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krisp

A NEW SARS-CoV-2 LINEAGE WITH MULTIPLE SPIKE MUTATIONS EMERGE AND SPREAD FAST IN SOUTH AFRICA

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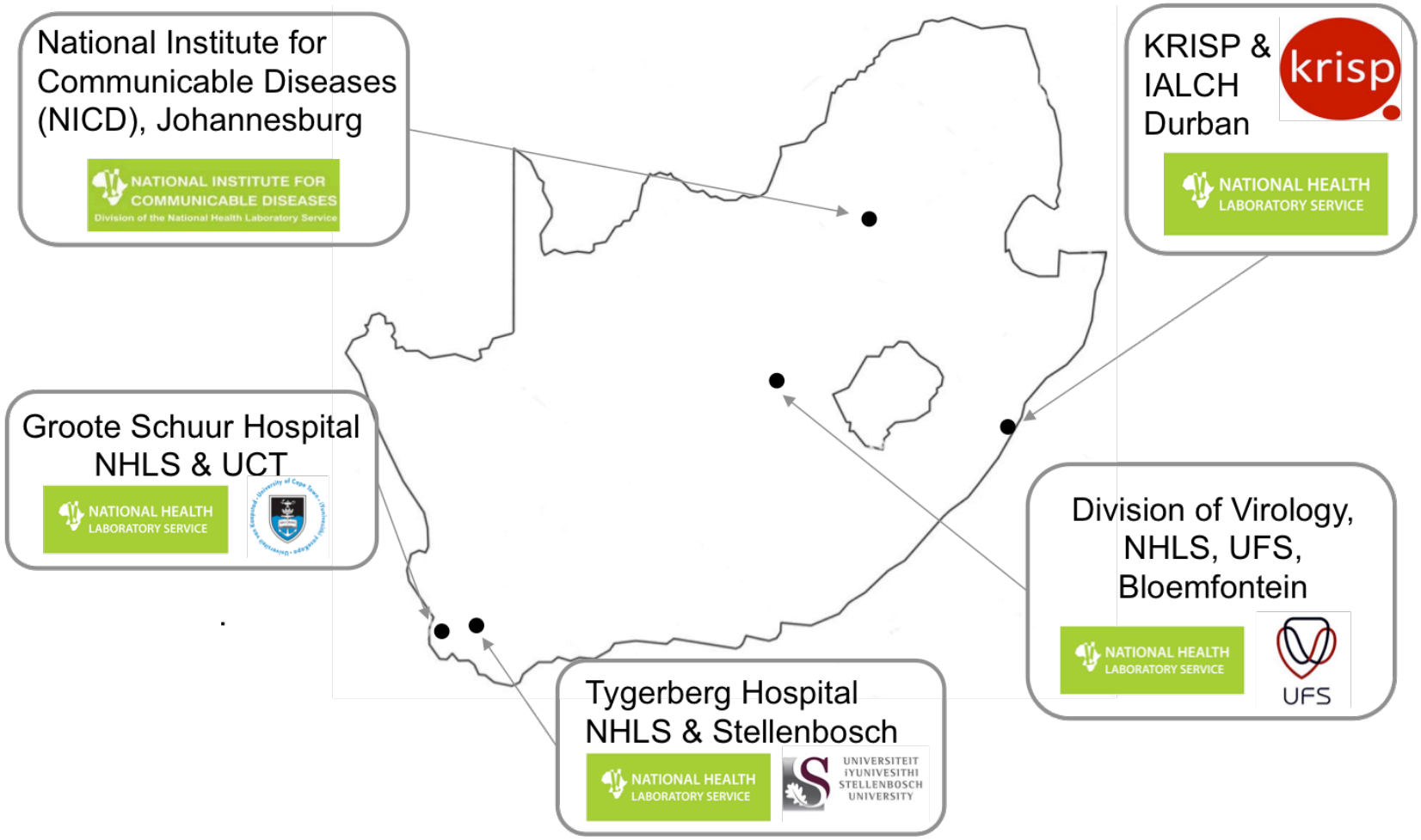
UKZN INSPIRING GREATNESS

Genomics a potent tool in the COVID-19 fight

- Used to discover the virus that caused COVID-19 (i.e. SARS-CoV-2)
- To develop diagnostics (i.e. qPCR)
- To develop vaccines (i.e. mRNA and vector vaccines)
- To track transmission (i.e. introductions, outbreaks, spread)
- To identify re-infection
- To understand the body interaction with the virus.

