Medical Xpress

In pursuit of a universal flu vaccine—study shows pros, cons for major strategy to create broadly protective shot

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Developing a universal flu vaccine that would protect against all seasonal and pandemic strains of the virus is no easy task, and new research suggests that one of the most promising strategies -- creating a vaccine that targets the "stalk" of a protein that covers the flu virus -- is a strong one, but isn't completely bulletproof. Researchers found that the stalk of the hemagglutinin protein can vary in response to pressure from the immune system. Credit: University of Rochester Medical Center

Flu shot season is here. But as you head to the doctor's office or pharmacy to get vaccinated, scientists are working to make this yearly ritual a thing of the past. Researchers around the world, including at the University of Rochester Medical Center (URMC), are pursuing a "universal" flu vaccine, one that would protect against most or all seasonal and pandemic strains of the flu virus.

This is no easy task, and a study out today in the journal *Scientific Reports* suggests that one of the most promising strategies - creating a vaccine that targets the "stalk" of a protein that covers the flu virus - is a strong one, but isn't completely bulletproof.

The hemagglutinin protein, which blankets the outside of the flu virus, looks a bit like a flower; it has a stalk (think stem) and a head (think petals). Current vaccines target the head, which is the part of the virus that's always changing in an effort to evade our immune defenses. The head sits on the stalk, and it's believed that the stalk stays relatively constant from one strain of flu to another. Directing a vaccine and the body's immune response towards the stalk is a seemingly logical strategy for creating a shot that would provide broad protection.

But, contrary to current assumptions, researchers at the URMC-based New York Influenza Center of Excellence (NYICE) found that the stalk can change, although not as easily or frequently as the head.

Using supercomputers at the University's Health Sciences Center for Computational Innovation, they analyzed the genetic sequences of human H1N1 flu viruses circulating since 1918. They found variations in both the head and the stalk, although variability was highest in the head region.

In the lab, they coupled the H1N1 virus with human antibodies - immune system soldiers that fight off foreign invaders. Not surprisingly,

repetitive exposure to the antibodies caused many mutations in the head, as it worked to escape the immune system's clutches. But, it led to a few modifications in the stalk, too. The results suggest that the stalk can vary in response to pressure from the immune system.

"The good news is that it's much more difficult to drive mutations in the stalk, but it's not impossible," said David J. Topham, Ph.D., study author and the Marie Curran Wilson and Joseph Chamberlain Wilson Professor in the department of Microbiology and Immunology at URMC. "A universal flu vaccine based on the stalk would be more broadly protective than the ones we use now, but this information should be taken into account as we move forward with research and development."

Despite efforts to vaccinate, the World Health Organization estimates that the flu virus results in 1 billion infections, 3 to 5 million cases of severe disease, and 300,000 to 500,000 deaths annually. Current vaccines, which require experts to pick the flu strains that they believe are going to circulate in a given year, are typically 40 to 70 percent effective in the U.S., though in some years protection is as low as 20 percent. Experts agree there is room for improvement and the National Institutes of Health is leading the charge in the creation of a universal vaccine.

More information: Christopher S. Anderson et al. Natural and directed antigenic drift of the H1 influenza virus hemagglutinin stalk domain, *Scientific Reports* (2017). DOI: 10.1038/s41598-017-14931-7

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