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Researchers map molecular details that encourage H1N1 transmission to humans

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The 2009 H1N1 pandemic influenza virus appears to have required certain mutations in order to be transmitted to humans, according to a paper in the September *Journal of Virology*. The research could prove extremely valuable for efforts to predict human outbreaks.

The 2009 influenza pandemic was caused by a swine influenza virus that mutated in a way that made it transmissible among humans. The researchers, led by Hualan Chen of the Harbin Veterinary Research Institute, Harbin, China, have determined the probable details of the mutations that led to human transmission.

In this study, Chen, who is director of the National Avian Influenza Reference Laboratory at the Institute, and her collaborators have shown that two specific mutations in each of two proteins appear to be critical to transmission to, and among humans. One of those mutations, of a single amino acid in the virus' hemagglutinin protein, gives the virus the ability to bind to human receptors, and enables transmission in mammals via droplets of respiratory fluids.

That amino acid, in the 226th slot in the protein, is glutamine. The researchers showed its importance by causing a mutation from glutamine, the amino acid in that position seen in viruses from infected humans, to argenine, as seen in swine. Working in cell cultures, the researchers showed that the switch dampened the virus' ability to bind the human receptor, while boosting its ability to bind to the avian receptor. They showed further that the change rendered the virus non-

transmissible via respiratory droplets in guinea pig models, and unable to replicate in the lungs of ferrets—results that suggest, but do not prove that the same may happen in humans.

Also in guinea pigs, changing an amino acid in the virus' PB2 protein abolished transmission in guinea pigs via respiratory droplets, while that change, plus another single amino acid change in the hemagglutinin protein, killed such transmission in ferrets.

It gets still more convoluted. The same amino acid in the PB2 protein that enables virus transmission via respiratory droplets, which is located at position 271 in that protein, can also encourage the afore-mentioned mutation in hemagglutinin position 226 to glutamine, which enables the virus to cleave to the human receptor.

The value of all this information, says Chen, is that it provides a means for predicting outbreaks of human-transmissible H1N1.

More information: Y. Zhang, et al., 2012. Key molecular factors in hemagglutinin and PB2 contribute to efficient transmission of the 2009 H1N1 pandemic influenza virus. *J. Virol*. 86:9666-9674. bit.ly/asmtip0912b

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