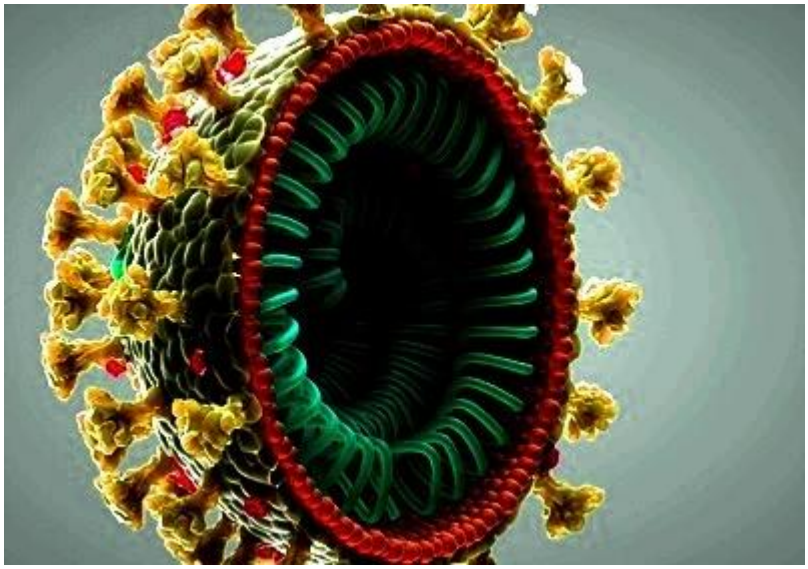
The XEC variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first identified in Germany in August 2024, is a recombinant lineage of KS.1.1 (JN.13.1.1.1) and KP.3.3 (JN.1.11.1.3.3) variants. In this study, researchers from Japan (the Sato Laboratory-Kei Sato) employed several methods to examine the virological characteristics of the SARS-CoV-2 XEC variant.

By the beginning of 2024, the SARS-CoV-2 JN.1 variant (BA.2.86.1.1), which arose from BA.2.86.1, outcompeted the previously dominant XBB lineages. The studies have demonstrated that BA.2.86 variant is phylogenetically distinct from the SARS-CoV-2 Omicron XBB lineages, and is highly immune evasive. Subsequently, the JN.1 diversified, resulting in the emergence of subvariants such as KP.2 (JN.1.11.1.2) and KP.3 (JN.1.11.1.3), which acquired additional spike (S) protein substitutions. From October 2024, JN.1 subvariants including KP.2 and KP.3 were outcompeted by KP.3.1.1 (JN.1.11.1.3.1.1), which is the predominant SARS-CoV-2 variant in the world. Compared to KP.3, XEC variant acquired two S substitutions, S:T22N and S:F59S.



About the Study and Results

The authors used a Bayesian multinomial logistic model to estimate the relative effective reproduction number (Re) of XEC variant based on genome surveillance data from the USA,

the United Kingdom, France, Canada, and Germany, where this variant has spread since August 2024. The results demonstrated that the relative Re of XEC was 1.13-fold higher than that of KP.3.1.1 in the United States. The other countries also showed higher Re values for XEC. Since the effective reproduction number describes the potential for epidemic spread of infectious agents, these results indicate that XEC has the potential to outcompete the other major lineages, including KP.3.1.1. and become the predominant lineage worldwide.

Additionally, the authors performed a Lentivirus-based pseudovirus assay which showed that the infectivity of KP.3.1.1 and XEC variants was significantly higher than that of KP.3. S:T22N did not affect the infectivity of the pseudovirus based on KP.3, but, S:F59S significantly increased it.

Researchers also performed neutralization assays using three types of human sera: sera from fully vaccinated individuals who had been infected with XBB.1.5 (n=13, one 2-dose vaccinated, three 3-dose vaccinated, five 4-dose vaccinated, three 5-dose vaccinated and one 6-dose vaccinated), sera from individuals who had been infected with JN.1 (n=12, one 2-dose vaccinated, two 3-dose vaccinated, two 7-dose vaccinated and seven unknown vaccine history) and sera from fully vaccinated individuals who had been infected with KP.3.3 (n=15, five 3-dose vaccinated, four 4-dose vaccinated, five 5-dose vaccinated and one 6-dose vaccinated). Assays for each serum sample were performed in quadruplicate to determine the 50% neutralization titer (NT50). In all serum groups, both, XEC and KP.3.1.1 variants showed immune resistance compared to KP.3, with statistically significant differences.

In the XBB.1.5 BTI sera and JN.1 infection sera, the NT50 of XEC and KP.3.1.1 were comparable. However, XEC exhibited more robust immune resistance to KP.3.3 BTI sera than KP.3.1.1. The NT50 of XEC was significantly (1.3-fold) lower than that of KP.3.1.1. S:T22N and S:F59S significantly increased the resistance to KP.3.3 BTI sera, by 1.5-fold and 1.6-fold, respectively.

Conclusion

The authors concluded that their investigation showed that the SARS-CoV-2 XEC variant exhibited a higher pseudovirus infectivity and immune evasion compared to KP.3. In particular, XEC exhibited a more robust immune resistance to KP.3.3 BTI sera compared to KP.3.1.1.

According to the authors, these results indicate that XEC will be a predominant SARS-CoV-2 variant in the near future.

This study has been published on a preprint server and is currently being peer-reviewed. bioRxiv preprint. https://doi.org/10.1101/2024.10.16.618773