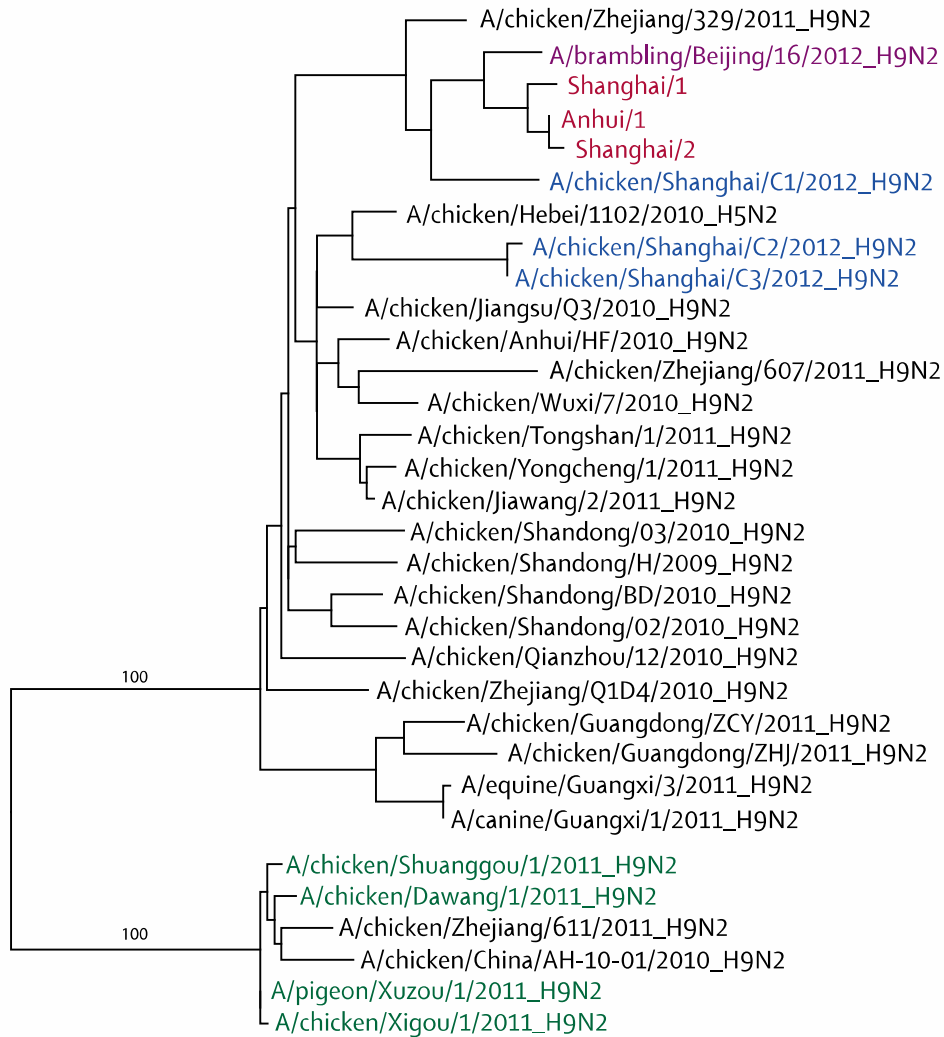


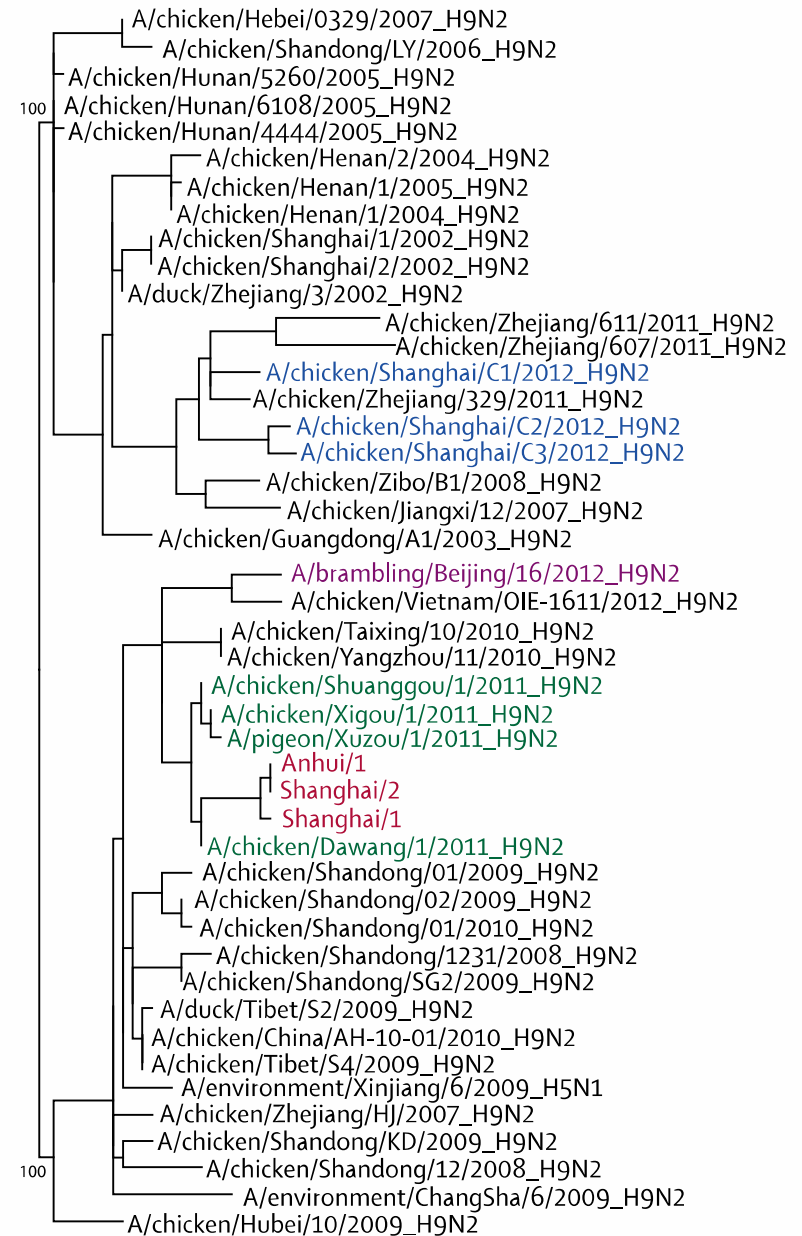
A

Different Neighbors



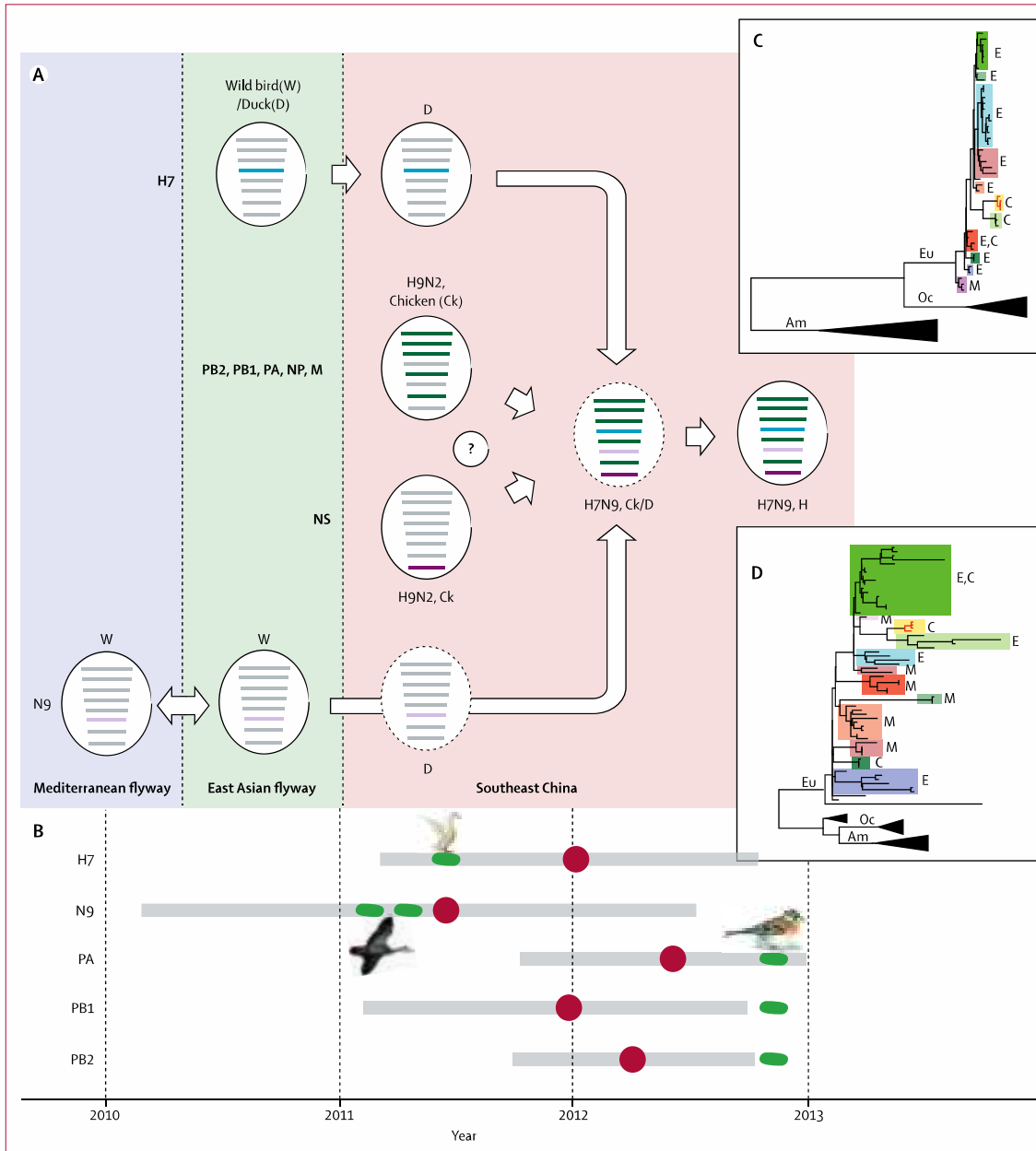
0.015

B



0.015

Spatial and temporal model of origin of novel avian influenza A H7N9 virus



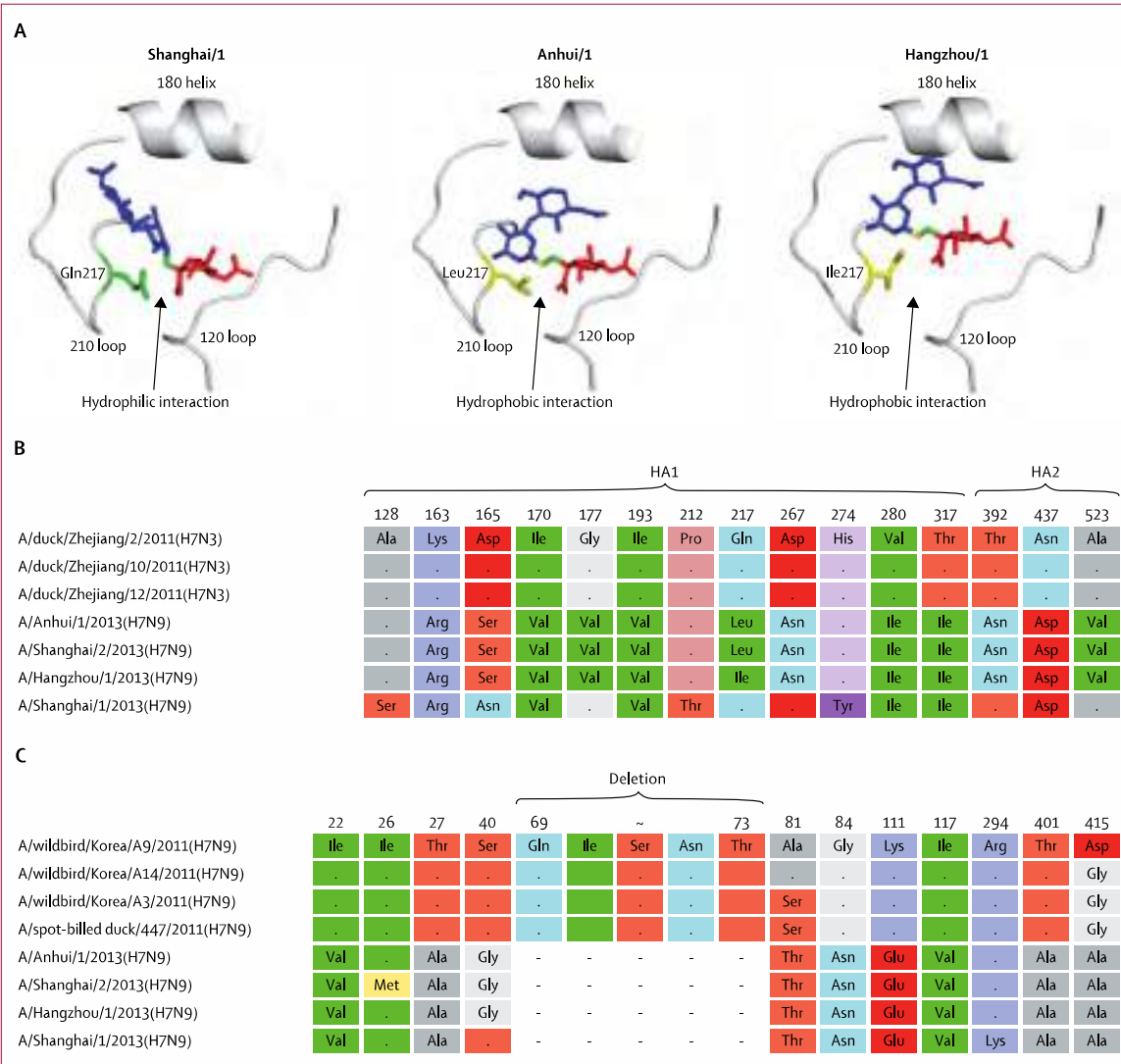
Conclusions:

