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Opinion

An Understanding of the New SARS-Cov-2 Variant-Arcturus, A Subvariant of Omicron

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Opinion

In late March 2023, a new subvariant of SARS-CoV-2 called XBB.1.16 or Arcturus, emerged and was detected in various countries. This subvariant is linked with a 1.27-fold and 1.17-fold increase in adequate Reproductive Number (Re) compared to the XBB.1 and XBB.1.5 subvariants, respectively, indicating its potential for rapid spread. Previously, the XBB.1.5 and XBB.1.9 subvariants of the Omicron variant, which contain the F486P substitution in their Spike Protein (S protein), were circulating widely across the world [1]. Following its detection in multiple countries, including India, on March 30, 2023, the World Health Organization (WHO) began monitoring XBB.1.16 due to its increased transmissibility. According to the GISAID database, XBB.1.16 has been the most prevalent SARS-CoV-2 variant in India since February 2023, which is attributed to the high immune evasion and hACE2 binding of XBB variants caused by an F486S amino acid substitution in the spike glycoprotein [2]. By the end of March 2023, XBB.1.16 had outcompeted other variants in India, leading to the WHO classifying it as a variant under monitoring on March 30, 2023 [1].

At present, the World Health Organization (WHO) is closely monitoring one Variant of Interest (VOI), XBB.1.5, and six Variants Under Monitoring (VUMs). The VUMs include BQ.1, BA.2.75, CH.1.1, XBB, XBF, and XBB.1.16, with XBB.1.16 being added to the list on March 22, 2023. XBB.1.16 is a recombinant of BA.2.10.1 and BA.2.75 and has three additional mutations in the SARS-CoV-2 spike protein (E180V, F486P, and K478R) compared to its parent lineage XBB, with the F486P mutation being shared with XBB.1.5. Mutations at position 478 of the SARS-CoV-2 spike protein have been associated with increased transmissibility, decreased antibody neutralization, and pathogenicity. Till March 27, 712 sequences of XBB.1.16 have been reported from 21 countries. However, current reports do not suggest an increase in hospitalizations, ICU admissions, or deaths due to XBB.1.16. Furthermore, there are no recent laboratory studies on markers of disease severity for XBB.1.16 [3].

A recent report extensively examines the virological characteristics of the SARS-CoV-2 Omicron XBB subvariant, XBB.1.16, through multiscale investigations. The current analysis indicates that the XBB.1.16 subvariant has two S substitutions, E180V and T478R, in the N-Terminal Domain (NTD) and Receptor-Binding Domain (RBD), respectively, compared to its predecessor mutant strains. Moreover, the Dissociation Constant (KD) of the XBB.1.16 RBD for the Angiotensin-Converting Enzyme 2 (ACE2) host receptor was 2.4-fold higher than that of XBB.1.5. However, the KD values of XBB.1.16 were considerably lower than that of XBB.1, indicating the binding affinities of this novel subvariant [1].

According to pseudo virus assays, the infectivity of XBB.1.16 was similar to that of XBB.1, but unlike XBB.1.5, which had higher infectivity than the parental XBB.1 mutant. Notably, the S: T478R and S: E180V substitution mutations significantly impact on the infectivity of this viral variant. While the S: T478R mutation enhances the infectivity of XBB.1.16, the S: E180V substitution markedly decreases its viral infectivity. It is likely that XBB.1.16 acquired both of these S protein mutations simultaneously as part of its evolutionary strategy. This phenomenon has been observed in other Omicron subvariants, such as BA.5 and XBB.1. In fact, XBB.1.16 follows the evolutionary trajectory of previously emerging Omicron subvariants [1].

Neutralization assays demonstrated that XBB.1.16 exhibited high resistance to sera from individuals who were reinfected with Omicron BA.2/BA.5, showing 18- and 37-fold greater resistance compared to Omicron B.1.1/B.1.1. However, this subvariant's sensitivity to convalescent sera from hamsters infected with XBB.1 was comparable to that of XBB.1/XBB.1.5 mutants. All six clinically available monoclonal antibodies for SARS-CoV-2 were highly ineffective against XBB.1.16, except for sotrovimab, which demonstrated weak antiviral activity. Additionally, antigenic cartography revealed that XBB.1.16 had antigenicity similar to that

of XBB.1 but significantly different from XBB.1.5. The extensive exploratory analyses conducted suggest that the SARS-CoV-2 Omicron XBB.1.16 subvariant has a more significant potential to spread and infect people worldwide compared to the XBB.1 and XBB.1.5 subvariants. Additionally, XBB.1.16 has a higher immune-evasion potential similar to that of XBB.1 and XBB.1.5. The authors hypothesize that XBB.1.16 has a higher fitness and growth advantage due to different antigenicity than XBB.1.5, and mutations in non-S SARS-CoV-2 proteins may also have contributed to its higher fitness [1].

For preventive measures, we need to follow all safety methods suggested by WHO and other international agencies. As we suggested earlier, physical activity, intake of micronutrients (minerals and vitamins) through consumption of healthy food (vegetables and fruits), avoid eating meat and meat products will be helpful to prevent the viruses at certain extent [4-8].

Acknowledgement

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Conflict of Interest

None.

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