Pathogenicity of SARS-CoV-2 Omicron BA.1.1 in hamsters

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New variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that have acquired different mutations which modulate viral transmissibility, pathogenicity, and antibody evasion continue to emerge. SARS-CoV-2 Omicron (PANGO lineage B.1.1.529) was first reported in November 2021 in South Africa and was quickly defined as the fifth Variant of Concern (VOC), after Alpha, Beta, Gamma, and Delta.[1] Omicron demonstrates robust transmissibility among the human population and has quickly replaced Delta as the predominant circulating SARS-CoV-2 variant. Continuous surveillance has revealed different sublineages of Omicron, such as BA.1, BA.1.1 (BA.1 with the spike R346K substitution), BA.2, and BA.3. Recent studies demonstrated that BA.1 is highly immunoevasive to antibodies elicited by previous infection and/or vaccines, and most clinically approved anti-SARS-CoV-2 monoclonal antibodies.[2] At the same time, the pathogenicity of BA.1 is substantially attenuated in animal models.[3–5] and clinical studies.[6] The pathogenicity of the other Omicron sublineages, including BA.1.1, BA.2, and BA.3, remain largely unexplored.

In a recent issue of *EBioMedicine*, Mohandas and colleagues investigated the replication and pathogenicity of Omicron BA.1.1 in the Syrian hamster model.[7] They showed that BA.1.1-infected hamsters had less body weight loss than Delta-infected hamsters. The serum samples of BA.1.1-infected hamsters neutralized other VOCs with substantially reduced efficiency, suggesting that the antibody response generated by BA.1.1 infection provided limited protection to other non-Omicron variants. BA.1.1 replicated less efficiently than Delta in the lower respiratory tract of the hamsters but the differences appeared to be less substantial than those between BA.1 and Delta reported in other studies.[3,5] The histopathological changes observed in the lungs of BA.1.1- and Delta-infected hamsters were comparable with similar cumulative histopathological scores. This finding is different from recent studies on BA.1, which demonstrated that BA.1 infection resulted in markedly attenuated lung histopathological changes in comparison to SARS-CoV-2 wildtype, Delta, or other VOCs, in both hamster and mouse models.[3–5]

Overall, the findings from the study indicate that despite less efficient virus replication and less body weight loss, Omicron BA.1.1-induced lung disease is not substantially attenuated in hamsters in comparison to Delta. These findings are interesting since BA.1.1 differs from BA.1 with the R346K substitution of the spike protein. Further investigations are warranted to reveal the mechanism of how this substitution at the spike receptor binding domain (RBD) modulates virus-induced lung disease *in vivo*. The results of the current study suggest that the sublineages of Omicron may differ in their virological characteristics. This is particularly important since BA.2 has now replaced BA.1 and BA.1.1 as the predominant circulating SARS-CoV-2 variant globally. Recent evidence suggests that the BA.2 transmits more efficiently than BA.1,[8] but has a similar capacity of antibody evasion.[9] However, the pathogenicity of BA.2 is currently unclear. Furthermore, recombinant variant of BA.1 and BA.2, known as XE, as well as recombinant variants of BA.1 and Delta, known as XD and XF, have recently emerged.[10] The virological features of these new variants should be further investigated. The information obtained will be important for optimizing the public health control measures of the ongoing COVID-19 pandemic.

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Declaration of interests

The authors declare no conflict of interest.

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