- 1: HA and NA were from different bird migratory pathways.
- 2: Six internal genes were from two sources of poultry in China.
- 3: The intermediate hosts are likely the domestic birds.
- 4: H7N9 virus has been emerged in poultry for at least one year.

Diversity & Dynamics

H7N9病毒多态性与动态重配过程？

功能位点多态性

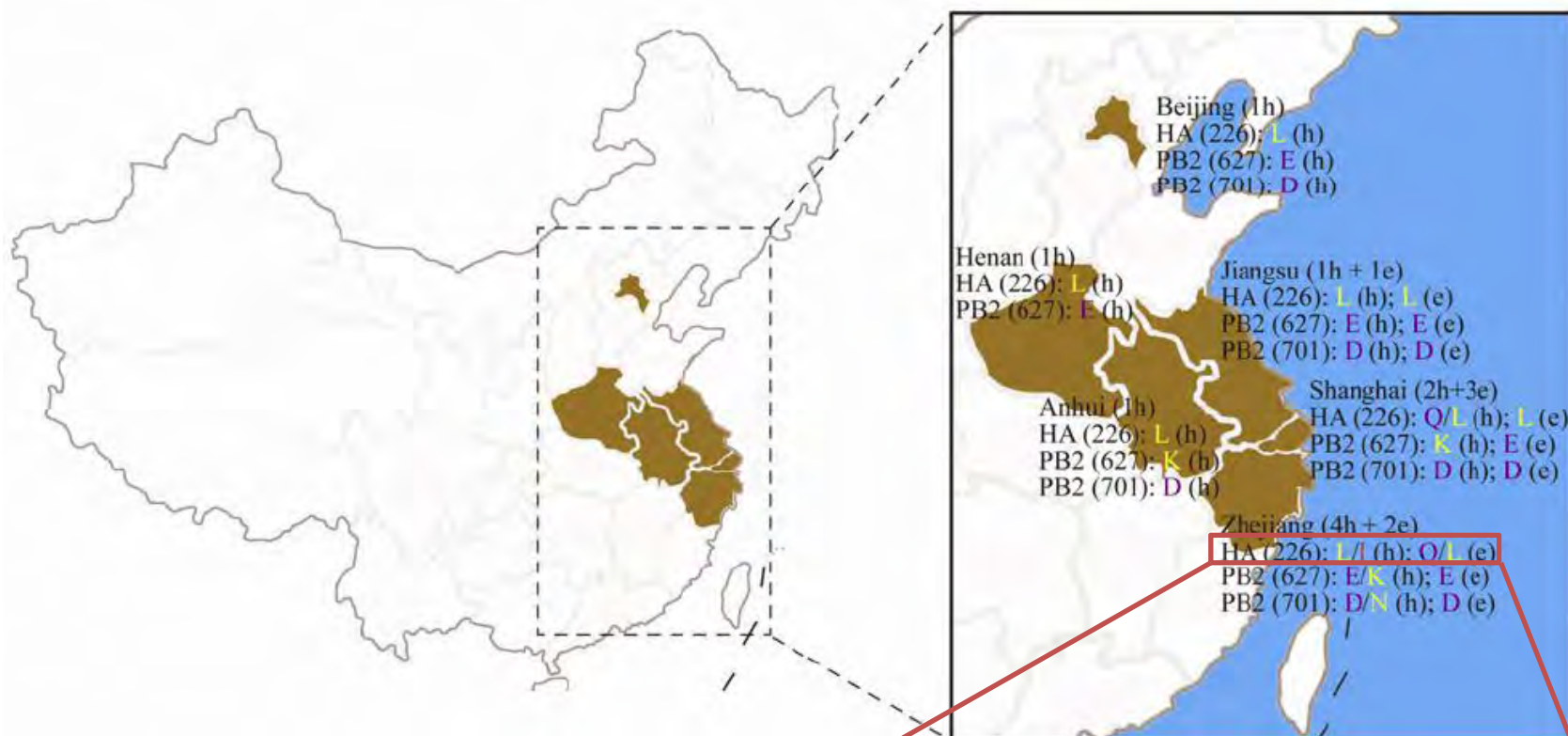


结论:

