Pandemic flu strain could point way to universal vaccine

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The search for a universal flu vaccine has received a boost from a surprising source: the 2009 H1N1 pandemic flu strain.

Several patients infected with the 2009 H1N1 strain developed antibodies that are protective against a variety of flu strains, scientists from Emory University School of Medicine and the University of Chicago have found. The results were published online Monday in the Journal of Experimental Medicine.

"Our data shows that infection with the 2009 pandemic influenza strain could induce broadly protective antibodies that are only rarely seen after seasonal flu infections or flu shots," says first author Jens Wrammert, PhD, assistant professor of microbiology and immunology at Emory University School of Medicine and the Emory Vaccine Center.

"These findings show that these types of antibodies can be induced in humans, if the immune system has the right stimulation, and suggest that a pan-influenza vaccine might be feasible."

The antibodies isolated from a group of patients who were infected with the 2009 H1N1 strain could guide researchers in efforts to design a vaccine that gives people long-lasting protection against a wide spectrum of flu viruses, say the researchers. Next, the research team is planning to examine the immune responses of people who were vaccinated against the 2009 H1N1 strain but did not get sick.

The research comes from a collaboration between the laboratories of Rafi Ahmed, PhD, at Emory and Patrick Wilson, PhD at the University of Chicago. Ahmed is director of the Emory Vaccine Center and a Georgia Research Alliance Eminent Scholar. Wilson is assistant professor of medicine at the University of Chicago's Knapp Center for Lupus and Immunology Research.

Scientists from Columbia, Harvard and the National Institutes of Health (NIH) also contributed to the study, which was funded by the National Institute of Allergy and Infectious Diseases, part of the NIH, and by the American Recovery and Reinvestment Act of 2009.

The nine patients studied were recruited through the Hope Clinic, the clinical division of the Emory Vaccine Center. They had a range of disease severities, from mild illness that waned after a few days to a severe case that required a two-month hospital stay including ventilator support. Most of the participants were in their 20s or 30s. Blood samples were usually taken about 10 days after the onset of symptoms.

The team of researchers identified white blood cells from the patients that made antibodies against flu virus, and then isolated the antibody genes from individual cells. They used the genes to produce antibodies in cell culture -- a total of 86 varieties -- and then tested which flu strains they reacted against.

Five antibodies isolated by the team could bind all the seasonal H1N1 flu strains from the last decade, the devastating "Spanish flu" strain from 1918 and also a pathogenic H5N1 avian flu strain.

Seasonal flu shots contain three inactivated viral strains, each grown in chicken eggs. Over the last decade, it was standard that one of the three is an H1N1 strain. However, vaccination with any one H1N1 strain doesn't usually result in protection against all of them – that's why the

2009 strain could make so many people sick.

Some of the antibodies the team identified stick to the "stalk" region of part of the virus (a protein called hemagglutinin). Because this part of the virus doesn't change as much as other regions, scientists have proposed to make it the basis of a vaccine that could provide broader protection.

"Previously, this type of broadly protective, stalk-reactive antibody was thought to be very rare," Wrammert says. "In contrast, in the patients we studied, these stalk-reactive antibodies were surprisingly abundant."

The team tested whether three of the antibodies they isolated could protect mice against the 2009 H1N1 strain or two other common lab strains. Two antibodies could protect mice against an otherwise lethal dose of any of the three strains, even when the antibody was given 60 hours after infection. However, one antibody only protected against the 2009 H1N1 strain.

The antibody that only reacted to the 2009 H1N1 strain came from the patient with the most severe illness. The antibody genes from that patient suggest that the patient had a complete lack of preexisting immunity to H1N1 viruses, the authors write. In cases where patients experienced a milder illness, it appears that immune cells that developed in response to previous seasonal flu shots or infections formed a foundation of response to 2009 strain.

"The result is something like the Holy Grail for flu-vaccine research," says study author Patrick Wilson, PhD, assistant professor of medicine at the University of Chicago. "It demonstrates how to make a single vaccine that could potentially provide permanent immunity to all influenza. The surprise was that such a very different influenza strain, as opposed to the most common strains, could lead us to something so

widely applicable."

Provided by Emory University