Medical Xpress

Synthetic DNA vaccine effective against influenza A virus subtype

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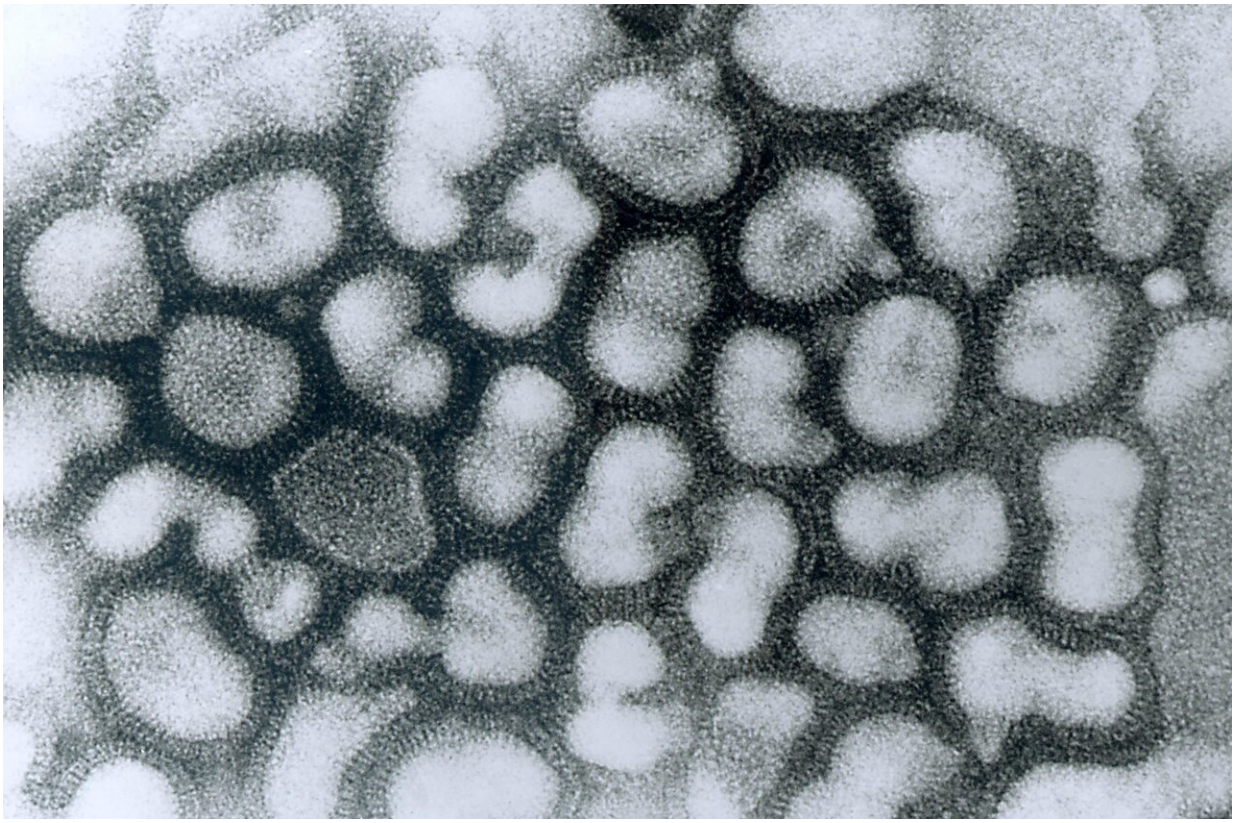

Transmission electron micrograph of influenza A virus, late passage. Credit: CDC

Currently available vaccines for the prevention of seasonal influenza virus infection have limited ability to induce immunity against diverse

H3N2 viruses, an influenza A subtype that has led to high morbidity and mortality in recent years.

Now, Wistar scientists have engineered a synthetic DNA vaccine shown to produce broad immune responses against these H3N2 viruses. Study results were published online in the journal *Human Gene Therapy*.

The recent severe influenza seasons in 2013/2014, 2014/2015 and 2017/2018 can be directly attributed to H3N2. Commercial vaccine efficacy against H3N2 in 2017/2018 was low and contributed to a greater rate of pneumonia and influenza-associated deaths.

"Current vaccine design and manufacturing to meet the antigenic diversity of H3N2 viruses is challenging, and with another flu season approaching there remains a pressing need for new vaccine approaches for influenza," said lead researcher David B. Weiner, Ph.D., executive vice president and director of the Vaccine & Immunotherapy Center at The Wistar Institute, and W.W. Smith Charitable Trust Professor in Cancer Research. "There is also a need for improvements in rapid selection and deployment against newly emergent viral strains and synthetic DNA vaccines represent an important tool to reach this goal."

To overcome the antigenic diversity of H3N2 viruses, Weiner and colleagues used H3N2 strains from 1968 to the present retrieved from the Influenza Research Database to generate four synthetic common sequences of the hemagglutinin antigen (HA), a protein present on the viral surface. These micro-consensus sequences were used to generate four DNA vaccines that were co-mixed to create a cocktail vaccine labeled pH3HA. The scientists administered the vaccine or placebo to mice and a booster vaccine two weeks later. Two weeks after the booster injection, they inoculated them with two representative influenza viruses.

Sarah Elliot, Ph.D., a senior postdoctoral fellow in the Weiner Lab, and colleagues monitored clinical signs, body weight and survival for two weeks after infection. All mice immunized with the synthetic DNA vaccine developed broad, robust antibody responses against HA and effective cellular immune responses including CD4 and CD8 T cell responses.

They were protected against lethal influenza A infection from two different challenge H3N2 viruses. Vaccination with pH3HA induced robust antibodies against the 1968 pandemic H3N2 as well as contemporary H3N2 strains that were components of commercially available vaccines from 2015/2016 and 2017/2018.

Compared with those who received placebo, immunized mice survived intranasal virus challenge with 10 times the median lethal dose; the placebo group succumbed to infection within six days of exposure to the challenge virus.

"The pH3HA vaccine represents a unique micro-consensus approach to producing immune responses to antigenically related—yet diverse, seasonal influenza A H3N2 viruses," Weiner said. "The overarching goals of this approach are to limit the number of vaccine reformulations that can be deployed to protect against novel H3N2 viruses."

More information: Sarah Elliott et al, A Synthetic Micro-Consensus DNA Vaccine Generates Comprehensive Influenza-A H3N2 Immunity and Protects Mice Against Lethal Challenge by Multiple H3N2 Viruses, *Human Gene Therapy* (2018). DOI: 10.1089/hum.2018.102

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