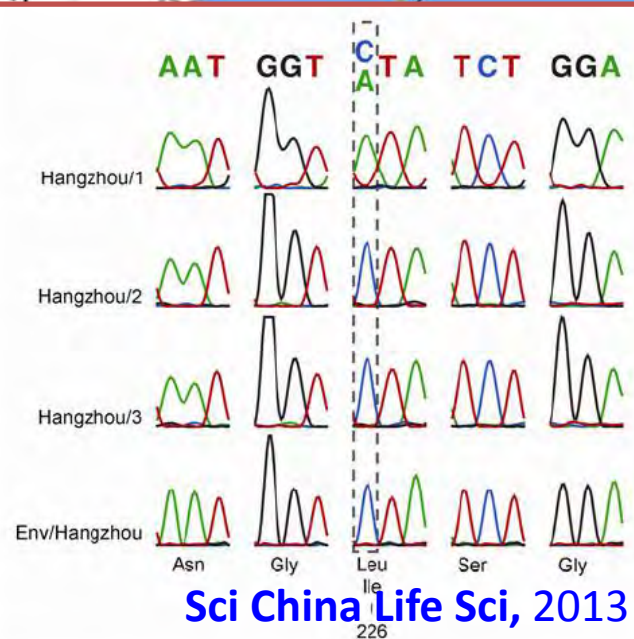
1: Anhui/1 具有哺乳动物特异性受体

2: Shanghai/1 与其他病毒在包括达菲耐药位点在内的多个位点存在差异性

3: H7N9在形成初期即存在有至少两种多态性

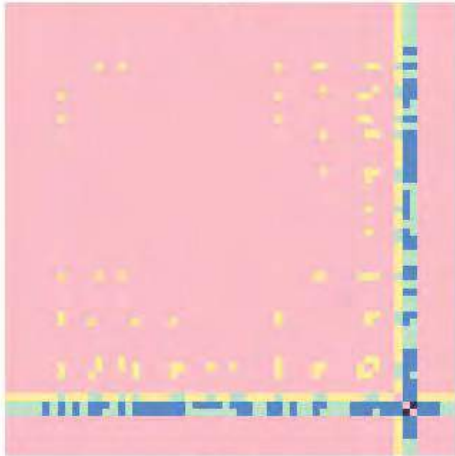


杭州的病毒HA出现了受体结合位点226I的变异，很有可能是一种新型的结合哺乳动物细胞的类型。

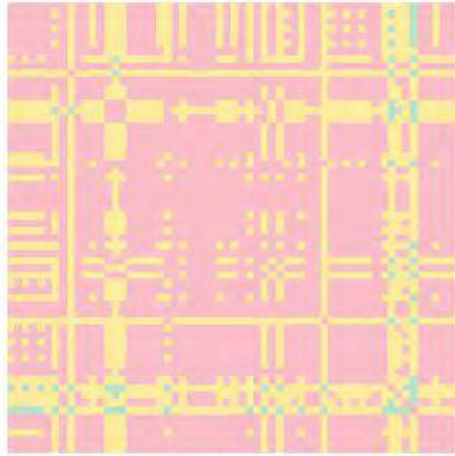


病毒的内部基因比表面基因表现出更复杂的多态性

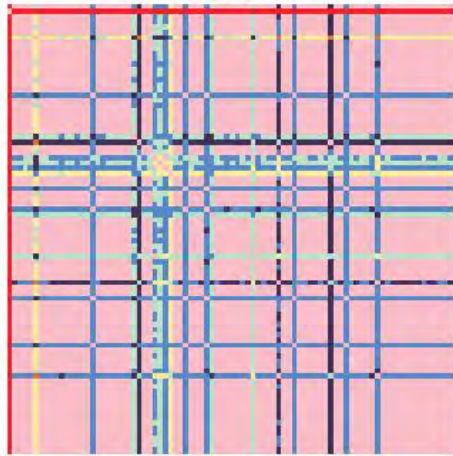
HA



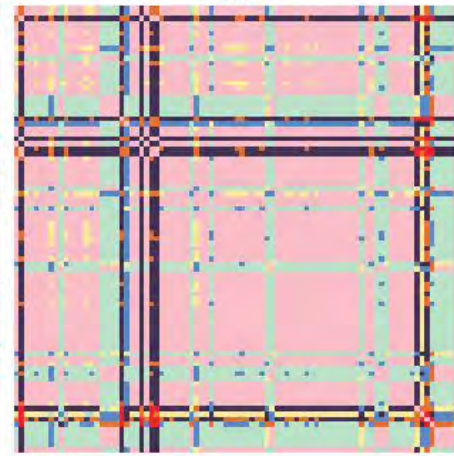
NA



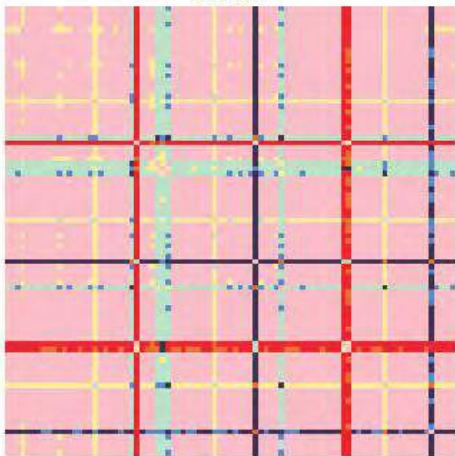
PA



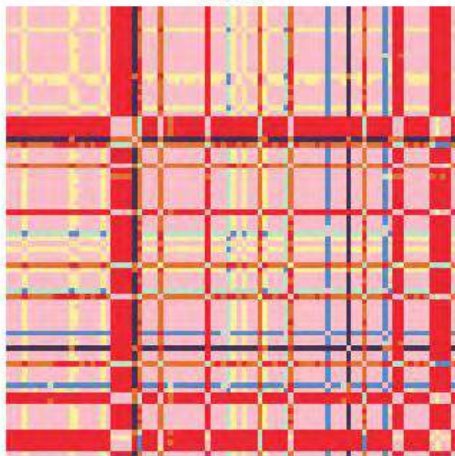
NP



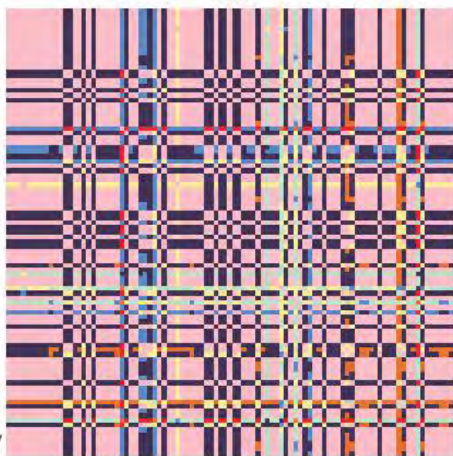
PB2



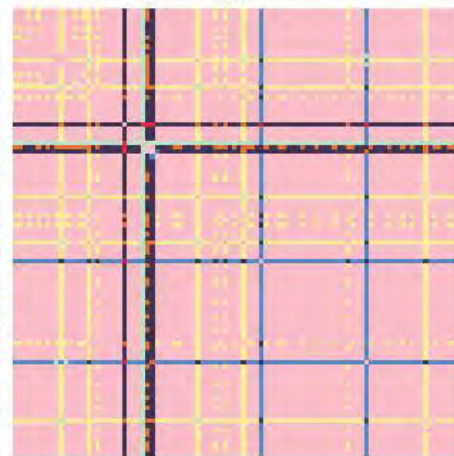
PB1

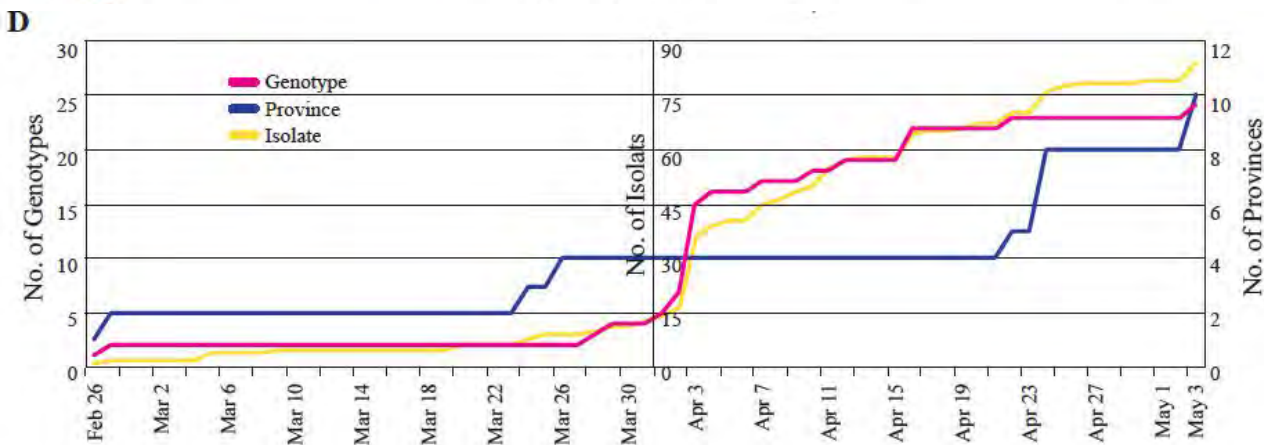
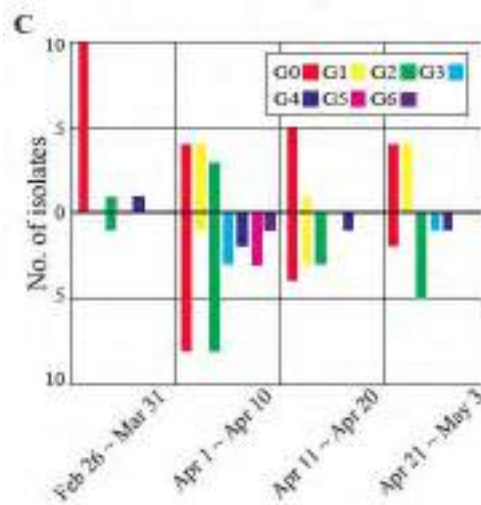
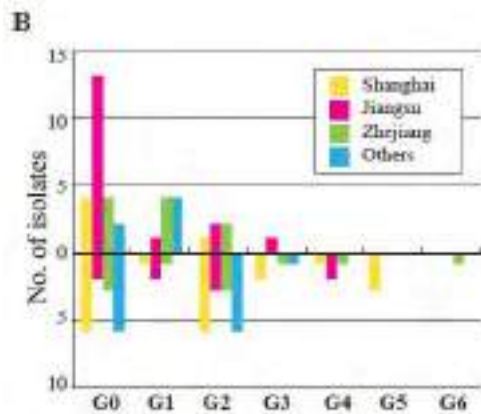
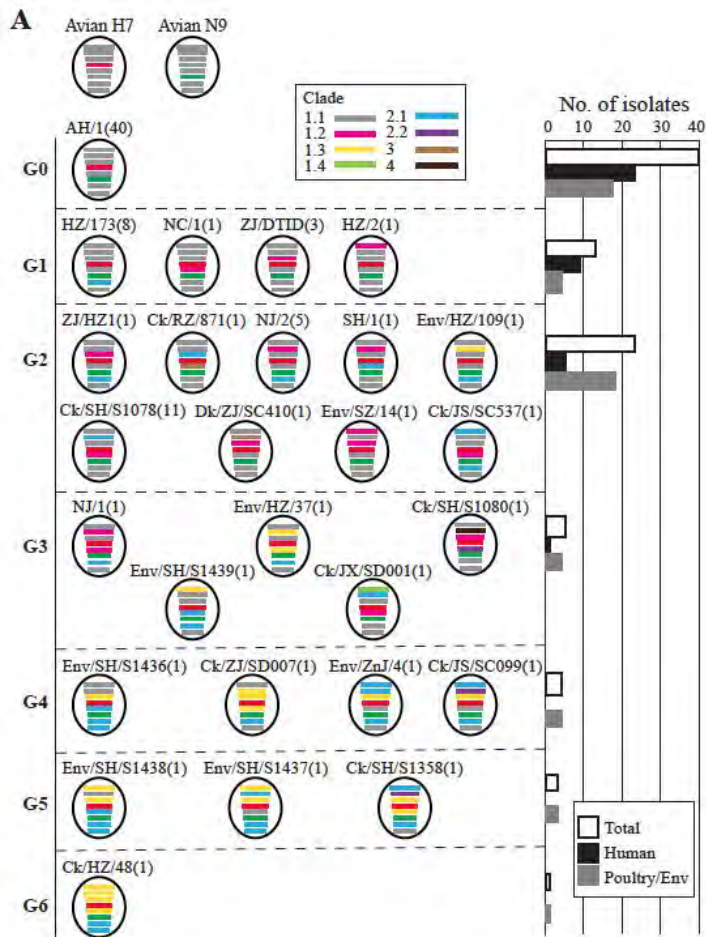


M

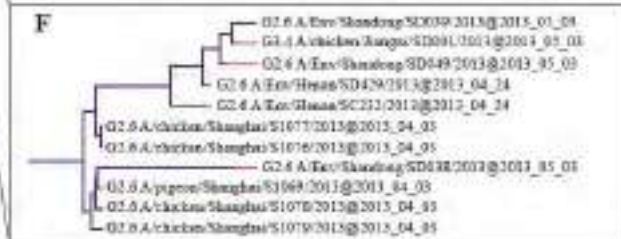
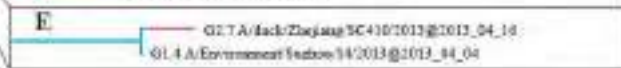
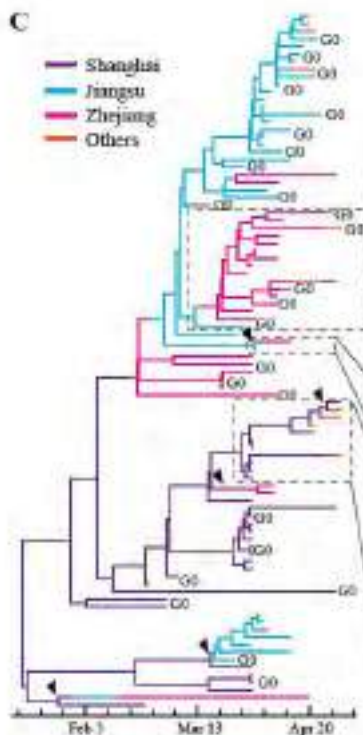
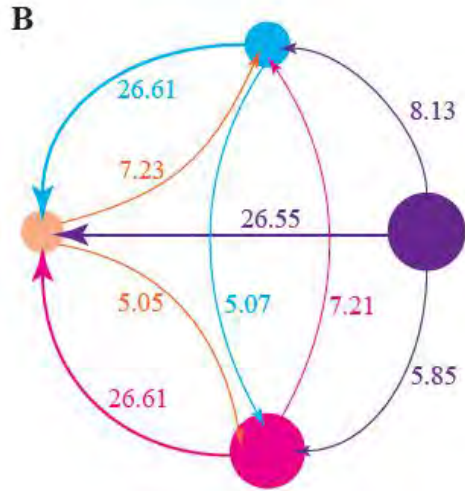


