Concepts to understand viral evolution in the context of surveillance and control

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HEALTH
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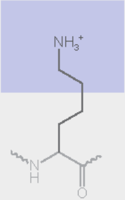
Viral evolution and genomic and phenotypic characterization

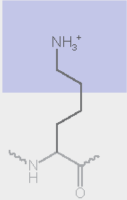
General considerations:

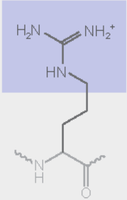
- Mutation is naturally expected in virus evolution and adaptation process.
- Usually, RNA viruses are more prone to generate mutations (low proofreading of the polymerases) and therefore, to generate genetic variants.
- There are different type of mutations, and some are more important than other

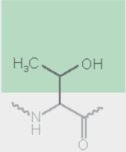
Viral evolution and genomic and phenotypic characterization

	No mutation	Point mutations			
		Silent	Nonsense	Missense	
				conservative	non-conservative
DNA level	TTC	TTT	ATC	TCC	TGC
mRNA level	AAG	AAA	UAG	AGG	ACG
protein level	Lys	Lys	STOP	Arg	Thr









basic 🟪
polar 🟩

Silent → Neutral

Nonsense → Deleterious

Missense → Either advantageous or not

Viral evolution and genomic and phenotypic characterization

Why viruses change? What are the consequences?

- The changes might lead advantages for the virus to *achieve its goals*:
  - Better capacity to enter the cells and then to replicate (spread)

Viral evolution and genomic and phenotypic characterization

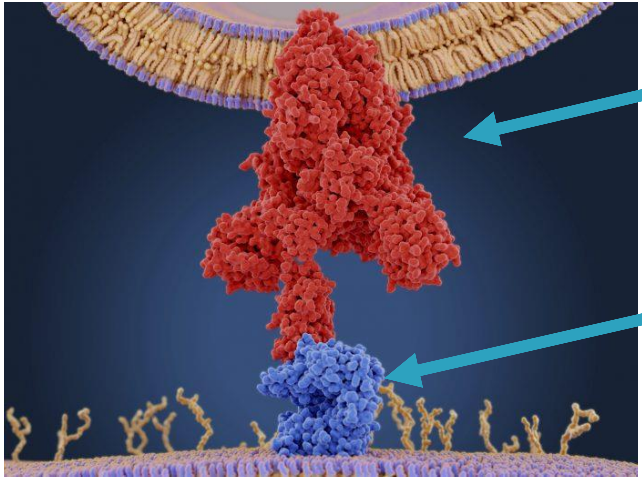
Why viruses change? What are the consequences?

- The changes might lead advantages for the virus to *achieve its goals*:
    - Better capacity to enter the cells and then to replicate (spread)
    - To escape the immune response (either natural or vaccine mediated)
    - To avoid antivirals

Usually do not evolve to become more lethal
It is not convenient to kill the host!

Viral evolution and genomic and phenotypic characterization

- Better capacity to enter the cells and then to replicate



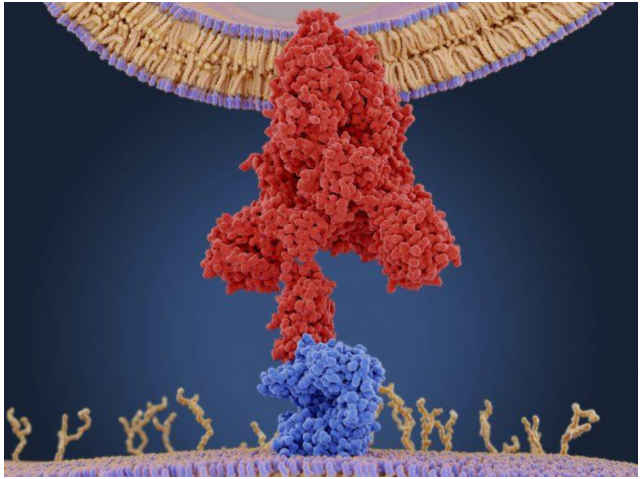
S Protein (Spike)

Angiotensin-Converting Enzyme (ACE) Receptor

https://www.clinicalomics.com/topics/patient-care/coronavirus/research-may-explain-why-men-are-more-susceptible-to-covid-19-than-women/

