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Swiss national RSV, SARS-CoV-2 and Influenza virus genomic surveillance program: February to March, 2025

Geneva Centre for Emerging Viral Diseases

Division of Infectious Diseases

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1. Summary:

This report covers the samples collected between January 9, 2025 and February 28, 2025, corresponding to the third sequencing batch of the integrated RSV, SARS-CoV-2 and influenza virus genomic surveillance program of the 2024/2025 season.

All samples (n=177) sent for sequencing originated from the Sentinella program, yielding a total number of 173 sequences: 6 SARS-CoV-2, 152 influenza (among which 94 IA (41 H1N1, 53 H3N2), 58 IB), and 15 RSV (7 RSV-A, 8 RSV-B).

SARS-CoV-2 lineages were represented by XEC and KP3.1.1 (Figure 1). For influenza virus, 38% of the sequences were influenza B and 62% were influenza A: of the influenza A sequences, 44% belonged to the H1N1pdm09 subtype, while 56% belonged to the H3N2 subtype. For RSV, 46% of the sequences were RSV-A, and 53% were RSV-B.

In the current batch, only 1 influenza A(H1N1pdm09) specimen, collected within the Sentinella network, carried the amino acid substitution H275Y associated with highly reduced susceptibility to oseltamivir. No other mutations linked resistance to oseltamivir nor baloxavir were observed. No resistance mutation to nirsevimab have been retrieved in circulating RSV samples. Similarly, no high-level nirmaltrelvir/ritonavir resistance mutation has been observed within circulating SARS-CoV-2 strains.

Note that the success rate for SARS-CoV-2 and influenza sequencing was 100% in the current sequencing batch, while 15/18 (83%) of RSV samples successfully led to a sequence.

Key numbers

Table 1: Origin of the samples and success of the sequencing.

	SARS-CoV-2	Influenza virus	RSV
Sentinella	6	153 (95 A, 58 B)	18 (8A, 10B)
Laboratory network	0	0	0
Total	6	153	18
Number of sequences successfully deposited in GISAID	6	152 (94 A (41 H1N1 and 53 H3N2), 58 B)	15 (7 A, 8 B)

Table 2: Sentinella positive specimens (from January 9 to February 28, 2024).

	SARS-CoV-2	Influenza virus	RSV
Total number of positive specimens	14	359 (222 A, 137 B)	52
Meeting sequencing criteria	7	158 (99 A, 59 B)	18
Included	6	153 (95A, 58B)	18

Sequencing criteria and reasons for non inclusion of samples in the sequencing batch are detailed in the methods section below.

Table 3: Detailed origin of samples by originating lab.

Site	SARS-CoV-2	Influenza virus	RSV
CHUV	0	0	
HUG*	6	153 (95 A, 58 B)	18
ICH	0	0	0
IFIK	0	0	0
IMV	0	0	0
USB	0	0	0
Total	0	0	0

*All samples provided by the HUG laboratory originate from the Sentinella network.

SARS-CoV-2 lineages

A very low number of SARS-Cov-2 sequences have been produced in the last sequencing batch (collected over January and February 2025), as only rare Sentinella samples tested positive for SARS-CoV-2.