NS





- ## H7N9基因型分析:
- 至少有27个基因型出现在这次H7N9的暴发过程中
 - 基因型的时空分布特点没有规律
 - G0主要出现在人感染病例中;
 - 在家禽中G0和G2.6共同作为主要基因型存在
 - H7N9病毒的基因型随着病毒的传播（省内传播和跨省传播）在持续增加



H7N9基因流和谱系分析:

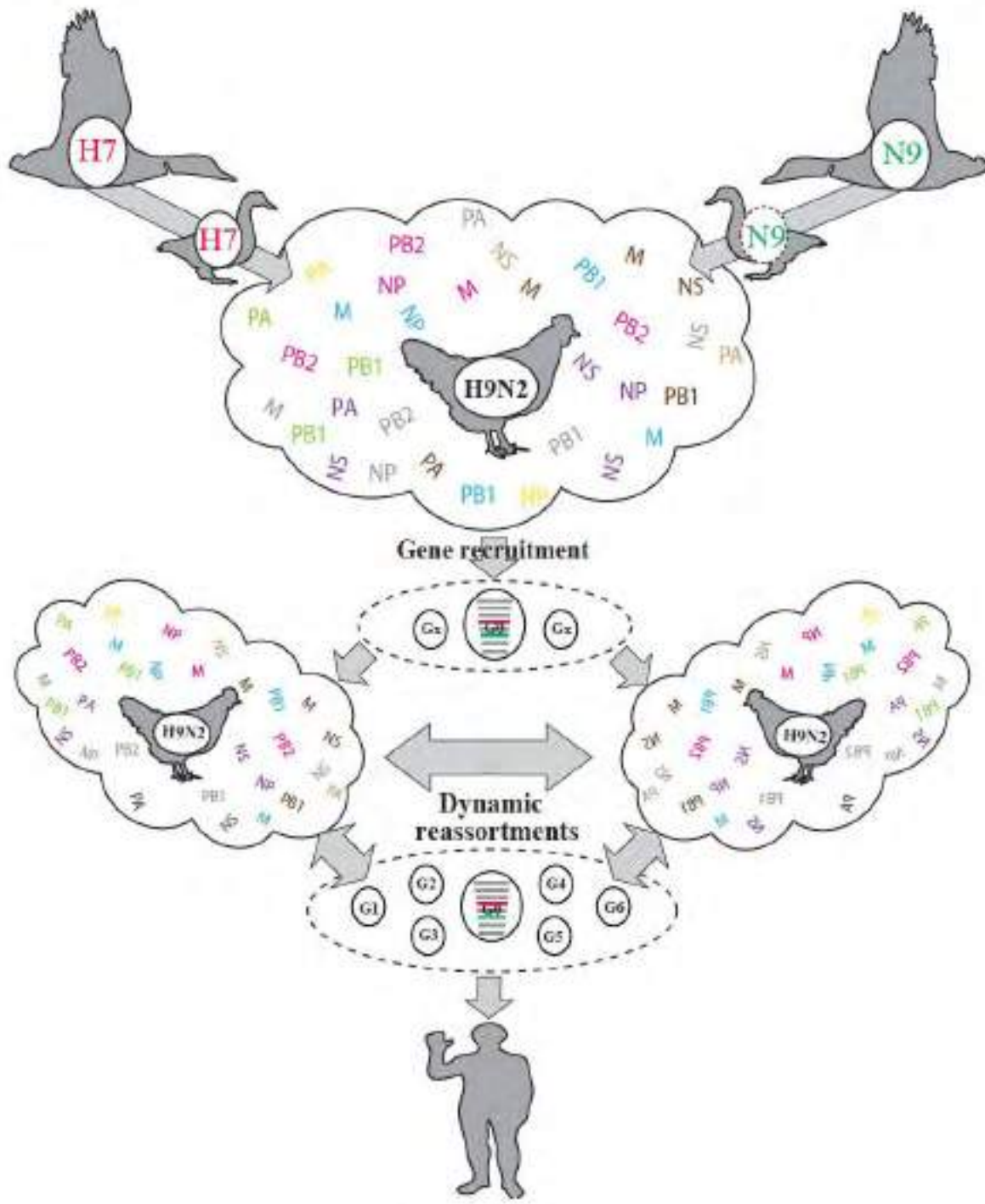
1: H7N9病毒源于长三角地区，之后向周边省市扩散

2: 各个省之间存在病毒的交互传播

3: 在传播过程中，产生了新的基因型

4: G0作为病毒传播过程中的最主要基因型

5: H7N9病毒中大部分基因型还不能很好的适应禽类宿主



H7N9动态重配模式：

1: H7N9病毒在H9N2病毒的基因库中招募不同的基因片段

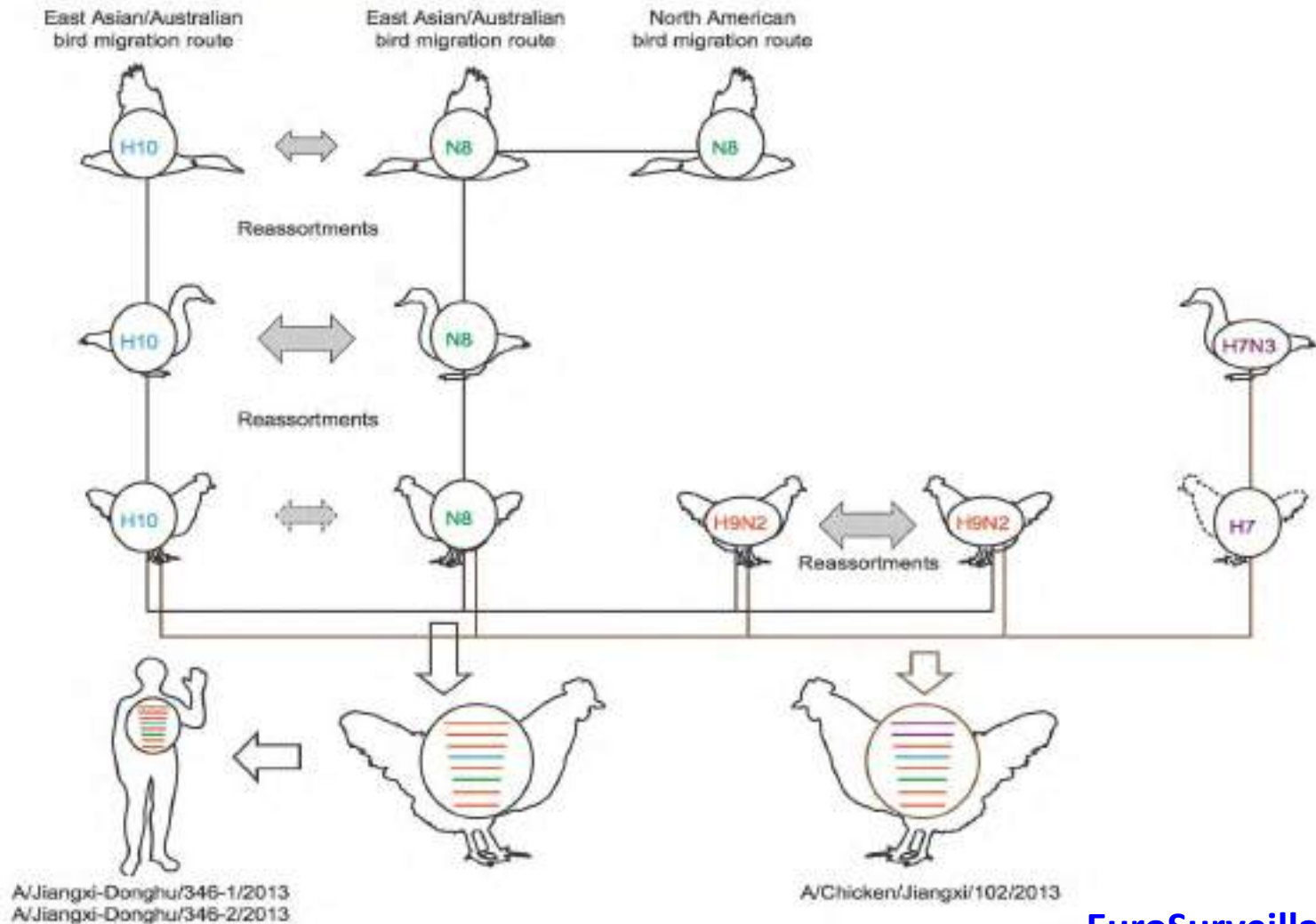
2: 通过基因型的改变从而改变对宿主的适应性

3: 通过家禽运输，一些H7N9病毒会进入新的病毒基因库，并招募新的基因片段，产生新的基因型

4: 新产生的基因型可能会对禽或人产生新的适应能力

5: 控制H7N9的动态重配对于病毒的防控至关重要

Genesis of the novel human-infecting influenza A(H10N8) virus and potential genetic diversity of the virus in poultry, China



A/Jiangxi-Donghu/346-1/2013
A/Jiangxi-Donghu/346-2/2013

A/Chicken/Jiangxi/102/2013

H7N9等禽流感病毒出现的原因？

LETTER

Phylogenetics of varied subtypes of avian influenza viruses in China: potential threat to humans

Dear Editor,

Since February 2013, infections with several novel avian-origin influenza viruses have occurred in Taiwan and the Mainland of China. The H7N9 influenza virus has caused 136 human infections with 44 deaths in the first influenza season, and has continued to cause infections during the current influenza season (Li et al., 2014). As of February 11th, 2014, a total of 331 human infections with 101 deaths in China have been reported (<http://www.nhfc.gov.cn>). During the outbreak of H7N9 in the Mainland of China, Taiwan reported the first human infection of avian H8N1 influenza virus, which again hit the public (Shi et al., 2013a; Wei et al., 2013). In November 2013, the first infection of H10N8 influenza virus was reported by Nanchang Center for Disease Control and Prevention (Chen et al., 2014). Questions

