

## Haunted with and hunting for viruses

George Fu GAO<sup>1,2,3\*</sup> & WU Ying<sup>2\*</sup>

<sup>1</sup>Chinese Center for Disease Control and Prevention, Beijing 102206, China;

<sup>2</sup>CAS Key Laboratory of Pathogenic Microbiology and Immunology, Institute of Microbiology, Chinese Academy of Sciences, Beijing 100101, China;

<sup>3</sup>Research Network of Immunity and Health, Beijing Institutes of Life Science, Chinese Academy of Sciences, Beijing 100101, China

Received July 5, 2013

---

**Citation:** Gao G F, Wu Y. Haunted with and hunting for viruses. *Sci China Life Sci*, 2013, 56: 675–677, doi: 10.1007/s11427-013-4525-x

---

Early this year, a subtype influenza A virus (H7N9), was found to cause severe human infections with a 29% case fatality rate (CFR) [1], making it a top-profile piece of news in the world ([www.who.org](http://www.who.org)). The infection was shortly confirmed to be related to live animal markets and poultry dealing [2–4], which led to a close-down of the markets and the outbreak has since been well controlled ([www.chinacdc.cn](http://www.chinacdc.cn)). This is the first case for low pathogenic avian influenza virus (LPAIV) to infect humans in population level, alerting the world that AIV could be a real threat to human beings, including the previous-reported highly pathogenic AIV (HPAIV) H5N1 subtype [5]. Meanwhile the 2012-emerged novel coronavirus in the Middle East has been re-emerging in 2013 with 77 cases of approximately 52% CFR as of 26 June ([www.who.org](http://www.who.org)) [6]. The virus, recently renamed as Middle East respiratory syndrome coronavirus (MERS-CoV), is closely related to severe acute respiratory syndrome coronavirus (SARS-CoV) [7,8]. The devastating outcome of the SARS-CoV in 2003–2004 is still vividly remembered by everyone. Here we also want to remind the world that the novel bunyavirus, severe fever with thrombocytopenia syndrome virus (SFTSV), first isolated in China, has been expanding its border to Japan and USA this year [9]. All of these stories tell that the human beings are haunted with unpredictable viruses.

Meanwhile, we are actively hunting for new viruses, es-

pecially with next-generation sequencing (NGS) for new virus genome discovery, e.g., Ruben Donis et al. [10] sequenced a bat-derived influenza virus genome by using NGS in 2012, raising a serious question as to whether or not our seasonal or pandemic flu might have another reservoir host. Chen and colleagues [11] confirmed the SFTSV independently by using NGS. Indeed, metagenomics analysis has yielded a great deal of new viruses, especially from the environment. Our actively hunting for new viruses has made some significant contributions for our understanding of virus ecology, pathogenesis and interspecies transmission.

*Science China Life Sciences* has focused on this hot topic in the event of the H7N9 outbreak after a comprehensive overview of the topic addressing HPAIV H5N1 in 2009 in the journal [12–14]. In this issue, six groups have been invited to present their recent findings on the emerging viruses, in addition to a previous report on H7N9 [3].

Shi [15] reviewed recent discoveries of new viruses or virus genomes from bat. Bat is believed to harbor many more viruses than we ever thought as a reservoir host or even a susceptible host [16]. After the SARS-CoV virus, we have been actively seeking for new coronaviruses from bat and have yielded many of them, including potential human infecting HKU-1, 4, 5 and 9 [17,18]. Recent MERS-CoV infection is another example for severe disease caused by used-to-be-less pathogenic coronaviruses. Shi and colleagues [19] by using NGS have discovered many unknown

---

\*Corresponding author (email: [gaofu@chinaacdc.cn](mailto:gaofu@chinaacdc.cn); [wuying@im.ac.cn](mailto:wuying@im.ac.cn))

animal viruses from bat, especially some important paramyxoviruses and reoviruses. Filovirus has also been identified in bat with potential severe outcomes. Lyssaviruses (with many genotypes, including rabies virus) in the Rhabdoviridae family have been linked with severe fatal human cases, even in the developed countries, including Australia, with the bites of bats in the city [20,21]. The potential roles of these viruses in bats for interspecies transmission are yet to be elucidated.

Tan and colleagues [22] specifically focused on the newly-emerged MERS-CoV. The virus was identified in 2012 in the Middle East with some exported cases to Europe. In 2013 the virus has been re-emerging and expanding its borders to more European countries. In the initial diagnosis, the pan-coronavirus real-time reverse transcription polymerase chain reaction (RT-PCR) assay played a very important role for the identification of the causative agents. By using this method, scientists detected an expected-size PCR fragment for the corresponding conserved region of ORF1b of the replicase gene of a coronavirus. This is another example that molecular biology methods played for the discovery of new pathogens. Soon the receptor used by MERS-CoV to enter the host cells was identified [23] and the molecular basis of the receptor binding to the virus was also elucidated recently [8].

