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創新、服務、生命守護

本所禽病診斷實驗室與美國康乃狄克大學合作之禽流感研究獲刊登於「Infection, Genetics and Evolution」科學期刊。

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本篇研究報告分析臺灣2015-2018年發生的高病原性禽流感H5Nx亞型病毒，將病毒的親緣關係、傳播途徑、重組及演化速度作完整之探討，希望可以讓大家更瞭解這一群病毒。

目前又快到了候鳥過境臺灣的高峰期，希望大家都能做好防疫準備並加強落實生物安全，不要再讓臺灣禽場發生可怕的疫情囉！

論文網址連結：

<https://www.sciencedirect.com/science/article/abs/pii/S1567134821001829>

謹以此項成果獻給所有克盡職責之動物防疫人員。

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## Infection, Genetics and Evolution

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Research paper

### Evolutionary history of H5 highly pathogenic avian influenza viruses (clade 2.3.4.4c) circulating in Taiwan during 2015–2018

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#### ABSTRACT

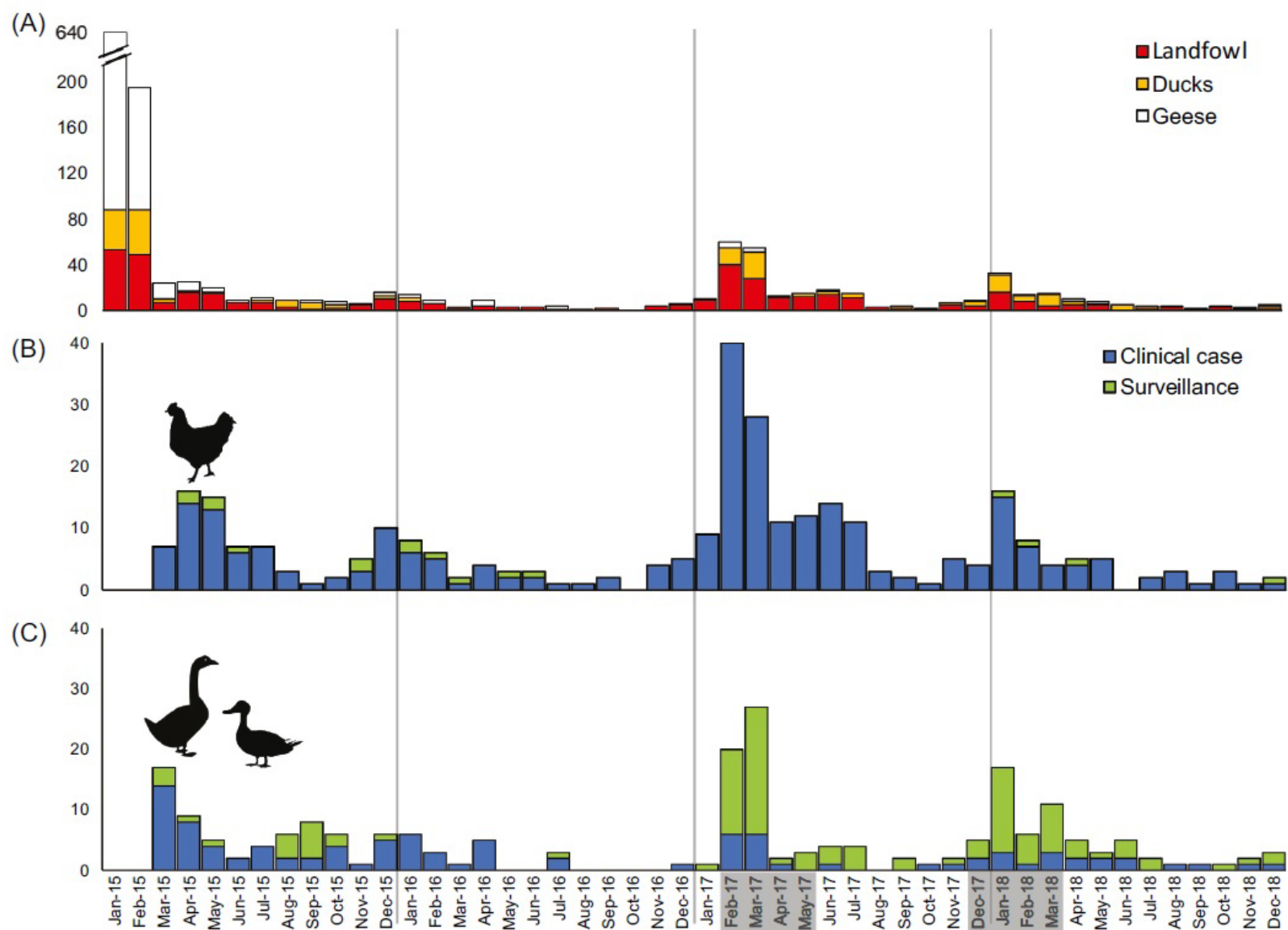
The highly pathogenic avian influenza (HPAI) virus A/goose/Guangdong/1/96 H5N1 (Gs/GD) lineage has been transmitted globally and has caused deaths in wild birds, poultry, and humans. Clade 2.3.4.4c, one of the sub-clades of the Gs/GD lineage, spread through Taiwan in late 2014 and become an endemic virus. We analyzed 239 newly sequenced HPAI clade H5Nx isolates to explore the phylogenetic relationships, divergence times, and evolutionary history of Taiwan HPAI H5Nx viruses from 2015 to 2018. Overall, 15 reassortant genotypes were identified among H5N2, H5N3, and H5N8 viruses. Maximum likelihood and Bayesian phylogenies