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SUBMISSION DEADLINE IS NOVEMBER 15, 2012
Immune response and effect of maternal antibody interference on vaccination with a bivalent swine influenza vaccine

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Introduction
Vaccination against swine influenza virus (SIV) is an important management tool. Maternally-derived antibodies (MDA) can be detected in pigs up to 16 weeks of age and may affect vaccination. The objective of this study was to investigate the immune response to a commercial bivalent SIV vaccine and the effect that the presence of MDA may have immunologically and on vaccine efficacy in pigs experimentally infected with a heterologous H1N1 SIV isolate.

Materials and methods
Ninety-six crossbred pigs were procured at 10-12 days of age from 2 herds serologically negative for PRRSV and Mycoplasma hypomunovaricaceae/appendicitis. The pigs were allocated to 2 challenge groups with MDA or without MDA determined by HI test at 3 or 5 wks of age. Two weeks after the second vaccination, a virulent classical H1N1 strain, A/swine/IA/40776/92, with minimal cross-reactivity with vaccine antibodies was administered intratracheally at the dose of 100 TCID50/ml (10 ml) to the challenged groups. Clinical signs, including cough, respiratory rate and rectal temperature were evaluated prior to challenge and daily for 7 days post infection (DPI). Pigs were necropsied at 5 and 21 DPI. Lesions consistent with SIV were evaluated on a standard diagnosis 2 and microscopic analysis of lung tissue and immunohistochemistry (IHC) for SIV antigen were performed. Nasal swabs were collected at 1, 3, 5, and 7 DPI for virus isolation. Bronchoalveolar lavage and nasal washes were assayed for SIV-isotype specific antibodies as previously described. Serum was collected prior to each vaccination, prior to challenge and at 5 and 20 DPI. SIV antibodies from swine serum were measured using HI assay. Analysis of variance was used to analyze the data. A P value < 0.05 was considered significant.

Results and discussion
Rectal temperatures on -1.1-7 DPI were significantly higher in all SIV challenged groups compared to the non-challenged groups (Figure 1). Vaccination in the absence of MDA significantly reduced the percentage of SIV-induced pneumonia at 5 DPI by macroscopic and microscopic evaluation (Table 2). Interestingly, the percentage of lung lesions was significantly higher in pigs with MDA at the time of the second vaccination (Figure 2). At 5 and 21 DPI, the SIV vaccinated and challenged group without MDA (group 6) had significantly lower levels of virus compared to the rest of the challenged groups. Pigs with MDA (group 8) had significantly increased levels of virus compared to group 6.

In the pigs without MDA, antibody levels to both virus antigens increased in response to vaccination and challenge (Figure 3 and 4). The non-vaccinated challenged pigs developed antibodies by 20 DPI and had higher titers to the challenge antigen than the vaccine antigen, although cross-reactivity with the vaccine virus occurred. By 20 DPI, the vaccinated MDA positive group had strong antibody responses to both viral antigens demonstrating that an anamnestic response occurred. Vaccination enhanced the local immunity in the respiratory tract of the challenged pigs as measured by SIV-specific IgG and IgA from BALs.

The increased disease observed in vaccinated pigs with MDAs on vaccine was unexpected and the exact mechanism for the increased severity of disease is unknown. This study shows that MDAs are not completely protective against pneumonia and confirm their impact on vaccine efficacy. These results indicate that vaccination in the presence of MDA appears to prime the immune system to respond more quickly to infection. The results of this study provide important information on the immune response to SIV vaccination in the presence of MDAs.

The results of this trial demonstrate that a bivalent SIV vaccine administered in the absence of MDA significantly reduced pneumonia and nasal viral load in pigs experimentally infected with a heterologous H1N1 SIV isolate. However, the presence of MDA during vaccination was shown to interfere with vaccine efficacy based on the percentage of SIV-induced pneumonia at 5 DPI and the amount of virus isolated from the nasal cavity.

Acknowledgments
The authors would like to thank Nancy Upchurch for technical support and the students from the Thacker Lab for their assistance with the animal work.

References
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Figure 1: Rectal temperature from pigs challenged with SIV

![Figure 1](image)

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![Figure 2](image)

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