Viral evolution and genomic and phenotypic characterization

- Better capacity to enter the cells and then to replicate



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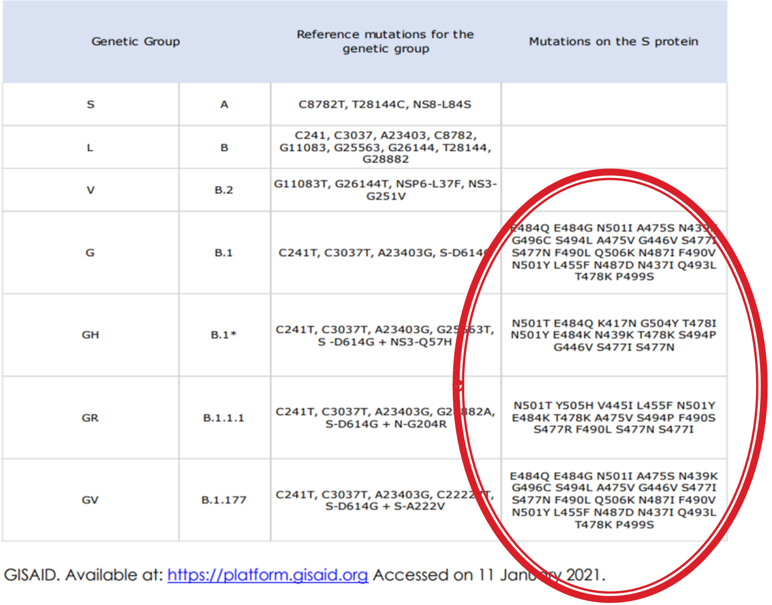
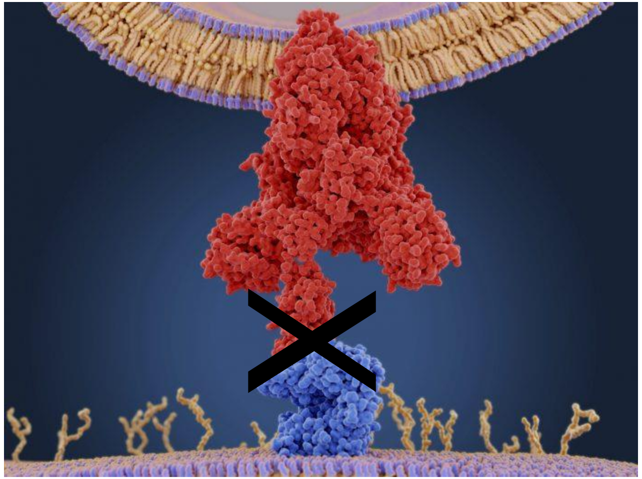


Genetic Group		Reference mutations for the genetic group	Mutations on the S protein
S	A	C8782T, T28144C, NS8-L84S	
L	B	C241, C3037, A23403, C8782, G11083, G25563, G26144, T28144, G28882	
V	B.2	G11083T, G26144T, NSP6-L37F, NS3-G251V	
G	B.1	C241T, C3037T, A23403G, S-D614[illegible]	E484Q E484G N501I A475S N43[illegible] G496C S494L A475V G446V S477I S477N F490L Q506K N487I F490V N501Y L455F N487D N437I Q493L T478K P499S
GH	B.1*	C241T, C3037T, A23403G, G25[illegible]63T, S -D614G + NS3-Q57H	N501T E484Q K417N G504Y T478I N501Y E484K N439K T478K S494P G446V S477I S477N
GR	B.1.1.1	C241T, C3037T, A23403G, G2[illegible]882A, S-D614G + N-G204R	N501T Y505H V445I L455F N501Y E484K T478K A475V S494P F490S S477R F490L S477N S477I
GV	B.1.177	C241T, C3037T, A23403G, C2222[illegible]T, S-D614G + S-A222V	E484Q E484G N501I A475S N439K G496C S494L A475V G446V S477I S477N F490L Q506K N487I F490V N501Y L455F N487D N437I Q493L T478K P499S

Source: GISAID. Available at: https://platform.gisaid.org Accessed on 11 Jan[illegible]y 2021.

