Genomic surveillance of SARS-CoV-2 in Belgium

Report of the National Reference Laboratory (UZ Leuven & KU Leuven)

Situation update – 26 of November 2021
(report 2021_56)

Executive summary

South Africa has communicated on 25/11/2021 the emergence of a new variant of concern (will probably be named Nu, corresponding to the pangolin lineage B.1.1.529). In this report, we discuss the current situation in South Africa and the world, and we assess the current situation in Belgium.

We report here the first case of B.1.1.529 infection in Belgium.

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Previous reports can be downloaded using the following link:
https://www.uzleuven.be/nl/laboratoriumgeneeskunde/genomic-surveillance-sars-cov-2-belgium

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1. Situation in South Africa

South Africa has one of the best genomic surveillance systems around the world, fueled by outstanding scientists and a very efficient network of collaborating laboratories. The data they share with the world is of outermost importance. Most other countries in the African continent still have very limited capacity to accurately and quickly identify emerging public health threats, and this situation should be regarded as a major problem at the global level.

South Africa is now experiencing a fourth wave of SARS-CoV-2 infections. The two last waves were caused by variants of concern, namely Beta (first described in South-Africa) and Delta (first described in India). The current wave is caused by a new variant of concern which has very recently been characterised as B.1.1.529 or variant Nu (Figure 1). This resurgence of infections occurs in the context of the summer (Southern Hemisphere) and of low baseline circulation of the Delta variant, suggesting that the new variant might be more transmissible than the Delta variant.