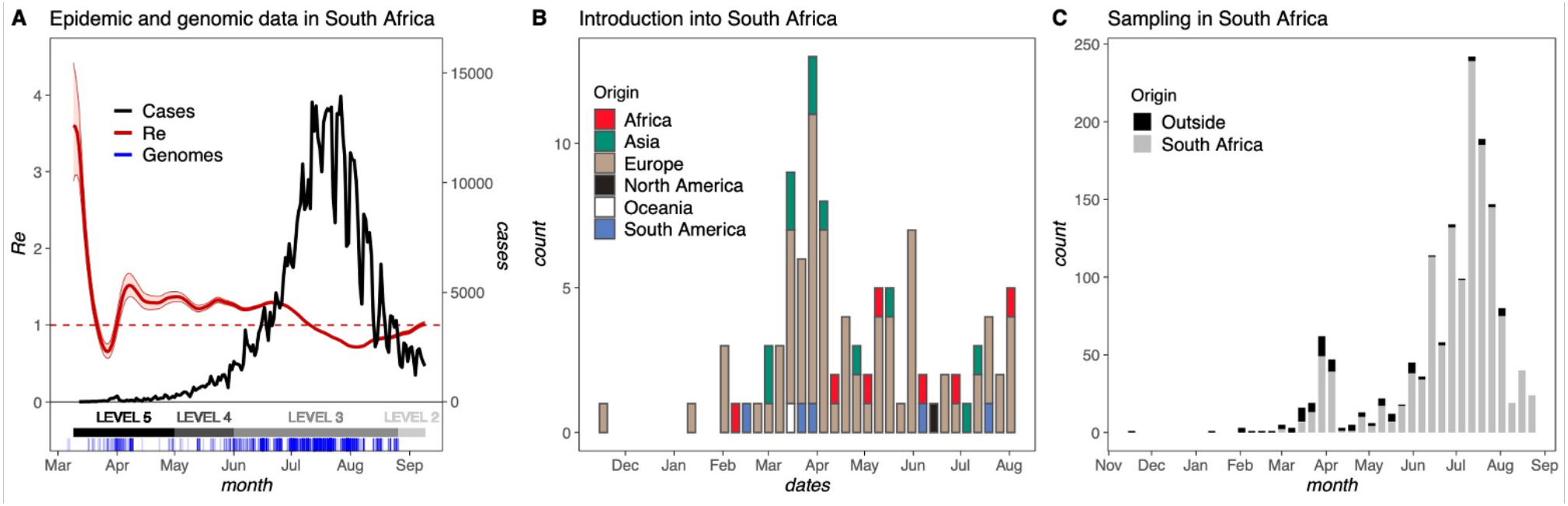
Over 250,000 genomes produced - 2,500 in South Africa

Network for Genomic Surveillance in South Africa (NGS-SA)



