

Omicron

Update 01-Dec-2021

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cov.lanl.gov

- 1) Data set and reference spike sequence.
- 2) Dynamics: Botswana and South Africa.
- 3) Evidence suggesting outlier B.1.1.529-related viruses may be recombinants.
- 4) dN/dS ratios in different regions of the SARS-CoV-2 genome and Spike, focus on Omicron.

Omicron: B.1.1.529

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9:30 mountain time 12/01/2021

Pango lineage designation changes since last 11/23/2021: B.1.1 → B.1.1.263 → B.1.1.529

B.1.1.529: 308 Viruses in GISAID

Botswana, 20 sequences, earliest 11/11/2021

South Africa, 172 sequences, earliest 11/09/2021

Nations with sequences in GISAID, many noted in GISAID to be travelers or targeted sampling:

- Botswana	20	- Belgium	2
- Ghana	32	- Czech Republic	2
- Reunion	1	- England	9
- South Africa	172	- Germany	5
		- Italy	4
- Hong Kong	7	- Netherlands	13
- Japan	2	- Portugal	13
- Israel	1	- Scotland	9
		- Spain	1
- Canada	2	- Sweden	1
- Australia	3		
- Brazil	2		

Omicron is highly mutated compared to other variants studied to date, see spread sheet.



Classification Group	Date of addition to website listing, newest entries highlighted in yellow	WHO designation, * means it is WHO listed for further monitoring as of Nov. 26, 2021	Pango lineage where the form of Spike is most commonly found, see columns L and M for complete list. Grey lettering with an underscore indicates an ancestral amino acid. Colors as in column E.	Most common Spike backbones of variant form. NTD supersite, RBD, positive charge near the furin cleavage site or H655Y. Liu et al. bioRxiv 2021, 10.1101/2021.08.12.456173 & Alba et al. bioRxiv 2021, 10.1101/2021.08.05.455290
WHO VOC*	Aug. 9, 2021	Alpha α	Alpha (B.1.1.7 + Q.* Pango sublineages)	H69-,V70-,Y144-,N501Y,A570D,D614G,P681H,T716I,S982A,D1118H
	Aug. 9, 2021	Beta β	B.1.351	D80A,D215G,L242-,A243-,L244-,K417N,E484K,N501Y,D614G,A701V
	Aug. 9, 2021	Gamma γ	P.1	L18F,T20N,P26S,D138Y,R190S,K417T,E484K,N501Y,D614G,H655Y,T1027I,V1176F
	Aug. 9, 2021	Delta δ	Delta (B.1.617.2 + AY.* Pango sublineages)	T19R,T95I,G142D,E156-,F157-,R158G,L452R,T478K,D614G,P681R,D950N
	Nov. 26, 2021	Omicron ο	B.1.1.529 (Previously called B.1.1)	A67V,H69-,V70-,T95I,G142D,V143-,Y144-,Y145-,N211-,L212I,+214EPE,G339D,S371L,S373P,S375F,K417N,N440K,G446S,S477N,T478K,E484A,Q493R,G496S,Q498R,N501Y,Y505H,T547K,D614G,H655Y,N679K,P681H,N764K,D796Y,N856K,Q954H,N969K,L981F
WHO VOI*	Aug. 9, 2021	Lambda Λ	C.37	G75V,T76I,R246N,S247-,Y248-,L249-,T250-,P251-,G252-,D253-,L452Q,F490S,D614G,T859N
	Aug. 9, 2021	Mu μ	B.1.621	T95I,+143T,Y144S,Y145N,R346K,E484K,N501Y,D614G,P681H,D950N
*WHO Variant of Concern or interest				
Rare but highly complex Spike variants recently identified in Africa				
Recent rare complex variants	Sept. 11, 2021	*	C.1.2	P9L,C136F,Y144-,R190S,D215G,A243-,L244-,Y449H,E484K,N501Y,D614G,H655Y,N679K,T716I,T859N
	Nov.18, 2021	*	B.1.640 (Previously called B.1 or B.1.576)	P9L,E96Q,C136-,N137-,D138-,P139-,F140-,L141-,G142-,V143-,Y144-,R190S,I210T,R346S,N394S,Y449N,F490R,N501Y,D614G,P681H,T859N,D936H

Other variants of interest and concern over 2021:

Earlier lineage expansion, but transient	Aug. 9, 2021	* Iota ι	B.1.526	L5F,T95I,D253G,E484K,D614G,A701V
	Aug. 9, 2021	* Eta η	B.1.525	Q52R,A67V,H69-,V70-,Y144-,E484K,D614G,Q677H,F888L
	Aug. 9, 2021	Zeta ζ	P.2	E484K,D614G,V1176F
	Aug. 9, 2021	Epsilon ε	B.1.429 (+B.1.427)	S13I,W152C,L452R,D614G
	Aug. 9, 2021		B.1.1.519	T478K,D614G,P681H,T732A
	Aug. 9, 2021		B.1.637 (previously grouped in B.1.526)	D80G,Y144-,F157S,L452R,D614G,T859N,D950H
	Aug. 9, 2021		C.36.3	S12F,H69-,V70-,W152R,R346S,L452R,D614G,Q677H,A899S
	Aug. 9, 2021		B.1.1.318 (B.1.1.318 + AZ.* Pango sublineages)	T95I,Y144-,E484K,D614G,P681H,D796H
	Nov.18, 2021	*	AZ.5 (Formerly a B.1.1.318 Pango sublineage)	D80Y,T95I,Y144-,W258L,E484K,D614G,P681H,D796H
	Aug. 9, 2021		B.1.619	I210T,N440K,E484K,D614G,D936N,S939F,T1027I
	Aug. 9, 2021		B.1.620	P26S,H69-,V70-,V126A,Y144-,L242-,A243-,L244-,H245Y,S477N,E484K,D614G,P681H,T1027I,D1118H
	Sept. 11, 2021		B.1	T19R,E484K,D614G,D950N
	Aug. 9, 2021	* Kappa κ	B.1.617.1	T95I,G142D,E154K,L452R,E484Q,D614G,P681R,Q1071H
	Aug. 9, 2021		A.23.1	F157L,V367F,Q613H,ancestral D614_,P681R
	Aug. 9, 2021		A.27	L18F,L452R,N501Y, ancestral D614_,A653V,H655Y,D796Y,G1219V
	Aug. 9, 2021		B.1.177.82	A222V,A262S,P272L,D614G
	Aug. 9, 2021		B.1.234	G142S,E180V,D614G Q677H
	Aug. 9, 2021		B.1.1.284	M153T,G184S,D614G,Q677H
	Aug. 9, 2021		B.1.466.2	N439K,D614G,P681R
	Aug. 9, 2021		R.1	W152L,E484K,D614G,G769V
	Aug. 9, 2021		B.1.258.17	H69-,V70-,L189F,N439K,D614G,V772I
	Aug. 9, 2021		B.1.575	S494P,D614G,P681H,T716I
	Aug. 9, 2021		B.1.214.2	+214TDR,Q414K,N450K,D614G,T716I
	Aug. 9, 2021		B.1.1.523	E156-,F157-,R158-,F306L,E484K,S494P,D614G,E780A,D839V,T1027I
	Aug. 9, 2021		P.4	G142V,N164K,Q173K,L452R,D614G,S704L,I720V,V1176F

Mutation list of the most common form of Spike among Omicron sequences



Note: This reference sequence was derived from a small set of sequences available 11/23/2021 from Botswana, South African and Hong Hong. By 11/29/2021 there were 176 sequences from a dozen countries available, and spikes with this set of mutations have remained the most commonly sampled form of Spike in the lineage in GISAID.

