | | | | |
| | | to wild type - a finding | | | | | |
| | | that was similar to that | | | | | |
| | | of the 3.4-fold resistance | | | | | |
| | | of the South Africa | | | | | |
| | | B.1.351 variant using | | | | | |
| | | the same assay. Neutral- | | | | | |
| | | ization by 3 Moderna | | | | | |
| | | vaccine sera 28 days | | | | | |
| | | post-booster was 5-fold | | | | | |
| | | resistant (vs. 2.2-fold | | | | | |
| | | for B.1.351). The re- | | | | | |
| | | sistance of B.1.617 was | | | | | |
| | | caused by the L452R | | | | | |
| | | and E484Q mutation, | | | | | |
| | | based on results from | | | | | |
| | | | | | | | |
| | | viruses pseudotyped | | | | | |
| | | for individual variants | | | | | |
| | | within B.1.617. | | | | | |



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| p.L452R | vaccine neutraliza- tion efficacy | Relative to B.1, Epsilon | AY.117, AY.3, | Wilhelm et al. | Depth 58812 | Allele 58805 | Frequency 1.0 |
|---------|--------------------------------------|--|--|----------------|----------------|-----------------|------------------|
| | | (B.1.417/429) shows 1.74x-2.35x decrease in neutralization efficiency by 18 vaccinee sera (BNT162b2 and mRNA1273). | AY.9, AY.57, AY.77, AY.21, AY.77, AY.21, AY.119.1, AY.126, AY.49, AY.120.1, AY.19, AY.34.1, AY.89, AY.16.1, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.87, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.4.2.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.38, AY.44, AY.17, AY.40, AY.14, AY.65, AY.94, AY.62, AY.88, AY.46.1, AY.113, AY.98.1, AY.113, AY.98.1, AY.110, AY.65, AY.94, AY.66, AY.88, AY.46.6, AY.124, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.26, AY.55, AY.54, AY.28, AY.45, AY.16, B.1.617.2, AY.110, AY.26, AY.55, AY.54, AY.28, AY.45, AY.16, B.1.617.2, AY.106, AY.107, AY.108, AY.82, AY.15, AY.108, AY.85, AY.60, AY.107, AY.108, AY.82, AY.15, AY.108, AY.82, AY.15, AY.108, AY.83, AY.29, AY.41, AY.106, AY.9.2, AY.25, AY.103, AY.105, AY.106, AY.9.2, AY.25, AY.103, AY.105, AY.67, AY.41, AY.106, AY.9.2, AY.25, AY.103, AY.105, AY.67, AY.41, AY.10, AY.39, AY.45, AY.41, AY.10, AY.39, AY.45, AY.41, AY.6, AY.42, AY.53, | (2021) | | | |
| | | | AY.25.1, AY.1, AY.116, AY.78, AY.2, AY.118, AY.93, AY.47, AY.100, AY.43.4, AY.86, AY.109, COMTACT WY.43, | | | | CIDGOH ® |

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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|----------------------------|--|------------------------|---------------------|-------------------|---------------------|------------------------|
| p.L452R | vaccinee plasma binding | This variant combination (representing lineage B.1.617) showed a 1.30x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously nonseroconverted subjects. 1.18x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. [exact variant list not provided in manuscript, is inferred fro common knowledge] | AY.70, AY.35, AY.98 | Gong et al. (2021) | 23 | 23 | 1.0 |
| p.L452R | viral load | In 9 infected ham- sters each for B.1 and B.1.617.1, no significant change in viral load or subgenomic RNA levels were detected. | AY.70, AY.35, AY.98 | Yadav et al. (2021) | 23 | 23 | 1.0 |



