Earlier Flu Viruses Provided Some Immunity to Current H1N1 Influenza, Study Shows

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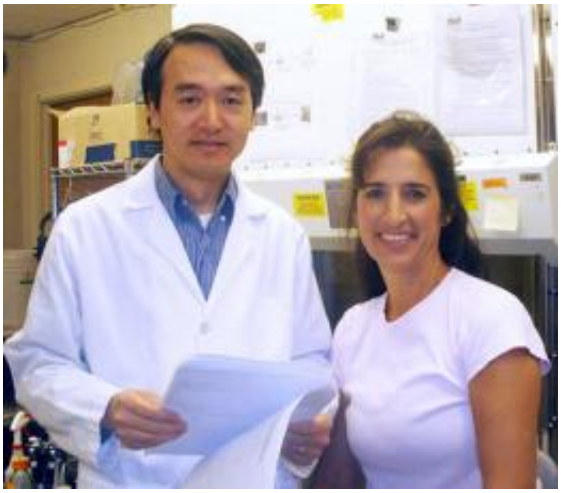

Researchers Zheng Xing, left, and Carol Cardona have identified a group of immunologically important sites on the virus that are also present in seasonal flu viruses that have been circulating for years. (UC Davis photo)

(PhysOrg.com) -- University of California, Davis, researchers studying the 2009 H1N1 influenza virus, formerly referred to as "swine flu," have identified a group of immunologically important sites on the virus that are also present in seasonal flu viruses that have been circulating for years. These molecular sites appear to result in some level of immunity to the new virus in people who were exposed to the earlier influenza viruses.

More than a dozen structural sites, or epitopes, in the virus may explain

why many people over the age of 60, who were likely exposed to similar viruses earlier in life, carry antibodies or other type of immunity against the new virus, immune responses that could be attributed to earlier flu exposure and vaccinations.

Researchers Zheng Xing, a project scientist, and Carol Cardona, a veterinarian and Cooperative Extension specialist, both of the UC Davis School of Veterinary Medicine, report their findings online in the journal of *Emerging Infectious Diseases*. The report will appear in the November print edition of the journal, published by the Centers for Disease Control and Prevention.

"These findings indicate that human populations may have some level of existing immunity to the pandemic H1N1 influenza and may explain why the 2009 H1N1-related symptoms have been generally mild," Cardona said.

"Our hypothesis, based on the application of data collected by other researchers, suggests that cell-mediated immunity, as opposed to antibody-mediated immunity, may play a key role in lowering the disease-causing ability, or pathogenicity, of the 2009 H1N1 influenza," Xing added.

He noted that immune responses based on production of specific cells, known as cytotoxic T-cells, have been largely neglected in evaluating the efficacy of flu vaccinations. In this type of immune response, the T-cells and the antiviral chemicals that they secrete attack the invading viruses.

About 2009 H1N1 influenza

The 2009 H1N1 virus is a new strain of influenza that first appeared in the United States in April 2009. Early on, it was referred to as "swine flu" because it was genetically similar to influenza viruses that normally

occur in pigs in North America. Further study, however, revealed that the virus actually included genes from viruses found in birds and humans, as well as pigs.

At first, this H1N1 influenza virus apparently caused a high number of deaths among patients in Mexico and among people with certain pre-existing medical conditions. But as it has progressed to become a pandemic or geographically widespread virus, H1N1 has caused relatively mild symptoms and few deaths.

One hallmark of this new influenza virus, according to the Centers for Disease Control and Prevention, has been the presence of pre-existing antibodies against the virus in about one third of H1N1 2009 patients over the age of 60, a phenomenon that suggested some levels of immunity may have existed to the new pandemic H1N1 virus.

To probe this phenomenon, the UC Davis researchers surveyed data from earlier studies of epitopes known to exist on different strains of seasonal influenza A. They found that these epitopes, present in other seasonal H1N1 influenza strains around the world and capable of triggering an immune response, were also present in the strains of H1N1 2009 that were found in California, Texas and New York.

Interestingly, although previous H1N1 viruses seem to have produced a protective antibody response in exposed people, these antibodies largely did not provide cross-protection for individuals infected with the H1N1 2009 strain of influenza. The researchers theorize that, rather than stimulating protective antibodies, the epitopes of the new H1N1 2009 virus produced an immune response by triggering production of cytotoxic T-cells, which boost a person's immune defenses by killing infected cells and attacking the invading viruses.

Humans can mount two types of immune responses. One type is

produced when the invading virus triggers production of protective antibodies that circulate in the bloodstream, and the other type, described above, is known as a cell-mediated immune response. It is produced when the invading virus triggers the activation of cytotoxic T-cells, a process that helps clear the virus from the body. Evidence from earlier studies suggests that cytotoxic T-cell immune immunity can be caused by either an active viral infection or by vaccination against such a virus.

Implications for avian influenza

The researchers note that about 80 percent of the epitopes found in seasonal influenza and flu vaccine viruses are also present in the highly pathogenic H5N1, or avian influenza, virus. They suggest that these epitopes may have protected some individuals infected with the highly pathogenic H5N1 virus through cytotoxic T-cell immunity.

However, the H5N1 virus rapidly reproduces itself and spreads so quickly within vital organs that the body may not be able to launch protective immunity, thus accounting for the high fatality rate of avian influenza.

Furthermore, only a fraction of the human population can recognize the specific epitopes necessary to cause the appropriate protective immune response, which may explain why the H1N1 2009 virus, as well as avian influenza, may vary in severity from person to person.

Xing and Cardona propose that immunity acquired from seasonal influenza or flu vaccinations may provide partial protection for patients infected with the avian influenza virus due to the shared epitopes essential for cytotoxic T-cell immunity.

This is supported by statistics from the World Health Organization

indicating that there have been fewer avian influenza infections in people 40 years and older than there were in people under that age, and that the fatality rate of avian influenza was just 32 percent in the older age group but 59 percent in the younger group.

The researchers, therefore, suggest that repeated exposure to seasonal influenza viruses or flu vaccinations may have resulted in cytotoxic T-cell immunity to avian influenza, and that the same type of immunity may also have developed in people exposed to the H1N1 virus.

Source: University of California - Davis