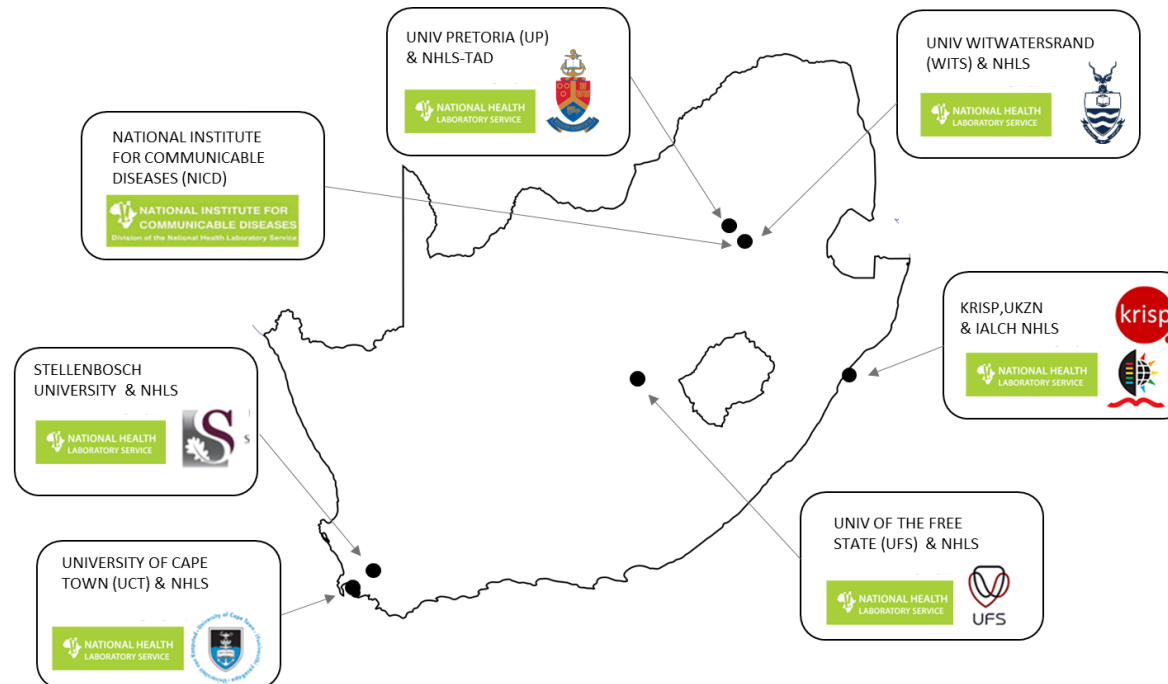


SARS-CoV-2 Sequencing Update 15 July 2022



Supported by the DSI and the SA MRC

Msomi N, Mlisana K, et al. Lancet Microbe 2020

The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 15 July 2022 at 15h28



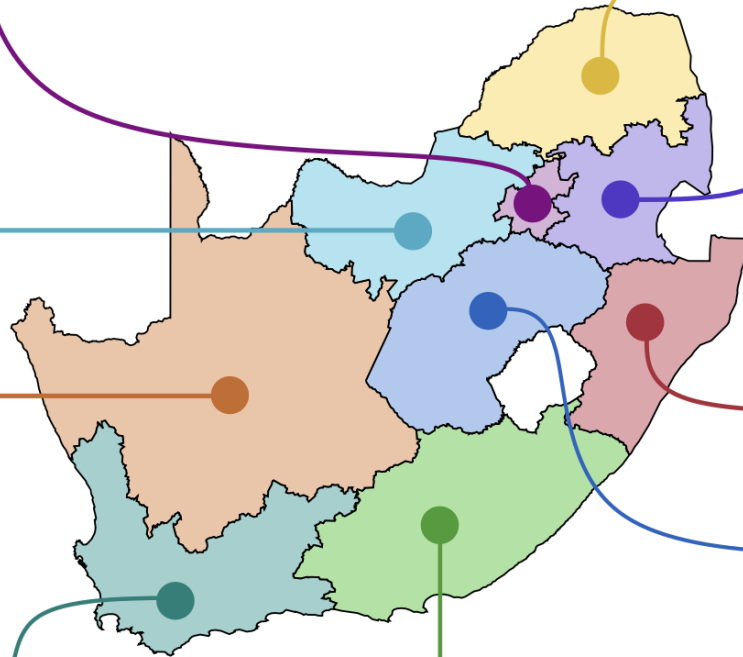
Data license: <https://www.gisaid.org/registration/terms-of-use/>

Elbe, S., and Buckland-Merrett, G. (2017) Data, disease and diplomacy: GISAID's innovative contribution to global health. *Global Challenges*, 1:33-46. DOI: 10.1002/gch2.1018 PMCID: 31565258

Shu, Y., McCauley, J. (2017) GISAID: Global initiative on sharing all influenza data – from vision to reality. *EuroSurveillance*, 22(13) DOI: 10.2807/1560-7917.ES.2017.22.13.30494 PMCID: PMC5388101

SARS-CoV-2

GENOMIC SURVEILLANCE epiweeks 39 (2021) - 27 (2022)



Gauteng ↑ PTP: 5.0%

Genomes Cases
5 443 (29.5%) 398 744 (37.0%)

Genomes deposited in the last week

1 2 44 29 4

North West - PTP: 3.5%

Genomes Cases
903 (4.9%) 50 130 (4.6%)

Genomes deposited in the last week

3 3

Northern Cape ↓ PTP: 1.9%

Genomes Cases
761 (4.1%) 24 632 (2.3%)

Genomes deposited in the last week

1 7 8

Western Cape - PTP: 6.4%

Genomes Cases
4 390 (23.8%) 188 561 (17.5%)

Genomes deposited in the last week

3 6 1 132 42

Eastern Cape - PTP: 3.6%

Genomes Cases
1 243 (6.7%) 73 569 (6.8%)

Genomes deposited in the last week

18 21 3

Limpopo - PTP: 4.8%

Genomes Cases
1 367 (7.4%) 36 317 (3.4%)

Genomes deposited in the last week

1 14 29 3

Mpumalanga - PTP: 5.6%

Genomes Cases
1 658 (9.0%) 50 102 (4.6%)

Genomes deposited in the last week

1 10 14 29

KwaZulu-Natal - PTP: 2.5%

Genomes Cases
2 032 (11.0%) 203 255 (18.8%)

Genomes deposited in the last week

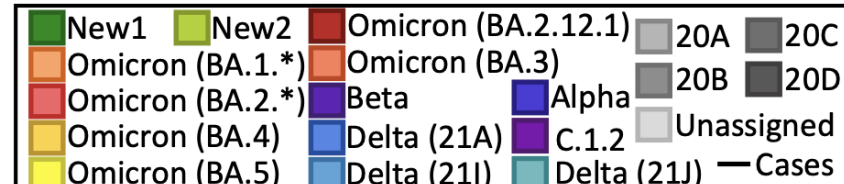
54 24 84 1

Free State - PTP: 4.6%

Genomes Cases
645 (3.5%) 53 689 (5.0%)

Genomes deposited in the last week

1



578 genomes added since the previous report

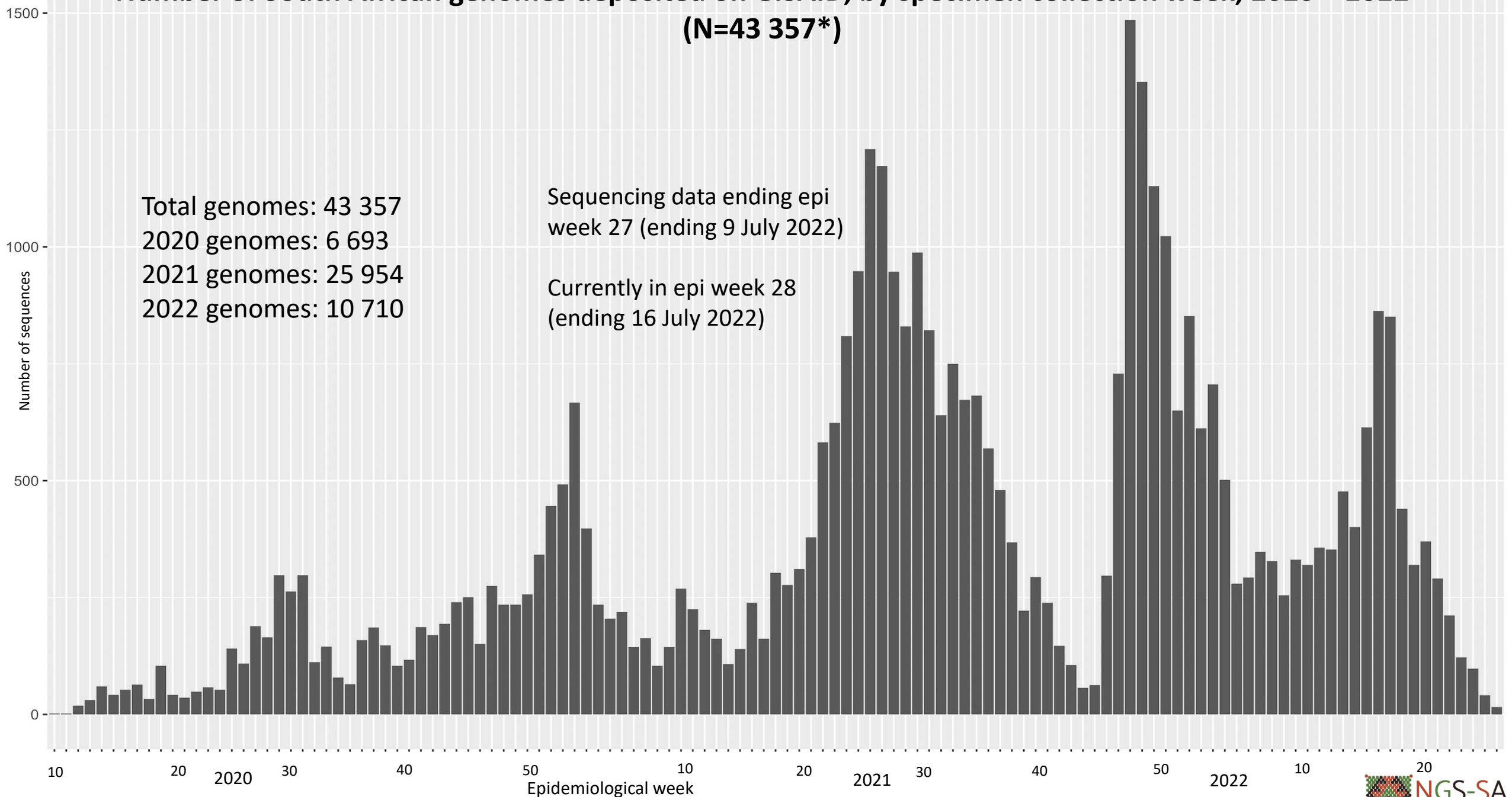


Bar graphs represent genomes sequenced per epiweek, with lines representing cases by collection date (weeks 39 [2021] – 27 [2022])

Genomes and cases presented as provincial total (percentage of national total) for epiweeks 39 (2021) – 27 (2022)

