

LETTER TO EDITOR



# Emergence and Characterization of the SARS-CoV-2 JN.1 Variant: Global Prevalence and Implications for Public Health

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## Abstract

The relentless evolution of SARS-CoV-2 variants remains a formidable challenge to global public health, thus prompting significant concern among health authorities due to emergent strains. One such “variant of interest” (VOI) recently identified by the World Health Organization (WHO) is JN.1, a distinct sub-lineage stemming from the BA.2.86 variant. Noteworthy mutations, including R3821K in ORF1a, L455S in the spike protein, and F19L in ORF7b, characterize JN.1\*, the prevalence of which is steadily surging worldwide, signaling a remarkable competitive advantage. While differing from its parent variant, BA.2.86, in terms of infectivity and immune evasion, current evidence does not support heightened pathogenicity associated with JN.1\*; however, the augmented immune evasion capabilities raise concerns about potential waves of infections, particularly among individuals previously exposed to earlier variants. Indeed, existing vaccines may offer limited protection against JN.1\* due to its distinct immunological profile. Consequently, a shift toward non-immunologic protective measures may become imperative to effectively curb transmission. As JN.1\* gains prominence, understanding its unique characteristics and adapting public health strategies accordingly are paramount in mitigating the impact on global health.

**Keywords:** SARS-CoV-2 Variant, Global Prevalence, Variant of Interest (VOI), Immune Evasion, International Cooperation in Pandemic Response

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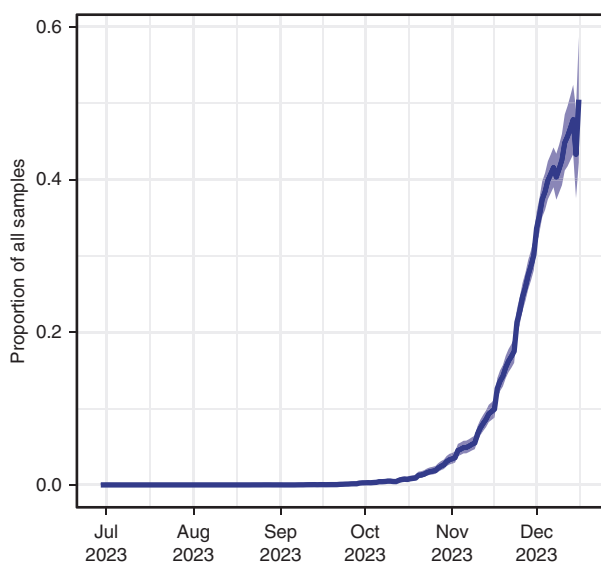
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Since its emergence almost 4 years ago, SARS-CoV-2 has triggered a profound global health crisis. To date there have been 772 million people infected with SARS-CoV-2, and nearly 7 million deaths have occurred according to statistics from World Health Organization (WHO) [1]. The virus has undergone continuous mutations during its transmission, spawning numerous variants that have sparked multiple global infection

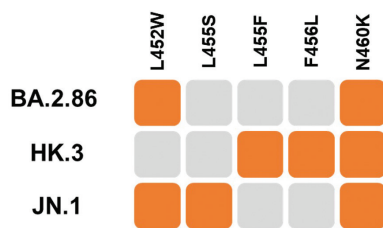
surges. Some of these variants have spread globally, leading to multiple global infection peaks. Notably, the emergence of the JN.1 variant, now designated a “variant of interest” (VOI) by the WHO as of 18 December 2023, has garnered significant attention due to its escalating prevalence and dominance in current infections [2].

JN.1 is also known as BA.2.86.1.1. The parent variant, BA.2.86, emerged in the second half of 2023 and swiftly spread

worldwide [3]. JN.1 is a sub-lineage of BA.2.86 with specific mutations. According to data from the website, cov-spectrum (<https://cov-spectrum.org>) [4], as of 26 December 2023 a total of 16,604 sequences of the JN.1\* variant (JN.1 variant and all descendant variants) have been detected globally, accounting for the highest proportion (47.9%) and showing a continuous upward trend (Fig. 1). This variant bears three distinct mutations, including R3821K in ORF1a, L455S in the S protein, and F19L in ORF7b, setting JN.1\* apart from BA.2.86. Among the three mutations, the L455 site in the S protein is located in the receptor-binding domain (RBD). Notably, in the “flip” variants, like HK.3 and GK.1, this site often manifests as L455F (Fig. 2). Preliminary research indicated that while the ability of JN.1\* to bind to host cells may be slightly weakened compared to the BA.2.86 variant, infectivity is heightened [5]. In addition, the JN.1\* variant has shown certain advantages in immune evasion, demonstrating stronger immune escape capabilities compared to variants, such as BA.2.86 and HK.3 [5,6]. The functional implications of other mutations await experimental



**FIGURE 1** | The weekly proportion of JN.1 variants. The figure was generated by <https://cov-spectrum.org/>.



**FIGURE 2** | Key mutations in spike protein of BA.2.86, HK.3, and JN.1 variants. Orange cube indicated the difference of amino acid in the site between individual variant and reference strain Wuhan-Hu-1 (GenBank accession No. NC\_045512.2). The mutations are marked on the top.

validation. The F19L mutation in ORF7b might impact interferon activation, potentially contributing to the spread of JN.1\* [7,8].

Currently, no evidence suggests that the JN.1\* variant is associated with more severe clinical symptoms or enhanced pathogenicity. However, the robust immune evasion raises concerns about reinfections in individuals previously infected with XBB-related variants, potentially triggering a new wave of infections. Indeed, there has been an upward trend in the number of infections reported. The global infection number by week 50 of 2023 (430.3k) increased 75.5% from the previous week (245.2k) [1], underscoring the urgency of proactive measures.

The currently available vaccines based on XBB-related variants are still expected to have effectiveness for the JN.1\* variant [9]. Considering the immune escape capability, non-immunologic protective measures may become the primary choice for interrupting transmission. This approach includes strengthening personal hygiene habits, such as frequent handwashing, mask-wearing, and maintaining social distancing, as well as enhancing disinfection and ventilation in public places. Additionally, strengthening virus testing and self-isolation measures are also important means to address the spread of the JN.1\* variant, enabling the prompt detection of infected individuals and the implementation of corresponding control measures. The development of variant-specific vaccines or booster strategies targeting the unique features of JN.1 should be explored to bolster immunity against this evolving threat.

Considering the persistent mutations and transmission of SARS-CoV-2, the collaborative efforts of global communities are imperative in data sharing, experiences exchange, and concerted scientific research, which will enable a more comprehensive understanding of emerging variants. This collective approach will also facilitate prompt responses and informed decision-making in deploying effective public health interventions.

#### ACKNOWLEDGEMENTS

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#### CONFLICTS OF INTEREST

The authors declare there are no competing interests.

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