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Geneva, August 03, 2021

Swiss national SARS-CoV-2 genomic and variants surveillance program: report of the month of June

1. Introduction: description of the Swiss national SARS-CoV-2 genomic and variants surveillance program.

Geneva Centre for Emerging Viral Diseases

Division of Infectious Diseases

Department of Medicine

Laboratory of virology

Division of Laboratory Medicine

Diagnostic Department

Currently, 8 diagnostic laboratories have joined the program, including university hospital centres in Switzerland (Geneva, Lausanne, Bern, Basel, Zurich, St-Gall, Ticino), in addition to private laboratories (Viollier, Dianalabs Genève), cantonal-based laboratories (Hôpitaux du Valais) and 3 high-throughput sequencing platforms (Health 2030 Genome Centre in Geneva, Functional Genomics Centre Zurich run by ETH Zürich and University of Zürich, Genomics Facility Basel run by ETH Zürich and University of Basel). Additional laboratories have been requested to join the program in order to fill sequencing gaps in some regions .

Processed sequencing data are shared openly within 14 days from positive PCR result through the GISAID platform (https://www.gisaid.org) and eventually through the Swiss Pathogen Surveillance Platform (SPSP). The centralized analysis of this National Surveillance will be performed by the groups of Pr. Neher, Pr. Stadler and Dr. Althaus, where variants of concern are counted, analyzed and all sequences scanned for new variants with potential changes in antibody-Spike interactions (https://nextstrain.org/groups/swiss, https://covariants.org/per-country, https://cov-spectrum.ethz.ch).

This work is done in close collaboration with the Swiss National COVID-19 Science Task Force and the Swiss Institute of Bioinformatic (SIB).

In order to complement the genomic surveillance based on patient samples, sequencing of SARS-CoV-2 in wastewater samples was also planned, initially for 6 months. Samples are collected daily in six wastewater treatment plants (WWTP), under the coordination of Eawag. Up to 50 samples per week over the first 26 weeks have been performed. The sequencing and analysis of these samples, including detection of variants, is done under the coordination of Prof Niko Beerenwinkel. It started in December 2020 for Lausanne and Zurich, and in February 2021 for all six WWTP (https://bsse.ethz.ch/cbg/research/computational-virology/sarscov2-variants-wastewater-surveillance.html). The analysis of wastewater samples is envisaged to run until the end of the surveillance program on 31.3.2022.

Immunological characterization of the variants within the surveillance program is coordinated by Professor Trono's team at EPFL.

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The list of the participants and collaborators of the program can be found at the end of this report in the appendix.

This report covers the period of May 31 to July 4 (weeks 22, 23, 24, 25, 26).

All data presented in this report are based on the sampling date.

2. Variants of concern, variant of interest and other surveilled variants: brief summary and special focus

Currently, 4 variants are considered variant of concerns (VOCs) by the WHO, B.1.1.7 (first identified in the UK – VOC Alpha, currently dominant in Switzerland), B.1.351 (first identified in South Africa – VOC Beta), P.1 (first identified in Brazil – VOC Gamma), and most recently B.1.617.2 (first identified in India, Delta), and their sub-lineages.

Two doses of the mRNA vaccines available in Switzerland have shown to keep a good effectiveness in real life observational studies against both symptomatic and severe disease due to the B.1.1.7 (Alpha) and B.1.617.2 (Delta) variants. One dose already seems to confer a good protection against severe disease, but has only minimal effect in protecting against symptomatic disease. A minimal decrease in protecting against infection has been showed against the B.1.351 (Beta) and B.1.617.2 (Delta) variants. (https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---29-june-2021).

Greater transmissibility and/or immune escape potential may lead to a renewed surge in infections despite the vaccination campaign. While we have identified some mutations that lead to greater transmissibility or reduced vaccine efficacy in vitro, there are many more such mutations or combinations of mutations which have not been identified. Therefore any variants displaying mutations known to be linked with either increased transmissibility and/or immune escape potential should be closely monitored, lest they acquire further enhancing mutations and develop into an even worse variant.

Therefore variants presented below will be particularly surveilled:

- variants classified as VOCs by the WHO
    - B.1.1.7 (Alpha) (and its sublineage with the E484K mutation)
    - B.1.351 (Beta)
    - P.1 (Gamma)
    - B.1.617.2 (Delta)

- new variants (until sufficient monitoring suggests they do not have a replicative/escape advantage) that include E484K + N501Y: higher transmissibility, immune escape risk, resistance to mAbs, such as: B.1.621 (N501Y + E484K), and B.1.315

- variants that include E484K alone due to immune escape risk and resistance to mAbs, such as: B.1.1.318, B.1.525 (eta), B.1.526 (part of the lineage carries E484K, the other S477N (iota)), B.1.620, B.1.621, P.3 (theta)

- variants that include L452R: slightly more transmissible relative to N501, resistance to mAbs, such as: C.36, C.37 (Lambda) and B.1.427/429 (epsilon)

-variants that include L452R + N501Y, such as A.27 and/or B.1.1.7 + L452R

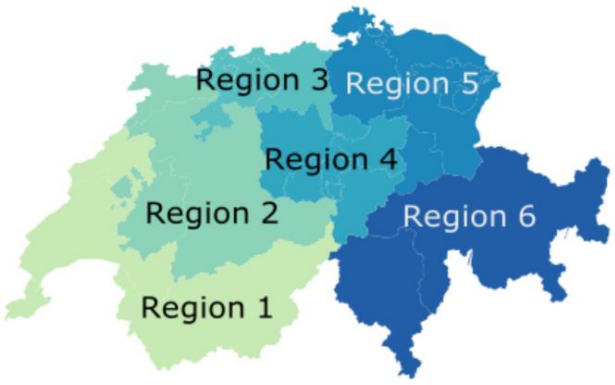
3. Epidemiology in Switzerland and number and origin of sequences produced through the program during the surveilled period

Data in this report comes from 3 sources: 1) The publicly available data on COVID-19 as reported by the FOPH (https://www.covid19.admin.ch), including data that is declared to the FOPH by the different laboratories in Switzerland; 2) data originating from laboratories participating in the surveillance program; and 3) sequences submitted to GISAID, for which the corresponding infected person was in Switzerland (resident or recent travel history to Switzerland).

General caveat: the numbers and denominators are fluid and variable over time; and are subject to change depending notably on the different databases used, and variable declaration delays. We aim to have a "harmonized" data set in the future with publicly available FOPH data and sequence data from SPSP. The overall goal of the program is to provide epidemiological trends and to highlight meaningful observations. In the current situation of decreasing number of cases detected in the country, the active investigation of specific clusters in some cantons can impact the precision of our observations.

The number and origin of sequences submitted to GISAID by each laboratory during January and February, 2021, prior to the start of the surveillance program can be found in the first report covering the months of March and April 2021.

Data will be presented here by regions, using the same region definitions that are used for the influenza sentinel surveillance system in Switzerland. Data are presented according to residency post-code.



Region 1 includes the cantons of Geneva, Neuchatel, Vaud and Wallis

Region 2 includes the cantons of Bern, Fribourg and Jura

Region 3 includes the cantons of Aargau, Basel (Basel-Stadt and Basel-Land) and Solothurn

Region 4 includes the cantons of Luzern, Unterwalden (Obwalden and Niedwalden), Schwitz, Uri and Zug

Region 5 includes the cantons of Appenzell (Appenzell Ausserrhoden and Appenzell Innerrhoden), Glarus, Sankt Gallen, Schaffhausen, Thurgau and Zurich.

