

Guangxiang Luo ORCID iD: 0000-0002-0354-6020

Editorial

Global Health Concern Stirred by Emerging Viral Infections

Guangxiang (George) Luo¹ and Shou-Jiang Gao²

¹Department of Microbiology, University of Alabama at Birmingham School of Medicine, Birmingham, AL35294, USA; ²UPMC Hillman Cancer Center, Department of Microbiology and Molecular Genetics, University of Pittsburgh, Pittsburgh, PA15213, USA

Keywords:

Coronavirus, Virus classification, Antiviral agents, Genetic variability, Evolution, Recombination, Evolution, Recombinant virus, Genetics, Tissue tropism, Pathogenesis

Emerging viral infections continue to pose a major threat to global public health. In 1997, a highly pathogenic avian influenza A (H5N1) virus was found to directly
This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/jmv.25683.

This article is protected by copyright. All rights reserved.

spread from poultry to humans unlike previously reported transmission routes of human-to-human and livestock-to-human, stirring a grave concern for a possible influenza pandemic¹. Several other avian influenza A virus subtypes (H7N9, H9N2, and H7N3) were also associated with human disease, raising an alarm that all subtypes of influenza A virus circulating in domestic and wild birds and livestock can potentially spill over to humans, resulting in pandemics²⁻⁴. In 1999, a newly emerged paramyxovirus termed Nipah virus was identified as the cause of a severe encephalitis outbreak occurred in Malaysia and Singapore⁵. Soon after, the outbreak of severe acute respiratory syndrome (SARS) happened during 2002-2003 in China was caused by a novel coronavirus designated SARS-CoV, spreading to 37 countries and resulting in a total of more than 8,000 infections and 774 deaths (9.6% mortality rate)⁶. More recent years have witnessed the emergence of several other important viral diseases, including a pandemic influenza caused by a swine H1N1 influenza A virus in 2009⁷, the Middle East respiratory syndrome (MERS) caused by a new deadly (>30% mortality) MERS-CoV in 2012⁸, the outbreak of a severe fever with thrombocytopenia syndrome (SFTS) resulted from the infection of a previously unrecognized SFTS bunyavirus in 2010⁹, the Ebola outbreak in West Africa during 2014-2016¹⁰, and the microcephaly crisis associated with Zika virus infection in 2015¹¹. Clearly, emerging and reemerging viral pathogens constantly pose a threat to public health.

The most recent outbreak of viral pneumonia in the city of Wuhan, China, which started in the middle of December, 2019 and now is spreading to many cities in China as well as to Hong Kong, Singapore, Thailand, and Japan, serves as an important reminder of our vulnerability to emerging viral infections. A total of 291 patients infected with the

newly identified coronavirus termed 2019-nCoV in China have been reported as of January 21, 2020. Initially, there was no clear evidence for person-to-person transmission. In the last few days, however, person-to-person spread of the 2019-nCoV has been confirmed, as shown by new cases of viral pneumonia among family members and health care providers through close contacts. In this issue, Lu, Stratton, and Tang have provided detailed clinical and epidemiological information about this new viral pneumonia outbreak in Wuhan, China¹².

In the last few weeks, rapid progresses have been made in the identification of viral etiology, isolation of infectious virus, and the development of diagnostic approaches, thanks to many dedicated scientists in China and also technology and infrastructure investment made by Chinese government in recent years since SARS outbreak in 2003. The novel 2019-nCoV was identified from patient samples by high-throughput sequencing of the viral RNA genome. More importantly, the infectious coronavirus was also isolated from one patient, which exhibits morphological characteristics of a typical coronavirus as determined by electronic microscopy. The availability of viral RNA genome sequence has fostered the development of new genetic tests based on the reverse-transcription polymerase chain reaction (RT-PCR) technology¹³. Several RT-PCR kits have been developed and are currently being used for diagnosis of the 2019-nCoV infection. In this issue, Zhang et al. review the recent advances made in the detection of emerging and reemerging viral infections¹³. A minireview by Chen et al. describes the properties of coronavirus and the underlying molecular mechanism of viral replication and pathogenesis. In another minireview, Li et al. provide an overview on the host immune response to coronavirus infection.

