Surveillance report

Surveillance generated by nf-ncov-voc for B.1.640.2 variant

Date

This report is generated on 2022-02-02 using 171066 number of genomes collected between 2020-02-25 and 2021-12-29

Pango Lineages

Pango Lineages in this report ['B.1.640']

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	p.D614G, p.N501Y, p.P681H, p.R190S
Immunity after natural infection	convalescent plasma escape, reinfection, humoral response durability	p.N501Y
Vaccines	vaccine neutralization efficacy	p.D614G, p.N501Y, p.P681H
Monoclonal antibodies	monoclonal antibody serial passage escape, pharmaceutical effectiveness	p.F490R, p.N501Y, p.R346S
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
p.D614G	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 2.52x increase in binding (KD) relative to D614G, mostly due to decreased in "off-rate" a.k.a. dissociation rate (Kdis). Compare to full Spike variant complements for major lineages containing this variant subset: 5.43x (B.1.1.7 aka Alpha), 3.56x (B.1.351 aka Beta), 4.24x (P.1 aka Gamma).	B.1.640	Gong et al. (2021)	5	A	G	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.	B.1.640	Gong et al. (2021)	5	A	G	1.0
p.D614G	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.82x increase in binding (KD) relative to D614G.	B.1.640	Gong et al. (2021)	5	A	G	1.0
p.D614G	ACE2 receptor binding affinity	In four cell lines (including 293T-hACE2 cells), this mutation combination increases infectivity vs D614G alone	B.1.640	Li et al. (2020)	5	A	G	1.0
p.D614G	convalescent plasma binding	1.65x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.640	Gong et al. (2021)	5	A	G	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
p.D614G	convalescent plasma binding	1.26x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.640	Gong et al. (2021)	5	A	G	1.0
p.D614G	convalescent plasma binding	1.09x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.640	Gong et al. (2021)	5	A	G	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.	B.1.640	Landis et al. (2021)	5	A	G	1.0
p.D614G	syncytium formation	Slight increase in Vero cell-cell membrane fusion assay under infection with VSV pseudotyped virus.	B.1.640	Kim et al. (2021)	5	A	G	1.0
p.D614G	syncytium formation	Slight increase in Vero cell-cell membrane fusion assay under infection with VSV pseudotyped virus relative to wild type, no change relative to D614G.	B.1.640	Kim et al. (2021)	5	A	G	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.	B.1.640	Planas et al. (2021)	5	A	G	1.0
p.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)	B.1.640	Barrett et al. (2021)	5	A	G	1.0
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 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.	B.1.640	Daniloski et al. (2021)	5	A	G	1.0
p.D614G	trafficking	No change in infectivity (24h) relative to D614G alone in Caco-2 cells, Vero or Calu-3.	B.1.640	Kim et al. (2021)	5	A	G	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).	B.1.640	Kim et al. (2021)	5	A	G	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
p.D614G	trafficking	More efficient infectivity (24h) compared to wild type, in Caco-2 cells extasciitilde9x, Vero extasciitilde8x, and Calu-3 extasciitilde8x. Compare to wild type at extasciitilde5x across cell types.	B.1.640	Kim et al. (2021)	5	A	G	1.0
p.D614G	trafficking	extasciitilde4x more efficient S2 domain cleavage compared to wild type, no change relative to D614G alone in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3).	B.1.640	Kim et al. (2021)	5	A	G	1.0
p.D614G	trafficking	9x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction.	B.1.640	Kuzmina et al. (2021)	10	A	G	1.0
p.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.	B.1.640	Ozono et al. (2020)	5	A	G	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.	B.1.640	Zhang et l. (2020)	5	A	G	1.0
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.	B.1.640	Garcia-Beltran et al. (2021)	5	A	G	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.	B.1.640	Kuzmina et al. (2021)	5	A	G	1.0
p.D614G	vaccine neutralization efficacy	This variant showed no change in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype).	B.1.640	Kuzmina et al. (2021)	5	A	G	1.0

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p.D614G	vaccine neutralization 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]	B.1.640	Zuckerman et al. (2021)	5	A	G	1.0
p.D614G	vaccinee plasma binding	1.17x 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 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.	B.1.640	Gong et al. (2021)	5	A	G	1.0
p.D614G	vaccinee plasma binding	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.	B.1.640	Gong et al. (2021)	5	A	G	1.0
p.D614G	vaccinee plasma binding	1.19x 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. 1.59x 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.	B.1.640	Gong et al. (2021)	5	A	G	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.	B.1.640	Plante et al. (2020)	5	A	G	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)	B.1.640	Spratt et al. (2021)	5	A	G	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.	B.1.640	Weissman et al. (2020)	5	A	G	1.0
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.	B.1.640	Yurkovetskiy et al. (2020)	5	A	G	1.0