Viral evolution and genomic and phenotypic characterization

- To escape the immune response (either natural or vaccine mediated)



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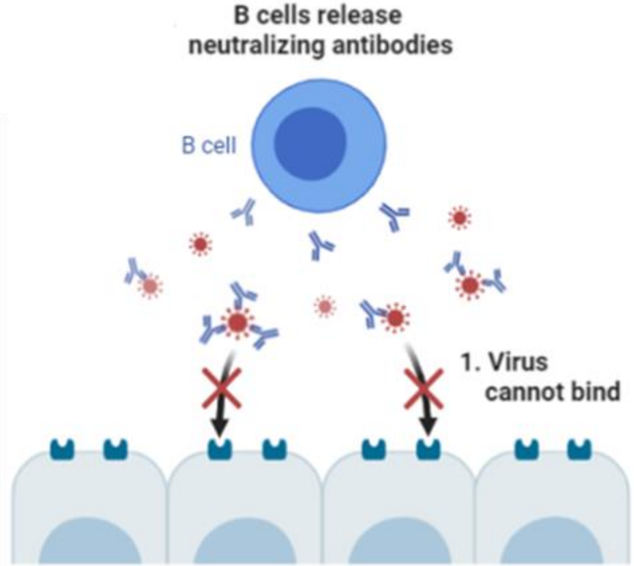
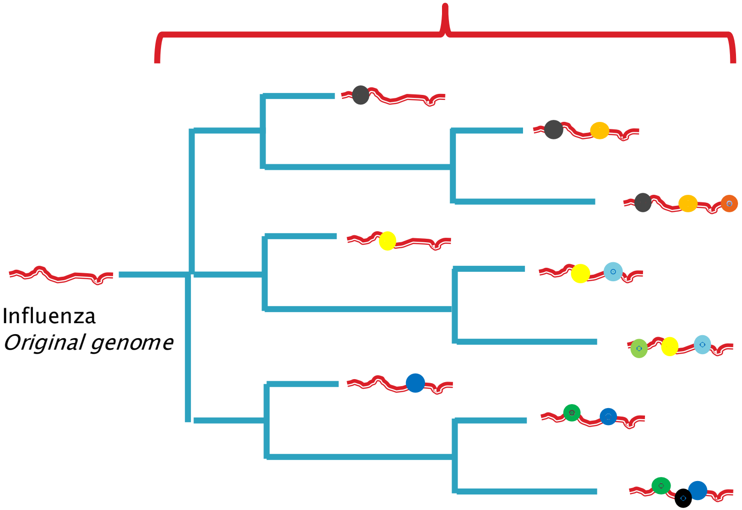


Genetic groups, Lineages, Variants...

Genomic



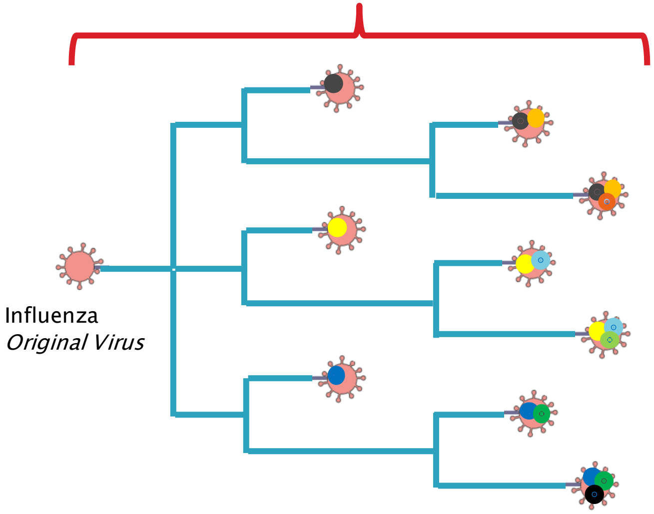
Influenza
Original genome

Genetic group

Lineage

Clades

Phenotipic



Influenza
Original Virus

Genetic group

Lineage

Clades

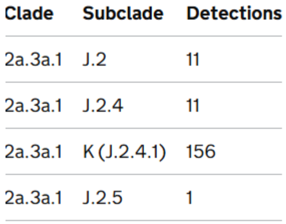
It is important to mention that the denominations as *clade*, *lineage*, *variant*, etc., are arbitrary and do not correspond to an official taxonomic hierarchy.

