SARS-CoV-2 Research Summary
Omicron BA.2.75

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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	x
L24S	x	x	x	x	x	x	x	x	x
25-27del	x	x	x	x	x	x	x	x	x
69/70del	x								
G142D	x	x	x	x	x	x	x	x	x
K147E			x	x	x	x	x	x	x
W152R			x	x	x	x	x	x	x
F157L			x	x	x	x	x	x	x
I210V			x	x	x	x	x	x	x
V213G	x	x	x	x	x	x	x	x	x
G257S			x	x	x	x	x	x	x
G339D	x	x							
G339H			x	x	x	x	x	x	x
R346T				*		x	x		
K356T									x
S371F	x	x	x	x	x	x	x	x	x
S373P	x	x	x	x	x	x	x	x	x
S375S	x	x	x	x	x	x	x	x	x
T376A	x	x	x	x	x	x	x	x	x
D405N	x	x	x	x	x	x	x	x	x
R408S	x	x	x	x	x	x	x	x	x
K417N	x	x	x	x	x	x	x	x	x
N440K	x	x	x	x	x	x	x	x	x
G446S			x	x	x	x	x	x	x
L452R	x							x	
N460K			x	x	x	x	x	x	x
S477N	x	x	x	x	x	x	x	x	x
T478K	x	x	x	x	x	x	x	x	x
E484A	x	x	x	x	x	x	x	x	x
F486V	x								
F486S				x			x		
F490S				*					
Q493R		x							
Q498R	x	x	x	x	x	x	x	x	x
N501Y	x	x	x	x	x	x	x	x	x
Y505H	x	x	x	x	x	x	x	x	x
D574V					x	x			
D614G	x	x	x	x	x	x	x	x	x
H655Y	x	x	x	x	x	x	x	x	x
N679K	x	x	x	x	x	x	x	x	x
P681H	x	x	x	x	x	x	x	x	x
N764K	x	x	x	x	x	x	x	x	x
D796Y	x	x	x	x	x	x	x	x	x
Q954H	x	x	x	x	x	x	x	x	x
N969K	x	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. Asterisk (*) indicates that a mutation is found in some but not all genomes. Note: lineage assignments are preliminary and may change as more genomes are sequenced.*

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Growth *in vitro*

Saito *et al.* reported growth efficiency of BA.2.75 in human alveolar epithelial cells was comparable to BA.5 but greater than BA.2[6].

Neutralization sensitivity (previous infection and vaccination)

Several reports examined the neutralization sensitivity of BA.2.75, concluding that while it exhibits enhanced neutralization resistance over BA.2, it is less resistant than BA.4/5 variants[2-8]. Neutralization sensitivity of BA.2.75 was also reported to be similar to that of BA.2.12.1[2]. Spike mutations G446S and N460K appear to be largely responsible for this enhanced resistance.

Therapeutics (monoclonals and antivirals)

Several reports evaluated the efficacy of therapeutic monoclonal antibodies (mAb)[1,2,7,9], concluding that while there was a slight increase in Bebtelovimab resitance, BA.2.75 remains largely sensitive to this mAb. BA.2.75 is also moderately susceptible to tixagevimab[8], cilgavimab[8], as well as Evisheld[7].

Saito *et al.* also reported that the clinically-available antiviral drugs (Paxlovid [Ritonavir and Nirmatrelvir], Remdesivir and Molnupiravir) were effective against BA.2.75[6].

Pathogenicity *in vivo*

Data on pathogenicity *in vivo* was mixed, with Saito *et al.* reporting that BA.2.75 pathogenicity in hamsters was comparable to BA.5 but greater than BA.2[6], whereas Uraki *et al.* reported that BA.2.75 replicated better than BA.5 and BA.2, suggesting that BA.2.75 could cause more severe disease[10].

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