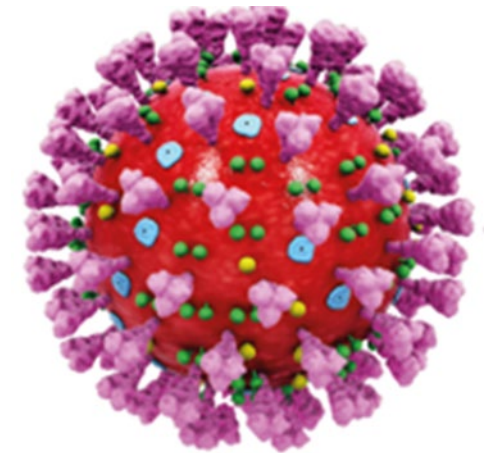


COVID update, Sept 2023

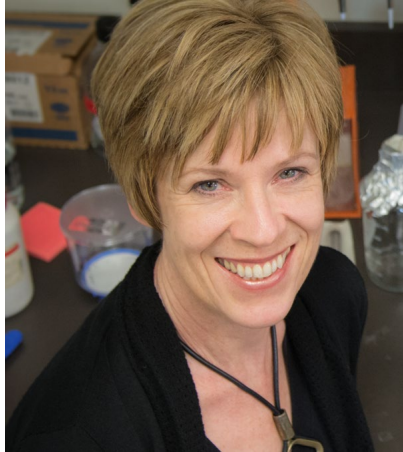
– focus on virus mutations

Paula Cannon, PhD
Professor, USC

LA City Health Commission
September 11th, 2023



Disclosures

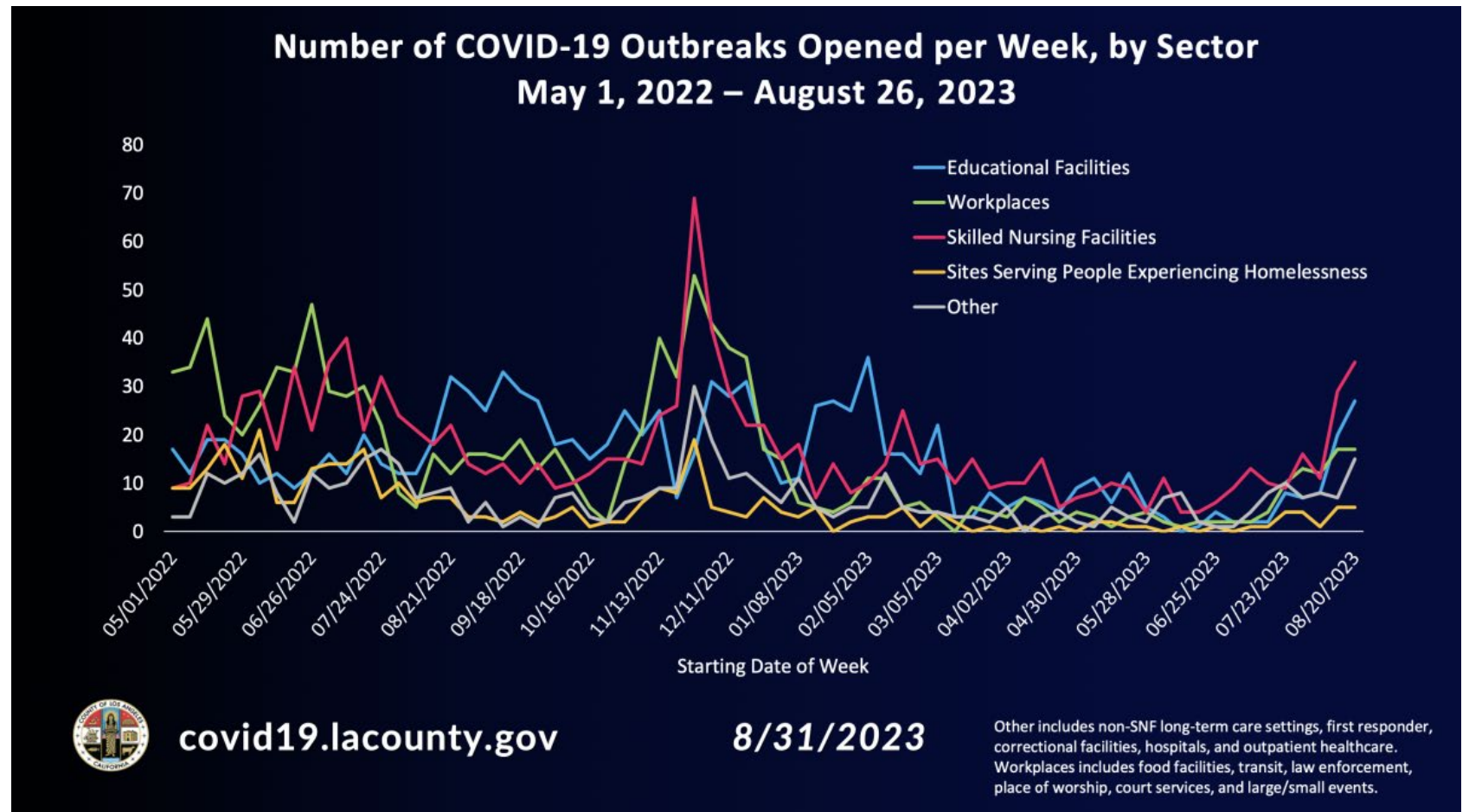


- Distinguished Professor of Molecular Microbiology & Immunology
Keck School of Medicine of USC
- I study viruses, including HIV and SARS-CoV-2, and my work is funded by the National Institutes of Health.
- I serve on Scientific Advisory Boards for Chroma Medicine and Immusoft, and on the Board of Directors for Blue Whale Bio. I also provide expert opinions to biotech companies and lawyers. None of these activities are related to SARS-CoV-2 and COVID, or any of the topics I will cover in this presentation.

