A vaccine based on conserved regions could prove radical

To keep pace with rapidly mutating flu viruses, scientists reformulate influenza vaccines annually. In the process, they must accurately predict which strains will circulate each flu season. Now, new research suggests that scientists might be able to design a more potent vaccine that can deliver immunity to multiple flu strains.

Previously, researchers had identified antibodies that neutralize multiple influenza virus strains (*Proc. Natl. Acad. Sci. USA* **105**, 5986–5991; 2008; *PLoS ONE* **3**, e3942; 2008). However, they had not determined precisely how the antibodies bound the virus, making it difficult to design vaccines that elicited the responses of these antibodies.

In February, two independent research teams described how a number of human antibodies latch onto and neutralize multiple influenza A strains, including the 1918 pandemic H1 virus and the H5 bird flu virus. The research teams showed that these antibodies bind the same genetically stable region on the 'neck' of the influenza hemagglutinin protein, thereby preventing the virus from fusing with human host cells. Scientists say that antibodies that target conserved regions of the virus could be combined with antiviral medicine to treat flu victims.

To identify such antibodies, the two groups used white blood cells from healthy immunized volunteers. "Both groups screened different libraries of human antibodies in search of those with neutralizing activity against a broad range of influenza virus subtypes," says Rachelle Salomon of the US National Institute of Allergy and Infectious Diseases (NIAID).

Although the two groups identified different antibodies, the antibodies bound the same general region of the flu virus. A team led by Wayne Marasco of the Dana-Farber Cancer Institute and Harvard Medical School in Boston identified multiple human antibodies that bound a genetically stable pocket in the neck of the hemagglutinin protein (*Nat. Struct. Mol. Biol.*, doi:10.1038/nsmb.1566; 2009). Similarly, Ian Wilson of the Scripps Research Institute in La Jolla, California and his colleagues reported that the CR6261 antibody bound the same region of the hemagglutinin protein as did the antibodies identified by Marasco's team (*Science*, doi:10.1126/science.1171491; 2009). Part of Wilson's team had previously identified CR6261 (*PLoS ONE* **3**, e3942; 2008). When tested in mice, CR6261 and three of the antibodies identified by Marasco's team protected the mice from multiple influenza A strains.

Although it is possible this research could lead to the development of more effective antibody-based drugs and influenza vaccines, NIAID director Anthony Fauci cautions that there is much more work to be done. This research "ultimately could have a big impact, but it has to go through the step-by-step processes," Fauci says. He explains that "at any step in the process, it may run into some substantial blocks."

Kirsten Dorans, New York

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Getting better: Flu vaccines might be improved

Broad-acting HPV vaccines explored to fight cancer

By focusing on a unique target within the shell that surrounds the human papillomavirus (HPV), scientists may be able to develop an affordable vaccine that targets additional strains of this cancer-causing virus. Doug Lowy of the US National Cancer Institute recently discussed the potential benefits of this approach in March at an HPV vaccine symposium in New York.

The two HPV vaccines currently marketed by Merck and GlaxoSmithKline are composed of virus-like particles. When injected into the body, these particles induce the formation of antibodies that target a protein known as L1 that encases the papillomavirus. Although these vaccines effectively neutralize two HPV strains that can cause cervical cancer, these strains only account for approximately 70% of cervical cancers (*Br. J. Cancer* **95**, 1459–1466; 2006; *Lancet* **367**, 1757–1765, 2008). As a result, even vaccinated women must still be screened for signs of cervical cancer.

In an effort to develop vaccines that target a broader range of HPV strains, researchers are looking at targeting another protein known as L2. Although it also helps to form the protein shell surrounding the papillomavirus, L2 is more highly conserved across HPV strains than the L1 protein.

Studies in mice conducted by Richard Roden of Johns Hopkins University and his colleagues have shown that vaccinations containing human HPV L2 proteins protect against more HPV strains than those based on the L1 virus-like particle (*Proc. Natl. Acad. Sci. USA* **105**, 5850–5855; 2008). Because bacteria can be engineered to produce L2 proteins in culture, L2 proteins might also be cheaper to produce than the L1 virus-like particles. However, vaccines based on L2 proteins might perhaps provide shorter protection against HPV compared with those containing L1 virus-like particles. Currently, Roden's team is tweaking and modifying L2 proteins in an attempt to broaden the range of HPV strains they neutralize.

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