Region 6 includes the cantons of Graubünden and Ticino.

Divisions of the different regions, from https://covariants.org/per-country

Number of cases processed by the laboratories participating in the surveillance program

During the period covered by the present report, the FOPH reported a total of 7 367 confirmed SARS-CoV-2 cases in Switzerland. Supplementary Table 1 provides an overview of the number and incidence of confirmed cases, the effective reproduction number R_e, the number and incidence of tests, test positivity, the number and proportion of sequenced samples, and the number and proportion of VOCs by canton, region and for Switzerland overall.

The laboratories participating in this program reported 2967 positive tests during the surveilled program, which represents about 40% of the total number of cases reported in Switzerland (including both PCR and antigen-based tests). Detailed data regarding the total number of tests performed each week by the laboratories participating in the surveillance program (including negative and positive tests numbers, and the number of the positive tests that have been sequenced) are available in appendix Table 3. Of note, antigen-based tests are by definition excluded of the surveillance, which applies only to PCR tests (although in some instance antigen positive cases may be asked to be re-tested by RT-PCR when part of VOC's clusters).

Number of SARS-CoV-2 sequences produced through the surveillance program

A total number of 1'970 SARS-CoV-2 sequences have been submitted to GISAID during this period. This represents 66.4% of the total number of the positive cases processed by the laboratories participating in the surveillance program (see Supplementary Table 2 and 3 in Appendix for details), and 27% of all cases detected in Switzerland during the surveilled period.

Table 1 shows the number of sequences successfully submitted to GISAID through the surveillance program during the surveilled period by calendar week.

Week	Date	Number of sequences successfully submitted to GISAID
22	May 31 to June 6	680
23	June 7 to 13	494
24	June 14 to 20	338
25	June 21 to 27	249
26	June 28 to July 4	209
	Total	1 970

Table 1: number of sequences submitted to GISAID through the surveillance program

The total number of SARS-CoV-2 sequences submitted to GISAID by each laboratory during the month of June is available in Supplementary Table 3 in the appendix.

Covering of sequencing in Switzerland and contribution of the national SARS-CoV-2 surveillance sequencing program

As shown in Figure 1, the total number of SARS-CoV-2 sequences submitted per week progressively decreased during the month of May (week 18 to 22), reflecting the decrease in cases within Switzerland, and continued to progressively decrease during the month of June (week 22 to 26). The vast majority of the sequences available in GISAID (green curve) and those on which the surveillance is conducted, come from the national surveillance program.

With the decrease number of positive cases each week, the fraction of the total number of positive sequenced cases increased in all regions, largely above the aim of the program (>10%), and reached 27% in average.

Figure 2 displays the fraction of SARS-CoV-2 cases sequenced for each Swiss region. Region 4 had the lowest total number of sequences and the lowest fraction of cases sequenced in Switzerland. At the beginning of the month of June, the fraction of cases sequenced in this region increased, and reached 10 %. An effort will be done in order to increase the covering of this region.

Figure 3 shows the covering of sequencing among the different Swiss cantons over the last 3 months, presented by fraction of cases sequenced among the total number of reported cases in the canton. It will be used to guide the contact with new laboratories in order to have a better covering of the country.

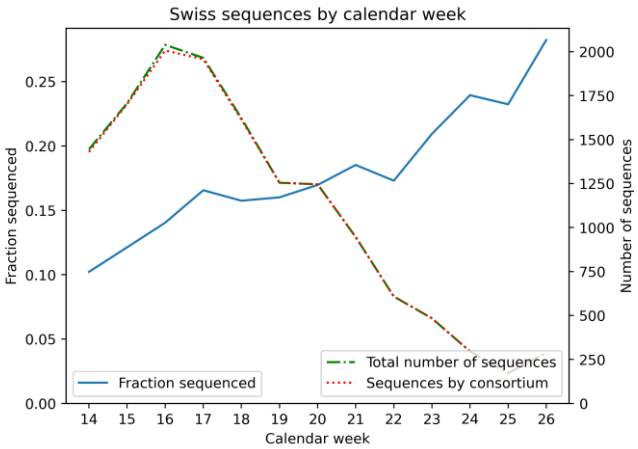


Figure 1: Number of SARS-CoV-2 sequences available for Switzerland (total available Swiss sequences in GISAID in green, Swiss sequences submitted through the program in dotted orange) and fraction of the total number of positive cases declared to the FOPH that have been sequenced (blue curve).

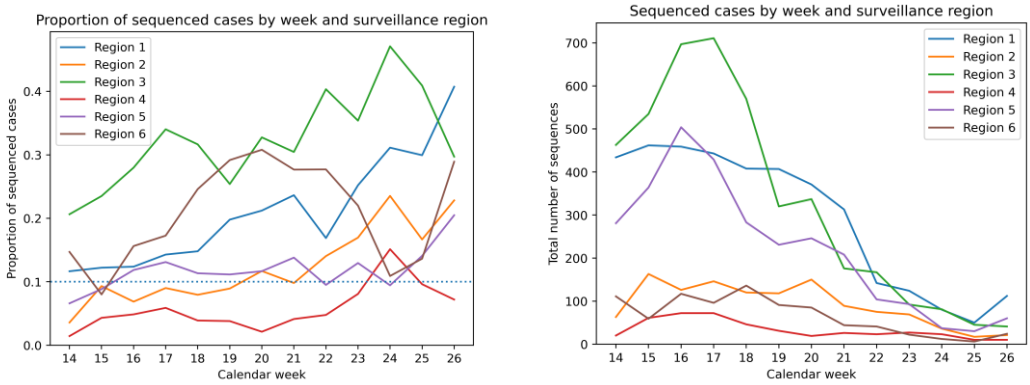


Figure 2: Covering of sequencing among the different Swiss regions per week, presented by fraction of cases sequenced (left) and by number of sequences (right)

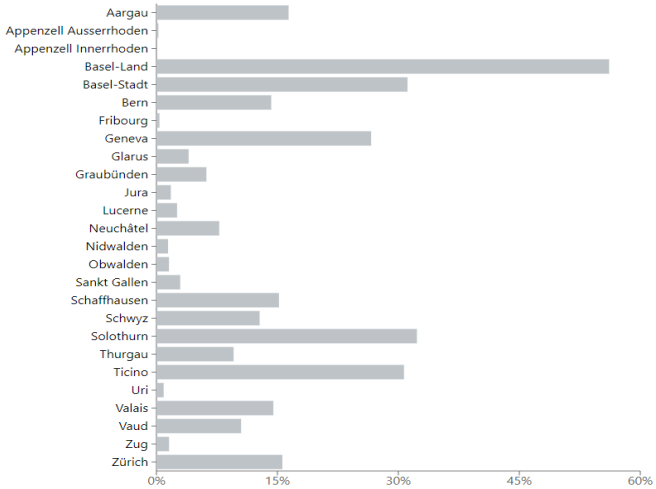


Figure 3: Covering of sequencing among the different Swiss cantons over the last 3 months, presented by fraction of cases sequenced. Screenshot form CoVspectrum website. Online dynamic navigation is available at https://cov-spectrum.ethz.ch/explore/Switzerland/AllSamples/Past3M/sequencing-coverage

4. Variants circulating in Switzerland since January 2021, with a focus on the surveilled period

Determination of the proportion of total number of sequences over time falling into defined variant groups is done by Emma Hodcroft's team and displayed on the CoVariant website (https://covariants.org/per-country). Those results are based on the total number of sequences submitted to GISAID over the time period for Switzerland. Those data mainly, but not exclusively, come from the national genomic surveillance program since its beginning (see Figure 1).

