

## It is not just AIV: From avian to swine-origin influenza virus

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In March and early April 2009, a new swine-origin influenza A (H1N1) virus (S-OIV) emerged in Mexico and the United States. The virus spreads worldwide by human-to-human transmission. Within a few weeks, it reached a pandemic level. The virus is a novel reassortment virus. It contains gene fragments of influenza virus of swine, avian and human emerged from a triple reassortant virus circulating in North American swine. The source triple-reassortant itself comprised genes derived from avian (PB2 and PA), human H3N2 (PB1) and classical swine (HA, NP and NS) lineages. In contrast, the NA and M gene segments have their origin in the Eurasian avian-like swine H1N1 lineage (Figure 1) [1].

Last year, a special issue in *Science in China Series C: Life Science* was published, which gave an overview of H5N1 avian influenza virus, esp. addressing the related research in China [2–10]. Yet, after the emergence of avian influenza virus we have swine-origin virus in 2009. Animal-origin zoonotic influenza viruses are historically a problem as even the 1918 flu pandemic had avian origin. In the special issue, SHU Yelong [2] from the China CDC and CHAN Paul K S [3] from the Chinese University of Hong Kong, reviewed the epidemiological, clinical, virological characteristics of H5N1 virus in the mainland and Hong Kong SAR, China, respectively. Clearly, the understanding on these aspects of H5N1 virus is the prerequisite to place the virus under close surveillance and control, and guarantees preparation for and dealing with a potential new pandemic. We [4] reviewed our current knowledge of interspe-

cies transmission and host factors involved in restriction of the interspecies transmission. The results indicate that not only the virus receptor usage but also numerous other host factors interacting with the virus or virus components are determinants for the viral host range and transmission restriction.

SHAW Pang-Chui *et al.* [5] from the Chinese University of Hong Kong revisited the structure of nucleoprotein (NP). Structural biology gives more direct and visible explanation of biological events. The revealed NP structure here enhances our understanding of the regions which may be involved in RNA binding and oligomerization properties of NP. LIU Yingfang and colleagues [6] from the Institute of Biophysics, Chinese Academy of Sciences, present crystal structures of some parts of the polymerase complex, PA alone or PA with part of PB1. This breakthrough fills the gap in our understanding of the most crucial parts in the replication of the influenza virus and satisfies our longing for learning the structurally and functionally important regions of this complex for inhibitor design. New drug target discovery is always our ultimate goal for the control of influenza virus as current-drug resistance is arising.

WANG Hongliang and JIANG Chengyu [7] from the Peking Union Medical College, Chinese Academy of Medical Sciences, described our current understanding of the molecule pathogenesis of H5N1 in human infection and present their work on the clathrin-dependent endocytosis of H5N1 influenza virus [8], which confirmed that H5N1 followed the same rule as other subtypes for endocytosis. CHEN Hualan from the Harbin Veterinary Research Institute, Chinese Academy of Agriculture Sciences, discusses the situa-