自2006年以来，我国各地家禽中存在有各种不同亚型的禽流感病毒

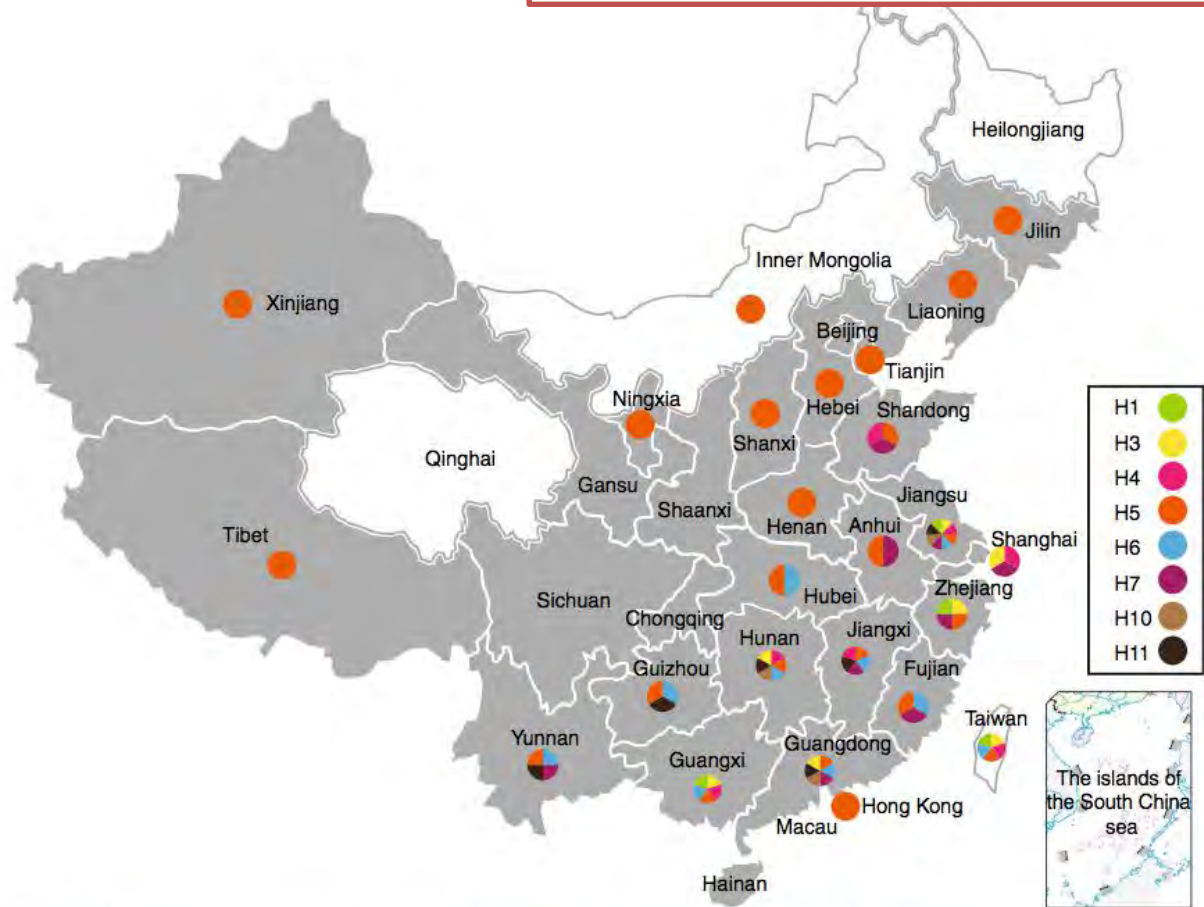


Figure 1. Distribution of varied subtypes of influenza viruses within poultry of China (based on NCBI deposits). Different colors depict different HA subtypes, and the shaded regions show the emergence of H9N2 virus within poultry in that province.

Poultry carrying H9N2 act as incubators for novel human avian influenza viruses

After being hit by avian influenza A H7N9 virus (134 individuals infected and 45 deaths in 2013, and 213 cases and 56 deaths as of Feb 23, 2014),¹ China had their first case of fatal H10N8 infection in a human being on Dec 17, 2013, in the Jiangxi Province, which has been followed by two more cases in the same province.²

The two novel influenza viruses that affect human beings, H7N9 and H10N8, have similar genetic lineage: the haemagglutinin (H) gene originated from ducks and the neuraminidase (N) gene from wild birds.^{1,4} Avian influenza viruses are often thought to be transmitted from wild birds to domestic birds and then to people. However, influenza viruses from wild birds could hardly ever adapt to and replicate well within domestic birds, since influenza virus from wild birds is rarely found to be prevalent in domestic hosts. Most influenza viruses from wild-bird origin would die within domestic hosts, preventing people from being infected by avian influenza virus.

probably enable H7N9 virus to survive and be transmitted within poultry, because dynamic reassortments of H7N9 with H9N2 genes have been observed,¹ suggesting that H7N9 virus evolved in poultry to become a virus that infects human beings. Hence, reassortment between the prevalent poultry H9N2 viruses (providing genetic components) and the

influenza make the to domest in live m role duric influenza Several viruses infecting next avia cause m Therefore carrying wild-bir would b prevent H infected v We call poultry n disinfect and any c markets. We discuss i Di Liu, Wu

- 1. Liu D, Shi W, Shi X, et al. Origin and diversity of novel avian influenza A H7N9 viruses causing human infections: phylogenetic, structural, and evolutionary analyses. *Lancet* 2013; **381**: 1976-87.
- 2. Shi W, Shi W, Li X, et al. Phylogenetics of novel subtypes of avian influenza viruses in China: potential threat to humans. *PLoS ONE* 2014; **9**: e87994.
- 3. Cui L, Liu D, Shi W, et al. Dynamic reassortments and genetic heterogeneity of the human-infecting influenza A (H7N9) virus. *Nat Commun* 2014; **5**: 3142.



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SCIENCE CHINA Life Sciences

• INSIGHT •

doi: 10.1007/s11427-014-4677-3

The new emerging H7N9 influenza virus indicates poultry as new mixing vessels

LIU Di^{1,2*} & GAO George F,^{1,2,3,4}

隐性带毒家禽是禽流感的“孵化器”和“混合器”

¹Office of Director-General, Chinese Center for Disease Control and Prevention, Beijing 102206, China

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Science China Life Sci, 2014

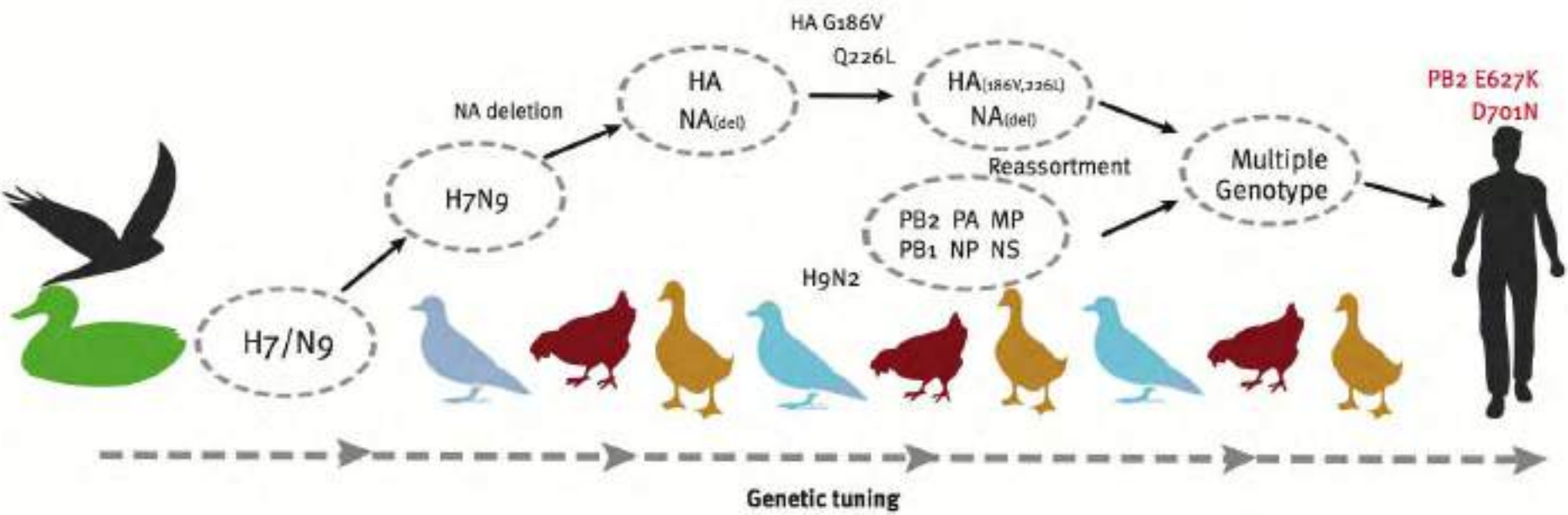
Mutation & Adaptation

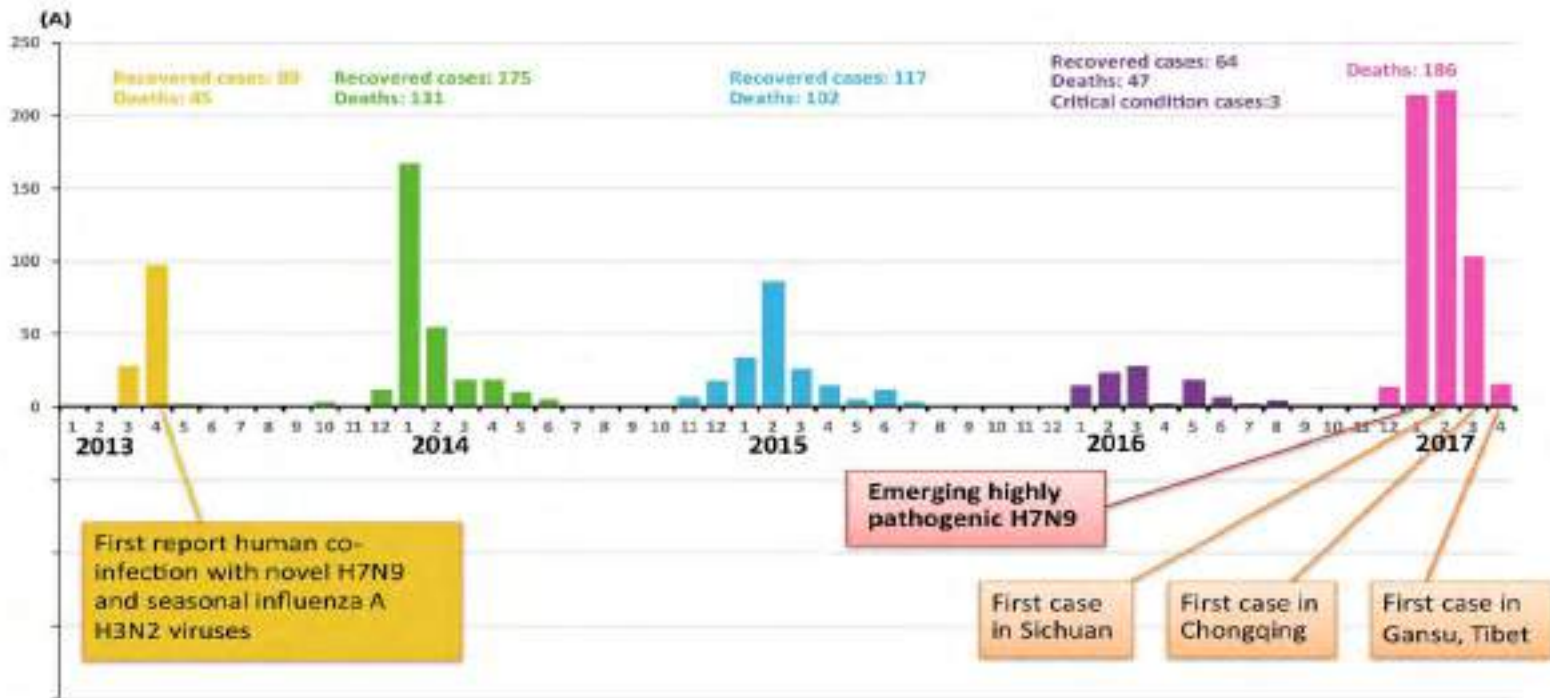
H7N9病毒是如何适应宿主的？

Genetic tuning of the novel avian influenza A(H7N9) virus during interspecies transmission, China, 2013

