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# 病原基因组学与进化

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# Pathogens Genomics

Pathogen infections are among the leading causes of infirmity and mortality among humans and other animals in the world. Until recently, it has been difficult to compile information to understand the generation of pathogen virulence factors as well as pathogen behaviour in a host environment. The study of **Pathogenomics** attempts to utilize genomic and metagenomics data gathered from high through-put technologies to understand microbe diversity and interaction as well as host-microbe interactions involved in disease states.

# 病原（菌）基因组学

- Causes of Genomic Diversity
  - Gene Loss / Genome Decay
  - Gene Gain/ Gene Duplication
  - Genome Rearrangement
  - Single Nucleotide Polymorphism
- Analysis of Genomic Diversity
  - Pan-genomes and core genomes
- Mobile Genetic Elements that Encode Virulence factors

# 病毒基因组学

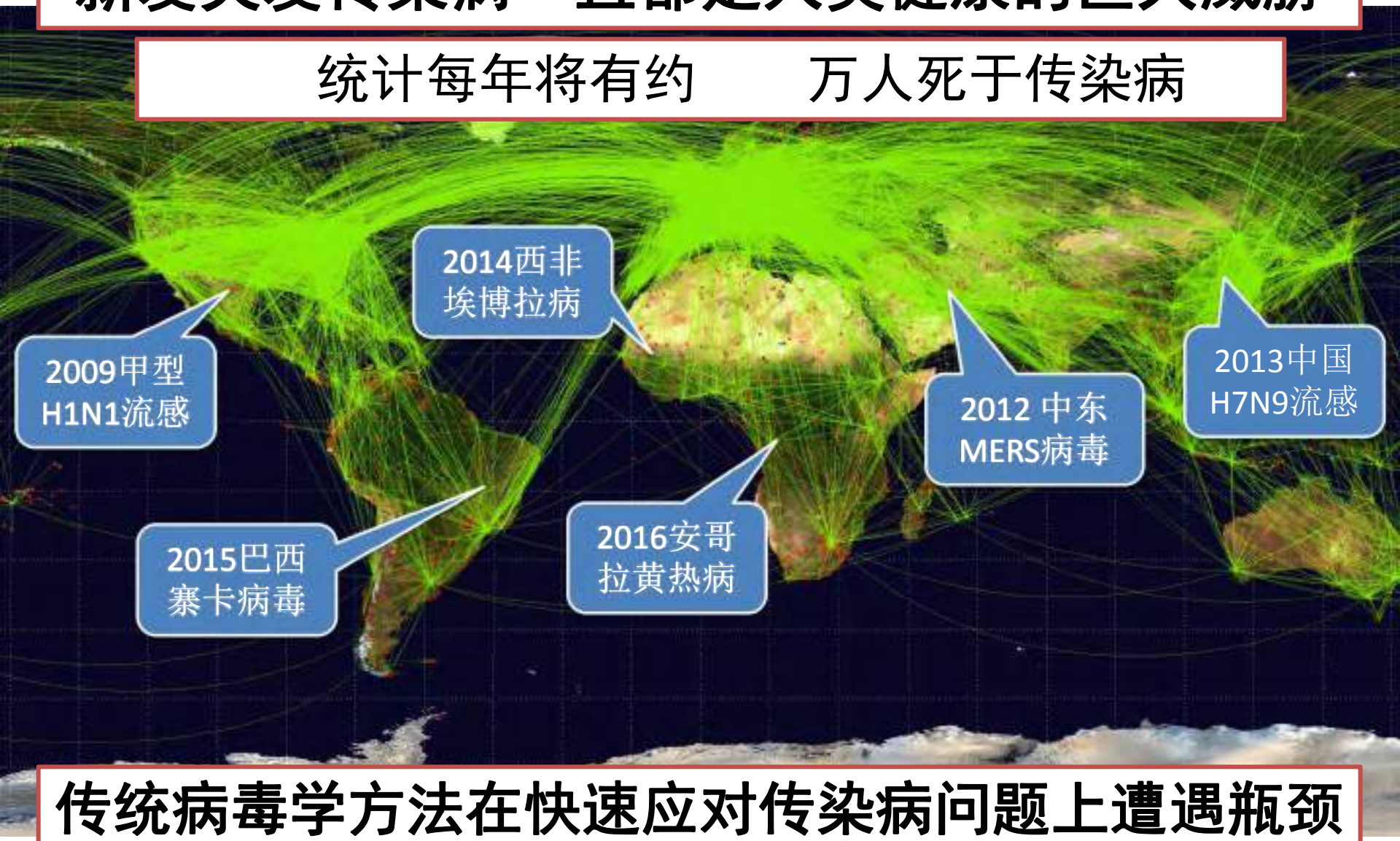
- Causes of Genomic Diversity
  - ~~– Gene Loss / Genome Decay~~
  - ~~– Gene Gain/ Gene Duplication~~
  - – Genome Rearrangement / Reassortment
  - – Single Nucleotide Polymorphism
- Analysis of Genomic Diversity
  - ~~– Pan-genomes and core genomes~~
- ~~Mobile Genetic Elements that Encode Virulence factors~~

