Brief Report

Emergence of the SARS-CoV-2 BA.3.2 Saltation Variant with a Distinct Mutation-Spectrum Profile Compared with BA.1 and BA.2.86

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Emergence of the SARS-CoV-2 BA.3.2 Saltation Variant with a Distinct Mutation-Spectrum Profile Compared with BA.1 and BA.2.86

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Abstract

Submissions of sequences consistent with SARS-CoV-2 BA.3.2, a newly observed saltation variant, have increased in GISAID since November 2025. Saltation events are often prioritized for monitoring due to extensive divergence. Using 12-category nucleotide substitution spectra and principal component analysis, we show that BA.3.2 has a mutation-spectrum profile distinct from BA.1 and BA.2.86, lacking pronounced transversion enrichment while retaining spike-focused substitution enrichment. Unlike BA.1, BA.3.2 shows no clear enrichment of basic residue-introducing substitutions in spike.

Keywords: SARS-CoV-2; BA.3.2; saltation; genomic surveillance; mutation spectrum

Background

BA.3.2 is a recent SARS-CoV-2 saltation variant with increased sequence submissions to GISAID since late 2025. In multiple countries, many sequences consistent with BA.3.2 or its descendants have been submitted under the BA.3 lineage designation, with a relatively large share of reported submissions coming from Australia. Early reports [1] indicate that BA.3.2 was first detected in late 2024, with a small number of sequences submitted from South Africa; these early detections did not immediately lead to sustained growth in submissions, and BA.3.2 remained infrequently observed for several months. The recent increase of BA.3.2 provides a timely opportunity to test whether saltation events share common nucleotide-level mutation-spectrum features, as BA.3.2 represents a large mutational jump relative to BA.3 and can be systematically compared using mutation-spectrum-based approach.

Highly divergent SARS-CoV-2 lineages with large constellations of substitutions have repeatedly emerged since late 2021. The most prominent examples include Omicron BA.1 [2,3] and BA.2.86 [4,5], both of which appeared with large mutational distances relative to their inferred ancestors. BA.1 caused a rapid global surge of infections, while BA.2.86 was followed by a subsequent surge of the JN.1 lineage after the acquisition of additional spike substitutions, including L455S. Saltation events are often discussed through the lens of a limited number of underlying evolutionary processes (e.g., prolonged replication under selective pressure [6]), yet it remains unclear whether they share a common mutational signature at the nucleotide level.

Lineage-to-Lineage Substitution Spectra

We constructed lineage-to-lineage substitution spectra for BA.3 → BA.3.2, B.1.1 → P.1 (Gamma variant), and B.1 → B.1.617.2 (Delta variant), and compared them with major mutation spectra reported previously [7], including B.1.1 within-lineage spectra, spectra observed in immunocompromised individuals [8–11], and lineage-to-lineage substitution spectra for B.1.1 → BA.1 and BA.2 → BA.2.86.1.

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Because relatively few sequences are currently assigned to BA.3.2, we used sequence data registered under the BA.3 and BA.3.2.2 lineage names. Notably, BA.3 sequences submitted in 2025 and later were all consistent with BA.3.2-related lineages. Since November 2025, submissions of BA.3.2-related sequences in the BA.3 category have increased rapidly, as shown in Figure 1A. BA.3 sequence data (n = 94, after excluding low-coverage genomes) were retrieved on 7 January 2026, and BA.3.2.2 sequence data (n = 71, after excluding low-coverage genomes; some of which were subsequently recategorized into the RE lineage) were retrieved on 9 January 2026. BA.3 sequences were further stratified into those submitted in 2021–22 (n = 76) and 2025–26 (n = 18). The complete list of sequence IDs is provided in the Supplementary Material.