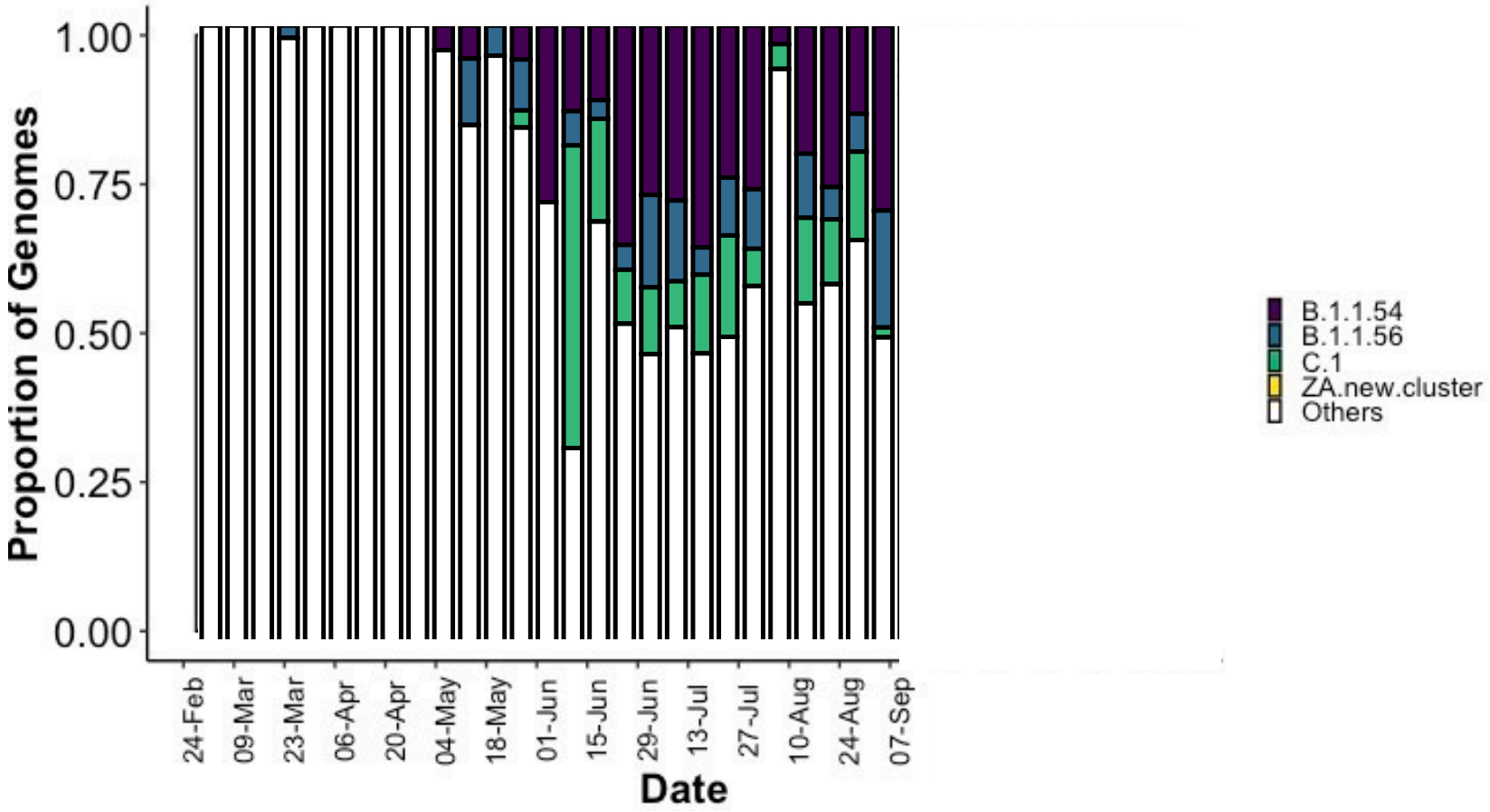
Initial funding from the Department of Science and Innovation (DSI) and the SAMRC

Introductions and local transmission of SARS-CoV-2 (first wave)