National flu and COVID-19 surveillance report - England: 13 November 2025 (week 46)

Influenza virus characterisation

Genetic characterisation

Number of influenza A(H3N2) viruses characterised by genetic analysis at the UKHSA Respiratory Virus Unit since week 35 2025



Clade	Subclade	Detections
2a.3a.1	J.2	11
2a.3a.1	J.2.4	11
2a.3a.1	K (J.2.4.1)	156
2a.3a.1	J.2.5	1

Antigenic characterisation

A(H3N2): 13 A(H3N2) viruses have been antigenically characterized:

- three (23%) were similar to reference viruses representative of the A/District of Columbia/27/2023 (H3N2)-like and A/Croatia/10136RV/2023 (H3N2)-like Northern Hemisphere 2025/26 (H3N2) vaccine strains.
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Oseltamivir and zanamivir antiviral susceptibility results of influenza positive samples tested at UKHSA-RVU since week 35 of 2025 using whole genome sequencing

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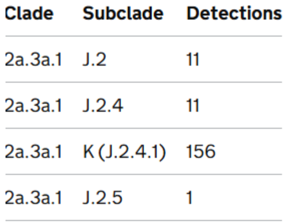

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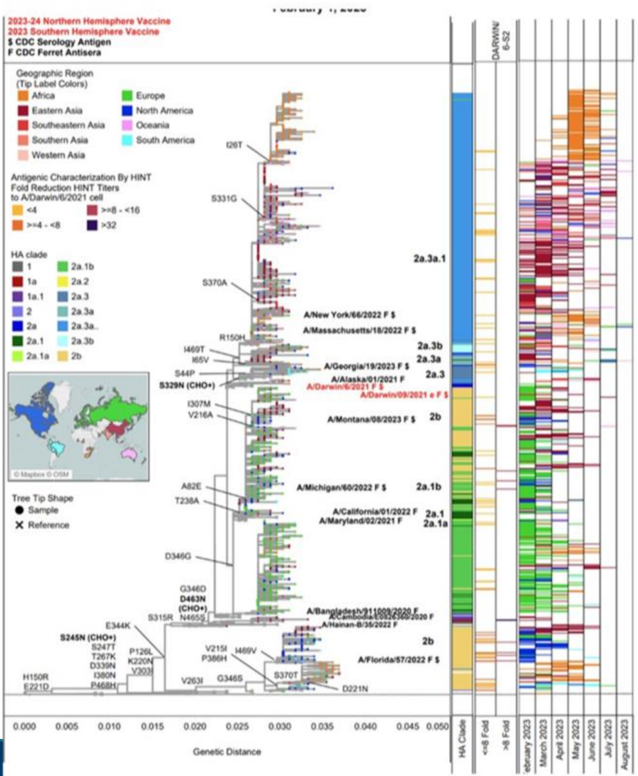
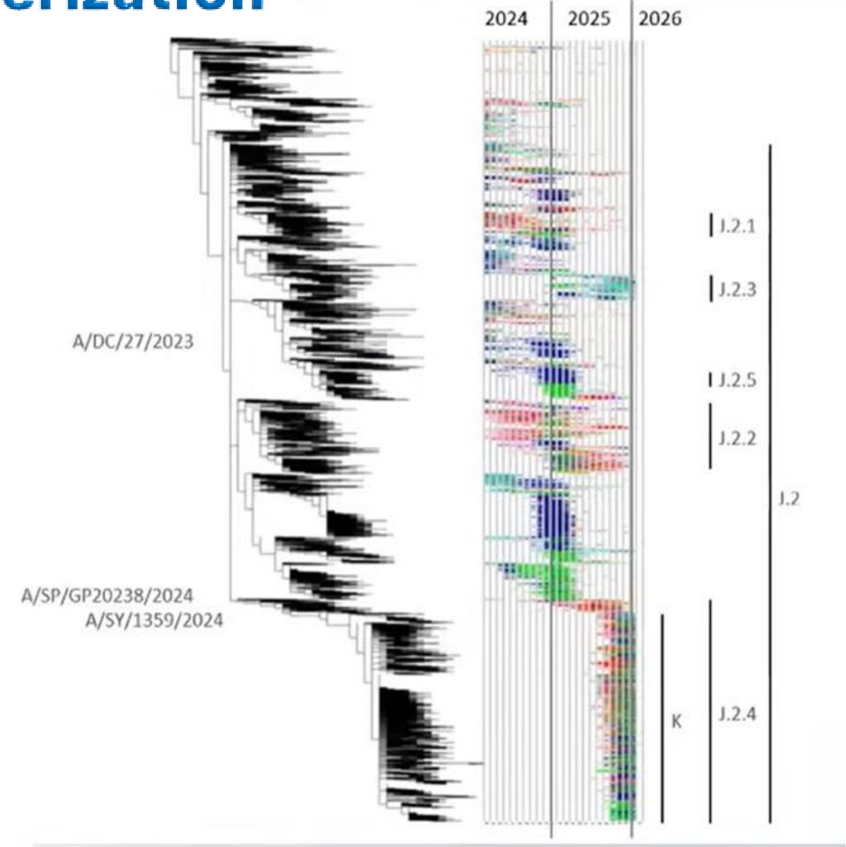
Viral evolution and genomic and phenotypic characterization





