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The Threat of COVID-19 Resurgence and Emergent Recombinant Variants: The Imperative of Securing Vaccine Sovereignty

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Abstract

In 2025, COVID-19 has been rapidly resurging across Asia—particularly in Hong Kong, China, and Thailand—raising growing concern over newly emerging recombinant variants, including XDV.1 and the NB.1.8.1 lineage. Of particular concern is XDV.1, a multi-recombinant variant combining the genetic material of both Omicron and Delta strains, which appears to exhibit heightened transmissibility and notable immune escape capabilities. NB.1.8.1, a sub-lineage of XDV.1, is currently spreading rapidly in several countries, including South Korea. Fortunately, the World Health Organization and Hong Kong health authorities have affirmed that vaccines based on the JN.1 lineage continue to elicit cross-neutralizing responses, a position also endorsed by Korea's Disease Control and Prevention Agency. However, in response to the virus's accelerated evolution, there is an emerging demand for next-generation multivalent vaccines that incorporate shared antigenic features such as those found in FLiRT mutations. Moreover, the capacity to design antigens through mRNA platforms and to establish domestic vaccine production capabilities is becoming a strategic imperative for national pandemic preparedness and bio-sovereignty. Proactive governmental investment in research and development is thus proving to be a critical inflection point in strengthening vaccine sovereignty.

Keywords

COVID-19, variants, resurgence, mRNA vaccine, vaccine sovereignty

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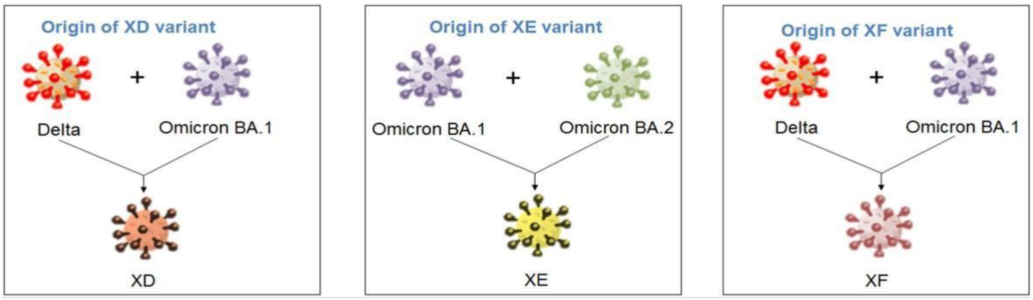
In recent weeks (mid-May), a rapid resurgence of COVID-19 has been observed not only in Greater China—including Hong Kong, Taiwan, and mainland China—but also across Thailand, Singapore, and broader Southeast Asia. This trend has prompted heightened vigilance and cautionary advisories from public health authorities and experts worldwide. The resurgence appears to have been triggered by the congregation of tens of thousands of international tourists during Thailand's Songkran Festival (April 12-16), one of the world's largest water festivals. The situation was further exacerbated by mass population movements during China's Labor Day holiday period (May 1-5), which is now being analyzed as a key factor accelerating the spread. These developments suggest that the current wave is not confined to East or Southeast Asia but may portend a more global resurgence. Indeed, on May 22, the U.S. Centers for Disease Control and Prevention (CDC) reported that variants of the XDV lineage, prevalent in Asia, had been detected among travelers arriving in the United States through airport surveillance programs.

Amid this resurgence, growing attention has turned to the newly emerged variants, particularly following reports of over 30 COVID-19-related deaths in Hong Kong. While Hong Kong health authorities have stated that the XDV variant exhibits high transmissibility but relatively low pathogenicity, concerns remain due to the rapid mutation rate and speed of transmission. South Korea’s public health authorities are also closely monitoring the situation, warning that “although the current domestic outbreak remains under control, the possibility of a summer resurgence cannot be ruled out.” In such a context, while strengthening surveillance and response systems remains vital, it is equally important to move beyond reactive measures. Raising public awareness of the trajectory of emerging variants and their potential implications for health security, as well as establishing more proactive and adaptive policy frameworks, has become an urgent priority.

