Surveillance report

Surveillance generated by nf-ncov-voc for Zeta variant

Date

This report is generated on 2023-03-04 using 459574 number of genomes collected between 2020-02-25 and 2023-02-16

Pango Lineages

Pango Lineages in this report ['P.2']

Indicator

This table contains key indicators identified

Indicator	Sub-categories from POKAY	Mutations
Transmissibility between humans	transmissibility	
Infection Severity	ACE2 receptor binding affinity, viral load, outcome hazard ratio	D614G, E484K, L5F, T95I
Immunity after natural infection	convalescent plasma escape, reinfection, humoral response durability	D614G, E484K
Vaccines	vaccine neutralization efficacy	D614G, E484K, V1176F
Monoclonal antibodies	monoclonal antibody serial passage escape, pharmaceutical effectiveness	E484K
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 Depth	Reference Allele	Alternate Allele	Alternate Frequency
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	P.2	Collier et al. (2021)	229	G	A	1.0
E484K	ACE2 receptor binding affinity	This variant appears twice in the experiments, with slightly different affinities (both extasciitilde1.2x decrease in binding relative to D614G) using flow cytometry and ACE2 ectodomains-Fc portion IgG complex.	P.2	Gong et al. (2021)	229	G	A	1.0
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.	P.2	Laffeber et al. (2021)	229	G	A	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
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.	P.2	Liu et al. (2021)	229	G	A	1.0
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).	P.2	Ramanathan et al. (2021)	229	G	A	1.0
E484K	ACE2 receptor binding affinity	Experimentally, ACE2 binding affinity increased 0.06 fold	P.2	Starr et al. (2020)	229	G	A	1.0
E484K	ACE2 receptor binding affinity	Reported moderate increase in affinity compared to wild-type RBD on the cell surface (Kd	P.2	Tian et al. (2021)	229	G	A	1.0
E484K	ACE2 receptor binding affinity	Reported slight increase in affinity compared to wild-type RBD on the cell surface (Kd	P.2	Tian et al. (2021)	229	G	A	1.0
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.	P.2	Vogel et al. (2021)	229	G	A	1.0
E484K	ACE2 receptor binding affinity	Among the first selected variants in an in vitro evolution experiment for ACE2 binding.	P.2	Zahradnik et al. (2021)	229	G	A	1.0
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.	P.2	Reynolds et al. (2021)	229	G	A	1.0
E484K	antibody epitope effects	Ablates Class 1 receptor-binding-motif targeting antibodies COV2-2050, 1B07, COVOX-384 and S2H58.	P.2	Chen et al. (2021)	229	G	A	1.0
E484K	antibody epitope effects	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.	P.2	Collier et al. (2021)	229	G	A	1.0
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.	P.2	Gaebler et al. (2021)	229	G	A	1.0
E484K	antibody epitope effects	Monoclonal antibodies 13G9 and 58G6 maintain fairly high neutralization potency, compared to others interfacing with E484K.	P.2	Li et al. (2021)	229	G	A	1.0

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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.	P.2	Liu et al. (2020)	229	G	A	1.0
E484K	antibody epitope effects	Massive reduction in binding efficiency vs wild type for mAb LY-CoV555.	P.2	Rappazzo et al. (2021)	229	G	A	1.0
E484K	antibody epitope effects	Complete loss of binding in ELISA by the variant against monoclonal antibody VH-Fc ab8	P.2	Sun et al. (2021)	229	G	A	1.0
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)	P.2	Wang et al. (2021)	229	G	A	1.0
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).	P.2	Wang et al. (2021)	229	G	A	1.0
E484K	convalescent plasma binding	1.42x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	P.2	Gong et al. (2021)	229	G	A	1.0
E484K	convalescent plasma escape	Average extasciitilde5-fold reduction in neutralization efficacy in convalescent sera of 16 health workers infected in Spring 2020.	P.2	Alenquer et al. (2021)	229	G	A	1.0
E484K	convalescent plasma escape	This mutation occurred in 100% of sequenced virions after 12 passages and led to a 4-fold decrease in convalescent plasma neutralization activity	P.2	Andreano et al. (2020)	229	G	A	1.0
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	P.2	Cele et al. (2021)	229	G	A	1.0
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.	P.2	Liu et al. (2021)	229	G	A	1.0
E484K	convalescent plasma escape	Escape mutant found after in passage in plasma pool of 26 convalescents mean 1.5 post symptom onset.	P.2	Schmidt et al. (2021)	229	G	A	1.0
E484K	convalescent plasma escape	The only mutation in the B.1.351 lineage that appears to contribute to neutralization reduction (extasciitilde1.7x across 10 convalescent sera from April 2020 infectees)	P.2	Tada et al. (2021)	229	G	A	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
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]	P.2	Tada et al. (2021)	229	G	A	1.0
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.	P.2	Tang et al. (2021)	229	G	A	1.0
E484K	convalescent plasma escape	The neutralizing activity of 15/20 convalescent sera was significantly lower against this pseudotyped virus model	P.2	Wang et al. (2021)	229	G	A	1.0
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	P.2	Wibmer et al. (2021)	229	G	A	1.0
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 direectly 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.	P.2	Wibmer et al. (2021)	229	G	A	1.0
E484K	convalescent plasma escape	Subtype of the B.1.526 "New York" lineage, lentivirus pseudotyped with this mutation combination in showed 3.3x reduction in IC50 serum dilution concentration for 6 convalescent sera.	P.2	Zhou et al. (2021)	229	G	A	1.0
E484K	monoclonal antibody serial passage escape	The engineered mutation cause 10-fold or more increase in the disassociation constant with many monoclonal antibodies (C144/C002/C121/C104/C110).	P.2	Barnes et al. (2020)	229	G	A	1.0
E484K	monoclonal antibody serial passage escape	Escape variant 100% appearance in 2 passages against Regeneron monoclonal antibody REGN10989 @ 50ug/mL (99% after one passage)	P.2	Baum et al. (2020)	229	G	A	1.0