The proportion of the B.1.617.2 Delta variant (in green in Figure 4) has been progressively increasing during the month of June all over Switzerland, and now accounts for the majority of cases in Switzerland. See Table 2 below for the number of the main VOCs/VOIs by region.

Over the month of June, the B.1.617.2 (Delta) variant progressively replaced all other circulating variants in Switzerland, and accounted for more than half of the sequences retrieved in the country at the end of the month (see Figure 5 and 6 and Table 2).

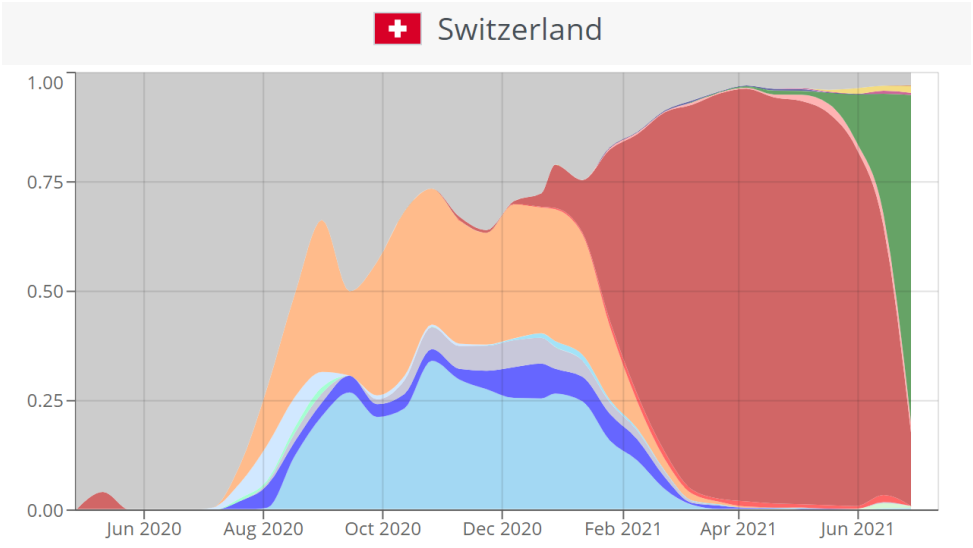
Its sublineage AY.1 (Delta + an additional 417N mutation) was detected in Switzerland for the first time at the end of May and increased at the beginning of June, reflecting a large cluster investigation in the Geneva area. This sublineage has not been detected during the last 2 weeks of June, when the B.1.617.2 variant progressively increased in proportion. (see Figure 6)

The B.1.351 (Beta) variant continued to be detected all over Switzerland at a very low level during the month of June.

The P.1 (Gamma) variant slightly increased in proportion at the end of June, but still at a very low level. This increase in proportion may be artificial, due to the overall decrease in the number of sequences over this period.

Other notable variants were detected in Switzerland over the month of June. Few cases of the C.37 (Lambda) variant have been detected at the end of the month, in regions 1, 2 and 3. Moreover, identification of B.1.621 was also noted in June, mainly in regions 1 and 5.

An estimate of the total number of VOCs circulating in Switzerland, corrected by taking in account the 12.5 % fraction of sequencing in Switzerland is available through the covSPECTRUM program developed at ETHZ at https://cov-spectrum.ethz.ch/explore/Switzerland.



Nexstrain Clade	Pango Lineage	WHO name
20I/501Y.V1	B.1.1.7	Alpha
20H/501Y.V2	B.1.351	Beta
20J/501Y.V3	P.1	Gamma
21A/S:478K	B.1.617.2	Delta
20C/S.452R	B.1.427/B.1.429	Epsilon
20A/S: 484K	B.1.525	Eta
20C/S: 484K	B.1.526	Iota
21A/S: 154K	B.1.617.1	Kappa
21G	C.37	Lambda
20A/S:439K	B.1.258	
20A/S:98F	B.1.221	
20E (EU1)	B.1.177	
20A.EU2	B.1.160	
21H	B.1.621	

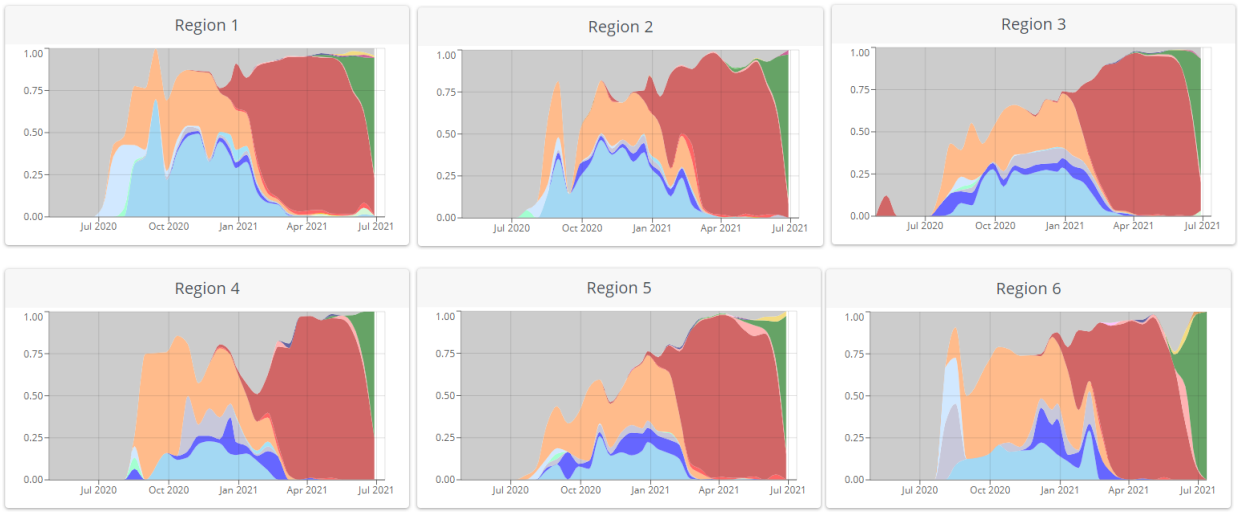


Figure 4: proportion of total number of sequences (not cases), over time, that fall into defined variant groups, for Switzerland. Screenshot from CoVariant website. Dynamic navigation is available at https://covariants.org/per-country. Dark red indicates lineage B.1.1.7 (Alpha). Note the rapid increase in prevalence and rise to dominance. Light red indicates B.1.351 (Beta). Green indicates lineage B.1.617.2 (Delta), detected since mid-April in Switzerland.

