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Virus like particle (VLP) forming DNA vaccine Encapsidated in Nonreplicable Baculovirus Nanocarrier

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Despite the advantages of DNA vaccines, overcoming their lower efficacy relative to that of conventional vaccines remains a challenge. Here, we constructed a human endogenous retrovirus (HERV) envelope-coated, nonreplicable, baculovirus-based virus like particle (VLP) forming DNA vaccine against swine influenza A/California/04/2009(H1N1). Previous we reported the efficacy of influenza HA DNA vaccine using a non-replicable baculoviral DNA vaccine (AcHERV-pdmH1N1 HA). However, AcHERV-pdmH1N1 HA vaccine only elicits an immune response against same HA antigen and limits the degree of immune response against whole viral antigen compare to the commercial killed vaccine. Here, we constructed a baculovirus carrying pdmH1N1 HA, NA and M gene for making VLP in host cell. Comparable to monovalent HA vaccine, AcHERV-pdmH1N1 HA-NA-M showed a strong humoral, cellular immune responses, and protected against pathogenic H1N1 virus in challenge test. Our AcHERV-pdmH1N1 VLP forming DNA vaccine could be a potential vaccine candidate to achieve an efficacy comparable to that of killed virus vaccines.

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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 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 transgene 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 noninvasive 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.

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