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E484K	monoclonal antibody 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	P.2	Greaney et al. (2020)	229	G	A	1.0
E484K	monoclonal antibody serial passage escape	Escape mutation against monoclonal antibody LY-CoV555 (antibody that forms the basis for Eli Lilly's bamlanivimab)	P.2	Starr et al. (2021)	229	G	A	1.0
E484K	monoclonal antibody serial passage escape	Class 2 antibodies C627, C602, C671, C643, and class 2/3 antibody C603 selected for the emergence of the E484K mutation in vitro.	P.2	Wang et al. (2021)	229	G	A	1.0
E484K	monoclonal antibody 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	P.2	Weisblum et al. (2020)	229	G	A	1.0
E484K	pharmaceutical effectiveness	Bamlanivimab (LY-CoV555) lost extasciitilde16x binding against this isolated mutation. Casirivimab lost extasciitilde16x binding against this isolated mutation.	P.2	Engelhart et al. (2021)	229	G	A	1.0
E484K	pharmaceutical effectiveness	Tixagevimab, Regdanvimab and COR-101 display reduced binding affinity to virus pseudotyped as RBD from B.1.351.	P.2	Engelhart et al. (2021)	229	G	A	1.0
E484K	pharmaceutical effectiveness	This mutated version of RBD completely abolishes the binding to a therapeutic antibody, Bamlanivimab, in vitro.	P.2	Liu et al. (2021)	229	G	A	1.0
E484K	trafficking	This variant alone shows a extasciitilde5x decrease in cell entry efficiency (RLU measurement in 293T cells) compared to D614G.	P.2	Ferriera et al (2021)	229	G	A	1.0
E484K	trafficking	extasciitilde2x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction.	P.2	Kuzmina et al. (2021)	229	G	A	1.0
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.	P.2	Tada et al. (2021)	229	G	A	1.0
E484K	vaccine neutralization efficacy	Nine stored sera from Pfizer BNT162b2 vaccinees were tested against a range of spike mutation bearing PV. E484K conferred a ten-fold reduction in neutralisation by vaccine sera.	P.2	Ferreira et al. (2021)	229	G	A	1.0
E484K	vaccine neutralization efficacy	Pseudotyped P.2 virus has reduced neutralization activity vs wild type: 5.8x (30 sera Pfizer median 9 days post 2nd dose) and 2.9x (35 sera Moderna median 18 days post 2nd dose). This was significant by ANOVA.	P.2	Garcia-Beltran et al. (2021)	229	G	A	1.0

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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 efficacy.	P.2	Ikegame et al. (2021)	229	G	A	1.0
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 high IgG ELISA titre neutralized this variant 2.6x less relative to reference USA-WA1/2020 strain.	P.2	Jangra et al. (2021)	229	G	A	1.0
E484K	vaccine neutralization efficacy	This variant showed only minor in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype).	P.2	Kuzmina et al. (2021)	229	G	A	1.0
E484K	vaccine neutralization 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).	P.2	Solfrosi et al. (2021)	229	G	A	1.0
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.	P.2	Tada et al. (2021)	229	G	A	1.0
E484K	vaccine neutralization 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.	P.2	Wang et al. (2021)	229	G	A	1.0

