Genomic surveillance of SARS-CoV-2 in Belgium

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

Situation update 19th of January 2021
(2nd report for 2021)

Executive summary

Genomic surveillance in Belgium is currently based on 3.163 genomic sequences available on GISAID, with a recent acceleration in sequencing capacity. Since the 1st of December 2020, a total of 1.215 sequences have been produced by 4 sequencing platforms. 130 501Y.V1 and 7 501Y.V2 VOCs have been identified.

Belgium has recently experienced multiple introductions of variants of concern (VOCs), particularly since the last days of 2020. The consolidated genomic and epidemiological data are consistent with a rapidly increasing number of events of local transmission. Based on the evolution of atypical PCR results ("S droputs"), we estimate that VOCs currently represent 5-10% of infectious cases in the country (increasing trend).

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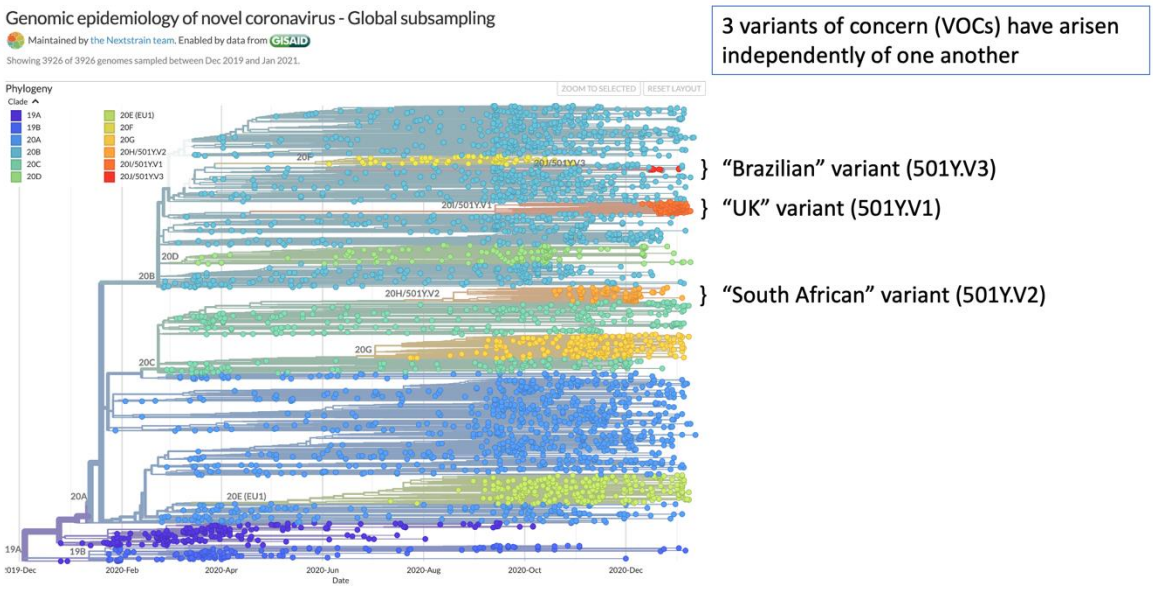
1. International context

Since the end of the year, 3 variants of concern (VOCs) have arisen independently of one another in the United Kingdom (501Y.V1), South Africa (501Y.V2) and Brazil (501Y.V3). These variants harbour a number of mutations and deletions associated with higher infectiousness and immune escape. All 3 variants are spreading internationally, with 501Y.V1 and 501Y.V2 having been detected in Belgium.

Global view on the 3 variants: 501Y.V1, 501Y.V2 and 501Y.V3



2. Methodology of the Belgian genomic surveillance

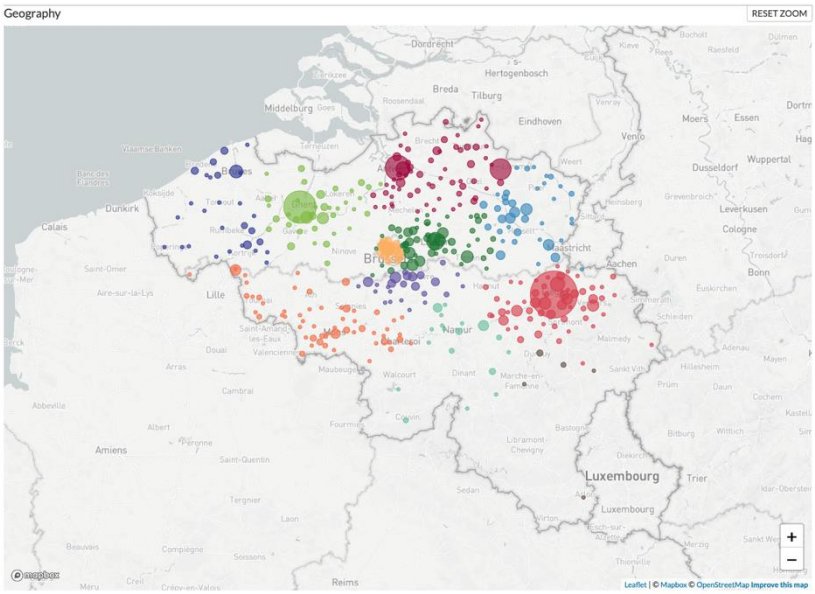
The National Reference Centre hosted at UZ Leuven – KU Leuven has put in place genomic surveillance at the national level since the first introduction of the virus in February. Other university centres, in particular the university of Liège and the University of Gent, have also contributed to surveillance through complementary initiatives. As the principle of genomic surveillance is based on the comparison over time and space of genomic sequences, three fundamental elements underlie this national genomic plan:

