Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases

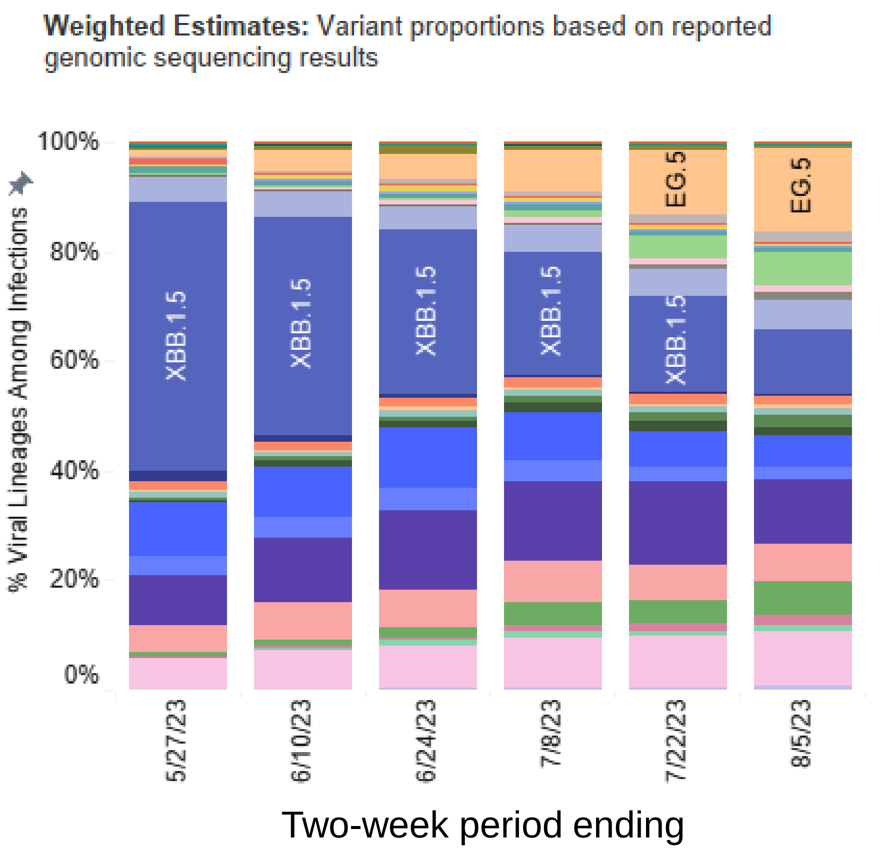
Current landscape of SARS-CoV-2 lineages

September 2023

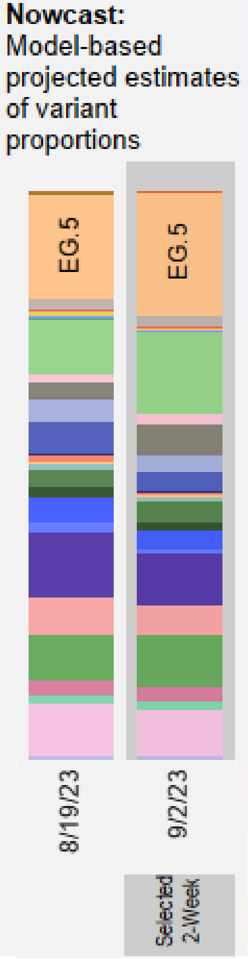
Natalie J. Thornburg, PhD
Chief, Laboratory Branch
Coronaviruses and Other Respiratory Viruses Division