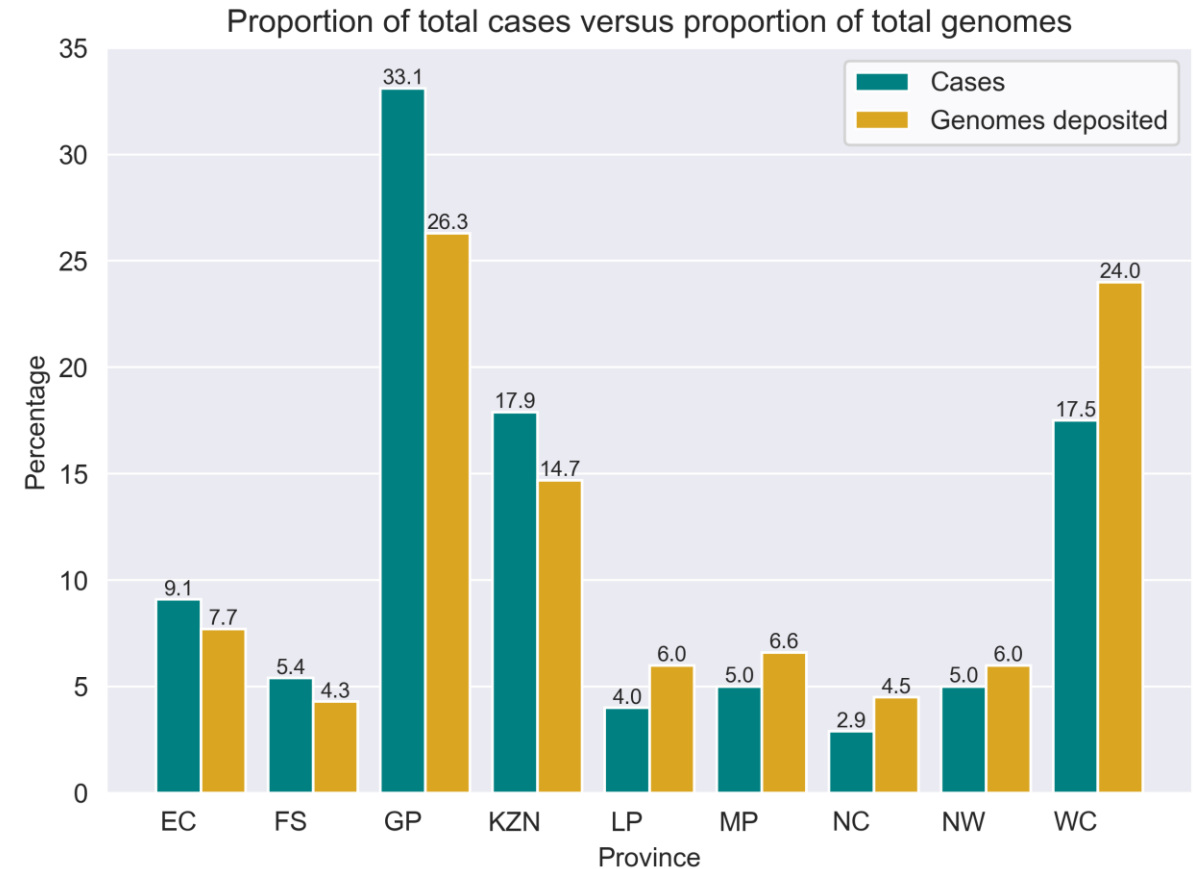
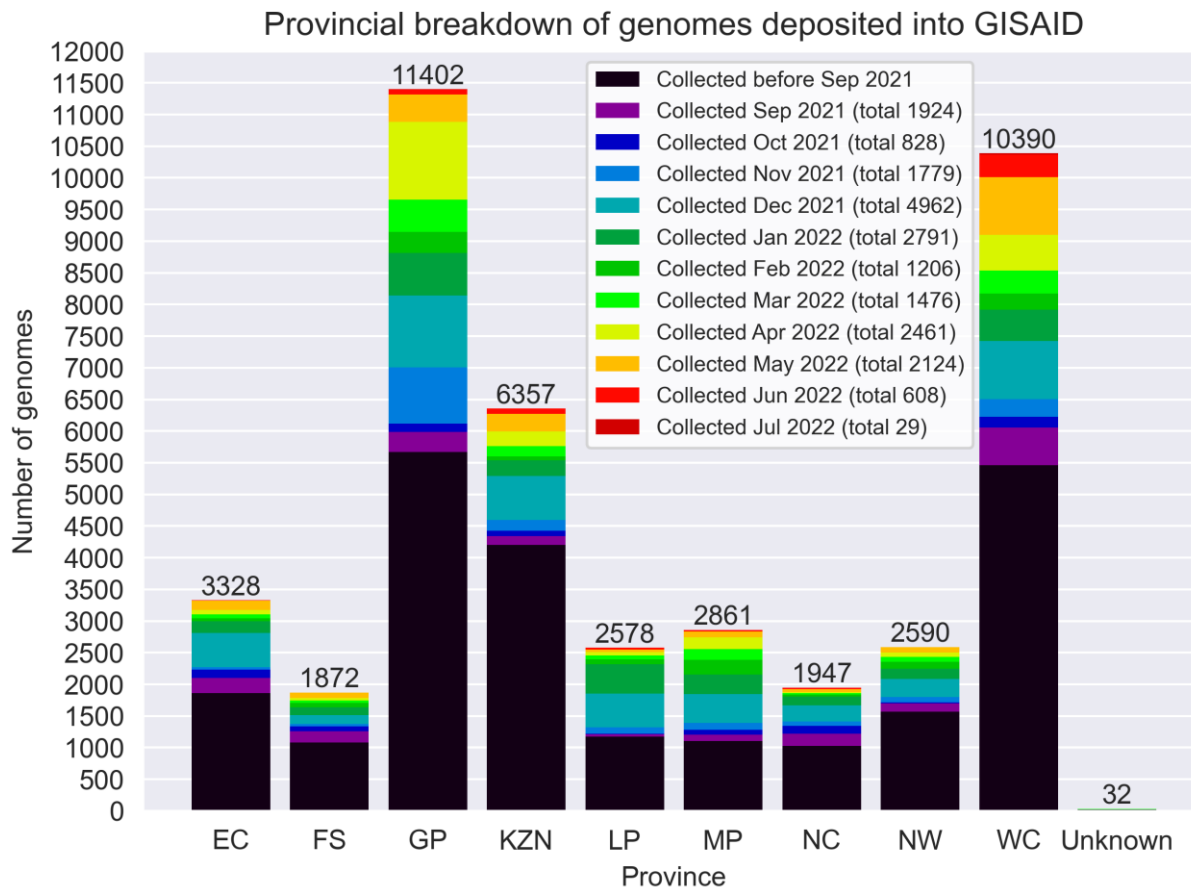
PTP: percentage testing positive in week 27 (03 July 2022 – 09 July 2022); arrow indicates direction of change since previous week (26 June 2022 – 02 July 2022) if change was significant ($P < 0.05$)

Number of South African genomes deposited on GISAID, by specimen collection week, 2020 – 2022 (N=43 357*)



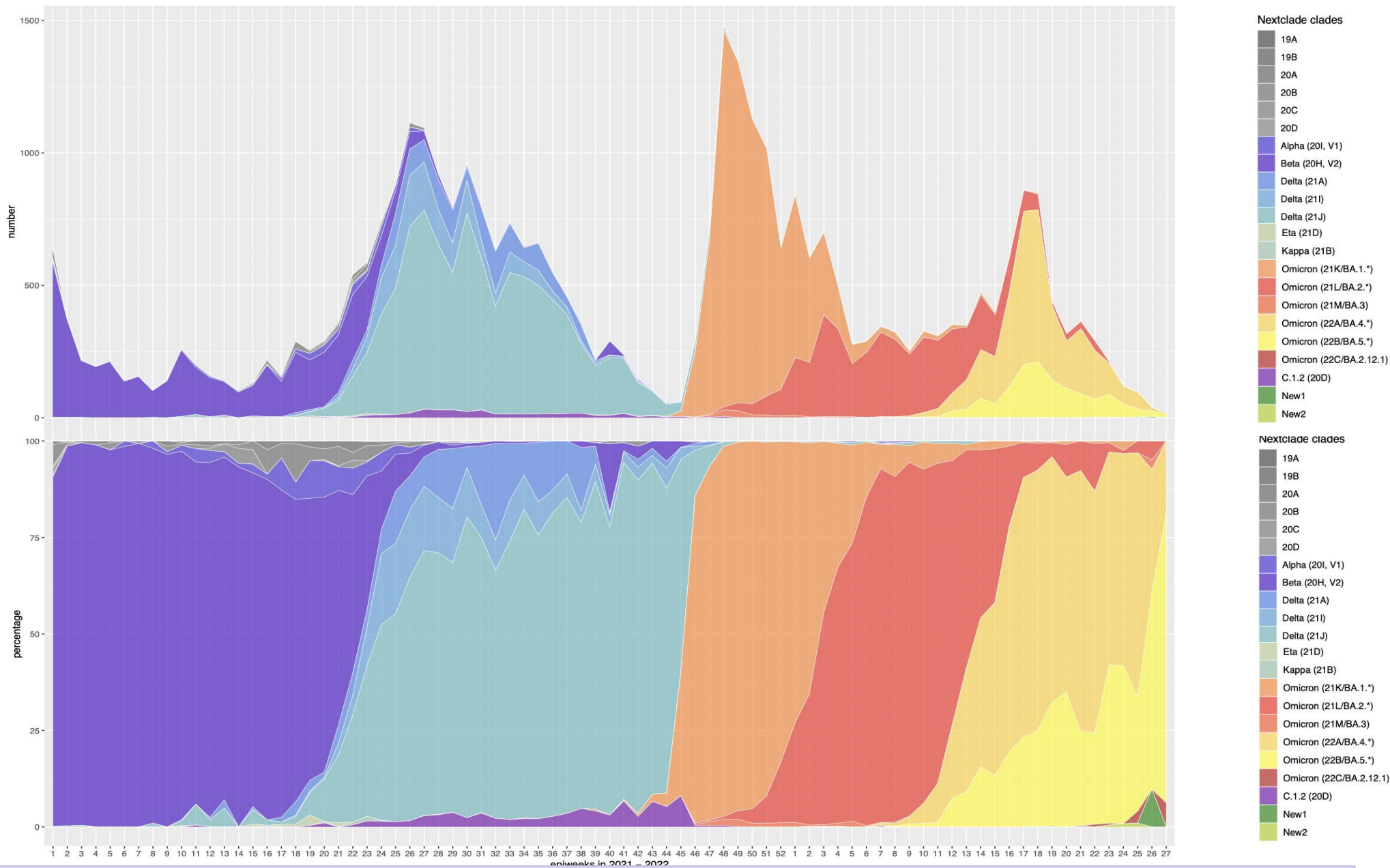
*This represents the cleaned, de-duplicated dataset of unique **National and Pneumonia Surveillance** sequences. This dataset will be used for all further figures.

GISAID genomes vs total cases, 2020 – 2022 (N=43 357)



All provinces, apart from GP, KZN and WC, have comparable percentages of overall cases and sequenced genomes. All provinces have contributed sequences for April, May, and June. July sequences are from WC and GP.

Number and percentage of clades by epiweek in South Africa, 2021 – 2022 (36 577*)



Sequencing data
ending epi week
27 (ending 9 July
2022)

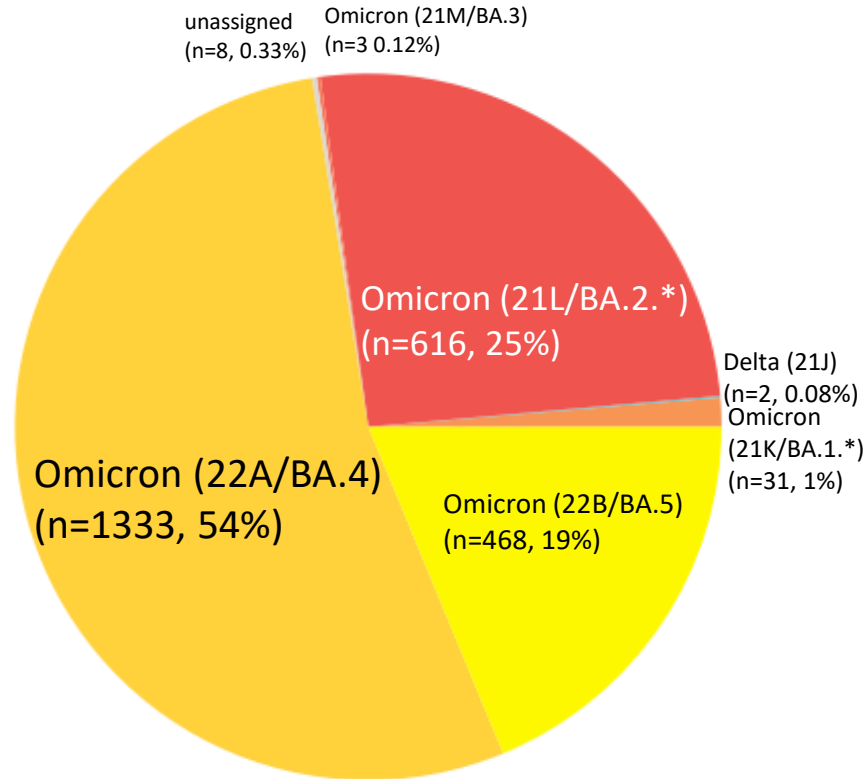
Currently in epi
week 28 (ending
16 July 2022)

*Excludes sequences
missing collection dates,
as well as those collected
January 1st and 2nd 2021
as they are part of
epiweek 53 of 2020.

Delta dominated in South Africa until October at >80%. Omicron has dominated from November onwards.