Current state in LA county – seeing an uptick

“We have been seeing a gradual and consistent rise in COVID-19 transmission over the past few weeks. Despite the increase, hospitalizations remain at near historic lows, and deaths are at their lowest point since the beginning of the pandemic.”

Los Angeles County Department of Public Health, 9/5/23



COVID-19 uptick also seen in wastewater sampling

Last 6 months



Year-over-year comparisons - same as '21 and '22

■ 2020-2021 ■ 2021-2022 ■ 2022-2023 ■ 2023-2024

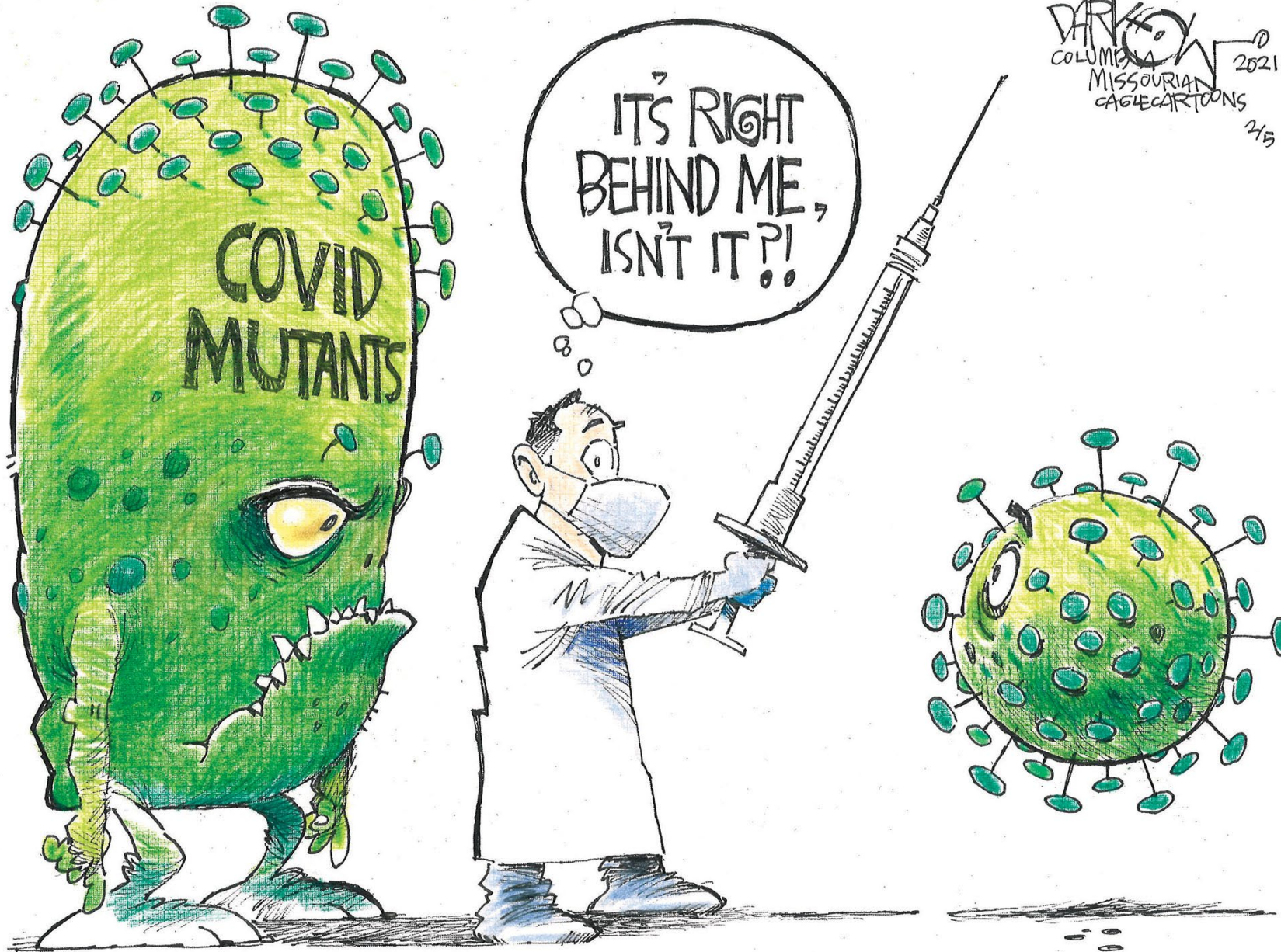


What drives an increase?

- Behavior, weather, vacation and travel, back-to-school
- Waning immunity (> 6 months after vaccine or infection)

What about the virus?

Concern that new waves could result from new variants, with increased ability to transmit, or override our immunity



COVID Mutants By John Darkow

WHO classification of COVID-19 variants (updated Aug 2023)

Variants Under Monitoring (VUMs)

- Mutations *suspected* to change virus characteristics¹
- Early signs of growth advantage, but impact still unclear.

