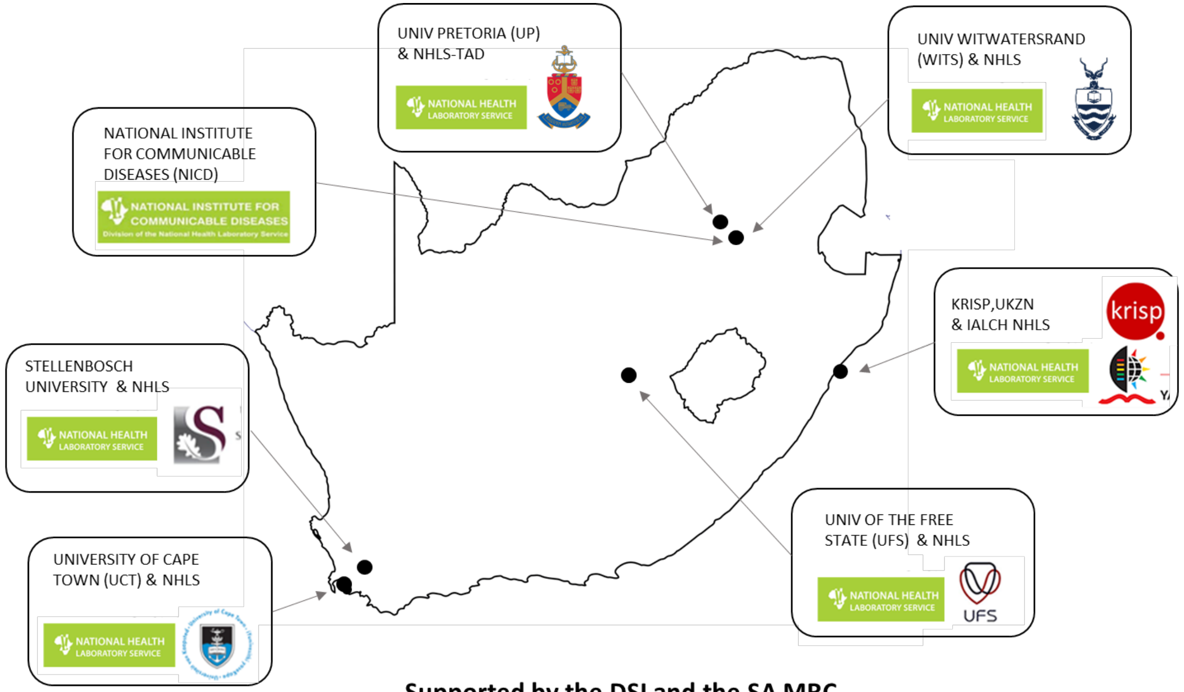
NGS-SA
Network for Genomic Surveillance in South Africa

Network for Genomic Surveillance South Africa (NGS-SA)