based on homologous hemagglutinin (HA) and matrix protein (MP) genes suggest that Taiwan HPAI H5Nx viruses share a most recent common ancestor that has diversified since October 2014 and is closely related to two HPAI H5N8 viruses identified from wild birds in Japan. Two waves of HPAI caused by multiple reassortants were identified, the first occurring in late 2014 and the second beginning in late 2016. The first wave consisted of seven H5Nx reassortants that spread through Taiwan. In the second wave, eight novel reassortants were detected which had newly introduced internal genes, mostly derived from the avian influenza virus gene pool maintained in wild birds in Asia. Phylodynamic reconstruction using the Bayesian Skygrid model revealed varied fluctuating patterns of relative genetic diversity among reassortants. The mean evolutionary rate also varied among reassortants and subtypes. The neuraminidase (NA) gene evolved faster than the HA gene in H5N2 viruses, while HA evolved faster than NA in H5N8 viruses. The HA mean evolutionary rate ranged from  $6.10 \times 10^{-3}$  to  $7.73 \times 10^{-3}$  and from  $5.81 \times 10^{-3}$  to  $9.45 \times 10^{-3}$  substitutions/site/year for H5N2 and H5N8 viruses, respectively. The continuous circulation of HPAI H5Nx variants and the emergence of novel reassortants in Taiwan highlight that the surveillance, biosecurity, and management systems of poultry farms need to be improved and carefully executed.