# (病毒) 进化

- 进化生物学是研究生命的起源及进化的过程、原因、机制、速率和方向的科学
- **起源（Origin）：** 从哪里来？
- **进程（Process/Route）：** 怎么来的？
- **原因（Causes）：** 为什么会来？
- **机制（Selection）：** 谁驱动它？
- **速率（Dynamics）：** 快？慢？
- **方向（Direction）：** 要去哪？

# 新发突发传染病一直都是人类健康的巨大威胁

统计每年将有约　　万人死于传染病




# 传统病毒学方法在快速应对传染病问题上遭遇瓶颈

# 基因组学和生物信息学成为病原研究的必要手段

本人研究重点

## 重要病原生物起源、传播与进化规律

1. 传染病病原是从哪里来的？
2. 传染病病原是如何传播的？
3. 病原进化规律和应对策略？

# H7N9 Avian Influenza Virus

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Human Infection with a Novel Avian-Origin Influenza A (H7N9) Virus

Rongbao Gao, M.D., Bin Cao, M.D., Yunwen Hu, M.D., Zijian Feng, M.D., M.P.H., Dayan Wang, M.D., Wanfu Hu, M.D., Jian Chen, M.D., Zhijun Jie, M.D., Haibo Qiu, M.D., Ph.D., Ke Xu, M.D., Xuewei Xu, M.D., Hongzhou Lu, M.D., Ph.D., Wenfei Zhu, M.D., Zhancheng Gao, M.D., Nijuan Xiang, M.D., Yinzhong Shen, M.D., Zebao He, M.D., Yong Gu, M.D., Zhiyong Zhang, M.D., Yi Yang, M.D., Ph.D., Xiang Zhao, M.D., Lei Zhou, M.D., Xiaodan Li, M.D., Shumei Zou, M.D., Ye Zhang, M.D., Xiyan Li, M.D., Lei Yang, M.D., Junfeng Guo, M.D., Jie Dong, M.D., Qun Li, M.D., Libo Dong, M.D., Yun Zhu, M.D., Tian Bai, M.D., Shiwen Wang, M.D., Pei Hao, M.D., Weizhong Yang, M.D., Yanping Zhang, M.D., Jun Han, M.D., Hongjie Yu, M.D., Dexin Li, M.D., George F. Gao, Ph.D., Guizhen Wu, M.D., Yu Wang, M.D., Zhenghong Yuan, Ph.D., and Yuelong Shu, Ph.D.

- 2013年2月26日, 上海第一例感染
- 3月31日, 确诊H7N9病毒感染
- 4月11日,国家CDC等单位在 *New England Journal of Medicine* 发表第一篇研究论文

Table 1. Demographic, Epidemiologic, and Virologic Characteristics and Complications, Treatment, and Clinical Outcomes of Three Patients Infected with Avian-Origin Influenza A (H7N9) Virus.*

| Characteristic | Patient 1 | Patient 2 | Patient 3 |
|---|---|---|---|
| Age (yr) | 87 | 27 | 35 |
| Sex | Male | Male | Female |
| Occupation | Retired | Butcher | Housewife |
| Underlying conditions | COPD, hypertension | Hepatitis B | Depression, hepatitis B, obesity |
| Area of origin | Shanghai | Shanghai | Anhui |
| Exposure to chicken market in past 7 days | No | Yes | Yes |
| Date of illness onset | February 18, 2013 | February 27, 2013 | March 13, 2013 |
| Date of admission | February 25, 2013 | March 4, 2013 | March 19, 2013 |
| Admission to ICU | None | March 6, 2013 | March 20, 2013 |
| Date of specimen collection | February 26, 2013 | March 5, 2013 | March 20, 2013 |
| Date of laboratory confirmation of virus | March 30, 2013 | March 30, 2013 | March 30, 2013 |
| Viral isolation | A/Shanghai/1/2013 (H7N9) | A/Shanghai/2/2013 (H7N9) | A/Anhui/1/2013 (H7N9) |
| Complications | | | |
| Septic shock | No | No | Yes |
| ARDS | Yes | Yes | Yes |
| Acute renal damage | No | No | Yes |
| Encephalopathy | Yes | No | Yes |
| Rhabdomyolysis | No | Yes | Yes |
| Secondary infections | No | Yes† | Yes† |
| Oxygen therapy | Mask‡ | Mechanical ventilation | Mechanical ventilation |
| Extracorporeal membrane oxygenation | No | No | Yes |
| Continuous renal-replacement therapy | No | No | Yes |
| Antibiotic therapy | Imipenem, moxifloxacin, and vancomycin | Cefoperazone–sulbactam, levofloxacin, and linezolid | Imipenem and vancomycin |
| Antiviral agent§ | Oseltamivir (started on day 7) | Oseltamivir and amantadine (started on day 7) | Oseltamivir (started on day 8) |
| Glucocorticoid therapy | Yes | Yes | Yes |
| Intravenous immune globulin therapy | Yes | Yes | Yes |
| Length of stay in hospital | 6 days | 6 days | 29 days |
| Date of death | March 4, 2013 | March 10, 2013 | April 9, 2013 |

