nf-ncov-voc 1 of 110

## Surveillance report

Surveillance generated by nf-ncov-voc for Delta variant

#### Date

This report is generated on 2022-01-21 using 164953 number of genomes collected between 2020-02-25 and 2021-12-29

## 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.61', 'AY.62', 'AY.62', 'AY.64', '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.85', 'AY.86', 'AY.87', 'AY.88', 'AY.89', 'AY.99', 'AY.99.2', 'AY.99.2'

#### 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.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	A	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	A	0.5



nf-ncov-voc 2 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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	A	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	A	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	A	0.5
p.V70del	convalescent plasma escape	Viruses containing the point mutations of B.1.1.7 showed that the single point mutations (\Delta 69-70 and N501Y) were neutralized as efficiently as D614G across 10 convalescent sera from April 2020 infectees.	AY.77	Tada et al. (2021)	2	A	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	A	0.5
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 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	A	0.5



nf-ncov-voc 3 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	
Mutations p.G142D	monoclonal antibody serial passage escape	Escape mutation against Spike N terminal domain antigenic supersite i mAbs S2M28, S2X28, S2X333	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.118, AY.103, AY.403, AY.409, AY.84, AY.23, AY.44, AY.34.1, AY.46.1, AY.191, AY.77, AY.61, AY.119.1, AY.77, AY.75, AY.40, AY.116.1, AY.117, AY.102, AY.116, AY.117, AY.101, AY.117, AY.102, AY.116, AY.117, AY.101, AY.117, AY.102, AY.116, AY.117, AY.104, AY.116, AY.117, AY.104, AY.116, AY.117, AY.105, AY.106, AY.116, AY.117, AY.40, AY.105, AY.106, AY.107, AY.60, AY.108, AY.108, AY.108, AY.109, AY.109, AY.109, AY.109, AY.109, AY.101, AY.109, AY.109, AY.109, AY.101, AY.109, AY.101, AY.109, AY.101, AY.107, AY.108, AY.109, AY.111, AY.127, AY.33, AY.42, AY.43, AY.43, AY.41, AY.43, AY.44, AY.43, AY.41, AY.43, AY.44, A	McCallum et al. (2021)	Sequence Depth 53643		Alternate Frequency TETA, ATT, AT
, week			AY.121,				

Contact Us CIDGOH

nf-ncov-voc 4 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
Mutations p.G142D	Sub-category  monoclonal antibody serial passage escape	Function  Selected twice in passage with mAb COV2-2489.	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.53, AY.73, AY.109, AY.43.4, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1,	Citation  Suryadevara et al. (2021)	Sequence Depth 53643	Allele	Alternate Frequency TETA,ATT,AT
			AY.46.1, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116,				
			AY.9, AY.70, AY.9.2.1, AY.37, AY.121.1, AY.43.3, AY.4.4, AY.47, AY.5, AY.65, AY.25, AY.120.1, AY.42, AY.74, AY.105, AY.104,				
			AY.126, AY.106, AY.114, AY.51, AY.46.4, AY.78, AY.3, AY.107, AY.6, AY.7.1, AY.99, AY.26, AY.68, AY.38, AY.46.6, AY.41, AY.99.2,				
			AY.46, AY.39, AY.4.2.1, AY.4.3, AY.35, AY.20, AY.110, AY.111, AY.127, AY.33, AY.57, AY.14, AY.4.2, AY.72, AY.85, AY.39.1, AY.21, AY.94, AY.98, AY.60,				
			AY.25.1, AY.1, AY.119, AY.4.5, AY.82, AY.121, AY.18, AY.4.2.2, AY.28, AY.93, AY.10, AY.5.3, AY.24, AY.16, AY.62, AY.122, AY.29, AY.83,				
O MESCA			AY.98.1, AY.9.2, AY.48, AY.4.6, AY.122.1, AY.55, AY.101, AY.100				CIDCOH®

Contact Us CIDGOH®

nf-ncov-voc 5 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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	Т	0.4
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.77, AY.46.4, AY.6, AY.35, AY.4.4	Gong et al. (2021)	31	Т	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.77, AY.46.4, AY.6, AY.35, AY.4.4	Gong et al. (2021)	31	Т	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.77, AY.46.4, AY.6, AY.35, AY.4.4	Gong et al. (2021)	31	Т	0.26
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	TGG,GGG	1.0
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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Gong et al. (2021)	13662	TGG,GGG	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	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Li et al. (2020)	13662	TGG,GGG	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	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Gong et al. (2021)	13662	TGG,GGG	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	TGG,GGG	1.0



nf-ncov-voc 6 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Wilhelm et al. (2021)	13662	TGG,GGG	1.0
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. Second case also includes N:p.A220V	AY.27, AY.38, AY.57, AY.70, AY.46	Brehm et al. (2021)	13501	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Landis et al. (2021)	13662	TGG,GGG	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.27, AY.38, AY.57, AY.70, AY.46	Brehm et al. (2021)	13501	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Kim et al. (2021)	13662	TGG,GGG	1.0



nf-ncov-voc 7 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Planas et al. (2021)	13662	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Barrett et al. (2021)	13662	TGG,GGG	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 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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Daniloski et al. (2021)	13662	TGG,GGG	1.0
p.D614G	trafficking	No change in infectivity (24h) relative to D614G alone in Caco-2 cells, Vero or Calu-3.	AY.27, AY.33, AY.38, AY.57, AY.70, AY.46	Kim et al. (2021)	13662	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Kim et al. (2021)	13662	TGG,GGG	1.0
p.D614G	trafficking	Among S variants tested, the D614G mutant shows the highest cell entry (extascitidle3.5x wild type), as supported by structural and binding analyses.	AY.27, AY.33, AY.38, AY.57, AY.70, AY.46	Ozono et al. (2020)	13662	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Tada et al. (2021)	13662	TGG,GGG	1.0



nf-ncov-voc 8 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Zhang et l. (2020)	13662	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Tada et al. (2021)	13662	TGG,GGG	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	TGG,GGG	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	TGG,GGG	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.	AY.27, AY.33, AY.38, AY.57, AY.70, AY.46	Garcia- Beltran et al. (2021)	13662	TGG,GGG	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	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Kuzmina et al. (2021)	13662	TGG,GGG	1.0



nf-ncov-voc 9 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Wilhelm et al. (2021)	13662	TGG,GGG	1.0
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 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)	8	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Gong et al. (2021)	13662	TGG,GGG	1.0



nf-ncov-voc 10 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Plante et al. (2020)	13662	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Spratt et al. (2021)	13662	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Weissman et al. (2020)	13662	TGG,GGG	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.	AY.27, AY.33, AY.38, AY.57, AY.70, AY.46	Yurkovetskiy et al. (2020)	13662	TGG,GGG	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.27, AY.33, AY.38, AY.57, AY.70, AY.46	Zhang et al. (2020)	13662	TGG,GGG	1.0
p.D614G	ACE2 receptor binding affinity	This variant appears twice in the experiments, with slightly different affinities (both extasciitide1.2x decrease in binding relative to D614G) using flow cytometry and ACE2 ectodomains-Fc portion IgG complex.	AY.77	Gong et al. (2021)	2	G	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	G	1.0



nf-ncov-voc 11 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence		Alternate
					Depth	Allele	Frequency
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	G	1.0



nf-ncov-voc 12 of 110

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.	AY.54, AY.46.2, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.13, AY.31, AY.33, AY.34, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.41, AY.46.1, AY.119.1, AY.77, AY.75, AY.49, B.1.617.2, AY.86, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.81, AY.161, AY.116, AY.111, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.111, AY.44, AY.120, AY.121, AY.42, AY.43, AY.43, AY.51, AY.46, AY.78, AY.36, AY.78, AY.36, AY.78, AY.36, AY.41, AY.92, AY.42, AY.43, AY.43, AY.40, AY.72, AY.85, AY.39, AY.42, AY.41, AY.42, AY.43, AY.42, AY.41, AY.42, AY.43, AY.44, AY.43, AY.45, AY.41, AY.42, AY.43, AY.41, AY.42, AY.43, AY.44, AY.42, AY.43, AY.44, AY.42, AY.43, AY.44, AY.45, AY.41, AY.41, AY.42, AY.43, AY.44, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.41, AY.41, AY.42, AY.43, AY.44, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.46, AY.41, AY.41, AY.42, AY.43, AY.44, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.44, AY.43, AY.44, AY.43, AY.44,	Gong et al. (2021)	45770	Allele	1.0
			AY.101, C <b>entace</b> Us				CIDGOH <sup>©</sup>

nf-ncov-voc 13 of 110

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.98, AY.35	Gong et al. (2021)	12	G	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.77, AY.46.4, AY.6, AY.35, AY.4.4	Gong et al. (2021)	31	G	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	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.	AY.5	Gong et al. (2021)	18	G	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.106, AY.114, AY.119.1, AY.77, AY.78, AY.107, AY.4, AY.1, AY.119, AY.4.5, B.1.617.2, AY.125, B.1.617.2, AY.121, AY.88, AY.4.2.2, AY.116.1, AY.117, AY.108, AY.5.3, AY.102, AY.118, AY.34, AY.118, AY.34, AY.116, AY.39, AY.4.2.1, AY.4.3, AY.121, AY.4.3, AY.121, AY.4.4, AY.19, AY.4.4, AY.109, AY.110, AY.110, AY.111, AY.127, AY.89, AY.36, AY.34.1, AY.4.2, AY.4.2, AY.4.2, AY.120, AY.4.3, AY.120, AY.4.3, AY.121, AY.4.3, AY.110, AY.111, AY.127, AY.89, AY.36, AY.34.1, AY.4.2, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.2, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.4.3, AY.120, AY.120, AY.120, AY.120, AY.121, AY.120, AY.121, AY.12	Gong et al. (2021)	4594	G	1.0



Contact Us  $\qquad \qquad$  CIDGOH  $^{\odot}$ 

nf-ncov-voc 14 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate Allele	Alternate
p.D614G	ACE2 receptor binding affinity	In four cell lines (including 293T-hACE2 cells), this mutation combination increases infectivity vs D614G alone	Lineages  AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.3.1, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.41, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.1161, AY.117, AY.102, AY.116, AY.117, AY.102, AY.116, AY.32, AY.34, AY.116, AY.92.1, AY.37, AY.121.1, AY.43.3, AY.2, AY.44, AY.47, AY.5, AY.65, AY.25, AY.120, AY.106, AY.114, AY.105, AY.126, AY.106, AY.114, AY.126, AY.106, AY.114, AY.126, AY.107, AY.126, AY.108, AY.107, AY.126, AY.108, AY.107, AY.108, AY.107, AY.108, AY.108, AY.109, AY.109, AY.109, AY.109, AY.109, AY.109, AY.110, AY.111, AY.127, AY.49, AY.42, AY.43, AY.43, AY.44, AY.43, AY.45, AY.41, AY.49, AY.42, AY.49, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.45, AY.41, AY.45, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.45, AY.41, AY.45, AY.45, AY.41, AY.45, AY.45, AY.41, AY.45, AY.45, AY.45, AY.46, AY.47, AY.48, AY.46, AY.47, AY.48, AY	Li et al. (2020)	Sequence Depth  45770	Alternate Allele G	Alternate Frequency 1.0
INTERFACE AND ADDRESS OF THE PARTY OF THE PA			AY.101, C <b>entace</b> Us				CIDGOH <sup>©</sup>

<u>nf-ncov-voc</u> 15 of 110

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	G	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	G	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	G	1.0



nf-ncov-voc 16 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Allele	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.54, AY.46.2, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.13, AY.31, AY.33, AY.34, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.41, AY.46.1, AY.119.1, AY.77, AY.75, AY.49, B.1.617.2, AY.86, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.81, AY.161, AY.116, AY.111, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.111, AY.44, AY.120, AY.121, AY.42, AY.43, AY.43, AY.51, AY.46, AY.78, AY.36, AY.78, AY.36, AY.78, AY.36, AY.41, AY.92, AY.42, AY.43, AY.43, AY.40, AY.72, AY.85, AY.39, AY.42, AY.41, AY.42, AY.43, AY.42, AY.41, AY.42, AY.43, AY.44, AY.43, AY.45, AY.41, AY.42, AY.43, AY.41, AY.42, AY.43, AY.44, AY.42, AY.43, AY.44, AY.42, AY.43, AY.44, AY.45, AY.41, AY.41, AY.42, AY.43, AY.44, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.41, AY.41, AY.42, AY.43, AY.44, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.46, AY.41, AY.41, AY.42, AY.43, AY.44, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.44, AY.43, AY.44, AY.43, AY.44,	Gong et al. (2021)	45770	Allele	Trequency 1.0
INTERPORT			AY.101, C <b>ôntá00</b> Us				CIDGOH <sup>©</sup>

<u>nf-ncov-voc</u> 17 of 110

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.98, AY.35	Gong et al. (2021)	12	G	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.77, AY.46.4, AY.6, AY.35, AY.4.4	Gong et al. (2021)	31	G	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	G	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	G	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.106, AY.114, AY.114, AY.119.1, AY.77, AY.48, AY.107, AY.4, AY.1, AY.119, AY.4.5, B.1.617.2, AY.125, B.1.617.2, AY.121, AY.88, AY.4.2.2, AY.116.1, AY.117, AY.108, AY.5.3, AY.102, AY.113, AY.118, AY.34, AY.116, AY.39, AY.4.2.1, AY.4.3, AY.121.1, AY.4.3, AY.121, AY.4.4, AY.109, AY.110, AY.111, AY.127, AY.109, AY.110, AY.111, AY.127, AY.34.1, AY.4.6, AY.92, AY.120, AY.4.2, AY.120, AY.4.2, AY.120, AY.4.3, AY.120, AY.4.3, AY.121, AY.4.4, AY.120, AY.4.5, AY.121, AY.4.5, AY.120, AY.4.5, AY.120, AY.4.5, AY.120, AY.4.5, AY.120, AY.4.2, AY.120, AY.4.3, AY.120,	Gong et al. (2021)	4594	G	



