Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern

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Why is Omicron causing such alarm?

Scientists are concerned for two main reasons. One is epidemiological and relates to the speed with which the variant that emerged this month is spreading in South Africa, particularly in Gauteng province.

Daily cases have more than tripled in South Africa since Tuesday, with 2,828 cases recorded on Friday. Early testing results indicated that 90 per cent of the new cases on Wednesday in Gauteng were caused by the new variant.

the R value, which measures an epidemic’s growth rate, was estimated at 1.93 for Gauteng, where Omicron is concentrated. This compared with 1.47 for South Africa as a whole.
What is the B.1.1.529 lineage?

This lineage possesses a high number of mutations previously seen in other SARS-CoV-2 variants of interest (VOI) or variants of concern (VOC) but also other mutations which are novel.

At the present, the B.1.1.529 lineage is relatively distinct from the C.1.2, Beta and Delta variants and has a different evolutionary pathway.

One of these changes can be detected through standard diagnostic tests that target the S gene, which allows detection of this lineage in South Africa without sequencing data.
PCR-based proxy for new variant

- Variant can be detected with one particular PCR assay (before whole genome sequencing)

- New increase in S-gene dropout noted by NHLS and private labs very recently - from mid-November

- Now rapidly increasing in most provinces

Figure 9: S-gene dropout (%) of cases with high \( \text{V} \) (Ct value<30 for ORF or N gene). The red bars are the number of tests reporting the presence of SARS-CoV-2 (daily) on the TaqPath assay. The solid blue line is the moving median of S-gene dropout (%).

*Current (end of Nov ’21) dramatically increasing trend in the proportion of SGTF (Ct value<30 for ORF or N gene)
## Mutation list

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**Mutation list**

- **Type**: The type of mutation (e.g., deletion, insertion, etc.)
- **Pos**: Position of the mutation
- **Ref**: Reference nucleotide
- **Alt**: Alternate nucleotide
- **Strand**: Strandedness of the mutation
- **End**: End position of the mutation
- **Name**: Name of the mutation
- **Start**: Start position of the mutation
- **Stop**: Stop position of the mutation
- **Cell line**: Cell line where the mutation was identified
- **Strain**: Strain of the organism
- **Organism**: Organism from which the mutation was identified
- **Source**: Source of the mutation
- **Refseq**: Reference sequence
- **Ensembl**: Ensembl accession number
- **Genome**: Genome accession number
- **Gencode**: Gencode accession number
- **Annotation**: Annotation details

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*Note: The table represents a sample from a larger dataset and does not cover all possible mutations.*

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*Table columns are separated by spaces.*

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*Row values are separated by tabs.*

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*Column widths are adjusted for readability.*
The 50 mutations on the new B.1.1.529 variant - The key mutations.

1. The combination of mutations at K417N, S477N, Q498R and N501Y is thought to be an antibody-evasion strategy.
2. Deletions at positions 69 & 70 mean the variant can be detected using some PCR tests without the need for full genomic sequencing.
3. Four new mutations at Q339D, S371L, S373P and S375F may create additional obstacles for certain antibodies.
4. Three mutations near the furin cleavage site at H655Y, N679K and P681H may be associated with increased transmissibility.
5. Three additional deletions at positions L105, S106 and G317 in NSP6, a protein that is not part of the spike, may aid in immune evasion.
6. In total there are 15 mutations in the receptor binding domain, the part of the spike that mediates how easily the virus attaches itself to cells.

Sources: Ulrich Elling; Björn Meyer; Kevin McCarthy; covariants.org
Receptor binding domain

• 15 of the mutations are on the “receptor binding domain” — which acts like a “grappling hook” for the Sars-Cov-2 virus to enter human cells.

• The Delta variant which accounts for almost all sequenced cases worldwide dented the effectiveness of vaccines with just three mutations in this region.
The B.11.529 lineage has a deletion (∆69-70) within the S gene that allowed for rapid identification of this variant in South Africa and will enable continued monitoring of this lineage irrespective of available sequence data. However, most other targets (including the N and RdRp genes) remain unaffected from specimens tested in over 100 specimens from testing laboratories in Gauteng so it is unlikely that overall PCR test sensitivity is affected. These PCR tests typically detect at least two different SARS-CoV-2 targets, which serves as a backup in the case of a mutation arising in one.

Analysis of the mutations in the nucleocapsid (N gene) of B.11.529 viruses suggests that rapid antigen tests should be unaffected, however verification of this is underway.
B.1.1.529 – potential impact of mutations

- Multiple RBD and NTD mutations associated with resistance to neutralizing antibodies (and therapeutic monoclonal antibodies)
- Cluster of mutations (H655Y + N679K + P681H) adjacent to S1/S2 furin cleavage site – associated with more efficient cell entry → enhanced transmissibility
- nsp6 deletion (Δ105-107) – similar to deletion to Alpha, Beta, Gamma, Lambda – may be associated with evasion of innate immunity (interferon antagonism) → could also enhance transmissibility
- R203K+G204R mutations in nucleocapsid - seen in Alpha, Gamma, Lambda – associated with increased infectivity
Does infection with B.1.1.529 result in similar symptoms as with other variants?

- Currently no unusual symptoms have been reported following infection with the B.1.1.529 variant and as with other variants some individuals are asymptomatic.
Will these mutations affect vaccine effectiveness, disease severity, and transmissibility?

- SARS-CoV-2, like all viruses, changes with time, with mutations that afford the virus some kind of advantage being selected for in recent infections.
- While some of the mutations in the B.1.1.529 lineage have arisen in other SARS-CoV-2 variants of concern or variants of interest, we are being cautious about the implications, while we gather more data to understand this lineage.
Will these mutations affect vaccine effectiveness, disease severity, and transmissibility?

- Based on our understanding of the mutations in this lineage, partial immune escape is likely, but it is likely that vaccines will still offer high levels of protection against hospitalisation and death.

- Vaccination remains critical to protect those in our communities at high risk of hospitalisation and death, to reduce strain on the health system, and to help slow transmission.

- Non-pharmaceutical interventions (NPIs) are still proven to prevent the spread of all SARS-CoV-2 viruses.
Take home message

Minister Phaahla stresses the importance of vaccination, as the more individuals who are vaccinated, the less opportunities there are for #COVID19 variants to emerge.

#NewVariant
#B11529

"The importance of non-pharmaceutical interventions remains unchanged and the public are urged to be responsible," says @Dr_Groome, Head of the Division of Public Health Surveillance and Response @nicd_sa