Nanoparticle vaccine offers universal protection against influenza A viruses, study finds

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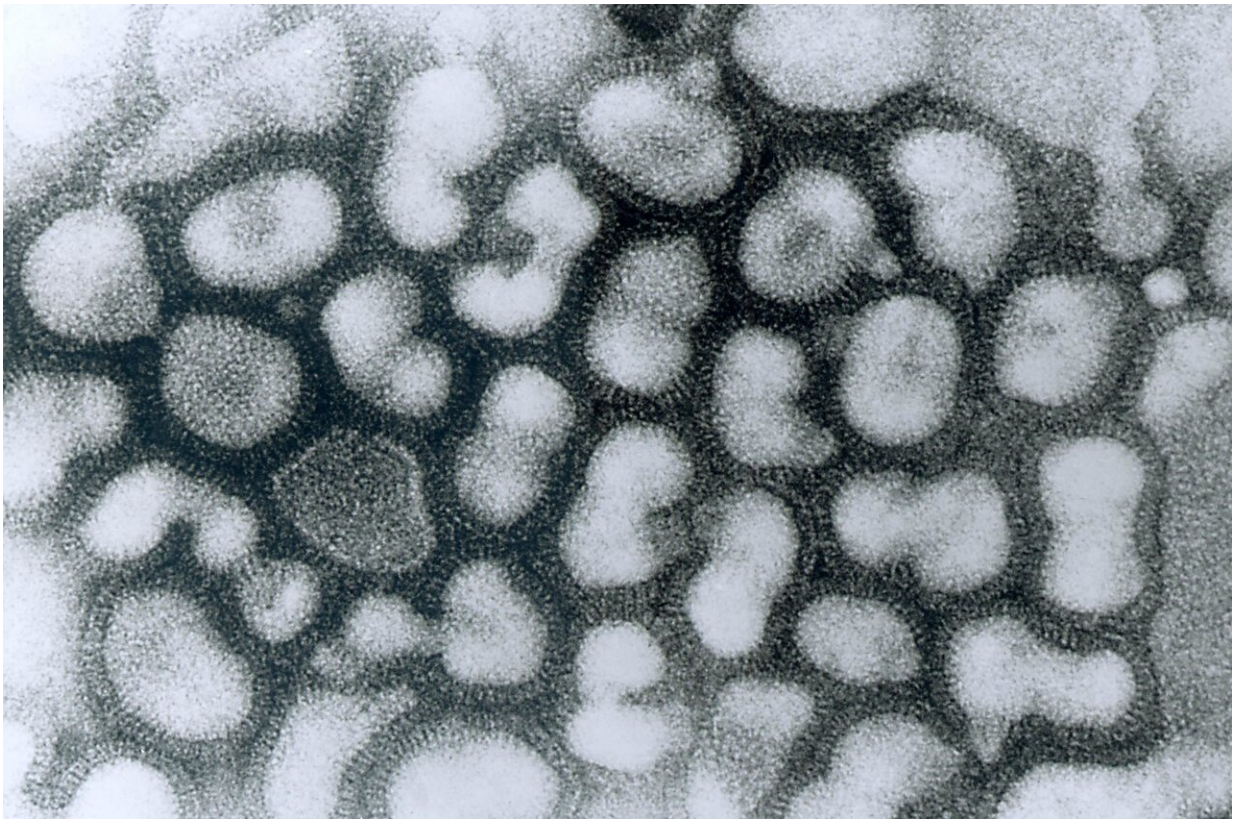

Transmission electron micrograph of influenza A virus, late passage. Credit: CDC

Researchers have developed a universal vaccine to combat influenza A

viruses that produces long-lasting immunity in mice and protects them against the limitations of seasonal flu vaccines, according to a study led by Georgia State University.

Influenza, a contagious respiratory illness that infects the nose, throat and lungs, is among the leading causes of death in the United States, according to the Centers for Disease Control and Prevention (CDC). The CDC estimates influenza has resulted in between 12,000 and 56,000 deaths annually in the U.S. since 2010.

Seasonal flu vaccines must be updated each year to match the influenza viruses that are predicted to be most common during the upcoming flu season, but protection doesn't always meet expectations or new viruses emerge and manufacturers incorrectly guess which viruses will end up spreading. In 2009, the H1N1 pandemic caused 200,000 deaths during the first 12 months, and low vaccine effectiveness was also observed during the 2014-15 and 2016-17 flu seasons. A universal flu vaccine that offers broad protection against various viruses is urgently needed and would eliminate the limitations of seasonal flu vaccines.

Seasonal flu vaccines provide protective immunity against influenza viruses by targeting the exterior head of the virus's surface protein, which is hemagglutinin (HA). The influenza virus trains the body to produce antibodies against inactivated virus particles containing the head of this protein, ideally preventing the head from attaching to receptors and stopping infection. However, the head is highly variable and is different for each virus, creating a need for better vaccines. This study uses a new approach and instead targets the inside portion of the HA protein known as the stalk, which is more conservative and offers the opportunity for universal protection.

In this study, the researchers found vaccinating mice with double-layered protein nanoparticles that target the stalk of this protein produces long-

lasting immunity and fully protects them against various influenza A viruses. The findings are published in the journal *Nature Communications*.

"Vaccination is the most effective way to prevent deaths from influenza virus, but the virus changes very fast and you have to receive a new vaccination each year," said Dr. Bao-Zhong Wang, associate professor in the Institute for Biomedical Sciences at Georgia State. "We're trying to develop a new vaccine approach that eliminates the need for vaccination every year. We're developing a universal influenza vaccine. You wouldn't need to change the vaccine type every year because it's universal and can protect against any influenza virus.

"What we wanted to do is to induce responses to this stalk part of the influenza surface glycoprotein, not the head part. This way you're protected against different viruses because all influenza viruses share this stalk domain. However, this stalk domain itself isn't stable, so we used a very special way to make this vaccine construct with the stalk domain and had success. We assembled this stalk domain into a protein nanoparticle as a vaccine. Once inside, the nanoparticle can protect this antigenic protein so it won't be degraded. Our immune cells have a good ability to take in this nanoparticle, so this nanoparticle is much, much better than a soluble protein to induce immune responses."

The nanoparticles are unique because they were generated to contain almost entirely the protein capable of inducing immune responses. The double layer also better retains the protein function.

To determine the effectiveness of the nanoparticle vaccine, the researchers immunized mice twice with an intramuscular shot. Then, the mice were exposed to several influenza viruses: H1N1, H3N2, H5N1 and H7N9. Immunization provided universal, complete protection against lethal virus exposure and dramatically reduced the amount of

virus in the lungs.

Next, the researchers would like to test the nanoparticle vaccine in ferrets, which are similar to humans in the orchestration of their respiratory system.

"This vaccine is composed of very conserved domains. That's the reason why the induced immunity can offer universal protection," said Dr. Lei Deng, first author of the study and a postdoctoral researcher in the Institute for Biomedical Sciences at Georgia State. "The seasonal influenza vaccines induce the dominant immune response against the head domain of the HA molecules, which is hypervariant. That is why we have to adopt new influenza strains for the new vaccine every year. Our vaccine overcomes this problem. For long-term protection, longevity of induced immunity in human still needs to be tested in further clinical tests."

Provided by Georgia State University