Contact Us  $\qquad \qquad$  CIDGOH  $^{\odot}$ 

<u>nf-ncov-voc</u> 18 of 110

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	G	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.98, AY.35	Tada et al. (2021)	12	G	1.0



nf-ncov-voc 19 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
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.54, AY.46.2, AY.45, AY.88, AY.108, AY.111, AY.113, AY.118, AY.13, AY.31, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.86, AY.16.1, AY.116.1, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.116, AY.116, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.120, AY.120, AY.120, AY.120, AY.120, AY.120, AY.104, AY.26, AY.26, AY.26, AY.106, AY.114, AY.51, AY.46.4, AY.43, AY.44, AY.43, AY.46, AY.41, AY.51, AY.46, AY.78, AY.64, AY.78, AY.65, AY.106, AY.114, AY.51, AY.46, AY.107, AY.108, AY.107, AY.40, AY.107, AY.40, AY.71, AY.99, AY.42, AY.43, AY.40, AY.72, AY.43, AY.40, AY.72, AY.43, AY.40, AY.73, AY.41, AY.42, AY.43, AY.44, AY.43, AY.45, AY.41, AY.49, AY.42, AY.41, AY.49, AY.42, AY.49, AY.41, AY.42, AY.49, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.41, AY.49, AY.45, AY.41, AY.49, AY.41, AY.49, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.47, AY.49, AY.47, AY.49, AY.49, AY.41, AY.49, AY.41, AY.41, AY.42, AY.40, AY.72, AY.48, AY.40, AY.73, AY.41, AY.42, AY.40, AY.73, AY.40, AY.41, AY.42, AY.43, AY.40, AY.43, AY.44,	Wilhelm et al. (2021)	Sequence Depth 45770	Allele	1.0
			AY.101, C <b>ô</b> Mtå00 Us				CIDGOH <sup>©</sup>

nf-ncov-voc 20 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
	-				Depth	Allele	Frequency
p.D614G	humoral response	27yo female nurse rein-	AY.119.1,	Brehm et al.	10039	G	1.0
	durability	fected in December 2020	AY.64, AY.75,	(2021)			
		(B.1.177) after initial in-	AY.60, AY.61,				
		fection in March 2020	AY.26, AY.59,				
		(B.3), i.e. with a 9	B.1.617.2,				
		month interval. Both	AY.68, AY.88,				
		cases were mild. No	AY.4.2.2,				
		significant differences in	AY.28, AY.67,				
		the neutralizing capacity	AY.10, AY.24,				
		of the two linages were	AY.62, AY.9,				
		observed in 4 sera taken	AY.4.2.1,				
		(1 pre-reinfection, three	AY.9.2.1,				
		post-reinfection). Neu-	AY.37, AY.73,				
		tralizing antibody titres	AY.2, AY.47,				
		(IC50) before and imme-	AY.9.2, AY.65,				
		diately after re-infection	AY.14, AY.4.2,				
		were <300 against both	AY.74, AY.55,				
		strains, and jumped >7x	AY.72, AY.21				
		upon re-infection. Viral					
		titres were also higher in					
		the second case. Sec-					
		ond case also includes					
		N:p.A220V					



nf-ncov-voc 21 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Allele	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.	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.111, AY.113, AY.118, AY.13, AY.31, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.119.1, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.16.1, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.120, AY.120, AY.120, AY.120, AY.120, AY.120, AY.120, AY.120, AY.104, AY.26, AY.26, AY.106, AY.114, AY.51, AY.46.4, AY.43, AY.64, AY.78, AY.64, AY.78, AY.64, AY.78, AY.66, AY.111, AY.105, AY.104, AY.105, AY.106, AY.114, AY.51, AY.46.4, AY.43, AY.64, AY.78, AY.64, AY.78, AY.65, AY.107, AY.66, AY.114, AY.51, AY.66, AY.114, AY.51, AY.66, AY.114, AY.51, AY.66, AY.71, AY.99, AY.42, AY.98, AY.40, AY.72, AY.85, AY.39, AY.42, AY.107, AY.49, AY.42, AY.49, AY.42, AY.49, AY.42, AY.49, AY.41, AY.42, AY.49, AY.42, AY.49, AY.41, AY.42, AY.40, AY.72, AY.48, AY.40, AY.73, AY.104, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.44, AY.47, AY.49, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.44, AY.47, AY.49, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.41, AY.42, AY.43, AY.44, AY.44, AY.44, AY.47, AY.49, AY.41, AY.41, AY.42, AY.43, AY.44, AY.41, AY.42, AY.43, AY.44, AY.44	Landis et al. (2021)	Depth 45770	Allele G	Alternate Frequency 1.0
INTER TO THE PARTY OF THE PARTY			AY.101, C <b>entae</b> Us				CIDGOH <sup>©</sup>

nf-ncov-voc 22 of 110

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.119.1, AY.64, AY.75, AY.60, AY.61, AY.26, AY.59, B.1.617.2, AY.68, AY.88, AY.4.2.2, AY.28, AY.67, AY.10, AY.24, AY.62, AY.9, AY.4.2.1, AY.9.2.1, AY.9.2.1, AY.9.2, AY.47, AY.9.2, AY.47, AY.9.2, AY.47, AY.9.2, AY.47, AY.9.2, AY.47, AY.74, AY.55, AY.74, AY.55, AY.72, AY.21	Brehm et al. (2021)	10039	G	1.0



nf-ncov-voc 23 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate
p.D614G	Sub-category syncytium formation	Function  Slight increase in Vero cell-cell membrane fusion assay under infection with VSV pseudotyped virus.	Lineages  AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.3.1, AY.53, AY.73, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.16, AY.116, AY.9, AY.9.2.1, AY.37, AY.121.1, AY.43.3, AY.2, AY.4.4, AY.47, AY.5, AY.65, AY.25, AY.65, AY.25, AY.106, AY.114, AY.105, AY.106, AY.114, AY.42, AY.42, AY.43, AY.120, AY.106, AY.114, AY.51, AY.46.4, AY.43, AY.64, AY.78, AY.120, AY.106, AY.114, AY.51, AY.46.4, AY.78, AY.120, AY.106, AY.114, AY.51, AY.46.4, AY.78, AY.38, AY.107, AY.66, AY.114, AY.99.2, AY.67, AY.89, AY.67, AY.89, AY.42.1, AY.42, AY.42, AY.43, AY.42, AY.43, AY.41, AY.99.2, AY.66, AY.41, AY.99.2, AY.67, AY.89, AY.42.1, AY.43, AY.42, AY.43, AY.42, AY.41, AY.99.2, AY.66, AY.41, AY.99.2, AY.67, AY.89, AY.42, AY.41, AY.99.2, AY.410, AY.72, AY.49, AY.42, AY.41, AY.99.2, AY.410, AY.111, AY.45, AY.410, AY.42, AY.49, AY.410, AY.42, AY.49, AY.410, AY.42, AY.410, AY.42, AY.410, AY.42, AY.43, AY.440, AY.72, AY.49, AY.49, AY.49, AY.49, AY.49, AY.49, AY.40, AY.72, AY.49, AY.41, AY.41, AY.42, AY.40, AY.72, AY.49, AY.41, AY.42, AY.40, AY.72, AY.49, AY.41, AY.42, AY.40, AY.72, AY.49, AY.41, AY.42, AY.40, AY.72, AY.40, AY.73, AY.41, AY.42, AY.40, AY.73, AY.41, AY.42, AY.40, AY.73, AY.41, AY.42, AY.40, AY.73, AY.41, AY.42, AY.40, AY.73, AY.41, AY.41, AY.42, AY.40, AY.73, AY.41, AY.42, AY.40, AY.73, AY.41, AY.42, AY.40, AY.73, AY.41, AY.42, AY.40, AY.73, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.4	Kim et al. (2021)	Sequence Depth 45770	Alternate Allele G	Alternate Frequency 1.0
			AY.55, AY.87, AY.101, CAYTACO Us				CIDGOH <sup>©</sup>

nf-ncov-voc 24 of 110

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 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.54, AY.46.2, AY.46.2, AY.45, AY.88, AY.1108, AY.113, AY.113, AY.118, AY.13, AY.31, AY.53, AY.73, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.191, AY.77, AY.75, AY.4, AY.119.1, AY.77, AY.125, AY.59, B.1.617.2, AY.86, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.92, AY.16, AY.110, AY.116, AY.111, AY.43.3, AY.2, AY.44, AY.47, AY.5, AY.65, AY.25, AY.120.1, AY.42, AY.40, AY.126, AY.106, AY.114, AY.105, AY.120, AY.104, AY.126, AY.106, AY.114, AY.51, AY.46.4, AY.47, AY.59, AY.67, AY.68, AY.41, AY.49, AY.107, AY.69, AY.104, AY.120, AY.104, AY.120, AY.104, AY.120, AY.104, AY.120, AY.104, AY.120, AY.105, AY.110, AY.111, AY.42, AY.43, AY.64, AY.43, AY.64, AY.71, AY.99, AY.42.1, AY.43, AY.40, AY.71, AY.99, AY.42.1, AY.43, AY.41, AY.42, AY.43, AY.41, AY.43, AY.41, AY.42, AY.43, AY.41, AY.43, AY.44, AY.45, AY.41, AY.41, AY.45, AY.41,	Planas et al. (2021)	45770	G G Allele	1.0
INTERTAL DESCRIPTION OF THE PROPERTY OF THE PR			AY.101, C <b>entace</b> Us				CIDGOH <sup>©</sup>

nf-ncov-voc 25 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
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)	AY.54, AY.46.2, AY.45, AY.46.3, AY.108, AY.113, AY.113, AY.113, AY.113, AY.13, AY.13, AY.103, AY.43.4, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.19.1, AY.77, AY.75, AY.4, AY.125, AY.99, B.1.617.2, AY.86, AY.116, AY.117, AY.102, AY.15, AY.31, AY.161, AY.117, AY.102, AY.15, AY.31, AY.41, AY.47, AY.54, AY.120.1, AY.47, AY.54, AY.105, AY.120.1, AY.42, AY.44, AY.47, AY.54, AY.105, AY.120, AY.106, AY.114, AY.105, AY.120, AY.106, AY.114, AY.105, AY.120, AY.106, AY.114, AY.105, AY.120, AY.106, AY.114, AY.42, AY.43, AY.64, AY.43, AY.65, AY.107, AY.66, AY.71, AY.99, AY.42, AY.43, AY.107, AY.66, AY.41, AY.42, AY.43, AY.40, AY.72, AY.40, AY.72, AY.48, AY.40, AY.72, AY.49, AY.41, AY.42, AY.40, AY.72, AY.49, AY.42, AY.41, AY.42, AY.43, AY.40, AY.72, AY.48, AY.40, AY.73, AY.40, AY.41, AY.41, AY.42, AY.43, AY.40, AY.42, AY.43, AY.40, AY.43, AY.44, AY.41, AY.42, AY.43, AY.44, AY.41, AY.41, AY.42, AY.43, AY.44, AY.41, AY.42, AY.41, AY.42, AY.41, A	Barrett et al. (2021)	Depth 45770	Allele G	Frequency 1.0
INTEGRAL			AY.101, C <b>ô</b> Ytả00 Us				CIDGOH ©

nf-ncov-voc 26 of 110

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.54, AY.46.2, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.113, AY.103, AY.43.4, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.84, AY.121.1, AY.117, AY.102, AY.15, AY.32, AY.86, AY.19, AY.116, AY.117, AY.102, AY.15, AY.32, AY.44, AY.47, AY.50, AY.21, AY.47, AY.50, AY.106, AY.114, AY.47, AY.51, AY.42, AY.44, AY.43, AY.64, AY.43, AY.64, AY.78, AY.65, AY.120, AY.106, AY.114, AY.51, AY.46, AY.107, AY.66, AY.114, AY.43, AY.64, AY.78, AY.36, AY.107, AY.66, AY.110, AY.111, AY.45, AY.46, AY.41, AY.99, AY.42, AY.43, AY.40, AY.71, AY.99, AY.42, AY.43, AY.40, AY.71, AY.99, AY.42, AY.43, AY.44, AY.43, AY.45, AY.41, AY.41, AY.45, AY.41, AY.42, AY.43, AY.44, AY.43, AY.45, AY.41, AY.45, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.45, AY.41, AY.42, AY.40, AY.71, AY.98, AY.40, AY.71, AY.98, AY.40, AY.72, AY.85, AY.41, AY.42, AY.40, AY.72, AY.85, AY.41, AY.42, AY.40, AY.72, AY.85, AY.4	Daniloski et al. (2021)	Depth 45770	Allele G	Frequency 1.0
INTERPORT			AY.101, Contact Us				CIDGOH ©

nf-ncov-voc 27 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
p.D614G	Trafficking trafficking	Function  No change in infectivity (24h) relative to D614G alone in Caco-2 cells, Vero or Calu-3.	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.113, AY.113, AY.118, AY.13, AY.3.1, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.19.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.I.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.84, AY.121.1, AY.43.3, AY.2.1, AY.43.3, AY.2.2, AY.44, AY.47, AY.55, AY.120.1, AY.42, AY.105, AY.120, AY.106, AY.114, AY.92, AY.106, AY.114, AY.93, AY.106, AY.114, AY.105, AY.106, AY.114, AY.107, AY.108, AY.106, AY.114, AY.107, AY.108, AY.108, AY.109, AY.109, AY.104, AY.105, AY.106, AY.114, AY.107, AY.107, AY.108, AY.107, AY.108, AY.108, AY.109, AY.109, AY.107, AY.108, AY.109, AY.114, AY.107, AY.107, AY.108, AY.109, AY.114, AY.107, AY.107, AY.108, AY.114, AY.107, AY.107, AY.108, AY.114, AY.107, AY.107, AY.108, AY.46.4, AY.78, AY.36, AY.46.4, AY.79, AY.48, AY.46, AY.71, AY.99, AY.42.1, AY.49, AY.42, AY.49, AY.42, AY.48, AY.41, AY.42, AY.49, AY.41, AY.42, AY.40, AY.72, AY.48, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.42, AY.44, AY.45, AY.40, AY.72, AY.48, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.42, AY.44, AY.43, AY.44, AY.45, AY.49, AY.41, AY.42, AY.48, AY.41, AY.42, AY.48, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.44, AY.44, AY.45, AY.46, AY.47, AY.48, AY.48, AY.49, AY.41, AY.42, AY.48, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.44, AY.44, AY.44, AY.44, AY.45, AY.46, AY.47, AY.48, AY.41, AY.41, AY.42, AY.48, AY.41, AY.42, AY.48, AY.41, AY.42, AY.48, AY.41, AY.41, AY.42, AY.43, AY.44,	Kim et al. (2021)	Sequence Depth 45770	Alternate Allele G	Alternate Frequency 1.0
INTERTO			AY.55, AY.87, AY.101, COMTACO Us				CIDGOH ©

