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VIRUS-HOST CELL INTERACTION: HOW INFLUENZA A VIRUSES CROSS THE SPECIES BARRIERS?

Mahmoud M. Naguib[1], Per Eriksson[1], Elinor Jax[2,3], Jonas Nilsson[4,5], Carina Sihlbom[6], Britt-Marie Olsson[6], Josanne Verhagen[7], Michelle Wille[8], Jonas Waldenström[7], Ola Blixt[9], Göran Larson[4,5], Robert Kraus[2,3] Åke Lundkvist[1], Björn Olsen[10], Josef D. Järhult[10]*, Patrik Ellström[10]*

[1]Zoonosis Science Center, Department of Medical Biochemistry and Microbiology, Uppsala University, Uppsala SE-75237, Sweden

[2]Department of Migration and Immuno-Ecology, Max Planck Institute for Ornithology, Radolfzell 78315, Germany

[3]Department of Biology, University of Konstanz, Konstanz 78457, Germany

[4]Department of Laboratory Medicine, University of Gothenburg, SE-405 30, Gothenburg, Sweden

[5]Laboratory of Clinical Chemistry, Sahlgrenska University Hospital, SE-405 30, Gothenburg, Sweden

[6]Proteomics Core Facility, Universoty of Gothenburg, Sahlgrenska Academy, SE-405 30, Gothenburg, Sweden

[7]Centre for Ecology and Evolution in Microbial Model Systems, Linnaeus University, SE-391 82 Kalmar, Sweden

[8]WHO Collaborating Centre for Reference and Research on Influenza, at The Peter Doherty Institute for Infection and Immunity, Melbourne 3000, Victoria, Australia

[9]Department of Chemistry, Chemical Biology, University of Copenhagen, 1871 Frederiksberg C, Denmark

[10]Zoonosis Science Center, Department of Medical Sciences, Uppsala University, Uppsala SE-75185, Sweden

*JJ and PE contributed equally to this publication

Influenza A virus (IAV) pandemics of the last 100 years have been associated with host switch events. Viruses causing these pandemics were partially or entirely originating from viruses of avian sources, which gained the ability for efficient human-to-human transmission. Transmission of influenza A viruses (IAV) from wild waterfowl (natural reservoir) to poultry is a key step in a chain of events that ultimately can lead to exposure and infection of domestic animals and humans. Key features for the outcome of IAV interspecies transmission are the molecular interactions between virus and host, including viral evolution in the face of host immunity, the interplay between virus surface antigens and host receptors, and host immune response to infection. Revealing these factors is essential to understand the interspecies transmission of influenza A viruses. To asses these questions a virus panel comprising eight different subtypes of mallard-derived AIV isolates were experimentally inoculated in chickens and tufted ducks. The outcome of virus challenge was highly dependent on virus subtype, and all mallard-derived IAVs could not produce infection in tufted ducks and/or chickens, whereas systemic spread was detected for other subtypes. Sialic acid containing glycans are host receptors for IAV and glycoproteomic analysis revealed that birds can indeed produce many of the structures that are also found in humans, e.g. longer sialyl Lewis structures and both N and O-linked Neu5Ac±2,6 terminating glycans. This suggests that receptor incompatibility as barrier for transmission between birds and humans is more complex than previously thought. The current study highlights the role of host species (donor vs. recipient), route of inoculation, virus subtype and phylogeny, and cell surface receptor structures as determinants for interspecies transmission.