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Prerequisites for the Acquisition of Mammalian Pathogenicity by Influenza A Virus with a Prototypic Avian PB2 Gene

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Abstract : The polymerase of avian influenza A virus (AIV) is a heterotrimer composed of PB2, PB1 and PA. PB2 plays a role in overcoming the host barrier; however, the genetic prerequisites for avian PB2 to acquire mammalian pathogenic mutations have not been well elucidated. Here, we demonstrated that key amino acid mutations (I66M, I109V and I133V, collectively referred to as MVV) of prototypic avian PB2 increase the replication efficiency of recombinant PR8 virus carrying the mutated PB2 in both avian and mammalian hosts. The MVV mutations caused no weight loss in mice, but they did allow replication in infected lungs, and the viruses acquired fatal mammalian pathogenic mutations such as Q591R/K, E627K, or D701N in the infected lungs. The MVV mutations are located at the interfaces of the trimer and are predicted to increase the strength of this structure. Thus, gaining MVV mutations might be the first step for AIV to acquire mammalian pathogenicity. These results provide new insights into the evolution of AIV in birds and mammals.

Keywords : avian influenza A virus, prototypic PB2, polymerase activity, mammalian pathogenicity, first-step mutations
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