Enterovirus has been known as serious human pathogens for a long time but their significance to the public health has been emphasized by the emergence of enterovirus 71 in 1998 as a serious pathogenic agents for children in Taiwan [24] and re-emerged in mainland China in 2008 [25]. In this issue, Duan and colleagues [26] summarized the findings of new enteroviruses by using NGS. Because of the application of new NGS technology they also challenged the Koch's postulates. A new model of Koch's postulates, named the metagenomic Koch's postulates, has provided guidance for the study of the pathogenicity of novel viruses. The review also provided a detailed description of the NGS and related molecular methods for the virus discovery followed by a list of new enteroviruses found in human feces. These include viruses in the family of Picornaviridae, Parvoviridae, Circoviridae, Astroviridae and Polyomaviridae.

Yu Xue-Jie and colleagues [27] reviewed the new bunyavirus, SFTSV, identified in China. As the virus discoverers, they have overviewed the whole process of the discovery, which is helpful and meaningful for the new virus discoveries in the future. The disease caused by SFTSV, with a CFR of 12%, had been in China for a couple of years before the causative agent was finally identified. There are still a lot of questions remained unknown for this new virus and vigorous studies are in great need. The transmission route of the virus has not been clarified but tick as vector is suspected. Domestic and wild animals, e.g., goats, boars, cattle and dogs, are believed to be the virus-amplifying hosts. Therefore the effective control measures are still under evaluation. Vaccines protecting the SFTSV infection are under

its way in Chinese Center for Disease Control and Prevention. Recently a similar virus has been identified in both Japan and USA (a new name of Heartland virus was proposed for the US virus) [9].

In addition to new viruses infecting human beings, some new viruses infecting animals but their public health significance needing to be further evaluated, have also been discovered. The new flavivirus, duck egg-drop syndrome virus (DEDSV), is a good example. Su and colleagues [28] reviewed the characterization of the DEDSV and its disease form in this issue. The virus was found closely-related to a long-time-known virus, Tembusu virus [29,30]. Initially, the disease was only found in egg-raising ducks but soon it was found in pigeons, chickens and geese [31,32]. Yet the transmission vector, though mosquitoes are suspected, has not been identified. Due to the public health concerns of its related viruses, potential human infection of DEDSV should be evaluated.

Research on insect viruses is reviving in recent years. In this issue, Zhou and colleagues [33] reviewed the newly-identified insect viruses in China. Insects are the largest group of animals on the Earth therefore they also carry many more viruses. Studies on these viruses can provide useful knowledge for our understanding about animal or human infecting viruses. More importantly, modification and application of insect-infecting viruses can be used as effective biologicals for the control of insect pest. The new viruses identified include Wuhan nodavirus (WhNV), a member of family Nodaviridae; *Dendrolimus punctatus* tetravirus (DpTV), a new member of the genus *Omegatetravirus* of the family Alphanodaviridae; *Ectropis obliqua* picorna-like virus (EoV), a positive-strand RNA virus causing a lethal granulosis infection in the larvae of the tea looper (*Ectropis obliqua*), the virus a member of the Flaviviridae family.

While we are enjoying ourselves with the civilization of modern societies, the ecology has ever been changing. Human beings encounter more ecology-climate-changing problems, including the zoonotic pathogens. We have to face some unknown pathogenic agents passively. To get ourselves well prepared we also ought to actively hunt for unknown pathogens. Prediction and pre-warning can only be realized by knowing more about the unknown. This is especially true for infectious agents.

- 1 Gao R B, Cao B, Hu Y W, et al. Human infection with a novel avian-origin influenza A (H7N9) virus. *N Engl J Med*, 2013, 368: 1888–1897
- 2 Chen Y, Liang W, Yang S, et al. Human infections with the emerging avian influenza A H7N9 virus from wet market poultry: clinical analysis and characterisation of viral genome. *Lancet*, 2013, 381: 1916–1925
- 3 Li J, Yu X F, Pu X Y, et al. Environmental connections of novel avian-origin H7N9 influenza virus infection and virus adaptation to the human. *Sci China Life Sci*, 2013, 56: 485–492
- 4 Liu D, Shi W F, Shi Y, et al. Origin and diversity of novel avian influenza A H7N9 viruses causing human infection: phylogenetic,