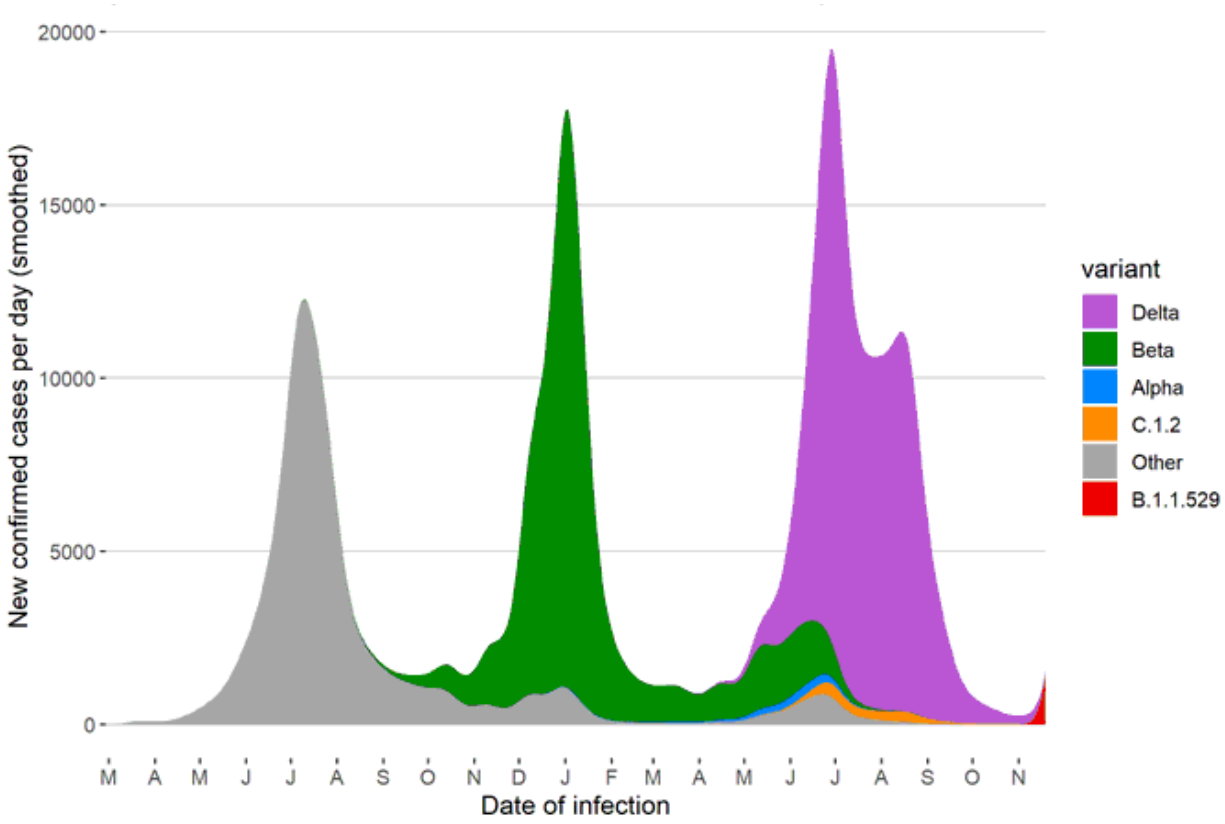

Figure 1 : New confirmed cases of SARS-CoV-2 per day and by variant in South Africa.

This potentially higher transmissibility of Nu compared to Delta seems to be confirmed in a multinomial fit analysis (Figure 2) based on the sequencing data and the data generated by the diagnostic PCR

laboratories (S gene target failure when using the TaqPath PCR). As the situation is rapidly evolving and the disease surveillance efforts in South Africa are highly focused on the detection of this new variant (active case finding is prioritized against baseline surveillance), the actual evolution of this variant may be overestimated. Nevertheless, even if this unprecedented growth rate advantage (currently estimated at 38% per day) would be lower, this new variant very probably still has the sufficient growth advantage to become the dominant variant in South Africa and the rest of the world. In other terms, this variant could have the potential to cause a new global wave of infections. The scale of this wave and its impact on the health of populations will be determined by the level of vaccination (on which we can act directly) and the still missing definitive assessment of this new variant with regard to vaccine efficacy, efficacy of antiviral therapies, transmissibility and virulence.

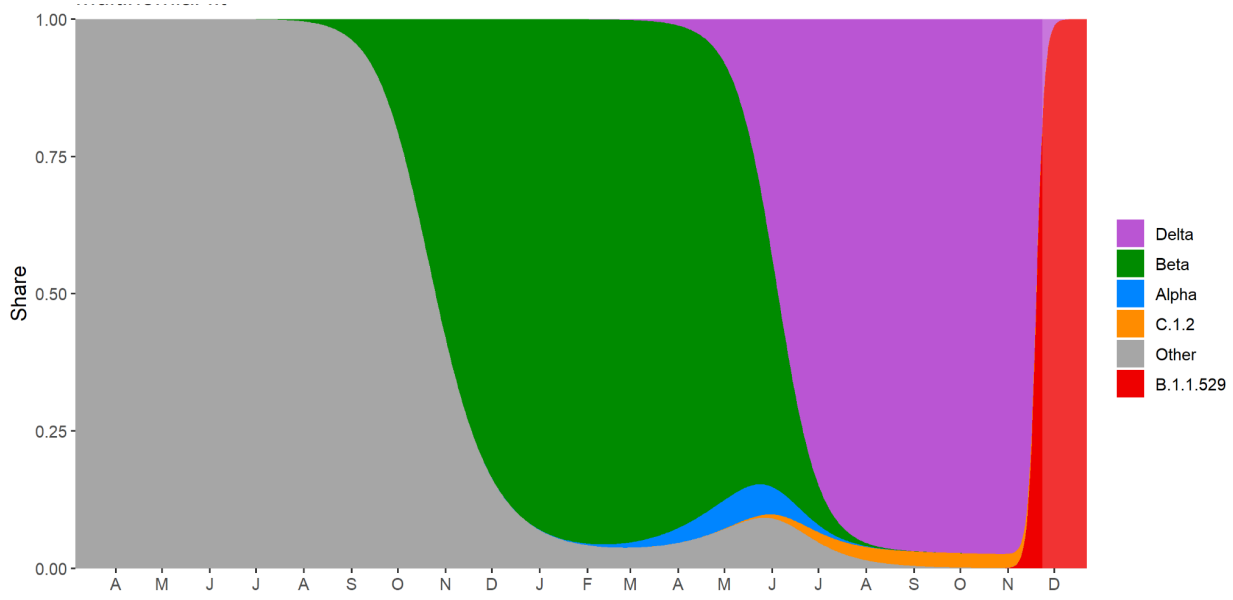

Figure 2: Current (dark red) and foreseen (red) share of the Nu variant in South Africa (multinomial fit), based on the data currently available. These projections may evolve based on upcoming data, as the current data are not yet fully representative of the situation.

