Genomic surveillance of SARS-CoV-2 in Belgium

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

Situation update - 17th of January 2021
(1th report for 2021)

Executive summary

Genomic surveillance has scaled-up as decided on 29th of December 2020, with over 1.100 recent viral genomes sequenced. Approximately 1/3 of these genomes could be analysed, highlighting that Belgium has recently experienced multiple introductions of variants of concern (VOCs). The consolidated epidemiological data are consistent with documented events of local transmission, including at least one large community outbreak.
The trend in "S dropouts" among PCR results obtained in the Federal Platform laboratories are consistent with a recent phenomenon steadily increasing over the recent days.

Contents of the document

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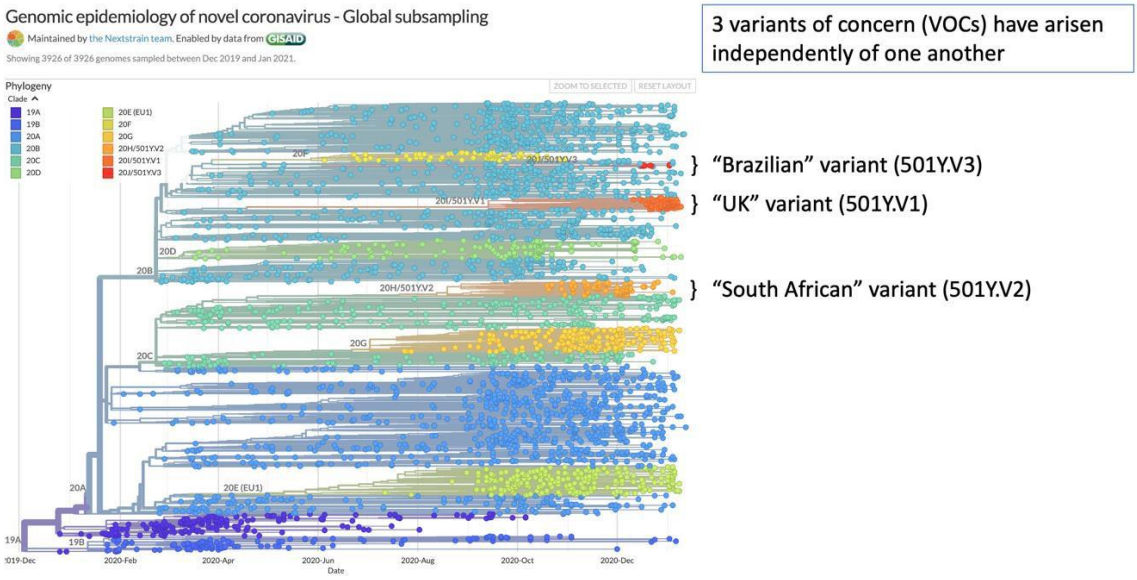
1. International context

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

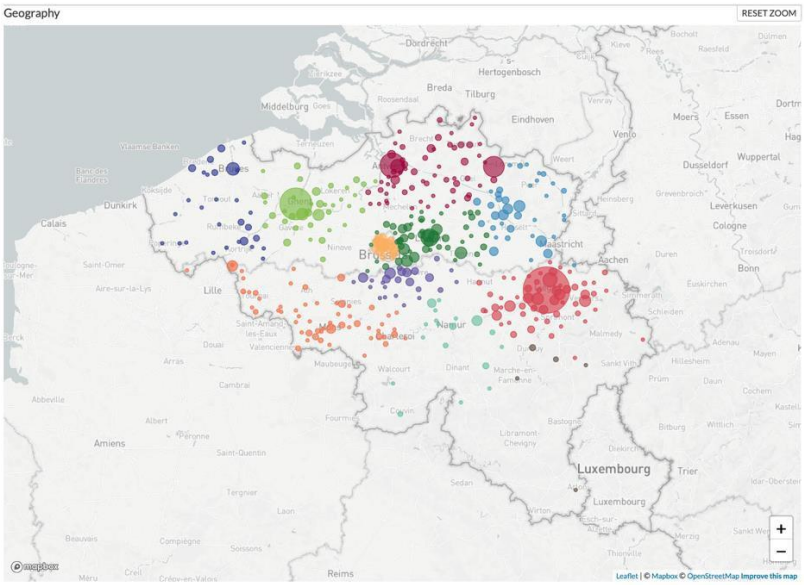
The National Reference Centre hosted at UZ Leuven – KU Leuven has put in place genomic surveillance at the national level since the first introduction of the virus in February. Other university centres, in particular the university of Liège and the University of Gent, have also contributed to surveillance 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. This delay explains that the analysis hereunder only includes roughly one third of the samples sequenced since early December. It is expected that several hundred sequences will be made available for analysis in the coming days, and may thus provide a different representation of the situation in the country. Further, it should be considered for the most recent data that there is an over-representation of sequences of VOCs as these have been prioritized for uploading. Additionally, associated metadata has been difficult to collect in the past weeks, but this issue is now being solved as a standardized sequencing form has been published by Sciensano. Finally, sequencing platforms in Belgium still have difficulties to get ethical clearance for uploading sequences. Therefore, a legal framework should be consolidated to make sure no delay or lack of completeness would be caused by these ethical considerations.

