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Short communication

A discernable increase in the severe acute respiratory syndrome coronavirus 2 R.1 lineage carrying an E484K spike protein mutation in Japan

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ABSTRACT

Three COVID-19 waves in Japan have been characterized by the presence of distinct PANGO lineages (B.1.1. 162, B.1.1.284, and B.1.1.214). Recently, in addition to the B.1.1.7 lineage, which shows 25% abundance, an R.1 lineage carrying the E484K mutation in the spike protein was found to show up to 40% predominance. E484K could be a pivotal amino acid substitution with the potential to mediate immune escape; thus, more attention should be paid to such potential variants of concern to avoid the emergence of mutants of concern. Such comprehensive real-time genome surveillance has become essential for the containment of COVID-19 clusters.

1. Introduction

As of March 31, 2021, Japan reported 475,043 cases and 9175 deaths due to coronavirus disease (COVID-19), some of which were caused by variants of concern (VOCs). We conducted genome surveillance for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with support from local public health centers or laboratory institutes (Itokawa et al., 2020; Sekizuka et al., 2020) and five airport quarantine stations (Narita, Haneda, Nagoya, Kansai, and Fukuoka airports; Sekizuka et al., 2021). During the surveillance, we monitored several VOCs of the PANGO lineage, namely B.1.1.7 (501Y.V1), B.1.351 (501Y.V2), and P.1 (501Y·V3; Fujino et al., 2021) which have emerged in the past months in all countries. As of March 31, 2021, a notable increase in imported VOC cases has been identified at the airport (123 cases) and domestic (678 cases) quarantines.

2. Materials and methods

COG-JP has consistently monitored the prevalence of PANGO lineages from the first COVID-19 case (January 15, 2020) to recent cases (March 6, 2021) [≥29 kb genome in size; in total, 28,350 isolates have been deposited in the Global Initiative on Sharing All Influenza Data (GISAID) EpiCoV database (Appendix Table 1)] (Itokawa et al., 2020; Sekizuka et al., 2020). Whole-genome sequences of SARS-CoV-2 isolates from domestic COVID-19-positive patients in Japan (n = 28,965) were assigned according to the PANGO lineage definition (2021/02/21 version; Rambaut et al., 2020). Phylogenetic analysis was performed using the Nextstrain analysis (Hadfield et al., 2018). The study protocol

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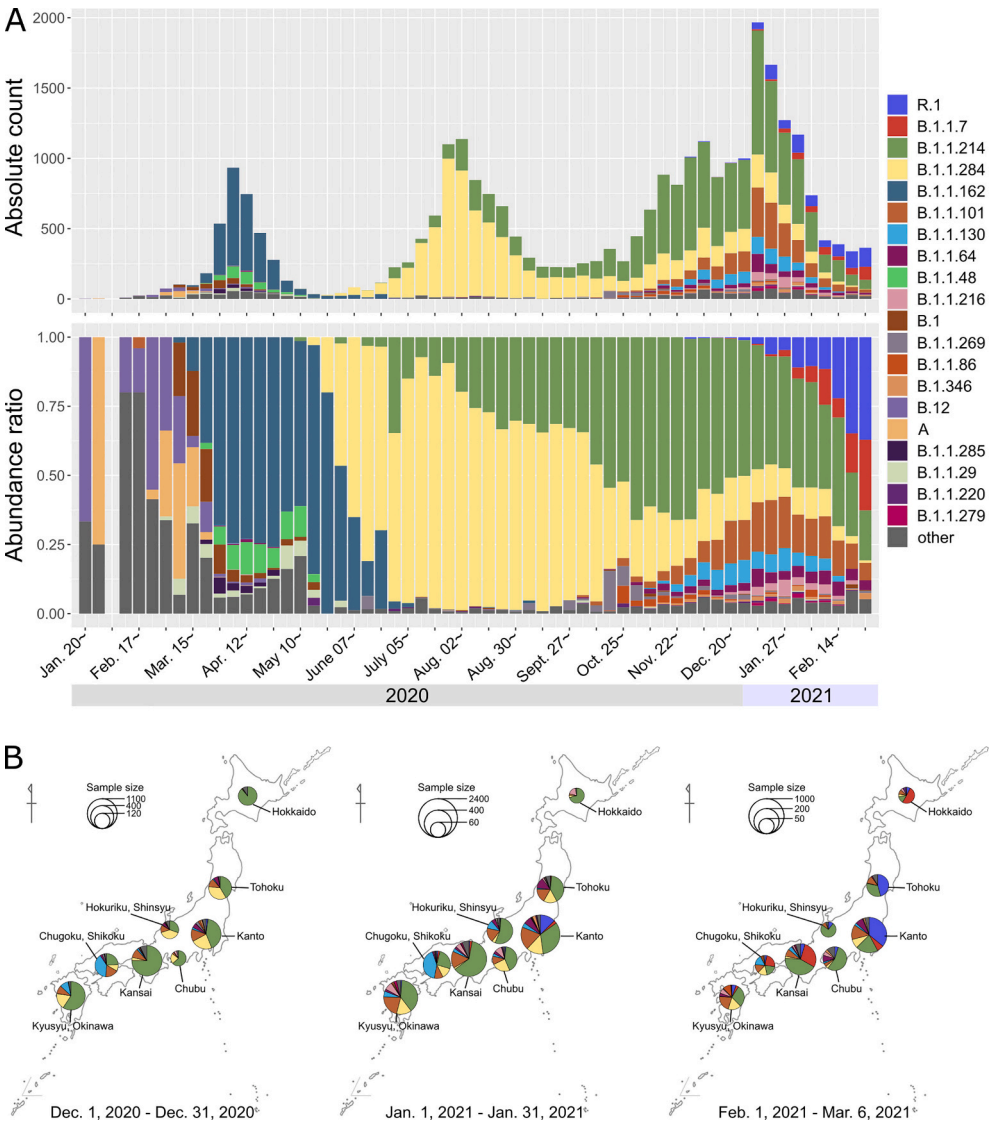