Codon aligned curated reference sequences in fasta files, that include B.1.1.529 can be found here:

GISAID -> EpiCoV -> Downloads -> LANL Alignments

NTD

A67V,**H69-**,**V70-**,T95I,**G142D**,**V143-**,**Y144-**,**Y145-**,**N211-**,L212I,+**214EPE**,

RBD

G339D,S371L,S373P,S375F,K417N,N440K,G446S,S477N,T478K,E484A,Q493R,G496S,Q498R,N501Y,Y505H,

T547K,D614G,**H655Y**,**N679K**,**P681H**,N764K,D796Y,N856K,**Q954H**,**N969K**,**L981F**

Furin cleavage enhancing

Heptad Repeat 1

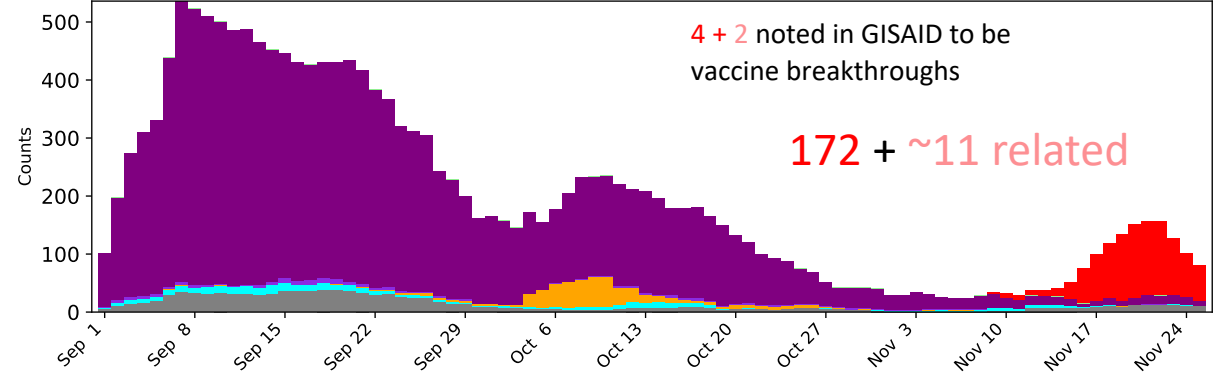
Omicron: B.1.1.529 South Africa

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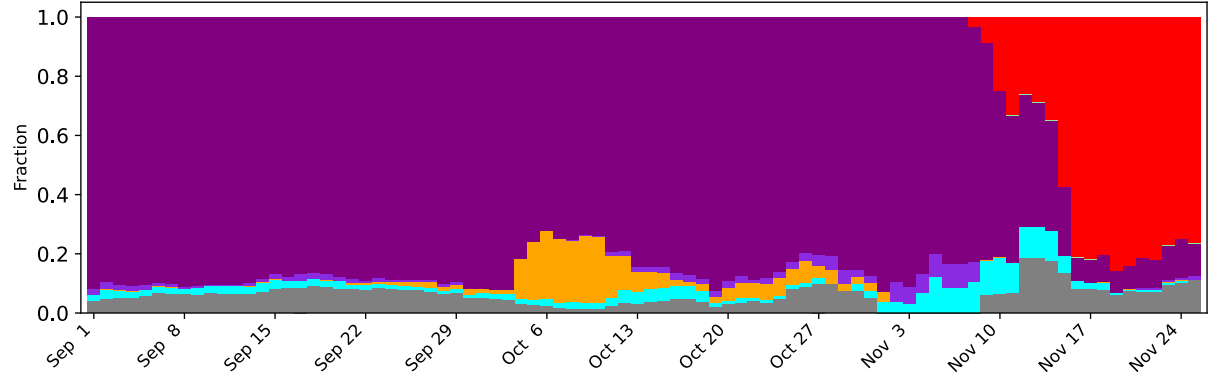


- █ Omicron
- █ Omicron-related
- █ B.1.640
- █ Delta_AY...
- █ Delta_B.1.617.2
- █ Beta
- █ C.1.2

