H1N1 flu virus used new biochemical trick to cause pandemic

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(PhysOrg.com) -- The influenza virus, scientists well know, is a crafty, shape-shifting organism, constantly changing form to evade host immune systems and jump from one species, like birds, to another, mammals.

Now, in a report in the current (Aug. 5) Public Library of Science Pathogens, an international team of scientists shows that the recent pandemic-causing H1N1 flu virus used a new biochemical trick to spread efficiently in humans.

The new work expands the repertoire of known factors flu viruses can use to hijack a host cell and amplify infection in mammals, including humans. The discovery not only yields new insight into the subtle biology of flu, but also reveals another genetic marker public health officials can use to presage pandemics.

"We have found why the pandemic H1N1 virus replicated so well in humans," says Yoshihiro Kawaoka, one of the world's leading influenza experts and a professor of pathobiological sciences at the University of Wisconsin-Madison's School of Veterinary Medicine.

The H1N1 flu virus caused a worldwide epidemic in 2009 and 2010, sickening as many as 34 million Americans and causing up to an estimated 6,000 deaths in the United States alone.

The H1N1 virus, Kawaoka explains, is really a combination of four

different avian and swine flu viruses that have emerged during the past 90 years, and even includes genetic residue of the 1918 pandemic virus, an influenza that killed as many as 20 million people.

Typically, the presence of two amino acids -- lysine and asparagines -- in specific sites on a key avian protein are required for a flu virus to make the jump from an animal host and replicate efficiently in human cells. The H1N1 virus lacked both of these amino acid building blocks, posing a puzzle for scientists.

The new study found that the lysine amino acid resides in a completely different location on the protein and is responsible for the H1N1 virus's ability to adapt to and co-opt human cells. "This pandemic H1N1 has this mutation and is why it can replicate so well in humans," says Kawaoka, who also is a professor at the University of Tokyo. "This gives us another marker to help predict the possibility of future flu pandemics."

The new PLoS Pathogens report also includes critical data for the three-dimensional structure of the H1N1 protein known as PB2, which originated from an avian virus. The structure was derived from an exquisite X-ray crystallographic study produced by the Seattle Structural Genomics Center for Infectious Disease (SSCGID), a consortium of Washington State-based organizations whose mission is to provide a "blueprint" for the development of new drugs, vaccines and diagnostics for deadly infectious diseases.

The structural data, says Kawaoka, provides essential insight into how the virus interacts with the host cell, and could help provide a basis for antiviral agents that could be used to thwart a future flu virus that uses the same amino acid trick to infect human cells. "Clearly, the host factors in human cells are doing something. The structure may help us better understand the interplay between the virus and the host human

cell."

According to Bart L. Staker of Emerald BioStructures Inc., a member of the SSCGID, the structural data also reveals changes in the surface shape of the avian virus protein in H1N1, which could, in turn, be responsible for thwarting factors in the human cell that would otherwise inhibit infection.

Peter Myler, a principal investigator at Seattle Biomedical Research Institute (Seattle BioMed) and leader of the SSCGID, says the structural data plays an essential role in shedding new light on the H1N1 virus. "By determining the three-dimensional structure of this protein, we have new information that can be used to develop much-needed new interventions for this deadly disease," explains Myler.

To date, the SSCGID has solved more than 200 protein structure from a number of bacterial, viral, fungal and protozoan pathogens.

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