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p.D614G	virion structure	Based on pseudotyped virus experiments, D614G may increase infectivity by assembling more functional S protein into the virion.	B.1.640	Zhang et al. (2020)	5	A	G	1.0
p.N501Y	ACE2 receptor binding affinity	The N501Y mutation had the biggest effect on ACE2 affinity of any VOC mutation tested, increasing the affinity extasciitilde10 fold to KD extasciitilde7 nM, by increasing the k(on) extasciitilde1.8 fold and decreasing the k(off) by extasciitilde 7 fold as measured by surface plasmon resonance.	B.1.640	Barton et al. (2021)	5	A	T	1.0
p.N501Y	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	B.1.640	Collier et al. (2021)	5	A	T	1.0
p.N501Y	ACE2 receptor binding affinity	The most frequent RBM mutation N501Y (165,519 instances) makes defective the atypical N-glycosylation sequon NGV 501-503, becoming a key RBM position for the interaction with hACE2-binding hotspot 353.	B.1.640	Gamez et al. (2021)	5	A	T	1.0
p.N501Y	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 2.52x increase in binding (KD) relative to D614G, mostly due to decreased in "off-rate" a.k.a. dissociation rate (Kdis). Compare to full Spike variant complements for major lineages containing this variant subset: 5.43x (B.1.1.7 aka Alpha), 3.56x (B.1.351 aka Beta), 4.24x (P.1 aka Gamma).	B.1.640	Gong et al. (2021)	5	A	T	1.0
p.N501Y	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.	B.1.640	Laffeber et al. (2021)	5	A	T	1.0
p.N501Y	ACE2 receptor binding affinity	Reported 10-fold increase in ACE2 binding vs wild-type (Kd	B.1.640	Liu et al. (2021)	5	A	T	1.0
p.N501Y	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.	B.1.640	Liu et al. (2021)	5	A	T	1.0

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p.N501Y	ACE2 receptor binding affinity	extasciitilde4-fold increase in binding affinity vs wild type.	B.1.640	Motozono et al. (2021)	5	A	T	1.0
p.N501Y	ACE2 receptor binding affinity	Using Microscale Thermopheresis, this variant binds ACE2 at nearly two-fold greater affinity than the original SARS-COV-2 RBD (203.7 nM vs 402.5 nM).	B.1.640	Ramanathan et al. (2021)	5	A	T	1.0
p.N501Y	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).	B.1.640	Ramanathan et al. (2021)	5	A	T	1.0
p.N501Y	ACE2 receptor binding affinity	In silico methods (PyMOL and PDBePISA) involving mutagenesis (N501Y mutation) and interface analysis focusing on the Spike RDB-ACE2 interaction showed that the SARS-CoV-2 N501Y mutant (lineage B.1.1.7) establishes a more significant number of interactions relating to the mutant residue Y501 (Spike RDB) with residues Y41 and K353 (ACE2). This finding shows that the increased infectivity of SARS-CoV-2 lineage B.1.1.7 is associated with the interaction force between the Spike RBD Y501 mutant residue with the ACE2 receptor, which in this strain is increased.	B.1.640	Santos and Passos (2021)	5	A	T	1.0
p.N501Y	ACE2 receptor binding affinity	Experimentally, ACE2 binding affinity increased 0.24 fold	B.1.640	Starr et al. (2020)	5	A	T	1.0
p.N501Y	ACE2 receptor binding affinity	This single mutation causes major increase in binding affinity vs. wild type as measured by IC50 vs pseudotyped lentivirus, but combined with the complete set of B.1.1.7 lineage variants no major change vs wild type affnity is observed.	B.1.640	Tada et al. (2021)	5	A	T	1.0
p.N501Y	ACE2 receptor binding affinity	Reported 4-fold increase in affinity compared to wild-type RBD on the cell surface (Kd	B.1.640	Tian et al. (2021)	5	A	T	1.0
p.N501Y	ACE2 receptor binding affinity	Reported slight increase in affinity compared to wild-type RBD on the cell surface (Kd	B.1.640	Tian et al. (2021)	5	A	T	1.0
p.N501Y	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.	B.1.640	Vogel et al. (2021)	5	A	T	1.0
p.N501Y	ACE2 receptor binding affinity	Among the first selected and fixed variants in an in vitro evolution experiment for ACE2 binding. Calculated disassociation constant for this variant is nearly four fold lower than wild type (Kd	B.1.640	Zahradnik et al. (2021)	5	A	T	1.0

