Immunovirological Aspects of Omicron Variant and Vaccine Efficacy

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Tracking SARS-CoV-2 variants: WHO

Currently circulating variants of concern (VOCs)

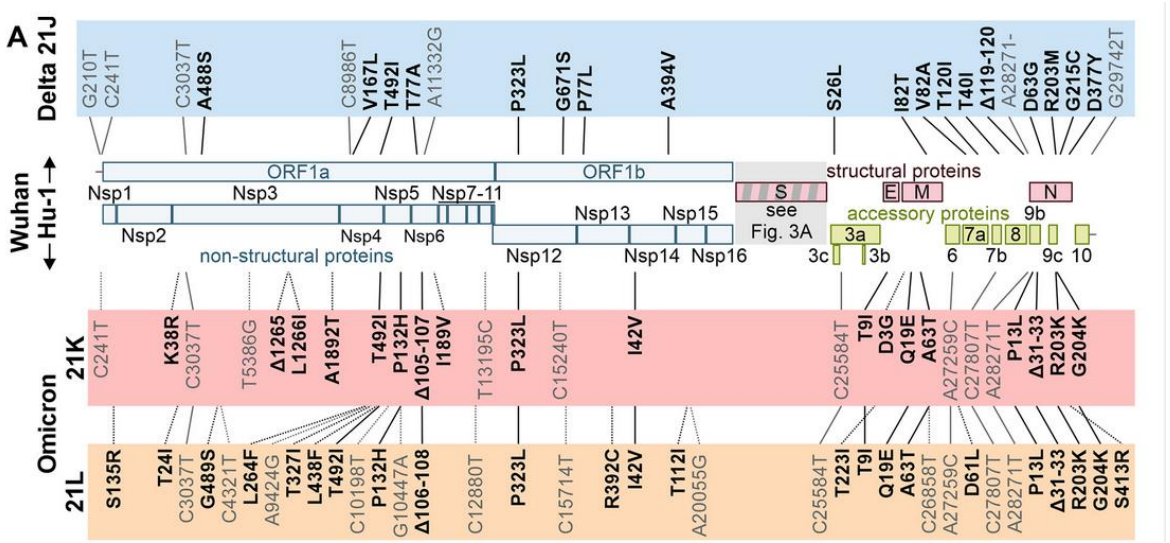
WHO label	Pango lineage•	GISAID clade	Nextstrain clade	Additional amino acid changes monitored°	Earliest documented samples	Date of designation
Delta	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:K417N +S:E484K	India, Oct-2020	VOI: 4-Apr-20 VOC: 11-May
Omicron*	B.1.1.529	GR/484A	21K, 21L, 21M	+S:R346K +S:L452R/Q +S:F486V	Multiple countries, Nov-2021	VUM: 24-Nov VOC: 26-Nov

Independent evolution of Omicron

- SARS-CoV-2: **30kb** genome: largest genome of all known RNA viruses.
- Proofreading function of the viral polymerase: **Nsp14+Nsp10**: exonuclease activity: reduces the accumulation of mutations.
- The genomes of different subtypes of HIV-1 may differ by up to 15% while the Omicron VOC differs in less than 0.2% of its nucleotides from the early pandemic Wuhan strain of SARS-CoV-2.
- Influenza viruses: **mutate at least four times faster.**
- Omicron: 55 mutations from the initial Wuhan Hu-1 strain.
- Delta: 21 to 44 substitutions.

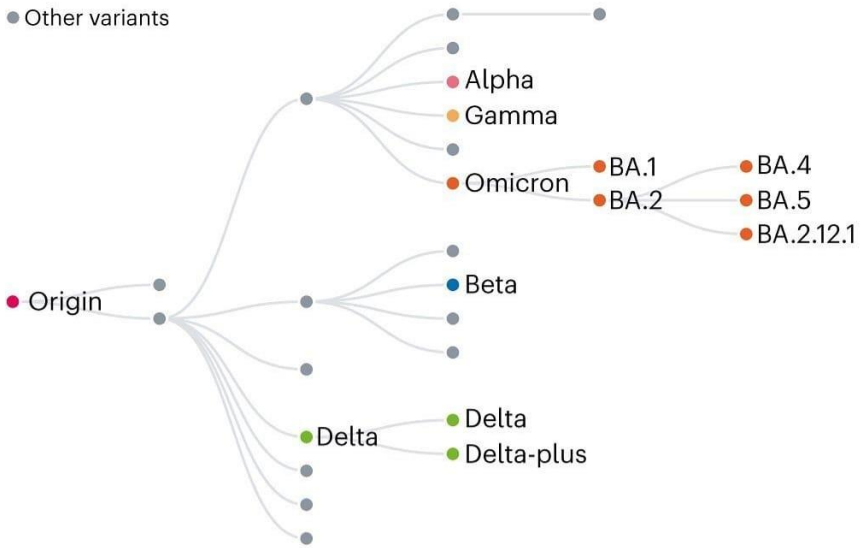
What is alarming about Omicron?

