

# Flu transmission work is urgent

**Yoshihiro Kawaoka** explains that research on transmissible avian flu viruses needs to continue if pandemics are to be prevented.

**H**ighly pathogenic avian H5N1 influenza viruses first proved lethal in humans in 1997 in Hong Kong. Since 2003, 578 confirmed infections have resulted in 340 deaths ([go.nature.com/epb7ts](http://go.nature.com/epb7ts)). Now widespread in parts of south-east Asia and the Middle East, H5N1 viruses have killed or led to the culling of hundreds of millions of birds.

To date, H5N1 viruses have not been transmitted between humans. Some experts have argued that it is impossible. But given the potential consequences of a global outbreak, it is crucial to know whether these viruses can ever become transmissible. Work by my group (accepted by *Nature*) and an independent study (accepted by *Science*) led by Ron Fouchier of the Erasmus Medical Center in Rotterdam, the Netherlands, suggest that H5N1 viruses have the potential to spread between mammals. As the risks of such research and its publication are debated by the community, I argue that we should pursue transmission studies of highly pathogenic avian influenza viruses with urgency.

To determine whether H5N1 viruses could be transmitted between humans, my team generated viruses that combined the H5 haemagglutinin (HA) gene with the remaining genes from a pandemic 2009 H1N1 influenza virus. Avian H5N1 and human pandemic 2009 viruses readily exchange genes in experimental settings, and those from a human virus may facilitate replication in mammals. Indeed, we identified a mutant H5 HA/2009 virus that spread between infected and uninfected ferrets (used as models to study the transmission of influenza in mammals) in separate cages via respiratory droplets in the air. Thus viruses possessing an H5 HA protein can transmit between mammals.

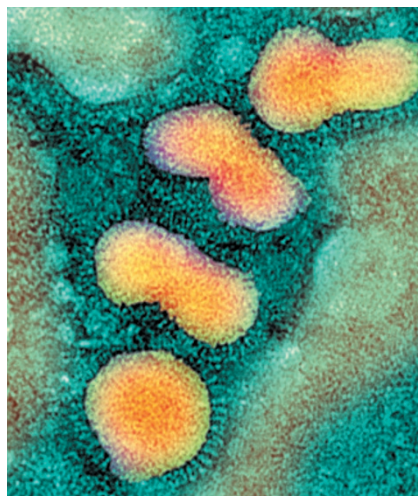
Our results also show that not all transmissible H5 HA-possessing viruses are lethal. In ferrets, our mutant H5 HA/2009 virus was no more pathogenic than the pandemic 2009 virus — it did not kill any of the infected animals. And, importantly, current vaccines and antiviral compounds are effective against it.

Fouchier and his team also generated a transmissible H5 HA-possessing virus — meaning that two independent studies have demonstrated the potential for transmissibility of H5 HA-possessing viruses between ferrets. Their mutant H5 HA virus, generated in the genetic background of an H5N1 virus, did kill infected ferrets.

Some people have argued that the risks

of such studies — misuse and accidental release, for example — outweigh the benefits. I counter that H5N1 viruses circulating in nature already pose a threat, because influenza viruses mutate constantly and can cause pandemics with great losses of life. Within the past century, ‘Spanish’ influenza, which stemmed from a virus of avian origin, killed between 20 million and 50 million people. Because H5N1 mutations that confer transmissibility in mammals may emerge in nature, I believe that it would be irresponsible not to study the underlying mechanisms.

The new work has implications for pan-



**H5N1 avian influenza virus particles.**

demic preparedness. There is an urgent need to expand development, production and distribution of vaccines against H5 viruses, and to stockpile antiviral compounds. Both studies identify specific mutations in HA that confer transmissibility in ferrets to H5 HA-possessing viruses. A subset of these mutations has been detected in H5N1 viruses circulating in certain countries. It is therefore imperative that these viruses are monitored closely so that eradication efforts and countermeasures (such as vaccine-strain selection) can be focused on them, should they acquire transmissibility.

Consequently, I believe that the benefits of these studies — the knowledge that H5 HA-possessing viruses pose a risk and the ability to monitor them and develop countermeasures — outweigh the risks. High biosafety and security standards can be met. Our experiments were carried out in a high-containment facility by a small group of highly trained individuals who

operate under strict procedures to prevent the accidental release of viruses.

However, the US National Science Advisory Board for Biosecurity (NSABB) has recommended that details of both studies (including the mutations that confer transmissibility) should be restricted, and released only to select individuals on a ‘need-to-know’ basis. I acknowledge the advisory role of the NSABB, but I do not concur with its decision.

The primary justification for the NSABB’s recommendation is that publication of our data “could enable replication of the experiments by those who would seek to do harm” ([go.nature.com/nywkdy](http://go.nature.com/nywkdy)). But redacting our papers will not eliminate that possibility — there is already enough information publicly available to allow someone to make a transmissible H5 HA-possessing virus.

The mechanism that the US government proposes for releasing data would also be unwieldy. Thousands of applications to access the research are likely to be filed, and potential background checks would create a huge administrative burden. We cannot afford to lose time if we are to combat emerging pandemic threats. Even if an efficient process can be established, it would be difficult to enforce continued confidentiality in the scientific community.

By contrast, wide data dissemination will attract researchers from other areas to contribute to the field. This is crucial, because new ideas are needed to answer some of the most urgent questions. For example, the specific mutations that we identified suggest that influenza transmission is more complex than anticipated and involves not only the receptor-binding properties of HA, but other biological and physical properties.

The redaction of our manuscript, intended to contain risk, will make it harder for legitimate scientists to get this information while failing to provide a barrier to those who would do harm. To find better solutions to dual-use concerns, the international community should convene to discuss how to minimize risk while supporting scientific discovery. Flu investigators (including me) have agreed to a 60-day moratorium on avian flu transmission research ([go.nature.com/ttivj5](http://go.nature.com/ttivj5)) because of the current controversy. But our work remains urgent — we cannot give up. ■

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