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

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We report that intranasal administration of an E1/E3-defective (ΔE1E3) adenovirus serotype 5 (Ad5)-vectored influenza vaccine could induce sero-conversion 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.

Biography

De-chu Christopher Tang is the Founder of VaxDome LLC and Vaxin Inc. He has obtained his PhD in Microbiology from Indiana University in 1989. He carried out his Post-doctoral work at Baylor College of Medicine, Duke University and University of Texas Southwestern Medical Center. He then joined the Faculty at University of Alabama at Birmingham (UAB) in 1994; subsequently founded Vaxin Inc. on UAB campus in 1997 and was responsible for Vaxin's daily operation as the Chief Scientific Officer until 2012. He was one of the pioneers during the development of DNA vaccines, non-invasive skin-patch vaccines, adenovirus-vectored nasal vaccines and adenovirus-vectored poultry vaccines as well as the protective innate-adaptive immunity duo platform technology. He has received the Wallace H. Coulter Award for innovation and entrepreneurship in 2000 and Vaxin Inc., was selected as a Tech Museum Awards Laureate in 2007. He was selected as a Distinguished Overseas Scientist by the South Korea KOFST Brain Pool Program in 2012; subsequently joined Chung-Ang University and International Vaccine Institute (IVI) in Seoul. He was also appointed as a Scientist at IVI after the Brain Pool Program Award expired in 2013. He founded VaxDome LLC in Birmingham, Alabama, USA in 2014.

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