Interestingly¹⁴, Ji et al. have performed an evolutionary sequence analysis suggesting that snake is the most likely reservoir for the 2019-nCoV¹⁵. Consistent with this novel idea, snake was indeed sold at the Huanan Seafood Wholesale Market where many initial patients had history of exposure to the virus prior to their illness¹². It will be interesting to determine if 2019-nCoV can be isolated and/or infect snakes. Other poultry and exotic animals such as bats and marmots were also sold in the Seafood Market and could potentially carry and spread the newly discovered 2019-nCoV to humans. Future investigations are warranted to further confirm animal reservoir of the 2019-nCoV. Another interesting finding from their sequence analysis is the identification of recombination of the bat coronavirus with an origin-unknown coronavirus within the spike glycoprotein, which may explain the reduced disease severity and limited person-to-person spread. The question arises whether adaptation of the 2019-nCoV in humans will enhance viral virulence and/or person-to-person spread.

Although rapid achievements were accomplished within such a short period, there are still many important questions remained to be answered. Further characterization of the isolated virus in cell culture and animal models will provide valuable information as to its causal relationship with the viral pneumonia outbreak. More significantly, the confirmation of animal reservoir for the 2019-nCoV is critical for intervention and prevention of the outbreak. It is of paramount importance to develop new diagnostic methods for rapid detection of viral infection, including immunoassay for quantification of virus-specific antibodies. Other important scientific questions include viral evolution, virulence factors, and the underlying molecular mechanism of viral replication and pathogenesis. The ultimate control of emerging viral infections requires the discovery and

development of effective vaccines and/or antiviral drugs, which may take years. However, it is possible that some of the licensed antiviral drugs for treatment of other viral infections may also have activity against the 2019-nCoV, as previously reported for MERS-CoV¹⁶. It is worthwhile to evaluate some of existing antiviral drugs in cell culture using the isolated 2019-nCoV. Any resulting drug inhibiting the 2019-nCoV can be used for treatment of 2019-nCoV-infected patients.

References

- 1 Claas, E. C. *et al.* Human influenza A H5N1 virus related to a highly pathogenic avian influenza virus. *The Lancet* **351**, 472-477 (1998).
- 2 Gao, R. *et al.* Human infection with a novel avian-origin influenza A (H7N9) virus. *New England Journal of Medicine* **368**, 1888-1897 (2013).
- 3 Peiris, M. *et al.* Human infection with influenza H9N2. *The Lancet* **354**, 916-917 (1999).
- 4 Tweed, S. A. *et al.* Human illness from avian influenza H7N3, British Columbia. *Emerging infectious diseases* **10**, 2196 (2004).
- 5 Chua, K. *et al.* Nipah virus: a recently emergent deadly paramyxovirus. *Science* **288**, 1432-1435 (2000).

-
- 6 Fouchier, R. A. *et al.* Aetiology: Koch's postulates fulfilled for SARS virus. *Nature* **423**, 240 (2003).
- 7 Vijaykrishna, D. *et al.* Reassortment of pandemic H1N1/2009 influenza A virus in swine. *Science* **328**, 1529-1529 (2010).
- 8 Zumla, A., Hui, D. S. & Perlman, S. Middle East respiratory syndrome. *The Lancet* **386**, 995-1007 (2015).
- 9 Yu, X. J. *et al.* Fever with thrombocytopenia associated with a novel bunyavirus in China. *N Engl J Med* **364**, 1523-1532, doi:10.1056/NEJMoa1010095 (2011).
- 10 Baseler, L., Chertow, D. S., Johnson, K. M., Feldmann, H. & Morens, D. M. The pathogenesis of Ebola virus disease. *Annual Review of Pathology: Mechanisms of Disease* **12**, 387-418 (2017).
- 11 Bogoch, I. I. *et al.* Anticipating the international spread of Zika virus from Brazil. *The Lancet* **387**, 335-336 (2016).
- 12 Lu, H., Stratton, C. W. & Tang, Y. W. Outbreak of Pneumonia of Unknown Etiology in Wuhan China: the Mystery and the Miracle. *J Med Virol*, doi:10.1002/jmv.25678 (2020).
- 13 Zhang, N. *et al.* Recent advances in the detection of respiratory virus infection in humans. *J Med Virol*, doi:10.1002/jmv.25674 (2020).

-
- 14 Geng Li, Y. F., Yanni Lai, Tiantian Han, Zonghui Li, Peiwen Zhou, Pan Pan, Wenbiao Wang, Dingwen Hu, Xiaohong Liu, Jianguo Wu. Coronavirus Infection and Immune Responses. *J Med Virol* (2020).
- 15 Wei Ji, Wei Wang, X. Z., Junjie Zai, Xingguang Li. Homologous recombination within the spike glycoprotein of the newly identified coronavirus may boost cross-species transmission from snake to human. *J Med Virol*, *JMV-20-7886* (2020).
- 16 Cong, Y. *et al.* MERS-CoV pathogenesis and antiviral efficacy of licensed drugs in human monocyte-derived antigen-presenting cells. *PloS one* **13** (2018).