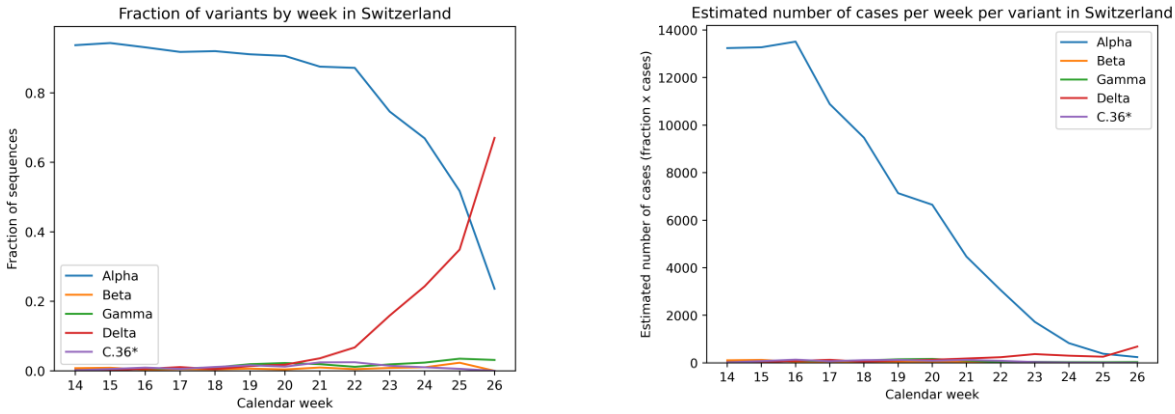


Figure 5:

(Left): Percentage of circulating VOCs and VOIs in Switzerland by week, over the 26 first weeks of 2021 (total number of B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), B.1.617.2 (Delta) and C.36 sequences from Switzerland and successfully submitted to GISAID are shown here).

(Right): Estimated number of sequences of the main VOCs/VOIs and variants under monitoring retrieved during the surveilled period.

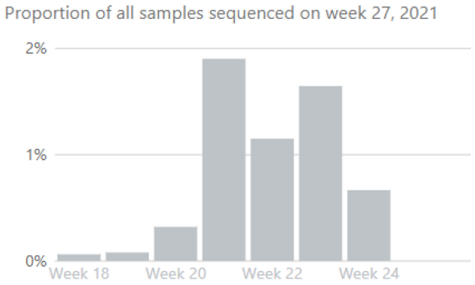


Figure 6: proportion of all AY.1 sequences among available sequenced cases over time

Region	C.36*	beta	delta	gamma	others	sequences	Cases	Proportion sequenced
Total	10	9	140	17	578	754	5253	0.144
1	2	3	53	2	127	187	1180	0.158
2	2	2	21	1	73	99	748	0.132
3	0	0	30	0	138	168	673	0.250
4	0	0	6	1	45	52	725	0.072
5	2	4	21	10	172	209	1595	0.131
6	4	0	8	3	19	34	332	0.102

Table 2: Number of variants of concerns (except B.1.1.7) and variant of interest C.36 by region, among the positive cases that have been successfully sequenced and analyzed by CoVspectrum.

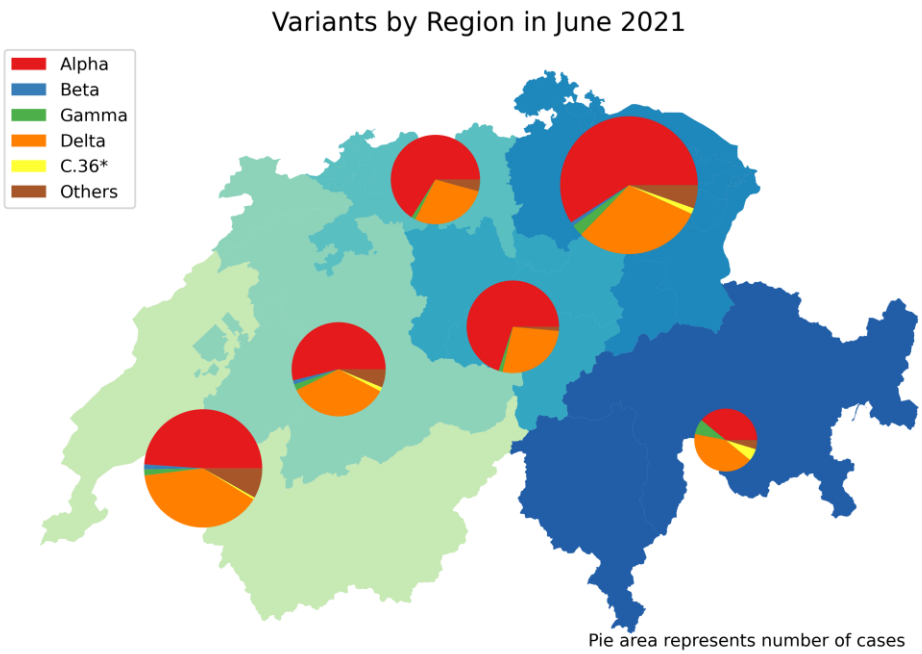


Figure 7: Distribution of variants per region, for June, shown on a map. The total number of sequences in that month, in the region, is shown in parentheses next to each region name. The size of the pie chart corresponds to the total number of sequences. Note that although Delta was dominant by the end of the month, Alpha was still dominant at the start of the month. Due to the decrease in the total number of cases during the month of June, the total number of Delta sequences was lower than the number of Alpha sequences, even if Delta was dominant in proportion at the end of the month.

5. Assessment of the competition between the different variants in Switzerland

The competition between different SARS-CoV-2 variants can be modelled using multinomial logistic regression. The analysis by Dr. Althaus' group is based on sequences retrieved from covSPECTRUM. The results highlight that Delta is expected to have become the single dominant SARS-CoV-2 variant in Switzerland in July 2021.