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)

3. Sequencing and preliminary reports from sequencing laboratories

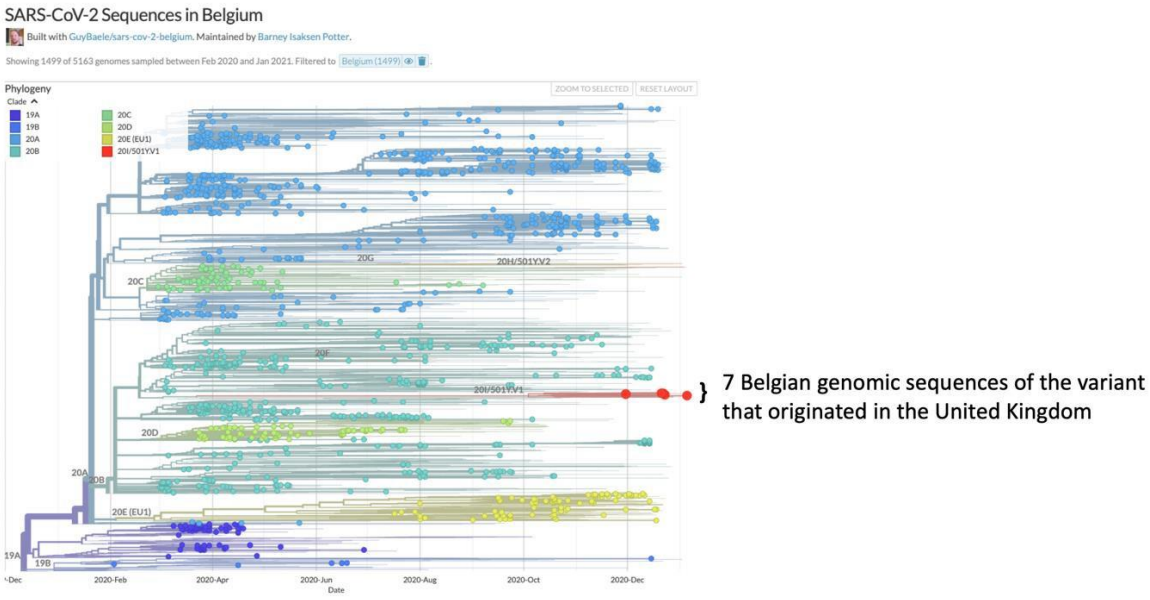
Since the 1st of December 2020, a total of 1.131 sequences have been produced and communicated by 4 sequencing platforms. While approximately 2/3 of the sequences are yet to be uploaded on GISAID or analysed, 91 501Y.V and 7 501Y.V2 VOCs have been identified. Most VOCs have been prioritized by the sequencing platforms for upload on GISAID.

1 dec - 17 jan	KUL	Gent	Liège	Antwerpe
Sequenced	561	277	261	32

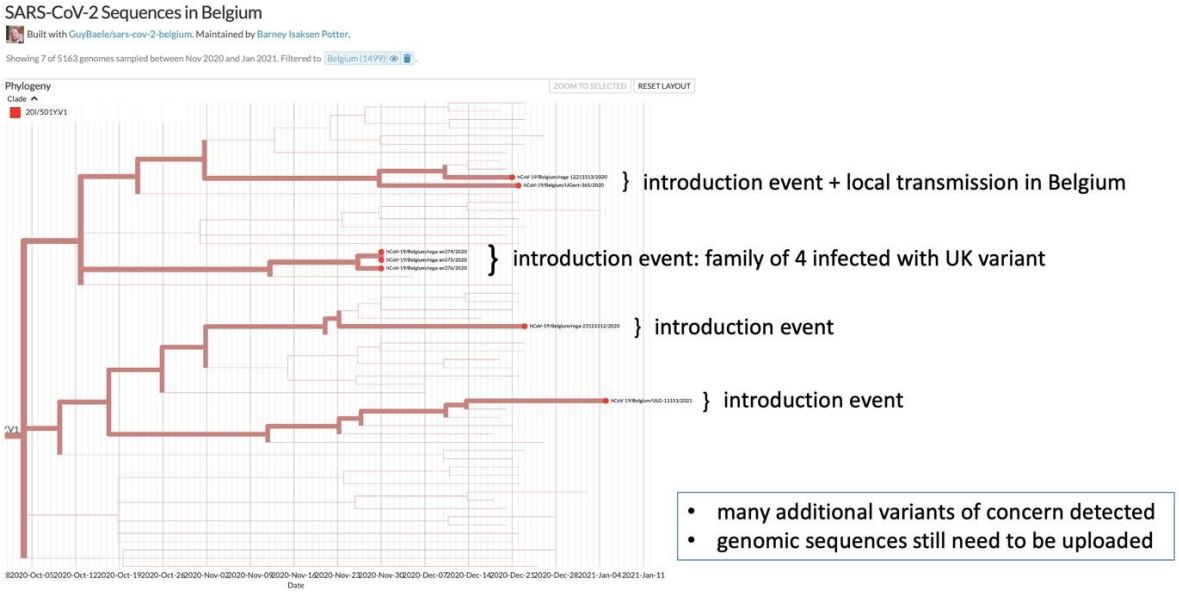
4. Recent introduction of VOCs in Belgium

