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The bat-borne influenza A virus H9N2 exhibits a set of unexpected pre-pandemic features

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Over the past years, bats have gained increasing attention as hosts for several emerging viruses of zoonotic concern, including Marburg, Ebola, SARS and MERS coronaviruses. Paradoxically, however, bats have long been neglected as a potential reservoir for influenza A viruses (IAVs). In 2017, a novel H9N2 IAV was isolated from fruit bats in Egypt. In the following years, similar viral sequences were also detected in bats in South Africa, suggesting a widespread circulation of bat H9N2 in Africa.
Here, we combined various in vivo and in vitro approaches to evaluate whether bat H9N2 is of zoonotic concern. Intranasal infection of ferrets demonstrated that bat H9N2 replicates efficiently in the upper respiratory tract and is rapidly transmitted to naive contact animals. Moreover, we found that bat H9N2 is able to replicate in human lung cultures to similar titers as human-adapted IAVs and that the human population lacks humoral immunity to bat H9N2. We also tested the ability of bat H9N2 to overcome restriction by human MxA, a crucial innate antiviral factor for zoonotic IAVs. While bat H9N2 was potently suppressed in MxA-overexpressing cells, infection of MxA-transgenic mice resulted in viral lung titers comparable to those of wild-type B6 mice. Western blot analysis revealed suppression of MxA induction in the MxA transgenic mice. Collectively, our data show that bat H9N2 meets key criteria for pre-pandemic IAVs.

Keywords

Bat influenza A viruses, IAV, H9N2, pandemic potential, risk assessment, MxA escape, ferret transmission, lack of humoral immunity

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Graduate Student

Junior Scientist Status

Yes, I am a Junior Scientist.

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