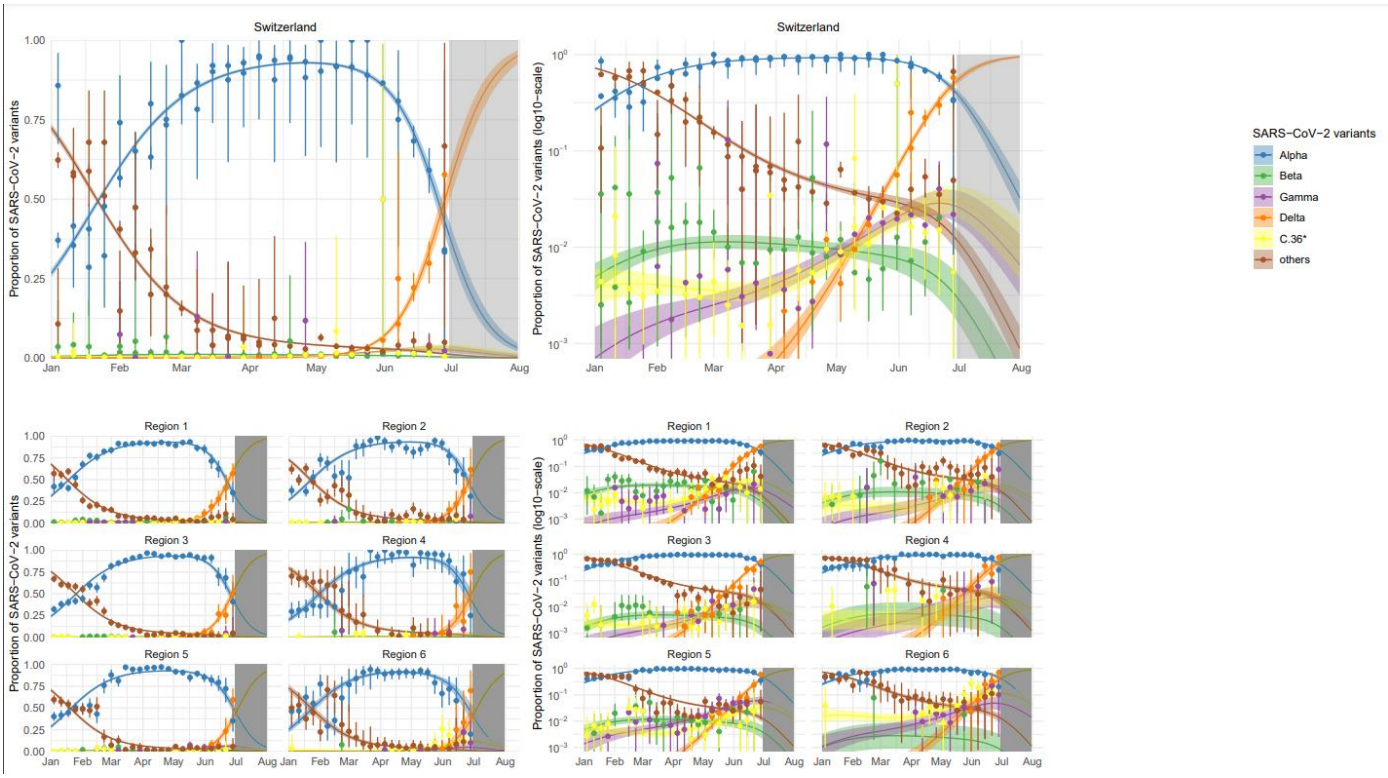


Figure 8: Observed and modeled proportion of SARS-CoV-2 variants over time in Switzerland. The proportion of Alpha and Beta started to grow in Switzerland in December 2020 and January 2021. Beta was subsequently outcompeted by Alpha in February and March 2021. In April and May 2021, Gamma and Delta started to replace Alpha, with Delta now outcompeting all other variants. At the end of June, more than half of the retrieved sequences in Switzerland were due to Delta. Model fits are based on a multinomial logistic regression with splines.

The estimated proportion of the Delta variant through time and its estimated transmission advantage is available on CoVspectrum:

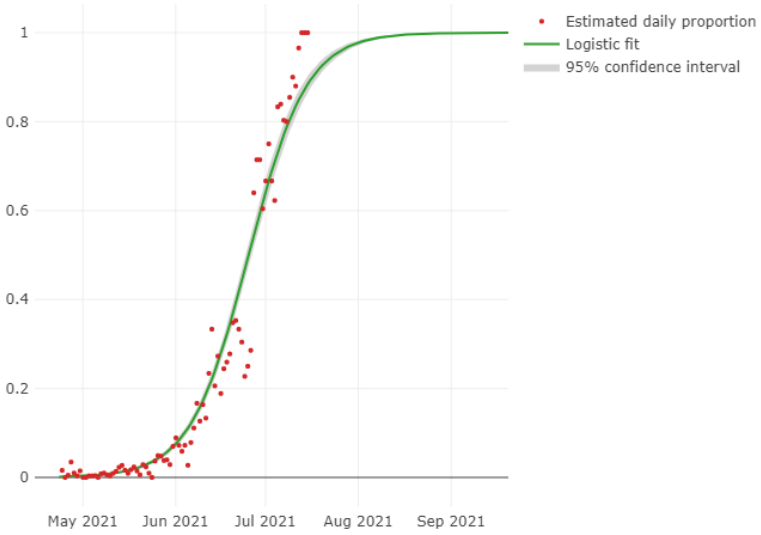


Figure 9: Estimated proportion of the Delta variant through time. The model assumes that the increase or decrease of the proportion of a variant follows a logistic function. It fits a logistic model to the data by optimizing the maximum likelihood to obtain the logistic growth rate a. From that, an estimate of the transmission advantage under a continuous (f_c) and discrete (f_d) model is derived. Dynamic navigation available at https://cov-spectrum.ethz.ch/

6. Wastewater surveillance program

Since February, an increased prevalence of the B.1.1.7 (Alpha) variant has been observed over time in all WWTPs tested. The B.1.617.2 (Delta) variant started to appear in wastewater samples around the beginning of June in all WWTPs. By mid-June it had reached the highest levels in Zurich (34%) and Laupen/Berne (47%).

