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Press Release

HKU Discovers Vaccinia Virus-Based Multivalent H5N1 Avian Influenza Vaccines

H5 Vaccine

The highly pathogenic H5N1 avian influenza A virus is now entrenched in poultry in many countries in Asia and Africa. Its repeated, though inefficient, transmission to humans continues to pose a pandemic threat. The severity of disease currently seen in human H5N1 disease highlights the fact that an H5N1 pandemic may have catastrophic consequences. It is believed that vaccines remain one of the most effective public health interventions to reduce the morbidity, mortality and the socio-economic disruption associated with an influenza pandemic. Such a vaccine should be safe and effective. Since embryonated hens eggs will be a limiting factor for a rapid scale-up of production in a pandemic emergency setting, such vaccines should be amenable to production in cell culture. Furthermore, if such a vaccine is be stockpiled in advance of pandemic emergence (pre-pandemic vaccines), it should be protective against a wide range of antigenically variant H5N1 virus clades and retain their stability over a long storage period. In a H5 pandemic situation, such vaccines may have to be deployed at short notice, the induction of good and rapid protective immune response after the first dose of vaccine is a major advantage. To address these issues, the team at the Department of Microbiology at The University of Hong Kong in collaboration with Dr. Liyanage P. Perera at the National Institutes of Health, USA has developed a novel vaccine strategy for the H5N1 virus by modifying a licensed smallpox vaccine. Results of this investigation have been published in the March 2009 issue of The Journal of Immunology.

Research methodology and major findings

In this investigation, the Wyeth New York Board of Health strain of vaccinia and modified vaccinia virus Ankara were used as the prototype vaccine strains. Vaccina virus-based vaccine candidates that express in tandem 5 genes of the clade 1 H5N1 strain of influenza A (A/Vietnam/1203/2004), namely, the H5 hemagglutinin gene, N1 neuraminidase gene, nuclear protein NP gene, and genes encoding the two matrix

polypeptides M1 and M2 of the A/Chicken/Indonesia/PS/03 (Clade 2.1, of Indonesian origin) were developed and tested in mice. Furthermore, we examined the effect of including the immunostimulatory IL-15 cytokine in this vaccine virus to act as an immune adjuvant (i.e. boost the immune response). These vaccines were demonstrated to provide potent and complete protection to mice subsequently challenged with a H5N1 viruses of a different clade (Clade 2.1). The incorporation of human IL-15 cytokine gene in these vaccinia-based vaccines resulted in the improvement of both antibody and cellular immune responses against H5N1 viruses in relation to both the magnitude of the responses and their long duration. A single dose of this new vaccine induced higher levels of specific H5N1 antibodies than those induced by the existing licensed commercial H5N1 vaccine.

Significance of the research

Findings from this study suggest the feasibility of a new and alternative strategy for H5 vaccine development. Our approach has the following advantages:

1. The vaccinia-based vaccine delivery vectors have a proven safety track record for vaccination;
2. Some of these live-attenuated vaccines can induce potent immune responses after a single vaccine dose without the risk of influenza virus gene reassortment inherent in live attenuated cold adapted influenza vaccines. They are also likely to be safe in immunocompromised patients.
3. The vaccines can be manufactured with existing vaccine production facilities and does not require high level biosafety containment for their production.
4. They can be produced using cell-culture methods thereby avoiding potential production bottlenecks which may apply to egg-based vaccines.
5. A single vaccine dose will provide rapid protective immune responses

In the future, the research team plans to extend these studies to further optimize and evaluate the efficacy of these vaccines. In addition, the team aims to explore this strategy to generate a “universal influenza vaccine” that provides protection against a range of influenza viruses subtypes covering a range of pandemic virus candidates.

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Please visit the website at http://web3.hku.hk/facmed/hkumed/news_list.php for press photos and supplementary information.

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