SARS-CoV-2 Sequencing Update
29 April 2022



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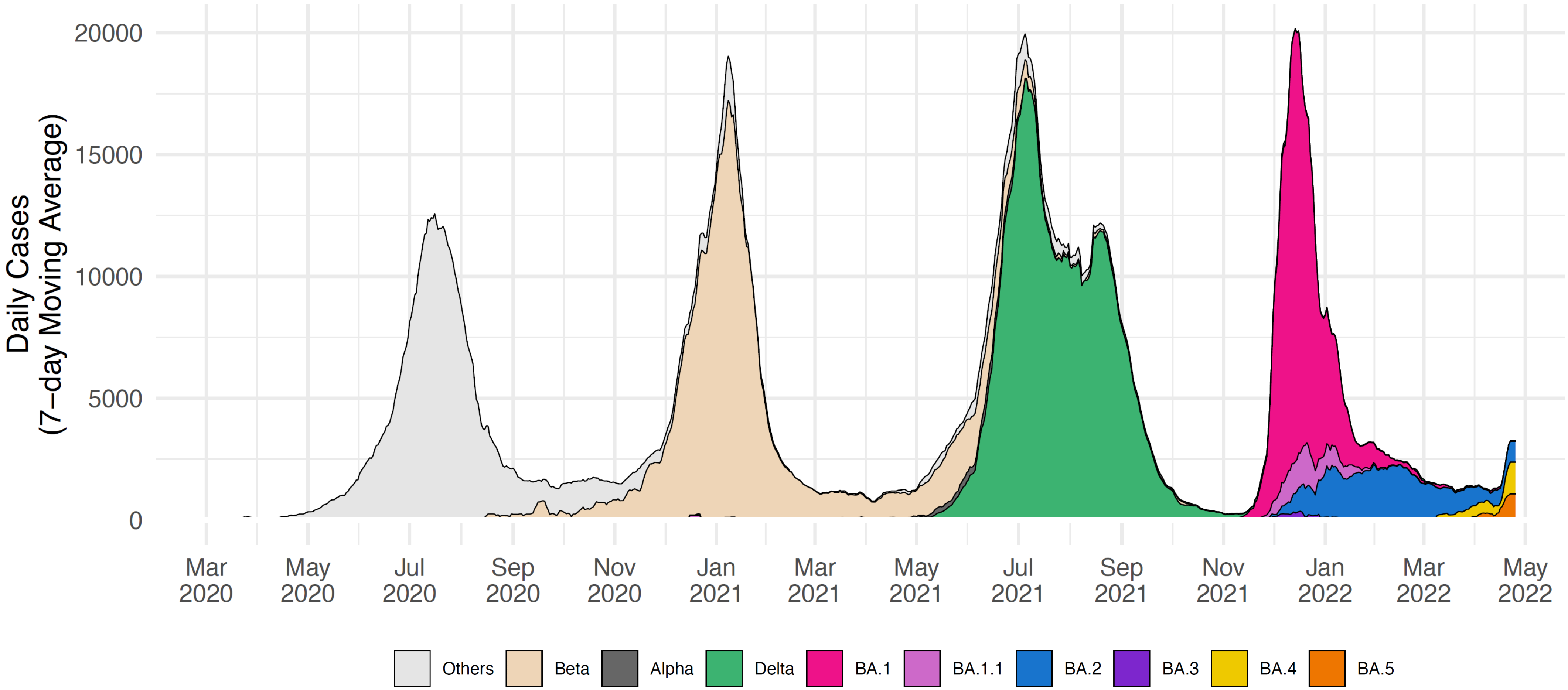
Supported by the DSI and the SA MRC

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

Summary of new Omicron lineages (BA.4 & BA.5)

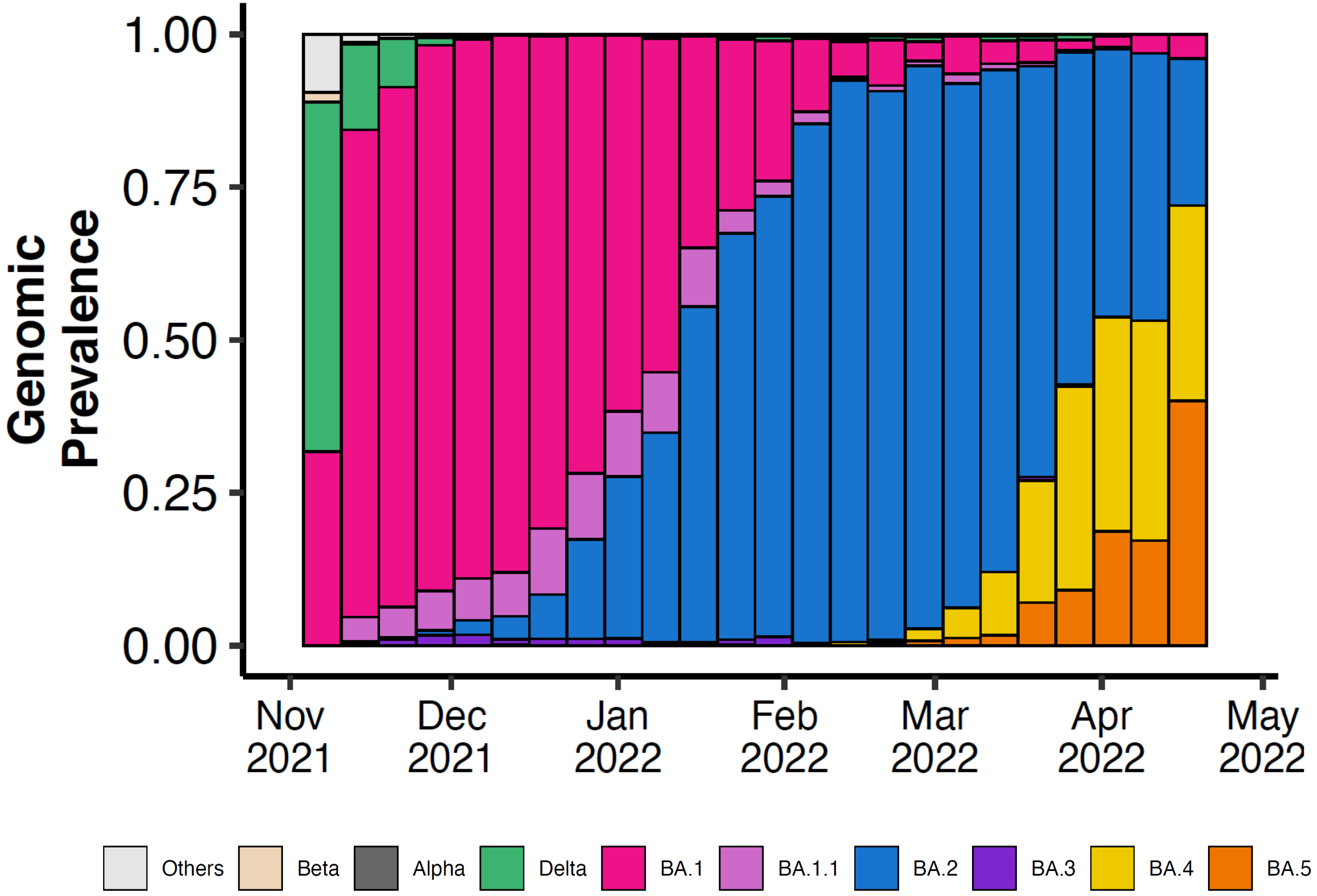
- **Omicron variant** is a family of different lineages (originally BA.1, BA.2 and BA.3)
- We have now identified **two new Omicron lineages** (**BA.4 & BA.5**)
- Although similar to BA.2, there are **important additional mutations**
- Genomic data and PCR test data suggest BA.4 and BA.5 are responsible for **an increasing share of cases in SA** since March and have a **growth advantage over BA.2**
- Now consistent indicators that this is associated with a change in epidemiology – **increasing cases & test positivity**, and **increase in hospital admissions in some provinces**