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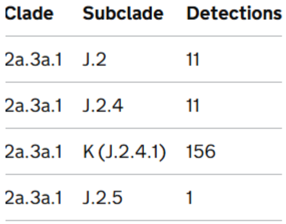

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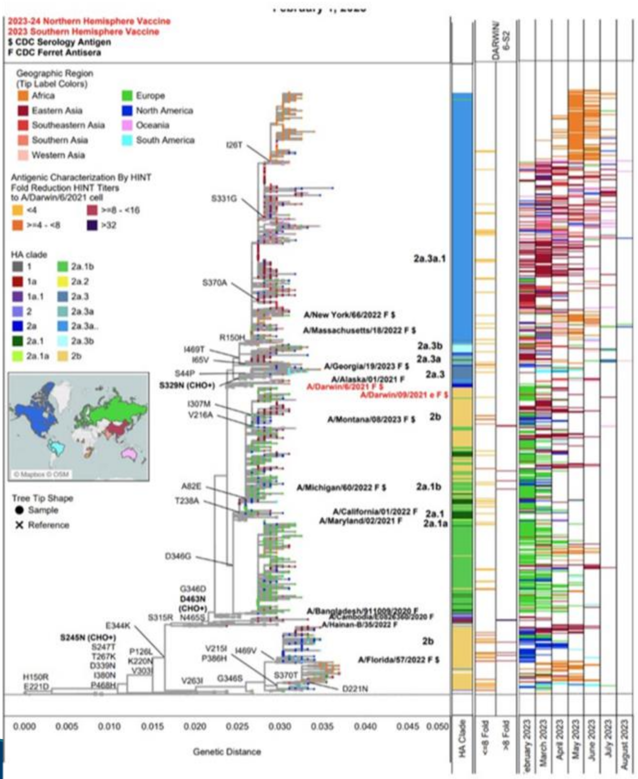

