Surveillance report

Surveillance generated by nf-ncov-voc for Epsilon variant

Date

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

Pango Lineages

Pango Lineages in this report ['B.1.427', 'B.1.429']

Indicator

This table contains key indicators identified

Indicator	Sub-categories from POKAY	Mutations
Transmissibility between humans	transmissibility	D614G, L452R, S13I, W152C
Infection Severity	ACE2 receptor binding affinity, viral load, outcome hazard ratio	D138Y, D614G, L452R, L5F, P26S, S13I, W152C
Immunity after natural infection	convalescent plasma escape, reinfection, humoral response durability	D614G, L452R, S13I, W152C
Vaccines	vaccine neutralization efficacy	D614G, L452R, S13I, W152C
Monoclonal antibodies	monoclonal antibody serial passage escape, pharmaceutical effectiveness	L452R, S443F
Diagnostics	clinical indicators, antigenic test failure, symptom prevalence	

Mutation Significance

This table contains key functional impacts of mutations identified

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
S13I	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.42x increase in binding (KD) relative to D614G.	B.1.427, B.1.429	Gong et al. (2021)	794	G	T	1.0
S13I	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant combination (representing lineage B.1.429 aka Epsilon) showed a 2.82x increase in binding (KD) relative to D614G, indicating a strong marginal effect for L452R.	B.1.427, B.1.429	Gong et al. (2021)	794	G	T	1.0
S13I	antibody epitope effects	The S13I mutation dampened binding of 5 mAbs and abrogated binding of 5 additional mAbs out of 11 neutralizing mAbs evaluated. Predicted to shift the signal peptide cleavage site from S13-Q14 to C15-V16, which can affect NTD conformation. PG: in saying S12F does not shift the signal peptide nor affect mAb binding, this manuscript appears to contradict the text of McCallum et al.'s earlier 2021 manuscript stating that S12F *does* affected some mAb binding via putative signal peptide shift.	B.1.427, B.1.429	McCallum et al. (2021)	794	G	T	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
S13I	antibody epitope effects	The B.1.427/B.1.429 S13I/W152C NTD did not bind to any NTD-directed neutralizing mAbs, which are known to target a single antigenic site (antigenic site i), whereas binding of the non-neutralizing S2L20 mAb to the NTD antigenic site iv was not affected by any mutants, confirming proper retention of folding.	B.1.427, B.1.429	McCallum et al. (2021)	794	G	T	1.0
S13I	antibody epitope effects	14 of 34 RBD-specific mAbs showed reduced neutralization to the B.1.427/B.1.429 variant pseudotype.	B.1.427, B.1.429	McCallum et al. (2021)	794	G	T	1.0
S13I	convalescent plasma binding	1.19x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.427, B.1.429	Gong et al. (2021)	794	G	T	1.0
S13I	convalescent plasma binding	This variant combination (representing lineage B.1.429 aka Epsilon) showed a 1.1x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset, indicating ablated marginal effect from L452R.	B.1.427, B.1.429	Gong et al. (2021)	794	G	T	1.0
S13I	convalescent plasma escape	Antibody neutralization assays showed 6.7-fold resistence against 7/8 convalescent plasma.	B.1.427, B.1.429	Deng et al. (2021)	794	G	T	1.0