Trends in weighted lineage proportion estimates & Nowcast

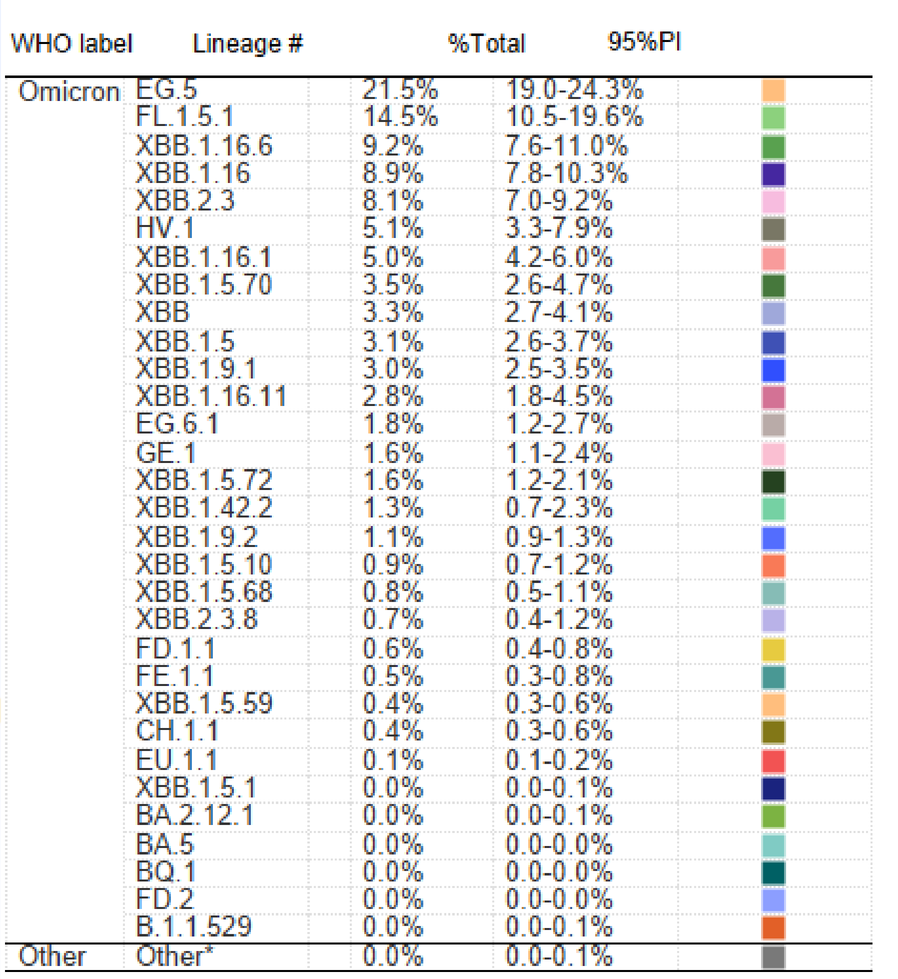
United States, May 27 – September 2, 2023



Weighted Estimates: Variant proportions based on reported genomic sequencing results



Nowcast: Model-based projected estimates of variant proportions



WHO label	Lineage #	%Total	95%PI	
Omicron	EG.5	21.5%	19.0-24.3%	🟧
	FL.1.5.1	14.5%	10.5-19.6%	🟩
	XBB.1.16.6	9.2%	7.6-11.0%	🟩
	XBB.1.16	8.9%	7.8-10.3%	🟪
	XBB.2.3	8.1%	7.0-9.2%	🟪
	HV.1	5.1%	3.3-7.9%	🟫
	XBB.1.16.1	5.0%	4.2-6.0%	🟥
	XBB.1.5.70	3.5%	2.6-4.7%	🟩
	XBB	3.3%	2.7-4.1%	🟦
	XBB.1.5	3.1%	2.6-3.7%	🟦
	XBB.1.9.1	3.0%	2.5-3.5%	🟦
	XBB.1.16.11	2.8%	1.8-4.5%	🟥
	EG.6.1	1.8%	1.2-2.7%	🟫
	GE.1	1.6%	1.1-2.4%	🟪
	XBB.1.5.72	1.6%	1.2-2.1%	🟩
	XBB.1.42.2	1.3%	0.7-2.3%	🟩
	XBB.1.9.2	1.1%	0.9-1.3%	🟦
	XBB.1.5.10	0.9%	0.7-1.2%	🟧
	XBB.1.5.68	0.8%	0.5-1.1%	🟩
	XBB.2.3.8	0.7%	0.4-1.2%	🟪
	FD.1.1	0.6%	0.4-0.8%	🟨
	FE.1.1	0.5%	0.3-0.8%	🟩
	XBB.1.5.59	0.4%	0.3-0.6%	🟧
	CH.1.1	0.4%	0.3-0.6%	🟫
	EU.1.1	0.1%	0.1-0.2%	🟥
	XBB.1.5.1	0.0%	0.0-0.1%	🟦
	BA.2.12.1	0.0%	0.0-0.1%	🟩
	BA.5	0.0%	0.0-0.0%	🟩
	BQ.1	0.0%	0.0-0.0%	🟩
	FD.2	0.0%	0.0-0.0%	🟦
	B.1.1.529	0.0%	0.0-0.1%	🟧
Other	Other*	0.0%	0.0-0.1%	⬛

https://covid.cdc.gov/covid-data-tracker/#variant-proportions Accessed 9/1/2023

Convergent Evolution of Different Omicron Sub-lineages:

