Virtual Training on **Antigen Surveillance: from Evolution to Immune Escape**

SARS-CoV-2 variants: increased fitness and immune evasion

Delphine PLANAS, PhD
March 23rd, 2026

Objectives

- SARS-CoV-2 pathogenesis
- Overview of mRNA-based vaccines and SARS-COV-2 variant emergence
- Distinct evolution of Omicron XBB and BA.2.86/JN.1 lineages
- Future challenges and novel vaccine strategies

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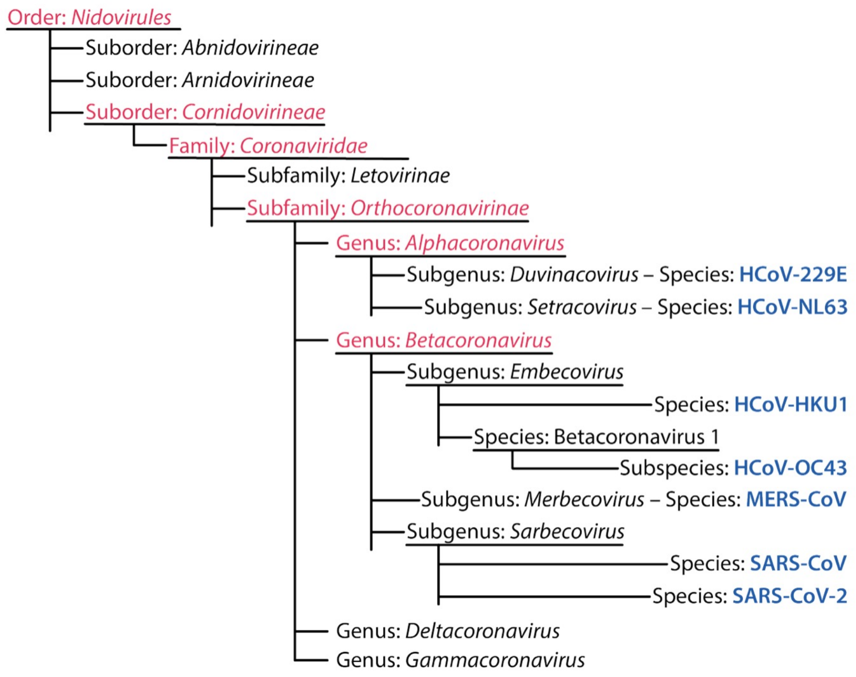
Emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

World Health Organization

Pneumonia of unknown cause – China

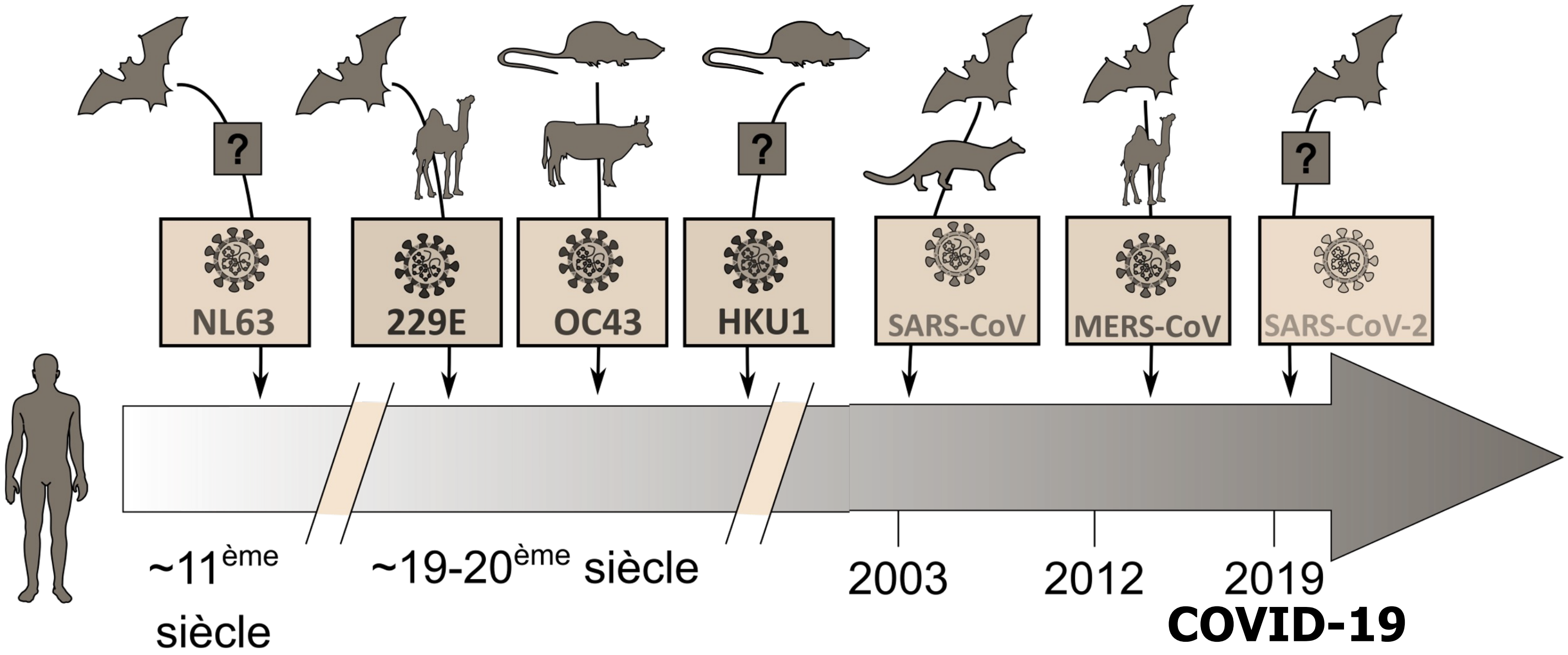
Disease outbreak news
5 January 2020

On 31 December 2019, the WHO China Country Office was informed of cases of pneumonia of unknown etiology (unknown cause) detected in Wuhan City, Hubei Province of China. As of 3 January 2020, a total of 44 patients with pneumonia of unknown etiology have been reported to WHO by the national authorities in China. Of the 44 cases reported, 11 are severely ill, while the remaining 33 patients are in stable condition. According to media reports, the concerned market in Wuhan was closed on 1 January 2020 for environmental sanitation and disinfection.



- Order: *Nidovirules*
  - Suborder: *Abnidovirineae*
  - Suborder: *Arnidovirineae*
  - Suborder: *Cornidovirineae*
    - Family: *Coronaviridae*
      - Subfamily: *Letovirinae*
      - Subfamily: *Orthocoronavirinae*
        - Genus: *Alphacoronavirus*
          - Subgenus: *Duvinacovirus* – Species: **HCoV-229E**
          - Subgenus: *Setracovirus* – Species: **HCoV-NL63**
        - Genus: *Betacoronavirus*
          - Subgenus: *Embecovirus*
            - Species: **HCoV-HKU1**
            - Species: Betacoronavirus 1
              - Subspecies: **HCoV-OC43**
          - Subgenus: *Merbecovirus* – Species: **MERS-CoV**
          - Subgenus: *Sarbecovirus*
            - Species: **SARS-CoV**
            - Species: **SARS-CoV-2**
        - Genus: *Deltacoronavirus*
        - Genus: *Gammacoronavirus*

Epidemic coronaviruses



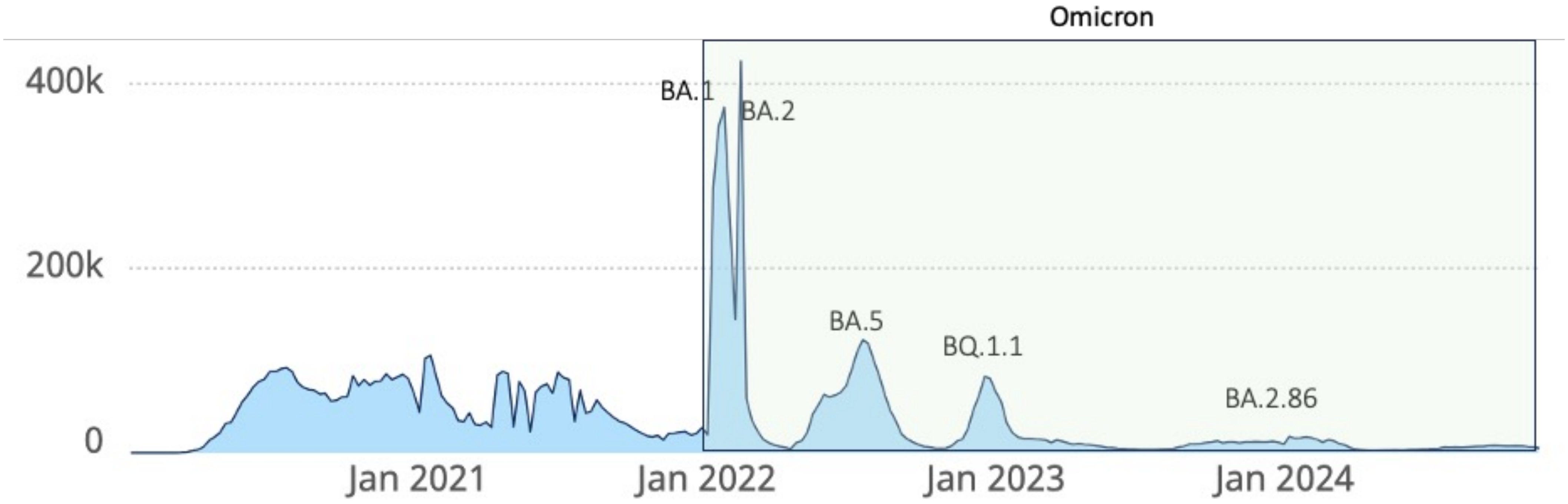
Asymptomatic or mild cold
Rare complications

Asymptomatic, mild or severe cold
Frequent complications > 65

Case fatality ratio:
SARS-CoV: 5-10%
MERS-CoV: 35%
SARS-CoV-2: 0.5-3% before vaccination

Evolution of the COVID-19 pandemic

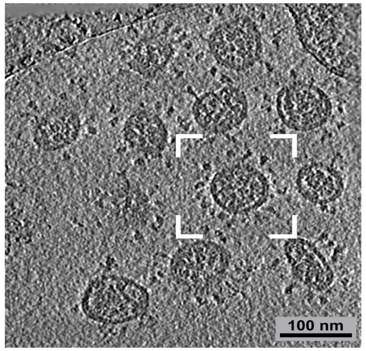
- Over 780 million people have been diagnosed with SARS-CoV-2 infection.
- 7 million deaths have been recorded.



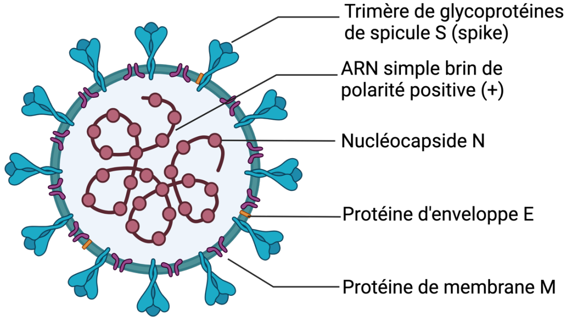
Data source: WHO COVID-19

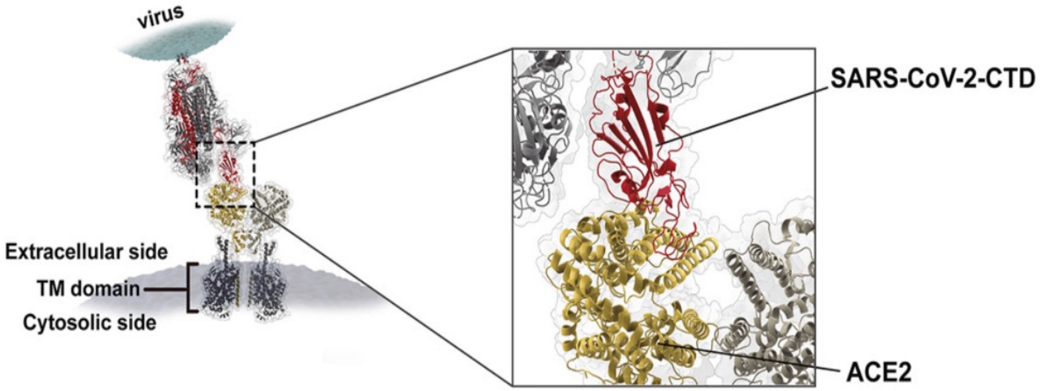
Source: Official data collated by Our World in Data, Johns Hopkins University CSSE COVID-19 Data