S13I	convalescent plasma escape	In 9 plasma collected 15 to 28 days after early 2020 infections, neutralization reduced 4.9-fold for B.1.427/B.1.429 compared to wildtype (D614G). In 13 plasma collected extascitilde1mo after B.1.1.7 infection (nursing home in Ticino, Switzerland), neutralization reduced to undetectable levels in many plasma for B.1.427/B.1.429 pseudotyped virus, as well as WT and other VOCs.	B.1.427, B.1.429	McCallum et al. (2021)	794	G	T	1.0
S13I	convalescent plasma escape	Loss of neutralizing activity (PsVNA50 assay) using 6 hyperimmune immunoglobulin preparations from convalescent plasma was minimal against B.1.249 (1.7-fold). Neutralization against 10 convalescent plasma was somewhat poorer (3.1-fold).	B.1.427, B.1.429	Tang et al. (2021)	794	G	T	1.0
S13I	transmissibility	Exhibits an estimated 18.6-24% increase in transmissibility relative to wild-type circulating strains. a.k.a. 20C/L452R or B.1.427/B.1.429.	B.1.427, B.1.429	Deng et al. (2021)	794	G	T	1.0
S13I	transmissibility	Lineages bearing these spike mutations comprised 54.4% of the total sequences from January, compared to 15.7% in November. Household contacts exposed to the "California" or "West Coast" variants (B.1.427 and B.1.429) were at higher risk of infection compared to household contacts exposed to lineages lacking these variants (0.36 vs 0.29, RR	B.1.427, B.1.429	Peng et al. (2021)	794	G	T	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
S13I	vaccine neutralization efficacy	Neutralization efficiency (ID50) against B.1.1.427/429 reduced 2.1x relative to D614G wildtype using pseudotyped VSV assay on 8 Moderna vaccinee sera one week post-booster.	B.1.427, B.1.429	Choi et al. (2021)	794	G	T	1.0
S13I	vaccine neutralization efficacy	6 of 11 (55%) vaccine recipients (Moderna or Pfizer), showed 2x reduction in neutralization to a B.1.429 lineage virus.	B.1.427, B.1.429	Deng et al. (2021)	794	G	T	1.0
S13I	vaccine neutralization efficacy	Pseudotyped B.1.1.429 virus has reduced neutralization activity vs wild type: 2.0x (30 sera Pfizer median 9 days post 2nd dose, 35 sera Moderna median 18 days post 2nd dose). This was NOT significant by ANOVA.	B.1.427, B.1.429	Garcia-Beltran et al. (2021)	794	G	T	1.0
S13I	vaccine neutralization efficacy	Using HIV pseudotype: Neutralization potency of 11 Moderna mRNA1273-elicited plasma (7-27 days post-2nd dose) was reduced extasciitilde2.8-fold compared to wildtype (D614G) S. It was reduced extasciitilde4-fold in 14 Pfizer/BioNtech BNT162b2-elicited plasma (7-27 days post-2nd dose). Using VSV pseudotype: we observed a 3-fold average reduction of Pfizer/BioNtech BNT162b2-elicited plasma neutralizing activity.	B.1.427, B.1.429	McCallum et al. (2021)	794	G	T	1.0
S13I	vaccine neutralization efficacy	Detectable antibodies against B.1.1.7 in all samples at Day 43 and Day 209 using pseudotyped lentivirus neutralization in Moderna vaccinee cohort.	B.1.427, B.1.429	Pegu et al (2021)	794	G	T	1.0
S13I	vaccinee plasma binding	1.08x 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. 1.27x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.427, B.1.429	Gong et al. (2021)	794	G	T	1.0
S13I	vaccinee plasma binding	This variant combination (representing lineage B.1.429 aka Epsilon) showed a 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 previously non-seroconverted subjects. [Stark contrast to 2.15x increase in binding by convalescent plasma 8 months post infection, presumably via memory B cell affinity maturation against L452R effects] 1.12x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.427, B.1.429	Gong et al. (2021)	794	G	T	1.0