Variants of Interest (VOIs)

- Mutations *predicted or known* to affect virus characteristics¹
- Apparent epidemiological impacts²

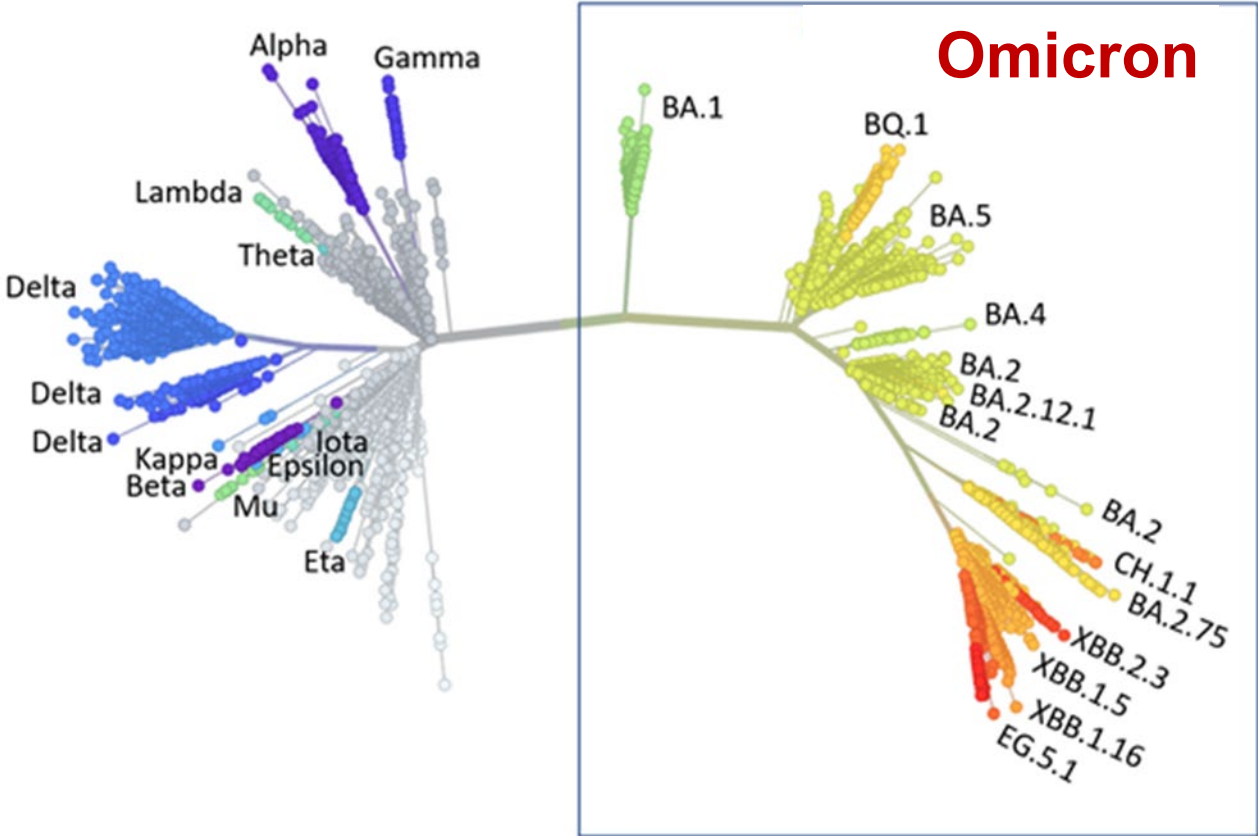
Variants of Concern (VOCs)

- Increase in transmissibility; OR Increase in virulence/change in disease manifestation, OR Decreased effectiveness of public health measures, diagnostics, vaccines, therapeutics

¹ Transmissibility, disease severity, immune escape, diagnostic escape, therapeutic escape

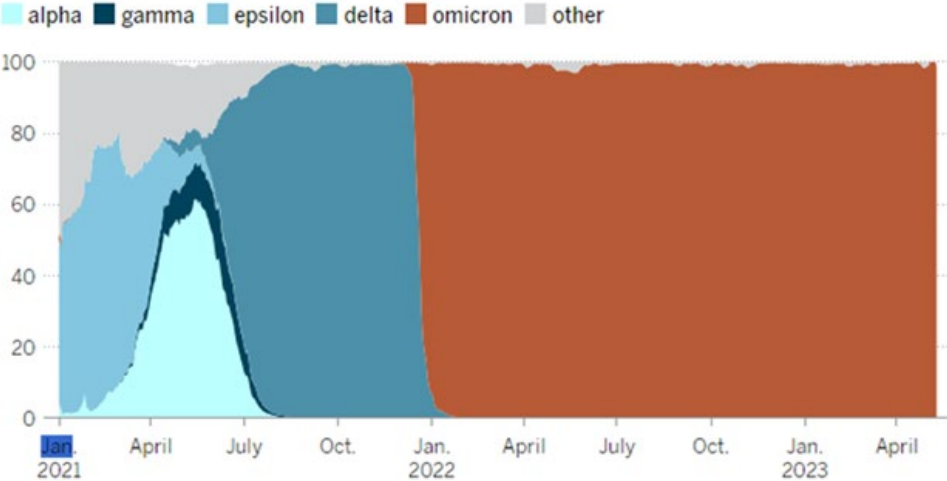
² Significant community transmission, multiple outbreaks in multiple countries, increasing over time