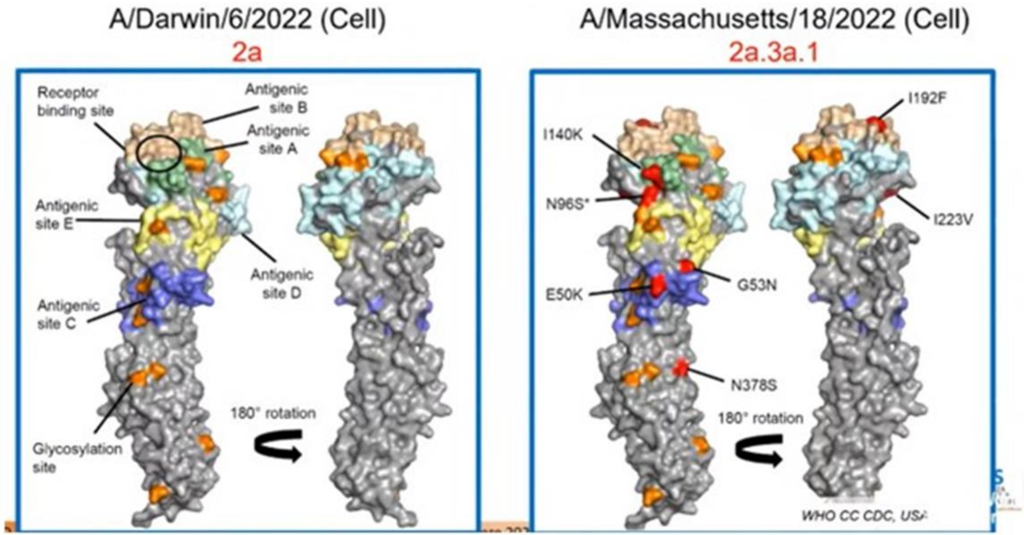

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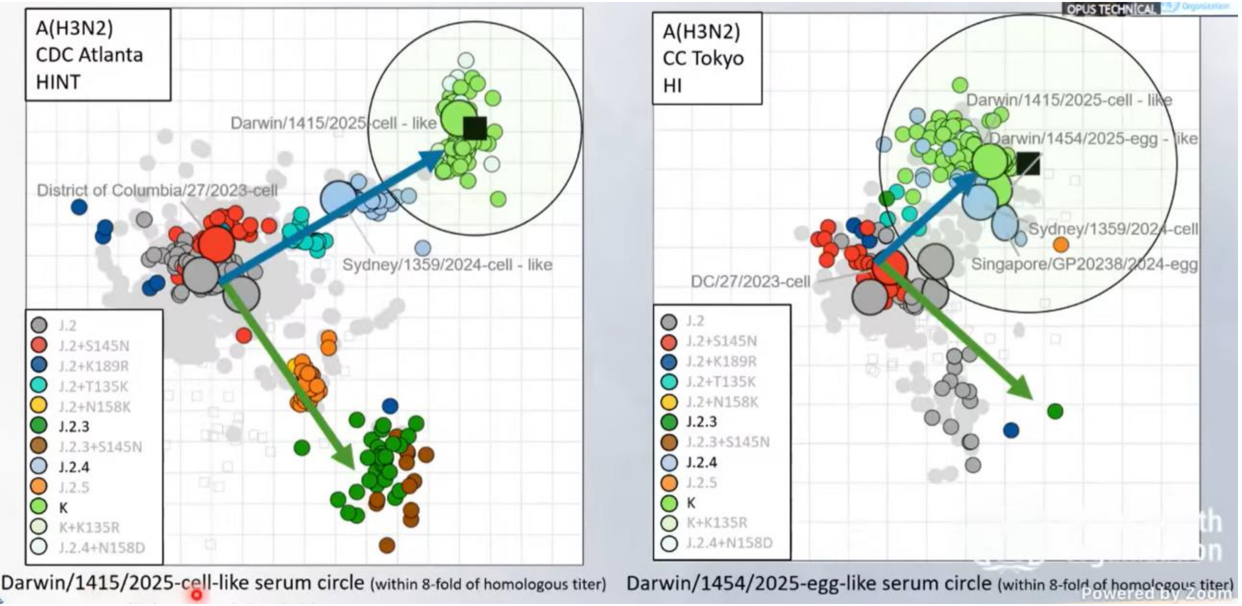


Darwin/1415/2025-cell-like serum circle (within 8-fold of homologous titer) Darwin/1454/2025-egg-like serum circle (within 8-fold of homologous titer)

Phenotypic analyses

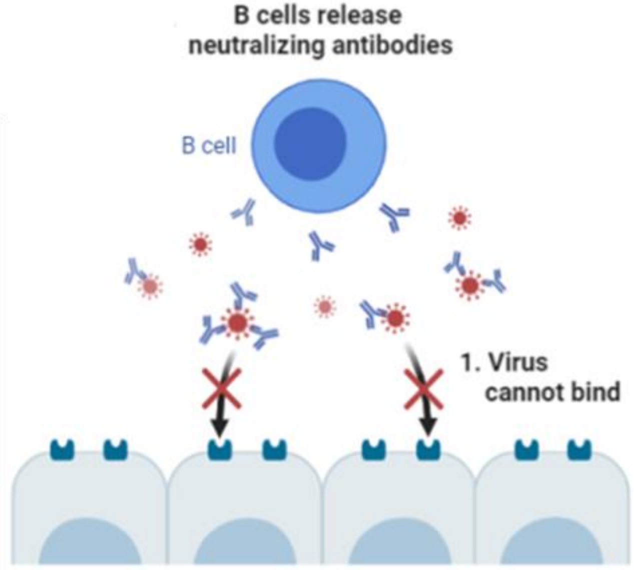
- Subclade K viruses and J.2.4 viruses with HA substitutions F79V, S144N (addition of a potential N-glycosylation site), N158D, I160K, T328A were better recognized by antisera raised against A/Darwin/1415/2025-like (subclade K) viruses.