Of the 91 501Y.V1 and 7 501Y.V2 identified by the sequencing platforms, only 7 501Y.V1 sequences were available on GISAID on the 16th of January. The phylogenetic analysis of these sequences show that these originated from 4 individual introduction events, with a first case of local transmission in Belgium. Although most of the VOC genomes are not yet included in the analysis hereunder, we know from the context of the latest VOCs detected that both 501Y.V1 and 501Y.V2 have generated secondary infections in Belgium and that 501Y.V1 has been involved in at least one large community outbreak.

UK variant 501Y.V1 sequenced in Belgium



Local transmission in Belgium of UK variant 501Y.V1



5. Active surveillance through “S dropouts”

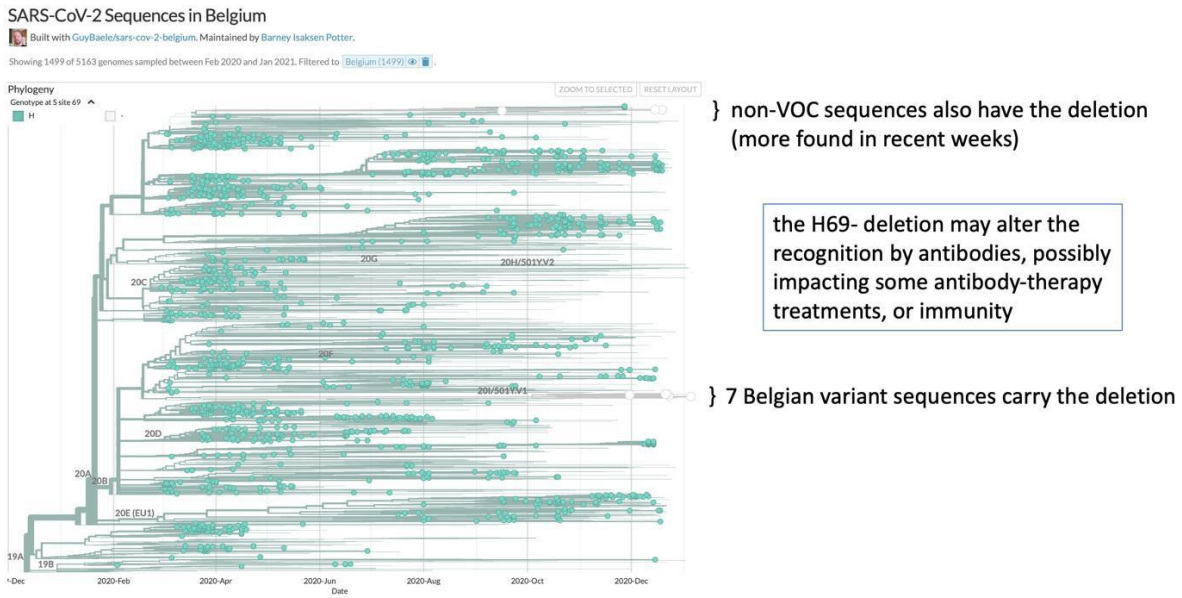
As shown below, the H69- deletion in the S gene, which generates the “S dropout” profile in the PCR used by the Belgian Federal Platform Bis laboratories, is not only present in the 501Y.V1, but also in non-VOC strains circulating in Belgium since several months. This is the reason why this signal cannot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

Another element that needs to be considered is that among Platform Bis laboratories, a variable proportion of “S dropouts” also show a weak Orf signal (see table below), what has not been typically described with the 501Y.V1.

Laboratory	Number of S-gene dropouts with ORF1ab Cq ≥30	Proportion of total
UMons	502	58,3%
UZ Gent	264	30,7%
UZA	90	10,5%
Saint LUC - UCL	3	0,3%
Namur	2	0,2%
ULB	0	0,0%
UZ Leuven	0	0,0%
ULG	0	0,0%
Total	**861**	

Nevertheless, considering the high number of travels between UK (and Ireland) and Belgium and that this VOC is already circulating since a number of months in the UK, using the evolution of the proportion of S dropouts among the positive PCR results is informative of the current situation in our country.

Few Belgian sequences with H69- deletion



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 travels during the Christmas holydays.