Key changes in the spike receptor binding domain (RBD) detected since September 2022

	Spike RBD (residues 333-527) amino acid substitutions											
Lineage	339 §	346 §,¶	368	444 §,¶	445 ¶	446 §,¶	452 §,¶	460 §,¶	478	486 §,¶	490 §,¶	521
Reference sequence: BA.4/BA.5	D	R	L	K	V	G	R	N	K	V	F	P
BA.4.6, BA.5.2.6, BF.7, BF.11	—	T	—	—	—	—	—	—	—	—	—	—
BQ.1	—	—	—	T	—	—	—	K	—	—	—	—
BQ.1.1	—	T	—	T	—	—	—	K	—	—	—	—
BA.2.75	H	—	—	—	—	S	L	K	—	F	—	—
BN.1	H	T	—	—	—	S	L	K	—	F	S	—
CH.1.1	H	T	—	T	—	S	—	K	—	S	—	—
XBB, XBB.1	H	T	I	—	P	S	L	K	—	S	S	—
XBB.1.5, XBB.1.5.1, FD.2, **XBB.1.9.1, XBB.1.9.2**	H	T	I	—	P	S	L	K	—	P	S	—
XBB.1.16, XBB.1.16.1	H	T	I	—	P	S	L	K	R	P	S	—
XBB.2.3	H	T	I	—	P	S	L	K	—	P	S	S

Ma et al. MMWR to be published on June 15, 2023

§ Indicates sites of independent substitutions in at least two different evolutionary lineages.

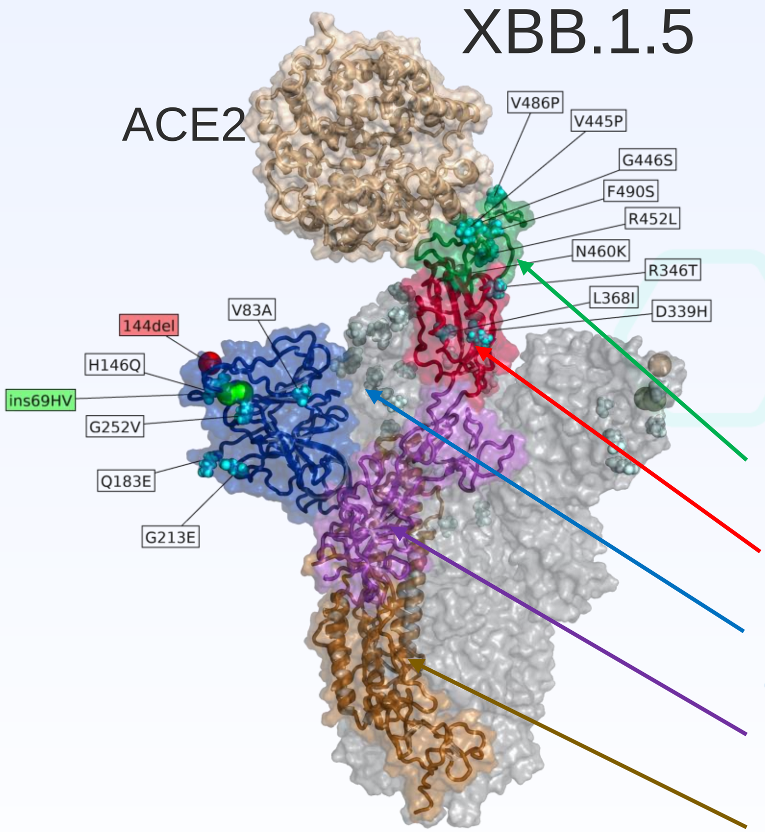
¶ Indicates sites identified in a previous study associated with *in vitro* reductions in binding by monoclonal antibodies that were previously FDA-authorized.