SARS-CoV-2 Spike protein binds to ACE2

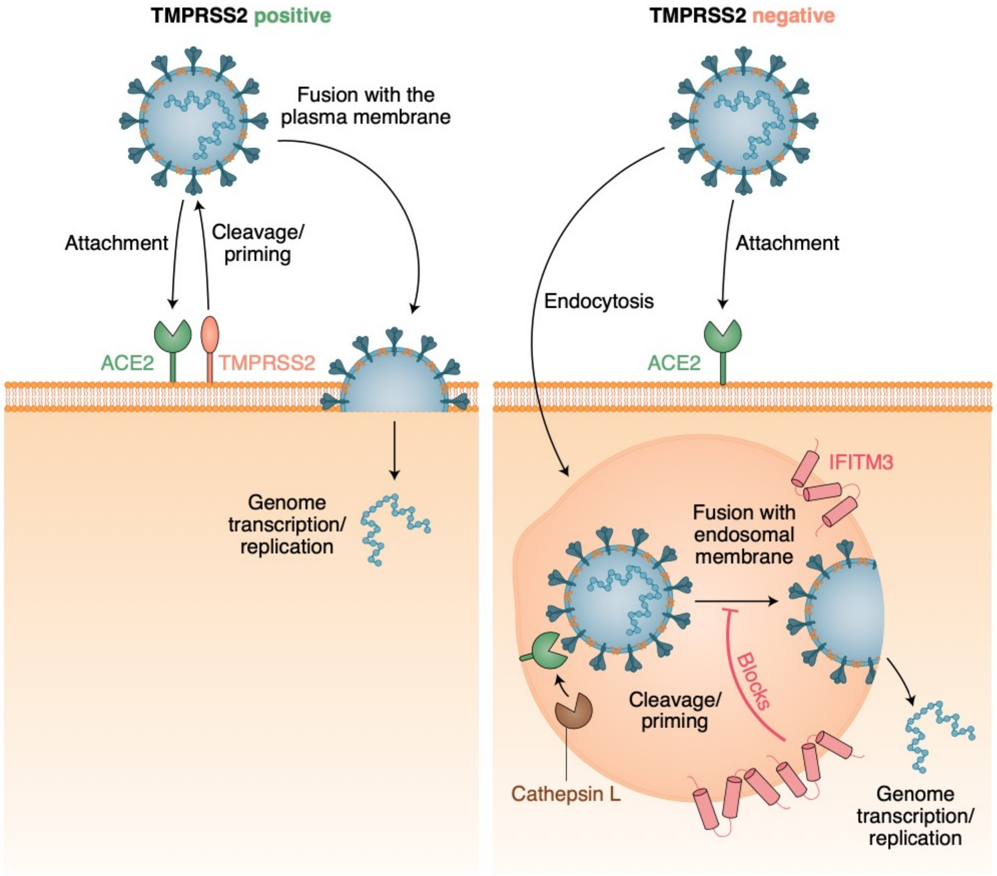


H. Yao *et al.*, 2020



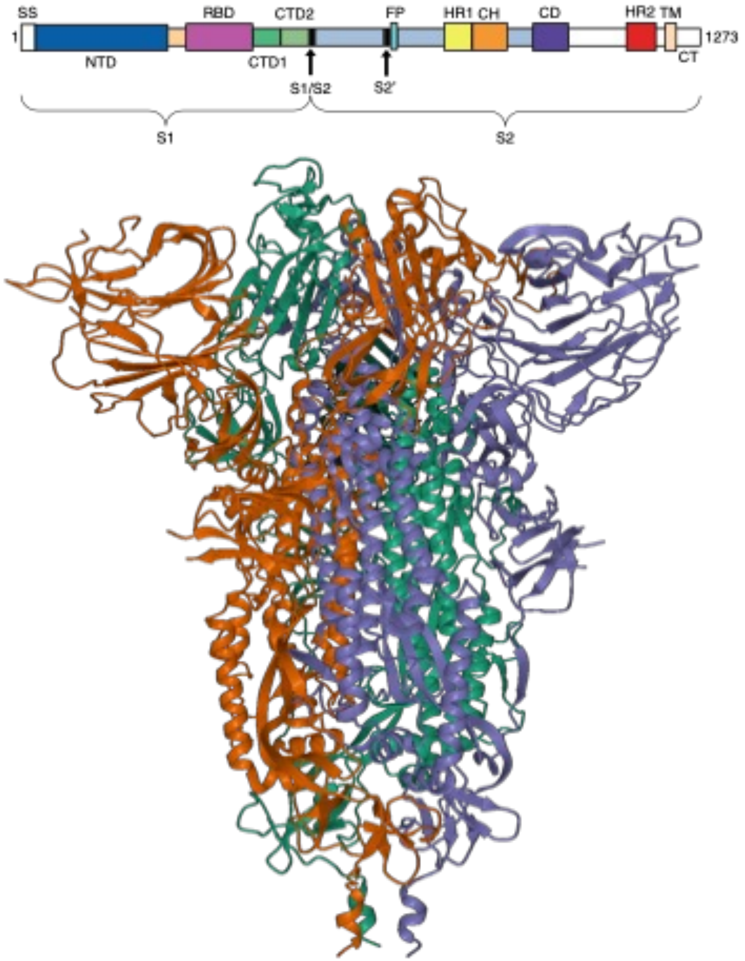


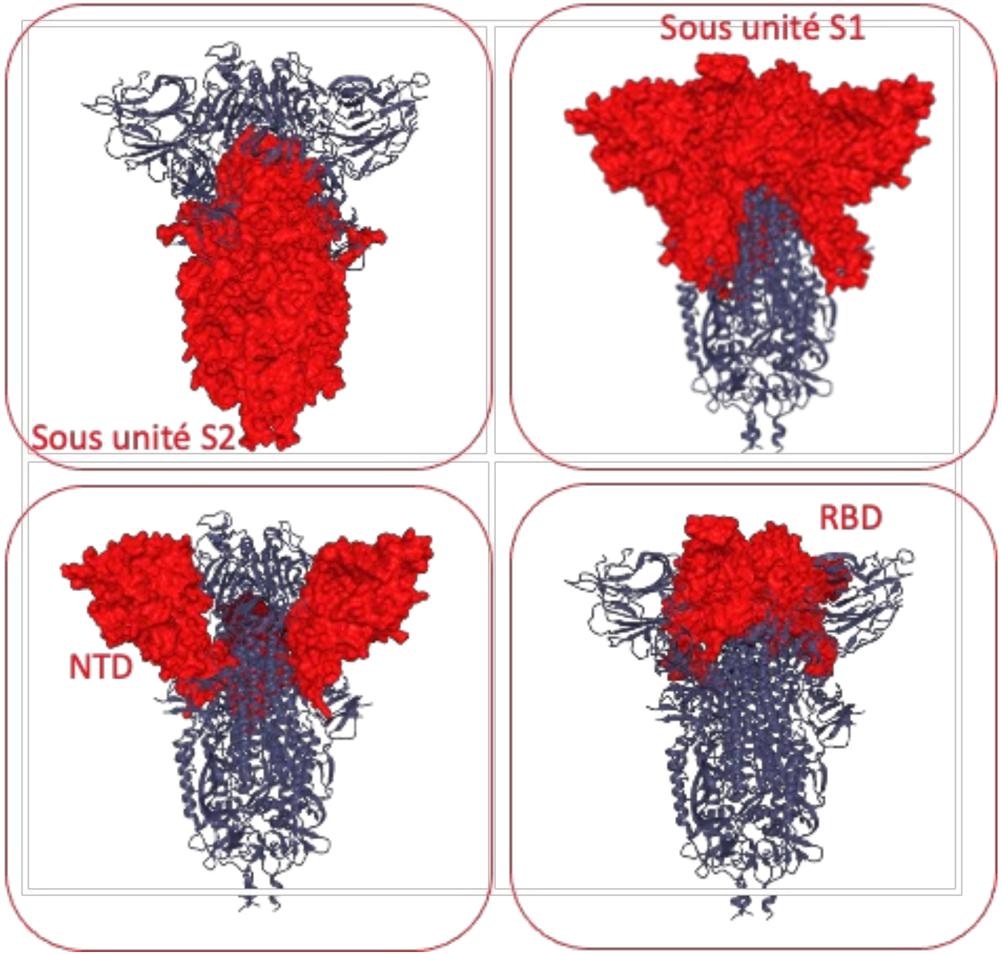
Wang *et al.*, Cell, 2020



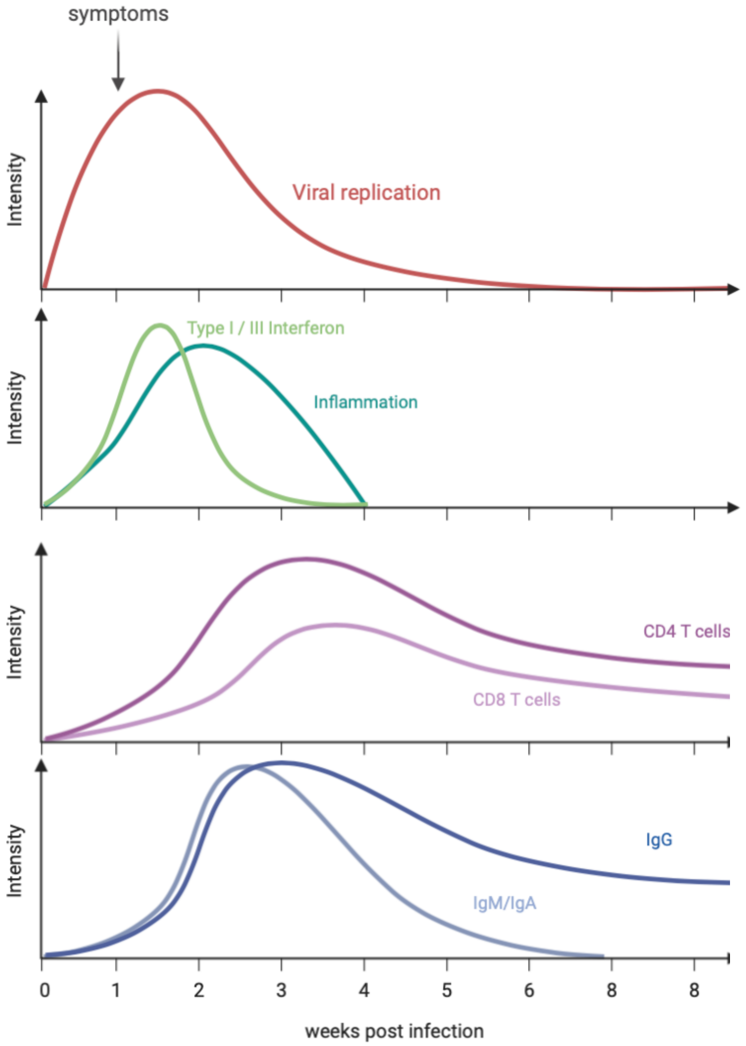
Markus Hoffmann and Stefan Pöhlmann., Nature Microbiology, 2021

SARS-CoV-2 Spike protein





Immune responses during COVID-19



Severe disease

Increased

Decreased

Increased

Increased

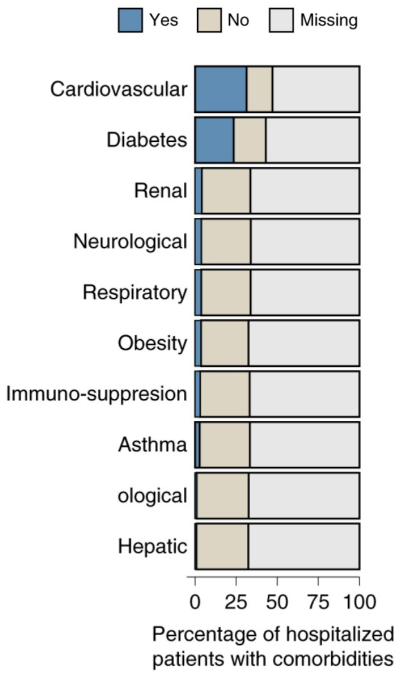
biomarker of infection and protective immunity

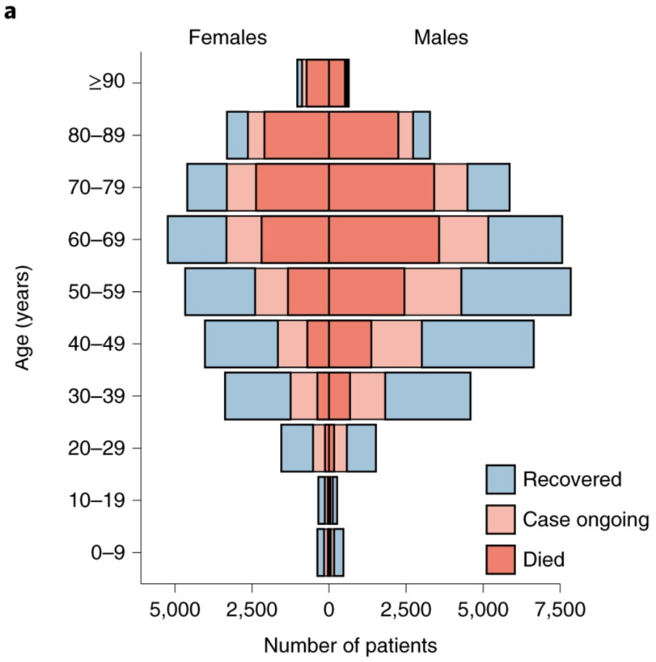
Increased

Adapted from Stephens and McElrath, JAMA, 2020 ; Zhang et al., Science 2020 ; Bastard et al., Science 2020 ; Hadjajd et al., Science 2020 ; Zheng et al., BMJ 2020; Sette and Crotty, Cell, 2021

Clinical features of COVID-19

Factors associated to severe disease

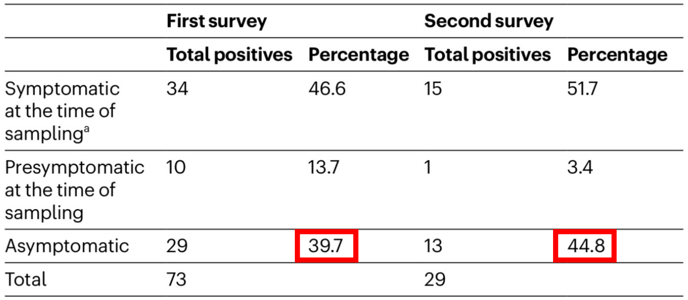




Marciel de Souza, Nat Hum Behav 2020

Asymptomatic infection

In Vo' (Italy), 40% of SARS-CoV-2-infected patients were asymptomatic.



	First survey		Second survey	
	Total positives	**Percentage**	**Total positives**	**Percentage**
Symptomatic at the time of sampling[a]	34	46.6	15	51.7
Presymptomatic at the time of sampling	10	13.7	1	3.4
Asymptomatic	29	39.7	13	44.8
Total	73		29	

Lavezzo et al., Nature, 2020

On the cruise ship *Diamond Princess*, 58% of infected individuals were asymptomatic.

Sakurai et al., NEJM, 2020

Correlates of protection (CoP) against SARS-CoV-2

Definition: A CoP is **an immune marker** that can be used to reliably **predict a vaccine's level of efficacy** in preventing a clinically relevant outcome.

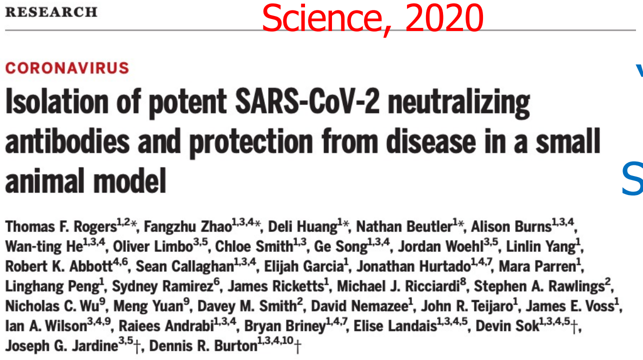
Article

Correlates of protection against SARS-CoV-2 in rhesus macaques

Nature, 2021

https://doi.org/10.1038/s41586-020-03041-6
Received: 5 September 2020
Accepted: 25 November 2020

Katherine McMahan[1,7], Jingyou Yu[1,7], Noe B. Mercado[1,7], Carolin Loos[2,3,7], Lisa H. Tostanoski[1,7], Abishek Chandrashekar[1,7], Jinyan Liu[1,7], Lauren Peter[1,7], Caroline Atyeo[2,4], Alex Zhu[2], Esther A. Bondzie[1], Gabriel Dagotto[1,4], Makda S. Gebre[1,4], Catherine Jacob-Dolan[1,4], Zhenfeng Li[1], Felix Nampanya[1], Shivani Patel[1], Laurent Pessaint[5], Alex Van Ry[5], Kelvin Blade[5], Jake Yalley-Ogunro[5], Mehtap Cabus[5], Renita Brown[5], Anthony Cook[5], Elyse Teow[5], Hanne Andersen[5], Mark G. Lewis[5], Douglas A. Lauffenburger[3], Galit Alter[2,6] & Dan H. Barouch[1,2,4,6] ✉



RESEARCH

Science, 2020

CORONAVIRUS

Isolation of potent SARS-CoV-2 neutralizing antibodies and protection from disease in a small animal model

Thomas F. Rogers[1,2]*, Fangzhu Zhao[1,3,4]*, Deli Huang[1]*, Nathan Beutler[1]*, Alison Burns[1,3,4], Wan-ting He[1,3,4], Oliver Limbo[3,5], Chloe Smith[1,3], Ge Song[1,3,4], Jordan Woehl[3,5], Linlin Yang[1], Robert K. Abbott[4,6], Sean Callaghan[1,3,4], Elijah Garcia[1], Jonathan Hurtado[1,4,7], Mara Parren[1], Linghang Peng[1], Sydney Ramirez[6], James Ricketts[1], Michael J. Ricciardi[8], Stephen A. Rawlings[2], Nicholas C. Wu[9], Meng Yuan[9], Davey M. Smith[2], David Nemazee[1], John R. Teijaro[1], James E. Voss[1], Ian A. Wilson[3,4,9], Raiees Andrabi[1,3,4], Bryan Briney[1,4,7], Elise Landais[1,3,4,5], Devin Sok[1,3,4,5]†, Joseph G. Jardine[3,5]†, Dennis R. Burton[1,3,4,10]†

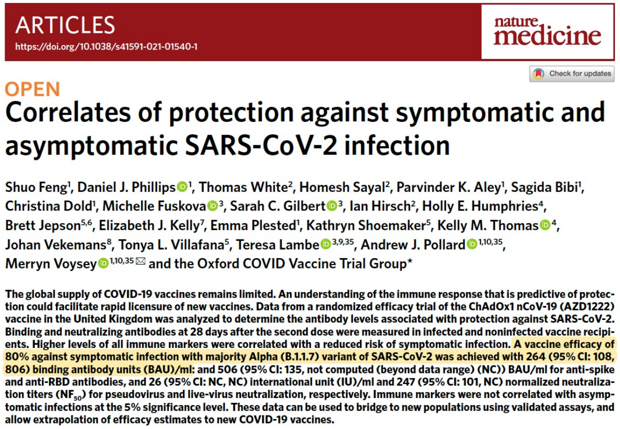
"Passive transfer of neutralizing antibodies can prevent severe SARS-CoV-2 infection in multiple animal models."

2021

nature medicine
ARTICLES
https://doi.org/10.1038/s41591-021-01377-8

Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection

David S. Khoury[1,9], Deborah Cromer[1,9], Arnold Reynaldi[1], Timothy E. Schlub[1,2], Adam K. Wheatley[3], Jennifer A. Juno[3], Kanta Subbarao[3,4], Stephen J. Kent[3,5,6], James A. Triccas[7,8] ✉ and Miles P. Davenport[1] ✉



ARTICLES
https://doi.org/10.1038/s41591-021-01540-1
nature medicine

OPEN

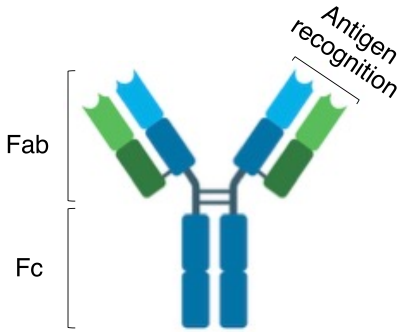
Correlates of protection against symptomatic and asymptomatic SARS-CoV-2 infection

Shuo Feng[1], Daniel J. Phillips[1], Thomas White[2], Homesh Sayal[2], Parvinder K. Aley[1], Sagida Bibi[1], Christina Dold[1], Michelle Fuskova[3], Sarah C. Gilbert[3], Ian Hirsch[2], Holly E. Humphries[4], Brett Jepson[5,6], Elizabeth J. Kelly[7], Emma Plested[1], Kathryn Shoemaker[5], Kelly M. Thomas[4], Johan Vekemans[8], Tonya L. Villafana[5], Teresa Lambe[3,9,35], Andrew J. Pollard[1,10,35], Merryn Voysey[1,10,35] ✉ and the Oxford COVID Vaccine Trial Group*

The global supply of COVID-19 vaccines remains limited. An understanding of the immune response that is predictive of protection could facilitate rapid licensure of new vaccines. Data from a randomized efficacy trial of the ChAdOx1 nCoV-19 (AZD1222) vaccine in the United Kingdom was analyzed to determine the antibody levels associated with protection against SARS-CoV-2. Binding and neutralizing antibodies at 28 days after the second dose were measured in infected and noninfected vaccine recipients. Higher levels of all immune markers were correlated with a reduced risk of symptomatic infection. A vaccine efficacy of 80% against symptomatic infection with majority Alpha (B.1.1.7) variant of SARS-CoV-2 was achieved with 264 (95% CI: 108, 806) binding antibody units (BAU)/ml: and 506 (95% CI: 135, not computed (beyond data range) (NC)) BAU/ml for anti-spike and anti-RBD antibodies, and 26 (95% CI: NC, NC) international unit (IU)/ml and 247 (95% CI: 101, NC) normalized neutralization titers (NF_{50}) for pseudovirus and live-virus neutralization, respectively. Immune markers were not correlated with asymptomatic infections at the 5% significance level. These data can be used to bridge to new populations using validated assays, and allow extrapolation of efficacy estimates to new COVID-19 vaccines.

