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Geneva Centre for
Emerging Viral Diseases

Division of Infectious
Diseases

Department of Medicine

Laboratory of virology

Division of Laboratory
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Diagnostic Department

**SARS-CoV-2 genomic surveillance in Geneva: weekly update
Focus on E484Q containing Delta sub-lineages and AY.4.2 (update)**

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

The number of tests (PCR and antigen tests) performed at the laboratory of virology of the Geneva University Hospitals represents around 18% of the total number of tests performed in the canton of Geneva during week 45 (2562/14652). Roughly **29% of the positive specimens collected in the Geneva area were processed at HUG (216/736) during week 45**. Tests performed at our outpatient testing center are either PCR-based or antigen-based. Most symptomatic patients are screened by RT-PCR and all positive antigen-based tests are confirmed by PCR, allowing screening for variants.

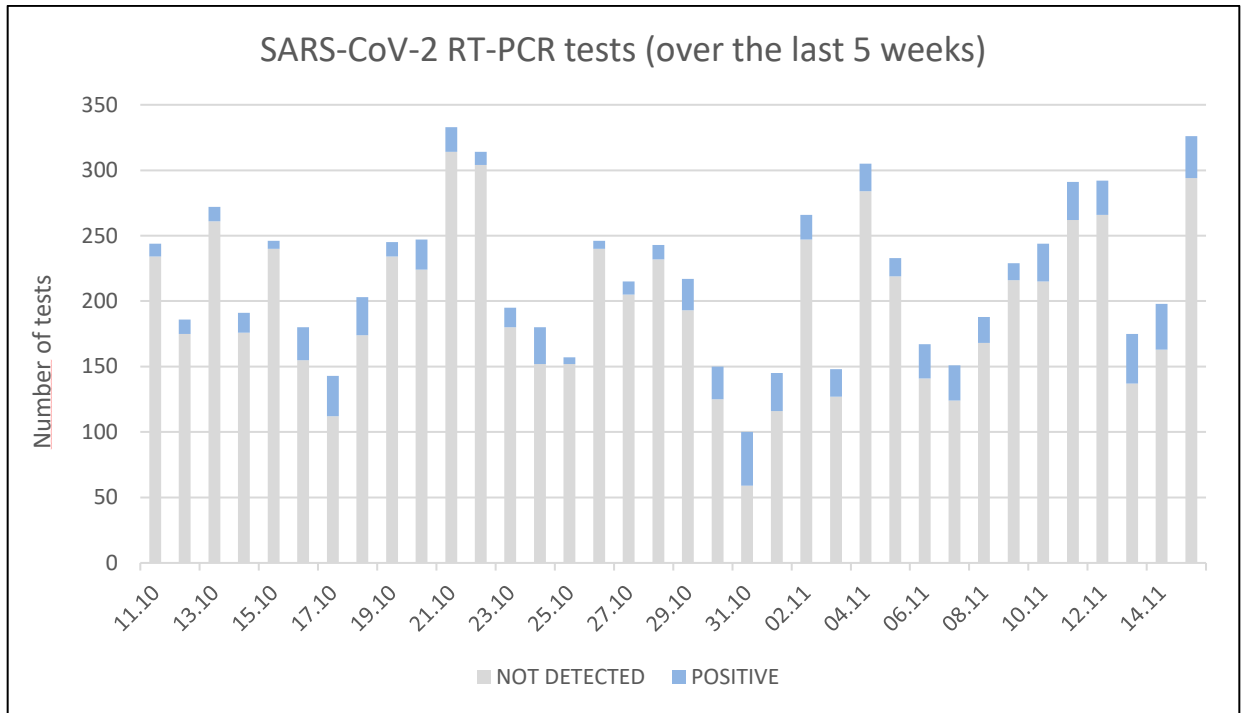
The number of positive tests in the canton and the total number of tests done during the surveilled week come from the website of the Direction Générale de la Santé in Geneva (available at <https://infocovid.smc.unige.ch/>), accessed November 16, at 08:00 pm.

