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Lung alert

A potential method for development of a bird flu vaccine

The mechanisms by which animal strains of the influenza virus adapt themselves to invade human hosts are not fully understood, leading to difficulty in effective immunisation and treatment. Attempts are now being made to use structurally modified mutants to develop vaccines and therapeutic antibodies to pre-empt the emergence of human-adapted H5N1 strains of the avian influenza virus.

The viral haemagglutinin (HA), which is defined as the receptor binding domain (RBD) of its spike, binds to specific sialic acid (SA) receptors in the respiratory epithelium. Avian virus particles which adapt to humans preferentially bind to α 2,6-SA receptors rather than α 2,3-SA receptors.

The authors created mutants with this altered recognition (pseudoviruses) by causing structural changes in amino acid sequences. Their infectivity was confirmed by inoculation into 293A renal epithelial cells. The SA specificity of the different HA mutants was then analysed by a modified glycan microarray method and a resialylated HA assay was used to confirm the SA recognition in the mutants. Immunogenic and antigenic differences were further identified by vaccination of mice and generation of monoclonal antibodies (mAbs).

They identified mutations in the avian H5 haemagglutinin that alter its SA specificity. Moreover, they induced mAbs which can more effectively inhibit these mutants. Whether this can lead to the development of a viable vaccine and mAbs for use in clinical practice remains uncertain. However, this attempt is unique in its novelty of approach and may have implications for further research which targets hitherto unexplored viral components.

- ▶ Zhi-Yong Yang, Chih-Jen Wei, Wing-Pui Kong, *et al*. Immunization by avian H5 influenza hemagglutinin mutants with altered receptor binding specificity. *Science* 2007;**317**:825–8

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