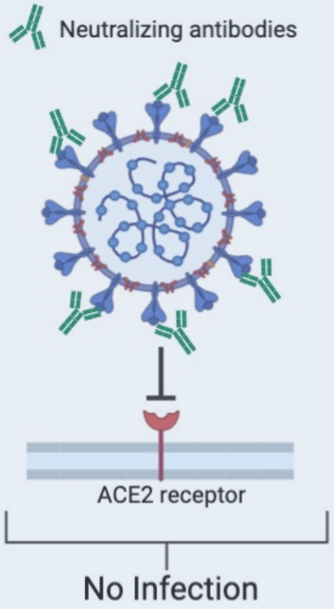
"Neutralizing antibodies levels are highly predictive of immune protection from symptomatic infection."

Immune properties of antibodies



- They often correlate with sterilizing immunity
- Their transfer may provide immune protection
- They are specific and target multiple epitopes

Neutralization

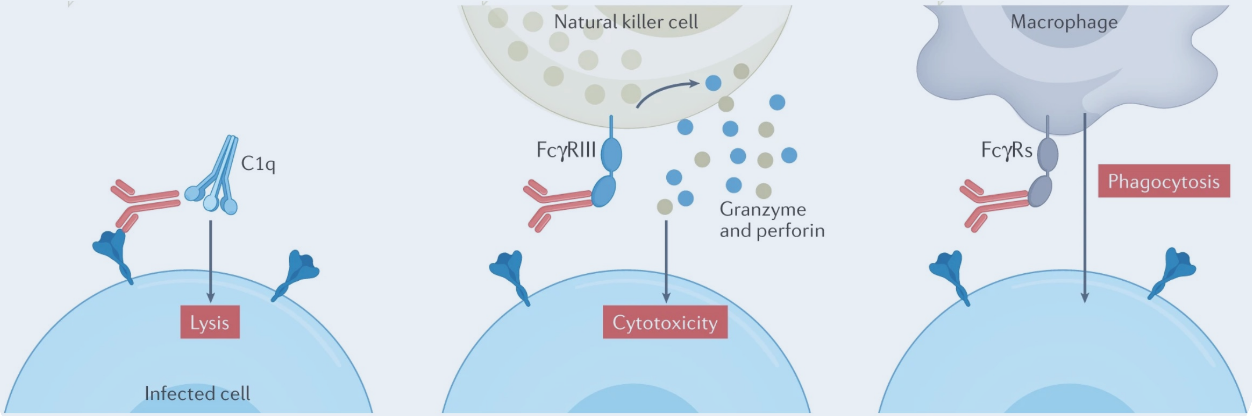


Fc-effector functions

Complement-dependent cytotoxicity

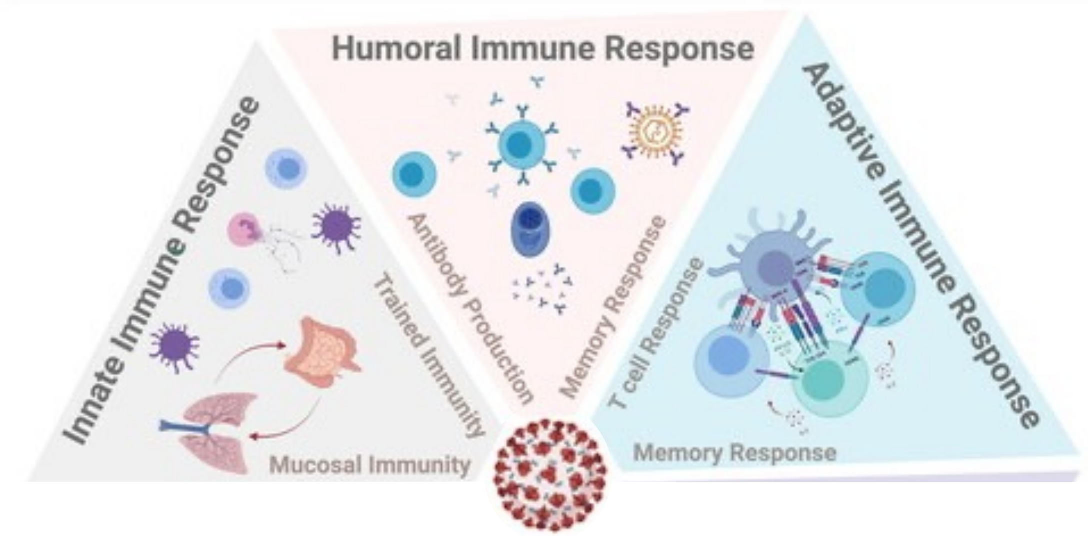
Antibody-dependent cellular cytotoxicity

Antibody-dependent phagocytosis



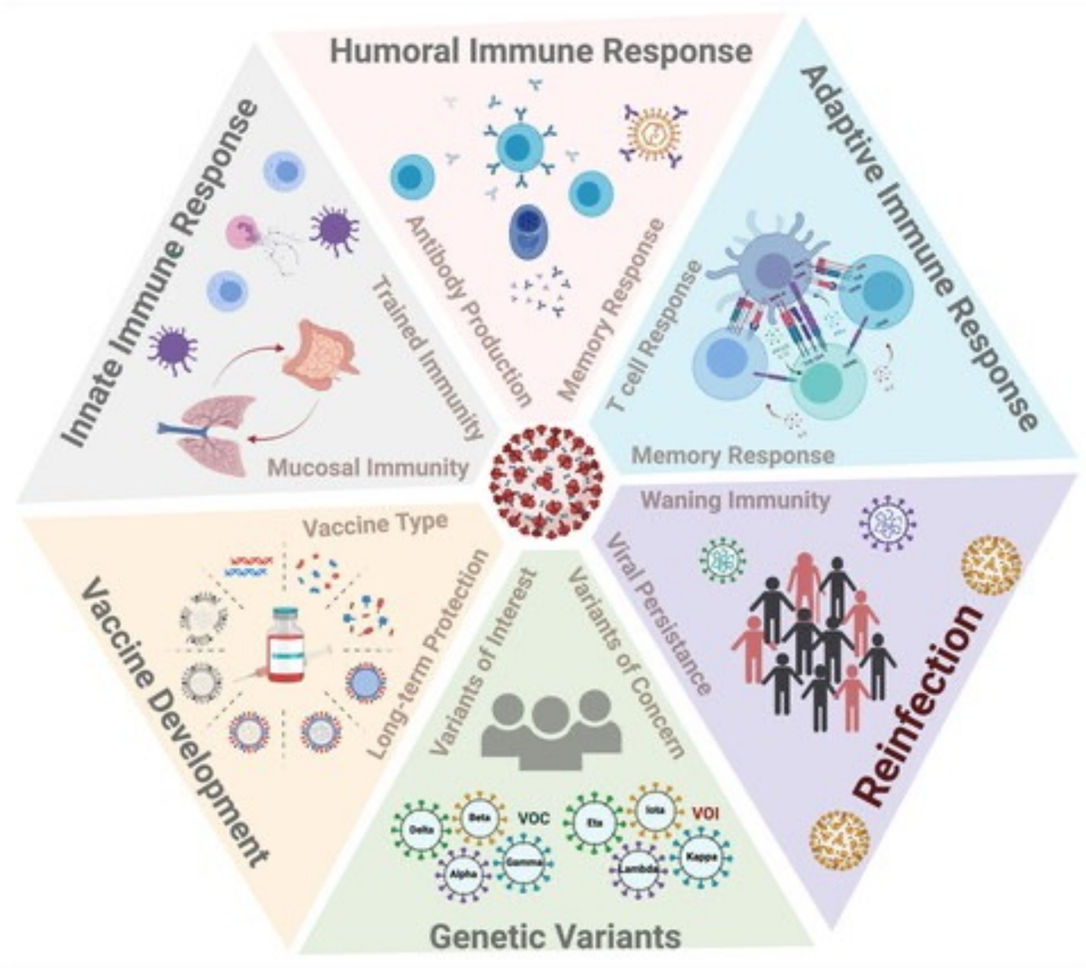
Pantaleo G et al., Nature, 2022

Protection against severe disease



Neema et al., Int Rev Immunol, 2022

Protection against severe disease



Neema et al., Int Rev Immunol, 2022

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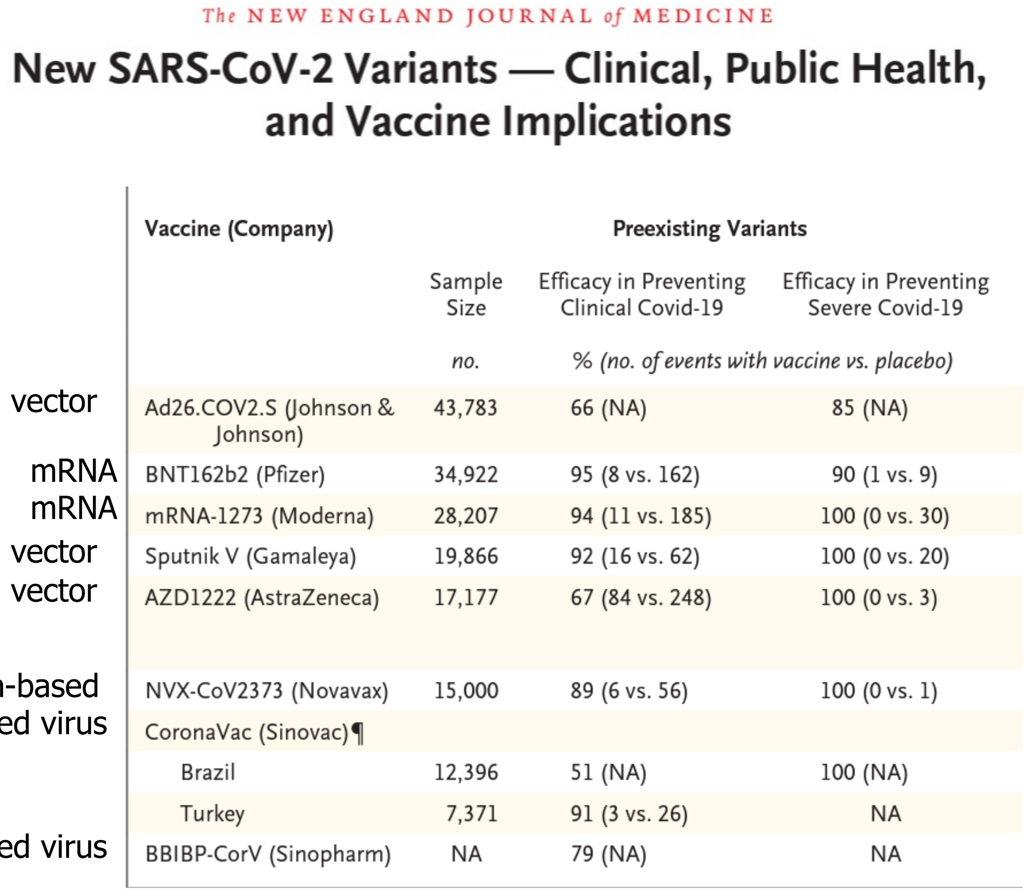
Beginning of 2021: Implementation of COVID-19 Vaccination



The NEW ENGLAND JOURNAL of MEDICINE

New SARS-CoV-2 Variants — Clinical, Public Health, and Vaccine Implications

	Vaccine (Company)	Preexisting Variants		
		Sample Size	Efficacy in Preventing Clinical Covid-19	Efficacy in Preventing Severe Covid-19
		no.	*% (no. of events with vaccine vs. placebo)*	
Viral vector	Ad26.COV2.S (Johnson & Johnson)	43,783	66 (NA)	85 (NA)
mRNA	BNT162b2 (Pfizer)	34,922	95 (8 vs. 162)	90 (1 vs. 9)
mRNA	mRNA-1273 (Moderna)	28,207	94 (11 vs. 185)	100 (0 vs. 30)
Viral vector	Sputnik V (Gamaleya)	19,866	92 (16 vs. 62)	100 (0 vs. 20)
Viral vector	AZD1222 (AstraZeneca)	17,177	67 (84 vs. 248)	100 (0 vs. 3)
Protein-based	NVX-CoV2373 (Novavax)	15,000	89 (6 vs. 56)	100 (0 vs. 1)
Inactivated virus	CoronaVac (Sinovac)¶			
	Brazil	12,396	51 (NA)	100 (NA)
	Turkey	7,371	91 (3 vs. 26)	NA
Inactivated virus	BBIBP-CorV (Sinopharm)	NA	79 (NA)	NA

Salim S Abdool Karim & Tulio de Oliveira, NEJM, 2021

Efficacy of vaccins

Nov 2023

Research

The Royal Society of Medicine

Journal of the Royal Society of Medicine; 0(0) 1–10
DOI: 10.1177/01410768231216332

Temporal changes to adult case fatality risk of COVID-19 after vaccination in England between May 2020 and February 2022: a national surveillance study

Florence Halford, Kathryn Yates, Tom Clare, Jamie Lopez-Bernal, Meaghan Kall and Hester Allen
COVID-19 Vaccines and Epidemiology Division, UK Health Security Agency, London NW9 5EQ, UK
Corresponding author: Hester Allen. Email: hester.allen@ukhsa.gov.uk

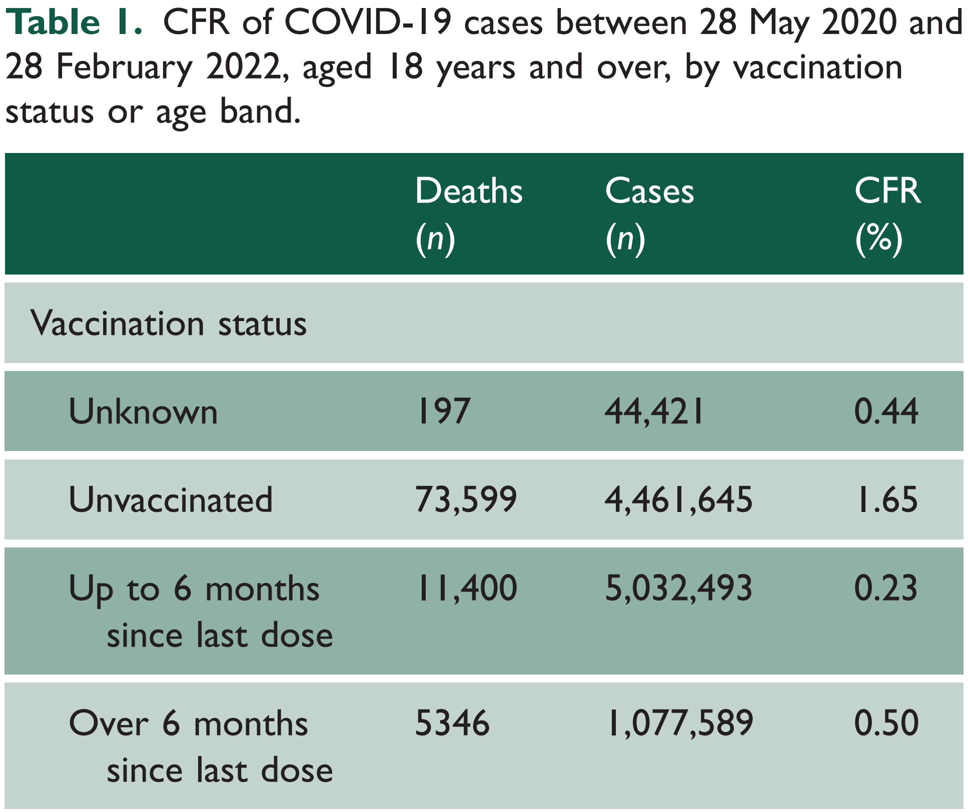
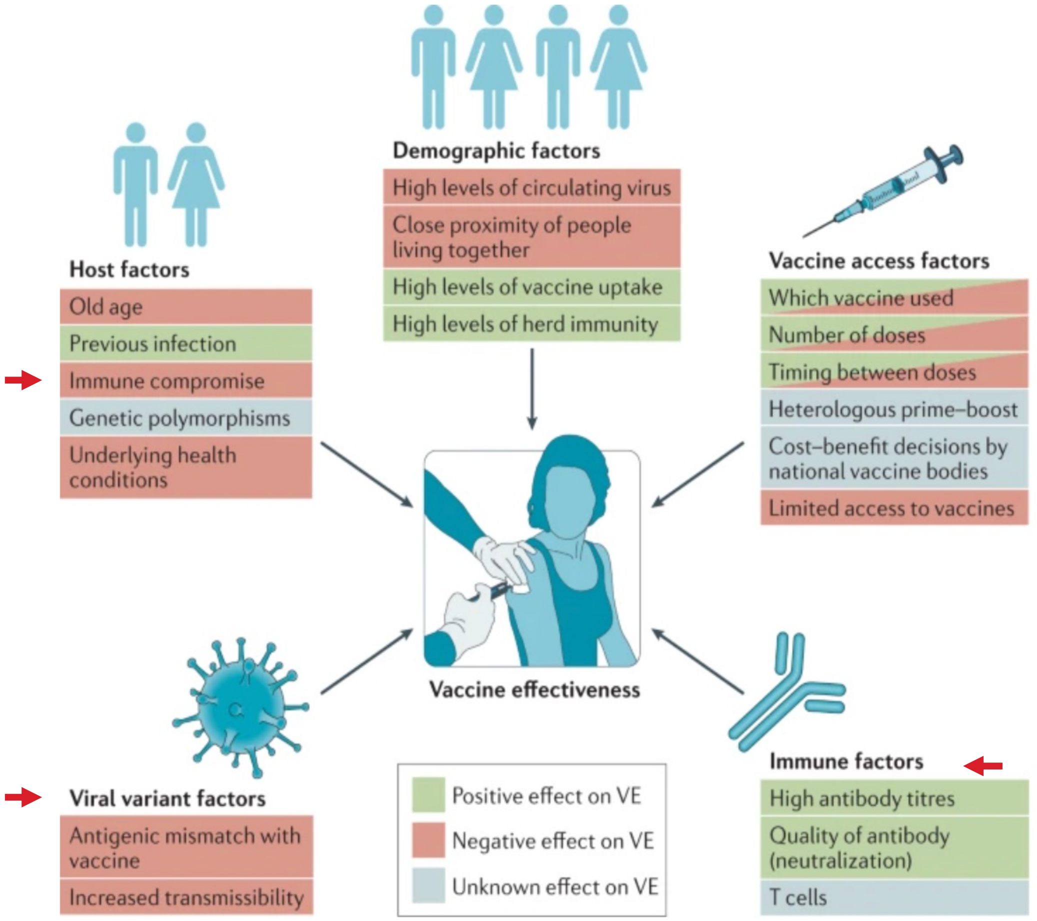


Table 1. CFR of COVID-19 cases between 28 May 2020 and 28 February 2022, aged 18 years and over, by vaccination status or age band.