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S13I	viral load	Swab samples N/NP viral RNA is approximately 2-fold higher in B.1.427/B.1.429 than in non-variant viruses.	B.1.427, B.1.429	Deng et al. (2021)	794	G	T	1.0
W152C	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.33x increase in binding (KD) relative to D614G.	B.1.427, B.1.429	Gong et al. (2021)	792	G	T	1.0
W152C	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant combination (representing lineage B.1.429 aka Epsilon) showed a 2.82x increase in binding (KD) relative to D614G, indicating a strong marginal effect for L452R.	B.1.427, B.1.429	Gong et al. (2021)	792	G	T	1.0
W152C	antibody epitope effects	The W152C mutation reduced recognition of six NTD neutralizing mAbs, including a complete loss of binding for two of them, with a complementary pattern to that observed for S13I (also found in lineage B.1.427/B.1.429) out of 11 neutralizing mAbs evaluated.	B.1.427, B.1.429	McCallum et al. (2021)	792	G	T	1.0
W152C	antibody epitope effects	The B.1.427/B.1.429 S13I/W152C NTD did not bind to any NTD-directed neutralizing mAbs, which are known to target a single antigenic site (antigenic site i), whereas binding of the non-neutralizing S2L20 mAb to the NTD antigenic site iv was not affected by any mutants, confirming proper retention of folding.	B.1.427, B.1.429	McCallum et al. (2021)	792	G	T	1.0
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W152C	convalescent plasma binding	1.15x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.427, B.1.429	Gong et al. (2021)	792	G	T	1.0
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W152C	trafficking	Pseudoviruses carrying the W152C mutation demonstrated small increases in cell entry compared to D614G alone in 293T cells and human airway organoids.	B.1.427, B.1.429	Deng et al. (2021)	792	G	T	1.0
W152C	transmissibility	Exhibits an estimated 18.6-24% increase in transmissibility relative to wild-type circulating strains. a.k.a. 20C/L452R or B.1.427/B.1.429.	B.1.427, B.1.429	Deng et al. (2021)	792	G	T	1.0
W152C	transmissibility	Lineages bearing these spike mutations comprised 54.4% of the total sequences from January, compared to 15.7% in November. Household contacts exposed to the "California" or "West Coast" variants (B.1.427 and B.1.429) were at higher risk of infection compared to household contacts exposed to lineages lacking these variants (0.36 vs 0.29, RR	B.1.427, B.1.429	Peng et al. (2021)	792	G	T	1.0
W152C	vaccine neutralization efficacy	Neutralization efficiency (ID50) against B.1.1.427/429 reduced 2.1x relative to D614G wildtype using pseudotyped VSV assay on 8 Moderna vaccinee sera one week post-booster.	B.1.427, B.1.429	Choi et al. (2021)	792	G	T	1.0
W152C	vaccine neutralization efficacy	6 of 11 (55%) vaccine recipients (Moderna or Pfizer), showed 2x reduction in neutralization to a B.1.429 lineage virus.	B.1.427, B.1.429	Deng et al. (2021)	792	G	T	1.0
W152C	vaccine neutralization efficacy	Pseudotyped B.1.1.429 virus has reduced neutralization activity vs wild type: 2.0x (30 sera Pfizer median 9 days post 2nd dose, 35 sera Moderna median 18 days post 2nd dose). This was NOT significant by ANOVA.	B.1.427, B.1.429	Garcia-Beltran et al. (2021)	792	G	T	1.0
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W152C	vaccinee plasma binding	1.03x 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. 1.32x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.427, B.1.429	Gong et al. (2021)	792	G	T	1.0
W152C	vaccinee plasma binding	This variant combination (representing lineage B.1.429 aka Epsilon) showed a 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 previously non-seroconverted subjects. [Stark contrast to 2.15x increase in binding by convalescent plasma 8 months post infection, presumably via memory B cell affinity maturation against L452R effects] 1.12x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.427, B.1.429	Gong et al. (2021)	792	G	T	1.0
W152C	viral load	Swab samples N/NP viral RNA is approximately 2-fold higher in B.1.427/B.1.429 than in non-variant viruses.	B.1.427, B.1.429	Deng et al. (2021)	792	G	T	1.0
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.	B.1.429	Gong et al. (2021)	749	A	G	1.0
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.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
D614G	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.1x decrease in binding (KD) relative to D614G.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
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.	B.1.429	Gong et al. (2021)	749	A	G	1.0
D614G	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.42x increase in binding (KD) relative to D614G.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
D614G	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant combination (representing lineage B.1.429 aka Epsilon) showed a 2.82x increase in binding (KD) relative to D614G, indicating a strong marginal effect for L452R.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0