Context - Fourth wave involved different Omicron lineages



Early Omicron wave dominated by BA.1 – wave prolonged by BA.2 but without significant resurgence in reported cases

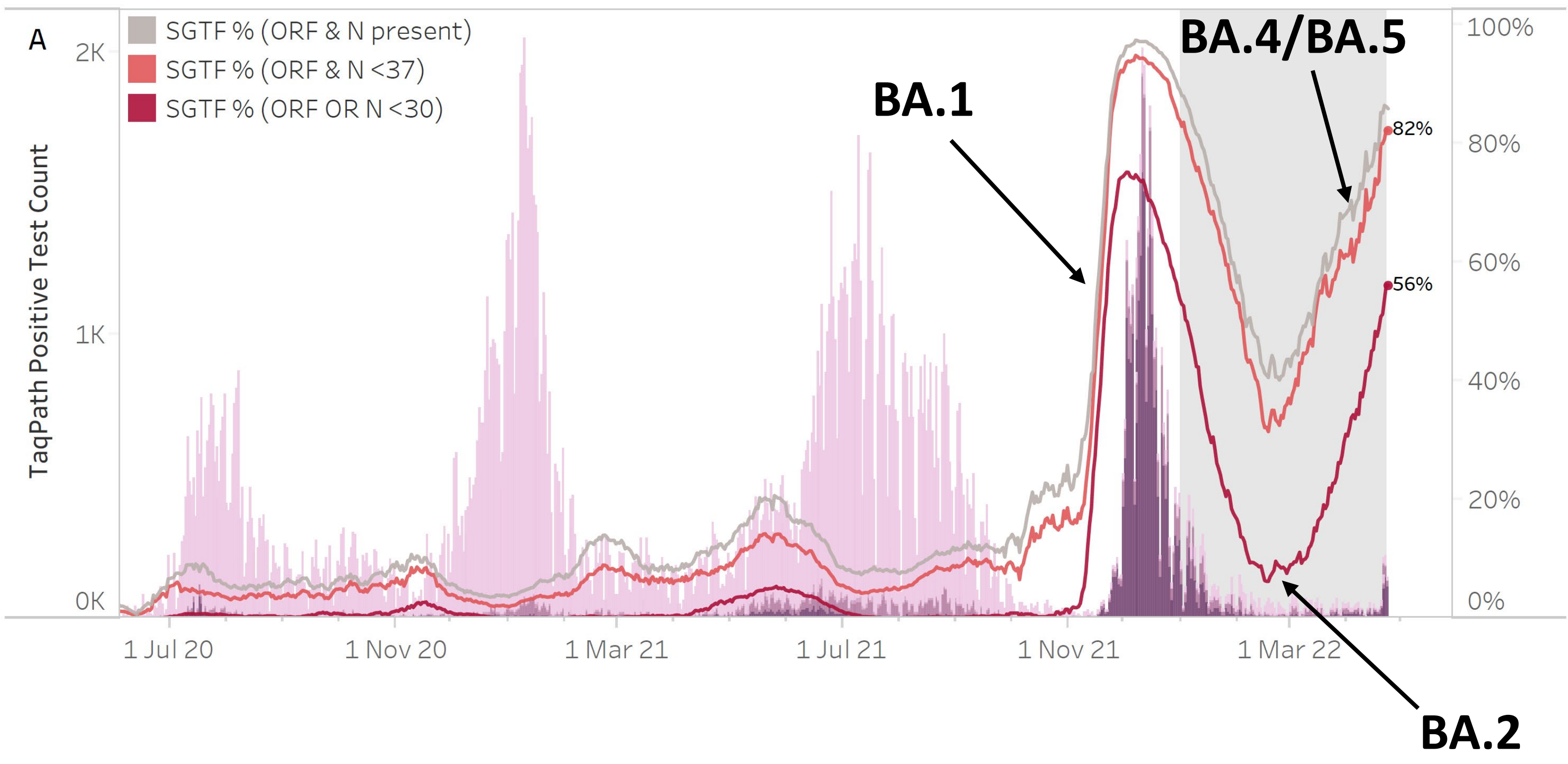
BA.4 & BA.5 increasing as a proportion of sequenced cases