Bolded sub-lineages are expanding in the United States as of June 10, 2023

More than 90% of circulating viruses have similar Spike receptor binding domain sequences

Lineage	**Spike RBD (residues 333-527) amino acid substitutions**						
	452	455	456	460	478	486	521
Reference sequence: XBB.1.5	L	L	F	K	K	P	P
XBB.1.9	—	—	—	—	—	S	—
XBB.1.5.70	—	F	L	—	—	—	—
XBB.1.16	—	—	—	—	R	—	—
EG, FL	—	—	L	—	—	—	—
EG.5, **EG.5.1.6**, **FL.1.5**	—	—	L	—	—	—	—
XBB.1.16.6, XBB.1.16.9, **FL.1.5.1, HN.1**	—	—	L	—	R	—	—
HV.1	R	—	L	—	—	—	—
HK.3	—	F	L	—	—	—	—
XBB.2.3	—	—	—	—	—	—	S
XBB.1.16, XBB.1.16.1	—	—	—	—	R	—	—

XBB.1.5 and XBB.1.16 Spike substitutions relative to BA.5



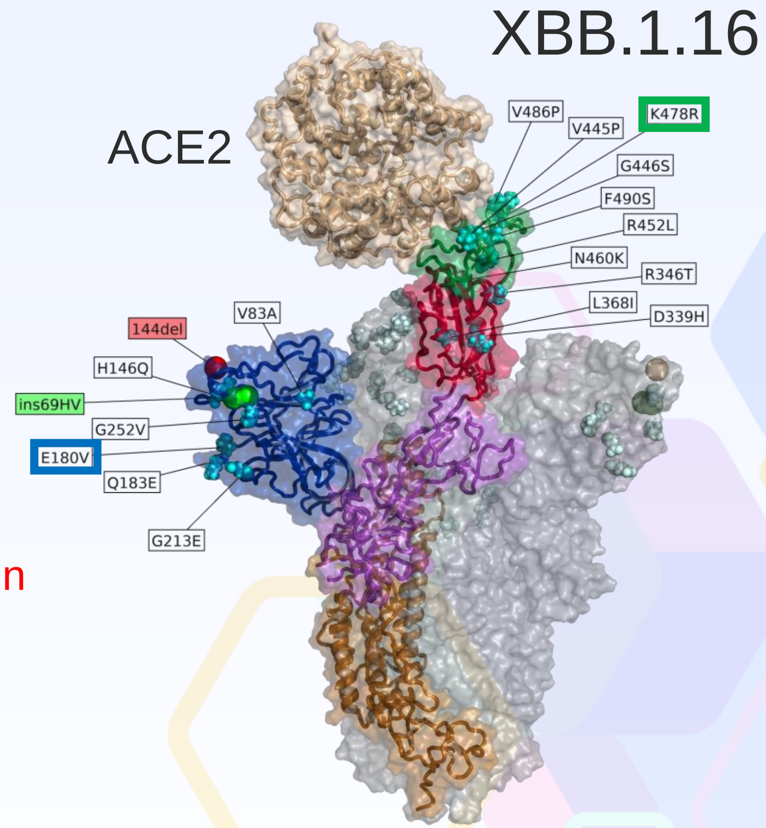
Receptor binding motif

Receptor binding domain

N-terminal domain

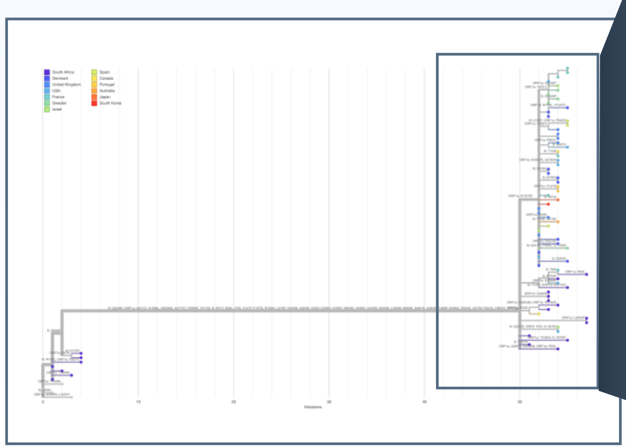
Remainder of S1

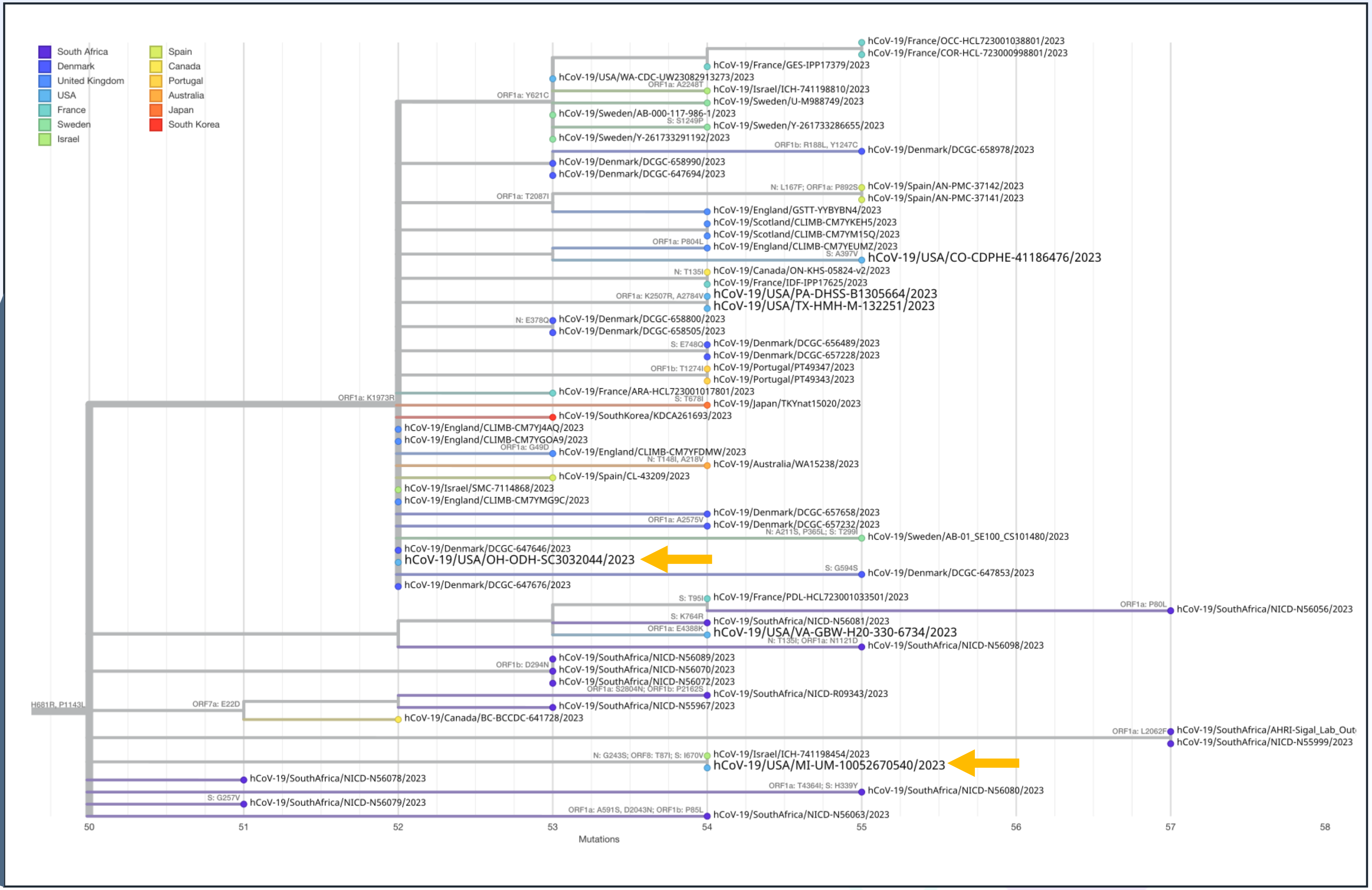
S2



BA.2.86 is a descendent of BA.2

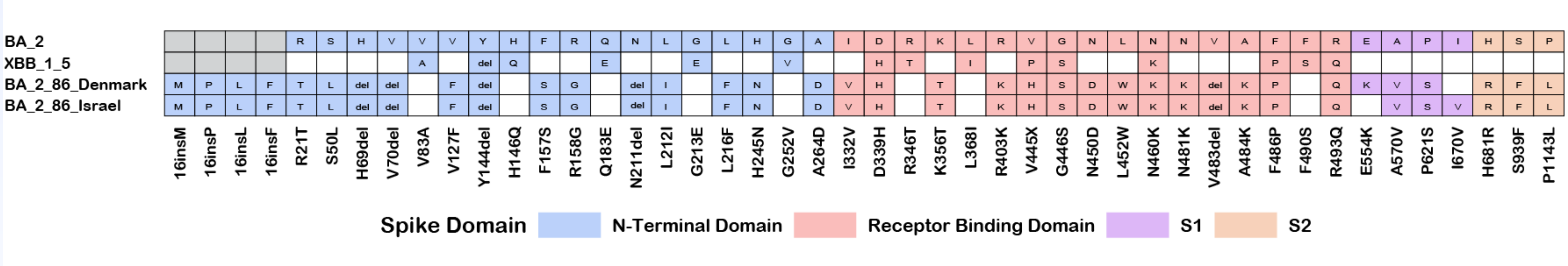
- Most closely related to BA.2
- BA.2 and its lineages circulated in spring 2022 before BA.5 viruses





Nexstrain (Roemer / Neher)

BA.2.86 has >30 amino acid substitions in spike in comparison to XBB.1.5



	16insM	16insP	16insL	16insF	R21T	S50L	H69del	V70del	V83A	V127F	Y144del	H146Q	F157S	R158G	Q183E
BA_2					R	S	H	V	V	V	Y	H	F	R	Q
XBB_1_5									A		del	Q			E
