ID der Kurzfassung : **145**

Genetic basis for animal influenza A virus escape from domestic mammalian interferon-induced Mx1 restriction factors

Inhalt

Since 2020, highly pathogenic avian H5N1 influenza A viruses (IAV) of clade 2.3.4.4b have expanded their host range to include domestic mammals such as dairy cattle and American mink. The human Mx1 interferon-induced protein is a major host-jump barrier, as Mx1-escape mutations on the viral nucleoprotein (NP) often incur a fitness cost. Swine Mx1 is less potent than human Mx1, facilitating the selection of mutations that promote escape from both. We investigate whether other domestic mammals, like swine, could serve as gateways for the pre-adaptation of avian IAV to humans through the selection of Mx1-escape mutations.

To this end, we use a Eurasian avian-like swine H1N2 virus (EAsw) as a zoonotic IAV model and we develop three complementary approaches: i) minigenome assays; ii) viral growth assays in cells stably expressing Mx1; and iii) a mutagenic screen of surface-exposed NP residues to identify combinations of mutations that can confer resistance to mammalian and human Mx1 proteins. To address biosafety for ii) and iii), we generated single-cycle, hemagglutinin (HA)-defective EAsw viruses that replicate only in transcomplementing MDCK-HA cells. Minigenome assays and growth curves reveal marked species-specific differences in anti-IAV activity.

These approaches should contribute to a better understanding of mammalian-adaptive mutations, which is essential for improving genomic surveillance and preventing the emergence of IAV with zoonotic and pandemic potential.

Keywords

Influenza A virus, Mx1, domestic mammals, viral escape, nucleoprotein, host-jump barriers

Registration ID

INF26-98

Professional status of the speaker

PhD student

Junior scientist status

Yes, I am a junior scientist.

Track Klassifizierung: Virus host cell interaction

Typ des Beitrags: Poster presentation