# Virological characteristics of the SARS-CoV-2 KP.3.1.1 variant

The SARS-CoV-2 JN.1 variant (BA.2.86.1.1), arising from BA.2.86.1 with spike protein (S) substitution S:L455S, outcompeted the previously predominant XBB lineages by the beginning of 2024.[1] Subsequently, JN.1 subvariants including KP.2 (JN.1.11.1.2) and KP.3 (JN.1.11.1.3), which acquired additional S substitutions (eg, S:R346T, S:F456L, and S:Q493E) have emerged concurrently (appendix pp 19–20).[2] Thereafter, JN.1 subvariants, such as LB.1 (JN.1.9.2.1), KP.2.3 (JN.1.11.1.2.3), and KP.3.1.1 (JN.1.11.1.3.1.1), which convergently acquired a deletion of serine at position 31 in S (S:S31del) in addition to the above substitutions, have emerged and have spread as of June 2024 (appendix pp 19–20). We recently reported the virological features of JN.1 subvariants including KP.2, KP.3, LB.1, and KP.2.3.[2,3] Here, we investigated the virological properties of KP.3.1.1.

First, we estimated the relative effective reproduction number ($R_e$) of KP.3.1.1 using a Bayesian multinomial logistic model[4] based on genome surveillance data from Spain, the USA, France, Canada, and the UK, where at least 40 sequences of KP.3.1.1 have been detected as of June 24, 2024 (appendix pp 9–18 [table] and 19–20 [figure]). In Spain, the $R_e$ of KP.3.1.1 is over 1·2-fold higher than that of JN.1 and even higher than those of KP.2, KP.3, LB.1, and KP.2.3 (appendix pp 19–20). Additionally, the other countries under investigation herein show higher $R_e$ for KP.3.1.1. However, it should be noted there is the possibility of overestimation in these countries due to limited KP.3.1.1 sequence numbers. These results suggest that KP.3.1.1 will spread worldwide along with other JN.1 sublineages.[2,3]

We then assessed the virological properties of KP.3.1.1 using pseudoviruses. Similar to LB.1 and KP.2.3,[3] the pseudovirus of KP.3.1.1 had significantly higher infectivity than of KP.3 (appendix pp 9–18), suggesting that S:S31del increases pseudovirus infectivity. Neutralisation of KP.3.1.1 was tested using (1) convalescent serum samples after breakthrough infection with XBB.1.5 or EG.5, (2) convalescent serum samples after the infection with HK.3 or JN.1, and (3) serum samples after monovalent XBB.1.5 vaccination. The 50% neutralisation titre ($NT_{50}$) against KP.3.1.1 was significantly lower than KP.3 (1·4–1·6-fold) in all four groups of convalescent serum samples tested (appendix pp 19–20). KP.3.1.1 also showed a 1·3-fold lower $NT_{50}$ against XBB.1.5 vaccine serum samples than KP.3 (appendix pp 19–20).[1–3,5] Moreover, KP.3.1.1 showed stronger resistance with a 1·3-fold lower $NT_{50}$ with statistical significances to the convalescent serum samples infected with EG.5 and HK.3 compared with KP.2.3 (appendix pp 19–20).

Altogether, KP.3.1.1 had a higher $R_e$, higher pseudovirus infectivity, and higher neutralisation evasion than KP.3. These results align with our recent report that the JN.1 subvariants with S:S31del (eg, KP.2.3 and LB.1) showed increased $R_e$, infectivity, and immune evasion compared with the other JN.1 subvariants without S:S31del (eg, JN.1, KP.2, and KP.3).[3] Our data highlight the evolutionary significance of S:S31del in the JN.1 lineages.

JI received consulting fees and honoraria for lectures from Takeda; consulting fees from Moderna and Takeda; and honoraria for lectures from Moderna and Shionogi. The other authors declare no competing interests. This study was supported in part by AMED ASPIRE Program (JP24jf0126002 to G2P-Japan Consortium and KS); AMED SCARDA Japan Initiative for World-leading Vaccine Research and Development Centers "UTOPIA" (JP243fa627001h0003 to KS); AMED SCARDA Program on R&D of new generation vaccine including new modality application (JP243fa727002 to KS); AMED Research Program on Emerging and Re-emerging Infectious Diseases (JP24fk0108690 to KS); JST PRESTO (JPMJPR22R1 to JI); JSPS KAKENHI Fund for the Promotion of Joint International Research (International Leading Research; JP23K20041 to G2P-Japan Consortium and KS); JSPS KAKENHI Grant-in-Aid for Early-Career Scientists (JP23K14526 to JI); JSPS KAKENHI Grant-in-Aid for Scientific Research A (JP24H00607 to KS); Mitsubishi UFJ Financial Group, Inc. Vaccine Development Grant (to JI and KS); and The Cooperative Research Program (Joint Usage/Research Center program) of Institute for Life and Medical Sciences, Kyoto University (to KS).

*Yu Kaku†, Keiya Uriu†, Kaho Okumura†, The Genotype to Phenotype Japan (G2P-Japan) Consortium, Jumpei Ito, *Kei Sato*
**KeiSato@g.ecc.u-tokyo.ac.jp**

†Contributed equally

Division of Systems Virology, Department of Microbiology and Immunology (YK, KU, KO, JI, KS), International Research Center for Infectious Diseases (JI, KS), International Vaccine Design Center, The Institute of Medical Science, The University of Tokyo, Tokyo 113-0033, Japan (KS); Faculty of Liberal Arts, Sophia University, Tokyo, Japan (KO); Graduate School of Medicine, The University of Tokyo, Tokyo, Japan (KS); Department of Computational Biology and Medical Sciences, Graduate School of Frontier Sciences, The University of Tokyo, Kashiwa, Japan (KS); Collaboration Unit for Infection, Joint Research Center for Human Retrovirus Infection, Kumamoto University, Kumamoto, Japan (KS); MRC-University of Glasgow Centre for Virus Research, Glasgow, Scotland, UK (KS)

1 Kaku Y, Okumura K, Padilla-Blanco M, et al. Virological characteristics of the SARS-CoV-2 JN.1 variant. *Lancet Infect Dis* 2024; **24:** e82.
2 Kaku Y, Uriu K, Kosugi Y, et al. Virological characteristics of the SARS-CoV-2 KP.2 variant. *Lancet Infect Dis* 2024; **24:** e416.
3 Kaku Y, Yo MS, Tolentino JE, et al. Virological characteristics of the SARS-CoV-2 KP.3, LB.1, and KP.2.3 variants. *Lancet Infect Dis* 2024; **24:** e482–83.
4 Yamasoba D, Kimura I, Nasser H, et al. Virological characteristics of the SARS-CoV-2 Omicron BA.2 spike. *Cell* 2022; **185:** 2103–15.e19.
5 Kosugi Y, Kaku Y, Hinay AAJ, et al. Antiviral humoral immunity against SARS-CoV-2 omicron subvariants induced by XBB.1.5 monovalent vaccine in infection-naive and XBB-infected individuals. *Lancet Infect Dis* 2024; **24:** e147–48.

*Lancet Infect Dis* 2024
Published **Online** August 16, 2024 https://doi.org/10.1016/S1473-3099(24)00505-X

See **Online** for appendix