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D614G	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.33x increase in binding (KD) relative to D614G.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
D614G	ACE2 receptor binding affinity	In four cell lines (including 293T-hACE2 cells), this mutation combination increases infectivity vs D614G alone	B.1.427, B.1.429	Li et al. (2020)	795	A	G	1.0
D614G	convalescent plasma binding	1.56x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.429	Gong et al. (2021)	749	A	G	1.0
D614G	convalescent plasma binding	2.15x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
D614G	convalescent plasma binding	No change in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
D614G	convalescent plasma binding	1.08x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.429	Gong et al. (2021)	749	A	G	1.0
D614G	convalescent plasma binding	1.19x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
D614G	convalescent plasma binding	This variant combination (representing lineage B.1.429 aka Epsilon) showed a 1.1x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset, indicating ablated marginal effect from L452R.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
D614G	convalescent plasma binding	1.15x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
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]	B.1.427, B.1.429	Wilhelm et al. (2021)	795	A	G	1.0
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	B.1.429	Brehm et al. (2021)	749	A	G	1.0
D614G	immunosuppression variant emergence	Studying 94 COVID-19 extended infection cases with genomics April 1 to October 17, 2020, one case developed 23 mutations in a 19 day period, including this combination in Spike.	B.1.427, B.1.429	Landis et al. (2021)	795	A	G	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
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	B.1.429	Brehm et al. (2021)	749	A	G	1.0
D614G	syncytium formation	Slight increase in Vero cell-cell membrane fusion assay under infection with VSV pseudotyped virus.	B.1.427, B.1.429	Kim et al. (2021)	795	A	G	1.0
D614G	tissue specific neutralization	The nasal mucosa of Pfizer vaccinees with time course collection was evaluated against VSV pseudotypes: results (only one nasal swab from different previously infected vacinee neutralizing at weeks 3 and 6 against B.1.1.7 and D614G) suggest that vaccinees probably do not elicit an early humoral response detectable at mucosal surfaces even though sera neutralization was observed. They strengthen the hypothesis that some vaccines may not protect against viral acquisition and infection of the oral–nasal region, but may prevent severe disease associated with viral dissemination in the lower respiratory tract.	B.1.427, B.1.429	Planas et al. (2021)	795	A	G	1.0
D614G	trafficking	Circulating variant shown in vitro to not have major defects or enhancement of cell surface protein trafficking (i.e. Spike cleavage or fusion required for cell entry)	B.1.427, B.1.429	Barrett et al. (2021)	795	A	G	1.0
D614G	trafficking	The increased transduction with Spike D614G ranged from 1.3- to 2.4-fold in Caco-2 and Calu-3 cells expressing endogenous ACE2 and from 1.5- to 7.7-fold in A549ACE2 and Huh7.5ACE2 overexpressing ACE2. Although there is minimal difference in ACE2 receptor binding between the D614 and G614 Spike variants, the G614 variant is more resistant to proteolytic cleavage, suggesting a possible mechanism for the increased transduction.	B.1.427, B.1.429	Daniloski et al. (2021)	795	A	G	1.0
D614G	trafficking	No change in infectivity (24h) relative to D614G alone in Caco-2 cells, Vero or Calu-3.	B.1.427, B.1.429	Kim et al. (2021)	795	A	G	1.0
D614G	trafficking	extasciitilde4x more efficient S2 domain cleavage compared to wild type in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3).	B.1.427, B.1.429	Kim et al. (2021)	795	A	G	1.0
D614G	trafficking	Among S variants tested, the D614G mutant shows the highest cell entry (extasciitilde3.5x wild type), as supported by structural and binding analyses.	B.1.427, B.1.429	Ozono et al. (2020)	795	A	G	1.0

