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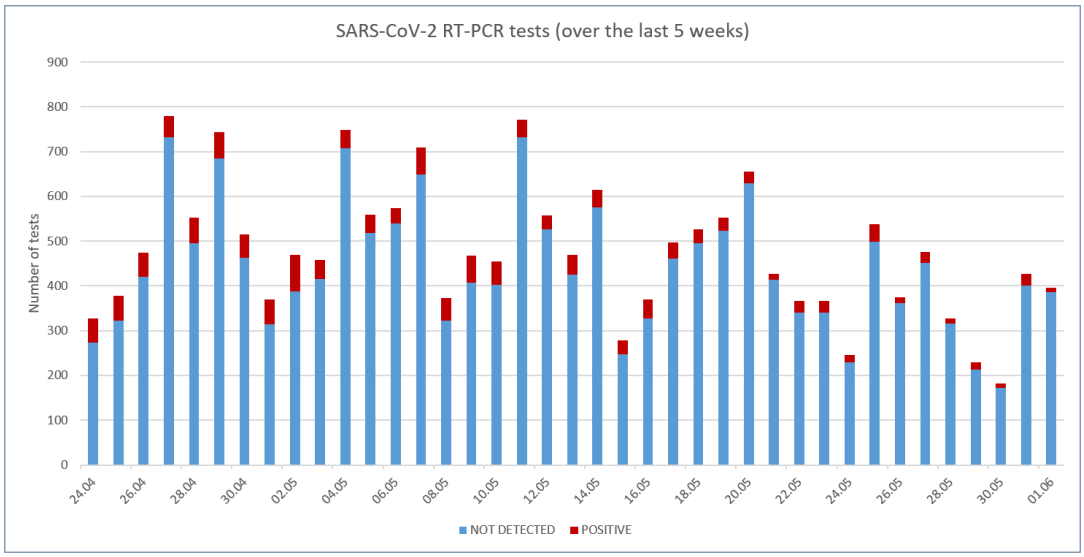
SARS-CoV-2 genomic and variants surveillance in Geneva: weekly update

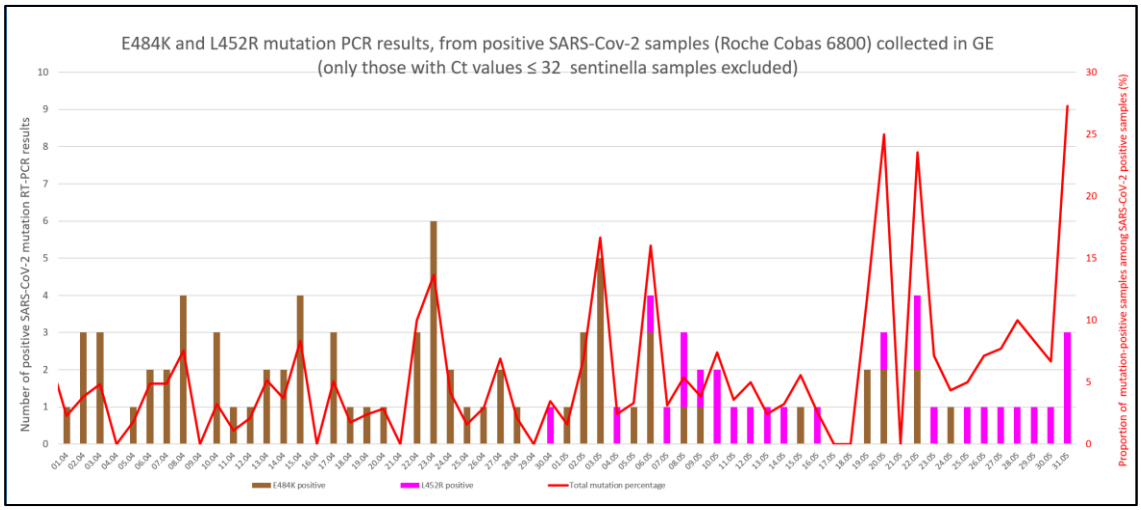
The laboratory of virology of the Geneva University Hospitals as a sentinel site for the Geneva area

The number of tests performed at the laboratory of virology of Geneva University Hospitals represents around 1/4 of the total number of tests performed in the canton of Geneva. Specimens analyzed in our laboratory come from the community (the majority: symptomatic patients and asymptomatic contacts), from hospital workers (systematic screening in case of any symptoms, cluster investigations and asymptomatic HCWs as part of hospital surveillance system), from asymptomatic travelers needing a screening test, and from hospitalized patients. All tests performed at our outpatient testing center (located in the Hospital but open to anyone from the community) are PCR-based and not antigen-based; of course many centers in the canton are using antigen-based tests for primary screening. WGS is carried out in close collaboration with the Health 2030 Genome Center in Geneva and Philippe Le Mercier from the Swiss Institute of Bioinformatics. Since March 1, 2021, the sequencing is done within the Swiss national SARS-CoV-2 genomic and variants surveillance program. With the decreased number of sars-CoV-2 positive cases, all specimen with a Ct value ≤ 32 are sequenced. In some instances, sequencing can be done in specimens sent by other laboratories in Switzerland. Phylogenetic analysis data are produced by Nextstrain, in collaboration with Richard Neher's group at the University of Basel.