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p.N501Y	ACE2 receptor binding affinity	N501Y residue inserts into a cavity at the binding interface near Y41 of ACE2. The additional interactions result in increased affinity of ACE2 for the N501Y mutant, accounting for its increased infectivity.	B.1.640	Zhu et al. (2021)	5	A	T	1.0
p.N501Y	T cell evasion	Vaccinated, but not post-infection sera, show decreased average T cell response to an N501Y peptide. When we primed transgenic mice expressing human HLA-DRB1*0401 with the Wuhan Hu-1 peptide pool, T cell responses to the B.1.1.7 variant peptide pool were significantly reduced (p	B.1.640	Reynolds et al. (2021)	5	A	T	1.0
p.N501Y	antibody epitope effects	Ablates Class 3 N-terminal domain targeting antibody COV2-2489, diminishes COV2-2676.	B.1.640	Chen et al. (2021)	5	A	T	1.0
p.N501Y	antibody epitope effects	Of 50 mAbs tested, major loss of neutralization observed for S2X128, S2D8, S2X192, S2D19, S2H14, S2H19.	B.1.640	Collier et al. (2021)	5	A	T	1.0
p.N501Y	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 3% to 1.2% (poorer immune recognition) Together with other B1.1.7 lineage mutational changes (Spike: Y144del, A570D, P681H, Nucleoprotein: D3L, S235F) resulted in only 2 or 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.	B.1.640	Haynes et al. (2021)	5	A	T	1.0
p.N501Y	antibody epitope effects	Contrary to other reports on N501Y containing lineages (i.e. with additional mutations), N501Y alone may have an even greater affinity for a human monoclonal antibody specific for wild type. These results suggest that the individual N501Y mutation does not contribute to altered viral properties by itself, but may contribute to a collective conformational shift produced by multiple mutations.	B.1.640	Klegerman et al. (2021)	5	A	T	1.0
p.N501Y	antibody epitope effects	Lowered the neutralization potency of mAb COVA1-12 to the limit of the assay. Decrease in potency was observed against the N501Y pseudotype for the cluster IX mAb COVA2-17.	B.1.640	Rees-Spear et al. (2021)	5	A	T	1.0
p.N501Y	antibody epitope effects	Reduction in neutralization by mAbs COVA1-18 (extasciitilde4x), COVA2-15 (extasciitilde9x), S309 (extasciitilde3x)	B.1.640	Shen et al. (2021)	5	A	T	1.0
p.N501Y	antibody epitope effects	4 antibodies tested were less potent against K417N by ten-fold or more, in both mAb classes 1 and 3	B.1.640	Wang et al. (2021)	5	A	T	1.0
p.N501Y	convalescent plasma binding	1.65x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.640	Gong et al. (2021)	5	A	T	1.0

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p.N501Y	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	B.1.640	Cele et al. (2021)	5	A	T	1.0
p.N501Y	convalescent plasma escape	0.7x reduction in neutralization by key variant in several variants of concern in sera collected from cohort of 10 with severe disease 21 to 63 days post-onset.	B.1.640	Kuzmina et al. (2021)	5	A	T	1.0
p.N501Y	convalescent plasma escape	In 30 samples collected 111 to 260 days post onset of symptoms, the covalescent plasma can neutralize both the reference USA-WA1/2020 strain and the mouse adapted strain that contains the N501Y spike mutation with similar efficiency.	B.1.640	Rathnasinghe et al. (2021)	5	A	T	1.0
p.N501Y	convalescent plasma escape	Neutralization activity of convalescent sera tested decreased extasciitilde2x with this B.1.1.7 pseudotyped virus.	B.1.640	Shen et al. (2021)	5	A	T	1.0
p.N501Y	convalescent plasma escape	Viruses containing the point mutations of B.1.1.7 showed that the single point mutations (Δ69-70 and N501Y) were neutralized as efficiently as D614G across 10 convalescent sera from April 2020 infectees.	B.1.640	Tada et al. (2021)	5	A	T	1.0
p.N501Y	convalescent plasma escape	As measured by surface plasmon resonance, RBD with the N501Y mutation alone showed a mean 2.1x decrease in binding affinity for six batches of hyperimmune immunoglobulin (hCoV-2IG) preparations generated from SARS-CoV-2 convalescent plasma.	B.1.640	Tang et al. (2021)	5	A	T	1.0
p.N501Y	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	B.1.640	Wibmer et al. (2021)	5	A	T	1.0
p.N501Y	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.	B.1.640	Wibmer et al. (2021)	5	A	T	1.0
p.N501Y	environmental condition stability	Relative to D614G, this mutation demonstrated significant increase in infectivity (i.e. heat stability) after incubation at 50C after 30 minutes or 1 hour	B.1.640	Tada et al. (2021)	5	A	T	1.0