In South Africa, where the majority of cases and genomic sequences are currently coming from, genome sequencing and other genetic analysis from Tulio de Oliveria's team found that the B.1.1.529 variant was responsible for all of 77 of the virus samples they analysed from Gauteng, South Africa, collected between 12 and 20 November. Prof. de Oliveira predicts an increase of B.1.1.529 that will soon be found in nearly 100% of genomic sequencing efforts (currently at 75%).

2. Available genomic data worldwide

Currently 66 B.1.1.529 genomes are available on GISAID: 6 from Botswana (including the 5 earliest available genomes), 58 from South Africa and 2 from Hong Kong. An initial Nextstrain build, as constructed by the Nextstrain Team (Figure 3), is available at: https://nextstrain.org/ncov/gisaid/africa. Furthermore, Israel has reported a first case today, a traveler returning from Malawi.

It's important to realise that data is still incoming and the total number of genomic sequences is small at the moment, only being available for 3 countries at the moment on GISAID. Israel has also just reported its first case, and we expect other countries to release similar information soon.

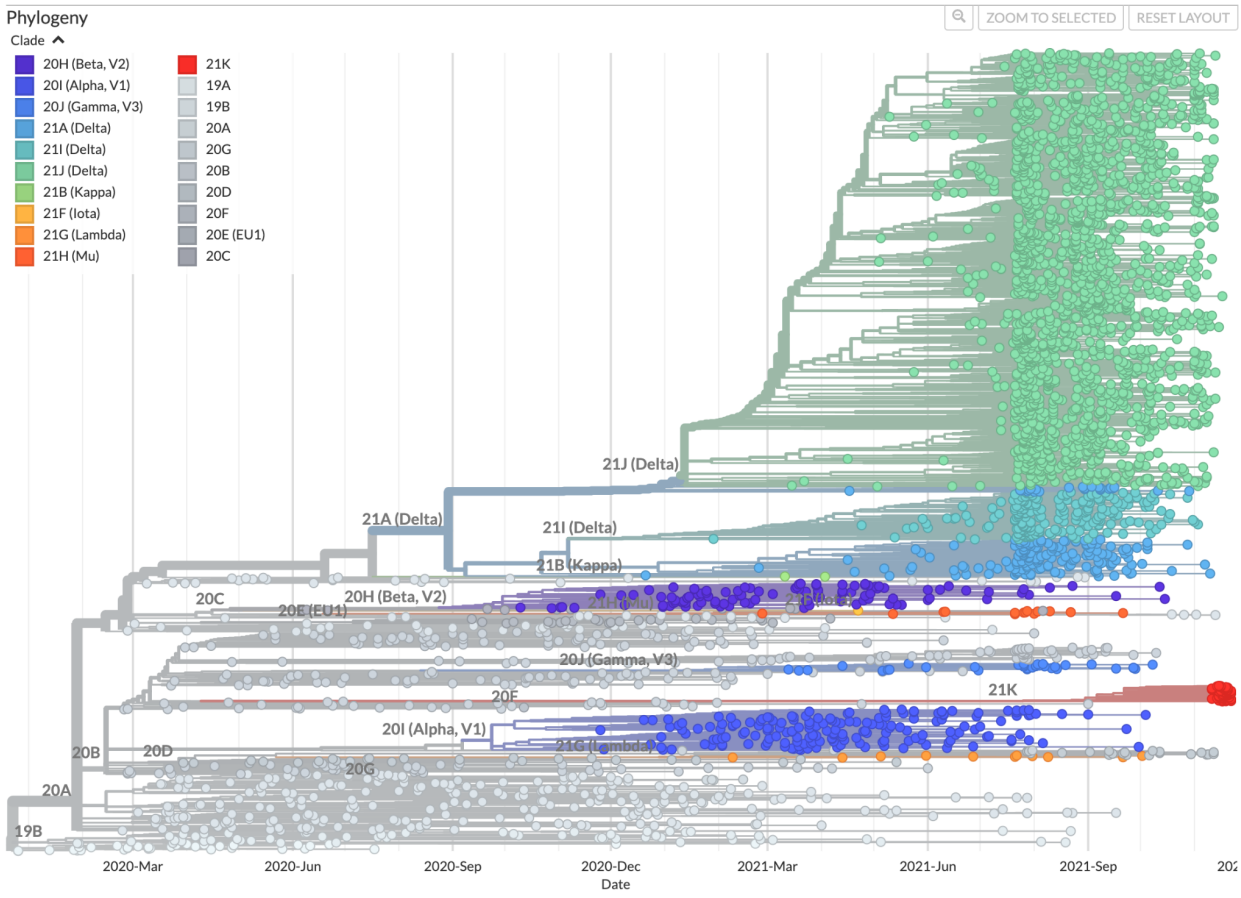

Figure 3. Phylogenetic analysis of B.1.1.529 (21K, shown in red) along with representatives of all other major variants (of concern). This shows that this lineage is very different from all other variants, with the long branch leading up to the clade representative of its high number of mutations.

