SARS-CoV-2 Sequencing Update
7 January 2022

Supported by the DSI and the SA MRC
Msmoi 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 7 January at 16h27.

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 – 2022
(N=26 719*)

Total genomes: 26 719
2020 genomes: 6 462
2021 genomes: 20 257

Sequencing data ending epi week 52 (ending 1 January 2022)
Currently in epi week 1 (ending 8 January 2022)

*This represents the cleaned, de-duplicated dataset of unique sequences. This dataset will be used for all further figures.
All provinces, apart from GP, NC and WC, have comparable percentages of overall cases and overall sequenced genomes.
Omicron sub-lineage spike mutation profiles

BA.1
21K

BA.2
21L

Lacks 69-70del
Not detectable by S-Gene Target Failure

BA.3
21M

Lineage definitions based on https://github.com/cov-lineages/pango-designation/issues/367
Images from https://covdb.stanford.edu/page/mutation-viewer/
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
Mutational profile of Omicron is largely shared amongst all sequences. Low mutation frequencies for N417N, N440K, G446S and N764K are most likely a result of poor coverage due to primer drop off.
Omicron has been detected in 122 countries across the globe (detections based on GISAID).
Delta dominated in South Africa until October at >80%. Omicron dominated November and early December at >95%.
The Delta variant dominated at >80% in October in South Africa, while Omicron was detected at 0.3% (2/768). Omicron dominated in November, at 84% (1141/1367) and continues to dominate in December (99%, 1057/1071).
Detection Rates: Beta, Delta, C.1.2 and Omicron

C.1.2 has been detected at ≤ 4% of sequences monthly since May 2021. Beta prevalence increased slightly in October but has since remained at low levels in November and December. Omicron has been dominant since November (>80% in November, >98% in December).
Free State Province, 2021-2022, n = 1070
Gauteng Province, 2021-2022, n = 5518

The diagram shows the distribution of cases over time, with a focus on specific variants such as Omicron and Delta. The x-axis represents the epiweek, and the y-axis shows the number of cases and the percent of genomes.}

[Diagram showing case distribution and genome percent over epiweeks]
Mpumalanga Province, 2021-2022, n = 1157

NGS-SA
Network for Genomic Surveillance in South Africa
Northern Cape Province, 2021-2022, n = 1377

Graph showing the number of genomes and cases over time in the Northern Cape Province from 2021 to 2022, with a total of 1377 cases.
North West Province, 2021, n = 1300

[Graph showing genomic surveillance data for the North West Province in 2021, with a total of 1300 cases. The graph includes a timeline of cases and a breakdown of different variants such as Omicron (21K), Omicron (21M), Beta (20H.V2), Delta (21A), and Alpha (20L.V1).]
Western Cape Province, 2021-2022, n = 4234

[Graph showing the number of genomes and percent of genomes over time for different variants, labeled with their respective dates and counts.]
Summary

• Variant of Concern Omicron
  • South Africa:
    • Dominated November sequencing data at 83.5% of genomes (n=1141/1367) and December sequencing data at 98.7% of genomes (n=1057/1071)
    • Detected in all provinces
    • BA.1 is dominant in South Africa. BA.2 has been detected at low levels since November 2021 and does not appear to be increasing; however, more sequencing data from recent weeks are needed to confirm this
  • Global:
    • Detected in 122 countries worldwide
    • Split into three lineages based on different mutational profiles: BA.1 (21K), BA.2 (21L), BA.3 (remains in 21M with parent lineage B.1.1.529 as does not meet requirements for new clade)
• Delta variant dominated in all provinces until end October
  • Delta sub-lineages varied by province
• C.1.2 lineage detected in all provinces of South Africa with prevalence of <4% of genomes per month and continues to be detected at low frequency
This project (RIA2020EF-3030) is part of the EDCTP2 programme supported by the European Union.
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Funders:
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G7 Global Health fund, Robert Koch Institute, Dr Fabian Leendertz

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GIZ/BMBF: African Network for improved diagnostics and epidemiology of common and emerging infectious agents (ANDEMIA)
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Multiple labs from NGS-SA and collaborating public and private laboratories are contributing to sequencing, both as originating and as submitting (pictured here) laboratories.
# Variants of Concern (VOC)

<table>
<thead>
<tr>
<th>WHO label</th>
<th>Pango lineage•</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>VOC: 11-May-2021</td>
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</tr>
<tr>
<td>Omicron*</td>
<td>B.1.1.529</td>
<td>GRA</td>
<td>21K, 21L</td>
<td>+S:R346K</td>
<td>Multiple countries, Nov-2021</td>
<td>VUM: 24-Nov-2021</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VOC: 26-Nov-2021</td>
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</tr>
</tbody>
</table>


* Includes all descendant lineages. See the cov-lineages.org and the Pango network websites for further details.
* See TAG-VE statement issued on 26 November 2021
* Only found in a subset of sequences
# Currently designated Variants of Interest (VOI)

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<th>Pango lineage*</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. 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.)