From, WHO Vaccine Composition Consultation, February 2026

Viral evolution and genomic and phenotypic characterization

- To escape the immune response (either natural or vaccine mediated)

Some mutations might change the structure, and the antibodies do not recognize the protein anymore…



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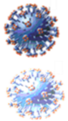
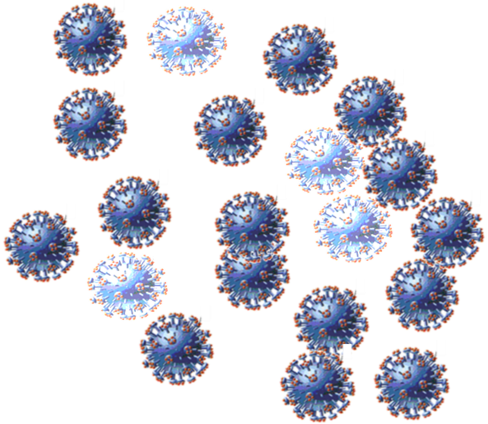
Viral evolution and genomic and phenotypic characterization: SARS-CoV-2

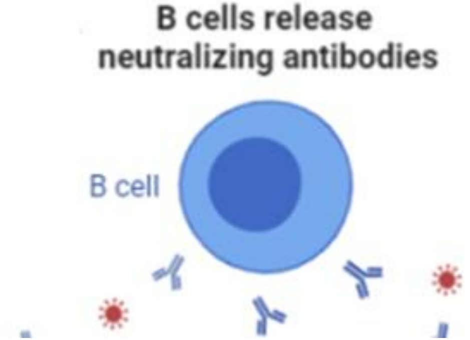


Variant 1

Variant 2

Circulating in a population





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Viral evolution and genomic and phenotypic characterization: SARS-CoV-2

Variant 1

Variant 2

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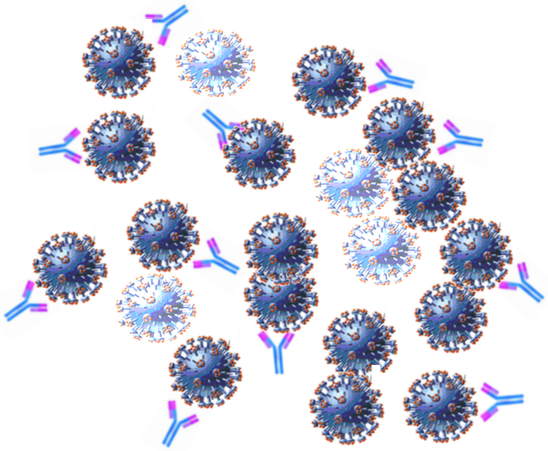

