International Forum on Ecology & Evolution of Avian Influenza

A webinar series over the period of 5/2021 - 12/2024

June 8, 2021, Tuesday, 9am - 10am, China
June 7, 2021, Monday, 9pm -10pm, EDT, USA

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http://cvm.cau.edu.cn/art/2017/9/12/art_19969_33.html

Haemagglutinin Mutation and Higher Neuraminidase Activity Enhanced the Adaption of H5N6 Avian Influenza Viruses to Mammalian Hosts

Clade 2.3.4.4 H5Nx virus, including H5N2, H5N6, and H5N8 show unprecedented intercontinental spread. Since 2014, human case of H5N6 avian influenza virus (AIV) infection have been reported in China. However, the critical molecular features that determined H5N6 virus infectivity in mammals remain unclear. Here, receptor binding assays demonstrated that these H5Nx viruses acquired the affinity for human-like SAα2,6Gal receptor and displayed a higher binding affinity for avian-like SAα2,3Gal receptors. Based on reverse genetics and crystallographic data, we confirmed that combined mutations at the receptor binding site (RBS) and deglycosylation site at residue 158 of haemagglutinin (HA) are responsible for the Clade 2.3.4.4 virus recognition of SAα2,6Gal receptor. We found that an amino acid (AA) deletion at HA position 130 functionally improves HA acid stability. Crystal structure of the 130 AA deleted H5 HA protein identified the creation of additional hydrogen bonds with the adjacent monomer at the 130-loop, and generation of positive charges in the vicinity of 129 histidine, which collectively increased HA acid stability. Unlike low-pH unstable H5N2 and H5N8 NA proteins, H5N6 NA also exhibits low-pH stability of sialidase activity. In vitro and in vivo (mice and ferrets) findings corroborated the functional importance of HA and NA stability in promoting infectivity and replication efficiency of H5N6 virus in mammals. Our findings provide a genetic and structural basis of the possible mechanism of how emerging H5N6 virus can cross species barrier to infect humans.

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Organizing Committee Chairs: Xiangming Xiao (University of Oklahoma, USA), and Yuelong Shu (Sun Yat-sen University, China)