



Novel Influenza A (H6N1) Virus That Infected a Person in Taiwan

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Dear Editor-in-Chief

Influenza A (H6N1) virus infection of domestic poultry and wild birds occurs worldwide (1-3), but there has been no report of a human A (H6N1) infection case before 2013. In May 2013, a 20-year-old female suffering from influenza-like symptoms and shortness of breath was admitted to a hospital in Taiwan, China. She was confirmed as being infected with a novel avian-originated influenza A (H6N1) virus by Taiwan Centers for Disease Control (4). The patient was fully recovered after receiving oseltamivir.

In order to monitor further the novel human H6N1 isolate (designated as A/Taiwan/2/2013) and to assess the variability among related strains, we conducted phylogenetic and molecular evolutionary analyses using reported sequence information of influenza A (H6N1) viruses isolated from multiple species. The genome sequences of A/Taiwan/2/2013 and other avian H6N1 strains were obtained from the Global Initiative on Sharing Avian Influenza Data (GISAID) database. A phylogenetic tree based on hemagglutinin (HA) gene sequences was generated using the neighbor-joining method with the MEGA software (version 5.05). Phylogenetic analysis showed that the H6N1 strains were clustered into four distinct branches (Fig. 1). The novel human influenza A/Taiwan/2/2013 was genetically similar to viruses isolated from chickens in Taiwan, but different from H6N1 isolates circulating in poultry in

the rest regions of Asia, Europe, and North America. Moreover, recent studies also demonstrated that all eight genes of the A/Taiwan/2/2013 isolate belonged to the Taiwan lineage (4-5). Molecular characterization of the novel human influenza A/Taiwan/2/2013 showed that it lacked multiple basic amino acids at the HA cleavage site, and had the avian-signature Q226 (H3 numbering is used throughout) in the HA receptor binding site, and E627 in PB2 (Table 1). These results concisely classify this H6N1 isolate as a putatively low-pathogenic avian-originated influenza virus. However, the human influenza A (H6N1) virus has one P186L substitution as compared with all the avian H6N1 strains, and E190V and G228S two substitutions as compared with all the H6N1 strains found outside of Taiwan in the HA receptor binding site (Table 1). These residue substitutions could increase the hydrophobicity of the receptor-binding site, indicating that the virus might have high affinity binding to human α 2-6 linked sialic acid receptor (6).

For the neuraminidase (NA) protein, the A/Taiwan/2/2013 isolate and almost all H6N1 viruses isolated from chickens in Taiwan since 2001 have three deletions (position 41-48, 50-53, and 68-69) in the NA stalk region. Reportedly, viruses with these deletions have a growth advantage over those with no deletion (1).