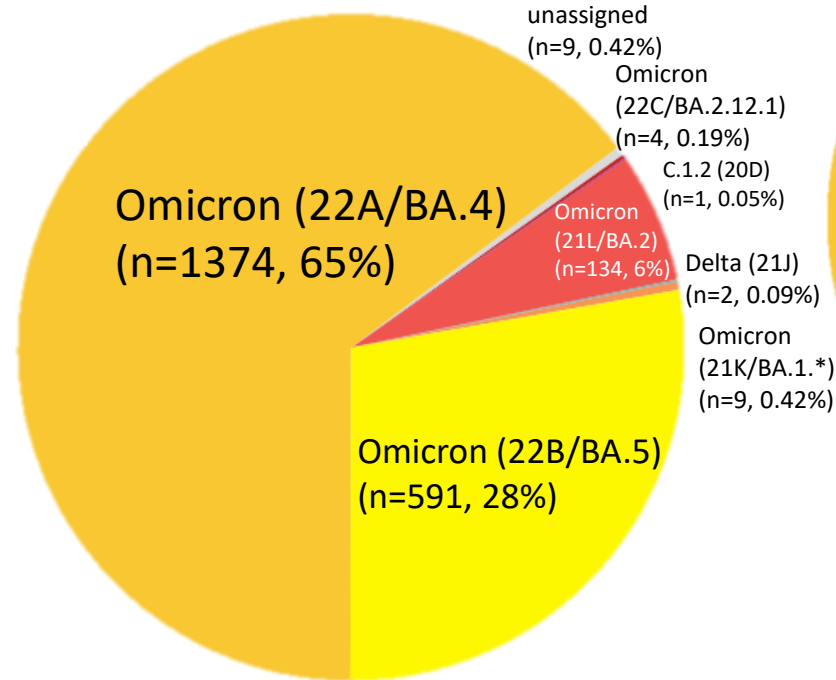
Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in April – June 2022

April (N=2461)



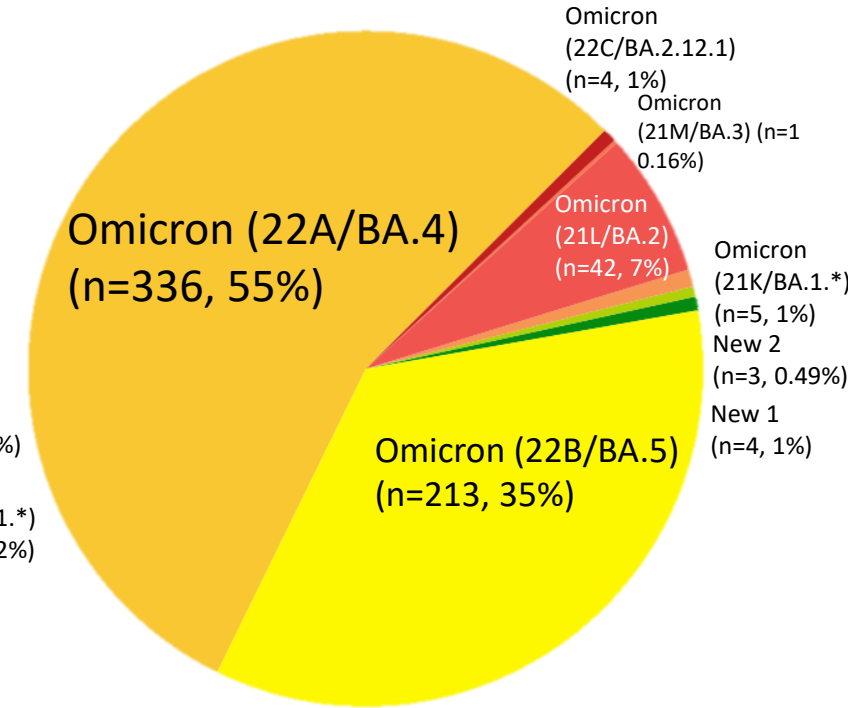
Total Omicron in Apr: 2451 (99.6%)

May (N=2124)



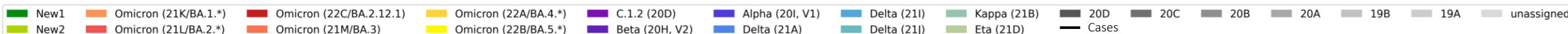
Total Omicron in May: 2112 (99.4%)

June (N=608)



Total Omicron in June: 601 (98.8%)

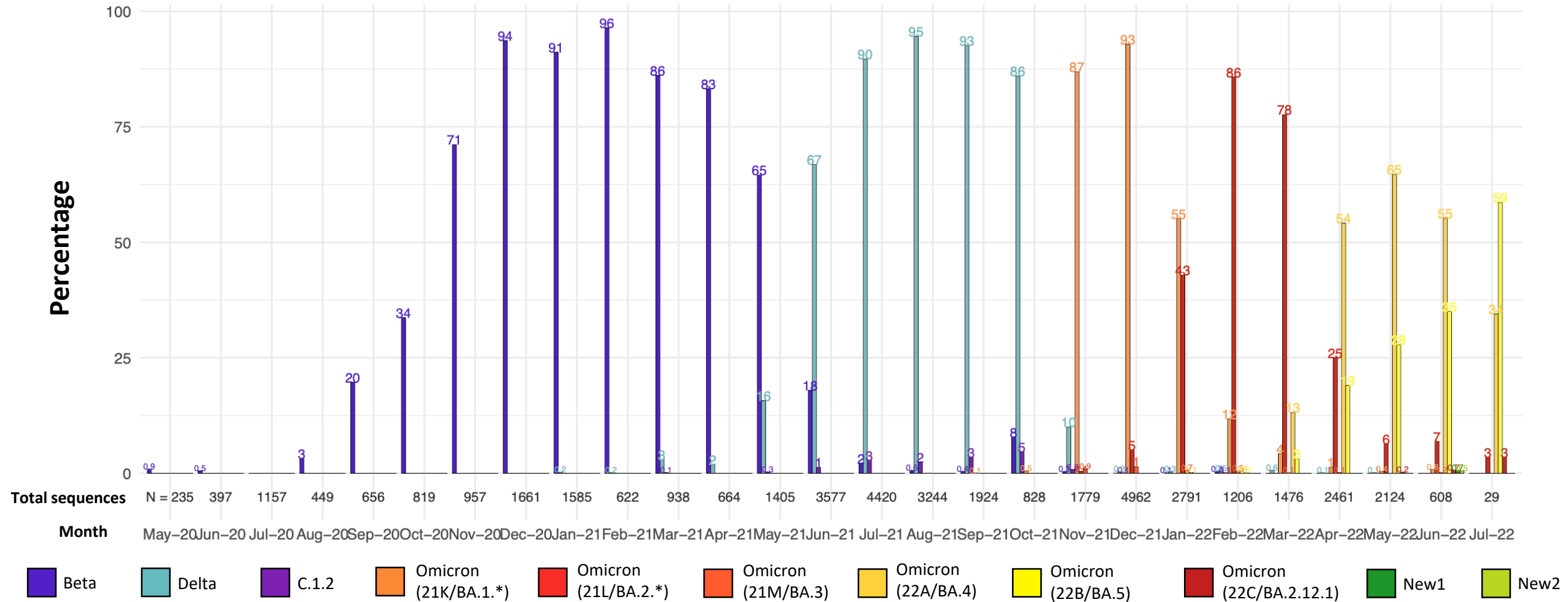
Clade key (bar graph)



Omicron dominated in April (99.6%, 2451/2461), May (99.4%, 2112/2124) and June (98.8%, 601/608). BA.4 and BA.5 together were dominant in April, May and June. BA.2.12.1 was detected at low levels in May and June.

Detection Rates: Beta, Delta, C.1.2 and Omicron

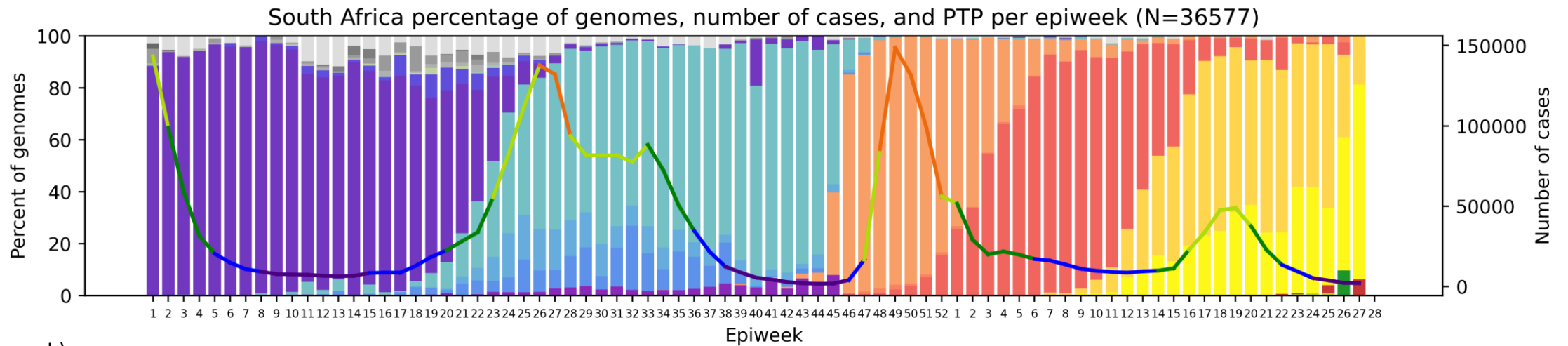
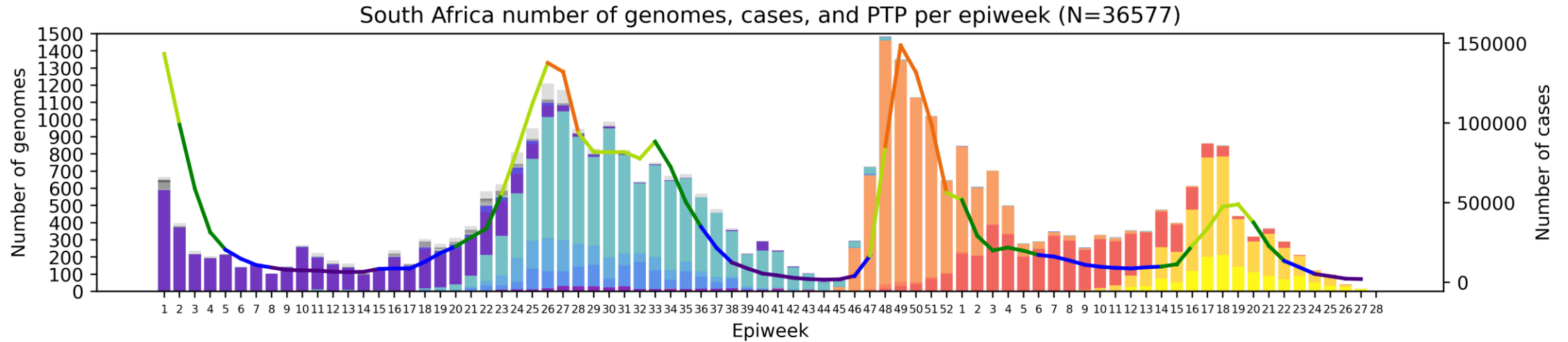
Detection rates of variants being monitored in South Africa



*Bars represent percentage prevalence of variant for the month; total number sequences collected for the month are given below the bar

Omicron has been dominant since November (>85% in November, >98% in December – July).
BA.4 and BA.5 together dominated in April at 73%, May at 93%, June at 90% and currently make up 93% of July sequences, although with a small number of genomes.

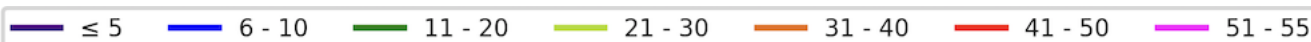
South Africa, 2021-2022, n = 36 577*



Clade key (bar graph)

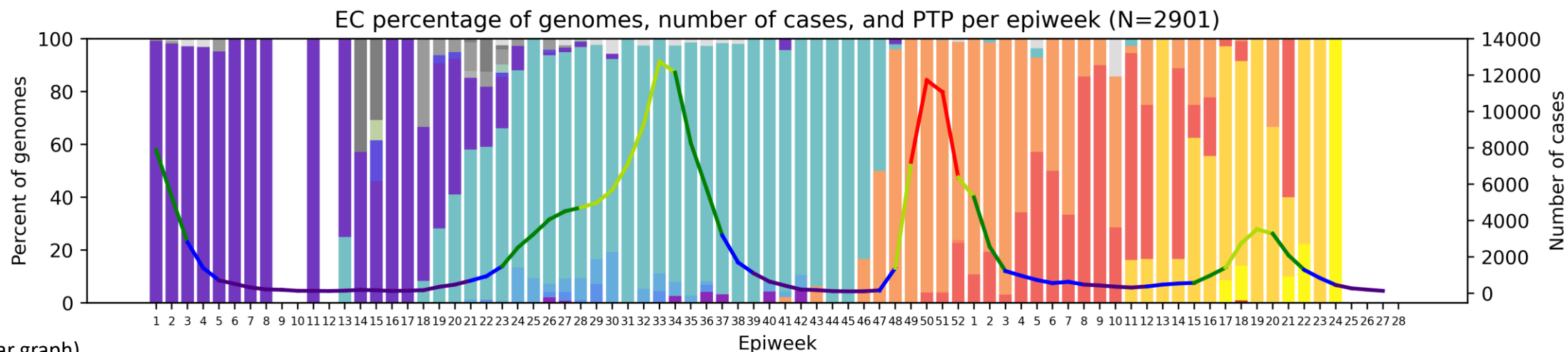
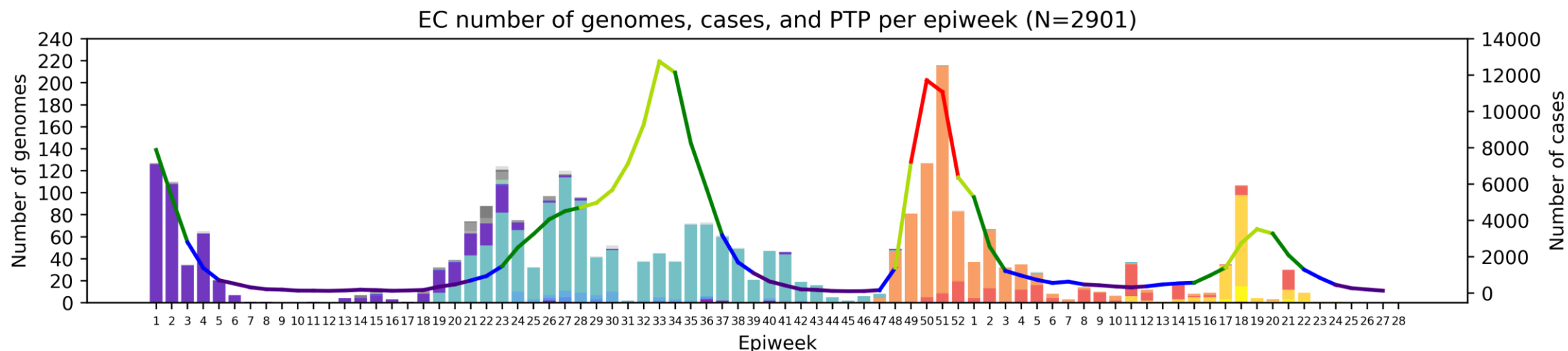


Weekly percentage testing positive key (line graph)



*Excludes sequences missing collection dates, as well as those collected January 1st and 2nd 2021 as they are part of epiweek 53 of 2020.