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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 non-seroconverted 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.	P.2	Gong et al. (2021)	229	G	A	1.0
E484K	virion structure	Estimated free energy change (ddG) for this variant is -0.6 kcal/mol (i.e. destabilizing relative to wild type)	P.2	Spratt et al. (2021)	229	G	A	1.0
D614G	ACE2 receptor binding affinity	This variant appears twice in the experiments, with slightly different affinities (both extasciitilde1.2x decrease in binding relative to D614G) using flow cytometry and ACE2 ectodomains-Fc portion IgG complex.	P.2	Gong et al. (2021)	229	A	G	1.0
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.	P.2	Gong et al. (2021)	229	A	G	1.0
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.	P.2	Gong et al. (2021)	229	A	G	1.0
D614G	ACE2 receptor binding affinity	In four cell lines (including 293T-hACE2 cells), this mutation combination increases infectivity vs D614G alone	P.2	Li et al. (2020)	229	A	G	1.0
D614G	convalescent plasma binding	1.42x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	P.2	Gong et al. (2021)	229	A	G	1.0
D614G	convalescent plasma binding	No change in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	P.2	Gong et al. (2021)	229	A	G	1.0
D614G	convalescent plasma binding	No change in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	P.2	Gong et al. (2021)	229	A	G	1.0
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]	P.2	Tada et al. (2021)	229	A	G	1.0
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.	P.2	Landis et al. (2021)	229	A	G	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
D614G	syncytium formation	Slight increase in Vero cell-cell membrane fusion assay under infection with VSV pseudotyped virus.	P.2	Kim et al. (2021)	229	A	G	1.0
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.	P.2	Planas et al. (2021)	229	A	G	1.0
D614G	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)	P.2	Barrett et al. (2021)	229	A	G	1.0
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 overexpressing 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.	P.2	Daniloski et al. (2021)	229	A	G	1.0
D614G	trafficking	No change in infectivity (24h) relative to D614G alone in Caco-2 cells, Vero or Calu-3.	P.2	Kim et al. (2021)	229	A	G	1.0
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).	P.2	Kim et al. (2021)	229	A	G	1.0
D614G	trafficking	extasciitilde2x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction.	P.2	Kuzmina et al. (2021)	229	A	G	1.0
D614G	trafficking	Among S variants tested, the D614G mutant shows the highest cell entry (extasciitilde3.5x wild type), as supported by structural and binding analyses.	P.2	Ozono et al. (2020)	229	A	G	1.0

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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.	P.2	Zhang et l. (2020)	229	A	G	1.0
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.	P.2	Garcia-Beltran et al. (2021)	229	A	G	1.0
D614G	vaccine neutralization efficacy	Pseudotyped P.2 virus has reduced neutralization activity vs wild type: 5.8x (30 sera Pfizer median 9 days post 2nd dose) and 2.9x (35 sera Moderna median 18 days post 2nd dose). This was significant by ANOVA.	P.2	Garcia-Beltran et al. (2021)	229	A	G	1.0
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.	P.2	Kuzmina et al. (2021)	229	A	G	1.0
D614G	vaccine neutralization efficacy	This variant showed only minor in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype).	P.2	Kuzmina et al. (2021)	229	A	G	1.0
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.	P.2	Tada et al. (2021)	229	A	G	1.0

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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 non-seroconverted 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.	P.2	Gong et al. (2021)	229	A	G	1.0
D614G	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 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.	P.2	Gong et al. (2021)	229	A	G	1.0
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 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.	P.2	Gong et al. (2021)	229	A	G	1.0
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.	P.2	Plante et al. (2020)	229	A	G	1.0
D614G	virion structure	Estimated free energy change (ddG) for this variant is 2.5 kcal/mol (i.e. stabilizing relative to wild type)	P.2	Spratt et al. (2021)	229	A	G	1.0
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.	P.2	Weissman et al. (2020)	229	A	G	1.0
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.	P.2	Yurkovetskiy et al. (2020)	229	A	G	1.0
D614G	virion structure	Based on pseudotyped virus experiments, D614G may increase infectivity by assembling more functional S protein into the virion.	P.2	Zhang et al. (2020)	229	A	G	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
V1176F	vaccine neutralization efficacy	Pseudotyped P.2 virus has reduced neutralization activity vs wild type: 5.8x (30 sera Pfizer median 9 days post 2nd dose) and 2.9x (35 sera Moderna median 18 days post 2nd dose). This was significant by ANOVA.	P.2	Garcia-Beltran et al. (2021)	230	G	T	1.0

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