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D614G	trafficking	We report here pseudoviruses carrying SG614 enter ACE2-expressing cells more efficiently than wild type (extasciitilde9-fold). This increased entry correlates with less S1-domain shedding and higher S-protein incorporation into the virion. D614G does not alter S-protein binding to ACE2 or neutralization sensitivity of pseudoviruses. Thus, D614G may increase infectivity by assembling more functional S protein into the virion.	B.1.427, B.1.429	Zhang et l. (2020)	795	A	G	1.0
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]	B.1.427, B.1.429	Tada et al. (2021)	795	A	G	1.0
D614G	vaccine neutralization efficacy	Neutralization efficiency (ID50) against B.1.1.427/429 reduced 2.1x relative to D614G wildtype using pseudotyped VSV assay on 8 Moderna vaccinee sera one week post-booster.	B.1.427, B.1.429	Choi et al. (2021)	795	A	G	1.0
D614G	vaccine neutralization efficacy	6 of 11 (55%) vaccine recipients (Moderna or Pfizer), showed 2x reduction in neutralization to a B.1.429 lineage virus.	B.1.427, B.1.429	Deng et al. (2021)	795	A	G	1.0
D614G	vaccine neutralization efficacy	Pseudotyped D614G virus has reduced neutralization activity vs wild type: 1.2x (37 sera Pfizer median 9 days post 2nd dose, 37 sera Moderna median 18 days post 2nd dose). This was NOT significant by ANOVA.	B.1.427, B.1.429	Garcia-Beltran et al. (2021)	795	A	G	1.0
D614G	vaccine neutralization efficacy	Pseudotyped B.1.1.429 virus has reduced neutralization activity vs wild type: 2.0x (30 sera Pfizer median 9 days post 2nd dose, 35 sera Moderna median 18 days post 2nd dose). This was NOT significant by ANOVA.	B.1.427, B.1.429	Garcia-Beltran et al. (2021)	795	A	G	1.0
D614G	vaccine neutralization efficacy	Using a lentivirus virus pseudotyped with D614G Spike, sera from vaccinated individuals who received the second dose (9–11 days post-second dose of Pfizer) exhibited a robust neutralizing potential, with a mean NT50 value of 99,000. This was an average of a 2-fold increase, relative to sera drawn from the individuals who received one dose of vaccination—mean NT50 dilution of 51,300. Importantly, a 6-fold increase in mean NT50 dilution was obtained when sera from the first vaccination dose was compared to convalescent sera from cohort with severe disease (NT50 51,000 vs 8,700) 21 to 63 days post-onset.	B.1.427, B.1.429	Kuzmina et al. (2021)	795	A	G	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
D614G	vaccine neutralization efficacy	Detectable antibodies against B.1.1.7 in all samples at Day 43 and Day 209 using pseudotyped lentivirus neutralization in Moderna vaccinee cohort.	B.1.427, B.1.429	Pegu et al (2021)	795	A	G	1.0
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).	B.1.427, B.1.429	Wilhelm et al. (2021)	795	A	G	1.0
D614G	vaccinee plasma binding	1.37x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.56x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.429	Gong et al. (2021)	749	A	G	1.0
D614G	vaccinee plasma binding	1.05x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.16x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
D614G	vaccinee plasma binding	1.23x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.1x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
D614G	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.	B.1.429	Gong et al. (2021)	749	A	G	1.0
D614G	vaccinee plasma binding	1.08x 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. 1.27x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
D614G	vaccinee plasma binding	This variant combination (representing lineage B.1.429 aka Epsilon) showed a 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 previously non-seroconverted subjects. [Stark contrast to 2.15x increase in binding by convalescent plasma 8 months post infection, presumably via memory B cell affinity maturation against L452R effects] 1.12x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
D614G	vaccinee plasma binding	1.03x 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. 1.32x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.427, B.1.429	Gong et al. (2021)	795	A	G	1.0