South-Africa: 2489 sequences



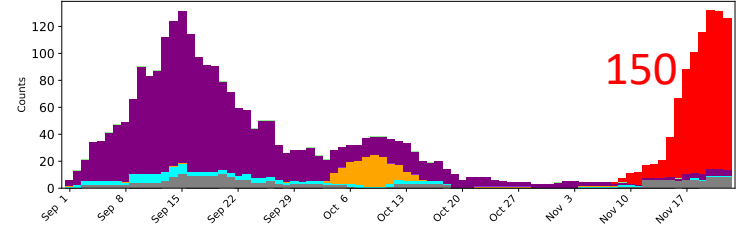
South-Africa: 2489 sequences



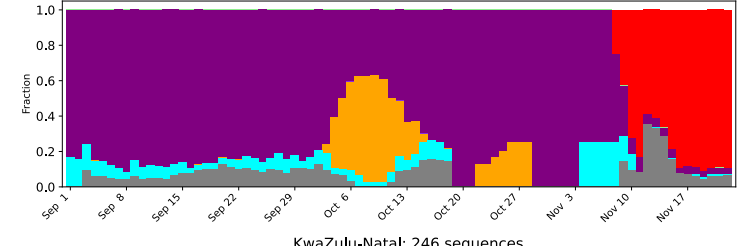
Western Cape 14



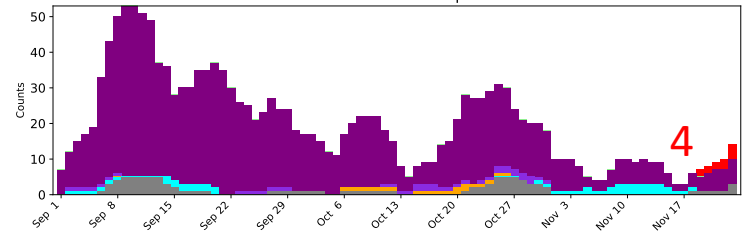
South-Africa.Gauteng: 519 sequences



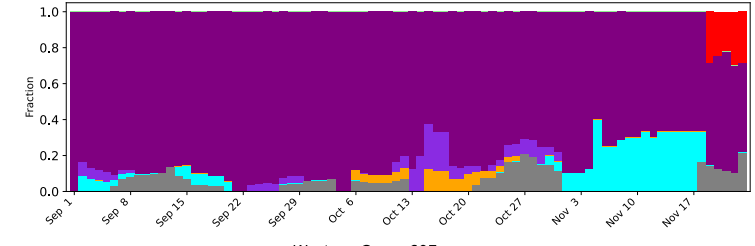
South-Africa.Gauteng: 519 sequences



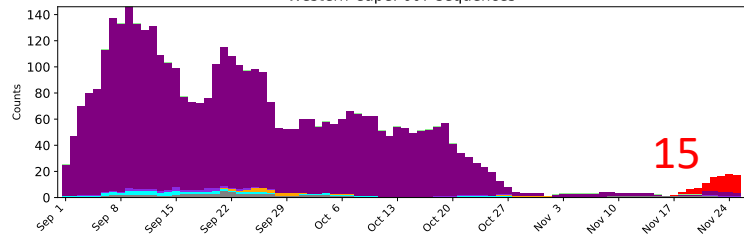
KwaZulu-Natal: 246 sequences



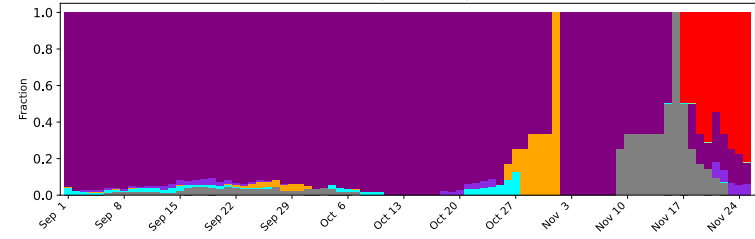
KwaZulu-Natal: 246 sequences



Western-Cape: 607 sequences



Western-Cape: 607 sequences



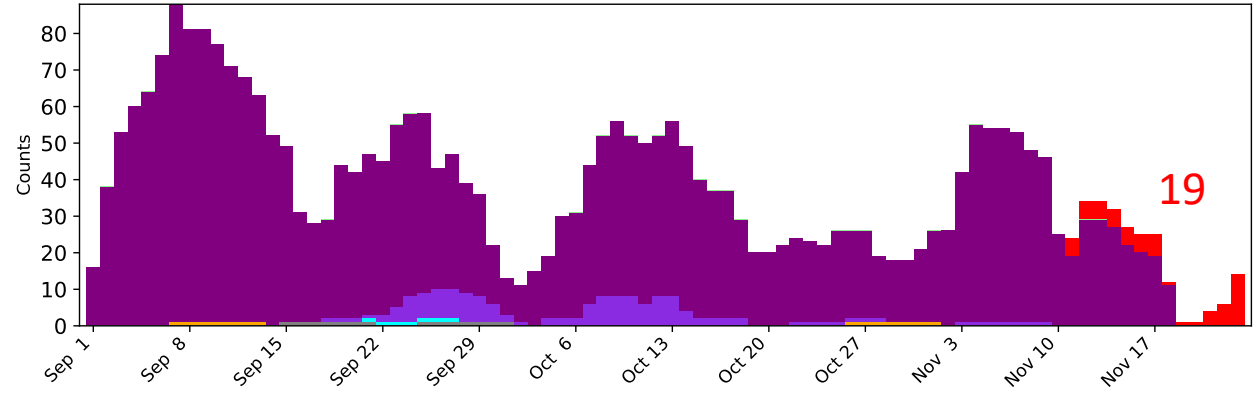
Omicron: B.1.1.529: Botswana

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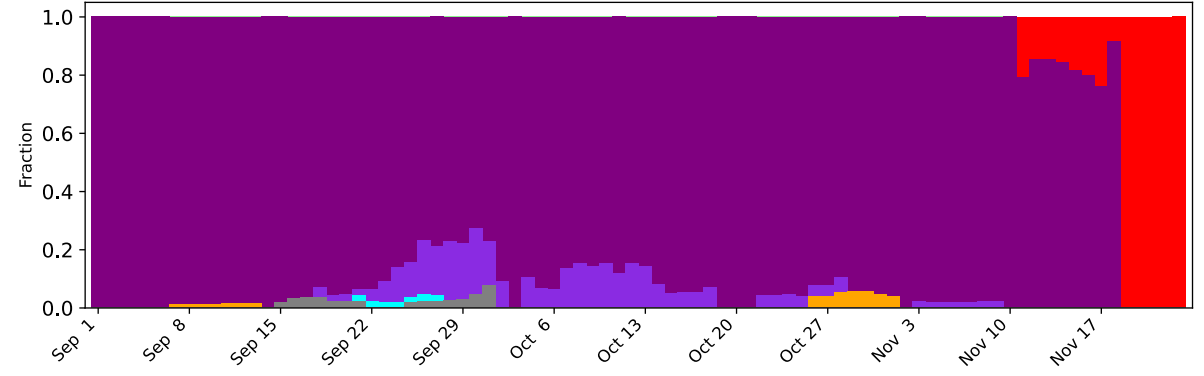


- █ Omicron
- █ Omicron-related
- █ B.1.640
- █ Delta_AY...
- █ Delta_B.1.617.2
- █ Beta
- █ C.1.2
- █ other