* ARDS denotes acute respiratory distress syndrome, and COPD chronic obstructive pulmonary disease.
† Patients 2 and 3 were infected with carbapenem-resistant *Acinetobacter baumannii*.
‡ This patient refused intubation and mechanical ventilation.
§ Oseltamivir was administered in Patient 1 on February 25, 2013; the viral sample was obtained after two doses of oseltamivir were administered. Oseltamivir was administered in Patient 2 on March 6, 2013, and in Patient 3 on March 21, 2013.

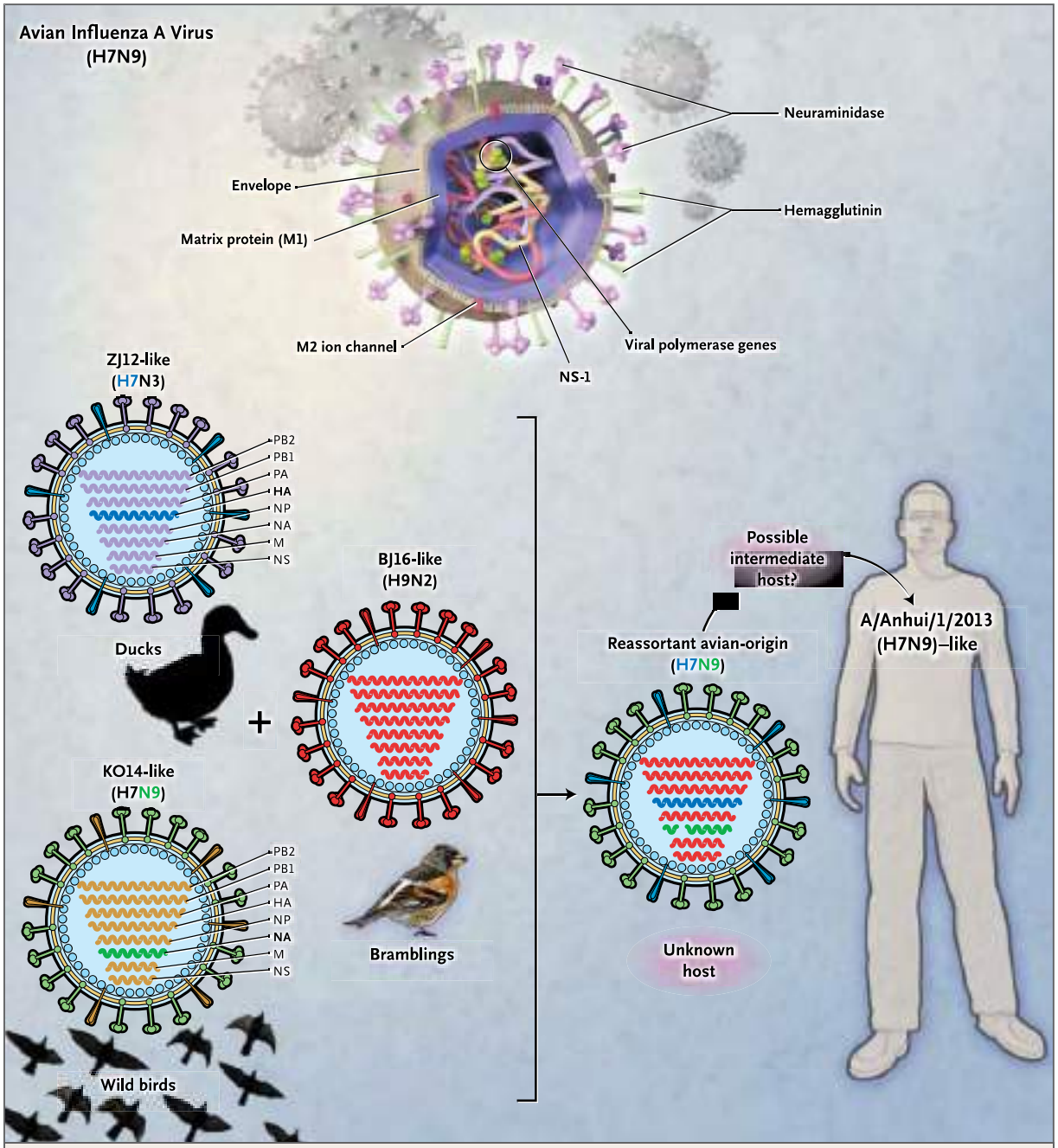



**Figure 2. Hypothetical Host and Lineage Origins of the Gene Segments of the Novel Reassortant Human Influenza A (H7N9) Viruses.**
The colors of the gene segments in the ovals indicate their origin. BJ16 denotes A/brambling/Beijing/16/2012, KO14 A/wild bird/Korea/A14/2011, and ZJ12 A/duck/Zhejiang/12/2011.

- HA基因最相近于浙江鸭群中的H7N3流感病毒
- NA基因最相近于经韩国野鸟中H7N9流感病毒
- 内部基因来源于禽类中H9N2流感病毒

Invited Article
Virology

Chinese Science Bulletin

June 2013 Vol.58 No.16: 1857–1863
doi: 10.1007/s11434-013-5873-4

# Isolation and characterization of H7N9 viruses from live poultry markets—Implication of the source of current H7N9 infection in humans

SHI JianZhong[1†], DENG GuoHua[1†], LIU PeiHong[2], ZHOU JinPing[2], GUAN LiZheng[1], LI WenHui[1], LI XuYong[1], GUO Jing[1], WANG GuoJun[1], FAN Jun[1], WANG JinLiang[1], LI YuanYuan[1], JIANG YongPing[1], LIU LiLing[1], TIAN GuoBin[1], LI ChengJun[1*] & CHEN HuaLan[1*]