a. **Sampling**: due to the fact that all positive samples cannot – and will not – be sequenced, emergence or evolution in the relative presence of viral variants will be noticed through the genomic surveillance system only if it has reached a significant size. While such surveillance should in principle include unbiased samples (baseline surveillance), it should be noted that the recent emergence of VOCs has generated a selection bias through a number of "active surveillance" strategies focusing mainly on returning travellers, abnormal PCR results (S dropouts) and large outbreaks. An over-representation of VOCs in sequencing results compared to their actual frequency implies that complementary indicators and analysis will be required to precisely follow the epidemiological evolution in Belgium.

b. **Geographic coverage**: until today, some provinces of the country are under sampled. It is part of the reinforced genomic surveillance plan to ensure a uniform coverage of the country in the coming weeks, including both retrospective and prospective analysis.

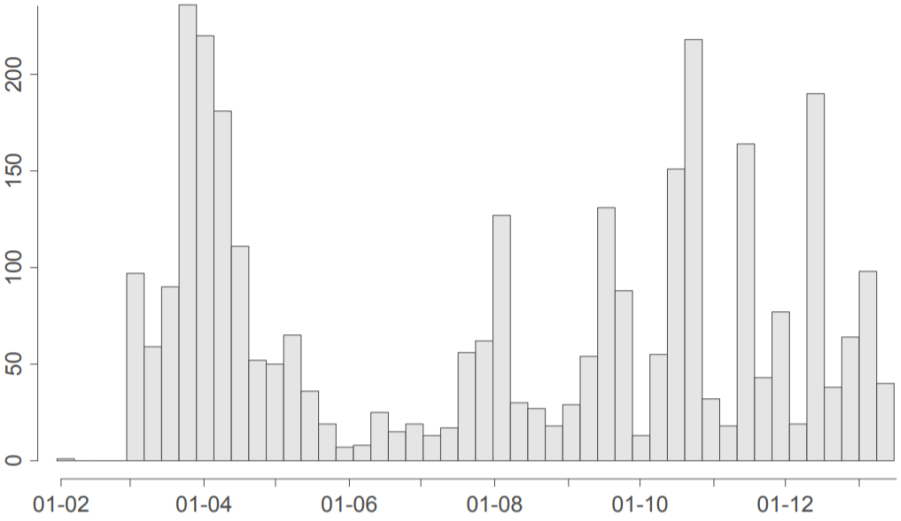
c. **Sharing of data**: genomic sequences are analysed and compared on the Belgian Nextstrain instance (publicly available online) after they have been submitted to GISAID. The process of uploading the data can take several days, and has been accelerated by the sequencing laboratories. From 15/1 to 18/1/2021, GISAID did not release the the uploaded sequences, so no phylogenetic analysis could be performed for this vi-weekly report. Sequencing laboratories request from the government a legal framework which authorizes the deposit of these viral sequences on GISAID.

Coverage by province of available sequences



- currently available Belgian genomic sequences
- undersampling in West Flanders, severe undersampling in Namur and Luxemburg
- many genomic sequences not available due to ethical reasons
- new sequences still to be uploaded (takes time to do + database processing time)

Number of SARS-CoV-2 genomic sequences deposited on GISAID by Belgian laboratories
(19-01-2020, total: 3,163; https://platform.gisaid.org; graphic generated by Simon Dellicour, ULB)



3. Sequencing and preliminary reports from sequencing laboratories

Since the 1st of December 2020, a total of 1.215 sequences have been produced and communicated by 4 sequencing platforms. 130 501Y.V1 and 7 501Y.V2 VOCs have been identified.

