Activation of protective innate-adaptive immunity duo for conferring rapid sustained broad protection of vaccines against pathogens

De-chu Christopher Tang
VaxDome LLC, USA

We report that intranasal administration of an E1/E3-defective (ΔE1E3) adenovirus serotype 5 (Ad5) vectored influenza vaccine could induce seroconversion in human volunteers without appreciable adverse effects even in subjects with pre-existing Ad5 immunity. Mice and ferrets were well protected against challenge by a lethal dose of an H5N1 avian influenza virus following intranasal instillation of an Ad5 vector encoding hemagglutinin (HA) in a single dose regimen. Moreover, the ΔE1E3 Ad5 particle itself without trans-gene could confer rapid sustained broad protection against influenza by inducing an anti-influenza state in a drug like manner, conceivably by activating a specific arm of innate immunity. An Ad5 vector encoding HA thus consolidates drug and vaccine into a single package which allows the Ad5 backbone to induce protective innate immunity capable of conferring nearly immediate and prolonged (e.g., 5 hours to 47 days) protection as the first wave against influenza followed by HA mediated adaptive immunity as the second wave before the innate immunity associated anti-influenza state declines away. In addition to ΔE1E3 Ad5_s capacity to rapidly induce an anti-influenza state, an Ad5 vector encoding a bioengineered Bacillus anthracis protective antigen (PA) could also confer rapid (e.g., 1-2 days) prophylactic or post-exposure anthrax therapy with synergy to antibiotic treatment in a murine model. Both rabbits and macaques were well protected by an Ad5-PA vectored nasal anthrax vaccine in a single dose regimen against inhalational anthrax following challenge with a lethal dose of Bacillus anthracis Ames spores. Overall, the work conceivably would foster the development of a novel non-invasive drug-vaccine duo platform technology capable of conferring rapid sustained broad protection against pathogens with neither the potential to induce drug resistance nor that to trigger harmful systemic inflammation.

dechutang@gmail.com

An H5N1 M2e vaccine provides protection against H7N9 infection

Bojian Zheng and Ho-Chuen Leung
The University of Hong Kong, Hong Kong

In March 2013, a patient infected with a novel avian influenza A H7N9 virus was reported in China. Since then, there have been 458 confirmed infection cases and 177 deaths. The virus contains several human adaptation markers indicating that H7N9 has pandemic potential. The outbreak of this new influenza virus highlighted the need for the development of universal influenza vaccines. Previously, we demonstrated that a tetrameric peptide vaccine based on the matrix protein 2 ectodomain (M2e) of the H5N1 virus (H5N1-M2e) could protect mice from lethal infection with different clades of H5N1 and 2009 pandemic H1N1 influenza viruses. In this study, we investigated the cross protection of H5N1-M2e against lethal infection with the new H7N9 virus. Although five amino acid differences existed at positions 13, 14, 18, 20 and 21 between M2e of H5N1 and H7N9, H5N1-M2e vaccination with either Freund’s adjuvant or the Sigma Adjuvant System (SAS) induced a high level of anti-M2e antibody which cross reacted with H7N9-M2e peptide. A mouse adapted H7N9 strain, A/Anhui/01/2013m was used for lethal challenge in animal experiments. H5N1-M2e vaccination provided potent cross protection against lethal challenge of the H7N9 virus. Reduced viral replication and histopathological damage of mouse lungs were also observed in the vaccinated mice. Our results suggest that the tetrameric H5N1-M2e peptide vaccine could protect against different subtypes of influenza virus infections. Therefore, this vaccine may be an ideal candidate for developing a universal vaccine to prevent the re-emergence of avian influenza A H7N9 virus and the emergence of potential novel reassortants of influenza virus.

bzheng@hkucc.hku.hk