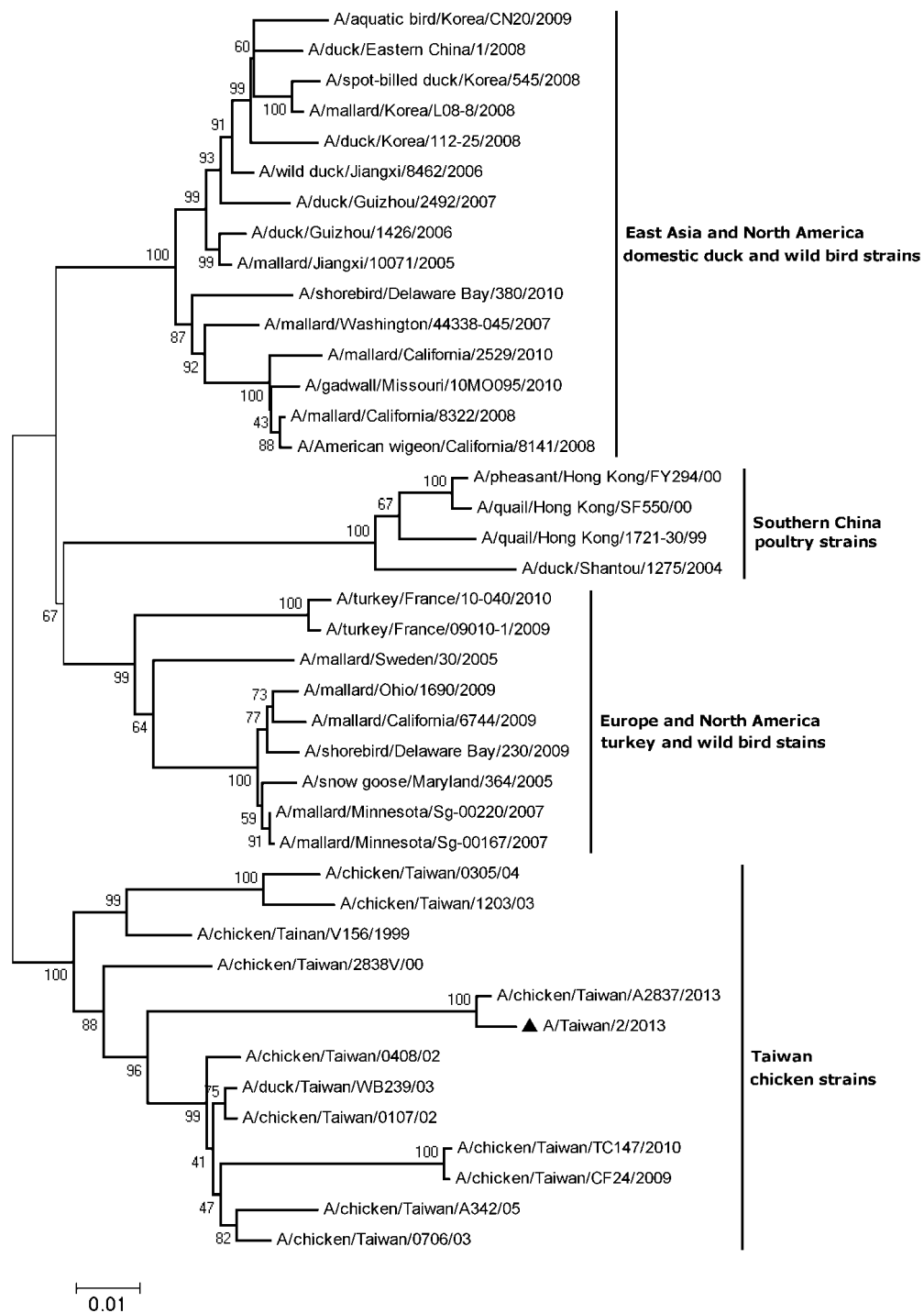


Fig. 1: Phylogenetic tree of influenza (A) H6N1 viruses based on the HA gene sequences, the novel human virus was marked with triangle

Table 1: Comparison of residue substitutions at different positions between novel human influenza A/Taiwan/2/2013 and other published avian H6N1 strains from different regions

Viruses	Receptor binding sites				Cleavage site of HA	NA deletion	PB2 627
	186	190	226	228			
A/Taiwan/2/2013	L	V	Q	S	PQIATR↓G	41-48, 50-53, 68-69	E
A/chicken/Taiwan/A2837/2013	P	V	Q	S	PQIATR↓G	41-48, 50-53, 68-69	E
A/chicken/Taiwan/0706/03	P	V	Q	S	PQIETR↓G	41-48, 50-53, 68-69	E
A/duck/Eastern China/1/2008	P	E	Q	G	PQIETR↓G	No deletion	E
A/aquatic bird/Korea/CN20/2009	P	E	Q	G	PQIETR↓G	No deletion	E
A/mallard/Washington/44338-045/2007	P	E	Q	G	PQIETR↓G	No deletion	E
A/turkey/France/10-040/2010	P	E	Q	G	PQIETR↓G	No deletion	E
A/quail/Hong Kong/1721-30/99	P	E	Q	G	PQIETR↓G	54-72	E

Altogether, the present study demonstrated that the influenza A (H6N1) viruses in Taiwan have established a stable sublineage, and accumulated critical site mutations increasing the risk of avian-to-human transmission. This study also highlights the need for systematic surveillance of influenza A virus in both animal and human populations in organizing for a possible pandemic potential.

Acknowledgment

The authors declare that there is no conflict of interests.

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