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Evaluation of Experimental Combination Vaccines for Protecting Pigs Against *Mycoplasma hyopneumoniae* and *Erysipelothrix rhusiopathiae* Challenge

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Introduction and Objectives

Experimental vaccines containing fractions of swine influenza virus (SIV) subtypes H1N1 and H3N2, in combination with *Mycoplasma hyopneumoniae* and *Erysipelas rhusiopathiae* have been developed. The objective of the studies reported here was to evaluate the ability of these combination vaccines to protect pigs against virulent challenge with *M. hyopneumoniae* or *E. rhusiopathiae*.

Materials and Methods

Two experimental studies were conducted to evaluate the efficacy of swine influenza (H1N1, H3N2), erysipelas, and mycoplasma combination vaccines in either a *M. hyopneumoniae* or an *E. rhusiopathiae* challenge.

Study 1. This study was conducted to evaluate the efficacy of combination vaccines incorporating 1-dose or 2-dose *M. hyopneumoniae* bacterins by comparing postvaccination responses to *M. hyopneumoniae* challenge in piglets. Pigs seronegative (S/P ratio < 0.5) by ELISA assay to *M. hyopneumoniae* were vaccinated with a swine influenza (H1N1, H3N2) and mycoplasma combination vaccine (*FluSure/RespiSure*) and a treatment control vaccine (*FluSure/ER Bac Plus*) at approximately 3 and 6 weeks of age. Pigs in a third treatment group received *FluSure/RespiSure-ONE/ER Bac Plus* at approximately 3 weeks of age followed by a dose of *FluSure/ER Bac Plus* at approximately 6 weeks of age. Piglets were then challenged intratracheally with a suspension of *M. hyopneumoniae* at approximately 10 weeks of age and were sacrificed and necropsied for the determination of pulmonary damage at approximately 14 weeks of age. Throughout the study, blood samples were routinely collected (Days 0, 21, 35, 49, and 77) from piglets to establish serum antibody titers to *M. hyopneumoniae*. Results of this efficacy study were then compared to the results of *M. hyopneumoniae* efficacy studies conducted with *RespiSure* and *RespiSure-ONE* to determine whether the combination products provided similar levels of protection against mycoplasma challenge.

Study 2. Pigs seronegative by ELISA assay to *E. rhusiopathiae* were vaccinated with a swine influenza (H1N1, H3N2) and erysipelas combination vaccine (*FluSure/ER Bac Plus*) and a treatment control vaccine (*FluSure/RespiSure)* at approximately 3 and 6 weeks of age. Pigs in a third treatment group received a swine influenza (H1N1, H3N2), erysipelas, and mycoplasma combination vaccine (*FluSure/RespiSure-ONE/ER Bac Plus*) at approximately 3 weeks of age followed by a dose of *FluSure/ER Bac Plus* at approximately 6 weeks of age. Available piglets were then challenged with virulent *E. rhusiopathiae* at approximately 10 weeks of age and were monitored for clinical signs (elevated body temperatures, metastatic skin lesions characteristic of erysipelas, or *E. rhusiopathiae* cultured from tissue samples). Blood samples were routinely collected (Days -3, 21, 35, and 50) and were assayed for serum antibodies to *E. rhusiopathiae*. Results from the study were compared to the results of an *E. rhusiopathiae* challenge study conducted with *ER Bac Plus* alone to determine whether the combination product provided similar levels of protection against *E. rhusiopathiae* challenge.

Results and Discussion

Study 1. As Table 1 shows, vaccination of piglets with combination vaccines incorporating either a 1-dose or 2-dose *M. hyopneumoniae* bacterin was effective in reducing the severity of mycoplasmal disease. In comparison with treatment control pigs, pigs receiving *FluSure/RespiSure-ONE/ER Bac Plus* had 82% less lung damage following mycoplasma challenge. Similarly, pulmonary damage was reduced by 89% in pigs vaccinated with *FluSure/RespiSure*. Serologic analysis showed that titers increased in both test groups vaccinated against *M. hyopneumoniae* and, in the face of bacterial exposure, increased further after challenge. No interference between the viral and bacterial components of the multivalent vaccines was apparent based on the challenge and serology results.