Methods and collaborations

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 has been done within the Swiss national SARS-CoV-2 genomic and variants surveillance program. All specimens collected at HUG with a Ct value ≤ 32 are sequenced. In some instances, sequencing can be done on specimens sent by other laboratories in Switzerland within the surveillance program. Phylogenetic analysis data are produced by Nextstrain, in collaboration with Richard Neher's group at the University of Basel.

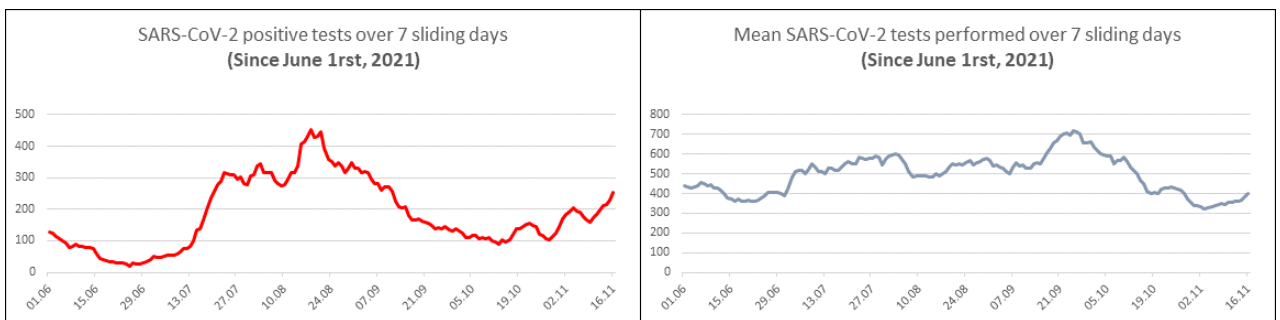
Geographic distribution, transmission advantage estimates and detailed number of available sequences over time in the canton of Geneva is available via CoVspectrum, maintained by the group of Tanja Stadler at ETH Zurich.

These reports are produced in collaboration with the Geneva Cantonal Physician team, which provides information on epidemiological links and post-vaccination infections (see below).

