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**Ecological and Genetic Landscapes of Global H12 Avian Influenza Viruses and Biological Characteristics of an H12N5 Virus Isolated from Wild Ducks in Eastern China**

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**Abstract:**

**Background/Objective:** Wild migratory birds are considered the central reservoirs of avian influenza viruses. H12 viruses are one of the 16 hemagglutinin (HA) subtypes of avian influenza viruses and are rarely reported because they are infrequently detected in birds. Consequently, the ecological and genetic profiles of H12 viruses and their adaptation in domestic birds and mammals remain unclear.

**Methods:** In this study, data statistical analysis, isolation and identification of viruses, genetic evolution analysis, and host adaptability study were used.

**Results:**Here, we found that H12N5 viruses were predominant in the nine identified H12NX subtypes, with the HA (H12) and neuraminidase (NA) (N5) genes showing combination bias in the categorized analysis of subtype combinations (H12 and N1–N9; H1–H12, H14, H15, and N5). These identified H12N5 viruses were primarily detected in birds of Anatidae and Scolopacidae in North America, excluding their possible characterization as chicken or mammalian viruses. The H12N5 viruses were divided into the North American lineage and Eurasian lineage according to their genetic differences, including the HA and NA surface genes and internal genes, although reassortment was observed between the two lineages. We isolated an Eurasian-lineage H12N5 virus from wild ducks in Eastern China, which was one of the 12 identified H12 viruses in China. Infectivity studies indicated that the H12N5 virus is poorly adapted to domestic ducks and chickens, although viral shedding could be detected in both inoculated and contact birds. Additionally, the naturally isolated H12N5 virus did not achieve good replication in mice.

**Conclusion:** These results indicate that the rare subtype of H12 viruses was mainly pooled in wild migratory birds and has an established phylogeography, with low risks of spillover into domestic birds and mammals.

**Keywords:** avian influenza viruses, H12N5, wild birds, ducks, chickens