	Deaths (*n*)	Cases (*n*)	CFR (%)
Vaccination status			
Unknown	197	44,421	0.44
Unvaccinated	73,599	4,461,645	1.65
Up to 6 months since last dose	11,400	5,032,493	0.23
Over 6 months since last dose	5346	1,077,589	0.50

Factors influencing vaccine effectiveness



Demographic factors
- High levels of circulating virus
- Close proximity of people living together
- High levels of vaccine uptake
- High levels of herd immunity

Host factors
- Old age
- Previous infection
- Immune compromise
- Genetic polymorphisms
- Underlying health conditions

Vaccine access factors
- Which vaccine used
- Number of doses
- Timing between doses
- Heterologous prime–boost
- Cost–benefit decisions by national vaccine bodies
- Limited access to vaccines

Vaccine effectiveness

Viral variant factors
- Antigenic mismatch with vaccine
- Increased transmissibility

🟩 Positive effect on VE
🟥 Negative effect on VE
🟦 Unknown effect on VE

Immune factors
- High antibody titres
- Quality of antibody (neutralization)
- T cells

Multiple factors can increase or decrease vaccine effectiveness (VE) at both the individual level and the population level.

John S. Tregoning et al., Nature, 2022

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Emergence of SARS-CoV-2 variants in 2021

Transmission of SARS-CoV-2 Lineage B.1.1.7 in England: Insights from linking epidemiological and genetic data

Erik Volz[1*+], Swapnil Mishra[1*], Meera Chand[4*], Jeffrey C. Barrett[5*], Robert Johnson[1*], Lily Geidelberg[1], Wes R Hinsley[1], Daniel J Laydon[1], Gavin Dabrera[4], Áine O'Toole[3], Roberto Amato[5], Manon Ragonnet-Cronin[1], Ian Harrison[4], Ben Jackson[3], Cristina V. Ariani[5], Olivia Boyd[1], Nicholas J Loman[4,6], John T McCrone[3], Sónia Gonçalves[5], David Jorgensen[1], Richard Myers[4], Verity Hill[3], David K. Jackson[5], Katy Gaythorpe[1], Natalie Groves[4], John Sillitoe[5], Dominic P. Kwiatkowski[5], The COVID-19 Genomics UK (COG-UK) consortium[7], Seth Flaxman[2], Oliver Ratmann[2], Samir Bhatt[1], Susan Hopkins[4], Axel Gandy[2*], Andrew Rambaut[3*], Neil M Ferguson[1*+]

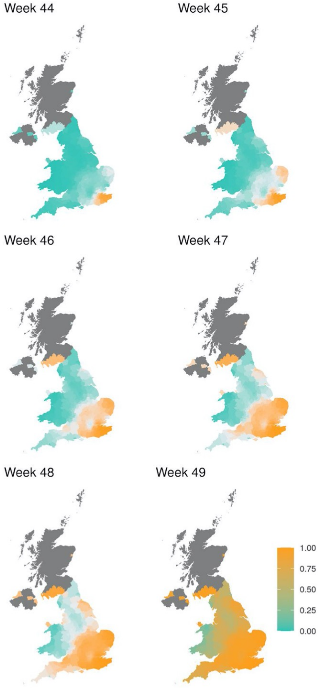
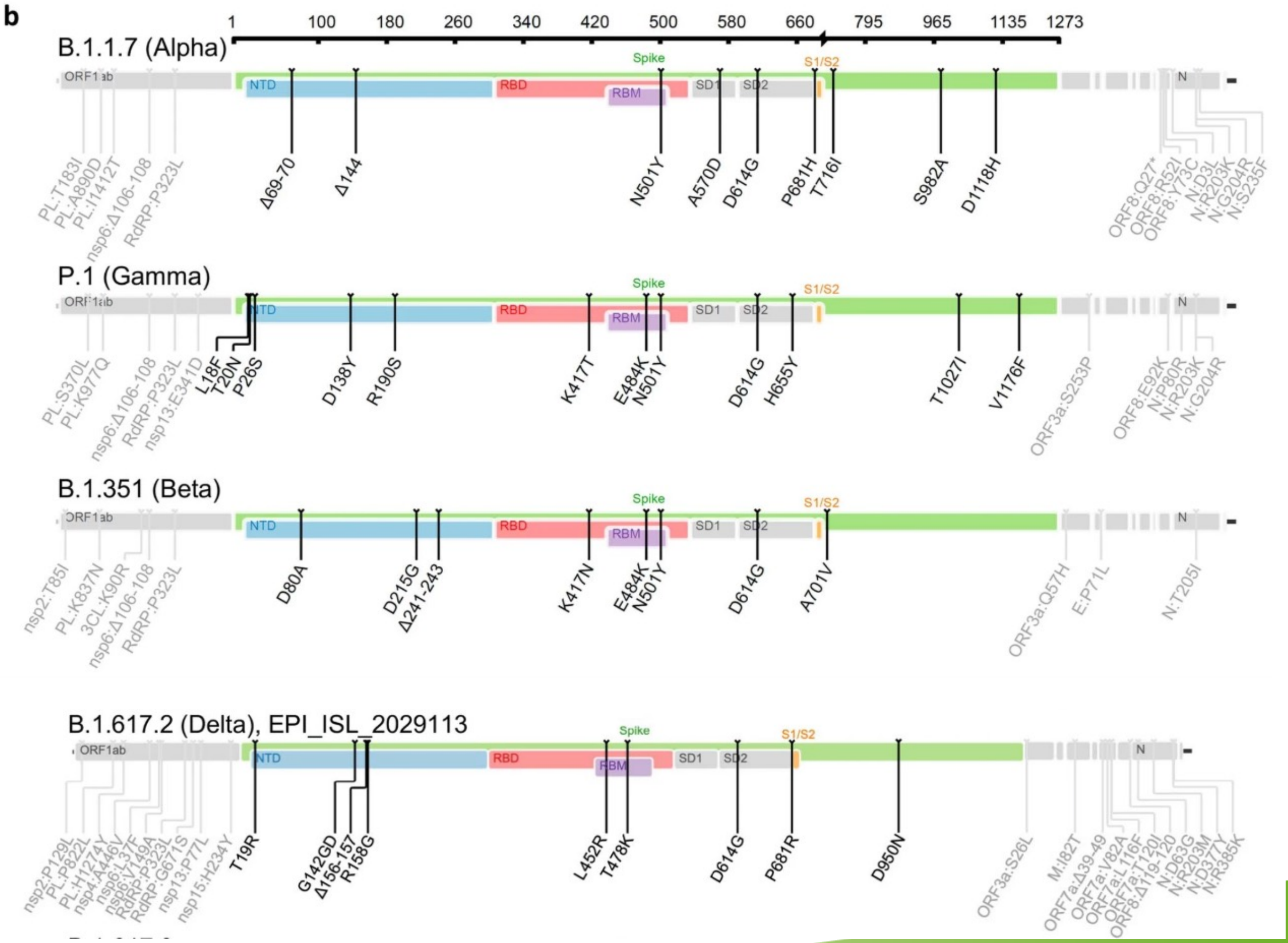
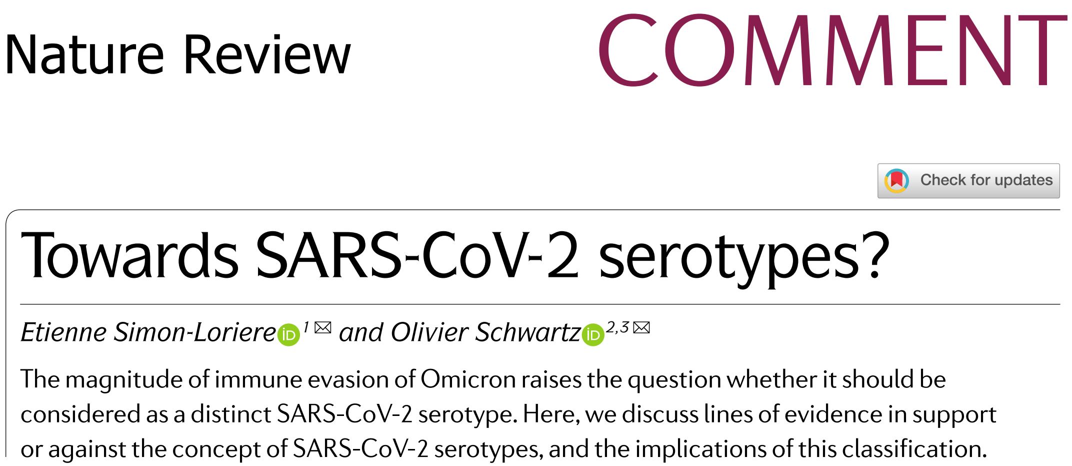


Figure S1 | Estimate of true positive rates for classification of B.1.1.7 infection given SGTF result (S-) as a function of time and UK region. The colour gradient shows the probability of sampling a B.1.1.7 sequence conditional on sampling any sequence with Δ69-70.



Emergence of Omicron variants

Nature Review



COMMENT

Check for updates

Towards SARS-CoV-2 serotypes?

Etienne Simon-Loriere[1] ✉ *and Olivier Schwartz*[2,3] ✉

The magnitude of immune evasion of Omicron raises the question whether it should be considered as a distinct SARS-CoV-2 serotype. Here, we discuss lines of evidence in support or against the concept of SARS-CoV-2 serotypes, and the implications of this classification.

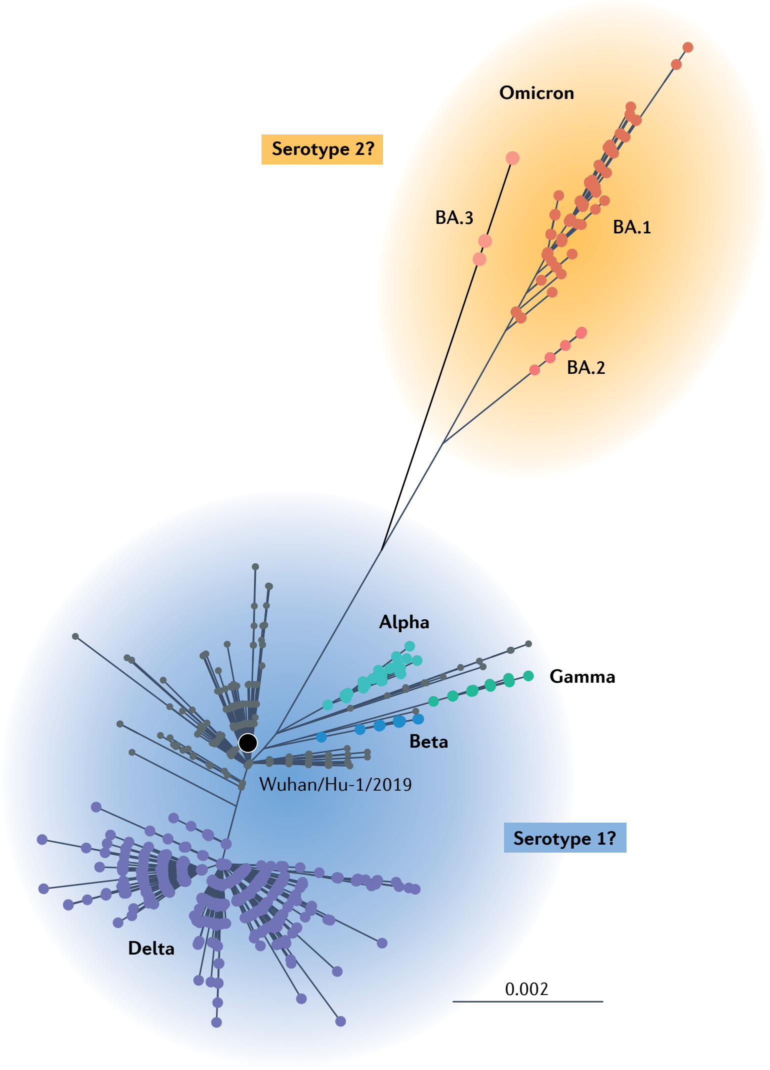
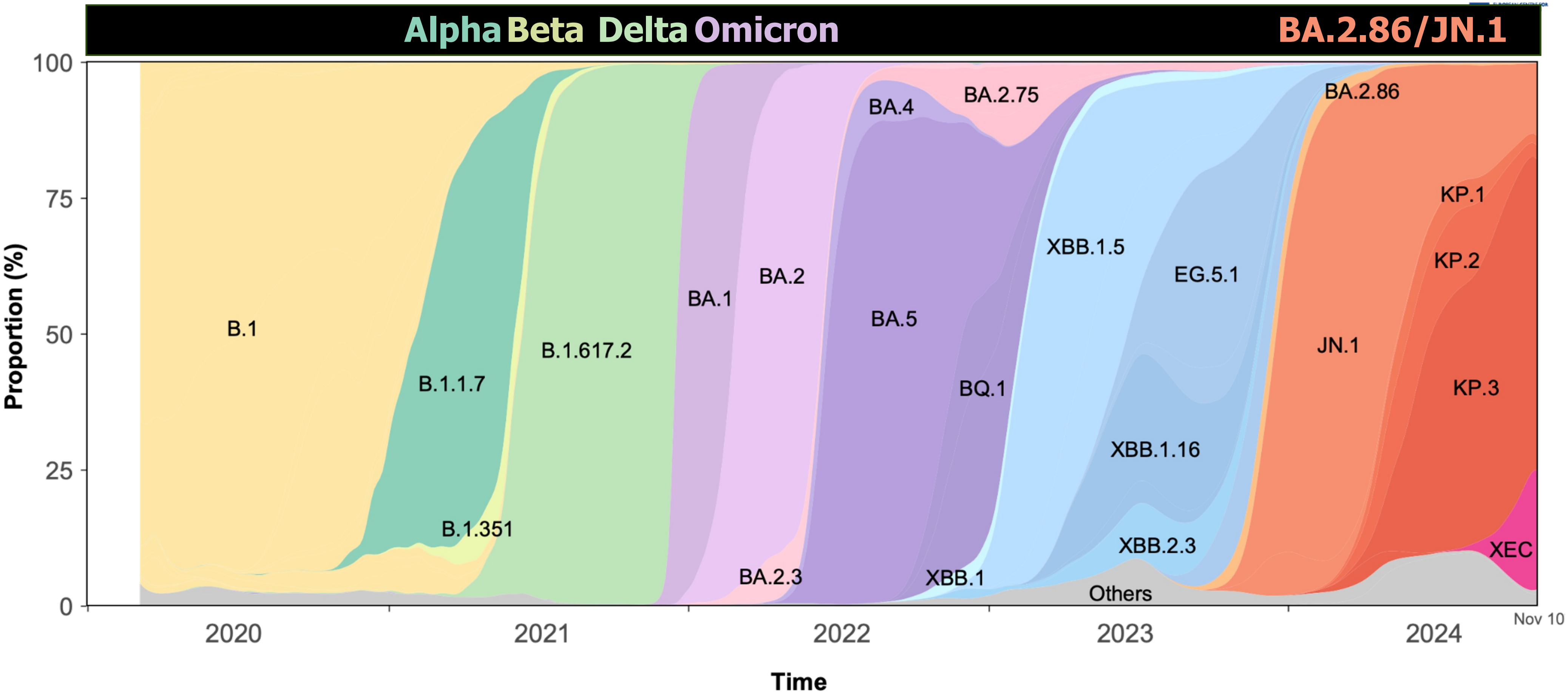


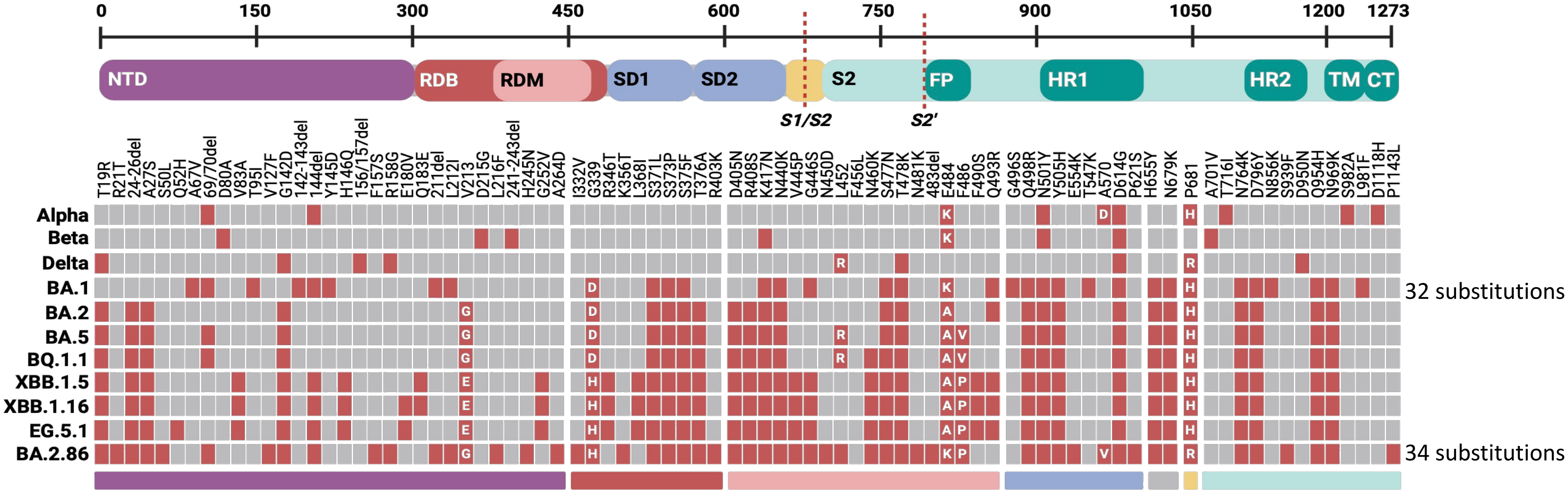
Fig. 1 | **SARS-CoV-2 global evolution and Omicron divergence.** Maximum likelihood phylogenies inferred from spike nucleotide sequences, scale corresponding to number of substitutions per site.