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p.N501Y	homoplasy	Variant within the six key residues in the receptor binding domain (RBD). Independently reported in UK, Australia (same origin as UK), and South Africa (independent origin).	B.1.640	Flores-Alanis et al. (2021)	5	A	T	1.0
p.N501Y	immunosuppression variant emergence	Appeared (day 128) and persisted in chronic (152 day) SARS-CoV-2 infection of immunocompromised patient with severe antiphospholipid syndrome	B.1.640	Choi et al. (2020)	5	A	T	1.0
p.N501Y	monoclonal antibody serial passage escape	In vitro selection against class 1 (Spike 'up' conformation) monoclonal antibody C663, and to a lesser extent C613.	B.1.640	Wang et al. (2021)	5	A	T	1.0
p.N501Y	pharmaceutical effectiveness	COR-101 lost extasciitilde8x binding against this isolated mutation. Regdanvimab lost extasciitilde6x binding against this isolated mutation.	B.1.640	Engelhart et al. (2021)	5	A	T	1.0
p.N501Y	pharmaceutical effectiveness	Tixagevimab, Regdanvimab and COR-101 display reduced binding affinity to virus pseudotyped as RBD from B.1.351.	B.1.640	Engelhart et al. (2021)	5	A	T	1.0
p.N501Y	pharmaceutical effectiveness	This mutated version of RBD completely abolishes the binding to a therapeutic antibody, Bamlanivimab, in vitro.	B.1.640	Liu et al. (2021)	5	A	T	1.0
p.N501Y	syncytium formation	Slight increase in Vero cell-cell membrane fusion assay under infection with VSV pseudotyped virus relative to wild type, no change relative to D614G.	B.1.640	Kim et al. (2021)	5	A	T	1.0
p.N501Y	trafficking	More efficient infectivity (24h) compared to wild type, in Caco-2 cells extasciitilde9x, Vero extasciitilde8x, and Calu-3 extasciitilde8x. Compare to wild type at extasciitilde5x across cell types.	B.1.640	Kim et al. (2021)	5	A	T	1.0
p.N501Y	trafficking	extasciitilde4x more efficient S2 domain cleavage compared to wild type, no change relative to D614G alone in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3).	B.1.640	Kim et al. (2021)	5	A	T	1.0
p.N501Y	trafficking	9x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction.	B.1.640	Kuzmina et al. (2021)	10	A	T	1.0
p.N501Y	trafficking	Decreased stability of RBD expression in yeast, suggesting decreased Spike protein stability.	B.1.640	Motozono et al. (2021)	5	A	T	1.0
p.N501Y	trafficking	Lentiviral pseudotyped with this individual mutation from B.1.1.7 was tested on ACE2.293T cells. Luciferase activity was measured two days post-infection, showing slightly increased infection rate amongst the cells. [in what is essentially a replicate experiment in the same paper, because each B.1.351 lineage variant was independetly evaluated and N501 is in both lineages, a significant decrease was observed, therefore the error bars described in this paper should be interpreted carefully]	B.1.640	Tada et al. (2021)	5	A	T	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
p.N501Y	vaccine neutralization efficacy	Observed 1.3-fold reduction in neutralization efficiency of Pfizer vaccinee sera (collected 14 days after second dose) against pseudotype B.1.1.7 key variant lentivirus. Compare to 2.6-fold reduction against cultured B.1.1.7 virus.	B.1.640	Bates et al. (2021)	5	A	T	1.0
p.N501Y	vaccine neutralization efficacy	1.2x drop in neutralization using sera collected from 14 healthy adult participants that received two injections of the mRNA-1273 (Moderna) vaccine at a dose of 100 µg (18-55 years: day 1 and day 14 post-2nd dose) against a recombinant single variant virus (modified replicating WA-1 cDNA clone) relative to contemporary circulating D614G variant (USA/GA-EHC-083E/2020) using a live-virus Focus Reduction Neutralization Test (FRNT) assay.	B.1.640	Edara et al. (2021)	5	A	T	1.0
p.N501Y	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.	B.1.640	Jacobson et al. (2021)	5	A	T	1.0
p.N501Y	vaccine neutralization efficacy	This variant showed no change in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype).	B.1.640	Kuzmina et al. (2021)	5	A	T	1.0
p.N501Y	vaccine neutralization efficacy	Human sera from 6 two-dose Pfizer vaccinated individuals (47-68 days post 1st-dose) can neutralize both the reference USA-WA1/2020 strain and the mouse adapted SARS-CoV-2 strain that contains the N501Y spike mutation with similar efficiency.	B.1.640	Rathnasinghe et al. (2021)	5	A	T	1.0
p.N501Y	vaccine neutralization efficacy	In a cohort of 20 patients 8+ weeks after second vaccine dose of Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) vaccines, a modest decrease in neutralization by vaccine plasma was observed.	B.1.640	Wang et al. (2021)	5	A	T	1.0
p.N501Y	vaccinee plasma binding	1.17x 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 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.	B.1.640	Gong et al. (2021)	5	A	T	1.0
p.N501Y	virion structure	Estimated free energy change (ddG) for this variant is 0.69 kcal/mol (i.e. stabilizing relative to wild type)	B.1.640	Spratt et al. (2021)	5	A	T	1.0
p.R346S	antibody epitope effects	Clonal somatic mutations of memory B cells at 6.2 months (evolving humoral immune response) show pronounced increase in binding to the variant.	B.1.640	Gaebler et al. (2021)	5	A	C	1.0

