Genomic surveillance of SARS-CoV-2 in Belgium

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

Situation update – 18th of February 2021
(report 2021_12)

Executive summary

Genomic surveillance in Belgium is organised around 3 different arms aiming to monitor the emergence and the further spread of specific viral populations (variants of concern, VOCs) which may impact disease control and/or vaccination strategies.

Through "baseline surveillance", an unbiased selection of positive samples from 24 sentinel labs (selected based on geographical dispersion and diversity of clinical patterns) are analysed in designated sequencing platforms. Currently, 5.526 Belgian sequences are available on GISAID. During weeks 5,6 and 7, 728 samples have been sequenced as part of the baseline surveillance, among which 249 were 20I/501Y.V1 (34%), 30 were 20H/501Y.V2 (4%) and 3 were 20J/501Y.V3 (0,4%).
Considering baseline and active surveillance together since Week 1, laboratories positively confirmed the presence of 1.339 VOCs in Belgium (1.183 20I/501Y.V1, 148 20H/501Y.V2 and 8 20J/501Y.V3).

In this report, we describe a new viral variant consistently detected in Belgium and probably originating from central African countries. This variant shows a combination of several mutations and deletions which may lead to competitive advantages and would explain why this strain seems to successfully spread in Belgium under the current – and extensive - disease control arsenal.

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1. International context

Since the end of the year, 4 variants of concern (VOCs) have arisen independently of one another in the United Kingdom (20I/501Y.V1), South Africa (20H/501Y.V2) and Brazil (20J/501Y.V3 and P.2). These variants harbour several mutations and deletions associated with higher infectiousness and immune escape. All variants are spreading internationally, with 3 VOCs having been detected to date in Belgium (1.183 for 20I/501Y.V1, 148 for 20H/501Y.V2 and 8 for 20J/501Y.V3).

2. Baseline surveillance

Since support was offered by the federal government end of December 2020, both the temporal coverage (number of sequences performed per week) and geographical coverage (number of collection sites) have improved. Currently, 5.526 Belgian sequences are available on GISAID.

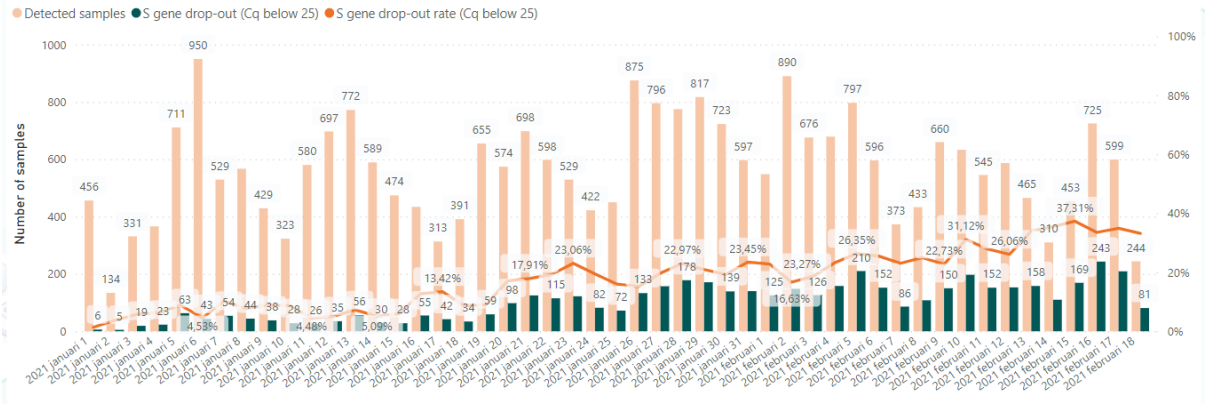

Figure 1: Evolution of the proportion of infectious samples detected among all positive tests diagnosed in the federal platform laboratories (Presence of the S dropout signal and Cq <25).

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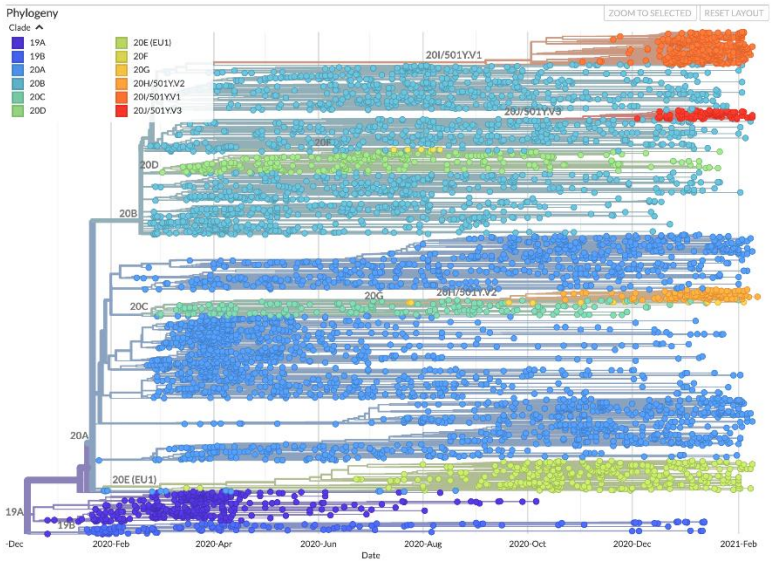

