Highly pathogenic avian influenza viruses (H5N1) that acquire human receptor specificity and anti-influenza drug discovery

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Pandemic influenza viruses can emerge through continuous evolution and acquisition of specific mutations or through reassortment between human and avian viruses. Highly pathogenic H5N1 influenza A viruses have spread to numerous countries in Asia, Europe and Africa infecting not only large numbers of poultry, but an increasing number of humans, often with lethal effects. Human influenza A viruses bind predominantly sialic acid (Sia) α2-6Galatose (Gal) linkages, whereas bird viruses bind Siaα2-3Gal predominantly. A conversion from Sia2-3Gal to Sia2-6Gal recognition is thought to be one of the changes that must occur before avian influenza viruses can replicate efficiently in humans and acquire the potential to cause human to human transmission and pandemic in human world. By identifying mutations in the receptor-binding hemagglutinin (HA) molecules that would enable avian H5N1 viruses to recognize human-type host cell receptors, it may be possible to predict the emergence of pandemic viruses.

We found that several H5N1 viruses from humans isolated in China, Thailand and Vietnam bound to human receptor, Siaα2-6Gal sugar chains and identified amino acids in HA which involve in the switching of receptor binding specificity from avian to human receptors. In the case of Lao PDR, all H5N1 viruses tested retained avian-like receptor specificity to α2-3-linked sialic acids, but some had altered affinities for Siaα2-3Gal because of mutations in HA glycoprotein at positions 133, 158, 183 (H3 numbering) . These results indicate that the avian H5N1 is now acquiring mutations causing human to human transmission. Many viral diseases are causing in Asian countries. These changes may contribute to emergence of a pandemic influenza strain and are critical for devising surveillance strategies and drug discovery. We developed new highly active influenza virus sialidase inhibitors and propose the introduction and development of a new frontier of “glycovirology”, and “glyco-drug discovery” into Asian countries.