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p.R346S	antibody epitope effects	Resistent to class 2/3 antibody C603.	B.1.640	Wang et al. (2021)	5	A	C	1.0
p.R346S	monoclonal antibody serial passage escape	Positive selection (up to 30% of supernatant sequences) under two rounds of C135 monoclonal antibody passage, overall 70% switch away from R346 to S, K or M	B.1.640	Weisblum et al. (2020)	5	A	C	1.0
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.	B.1.640	Gong et al. (2021)	5	C	A	1.0
p.P681H	antibody epitope effects	Ablates Class 3 N-terminal domain targeting antibody COV2-2489, diminishes COV2-2676.	B.1.640	Chen et al. (2021)	5	C	A	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.	B.1.640	Haynes et al. (2021)	5	C	A	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.	B.1.640	Johnson et al. (2020)	5	C	A	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.	B.1.640	Gong et al. (2021)	5	C	A	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).	B.1.640	Lubinski et al. (2021)	5	C	A	1.0
p.P681H	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 S680. In a homologuous site in Infectious Bronchitis Virus (IBV, Gammacoronaviruses), abolition of S680 phosphorylation improves furin cleavage (and presumably cell entry).	B.1.640	Maaroufi (2021)	5	C	A	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
p.P681H	trafficking	Lentiviral pseudotyped with this individual mutation from B.1.1.7 was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing NO statistically significant 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.	B.1.640	Tada et al. (2021)	5	C	A	1.0
p.P681H	vaccine neutralization 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]	B.1.640	Zuckerman et al. (2021)	5	C	A	1.0
p.P681H	vaccinee plasma binding	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.	B.1.640	Gong et al. (2021)	5	C	A	1.0
p.P681H	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.	B.1.640	Tada et al. (2021)	5	C	A	1.0
p.F490R	monoclonal antibody serial passage escape	Mildly effective mutant against this position in the RBD for highly neutralizing COV2-2050 monoclonal antibody Mildly effective mutant against this position in the RBD for highly neutralizing COV2-2479 monoclonal antibody	B.1.640	Greaney et al. (2020)	5	TT	CG	1.0
p.R190S	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.82x increase in binding (KD) relative to D614G.	B.1.640	Gong et al. (2021)	4	G	T	1.0
p.R190S	convalescent plasma binding	1.09x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.640	Gong et al. (2021)	4	G	T	1.0
p.R190S	vaccinee plasma binding	1.19x 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. 1.59x 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.	B.1.640	Gong et al. (2021)	4	G	T	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
p.R190S	virion structure	Estimated free energy change (ddG) for this variant is -0.69 kcal/mol (i.e. destabilizing relative to wild type)	B.1.640	Spratt et al. (2021)	4	G	T	1.0

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)