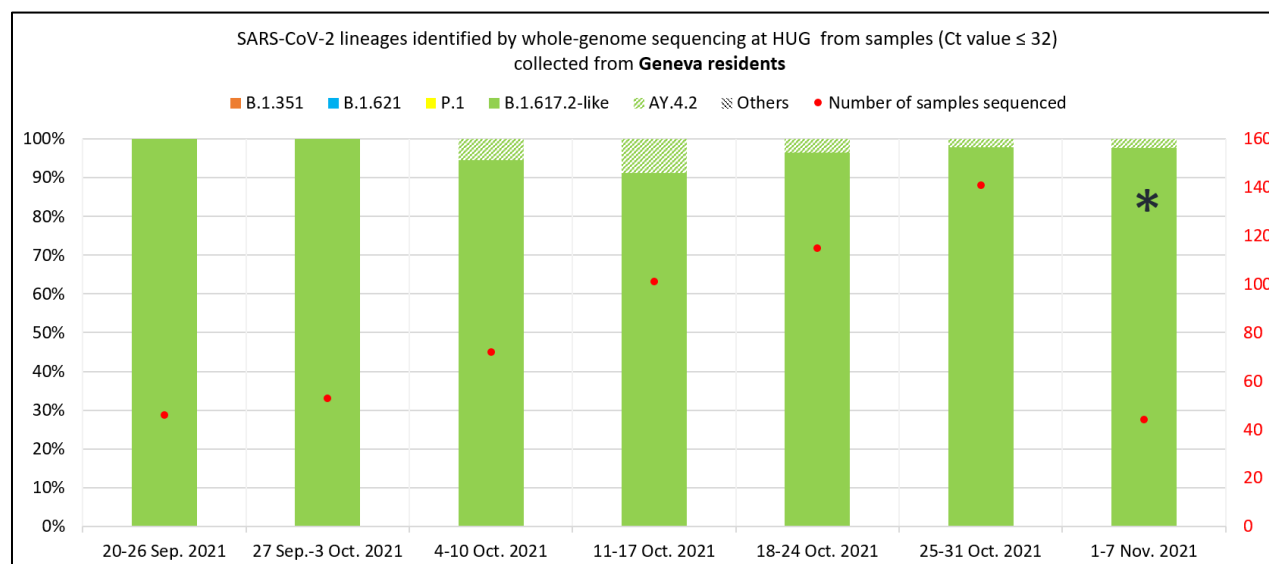


During week 45, the absolute number of positive SARS-CoV-2 tests continued to increase, and the mean positivity rate over 7 sliding days stayed high at 8.5%.

Similarly, at our outpatient symptomatic testing center, the mean positivity rate reached 20% on average for the second week in a row.



SARS-CoV-2 lineages identified by whole-genome sequencing at HUG from samples (Ct value ≤32) collected from Geneva residents



Results of WGS of 572 sequences submitted to GISAID between September 20 and November 7, 2021.

Note: due to a technical problem encountered during the WGS process, a total of 76 SARS-CoV-2 positive samples collected between September 23 and 28 could not be sequenced. This partly explains the drop in the number of sequences available during this period.

* Partial data for week 44 (November 1 to November 7), as sequencing is still ongoing. Numbers will be updated in the next report.

Since mid-July, the Delta B.1.617.2 variant replaced all other circulating variants. Exclusively Delta (B.1.617.2) or one of its sub-lineages sequences have been identified in samples collected from Geneva residents over the last 2 months. Worldwide, Delta or one of its sub-lineage has been identified in more than 98% of the available SARS-CoV-2 sequences collected over the last 2 months.

Focus on the Delta sub-lineage AY.4.2:

Four new sequences of the Delta sub-lineage AY.4.2 (a Variant under Investigation/Variant under Monitoring) **have been identified in the last sequencing batch.** The last identified sequence was collected on November 1st.

Epidemiological links: Among those 4 cases, one child was related to a known cluster (however, no sequencing result is available for the other cases belonging to this cluster). For the additional 3 cases, the source of contamination was not identified and therefore community transmission is likely.

A total of 27 sequences were retrieved in the whole Geneva area since the beginning of October: 1 additional sequence sampled in a currently hospitalized patient infected abroad and repatriated, and 5 more sequences, retrieved within the Swiss national SARS-CoV-2 genomic and variants surveillance program were sent from a private laboratory participating to the program. **This represents a proportion of 4% (27/625) of the sequences available for the Canton of Geneva from October 1 to November 15.** Of note, because of inherent delay due to sequencing and to the gathering of breakthrough vaccine infections primarily tested outside of our laboratory, we expect additional sequences to be available for the whole canton over this time period.

Focus on Delta sub-lineages carrying the E484Q mutation:

In the last sequencing batch, **5 more sequences** (among 181; 2.7%) **carrying the 3 mutations delineating the specific E484Q Delta sub-lineage first identified in Geneva** (Spike mutations E484Q, V687I and T859N), have been retrieved. For detailed information regarding the mutations present in this variant, please refer to the report of week 44, posted on November 10, 2021. Note that no Pango designation has yet been assigned for this Delta sub-lineage.

Epidemiological links: Among the 5 new cases, 2 were epidemiologically related to 2 other patients previously identified with this sub-lineage, 1 belonged to an identified cluster (however no sequencing result are available for the other cases) and 2 had recently travelled to Spain but may have been contaminated in the Geneva area.