1 dec - 19 jan	KUL	Gent	Liège	Antwerper	Consortiur
Sequenced	645	277	261	32	1215

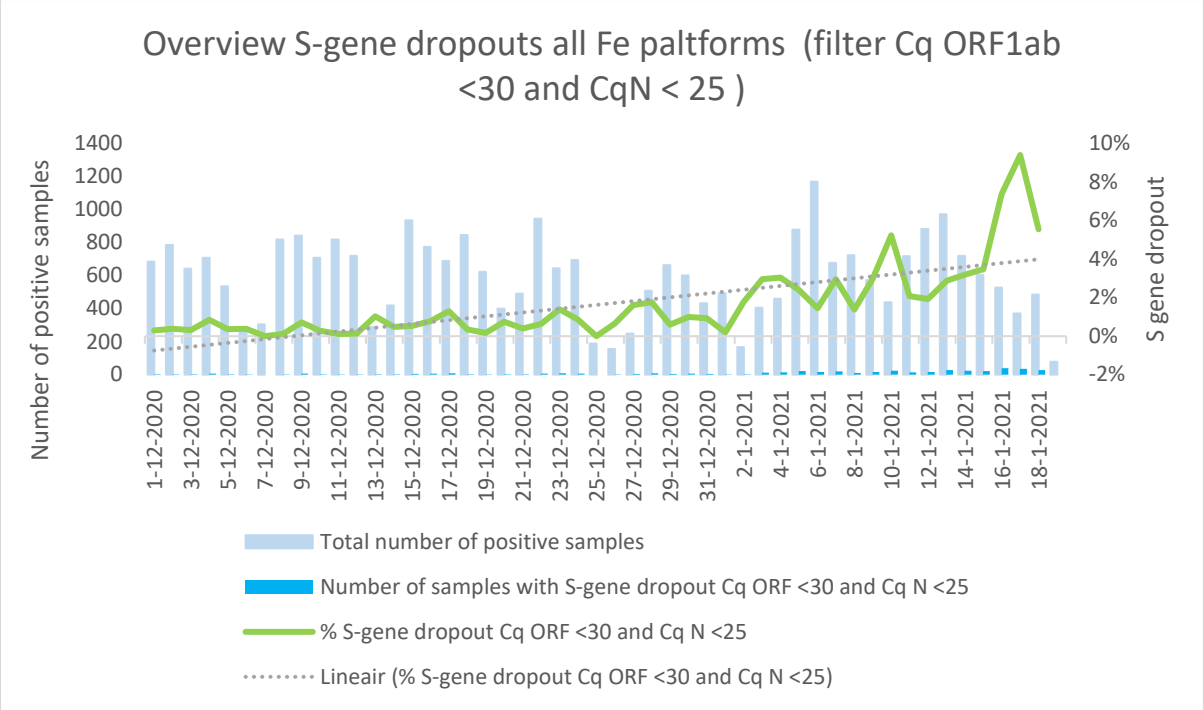
4. Active surveillance through "S dropouts"

The H69- deletion in the S gene, which generates the "S dropout" profile in the PCR used by the Belgian Federal Platform Bis laboratories, is not only present in the 501Y.V1, but also in non-VOC strains circulating in Belgium since several months. This is the reason why this signal cannot be considered as specific for VOCs, nor highly sensitive, considering that 501Y.V2 and 501Y.V3 do not present this deletion.

Nevertheless, considering the high number of international travels and that this VOC is already widely circulating in numerous countries, using the evolution of the proportion of S dropouts among the positive PCR results is informative of the current situation in our country.

When looking at the proportion of S-gene dropouts (Orf & N genes detected, restricting to results where both genes show a strong signal) against all positive results in the National Platform laboratories, we observe a significant increase which has started during the recent weeks, and thus compatible with the higher number of importations and secondary infections related to travels during the Christmas holydays.

Currently, all "S dropouts" are being confirmed by whole genome sequencing. The need for confirmatory tests will be maintained as long as these variants do not represent the vast majority of circulating strains in Belgium. To preserve the sequencing capacity for surveillance purposes, the National Reference Laboratory has asked INAMI-RIZIV to consider including in the nomenclature PCRs identifying the 501Y and the 484K mutations. This should allow a more dynamic system and support preventive measures aiming to control the further spread of VOCs in Belgium.


Overview S-gene dropouts all Fe paltforms (filter Cq ORF1ab <30 and CqN < 25)
Number of positive samples
S gene dropout
1400
1200
1000
800
600
400
200
0
10%
8%
6%
4%
2%
0%
-2%
1-12-2020
3-12-2020
5-12-2020
7-12-2020
9-12-2020
11-12-2020
13-12-2020
15-12-2020
17-12-2020
19-12-2020
21-12-2020
23-12-2020
25-12-2020
27-12-2020
29-12-2020
31-12-2020
2-1-2021
4-1-2021
6-1-2021
8-1-2021
10-1-2021
12-1-2021
14-1-2021
16-1-2021
18-1-2021
Total number of positive samples
Number of samples with S-gene dropout Cq ORF <30 and Cq N <25
% S-gene dropout Cq ORF <30 and Cq N <25
Lineair (% S-gene dropout Cq ORF <30 and Cq N <25)