Nuclear Transport as an Interspecies Barrier of Avian Influenza Viruses

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Migratory waterfowls are the natural reservoir of influenza A viruses. Numerous and highly diverse avian influenza viruses are harbored in those avian species. Avian influenza viruses are occasionally transmitted to mammalian species including humans. Successful transmission of an avian influenza virus to human population can cause a global outbreak known as influenza pandemic, which may kill millions of people. Most avian influenza viruses do not infect humans or mammals efficiently. Differences in viral-host interactions in avian and mammalian species form interspecies barrier that prevent effective transmission across species. The most well known component of the barrier is the difference in the selective usage of sialic acid types as receptor between avian and seasonal influenza viruses. Trapping of viruses by respiratory mucus with corresponding sialic acid is also believed to play some role. However, our recent data on sialic acid content in human saliva suggested otherwise. Other interspecies barriers have been proposed. Influenza viruses replicate their genome and produce mRNA in the nucleus. They therefore need mechanisms for the transportation of viral proteins and ribonucleoprotein complex across nuclear membrane in both directions. These mechanisms require interaction between viral proteins and specific host factors and machinery for the nuclear transporation. These host factors may differ among different cell types and species. It was proposed that the requirement for compatibility between viral and host factors for nuclear importation constitutes an additional layer of interspecies barrier. In addition, our recent data suggest that the nuclear export may also play a role in the interspecies barrier. A human cell-specific nuclear export defect was observed in an avian influenza virus. This suggests that some avian influenza viruses may need to adapt their nuclear transport machinery to match that of the new host species in order to cross the interspecies barrier.