Universal influenza B vaccine induces broad, sustained protection, researchers find

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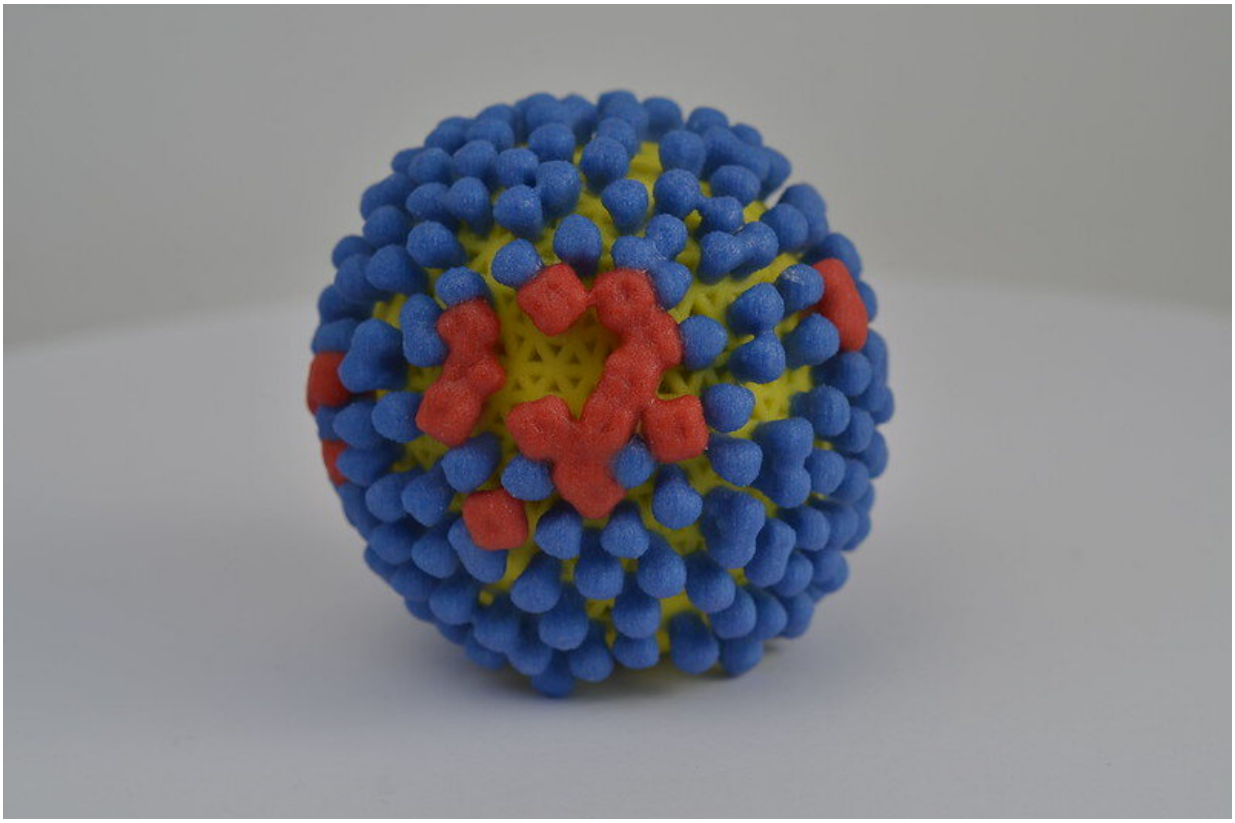

3D print of influenza virus. The virus surface (yellow) is covered with proteins called hemagglutinin (blue) and neuraminidase (red) that enable the virus to enter and infect human cells. Credit: NIH

A new universal flu vaccine protects against influenza B viruses, offering broad defense against different strains and improved immune protection,

according to a new study by researchers in the Institute for Biomedical Sciences at Georgia State University.

The double-layered protein nanoparticle vaccine, which is constructed with a stabilized portion of the influenza virus (the hemagglutinin (HA) stalk), induced broadly reactive immune responses and conferred robust and sustained cross-immune protection against influenza B virus strains of both lineages. The findings are published in the journal *Biomaterials*.

Influenza epidemics pose a major threat to public health, and type B influenza has coincided with several severe flu outbreaks. About one-fourth of clinical infection cases are caused by influenza B viruses each year. Influenza B viruses are sometimes the dominant circulating strains during influenza seasons, such as the 2019-20 U.S. flu season when influenza B caused more than 50 percent of the infections.

Influenza B has two lineages that are genetically distinct and trigger different immune responses. Seasonal flu vaccines are developed with one or both lineages of influenza B viruses, but they're limited by the ability of circulating strains to escape the immune system or vaccination. These vaccines are often ineffective because the variable portion of the influenza virus (the HA head) evolves. As a result, seasonal influenza vaccines need to be reformulated and updated frequently. To overcome these limitations, a universal influenza vaccine containing conserved parts of the virus and providing substantial broad cross-protection against diverse virus strains is urgently needed.

"In this study, we generated structure-stabilized HA stalk antigens from influenza B and fabricated double-layered protein nanoparticles as universal influenza B vaccine candidates," said Dr. Baozhong Wang, senior author of the study and Distinguished University Professor in the Institute for Biomedical Sciences at Georgia State University. "We found that layered protein nanoparticles incorporated with structure-

stabilized constant antigens have potential as a universal influenza vaccine with improved immune protective potency and breadth."

The nanoparticle vaccine was tested in cell culture and in mice. Studies in cell culture found the protein nanoparticles were effectively taken up to activate dendritic cells, which are critical for inducing protective immune responses against pathogens. The vaccine was found to be safe, biocompatible, biodegradable and highly immunogenic in animals.

"Our next aim is to combine the influenza A nanoparticles from our previous study with the influenza B nanoparticles we have fabricated and tested here to create a multivalent universal influenza nanoparticle vaccine against both influenza A and B," Wang said.

Co-authors of the study include Yufeng Song (first author), Wandi Zhu, Ye Wang, Lei Deng, Yao Ma, Chunhong Dong, Gilbert X. Gonzalez, Joo Kim, Lai Wei, Sang-Moo Kang and Bao-Zhong Wang of the Center for Inflammation, Immunity & Infection in the Institute for Biomedical Sciences at Georgia State. Deng is also affiliated with Hunan University in Changsha, China.

More information: Yufeng Song et al, Layered protein nanoparticles containing influenza B HA stalk induced sustained cross-protection against viruses spanning both viral lineages, *Biomaterials* (2022). DOI: 10.1016/j.biomaterials.2022.121664

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