

# THIS WEEK

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## Handle with care

*The possibility that H7N9 avian influenza may evolve sufficiently to cause a pandemic has scientists turning again to controversial research — they must be careful how they justify the risks taken.*

The H7N9 avian flu virus first reported in China in March has so far infected at least 134 people, and killed 43 of them. Thankfully, there are no signs yet that it can easily be transmitted between people — instead it is sporadically being caught by humans through contact with chickens and other fowl.

Researchers now want to make genetically engineered versions of H7N9 that are more transmissible and pathogenic in mammals. In a Correspondence published jointly this week in *Nature* and *Science* (see page 150), 22 scientists, including Ron Fouchier of the Erasmus Medical Center in Rotterdam, the Netherlands, and Yoshihiro Kawaoka of the University of Wisconsin-Madison, argue that such research can help to assess the 'pandemic potential' of H7N9. The dilemma is that should such engineered strains be accidentally or deliberately released from a lab, they could spark a flu pandemic.

The announcement is likely to prompt some replay of last year's debate over the creation by Fouchier and Kawaoka of lab strains of H5N1 that could transmit between ferrets. And it offers the first test of some of the review and oversight structures put in place for this 'gain-of-function' flu research. As this journal has said before, scientists who push for such research should be wary of over-selling the benefits to public health, at least in the short term, as a way to justify the risks taken.

A sense of perspective is crucial here. The long-term benefits of such work are clear — as long as it is done to the highest biosafety standards. It will shed light on, for example, the mechanisms of virus transmissibility and pathogenicity. But the immediate benefits to public health and our short-term ability to counter the threat of H7N9 are less clear-cut. Scientists cannot predict pandemics, so to assess the pandemic potential of viruses — and to decide which strains warrant the manufacture

of trial vaccines — comes down to judgements of relative risk.

Tests of how flu viruses behave in animal models such as ferrets can certainly provide information on the risk of transmissibility and pathogenicity, although it can be difficult to extrapolate those results to humans. A rash of papers this year has shown that H7N9 does have limited airborne transmissibility in ferrets, although the virus is not transmitting between people in the current outbreak in China.

Another way to assess pandemic potential is to monitor wild-type viruses for mutations that allow the virus more ready access to human cells. H7N9 has already acquired some of these mutations, which is why it infects humans more easily than does H5N1. But as researchers pointed out in June, there is no scientific evidence that such mutations predict the risk of a pandemic (D. M. Morens *et al.* *N. Engl. J. Med.* **368**, 2345–2348; 2013). Transmissibility is more complex than that.

In creating mammalian-transmissible versions of H7N9, scientists would go a step further and hope to identify combinations of mutations that could increase virus transmissibility in ferrets or other models. Such work could yield information on the biological principles affecting transmission. But nature could well come up with combinations for transmission that are different from those obtained in experiments.

Following the H5N1 controversy, the US Department of Health and Human Services has introduced an extra layer of review that will apply to anyone seeking funding for work to make mammalian-transmissible strains of H7N9 (see page 151). The risks and benefits of the work will be assessed by a panel of experts in public health, security, risk assessment, law and ethics, and, importantly, any extra steps needed to mitigate biosafety risks will be considered. The way the review handles H7N9 will be an important test of the effectiveness and transparency of this new approach. ■

## Blood ties

*Scientists should give donors more information about how their biospecimens are used.*

The family of Henrietta Lacks is finally getting a say in how researchers can use her cells, six decades after her fatal cervical tumour spawned the HeLa cell line. There is little doubt that the controversy over the case contributed to the decision by the US National Institutes of Health to consult her relatives about the future use of her genome information (see pages 132 and 141). But people who donate samples to biomedical research today are unlikely to find out what happens to their material.

Standards of informed consent have improved since scientists

established HeLa without approval from Lacks or her family. But research participants still have little control over how their tissues and data are used, and often never hear from the researchers again.

Increasingly, volunteers are asked to give 'broad consent' for samples and data to be used in studies that may not have been conceived at the time of donation. In exchange, donors should have the option to learn how their specimens are being used — and even to withdraw consent.

This already happens informally in some studies, but digital technologies could allow researchers to keep patients updated. Imagine the thrill of giving a sample, logging on to a secure website years later and discovering that your specimen helped to develop a skin-cancer treatment.

This continued contact with donors raises issues — not least how to ensure their anonymity. But researchers must also be honest and tell donors that privacy cannot be guaranteed, particularly for highly identifiable genomic information. Some volunteers and their families are rightly proud that they are directly contributing to research. Funders and researchers should give more of them the chance to stay involved. ■