

REASSORTMENT BETWEEN AVIAN AND HUMAN H3 INFLUENZA STRAINS: WHICH SEGMENTS DO THE AVIAN HEMAGGLUTININ FOLLOW?

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Background. Reassortment of influenza A viruses is the underlying mechanism of antigenic shift having led to pandemics in the past. However, the molecular compatibility of the hemagglutinin (HA) gene of avian viruses with the genes of a human acceptor virus has remained unclear. Here, we studied which genes of an avian strain co-segregate with the HA gene after double-infection of mammalian cells with a human strain.

Methods. Via reverse genetics, we generated an elastase-dependent HA cleavage-site mutant from A/Hongkong/1/68 (H3N2) (Hk68) and performed co-infections of A549 cells with the avian strain A/Duck/Ukraine/1/63 (H3N8) (DkUkr63) in absence of elastase but presence of trypsin in order to force selection of reassortants carrying the HA from DkUkr63. From plaque-purified reassortants, their segment composition, plaque morphology, and growth curves were determined.

Results. Genotyping of 21 plaques revealed that 16 were reassortants carrying the avian HA - either alone or in combination with other avian segments. Among these reassortants, the half contained the avian NA segment and formed large plaques like DkUkr63. Remarkably, sometimes the DkUkr63 PB1 and NP segregated together with the DkUkr63 HA whereas PB2 and PA always originated from Hk68.

Conclusions. A/Duck/Ukraine/1/63 and A/HongKong/1/68 easily form DkUkr63-HA-carrying reassortants with different gene constellations. Moreover, usage of an elastase-dependent mutant of a human strain as acceptor model allows to assess both molecular correlates of gene segment compatibility and the ability of an avian strain to donate its HA segment to circulating human strains creating novel reassortants with pandemic potential.



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