In genomic surveillance, BA.4 and BA.5 have been growing in prevalence since early March

BA.4 and BA.5 are replacing BA.2 - together responsible for over half the genomically sequenced cases since early April

Increase in PCR S-gene target failure (SGTF) since early March

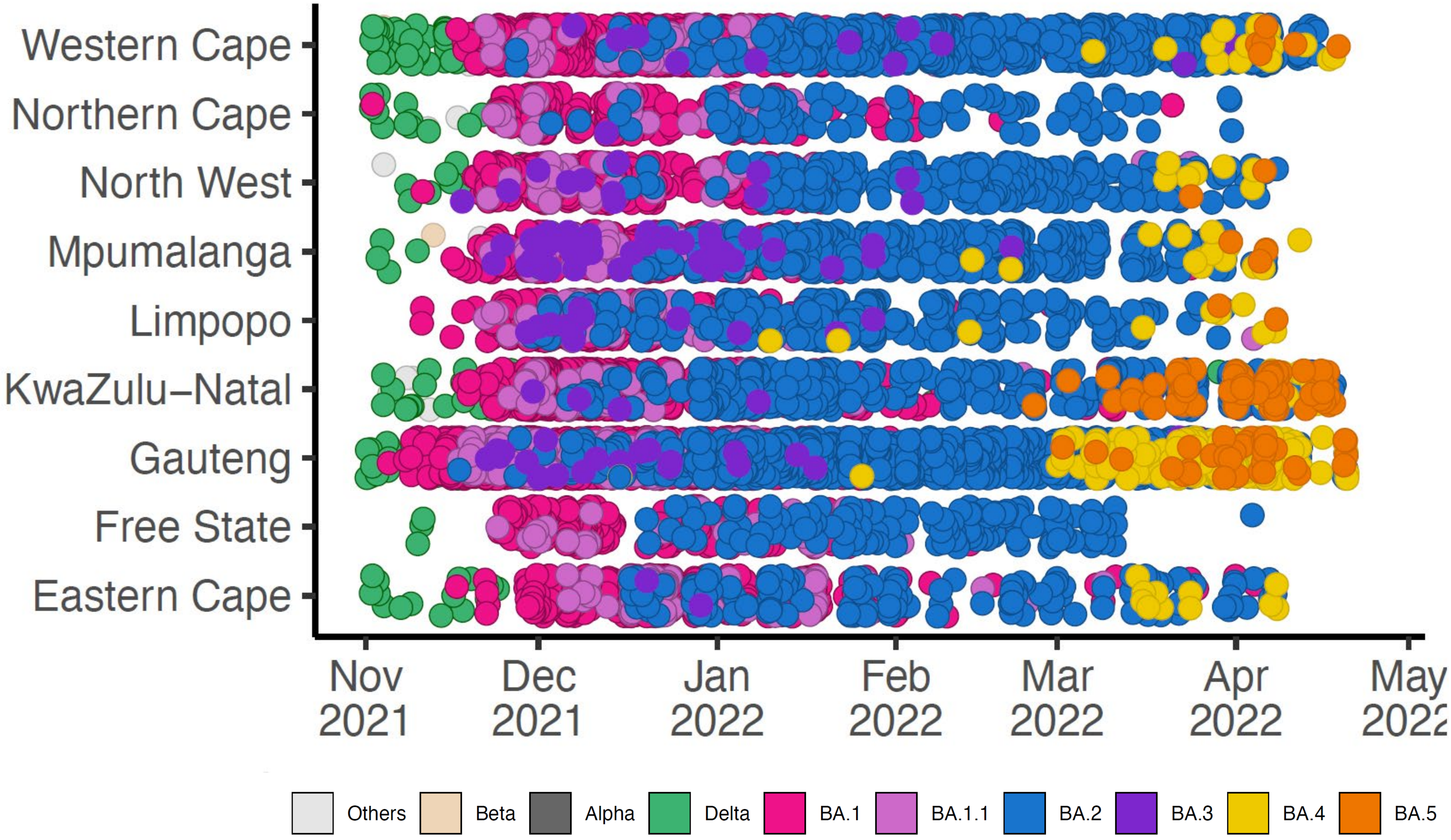


S-gene target failure is due to the 69-70 deletion in the spike protein – this is present in BA.1, BA.4 and BA.5 but not generally in BA.2

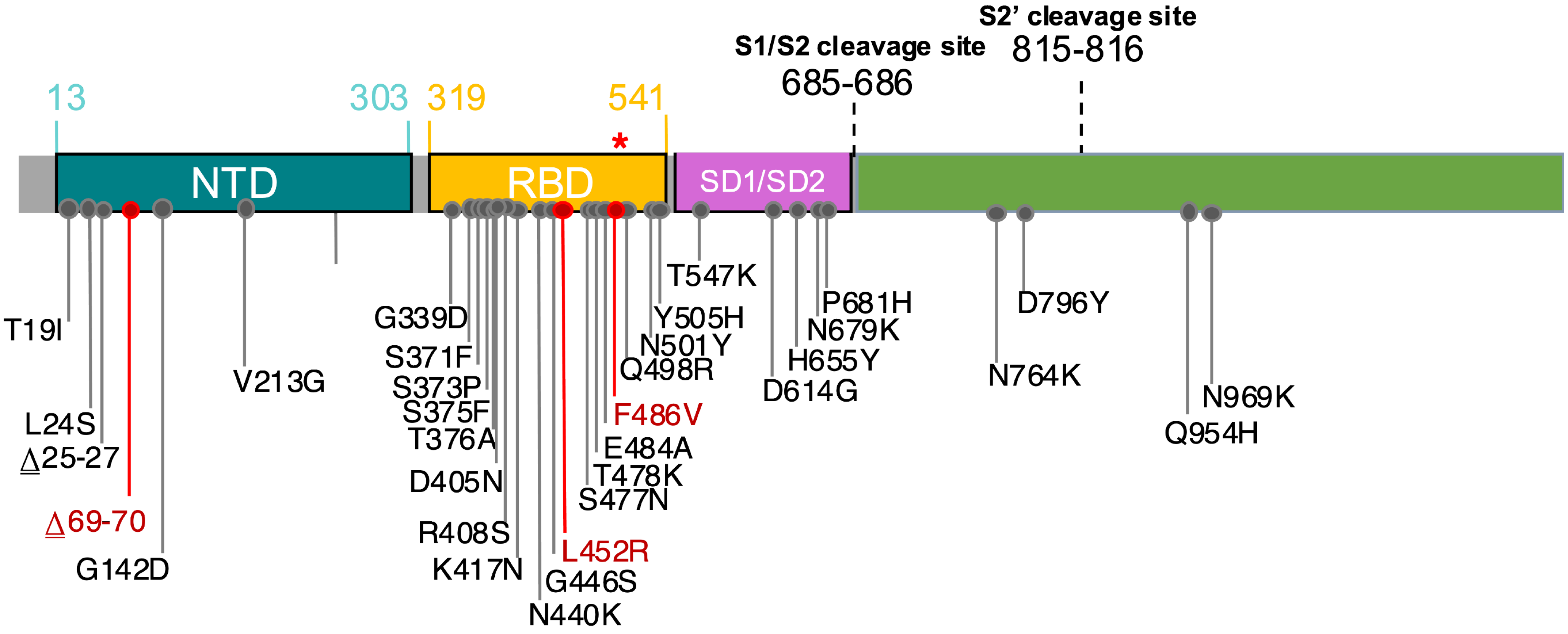
- In NHLS data, proportion of positive tests with SGTF increasing since early March
- SGTF pattern heterogeneous across provinces (and volume of testing with TaqPath assay differs by province)
- Similar reports from private laboratories