Global transitions in major variants



Planas D et al. Nature Commun, 2024

Evolutionary jump



	T19R	R21T	24-26del	A27S	S50L	Q52H	A67V	69/70del	D80A	V83A	T95I	V127F	G142D	142-143del	144del	Y145D
Alpha								🟥							🟥	
Beta									🟥							
Delta	🟥												🟥			
BA.1							🟥	🟥			🟥			🟥	🟥	🟥
BA.2	🟥		🟥	🟥									🟥			
BA.5	🟥		🟥	🟥				🟥					🟥			
BQ.1.1	🟥		🟥	🟥				🟥					🟥			
XBB.1.5	🟥		🟥	🟥						🟥			🟥		🟥	
XBB.1.16	🟥		🟥	🟥						🟥			🟥		🟥	
EG.5.1	🟥		🟥	🟥		🟥				🟥			🟥		🟥	
BA.2.86	🟥	🟥	🟥	🟥	🟥			🟥				🟥	🟥		🟥	

	H146Q	156/157del	F157S	R158G	E180V	Q183E	211del	L212I	V213	D215G	L216F	241-243del	H245N	G252V	A264D
Alpha															
Beta										🟥		🟥			
Delta		🟥		🟥											
BA.1							🟥	🟥							
BA.2									G						
BA.5									G						
BQ.1.1									G						
XBB.1.5	🟥					🟥			E					🟥	
XBB.1.16	🟥				🟥	🟥			E					🟥	
EG.5.1	🟥				🟥				E					🟥	
BA.2.86			🟥	🟥			🟥	🟥	G		🟥		🟥		🟥

	I332V	G339	R346T	K356T	L368I	S371L	S373P	S375F	T376A	R403K
Alpha										
Beta										
Delta										
BA.1		D				🟥	🟥	🟥		
BA.2		D				🟥	🟥	🟥	🟥	
BA.5		D				🟥	🟥	🟥	🟥	
BQ.1.1		D				🟥	🟥	🟥	🟥	
XBB.1.5		H	🟥		🟥	🟥	🟥	🟥	🟥	
XBB.1.16		H	🟥		🟥	🟥	🟥	🟥	🟥	
EG.5.1		H	🟥		🟥	🟥	🟥	🟥	🟥	
BA.2.86	🟥	H		🟥		🟥	🟥	🟥	🟥	🟥

	D405N	R408S	K417N	N440K	V445P	G446S	N450D	L452	F456L
Alpha									
Beta			🟥						
Delta								R	
BA.1			🟥	🟥		🟥			
BA.2	🟥	🟥	🟥	🟥					
BA.5	🟥	🟥	🟥	🟥				R	
BQ.1.1	🟥	🟥	🟥	🟥				R	
XBB.1.5	🟥	🟥	🟥	🟥	🟥	🟥			
XBB.1.16	🟥	🟥	🟥	🟥	🟥	🟥			
EG.5.1	🟥	🟥	🟥	🟥	🟥	🟥			
BA.2.86	🟥	🟥	🟥	🟥	🟥	🟥	🟥	🟥	

	N460K	S477N	T478K	N481K	483del	E484	F486	F490S	Q493R
Alpha						K			
Beta						K			
Delta			🟥						
BA.1		🟥	🟥			K			🟥
BA.2		🟥	🟥			A			🟥
BA.5		🟥	🟥			A	V		
BQ.1.1	🟥	🟥	🟥			A	V		
XBB.1.5	🟥	🟥	🟥			A	P	🟥	🟥
XBB.1.16	🟥	🟥	🟥			A	P	🟥	🟥
EG.5.1	🟥	🟥	🟥			A	P	🟥	🟥
BA.2.86	🟥	🟥	🟥	🟥	🟥	K	P		

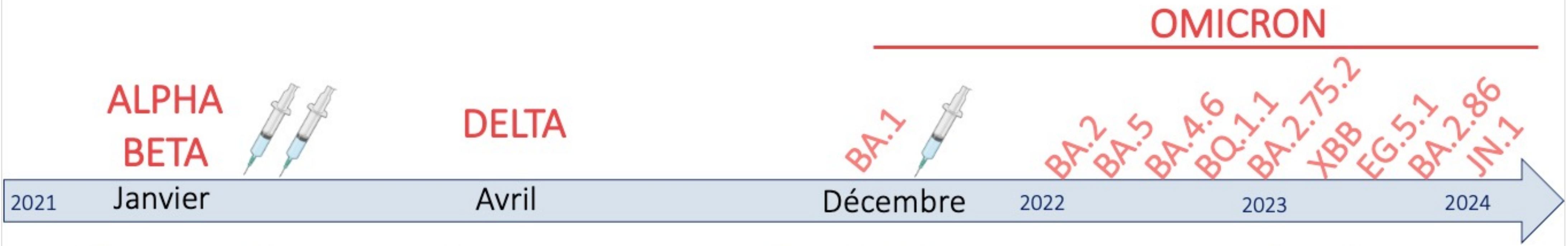
	G496S	Q498R	N501Y	Y505H	E554K	T547K	A570	D614G	P621S	H655Y	N679K	P681
Alpha			🟥				D	🟥				H
Beta			🟥					🟥				
Delta								🟥				R
BA.1	🟥	🟥	🟥	🟥		🟥		🟥		🟥	🟥	H
BA.2		🟥	🟥	🟥				🟥		🟥	🟥	H
BA.5		🟥	🟥	🟥				🟥		🟥	🟥	H
BQ.1.1		🟥	🟥	🟥				🟥		🟥	🟥	H
XBB.1.5		🟥	🟥	🟥				🟥		🟥	🟥	H
XBB.1.16		🟥	🟥	🟥				🟥		🟥	🟥	H
EG.5.1		🟥	🟥	🟥				🟥		🟥	🟥	H
BA.2.86		🟥	🟥	🟥	🟥		V	🟥	🟥	🟥	🟥	R

	A701V	T716I	N764K	D796Y	N856K	S939F	D950N	Q954H	N969K	S982A	L981F	D1118H	P1143L	
Alpha		🟥								🟥		🟥		
Beta	🟥													
Delta							🟥							
BA.1			🟥	🟥	🟥			🟥	🟥		🟥			32 substitutions
BA.2			🟥	🟥				🟥	🟥					
BA.5			🟥	🟥				🟥	🟥					
BQ.1.1			🟥	🟥				🟥	🟥					
XBB.1.5			🟥	🟥				🟥	🟥					
XBB.1.16			🟥	🟥				🟥	🟥					
EG.5.1			🟥	🟥				🟥	🟥					
BA.2.86			🟥	🟥		🟥		🟥	🟥				🟥	34 substitutions

Mutations can effect different properties of the Spike:

- Binding affinity to the receptor ACE2.
- Spike fusogenicity – S1/S2 cleavage, conformational changes, receptor affinity.
- Evasion from the immune system e.g. neutralizing antibodies from previous infections or vaccina

“Real-time” evaluation of SARS-CoV-2 antibody evasion



Need for a second dose against Alpha and Beta

Collier DA. et al., Nature, 2021
Graham C. et al., Immunity, 2021
Muik, A. et al., Science, 2021
Wang, P. et al., Nature, 2021
Xie, X. et al., Nat. Med., 2021
Planas D. et al., Nature Med, 2021

Need to vaccinate convalescent individuals

Edara, V.-V. et al. NEJM, 2021
Liu, J. et al., Nature, 2021
Wall EC., The Lancet, 2021
Saito A et al., Nautre, 2021
Planas D. *et al.*, Nature, 2021

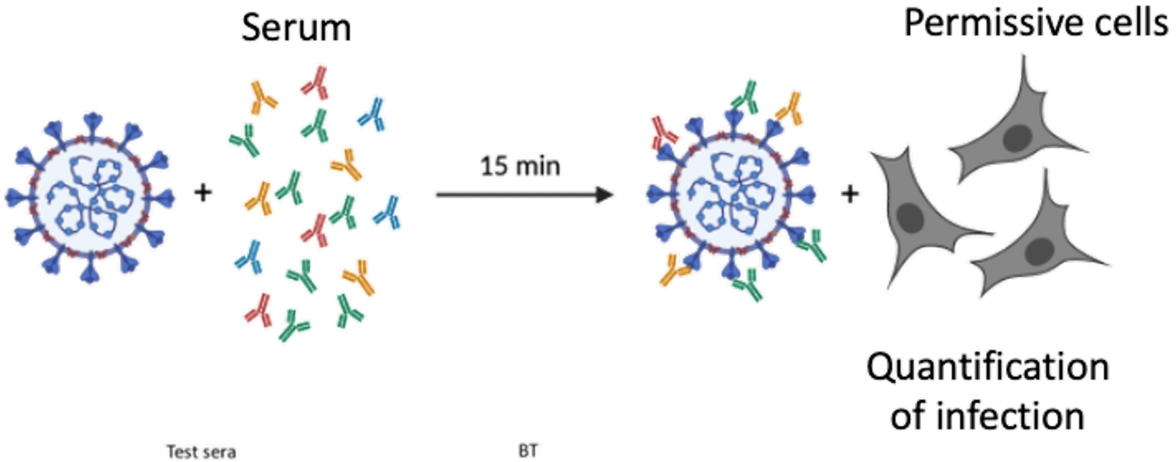
Need for a third dose against Omicron

Cao Y. et al., Nature , 2022
Cele et al., Nature, 2022
Hoffmaan M. et al., Cell, 2022
Dejnirattisai W. et al., Cell, 2022
Planas D. *et al.*, Nature, 2022

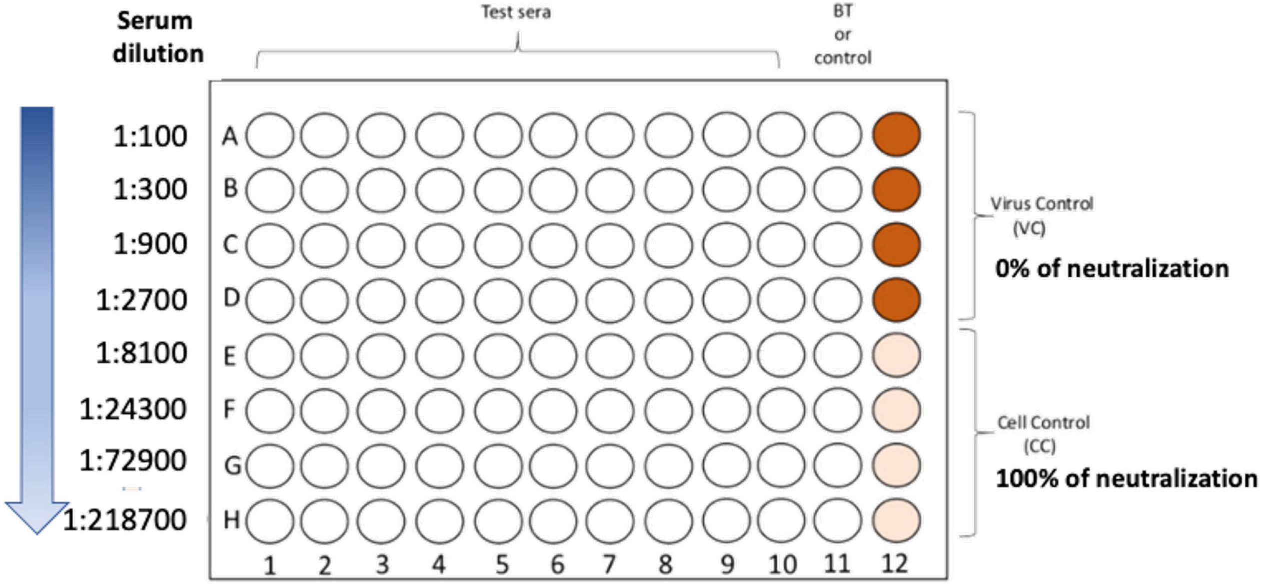
Escape from therapeutic monoclonal antibodies

Adaptation of vaccines to circulating variants

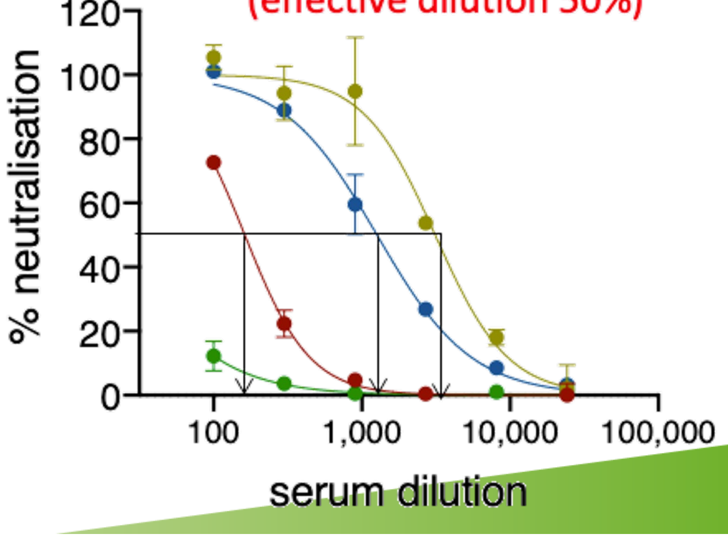
Principle of neutralization assay



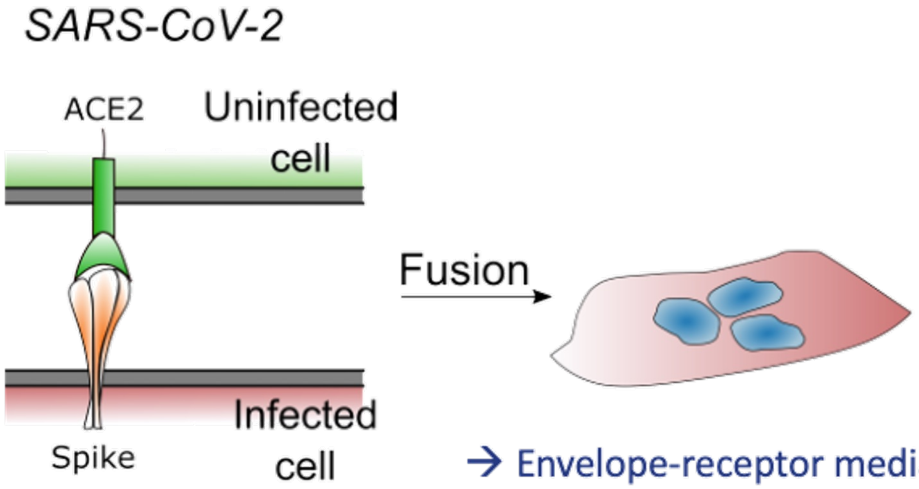
Cytopathic effect
Detection of viral protein
Detection of viral RNA
Reporter system (pseudotype)



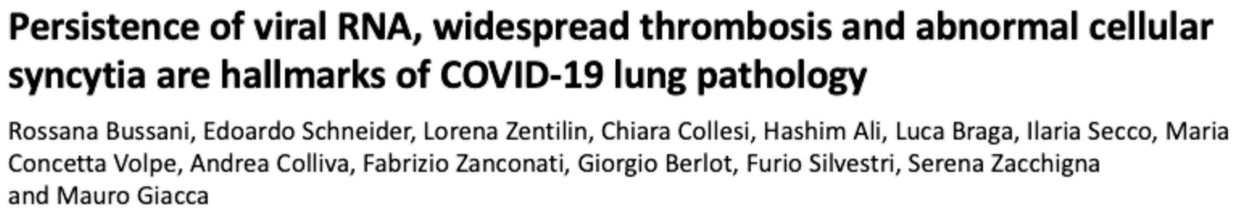
Calculation of ED50
(effective dilution 50%)



