

Reaction Times in Modern Virology: “This is not a Drill”

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The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant of interest BA.2.87.1 has not driven any Coronavirus disease 2019 (COVID-19) pandemic wave. Nevertheless, it has served to test the reaction times of modern virology laboratories. In this commentary, we highlight how fast the reaction has been at characterizing this sublineage, leading at an unprecedented pace to almost as many papers as the number of viral sequences.

Keywords: SARS-CoV-2; BA.2.87.1; pseudoviruses; neutralization assays; emerging pathogens

At the beginning of 2024, the world was concerned about a salutation lineage of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) harbouring more than 100 novel mutations compared to the parental BA.2. The strain was detected in 8 patients, swabbed from September 20 to November 29, 2023, in Limpopo districts of South Africa. The news was tweeted on Twitter/X on February 1, 2024, and on the same day, the PANGOLIN working group designated the sublineage as BA.2.87.1.

As depicted in Fig. 1, it took just 1 month for 8 virology laboratories around the globe to fully characterize the lineage [1–8]. Findings included infectiousness in respiratory or gastrointestinal cell lines [1,8], fusogenicity [1,8], Spike protein density at the cell surface [1], angiotensin-converting enzyme 2 (ACE2) affinity [8], and *in vitro* sensitivity to anti-Spike monoclonal antibodies [2,8] and convalescent sera or vaccine-elicited sera [3–7]. In regard to the last feature, which is of utmost interest to the general public, the reduction in vaccine-induced immunity was estimated as a 2–3 fold reduction in the 50% neutralizing antibody titer compared to the JN.1 lineage dominant at that time.

Overall, these findings were reassuring about the immune escape and pandemic potential of this sublineage. Notably, this effort resulted in a number of papers identical to the number of detected viral sequences, i.e., 8. Although BA.2.87.1 remained epidemiologically irrelevant (with no sequence found outside that district of that country), this experience worked as a large-scale practice to test the reaction times of modern virology and provided several hints.

First, pseudovirus assays have revolutionized virology, with laboratories around the globe able to run tests without accessing the rare viral isolate. In a world premiere for virology, 7 different renowned virology laboratories from 3 different continents (America, Europe, and

Asia) were able to extensively characterize a viral sequence exclusively found in another continent (Africa) in less than 2 months. Although BA.2.87.1 practices were favoured by former knowledge of the viral backbone, it should be noted that almost 10% of the BA.2.87.1 Spike sequence diverged from the parental line.

Second, preprint servers had a key role in disseminating research results, anticipating all but one [7] of the publications: at the time of writing, 5 of the 6 preprints had been finally e-published and indexed in PubMed [6,9–12]. For all 5 papers, the peer-review process largely consisted of minimal formal corrections without altering the main findings of the respective preprint [1–4,8]. Despite we are now almost out of the pandemic, time-to-publication is still lagging during the pandemic [13], and preprint servers continue to serve as reliable sources of original research, especially when released from high-reputation laboratories. Nevertheless, some caveats still persist, since a relevant amount of preprints never reached publication.

In conclusion, several lessons can be drawn from the BA.2.87.1 story: (1) viral sequence sharing by laboratories on freely accessible online repositories has made possible the precious work of volunteer variant seekers; (2) lineage designation by the PANGOLIN group remains a fundamental task to facilitate communication; (3) in this context, social media can have a positive use; (4) modern virology has the tools to inform epidemiological and therapeutic strategies; (5) although the peer-review process continues to play a central role in the value and validity of scientific publications, the reputation of investigating laboratories can render this process less crucial in an emergency context. The rate-limiting factor in this virtuous chain still remains genomic surveillance in low-to-middle-income countries, which has dramatically dropped and leaves several continents almost devoid of SARS-CoV-2 sequences. The molecular sig-