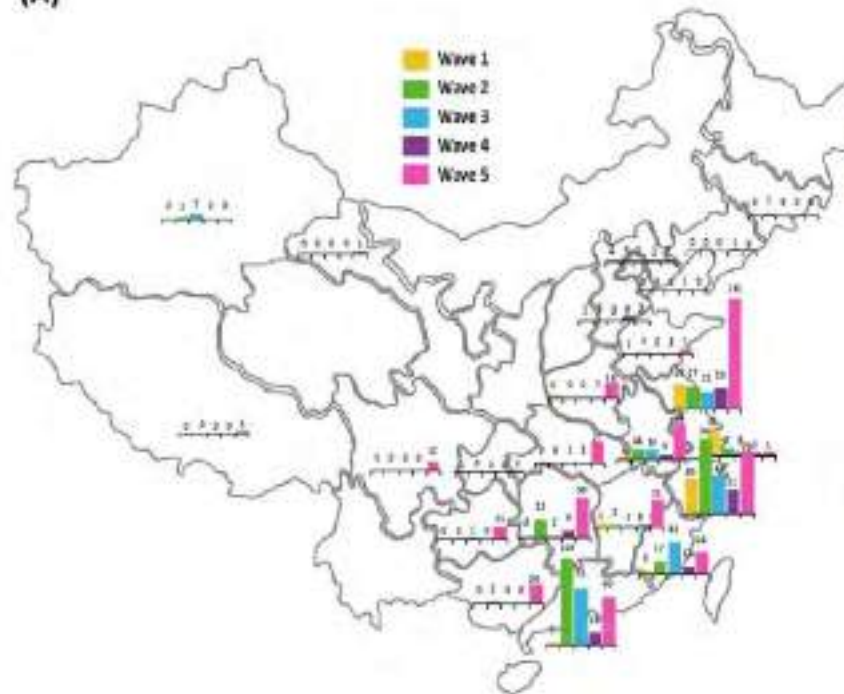
FIGURE 4

Proposed genetic tuning mechanism of avian influenza A(H7N9) viruses during interspecies transmission

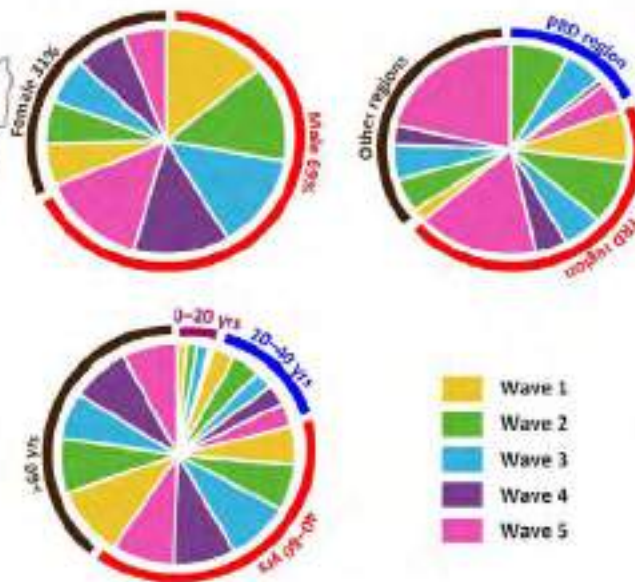




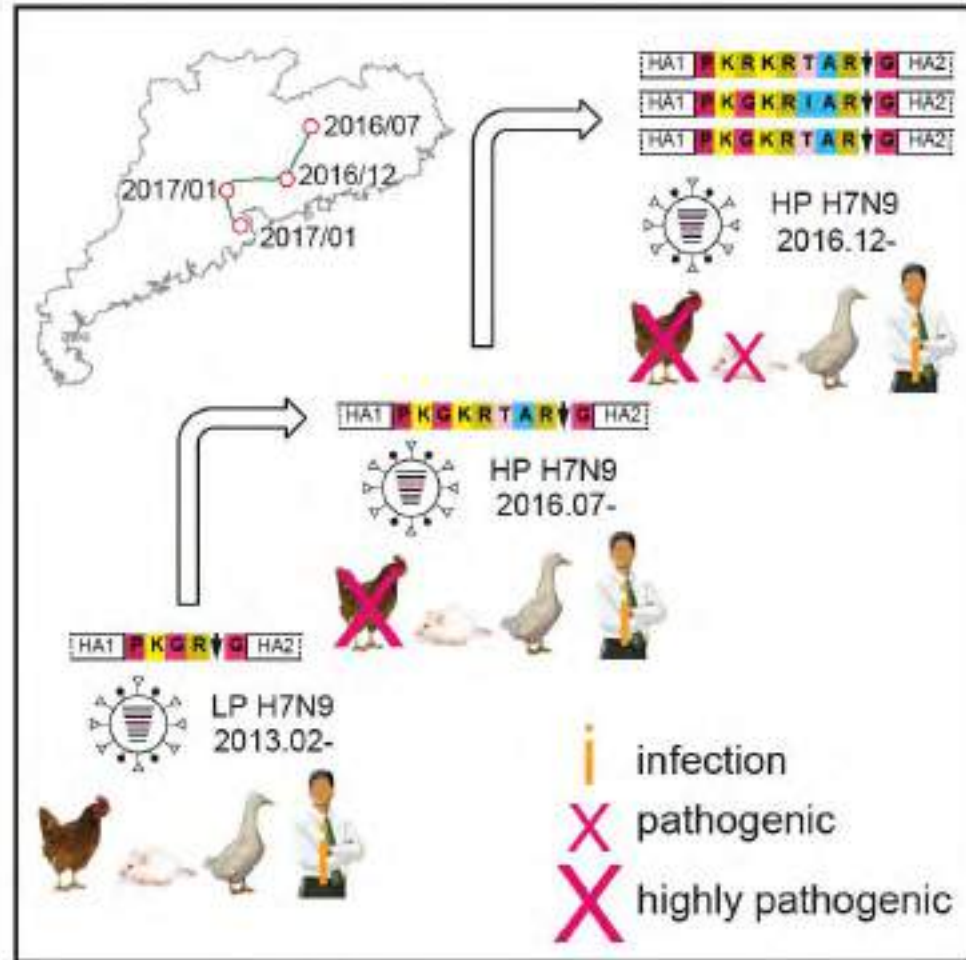
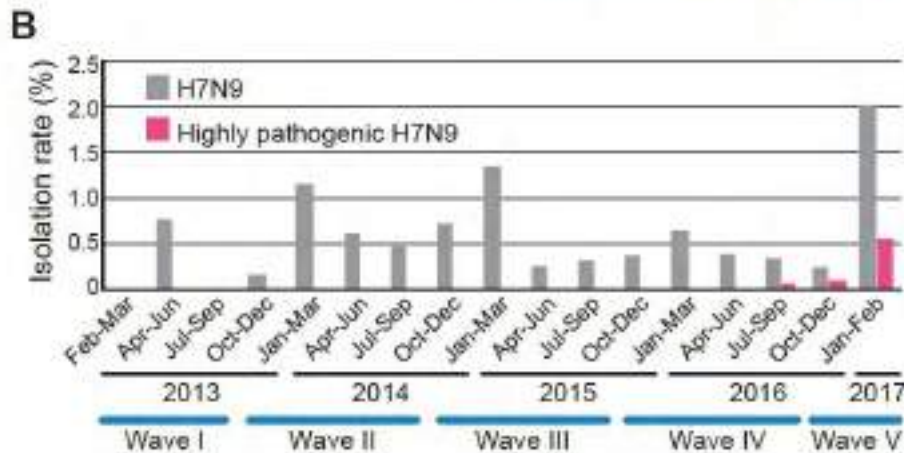
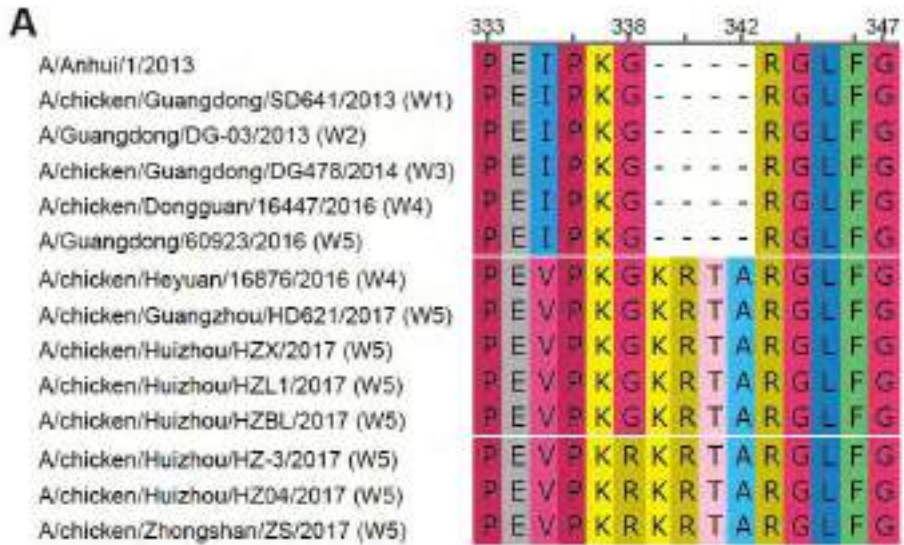
(A)



(B)