D614G	viral load	Hamsters infected with SARS-CoV-2 expressing spike(D614G) (G614 virus) produced higher infectious titres in nasal washes and the trachea, but not in the lungs, supporting clinical evidence showing that the mutation enhances viral loads in the upper respiratory tract of COVID-19 patients and may increase transmission.	B.1.427, B.1.429	Plante et al. (2020)	795	A	G	1.0
D614G	virion structure	Estimated free energy change (ddG) for this variant is 2.5 kcal/mol (i.e. stabilizing relative to wild type)	B.1.427, B.1.429	Spratt et al. (2021)	795	A	G	1.0
D614G	virion structure	Negative stain EM shows increased proportion of "one-up" trimer conformation of Spike proteins on the surface of virions, where the up conformation is presumed to be more likely to bind ACE2.	B.1.427, B.1.429	Weissman et al. (2020)	795	A	G	1.0
D614G	virion structure	CryoEM shows increased proportion of "one-up" trimer conformation of Spike proteins on the surface of virions, where the up conformation is presumed to be more likely to bind ACE2.	B.1.427, B.1.429	Yurkovetskiy et al. (2020)	795	A	G	1.0
D614G	virion structure	Based on pseudotyped virus experiments, D614G may increase infectivity by assembling more functional S protein into the virion.	B.1.427, B.1.429	Zhang et al. (2020)	795	A	G	1.0
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.	B.1.427, B.1.429	Gong et al. (2021)	793	T	G	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
L452R	ACE2 receptor binding affinity	Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant combination (representing lineage B.1.429 aka Epsilon) showed a 2.82x increase in binding (KD) relative to D614G, indicating a strong marginal effect for L452R.	B.1.427, B.1.429	Gong et al. (2021)	793	T	G	1.0
L452R	ACE2 receptor binding affinity	extasciitilde1.7-fold increase in binding affinity vs wild type.	B.1.427, B.1.429	Motozono et al. (2021)	793	T	G	1.0
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).	B.1.427, B.1.429	Motozono et al. (2021)	793	T	G	1.0
L452R	antibody epitope effects	Resistent to some neutralizing antibodies: mAbs X593 and P2B-2F6	B.1.427, B.1.429	Li et al. (2020)	793	T	G	1.0
L452R	antibody epitope effects	Mutant screen in neutralization assay with a broad range of monoclonal antibodies shows resistence to more than one antibody.	B.1.427, B.1.429	Liu et al. (2021)	793	T	G	1.0
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.	B.1.427, B.1.429	McCallum et al. (2021)	793	T	G	1.0
L452R	antibody epitope effects	14 of 34 RBD-specific mAbs showed reduced neutralization to the B.1.427/B.1.429 variant pseudotype.	B.1.427, B.1.429	McCallum et al. (2021)	793	T	G	1.0
L452R	antibody epitope effects	extasciitilde20% (ELISA significance threshold) drop in antibody binding (ELISA) by this variant against monoclonal antibody VH ab6.	B.1.427, B.1.429	Sun et al. (2021)	793	T	G	1.0
L452R	convalescent plasma binding	2.15x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.	B.1.427, B.1.429	Gong et al. (2021)	793	T	G	1.0
L452R	convalescent plasma binding	This variant combination (representing lineage B.1.429 aka Epsilon) showed a 1.1x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset, indicating ablated marginal effect from L452R.	B.1.427, B.1.429	Gong et al. (2021)	793	T	G	1.0
L452R	convalescent plasma escape	Observed extasciitilde2x decrease on average in 16 health workers' convalescent sera.	B.1.427, B.1.429	Alenquer et al. (2021)	793	T	G	1.0
L452R	convalescent plasma escape	Antibody neutralization assays showed 6.7-fold resistence against 7/8 convalescent plasma.	B.1.427, B.1.429	Deng et al. (2021)	793	T	G	1.0
L452R	convalescent plasma escape	Ablation of neutralization capability of 3 of 4 convalescent sera tested, the other is significantly hindered.	B.1.427, B.1.429	Liu et al. (2021)	793	T	G	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
L452R	convalescent plasma escape	In 9 plasma collected 15 to 28 days after early 2020 infections, neutralization reduced 4.9-fold for B.1.427/B.1.429 compared to wildtype (D614G). In 13 plasma collected extasciitilde1mo after B.1.1.7 infection (nursing home in Ticino, Switzerland), neutralization reduced to undetectable levels in many plasma for B.1.427/B.1.429 pseudotyped virus, as well as WT and other VOCs.	B.1.427, B.1.429	McCallum et al. (2021)	793	T	G	1.0