nf-ncov-voc 28 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
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.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.31, AY.53, AY.73, AY.1009, AY.84, AY.23, AY.89, AY.36, AY.44, AY.36, AY.45, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.31, AY.116, AY.119.1, AY.71, AY.102, AY.15, AY.32, AY.34, AY.116, AY.111, AY.43, AY.120.1, AY.42, AY.47, AY.59, AY.120.1, AY.42, AY.47, AY.59, AY.120.1, AY.42, AY.47, AY.59, AY.104, AY.120, AY.105, AY.120, AY.104, AY.120, AY.105, AY.120, AY.104, AY.120, AY.104, AY.120, AY.105, AY.120, AY.104, AY.120, AY.104, AY.126, AY.105, AY.107, AY.42, AY.43, AY.43, AY.44, AY.43, AY.45, AY.46, AY.78, AY.46, AY.78, AY.36, AY.78, AY.36, AY.79, AY.40, AY.79, AY.40, AY.79, AY.40, AY.79, AY.40, AY.79, AY.40, AY.79, AY.40, AY.71, AY.98, AY.40, AY.72, AY.85, AY.30, AY.101, AY.41, AY.42, AY.43, AY.40, AY.72, AY.85, AY.30, AY.104, AY.73, AY.40, AY.72, AY.85, AY.30, AY.104, AY.42, AY.40, AY.72, AY.88, AY.40, AY.73, AY.104, AY.114, AY.416, AY.42, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.44, AY.45, AY.40, AY.73, AY.40,	Kim et al. (2021)	45770	Allele	1.0
INFECTION OF			AY.101, C <b>entace</b> Us				CIDGOH ®

nf-ncov-voc 29 of 110

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	G	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	G	1.0



nf-ncov-voc 30 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
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.	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.113, AY.103, AY.103, AY.124, AY.109, AY.84, AY.23, AY.86, AY.44, AY.34.1, AY.119.1, AY.77, AY.75, AY.4, AY.119.1, AY.710, AY.116.1, AY.117, AY.102, AY.116, AY.117, AY.103, AY.21, AY.33, AY.2, AY.44, AY.47, AY.55, AY.120.1, AY.42, AY.74, AY.105, AY.106, AY.114, AY.106, AY.114, AY.106, AY.114, AY.106, AY.114, AY.107, AY.108, AY.108, AY.109, AY.109, AY.109, AY.109, AY.109, AY.109, AY.101, AY.111, AY.106, AY.111, AY.107, AY.107, AY.108, AY.109, AY.109, AY.110, AY.111, AY.107, AY.108, AY.109, AY.110, AY.111, AY.107, AY.111, AY.107, AY.40, AY.110, AY.111, AY.117, AY.42, AY.42, AY.43, AY.46, AY.41, AY.42, AY.40, AY.73, AY.42, AY.41, AY.42, AY.40, AY.73, AY.41, AY.42, AY.41, AY.42, AY.40, AY.73, AY.41, AY.42, AY.40, AY.42, AY.41, AY.42, AY.40,	Ozono et al. (2020)	Depth 45770	Allele G	Frequency 1.0
			AY.101, C <b>ônta00</b> Us				CIDGOH <sup>©</sup>

<u>nf-ncov-voc</u> 31 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.13, AY.3.1, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.41, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.16.1, AY.117, AY.102, AY.16.1, AY.119.1, AY.77, AY.65, AY.32, AY.34, AY.104, AY.105, AY.106, AY.114, AY.105, AY.120, AY.106, AY.120, AY.106, AY.114, AY.126, AY.106, AY.114, AY.126, AY.106, AY.114, AY.126, AY.106, AY.114, AY.126, AY.107, AY.64, AY.78, AY.37, AY.120, AY.104, AY.120, AY.105, AY.120, AY.106, AY.114, AY.127, AY.49, AY.42, AY.43, AY.46.4, AY.43, AY.46.4, AY.43, AY.46.4, AY.43, AY.46.4, AY.78, AY.37, AY.107, AY.66, AY.71, AY.99, AY.26, AY.110, AY.111, AY.127, AY.49, AY.42, AY.43, AY.40, AY.72, AY.49, AY.42, AY.43, AY.41, AY.99, AY.42, AY.43, AY.41, AY.99, AY.41, AY.99, AY.42, AY.43, AY.41, AY.99, AY.41, AY.43, AY.41, AY.99, AY.41, AY.43, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.410, AY.75, AY.85, AY.87, AY.101, AY.100, AY.110, AY.87, AY.100	Tada et al. (2021)	45752	G	1.0
See See Ba			Contact He				CIDCOH ®

Contact Us CIDGOH

nf-ncov-voc 32 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence		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.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.3.1, AY.53, AY.73, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.116, AY.9.2.1, AY.37, AY.121.1, AY.37, AY.121.1, AY.43.3, AY.2, AY.44, AY.47, AY.5, AY.65, AY.25, AY.120.1, AY.42, AY.74, AY.105, AY.106, AY.114, AY.51, AY.106, AY.114, AY.51, AY.42, AY.106, AY.106, AY.114, AY.51, AY.42, AY.43, AY.64, AY.78, AY.64, AY.78, AY.65, AY.106, AY.111, AY.42, AY.106, AY.111, AY.43, AY.42, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.41, AY.49, AY.42, AY.41, AY.49, AY.42, AY.41, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.41, AY.42, AY.43, AY.44, AY.42, AY.44, AY.47, AY.49, AY.49, AY.41, AY.49, AY.41, AY.41, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.43, AY.43, AY.44, AY.43, AY.44, AY.44, AY.44, AY.45, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.41, AY.41, AY.42, AY.41, AY.42, AY.43, AY.43, AY.44, AY.43, AY.44, AY.44, AY.45, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.45, AY.45, AY.48, AY.	Zhang et 1. (2020)	Depth 45770	Allele G	Frequency 1.0
			AY.101, C <b>antale</b> Us				CIDGOH <sup>©</sup>

nf-ncov-voc 33 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Allele	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.54, AY.46.2, AY.45, AY.46.2, AY.45, AY.108, AY.11, AY.113, AY.118, AY.113, AY.118, AY.109, AY.43.4, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.19.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.84, AY.121, AY.47, AY.102, AY.15, AY.32, AY.34, AY.116, AY.17, AY.102, AY.15, AY.31, AY.41, AY.47, AY.54, AY.105, AY.120, AY.106, AY.114, AY.51, AY.42, AY.43, AY.64, AY.41, AY.42, AY.43, AY.40, AY.72, AY.43, AY.40, AY.72, AY.43, AY.40, AY.72, AY.40, AY.73, AY.10, AY.111, AY.42, AY.43, AY.40, AY.73, AY.40, AY.72, AY.48, AY.40, AY.72, AY.48, AY.40, AY.73, AY.40, AY.73, AY.10, AY.111, AY.42, AY.43, AY.40, AY.73, AY.40, AY.41, AY.42, AY.43, AY.40, AY.42, AY.43, AY.40, AY.43, AY.40, AY.43, AY.40, AY.43, AY.40, AY.41, AY.42, AY.43, AY.44, AY.41, AY.42, AY.40, AY.42, AY.43, AY.44, AY.41, AY.42, AY.43, AY.44, AY.41, AY.42, AY.43, AY.44, AY.41, AY.42, AY.43, AY.40, AY.41, AY.42, AY.43, AY.40, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.43, AY.40, AY.42, AY.44, AY.41, AY.42, AY.41,	Tada et al. (2021)	Depth 45770	Allele G	Frequency 1.0
			AY.101, C <b>entae</b> Us				CIDGOH <sup>©</sup>

nf-ncov-voc 34 of 110

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.98, AY.35	Tada et al. (2021)	12	G	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.98, AY.35	Tada et al. (2021)	12	G	1.0



nf-ncov-voc 35 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Allele	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.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.13, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.84, AY.23, AY.44, AY.19.1, AY.77, AY.75, AY.4, AY.19.1, AY.77, AY.16.1, AY.116.1, AY.117, AY.116, AY.111, AY.43.3, AY.2, AY.44, AY.47, AY.55, AY.65, AY.120, AY.104, AY.126, AY.106, AY.114, AY.105, AY.106, AY.114, AY.105, AY.106, AY.114, AY.51, AY.46.4, AY.43, AY.64, AY.78, AY.65, AY.106, AY.114, AY.105, AY.106, AY.114, AY.105, AY.106, AY.114, AY.107, AY.40, AY.107, AY.68, AY.40, AY.110, AY.111, AY.41, AY.42, AY.42, AY.43, AY.42, AY.43, AY.40, AY.72, AY.85, AY.39, AY.42.1, AY.49, AY.49, AY.49, AY.49, AY.49, AY.49, AY.41, AY.41, AY.41, AY.42, AY.43, AY.40, AY.71, AY.98, AY.61, AY.45, AY.111, AY.161, AY.161, AY.161, AY.17, AY.98, AY.20, AY.110, AY.111, AY.127, AY.49, AY.99, AY.42, AY.110, AY.111, AY.127, AY.49, AY.49, AY.49, AY.40, AY.72, AY.85, AY.39, AY.40, AY.72, AY.85, AY.39, AY.10, AY.111, AY.127, AY.98, AY.40, AY.72, AY.88, AY.40, AY.72, AY.88, AY.40, AY.72, AY.88, AY.107, AY.89, AY.40, AY.71, AY.99, AY.40, AY.71, AY.99, AY.41, AY.42, AY.43, AY.40, AY.72, AY.85, AY.39, AY.10, AY.111, AY.45, AY.41, AY.45, AY.45, AY.41, AY.45, AY.41, AY.45, AY.45, AY.48, AY.48	Garcia-Beltran et al. (2021)	Depth 45770	Allele G	Frequency 1.0
			AY.101, C <b>0</b> Yt400 Us				CIDGOH ®

nf-ncov-voc 36 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
p.D614G	vaccine neutralization 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 vaccines)	AY.98, AY.35	Gong et al. (2021)	12	G	1.0



nf-ncov-voc 37 of 110

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.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.113, AY.13, AY.31, AY.53, AY.703, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.41, AY.46.1, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.116.1, AY.117, AY.116.1, AY.117, AY.102, AY.116, AY.116, AY.116, AY.117, AY.102, AY.116, AY.117, AY.102, AY.116, AY.119, AY.116, AY.117, AY.102, AY.116, AY.119, AY.116, AY.111, AY.117, AY.43, AY.2, AY.43, AY.20, AY.120, AY.104, AY.105, AY.106, AY.114, AY.105, AY.106, AY.114, AY.105, AY.106, AY.114, AY.107, AY.66, AY.108, AY.108, AY.109, AY.109, AY.104, AY.111, AY.127, AY.49, AY.40, AY.71, AY.49, AY.40, AY.71, AY.49, AY.40, AY.71, AY.49, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.45, AY.41, AY.49, AY.41, AY.49, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.45, AY.46, AY.47, AY.48, AY.49, AY.49, AY.49, AY.49, AY.49, AY.40, AY.51, AY.41, AY.41, AY.42, AY.43, AY.44, AY.45, AY.41, AY.47, AY.48, AY.41, AY.49, AY.49, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44,	Kuzmina et al. (2021)	Depth 45770	G G	Frequency
			AY.101, C <b>entace</b> Us				CIDGOH <sup>©</sup>

nf-ncov-voc 38 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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.77	Kuzmina et al. (2021)	2	G	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	G	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	G	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.98, AY.35	Tada et al. (2021)	12	G	1.0



Contact Us CIDGOH <sup>©</sup>

nf-ncov-voc 39 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Allele	Alternate
p.D614G	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.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.31, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.41, AY.19.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.9.2.1, AY.37, AY.121.1, AY.43.3, AY.2, AY.4.4, AY.47, AY.5, AY.65, AY.25, AY.120, AY.104, AY.126, AY.105, AY.120, AY.104, AY.126, AY.105, AY.120, AY.106, AY.114, AY.51, AY.46.4, AY.47, AY.5, AY.68, AY.41, AY.49, AY.99.2, AY.67, AY.106, AY.114, AY.105, AY.110, AY.111, AY.126, AY.106, AY.114, AY.51, AY.46.4, AY.43, AY.64, AY.71, AY.99, AY.65, AY.106, AY.111, AY.126, AY.106, AY.111, AY.127, AY.99, AY.26, AY.40, AY.71, AY.99, AY.42.1, AY.43, AY.43, AY.44, AY.43, AY.45, AY.41, AY.45, AY.45, AY.46, AY.47, AY.48, AY.41, AY.48, AY.41, AY.48, AY.49, AY.49	Wilhelm et al. (2021)	45770	Allele	Trequency  1.0
NAME OF THE PARTY			AY.101, C <b>ontace</b> Us				CIDGOH <sup>©</sup>

nf-ncov-voc 40 of 110

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	G	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	G	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	G	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 nonseroconverted 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	G	1.0



Contact Us CIDGOH  $^{\odot}$ 

nf-ncov-voc 41 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
p.D614G	vaccinee binding plasma	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.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.3.1, AY.53, AY.73, AY.109, AY.84, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.9.2.1, AY.37, AY.121.1, AY.47, AY.5, AY.65, AY.25, AY.120.1, AY.42, AY.44, AY.47, AY.5, AY.65, AY.25, AY.120.1, AY.42, AY.74, AY.105, AY.104, AY.114, AY.51, AY.46.4, AY.43, AY.107, AY.66, AY.114, AY.47, AY.99, AY.40, AY.111, AY.127, AY.49, AY.49, AY.49, AY.49, AY.49, AY.41, AY.41, AY.42, AY.41, AY.42, AY.43, AY.45, AY.41, AY.41, AY.45, AY.41, AY.45, AY.41, AY.45, AY.41, AY.45, AY.41, AY.45, AY.45, AY.41, AY.45, AY.45, AY.41, AY.45, A	Gong et al. (2021)	Depth 45770	Allele G	Frequency 1.0
INFECTION IN			AY.101, C <b>entace</b> Us				CIDGOH <sup>©</sup>

nf-ncov-voc 42 of 110

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.98, AY.35	Gong et al. (2021)	12	G	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.77, AY.46.4, AY.6, AY.35, AY.4.4	Gong et al. (2021)	31	G	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 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	G	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 nonseroconverted 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	G	1.0