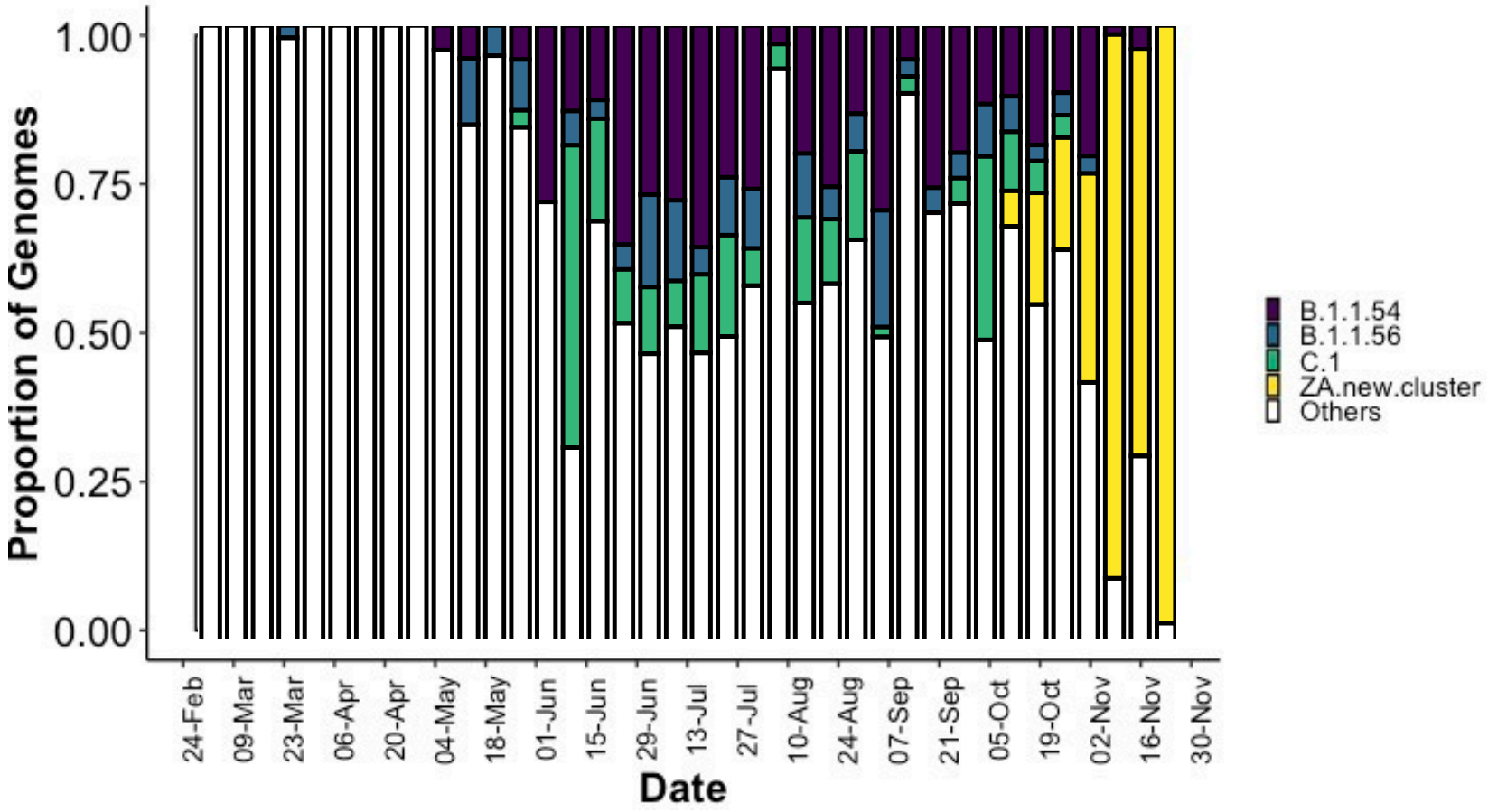
Tegally et al. *Nature Med* 2020 (in press)