L452R	convalescent plasma escape	Loss of neutralizing activity (PsVNA50 assay) using 6 hyperimmune immunoglobulin preparations from convalescent plasma was minimal against B.1.249 (1.7-fold). Neutralization against 10 convalescent plasma was somewhat poorer (3.1-fold).	B.1.427, B.1.429	Tang et al. (2021)	793	T	G	1.0
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]	B.1.427, B.1.429	Wilhelm et al. (2021)	793	T	G	1.0
L452R	gene expression increase	Experimentally, Spike gene expression increased 0.32 fold	B.1.427, B.1.429	Starr et al. (2020)	793	T	G	1.0
L452R	monoclonal antibody serial passage escape	Ranked effective mutant against this position in the RBD for highly neutralizing COV2-2096	B.1.427, B.1.429	Greaney et al. (2020)	793	T	G	1.0
L452R	monoclonal antibody serial passage escape	Escape mutation against monoclonal antibody LY-CoV555 (antibody that forms the basis for Eli Lilly's bamlanivimab)	B.1.427, B.1.429	Starr et al. (2021)	793	T	G	1.0
L452R	monoclonal antibody serial passage escape	Class 2/3 antibody C628 and class 2 antibody C643 selected for the emergence of the L452R mutation in vitro.	B.1.427, B.1.429	Wang et al. (2021)	793	T	G	1.0
L452R	pharmaceutical effectiveness	Bamlanivimab (LY-CoV555) lost extasciitilde5x binding against this isolated mutation. Cligavimab lost extasciitilde4x binding against this isolated mutation. Regdanvimab lost extasciitilde4x binding against this isolated mutation.	B.1.427, B.1.429	Engelhart et al. (2021)	793	T	G	1.0
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.	B.1.427, B.1.429	McCallum et al. (2021)	793	T	G	1.0
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.	B.1.427, B.1.429	Deng et al. (2021)	793	T	G	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
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]	B.1.427, B.1.429	Ferriera et al (2021)	793	T	G	1.0
L452R	trafficking	Increased stability of RBD expression in yeast, suggesting increased Spike protein stability.	B.1.427, B.1.429	Motozono et al. (2021)	793	T	G	1.0
L452R	transmissibility	Exhibits an estimated 18.6-24% increase in transmissibility relative to wild-type circulating strains. a.k.a. 20C/L452R or B.1.427/B.1.429.	B.1.427, B.1.429	Deng et al. (2021)	793	T	G	1.0
L452R	transmissibility	Lineages bearing these spike mutations comprised 54.4% of the total sequences from January, compared to 15.7% in November. Household contacts exposed to the "California" or "West Coast" variants (B.1.427 and B.1.429) were at higher risk of infection compared to household contacts exposed to lineages lacking these variants (0.36 vs 0.29, RR	B.1.427, B.1.429	Peng et al. (2021)	793	T	G	1.0
L452R	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]	B.1.427, B.1.429	Tada et al. (2021)	793	T	G	1.0
L452R	vaccine neutralization efficacy	Neutralization efficiency (ID50) against B.1.1.427/429 reduced 2.1x relative to D614G wildtype using pseudotyped VSV assay on 8 Moderna vaccinee sera one week post-booster.	B.1.427, B.1.429	Choi et al. (2021)	793	T	G	1.0
L452R	vaccine neutralization efficacy	6 of 11 (55%) vaccine recipients (Moderna or Pfizer), showed 2x reduction in neutralization to a B.1.429 lineage virus.	B.1.427, B.1.429	Deng et al. (2021)	793	T	G	1.0
L452R	vaccine neutralization efficacy	Nine stored sera from Pfizer BNT162b2 vaccinees were tested against a range of spike mutation bearing PV. L452R conferred about a two-fold reduction in neutralisation by vaccine sera, but was not statistically significant with this sample size.	B.1.427, B.1.429	Ferreira et al. (2021)	793	T	G	1.0
L452R	vaccine neutralization efficacy	Pseudotyped B.1.1.429 virus has reduced neutralization activity vs wild type: 2.0x (30 sera Pfizer median 9 days post 2nd dose, 35 sera Moderna median 18 days post 2nd dose). This was NOT significant by ANOVA.	B.1.427, B.1.429	Garcia-Beltran et al. (2021)	793	T	G	1.0
L452R	vaccine neutralization efficacy	The presence of this variant in 189 post-mRNA-vaccination COVID-19 cases was proportionally in line with lineage prevalence in Northen California during the study period, suggesting no effect of these variants on immune escape.	B.1.427, B.1.429	Jacobson et al. (2021)	793	T	G	1.0