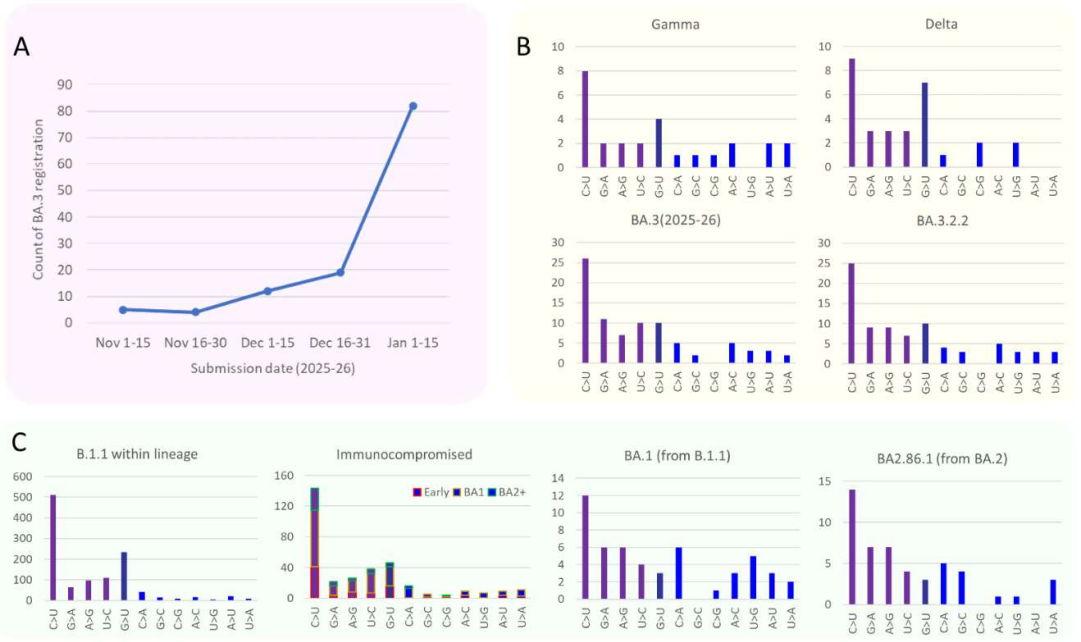

Figure 1. Contextualization of the BA.3.2 saltation event. (A) Temporal trend of SARS-CoV-2 sequences labeled as BA.3 by submission date. All sequences submitted as BA.3 in 2025 or later are consistent with BA.3.2-related genomic features. (B) Lineage-to-lineage nucleotide substitution spectra for B.1.1 → P.1 (Gamma), B.1 → B.1.617.2 (Delta), BA.3 (2021–22) → BA.3 (2025–26), and BA.3 (2021–22) → BA.3.2.2. Substitutions are classified using the standard 12-category framework. (C) Reference spectra from a previous study [7], including B.1.1 within-lineage spectra, spectra observed in immunocompromised individuals in pre-Omicron period (early), BA.1-prevalent period, and BA.2-prevalent period and thereafter [8–11], and lineage-to-lineage substitution spectra for B.1.1 → BA.1 and BA.2 → BA.2.86.1.

Consensus genome-wide nucleotide substitutions and spike amino-acid substitutions were extracted for BA.3 (2021–22), BA.3 (2025–26), and BA.3.2.2. Consensus mutations were defined as those present in ≥50% of sequences. Spike amino-acid substitutions were identical between the BA.3 (2021–22) → BA.3 (2025–26) and BA.3 (2021–22) → BA.3.2.2 comparisons. Additional methodological details are provided in the Supplementary Material.

For B.1, B.1.1, P.1, and B.1.617.2, sequence data were retrieved from GenBank. Consensus sequences and substitution spectra for B.1.1 → P.1 (Gamma) and B.1 → B.1.617.2 (Delta) were generated following the method described by Kakeya and Nitta [7]. Gamma and Delta were included for comparison because they harbor about 30 substitutions relative to their inferred ancestors, representing large mutational steps among early variants of concern, although smaller than those observed for B.1.1 → BA.1 and BA.2 → BA.2.86.1, each of which involves approximately 50 substitutions.