Both the absolute number of positive cases diagnosed at HUG (10-30 cases per day over the last week) and the positivity rate (around 5% over the last week) have continued their progressive decline since the beginning of May.

Specific mutations screening by RT-PCR among SARS-CoV-2 positive samples collected in GE and sent to our laboratory for primary diagnosis



Starting date of E484K/Q mutation screening: January, 27, 2021. Starting date of 417N/T mutation screening: March, 3, 2021. This 417N/T screening is done on E484K-positive samples, and presumably allows distinguishing between B.1.351 and P.1 (not depicted on this graph). Starting date of L452R mutation screening: May, 4, 2021. This graph only displays positive results of specific mutations looked for in samples sent for primary diagnostic with Ct values <32, and does not include mutations results obtained in SARS-CoV-2-positive samples sent from other laboratories. Results are presented by sampling date.

Mutation E484Q is no longer represented in this graph. In fact, sequencing revealed that the "E484Q melting curve" previously identified was due to neighboring point mutations, all found on the B.1.1.7 backbone.

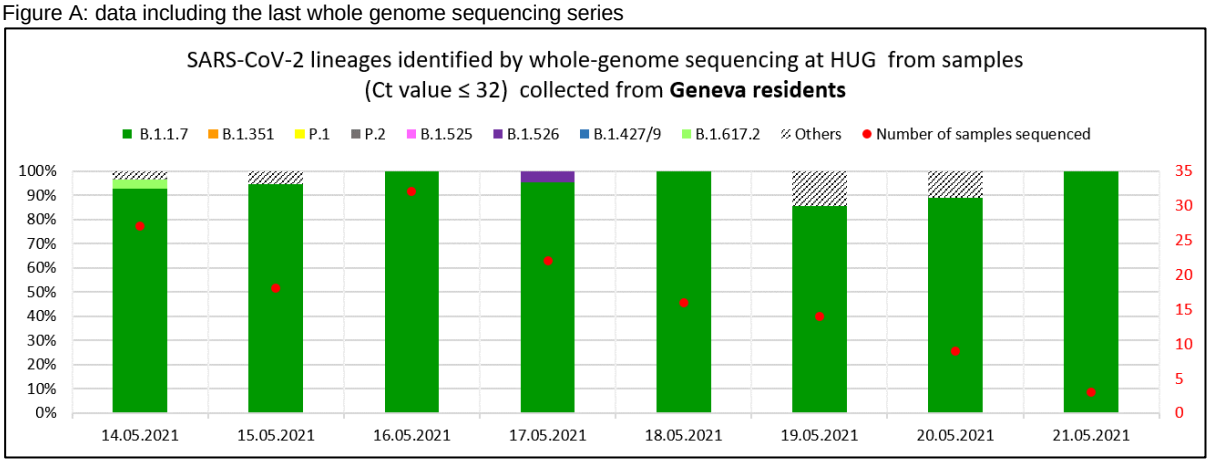
The proportion of positive samples carrying a mutation of interest (E484K, L452R) is increasing. Among them, over the last week, only specimens carrying the 452R mutation have been detected at a low level, and no 484K-containing sample has been identified. In Geneva, 2 different variants containing the 452R mutation are circulating at a low level: the variant of concern (VOC) B.1.617.2, now called "delta", and the variant under monitoring C.36. Precise variant typing is provided each week by ongoing whole genome sequencing.

Whether 484K containing variants are less frequently observed over the last 3 weeks because their circulation in the community has been effectively controlled, or whether they are being replaced by 452R containing variants remains to be determined. These numbers are too small to draw any definitive conclusions regarding a possible replacement of variants containing 484K mutations by variants containing the 452R mutation. Of note, the denominators used to construct this graph vary over the last week are between 10 and 20 specimens only.

Over the last week, variants which don't contain the 452R and/or 484K mutations were still generating most of the new infections in the Geneva area.

