RESEARCH ABSTRACT

SWINE HEALTH

Title: Improvement of vaccine protection against swine influenza: Proof-of-concept - **NPB #08-261**

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Scientific Abstract

Swine influenza is a growing and re-emerging concern in the U.S. swine industry. Historically, swine influenza in the U.S. had been only due to classical H1N1 (i.e., α clade) swine influenza virus (SIV) and can be relatively well controlled through vaccination using an inactivated virus. However, such stability was disturbed after introduction of H3N2 SIV, which resulted in the emergence of numerous reassortants between H1N1 and H3N2 and increased antigenic changes within each subtype. All these occurrences have negatively impacted the efficacy of current commercial vaccines. Such an inferior effectiveness of current inactivated virus vaccines raises the need for better vaccination strategies for SIV. It was then our hypothesis that the delivery of multiple exogenous and endogenous SIV antigens/genes in an organized manner (i.e., mimicking natural infection) induces effective and balanced humoral and cell-mediated immune responses in immunized animals. The main objective of the study was to generate an immunization vector capable of providing the source of both immunogenic endogenous and exogenous antigens for the balanced stimulation of the immune system.

The proposed work started with constructing a recombinant baculovirus (*Autographa californica* nucleopolyhedrovirus, AcMNPV) that can serve as multiple SIV antigen exchange vector for surface display (i.e., pseudotyping antigen) as well as endogenous expression of targeted antigens using gene cloning and baculovirus recombinant techniques. The target antigens were hemagglutinin (HA) for surface display and matrix (M) protein for endogenous expression based on our recent assessment of their role in the SIV immunity. A classical H1N1 SIV isolate (A/Sw/IA/1992) was used as the donor of the target genes. The resulting recombinant baculovirus was then used as immunogen (i.e., vaccine) and evaluated in animal trials measuring parameters associated with humoral and cell-mediated immune responses in comparison to pigs inoculated with SIV (A/Sw/IA/1992) and wild type baculovirus.

A viable recombinant baculovirus which displayed the immunologically recognizable HA protein on the surface and harbored functional M gene was successfully constructed. When injected with the recombinant baculovirus twice, pigs developed antibodies against the HA protein which were measurable by HI, ELISA and SN tests. The antibody kinetic was comparable with that in pigs inoculated with SIV itself. Pigs inoculated with wild type baculovirus did not produce antibody specific for the HA protein. However, antigen-specific CMI response (blastogenesis and interferon-γ production) was much weaker or minimal in the immunized pigs as compared to that in challenged pigs. Although optimal CMI response could not be obtained in pigs and further work remains to address that issue, the proposed work demonstrated a new approach combining the capability of surface display, mammalian cell transduction and the sequential endogenous antigen expression in the same baculovirus vector, mimicking the natural infection pathway of the virus on host cells. Therefore, a similar approach might provide a new tool for safe antigen delivery, which in turn enhances protective immunity by inducing both humoral and CMI responses against SIV.