Lineage-to-lineage substitution spectra were generated by counting differences between the consensus mutation lists of the two groups (Figure 1B). The BA.3 (2021–22) → BA.3 (2025–26) and

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BA.3 (2021–22) → BA.3.2.2 comparisons showed 84 and 81 nucleotide substitutions, respectively. Although the spectra for these two comparisons differed slightly, transitions and G→U transversions consistently dominated over non-G→U transversions. This pattern aligns with mutations observed within lineages or within immunocompromised hosts, and with lineage-to-lineage spectra for B.1.1 → P.1 and B.1 → B.1.617.2. In contrast, it significantly deviates from previous saltation events, including B.1.1 → BA.1 and BA.2 → BA.2.86.1, which show pronounced transversion enrichment (Figure 1C).

PCA Visualization

Principal component analysis (PCA) was used to compare similarities among mutation spectra. The newly obtained substitution spectra were plotted together with spectra analyzed in a previous study. To emphasize spectrum shape rather than absolute mutation counts, all spectra were L2-normalized prior to PCA. Saltation spectra were visualized alongside reference spectra [7] representing typical human within-lineage substitutions, reported immunocompromised-host spectra (as context for chronic infection-associated patterns) [8–11], and representative animal spectra [12].

PCA places the BA.3.2 spectrum as distinct from those of BA.1 and BA.2.86.1 and closer to the Gamma and Delta variants, which exhibit a moderately large number of substitutions (Figure 2). In the PCA of L2-normalized spectra, BA.1 and BA.2.86.1 are located in a region separate from typical human within-lineage and immunocompromised-host spectra, whereas BA.3.2 occupies a distinct position closer to, but not overlapping with, the human spectrum region. BA.3.2 is also clearly separated from reference animal spectra, indicating that its mutation spectrum is not simply a recapitulation of these patterns in this low-dimensional embedding. This separation supports heterogeneity among SARS-CoV-2 saltation spectra.

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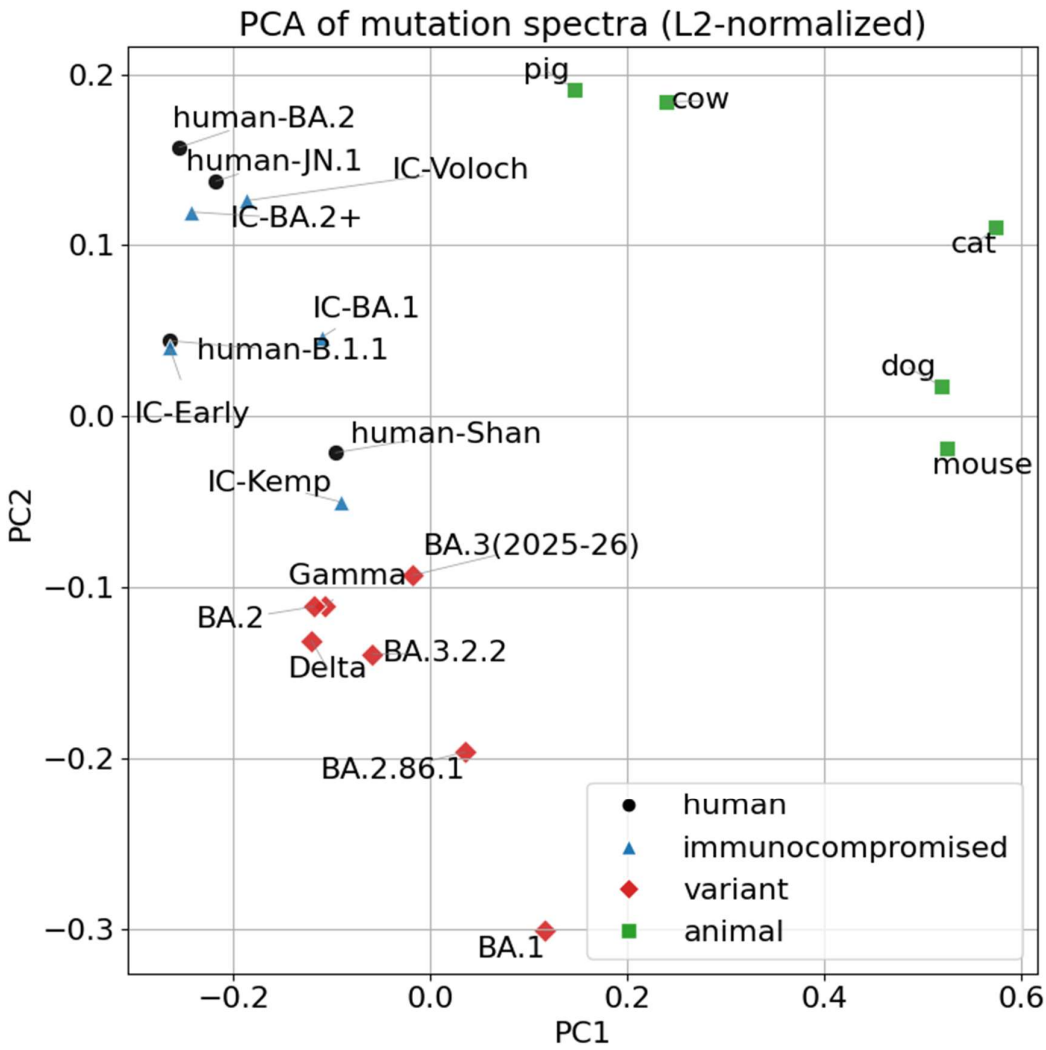