Multiple lineages circulating in South Africa



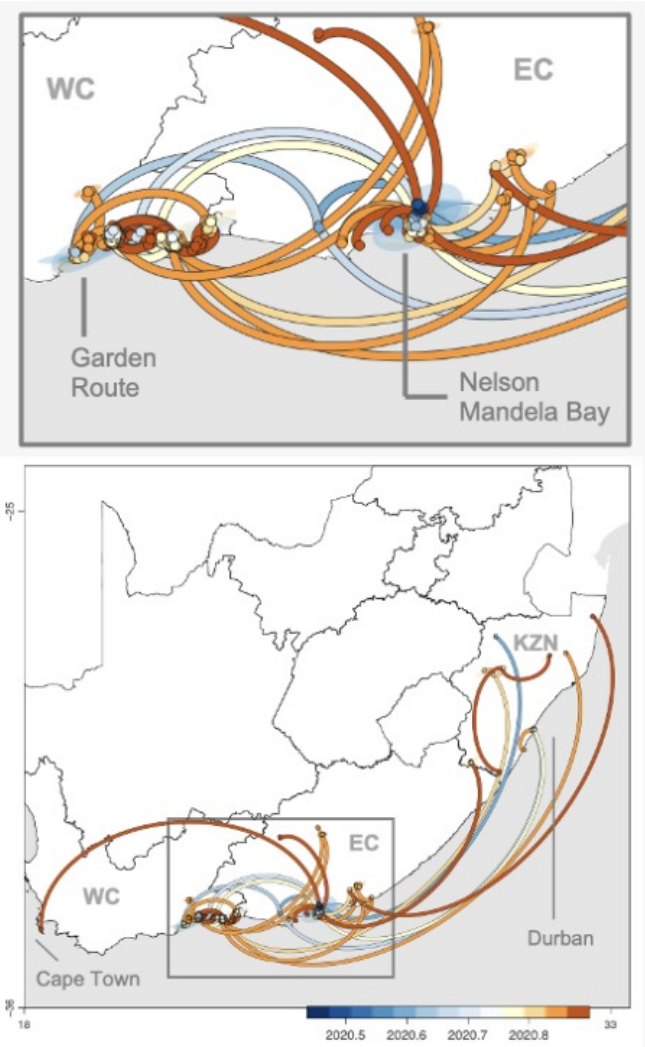
In the first wave, we had multiple lineages circulating
(Three lineages responsible for 42% of infection)

New lineage rapidly become the dominant



Since early November, the new lineage has rapidly become the **dominant lineage** in the sampled locations
(>90% of sequences in week beginning 16 Nov)

New lineage emerged in NMB and spread quickly to Garden Route and KZN.