Fig. 1. A spatiotemporal analysis of the SARS-CoV-2 PANGO lineage in Japan.
A) Numbers and B) abundance ratios of whole-genome sequences of SARS-CoV-2 isolates from domestic COVID-19-positive patients in Japan (n = 28,965) were assigned as per the PANGO lineage definition (2021/02/21 version; Rambaut et al., 2020). Top 20 PANGO lineages have been highlighted as per the colors on the right. C) Area-specific lineage percentage is displayed using colored pie charts (shown in panel A and B) from December 2020 to February 2021.

was approved by the National Institute of Infectious Diseases, Japan (approval no. 1091). The ethics committee waived the requirement for written consent for research on viral genome sequences.

3. Results and discussion

We found a notable distribution of the PANGO lineage during each COVID-19 wave. Specifically, B.1.1.162, B.1.1.284, and B.1.1.214 were predominant during the first, second, and third waves, respectively (Fig. 1). After the first wave (March to April 2020), an effort to monitor airport quarantine was initiated; this measure was successful in reducing the number of imported cases (Sekizuka et al., 2021). Domestic lineages (B.1.1.284 and B.1.1.214), which may have been derived phylogenetically from B.1.1.162 during the first wave, were predominant during the second s wave (July to September 2020), however, only the domestic lineages were predominant and not the imported ones. Moreover, B.1.1.214 was the predominant lineage during the peak of the third wave (October 2020 to January 2021; Fig. 1).

Recently, a new R.1 lineage carrying the spike protein mutation E484K has been detected in 5–37.6% of all COVID-19-positive cases within a span of six weeks (mid-January to early March 2021), and there has been a sharp increase in the number of cases (Fig. 1). The spatiotemporal distribution of the PANGO lineage showed that R.1 cases appeared to be predominant in the Kanto and northern Tohoku areas. Therefore, our study highlights the region-specific transmission of COVID-19. Indeed, B.1.1.7 cases have been especially predominant in the Kansai area; however, data from the ongoing surveillance of other VOCs will be required to confirm the extensive transmission of B.1.1.7.

As a notable feature of VOCs, the B.1.1.7 variant is susceptible to neutralizing antibodies elicited by vaccines using the ancestral spike protein (Shen et al., 2021). However, there is a greater concern about other immune evasion mutations, such as the E484K (Glu484 → Lys) mutation in the spike (S) protein found in B.1.351 (501Y·V2) variant that emerged in South Africa, and P.1 (501Y·V3) variant in Brazil (Altmann et al., 2021). Indeed, E484K could be a pivotal amino acid substitution with the potential to mediate immune escape. Thus far, B.1.1.318, B.1.525, R.1, R.2, and P.2 have been reported as variants carrying the E484K single mutation in the receptor-binding domain. R.1 has been mostly identified in the USA (first found on October 24, 2020) and Japan (first found on November 30, 2020). In fact, phylogenetic analysis indicated that both R.1 isolates were highly similar. Thus, the Japanese R.1 isolate might have originated from the R.1 isolate from the USA. Conversely, it is possible that the isolates in both countries were imported from an uncharacterized source in another country, where a potential common ancestor (B.1.1.316) was circulating (Fig. 2).