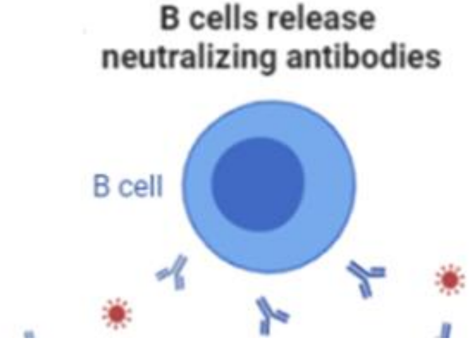

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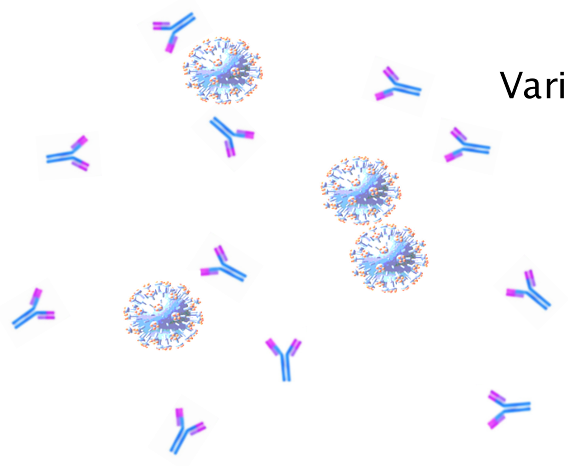
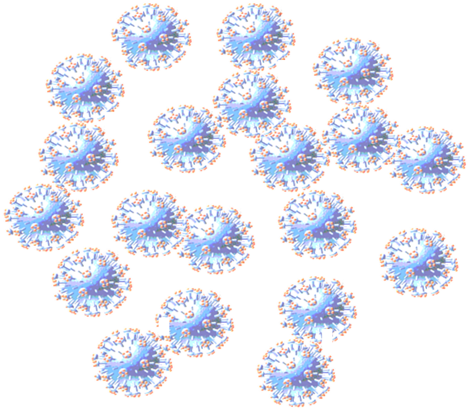


Variant 2 can replicate and increase population

Viral evolution and genomic and phenotypic characterization: SARS-CoV-2

● Variant 1
● Variant 2

Circulating in a population



E484K, K417N and **Δ69–70** contribute to immune response evasion (still to confirm the impact)

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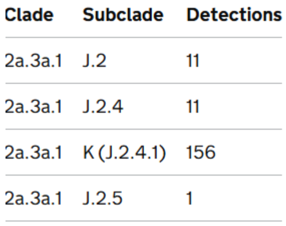

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Viral evolution and genomic and phenotypic characterization: Influenza

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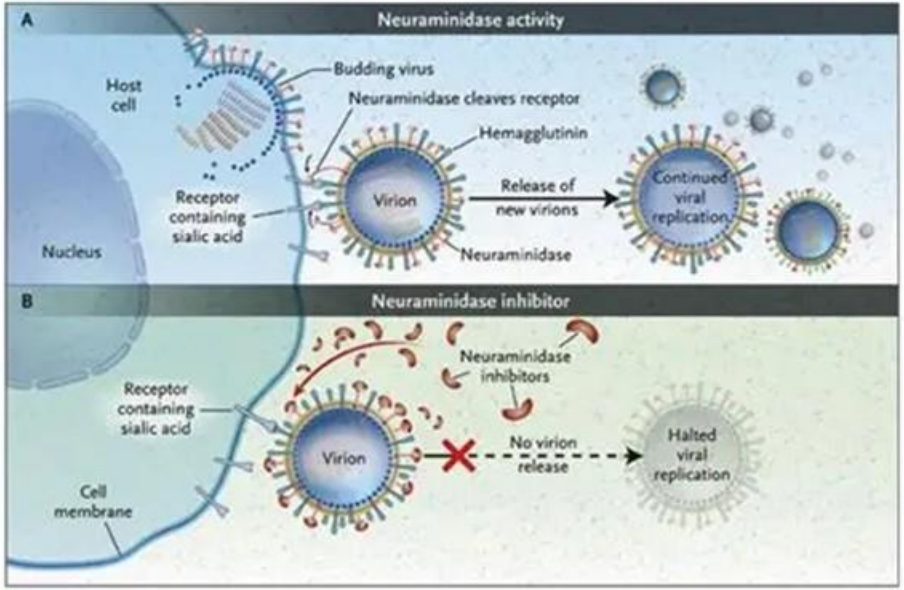

Demonstrates in vitro that the antiviral(neuraminidase inhibitor) works in a particular strain

Viral evolution and genomic and phenotypic characterization

Final remarks:

- Mutations are naturally expected in the virus evolution and adaptation process.
- Although some have demonstrated enhanced capacity to replicate and transmit, they are not necessarily more aggressive or severe.
- The impact on immune response should be assessed: Antigen characterization
- The more the virus is transmitted, the more the chance to generate mutations: More variants are expected to emerge (vaccine selection and evolution pressure)
- Maintain all the public health measures and strengthen the surveillance (epi and genetic)

THANK YOU!