Since the beginning of October, a total of 23 sequences of this Delta sub-lineage additionally have been identified from samples originating from Geneva residents and processed by HUG. The last identified sequence was collected on October 31. Most (60%) were post-vaccination infections (see below).

A total of 28 sequences have been retrieved in the whole canton, accounting for 4% (28/625) of available sequences collected since October 1. Note that as stated above, this proportion may change because of inherent delay due to sequencing.

In order to quickly identify and follow this sub-lineage, **a specific E484Q RT-PCR has been implemented since November 10, 2021, on samples tested for primary diagnostic at the laboratory of virology of HUG** and collected between October 9 and 11. Only 1 positive specimen was positive among 80 samples tested over this timeframe. Results of the systematic research of the E484Q mutation during week 45 and 46 will be displayed in the next report.

No more sequence of the Delta sub-lineage carrying the V1104L in addition to the E484Q mutation, and epidemiologically linked to vaccinated travelers returning from India has been retrieved since the last positive case collected on October 7.

There is an early signal for community transmission of both AY.4.2 and the specific E484Q Delta sub-lineage first identified in Geneva, as all cases are not linked together.

Post-vaccination infections in the canton of Geneva

Post-vaccination infection is defined here as a positive SARS-CoV-2 test occurring more than 14 days after the second vaccine dose. This surveillance is done in collaboration with the Direction Générale de la Santé (DGS) of Geneva. Data are collected by the DGS of Geneva during contact tracing calls after having obtained informed consent from SARS-CoV-2 positive patients. The list of patients with post-vaccination infections is sent weekly to HUG virology laboratory, which makes an effort to retrieve initial diagnostic samples in order to ensure sequencing, as recommended by FOPH.

Among the 748 new COVID-19 cases reported by the Direction Générale de la Santé in Geneva over week 45, 238 (32%) have been identified as post-vaccination infections.

As expected with the increased number of vaccinated people and the non-sterilizing immunity conferred by the vaccine, the proportion of post-vaccination infections is increasing over time.

Infections with AY.4.2 were predominantly documented in vaccinated individuals > 50% (12/21 for whom vaccination status is known).

Similarly, 15/23 for whom vaccination status is known (63%) of documented infections with a sequence carrying the three mutations E484Q V687I and T859N were identified in previously vaccinated individuals.

Whether these proportions are high because of immune escape properties of the variants or because of specific behavioral events and exposure bias (see report from week 44 posted on November 10) remains uncertain.

No data is available so far regarding possible immune escape of the Delta sub-lineages with additional 484Q, V687I and T859N mutations. More information is expected to follow in the next weeks while isolation and immunological characterization of this variant is ongoing.

Conclusions

- The **absolute number of positive tests continued to increase** during the last week, and the **mean positivity rate remains at a high level**.
- Delta or its sub-lineage is predominant since July and is exclusively causing all new identified infections in the canton of Geneva since mid-September.
- As expected with the increased number of vaccinees, the proportion of post-vaccination infections is increasing over time.
- The Delta sub-lineage **AY.4.2 is circulating in the community at a low level** and represents 4% of the available sequences of the Canton since the beginning of October.
- **The E484Q Delta sub-lineage first identified in Geneva** (with Spike mutations E484Q, V687I and T859N) is also **circulating in the community at a low level since the beginning of the month of October**. It was identified in a low proportion (4%) of the available sequences collected in the canton since October 1st. For detailed information regarding the mutations present in this variant, please refer to the report of week 44, posted on November 10, 2021.
- In order to quickly identify and follow the spread of this E484Q containing Delta sub-lineage, **a specific E484Q RT-PCR has been implemented since November 10, 2021**, on samples tested for primary diagnostic at the laboratory of virology of HUG.
- **Isolation** (Pr Eckerle group at Unige) **and immunological characterization** (Pr Eckerle and Trono groups at EPFL) **of this E484Q containing Delta sub-lineage is ongoing**. No Pango designation has yet been assigned.



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