- About 30 of mutations being located in the viral Spike gene that is critical for **virus infection** and the key target of **protective immune responses**.
- Most nucleotide changes are nonsynonymous.
- **Nonsynonymous** mutations change the protein sequences and are frequently subjected to natural selection.



Omicron sub-lineages

This diagram shows how the coronavirus SARS-CoV-2 has evolved to spawn several related variants. The latest are BA.4 and BA.5 along the Omicron lineage, which has dominated infections this year.



Based on data from NextStrain.

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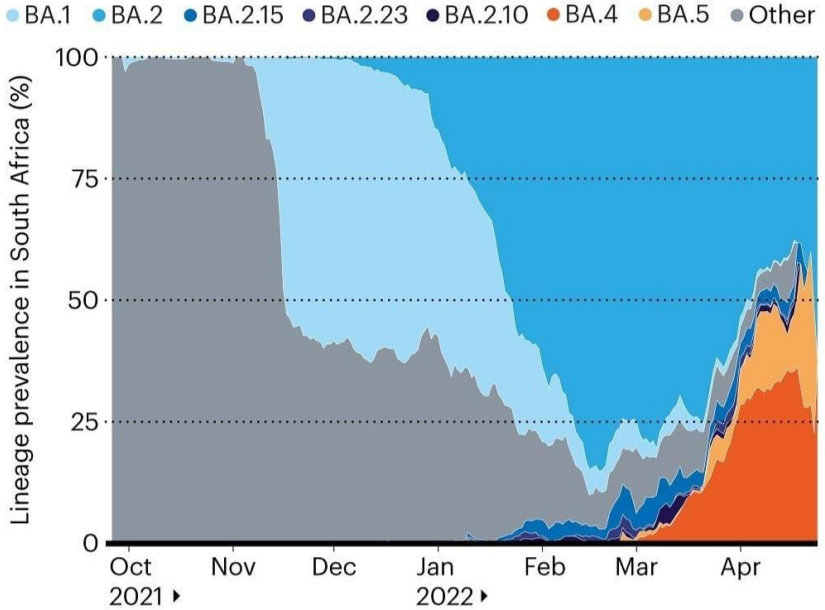
Graphics of the week

BA.4 and BA.5 spread faster than previous Omicron variants and are accounting for a growing proportion of COVID-19 cases in South Africa.



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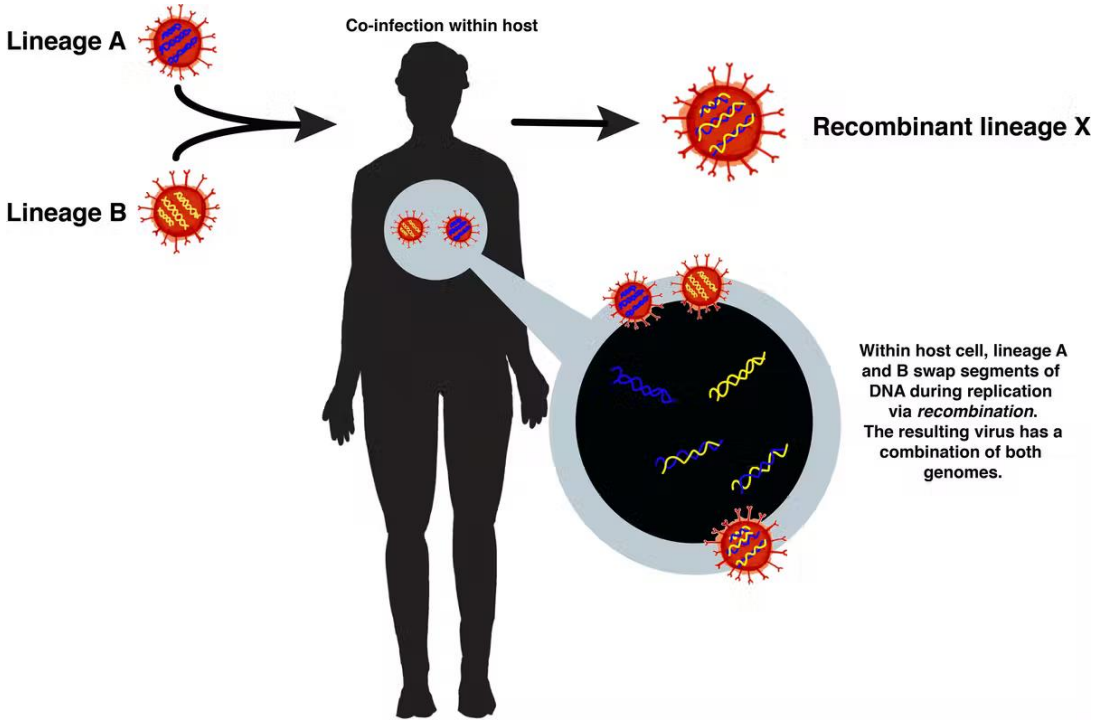
Graphics of the week