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| Decided Deci |
|--|
| AY.121, AY.85, AY.60, AY.107, AY.108, AY.105, AY.75, AY.33, AY.23, AY.29, AY.4.2, AY.99, AY.104, AY.9.2, AY.25, AY.105, AY.106, AY.106, AY.9.2.1, AY.18, AY.27, AY.41, AY.10, AY.39, AY.45, AY.4, AY.6, AY.32, AY.45, AY.4, AY.6, AY.33, AY.25, AY.41, AY.116, AY.78, AY.118, AY.93, AY.47, AY.100, AY.43, AY.86, |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|---|---|---|---------------------------|-------------------|---------------------|------------------------|
| p.G142D | monoclonal antibody serial passage escape | Function Selected twice in passage with mAb COV2-2489. | AY.117, AY.3, AY.9, AY.57, AY.77, AY.21, AY.119.1, AY.126, AY.120.1, AY.34.1, AY.89, AY.74, AY.24, AY.84, AY.116.1, AY.83, AY.72, AY.4.4, AY.114, AY.122.1, AY.64, AY.70, AY.42, AY.59, AY.101, AY.37, AY.99.2, AY.5, AY.46.2, AY.119, AY.46.4, AY.112.1, AY.98, AY.36, AY.102, AY.51, AY.111, AY.121.1, AY.20, AY.4.3, AY.48, AY.122, AY.35, AY.73, AY.38, AY.44, AY.65, AY.94, AY.62, AY.88, AY.46.6, AY.124, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.65, AY.94, AY.66, AY.124, AY.13, AY.113, AY.98.1, AY.110, AY.31, AY.127, AY.110, AY.31, AY.26, AY.55, AY.28, AY.46.6, AY.124, AY.43.3, AY.127, AY.110, AY.31, AY.26, AY.55, AY.28, AY.45, AY.16, B.1.617.2, AY.110, AY.31, AY.26, AY.45, AY.16, B.1.617.2, AY.104, AY.45, AY.105, AY.105, AY.105, AY.104, AY.92, AY.25, AY.103, AY.105, AY.104, AY.92, AY.41, AY.10, AY.39, AY.42, AY.45, AY.41, AY.10, AY.33, AY.105, AY.104, AY.99, AY.41, AY.10, AY.39, AY.45, AY.41, AY.66, AY.32, | Suryadevara et al. (2021) | | | Frequency |
| | | | AY.28, AY.54, AY.4.5, AY.16, B.1.617.2, AY.121, AY.85, AY.60, AY.107, AY.108, AY.82, AY.15, AY.75, AY.33, AY.23, AY.29, AY.4.2, AY.99, AY.104, AY.9.2, AY.25, AY.105, AY.106, AY.9.2.1, AY.18, AY.27, AY.41, AY.10, AY.39, AY.45, AY.4, | | | | |
| | | | AY.6, AY.32, AY.4.2.2, AY.5.3, AY.53, AY.25.1, AY.1, AY.116, AY.78, AY.118, AY.93, AY.47, AY.100, AY.43.4, AY.86, AY.109, AY.4.6, AY.43, AY.11, AY.34, AY.125, AY.13, AY.46 | | | | |



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| Mutations | Sub-category | Function | Lineages | Citation | Sequence Depth | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|----------|-----------------------|-------------------|---------------------|------------------------|
| p.P26S | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.58x increase in binding (KD) relative to D614G. | AY.4.3 | Gong et al. (2021) | 1 | 1 | 1.0 |
| p.P26S | convalescent plasma binding | 1.08x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom- onset. | AY.4.3 | Gong et al. (2021) | 1 | 1 | 1.0 |
| p.P26S | vaccinee plasma binding | 1.23x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.37x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | AY.4.3 | Gong et al. (2021) | 1 | 1 | 1.0 |



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The results here are in whole or part based upon data hosted at the Canadian VirusSeq Data Portal: https://virusseq-dataportal.ca/.We wish to acknowledge the following organisations/laboratories for contributing data to the Portal: Canadian Public Health Laboratory Network (CPHLN), CanCOGGeN VirusSeq and the list of labs available at https://virusseq-dataportal.ca/acknowledgements)



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