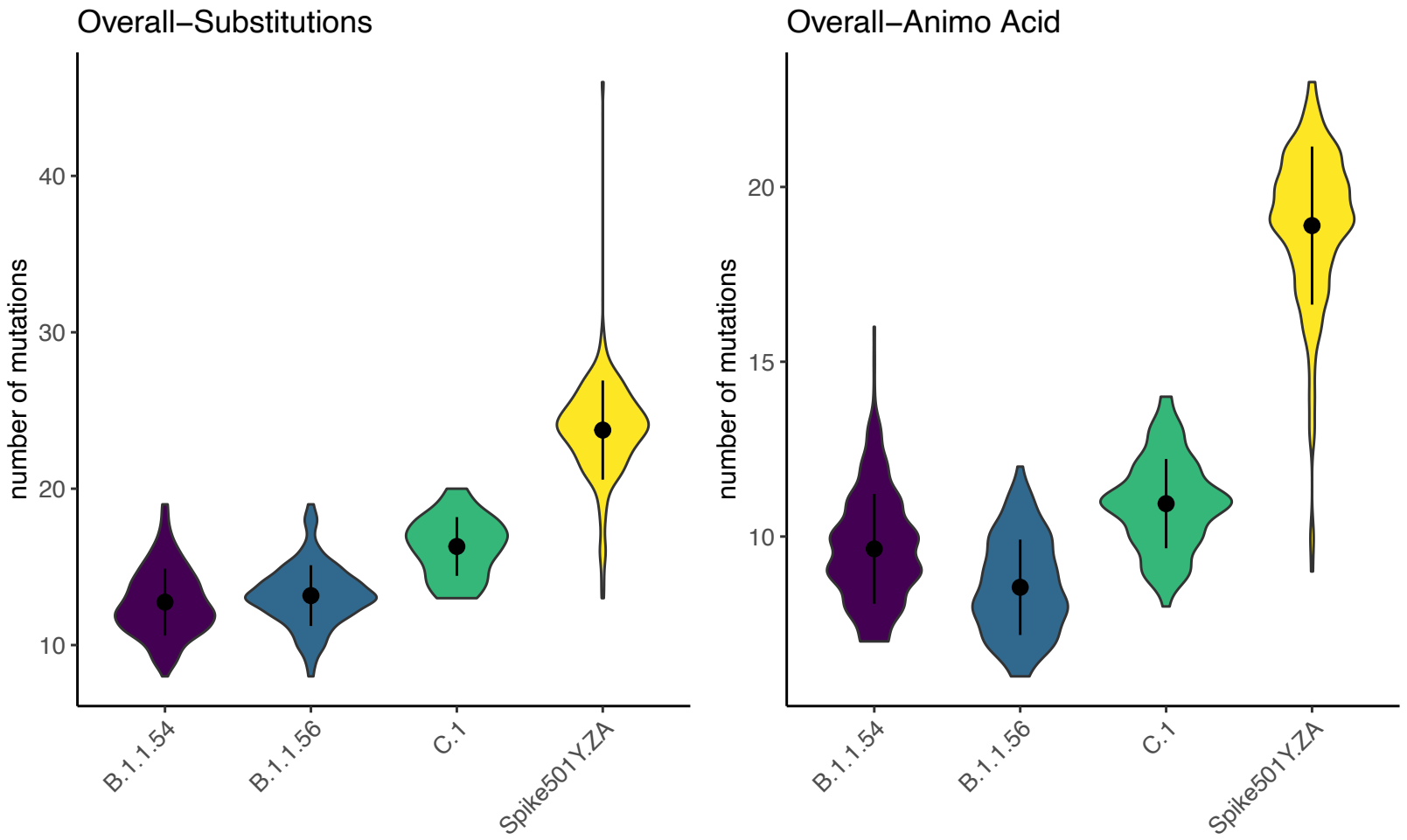


Our analysis suggests that this lineage emerged in Nelson Mandela Bay then spread to other districts in EC, to Garden Route and to multiple locations in KZN

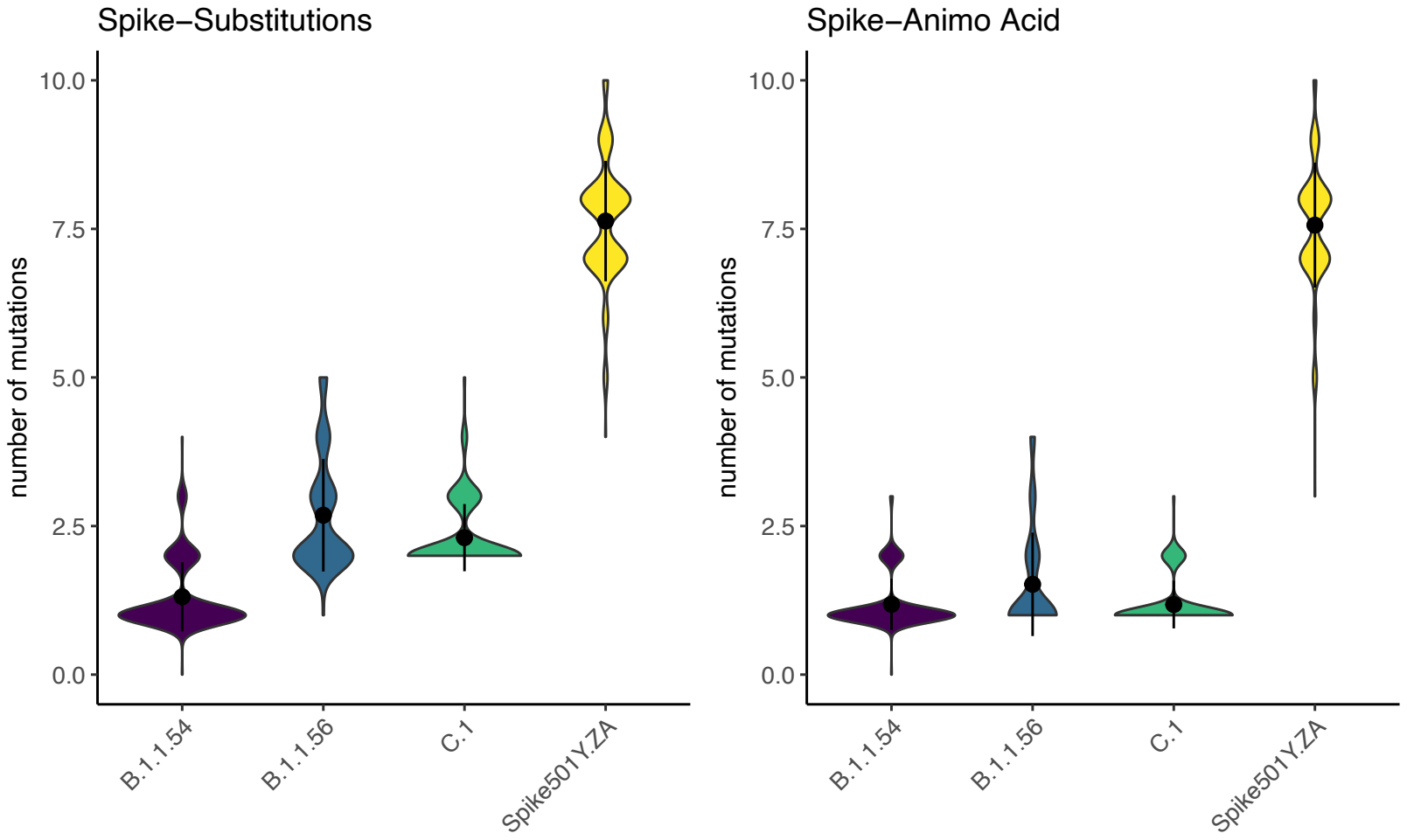
We have detected this lineage in **196 genomes** collected **15 Oct – 25 Nov** originating from:

- 25 different health facilities in 3 districts of EC
- 10 different health facilities in 6 districts of KZN
- 17 different health facilities in 4 local municipalities of Garden Route District
- 1 health facility in City of Cape Town*

New lineage has many more mutations (especially amino-acid ones)

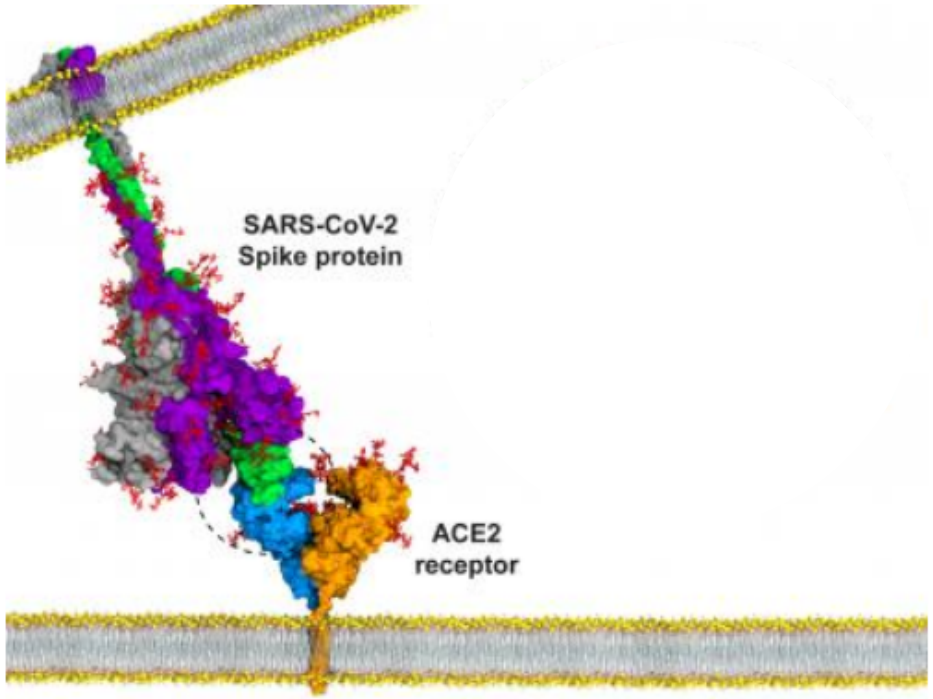


New lineage mutations concentrate in the Spike protein (all mutations change amino-acid)