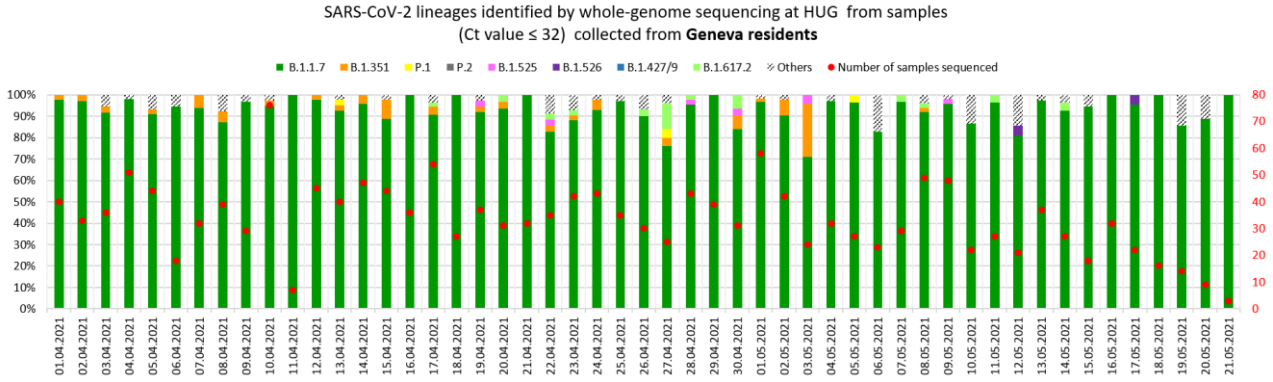
Whole genome sequencing results performed on SARS-CoV-2 positive samples collected in GE and sent to our laboratory

Figure A: data including the last whole genome sequencing series



This graph displays the sequences with 95% of positions covered ≥ 15x and submitted to GISAID (177 sequences obtained from samples collected from May, 14 to May, 21, 2021).

Figure B: whole genome sequencing results on SARS-CoV-2 positive samples over the last 5 weeks



This graph displays the sequences with 95% of positions covered ≥ 15x and submitted to GISAID (1 845 sequences obtained from samples collected from April, 1 to May, 21, 2021).

We continue to observe a low-level circulation of variants carrying the 484K mutation in the last sequencing batch, covering the period of May 14 to May 21, 2021, although not from VOCs:
-No new B.1.351 (beta) or P.1 (gamma) sequences has been identified
-3 sequences have been identified as B.1.620 (considered a VOI)
-and one B.1.526 (only considered a variant under monitoring, first detected in the US in December 2020)

The sequencing confirms that less variants containing the 484K mutation are circulating in the Geneva area since mid-May 2021, and identified variants are not VOCs.

One more case of the B.1.617.2 (first detected in India, now called delta) variant collected over the time period surveilled in this report has been confirmed by sequencing (Figure A), and is linked to a previously known cluster, according to the cantonal physician team. A total of 16 B.1.617.2 cases have been confirmed by whole-genome sequencing since mid-April (Figure B). Three more sequences of the C.36 variant (not a VOC nor a VOI but also carrying the 452R mutation) have been identified.

As the number of positive cases is declining, the number of sequences decreases each week. The laboratory of virology of the HUG still tests 1/4 to 1/3 of all positive cases in the canton each week, but as the absolute numbers of positive cases decline, the representativeness of the sequencing may also decrease. The Swiss national SARS-CoV-2 genomic and variant surveillance program launched March 1, 2021 aims to sequence 10% of the total number of positive cases in Switzerland (see first report covering the months of March and April). Other Geneva based laboratories are on the verge of joining the program to assure a substantial coverage, to achieve representative sequencing across the canton.

Moreover, with the number of total cases declining, and the intensive contact tracing done around the variants containing the 452R and E484K mutations, an effort will be made with the cantonal physician team to identify whether VOCs and VOIs are linked to specific clusters.

Conclusions

- The absolute number of SARS-CoV-2-positive samples and the positivity rate since the end of April, 2021 in the Geneva area continue to decrease over time.
- The B.1.1.7 variant still represents the vast majority of new SARS-CoV-2 infections in the Geneva area. No variant seems to be able to outcompete it so far.
- Variants carrying the 484K mutation have been less frequent since the past 3 weeks, and in the last sequencing batch no P.1 (gamma) or B.1.351 (delta) have been identified.
- Over the last week, no new cases containing the 484K mutation have been detected. The 452R mutation is detected in new cases every day, at low absolute numbers but in increasing proportion over time as the total of number of cases decreases.
- Whether 484K containing variants are less frequently observed over the last 3 weeks because their circulation has been effectively controlled in the community (intensive backward and forward tracing), or whether they are being replaced by 452R containing variants remains to be determined – numbers are too small over a limited period of time to draw any definitive conclusion on a possible replacement of variants containing 484K mutations by variants containing the 452R mutation.
- As of today, 16 cases of B.1.617.2 have been identified in Geneva and confirmed by whole genome sequencing; only one additional case was detected, linked to previously known cluster according to the cantonal physician team.

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