XE: A hybrid variant of Omicron

- Mutation is not the only way variants can emerge.
- XE is **a recombinant virus** (coinfection by BA.1 and BA.2).
- It was **first detected in the UK** in mid-Jan.
- XE: **10% more transmissible than BA.2**
- **Other recombined virus: Deltacron**



Omicron sub-lineages BA.4/BA.5 escape BA.1 infection elicited neutralizing immunity (Re-infection)

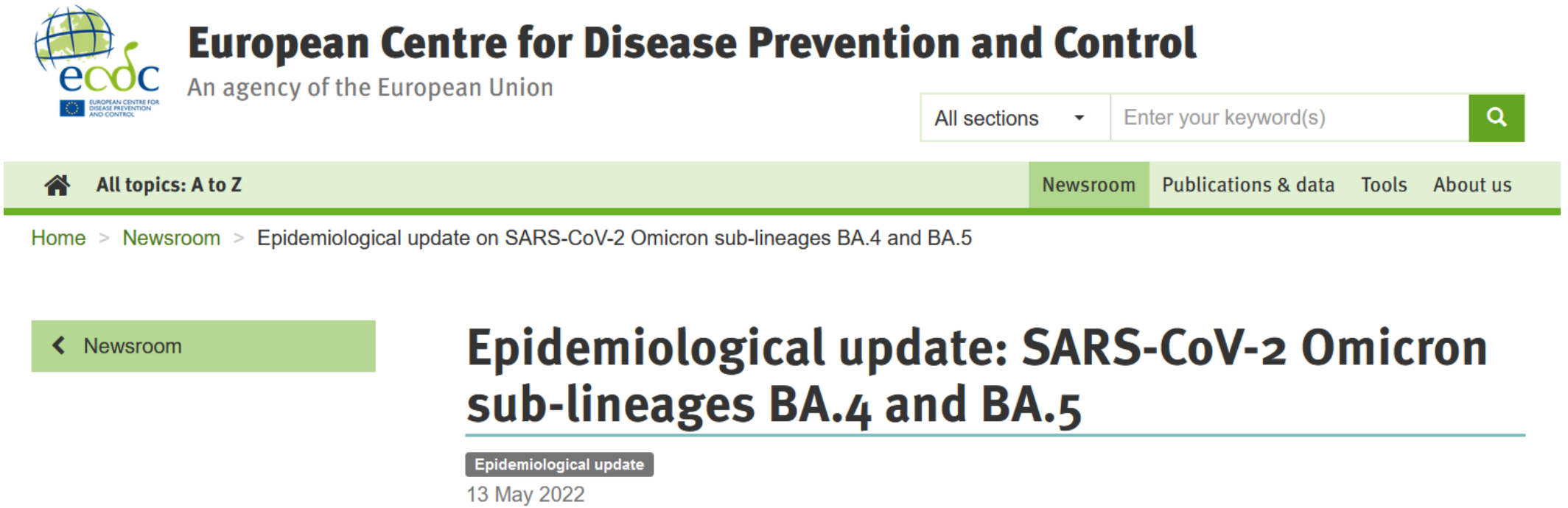
Two new sub-lineages, BA.4 and BA.5, are now emerging in South Africa with changes relative to BA.1, including L452R and F486V mutations in the spike receptor binding domain.

The observed escape of BA.4 and BA.5 from BA.1 elicited immunity is more moderate than of BA.1 against previous immunity.

In vaccinated BA.1 breakthroughs, FRNT50 declined from 507 for BA.1 to 158 for BA.4 (**3.2-fold**) and 198 for BA.5 (**2.6-fold**).