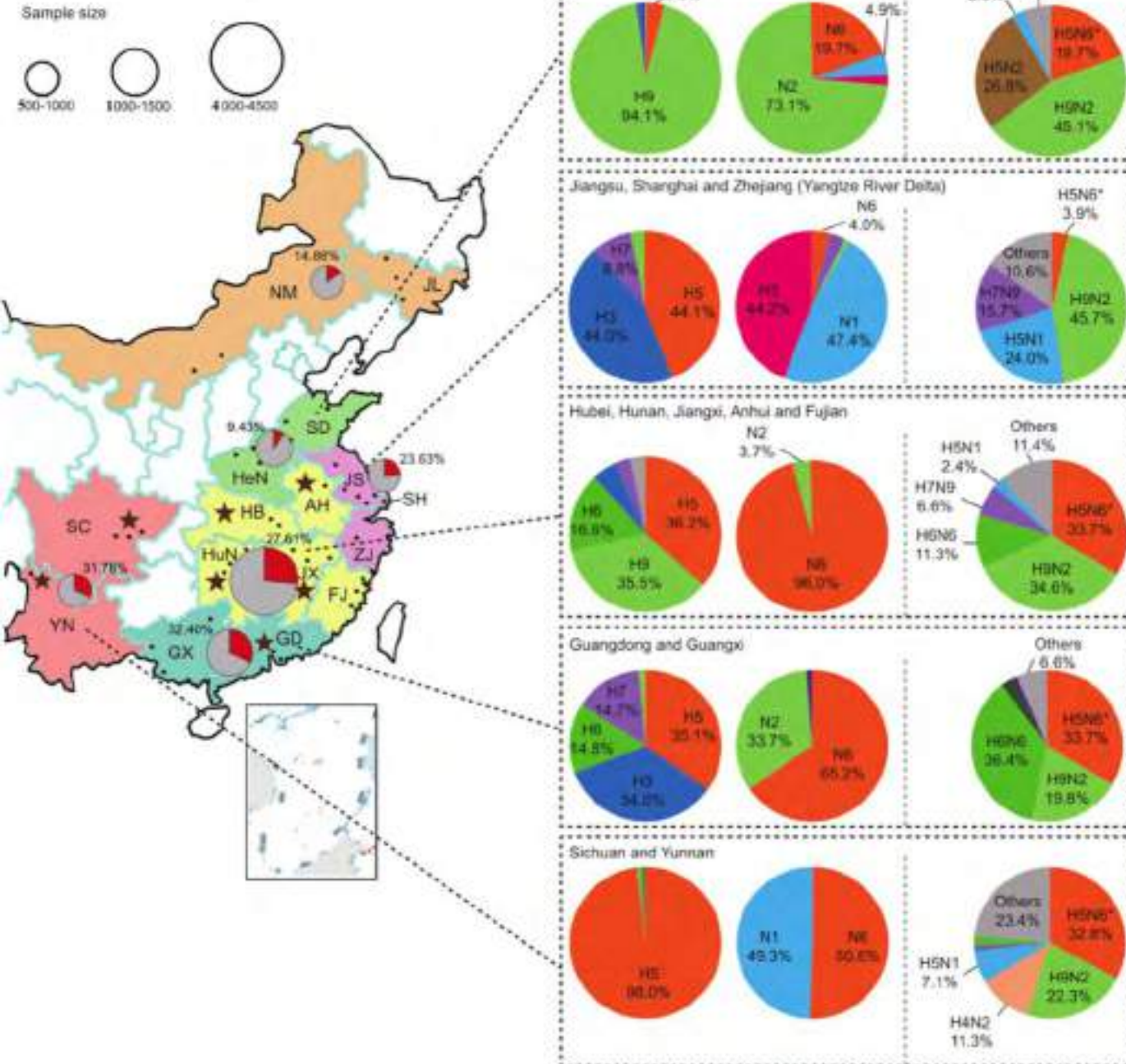


H7N9的HA裂解位点插入性变异



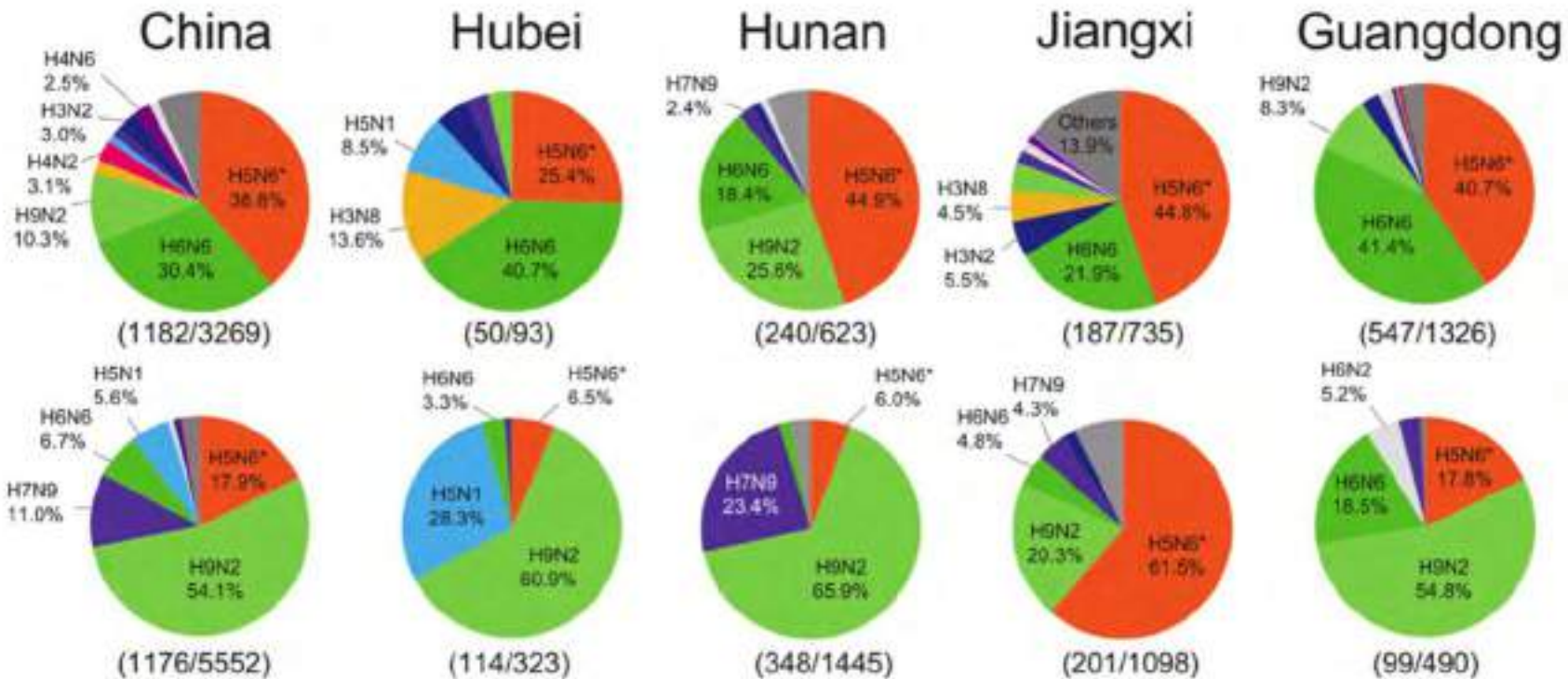
Post-H7N9?

Distribution of AIVs in China from 2014-2016

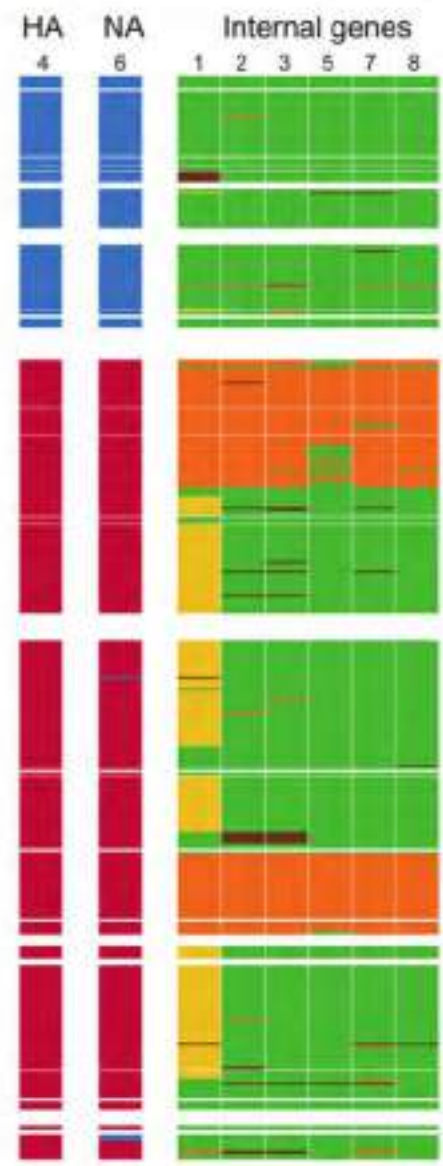
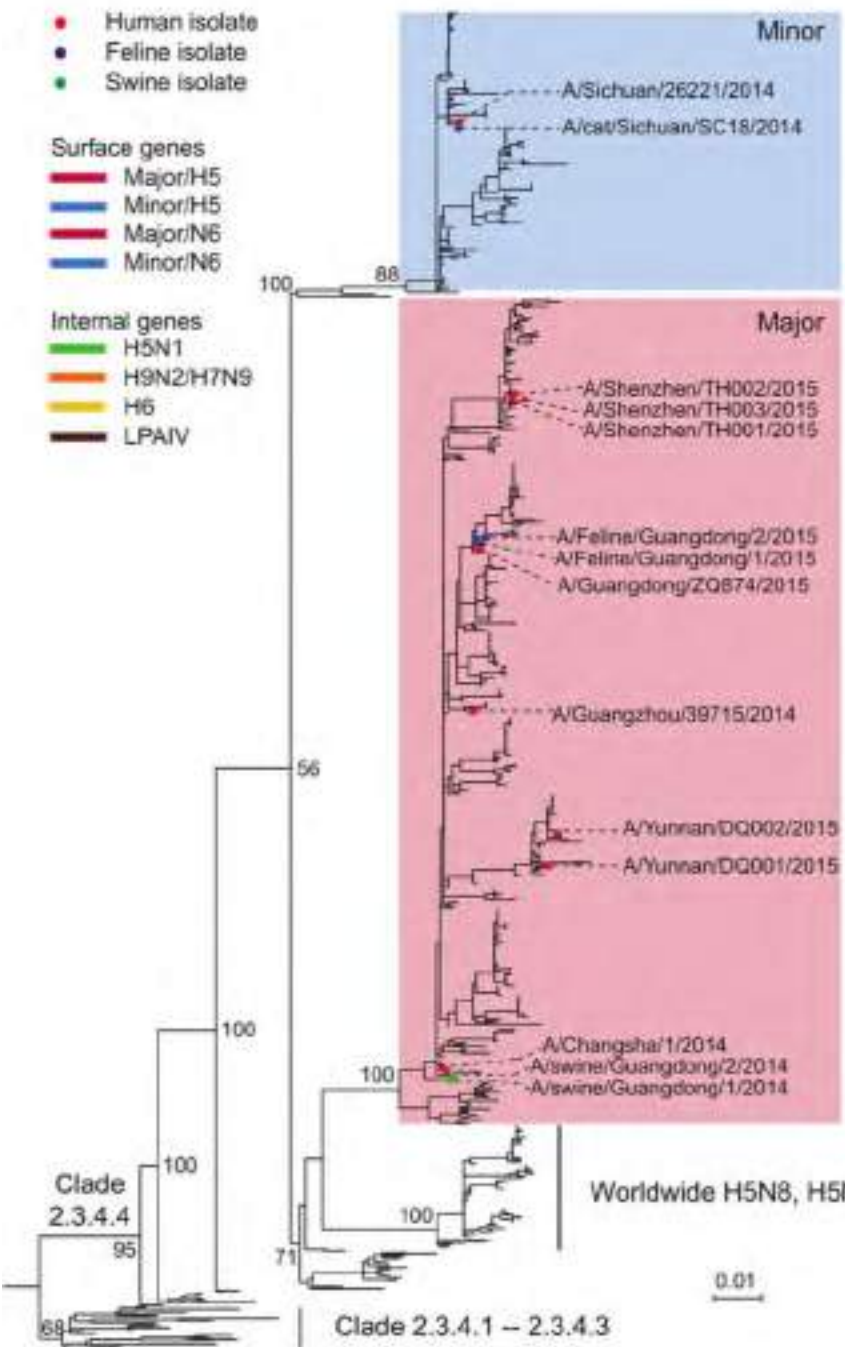