Laboratory Diagnostics Cycle Threshold (Ct) Value Update: Data to 23 Apr 2022
NHLS centralised data

BA.4 and/or BA.5 detected in seven provinces



Spike mutation profile for BA.4 & BA.5



BA.4 and BA.5 have identical spike mutations – closest sister lineage genetically is BA.2 - but there are some important differences

- Additional mutations: **69-70del**, **L452R**, **F486V**
- No mutation (wild type) at **Q493** (cf. Q493R in BA.1, BA.2 and BA.3)

BA.4 & BA.5 - potential impact of additional spike mutations

- **L452R** was present in Delta, Kappa & Epsilon variants
  - Associated with **increased virus replication and infectivity**
  - Associated with **resistance to neutralizing antibodies** and **polyclonal sera**
  - Other Omicron lineages with L452 mutations spreading in other parts of the world (e.g. BA.2.12 in the United States)
- **F486V** is an uncommon mutation in the receptor-binding domain
  - Mutations at that position are associated with **resistance to neutralizing antibodies** and **polyclonal sera**
- Impact of each single mutation or constellation of mutations **difficult to predict** – work underway to understand how these changes affect the virus properties (particularly how well it evades immunity and whether it changes disease severity)

Greaney A, et al. Nat Commun 2021
Greaney A, et al. Cell Host Microbe 2021
Greaney A, et al. Virus Evol 2022

Evolving virus and immunity

- **Complex mix of immunity in South Africa** - acquired from vaccines and infections with WT, Beta, Delta, Omicron (BA.1 & BA.2)
- Growth of BA.4/BA.5 could relate to **different capacity to get around immunity against infection**
- **Waning immunity against infection** may also be contributing to resurgence
- **Immune protection against severe disease is different** (involves multiple parts of immune system) – waning less prominent, and harder for evolving virus to get around this
- Key public health measure against all variants/lineages is and will always be **vaccination to prevent severe disease (first, second and third doses**)

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More details in manuscript submitted for peer review

Continued Emergence and Evolution of Omicron in South Africa: New BA.4 and BA.5 lineages

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- Manuscript submitted for peer review
- Preprint available at KRISP and CERI websites
- https://www.krisp.org.za/publications.php?pubid=392
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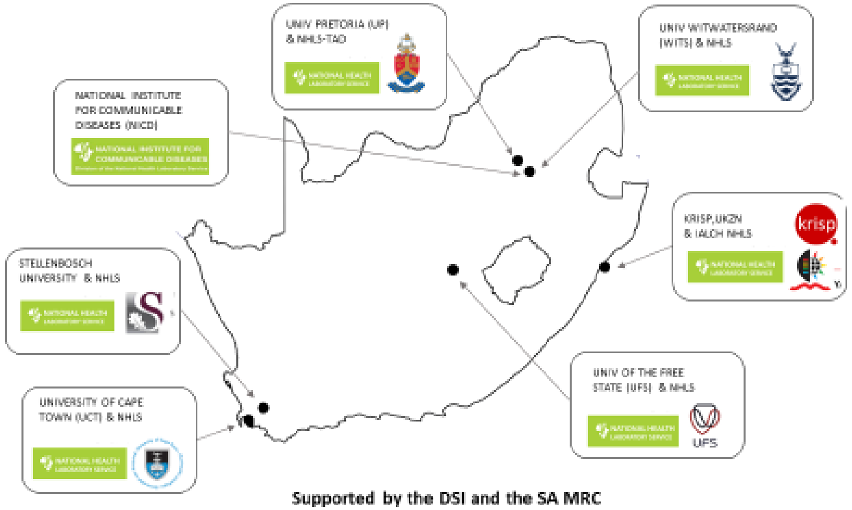

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