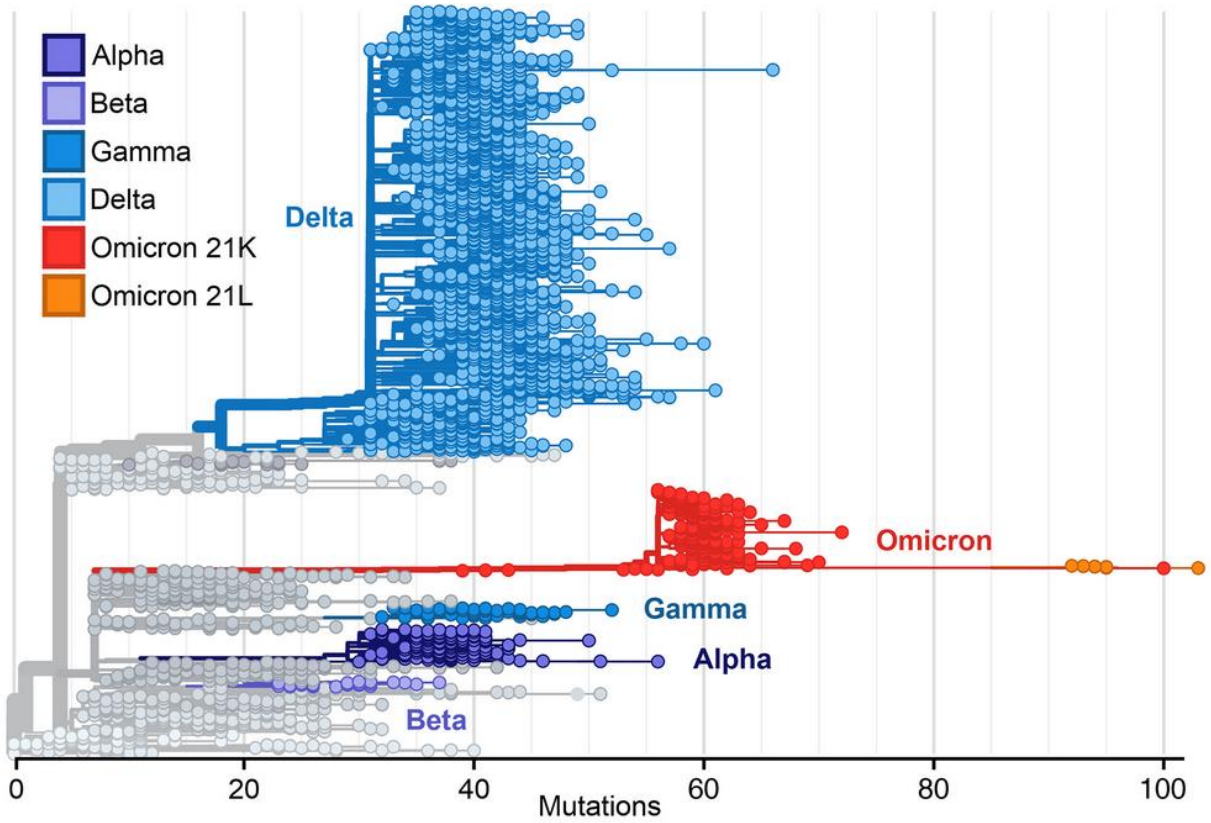
However, the low absolute neutralization levels for BA.4 and BA.5, **particularly in the unvaccinated group**, are unlikely to protect well against symptomatic infection.

As of 12 May 2022, ECDC has reclassified Omicron sub-lineages BA.4 and BA.5 from variants of interest to variants of concern.



Phylogenetic analysis

Omicron VOC clearly did not emerge from other VOCs, including the Delta VOC.



Theories of variants evolution

Phylogenetic analysis suggests that variants evolved independently by convergent evolution.

