New vaccine may give long-term defense against deadly bird flu and its variant forms

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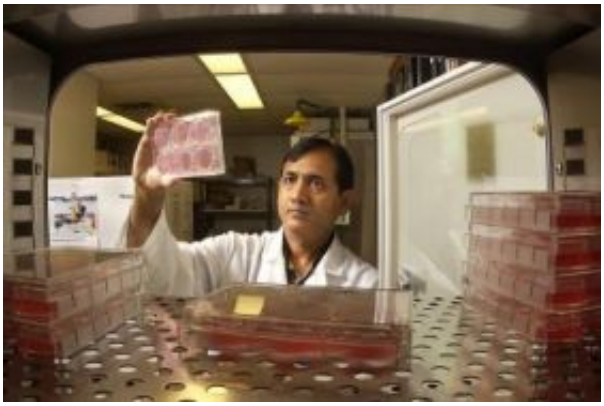

A new vaccine that apparently can provide long-lasting protection for pathogenic bird flu, H5N1, and its mutations, has been developed by Purdue researchers in collaboration with the US Centers for Disease Control and Prevention. Purdue virologist Suresh Mittal said that compared to traditional vaccines, the new vaccine would have the advantages of not being based on eggs, would be easy and fast to produce, and could easily be modified to changes in the flu virus. Credit: Purdue Agricultural Communication photo/Tom Campbell

A new vaccine under development may provide protection against highly pathogenic bird flu and its evolving forms, according to researchers at Purdue University and the Centers for Disease Control and Prevention who discovered the new preventative drug and have tested it in mice.

Unlike traditional influenza vaccines, the new vaccine could be produced quickly and stored for long periods in preparation for a pandemic of

dangerous disease-causing avian influenza - H5N1 - and its variants, said Suresh Mittal, a Purdue virologist. In an earlier study with mice, he and his colleagues found that the vaccine protected against H5N1 for a year or longer. Because the studies have only been done in mice, it's not yet known whether the same results will be obtained in humans.

"We want to have a vaccine that can be stored in advance and have the potential to provide protection for a period of time until we can change the vaccine to match the latest form of avian influenza," Mittal said. "The combination of flu genes that we've used to produce the vaccine, I think, will provide that capability."

The importance of having a long-lasting, broadly protective vaccine is that it would give some cross-protection against new viruses with pandemic potential caused by mutations in currently circulating H5N1 viruses. This would give scientists time to develop a better vaccine that would match the latest form of the bird flu.

Mittal and his colleagues, including Suryaprakash Sambhara, the CDC principal investigator on the project, report their findings on the vaccine in the April 15 issue of *The Journal of Infectious Diseases*. In the December issue of Clinical Pharmacology and Therapeutics, Mittal, Sambhara and their collaborators published their findings of the long-lasting capabilities of the vaccine.

"In humans we want a vaccine to be fully effective for at least a year," said Mittal, a professor of comparative pathobiology. "How long it will last in humans, we don't know yet."

To produce the new vaccine, the scientists used a mutated common cold virus, known as an adenovirus, as a delivery system for important genes from two types of the H5N1 avian influenza. The adenovirus is incapable of multiplying and so cannot cause illness to people. By using

the adenovirus vector technology, a couple of problems with existing vaccines used to fight annual flu outbreaks are solved.

Problems with current influenza vaccines include that they are made from eggs, a process that can take as long as six months. The vaccine Mittal and his research team has developed isn't grown in eggs, making vaccine production much faster.

Additionally it would be difficult under normal conditions to produce the hundreds of millions of doses needed to protect everyone at risk for highly pathogenic forms of bird flu. With the beginning of a pandemic, since H5N1 decimates poultry populations, the egg supply needed to produce vaccines would be drastically cut.

The new vaccine uses an adjuvant, molecules added to the vaccine that stimulate the body's immune system, so that lower doses of the vaccine can be used. The adjuvant also allows the vaccine to be stockpiled so more people can be vaccinated, and it helps the vaccine protect against variant forms of the H5N1. The only FDA-approved H5N1 vaccine protects against only that specific strain of flu and only works in about 60 percent of those immunized with a high dose.

"Adenoviral vector-based pandemic vaccines are an attractive option for developing countries where egg-independent cell-based vaccine technologies for other vaccines already are available," Sambhara said. "Since this process is already in place, our vaccine could be produced locally at an affordable price."

Since H5N1 has been known, it has changed so that there are now two main subgroups, called clades. Within one of the clades, five subclades have emerged. This has complicated the task of developing a "perfect match" vaccine for the highly pathogenic bird flu. Other avian influenza viruses exist, but they have not proved to be as lethal to humans or other

animals as has H5N1.

Influenza viruses are classified according to the combination of two types of proteins found on the virus cell surface. Different combinations of the 16 types of hemagglutinin (H) protein and nine types of neuraminidase (N) protein form a large number of influenza viruses for which birds are the natural hosts.

New, often more dangerous flu strains develop when the H and N combinations change and combine with other genes from circulating influenza viruses. When the genes of a human or swine influenza mix with an avian variety, a highly pathogenic human flu likely will result, Mittal said.

The first bird-to-human H5N1 case was recorded in 1997 in Hong Kong. The deadly virus has been documented in more than 60 countries, according to the World Health Organization (WHO). Though it mainly has struck wild birds and poultry, there have been more than 300 human cases in 14 countries in the past decade with a 60 percent fatality rate. Most of the human cases have occurred in people who live and work closely with their poultry, but a few cases have been documented of the disease spreading from person to person.

In a typical case, WHO this week reported the most recent fatality - the death of a 30-year-old Egyptian woman who became ill on April 2 after handling sick birds. She did not respond to the antiviral treatment Tamiflu, which can be given after contact with a flu carrier.

The next step in the bird flu vaccine project will be to test the vaccine on new viruses that are appearing, Mittal said.

The scientific team's vaccine work is being developed by PaxVax Inc., which has licensed the technology. Mittal is a scientific adviser for the

company but has no financial stake in the commercial development of the vaccine, nor do his colleagues.

Source: Purdue University