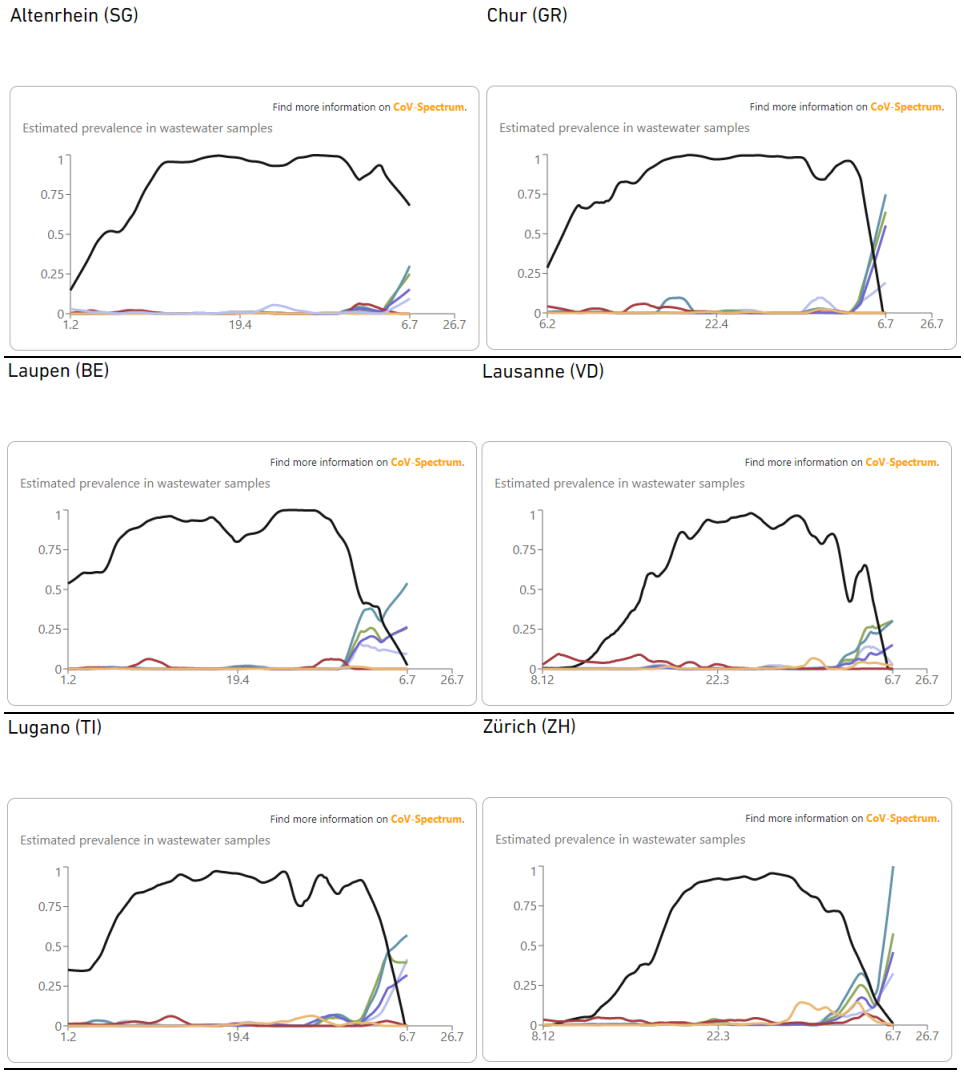


Figure 10 : Prevalence of different genomic variants of SARS-CoV-2 obtained from wastewater samples in different Swiss cantons. Samples are collected daily at six Swiss wastewater treatment plants. C.36.3 is represented in light blue, B.1.617.1 in green, B.1.617.2 (Delta) in dark blue, B.1.617.3 in purple, B.1.1.7 (Alpha) in black, B.1.351 (Beta) in red, P.1 (Gamma) in orange. Screenshot from the website of ETH Zürich. Online dynamic navigation available at https://bsse.ethz.ch/cbg/research/computational-virology/sarscov2-variants-wastewater-surveillance.html.

7. Immunological characterization of variants

The goal of the Swiss national SARS-CoV-2 genomic and variants surveillance program is to monitor the emergence and spread of new variants, be they known variants of interest (VOI) or variants of concern (VOC), or strains so far detected elsewhere in the world.
It includes a basic immunological characterization effort, whereby prototypic viral variants (i.e. presenting with significant sequence deviation in spike-coding region compared with previously prevalent strains) are tested for their sensitivity to neutralization by sera from previously infected or vaccinated individuals and by therapeutic / preventive monoclonal antibodies, some already FDA approved and some in development. For this, their spike proteins (the target of antibodies neutralization) is synthesized based on its RNA sequence and analyzed through cell-based or cell-free neutralization assays, i.e. with wild-type replicating isolates, viral pseudotypes or high-throughput surrogate spike-ACE2 (S^3-ACE2) binding assays using a collection of convalescent sera, post-vaccination sera and commercially available or in-house neutralizing monoclonal antibodies. Of note, the cell-free surrogate neutralization assay also provides semi-quantitative information on the relative affinity of each spike variants for the ACE2 viral receptor, which likely plays an important role in viral infectivity and transmission. This analysis through a well-established and streamlined pipeline instantly provides essential information on the immunological characteristics of the variants circulating in Switzerland, allowing for immediate strategic adjustments.
The cell-free neutralization assay, developed through a joined effort of EPFL and CHUV teams, is described in Fig. 11.

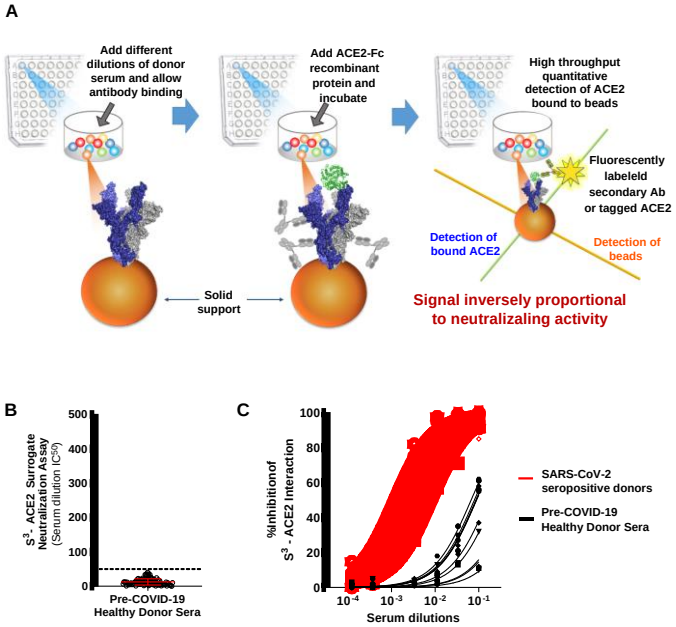


Figure 11: Outline and validation of a cell-free SARS-CoV-2 spike protein trimer-ACE2 surrogate neutralization assay. (A) A schematic outline of the S^3-ACE2 neutralization assay is shown. Anti-SARS-CoV-2 serum antibodies are monitored for their capacity in blocking the S^3-ACE2 interaction. ACE2 binding to spike protein was detected though use of a fluorescently labeled secondary antibody and the signal intensities are inversely proportional to the neutralizing potential of the anti-spike protein antibodies. (B) Serum dilution IC_{50} values were calculated for 104 healthy adult donor samples collected prior to November 2019 (pre-COVID-19 pandemic). The mean IC_{50} values and SD were used to establish a lower limit cutoff of 50 indicated by the dashed line. (C) Representative concentration response curves for ten healthy donor serum samples and ten SARS-CoV-2 seropositive donors with varying abundance of anti-spike protein IgG antibody are shown with black and red curves, respectively. Mean ± SD are shown in (B).

So far, the Spike proteins listed in Table 3 are available for use in neutralization assays based on either the cell-free system described in Fig. 1 or on lentivector pseudotypes. Additional proteins will be generated as new mutants and variants are identified through the national genetic surveillance program.

LV	Protein	MUTATIONS	LINEAGE
		D614G + L5F	
		D614G + L18F	
		D614G + del69-70	B.1.388
		D614G + D80Y	B.1.367
		D614G + W152R	
		D614G + M153T	
		D614G + M153I	
		A222V-EU1	B.1.177
		D614G + K417N	
		D614G + D80A / K417N	
		D614G + N439K	B.1.258.24
		D614G + del69-70 / N439K	
		D614G + L452R	B.1.427 / epsilon
		D614G + Y453F	
		D614G + del69-70 / Y453F	
		D614G + S459Y	
		S477N_EU2	B.1.160
		D614G + S477R	
		D614G + E484K	B.1.1.345
		D614G + E484K/ N501Y	
		D614G + K417N / E484K / N501Y	B1.177.31
		D614G + E484Q	
		D614G + L452R /E484Q	
		D614G + F486L	
		D614G + N501T	
		D614G + N501Y	Ap.1
		D614G + del69-70 / N501Y / P681H	
		D614G + del69-70 / del144 / N501Y / A570D / P681H	
		D614G	
		D614G + P681H	
		D614G + P681R	
		D614G + A701V	
		del69-70 / del144 / N501Y / A570D / D614G / P681H / T716I / S982A /D1118H	B.1.1.7 / alpha
		del69-70 / del144/ E484K/ N501Y / A570D / D614G / P681H / T716I / S982A / D1118H	B.1.1.7 + E484K
		L18F / D80A / D215G / del242-244 / R246I / K417N / E484K / N501Y / D614G / A701V	B.1.351 / beta
		D80A / D215G / del242-244 / R246I / K417N / E484K / N501Y / D614G / A701V	B.1.351 w/o L18F
		L18F / T20N / P26S / D138Y / R190S / K417T / E484K / N501Y / D614G / H655Y / T1027I / V1176F	B.11.28.1 / gamma
		T20N / P26S / D138Y / R190S / K417T / E484K / N501Y / D614G / H655Y / T1027I / V1176F	B.11.28.1 w/o L18F
		L18F / T20N / P26S /D138Y / R190S / K417T / E484K / N501Y / D614G	
		Q52R / del69-70 / E484K / Q677H / F888L	B.1.525 / eta
		H66D / G142V / del144 / D614G / G669S / N1187D	
		H66D / G142V / del144 / D215G / V483A / D614G / H655Y / G669S / Q949R / N1187D	Brittany
		T95I / D253G / D614G / A701V	
		L5F / T95I / D253G / E484K / D614G / A701V	B.1.526 / iota

