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Efficacy and Cross-protection of a Bivalent H1N1/H3N2 Swine Influenza Vaccine in Swine Challenged with Swine Influenza Virus Subtype H3N2

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Introduction

Numerous isolations of H3N2 swine influenza virus (SIV) from U.S. swine herds since 1998 has led to the development of SIV vaccines against both subtypes H1N1 and H3N2. This study examines the serological cross-reactions of swine vaccinated with a bivalent H1N1/H3N2 SIV vaccine against heterologous domestic H3N2 isolates as well as ability of the vaccine to protect swine against challenge with a virulent heterologous H3N2 virus.

Materials and Methods

Vaccines and Vaccination: The vaccine was prepared from inactivated H1N1 and H3N2 antigen fluids standardized to contain a minimum H3N2 antigen dose and adjuvanted with Emunade®, Schering-Plough Animal Health's proprietary dual adjuvant system. Four-to-five week-old swine from a high-health herd free of swine influenza, *Mycoplasma hyopneumoniae*, PRRS, and pseudorabies, were randomized into treatment groups and vaccinated twice, 14 days apart, with 2 mL intramuscularly.

Hemagglutination Inhibition (HI) Antibodies: To evaluate cross-reactions among H3N2 isolates, sera from vaccinated swine were tested for HI antibodies to antigens prepared to several unrelated H3N2 isolates from the U.S.A. Antigens and antisera to the Texas/4199-2/98 and NorthCarolina/35922/98 isolates were obtained from the National Veterinary Services Laboratory.

Challenge and Post-challenge Procedures: Swine were inoculated intranasally with a virulent H3N2 challenge virus heterologous to the vaccine strain. On day 5 post-challenge, swine were euthanized; lungs were scored for gross lesions and samples frozen for virus isolation. Lung consolidation scores and virus isolation from lungs were evaluated by the Wilcoxon (Mann-Whitney) Exact Rank Sum Tests.

Results and Conclusions

Lung Scores and Virus Isolation: The H3N2 SIV challenge was severe, producing a median lung consolidation score in the nonvaccinated swine of 10.2%. There was a highly significant reduction in lung lesions in vaccinated swine (median score 1.3%; $P < 0.0001$). The percentage of lung samples from which virus could be isolated was also significantly reduced in vaccinated swine ($P = 0.01$).

HI Antibody Titers: All swine were negative (titer < 10) to H3N2 prior to vaccination and the nonvaccinated swine remained serologically negative prior to challenge. Vaccinates developed significant H3N2 titers to both the vaccine and challenge virus, and to the other contemporary U.S. isolates evaluated. These serological data are consistent with previously reported data demonstrating genetic and antigenic similarity of the hemagglutinin genes of these viruses (1-4) and support a prediction that the vaccine would protect against the prevalent H3N2 isolates in the U.S. swine population.

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