I. Efficient replication in an immunocompromised individual over a long period of time.

II. Circulating in the human population for some time.

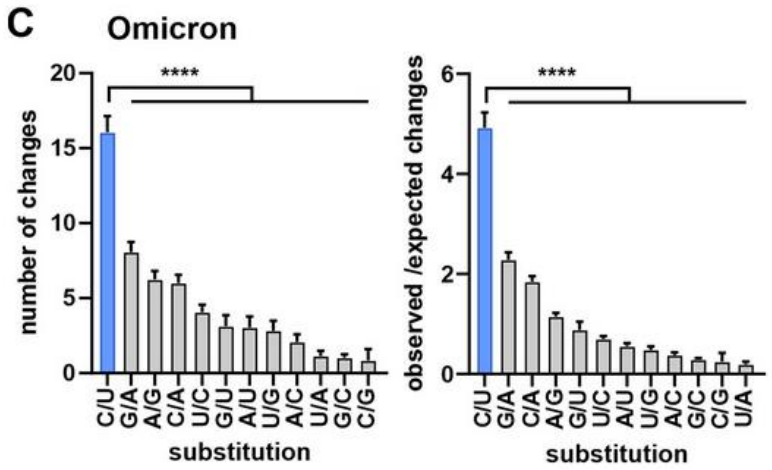
III. Omicron may have evolved in a nonhuman species from which it spilled back to humans (cross species barriers).

Possible causes of the mutations

APOBEC proteins deaminate cytosine to uracil, resulting in C-to-U or G-to-A changes.

About 30% of all nucleotide substitutions in the Delta and Omicron VOC compared to an early pandemic reference strain are C to U.

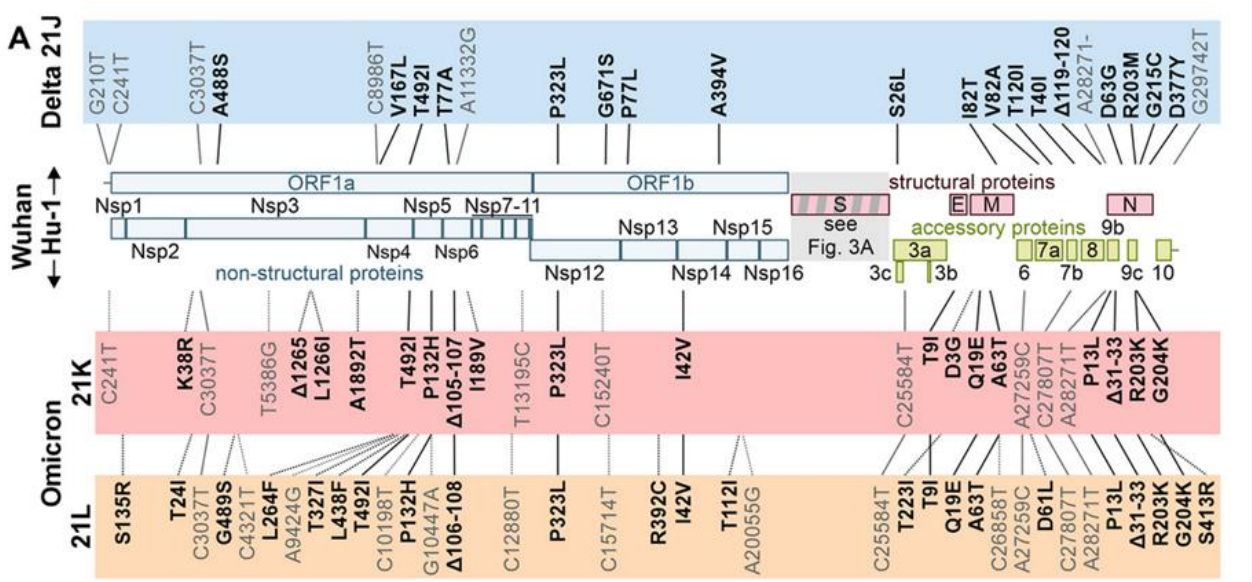
G-to-A changes are also very common and occur at a 2-fold-increased frequency.



Non-spike alterations in the genome

A total of 18 amino acid-changing mutations in the genome of more common 21K clade of the Omicron VOC are located outside the Spike gene.