ONGOING

LV	Protein	MUTATIONS	LINEAGE
		D614G + E154K	
		D614G + Q1071H	
		E154K / L452R / E484Q / D614G / P681R / Q1071H	B.1.617.1 / kappa
		D614G + T19R	
		D614G + del156-157 / R158G	
		D614G + L452R / P681R	
		D614G + T478K	
		D614G + D950N	
		T19R/ del156-157 / R158G / L452R / T478K / D614G / P681R / D950N	B.1.617.2 / delta

Table 3: Spike proteins synthesized for lentivector pseudotype-based (LV) or cell-free (Protein) neutralization assays. Mutations are depicted using single letter amino acid code. Corresponding virus lineages are indicated to the right when relevant.

In a first round of tests, samples collected through a Geneva-based serological survey (*L'Huillier* et al., Clin Microbiol Infect 2021, https://doi.org/10.1016/j.cmi.2021.01.005) were run through the cell-free assay as depicted in Fig. 12.

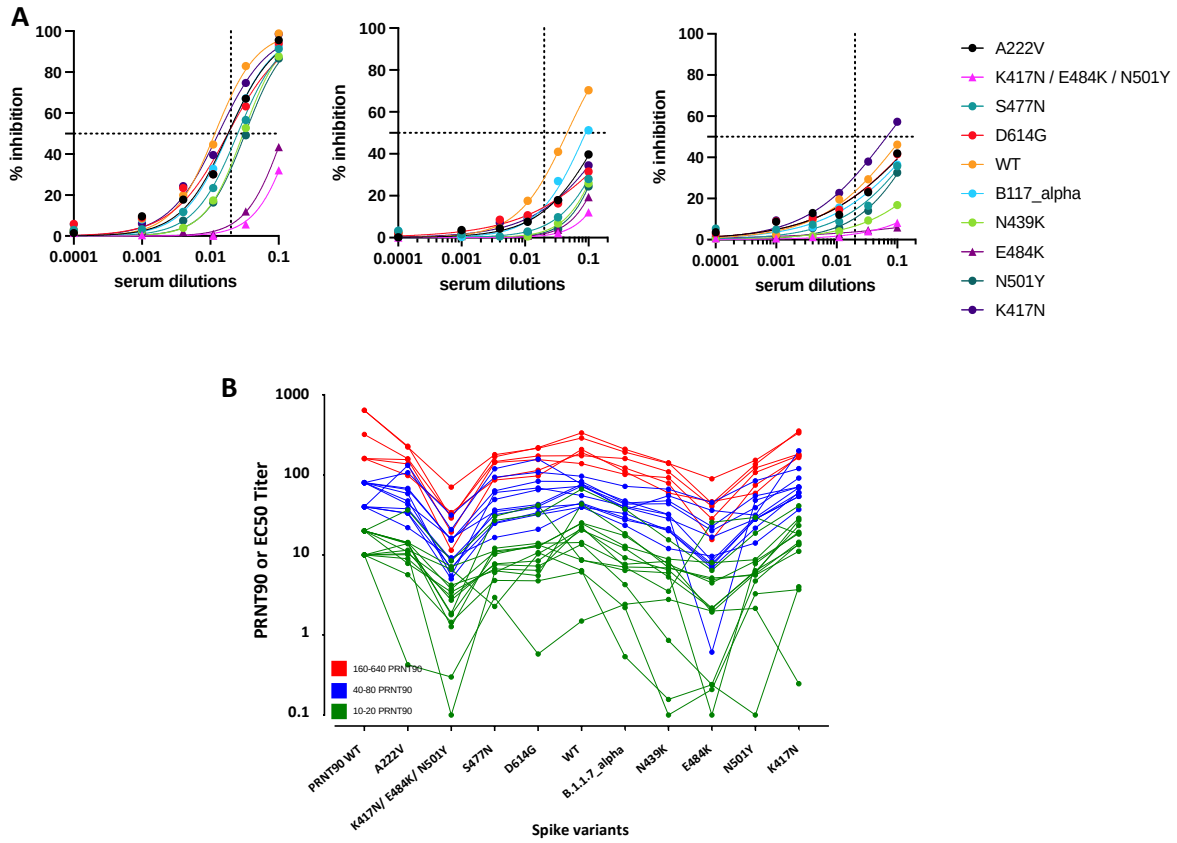


Fig. 12. Testing serums through cell-free SARS-CoV-2 neutralization assay. TOP panels: examples of neutralizations monitored with the S^3-ACE2 luminex-based assay using sera from 3 different donors and illustrating the heterogeneity in strength and breadth of the sera from recovered patients against various spike variants. BOTTOM: Sera were classified in 3 groups depending on the dilution needed to reach a reduction of 90% of the plaques in a conventional plaque reduction neutralization test (PRNT): low neutralizing ability in green (dilution 10-20x), middle in blue (dilution 40-80x) and high in red (dilution 160-640) and their neutralizing activities against the indicated spike variants were quantified in a S^3-ACE2 luminex-based assay. The serum dilutions necessary to achieve a 50% inhibition of ACE2 binding to each spike variant is represented (EC50).

The cell-free assay was also used to measure serially neutralization activity in the serum of a recently described case of re-infection (*Vetter* et al. Clin Microbiol Infect 2021, https://doi.org/10.1016/j.cmi.2021.02.010) (Fig. 13).

