Correlation between Resistance to Non-Specific Inhibitor and Mammalian Pathogenicity of an Egg Adapted H9N2 Virus

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Abstract : A/chicken/Korea/01310/2001 (H9N2) (01310) was passaged through embryonated chicken eggs (ECEs) by 20 times (01310-E20), and it has been used for an inactivated oil emulsion vaccine in Korea. After sequential passages, 01310-E20 showed higher pathogenicity in ECEs and acquired multiple mutations including a potential N-glycosylation at position 133 (H3 numbering) in HA and 18aa-deletion in NA stalk. To evaluate the effect of these mutations on the mammalian pathogenicity and resistance to non-specific inhibitors, we generated four PR8-derived recombinant viruses with different combinations of HA and NA from 01310-E2 and 01310-E20 (rH2N2, rH2N20, rH20N2, and rH20N20). According to our results, recombinant viruses containing 01310 E20 HA showed higher growth property in MDCK cells and higher virulence on mice than those containing 01310 E2 HA regardless of NA. The hemagglutination activity of rH20N20 was less inhibited by egg white and mouse lung extract than that of other recombinant viruses. Thus, the increased pathogenicity of 01310-E20 may be related to both higher replication efficiency and resistance to non-specific inhibitors in mice.

Keywords: avian influenza virus, egg adaptation, H9N2, N-glycosylation, stalk deletion of neuraminidase

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