Syncytia formation in COVID-19 patients

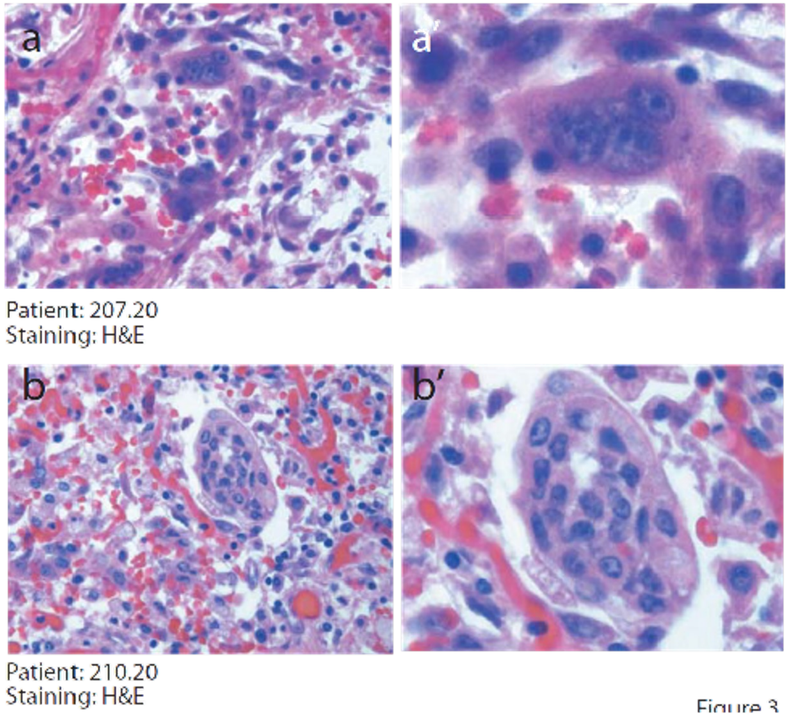


→ Envelope-receptor mediated fusion


Persistence of viral RNA, widespread thrombosis and abnormal cellular syncytia are hallmarks of COVID-19 lung pathology

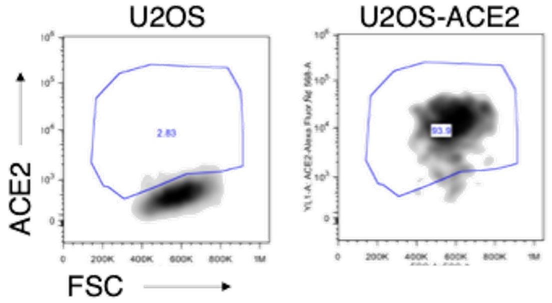
Rossana Bussani, Edoardo Schneider, Lorena Zentilin, Chiara Collesi, Hashim Ali, Luca Braga, Ilaria Secco, Maria Concetta Volpe, Andrea Colliva, Fabrizio Zanconati, Giorgio Berlot, Furio Silvestri, Serena Zacchigna and Mauro Giacca

- **Infected pneumocyte syncytia**
  - *Large number:* 20/41 (49%) patients
  - *Occasional:* 16/41 (39%) patients

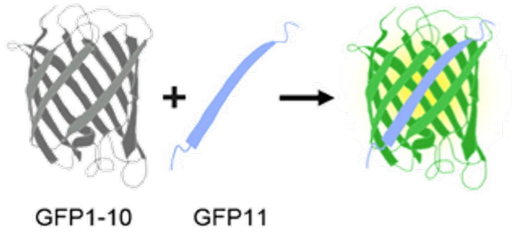


Bussani et al. EBioMedicine, 2020
Braga et al. Nature, 2021

Cell reporter system of SARS-CoV-2 infection



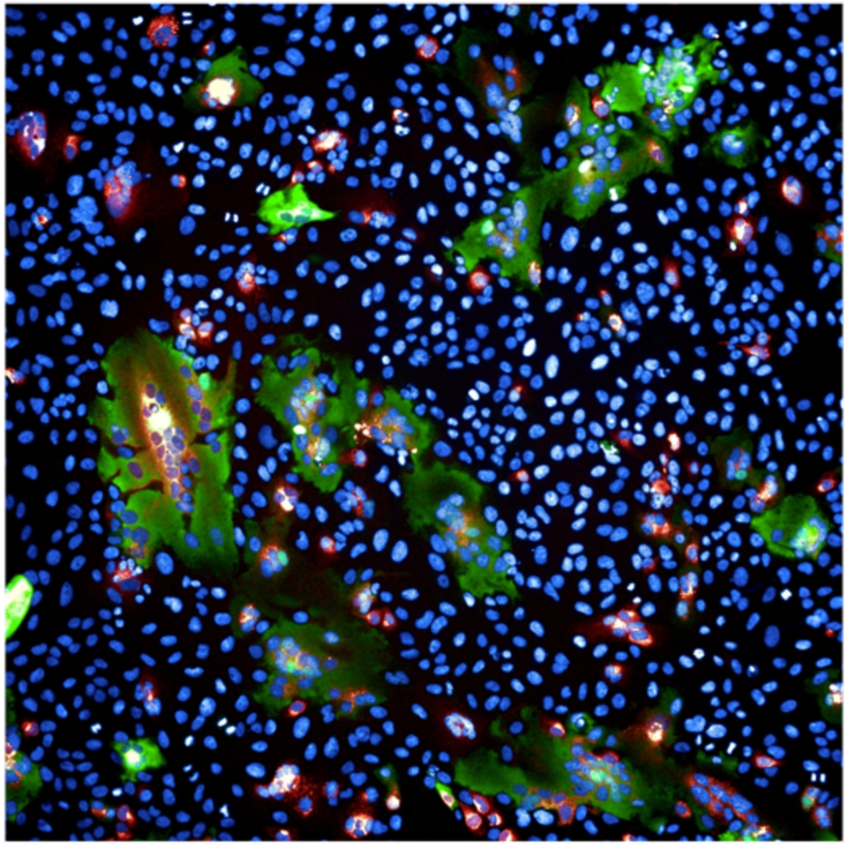
GFP split system



S-Fuse cells:

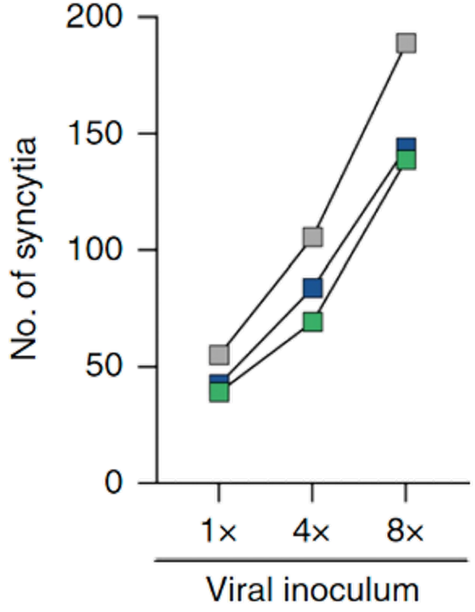
U2OS – ACE2 – GFP1-10
+
U2OS – ACE2 – GFP11

MOI 0.2 24h post-infection



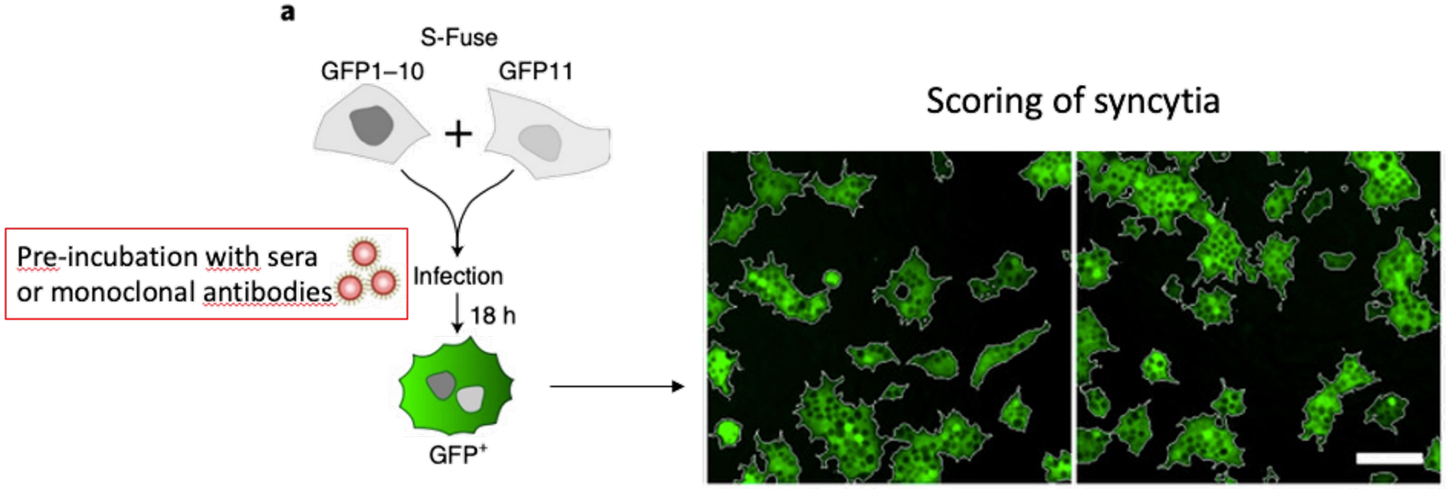
GFPSplit SARS-CoV-S DAPI

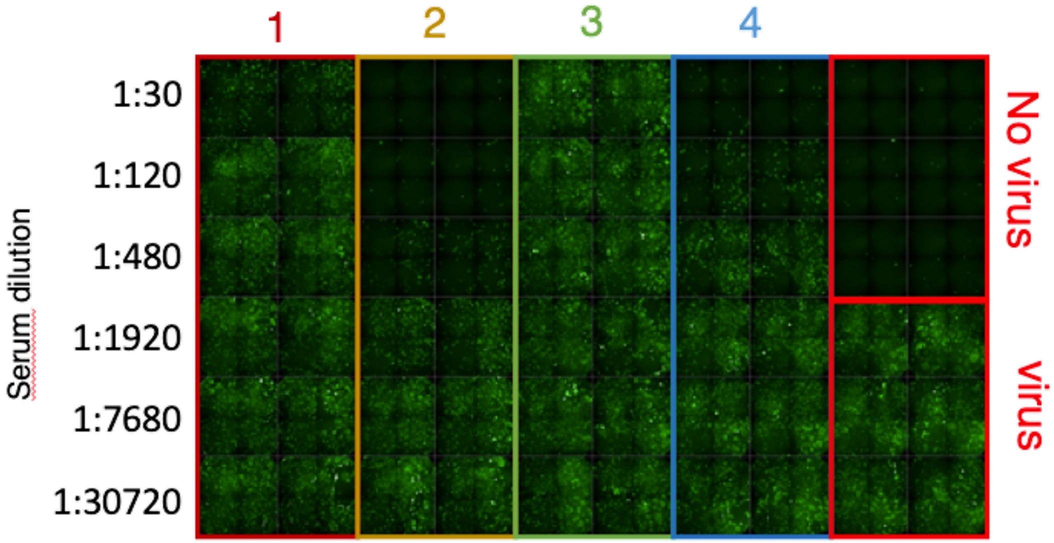
Buchrieser J et al., EMBO, 2021

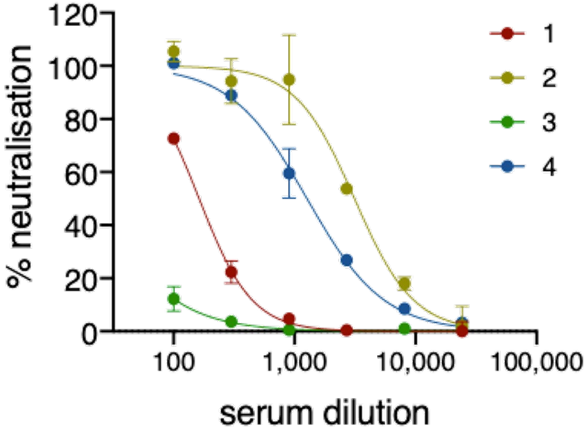


Planas D et al., Nature Med, 2021

S-Fuse neutralizing assay



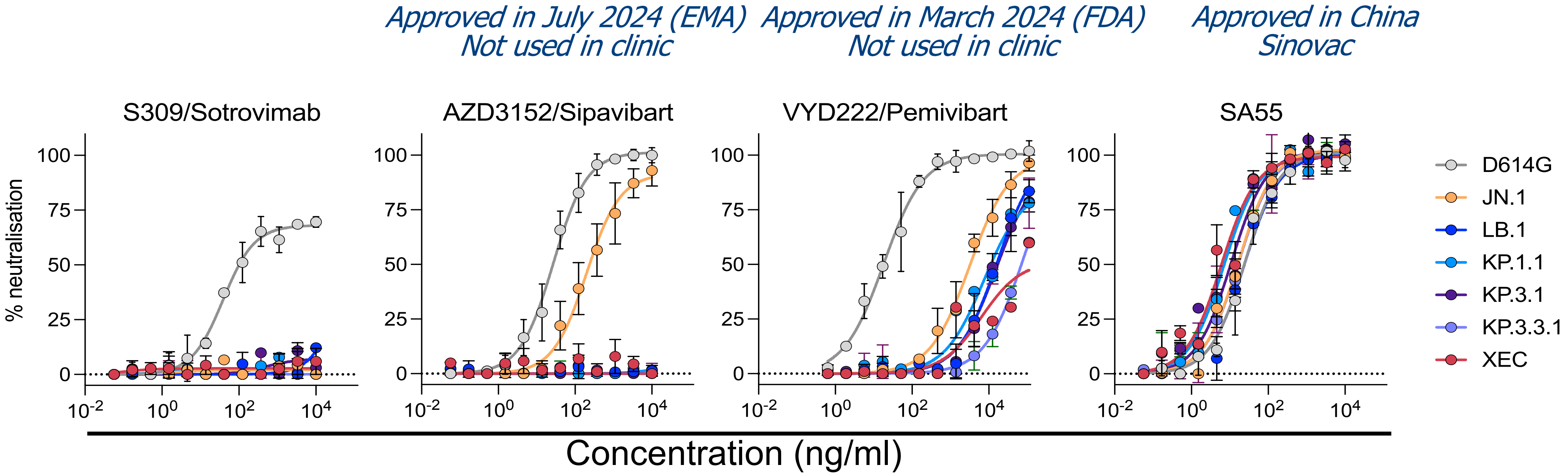




Advantages:
Live-virus
GFP is read 18hours
post-infection
No staining is necessary

Disadvantages:
BSL3 laboratory

Escape of JN.1 subvariants including XEC to recently approved mAb



Planas D *et al., Pathogens and Immunity*, 2024

Objectives

- SARS-CoV-2 pathogenesis
- Overview of mRNA-based vaccines and SARS-COV-2 variant emergence
- **Distinct evolution of Omicron XBB and BA.2.86/JN.1 lineages**
- Future challenges and novel vaccine strategies

Article | Open access | Published: 13 March 2024

Distinct evolution of SARS-CoV-2 Omicron XBB and BA.2.86/JN.1 lineages combining increased fitness and antibody evasion

Delphine Planas, Isabelle Staropoli, Vincent Michel, Frederic Lemoine, Flora Donati, Matthieu Prot, Francoise Porrot, Florence Guivel-Benhassine, Banujaa Jeyarajah, Angela Brisebarre, Océane Dehan, Léa Avon, William Henry Bolland, Mathieu Hubert, Julian Buchrieser, Thibault Vanhoucke, Pierre Rosenbaum, David Veyer, Hélène Péré, Bruno Lina, Sophie Trouillet-Assant, Laurent Hocqueloux, Thierry Prazuck, Etienne Simon-Loriere & Olivier Schwartz

Nature Communications **15**, Article number: 2254 (2024) | Cite this article

15k Accesses | **231** Citations | **72** Altmetric | Metrics

Aim:
Characterization of current SARS-CoV-2 variants:
a model for the diversification of an emerging virus.