BA_2_86_Denmark	M	P	L	F	T	L	del	del		F	del		S	G	
BA_2_86_Israel	M	P	L	F	T	L	del	del		F	del		S	G	

	N211del	L212I	G213E	L216F	H245N	G252V	A264D	I332V	D339H	R346T	K356T	L368I	R403K	V445X	G446S
BA_2	N	L	G	L	H	G	A	I	D	R	K	L	R	V	G
XBB_1_5			E			V			H	T		I		P	S
BA_2_86_Denmark	del	I		F	N		D	V	H		T		K	H	S
BA_2_86_Israel	del	I		F	N		D	V	H		T		K	H	S

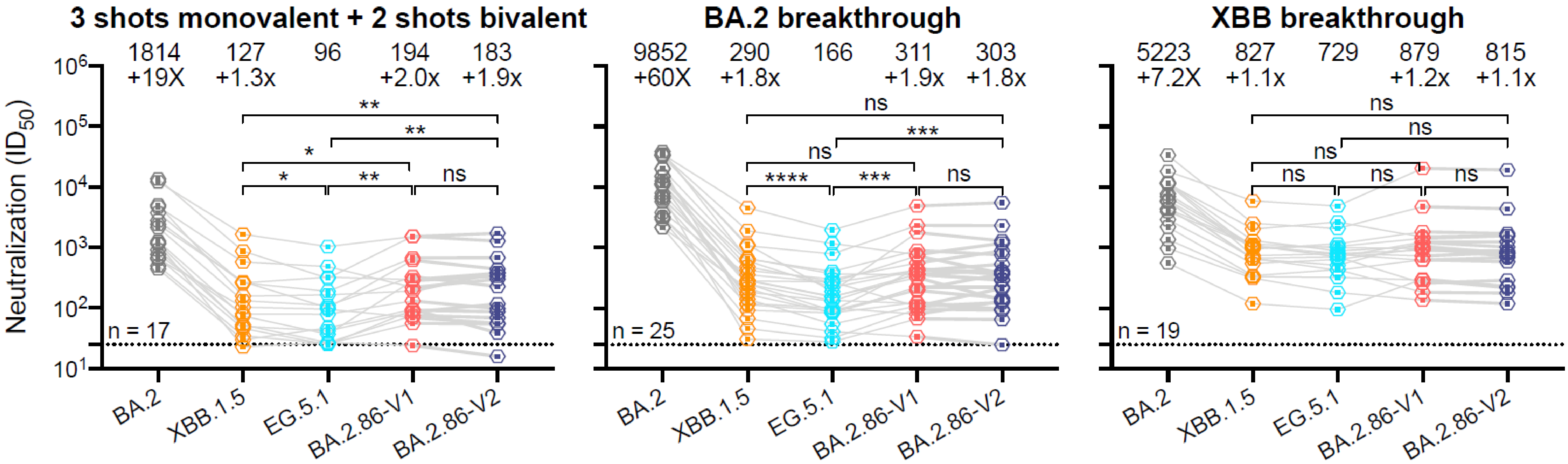
	N450D	L452W	N460K	N481K	V483del	A484K	F486P	F490S	R493Q	E554K	A570V	P621S	I670V	H681R	S939F	P1143L
BA_2	N	L	N	N	V	A	F	F	R	E	A	P	I	H	S	P
XBB_1_5			K				P	S	Q							
BA_2_86_Denmark	D	W	K	K	del	K	P		Q	K	V	S		R	F	L
BA_2_86_Israel	D	W	K	K	del	K	P		Q		V	S	V	R	F	L