資料來源：Infection, Genetics and Evolution

<https://www.sciencedirect.com/science/article/abs/pii/S1567134821001829>

高病原性家禽流行性感冒 (HPAI) 是全世界非常重視的家禽疾病，甚至有些分支的病毒會造成人類的感染及死亡。很不幸的是，臺灣禽場也在2015年時發生嚴重的HPAI疫情，所分離到的病毒與日本病毒具有高度的親緣關係，均屬於2.3.4.4c分支。在這一研究報告中，我們將2015-2018年在台灣所分離到的239株病毒利用次世代定序儀讀取病毒全長核酸序列，一共發現了15種不同的重組基因型，而這些重組主要是發生在2014年以及2016年兩個時間點，重組的基因主要是來自於亞洲野鳥禽流感病毒基因庫 (gene pool)。

病毒HA基因的演化速率約為千分之5.81~9.45 substitutions/site/year。我們需要做好禽場的監測、生物安全及管理，以避免病毒持續演化及重組而造成更大的危害。

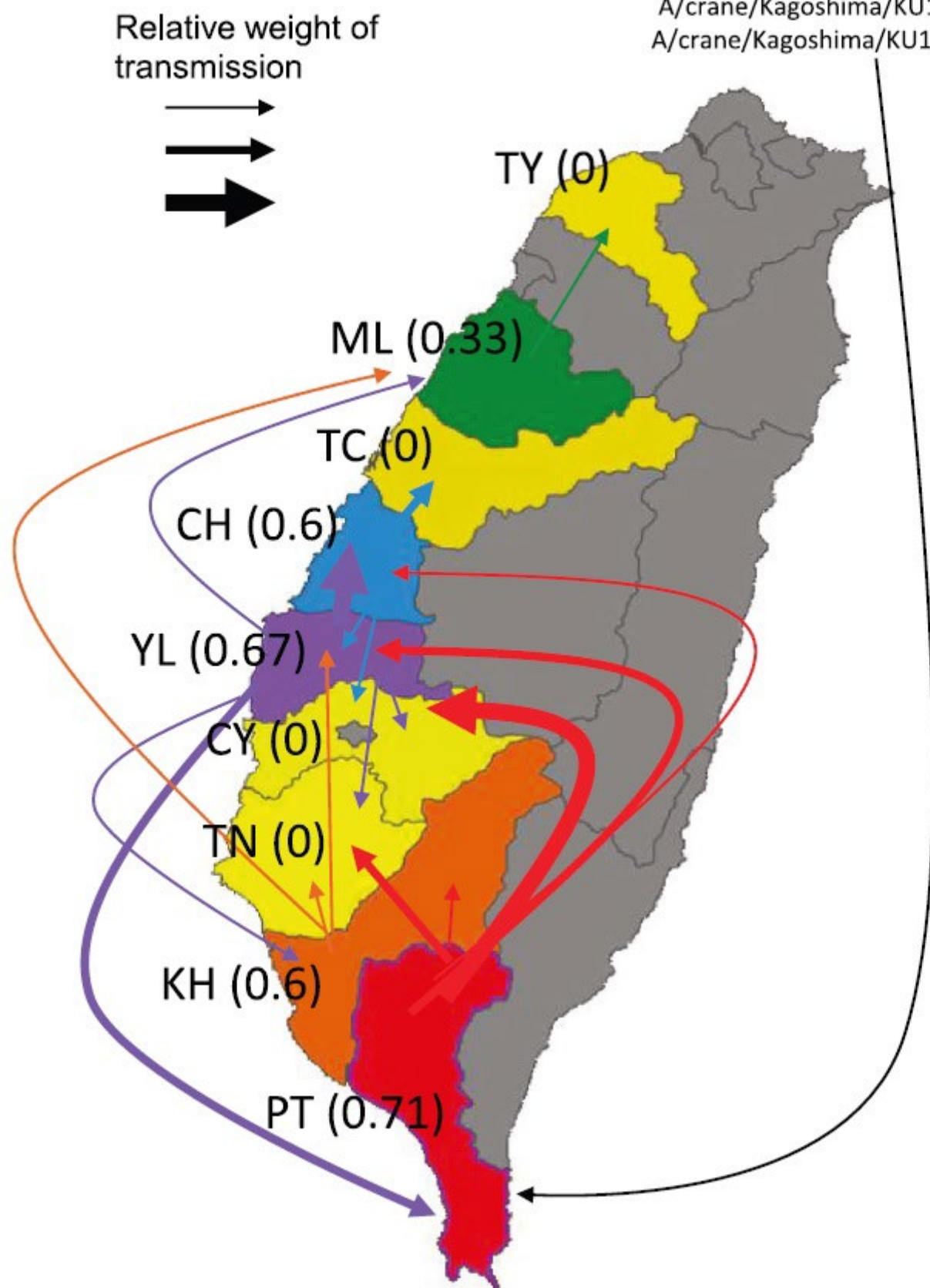


**Fig. 1.** Number of confirmed highly pathogenic avian influenza virus clade 2.3.4.4 H5Nx cases in Taiwan during 2015–2018. (A) Total number of confirmed clade 2.3.4.4 H5Nx cases that categorized by landfowl (colored in red), ducks (yellow), and geese (white). Number of confirmed clade 2.3.4.4 H5Nx cases of (B) landfowl and (C) waterfowl from clinical samples (from farm and slaughterhouse, colored in blue) and surveillance samples (light green). The gray shaded months indicate enhanced surveillance program applied after HPAI H5N6 detection.