- H5N6 became dominant in some regions
- H9N2 is still prevalent

Host preference of AIVs

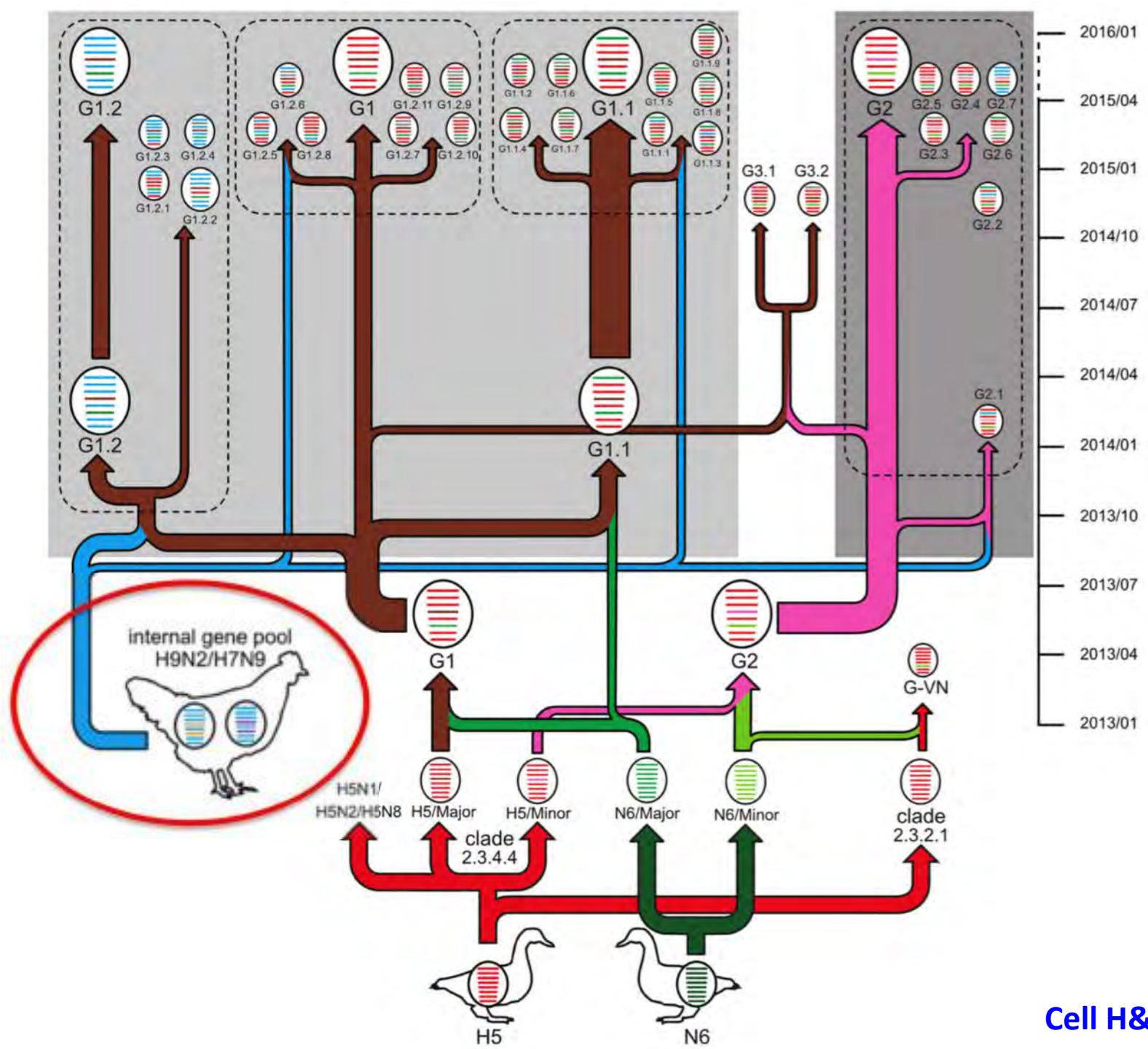


C



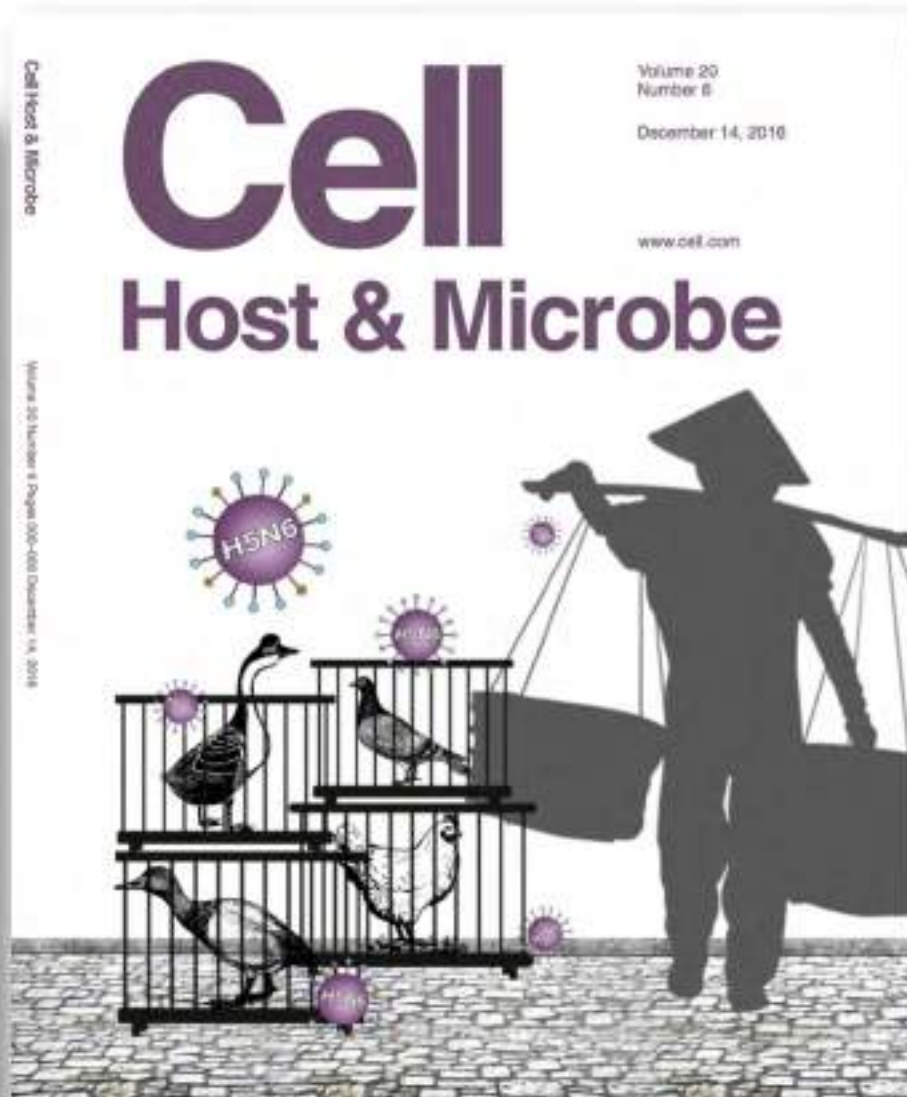
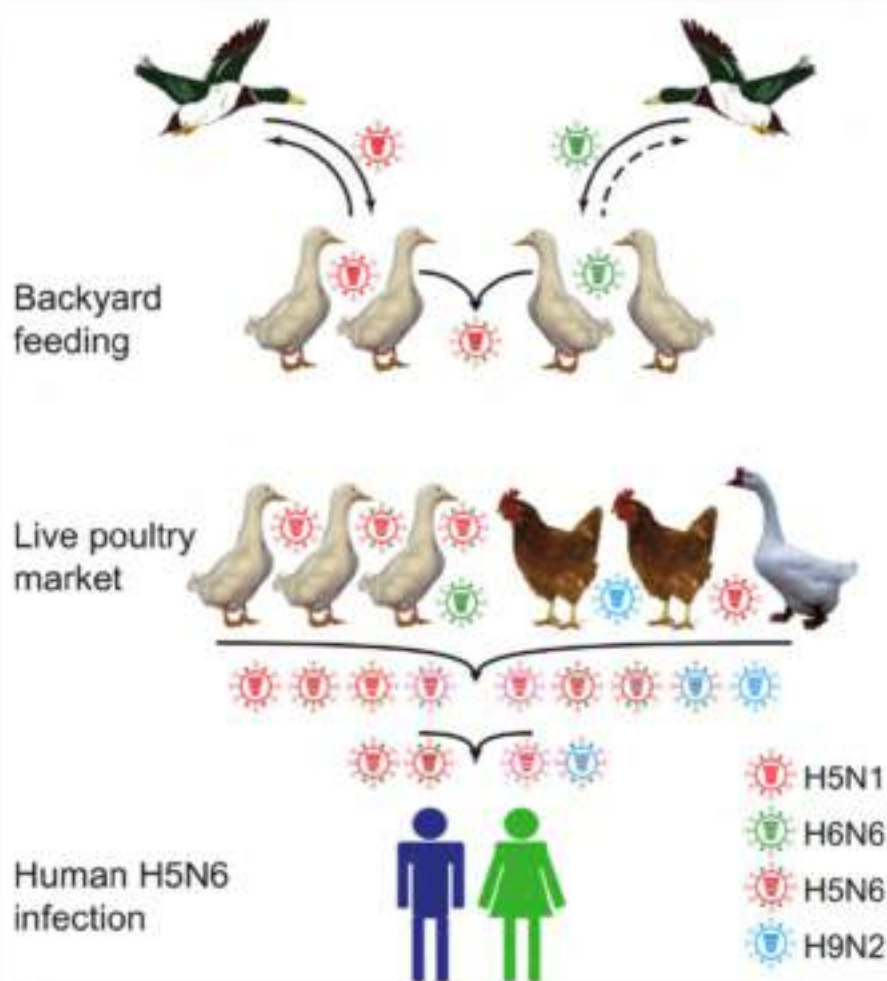
HA & NA Matching

- Major::Major: 75.6%
- Minor::Minor: 23.5%
- Major::Minor: 0.7%



Cell Host & Microbe

Genesis, Evolution and Prevalence of H5N6 Avian Influenza Viruses in China



禽流感病毒进化特征小结

- H7N9依野生候鸟→家养水禽→家养陆禽→哺乳动物/人为主的传播路径进行起源与进化
- 禽流感病毒借助家禽运输和活禽交易快速扩散，通过动态重配进行快速变异
- H9N2带毒家禽对禽流感病毒起源与进化起关键作用，是“孵化器”和“混合器”
- H7N9病毒在禽类宿主中进行“遗传调频”获得适应性变异
- 鸡源与鸭源禽流感病毒的交互重配很可能会导致新型禽流感病毒的出现

致 谢

- 中国科学院微生物研究所，天津生物工程研究所
- 中国科学院病原微生物与免疫学重点实验室
- 中国科学院流感预警与研究中心
- 国家CDC病毒病研究所；江苏省CDC
- 华南农业大学；泰山医学院
- 军事医学科学院2所、5所
- 北京地坛医院，首都医科大学传染病研究所
- 项目资助：MOST、NSFC、CAS