

International Conference on **Influenza**

August 24-26, 2015 London, UK

Novel coated nanoclusters from structure-stabilized influenza H7N9 HA induce enhanced protective immunity

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Nanoparticles from antigenic proteins are highly immunogenic because of the novel quality brought from their particulate structures. We developed a two-step procedure to generate protein nanoparticles (nanoclusters) from recombinant trimeric structure-stabilized H7N9 HA (stHA). These nanoclusters have an average diameter of 273.6 nm with a similar Zeta potential to the soluble protein, demonstrating their comparable solution stability. In a dendritic cell culture, these nanoclusters were reactive to upregulate the CD86 expression and stimulate the production of TNF- α . To evaluate the immunogenicity of the nanoclusters, mice were immunized with either intramuscular (i.m.) or intranasal (i.n.) route. We found that these nanoclusters induced extremely high levels of serum IgG with high neutralization activity as well by i.m. route. One i.m. immunization with 10 μ g of the nanoclusters provided complete protection against a 10 LD₅₀ live H7N9 virus challenge with slight bodyweight loss decreases. Two immunizations with either i.m. or i.n. route protected immunized mice against virus challenges without any disease symptoms. Systemic antibody responses were found to be durable up to six month: IgG levels were not significantly different in the first three months but dropped in six months. However, the neutralization activity and hemagglutination inhibition (HAI) titers were not dropped significantly, demonstrating the durability of the protective antibodies. Because of the high immunogenicity and time-efficient egg-independent production (a few weeks not several months), stHA nanoclusters have potentials to be developed into a new generation of influenza vaccines, particularly for fighting an emerging influenza pandemic.

Biography

Bao-Zhong Wang has completed his PhD in the year of 2003 from Shanghai Institute of Biochemistry, Chinese Academy of Sciences, Shanghai, China. He is an Assistant Professor in the Department of Microbiology and Immunology, Emory University School of Medicine. He has published more than 35 peer viewed papers.

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