Contact Us CIDGOH <sup>®</sup>

nf-ncov-voc 43 of 110

Mutations	Sub-category	Func	tion	Lineages	Citatio	n	Sequence Depth	Alternate Allele	Alternate Frequency
p.D614G	vaccinee binding pla	bindi D614 plasm weeks of BNT in seroc 1.02x bindi D614 plasn weeks	G alone) by 5 na collected 3 s after one dose Pfizer/BioNtech 162b2 vaccine previously nononverted subjects. decrease in Spike ng (relative to G alone) by 5	AY.106, AY.114, AY.119.1, AY.77, AY.4, AY.107, AY.4, AY.1, AY.119, AY.4.5, B.1.617.2, AY.121, AY.88, AY.4.2.2, AY.116.1, AY.117, AY.108, AY.5.3, AY.102, AY.113, AY.118, AY.34, AY.116, AY.39, AY.4.2.1, AY.4.3, AY.121.1, AY.29, AY.124, AY.4.4, AY.20, AY.4.3, AY.109, AY.110, AY.111, AY.109, AY.111, AY.109, AY.111, AY.127, AY.89, AY.34.1, AY.4.6, AY.92, AY.120.1, AY.4.20, AY.4.20, AY.4.20, AY.4.30, AY.4.31, AY.109, AY.111, AY.109, AY.110, AY.111, AY.127, AY.89, AY.36, AY.34.1, AY.4.2, AY.4.2, AY.120, AY.4.20, AY.4.30, AY.120	Gong (2021)	et al.	4594	G	1.0



nf-ncov-voc 44 of 110

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.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.3.1, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.9.2.1, AY.37, AY.121.1, AY.47, AY.5, AY.65, AY.25, AY.120.1, AY.42, AY.44, AY.105, AY.104, AY.105, AY.106, AY.111, AY.46.4, AY.43, AY.64, AY.78, AY.39, AY.107, AY.6, AY.107, AY.6, AY.110, AY.111, AY.41, AY.42, AY.42, AY.43, AY.42, AY.43, AY.40, AY.72, AY.49, AY.42, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.43, AY.41, AY.42, AY.41, AY.42, AY.43, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.42, AY.49, AY.49, AY.49, AY.49, AY.41, AY.41, AY.45, AY.41, AY.41, AY.45, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.44, AY.45, AY.45, AY.41, AY.45, AY.45, AY.41, AY.45, AY.45	Plante et al. (2020)	Depth 45770	G	Frequency 1.0
			AY.101, C <b>entaee</b> Us				CIDGOH <sup>©</sup>

nf-ncov-voc 45 of 110

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.54, AY.46.2, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.31, AY.53, AY.709, AY.84, AY.109, AY.84, AY.23, AY.89, AY.36, AY.411, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.16, AY.116, AY.116, AY.111, AY.117, AY.102, AY.15, AY.37, AY.116, AY.116, AY.111, AY.43.3, AY.2, AY.44, AY.47, AY.5, AY.65, AY.25, AY.120.1, AY.42, AY.106, AY.114, AY.105, AY.120, AY.104, AY.126, AY.106, AY.114, AY.51, AY.46.4, AY.47, AY.59, AY.67, AY.68, AY.41, AY.49, AY.106, AY.114, AY.51, AY.46.4, AY.105, AY.106, AY.114, AY.107, AY.108, AY.107, AY.69, AY.104, AY.120, AY.110, AY.111, AY.127, AY.49, AY.40, AY.71, AY.99, AY.42, AY.43, AY.40, AY.72, AY.85, AY.39, AY.40, AY.71, AY.98, AY.60, AY.21, AY.41, AY.42, AY.43, AY.40, AY.72, AY.85, AY.39, AY.40, AY.71, AY.98, AY.60, AY.21, AY.41, AY.42, AY.43, AY.40, AY.72, AY.84, AY.43, AY.40, AY.72, AY.88, AY.40, AY.72, AY.88, AY.40, AY.72, AY.88, AY.40, AY.72, AY.88, AY.99, AY.41, AY.45, AY.41, AY.45, AY.45, AY.45, AY.41, AY.45, AY.45, AY.41, AY.45, AY.45, AY.48,	Spratt et al. (2021)	Depth 45770	Allele G	Frequency 1.0
1811017			AY.101, C <b>o</b> Yta@ Us				CIDGOH ®

nf-ncov-voc 46 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
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.54, AY.46.2, AY.45, AY.46.3, AY.108, AY.113, AY.113, AY.113, AY.113, AY.13, AY.13, AY.103, AY.43.4, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.19.1, AY.77, AY.75, AY.4, AY.125, AY.99, B.1.617.2, AY.86, AY.116, AY.117, AY.102, AY.15, AY.31, AY.161, AY.117, AY.102, AY.15, AY.31, AY.41, AY.47, AY.54, AY.120.1, AY.47, AY.54, AY.105, AY.120.1, AY.42, AY.44, AY.47, AY.54, AY.105, AY.120, AY.106, AY.114, AY.105, AY.120, AY.106, AY.114, AY.105, AY.120, AY.106, AY.114, AY.105, AY.120, AY.106, AY.114, AY.42, AY.43, AY.64, AY.43, AY.65, AY.107, AY.66, AY.71, AY.99, AY.42, AY.43, AY.107, AY.66, AY.41, AY.42, AY.43, AY.40, AY.72, AY.40, AY.72, AY.48, AY.40, AY.72, AY.49, AY.41, AY.42, AY.40, AY.72, AY.49, AY.42, AY.41, AY.42, AY.43, AY.40, AY.72, AY.48, AY.40, AY.72, AY.88, AY.40, AY.72, AY.88, AY.40, AY.72, AY.88, AY.40, AY.72, AY.88, AY.40, AY.73, AY.10, AY.111, AY.161, AY.40, AY.72, AY.88, AY.40, AY.72, AY.88, AY.40, AY.73, AY.40, AY.73, AY.40, AY.73, AY.40, AY.41, AY.42, AY.43, AY.40, AY.41, AY.42, AY.43, AY.40, AY.42, AY.43, AY.44, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.41, AY.42, AY.44, AY.41, AY.42, AY.41,	Weissman et al. (2020)	Depth 45770	Allele G	Frequency 1.0
INFECTION AND AND AND AND AND AND AND AND AND AN			AY.101, C <b>ô</b> Mtå00 Us				CIDGOH <sup>©</sup>

nf-ncov-voc 47 of 110

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.54, AY.46, AY.46, AY.46, AY.45, AY.48, AY.108, AY.11, AY.113, AY.113, AY.113, AY.103, AY.43.4, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.86, AY.19, AY.116, AY.117, AY.102, AY.15, AY.32, AY.86, AY.19, AY.116, AY.117, AY.102, AY.15, AY.32, AY.44, AY.47, AY.59, AY.92.1, AY.37, AY.121, AY.43, AY.21, AY.47, AY.56, AY.25, AY.120, AY.106, AY.114, AY.120, AY.106, AY.114, AY.43, AY.64, AY.43, AY.64, AY.43, AY.64, AY.43, AY.64, AY.43, AY.64, AY.43, AY.64, AY.78, AY.36, AY.106, AY.114, AY.51, AY.46, AY.107, AY.69, AY.108, AY.107, AY.69, AY.107, AY.69, AY.110, AY.111, AY.51, AY.40, AY.71, AY.99, AY.42, AY.43, AY.40, AY.71, AY.99, AY.42, AY.43, AY.40, AY.71, AY.99, AY.42, AY.43, AY.40, AY.72, AY.43, AY.40, AY.71, AY.98, AY.40, AY.72, AY.43, AY.41, AY.42, AY.43, AY.42, AY.43, AY.42, AY.43, AY.42, AY.43, AY.40, AY.71, AY.98, AY.40, AY.71, AY.98, AY.40, AY.72, AY.85, AY.30, AY.110, AY.111, AY.45, AY.41, AY.42, AY.40, AY.72, AY.85, AY.30, AY.110, AY.111, AY.45, AY.41, AY.42, AY.40, AY.72, AY.85, AY.30, AY.104, AY.110, AY.111, AY.127, AY.49, AY.42, AY.43, AY.40, AY.72, AY.85, AY.30, AY.110, AY.111, AY.127, AY.49, AY.42, AY.40, AY.72, AY.85, AY.30, AY.110, AY.111, AY.127, AY.49, AY.42, AY.40, AY.72, AY.85, AY.30, AY.40, AY.72, AY.85, AY.30, AY.10, AY.111, AY.127, AY.49, AY.42, AY.43, AY.40, AY.72, AY.85, AY.30, AY.40, AY.72, AY.85, AY.40, AY.73, AY.40, AY.73, AY.40, AY.73, AY.40, AY.71, AY.81, AY.41, AY.42, AY.44, AY.42, AY.44, AY.42, AY.44, AY.42, AY.44, AY.42, AY.4	Yurkovetskiy et al. (2020)	Depth 45770	G	Frequency 1.0
INTEGOTION OF THE PARTY OF THE			AY.101, C <b>entae</b> Us				CIDGOH <sup>©</sup>

nf-ncov-voc 48 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
p.D614G	virion structure	Based on pseudotyped virus experiments, D614G may increase infectivity by assembling more functional S protein into the virion.	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.111, AY.113, AY.118, AY.13, AY.31, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.75, AY.4, AY.125, AY.86, AY.116.1, AY.116.1, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.121.1, AY.47, AY.5, AY.65, AY.21, AY.47, AY.120.1, AY.42, AY.44, AY.47, AY.5, AY.65, AY.25, AY.120, AY.104, AY.120, AY.104, AY.120, AY.104, AY.120, AY.104, AY.120, AY.104, AY.120, AY.105, AY.120, AY.104, AY.121, AY.43, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.41, AY.49, AY.42, AY.43, AY.44, AY.49, AY.45, AY.41, AY.49, AY.49, AY.41, AY.49, AY.49, AY.41, AY.49, AY.49, AY.41, AY.49, AY.49, AY.41, AY.41, AY.42, AY.49, AY.41, AY.42, AY.40, AY.72, AY.48, AY.40, AY.73, AY.104, AY.41, AY.49, AY.41, AY.42, AY.40, AY.73, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.46, AY.47, AY.49, AY.49, AY.41, AY.41, AY.42, AY.40, AY.73, AY.41, AY.41, AY.42, AY.40, AY.73, AY.41, AY.41, AY.42, AY.40, AY.73, AY.41, AY.42, AY.40, AY.73, AY.41, AY.41, AY.42, AY.40, AY.73, AY.41, AY.41, AY.42, AY.40, AY.42, AY.40, AY.42, AY.40, AY.43, AY.40, AY.43, AY.40, AY.41, AY.41, AY.41, AY.41, AY.42, AY.40, AY.42, AY.40, AY.43, AY.44, AY.44, AY.44, AY.44, AY.44, AY.44, AY.45, AY.45, AY.46, AY.41, AY.41, AY.42, AY.40, AY.42, AY.43, AY.44, AY	Zhang et al. (2020)	depth 45770	Allele	Frequency 1.0
INFECTION AND ADDRESS OF THE PARTY OF THE PA			AY.101, C <b>ô</b> Yt <b>ả00</b> Us				CIDGOH <sup>©</sup>

nf-ncov-voc 49 of 110

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.3.1	Gong et al. (2021)	22	TG,CG	1.0
p.L452R	ACE2 receptor binding affinity	extasciitilde1.7-fold increase in binding affinity vs wild type.	AY.3.1	Motozono et al. (2021)	22	TG,CG	1.0
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)	22	TG,CG	1.0
p.L452R	antibody epitope effects	Resistent to some neutralizing antibodies: mAbs X593 and P2B- 2F6	AY.3.1	Li et al. (2020)	22	TG,CG	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)	22	TG,CG	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)	22	TG,CG	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)	22	TG,CG	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)	22	TG,CG	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)	22	TG,CG	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)	22	TG,CG	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)	22	TG,CG	1.0
p.L452R	gene expression in- crease	Experimentally, Spike gene expression in- creased 0.32 fold	AY.3.1	Starr et al. (2020)	22	TG,CG	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)	22	TG,CG	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)	22	TG,CG	1.0



Contact Us CIDGOH <sup>©</sup>

nf-ncov-voc 50 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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)	22	TG,CG	1.0
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 extasciitilde4x binding against this isolated mutation.	AY.3.1	Engelhart et al. (2021)	22	TG,CG	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)	22	TG,CG	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)	22	TG,CG	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)	22	TG,CG	1.0
p.L452R	trafficking	Increased stability of RBD expression in yeast, suggesting in- creased Spike protein stability.	AY.3.1	Motozono et al. (2021)	22	TG,CG	1.0
p.L452R	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.3.1	Tada et al. (2021)	22	TG,CG	1.0
p.L452R	vaccine neutraliza- tion 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)	22	TG,CG	1.0
p.L452R	vaccine neutraliza- tion 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)	22	TG,CG	1.0



Contact Us CIDGOH <sup>©</sup>

nf-ncov-voc 51 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
p.L452R	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.3.1	Wilhelm et al. (2021)	22	TG,CG	1.0
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)	22	TG,CG	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)	22	TG,CG	1.0



Contact Us CIDGOH <sup>®</sup>

nf-ncov-voc 52 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth		Alternate Frequency
Mutations 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.	Lineages  AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.113, AY.113, AY.113, AY.13, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.75, AY.41, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.47, AY.37, AY.121, AY.43, AY.2, AY.44, AY.47, AY.5, AY.65, AY.25, AY.120, AY.104, AY.105, AY.107, AY.99, AY.40, AY.71, AY.99, AY.40, AY.71, AY.99, AY.41, AY.99, AY.41, AY.99, AY.42, AY.43, AY.40, AY.72, AY.85, AY.39, AY.40, AY.71, AY.98, AY.40, AY.72, AY.85, AY.31, AY.11, AY.45, AY.41, AY.91, AY.45, AY.41, AY.92, AY.110, AY.111, AY.45, AY.41, AY.93, AY.40, AY.72, AY.85, AY.31, AY.41, AY.94, AY.73, AY.94, AY.17, AY.98, AY.40, AY.72, AY.85, AY.110, AY.111, AY.45, AY.121, AY.47, AY.85, AY.110, AY.111, AY.47, AY.98, AY.40, AY.73, AY.	Gong et al. (2021)	Sequence Depth 59423	Alternate Allele G	Alternate Frequency 1.0
O INFECTION			AY.122, AY.29, AY.83, AY.98.1,				
Ann out			AY.98.1, Contact Us AY.48, AY.4.6, AY.122.1,				CIDGOH <sup>©</sup>

nf-ncov-voc 53 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
					Depth	Allele	Frequency
p.L452R	ACE2 receptor bind-	Using flow cytometry	AY.98, AY.35,	Gong et al.	24	G	1.0
_	ing affinity	and ACE2 ectodomains-	AY.70	(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					



