

The overlooked role of mucus as a species-specific infection barrier

Inhalt

Contemporary swine influenza A viruses (IAV-S) of the Eurasian-avian lineage (EAav) present a pandemic threat by being antigenically largely distinct from the IAV-S that caused the 2009 pandemic (Pdm09). Cross-species transmission only rarely occurs and the role of respiratory mucus as a decoy receptor-loaden species barrier is understudied. IAV infection requires binding to specific sialic acids (Sia) receptors at the epithelial cell surface that likely differ from the decoy receptors present on respiratory mucins. Sia binding to the viral hemagglutinin (HA) needs to be compensated by sialidase activity of the viral neuraminidase (NA) to promote traversal of the mucus and to remain motile on the cell surface.

Penetration of mucus overlaying primary swine and human tracheal cultures was absolutely dependent on NA activity while efficient infection also required NA activity on cell surface receptors. Importantly, large differences exist in decoy effects between swine and human mucus, likely caused by marked differences between their sialoglycomes. Glycoengineered HEK293 cells expressing defined sialylated glycotopes were used to quantify virus binding and NA-mediated release and correlated to infectivity of HEK293 cells and primary cells. Swine and human tracheal mucus was added to dissect species-specific inhibition patterns. We hypothesize that the balance between these parameters is, more than the individual parameters, determining infection efficiency.

Keywords

Swine influenza A virus (swIAV), Mucus glycome, Sialic acid receptors, Hemagglutinin–neuraminidase balance (HA–NA balance), host adaptation, cross-species transmission, Glycoengineering, Zoonotic potential

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