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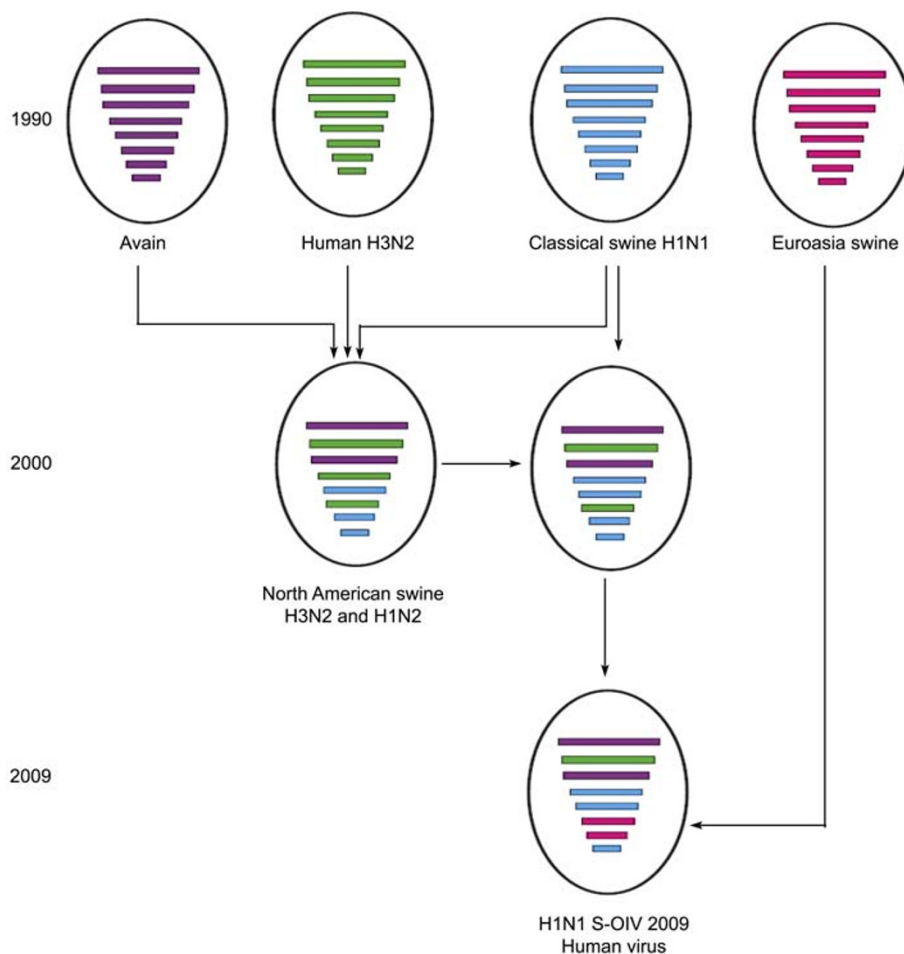
tion of animal infection and the control in China [9]. LIU Di *et al.* [10] from the CAS Key Laboratory of Pathogenic Microbiology and Immunology, described the construction of the website for Avian Flu Information to provide influenza virus sequence database and a bioinformatic platform. This effort facilitates the fighting against H5N1 avian influenza in a comprehensive way and helps for the combat of the current H1N1 as well.

It is not a surprise that we have to experience the swine-origin influenza pandemic after the avian-origin H5N1 influenza breakout as the influenza virus infection in the swine population has been frequently detected [11]. The remarkable ability of influenza virus to mutate (antigen drift) as a RNA virus and its special reassortment mechanism (antigen shift) enable it adapt to novel hosts. While the 1918 virus was derived from avian virus mutation, the 1957 and 1968 pandemic viruses were all generated by reassortment of avian virus with human virus [12,13]. Domestic pigs have been described as a hypothetical 'mixing-vessel', mediating the emergence of new influenza viruses with avian or avian-like genes into the human population by reassortment, and triggering a pandemic associated with antigenic

shift [14]. So the nature of influenza virus determines that the occurrence of influenza pandemic is inevitable.

Although 2009 H1N1 S-OIV emerged as a new pandemic influenza virus, the production of vaccine is timely enough to combat it. In China, till now more than 20 million people have accepted vaccination. In the effort to develop vaccine against the 2009 A(H1N1) influenza viruses, an exciting achievement was made by ZHU Fengcai's group from the Jiangsu Provincial Center for Disease Control and Prevention, who organized a large clinical trail to evaluate the safety and of immunogenicity of an inactivated split-virus vaccine. The results of this trail were reported in *New England Journal of Medicine*, showing that the vaccine was tolerated well and induced high titer of antibodies [15].

Recently, a mutation (D225G/E) in HA protein of 2009 H1N1 S-OIV has been identified. This mutation may make the virus bind to 2, 3-linkage receptors. Since 2, 3-linkage receptors distribute mainly in human lung [16], the mutated virus tends to infect lung instead of the upper respiratory tract. This mutation may also reduce the transmission of the virus, as in the case of H5N1 virus. The real significance of this mutation remains to be elucidated.



**Figure 1** Reassortment events in the evolution of the 2009 influenza A (H1N1) virus

As discussed above, another influenza pandemic is an inevitable scenario in the future, and therefore comprehensive strategies should be applied. Vaccine is still the most promising way to fight against a pandemic. The current vaccine strategy utilizes inactivated vaccines which are made from growing viruses in the allantoic cavity of embryonated hen's eggs. This technology is constrained by the need for specialized egg-based production facilities and long production times required for the creation of a new vaccine. Recent advances include the use of reverse genetics to express the HA and NA of extremely-virulent viruses, such as H5N1, with the internal proteins of standard vaccine strains in order to enable the virus to replicate without killing the chick embryo, as well as the development of cell culture systems for high-titer virus growth [17]. To make full preparation for a new pandemic, we should combine all strategies including vaccine development, drug stock-piling and close surveillance worldwide.

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