Mutations	Sub-category	Function	Lineages	Citation	Sequence Depth	Reference Allele	Alternate Allele	Alternate Frequency
L452R	vaccine neutralization efficacy	Using HIV pseudotype: Neutralization potency of 11 Moderna mRNA1273-elicited plasma (7-27 days post-2nd dose) was reduced extasciitilde2.8-fold compared to wildtype (D614G) S. It was reduced extasciitilde4-fold in 14 Pfizer/BioNtech BNT162b2-elicited plasma (7-27 days post-2nd dose). Using VSV pseudotype: we observed a 3-fold average reduction of Pfizer/BioNtech BNT162b2-elicited plasma neutralizing activity.	B.1.427, B.1.429	McCallum et al. (2021)	793	T	G	1.0
L452R	vaccine neutralization efficacy	Detectable antibodies against B.1.1.7 in all samples at Day 43 and Day 209 using pseudotyped lentivirus neutralization in Moderna vaccinee cohort.	B.1.427, B.1.429	Pegu et al (2021)	793	T	G	1.0
L452R	vaccine neutralization efficacy	Relative to B.1, Epsilon (B.1.417/429) shows 1.74x-2.35x decrease in neutralization efficiency by 18 vaccinee sera (BNT162b2 and mRNA1273).	B.1.427, B.1.429	Wilhelm et al. (2021)	793	T	G	1.0
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 non-seroconverted subjects. 1.16x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.427, B.1.429	Gong et al. (2021)	793	T	G	1.0
L452R	vaccinee plasma binding	This variant combination (representing lineage B.1.429 aka Epsilon) showed a 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 previously non-seroconverted subjects. [Stark contrast to 2.15x increase in binding by convalescent plasma 8 months post infection, presumably via memory B cell affinity maturation against L452R effects] 1.12x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.	B.1.427, B.1.429	Gong et al. (2021)	793	T	G	1.0
L452R	viral load	Swab samples N/NP viral RNA is approximately 2-fold higher in B.1.427/B.1.429 than in non-variant viruses.	B.1.427, B.1.429	Deng et al. (2021)	793	T	G	1.0
L452R	virion structure	Estimated free energy change (ddG) for this variant is -0.67 kcal/mol (i.e. destabilizing relative to wild type)	B.1.427, B.1.429	Spratt et al. (2021)	793	T	G	1.0

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