Figure 2. Principal component analysis (PCA) of L2-normalized 12-category nucleotide substitution spectra (PC1 explained variance: 0.576; PC2 explained variance: 0.152). Points represent human lineages, immunocompromised-host spectra, lineage-shift variants, and animal-associated spectra. BA.3 (2025–26) and BA.3.2.2 cluster with transition-dominant, non-saltation lineage shifts such as P.1 and B.1.617.2, and are distinct from BA.1 and BA.2.86.1, which occupy regions characterized by elevated transversion frequencies.

Additional Genomic Distribution Metrics

Where applicable, additional genomic distribution metrics were summarized, including the concentration of substitutions across the genome (spike-focused enrichment) and shifts in amino-acid properties (basic residue-introducing substitutions), using the same definitions as described by Kakeya and Nitta [7].

Consistent with BA.1 and BA.2.86, BA.3.2 shows enrichment of substitutions in spike, indicating convergent selective focus on spike despite differences in nucleotide-level mutation-spectrum signatures. In contrast, the Delta variant, which exhibits mutation-spectrum profiles more similar to BA.3.2, does not show spike-focused substitution enrichment (Figure 3). Together, these results indicate that saltation and non-saltation variants can share similar mutation-spectrum shapes while differing in the genomic distribution of substitutions, highlighting heterogeneity in the mutational and selective processes underlying SARS-CoV-2 variant emergence.

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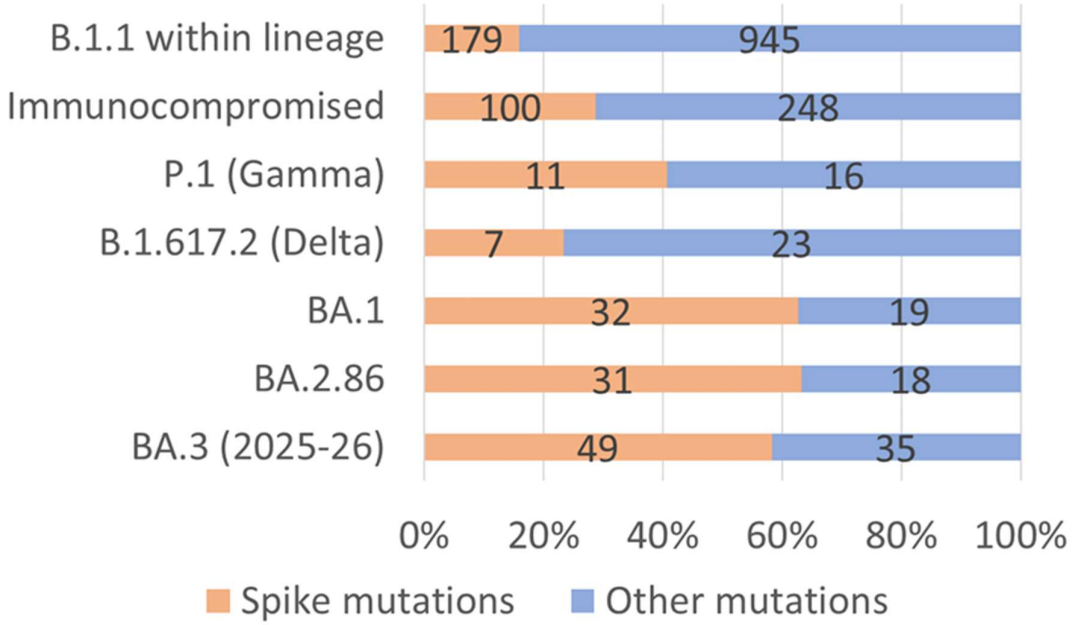