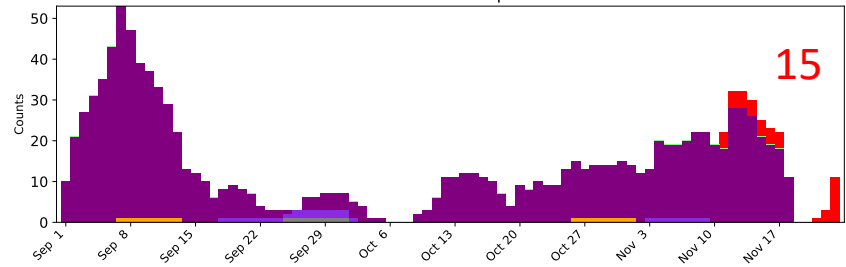
Botswana: 465 sequences



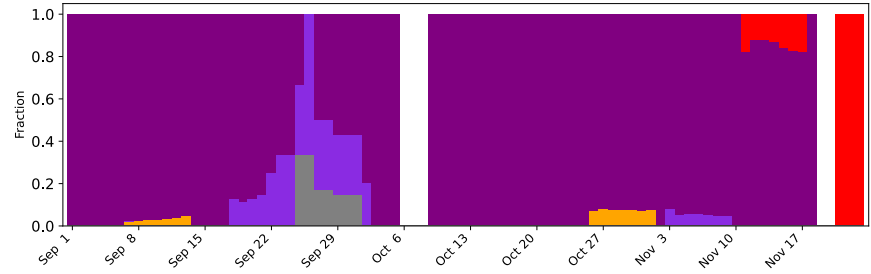
Botswana: 465 sequences



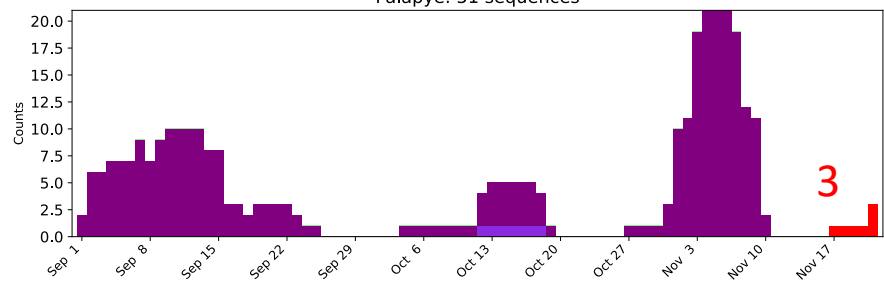
Gaborone: 178 sequences



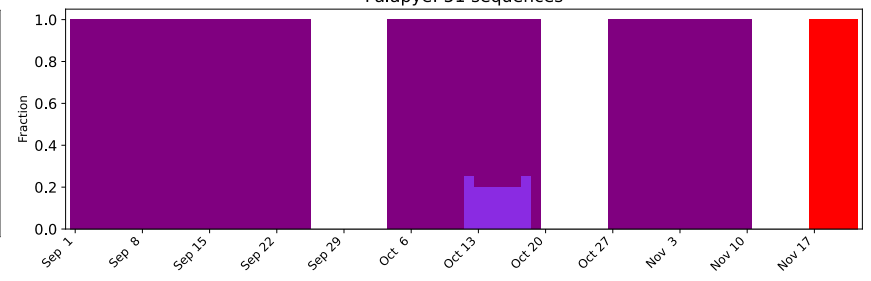
Gaborone: 178 sequences



Palapye: 51 sequences

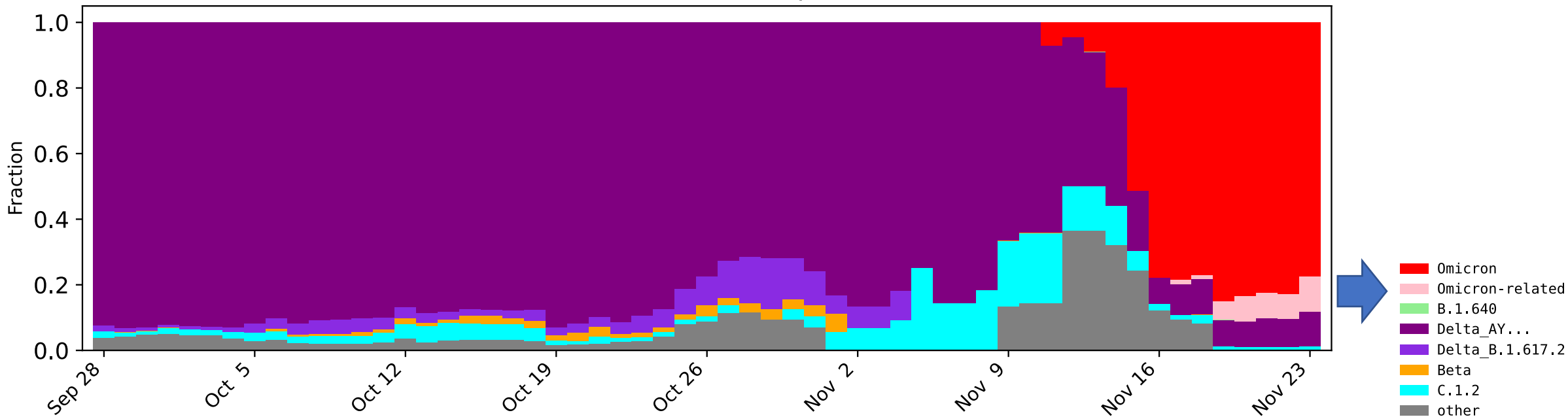


Palapye: 51 sequences



From 11/28/2021:

South-Africa: 693 sequences



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Omicron: 10 sequences that are B.1.1.529-related, but not designated as such, were found. Some may be recombinants.