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[2] *Shanghai Animal Disease Control Center, Shanghai 201103, China*

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- 4月18日，科学通报发表了哈兽研陈华兰教授团队的工作。在活禽市场发现病毒。
- 4月25日,李兰娟院士团队在*Lancet*杂志报道了新的H7N9病例。同时，在家禽市场中也分离到了病毒。
- 提出并确认了由禽到人的传播路径

# Human infections with the emerging avian influenza A H7N9 virus from wet market poultry: clinical analysis and characterisation of viral genome

*Yu Chen*, Weifeng Liang*, Shigui Yang*, Nanping Wu*, Hainv Gao, Jifang Sheng, Hangping Yao, Jianer Wo, Qiang Fang, Dawei Cui, Yongcheng Li, Xing Yao, Yuntao Zhang, Haibo Wu, Shufa Zheng, Hongyan Diao, Shichang Xia, Yanjun Zhang, Kwok-Hung Chan, Hoi-Wah Tsoi, Jade Lee-Lee Teng, Wenjun Song, Pui Wang, Siu-Ying Lau, Min Zheng, Jasper Fuk-Woo Chan, Kelvin Kai-Wang To, Honglin Chen, Lanjuan Li, Kwok-Yung Yuen*

## Summary

**Background** Human infection with avian influenza A H7N9 virus emerged in eastern China in February, 2013, and has been associated with exposure to poultry. We report the clinical and microbiological features of patients infected with influenza A H7N9 virus and compare genomic features of the human virus with those of the virus in market poultry in Zhejiang, China.

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*These authors contributed equally to this work