Emergence of Recombinant Variants

In 2022, global health experts began raising concerns over the possibility of co-infections involving the Delta variant (Delta, known for its high lethality) and the Omicron variant (Omicron, known for its extensive mutations) among immunocompromised populations. Such co-infections subsequently led to the informal designation of "Deltacron," a hybrid strain that served as an early indicator of recombinant SARS-CoV-2 variants. When two or more variants simultaneously infect a single host, their genetic material may intermingle during viral replication, producing a novel genomic composition. This phenomenon is referred to as the emergence of a *recombinant variant*—a genetically distinct strain formed through the recombination of multiple existing lineages within a host organism.



〈Figure 1.〉 Examples of SARS-CoV-2 Viral Recombination[1)]

As illustrated in Figure 1, the XD lineage represents a prototypical case of the so-called “Deltacron” recombinant variant. Its spike protein is derived from the Omicron subvariant BA.1, while its non-spike genomic regions originate from the Delta lineage AY.4. As a result, the XD variant was initially a cause for significant concern, as it appeared to combine Omicron’s high transmissibility and mutational capacity with Delta-derived genes associated with increased disease severity. However, to date, no evidence of widespread transmission has been observed. In contrast, the XE lineage is a recombinant of two Omicron subvariants—BA.1 and BA.2—featuring a spike protein from BA.2 and the remainder of its genome from BA.1. This variant demonstrates a slight increase in transmissibility compared to its parental lineages but retains a pathogenic profile similar to that of the original Omicron strains. The XF lineage, another recombinant of Delta and BA.1, differs from XD in the specific genomic recombination sites and structural composition. As of now, XF has been removed from the World Health Organization (WHO) monitoring list due to its limited public health impact.

Lineage and Characteristics of Recombinant Variants

Among the major variants currently circulating across Asia—including China, Hong Kong, and Thailand—the NB.1.8.1 sublineage of the XDV.1 recombinant lineage has emerged as particularly noteworthy. Unlike simple recombinants between Omicron subvariants, XDV.1 is characterized as a multi-recombinant variant, formed through the convergence of genetic material from multiple SARS-CoV-2 lineages. Specifically, XDV.1 incorporates genomic elements from the XBB lineage—a recombinant of

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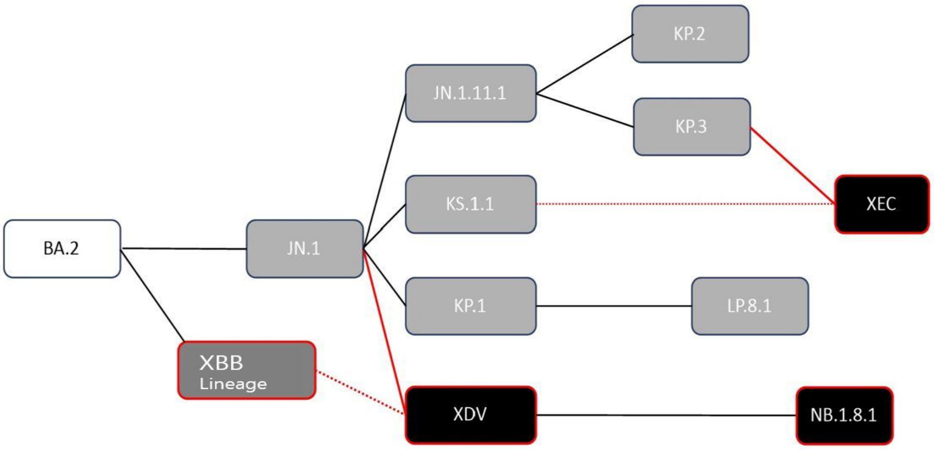
1) Chiranjib Chakraborty et al. “Recombinant SARS-CoV-2 variants XD, XE, and XF: The emergence of recombinant variants requires an urgent call for research - Correspondence,” *International Journal of Surgery,* (June 2022;102:106670). DOI: 10.1016/j.ijsu.2022.106670

Omicron BA.2 subvariants BA.2.10.1 and BA.2.75—as well as the spike protein of the JN.1 lineage (itself derived from BA.2), and even genetic features associated with the Delta variant. Due to this complex genetic architecture, XDV.1 is considered a novel threat in terms of transmissibility, immune evasion, and potential virulence. Notably, the XBB lineage, from which part of XDV.1 descends, exhibited the strongest immune escape capacity among post-Omicron variants and became the globally dominant strain during the latter half of 2023, significantly contributing to renewed waves of infection. The fusion of such immune-evasive properties with the virulence characteristics of the Delta variant in XDV.1 renders it an unusually distinct and potentially high-risk variant.



