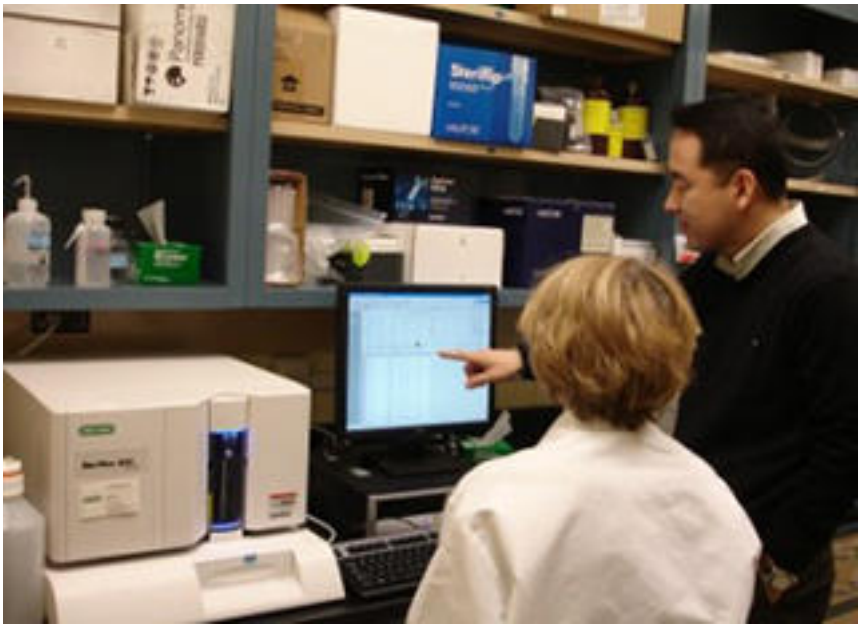
Developing a Universal Flu Vaccine

Ohio State University



WOOSTER, OH — As public health officials keep a wary eye for signs of resurgence of a deadly flu strain that emerged in China last spring, an Ohio State University researcher is working on a new type of flu vaccine that would vastly improve the odds of protecting both humans and animals from the flu virus.

Chang-Won Lee, an associate professor in the Food Animal Health Research Program of the College of Food, Agricultural, and Environmental Sciences (CFAES [1]), received a five-year, $2.2 million grant earlier this year from a special joint program [2] between the National Institutes of Health and the U.S. Department of Agriculture.

The program funds medical research that uses relevant farm animal models with an aim to improve both human and animal health.

Lee's project is using swine and chickens in addition to mice as models to develop a universal flu vaccine.

New flu vaccines for humans are usually tested in mice because "they're easy to work with," Lee said. "But if you get good results in mice, can you extrapolate that to humans? Not always. We are not developing a mouse vaccine. Swine is a better model to use for several human infectious diseases."

Other researchers have worked on developing a universal flu vaccine, but most have used the mouse as their model, Lee said.

"The mouse is an animal that is very easy to protect against the flu, but that doesn't

mean the vaccine works in humans. If you can show that something works in a large animal, especially swine, which is anatomically, physiologically and immunologically similar to humans, then there is much more of a chance that it will work in humans.

"And since swine and poultry are the top two types of animals affected by the flu and sporadically transmit the virus to humans, you get a dual benefit from this research."

Currently available flu vaccines are effective against only a few strains at a time, and they're not always targeted against the strains that end up circulating during flu season. That's one reason why more than 200,000 people are hospitalized due to seasonal flu every year in the U.S., with thousands of deaths.

In addition, flu viruses mutate easily, developing new pandemic strains that humans have little to no immunity against. They often pass between animals and humans. For example, a new avian influenza, H7N9, was discovered in China in spring 2013. Of the 130 human infections, 43 were fatal. Direct contact with poultry was blamed for most of the infections, although the first evidence of human-to-human transmission — a key step in the emergence of pandemic flu — was recently identified in research [3] published in the *British Medical Journal*.

A universal flu vaccine would work against a broad array of flu strains and would not need to be reformulated annually.

"Agricultural and medical researchers don't normally work together, but we should," Lee said. In this project, Lee is working with Xi (Jason) Jiang at the University of Cincinnati College of Medicine. In 2010, Jiang led a team of researchers in discovering an important property of norovirus protein that is being used in the current project.

The norovirus P particle is a protein that's highly immunogenic — that is, it provokes an immune response in the body. Lee's team is working with the genes in norovirus that produce the P particle and recombining them with genes that produce a flu antigen that would work against most strains of flu.

"When we get to the final product, the flu antigen is on the surface — it's beautifully expressed on the surface of the P protein," Lee said. "You can think of it as a flower — the stem is the P protein, and the outside flower is the flu antigen. That way, the host system should efficiently recognize this as a flu protein and develop an immune response."

The norovirus P particle is easy to work with, Lee said, as it is readily produced in harmless types of *E. coli* bacteria, which are often used in lab work. It's also highly stable, which would allow the vaccine to be transported and stored without the need for refrigeration — critical for vaccination programs in remote areas and developing countries.

The new vaccine would combine an HA2-based vaccine, which prevents the virus from attaching to a cell -- thus restricting it from replicating -- with an M2e-based

vaccine, which blocks the key step for the flu virus to replicate in the cell. "We are working separately first, and then we'll combine them to see the synergism between the two," Lee said.

Lee is testing the new vaccine in both swine and poultry at the Ohio Agricultural Research and Development Center's campus in Wooster, Ohio. OARDC is the research arm of CFAES. Meanwhile, Jiang's lab is testing the new vaccine in a traditional mouse model.

"So far, we have shown that our construct is highly immunogenic in those three species," Lee said. "We are now working on two more things: studying how effective this is against different flu strains, and looking in more detail for the protective immune correlates. That is, we are not just looking to see if our new vaccine is protective or not, we want to answer how it works — the mechanism of action."

Currently, the researchers are working with low-pathogenic flu strains — the type that cause mild illness — but plan to examine the vaccine's effectiveness against highly pathogenic strains, which can cause severe disease, in years three and four of the study using the newly constructed high-level biosecurity facility [4] at OARDC.

Also working on the project, officially called "Universal Flu Vaccine by a Norovirus P Particle Platform," is Renukaradhya Gourapura, an immunologist with OARDC's Food Animal Health Research Program [5].

Links:
[1] http://cfaes.osu.edu
[2] http://grants.nih.gov/grants/guide/pa-files/PAR-10-276.html
[3] http://www.nlm.nih.gov/medlineplus/news/fullstory_139516.html
[4] http://oardc.osu.edu/paar
[5] http://oardc.osu.edu/fahrp