Pango lineage

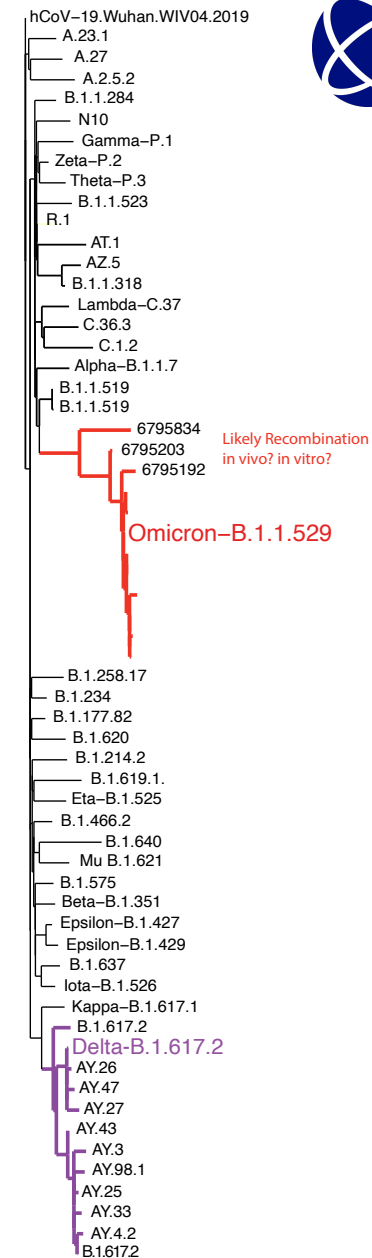
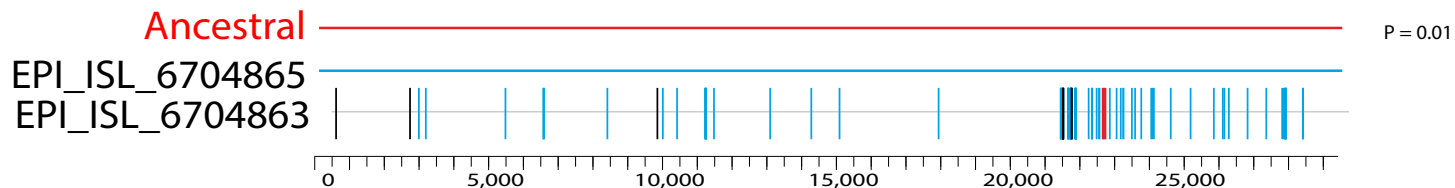
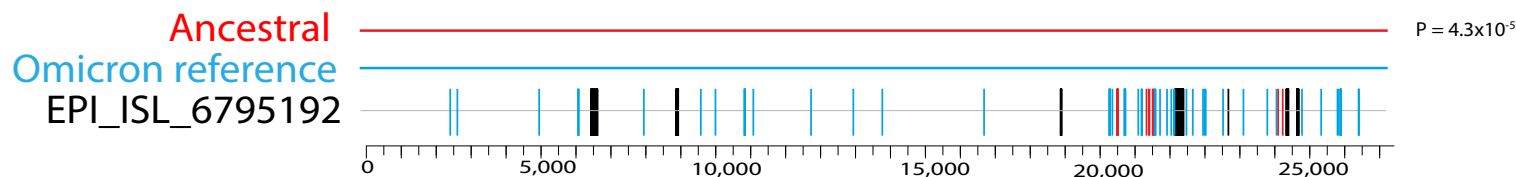
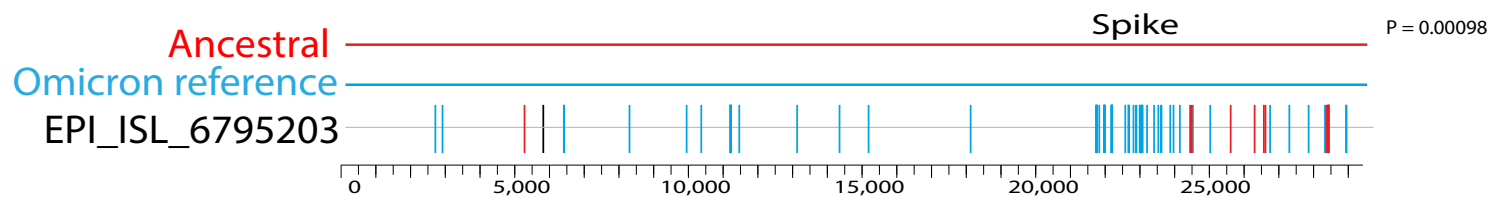
EPI_ISL	Date	Location	Pango Lineage
EPI_ISL_6795834	2021-11-17	Africa / South Africa / Gauteng / Tshwane	B.1.1.37
EPI_ISL_6795203	2021-11-23	Africa / South Africa / KwaZulu-Natal	B.1.1.263
EPI_ISL_6704863	2021-11-19	Africa / South Africa / Gauteng / Pretoria	None
EPI_ISL_6704865	2021-11-19	Africa / South Africa / Gauteng / Pretoria	None
EPI_ISL_6704866	2021-11-19	Africa / South Africa / Gauteng / Pretoria	None
EPI_ISL_6704868	2021-11-20	Africa / South Africa / Gauteng / Pretoria	None
EPI_ISL_6704869	2021-11-20	Africa / South Africa / Gauteng / Pretoria	None
EPI_ISL_6704876	2021-11-20	Africa / South Africa / Gauteng / Pretoria	None
EPI_ISL_6795192	2021-11-09	Africa / South Africa / Gauteng / Pretoria	None
EPI_ISL_6810486	2021-11-19	Africa / South Africa / Gauteng / Pretoria	None

None -> "B.1.1.529 (probable)"

Vaccine Breakthrough

Vaccine Breakthrough

Full Genome Evidence for Recombination

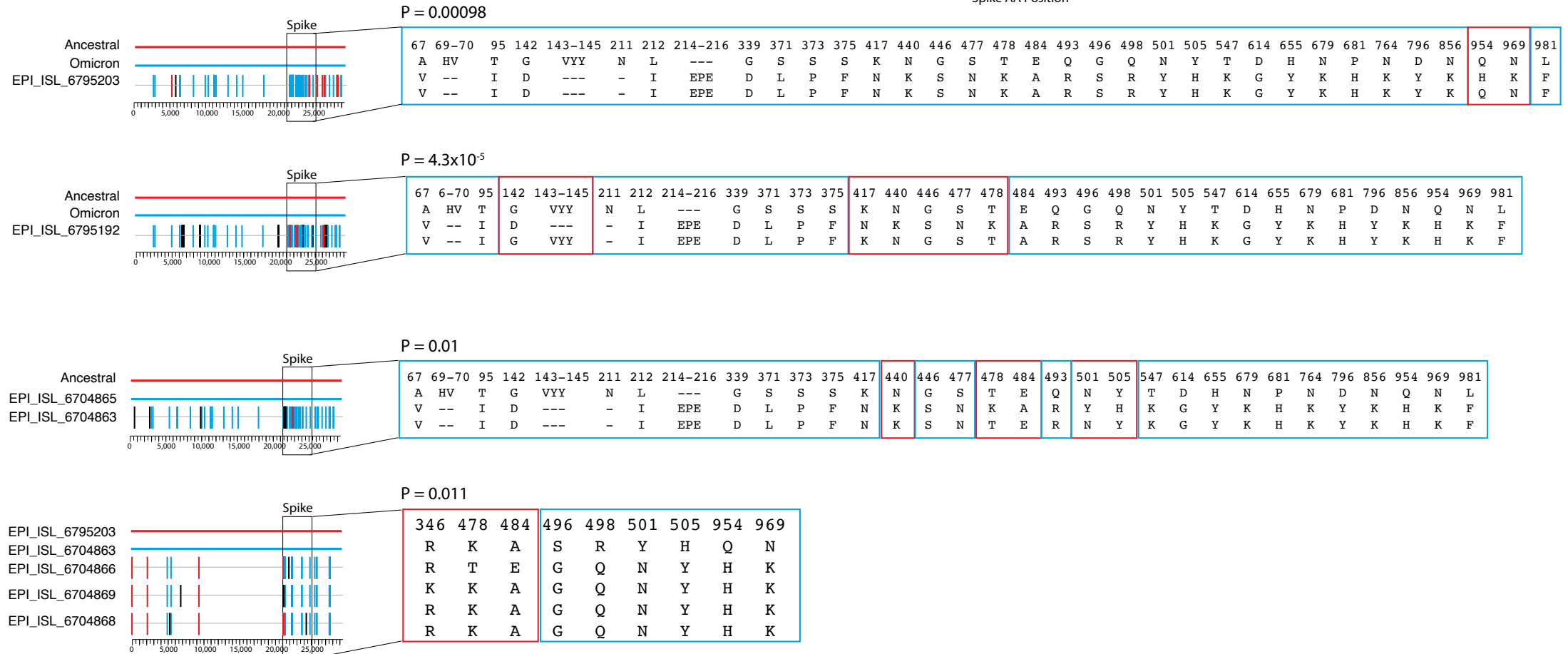


Every difference between the ancestral Wuhan sequence and the Omicron reference sequence is marked with a bar. Red matches ancestral, blue the Omicron reference, blacks are unique to the variant.