- structural, and coalescent analyses. *Lancet*, 2013, 381: 1926–1932
- 5 Gao G F, Sun Y. It is not just AIV: from avian to swine-origin influenza virus. *Sci China Life Sci*, 2010, 53: 151–153
  - 6 Zaki A M, van Boheemen S, Bestebroer T M, et al. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med*, 2012, 367: 1814–1820
  - 7 Lu G, Liu D. SARS-like virus in the Middle East: a truly bat-related coronavirus causing human diseases. *Protein Cell*, 2012, 3: 803–805
  - 8 Lu G, Hu Y, Wang Q H, et al. Molecular basis of novel human coronavirus MERS-CoV bound to its receptor CD26. *Nature*, 2013, doi: 10.1038/nature12328
  - 9 Wu Y, Gao G F. Severe fever with thrombocytopenia syndrome virus expands its borders. *Emerg Microbes Infect*, 2013, in press
  - 10 Tong S, Li Y, Rivaller P, et al. A distinct lineage of influenza A virus from bats. *Proc Natl Acad Sci USA*, 2012, 109: 4269–4274
  - 11 Xu B L, Liu L C, Huang X Y, et al. Metagenomic analysis of fever, thrombocytopenia and leukopenia syndrome (FTLS) in Henan Province, China: discovery of a new bunyavirus. *PLoS Pathog*, 2011, 7: e1002369
  - 12 Chen H L. H5N1 avian influenza in China. *Sci China Ser C-Life Sci*, 2009, 52: 419–427
  - 13 Liu D, Liu Q H, Wu L H, et al. Website for avian flu information and bioinformatics. *Sci China Ser C-Life Sci*, 2009, 52: 470–473
  - 14 Liu D, Liu X L, Yan J H, et al. Interspecies transmission and host restriction of avian H5N1 influenza virus. *Sci China Ser C-Life Sci*, 2009, 52: 428–438
  - 15 Shi Z L. Emerging infectious diseases associated with bat viruses. *Sci China Life Sci*, 2013, 56: 678–682
  - 16 Shi Z L. Bat and virus. *Protein Cell*, 2010, 1: 109–114
  - 17 Woo P C, Lau S K, Lam C S, et al. Discovery of seven novel mammalian and avian coronaviruses in the genus *Deltacoronavirus* supports bat coronaviruses as the gene source of Alphacoronavirus and Betacoronavirus and avian coronaviruses as the gene source of Gammacoronavirus and Deltacoronavirus. *J Virol*, 2012, 86: 3995–4008
  - 18 Woo P C, Wang M, Lau S K, et al. Comparative analysis of twelve genomes of three novel group 2c and group 2d coronaviruses reveals unique group and subgroup features. *J Virol*, 2007, 81: 1574–1585
  - 19 Ge X Y, Li Y, Yang X L, et al. Metagenomic analysis of viruses from bat fecal samples reveals many novel viruses in insectivorous bats in China. *J Virol*, 2012, 86: 4620–4630
  - 20 Johnson N, Vos A, Freuling C, et al. Human rabies due to lyssavirus infection of bat origin. *Vet Microbiol*, 2010, 142: 151–159
  - 21 Rupprecht C E, Turmelle A, Kuzmin I V. A perspective on lyssavirus emergence and perpetuation. *Curr Opin Virol*, 2011, 1: 662–670
  - 22 Geng H Y, Tan W J. A novel human coronavirus: Middle East respiratory syndrome human coronavirus (MERS-CoV). *Sci China Life Sci*, 2013, 56: 683–687
  - 23 Raj V S, Mou H, Smits S L, et al. Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. *Nature*, 2013, 495: 251–254
  - 24 Yang F, Jin Q, He Y Q, et al. The complete genome of Enterovirus 71 China strain. *Sci China Ser C-Life Sci*, 2001, 44: 178–183
  - 25 Yang F, Ren L L, Xiong Z H, et al. Enterovirus 71 outbreak in the People's Republic of China in 2008. *J Clin Microbiol*, 2009, 47: 2351–2352
  - 26 Xie G Y, Duan J Z. New strategy for virus discovery: viruses identified in human feces in the last decade. *Sci China Life Sci*, 2013, 56: 688–696
  - 27 Zhang X S, Liu Y, Zhao L, et al. An emerging hemorrhagic fever in China caused by a novel bunyavirus SFTSV. *Sci China Life Sci*, 2013, 56: 697–700
  - 28 Liu P P, Lu H, Li S, et al. Duck egg drop syndrome virus (DEDSV): an emerging Tembusu-related flavivirus in China. *Sci China Life Sci*, 2013, 56: 701–710
  - 29 Liu P P, Lu H, Li S, et al. Genomic and antigenic characterization of the newly emerging Chinese duck egg-drop syndrome flavivirus: genomic comparison with Tembusu and Sitiawan viruses. *J Gen Virol*, 2012, 93(Pt 10): 2158–2170
  - 30 Su J L, Li S, Hu X D, et al. Duck egg-drop syndrome caused by BYD virus, a new Tembusu-related flavivirus. *PLoS ONE*, 2011, 6: e18106
  - 31 Liu M, Chen S Y, Chen Y H, et al. Adapted Tembusu-like virus in chickens and geese in China. *J Clin Microbiol*, 2012, 50: 2807–2809
  - 32 Tang Y, Diao Y, Yu C, et al. Characterization of a Tembusu virus isolated from naturally infected house sparrows (*Passer domesticus*) in Northern China. *Transbound Emerg Dis*, 2012, doi: 10.1111/j.1865-1682.2012.01328.x
  - 33 Qiu Y, Wang Z W, Liu Y X, et al. Newly discovered insect RNA viruses in China. *Sci China Life Sci*, 2013, 56: 711–714

**Open Access** This article is distributed under the terms of the Creative Commons Attribution License which permits any use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.