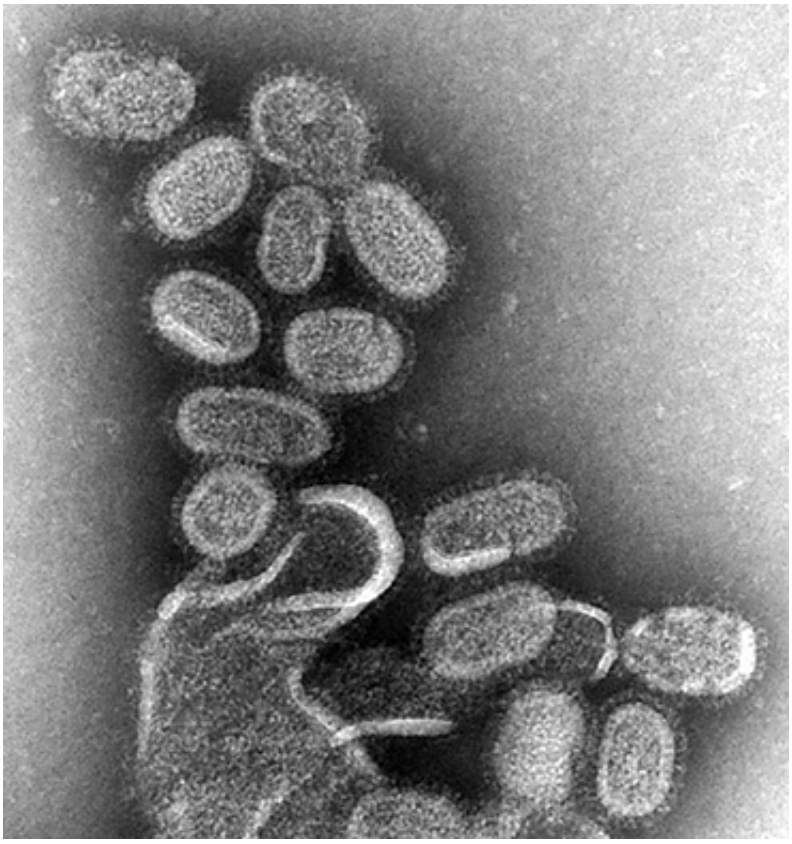
Nanoparticle vaccine made with peptides effective against influenza virus, study finds

July 30 2018



Electron microscopy of influenza virus. Credit: CDC

A new, double-layered nanoparticle vaccine made with peptides has been found to effectively protect mice against influenza A virus, according to a study led by Georgia State University.

Influenza, a contagious respiratory illness that infects the nose, throat and lungs, is a persistent threat to public health and is among the leading causes of death in the United States. The Centers for Disease Control and Prevention reports the 2017-18 flu season was a high severity season with record-breaking levels of influenza-like illness and hospitalization rates.

Universal flu vaccines that can induce broad and effective protection against a wide range of influenza viruses are urgently needed. Scientists now must update seasonal flu vaccines every year by predicting which strains will be the most common during the upcoming flu season. If seasonal flu vaccines are mismatched against circulating influenza strains , they provide low effectiveness and limited protection, which could lead to influenza epidemics and pandemics. Nanotechnology provides a promising approach for developing new influenza vaccines, and the double-layered nanoparticle vaccine created in this study shows strong potential for combatting influenza viruses.

To construct the nanoparticles (nanoscale-sized particles) for this vaccine, the researchers used peptides, compounds consisting of two or more amino acids linked in a chain, because they are much smaller than proteins. The nanoparticles mimic the biological cues of viruses and initiate danger signals that activate immune responses.

Each double-layered nanoparticle has a core made of peptides from nucleoprotein (NP), an internal influenza protein that has been found to produce cross-protection against influenza virus by inducing T-cell immune responses. The nanoparticle also has an outside coating made of four peptides from the ectodomain of the influenza A M2 protein (M2e), an evolutionarily conserved region in most human seasonal influenza A viruses and a promising target for universal flu vaccines. The M2e sequences came from human, swine and avian influenza strains.

The peptide-only, double-layered nanoparticles, which were delivered by skin vaccination with a dissolvable microneedle patch, induced robust, long-lasting protective immunity and guarded mice against exposure to influenza A virus. The findings are published in the journal *Proceedings of the National Academy of Sciences*.

Dr. Lei Deng, a postdoctoral researcher in the Institute for Biomedical Sciences at Georgia State, is first author of the study. The study is a collaboration among Georgia State, the Georgia Institute of Technology, Emory University and Henan Normal University in Henan, China.

"The adaptive immune system includes B lymphocytes mediating antibody responses and T lymphocytes mediating cellular responses," said Dr. Bao-Zhong Wang, leader and senior author of the study and associate professor in the Institute for Biomedical Sciences at Georgia State. "Our novel nanoparticles trigger immune responses of both immune branches. We have seen the synergistic role of the two branches in providing broad cross-protection against a wide range of diverse influenza virus challenges after vaccination with these layered peptide nanoparticles. The immune protection has also been improved by using a new syringe-free, painless, thermostable and self-applicable microneedle patch. No doubt, these findings will open a new vision for the development of an affordable universal influenza vaccine."

The researchers administered the double-layered nanoparticle vaccine to mice using a microneedle patch, which offers advantages over traditional, intramuscular injection, and then exposed them to influenza A virus to see if the vaccine induced protection against the virus.

They found that mice that received the nanoparticle vaccines completely survived various influenza A virus exposures while all mice that received a placebo died within one week.

The researchers based their vaccine design on findings from previous studies. Other researchers have found that NP can induce T-cell immune responses. Also, this team, along with other scientists, have found that M2e enhances immune responses.

In future studies, the researchers plan to build upon this double-layered nanoparticle vaccine by adding the inside portion of the influenza virus's surface protein, which is known as the stalk, to the nanoparticle vaccine coating. Seasonal flu vaccines provide protective immunity against influenza viruses by targeting the exterior head of this surface protein, hemagglutinin. The exterior head is highly variable and different for each virus. The stalk, on the other hand, is more conserved and offers the opportunity for universal protection. This group's previous studies have shown the stalk is effective in protecting against the flu.

The researchers hope to administer the vaccine using a microneedle patch. Their goal is to make a strong universal vaccine with a better delivery approach.

This vaccine approach could also be used to develop vaccines for other pathogens and cancers. The layered, peptide nanoparticles were found to be potent and stable, which indicates potential applications for other peptide-based vaccines and peptide drug delivery.

More information: Lei Deng el al., "Heterosubtypic influenza protection elicited by double-layered polypeptide nanoparticles in mice," *PNAS* (2018). www.pnas.org/cgi/doi/10.1073/pnas.1805713115

Provided by Georgia State University

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