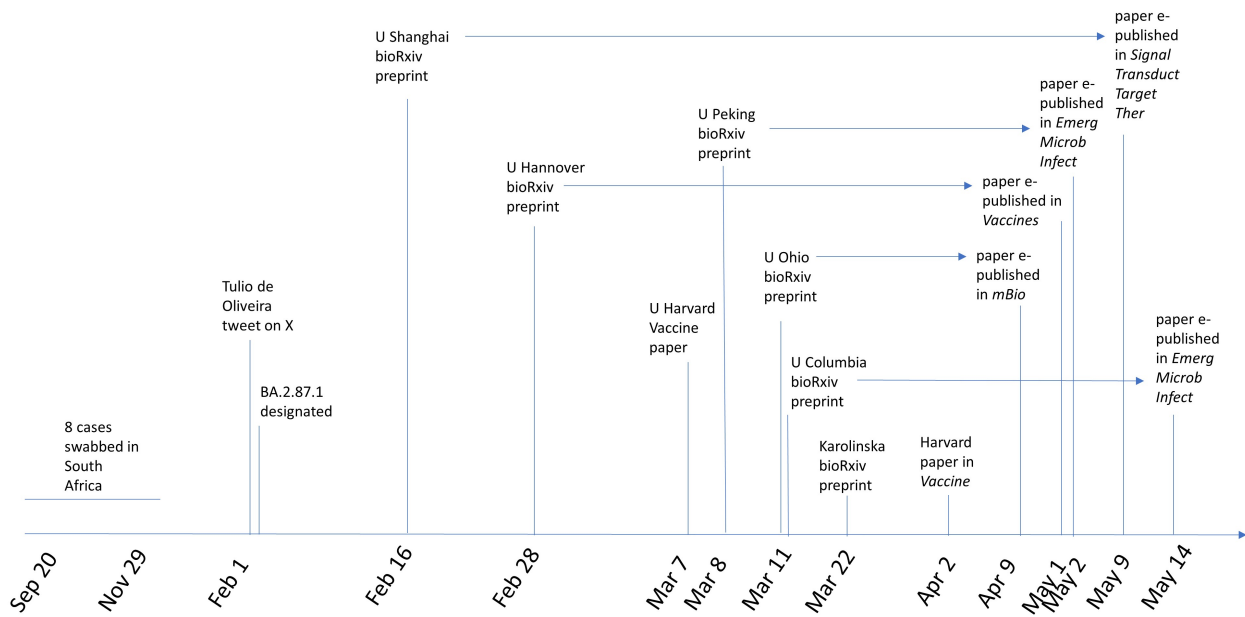


Fig. 1. Timeline of BA.2.87.1 research.

nature of BA.2.87.1 suggests its origin in persistently infected immunocompromised patients, so the next event could happen everywhere and drive clinically significant waves. Paraphrasing the title of the last Roger Waters’ tour, modern virology “is not a drill”.

Availability of Data and Materials

Not applicable.

Author Contributions

DF contributed to the conceptualization, visualization, and data curation. FM contributed to the conceptualization and validation. DF wrote the first draft, and FM revised the manuscript. Both authors have agreed to the publication of the final version of the manuscript, and to be accountable for all aspects of this work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Li P, Liu Y, Faraone JN, Hsu CC, Chamblee M, Zheng YM, *et al.* Distinct patterns of SARS-CoV-2 BA.2.87.1 and JN.1 variants in immune evasion, antigenicity, and cell-cell fusion. *bioRxiv*. 2024. (preprint)
- [2] Yang S, Yu Y, Jian F, Yisimayi A, Song W, Liu J, *et al.* Antigenicity assessment of SARS-CoV-2 saltation variant BA.2.87.1. *Emerging Microbes & Infections*. *bioRxiv*. 2024. (preprint)
- [3] Wang Q, Guo Y, Schwanz LT, Mellis IA, Sun Y, Qu Y, *et al.* SARS-CoV-2 omicron BA.2.87.1 exhibits higher susceptibility to serum neutralization than EG.5.1 and JN.1. *Emerging Microbes & Infections*. *bioRxiv*. 2024. (preprint)
- [4] Wang X, Jiang S, Ma W, Zhang Y, Wang P. Robust neutralization of SARS-CoV-2 variants including JN.1 and BA.2.87.1 by trivalent XBB vaccine-induced antibodies. *bioRxiv*. 2024. (preprint)
- [5] Sheward DJ, Marking U, Bladh O, Held S, Looyens E, Vandenaabee L, *et al.* Neutralisation sensitivity of the SARS-CoV-2 BA.2.87.1 variant. *bioRxiv*. 2024. (preprint)
- [6] Yang S, Yu Y, Jian F, Yisimayi A, Song W, Liu J, *et al.* Antigenicity assessment of SARS-CoV-2 saltation variant BA.2.87.1. *Emerging Microbes & Infections*. 2024; 13: 2343909.
- [7] Lasrado N, Rössler A, Rowe M, Collier ARY, Barouch DH.

Neutralization of SARS-CoV-2 Omicron subvariant BA.2.87.1. *Vaccine*. 2024; 42: 2117–2121.

- [8] Zhang L, Dopfer-Jablonka A, Nehlmeier I, Kempf A, Graichen L, Calderón Hampel N, *et al*. Virological Traits of the SARS-CoV-2 BA.2.87.1 Lineage. *bioRxiv*. 2024. (preprint)
- [9] Wang X, Jiang S, Ma W, Zhang Y, Wang P. Robust neutralization of SARS-CoV-2 variants including JN.1 and BA.2.87.1 by trivalent XBB vaccine-induced antibodies. *Signal Transduction and Targeted Therapy*. 2024; 9: 123.
- [10] Li P, Liu Y, Faraone JN, Hsu CC, Chamblee M, Zheng YM, *et al*. Distinct patterns of SARS-CoV-2 BA.2.87.1 and JN.1 variants in immune evasion, antigenicity, and cell-cell fusion. *mBio*. 2024; 15: e0075124.
- [11] Wang Q, Guo Y, Schwanz LT, Mellis IA, Sun Y, Qu Y, *et al*. SARS-CoV-2 omicron BA.2.87.1 exhibits higher susceptibility to serum neutralization than EG.5.1 and JN.1. *Emerging Microbes & Infections*. 2024; 13: 2359004.
- [12] Zhang L, Dopfer-Jablonka A, Nehlmeier I, Kempf A, Graichen L, Calderón Hampel N, *et al*. Virological Traits of the SARS-CoV-2 BA.2.87.1 Lineage. *Vaccines*. 2024; 12: 487.
- [13] Maggio LA, Costello JA, Brown KR, Artino Jr AR, Durning SJ, Ma T. Time to publication in medical education journals: An analysis of publication timelines during COVID-19 (2019-2022). *medRxiv*. 2024. (preprint)