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Flu shot might also offer some protection against H5N1

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The yearly influenza vaccine that health officials urge people to get each fall might also offer certain individuals some cross protection against the H5N1 virus, commonly known as bird flu, according to investigators at St. Jude Children's Research Hospital.

The investigators found that a protein present in the annual influenza shot can act as a vaccine itself and trigger some cross protection against H5N1 in mice; and that some human volunteers already had antibodies directed against the same part of this virus. Cross protection occurs when the immune response triggered by a vaccine designed to protect against one germ also offers some protection against a different germ.

The finding also suggests that the annual influenza vaccine might be especially beneficial to populations in areas of the world where H5N1 routinely infects birds and poses a threat to people.

"The jury is still out on whether the seasonal flu vaccine is definitely a reliable way to offer people some protection from H5N1," said Richard J. Webby, Ph.D., assistant member in the Virology division of the Department of Infectious Diseases at St. Jude. "But our initial results suggest that this is a research trail worth following." Webby is senior author of the report that appears in the Feb. 13 issue of the online journal *PLoS Medicine*.

The key to the apparent cross protection against H5N1 provided by the human influenza vaccine appears to be the antibodies produced in

response to a protein called neuraminidase on the surface of the virus. Neuraminidase, which is noted as "N" in the names of viruses, is one of the major proteins on the surface of human and avian influenza viruses; and it can often be found in human influenza vaccines. However, the amount of "N" in an influenza vaccine can vary widely depending on the company that produces it.

The other protein is hemagglutinin, or "H." The variations of "H" and "N" found on viruses are numbered; and in the case of the avian influenza virus, considered by experts to be a major threat to humans, the proteins are designated H5 and N1.

"The presence of the N1 protein in both the human flu and the bird flu virus helped to convince us to look for evidence that immunity to human strains of flu might also trigger some antibody response to H5N1," Webby said.

The investigators first vaccinated mice using DNA that coded for N1 from a human influenza virus. This ensured that the mice would make only N1 and not one of the hemagglutinin proteins, thus eliminating any chance of confusion over whether their immune systems were vaccinated against hemagglutinin, neuraminidase or both.

The team showed that all 11 vaccinated mice survived infection with a virus genetically modified to make human N1, while half of another group of vaccinated mice survived infection with H5N1 itself.

The St. Jude investigators then showed that the antibodies made against N1 protected the mice against the challenges. Specifically, the team collected the serum, the antibody-containing liquid of blood, from vaccinated mice and injected it into unvaccinated mice. Six of 13 mice getting the antibody-containing serum survived infection with the H5N1 virus, indicating that antibodies against human N1 from the vaccinated

mice offered some protection against H5N1.

Finally, the team tested samples of serum from human volunteers to see if they contained antibodies that reacted against the N1 of H5N1. Sera from 31 of 38 volunteers reacted against the N1 of the human influenza virus H1N1, while serum from nine of these individuals showed low activity against the N1 protein of an H5N1 from Vietnam. It was not clear whether these individuals had developed antibodies from previous seasonal vaccination or from exposure to influenza viruses that carried N1.

"Although the number of human donors in this study was limited, the results show that some individuals have levels of antibodies that are high enough to react against H5N1," Webby said.

If the initial findings of the St. Jude study are confirmed in the future, there may be a greater interest in examining the amount of neuraminidase in yearly influenza vaccines, according to Matthew Sandbulte, Ph.D., a postdoctoral fellow at the Food and Drug Administration, who did much of the work on this project.

"Hemagglutinin is more abundant than neuraminidase on viruses and is a better target for protective immunity, so current vaccines are designed to trigger immune responses mostly to hemagglutinin," Sandbulte said. "That is why vaccines contain standard amounts of hemagglutinin, but varying amounts of neuraminidase. But if further research confirms that the N1 part of the influenza vaccine offers some cross protection against H5N1, it will be desirable to have a better idea of the amount of N1 present in these vaccines."

An implication of the ability of N1 immunity conferring some degree of protection against H5N1 is that younger people who have a shorter history of exposure to the human influenza virus H1N1 might have less

existing immune protection against this virus. "That could mean such people are more susceptible to H5N1 infection than adults," Sandbulte said.

Source: St. Jude Children's Research Hospital