Contact Us CIDGOH <sup>©</sup>

nf-ncov-voc 54 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
Mutations p.L452R	Sub-category  ACE2 receptor binding affinity	Function  extasciitilde1.7-fold increase in binding affinity vs wild type.	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.13, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.66, AY.125, AY.59, B.1.617.2, AY.86, AY.19,	Citation  Motozono et al. (2021)	Sequence Depth 59425	Alternate Allele G	Alternate Frequency 1.0
		AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.70, AY.9.2.1, AY.37,					
			AY.121.1, AY.43.3, AY.2, AY.4.4, AY.47, AY.5, AY.65, AY.25, AY.120.1, AY.42, AY.74, AY.105,				
			AY.120, AY.104, AY.126, AY.106, AY.114, AY.51, AY.46.4, AY.43, AY.64, AY.78, AY.3,				
			AY.107, AY.107, AY.6, AY.7.1, AY.99, AY.26, AY.68, AY.38, AY.46.6, AY.41, AY.99.2, AY.46,				
			AY.67, AY.39, AY.4.2.1, AY.4.3, AY.35, AY.20, AY.110, AY.111, AY.127,				
			AY.33, AY.49, AY.57, AY.92, AY.14, AY.4.2, AY.40, AY.72, AY.85, AY.39.1, AY.21, AY.94, AY.17,				
			AY.98, AY.60, AY.25.1, AY.1, AY.119, AY.4.5, AY.61, AY.82, AY.121, AY.16.1, AY.56, AY.18,				
38 1875C7706_			AY.30, AY.18, AY.4.2.2, AY.28, AY.93, AY.10, AY.5.3, AY.24, AY.16, AY.62, AY.122, AY.29, AY.83,				
			AY.29, AY.83, CentaletiUs AY.9.2, AY.48, AY.4.6,				CIDGOH 6

nf-ncov-voc 55 of 110

nf-ncov-voc 56 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
Mutations p.L452R	antibody epitope effects	Resistent to some neutralizing antibodies: mAbs X593 and P2B-2F6	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.66, AY.125, AY.59, B.1.617.2, AY.86, AY.116.1, AY.117, AY.102, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.37, AY.116, AY.9, AY.116, AY.9, AY.110, AY.9, AY.120.1, AY.42, AY.43, AY.20, AY.104, AY.105, AY.120.1, AY.42, AY.43, AY.43, AY.44, AY.47, AY.51, AY.46, AY.106, AY.114, AY.51, AY.46, AY.107, AY.66, AY.114, AY.51, AY.46, AY.107, AY.67, AY.68, AY.71, AY.99, AY.68, AY.71, AY.99, AY.69, AY.104, AY.107, AY.69, AY.107, AY.69, AY.107, AY.69, AY.107, AY.69, AY.41, AY.99, AY.42, AY.43, AY.40, AY.43, AY.43, AY.43, AY.44, AY.43, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.45, AY.46, AY.47, AY.49, AY.41, AY.49, AY.41, AY.49, AY.49, AY.41, AY.49, AY.49, AY.49, AY.57, AY.99, AY.41, AY.49, AY.49, AY.57, AY.99, AY.14,	Li et al. (2020)			
		AY.4.3, AY.35, AY.20, AY.110, AY.111, AY.127, AY.33, AY.49, AY.57, AY.92, AY.14, AY.4.2, AY.40, AY.72, AY.85, AY.39.1, AY.21, AY.94, AY.17, AY.98, AY.60,					
			AY.25.1, AY.1, AY.119, AY.4.5, AY.61, AY.82, AY.121, AY.16.1, AY.56, AY.18, AY.4.2.2, AY.28, AY.93, AY.10, AY.5.3, AY.24, AY.16, AY.62, AY.122,				
NINTECTOR			AY.29, AY.83, ContactiUs AY.9.2, AY.48, AY.4.6,				CIDGOH (

<u>nf-ncov-voc</u> 57 of 110

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.54, AY.46.2, AY.45, AY.88, AY.108, AY.111, AY.113, AY.118, AY.103, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.41, AY.77, AY.27, AY.75, AY.46, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.70, AY.9.2.1, AY.37, AY.121.1, AY.43.3, AY.2, AY.44, AY.42, AY.42, AY.44, AY.105, AY.106, AY.114, AY.105, AY.106, AY.114, AY.107, AY.42, AY.43, AY.44, AY.44, AY.47, AY.51, AY.46, AY.106, AY.114, AY.107, AY.108, AY.109, AY.104, AY.120, AY.104, AY.120, AY.104, AY.120, AY.105, AY.120, AY.104, AY.120, AY.104, AY.120, AY.105, AY.120, AY.114, AY.51, AY.42, AY.43, AY.44, AY.43, AY.44, AY.47, AY.38, AY.46, AY.41, AY.49, AY.41, AY.49, AY.41, AY.42, AY.41, AY.42, AY.43, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.49, AY.47, AY.49, AY.41, AY.49, AY.41, AY.41, AY.42, AY.41, AY.42, AY.43, AY.43, AY.44, AY.43, AY.44, AY.45, AY.41, AY.45, AY.41, AY.47, AY.49, AY.41, AY.49, AY.41, AY.41, AY.42, AY.41, AY.42, AY.43, AY.43, AY.44, AY.47, AY.49, AY.41, AY.42, AY.41, AY.43, AY.44, AY.47, AY.49, AY.41, AY.41, AY.42, AY.43, AY.43, AY.44, AY.43, AY.44, AY.45, AY.49, AY.47, AY.49, AY.47, AY.49, AY.49, AY.41, AY.41, AY.41, AY.42, AY.43, AY.43, AY.43, AY.44, AY.43, AY.44, AY.45, AY.49, AY.47, AY.49, AY.47, AY.49, AY.49, AY.49, AY.49, AY.49, AY.57, AY.99, AY.40, AY.71, AY.98, AY.40, AY.72, AY.85, AY.40, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.45, AY.49, AY.51,	Liu et al. (2021)			
LOS INFECTIONS			AY.62, AY.122, AY.29, AY.83,				<del> </del>
			Contact Us AY.9.2, AY.48, AY.4.6,				CIDGOH ©

nf-ncov-voc 58 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
p.L452R	antibody epitope effects	10 of 14 RBD-specific mAbs that showed	AY.54, AY.46.2,	McCallum et al. (2021)	59425	G	1.0
	10000	at least 10-fold re-	AY.45, AY.88,	(2021)			
		duced neutralization of B.1.427/B.1.429 vari-	AY.108, AY.11,				
		ant pseudotype (S13I, W152C, and L452R)	AY.113, AY.118,				
		were also found to poorly bind to just a	AY.13, AY.53, AY.73,				
	L452R RBD mutant,	AY.103,					
		demonstrating a role for this mutation as an	AY.43.4, AY.124,				
		escape mechanism for certain RBD-targeting	AY.109, AY.84,				
		mAbs.	AY.23, AY.89, AY.36, AY.44,				
			AY.34.1,				
			AY.46.1, AY.119.1,				
			AY.77, AY.27, AY.75, AY.4,				
			AY.66, AY.125,				
			AY.59,				
			B.1.617.2, AY.86, AY.19,				
			AY.116.1, AY.117,				
			AY.102,				
			AY.15, AY.32, AY.34,				
			AY.116, AY.9, AY.70,				
			AY.9.2.1, AY.37,				
			AY.121.1, AY.43.3,				
			AY.2, AY.4.4,				
			AY.47, AY.5, AY.65, AY.25,				
			AY.120.1, AY.42, AY.74,				
			AY.105,				
			AY.120, AY.104,				
			AY.126, AY.106,				
			AY.114, AY.51,				
			AY.46.4,				
			AY.43, AY.64, AY.78, AY.3,				
			AY.107, AY.6, AY.7.1,				
			AY.99, AY.26, AY.68, AY.38,				
			AY.46.6,				
			AY.41, AY.99.2,				
			AY.46, AY.67, AY.39,				
			AY.4.2.1, AY.4.3,				
			AY.35, AY.20,				
			AY.110, AY.111,				
			AY.127, AY.33,				
			AY.49, AY.57, AY.92, AY.14,				
			AY.4.2, AY.40,				
			AY.72, AY.85, AY.39.1,				
			AY.21, AY.94, AY.17,				
			AY.98, AY.60, AY.25.1, AY.1,				
			AY.119,				
			AY.4.5, AY.61, AY.82,				
			AY.121, AY.16.1,				
			AY.56, AY.18,				
			AY.4.2.2, AY.28, AY.93,				
			AY.10, AY.5.3, AY.24, AY.16,				
			AY.62, AY.122,				
INTECT/O			AY.29, AY.83,				GID ~ ~ ~ ~ ^
			ContactiUs AY.9.2,				CIDGOH <sup>©</sup>
A CAND ONE			AY.48, AY.4.6,			<u> </u>	

nf-ncov-voc 59 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
p.L452R	Sub-category antibody epitope effects	extasciitilde20% (ELISA significance threshold) drop in antibody binding (ELISA) by this variant against monoclonal antibody VH ab6.	Lineages  AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.13, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.66, AY.125, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.86, AY.121, AY.43.3, AY.2, AY.44, AY.47, AY.5, AY.121.1, AY.43.3, AY.2, AY.44, AY.47, AY.5, AY.120, AY.106, AY.114, AY.107, AY.108, AY.107, AY.108, AY.108, AY.108, AY.109, AY.109, AY.109, AY.101, AY.106, AY.111, AY.43, AY.106, AY.114, AY.107, AY.108, AY.108, AY.109, AY.109, AY.109, AY.109, AY.109, AY.109, AY.109, AY.101, AY.106, AY.111, AY.43, AY.43, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.46, AY.41, AY.43, AY.45, AY.40, AY.72, AY.43, AY.40, AY.72, AY.43, AY.42, AY.43, AY.44, AY.43, AY.45, AY.40, AY.72, AY.43, AY.45, AY.40, AY.72, AY.48, AY.49, AY.41, AY.49, AY.41, AY.42, AY.40, AY.72, AY.43, AY.45, AY.40, AY.72, AY.85, AY.40, AY.71, AY.98, AY.40, AY.72, AY.85, AY.41, AY.41, AY.42, AY.40, AY.72, AY.85, AY.41, AY.43, AY.45, AY.41, AY.45, AY.41, AY.47, AY.85, AY.40, AY.72, AY.85, AY.40, AY.73, AY.85, AY.80,	Citation  Sun et al. (2021)			
or INFECTION.			AY.24, AY.16, AY.62, AY.122, AY.29, AY.83,				
			ContactiUs AY.9.2, AY.48, AY.4.6,				CIDGOH ©

nf-ncov-voc 60 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
p.L452R	convalescent plasma binding	Function  2.15x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptomonset.	Lineages  AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.113, AY.113, AY.113, AY.113, AY.103, AY.43.4, AY.109, AY.84, AY.23, AY.89, AY.36, AY.41, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.116.1, AY.117, AY.102, AY.116, AY.9, AY.34, AY.116, AY.9, AY.34, AY.116, AY.9, AY.70, AY.92.1, AY.43, AY.121.1, AY.43, AY.2, AY.44, AY.47, AY.5, AY.65, AY.25, AY.120.1, AY.42, AY.44, AY.105, AY.104, AY.105, AY.107, AY.40, AY.107, AY.40, AY.71, AY.99, AY.41, AY.99, AY.42, AY.43, AY.40, AY.72, AY.33, AY.49, AY.41, AY.99.2, AY.41, AY.43, AY.40, AY.71, AY.98, AY.40, AY.71, AY.99, AY.41, AY.42, AY.43, AY.41, AY.99.2, AY.44, AY.43, AY.40, AY.71, AY.99, AY.41, AY.43, AY.40, AY.72, AY.85, AY.39, AY.40, AY.71, AY.98, AY.60, AY.25, AY.110, AY.111, AY.119, AY.42, AY.43, AY.44, AY.47, AY.85, AY.39, AY.49, AY.40, AY.72, AY.85, AY.39, AY.40, AY.71, AY.98, AY.60, AY.25, AY.110, AY.111, AY.119, AY.42, AY.10, AY.43, AY.44, AY.43, AY.44, AY.47, AY.85, AY.39, AY.40, AY.71, AY.98, AY.60, AY.25, AY.110, AY.111, AY.119, AY.45, AY.41, AY.99, AY.45, AY.40, AY.57, AY.85, AY.39, AY.40, AY.57, AY.85, AY.39, AY.40, AY.57, AY.85, AY.39, AY.40, AY.51, AY.40, AY	Gong et al. (2021)			
ASK INFECT/OUT			AY.122, AY.29, AY.83, AY.98.1,				CIDGOH <sup>©</sup>

nf-ncov-voc 61 of 110

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.98, AY.35, AY.70	Gong et al. (2021)	24	G	1.0