WHO Variants of Concern



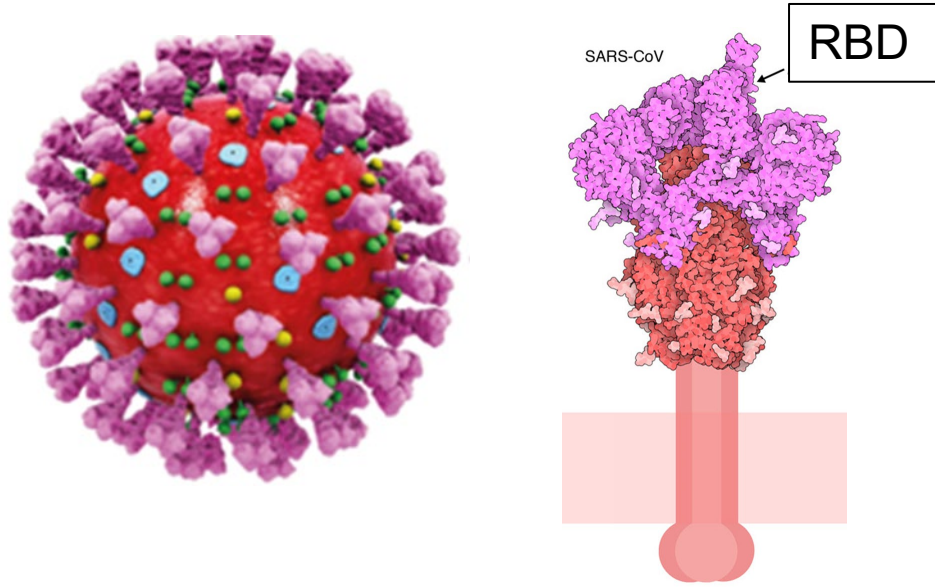
Source: Nextstrain.org

California waves, 2021- present

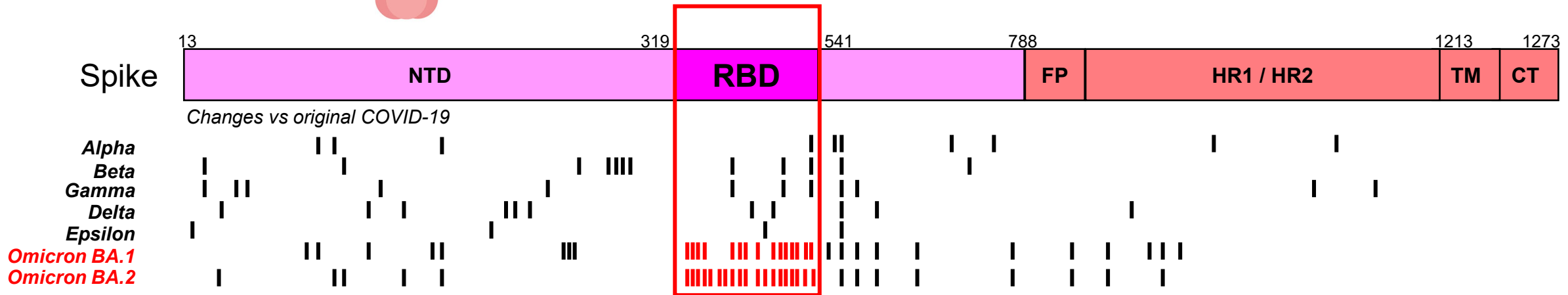


LA Times

Why Omicron was such a game changer



- Receptor binding domain (RBD) is critical part of Spike that lets virus bind to its receptor (ACE2)
- Antibodies** that bind here can 'neutralize' the virus
- Spike mutations help get around antibody effectiveness



**Antibodies are made in response to natural infections and vaccines, or can be given as a therapy (monoclonal antibodies)

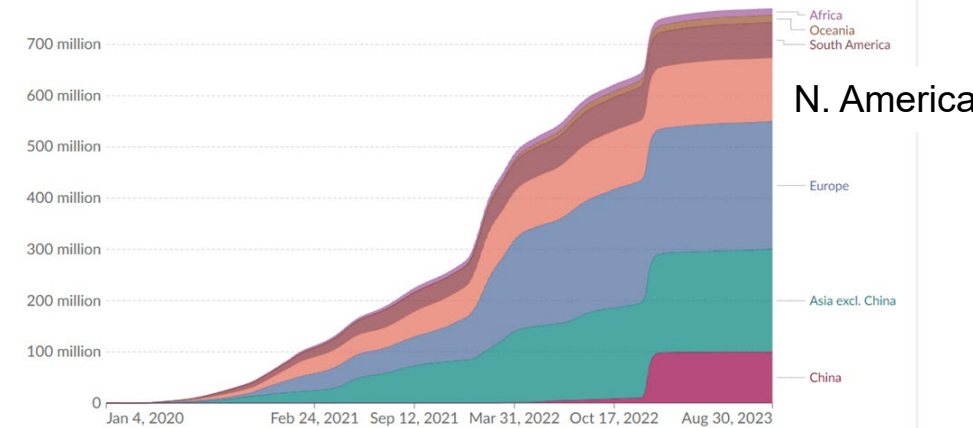
Why does SARS-CoV-2 mutate so much?

- It's not especially mutagenic - but a huge number of people have been infected (770M to date).
- It's a new-to-humans virus, so still optimizing its design
 - to be more infectious
 - to be more resistant to antibodies
- Co-infection by two different viruses in one person can result in a new recombinant (mixed) virus
- Opportunity to evolve over longer periods in people with weaker immune systems

Cumulative confirmed COVID-19 cases by world region

7-day rolling average. Due to limited testing, the number of confirmed cases is lower than the true number of infections.

