Rapid Reassortment of Internal Genes in Avian Influenza A(H7N9) Virus

To the Editor—H7N9 is a novel avian virus recently first reported from Shanghai in China. Very recently an isolate from Taiwan was also reported [1]. H7N9 is able to infect humans and has caused many fatal cases [2, 3]. Determining the origin and evolution of these disease-causing viruses is important for surveillance and prevention of the influenza epidemics. With more and more reported pathogenic H7N9 isolates reported, it is important to reexamine whether these disease-causing H7N9 isolates all came from the same common ancestor and whether they have undergone further reassortments.

Previous studies indicated that the 6 H7N9 internal genes were from a single avian H9N2 strain [3] or from a reassortment of 2 separate H9N2 strains: the NS gene was from an H9N2 strain in the Jiangsu area, whereas the other 5 genes, M, NP, PA, PB1, and PB2, were from the other H9N2 strain in the Zhejiang area [4]. Our results are consistent with the previous results regarding the origins of HA, NA, and NS; however, we found that the remaining 5 internal genes (M, NP, PA, PB1, and PB2) appeared to come from multiple sources as they were grouped into 2 or 3 clusters in the phylogenetic trees (Figure 1). However, for M, PA, PB1, and PB2, each has a cluster together with the A/brambling/Beijing/16/2012, suggesting that they may have originated from the brambling, and each of them has another cluster due to rapid assortments. Based on these different clusters, the current H7N9 isolates can be grouped into 9 lineages or genotypes (Figure 1*I*).

The phylogenetic tree of the H7N9 M gene has 2 separate clusters, with Shanghai/Patient4, Hangzhou/3, Shanghai/Patient2, Shanghai/Patient5, and Taiwan/1 in one cluster closing the A/brambling/Beijing/16/2012, and the remaining H7N9 strains forming the other cluster (Figure 1*D*). This observation indicates that the M genes in these 2 clusters may have originated from 2 different H9N2 strains.

We also calculated the nucleotide substitution rate for each gene of H7N9. The nucleotide substitution rates for the 3 single-origin genes HA, NA, and NS (approximately 0.0068) are lower than the

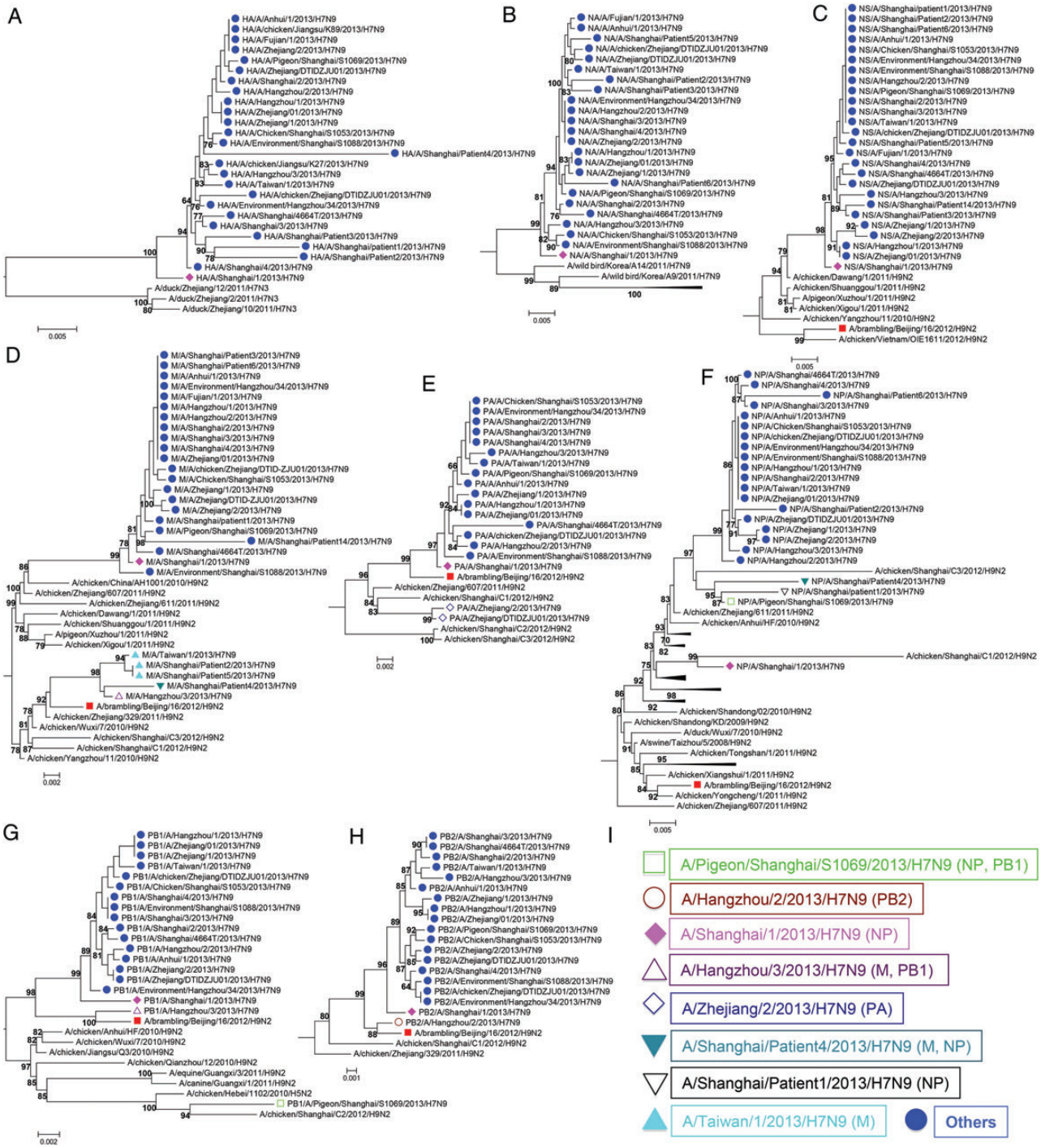

Figure 1. The maximum likelihood phylogenetic trees of the genes HA (*A*), NA (*B*), NS (*C*), M (*D*), PA (*E*), NP (*F*), PB1 (*G*), and PB2 (*H*) with approximately-maximum-likelihood method. *I*, The 26 H7N9 isolates can be divided into 9 genotypes. On each tree, different genotypes of H7N9 strains are represented with different symbol shapes. The H9N2 strain A/brambling/Beijing/16/2012 is also denoted with the filled rectangle for distinction from other H9N2 strains.

remaining internal genes (approximately 0.0124) except for PB2. For PB2, although 2 clusters were observed in the tree, they were genetically close and accordingly the substitution rate was also lower. The higher substitution rates for PB1, NP, M, and PA1 may be caused by multiple causes. For example, after removing the lineage A/Pigeon/Shanghai

from the PB1 dataset, which forms a separate cluster on the tree, the rate of the remaining PB1 sequences is 0.00843, much lower than the original one, 0.01723.

Overall, these results suggest that the current pathogenic H7N9 viruses may have originated through multiple reassortments with different lineages of H9N2 viruses. Reassortments enable the viruses to change their genetic architectures very quickly, which may in turn increase their capacity to infect humans. Thus, it is essential to watch the ongoing infection closely and perform timely analysis of available data, which will help reveal the accurate picture of virus genetic diversity, and to take effective measures to prevent potential infection outbreaks.

Notes

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