Contact Us CIDGOH <sup>©</sup>

nf-ncov-voc 62 of 110

Mutations	Sub-category	Function	Lineages	Citation		Alternate Allele	Alternate Frequency
Mutations p.L452R	Sub-category  convalescent plasma escape	Function  Observed extasciitilde2x decrease on average in 16 health workers' convalescent sera.	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.66, AY.125, AY.59, B.1.617.2, AY.86, AY.19,	Alenquer et al. (2021)	Sequence Depth 59425	Alternate Allele G	Alternate Frequency 1.0
			AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.70,				
			AY.9.2.1, AY.37, AY.121.1, AY.43.3, AY.2, AY.4.4, AY.47, AY.5, AY.65, AY.25, AY.120.1,				
			AY.126, AY.105, AY.104, AY.106, AY.106, AY.106, AY.114, AY.51,				
			AY.46.4, AY.43, AY.64, AY.78, AY.3, AY.107, AY.6, AY.7.1, AY.99, AY.26, AY.68, AY.38,				
			AY.46.6, AY.41, AY.99.2, AY.46, AY.67, AY.39, AY.4.2.1, AY.4.3, AY.35, AY.30				
			AY.35, AY.20, AY.110, AY.111, AY.127, AY.33, AY.49, AY.57, AY.92, AY.14, AY.4.2, AY.40,				
			AY.72, AY.85, AY.39.1, AY.21, AY.94, AY.17, AY.98, AY.60, AY.25.1, AY.1, AY.119,				
			AY.4.5, AY.61, AY.82, AY.121, AY.16.1, AY.56, AY.18, AY.4.2.2, AY.28, AY.93, AY.10, AY.5.3,				
g INTECTACY OF THE PROPERTY OF			AY.10, AY.5.3, AY.24, AY.16, AY.62, AY.122, AY.29, AY.83, Contaget Us AY.9.2,				CIDGOH

nf-ncov-voc 63 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
Mutations p.L452R	convalescent plasma escape	Ablation of neutralization capability of 3 of 4 convalescent sera tested, the other is significantly hindered.	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.13, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.66, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.116, AY.9, AY.70, AY.92.1, AY.37, AY.121.1, AY.43.3, AY.2, AY.44, AY.43, AY.40, AY.105, AY.106, AY.106, AY.114, AY.105, AY.106, AY.114, AY.105, AY.106, AY.114, AY.105, AY.106, AY.114, AY.106, AY.114, AY.107, AY.68, AY.74, AY.106, AY.114, AY.107, AY.69, AY.106, AY.114, AY.107, AY.60, AY.108, AY.109, AY.109, AY.106, AY.111, AY.43, AY.44, AY.43, AY.44, AY.43, AY.46, AY.41, AY.43, AY.46, AY.41, AY.41, AY.41, AY.42, AY.43, AY.42, AY.43, AY.44, AY.42, AY.44, AY.42, AY.44, AY.42, AY.44, AY.42, AY.44, AY.42, AY.44, AY.43, AY.44, AY.42, AY.44, AY.43, AY.44, AY.42, AY.44, AY.42, AY.44, AY.43, AY.44, AY.43, AY.44, AY.42, AY.44, AY.42, AY.44, AY.43, AY.43, AY.44, AY.43, AY.44, AY.42, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.42, AY.44, AY.43, AY.44, AY.42, AY.44, AY.42, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.42, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44,	Liu et al. (2021)	Sequence Depth 59425	Alternate Allele G	Alternate Frequency 1.0
			AY.4.2, AY.40, AY.72, AY.85, AY.39.1,				
			AY.4.2.2, AY.28, AY.93, AY.10, AY.5.3, AY.24, AY.16, AY.62, AY.122, AY.29, AY.83,				CIDGOH

nf-ncov-voc 64 of 110

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.98, AY.35, AY.70	Tada et al. (2021)	24	G	1.0



Contact Us CIDGOH <sup>®</sup>

nf-ncov-voc 65 of 110

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.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.53, AY.73, AY.109, AY.84, AY.124, AY.109, AY.84, AY.23, AY.89, AY.46.1, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.70, AY.9.2.1, AY.37, AY.121.1, AY.43.3, AY.2, AY.44, AY.47, AY.5, AY.65, AY.25, AY.120, AY.106, AY.114, AY.105, AY.106, AY.114, AY.107, AY.60, AY.104, AY.126, AY.106, AY.114, AY.107, AY.60, AY.107, AY.60, AY.108, AY.108, AY.108, AY.109, AY.109, AY.109, AY.109, AY.109, AY.101, AY.120, AY.101, AY.120, AY.104, AY.120, AY.105, AY.120, AY.104, AY.126, AY.107, AY.60, AY.114, AY.107, AY.60, AY.114, AY.117, AY.107, AY.60, AY.111, AY.127, AY.43, AY.40, AY.71, AY.49, AY.42, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.43, AY.43, AY.44, AY.43, AY.45, AY.37, AY.49, AY.41, AY.49, AY.41, AY.42, AY.40, AY.72, AY.43, AY.49, AY.41, AY.41, AY.41, AY.42, AY.40, AY.72, AY.43, AY.41, AY.41, AY.41, AY.41, AY.42, AY.41, AY.42, AY.41, AY.43, AY.43, AY.44, AY.45, AY.41, AY.49, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.41, AY.42, AY.41, AY.43, AY.44, AY.45, AY.41, AY.49, AY.41, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.41, AY.42, AY.41, AY.43, AY.44, AY.45, AY.41, AY.41, AY.41, AY.41, AY.42, AY.41, AY.42, AY.41, AY.43, AY.44, AY.45, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.41, AY.42, AY.41, AY.43, AY.44, AY.45, AY.41, AY.41, AY.41, AY.41, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.41, AY.43, AY.44, AY.45, AY.41, AY.41	Wilhelm et al. (2021)	Sequence Depth 59423	Alternate Allele G	Alternate Frequency 1.0
			AY.16.1, AY.56, AY.18, AY.4.2.2, AY.28, AY.93, AY.10, AY.5.3, AY.62, AY.122, AY.29, AY.83, AY.98.1, Contage Us AY.48, AY.4.6, AY.122.1,				CIDGOH

nf-ncov-voc 66 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
p.L452R	gene expression in- crease	Experimentally, Spike gene expression in- creased 0.32 fold	AY.54, AY.46.2, AY.45, AY.88,	Starr et al. (2020)	59425	G	1.0
			AY.108, AY.11,				
			AY.113, AY.118,				
			AY.13, AY.53, AY.73,				
			AY.103, AY.43.4,				
			AY.124, AY.109,				
			AY.84, AY.23, AY.89,				
			AY.36, AY.44, AY.34.1,				
			AY.46.1, AY.119.1,				
			AY.77, AY.27, AY.75, AY.4,				
			AY.66, AY.125,				
			AY.59, B.1.617.2,				
			AY.86, AY.19, AY.116.1,				
			AY.117, AY.102,				
			AY.15, AY.32, AY.34,				
			AY.116, AY.9, AY.70,				
			AY.9.2.1, AY.37,				
			AY.121.1, AY.43.3,				
			AY.2, AY.4.4, AY.47, AY.5,				
			AY.65, AY.25, AY.120.1,				
			AY.42, AY.74, AY.105,				
			AY.120, AY.104,				
			AY.126, AY.106,				
			AY.114, AY.51,				
			AY.46.4, AY.43, AY.64,				
			AY.78, AY.3, AY.107,				
			AY.6, AY.7.1, AY.99, AY.26,				
			AY.68, AY.38, AY.46.6,				
			AY.41, AY.99.2,				
			AY.46, AY.67, AY.39,				
			AY.4.2.1, AY.4.3,				
			AY.35, AY.20, AY.110,				
			AY.111, AY.127,				
			AY.33, AY.49, AY.57,				
			AY.92, AY.14, AY.4.2, AY.40,				
			AY.72, AY.85, AY.39.1,				
			AY.21, AY.94, AY.17,				
			AY.98, AY.60, AY.25.1, AY.1,				
			AY.119, AY.4.5,				
			AY.61, AY.82, AY.121,				
			AY.16.1, AY.56, AY.18,				
			AY.4.2.2, AY.28, AY.93,				
			AY.10, AY.5.3, AY.24, AY.16,				
			AY.62, AY.122,				
INFECTION AND AND AND AND AND AND AND AND AND AN			AY.29, AY.83, C <b>AYt 28t</b> 1,Us				CIDGOH
			AY.9.2, AY.48, AY.4.6,				

nf-ncov-voc 67 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	
Mutations p.L452R	monoclonal antibody serial passage escape	Ranked effective mutant against this position in the RBD for highly neutralizing COV2-2096	AY.54, AY.46.2, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.13, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.75, AY.4, AY.66, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.117, AY.117, AY.116, AY.117, AY.116, AY.117, AY.117, AY.117, AY.118, AY.118, AY.119, AY.1118, AY.119, AY.1118, AY.119, AY.1101, AY.1102, AY.1103, AY.1104, AY.1105, AY.1101, AY.1105, AY.120, AY.1104, AY.1106, AY.1006, AY.1106, AY.114, AY.43, AY.644, AY.43, AY.644,	Greaney et al. (2020)	Sequence Depth 59425	Alternate Allele G	Alternate Frequency 1.0
			AY.47, AY.5, AY.65, AY.25, AY.120.1, AY.42, AY.74, AY.105, AY.120, AY.104, AY.126, AY.106, AY.114, AY.51, AY.46.4,				
			AY.41, AY.99.2, AY.46, AY.67, AY.39, AY.4.2.1, AY.4.3, AY.35, AY.20, AY.110, AY.111, AY.127, AY.33, AY.49, AY.57, AY.92, AY.14, AY.4.2, AY.40,				
			AY.72, AY.85, AY.39.1, AY.94, AY.17, AY.98, AY.60, AY.25.1, AY.1, AY.119, AY.4.5, AY.61, AY.82, AY.121, AY.16.1, AY.56, AY.18, AY.4.2.2,				
INFECTION OF THE PROPERTY OF T			AY.4.2.2, AY.28, AY.93, AY.10, AY.5.3, AY.24, AY.16, AY.62, AY.122, AY.29, AY.83, Cent.98t1.Us AY.9.2,				CIDGOH <sup>©</sup>

nf-ncov-voc 68 of 110

D.L.   Demoncional anti-beam   Demoncional antibody   Serial passage   Demoncional antibody   D.Y.   D.Y.   Demoncional antibody   D.Y.   D.Y.	s Sub-category	Sequence Alternate Alternate Depth Allele Frequency
AY.4.5, AY.61, AY.82, AY.121, AY.16.1, AY.56, AY.18, AY.4.2.2,	monoclonal body serial pas	Depth Allele Frequency
AY.28, AY.93, AY.10, AY.5.3, AY.24, AY.16, AY.62,		
AY.192, AY.29, AY.83,		CIDGOH

nf-ncov-voc 69 of 110

D.143/9ft bootsystrial passage body serial passages of the Lat/2R mutation in vitro.  Class 2/3 carried by Serial passage occups of the Lat/2R mutation in vitro.  Avia,	Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth		Alternate Frequency
AY.24, AY.16, AY.62, AY.122, AY.29. AY.83.		monoclonal anti- body serial passage	Class 2/3 antibody C628 and class 2 antibody C643 selected for the emergence of the L452R	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.66, AY.125, AY.59, B.1.617.2, AY.86, AY.116.1, AY.117, AY.1102, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.70, AY.9.2.1, AY.37, AY.121.1, AY.43.3, AY.2, AY.44, AY.47, AY.5, AY.65, AY.55, AY.120, AY.106, AY.114, AY.105, AY.106, AY.114, AY.105, AY.106, AY.114, AY.106, AY.114, AY.107, AY.108, AY.107, AY.108, AY.109, AY.109, AY.109, AY.109, AY.109, AY.104, AY.114, AY.105, AY.107, AY.46.4, AY.43, AY.46, AY.78, AY.46, AY.79, AY.46, AY.71, AY.46, AY.71, AY.99, AY.46, AY.71, AY.99, AY.46, AY.71, AY.99, AY.46, AY.71, AY.99, AY.41, AY.43, AY.43, AY.43, AY.44, AY.43, AY.45, AY.41, AY.43, AY.45, AY.41, AY.49, AY.41, AY.42, AY.40, AY.72, AY.43, AY.45, AY.41, AY.41, AY.42, AY.40, AY.72, AY.43, AY.41, AY.42, AY.40, AY.72, AY.43, AY.41, AY.41, AY.42, AY.41, AY.42, AY.41, AY.43, AY.44, AY.47, AY.48, AY.47, AY.48, AY.49, AY.57, AY.99, AY.41, AY.41, AY.42, AY.41, AY.42, AY.43, AY.43, AY.44, AY.47, AY.43, AY.45, AY.41, AY.41, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.43, AY.43, AY.44, AY.47, AY.43, AY.45, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.47, AY.48, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.47, AY.43, AY.44, AY.47, AY.48, AY.41, AY.49, AY.57, AY.40, AY.57, AY.40, AY.57, AY.40, AY.57, AY.40, AY.57, AY.40, A	Wang et al.	Depth	Allele	Frequency
Centaguus Cidentia	CA INFECTION OF SA			AY.122, AY.29, AY.83,				CIDGOH <sup>©</sup>

nf-ncov-voc 70 of 110

pharmaconical effectiveness of CoSS) into transport of the control of the cost	Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
AY.10, AY.5.3, AY.24, AY.16, AY.62.		pharmaceutical	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	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.113, AY.103, AY.403, AY.409, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.66, AY.125, AY.59, B.1.617.2, AY.86, AY.117, AY.1102, AY.116.1, AY.117, AY.1102, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.120, AY.15, AY.37, AY.120.1, AY.43, AY.47, AY.55, AY.65, AY.25, AY.120, AY.104, AY.120, AY.104, AY.120, AY.105, AY.120, AY.104, AY.120, AY.105, AY.120, AY.104, AY.120, AY.104, AY.126, AY.106, AY.111, AY.42, AY.43, AY.64, AY.43, AY.65, AY.120, AY.104, AY.126, AY.106, AY.114, AY.41, AY.42, AY.43, AY.46, AY.41, AY.49, AY.41, AY.49, AY.41, AY.99.2, AY.46, AY.41, AY.99.2, AY.41, AY.43, AY.40, AY.72, AY.38, AY.40, AY.71, AY.98, AY.40, AY.71, AY.98, AY.40, AY.72, AY.85, AY.39.1, AY.111, AY.119, AY.42, AY.110, AY.111, AY.119, AY.43, AY.41, AY.99, AY.45, AY.39, AY.41, AY.99, AY.41, AY.99, AY.41, AY.99, AY.41, AY.99, AY.42, AY.110, AY.111, AY.117, AY.98, AY.40, AY.72, AY.85, AY.39.1, AY.94, AY.17, AY.98, AY.61, AY.41, AY.99, AY.41, AY.99, AY.41, AY.99, AY.41, AY.99, AY.42, AY.110, AY.111, AY.11	Engelhart et	Depth	Allele	Frequency
AY.29, AY.83,	INTECTOOR			AY.62, AY.122,				CIDGOH <sup>©</sup>