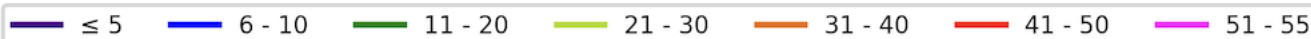
Eastern Cape Province, 2021-2022, n = 2901



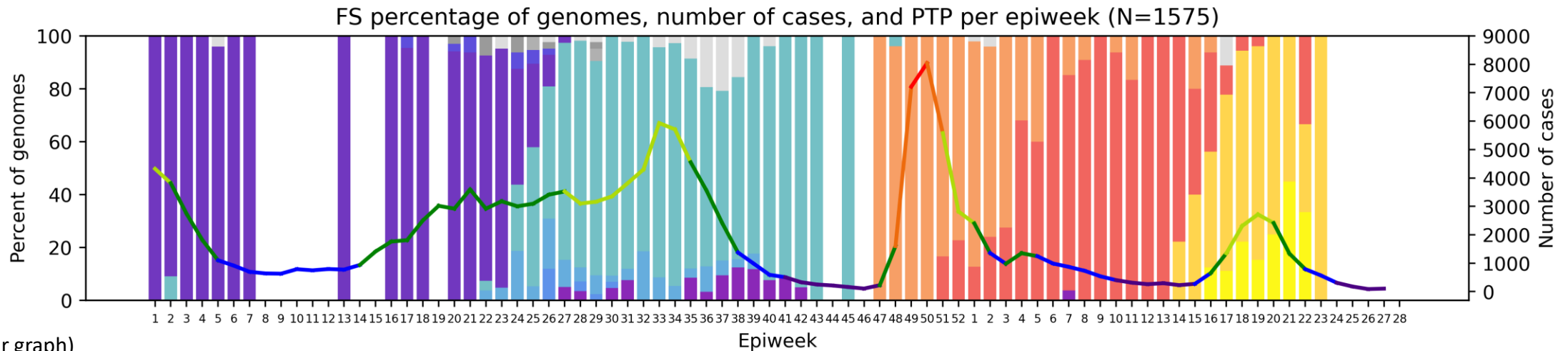
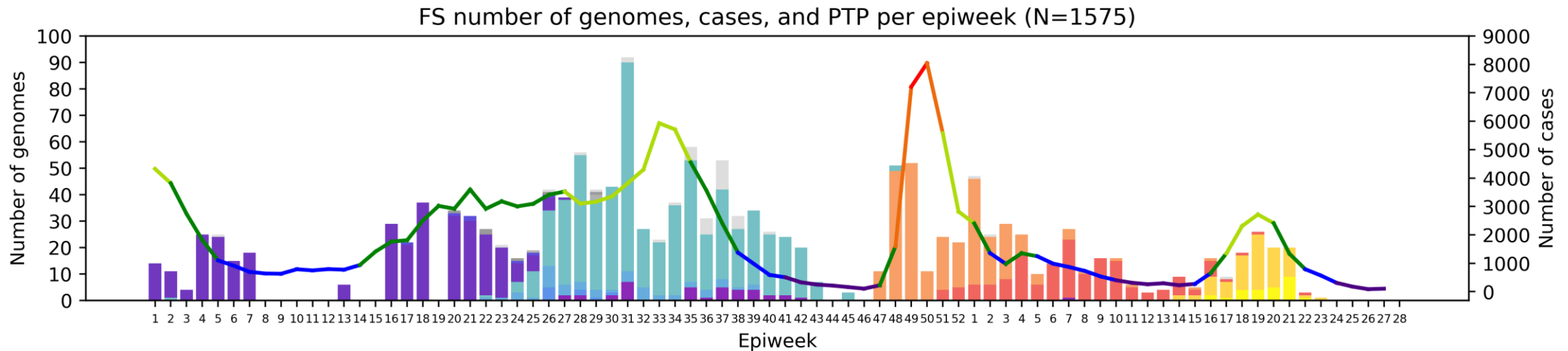
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



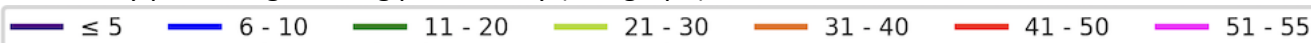
Free State Province, 2021-2022, n = 1575



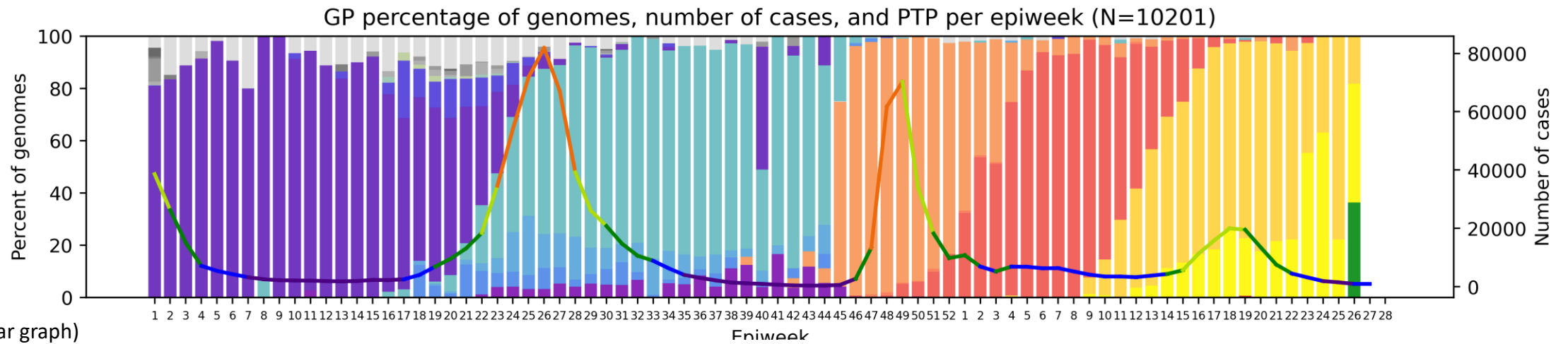
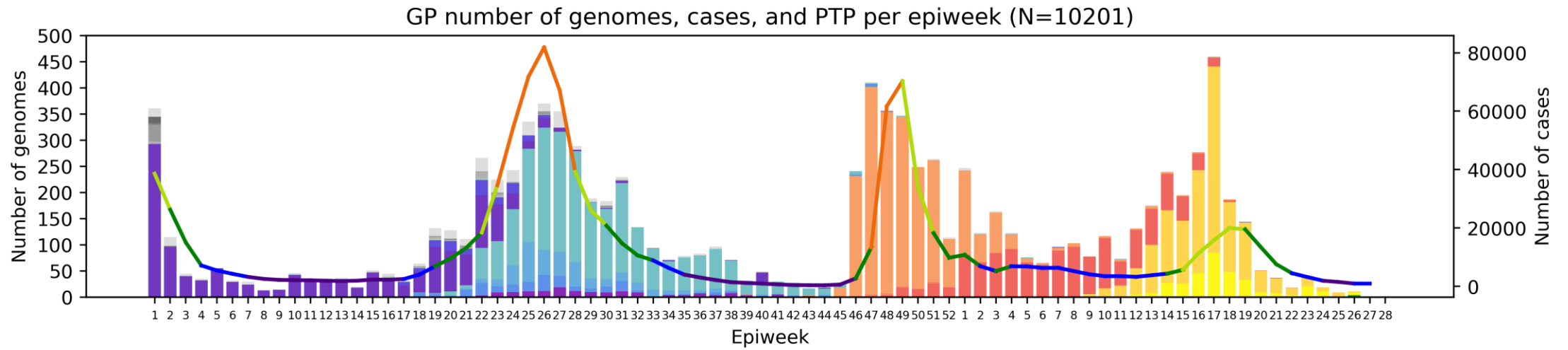
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



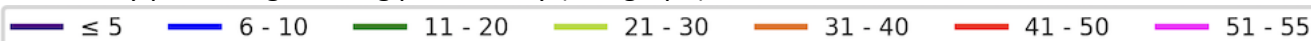
Gauteng Province, 2021-2022, n = 10 201



Clade key (bar graph)

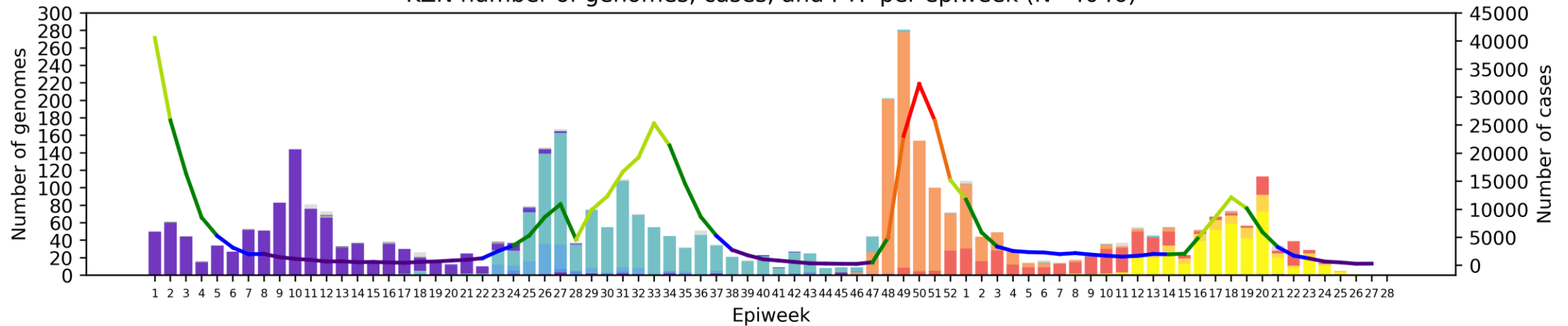


Weekly percentage testing positive key (line graph)

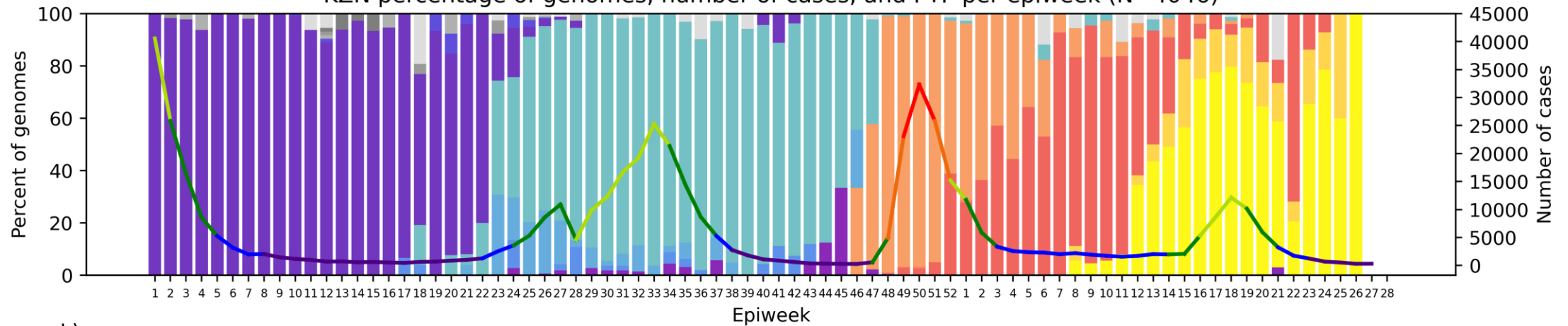


KwaZulu-Natal Province, 2021-2022, n = 4046

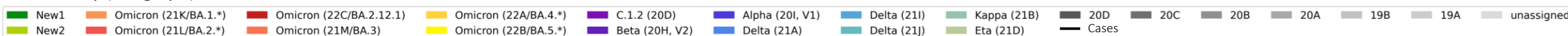
KZN number of genomes, cases, and PTP per epiweek (N=4046)



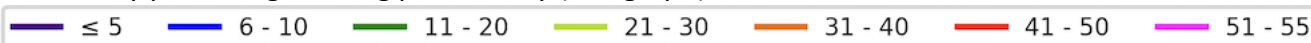
KZN percentage of genomes, number of cases, and PTP per epiweek (N=4046)