These results are similar to those obtained in challenge-of-immunity studies conducted with *RespiSure* and *RespiSure-ONE*. In previous *RespiSure* studies, pigs vaccinated with two doses of the mycoplasma vaccine and then challenged with a homologous strain of *M.*

hyopneumoniae had a mean percentage of lung damage of 4.98% compared to 27.91% in controls, which represented an 82.16% reduction in lung damage in vaccinates. Mean lung damage score for pigs challenged with a heterologous strain of *M. hyopneumoniae* was 1.81% for the *RespiSure* vaccinates and 19.24% for the controls, a 90.6% reduction in lung damage in vaccinates. In an independent challenge-of-immunity study conducted at Iowa State University, pigs vaccinated at approximately 6 weeks and again at 8 weeks of age with *RespiSure* showed evidence of less severe *M. hyopneumoniae* infection (1.9% mean percentage of lung damage) than nonvaccinated controls (7.9% mean percentage of lung damage), representing a 75.9% reduction in lung damage in vaccinates. In each of these studies, the level of protection against antibodies to *E. rhusiopathiae* increased substantially in the two treatment groups vaccinated against erysipelas. Additionally, titers against SIV H1N1, SIV H3N2, and *M. hyopneumoniae* increased in all vaccination groups, further illustrating lack of interference between the combination vaccines' bacterial and viral components.

Results obtained in this *E. rhusiopathiae* challenge study conducted with multiple-antigen *FluSure/RespiSure-ONE/ER Bac Plus* and *FluSure/ER Bac Plus* vaccines did not differ substantially from those obtained in a previous duration-of-immunity study conducted with single-antigen *ER Bac Plus*. In the latter study, pigs were vaccinated at approximately 3 and 6 weeks of age and then challenged with virulent *E. rhusiopathiae* 20 weeks after the second vaccination. While 9 of 10 (90%) control pigs showed clinical signs following challenge, 15 of 20 (75%) vaccinated pigs showed no signs.

These studies demonstrated that the vaccination of piglets with multivalent vaccines incorporating swine influenza (H1N1, H3N2), erysipelas, and mycoplasma antigens were effective in reducing the incidence of lung lesions after *M. hyopneumoniae* challenge and in protecting pigs from clinical disease induced by *E. rhusiopathiae* challenge.

mycoplasma challenge stimulated by vaccination with single-antigen *RespiSure* was similar to the level of protection against mycoplasma challenge established by vaccination with the multiple-antigen *FluSure/RespiSure-ONE/ER Bac Plus* and *FluSure/RespiSure* combination vaccines.

Study 2. As Table 2 shows, immunization of pigs with multivalent vaccines incorporating an *E. rhusiopathiae* bacterin was highly effective in preventing the clinical signs of erysipelas following challenge with virulent *E. rhusiopathiae*. Whereas 100% of the treatment control pigs showed signs of disease after challenge, 0% of vaccinates showed signs. Serologic analysis showed that

Table 1—Summary of *Mycoplasma challenge* results following vaccination with multivalent vaccines*

Vaccine	No. Pigs	Vaccination (age in wks)	Lung Lesions†	Percent Reduction	Mean Serum *Mycoplasma* Titer (Study Day) Day 0	Day 21	Day 35	Day 49	Day 77
FluSure/ER Bac Plus (control)	23	3/6	9.9[a]	—	0.03	0.04[a]	0.03[a]	0.07[a]	0.18[a]
FluSure/RespiSure-ONE/ER Bac Plus	24	3‡	1.8[b]	82	0.03	0.05[a]	0.04[a]	0.08[a]	0.71[b]
FluSure/RespiSure	24	3/6	1.1[b]	89	0.03	0.05[a]	0.23[b]	0.23[b]	0.80[b]

**M. hyopneumoniae* challenge was 10 mL of 10^5 CCU/mL, administered intratracheally 7 weeks after primary vaccination.
†Lung lesions evaluated 4 weeks after challenge.
‡*FluSure/ER Bac Plus* was also administered to pigs at 6 weeks of age.
[a,b]Values in the same column with different lower-case superscripts are significantly ($P \leq 0.05$) different.

Table 2—Summary of

Vaccine	No. Pigs	Vaccination (age in wks)	*E. rhusiopathiae* Titer Day 21	Day 35	Day 50	Percent with clinical signs
FluSure/RespiSure (control)	10	3/6	87[a]	57[a]	82[a]	100
FluSure/RespiSure-ONE/ER Bac Plus	20	3†	183[b]	6532[b]	3035[b]	0
FluSure/ER Bac Plus	20	3/6	235[b]	5902[c]	3510[b]	0

**E. rhusiopathiae* challenge was 2 mL of 2×10^8 CFU/mL, administered intramuscularly 7 weeks after primary vaccination.
†*FluSure/ER Bac Plus* was also administered to pigs at 6 weeks of age.
[a,b,c]Values in the same column with different lower-case superscripts are significantly ($P \leq 0.05$) different.