nf-ncov-voc 71 of 110

Sharmacentical effectiveness   C   Sharmacentrical effectiveness   C   Sharmacentrical effectiveness   Sharmacentrical effec	Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
AY.10, AY.5.3,	p.L452R	pharmaceutical	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	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.113, AY.103, AY.403, AY.409, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.66, AY.125, AY.59, B.1.617.2, AY.86, AY.117, AY.102, AY.116.1, AY.117, AY.1102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.116.1, AY.111, AY.112, AY.116, AY.9, AY.120, AY.120, AY.15, AY.43, AY.120, AY.104, AY.126, AY.105, AY.120, AY.104, AY.126, AY.106, AY.111, AY.46.4, AY.43, AY.65, AY.39, AY.46.4, AY.43, AY.66, AY.71, AY.99, AY.46, AY.106, AY.114, AY.99, AY.46, AY.107, AY.66, AY.71, AY.99, AY.46, AY.78, AY.38, AY.40, AY.110, AY.111, AY.43, AY.40, AY.72, AY.38, AY.40, AY.71, AY.99, AY.41, AY.99, AY.42, AY.43, AY.41, AY.99, AY.42, AY.43, AY.43, AY.44, AY.43, AY.45, AY.35, AY.39, AY.41, AY.99, AY.46, AY.41, AY.99, AY.41, AY.99, AY.41, AY.99, AY.42, AY.43, AY.41, AY.99, AY.41, AY.99, AY.41, AY.99, AY.41, AY.99, AY.42, AY.43, AY.41, AY.99, AY.41, AY.99, AY.41, AY.99, AY.42, AY.41, AY.99, AY.43, AY.41, AY.99, AY.41, AY.99, AY.41, AY.99, AY.41, AY.99, AY.42, AY.41, AY.99, AY.43, AY.41, AY.99, AY.41, AY.99, AY.41, AY.99, AY.42, AY.41, AY.99, AY.43, AY.43, AY.44, AY.47, AY.49, AY.47, AY.49, AY.47, AY.49, AY.41, AY.99, AY.41, AY.91, AY.41, AY.91, AY.41, AY.91, AY.42, AY.111,			Allele	Frequency
AY.62, AY.122, AY.29, AY.83.	OS INFECTION			AY.62, AY.122,				CIDGOH <sup>©</sup>

nf-ncov-voc 72 of 110

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.98, AY.35, AY.70	Yadav et al. (2021)	24	G	1.0



Contact Us CIDGOH <sup>©</sup>

nf-ncov-voc 73 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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.54, AY.46.2, AY.45, AY.88, AY.108, AY.111, AY.113, AY.118, AY.13, AY.53, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.27, AY.75, AY.46.1, AY.119.1, AY.77, AY.75, AY.46, AY.119.1, AY.117, AY.102, AY.16, AY.116, AY.117, AY.102, AY.116, AY.117, AY.102, AY.116, AY.117, AY.102, AY.116, AY.9, AY.116, AY.9, AY.116, AY.9, AY.116, AY.9, AY.106, AY.120, AY.120, AY.120, AY.120, AY.120, AY.42, AY.44, AY.43, AY.45, AY.65, AY.25, AY.120.1, AY.42, AY.44, AY.43, AY.105, AY.106, AY.114, AY.105, AY.106, AY.114, AY.105, AY.106, AY.111, AY.42, AY.43, AY.46, AY.41, AY.43, AY.46, AY.43, AY.64, AY.43, AY.64, AY.44, AY.43, AY.64, AY.43, AY.64, AY.44, AY.43, AY.64, AY.43, AY.107, AY.66, AY.111, AY.45, AY.46, AY.41, AY.42, AY.46, AY.47, AY.48, AY.48, AY.49, AY.57, AY.49, AY.41, AY.42, AY.40, AY.72, AY.85, AY.40, AY.72, AY.85, AY.40, AY.72, AY.85, AY.40, AY.72, AY.85, AY.41, AY.42, AY.40, AY.72, AY.85, AY.40, AY.72, AY.85, AY.41, AY.42, AY.40, AY.72, AY.85, AY.41, AY.42, AY.40, AY.72, AY.85, AY.41, AY.42, AY.40, AY.72, AY.85, AY.40, AY.72, AY.85, AY.41, AY.42, AY.40, AY.73, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.44, AY.44, AY.45, AY.46, AY.47, AY.47, AY.48, AY.48, AY.49, AY.49, AY.47, AY.49, AY.47, AY.49, AY.47, AY.48, AY.48, AY.49, AY.49, AY.41, AY.42, AY.40, AY.72, AY.85, AY.40, AY.73, AY.40, AY.73, AY.40, AY.73, AY.40, AY.73, AY.40, AY.73, AY.40, AY.73, AY.40, AY.74, AY.40, A	Deng et al. (2021)			
INFECTION OF			AY.62, AY.122, AY.29, AY.83,				
			Contactius AY.9.2,				CIDGOH <sup>©</sup>

nf-ncov-voc 74 of 110

n. This ventual alono above as exeminating the state of t	Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth		Alternate Frequency
AY.24, AY.16, AY.62, AY.122,			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.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.113, AY.113, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.27, AY.75, AY.4, AY.66, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.116.1, AY.117, AY.102, AY.116.1, AY.117, AY.102, AY.37, AY.121.1, AY.33, AY.2, AY.44, AY.47, AY.5, AY.65, AY.25, AY.120, AY.120, AY.104, AY.126, AY.105, AY.120, AY.104, AY.126, AY.105, AY.120, AY.104, AY.126, AY.105, AY.120, AY.106, AY.114, AY.126, AY.106, AY.114, AY.126, AY.107, AY.46.4, AY.47, AY.51, AY.46.4, AY.48, AY.49, AY.51, AY.46.4, AY.49, AY.51, AY.46.4, AY.41, AY.49, AY.41, AY.49, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.45, AY.46, AY.41, AY.49, AY.41, AY.49, AY.41, AY.42, AY.44, AY.43, AY.45, AY.41, AY.42, AY.44, AY.43, AY.46, AY.41, AY.49, AY.57, AY.46, AY.41, AY.49, AY.57, AY.46, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.44, AY.43, AY.45, AY.41, AY.42, AY.44, AY.47, AY.49, AY.57, AY.49, AY.51, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.43, AY.45, AY.41, AY.42, AY.41, AY.42, AY.41, AY.42, AY.43, AY.44, AY.47, AY.49, AY.57, AY.49, AY.57	Ferriera et al	Depth	Allele	Frequency
AV 20 AV 99	A INFECTION			AY.62,				

nf-ncov-voc 75 of 110

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	G	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	G	1.0



nf-ncov-voc 76 of 110

	Motozono et al. (2021)	Depth 59425	Allele G	Frequency 1.0
AY.67, AY.39, AY.4.2.1, AY.4.3, AY.35, AY.20, AY.110, AY.111, AY.127, AY.33, AY.49, AY.57, AY.92, AY.14, AY.4.2, AY.40, AY.72, AY.85, AY.39.1, AY.21, AY.94, AY.17, AY.98, AY.60, AY.25.1, AY.1, AY.119, AY.4.5, AY.61, AY.82, AY.121, AY.16.1, AY.16.1, AY.56, AY.18, AY.4.2.2, AY.4.2.2, AY.28, AY.93, AY.10, AY.5.3,				
AY.62, AY.122, AY.29, AY.83, Cont.98t.Us				CIDGOH ®

nf-ncov-voc 77 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
P.L452R	Sub-category transmissibility	Function  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]	Lineages  AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.44, AY.34.1, AY.119.1, AY.77, AY.27, AY.75, AY.41, AY.116.1, AY.117, AY.102, AY.16.1, AY.116.1, AY.117, AY.102, AY.16.1, AY.1102, AY.16.1, AY.1102, AY.15, AY.37, AY.101, AY.104, AY.105, AY.120, AY.104, AY.126, AY.105, AY.120, AY.104, AY.126, AY.106, AY.114, AY.51, AY.46.4, AY.43, AY.64, AY.43, AY.65, AY.39, AY.46, AY.41, AY.99, AY.46, AY.41, AY.99, AY.46, AY.41, AY.99, AY.46, AY.41, AY.99, AY.46, AY.41, AY.49, AY.41, AY.41, AY.41, AY.42, AY.40, AY.72, AY.33, AY.49, AY.41, AY.41, AY.41, AY.42, AY.40, AY.72, AY.38, AY.40, AY.71, AY.98, AY.40, AY.71, AY.98, AY.40, AY.72, AY.85, AY.39.1, AY.41, AY.42, AY.40, AY.73, AY.40, AY.71, AY.98, AY.40, AY.71, AY.98, AY.40, AY.71, AY.98, AY.40, AY.72, AY.85, AY.39.1, AY.41, AY.42, AY.40, AY.73, AY.40, AY.74, AY.40, AY.75, AY.85, AY.30, AY.41, AY.42, AY.40, AY.73, AY.40, AY.73, AY.40, AY.74, AY.40, AY.74, AY.40, AY.75, AY.85, AY.30, AY.41, AY.42, AY.40, AY.73, AY.40, AY.74, AY.40, AY.73, AY.40, AY.74, AY.40, AY.75, AY.30, AY.41, AY.41, AY.42, AY.40, AY.73, AY.40, AY.74, AY.40, AY.74, AY.40, AY.75, AY.30, AY.41, AY.41, AY.42, AY.40, AY.71, AY.43, AY.44, AY.41, AY.42, AY.40, AY.72, AY.85, AY.30, AY.41, AY.42, AY.40, AY.73, AY.40, AY.71, AY.42, AY.40, AY.71, AY.43, AY.44, AY.47, AY.40, AY.71, AY.40, AY.	Tada et al. (2021)	Sequence Depth 59423	Alternate Allele G	Alternate Frequency 1.0
INFECTION OF SECOND			AY.122, AY.29, AY.83, AY.98.1, CAMTAGE Us				CIDGOH ®

<u>nf-ncov-voc</u> 78 of 110

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.98, AY.35, AY.70	Tada et al. (2021)	24	G	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.98, AY.35, AY.70	Tada et al. (2021)	24	G	1.0



nf-ncov-voc 79 of 110

nf-ncov-voc 80 of 110

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.98, AY.35, AY.70	Ferreira et al. (2021)	24	G	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.98, AY.35, AY.70	Gong et al. (2021)	24	G	1.0



nf-ncov-voc 81 of 110

nf-ncov-voc 82 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
p.L452R	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.98, AY.35, AY.70	Tada et al. (2021)	24	G	1.0



Contact Us  $\qquad \qquad$  CIDGOH  $^{\odot}$ 

nf-ncov-voc 83 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
p.L452R	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.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.41, AY.19.1, AY.77, AY.27, AY.75, AY.4, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116.1, AY.117, AY.102, AY.15, AY.32, AY.34, AY.116, AY.9, AY.70, AY.9.2.1, AY.43, AY.47, AY.5, AY.65, AY.25, AY.120.1, AY.42, AY.44, AY.47, AY.5, AY.104, AY.105, AY.104, AY.105, AY.106, AY.114, AY.47, AY.105, AY.106, AY.114, AY.47, AY.105, AY.106, AY.111, AY.43, AY.44, AY.47, AY.51, AY.46.4, AY.48, AY.49, AY.78, AY.39, AY.107, AY.6, AY.71, AY.99, AY.46, AY.78, AY.39, AY.107, AY.6, AY.71, AY.99, AY.40, AY.72, AY.33, AY.40, AY.71, AY.99, AY.41, AY.99, AY.41, AY.99, AY.42, AY.43, AY.43, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.41, AY.99, AY.46, AY.47, AY.99, AY.41, AY.49, AY.71, AY.99, AY.41, AY.49, AY.71, AY.99, AY.41, AY.42, AY.41, AY.43, AY.41, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.41, AY.49, AY.47, AY.48, AY.41, AY.49, AY.41, AY.49, AY.41, AY.41, AY.41, AY.42, AY.41, AY.43, AY.41, AY.43, AY.44, AY.44, AY.43, AY.44, AY.43, AY.44, AY	Wilhelm et al. (2021)	Sequence Depth 59423	Allele G	Alternate Frequency 1.0
			AY.62, AY.122, AY.29, AY.83,				

nf-ncov-voc 84 of 110

<u>nf-ncov-voc</u> 85 of 110

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.98, AY.35, AY.70	Gong et al. (2021)	24	G	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.98, AY.35, AY.70	Yadav et al. (2021)	24	G	1.0



Contact Us  $\qquad \qquad \text{CIDGOH}^{\, \odot}$ 

nf-ncov-voc 86 of 110

<u>nf-ncov-voc</u> 87 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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	A	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	A	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	A	0.5
p.H69del	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	A	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	A	0.5
p.H69del	convalescent plasma escape	Viruses containing the point mutations of B.1.1.7 showed that the single point mutations $(\Delta 69\text{-}70 \text{ and } \text{N501Y})$ were neutralized as efficiently as D614G across 10 convalescent sera from April 2020 infectees.	AY.77	Tada et al. (2021)	2	A	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	A	0.5
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 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	AY.77	Gong et al. (2021)	2	A	0.5
p.K458N	convalescent plasma escape	post-infection vaccinees. Resistant to a pool of 10 convalescent sera (but less than 4x, a typical threshold for definition	AY.46.1	Li et al. (2020)	4	C	1.0



