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Omicron subvariant BA.5 efficiently infects lung cells

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Zoonotic transmission of animal sarbecoviruses threatens public health, as evidenced by the SARS epidemic and the COVID-19 pandemic. The attenuated Omicron variant dominates the COVID-19 pandemic since winter 2021 and attenuation is believed to be at least partially due to inefficient infection of lung cells. Here, we investigated whether reduced capacity to spread in the lung has been preserved during evolution of Omicron subvariants. We report that the spike proteins of Omicron subvariants BA.4 and BA.5, which are identical at the amino acid level, show increased cleavage by host cell proteases and augmented capacity to drive cell-cell fusion. Furthermore, BA.4/BA.5 spike facilitated increased entry into Calu-3 lung cells and augmented entry was due to deletion of H69 and V70 but was not associated with altered TMPRSS2 usage. Furthermore, increased Calu-3 cell entry of pseudotypes bearing BA.5 spike translated into augmented Calu-3 cells infection by authentic BA.5 virus. Finally, BA.5 spread in the nasal epithelium of ferrets and in the lungs of mice with much higher efficiency than previously circulating Omicron subvariants. These results indicate that attenuation of the Omicron variant can at least by partially lost during evolution of subvariants.

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Professional Status of the Speaker

Professor

Junior Scientist Status

No, I am not a Junior Scientist.

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