The impact of recombination on Spike

A Full Genome Evidence for Recombination



B Effect of Recombination on Spike

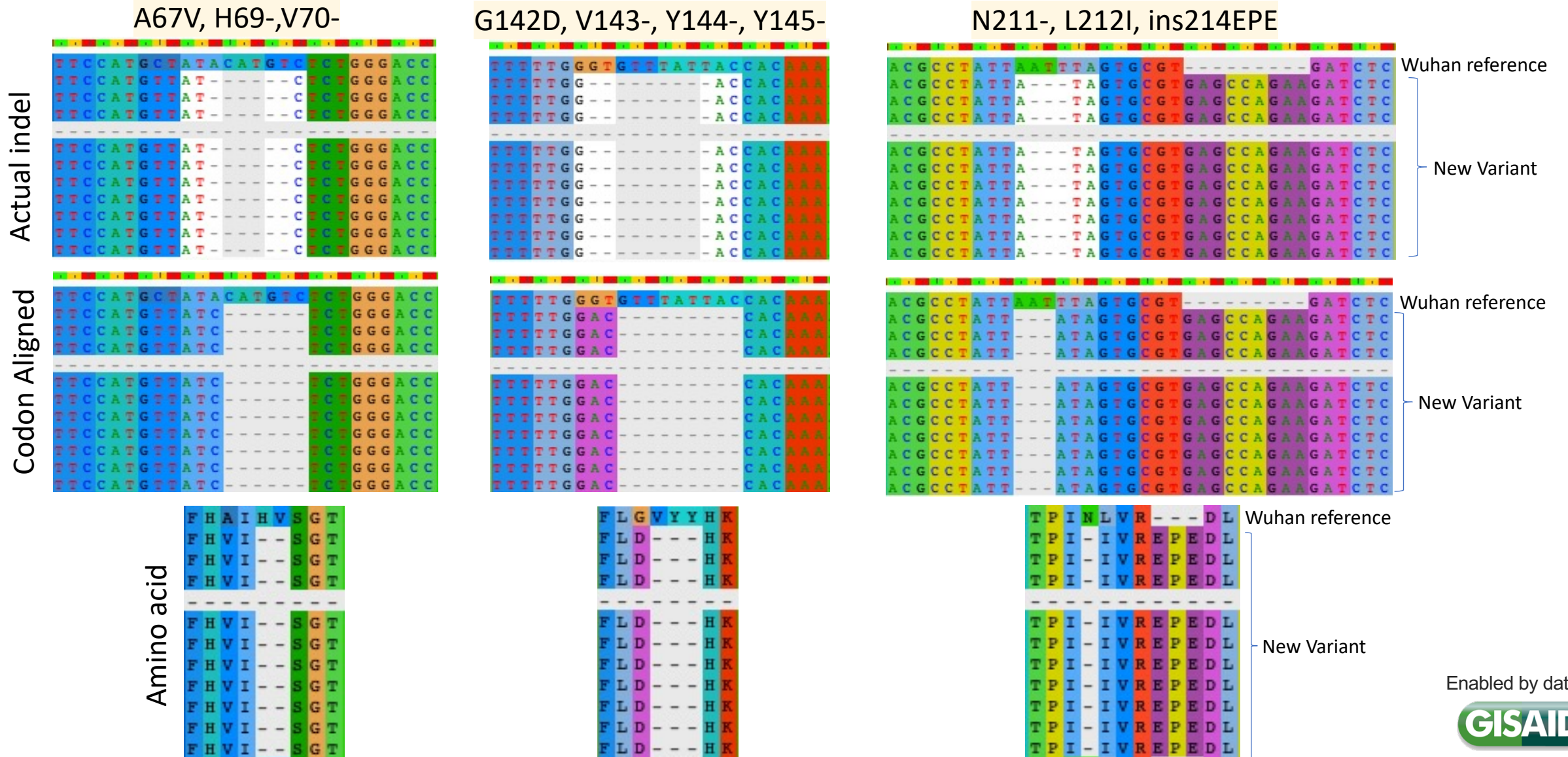
Spike AA Position

New B.1.1.529 variant from Botswana/South Africa, Insertions and Deletions



B.1.1.:

A67V, H69-, V70-, T95I, G142D, V143-, Y144-, Y145-, N211-, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F