All together Relative



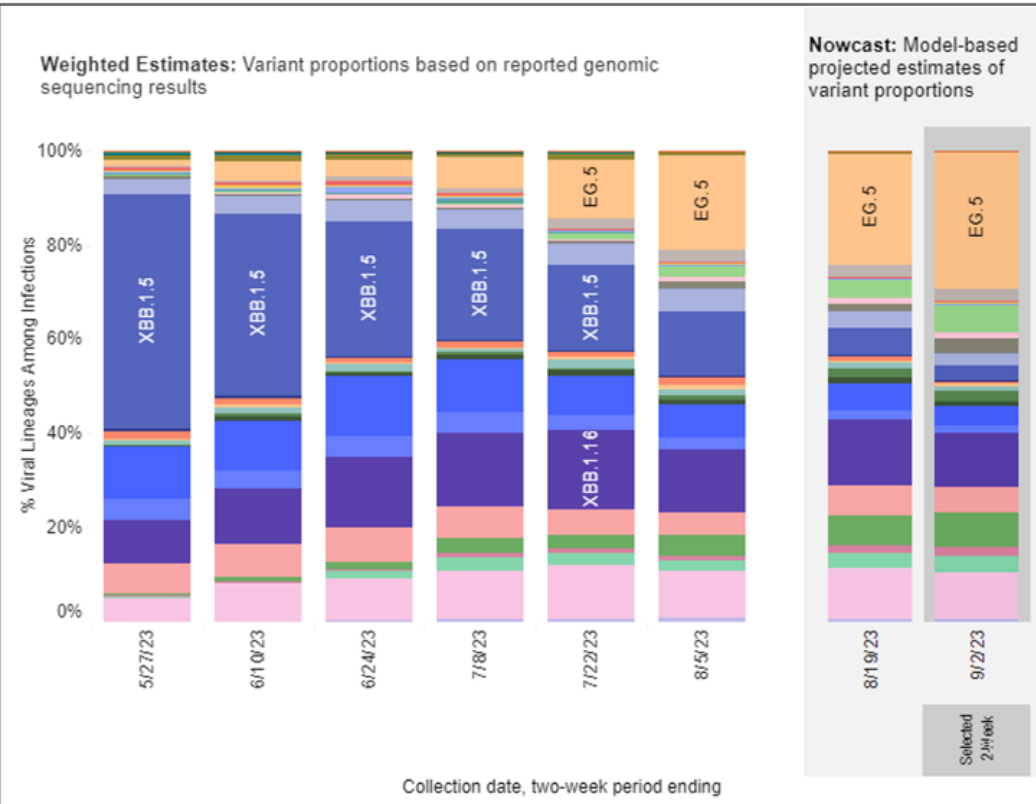
Source: WHO COVID-19 Dashboard

OurWorldInData.org/coronavirus • CC BY

Current circulating variants and trends in CA (Region 9)

Weighted Estimates in HHS Region 9 for 2-Week Periods in 5/14/2023 – 9/2/2023

Hover over (or tap in mobile) any lineage of interest to see the amount of uncertainty in that lineage's estimate.



Nowcast Estimates in HHS Region 9 for 8/20/2023 – 9/2/2023

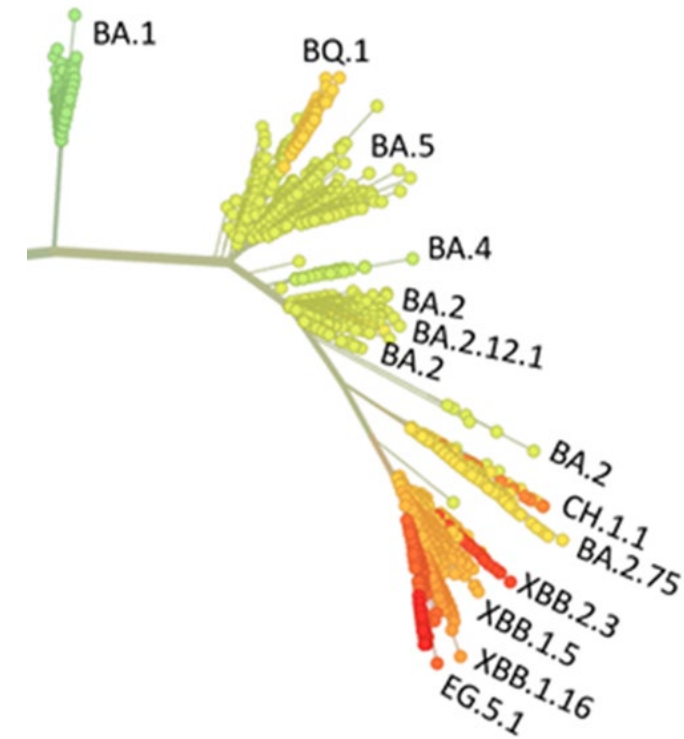
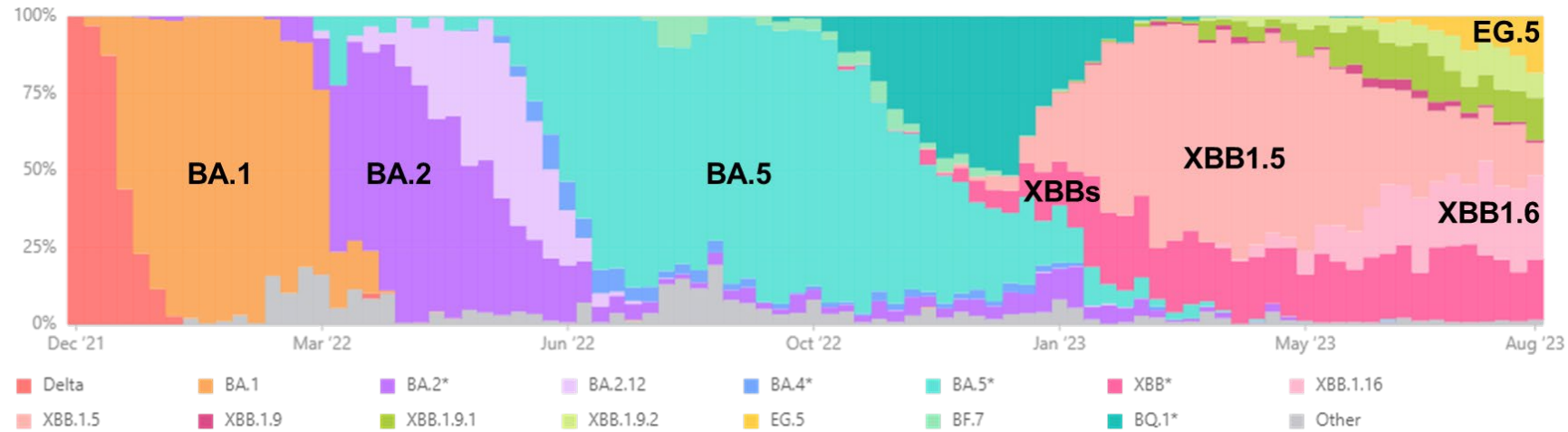
Region 9 - Arizona, California, Hawaii, Nevada, American Samoa, Commonwealth of the Northern Mariana Islands, Federated States of Micronesia, Guam, Marshall Islands, and Republic of Palau