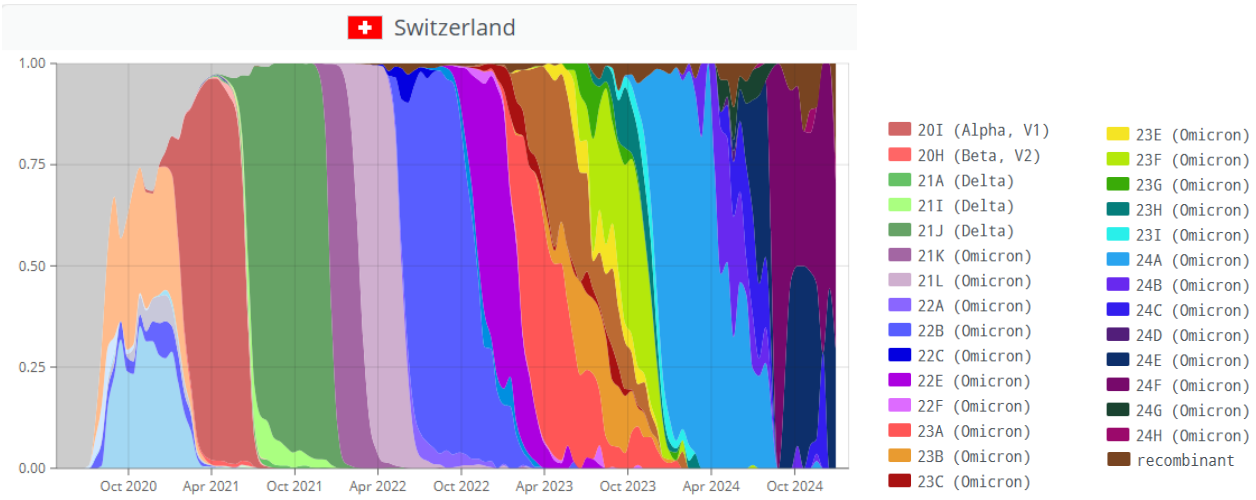

Figure 1: Proportion of Swiss sequences belonging to each pango lineage. XEC (24F) and KP.3.1.1 (24E) still dominated in the last sequencing batch. Source: www.covariants.org.

Escape mutation prevalence

Currently, no monoclonal antibodies available in Switzerland are effective at neutralizing most of the SARS-CoV-2 sub-lineages circulating in Switzerland and the rest of the world. The 3CL protease inhibitor, nirmatrelvir/ritonavir Paxlovid®, remains effective against SARS-CoV-2, and we are monitoring the prevalence of mutations that have been shown to reduce its efficacy by 5-fold or more (Table 4).

No resistance mutations were spotted in Switzerland.

Table 4: Prevalence NSP5 mutations of SARS-CoV-2 leading to resistance from nirmatrelvir/ritonavir Paxlovid®.

Mutation	Switzerland	Europe	Mutation	Switzerland	Europe
T25A	0	0	P168Del	0	0
F140L/S	0	0	H172L/N/Q/Y	0	0
G143S	0	0	A173V	0	0
S144A/E/L/P	0	0	R188G	0	0
M165R/T	0	0	Q189K	0	0
E166A/G/K/V	0	0	Q192A/C/D/E/F/G/H/I/K/L/P/R/S/T/V/W/Y	0	0
L167F	0	0	P252L	0	0

Data based on the Stanford University 3CLpro inhibitors mutation list, available at https://covdb.stanford.edu/ (only mutations causing more than a 5 fold reduction in nirsevimab susceptibility are depicted here).

Influenza virus lineages

Among samples retrieved within the Sentinella program since January, most H1N1 samples clustered within clade 5a.2a and a minor group within 5a.2a.1. All H3N2 samples except one belonged to clade 2a.3a.1. The remaining sample clustered within 2a.3b clade. All the B specimens clustered within clade V1A.3a.2.

For a graphical representation of the different clades circulating in Switzerland, see the Nextstrain group space for the WHO-Euro region maintained by the World Wide Influenza centre in London and the group of Richard Neher: https://nextstrain.org/groups/WHO-euro-flu.

Escape mutation prevalence

Table 5: Resistance mutations to influenza antivirals mostly used in Switzerland.

A(H1N1)pdm09			A (H3N2)			Influenza B		
Mutation	Switzerland	Europe	Mutation	Switzerland	Europe	Mutation	Switzerland	Europe
NAI : Oseltamivir			NAI : Oseltamivir			NAI : Oseltamivir		
S110F	0	0	**E119I/V**	0	2	**G104E**	0	0
E119A/D/V	0	1	D151E	0	0	E105K	0	0
R152K	0	0	**R224K**	0	0	**G108E**	0	0
D199E/G/Y	0	1	N245Y	0	0	**E117A/D/G/V**	0	0
I223K/L/R/T	0	1 (T)	**Del245-248f**	0	0	**P139S**	0	0
S247G/R	0	0	**Del247-250f**	0	0	**G140R**	0	0
H275Y	**1**	23	K249E	0	2	T146K/P	0	0
R293K	0	0	E276D	0	0	**R150K**	0	0
N295S	0	0	**R292K**	0	0	K152M/N	0	0
I427T	0	0	**N294S**	0	0	D197E/N/**Y**	0	2
I436N	0	0	N329K/R	0	0	A200T	0	0
P458T	0	0	S331R	0	16	**I221L/N/T**	0	0
			R371K	0	0	A245T	0	0
			Q391K+K249E	0	0	H273Y	0	2
			E119V+T148I	0	0	**R292K**	0	0
			E119V+I222L/V	0	0	N294S	0	0
						R374K	0	0
						A395E	0	0
						H439P	0	0
						Y142H+G145R	0	0
						T146P+N169S	0	0
PAI: Baloxavir			PAI: Baloxavir			PAI: Baloxavir		
I38S/T	0	0	**I38T**	0	0	I38F/M/T/V	0	2
I38F/L/M/V	0	0	I38F/L/M/N/S/V	0	1			
			L28P	0	0			
E23 G/K/R	0	0	E23G/K/R	0	0	E23K	0	0
K34R	0	0	K34R	0	0			
			A36V	0	0			
A37T	0	1	A37T	0	0			
			E119D	0	0			
E198 K	0	0	E198K	0	0			
E199D/G	0	0	E199G	0	0			
						E120De	0	1
						G199R	0	1