Figure 2: Nextrain build of currently available sequences from Belgium. VOCs are highlighted in dark orange (20I/501Y.V1), light orange (20H/501Y.V2) and red (20J/501Y.V3). Warning: this phylogeny tree is not representative is biased due to including all sequenced VOCs

Considering baseline and active surveillance together since Week 1, laboratories positively confirmed the presence of 1.339 VOCs in Belgium (1.183 20I/501Y.V1, 148 20H/501Y.V2 and 8 20J/501Y.V3). Currently, all 20J/501Y.V3 strains detected in Belgium seem to be clustered when comparing with other strains detected internationally, in particular in Europe. Nevertheless, the information collected by health inspectors to date do not allow to find a clear link between all these patients. This suggests that the cluster is actually much wider than the one described hereunder and that backward contact tracing must be pursued and intensified in order to contain this emerging chain of transmission.

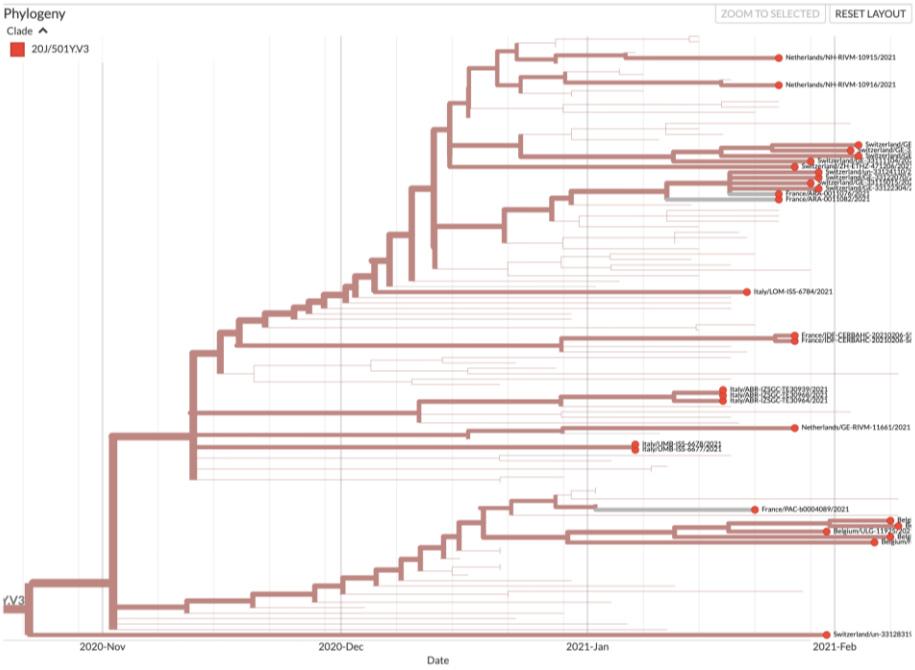

Figure 3: Currently, it the 8 20J/501Y.V3 strains detected in Belgium seem to be clustered when comparing with other strains detected internationally, in particular in Europe. Nevertheless, the information collected by health inspectors to date do not allow to find a clear link between all these patients. This suggests that the cluster is actually much wider than the one described hereunder and that backward contact tracing must be pursued and intensified in order to contain this emerging chain of transmission.

3. Variant of interest B1.525

This variant of interest was first described mid-December in England (England/CAMC-C769B3/2020) and has since then been described in 11 countries: England (28), Nigeria (7), USA (7), France (5), Canada (4), Ghana (4), Japan (4), Jordan (2), **Belgium (1)**, Italy (1) and Spain (1).

This variant is characterised by mutations: S:E484K, S:Q677H, S:F888L, S:69-70 deletion, and S:144 deletion, and a 9 nucleotide mutation in nsp6 (as seen in B.1.1.7, B.1.351, P.1). (https://github.com/cov-lineages/pango-designation/issues/4).