WHO label	Lineage #	%Total	95%PI
Omicron	EG.5	28.7%	25.6-32.1%
	XBB.1.16	11.6%	9.8-13.7%
	XBB.2.3	9.8%	8.3-11.4%
	XBB.1.16.6	7.3%	5.0-10.5%
	FL.1.5.1	6.0%	4.3-8.3%
	XBB.1.16.1	5.5%	4.5-6.6%
	XBB.1.9.1	4.2%	3.4-5.3%
	XBB.1.42.2	3.4%	1.8-6.2%
	XBB.1.5	3.3%	2.5-4.2%
	HV.1	3.0%	1.6-5.1%
	EG.6.1	2.7%	1.4-5.0%
	XBB	2.7%	2.0-3.5%
	XBB.1.5.70	2.3%	1.5-3.3%
	XBB.1.16.11	1.9%	1.1-3.4%
	XBB.1.9.2	1.4%	1.0-1.8%
	GE.1	1.2%	0.7-1.9%
	XBB.1.5.72	1.1%	0.7-1.8%
	XBB.1.5.68	0.9%	0.6-1.3%
	XBB.1.5.10	0.7%	0.5-1.0%
	XBB.2.3.8	0.7%	0.2-1.8%
	CH.1.1	0.5%	0.3-0.7%
	XBB.1.5.59	0.4%	0.2-0.7%
	FD.1.1	0.3%	0.2-0.5%
	FE.1.1	0.2%	0.1-0.4%
	EU.1.1	0.1%	0.1-0.2%
	XBB.1.5.1	0.0%	0.0-0.1%
	FD.2	0.0%	0.0-0.0%
	BA.5	0.0%	0.0-0.0%
	BQ.1	0.0%	0.0-0.1%
	BA.2.12.1	0.0%	0.0-0.0%
	B.1.1.529	0.0%	0.0-0.0%
Other	Other*	0.1%	0.0-0.1%

Top variants

- EG.5 (Eris)
- XBB.1.5 (Kraken)
- XBB.1.16
- FL.1.5.1

Current circulating variants from wastewater



Percentage of variant lineage sequenced from SARS-CoV-2 genomes in wastewater (Western region)
- <https://biobot.io/data/>



BA.2.86 (Pirola)

Health

Highly mutated COVID virus variant BA.2.86 showing up in multiple countries



Handful of cases from Israel, Denmark, U.S., U.K.; none yet in Canada

A new COVID variant, BA.2.86, has emerged around the world as cases of COVID-19 climb. Should you be worried about BA.2.86?

Infectious disease experts are keeping a close eye on BA.2.86 since it's possible that it will become super-contagious

By: Katie Kerwin McCrimmon, UCHealth | Aug. 31, 2023

Share     

Former FDA boss says he's 'pretty concerned' about new COVID variant BA.2.86

- Dr Scott Gottlieb warned the new strain was a 'highly-mutated' virus
- White House planning to urge ALL Americans to get Covid boosters this year
- [READ MORE: New Covid variant 'Pirola' has been spotted in the United States](#)

By LUKE ANDREWS HEALTH REPORTER FOR DAILYMAIL.COM

UPDATED: 12:38 EDT, 21 August 2023

New Covid variant causing concern among scientists detected in London

It is unclear whether BA.2.86 causes more severe disease but its detection in several countries has put scientists on alert

BA.2.86 in 10 countries, 4 US states

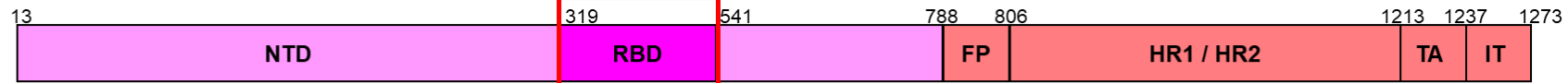
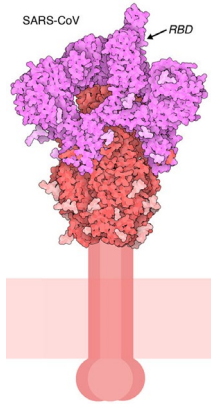


- First reported 24 July 2023
- Simultaneous appearance in multiple countries suggests it has been spreading undetected

Built with [corneliusroemer/ncov-simplest](#). Maintained by [Cornelius Roemer](#) and [Richard Neher](#).
Enabled by data from GISAID, 42 genomes.

