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Scientists create hybrid flu that can go airborne

H5N1 virus with genes from H1N1 can spread through the air between mammals.

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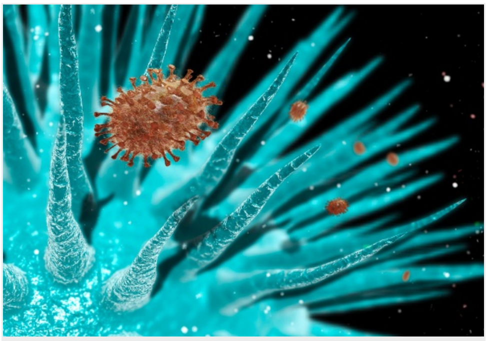
As the world is transfixed by a new H7N9 bird flu virus spreading through China, a study reminds us that a different avian influenza — H5N1 — still poses a pandemic threat.



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Researchers have crossed two strains of avian flu virus to create one that can be transmitted through the air — and possibly settle on the cilia of lung cells as in this conceptual image.

A team of scientists in China has created hybrid viruses by mixing genes from H5N1 and the H1N1 strain behind the 2009 swine flu pandemic, and showed that some of the hybrids can spread through the air between guinea pigs. The results are published in *Science*[1].

Flu hybrids can arise naturally when two viral strains infect the same cell and exchange genes. This process, known as reassortment, produced the strains responsible for at least three past flu pandemics, including the one in 2009.

There is no evidence that H5N1 and H1N1 have reassorted naturally yet, but they have many opportunities to do so. The viruses overlap both in their geographical range and in the species they infect, and although H5N1 tends mostly to swap genes in its own lineage, the pandemic H1N1 strain seems to be particularly prone to reassortment.

“If these mammalian-transmissible H5N1 viruses are generated in nature, a pandemic will be highly likely,” says Hualan Chen, a virologist at the Harbin Veterinary Research Institute of the Chinese Academy of Sciences, who led the study.

“It's remarkable work and clearly shows how the continued circulation of H5N1 strains in Asia and Egypt continues to pose a very real threat for human and animal health,” says Jeremy Farrar, director of the Oxford University Clinical Research Unit in Ho Chi Minh City, Vietnam.

Flu fears

Chen's results are likely to reignite the controversy that plagued the flu community last year, when two groups found that H5N1 could go airborne if it carried certain mutations in a gene that produced a protein called haemagglutinin (HA)[2, 3]. Following heated debate over biosecurity issues raised by the work, the flu community instigated a voluntary year-long moratorium on research that would produce further transmissible strains. Chen’s experiments were all finished before the hiatus came into effect, but more work of this nature can be expected now that the moratorium has been lifted.

“I do believe such research is critical to our understanding of influenza,” says Farrar. “But such work, anywhere in the world, needs to be tightly regulated and conducted in the most secure facilities, which are registered and certified to a common international standard.”

Virologists have created H5N1 reassortants before. One study found that H5N1 did not produce transmissible hybrids when it reassorts with a flu strain called H3N2[4]. But in 2011, Stacey Schultz-Cherry, a virologist at St. Jude Children's Research Hospital in Memphis, Tennessee, showed that pandemic H1N1 becomes more virulent if it carries the HA gene from H5N1[5].

Chen’s team mixed and matched seven gene segments from H5N1 and H1N1 in every possible combination, to create 127 reassortant viruses, all with H5N1’s HA gene. Some of these hybrids could spread through the air between guinea pigs in adjacent cages, as long as they carried either or both of two genes from H1N1 called PA and NS. Two further genes from H1N1, NA and M, promoted airborne transmission to a lesser extent, and another, the NP gene, did so in combination with PA.

“It’s a very extensive paper,” says Schultz-Cherry. “It really shows that it’s more than just the HA. The other proteins are just as important and can drive transmission.” Chen says that health organisations should monitor wild viruses for the gene combinations that her team identified in the latest study. “If those kinds of reassortants are found, we’d need to pay high attention.”

Knowledge gap

It is unclear how the results apply to humans. Guinea pigs have bird-like receptor proteins in their upper airways in addition to mammalian ones, so reassortant viruses might bind in them more easily than they would in humans.

And scientists do not know whether the hybrid viruses are as deadly as the parent H5N1. The hybrids did not kill any of the guinea pigs they spread to, but Chen says that these rodents are not good models for pathogenicity in humans.

There is also a chance that worldwide exposure that already occurred to the pandemic H1N1 strain might actually mitigate the risk of a future pandemic by providing people with some immunity against reassortants with H5N1. In an earlier study, Chen and her colleagues showed that a vaccine made from pandemic H1N1 provided some protection against H5N1 infections in mice[6].

“If you take [antibodies] from people who have been vaccinated or naturally infected, will they cross-react with these viruses?” asks Schultz-Cherry. “That’s an important study that would need to be done.”

Ironically, Chen’s team is now too busy reacting to the emerging threat of a different bird flu — H7N9. Research on H5N1 will have to wait.

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References

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