Contact Us  $\qquad \qquad$  CIDGOH  $^{\odot}$ 

nf-ncov-voc 88 of 110

	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
p.R158G	monoclonal antibody serial passage escape	Escape mutation against Spike N terminal domain antigenic supersite i mAb S2X28	AY.54, AY.46.2, AY.45, AY.88, AY.108, AY.11, AY.113, AY.118, AY.13, AY.31, AY.53, AY.109, AY.84, AY.124, AY.109, AY.84, AY.23, AY.89, AY.36, AY.41, AY.17, AY.17, AY.75, AY.46, AY.191, AY.166, AY.125, AY.59, B.1.617.2, AY.86, AY.19, AY.116, AY.117, AY.102, AY.15, AY.32, AY.16, AY.116, AY.117, AY.102, AY.16, AY.116, AY.9, AY.70, AY.92.1, AY.37, AY.121.1, AY.43.3, AY.2, AY.44, AY.47, AY.5, AY.65, AY.120, AY.106, AY.114, AY.105, AY.106, AY.114, AY.51, AY.42, AY.43, AY.64, AY.43, AY.64, AY.78, AY.65, AY.106, AY.114, AY.51, AY.46, AY.106, AY.114, AY.51, AY.46, AY.78, AY.39, AY.42, AY.43, AY.40, AY.106, AY.111, AY.41, AY.51, AY.46, AY.43, AY.40, AY.41, AY.41, AY.41, AY.42, AY.42, AY.43, AY.43, AY.44, AY.43, AY.45, AY.41, AY.41, AY.41, AY.42, AY.42, AY.43, AY.44, AY.43, AY.45, AY.41, AY.41, AY.41, AY.41, AY.42, AY.42, AY.43, AY.44, AY.43, AY.45, AY.41, AY.41, AY.41, AY.42, AY.41, AY.42, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.45, AY.41, AY.45, AY.41, AY.41, AY.41, AY.41, AY.42, AY.43, AY.44, AY.43, AY.44, AY.44, AY.45, AY.41, AY.41, AY.41, AY.41, AY.42, AY.42, AY.43, AY.44, AY.43, AY.44, AY.44, AY.43, AY.45, AY.41, AY.41, AY.41, AY.41, AY.42, AY.42, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.41, AY.41, AY.41, AY.41, AY.42, AY.42, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.41, AY.41, AY.41, AY.41, AY.42, AY.42, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, 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.42, AY.43, AY.43, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44,	McCallum et al. (2021)	58632	Allele G	
			AY.10, AY.5.3, AY.24, AY.16,				
			AY.62, AY.122,				

nf-ncov-voc 89 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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)	116	Т	0.69
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	Т	1.0
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	A,C	1.0
p.E484K	ACE2 receptor binding affinity	This variant appears twice in the experiments, with slightly different affinities (both extasciitide1.2x decrease in binding relative to D614G) using flow cytometry and ACE2 ectodomains-Fc portion IgG complex.	AY.77	Gong et al. (2021)	2	A,C	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	A,C	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	A,C	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	A,C	1.0
p.E484K	ACE2 receptor binding affinity	Experimentally, ACE2 binding affinity in- creased 0.06 fold	AY.77	Starr et al. (2020)	2	A,C	1.0
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	A,C	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	A,C	1.0



nf-ncov-voc 90 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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	A,C	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	A,C	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	A,C	1.0
p.E484K	antibody epitope effects	Ablates Class 1 receptor- binding-motif targeting antibodies COV2-2050, 1B07, COVOX-384 and S2H58.	AY.77	Chen et al. (2021)	2	A,C	1.0
p.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.	AY.77	Collier et al. (2021)	2	A,C	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	A,C	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	A,C	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	A,C	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	A,C	1.0
p.E484K	antibody epitope effects	Complete loss of binding in ELISA by the variant against monoclonal anti- body VH-Fc ab8	AY.77	Sun et al. (2021)	2	A,C	1.0
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	A,C	1.0



nf-ncov-voc 91 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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	A,C	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	A,C	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	A,C	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	A,C	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	A,C	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	A,C	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	A,C	1.0
p.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)	AY.77	Tada et al. (2021)	2	A,C	1.0



nf-ncov-voc 92 of 110

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	A,C	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	A,C	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	A,C	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	A,C	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	A,C	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	A,C	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	A,C	1.0



nf-ncov-voc 93 of 110

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	A,C	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	A,C	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	A,C	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	A,C	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	A,C	1.0
p.E484K	pharmaceutical effectiveness	Bamlanivimab (LY-CoV555) lost extasciitilde16x binding against this isolated mutation. Casirivimab lost extasciitilde16x binding against this isolated mutation.	AY.77	Engelhart et al. (2021)	2	A,C	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	A,C	1.0
p.E484K	pharmaceutical effectiveness	This mutated version of RBD completely abol- ishes the binding to a therapeutic antibody, Bamlanivimab, in vitro.	AY.77	Liu et al. (2021)	2	A,C	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	A,C	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	A,C	1.0
p.E484K	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	A,C	1.0



nf-ncov-voc 94 of 110

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	A,C	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	A,C	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	A,C	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	A,C	1.0
p.E484K	vaccine neutralization efficacy	Human sera from 5 two- dose Pfizer vaccinated individuals (47-68 days post 1st-dose) neutral- ized this variant 3.4x less relative to refer- ence 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 neutral- ized this variant 4.2x less relative to refer- ence USA-WA1/2020 strain. 11 convalescent plasma with high IgG ELISA titre neutral- ized this variant 2.6x less relative to reference USA-WA1/2020 strain.	AY.77	Jangra et al. (2021)	2	A,C	1.0
p.E484K	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	A,C	1.0
p.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).	AY.77	Solfrosi et al. (2021)	2	A,C	1.0



nf-ncov-voc 95 of 110

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	A,C	1.0
p.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.	AY.77	Wang et al. (2021)	2	A,C	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	A,C	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	A,C	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	Т	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	Т	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	Т	0.33



<u>nf-ncov-voc</u> 96 of 110

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	T	0.33	
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 S680. In a homologuous site in Infectious Bronchitis Virus (IBV, Gammacoronaviruses), abolition of S680 phosphorylation improves furin cleavage (and presumably cell entry). [Inference from similar positively charged substitution P681H actually described in the work]	AY.127, AY.88, AY.114, AY.65	Maaroufi (2021)	217	TTCG,CTCG	,TM©GTCGG,C	TCGTCGT,CTCGT
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.127, AY.88, AY.114, AY.65	Tada et al. (2021)	217	TTCG,CTCG	,TINCGTCGG,C	TCGTCGT,CTCGT
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.127, AY.88, AY.114, AY.65	Tada et al. (2021)	217	TTCG,CTCG	,TINCGTCGG,C	TCGTCGT,CTCGT
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 space, interstitial space, interstitial space, interstitial spetal thickening, consolidation and pneumocyte hyperplasia were observed with B.1.617.1 variant consistently.	AY.98, AY.35, AY.70	Yadav et al. (2021)	20	ס	1.0	



<u>nf-ncov-voc</u> 97 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
p.P681R	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	G	1.0



nf-ncov-voc 98 of 110

nf-ncov-voc 99 of 110

nf-ncov-voc 100 of 110

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.98, AY.35, AY.70	Tada et al. (2021)	20	G	1.0
p.P681R	viral load	In 9 infected hamsters each for B.1 and B.1.617.1, no significant change in viral load or subgenomic RNA levels were detected.	AY.98, AY.35, AY.70	Yadav et al. (2021)	20	G	1.0



nf-ncov-voc 101 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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.54, AY.46.2, AY.46.2, AY.45, AY.108, AY.11, AY.113, AY.118, AY.13, AY.53, AY.73, AY.103, AY.43.4, AY.124, AY.109, AY.84, AY.23, AY.44, AY.34.1, AY.46.1, AY.119.1, AY.77, AY.75, AY.46, AY.125, AY.59, B.1.617.2, AY.86, AY.116.1, AY.117, AY.102, AY.116.1, AY.117, AY.102, AY.15, AY.37, AY.116, AY.9, AY.37, AY.116, AY.9, AY.43.3, AY.2, AY.44, AY.47, AY.25, AY.120, AY.104, AY.126, AY.106, AY.106, AY.106, AY.106, AY.107, AY.108, AY.108, AY.108, AY.108, AY.109, AY.109, AY.109, AY.101, AY.101, AY.105, AY.106, AY.106, AY.107, AY.108, AY.108, AY.109, AY.109, AY.109, AY.109, AY.109, AY.109, AY.109, AY.109, AY.110, AY.111, AY.43, AY.42, AY.43, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.107, AY.46, AY.78, AY.39, AY.41, AY.49, AY.21, AY.41, AY.42, AY.43, AY.41, AY.42, AY.41, AY.42, AY.43, AY.41, AY.43, AY.49, AY.57, AY.99, AY.46, AY.61, AY.61, AY.41, AY.42, AY.41, AY.42, AY.43, AY.41, AY.43, AY.44, AY.43, AY.44, AY.43, AY.44, AY.43, AY.45, AY.41, AY.45, AY.41, AY.49, AY.56, AY.11, AY.45, AY.41, AY.45, AY.41, AY.45, AY.41, AY.42, AY.41, AY.42, AY.43, AY.43, AY.44, AY.44, AY.43, AY.44, AY.	Tada et al. (2021)	Depth 59202	Allele G,GTCGT,G'	
			AY.9.2,			1	

nf-ncov-voc 102 of 110

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	Т	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	Т	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	T	1.0
р.Р681Н	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	GTCGT,ATC	G <b>G</b> ØTCGG
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	GTCGT,ATC	G <b>G</b> ,GTCGG
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	GTCGT ATC	
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	GTCGT,ATC	
р.Р681Н	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	GTCGT,ATC	GήTCGG



Contact Us  $\qquad \qquad$  CIDGOH  $^{\odot}$ 

nf-ncov-voc 103 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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	GTCGT,ATC	
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).	AY.5	Maaroufi (2021)	18	GTCGT,ATC	GGIGTCGG
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.	AY.5	Tada et al. (2021)	18	GTCGT,ATC	GC:ICTCGG
р.Р681Н	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	GTCGT,ATC	GGGTCGG
р.Р681Н	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 nonseroconverted 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	GTCGT,ATC	
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.	AY.5	Tada et al. (2021)	18	GTCGT,ATC	G <b>G</b> IGTCGG



nf-ncov-voc 104 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
o.T95I	ACE2 receptor bind-	Using flow cytometry	AY.106,	Gong et al.	Depth 4187	T	0.67
5.1951	ing affinity and ACE2 ectodomains-	AY.114,	(2021)	4107	1	0.07	
		Fc portion IgG complex, this variant showed a 1.33x decrease in binding	AY.119.1,				
			AY.77, AY.78,				
			AY.107, AY.4,				
			AY.1, AY.119,				
		()	AY.4.5,				
			AY.125,				
			B.1.617.2,				
			AY.121,				
			AY.88,				
			AY.4.2.2,				
			AY.116.1,				
			AY.117,				
			AY.108,				
			AY.5.3,				
			AY.102,				
			AY.113,				
			AY.118, AY.34,				
			AY.116,				
			AY.39,				
			AY.4.2.1,				
			AY.4.3,				
			AY.121.1,				
			AY.29,				
			AY.124,				
			AY.4.4, AY.20,				
			AY.43.4,				
			AY.109,				
			AY.110,				
			AY.111,				
			AY.127,				
			AY.89, AY.36,				
			AY.34.1,				
			AY.4.6, AY.92,				
			AY.120.1, AY.4.2, AY.42,				
			AY.120,				
			AY.85,				
			AY.104,				
			AY.39.1,				
			AY.101,				
			AY.126,				
			AY.100				



nf-ncov-voc 105 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
TROET.		N 1	137.100	G . 1	Depth	Allele	Frequency
p.T95I	binding ing (relative to D614G AY	AY.106,	Gong et al.	4187	Т	0.67	
		alone) by 5 plasma col-	AY.114, AY.119.1,	(2021)			
		lected 8 months post-	AY.77, AY.78,				
			AY.107, AY.4,				
		symptom-onset.	AY.1, AY.119,				
			AY.4.5,				
			AY.125,				
			B.1.617.2,				
			AY.121,				
			AY.88,				
			AY.4.2.2,				
			AY.116.1,				
			AY.117,				
			AY.108,				
			AY.5.3,				
			AY.102,				
			AY.113,				
			AY.118,				
			AY.34,				
			AY.116,				
			AY.39,				
			AY.4.2.1,				
			AY.4.3,				
			AY.121.1,				
			AY.29, AY.124,				
			AY.4.4, AY.20,				
			AY.43.4, AY.43.4,				
			AY.109,				
			AY.110,				
			AY.111,				
			AY.127,				
			AY.89, AY.36,				
			AY.34.1,				
			AY.4.6, AY.92,				
			AY.120.1,				
			AY.4.2, AY.42,				
			AY.120,				
			AY.85,				
			AY.104,				
			AY.39.1,				
			AY.101,				
			AY.126,				
			AY.100				



nf-ncov-voc 106 of 110

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.106, AY.114, AY.119.1, AY.77, AY.4, AY.107, AY.4, AY.1, AY.119, AY.4.5, B.1.617.2, AY.121, AY.88, AY.4.2.2, AY.116.1, AY.117, AY.108, AY.5.3, AY.102, AY.113, AY.116, AY.34, AY.116, AY.34, AY.116, AY.39, AY.4.2.1, AY.4.3, AY.121.1, AY.4.3, AY.121.1, AY.4.3, AY.121.1, AY.4.4, AY.4.4, AY.109, AY.110, AY.110, AY.111, AY.110, AY.111, AY.127, AY.89, AY.36, AY.34.1, AY.4.2, AY.42, AY.4.2, AY.42, AY.4.2, AY.42, AY.120, AY.85, AY.101, AY.85, AY.101, AY.101, AY.101, AY.101, AY.110, AY.110, AY.110, AY.110, AY.1126, AY.100	Gong et al. (2021)	4187	Т	0.67
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	T	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	Т	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	Т	1.0



Contact Us  $\qquad \qquad$  CIDGOH  $^{\odot}$ 

nf-ncov-voc 107 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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	T	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	T	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	Т	1.0
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	Т	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	Т	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	Т	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	Т	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	Т	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	T	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-	AY.2, AY.1	Gong et al. (2021)	10	Т	1.0



nf-ncov-voc 108 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Alternate Allele	Alternate Frequency
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	Т	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	T	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	Т	1.0
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	Т	1.0
p.K417N	gene expression in- crease	Experimentally, Spike gene expression in- creased 0.1 fold	AY.2, AY.1	Starr et al. (2020)	10	Т	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	Т	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	Т	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	Т	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	T	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	Т	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	Т	1.0



nf-ncov-voc 109 of 110

Mutations	Sub-category	Function	Lineages	Citation	Sequence	Alternate	Alternate
Mutations	Sub-category	runction	Lineages	Citation	Depth	Allele	Frequency
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	AY.2, AY.1	Tada et al. (2021)	Deptn 10	T	1.0
p.K417N	vaccine neutralization efficacy	fitness.  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	Т	1.0
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 nonseroconverted 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	T	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	T	1.0



Contact Us  $\qquad \qquad$  CIDGOH  $^{\odot}$ 

nf-ncov-voc 110 of 110

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)

