Seasonal flu vaccine induces antibodies that protect against H7N9 avian flu

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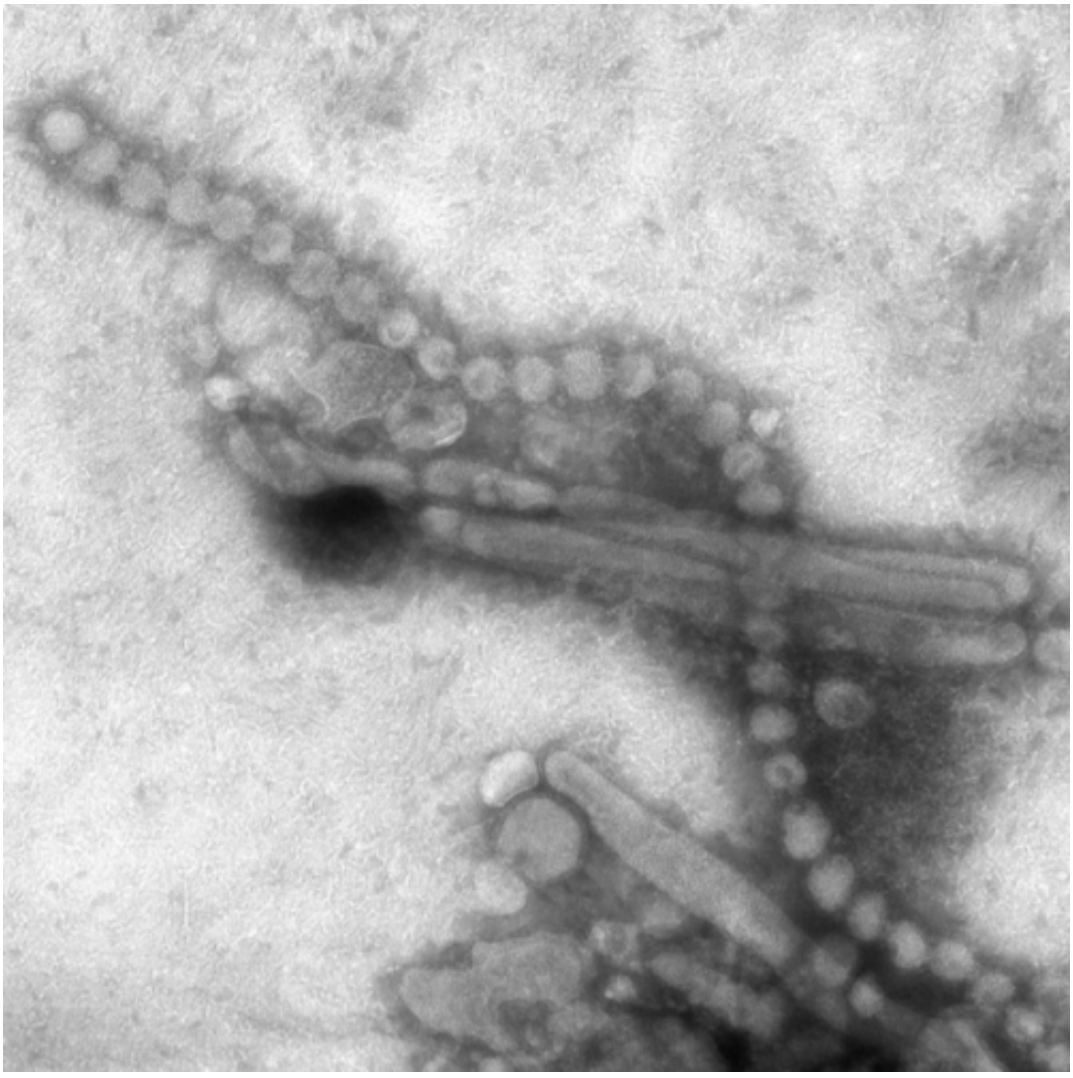

Influenza A (H7N9) as viewed through an electron microscope. Both filaments and spheres are observed in this photo. Credit: CDC

Antibodies that protect against H7N9 avian flu, which emerged in China in 2013 and sparked fears of a global pandemic, have been isolated in individuals who received seasonal flu vaccinations. These antibodies account for a small percentage of the total immune response, but appear to broadly neutralize H7 viruses and represent promising new targets for therapeutic development against a wide range of influenza strains, report scientists from the University of Chicago and Icahn School of Medicine at Mount Sinai in the *Journal of Clinical Investigation* on Feb 17.

"We have clear evidence that a normal immune response to flu vaccination offers protection against dangerous and highly unique strains of influenza such as H7N9," said co-senior author Patrick Wilson, PhD, associate professor of medicine at the University of Chicago. "We now need to develop ways of amplifying this response."

With a mortality rate of roughly 30 percent, avian influenza A (H7N9) is unusually dangerous for humans. To search for potential therapeutics against the virus, Wilson and his colleagues focused on annual seasonal flu vaccinations. The vaccine causes the immune system to produce antibodies - proteins that bind to and neutralize foreign invaders - against common flu strains.

The researchers studied whether seasonal vaccinations would also induce the production of antibodies against rare flu strains. They selected 83 antibodies - isolated from 28 vaccinated individuals - that reacted with H3N2, a common human flu strain. When tested, seven percent of these antibodies reacted against rare H7 strains, even though H7 strains were not included in the vaccines the subjects received.

Of these, three antibodies appeared to completely neutralize H7N9 avian flu. To verify their findings, the team treated mice with each antibody before exposing them to a lethal dose of H7N9 virus. All three antibodies prevented death in these subjects, compared to controls which

succumbed to infection. When the antibodies were tested as a therapeutic and administered 24 hours after infection, mice were again protected.

"It appears more common than previously thought for antibodies induced by flu vaccination to offer cross-protection against H7N9," said study author Carole Henry, PhD, postdoctoral fellow at the University of Chicago. "Although they are not always protective, H7-reactive antibodies can be found in almost everyone that's been vaccinated."

The researchers also tested the three antibodies for reactivity against other influenza viruses, and found H3 and other H7 strains could be neutralized as well. This broad-reactivity is likely due to the location on the influenza virus to which the antibodies bound - highly conserved regions that differ little between strains. Binding to these sites allows the antibodies to neutralize a range of influenza strains, despite the virus's notorious ability to mutate and evade vaccines. Even if mutations occur at these conserved regions, the team found that the virus was significantly less infectious.

Despite the efficacy of these antibodies, it is still unclear why they are produced in relatively low amounts. The team is now working to better understand this process and to develop therapeutic approaches based on these antibodies.

"The challenge is to exploit this response on a larger scale to make vaccines or therapeutics that offer broad protection against influenza strains," Wilson said. "For now, it's clear that seasonal flu vaccination provides defense against more than just common strains. Everyone should be vaccinated."

More information: "Preexisting human antibodies neutralize recently emerged H7N9 influenza strains," *Journal of Clinical Investigation*, 2015.

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