Team develops new broadly protective vaccines for H3N2 influenza

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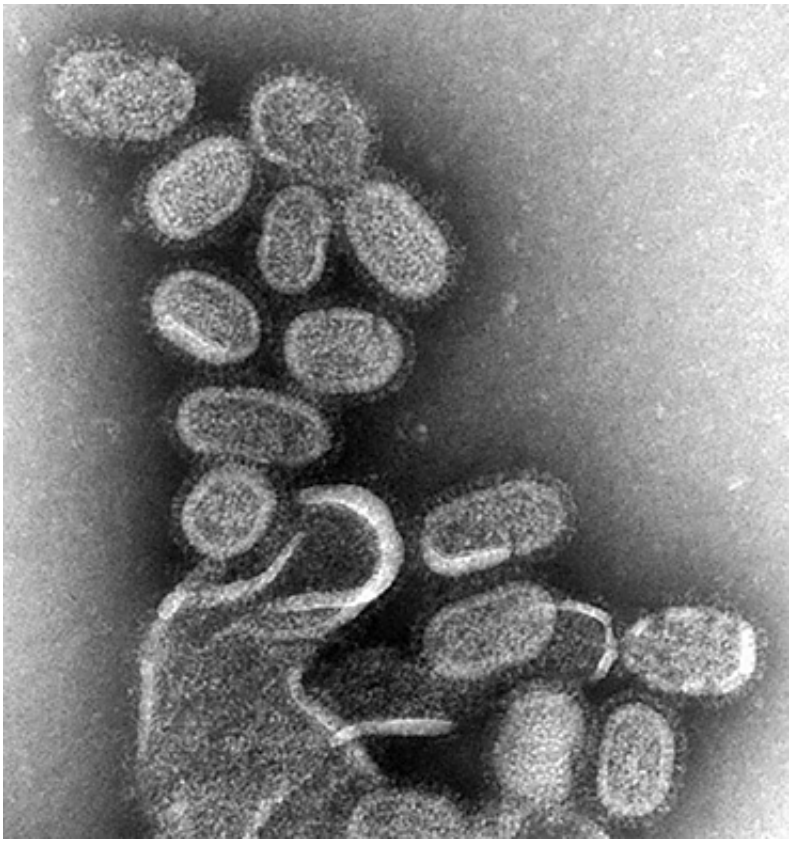

Electron microscopy of influenza virus. Credit: CDC

A collaborative research and development partnership between researchers at the University of Georgia and Sanofi Pasteur, the largest influenza vaccine manufacturer in the world, has resulted in the identification of a vaccine candidate that protects against multiple co-

circulating strains of H3N2 influenza isolated over five seasons following testing in mouse and ferret models. The team presented its data at the International Society for Vaccines Congress in Paris, France, and the findings are published in the *Journal of Virology*.

"One of the problems with current influenza vaccines is that the vaccine takes over six months to produce so vaccine manufacturers have to start well before flu season begins. Educated guesses are made by public-health authorities about which virus strains will be most prevalent during the upcoming flu season," said Ted M. Ross, director of UGA's Center for Vaccines and Immunology and Georgia Research Alliance Eminent Scholar in Infectious Diseases in the College of Veterinary Medicine. "They look at which flu viruses are circulating in the Southern Hemisphere during their winter months (May-September), as a preview for what we in the Northern hemisphere could see in our upcoming flu season each year. This year, it was a particularly bad flu season in Australia with H3N2 strains being most prevalent. What our group has developed is a vaccine that protects against all co-circulating strains of H3N2 viruses, so we might be able to one day replace the seasonal flu vaccine with this more broadly cross-protective vaccine."

The H3N2 influenza viruses evolve rapidly each year and the viruses at the start of a flu season may be well matched to the vaccine, but a few months later they may have drifted and able to evade the vaccine-induced immune response. Using a technique called Computationally Optimized Broadly Reactive Antigen, or COBRA, UGA researchers Terianne Wong, James Allen, Anne Bebin-Blackwell, Donald Carter, along with Ross, created 17 prototype vaccine candidates constructed using genetic sequences from multiple influenza virus strains.

These COBRA vaccines were designed to recognize all H3N2 circulating strains over multiple seasons. The current standard-of-care seasonal flu vaccines elicit antibodies that recognize the most dominant viruses

within a season. However, the COBRA vaccines elicited antibodies that neutralized 100 percent of the H3N2 viruses circulating over a five-year period, Ross said. That may allow for year-round manufacturing of the vaccine, as manufacturers would not have to halt production every year while the most prevalent strains are being identified by the health authorities.

This research is part of a broader effort to create a universal influenza vaccine, which would protect against all strains of the virus.

"This is progress, but we still have work to do before we get a truly universal flu vaccine," Ross said. "We need to determine how many seasons this H3 COBRA vaccine will protect against all H3N2 viruses into the future in all populations of people."

Commonly, vaccine candidates are tested in immunologically naïve model systems that do not have anti-influenza immune responses. However, most people have pre-existing immunity to influenza from a lifetime of previous infections and vaccinations. Therefore, a follow-up study by Donald Carter, Scott Johnson, Michael Carlock, Greg Kirchenbaum, James Allen and Ross investigated how pre-existing antibodies to historical influenza viruses influenced vaccine efficacy. The results show these broadly protective vaccine candidates are even more effective in hosts with pre-existing anti-influenza immunity, which bodes well for the use of these vaccines in people.

More information: Terianne M. Wong et al, COBRA HA elicits hemagglutination-inhibition antibodies against a panel of H3N2 influenza virus co-circulating variants., *Journal of Virology* (2017). DOI: 10.1128/JVI.01581-17

Donald M. Carter et al. Elicitation of protective antibodies against a broad panel of H1N1 viruses in ferrets pre-immune to historical H1N1

influenza viruses, *Journal of Virology* (2017). DOI: 10.1128/JVI.01283-17