Despite the earliest samples being available from Botswana (5 from the 11th of November, 2021), the available genomic data suggests that the cases in Botswana stem from infections in South Africa, with news reports having already linked the 2 infections in Hong Kong to South Africa as well. Importantly, **this does not necessarily mean that South Africa is the country where B.1.1.529 emerged**, although it does currently have the highest number of confirmed and suspected cases.

3. Genetic profile of B.1.1.529

B.1.1.529 is characterised by the following mutations in the spike protein: A67V, **D614G**, D796Y, **E484A**, G142D, G339D, G446S, G496S, **H69del, V70del**, H655Y, ins214EPE, **K417N**, L212I, L981F, N211del, **N440K**, **N501Y**, N679K, N764K, N856K, N969K, P681H, Q493R, Q498R, Q954H, S371L, S373P, S375F, **S477N**, T95I, **T478K**, T547K, V143del, Y144del, Y145del, Y505H (Figure 4). Several of these mutations and positions within spike have been the subject of investigation while studying other variants of concern (VOCs; Beta and Delta; in bold). However, many of the mutations listed are not shared with other VOCs, increasing worries about the vaccine efficacy and transmissibility of B.1.1.529.

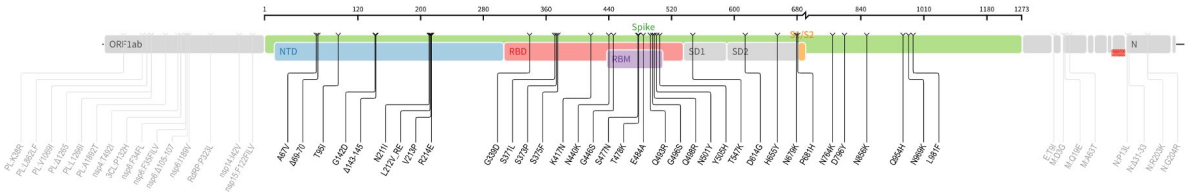

Figure 4. Mutational profile of B.1.1.529, focusing on the 30 mutations in the spike protein (source: Tulio de Oliveira, Stellenbosch University, South Africa).

