Jimmy Kwang, J Vaccines Vaccin 2012, 3:4
http://dx.doi.org/10.4172/2157-7560.S1.011

OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Vaccines and Vaccination

August 20-22, 2012 Hilton Chicago/Northbrook, USA

Baculovirus surface displayed hemagglutinin as a mucosal vaccine vector against H5N1 in mice

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Recent reports of baculovirus-mediated transductions of viral glycoprotein genes into mammalian cells and their efficient gene delivery in animal models have gained special attention. Here, we described the construction of baculovirus expressing Heamagglutinin (HA) under the control of the immediate-early promoter 1 (ie1) derived from the white spot syndrome virus (WSSV) genome, which enables the expression of hemagglutinin at the early stage of infection in insect cells, thereby enhancing the display of HA on the baculovirus envelope. Along with this suitable vaccine, the route of administration of the vaccine has a profound effect in controlling mucosally acquired infections such as influenza. Induction of mucosal immunity through nasal/oral immunization is an effective way to control influenza infection. In this study, we evaluated the oral vaccination of ie1 promoter based baculovirus displayed hemagglutinin (BacHA) against highly pathogenic H5N1 virus infection in a mouse model. Oral administration of live BacHA significantly induced strong cross-clade neutralization antibodies, both systemic and mucosal immune responses, against a challenge of 100 TCID50 of heterologous H5N1 strains (clade 1.0, 2.1, 2.3 and clade 8.0) infections. As an alternative approach, inactivated baculovirus was encapsulated within a reverse-micelle structure of phosphatidyl choline and delivered into the gastrointestinal tract of mice. Interestingly, oral administration of encapsulated BacHA significantly enhanced both systemic and mucosal immune response. The level of immune response obtained with encapsulated inactive form of baculovirus was equivalent with those obtained with live baculovirus, suggesting the potential of baculovirus as live and inactivated vaccine. Also, intranasal administration of baculovirus surface displayed HA showed that high level of HA specific mucosal and systemic immunity in mice. Moreover, the combination of BacHA with recombinant CTB mucosal adjuvant forms an effective mucosal vaccine and which provided 100% protection against 10 MLD50 of H5N1 infections. The baculovirus surface-displayed HA vaccine is efficacious in inducing mucosal immune responses as well as systemic immune responses and does not require either sophisticated biocontainment infrastructure or downstream purification processes for mass production. Further, oral or intranasal vaccinations are non invasive, pain free and affordable with improved logistics and immunization coverage during pre pandemic or pandemic situation.

Keywords: Influenza H5N1, baculovirus, recombinant baculovirus, immediate-early promoter 1, Hemagglutinin, mucosal vaccine

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