BA.2.86 has ~30 new changes in Spike

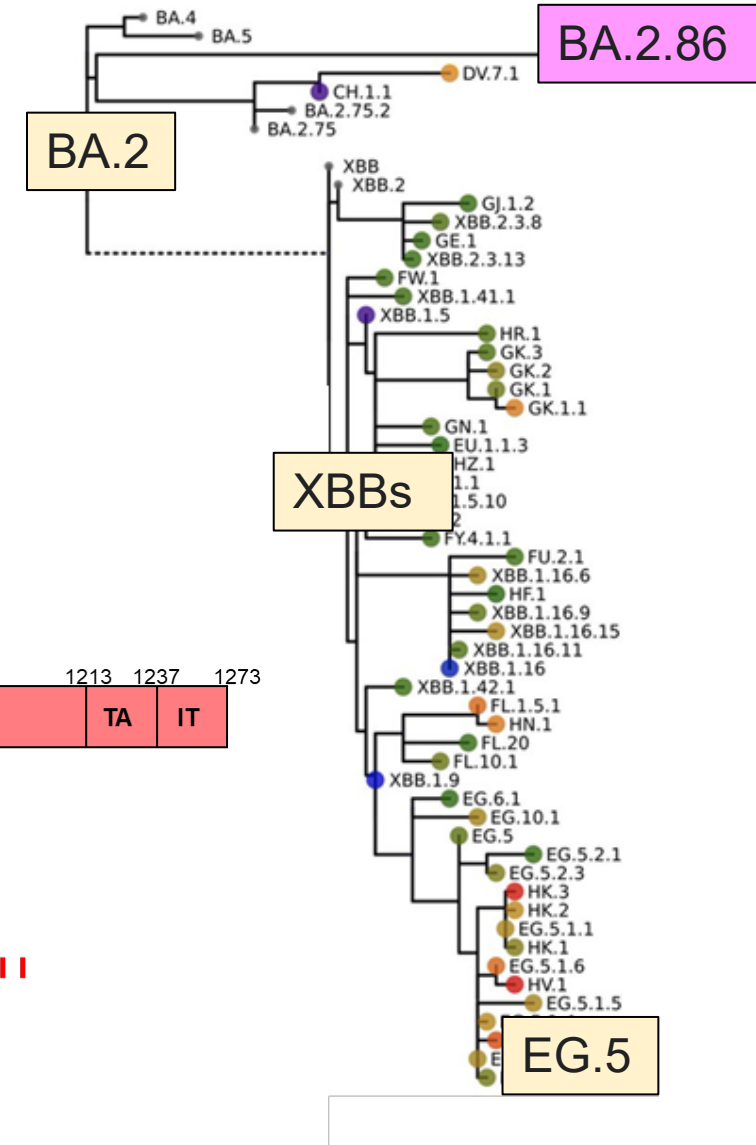
- This large jump is on par with the first appearance of the Omicron lineage
- It is closer to an earlier Omicron (BA.2)
- Designated Variant Under Monitoring by WHO on 17 August 2023



Changes BA.2 vs original



Changes BA.2.86 vs BA.2



BA.2.86 questions



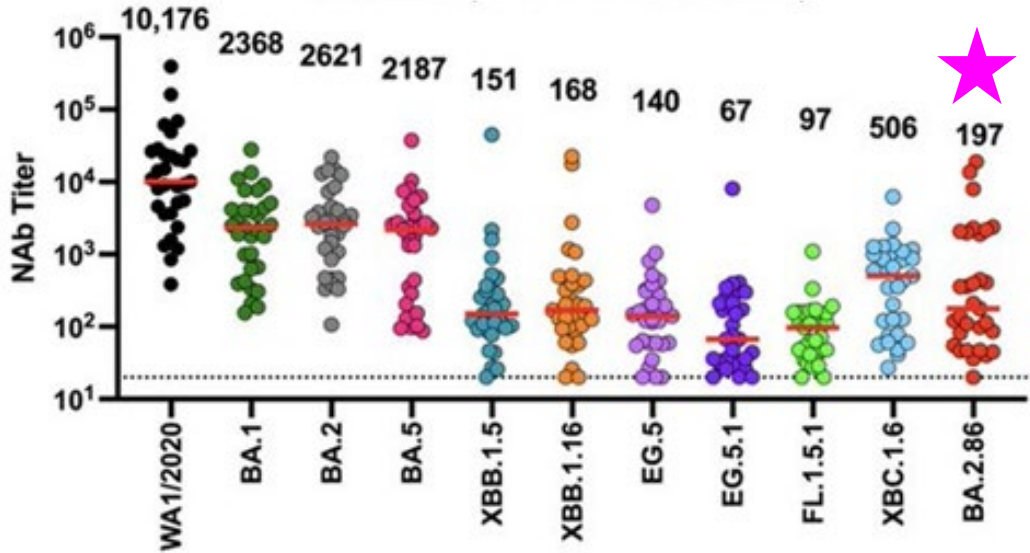
- Is it more transmissible, or more virulent?
- Is it more antibody-resistant, and therefore more likely to break through the protection conferred by prior infections and/or vaccinations?
- Implications for the new Fall booster vaccine

CDC Variants of Concern (VOCs)