Clade key (bar graph)

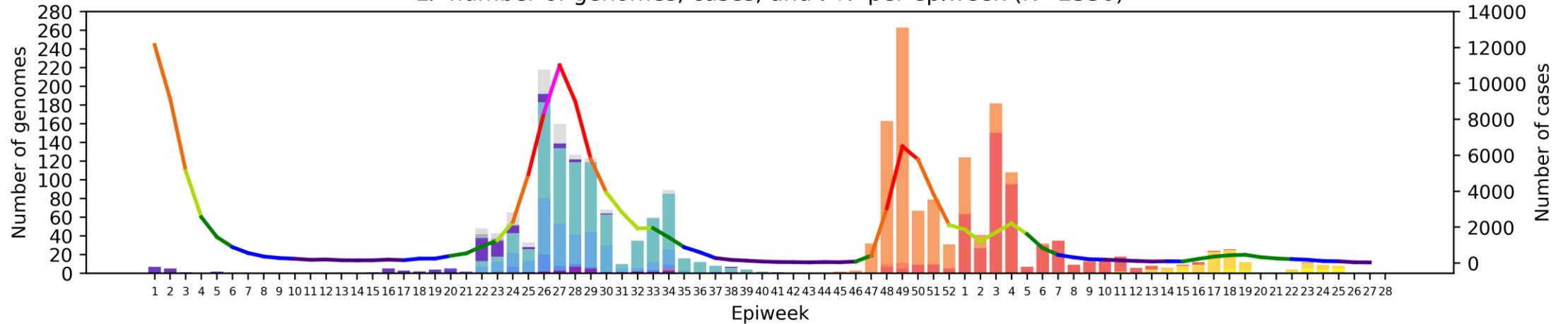


Weekly percentage testing positive key (line graph)

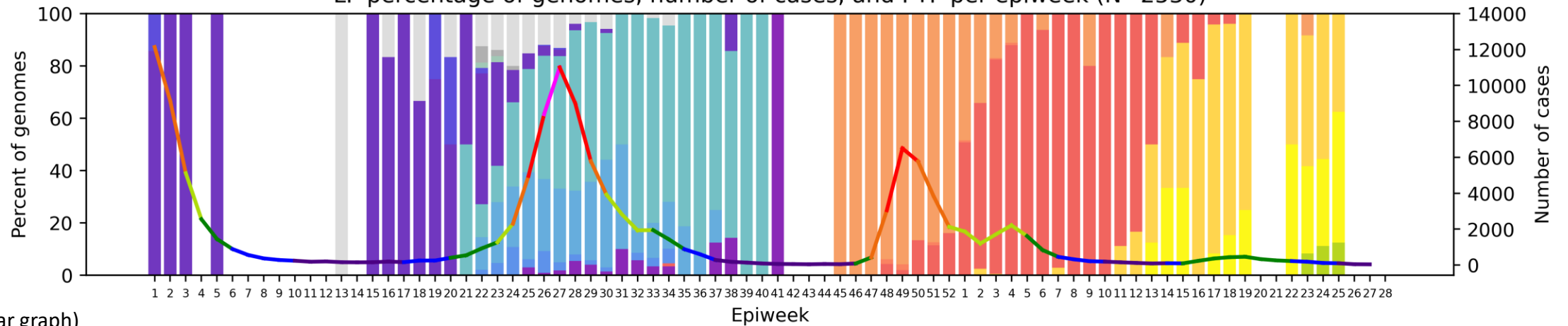


Limpopo Province, 2021-2022, n = 2530

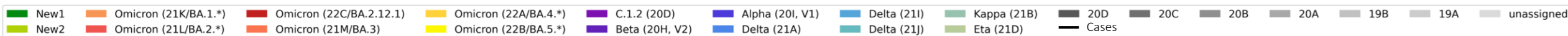
LP number of genomes, cases, and PTP per epiweek (N=2530)



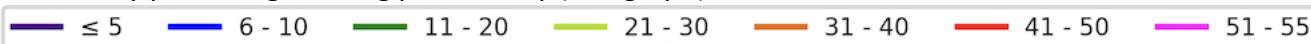
LP percentage of genomes, number of cases, and PTP per epiweek (N=2530)



Clade key (bar graph)

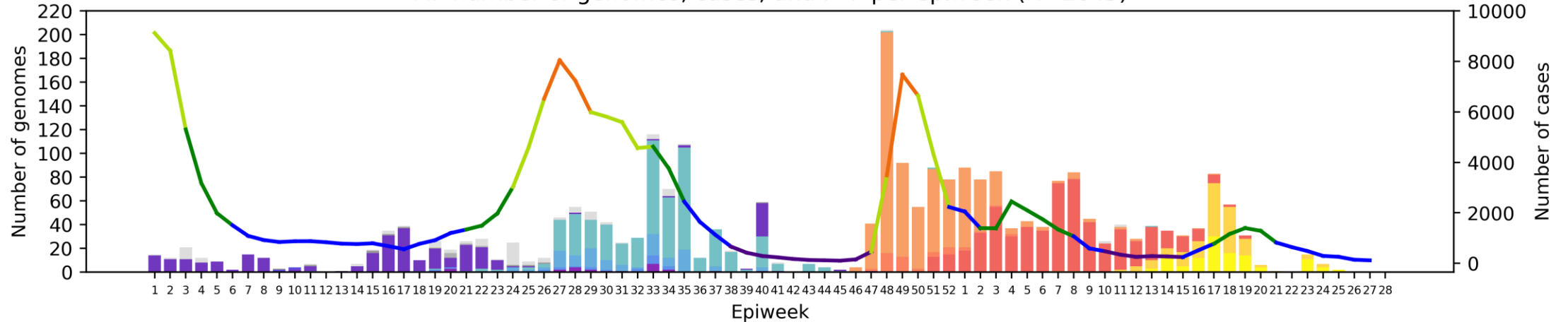


Weekly percentage testing positive key (line graph)

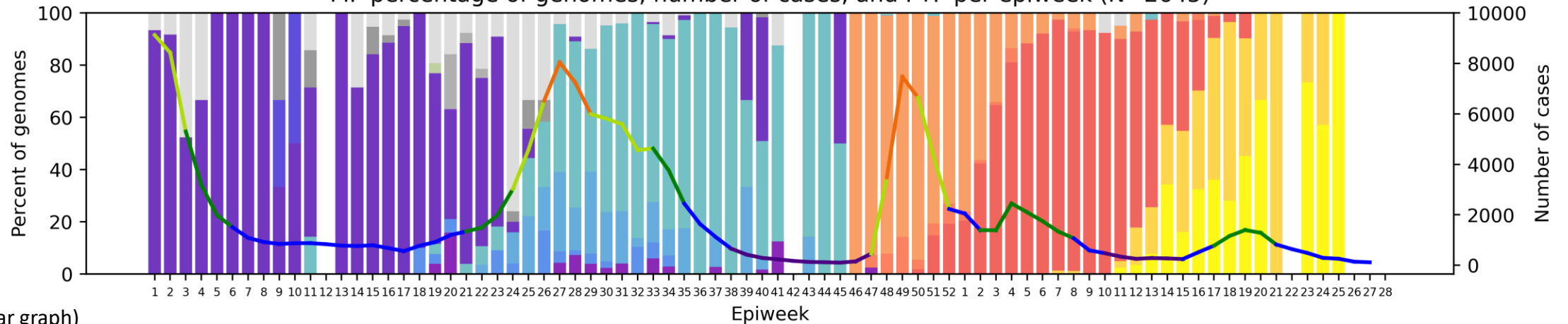


Mpumalanga Province, 2021-2022, n = 2645

MP number of genomes, cases, and PTP per epiweek (N=2645)



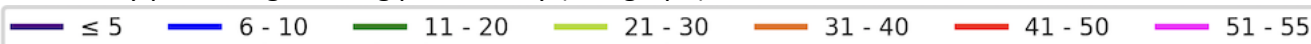
MP percentage of genomes, number of cases, and PTP per epiweek (N=2645)



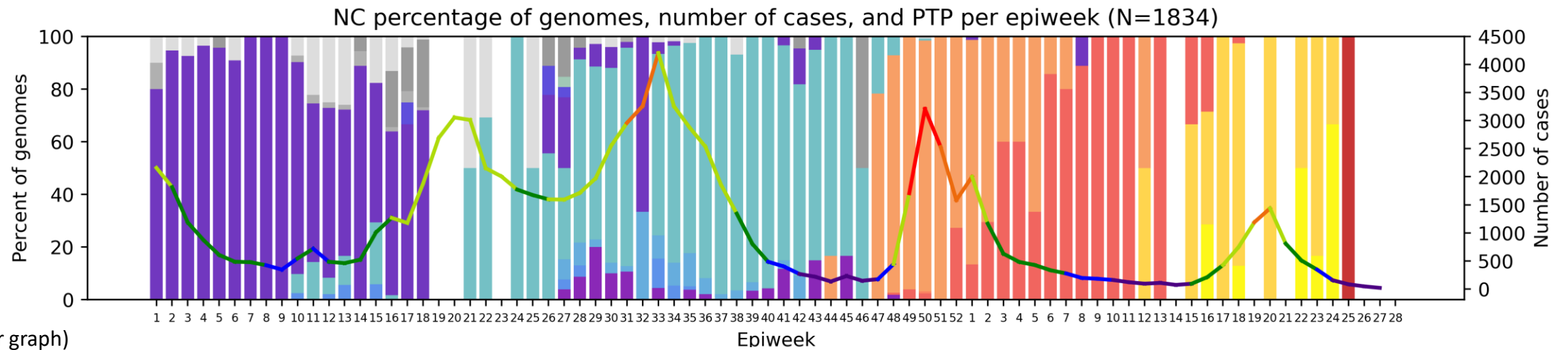
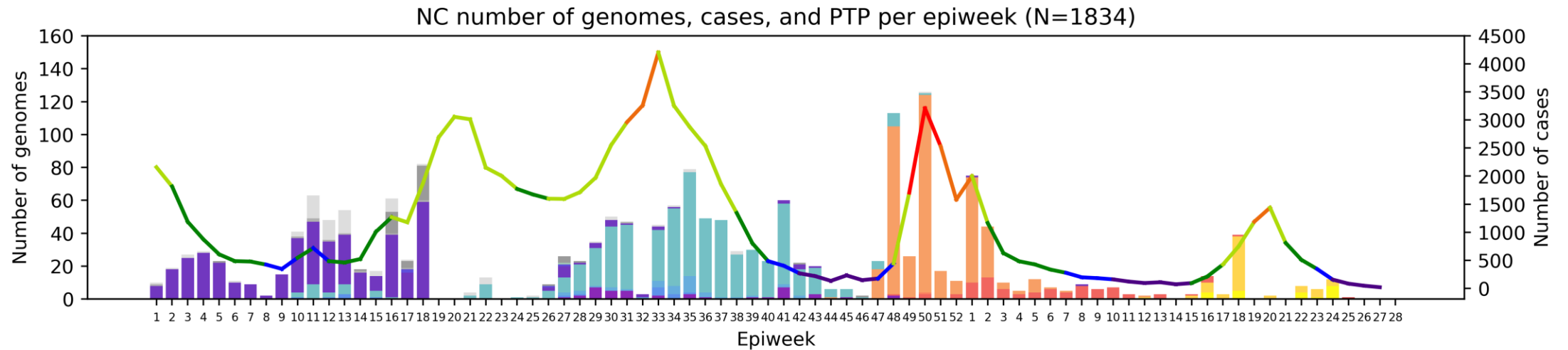
Clade key (bar graph)



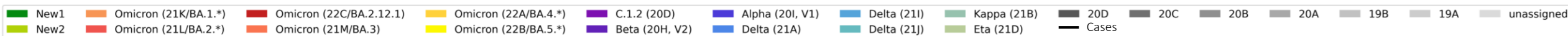
Weekly percentage testing positive key (line graph)



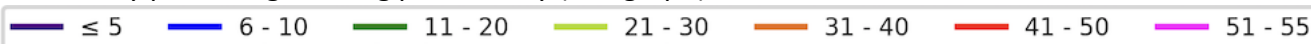
Northern Cape Province, 2021-2022, n = 1834