〈Figure 2.〉 Phylogenetic Tree of Currently Circulating or Dominant Lineages

Moreover, NB.1.8.1—a subvariant that has emerged through additional mutations of XDV.1—remains under scientific scrutiny. To date, comprehensive assessments of its transmissibility and pathogenicity are still lacking, underscoring the need for ongoing monitoring and evaluation.2)

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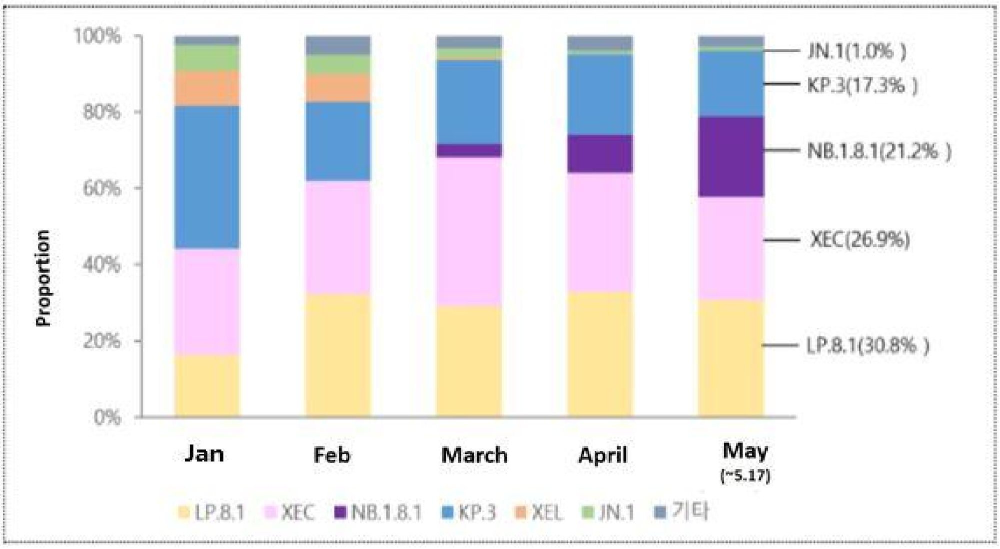
2) Korea Disease Control and Prevention Agency (KDCA), “Increase in COVID-19 Cases in Neighboring Countries; Public Urged to Follow Daily Prevention Guidelines and High-Risk Groups

Potential for Domestic Resurgence of Variants and Current Situation

According to the latest statistics released by the Korea Disease Control and Prevention Agency (KDCA), most sublineages of the JN.1 variant are currently in decline, with the exception of KP.3 and LP.8.1. Notably, since February 2024, the detection rate of the NB.1.8.1 variant has risen above 20% within South Korea, making it the most prominent emerging lineage of interest. As of mid-May 2025, KP.3 and LP.8.1 remain classified as dominant variants; however, recombinant variants that possess both high transmissibility and immune escape capacity—most notably XEC and NB.1.8.1—are rapidly replacing the previously dominant JN.1-related lineages.



〈Figure 3.〉 Proportional Distribution of SARS-CoV-2 Sublineages in South Korea (as of May 17, 2025)[3]

This ongoing shift indicates a critical juncture at which not only the antigenic composition of existing vaccines but also broader public health strategies must be re-evaluated and adjusted.

Encouraged to Get Vaccinated," Press Release, May 23, 2025.

3) Korea Disease Control and Prevention Agency, (2005.05.23.) Ibid.