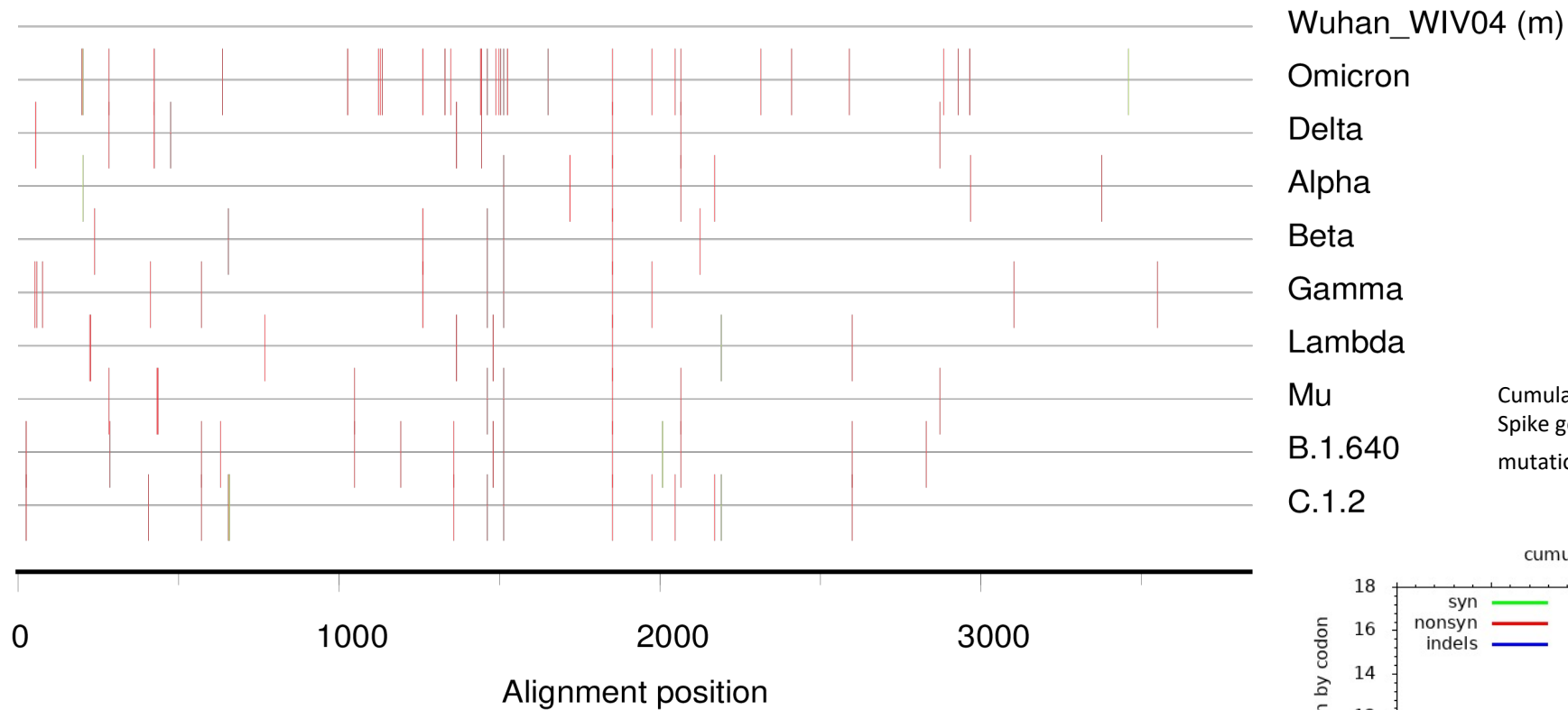




A view of synonymous and nonsynonymous substitutions in Spike and a simple dN/dS comparing VOI/VOC sequences to the ancestral virus.

dN/dS

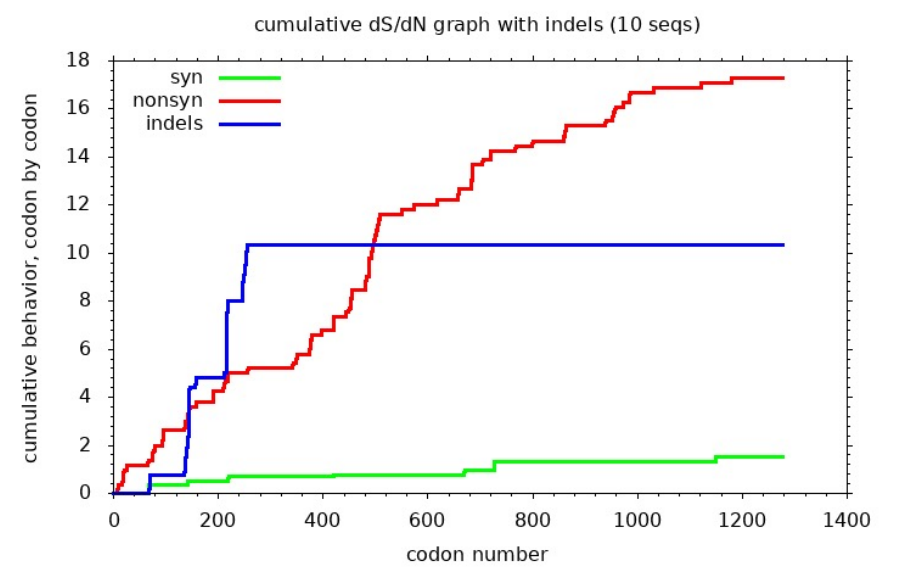
Silent and Non-silent Mutations compared to the Wuhan reference sequence



Omicron: dN/dS = 2.95
 Observed:
 Silent: 3/842 possible
 Nonsilent: 31/2961 possible

Cumulative silent and non-silent mutations in codons across the Spike gene show regions in Spike were nonsynonymous mutations cluster (steep red line) or are rare (flat sections).

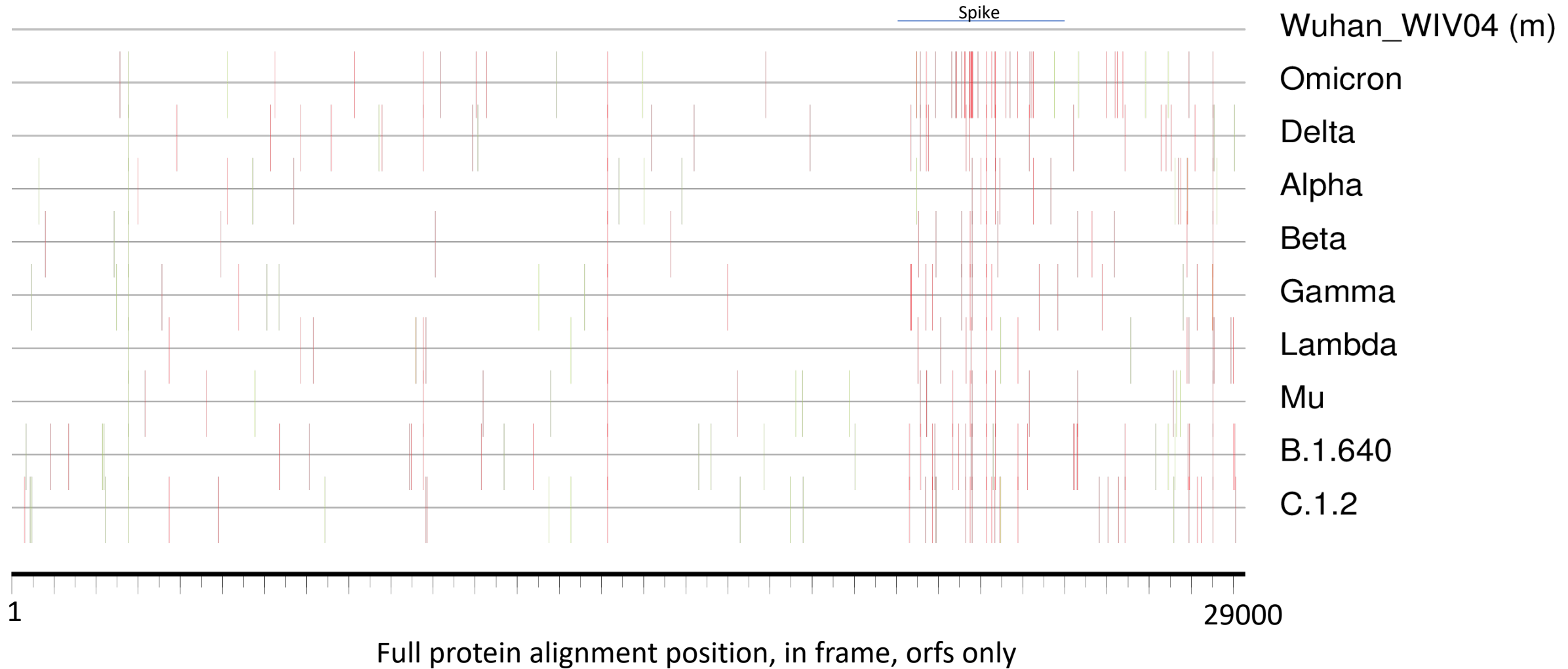
Average dN/dS for each reference strain to Wuhan is 2.4





