

# Rapid Development of Efficacious Swine Vaccines for Pandemic H1N1

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Ryan Vander Veen, graduate student; Mark Mogler, graduate student; Kurt Kamrud, collaborator associate professor of animal science; D.L. (Hank) Harris, professor of animal science

### Summary and Implications

Pandemic H1N1 (pH1N1) influenza was first reported in the United States in April 2009. Since then, the virus has spread worldwide in both human and swine populations. Currently, pH1N1 influenza is the most common H1N1 virus infecting pigs in the United States. Vaccination of swine against pH1N1 represents the single best method of protecting against infection.

### Introduction

The recent outbreak of pH1N1 highlights the zoonotic potential of influenza viruses. In addition to the pH1N1 virus, several studies have reported zoonotic transmission of swine influenza viruses to humans. Swine may play an important role in the creation of novel reassortant influenza viruses that may have human health implications. Vaccination of swine against influenza can significantly decrease morbidity and therefore decrease the zoonotic potential of swine influenza viruses. In this study we demonstrate a rapid response to the pH1N1 outbreak by producing a vaccine based on the alphavirus replicon technology in less than two months after the initial report. We also demonstrate vaccine efficacy of recombinant hemagglutinin (HA) and replicon particle vaccines following homologous pH1N1 influenza challenge.

### Materials and Methods

The HA gene from pH1N1 was commercially synthesized and inserted into the alphavirus replicon vector using previously described methods. Both recombinant HA protein and replicon particles expressing the HA protein were produced and used in a vaccination-challenge animal study. Twenty-five total pigs were divided equally among five treatment groups. The group treatments were: 1) sham; 2) HA RP; 3) recombinant HA high-dose; 4) recombinant HA mid-dose; and 5) recombinant HA low-dose. Pigs received respective vaccination treatment on study days 0 and 21. All animals were challenged intratracheally with

pH1N1 virus on study day 47 and were necropsied 5 days post-challenge. Sera were collected throughout the study for hemagglutination inhibition (HI) serum antibody testing. Nasal swabs were collected daily post-challenge for quantification of live virus shedding. At necropsy, pig lungs were grossly examined for lesions typical of swine influenza, and samples were also collected for histopathological analysis. Animal weights were taken prior to challenge and again at necropsy for determination of average daily gain (ADG) post-challenge. All animal work was approved by the ISU IACUC.

### Results and Discussion

All pigs receiving either the HA RP or any dose of recombinant HA vaccine developed positive HI antibody titers post-vaccination. Following challenge, all vaccinated groups had significantly lower gross lung scores than the sham group. These results correlated with microscopic analysis of lung samples which also indicated that vaccinated animals had significantly lower histopathological scores than the sham animals. No live virus was detected from nasal swab samples collected from HA RP and recombinant HA high-dose vaccinated animals at any time point post-challenge while all animals in the sham group were positive by day 3 post-challenge. The mid- and low-dose recombinant HA groups shed significantly less virus than the sham group at days 4 and 5 post-challenge. All vaccinated groups demonstrated higher ADG than the sham group.

These results demonstrate that alphavirus replicon-based HA vaccine are efficacious against pH1N1. Of importance, all vaccinated groups had higher ADG values, and decreased nasal shedding of the virus and decreased pulmonary disease when compared to the sham group. In addition, we demonstrated that this technology could be utilized rapidly to produce vaccines against an emerging virus.

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