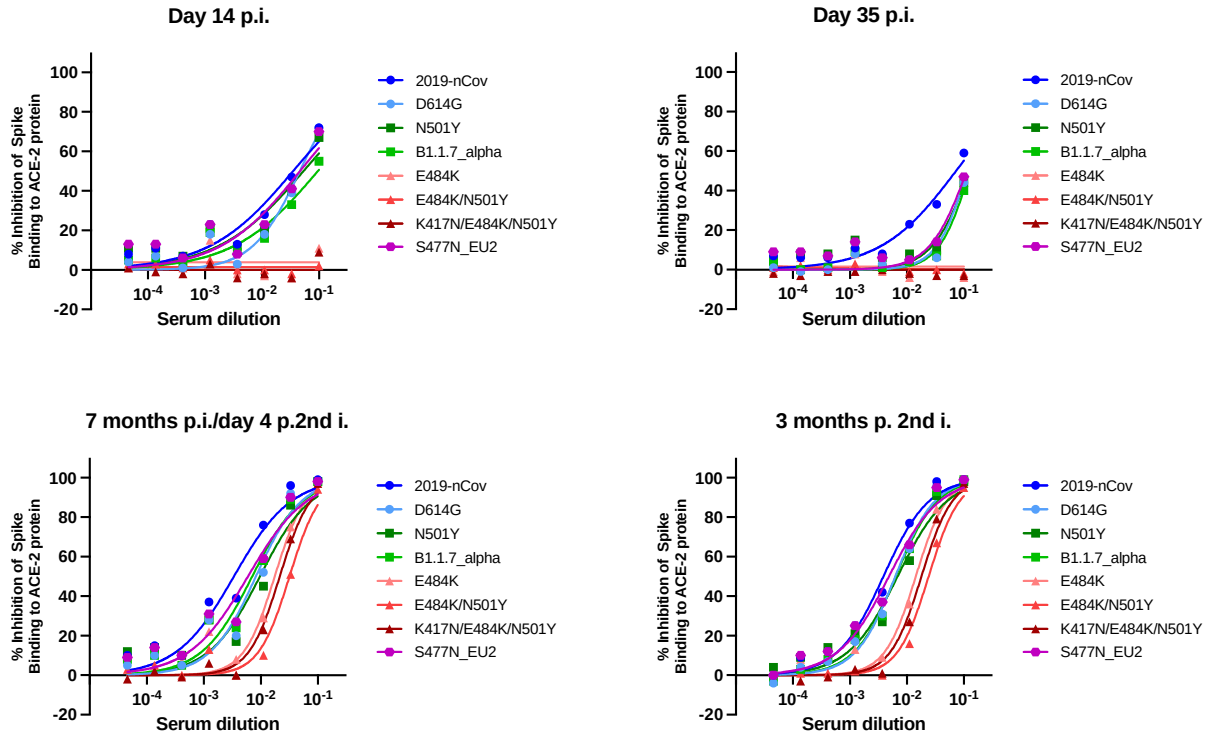


Fig. 13. Neutralization activity against indicated SARS-CoV2 variants in serum from a health care worker infected 7 months apart during Swiss first and second waves. Samples correspond to 14 (top left) or 35 (top right) days after first infection and 4 days (bottom left) or 3 months (bottom right) after second infection with an European S477N strain (EU-2). Notice how neutralization activity was relatively weak and narrow after first COVID episode but immediately boosted in both strength and breadth by second episode.

Taking advantage of the ongoing serological monitoring of the population in the canton of Geneva, we are now establishing biobanks of sera from previously infected or vaccinated individuals, aiming at a representative sampling of age groups, infecting variants and vaccine types. We are also constituting a collection of SARS-CoV-2 monoclonal antibodies, whether from commercial sources or developed in-house.

These sera and antibodies will serve to test the neutralization sensitivity of variants and mutants identified by the genetic surveillance program in the months to come.

Conclusion

In June, approximately 2000 sequences were obtained through this surveillance program. Each week since this surveillance program started, it has contributed almost all of the Swiss SARS-CoV-2 sequences available on GISAID. In June, around 27% of the cases reported in Switzerland were sequenced each week. Region 4 is still the least represented geographical area. Additional laboratories have been asked to join the program to ensure a substantial coverage, especially while the total number of new cases are declining, to achieve representative sequencing across the country. The FOPH may have to require participation of additional hospital-based and/or private laboratories in order to reach at least a 10% of sequence coverage in every region of Switzerland.

The B.1.1.7 (Alpha) variant was still dominant at the start of June, but was displaced by the B.1.617.2 (Delta) variant in Switzerland by the end of June over a short period of time, with a relatively homogenous representation over the different Swiss regions.

B.1.351 (Beta) continued to circulate at low levels throughout the whole surveilled period, without increasing trends.

An increase in the fraction and absolute number of the P.1 (Gamma) variant was observed during the month of June, with its fraction peaking at week 25. Most cases originate from region 5 and 6. Its proportion among the sequenced cases was, however, still relatively low (<5%), and the absolute number of sequences also remains low.

B.1.617.2 (Delta) has been detected at significant levels in almost all regions, and has been progressively increasing in proportion since its first detection in April, when it represented around 3% of the sequences, with a sharp and progressive increase during June. Similar results have been observed from wastewater samples. It is now dominant variant in Switzerland as of mid-June, 2021, and continues to circulate robustly. Its sub-lineage AY.1 (Delta + 417N) has not been detected after mid-June, and its circulation appears to be limited in Switzerland.

Notably, sequencing showed the presence of the B.1.621 variant, (considered a VOI), which was detected for the first time in June, and is now present at a low level in Switzerland.

Furthermore, C.37 (Lambda), another VOI, has been detected only a few times with no evidence of substantial circulation in the community.

No important geographical breakdown of a particular variant has been noticed.

An estimate of the total number of VOCs circulating in Switzerland, corrected by taking in account the fraction of sequencing in Switzerland is available at https://cov-spectrum.ethz.ch/explore/Switzerland.

As the number of cases of SARS-CoV-2 declines, an effort will be made to add more laboratories to the program in order to maintain representative sequencing throughout the country.

Acknowledgements:

https://bsse.ethz.ch/cevo/research/sars-cov-2/swiss-sars-cov-2-sequencing-consortium.html

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Appendix :

SARS-CoV-2 epidemiology in Switzerland:

We used publicly available data on COVID-19 as reported by FOPH (https://www.covid19.admin.ch) and sequence data submitted to GISAID to provide a summary of the SARS-CoV-2 epidemiology in Switzerland.

sup_table_overview_Jun.xlsx

Supplementary Table 1: Epidemiological data for Switzerland, its regions and cantons in June 2021: population, number and incidence of confirmed cases, effective reproduction number R_e, number and incidence of tests, test positivity, number and proportion of sequenced samples, and number and proportion of VOCs. R_e by region is represented as the median and range of the daily R_e values for all cantons within a region.

week	date	Total PCR tests	Positive tests	Sequenced	% positives	% positives sequenced
22	May 31 - June 6	22 900	1 091	680	4.76%	62.33%
23	June 7 to 13	18 596	771	494	4.15%	64.07%
24	June 14 to 20	16 259	419	338	2.58%	80.67%
25	June 21 to 27	17 550	354	249	2.02%	70.34%
26	June 28 - July 4	16 505	332	209	2.01%	62.95%
	Total	91 810	2 967	1 934	3.23%	66.40%

Supplementary Table 2: Total number of tests performed by the laboratories participating in the surveillance program from May 3 to May 30, 2021.

		Basic Surveillance		Augmented Surveillance						Sentinella Laboratories		
Week	Date	EOC	St-Gallen	UBS	IFIK	Dianalabs Genève	CHUV*	UZH*	ICH-VS**	HUG	ETH/Viollier*	All
22	May 31 - June 6	46	96	42	12	41	27	36	56	72	252	680
23	June 7 to 13	0	47	44	20	20	19	37	32	71	204	494
24	June 14 to 20	0	48	21	34	0	26	35	23	35	116	338
25	June 21 to 27	18	27	20	16	14	17	45	8	16	68	249
26	June 28 - July 4	10	12	10	6	5	19	27	19	42	59	209
	Total	74	230	137	88	80	108	180	138	236	699	1970

*Supplementary Table 3: number of sequences submitted to GISAID by each laboratory during the surveilled period (May 31-July 4, 2021). *including sequencing sent to high-throughput platforms ** Samples sent to high throughput platform*

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