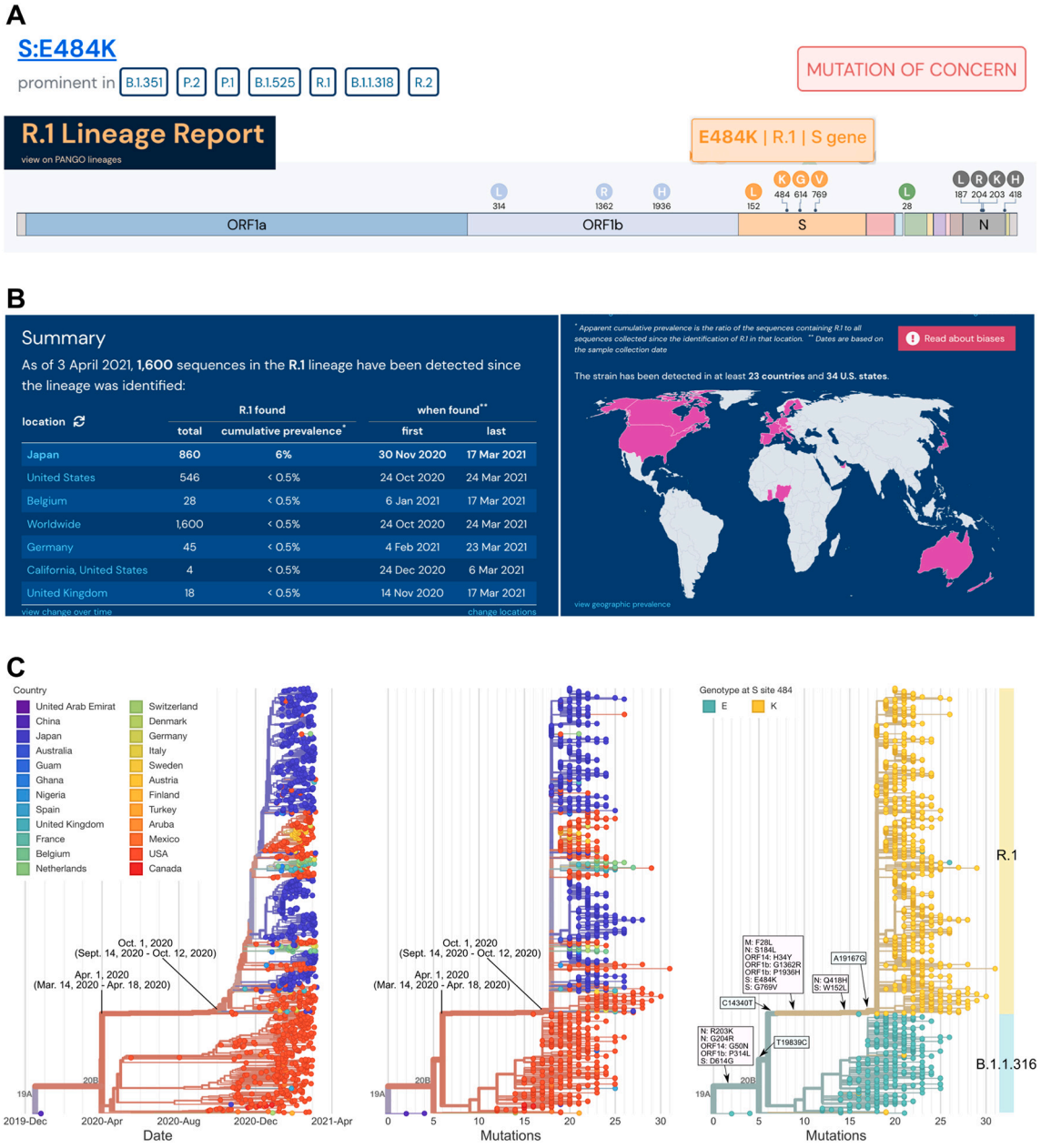

Fig. 2. Summary of SARS-CoV-2 R.1 lineage (April 3rd, 2021).
A) The R.1 lineage has a mutation of concern. The R.1 lineage carries the E484K mutation in the S protein; common genetic features are highlighted above the schematic representation of the SARS-CoV-2 genome structure. B) Current information on the number of cases, country, and first detection date for the R.1 lineage (Julia L. Mullen, 2020). C) Phylogenetic analysis of the R.1 lineage by Nextstrain analysis, along with the B.1.1.316 lineage which is the most recent common ancestor (Hadfield et al., 2018).

4. Conclusion

Although VOCs have a marked impact on the number of cases and severity of COVID-19 across many countries, mutants of concern carrying pivotal mutations should not be disregarded if the latent distribution has been found across the community. We should pay more attention to such potential VOCs to avoid the emergence of mutants of concern. Based on the current epidemiological situation in Japan, with an increase in the circulation of more transmissible lineages, immediate, strong, and decisive public health interventions such as contact tracing, strict quarantine monitoring, and comprehensive real-time genome surveillance have become essential for containment of COVID-19 clusters.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.meegid.2021.105013.

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