Researchers spotted B.1.1.529 in genome-sequencing data from Botswana. The variant stood out because it contains more than 30 changes to the spike protein — the SARS-CoV-2 protein that recognizes host cells and is the main target of the body's immune responses. Many of the changes have been found in variants such as Delta and Alpha and are linked to heightened infectivity and the ability to evade infection-blocking antibodies. The lab of Penny Moore, a virologist at the University of Witwatersrand in Johannesburg, is gauging the variant's potential to dodge immunity from vaccines and previous infections. There are anecdotal reports of reinfections and cases in vaccinated individuals, but "at this stage it's too early to tell anything". Her team hopes to have its first results in two weeks (source: Nature News, 25th of November, 2021: https://doi.org/10.1038/d41586-021-03552-w).

4. High-throughput deep mutational scanning

This information comes from the lab of Jesse Bloom at the Fred Hutch Research Center and the Genome Sciences department at the University of Washington. We here summarize the earlier communication from the Bloom lab on social media. Their results build on previously published work (by the Bloom lab) on 'Mapping mutations to the SARS-CoV-2 RBD that escape binding by different classes of antibodies': https://www.nature.com/articles/s41467-021-24435-8

Importantly, and as clearly stated by Jesse Bloom, all these results come from high-throughput deep mutational scanning and **need to be validated in traditional lab experiments** for high confidence.

We here list the mutations in the spike protein of B.1.1.529 again: A67V, D614G, D796Y, E484A, G142D, G339D, G446S, G496S, H69del, V70del, H655Y, ins214EPE, K417N, L212I, L981F, N211del, N440K, N501Y, N679K, N764K, N856K, N969K, P681H, Q493R, Q498R, Q954H, S371L, S373P, S375F, S477N, T95I, T478K, T547K, V143del, Y144del, Y145del, Y505H. Based on deep-mutational scanning experiments, the mutations in B.1.1.529 will affect polyclonal and monoclonal antibodies targeting the receptor-binding domain (RBD). This variant has a lot of antigenic change, which does not mean this variant will necessarily spread and outcompete other variants. In Figure 5, it's shown how mutations relate to polyclonal escape averaged over 36 human antibodies. Many mutations occur at peak escape sites, especially E484, G446, K417, and Q493.

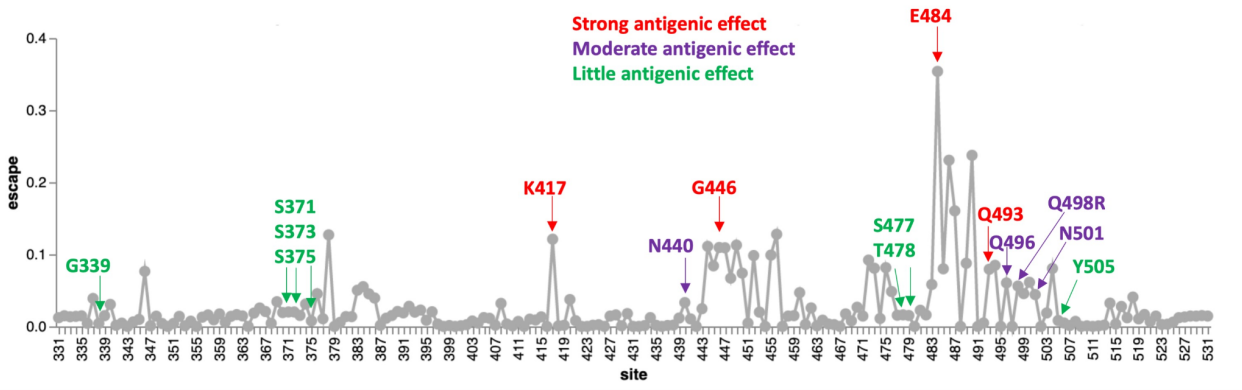

Figure 5. Antigenic effect of the mutations identified in B.1.1.529, based on deep mutational scanning.

5. Situation in Belgium

Following the communication from South Africa, the National Reference Laboratory has sent a communication to all diagnostic laboratories of the country to increase the vigilance and inform about the necessary confirmatory steps required in case of a returning traveller from the Southern African region or the detection of an S gene target failure (SGTF) on the Thermofisher TaqPath PCR assay.

