SARS-CoV-2 Sequencing Update
1 December 2021

Supported by the DSI and the SA MRC

Prepared by the National Institute for Communicable Diseases (NICD) of the National Health Laboratory (NHLS) on behalf of the Network for Genomics Surveillance in South Africa (NGS-SA)
The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 1 December at 08h48

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


Case data is based on specimen collection date. Cases from https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-epidemiological-brief/ Test data from https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-testing-summary/
Number of South African genomes deposited on GISAID, by specimen collection week, 2020 and 2021 (N=23,972*)

Total genomes: 23,972
2020 genomes: 6,353
2021 genomes: 17,619

Sequencing data ending epi week 47 (ending 27 November 2021)
Currently in epi week 48 (ending 4 December 2021)

*This represents the cleaned, de-duplicated dataset of unique sequences. This dataset will be used for all further figures.
All provinces, apart from GP, KZN, NC and WC, have comparable percentage of overall cases and overall sequenced genomes. The majority of November sequencing data is from Gauteng.
Omicron lineage mutation profile

- 45-52 amino acid changes (including deletions) across the whole GENOME
  - 26-32 changes in SPIKE
- Does not possess the RdRp G671S change associated with a decrease in Ct value for Delta variants
- Does possess the Spike Δ69-70, which causes the S-Gene Target Failure (SGTF) and was previously seen in the Alpha VOC
- Nucleocapsid mutations not predicted to affect antigen rapid diagnostic tests
### Omicron spike mutations compared to other VOC/VOIs

<table>
<thead>
<tr>
<th>Variant</th>
<th>Spike mutations</th>
<th>Mutations with unknown or unconfirmed impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omicron</td>
<td></td>
<td>Mutations observed in</td>
</tr>
<tr>
<td>C.1.2</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Beta</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Alpha</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Alpha+E484K</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Gamma</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Delta</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Kappa</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Eta</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Iota</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Lambda</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Mu</td>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>

- 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

#### Spike mutations

<table>
<thead>
<tr>
<th>Spike mutations</th>
<th>Mutation observed in</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥ 50% sequences</td>
</tr>
<tr>
<td></td>
<td>5 - 50% sequences</td>
</tr>
<tr>
<td></td>
<td>&lt;5% sequences</td>
</tr>
</tbody>
</table>

**NGS-SA**

Network for Genomic Surveillance in South Africa
Omicron has been detected in 19 countries across the globe (detections based on GISAID).
Delta dominated South Africa’s third wave with >90% frequency in October, with C.1.2 detection remaining <4%. Omicron dominates November sequencing data but sequencing is ongoing to determine its true prevalence.
Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in September – November 2021

The Delta variant dominated in September and October in South Africa. Omicron was first detected in South Africa in November and dominates comprising 74% (183/249) of sequences.
Detection Rates: Beta, Delta, C.1.2 and Omicron

C.1.2 continues to be detected at ≤ 4% of sequences in November. Prevalence of Beta increased in October but has not been detected in November. Omicron was first detected in South Africa on November 8th and accounts for 74% (n=183/249) of these genomes.
Eastern Cape Province, 2021, n = 1673
Free State Province, 2021, n = 930
Gauteng Province, 2021, n = 4745
KwaZulu-Natal Province, 2021, n = 2134
Limpopo Province, 2021, n = 1133
Mpumalanga Province, 2021, n = 1064
Northern Cape Province, 2021, n = 1202
North West Province, 2021, n = 1152
Summary

• New B.1.1.529 (21K) lineage has been designated Variant of Concern Omicron
  • Earliest detection in South Africa: 8 November, Gauteng
  • Omicron dominates November sequencing data at 74% of genomes (n=183/249). Sequencing is ongoing to determine prevalence of Omicron in other provinces.
  • Omicron has now been detected in 19 countries worldwide
  • More information can be found at https://www.nicd.ac.za/frequently-asked-questions-for-the-b-1-1-529-mutated-sars-cov-2-lineage-in-south-africa/

• Delta variant dominated in all provinces until end October
  • The Delta sub-lineages vary by province

• C.1.2 lineage detected in all provinces of South Africa with prevalence of <4% of genomes per month
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Multiple labs from NGS-SA and collaborating private laboratories are contributing to the sequencing effort.

**NGS-SA Labs**
- CERI: Centre for Epidemic Response and Innovation
- KRISP: KZN Research Innovation and Sequencing Platform
- 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

*NGS-SAs laboratories
<table>
<thead>
<tr>
<th>WHO label</th>
<th>Pango lineages*</th>
<th>GISAID clade</th>
<th>Nextstrain clade</th>
<th>Additional amino acid changes monitored*</th>
<th>Earliest documented samples</th>
<th>Date of designation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha</td>
<td>B.1.1.7#</td>
<td>GRY</td>
<td>20I (V1)</td>
<td>+S:484K, +S:452R</td>
<td>United Kingdom, Sep-2020</td>
<td>18-Dec-2020</td>
</tr>
<tr>
<td>Gamma</td>
<td>P.1</td>
<td>GR/501Y.V3</td>
<td>20J (V3)</td>
<td>+S:681H</td>
<td>Brazil, Nov-2020</td>
<td>11-Jan-2021</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VOC: 11-May-2021</td>
</tr>
<tr>
<td>Omicron*</td>
<td>B.1.1.529</td>
<td>GR/484A</td>
<td>21K</td>
<td>-</td>
<td>Multiple countries, Nov-2021</td>
<td>VUM: 24-Nov-2021</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>VOC: 26-Nov-2021</td>
</tr>
</tbody>
</table>

[Accessed 1 December 2021](https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/)

*Notable spike (S) amino acid changes under monitoring, which are currently reported in a minority of sequenced samples
*Includes all descendant lineages.
#Includes all Q.* lineages in the PANGO nomenclature system.
§Includes all AY.* lineages in the PANGO nomenclature system.
## Currently designated Variants of Interest (VOI)

<table>
<thead>
<tr>
<th>WHO label</th>
<th>Pango* lineages</th>
<th>GISAID clade</th>
<th>Nextstrain clade</th>
<th>Earliest documented samples</th>
<th>Date of designation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lambda</td>
<td>C.37</td>
<td>GR/452Q.V1</td>
<td>21G</td>
<td>Peru, Dec-2020</td>
<td>14-Jun-2021</td>
</tr>
<tr>
<td>Mu</td>
<td>B.1.631</td>
<td>GH</td>
<td>21H</td>
<td>Colombia, Jan-2021</td>
<td>30-Aug-2021</td>
</tr>
</tbody>
</table>

*Includes all descendant lineages.

[https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/] accessed 1 December 2021
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.)