Importance of the spike glycoprotein and receptor-binding domain

Virus



Human cell

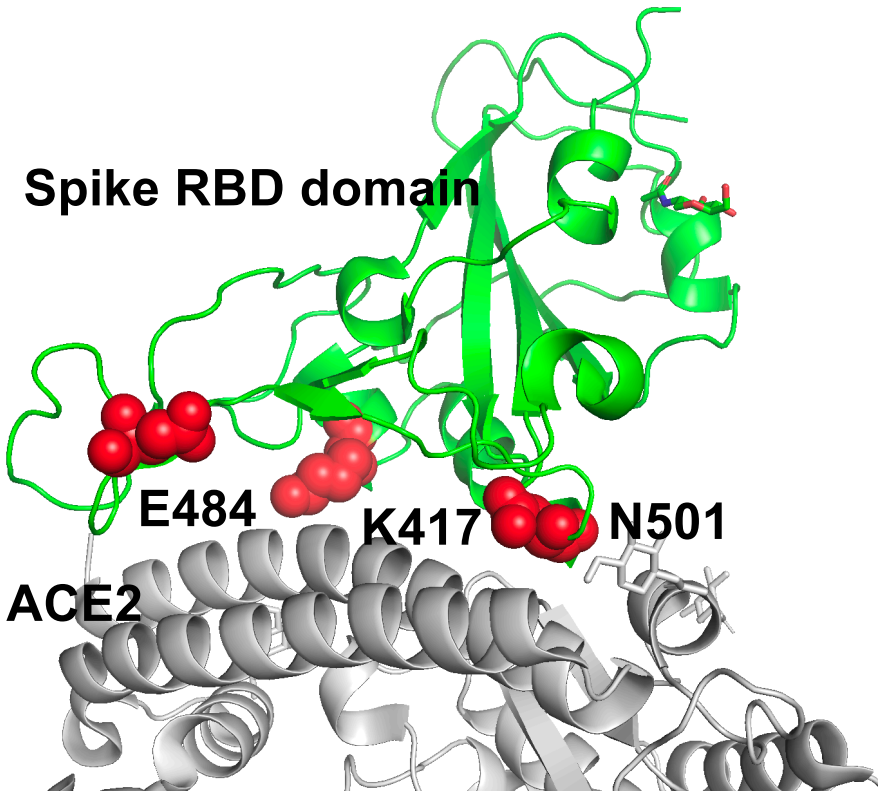
The **spike protein** attaches to the **ACE2 receptor** on host cells

Mutations may therefore affect ACE2 binding and/or neutralization

The **receptor-binding domain** (**RBD**) which is what directly interacts with the ACE2 receptor is also the main target for **neutralizing antibodies and vaccines**

Image courtesy of: https://www.sciencemuseumgroup.org.uk/blog/coronavirus-the-spike/

Structural visualization of spike RBD-hACE2 complex



<u>The three RBD mutations are at key residues interacting with the human ACE2 receptor and with neutralizing antibodies (NAbs)</u>

N501Y enhances binding affinity to ACE2

E484K enhances binding affinity to ACE2 and confers resistance to class 2 NAbs

K417N would abolish key interactions with class 1 NAbs, and likely contributes toward immune evasion at this site

Next steps

- A key task now is to get a better understanding of whether there is any clinical and epidemiological evidence to suggest phenotypic impact:
  - **Increased transmissibility** – very plausible from the data
  - **Increased pathogenicity** - different disease profile/progression
  - **Escape from neutralizing antibodies** - re-infection

- At the same time we are growing the virus and conducting experiments to assess the functional effect of these spike mutations
  - **Infectivity** of the virus in a cell system
  - **Neutralization** assays with antibodies from patients infected with other circulating strains (without the spike mutations)

Expanding and strengthening genomic surveillance

- We intend to intensify sampling from other districts of Eastern Cape, Western Cape and KwaZulu-Natal to understand the persistence of this lineage
- We should expand sampling to other provinces to assess the extent of its dissemination within the country
- We should also link with clinical investigations of cases of suspected re-infection and severe disease development

Conclusion

- Genomic surveillance is a critical component of the public health response – exemplified by early detection and tracking of this new lineage
- We have detected a new lineage with mutations at key sites in spike glycoprotein, which shows evidence of rapid and diffuse spread through three provinces
- The full significance of the mutations is yet to be determined and work is ongoing to characterize the phenotypic impact

Questions?

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