# Origin

H7N9禽流感病毒是如何形成的？


A
A/duck/Korea/BC10/2007_H7N3
A/northern pintail/Aomori/1001/2008_H7N7
A/northern pintail/Akita/1367/2008_H7N7
A/duck/Tsukuba/922/2008_H7N7
A/duck/Tsukuba/30/2007_H7N7
A/mallard/Korea/GG2/2007_H7N7
A/wild bird faeces/Korea/HDR22/2006_H7N7
D
A/wild bird faeces/Shihwa/21/2006_H7N3
A/duck/Mongolia/119/2008_H7N9
D
A/duck/Tsukuba/664/2007_H7N7
A/duck/Tsukuba/700/2007_H7N7
A/Northern shoveler/Seongdong/175/2008_H7N3
A/mallard/Korea/GH170/2007_H7N7
A/mallard/Korea/21-9/2008_H7N8
A/duck/Korea/A349/2009_H7N2
A/duck/Korea/A79/2010_H7N7
A/duck/Chiba/20/2009_H7N7
A/duck/Hokkaido/1/2010_H7N7
A/wild bird/Korea/A72/2010_H7N7
A/wild bird/Korea/A330/2009_H7N7
D
A/duck/Shimane/18/2006_H7N7
A/duck/Shiga/B149/2007_H7N7
A/duck/Korea/GJ56/2007_H7N8
A/quail/Thailand/CU-J2882/2009_H7N1
A/duck/Thailand/CU-LM7297T/2010_H7N6
D
A/duck/Shimane/83/2006_H7N3
A/mallard/Korea/5-80/2005_H7N8
W
H
D
A/duck/Jiangxi/1814/2003_H7N7
A/duck/Taiwan/4201/1999_H7N7
A/duck/Hokkaido/143/2003_H7N1
D
A/wild bird faeces/Nakdonggang/2-14/2004_H7N2
A/wild bird faeces/Korea/HDR16/2003_H7N2
W
A/duck/Hokkaido/Vac-2/2004_H7N7
A/duck/Mongolia/867/2002_H7N1
D
A/turkey/Italy/1265/1999_H7N1
A/mallard/Netherlands/12/2000_H7N3
A/turkey/Germany/R11/2001_H7N7
W,T
Long Branch
0·01
B
A/duck/Vietnam/G32/2008_H11N9
A/duck/Vietnam/G30/2008_H11N9
A/wild duck/Korea/SH20-27/2008_H7N9
A/duck/Vietnam/LBM81/2012_H11N9
A/northern pintail/Aomori/1192/2008_H5N9
A/duck/Tsukuba/239/2005_H11N9
A/duck/Tsukuba/164/2005_H11N9
A/sharp-tailed sandpiper/Australia/10/2004_H11N9
A/shore bird/Korea/S8/2006_H11N9
A/sharp-tailed sandpiper/Australia/6/2004_H11N9
A/duck/Hokkaido/W245/2004_H11N9
A/duck/Tsukuba/441/2005_H11N9
A/duck/Chiba/7/2006_H11N9
A/duck/Chiba/11/2006_H11N9
A/duck/Chiba/23/2006_H11N9
A/duck/Chiba/21/2006_H11N9
D
W
A/wild bird/Korea/A3/2011_H7N9
A/spot-billed duck/Korea/47/2011_H7N9
A/mallard/Korea/LBM616/2007_H11N9
A/muscovy duck/Thailand/CU-LM1984/2009_H4N9
A/duck/Hunan/1590/2007_H6N9
D
A/Anas crecca/Spain/1460/2008_H7N9
A/mallard/PT/26153/2007_H11N9
W
A/mallard/Switzerland/WV1071028/2007_H11N9
A/mallard/Czech Republic/15962-1T/2010_H6N9
A/mallard/Czech Republic/15902-18K/2009_H11N9
A/goose/Czech Republic/1848-T14/2009_H7N9
A/goose/Czech Republic/1848-K9/2009_H7N9
W,G
A/goose/Zambia/2009_H11N9
A/duck/Zambia/11/2009_H11N9
D,G
A/mallard/Sweden/65/2002_H10N9
A/mallard/Sweden/36/2003_H11N9
A/mallard/Sweden/103/2005_H2N9
A/mallard/Netherlands/42/2006_H11N9
A/mallard/Sweden/49/2005_H2N9
A/mallard/Sweden/90/2005_H11N9
A/mallard/Sweden/72/2005_H2N9
A/mallard/Sweden/49/2002_H5N9
A/mallard/Sweden/48/2002_H11N9
W
A/mallard/Netherlands/13/2001_H2N9
A/mallard/Netherlands/12/1999_H2N9
A/mallard/Netherlands/11/1999_H2N9
A/mallard/Netherlands/11/1999_mixed
W
A/duck/Nanchang/4-184/2000_H2N9
A/duck/Nanchang/2-0486/2000_H2N9
A/duck/Nanchang/2-0485/2000_H2N9
D
A/pintail/Shimane/324/1998_H1N9
A/swan/Shimane/227/2001_H3N9
A/swan/Shimane/190/2001_H6N9
A/wild duck/Shantou/311/2001_H6N9
A/mallard/New Zealand/1365-350/2005_H6N9
A/mallard/New Zealand/1440-365/2005_H11N9
W
A/common teal/Netherlands/9/2000_H11N9
A/duck/Siberia/700/1996_H11N9
A/duck/Vietnam/OIE-2386/2009_H11N9
0·02

**Lancet**, 2013