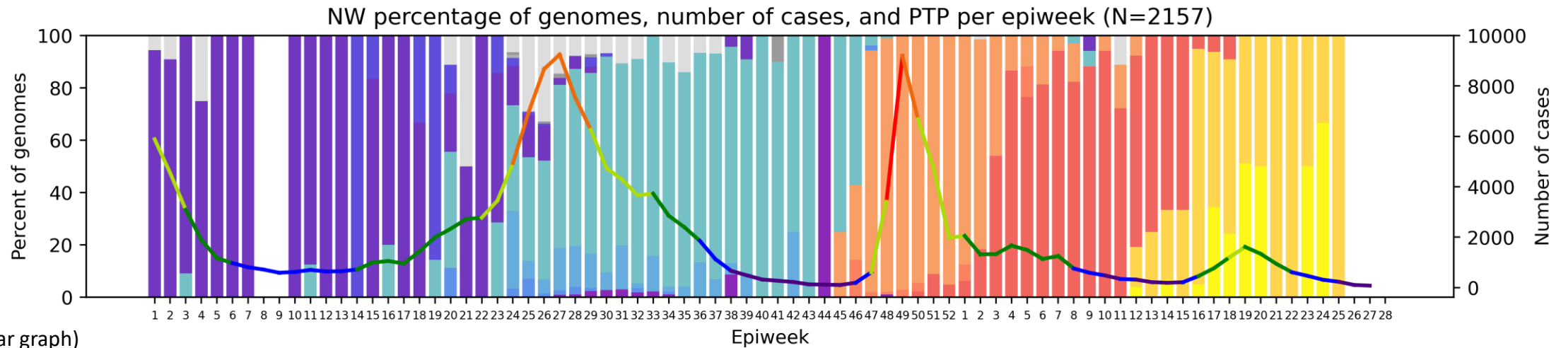
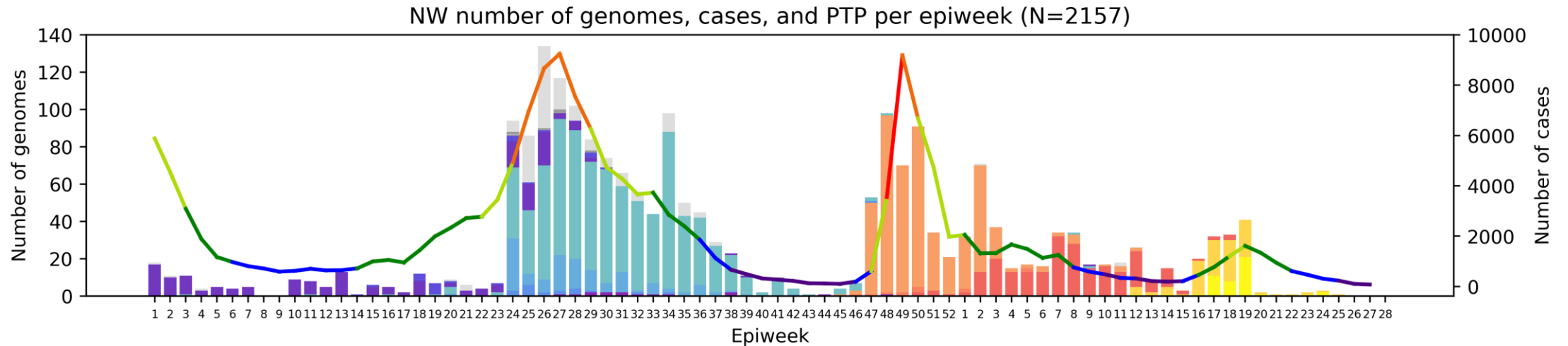
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



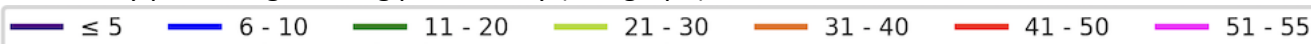
North West Province, 2021-2022, n = 2157



Clade key (bar graph)

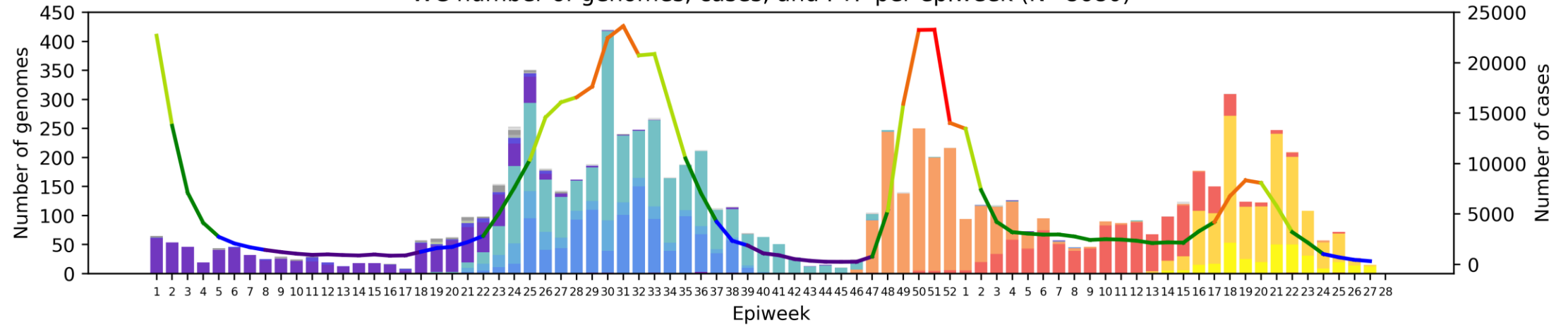


Weekly percentage testing positive key (line graph)

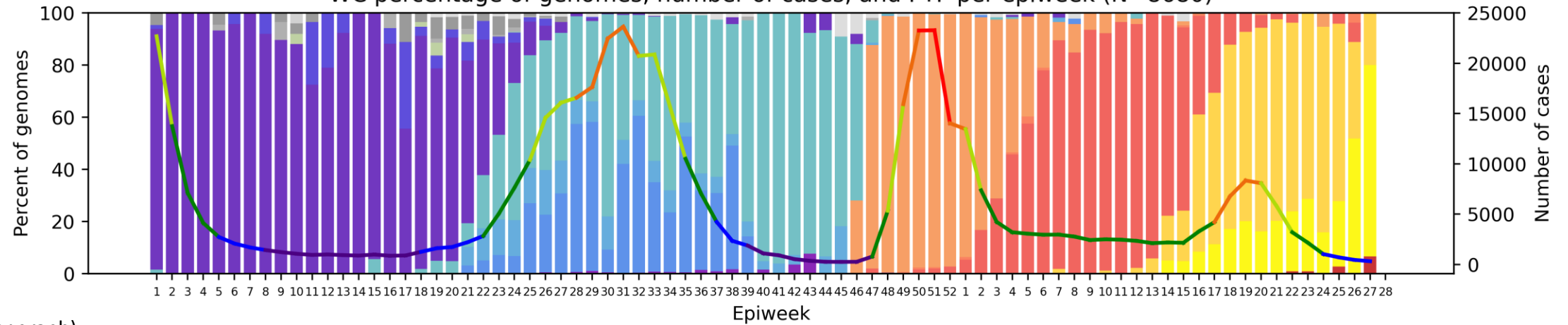


Western Cape Province, 2021-2022, n = 8680

WC number of genomes, cases, and PTP per epiweek (N=8680)



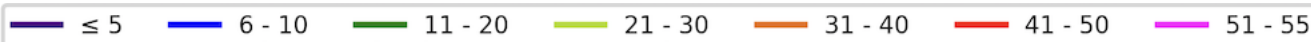
WC percentage of genomes, number of cases, and PTP per epiweek (N=8680)



Clade key (bar graph)

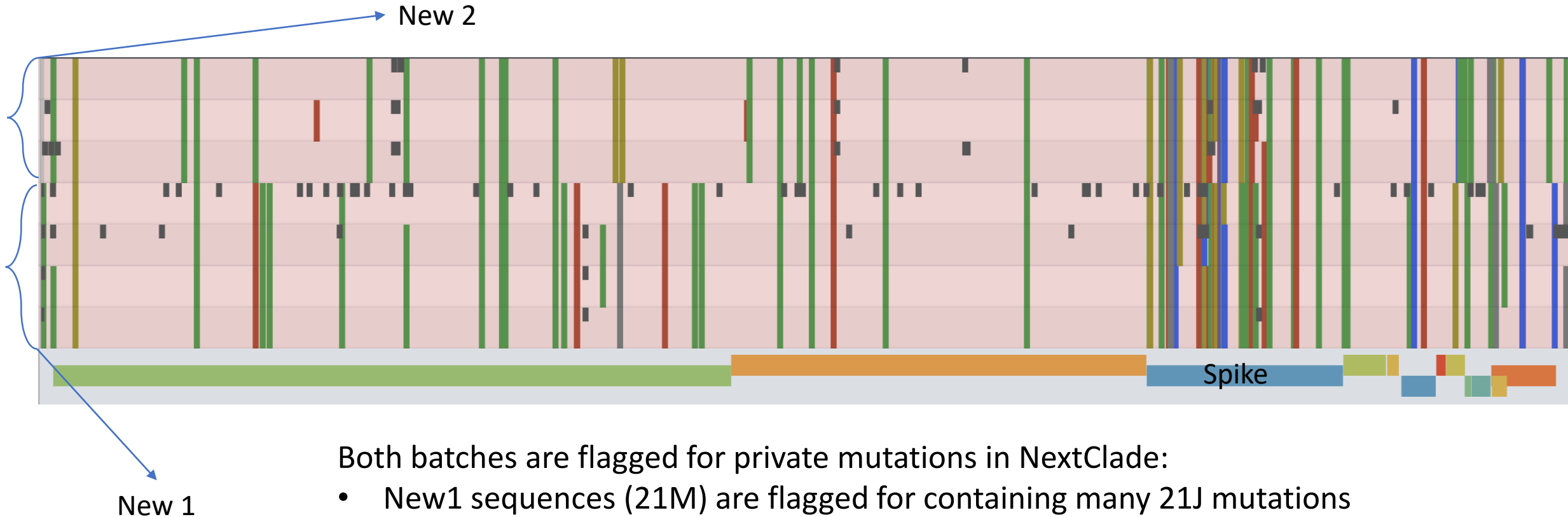


Weekly percentage testing positive key (line graph)



7 SARS-CoV-2 SGTP (S-gene target positive) sequences with novel mutations

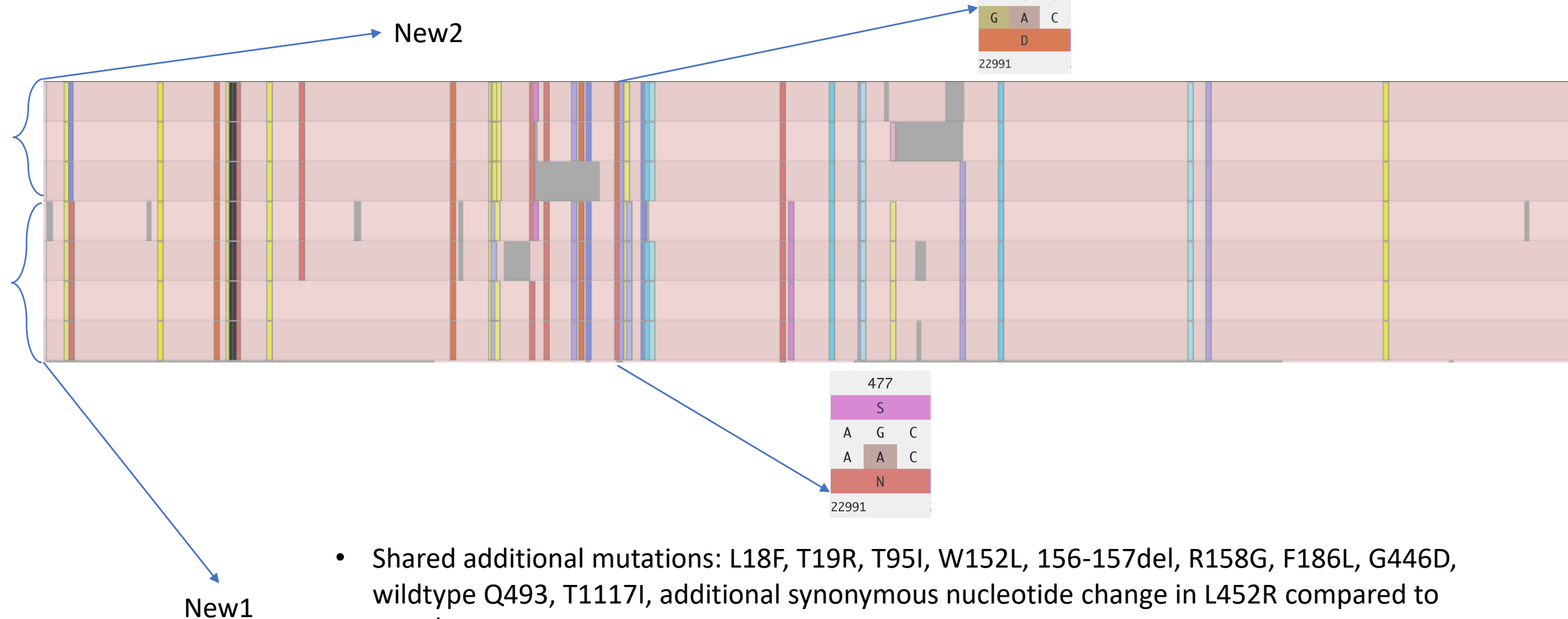
Whole genome profiles



Both batches are flagged for private mutations in NextClade:

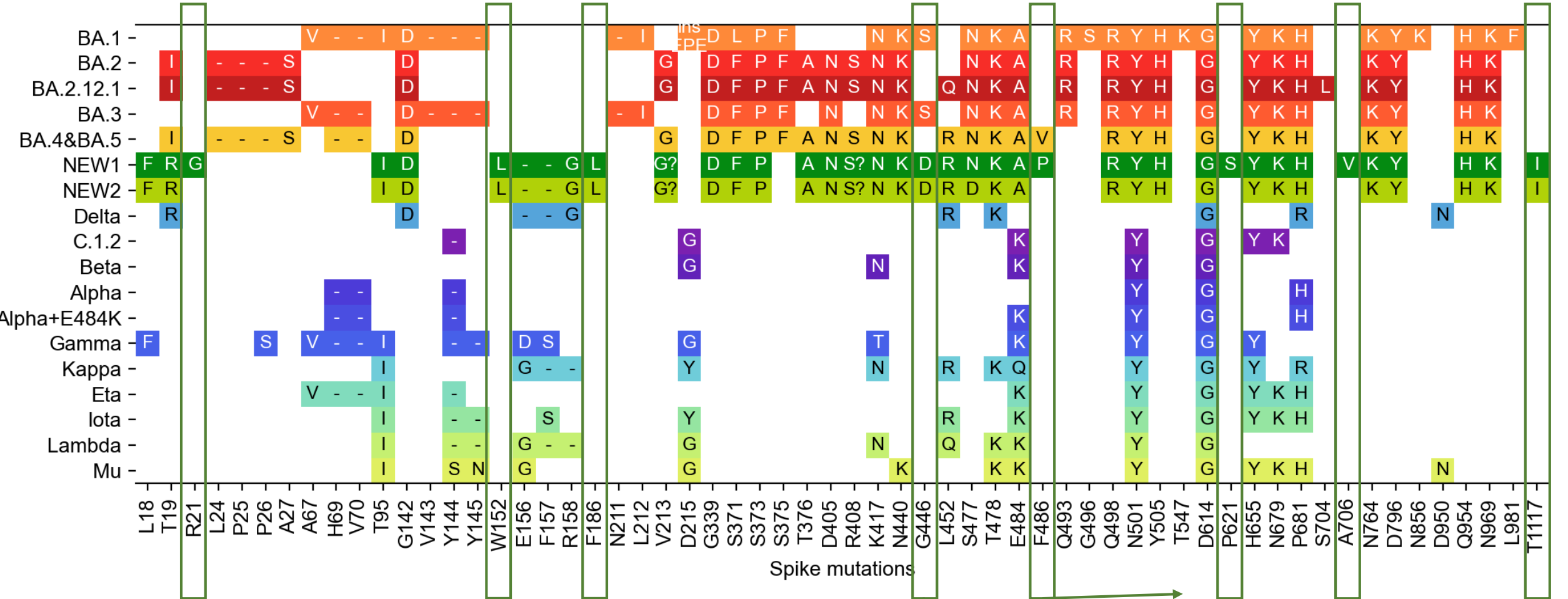
- New1 sequences (21M) are flagged for containing many 21J mutations
- New2 samples (21J) are flagged for containing many 21K and 21L mutations
- Sequences contain a mixture of mutations from Omicron and Delta

Spike protein profiles



- Shared additional mutations: L18F, T19R, T95I, W152L, 156-157del, R158G, F186L, G446D, wildtype Q493, T1117I, additional synonymous nucleotide change in L452R compared to BA.4/5
- Unique to New1 batch: R21G, F486P, A706V (A706T present in 1 surveillance sample but different nucleotide change in different position)
- Unique to New2 batch: S477D instead of S477N

Spike protein mutation profile (1)*



Seen in 1,424
seqs on GISAID

Seen in 578 seqs on GISAID

Seen in 485 seqs on GISAID
Different aa to BA.1
High predicted Ab escape (Bloom lab)

Seen in 9 seqs on GISAID

- 7 human, 2 bat

Different aa to BA.4/5

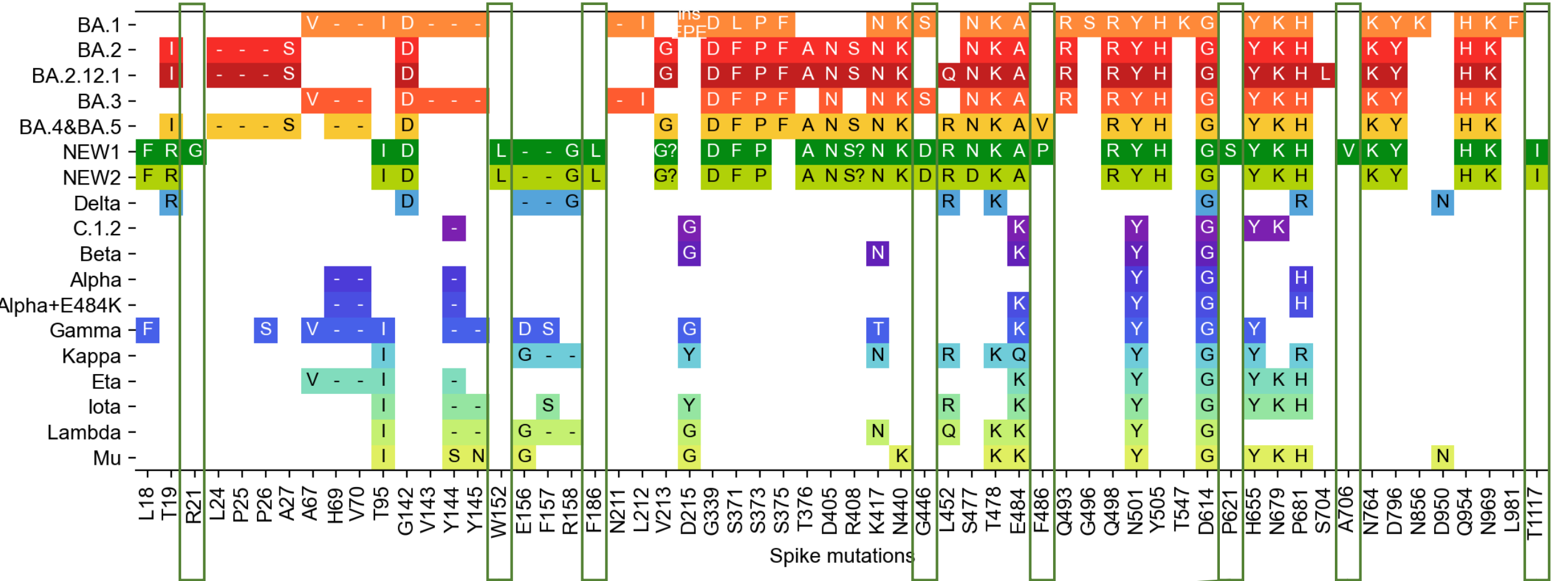
High predicted Ab escape (Bloom lab)

– know immune escape in BA.4/5 when F→V

486
F
T T T
C C T
P

*Only mutations present in Omicron, Delta, or the new SGTP sequences are pictured

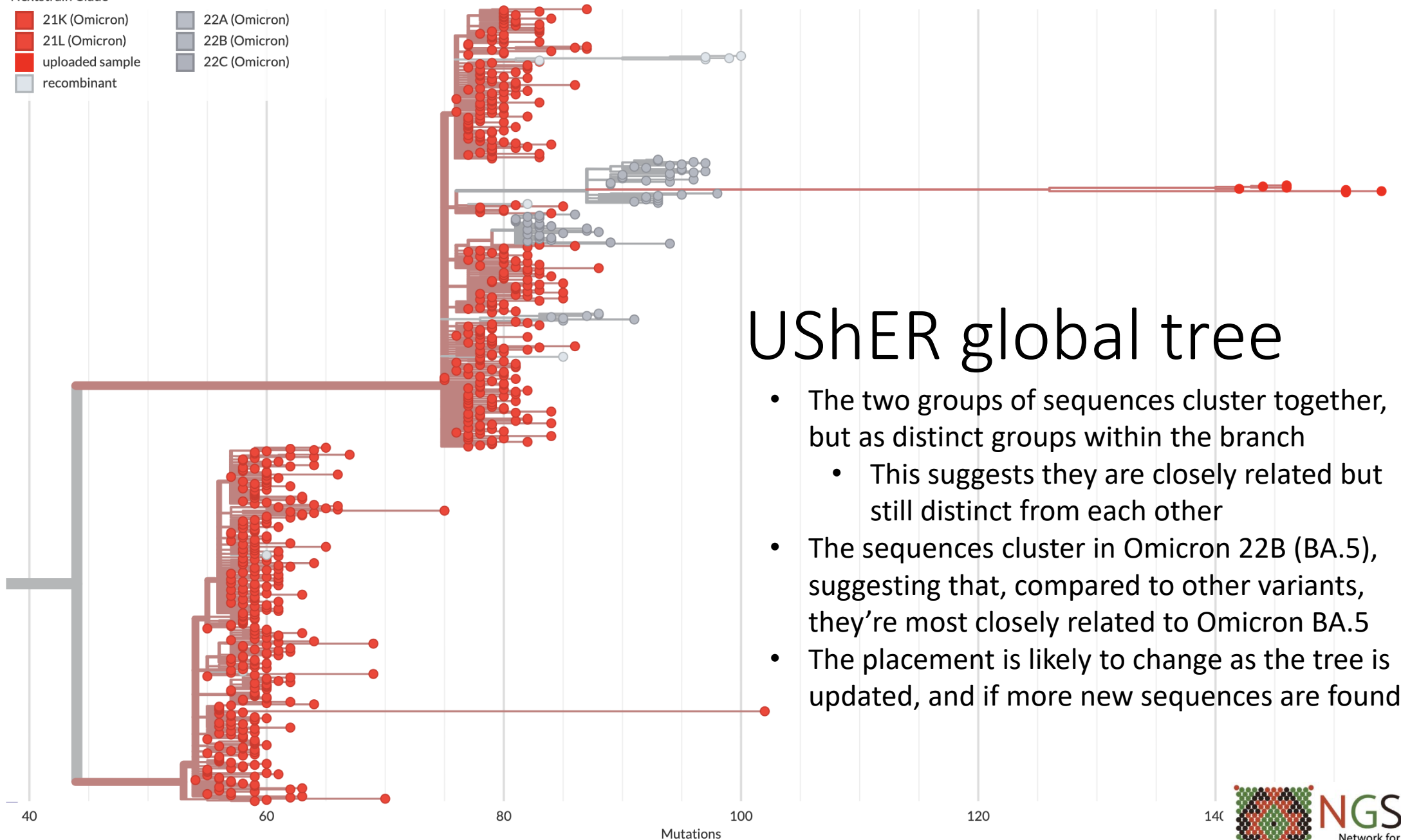
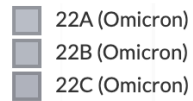
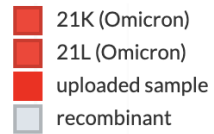
Spike protein mutation profile (2)*



Note V213, S375, D405 and R408 sometimes drop out on Ion Torrent – need confirmation on different platform

*Only mutations present in Omicron, Delta, or the SGTP sequences are pictured

Nextstrain Clade ^



UShER global tree

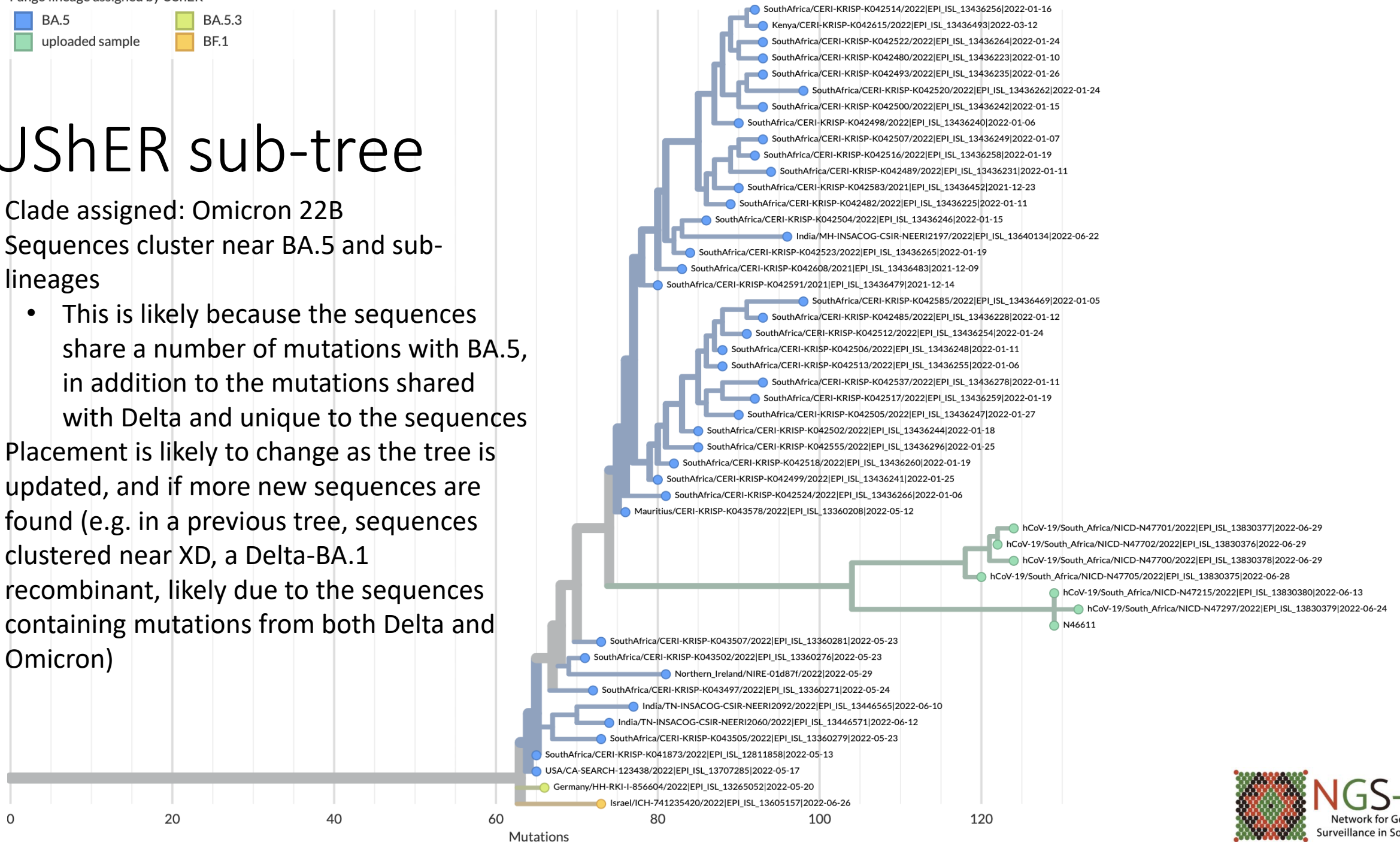
- The two groups of sequences cluster together, but as distinct groups within the branch
 - This suggests they are closely related but still distinct from each other
- The sequences cluster in Omicron 22B (BA.5), suggesting that, compared to other variants, they're most closely related to Omicron BA.5
- The placement is likely to change as the tree is updated, and if more new sequences are found