4. Variant of interest with Spike Insertion (VOI-SI)

A key feature of the recently identified VOCs is a suite of single base pair mutations that generate amino acid changes at key points within the spike protein. In addition to these single base pair changes, a number of sometimes overlapping short deletions have been observed in the different VOCs [1], both within spike and other viral genes [2].

The lineage B.1.1.7 (20I/501Y.V1), which arose in the United Kingdom in late 2020 [3] and the recently described B.1.525 lineage [2], carry deletions in spike affecting amino acid positions 69-70 & 144, while the B.1.351 lineage (20H/501Y.V2), originally identified in South Africa [4] carries a deletion of three amino acids (positions 242 to 244) in spike. In contrast, the P.1 lineage (20J/501Y.V3) [5] does not carry any deletions in the spike protein, however, all four carry a three amino acid deletion in the nsp6 protein.

In contrast to spike deletions, the frequency of insertions in the SARS-CoV-2 spike gene appears rare. Garry et al [1] examined ~350,000 SARS-CoV-2 sequences from the GISAID database, identifying only two examples with insertions at amino acid R214. In the same report they also point out that passage of SARS-CoV-2 in cell culture (Vero cells) can generate amino acid insertions in the same spike region [1], indicating that in some contexts such insertions are advantageous.

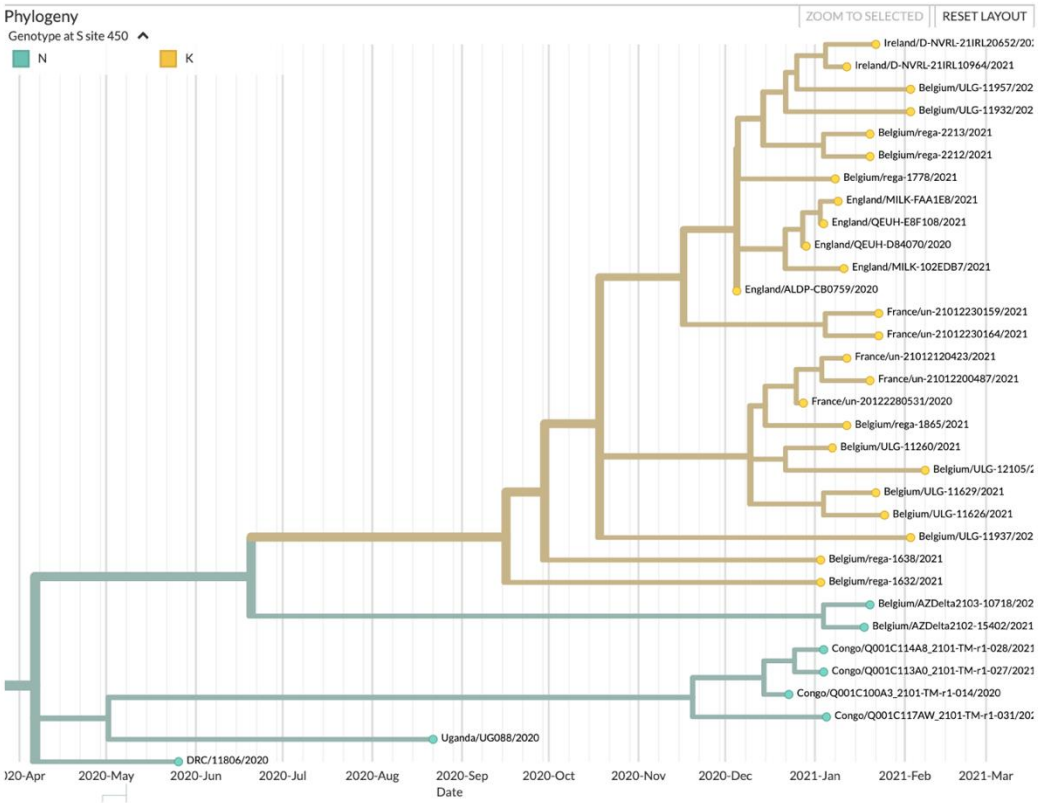

Figure 4: VOI-SI which also harbour the N450K amino acid change (shown in yellow) cluster together, the Belgian samples fall across the cluster indicating multiple independent introductions.

Baseline surveillance of SARS-CoV-2 genomes carried out at the University of Liège highlighted a Belgian genome carrying a spike insertion, which we will refer to as Variant of Interest with Spike Insertion (VOI-SI). The sample was collected on the 7th January, in an individual hospitalised for COVID-19, who recently returned from travel in the Congo. In the subsequent weeks additional similar genomes have been identified by both ULiège and UZ Leuven/KU Leuven, while genomes from the same lineage have been deposited in the GISAID database with origins in the UK, Ireland and France.