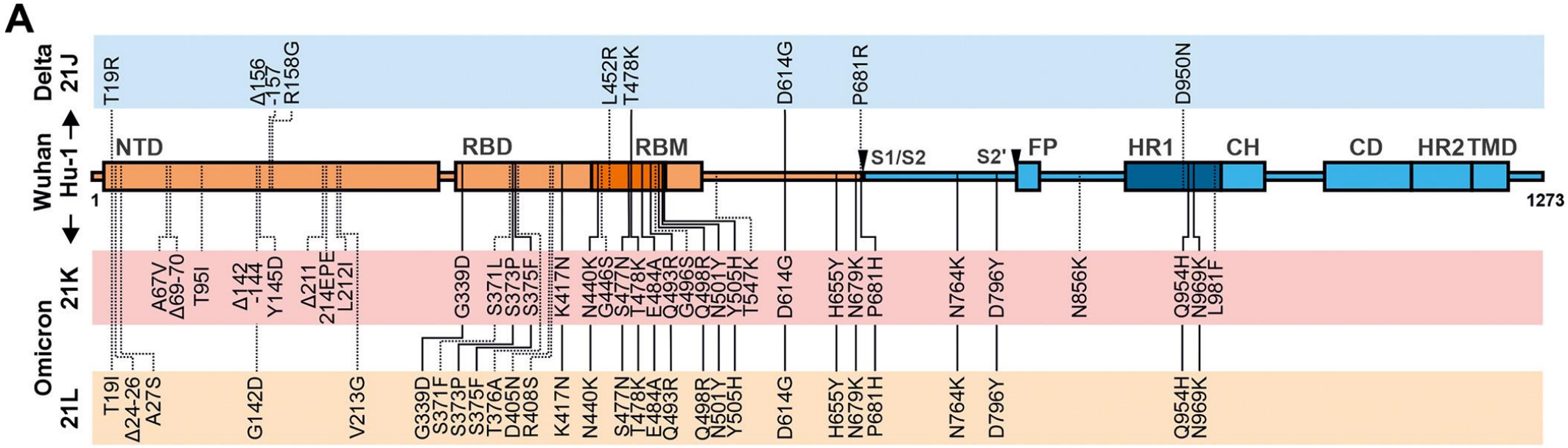
Two-thirds of the genome of SARS-CoV-2 encode 16 nonstructural proteins with functions including **innate immune evasion**, **viral RNA replication**, **proteolytic activity**, and **proofreading function**.



Alterations in the spike protein

Contains >60% of all mutations (over 30 mutations in spike with 15 in RBD).

The Spike protein is the key determinant of **virus transmission** and **immune evasion.**



Immune evasion

- Numerous recent studies show that the Omicron VOC evades many but not all neutralizing antibodies induced by vaccination or previous SARS-CoV-2 infection.
- An up-to-40-fold-decreased efficiency of neutralizing sera against the Omicron VOC.
- Sera from individuals boosted with RNA vaccines showed **substantial neutralizing activity** against the Omicron VOC.
- A panel of 247 human RBD-targeted mAbs, 85% fail to bind Omicron.
- Pre-existing cellular and innate immunity
- Non-neutralizing antibodies and residual NAs

Summary of the studies related to booster dose efficacy against Omicron variant

- The risk of hospitalization is lower for Omicron cases after the second and third doses of vaccine, with an 81% (77%–85%) reduction in the risk of hospitalization after three doses compared with unvaccinated Omicron cases. (UK Health Agency)

- A booster dose of BNT162b2 (Pfizer BioNTech) or mRNA-1273(Moderna) vaccine after either the ChAdOx1 nCoV-19 (Oxford–AstraZeneca) or BNT162b2 primary course **substantially increased protection against Omicron.**

Summary of the studies related to booster dose efficacy against Omicron variant

- COV-BOOST is a multicenter, randomized, controlled phase 2 trial of **third-dose booster** vaccination against COVID-19.

- All the seven vaccines in the study yielded **a great escalation of antibodies and cellular immune responses** after ChAd/ChAd (Oxford–AstraZeneca) initial course and all, except one, after BNT/BNT (Pfizer BioNTech), with no safety concerns.

Summary of the studies related to booster dose efficacy against Omicron variant

- Booster-dose vaccine effectiveness was evaluated at least after 7 days of receiving the third dose, compared with receiving only 2 doses 5 months ago, was estimated to be **93% for hospitalization**, **92% for severe COVID-19** disease, and **81% for COVID-19 mortality**.

- Persons who had received the booster dose of mRNA COVID-19 vaccine (compared with unvaccinated and those who received of two doses) **were less likely among cases with symptomatic SARS-CoV-2 infection compared with test-negative controls.**

Summary of the studies related to booster dose efficacy against Omicron variant

- A booster dose of **BBIBP-CorV** (Sinopharm Beijing Institute of Biological Products COVID-19 vaccine) led to a significant rebound in neutralizing immune response against SARS-CoV-2, while **the Omicron variant showed extensive but incomplete escape from booster-enhanced neutralization.**

- A homologous inactivated vaccine booster or a heterologous booster with a protein subunit vaccine (ZF2001) **significantly increased neutralization titers to both WT and Omicron variant.**


“thank you for your ATTENTION :)”


COVID-19
VACCINE