1

2

3

SARS-CoV-2 Research Summary
Omicron BA.2.75

Prepared by:
Anna Maria Niewiadomska
& Richard H. Scheuermann

(Updated September 2022)

Summary

BA.2.75 is a sublineage that was first detected in India (Dec. 2021) with 9 additional substitutions in spike compared to BA.2. Rapid evaluation has shown that BA.2.75 may have a higher reproduction number and ACE-2 binding affinity than BA.5. However, although fusogenicity, spike stability, growth *in vitro*, and neutralization sensitivity was greater than that of BA.2, it was less than those for BA.5. In addition, BA.2.75 remains largely susceptible to currently used therapeutic antibodies and antivirals. Data on pathogenicity in hamsters was mixed.
Overall results suggest that BA.2.75 may have a slight competitive advantage over BA.4/BA.5, despite having less immune evasion than BA.4/5.

Reproduction number

Xie *et al.* report that the effective reproduction number of BA.2.75 is greater than that of BA.5[6].

Affinity to spike

There are 4 reports demonstrating that BA.2.75 has significantly higher ACE-2-binding affinity than BA.2 and BA.5[2,6,7,11].

Fusogenicity (*in vitro* Alveolar cells)

Saito *et al.* reported BA.2.75 had greater fusogenicity than BA.2[6]. Qu *et al.* reported that while BA.2.75 fusogenicity was comparable to BA.5, it was greater than BA.2[8]. This may be due to the S:N460K mutation, which enhances Spike protein processing.

Spike stability

Cao *et al.* showed that BA.2.75 spike had decreased thermostability and increased “up” RBD conformation in acidic conditions[7]. This may enhance viral entry through endosomal fusion pathway.

	BA.5	BA.2	BA.2.75 BA.2.75.3 BM.1	BA.2.75.1	BL.1	BA.2.75.2	BA.2.75.4	BA.2.75.5
T19I	x	x	x	x	x	x	x	x
L24S	x	x	x	x	x	x	x	x
25-27del	x	x	x	x	x	x	x	x
69/70del	x							
G142D	x	x	x	x	x	x	x	x
K147E			x	x	x	x	x	x
W152R			x	x	x	x	x	x
F157L			x	x	x	x	x	x
I210V			x	x	x	x	x	x
V213G	x	x	x	x	x	x	x	x
G257S			x	x	x	x	x	x
G339D	x	x						
G339H			x	x	x	x	x	x
R346T					x	x		
K356T								x
S371F	x	x	x	x	x	x	x	x
S373P	x	x	x	x	x	x	x	x
S375S	x	x	x	x	x	x	x	x
T376A	x	x	x	x	x	x	x	x
D405N	x	x	x	x	x	x	x	x
R408S	x	x	x	x	x	x	x	x
K417N	x	x	x	x	x	x	x	x
N440K	x	x	x	x	x	x	x	x
G446S			x	x	x	x	x	x
L452R	x						x	
N460K			x	x	x	x	x	x
S477N	x	x	x	x	x	x	x	x
T478K	x	x	x	x	x	x	x	x
E484A	x	x	x	x	x	x	x	x
F486V	x							
F486S						x		
Q493R		x						
Q498R	x	x	x	x	x	x	x	x
N501Y	x	x	x	x	x	x	x	x
Y505H	x	x	x	x	x	x	x	x
D574V				x				
D614G	x	x	x	x	x	x	x	x
H655Y	x	x	x	x	x	x	x	x
N679K	x	x	x	x	x	x	x	x
P681H	x	x	x	x	x	x	x	x
N764K	x	x	x	x	x	x	x	x
D796Y	x	x	x	x	x	x	x	x
Q954H	x	x	x	x	x	x	x	x
N969K	x	x	x	x	x	x	x	x
D1199N						x		

Table 1: *This table compares the spike mutations found in BA.2 and BA.5 with BA.2.75 sub-lineages, with differences highlighted in blue. BA.2.75 now has 7 designated sub-lineages. BL.1 is a sublineage of BA.2.75.1, and BM.1 is a sublineage of BA.2.75.3.*

References

1. Yamasoba, D. *et al.* Neutralisation sensitivity of SARS-CoV-2 omicron subvariants to therapeutic monoclonal antibodies. *Lancet Infect. Dis.* **22**, 942–943 (2022).
2. Wang, Q. *et al.* Antigenic characterization of the SARS-CoV-2 Omicron subvariant BA.2.75. *bioRxiv* 2022.07.31.502235 (2022) doi:10.1101/2022.07.31.502235.
3. Gruell, H. *et al.* Neutralization sensitivity of the SARS-CoV-2 Omicron BA.2.75 sublineage. *bioRxiv* 2022.08.04.502609 (2022) doi:10.1101/2022.08.04.502609.
4. Wang, X. *et al.* Neutralization of Omicron BA.4/BA.5 and BA.2.75 by Booster Vaccination or BA.2 Breakthrough Infection Sera. *bioRxiv* 2022.08.04.502716 (2022) doi:10.1101/2022.08.04.502716.
5. Xie, X. *et al.* Neutralization of SARS-CoV-2 Omicron sublineages by 4 doses of mRNA vaccine. *bioRxiv* 2022.07.29.502055 (2022) doi:10.1101/2022.07.29.502055.
6. Saito, A. *et al.* Virological characteristics of the SARS-CoV-2 Omicron BA.2 spike. *Cell* **185**, 2103-2115.e19 (2022).
7. Cao, Y. *et al.* Characterizations of enhanced infectivity and antibody evasion of Omicron BA.2.75. *bioRxiv* 2022.07.18.500332 (2022) doi:10.1101/2022.07.18.500332.
8. Qu, P. *et al.* Evasion of Neutralizing Antibody Response by the SARS-CoV-2 BA.2.75 Variant. *bioRxiv* 2022.08.14.503921 (2022) doi:10.1101/2022.08.14.503921.
9. Shrwani, D. J. *et al.* Evasion of neutralizing antibodies by Omicron sublineage BA.2.75. *bioRxiv* 2022.07.19.500716 (2022) doi:10.1101/2022.07.19.500716.
10. Uraki, R. *et al.* Characterization of SARS-CoV-2 Omicron BA.2.75 clinical isolates. *bioRxiv* 2022.08.26.505450 (2022) doi:10.1101/2022.08.26.505450.
11. Sugano, A. *et al.* SARS-CoV-2 Omicron BA.2.75 variant may be much more infective than preexisting variants. *bioRxiv* 2022.08.25.505217 (2022) doi:10.1101/2022.08.25.505217.

Click to add speaker notes