Mutations depicted in this table cause reduced inhibition (RI) (for influenza A: 10-to-100-fold increase in IC_{50} values; for influenza B: 5 to 50 fold increase in IC_{50} values), or highly reduced inhibition, in bold (HRI) (for influenza A: >100 fold increase in IC_{50} value; for influenza B: > 50 fold increase in IC_{50} value). NAI: neuraminidase inhibitor (resistance mutation located in the neuraminidase protein). PAI: inhibitor of the cap endonuclease of the acidic protein baloxavir (resistance mutation located in the PA). Data based on last WHO algorithm (v2024). *Result based on sequences originating from Sentinella only.

RSV

RSV-A and RSV-B were retrieved almost in the same proportion in this sequencing batch. For a graphical representation of the different strains circulating in Switzerland, see www.nextstrain.org/rsv.

Escape mutation prevalence

Two monoclonal antibodies are available for use as a pre-exposure prophylaxis treatment: palivizumab and nirsevimab.
No mutation associated with a significant decrease in neutralization of the two main anti-RSV existing monoclonal antibodies have been detected in Switzerland.

Table 6 : Resistance mutations to monoclonal antibodies available in Switzerland with an anti-RSV activity.

RSV-A		
Mutation	Switzerland	Europe
Resistance to nirsevimab		
N67T + N208Y	0	0
K68E	0	0
Resistance to palivizumab		
K272 M/T	0	0
S275F	0	0

RSV-B		
Mutation	Switzerland	Europe
Resistance to nirsevimab		
I64T	0	0
I64M + K65R	0	0
K68E/Q	0	0
K68N	0	0
N201S/T	0	0
N208S/D	0	0
K65Q/T	0	0
Resistance to palivizumab		
K272N/Q	0	0
K272R	0	0
KN63R	0	0

Mutations depicted in this table have shown to cause a proven resistance to the mAb (highlighted in bold), or to possibly reduce the neutralization by the mAb. Only resistance causing more than a 5 fold reduced neutralization are presented here. List of mutations originates from the last ANRS – MIE Respiratory viruses group mutation list combined with literature review (https://virusfrenchresistance.org/virus-french-resistance-rsv/, *Fourati*, Lancet, 2024).

Methods:

Samples primarily originate from the **Sentinella** surveillance network, which reflects the circulation of viruses in the community. These are complemented by samples collected from six major tertiary hospital laboratories: **Institut für Medizinische Virologie (IMV)** in Zurich, **Centre Hospitalier Universitaire Vaudois (CHUV)** in Lausanne, **Hôpitaux Universitaires de Genève (HUG)** in Geneva, **Universitätsspital Basel (USB)**, **Institut Central des Hôpitaux (ICH)** in Sion, and **Institut für Infektionskrankheiten (IFIK)** in Bern. Samples are obtained from both outpatient departments and hospital wards to reach a predefined target of approximately **200 samples per batch**.
Only samples that meet the **sequencing criteria*** are sent for sequencing.

Note that all Sentinella specimen are processed at the Geneva University Hospitals, Laboratory of Virology.

Sequencing criteria

- Influenza virus A/B and RSV A/B: Ct values < 25; SARS-CoV-2: Ct value < 28
- AND (if documented) absence of co-infection with another respiratory virus

Reasons for Sentinella specimen meeting sequencing criteria not to be sent to sequencing: missing tube, not enough volume, other reason

Samples are processed with the Illumina Respiratory Virus Oligo Panel (Illumina) according to manufacturer's instructions. Analyses are performed by the 2030 Health Genome Center and transferred to the Swiss Pathogen Surveillance platform (SPSP) before submission in GISAID, as recommended by WHO.

Analysis of resistance mutation is performed by the team of Richard Neher, based on specific mutations list for each virus determined either by WHO documentation, literature review, or other available algorithms. For Influenza, this analysis covers all data in GISAID, for RSV and SARS-CoV-2 these data are restricted to data in NCBI.

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

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