Pango lineage assigned by UShER

BA.5	BA.5.3
uploaded sample	BF.1

UShER sub-tree

- Clade assigned: Omicron 22B
- Sequences cluster near BA.5 and sub-lineages
 - This is likely because the sequences share a number of mutations with BA.5, in addition to the mutations shared with Delta and unique to the sequences
- Placement is likely to change as the tree is updated, and if more new sequences are found (e.g. in a previous tree, sequences clustered near XD, a Delta-BA.1 recombinant, likely due to the sequences containing mutations from both Delta and Omicron)

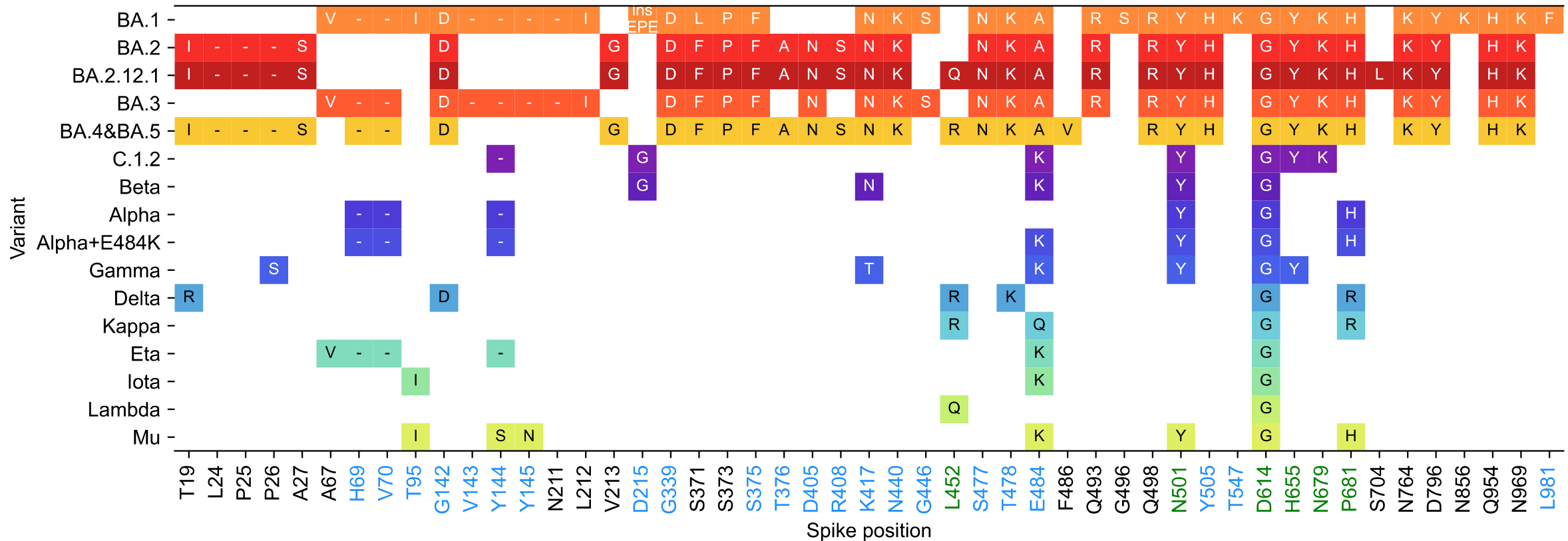


Summary

- **N=7 sequences with novel mutational profile**
 - NGS-SA teams are currently analysing the data to confirm the mutational profile
- **Variant of Concern Omicron in South Africa**
 - Dominates 2022 sequencing data at >98% of genomes.
 - While BA.1 was the predominant lineage in January (55%), BA.2 dominated in February (86%) and March (78%).
 - Omicron lineages BA.4 and BA.5 increased in prevalence in March (16%), and together are dominant in April (73%), May (93%) and June (90%).
 - BA.2.12.1 was detected in South Africa at low prevalence in May and June (<1%)

¹ <https://github.com/cov-lineages/pango-designation/releases/tag/v1.3>

Omicron spike mutations compared to other VOC/VOIs



- Multiple changes within the two immunogenic regions in S1 (NTD and RBD)
 - Including a three amino acid insertion
- Accumulation of mutations surrounding the furin cleavage site
 - Including combination of N679K and P681H
- Effect of most spike S2 subunit changes have not been defined, but may be linked to immune escape

Only lineage-defining mutations are pictured.



Supported by the DSI and the SA MRC



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YAKWAZULU-NATALI



EDCTP

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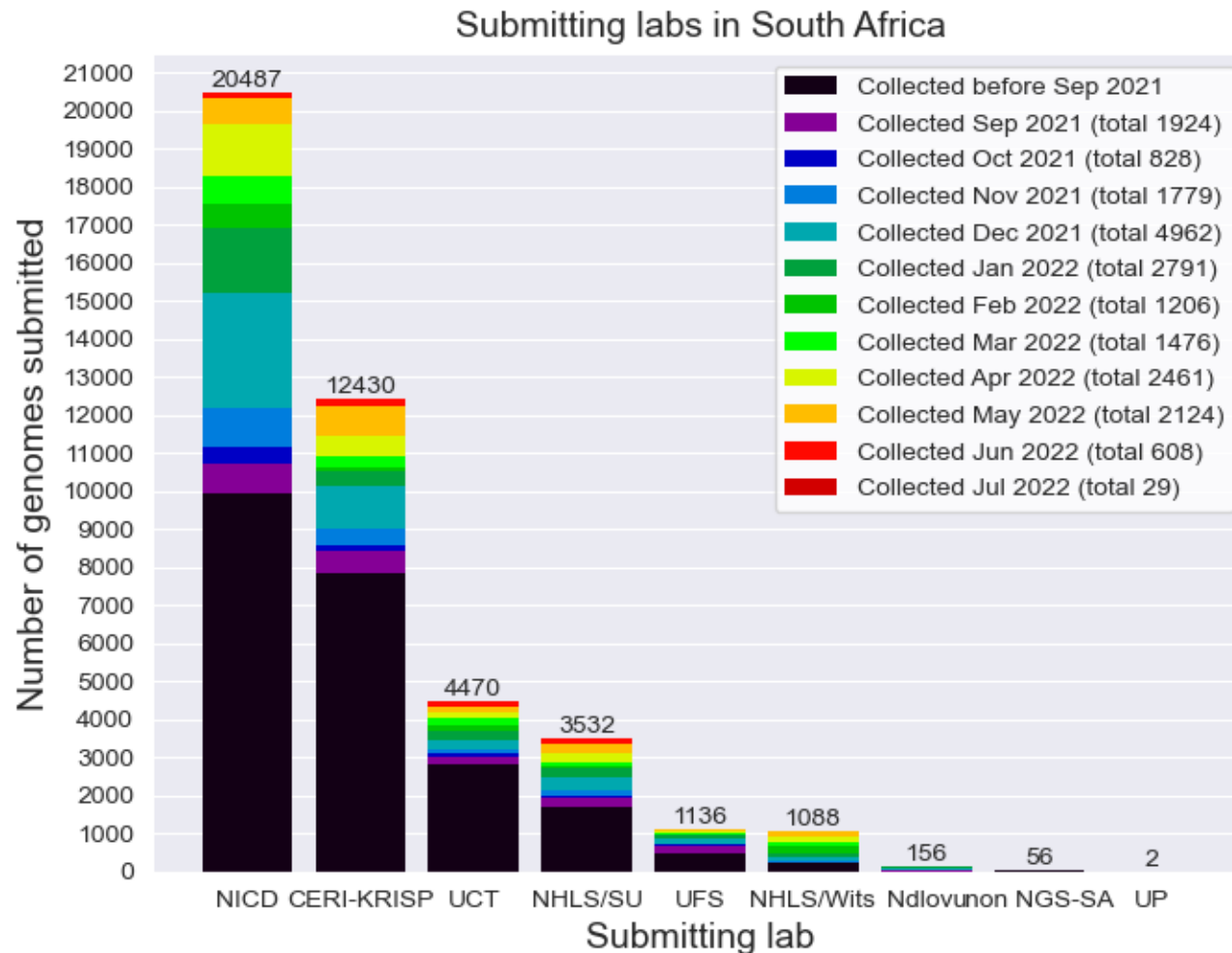
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South African genomes submitted per submitting lab, 2020 - 2022 (N=43 357)



NGS-SA Labs

CERi: Centre for Epidemic Response and Innovation

KRISP: KZN Research Innovation and Sequencing Platform

NDLOVU: Ndlovu Research Laboratories

NICD: National Institute for Communicable Diseases

NHLS: National Health Laboratory Service

SU: Stellenbosch University

UCT: University of Cape Town

UFS: University of the Free State

UP: University of Pretoria

Multiple labs from NGS-SA and collaborating public and private laboratories are contributing to sequencing, both as originating and as submitting (pictured here) laboratories.

Currently circulating Variants of Concern (VOC)

WHO label	Pango lineage●	GISAID clade	Nextstrain clade	Additional amino acid changes monitored°	Earliest documented samples	Date of designation
Delta	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:K417N +S:K484K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron*	B.1.1.529	GR/484A	21K	+S:R346K	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

<https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/> accessed 18 March 2022

●Includes all descendant lineages. See the cov-lineages.org and the Pango network websites for further details.

° Only found in a subset of sequences

Previously circulating Variants of Concern

WHO label	Pango lineage•	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	United Kingdom, Sep-2020	VOC: 18-Dec-2020 Previous VOC: 09-Mar-2022
Beta	B.1.351	GH/501Y.V2	20H (V2)	South Africa, May-2020	VOC: 18-Dec-2020 Previous VOC: 09-Mar-2022
Gamma	P.1	GR/501Y.V3	20J (V3)	Brazil, Nov-2020	VOC: 11-Jan-2021 Previous VOC: 09-Mar-2022

<https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/> accessed 18 March 2022

- Includes all descendant lineages. See the cov-lineages.org and the Pango network websites for further details.

Submission of routine specimens for sequencing

- representative of multiple geographic regions (provinces/districts/health facilities) from individuals of
 - all ages
 - over as many time periods during the SARS-CoV-2 epidemic in South Africa
- requested that testing laboratories in both the private and public sectors, submit respiratory samples to their closest NGS-SA sequencing laboratory on a routine basis (ideally every week) as follows, depending on the capacity of the testing laboratory:
 - All positives samples should be sent every week (NGS-SA laboratory will perform random sampling as described below) **OR**
 - A weekly selection of approximately 10%-20% of randomly selected positive samples should be sent every week. Number of selected samples will depend on the size of laboratory and how many other laboratories are drained by the submitting laboratory.

Submission of special interest specimens for sequencing

In addition to routine samples mentioned above, please send specimens separately to above and clearly marked if:

- Suspected vaccine breakthrough (≥ 14 days after vaccine), especially if hospitalised and clinically severe
- Suspected re-infection (≥ 90 days after previous episode), especially if hospitalised and clinically severe
- Prolonged shedding with high SARS-CoV-2 viral loads (i.e. Ct values less than 30 for more than 1 month post-primary diagnosis) in immunocompromised individuals
- Possible animal-to-human transmission
- Suspected cases of importation from another country, especially countries known to harbour SARS-CoV-2 variants of concern or countries with little available information
- Clusters of “unusual” cases (e.g., in terms of disease presentation, patient groups affected, etc.)