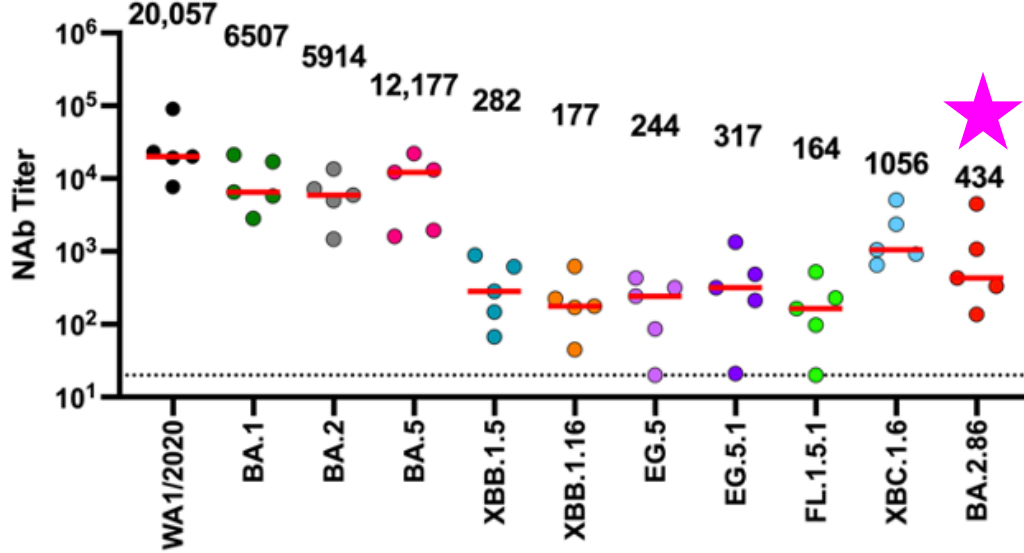
- Increase in transmissibility; OR Increase in virulence/change in disease manifestation, OR Decreased effectiveness of public health measures, diagnostics, vaccines, therapeutics

BA.2.86 – sensitivity to antibodies similar to other circulating viral variants

6 mths after Bivalent booster



6 mths after XBB infection



KEY: Abs work better against variants

MODERNA press release, 9/6/2023

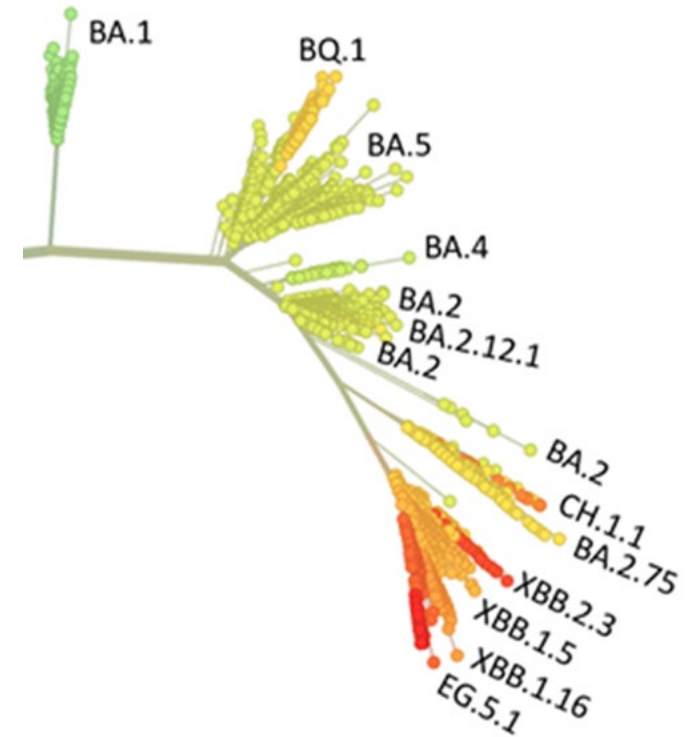
MODERNA CLINICAL TRIAL DATA CONFIRM ITS **UPDATED COVID-19 VACCINE GENERATES STRONG IMMUNE RESPONSE IN HUMANS AGAINST BA.2.86**

“....generates a strong human immune response against the highly mutated BA.2.86 variant.showing a similarly effective response against EG.5 and FL.1.5.1 variants”

“.....generates an 8.7-fold increase in neutralizing antibodies in humans against BA.2.86 (Pirola), a variant under monitoring.”

Update on vaccines

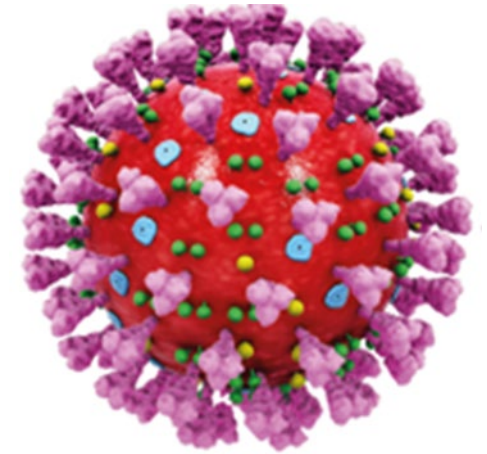
- **Initial vaccines** based on Spike from original Wuhan variant
- Last Fall's **bivalent vaccine** also included the BA.5 Spike
- In June, FDA panel recommended an **updated Fall booster** based on XBB.1.5 Spike
- **Pfizer and Moderna's** updated mRNA vaccines look good against current variants such as XBB.1.16., XBB.2.3 and EG.5.
- Expected to be approved immediately after CDC advisory committee meeting, Sept. 12
- **Novavax vaccine**, different technology (not mRNA), also looks promising and will likely be ready later in the Fall



Final thoughts

- Circulating variants are still Omicron, so virus might be moving towards an endemic endgame
- However, BA.2.86 coming 'out of the blue' suggests the virus can still evolve in an unseen manner eg in an immunocompromised person with prolonged illness, through coinfection and recombination of distinct variants, or by evolution in an animal host and then re-infecting humans
- Wastewater monitoring is a good predictor of new waves of infection and new variants. The appearance of BA.2.86 tells us why we should keep doing this
- Choice of the new Fall vaccine (based on XBB.1.5 Spike) looks like a very good decision
- Neutralizing antibodies still provide the best protection against infection, even when partially escaped by current variants. However, our immune system makes a much broader response that protects against severe disease, even for very distinct variants.

Recommendations for now



- Be aware - is Covid going up?
- Be prepared to test – any symptoms could be COVID
- If you are infected, isolate, get Paxlovid if eligible
- **Get the new Fall vaccine, if not recently infected or vaccinated**