Spike Domain 🟦 N-Terminal Domain 🟥 Receptor Binding Domain 🟪 S1 🟧 S2

- >30 amino acid substitutions in Spike in comparison to XBB.1.5
  - Variation between sequences due to missing data and sequencing artifacts

- First detected in specimen collected in late July, 2023
- As of 9/6 detected in 7 clinical specimens in 7 US states and 1 additional state in waste water
- Detected in 10 countries
- Small number of sequences

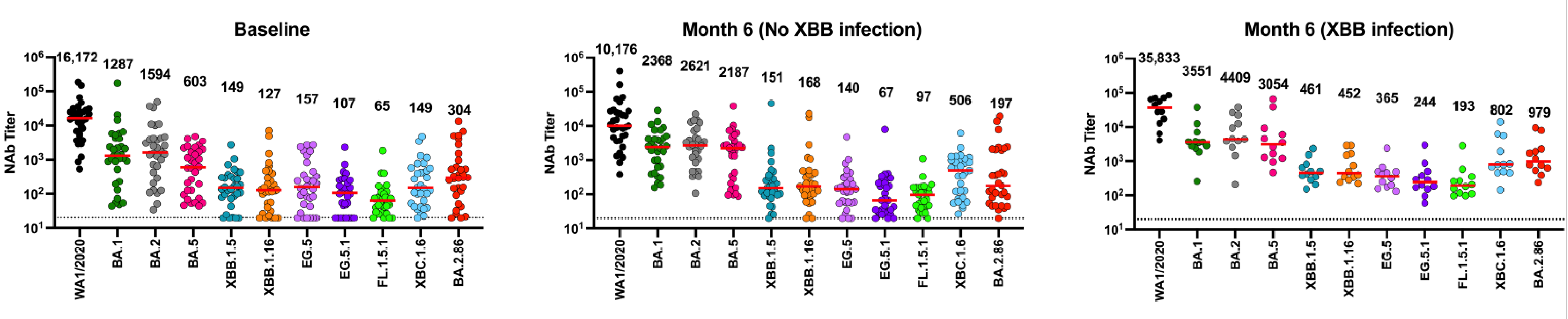
Reduction in pseudovirus neutralization is not detected using sera from people infected with XBB lineage viruses



Qian Wang
Dr. David D. Ho lab

No reduction in BA.2.86 pseudovirus neutralization is observed after bivalent vaccination, or after 6 months with or without XBB infection

SAVE
SARS-COV-2 ASSESSMENT OF VIRAL EVOLUTION



Lasrado et al. [Neutralization Escape by SARS-CoV-2 Omicron Subvariant BA.2.86 | bioRxiv]

Data generation with authentic viruses

- More than 90% of currently circulating viruses are XBB lineage viruses with 1-2 additional substitutions in RBD in comparison to XBB.1.5

- BA.2.86 is a newly detected lineage with > 30 amino acid substitutions in spike
  - Thus far, the number of viruses detected is still low
  - Sequence numbers are too low to calculate proportion (<0.05%)

- Preliminary pseudovirus neutralization data generated by multiple labs do not indicate a large reduction in neutralizing activity against BA.2.86

- CDC has generated a BA.2.86 isolates, is currently working on titrations before neutralization and will distribute to external laboratories for further examination

Summary

- More than 90% of currently circulating viruses are XBB lineage viruses with 1-2 additional substitutions in RBD in comparison to XBB.1.5

- BA.2.86 is a newly detected lineage with > 30 amino acid substitutions in spike
  - Thus far, the number of viruses detected is still low
  - Sequence numbers are too low to calculate proportion (<0.05%)

- Preliminary pseudovirus neutralization data generated by multiple labs do not indicate a large reduction in neutralizing activity against BA.2.86

- CDC has generated a BA.2.86 isolate, is currently working on titrations before neutralization and has begun distribution to external laboratories for further examination

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov