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Studies showing how bird flu viruses could adapt to humans offer surveillance and vaccine strategies

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Bird flu viruses are potentially highly lethal and pose a global threat, but relatively little is known about why certain strains spread more easily to humans than others. Two studies published today in the journal *Cell* identify mutations that increase the infectivity of H5N1 and H7N9 viruses through improved binding to receptors in the human respiratory tract. The findings offer much-needed strategies for monitoring the emergence of dangerous bird flu strains capable of infecting humans and for developing more effective vaccines.

"Avian influenza viruses evolve rapidly, and there are many subtypes of these viruses that we need to be concerned about because, in many cases, humans do not have immunity to these newer strains," says senior study author Ram Sasisekharan of the Singapore-MIT Alliance for Research and Technology. "Our findings can be put to use to monitor the evolution of H5N1 and H7N9 viruses in the field as well as in the clinic if and when there is an outbreak."

In the past 10 years, the H5N1 virus has infected nearly 600 individuals in several outbreaks around the world, killing about 60% of those infected. And over the past few months, a lethal subtype of the H7N9 virus has been found in at least 131 people, mostly in mainland China. Although these viruses do not normally infect humans, over time they can adapt to humans and gain the ability to spread more easily from person to person, underscoring the importance of finding out which

mutations could enhance the ability of these viruses to infect humans.

To address this question, Sasisekharan and his team analyzed the structure of the H5N1 and H7N9 viruses, focusing on hemagglutinin (HA)—a type of viral protein that binds to cell receptors in the respiratory tract of hosts. They characterized the set of HA mutations required to increase the preference of the viruses for human receptors, discovering that only a single amino acid change in the HA sequence is necessary for this to occur. Moreover, they found that distinct HA mutations are evolving in the H7N9 virus indicating that currently recommended H7 vaccines would not be effective against this newly emerged virus.

"Right now, there is no vaccine to protect against the H7N9 virus, and our findings could guide efforts to develop effective vaccine strategies," Sasisekharan says.

More information: Tharakaraman et al.: "Glycan Receptor Binding of the Influenza A Virus H7N9 Hemagglutinin." *Cell*, dx.doi.org/10.1016/j.cell.2013.05.034

Tharakaraman et al.: "Structural Determinants for Naturally Evolving H5N1 Hemagglutinin to Switch its Receptor Specificity." *Cell*, dx.doi.org/10.1016/j.cell.2013.05.035

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