Special Topic

• Editorial •

The challenges of avian influenza virus: mechanism, epidemiology and control

Early 2009, eight human infection cases of H5N1 highly pathogenic avian influenza (HPAI) virus, with 5 death cases, were reported in China. This again made the world alert on a possible pandemic worldwide, probably caused by avian-origin influenza virus. Again H5N1 is in the spotlight of the world, not only for the scientists but also for the ordinary people. How much do we know about this virus? Where will this virus go and where did it come? Can we avoid a possible pandemic of influenza? Will the human beings conquer this devastating agent? Obviously we can list more questions than we know the answers.

Influenza virus, as a pathogenic entity for chickens, has been known since the 19th century. However in 1997, the first human infection case with fatality and the virus identified as strain H5N1 were found in Hong Kong SAR (Special Administrative Region), China, reminding us the virus is expanding its host range from birds to mammals. In 2003, during the outbreak of SARS (Severe acute respiratory syndrome), one human fatal case was surprisingly diagnosed with an H5N1 virus isolation. This is the first human infection case in the mainland China. Now we know many countries (15 countries up to early 2009) have human infections of H5N1 influenza virus. These countries have become epicenters of influenza viruses, including seasonal influenza in addition to the H5N1 virus. In 2005, even the natural reservoir host, migratory birds were found infected with an outbreak of more than 6000 dead birds involved. Therefore in this special topic, we invite scientists from Hong Kong and mainland China to review recent progress in the H5N1-related research field with seven reviews and one manuscript of original studies on endocytosis and H5N1 influenza virus. The Website for Avian Flu Information consisting of avian influenza information from broad aspects is also introduced. It is not only a database and a platform for the researchers but also a knowledgebase for the public.

First we invite two prominent scientists, Yuelong SHU and Paul CHAN, from China CDC and the Chinese University of Hong Kong respectively to overview the situation of human infection of H5N1 in mainland China and the experience in Hong Kong. They summarize the frontline epidemiological, clinical and virological characteristics of human avian influenza virus infections based on the national surveillance system in mainland China and give a chronological and archival description of the events in Hong Kong. These accounts would greatly be appreciated for the future preparedness of possible pandemics. From the current human reported H5N1 virus infection cases, most of the patients could trace back with contacts of birds (chicken or ducks) though there were some reports with evidence of limited human-to-human transmission. Therefore domestic or wild bird infection control is the key for the H5N1 human infection. Hualan CHEN from Harbin Veterinary Research Institute, Chinese Academy of Agricultural Sciences, discusses the situation of animal infection and the control in China.

As we know more and more species, especially some mammalian species such as cats and tigers, are found victims or carriers of H5N1, the expansion of the host range and interspecies transmission of H5N1 virus is worrisome. The mechanism underlying this change is elusive and scientists are working together to tackle this problem from our understanding of the virus itself and the host factors affecting this change. George F. GAO, Frank LIU and colleagues from CAS Key Laboratory of Pathogenic Microbiology and Immunology review our current knowledge of the interspecies transmission and host factors involved: from virus receptor usage to host proteins interacting with the virus or virus components.

Basic research always gives us some tantalizing hope for the control of virus infection. Nucleoprotein (NP) is an important structural protein of influenza virus, being the key component of the ribonucleoprotein complex. The structure of NP is revisited by Andy NG, Jia-Huai WANG and Pang-Chui SHAW from Dana-Farber Cancer Institute and the Chinese University of Hong Kong. Correlations are made between the sequence conservation and the atomic structure. This provides the basis for identifying structurally and functionally important regions for inhibitor design. Crystal structures of some parts of the polymerase complex, PA alone or PA with part of PB1, have been solved. Zihe

RAO, Yingfang LIU and colleagues from Institute of Biophysics, CAS, Tsinghua University and Nankai University, provide an overview of the structure and potential target for the new drug design. For a long time the drug target for influenza viruses was basically limited to two proteins, hemagglutinin (HA) and neuraminidase (NA). Hopefully, the basic findings on nucleoprotein and polymerase will lead to some new drug leads.

Clinically the human cases of H5N1 infection manifest some ARDS (acute respiratory distress syndrome) symptoms, similar to SARS infection. Therefore unraveling the molecular pathogenesis mechanism will help save life. Chengyu JIANG, from Peking Union Medical College, Chinese Academy of Medical Sciences, who has long been involved in the study of molecular pathogenesis of SARS, describes our current understanding of the molecular pathogenesis of H5N1 in human infection and presents their recent work on the clathrin-dependent endocytosis of H5N1 influenza virus.

H5N1 virus research is a scientifically fascinating field and a much-needed field for life-saving. In the future we ought to know why and how H5N1 virus expands its host range. Compared to SARS, H5N1 is more complicated. Is there any chance human beings will be in a position to conquer this devastating virus? The understanding of H5N1 virus also helps us to combat other influenza viruses, such as the swine flu that has recently surfaced from Mexico. Though readers would see we have made some progress in the field, this tantalizing record is far from our ultimate goal of control of this virus. Molecular pathogenesis, virus evolution, human immune response and vaccine development, drug discovery and other basic research must be addressed.

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Professor George F. GAO obtained his Ph.D (DPhil) degree from Oxford University, UK and did his postdoc work in both Oxford University and Harvard University. He is now professor and director in CAS Key Laboratory of Pathogenic Microbiology and Immunology, Institute of Microbiology, Chinese Academy of Sciences. He is also the deputy director-general of Beijing Institutes of Life Science, Chinese Academy of Sciences, and executive vice-president of Chinese Society of Biotechnology. His research interests include the molecular mechanism of interspecies transmission of pathogens, molecular virology and molecular immunology. His group research is now focusing on the avian influenza virus and the molecular/structural basis of recognition of T cell receptors to peptide-MHC complexes. He has published more than 110 refereed papers, several books or book chapters and has obtained 12 UK, US and Chinese patents.

Professor P.C. SHAW obtained his Ph.D degree from Imperial College, University of London, UK. He is now professor and Chairman in Department of Biochemistry of the Chinese University of Hong Kong. He is also the director of Centre for Protein Science and Crystallography and deputy director of the Institute of Chinese Medicine. His research interests include the structure-function study of proteins with pharmacological significance and the quality control of Chinese medicinal material. His group is now employing a battery of biochemical and biophysical techniques to find and characterize selected influenza proteins and their interacting partners. He has published more than 150 refereed papers, two books and has obtained two US and two Chinese patents.

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