Fortunately, at present, there appears to be limited need for stand-alone vaccine development targeting XDV or NB.1.8.1. A recent report by the World Health Organization (WHO) confirms that both XDV and NB.1.8.1 elicit cross-neutralizing responses in sera from individuals vaccinated with or previously infected by JN.1. Specifically, NB.1.8.1 has been identified within the same antigenic cluster as LP.8.1 and XEC, all of which are JN.1 sublineages4)

Similarly, the Hong Kong Department of Health has classified XDV as a sublineage of JN.1 and reported that the currently deployed JN.1-based vaccines are eliciting effective immune responses against XDV. As a result, instead of initiating development of a new vaccine, authorities have emphasized the urgent need to boost vaccination coverage, particularly among high-risk populations5)

South Korea's KDCA has also reaffirmed that the JN.1-based vaccines currently in use remain effective in inducing significant immune responses and preventive efficacy against the circulating sublineages such as XEC and LP.8.1. Nevertheless, considering the continual emergence of recombinant variants, the current vaccine antigen design—centered on the JN.1 lineage—may soon face inherent limitations. In particular, given the recurring appearance of immune-evasive mutations, such as those associated with the FLiRT family, in major variants like XDV and NB.1.8.1, urgent consideration should be given to the development and deployment of next-generation multivalent vaccines that incorporate these shared antigenic features.

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4) WHO, "Statement on the Antigen Composition of COVID-19 Vaccines," tag-co-vac-annex_15052025, May 1, 2025

5) The Government of the Hong Kong Special Administrative Region, "DH urges high-risk individuals to receive COVID-19 vaccines as soon as possible as COVID-19 activity hits one-year high in Hong Kong," Press Release, May 15, 2025

The Need to Secure Vaccine Sovereignty to Contain Variant Spread

The interaction between SARS-CoV-2 variants and humanity can be likened to a contest between sword and shield. The virus continues to evolve through ongoing genetic mutations, aiming to enhance its transmissibility, immune evasion capabilities, and pathogenicity. In response, humanity has deployed defensive strategies such as the development of vaccines and therapeutics to curb the spread of disease. Since the emergence of the Omicron variant, the mutation cycle of SARS-CoV-2 has shortened considerably, accompanied by an increasing antigenic distance among variants. This trend underscores the strategic necessity of regularly updating vaccine antigen compositions.

In recognition of this need, public health authorities in advanced economies—including the U.S. Food and Drug Administration (FDA)—are institutionalizing a systematic approach to SARS-CoV-2 vaccine updates, akin to that of seasonal influenza vaccines. These efforts are predicated on adaptable vaccine platforms capable of rapid antigenic shifts, such as mRNA technologies.

Against this backdrop, securing an independent mRNA vaccine platform is no longer optional but essential for South Korea to establish itself as a globally autonomous actor in infectious disease response. For instance, in scenarios where immune-evasive variants like NB.1.8.1 rapidly proliferate within a specific region, the antigenic composition of vaccines developed by global pharmaceutical firms may not align with the dominant strains in that country. To preemptively address such mismatches, it is imperative to possess a domestic platform capable of designing and producing tailored antigens.

Countries such as the United States, Germany, and China, which currently possess mRNA vaccine platforms, are recognized as strategic actors with vaccine sovereignty. These nations occupy central positions in global health diplomacy and pandemic response, and are pursuing a "100-day mission" to develop and manufacture vaccines against emerging pathogens or variants within 100 days of detection.

For South Korea, the urgent task at hand is to establish a robust strategic foundation for vaccine sovereignty. This requires fostering and supporting domestic vaccine enterprises to internalize full-cycle technological capabilities across mRNA/LNP vaccine development—including antigen design, lipid nanoparticle (LNP) synthesis, purification, packaging, and large-scale production. Encouragingly, the Korean government has launched a national R&D program, allocating a total of 502.5 billion KRW (approximately USD 370 million) between 2024 and 2028 to support the development of mRNA vaccines for COVID-19. This initiative marks a critical inflection point at which South Korea may transition from a vaccine-importing country to a strategic nation with self-sufficient antigen design and production capabilities.