Non-synonymous mutations tend to cluster in Spike relative to the other sections of the proteome.
Omicron isn't particularly highly mutated relative to other variants outside of Spike.

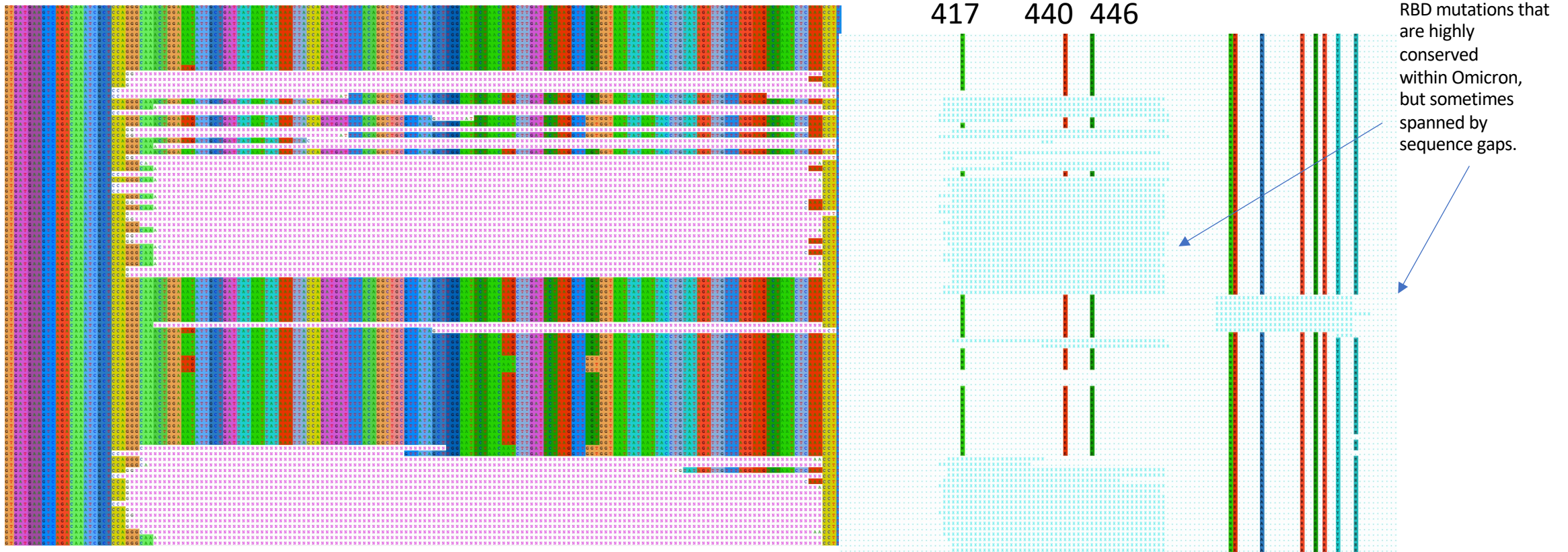
Silent and Non-silent Mutations compared to the Wuhan reference sequence



Two things to be mindful of for determining reference strains: currently there are still lots of gappy sequences, so an Omicron consensus sequence derived treating N's as ancestral will undercount mutation frequencies in the lineage.



Sequence gaps in Spike at the DNA level (left, pink N's) and protein level (right, blue x's)



Vertical stripes are amino acid changes in Omicron relative to the Wuhan sequence

Also there is an insertion in Omicron at Spike 214.



The discovery of Omicron and the analysis presented here relied upon the work of many, acknowledged here are contributors of some of the first key sequences in GISAID:

B.1.1.529 GISAID:

Botswana Harvard HIV Reference Laboratory: Sikhulile Moyo, Wonderful T. Choga, Dorcas Maruapula, Keoratile Ntshambiwa, Sefetogi Ramaologa, Thongbotho Mphoyakgosi, Boitumelo Zuze, Botshelo Radibe, Legodile Kooepile, Ontlametse T. Bareng, Pamela Smith-Lawrence, Kgomotso Moruisi, Roger Shapiro, Shahin Lockman, Joseph Makhema, Mphaphi B. Mbulawa, Mosepele Mosepele, Simani Gaseitsiwe

South Africa:

LANCET LABORATORY National Institute for Communicable Diseases of the National Health Laboratory Service: Amoako DG, Everatt J, Scheepers C, Glass A, Viana R, Mohale T, Ntuli N, Mahlangu B, Mnguni A, Ismail A, Bhiman JN

Division of Medical Virology, National Health Laboratory Service (NHLS), Tygerberg Hospital / Stellenbosch University:

Jean Maritz, Nadine Cronje, Petra Raimond, Tongai Maponga, Shannon Wilson, Kamela Mahlakwane, Tania Stander, Gert van Zyl, Wolfgang Preiser

CERI, Centre for Epidemic Response and Innovation, Stellenbosch University and KRISP, KZN Research Innovation and Sequencing Platform, UKZN

Amy Strydom, Adriano Mendes, Micheala Davids, Sim Mayaphi and Marietjie Venter, NGS-SA (Scheepers C, Hsiao M, von Gottberg A, Bhiman J, Lessells R, Bester P, Engelbrecht S, Preiser W, Mdlalose N, Mlisana K, Goedhals D, Everatt J, Amoaka D, Makatini Z, Hardie D, Maponga T, Iranzadeh A, Williamson C, Venter M, Oluwakemi M, Nyaga M) Giandhari J, Pillay S, Naidoo Y, Ramphal U, Ramphal Y, Arisha Maharaj, Moir M, San JE, Tshiabuila D, Tegally H, Wilkinson E, de Oliveira T

With thanks also to the many others whose work enabled the resolution of this variant new and its early trajectory

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