Figure 3. Proportion of spike versus non-spike substitutions for mutations observed in immunocompromised hosts, selected lineages, and lineage shifts. BA.3 (2025–26) shows spike-focused substitution enrichment comparable to BA.1 and BA.2.86, despite differing mutation-spectrum characteristics.

Previous analyses have reported enrichment of basic residue-introducing substitutions in spike for BA.1 [13,14], facilitating attachment and entry in the upper airway epithelium [15]. Unlike BA.1, BA.3.2 shows no clear enrichment of spike substitutions introducing basic residues (H/K/R). For spike amino-acid substitutions, the numbers of changes from non-basic to basic, basic to non-basic, and basic to basic residues were 12/2/0 (out of 27) for B.1.1 → BA.1 and 6/6/4 (out of 39) for BA.3 (2021–22) → BA.3 (2025–26), respectively.

Public Health Implications

Based on the findings reported above, key genomic features of P.1, B.1.617.2, BA.1, BA.2.86, and BA.3.2 are summarized in Table 1. Saltation events are often treated as inherently high-risk genomic signals because they involve large mutational distances and may coincide with antigenic change. Our findings indicate that saltation events are heterogeneous at the level of mutation spectra and genomic substitution patterns.

Table 1. Comparison of mutation-spectrum characteristics, spike substitution patterns, and early detection features across representative SARS-CoV-2 lineage shifts (P.1, B.1.617.2) and saltation variants (BA.1, BA.2.86, BA.3.2). Qualitative categories are based on publicly available sequence data at the time of analysis and are intended for comparative context rather than absolute risk classification.

Feature	P.1	B.1.617.2	BA.1	BA.2.86	BA.3.2
Ancestral lineage	B.1.1	B.1	B.1.1	BA.2	BA.3
Lineage-to-lineage substitution count	27	30	51	49 (BA.2.86.1)	81-84
Emergence period	Late 2020	Late 2020	Late 2021	Mid 2023	Late 2024

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Transversion enrichment	Weak	Weak	Pronounced	Pronounced	Weak
Spike-focused substitution enrichment	Moderate	Low	High	High	High
Basic residue enrichment in spike (vs ancestor)	Limited	Moderate	Marked	Not evident	Not evident
Location of early detection	Brazil	India	Multi-region	Multi-region	South Africa → Australia
Epidemiological impact	Regional expansion	Global expansion	Rapid global expansion	Later global expansion (via JN.1)	Limited to date

Qualitative categories are intended for comparative context.

For genomic surveillance, this supports incorporating mutation-spectrum metrics, alongside mutation counts and long-branch detection, to contextualize newly detected saltation events at an early stage, before phenotypic data are available. Such contextualization may help prioritize follow-up investigations, temper risk assessments based on divergence alone, and flag highly divergent saltation events that also carry mutation signatures linked to rapid spread or immune escape.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

Funding: Not applicable.

Institutional Review Board Statement: Ethical approval was not required for this study as it was performed using only publicly available data.

Data Availability Statement: All data used in this study are publicly available from GISAID and GenBank. The source code used in this study is available at https://github.com/visual-media-lab/BA3 The complete list of GISAID Accession IDs analyzed in this study is also available at the above site and in the Supplementary Material.

Use of Artificial Intelligence Tools: ChatGPT (OpenAI; version 5.2) was used as a coding assistant for general guidance and debugging of python scripts in this project. All generated code was reviewed, tested, and modified for accuracy and relevance by the author, who assumes full responsibility for the final work.

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Conflicts of Interest: None declared.

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