The earliest example of a VOI-SI was isolated in the UK on the 5th of December and was one of the spike insertions identified by Garry et al [1]. To date that number has grown to 43, with the majority (30) isolated in Belgium. The Pangolin COVID-19 Lineage Assigner (https://pangolin.cog-uk.io/) assigns the majority of the VOI-SI to lineage B.1.214 which is most commonly found in the Democratic Republic of the Congo. A Nextrain build using the available VOI-SI shows them to cluster together and indicates that the lineage has been introduced to Belgium multiple times **(Figure 4).**

In addition to the insertion in spike the lineage also carries a number of other amino acid changes in spike (Q414K, N450K, D614G, T716I) as well as a 30bp deletion in ORF3a (I20-, K21-, D22-, A23-, T24-, P25-, S26-, D27-, F28-, V29-). This lineage does not have the N501Y or E484K, changes found in the majority of VOCs, although the T716I amino acid change is also found in the B.1.1.7 lineage. One of the main reasons for concern regarding the B.1.351, P.1 and B.1.525 lineages is the presence of E484K which has been shown to impact antibody binding [6]. The same work highlighted that mutation in the 443-450 loop region can have a large impact on antibody binding [6], which makes the N450K change observed in the VOI-SI concerning.

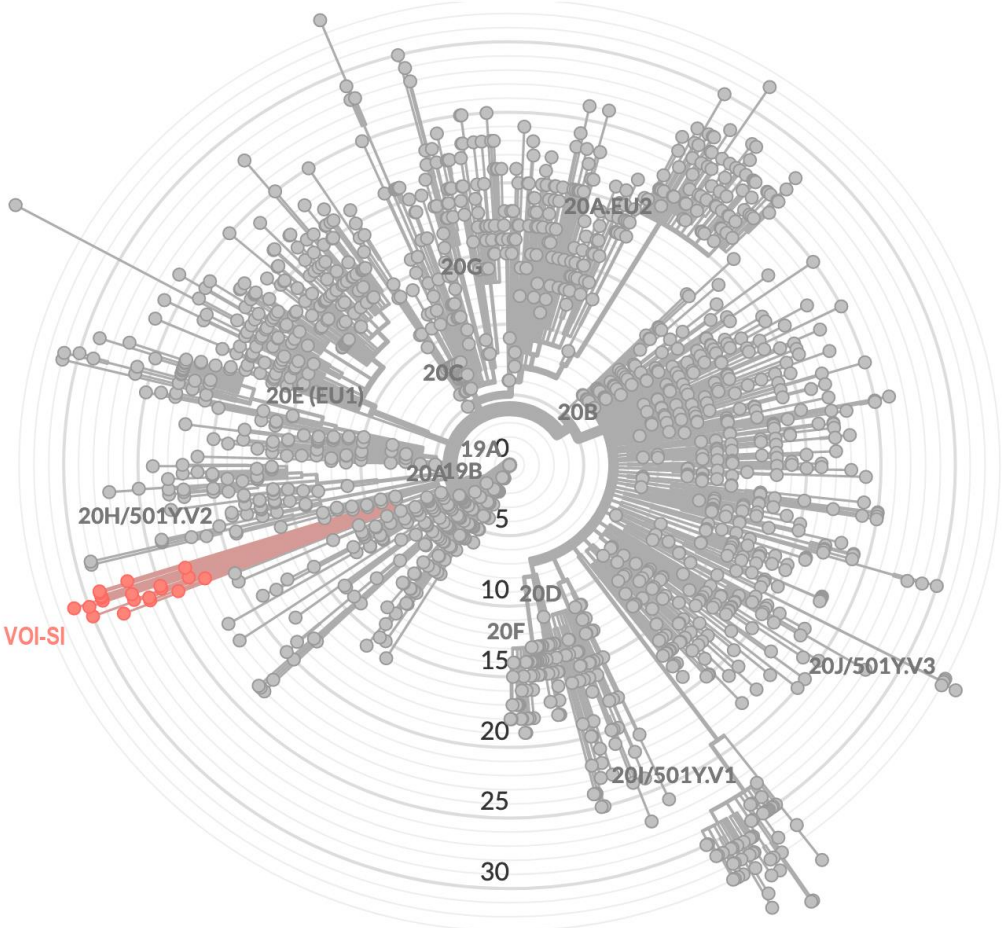

Figure 5: VOI-SI forms a separate clade among international SARS-CoV-2 sequences.

Finally, nearly half of the VOI-SI genomes submitted to date carry a three amino acid deletion in nsp6. The same deletion is observed in the VOC lineages B.1.1.7, B.1.351, B.1.525 and P.1, suggesting epistatic interactions between this deletion and changes in spike.

References

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