圖表為不同禽種的高病原性禽流感(HPAI)陽性病例及監測統計。

可怕的HPAI疫情剛爆發時，大量鵝場爆發疾病並進行撲殺，甚至讓我們都沒有鵝肉可以吃。HPAI在雞會有很嚴重的臨床症狀，當雞農發現雞隻有異常症狀及死亡率時可以即時通報。HPAI在鴨則就不一定有明顯的症狀，需要靠主動或被動監測來抓出潛在的病毒兇手。

The most closely related isolates to Taiwan HPAI H5Nx  
A/crane/Kagoshima/KU1/2014 (H5N8)  
A/crane/Kagoshima/KU13/2014 (H5N8)



圖為病毒的傳播路徑模擬，可以看到病毒在臺灣中南部縣市的感染途徑，凡走過必留下痕跡。

Genotype	Isolate of Recombinant	Date	No. of Isolate	HA	NA	PB2	PB1	PA	NP	MP	NS		
	A/crane/Kagoshima/KU1/2014 (H5N8)	11/23/2014	1	■	■	■	1	1	1	■	■		
	A/crane/Kagoshima/KU13/2014 (H5N8)	12/7/2014	1	■	■	■	1	1	1	■	■		
H5N3 G1	A/goose/TW/01038/2015 (H5N3)	1/12/2015	5	■	■	1	4	1	2	■	■		
H5N3 G2	A/duck/PT/15010157-1/2015 (H5N3)	1/14/2015	1	■	■	■	4	1	1	■	■		
H5N8 G1	A/goose/TW/01003/2015 (H5N8)	1/8/2015	21	■	■	■	3	1	2	■	■		
H5N8 G2	A/goose/TW/01039/2015 (H5N8)	1/10/2015	35	■	■	■	1	1	1	■	■		
H5N8 G3	A/goose/TW/01026/2015 (H5N8)	1/11/2015	1	■	■	■	1	1	1	■	■	2	
H5N8 G4	A/duck/TW/01068/2015 (H5N8)	1/12/2015	36	※	■	1	4	1	2	■	■	■	
H5N8 G5	A/chicken/TC/16110017-3/2016 (H5N8)	11/16/2016	1	■	■	■	3	3	3	■	■	3	
H5N8 G6	A/chicken/YL/17010001/2017 (H5N8)	1/1/2017	1	■	■	■	3	1	3	■	■	3	
H5N2 G0	A/goose/TW/15010004/2015 (H5N2)	1/7/2015	155	■	■	1	2	2	2	■	■	2	
H5N2 G1	A/goose/CY/17040014/2017 (H5N2)	4/6/2017	1	※	■	1	2	2	4	■	■	2	
H5N2 G2	A/duck/YL/17110001/2017 (H5N2)	11/1/2017	9	■	■	1	2	2	4	■	■	2	
H5N2 G3	A/goose/YL/18030020-1/2018 (H5N2)	3/30/2018	3	■	■	2	1	2	5	■	■	2	EastAsia
H5N2 G4	A/chicken/PT/18050006-1/2018 (H5N2)	5/7/2018	4	■	■	2	5	4	4	■	■	3	Asia
H5N2 G5	A/chicken/TP/18050007-1/2018 (H5N2)	5/9/2018	6	■	■	3	2	4	6	■	■	4	EuroAsia
H5N2 G6	A/chicken/PT/18080001-1/2018 (H5N2)	8/8/2018	5	■	■	3	■	■	2	■	■	2	America

※ The HA gene of H5N2 G1 was derived from Taiwan H5N8 G4.

Fig. 4. Genotype of reassortant identification using phylogeny-based methods. (A) Maximum likelihood phylogeny of internal genes. Sequences of top 100 GISAID blast hits of internal gene of each genotype of the Taiwan highly pathogenic avian influenza H5Nx viruses were retrieved to reconstruct phylogeny. (B) The identified genotypes of the Taiwan highly pathogenic avian influenza H5Nx viruses. Each genetic segment was colored by geographic origins. Distinct phylogenetic clades in the same geographic region were further indicated by numbers.

圖為病毒詳細的重組基因型，複雜多樣的重組型代表不斷潛伏伺機肆虐的病毒分身，應該更加留意禽場生物安全，早日將這些病毒一網打盡。