To have a first insight on the possible presence of the B.1.1.529 variant in the country, we looked at the last 150.000 PCR test results generated by the Federal Platform Laboratories, representing a period of one month. Among these, 2.2% presented an SGTF. The vast majority of the SGTF identified were associated with a very low viral load, and can therefore be considered as an artefact (possible cases, but with very low level of suspicion).

Over the last month, we identified 47 positive test results associated with both a Cq <26 and a SGTF. These samples were distributed over the last 23 days, with a higher frequency during the last week (Figure 6). These samples were analyzed in the 8 different federal platform laboratories.

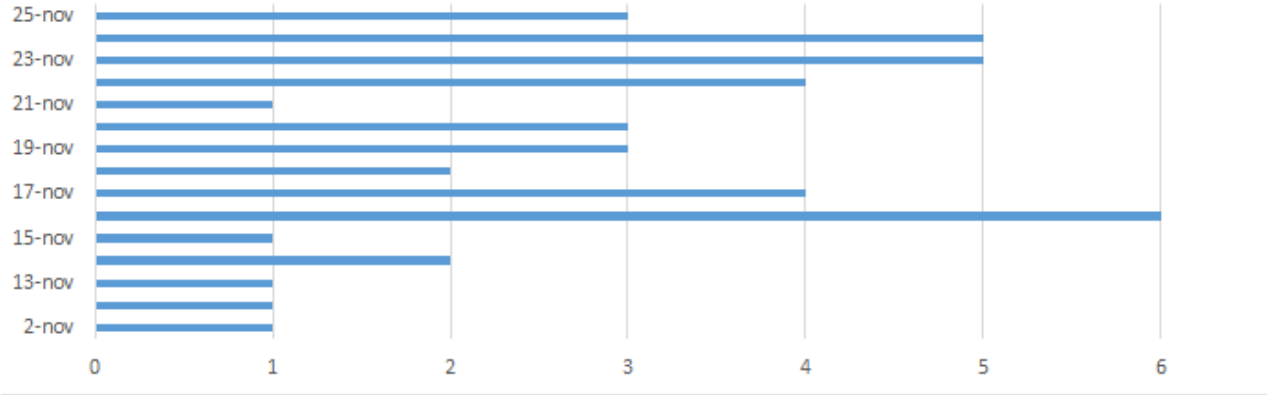

Figure 6: Number of positive (Cq < 26) PCR results from the 8 federal platform laboratories which show a SGTF. SGTF is typically caused by a 69-70 deletion in the Spike gene, which is systematically present in the Alpha and Nu variants, but also occasionally among other variants of concern. The numbers above cannot be considered as B.1.1.529 alone.

These samples will be systematically investigated in the coming days.

6. First case of B.1.1.529 in Belgium

Two possible cases (based on presence of SGTF at a federal testing platform) have been sequenced on 26/11/2021. Among these, one was identified as a Delta variant presenting the Del69/70, and the second was confirmed to be B.1.1.529.

The patient infected with B.1.1.529 is a young adult woman who developed symptoms 11 days after travelling to Egypt via Turkey. The patient had a high viral load at the time of diagnosis (Cq of 14,2) The patient did not report any link with South Africa or other Southern African countries. This patient had not previously been vaccinated and had not yet been infected. She developed flu-like symptoms, but does not present at this stage signs of severe disease.

The patient did not report high risk contacts outside her household. None of her household members have developed symptoms, but have nevertheless been referred for testing. An extended investigation will be launched.

7. Recommendations

The identification of a first B.1.1.529 positive case in Belgium (but also at the European level) highlights the rapid international spread of this variant.

Risk mitigation strategies should include travel restrictions or reinforced screening procedures at the international level (not only travels linked to South Africa), accelerating vaccination campaigns worldwide and accelerating the delivery of booster doses for the most fragile populations, reinforcing disease control interventions at all levels. Further, offering maximal support to African countries to ensure reinforced disease surveillance and control remains a high priority.

These standard recommendations should shortly be updated based on the evolution of our understanding of the impact of this variant with regard to virulence, infectiousness, vaccine efficacy and activity of existing antivirals.