Intranasal influenza vaccine enhances immune response and offers broad protection, researchers find

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An influenza vaccine that is made of nanoparticles and administered through the nose enhances the body's immune response to influenza virus infection and offers broad protection against different viral strains, according to researchers in the Institute for Biomedical Sciences at Georgia State University.

Recurring seasonal flu epidemics and potential pandemics are among the most severe threats to public health. Current seasonal influenza vaccines induce strain-specific immunity and are less effective against mismatched strains. Broadly protective influenza vaccines are urgently needed.

Intranasal vaccines are a promising strategy for combatting infectious respiratory diseases, such as influenza. They are more effective than vaccines injected into a muscle because they can induce mucosal immune responses in respiratory tracts, preventing infection at the portal of virus entry. They can also stimulate systemic immune responses throughout the body.

Scientists can overcome vaccine safety concerns and the long production phase of virus-based influenza vaccines by constructing intranasal vaccines with recombinant proteins or peptides. However, these vaccines are poor at producing immune responses, so it's necessary to have potent mucosal adjuvants, substances that enhance the body's immune response to antigens (the molecular structures on pathogens). The absence of appropriate mucosal adjuvants currently hinders the development of such a vaccine.

In this study, the researchers developed an intranasal influenza vaccine using recombinant hemagglutinin (HA), a protein found on the surface of influenza viruses, as the antigen component of the vaccine. HA is integral to the ability of influenza virus to cause infection.

They also created a two-dimensional nanomaterial (polyethyleneimine-functionalized graphene oxide nanoparticles) and found that it displayed potent adjuvant (immunoenhancing) effects on influenza vaccines delivered intranasally. The findings are published in the journal *Proceedings of the National Academy of Sciences.*

"Conventional flu vaccines predominantly induce antibody responses," said Dr. Baozhong Wang, senior author of the study, principal investigator of the National Institutes of Health grant supporting the study and a professor in the Institute for Biomedical Sciences. "However, recent research demonstrates that lung resident memory T cell responses are indispensable for optimal cross-protection against pulmonary influenza infection. The development of lung resident T cell responses requires vaccination by a respiratory route or influenza virus infection. Our research opens a new

path for the development of needle-free and logistically simplified intranasal flu vaccines for cross-protection."

"In our study, we reported for the first time that two-dimensional graphene oxide nanomaterials had a potent adjuvant effect in boosting the immune responses of intranasal hemagglutinin (HA) vaccines," said Dr. Chunhong Dong, lead author of the study and a postdoctoral research Fellow in Dr. Baozhong Wang's lab in the Institute for Biomedical Sciences.

"This study gives new insights into developing high performance intranasal vaccine systems with two-dimensional sheet-like nanoparticles," Dong said. "The graphene oxide nanoparticles have extraordinary attributes for drug delivery or vaccine development, such as the ultra-large surface area for high-density antigen loading, and the vaccine showed superior immunoenhancing properties in vitro and in vivo. The nanoplatform could be easily adapted for constructing mucosal vaccines for different respiratory pathogens."

The study, conducted in mice and cell culture, found the nanoparticles significantly enhanced immune responses at mucosal surfaces and throughout the body in mice. The robust immune responses conferred immune protection against influenza virus challenges by homologous (same) virus strains and heterologous (different) virus strains.

The results are also promising because needle-free, intranasal influenza vaccines possess superior logistical advantages over traditional injectable vaccines, such as easy administration with high acceptance for recipients and the avoidance of biohazardous waste.

More information: Chunhong Dong el al., "Intranasal vaccination with influenza HA/GO-PEI nanoparticles provides immune protection against homo- and heterologous strains," *PNAS* (2021). www.pnas.org/cgi/doi/10.1073/pnas.2024998118

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