Epidemiology and genetic evolution

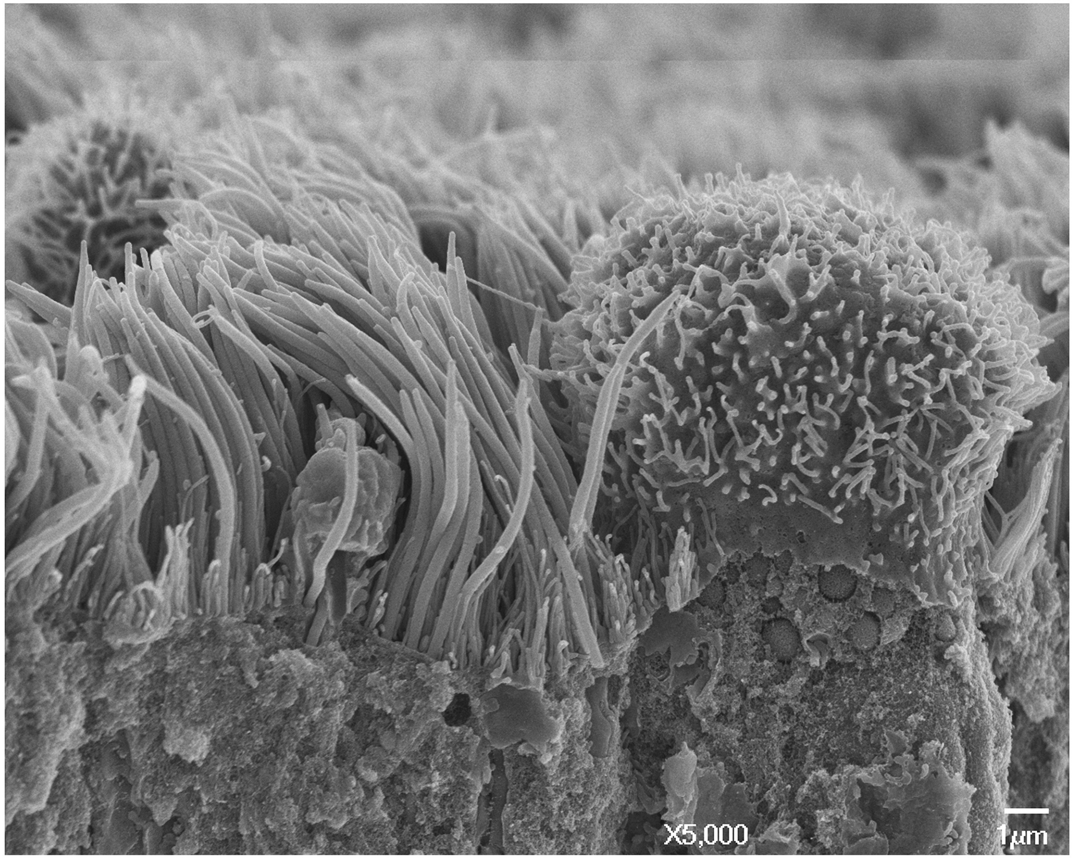
Viral replication and fitness

Model of cell line to characterized SARS-CoV-2 variants:

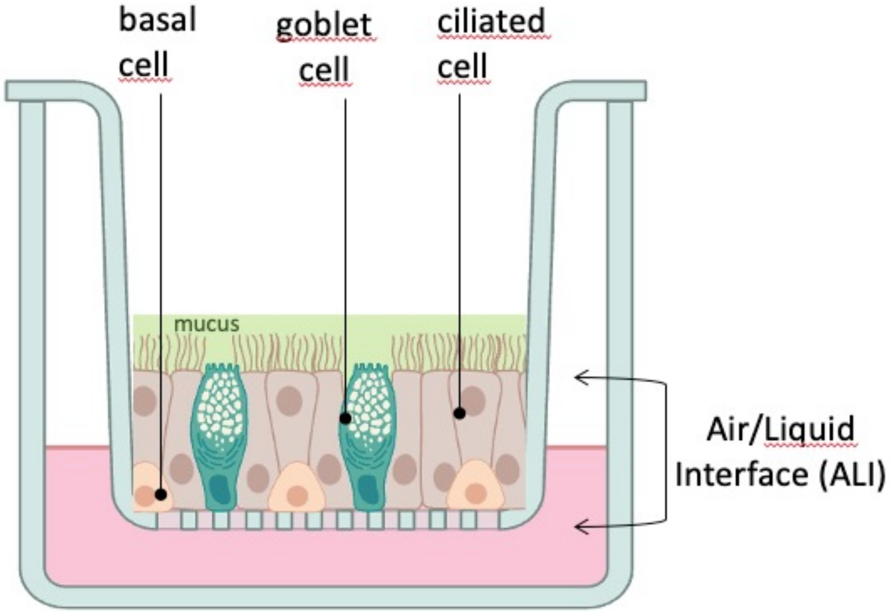
- *ACE2 affinity*
- *Spike fusogenicity*
- *Sensitivity to antiviral drugs*

Neutralizing Antibody escape

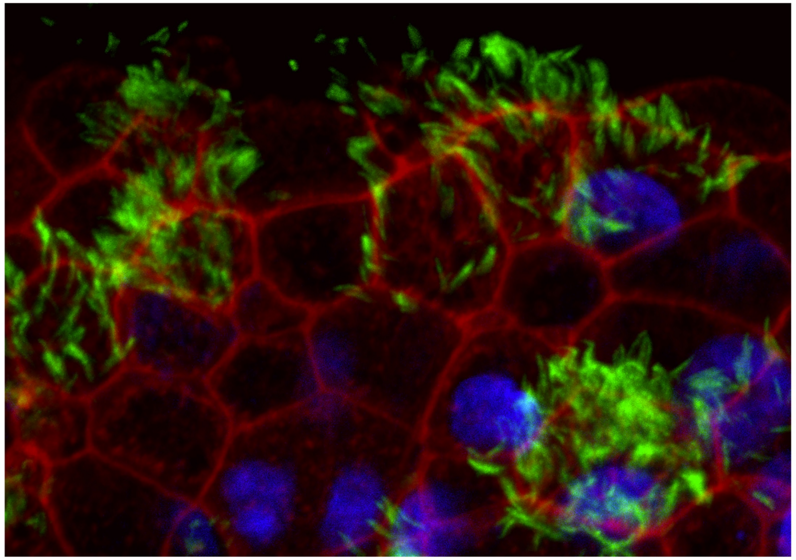
Multiplication of SARS-CoV-2 in airway epithelium model



Vincent Michel @Institut Pasteur

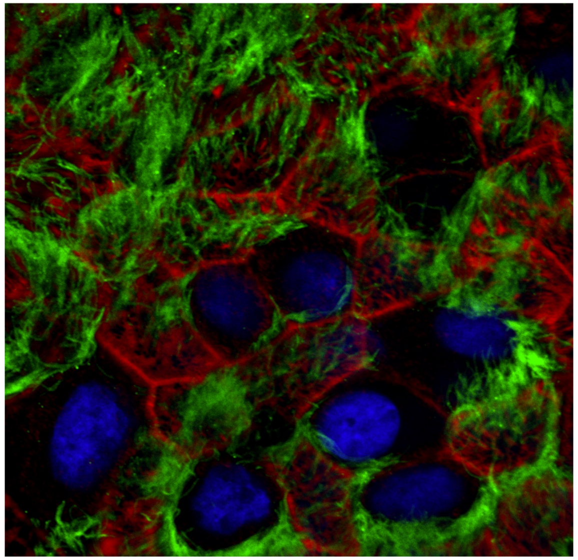


ACE2 and TMPRSS2 expression in human nasal epithelial cells (hNECs)



ACE2

ACE2
Actine
DAPI

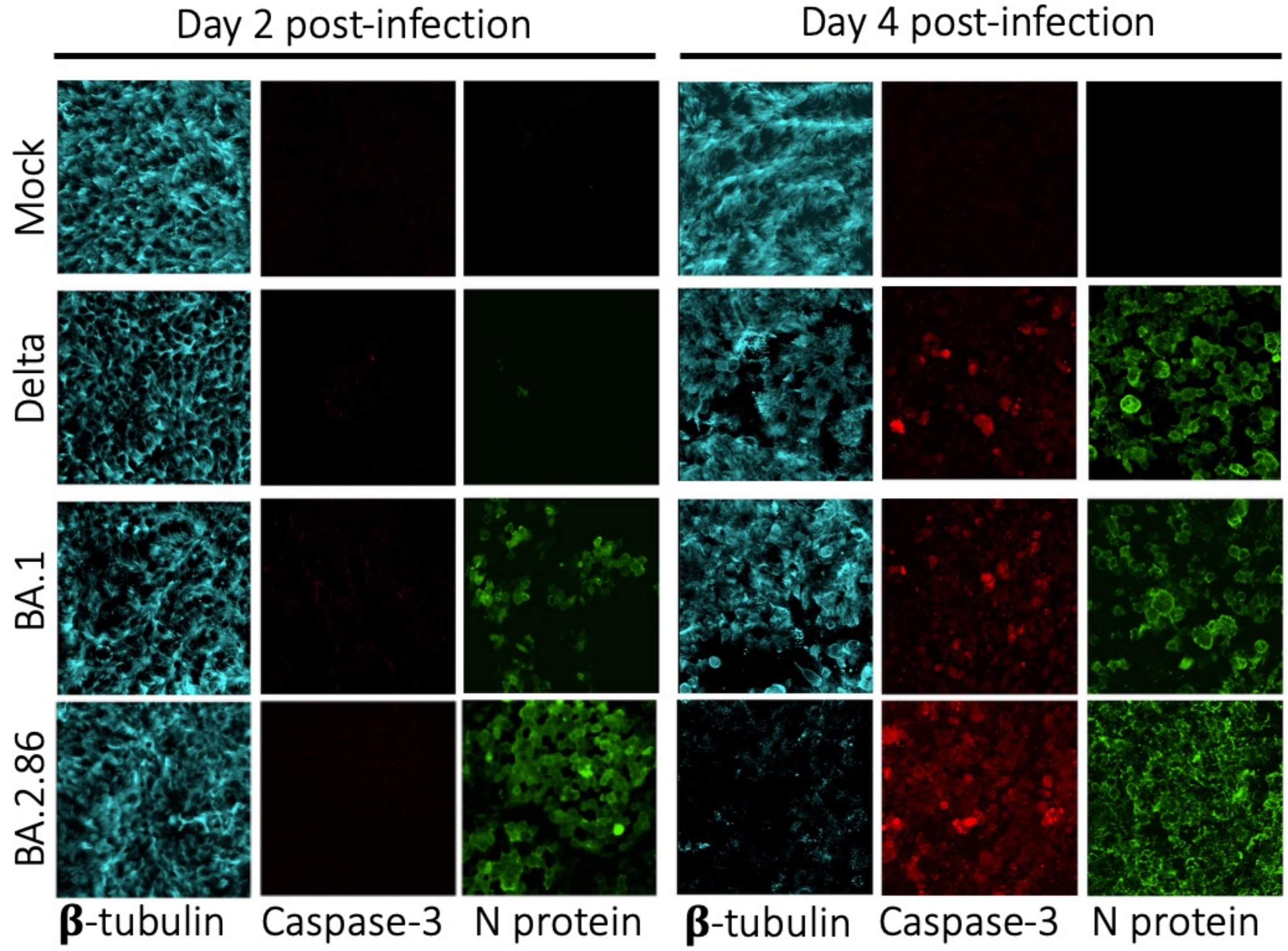


TMPRSS2

TMPRSS2
Actine
DAPI

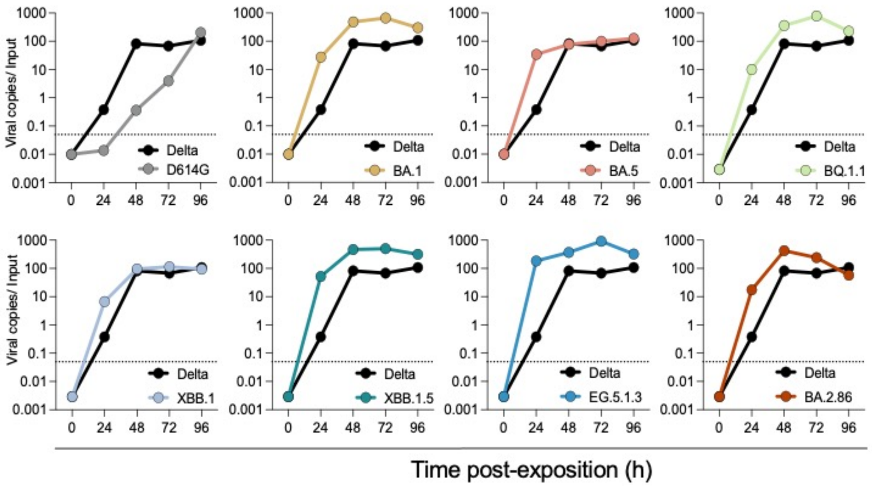
BA.2.86.1 seems to replicates faster than BA.1 and Delta variants

Viral input:
2.10^3 infectious particules/mL

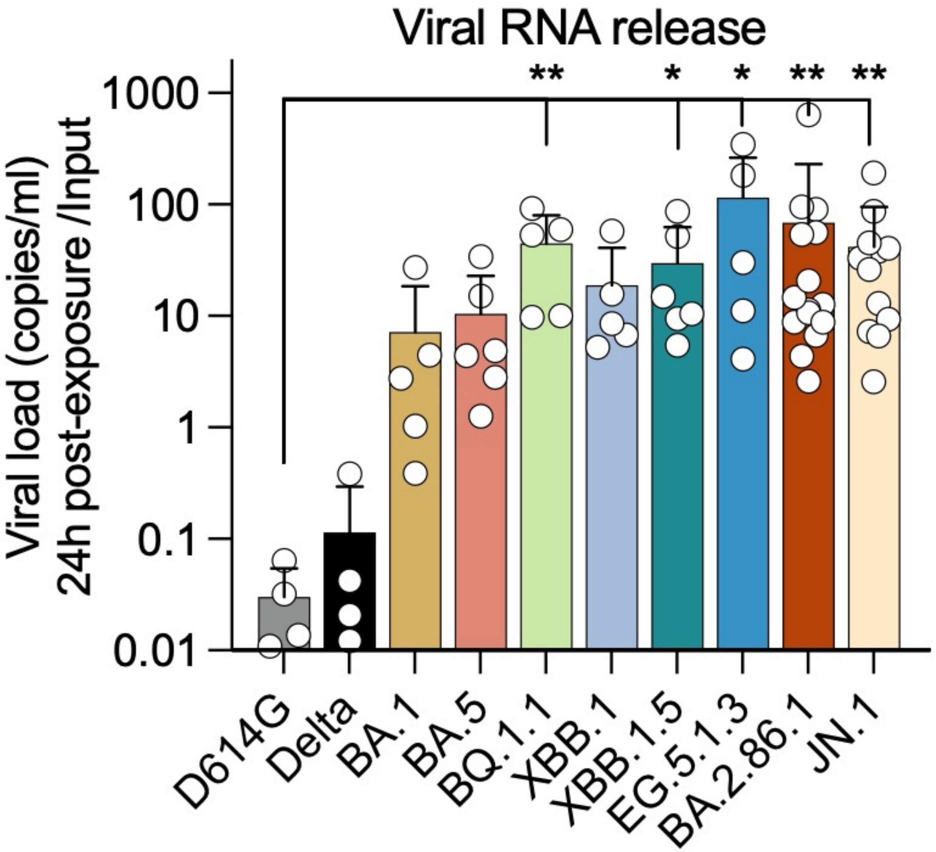


Post-Omicron variants replicate faster and higher compared to D614G and Delta.

Viral input: 2.10^3 infectious particules/mL



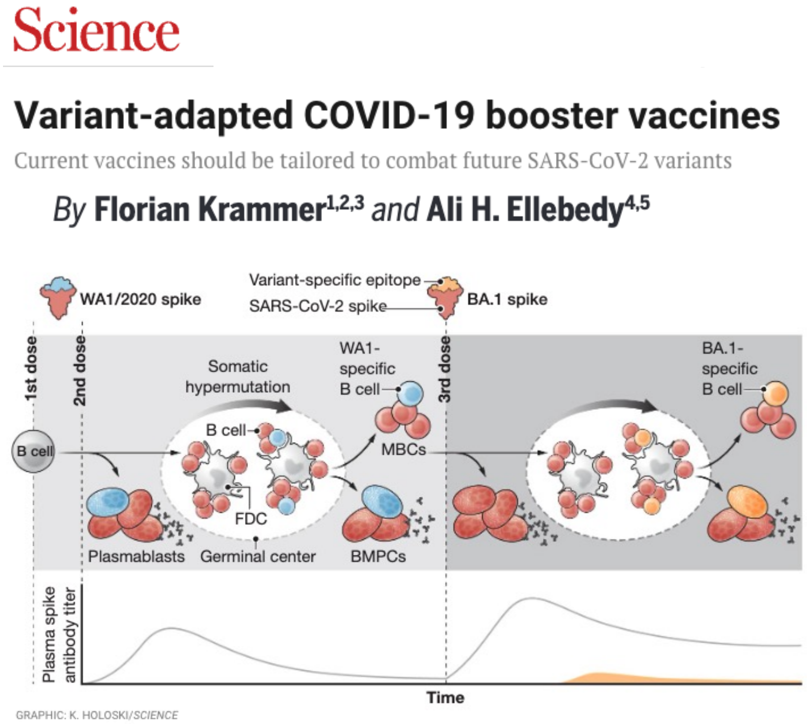
One representative experiment out of 3-5 experiments



Objectives

- SARS-CoV-2 pathogenesis
- Overview of mRNA-based vaccines and SARS-COV-2 variant emergence
- Distinct evolution of Omicron XBB and BA.2.86/JN.1 lineages
- **Future challenges and novel vaccine strategies**

Variant-adapted vaccines



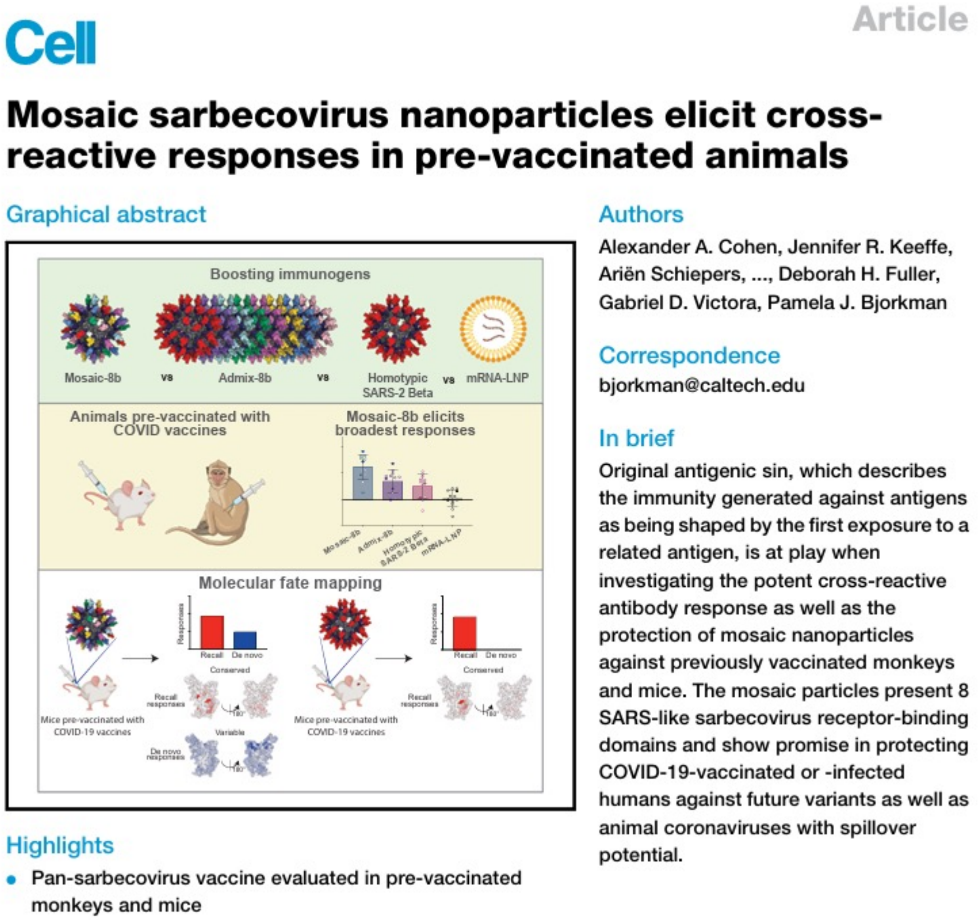
Science

Variant-adapted COVID-19 booster vaccines

Current vaccines should be tailored to combat future SARS-CoV-2 variants

By **Florian Krammer**[1,2,3] *and* **Ali H. Ellebedy**[4,5]

GRAPHIC: K. HOLOSKI/*SCIENCE*



Cell

Article

Mosaic sarbecovirus nanoparticles elicit cross-reactive responses in pre-vaccinated animals

Graphical abstract

Highlights

- Pan-sarbecovirus vaccine evaluated in pre-vaccinated monkeys and mice

Authors

Alexander A. Cohen, Jennifer R. Keeffe, Ariën Schiepers, ..., Deborah H. Fuller, Gabriel D. Victora, Pamela J. Bjorkman

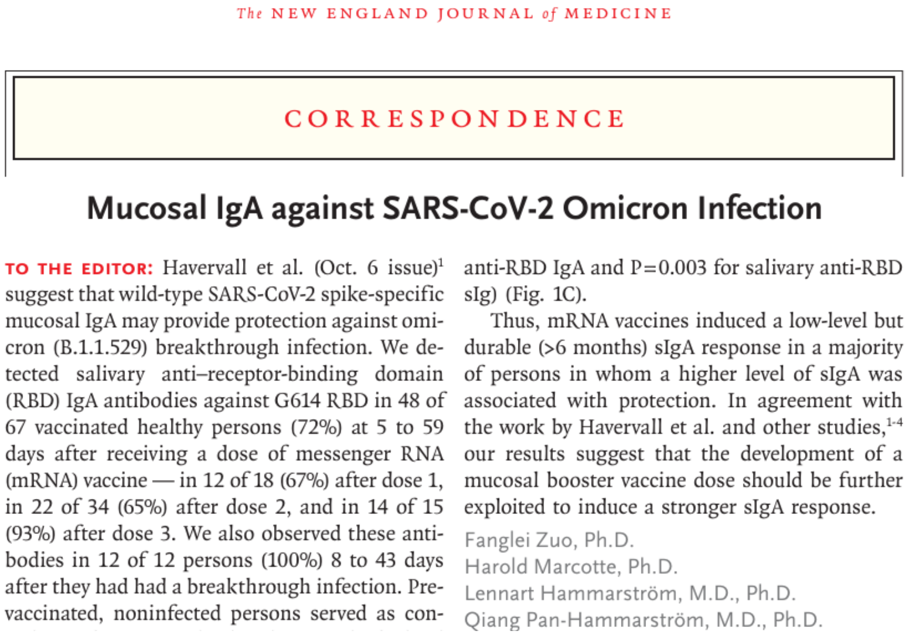
Correspondence

bjorkman@caltech.edu

In brief

Original antigenic sin, which describes the immunity generated against antigens as being shaped by the first exposure to a related antigen, is at play when investigating the potent cross-reactive antibody response as well as the protection of mosaic nanoparticles against previously vaccinated monkeys and mice. The mosaic particles present 8 SARS-like sarbecovirus receptor-binding domains and show promise in protecting COVID-19-vaccinated or -infected humans against future variants as well as animal coronaviruses with spillover potential.

Mucosal vaccines



The NEW ENGLAND JOURNAL *of* MEDICINE

CORRESPONDENCE

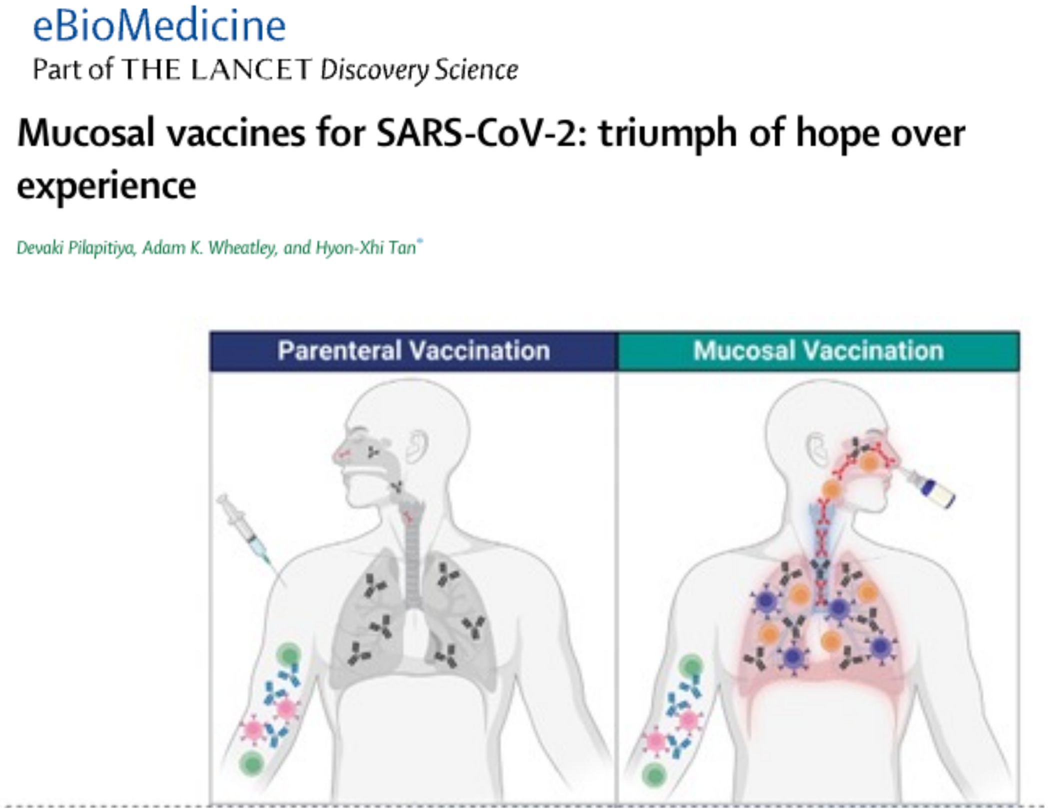
Mucosal IgA against SARS-CoV-2 Omicron Infection

TO THE EDITOR: Havervall et al. (Oct. 6 issue)[1] suggest that wild-type SARS-CoV-2 spike-specific mucosal IgA may provide protection against omicron (B.1.1.529) breakthrough infection. We detected salivary anti–receptor-binding domain (RBD) IgA antibodies against G614 RBD in 48 of 67 vaccinated healthy persons (72%) at 5 to 59 days after receiving a dose of messenger RNA (mRNA) vaccine — in 12 of 18 (67%) after dose 1, in 22 of 34 (65%) after dose 2, and in 14 of 15 (93%) after dose 3. We also observed these antibodies in 12 of 12 persons (100%) 8 to 43 days after they had had a breakthrough infection. Prevaccinated, noninfected persons served as con-

anti-RBD IgA and P=0.003 for salivary anti-RBD sIg) (Fig. 1C).

Thus, mRNA vaccines induced a low-level but durable (>6 months) sIgA response in a majority of persons in whom a higher level of sIgA was associated with protection. In agreement with the work by Havervall et al. and other studies,[1-4] our results suggest that the development of a mucosal booster vaccine dose should be further exploited to induce a stronger sIgA response.

Fanglei Zuo, Ph.D.
Harold Marcotte, Ph.D.
Lennart Hammarström, M.D., Ph.D.
Qiang Pan-Hammarström, M.D., Ph.D.

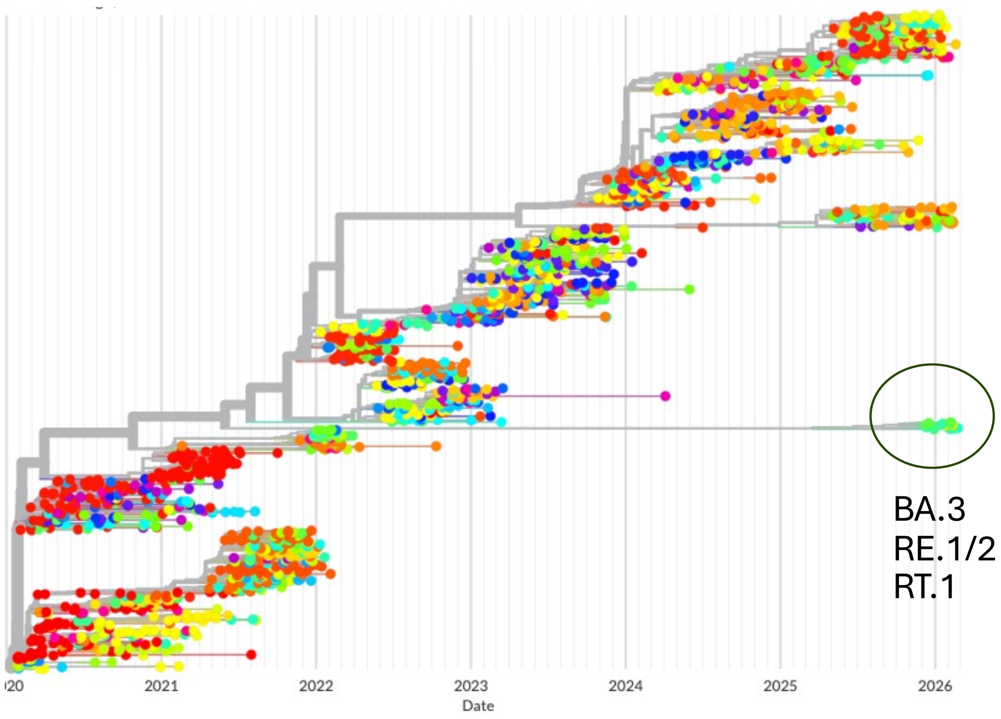


eBioMedicine
Part of THE LANCET *Discovery Science*

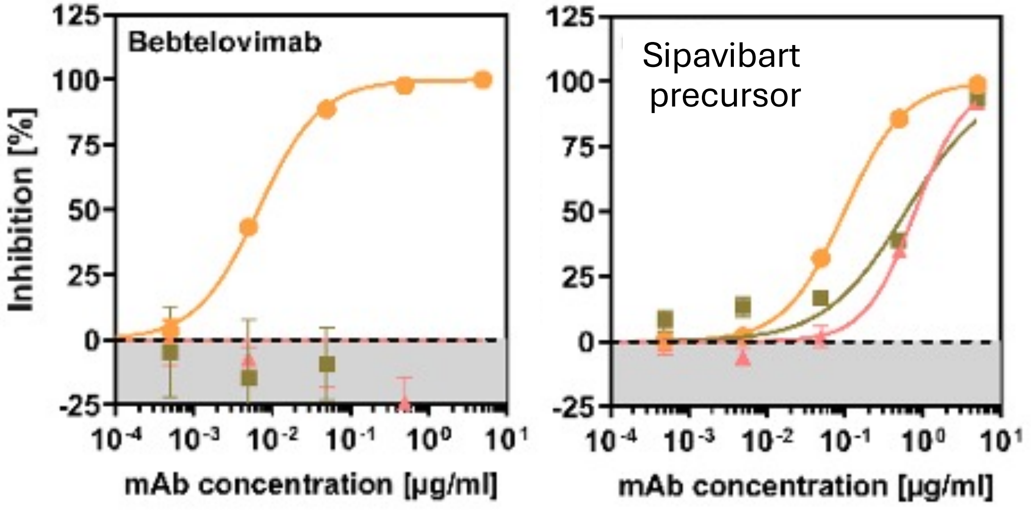
Mucosal vaccines for SARS-CoV-2: triumph of hope over experience

Devaki Pilapitiya, Adam K. Wheatley, and Hyon-Xhi Tan

Emerging SARS-CoV-2 variant BA.3.2



BA.3
RE.1/2
RT.1



Lu Zhang *et al.*, *Lancet Microbes*, 2026

LETTER ▸ New Microbes New Infect. 2026 Feb 18;70:101727. doi: 10.1016/j.nmni.2026.101727

SARS-CoV-2 BA.3.2: epidemiological trends and implications for prophylactic antibodies

Slim Fourati [a], Paul Loubet [b,*]

In summary

Emerging variants are often:

- more fit than previous variants
- less sensitive to sera from vaccinated individuals
- escape binding and neutralization by most therapeutic mAbs
- remain sensitive to Nirmatrelvir, Molnupiravir & Remdesivir

Remaining challenges

Fitness and tropism
Longer surveillance periods, impact and frequency of booster dose
Correlation between antibody levels, neutralizing titers and vaccine effectiveness
Local and systemic humoral responses in vaccine efficacy
Cellular immunity

Acknowledgements

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VACCINE RESEARCH INSTITUTE

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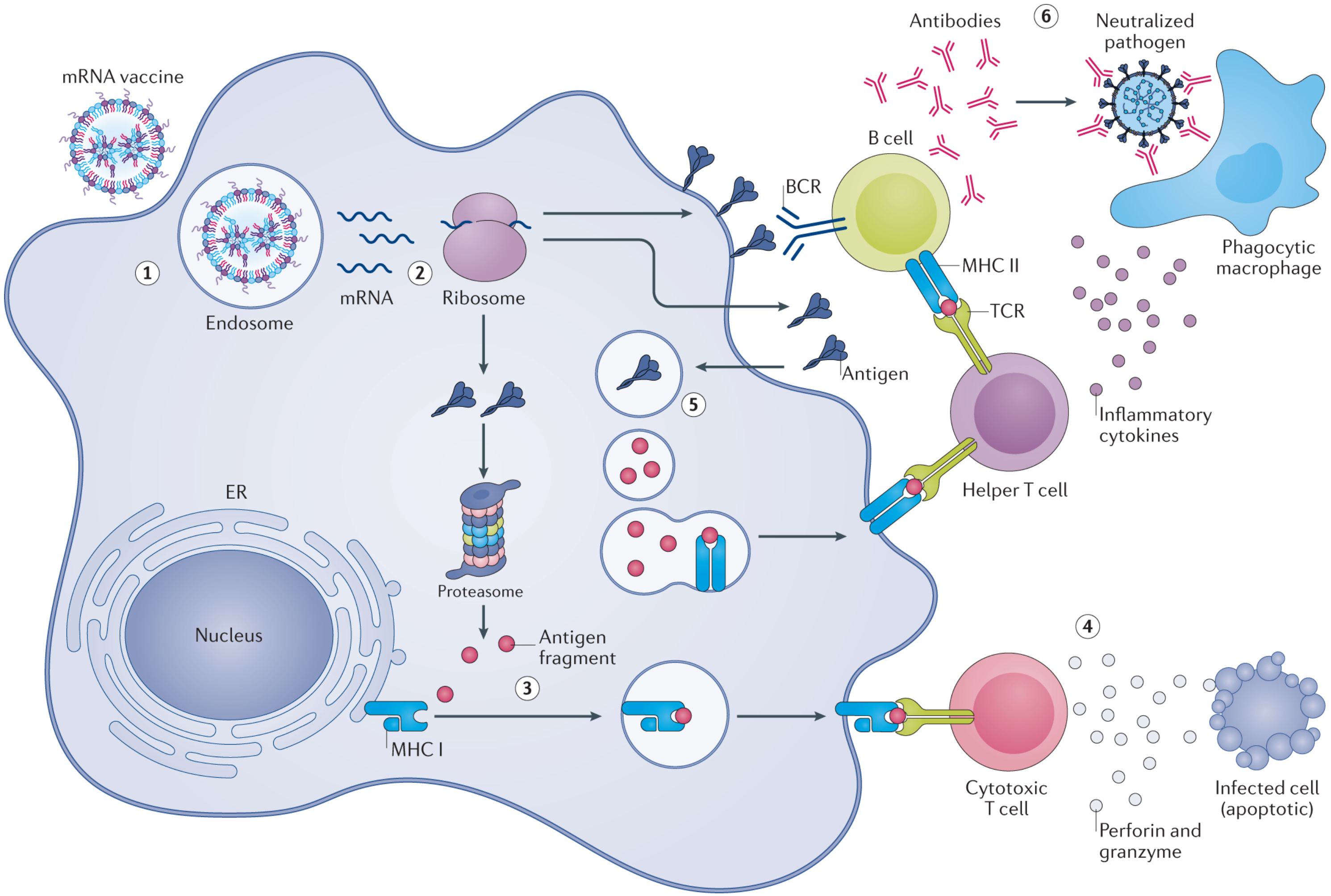
anrs

ANR

mRNA vaccines for infectious diseases



Chaudhary et al., Nature Reviews Drug Discovery, 2021