

Replicon Particle Administration Prior to Challenge Reduces PRRSV Viremia

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Summary and Implications

Vaccination of swine with an alphavirus-derived replicon particle vaccine stimulates a non-specific immune response. This effect was seen when animals were challenged with PRRSV at 24 hours post-vaccination. Animals that received vaccine had reduced viremia as measured by quantitative RT-PCR when compared to placebo. These results highlight the potential of replicon particle vaccines to induce robust immune responses in swine.

Introduction

Porcine reproductive and respiratory syndrome virus (PRRSV) is the most economically significant viral pathogen of swine in the United States. Current control measures and vaccines have significant drawbacks. Enhanced understanding of host immunity is necessary to develop more effective vaccines and therapeutics. Alphavirus-derived replicon particles (RP) are single-cycle, propagation-defective viral vectors. Numerous studies in a wide range of species have demonstrated the safety and efficacy of RP as a vaccine platform. In addition to vaccine antigen expression, RP have been used to deliver cytokines, such as Interleukin-12 and Type I interferon. Other investigators have demonstrated that RP enhance innate immune responses following administration. Our group is developing veterinary vaccines utilizing RP technology. One vaccine candidate under development expresses the hemagglutinin gene from swine influenza virus H3N2 (H3-RP). The H3-RP was chosen to examine the possible anti-PRRSV effects of RP vaccines using a young pig challenge model.

Materials and Methods

Study 1

Three-week-old pigs (n=12) were obtained from a commercial herd historically free of PRRSV and swine influenza virus. Pigs were randomized into groups of six animals, and housed together in BSL-2 animal facilities. At approximately four weeks of age, pigs were injected with either H3-RP or vaccine diluent (placebo). The titer of H3-

RP was determined to be 1×10^9 RP/dose by immunofluorescence assay. Challenge occurred 24 hours post-treatment via intranasal inoculation with 2×10^5 TCID₅₀ PRRSV in a 2 ml volume. Pigs were monitored for clinical signs and bled periodically for 21 days post-challenge. Serum samples were assayed for PRRSV viral RNA by quantitative real-time RT-PCR (Applied Biosystems).

Study 2

Three-week-old pigs (n=18) were obtained from the same source as in Study 1 and randomized into groups of six animals. At approximately four weeks of age, two groups of pigs were injected with H3-RP either 72 hours or 24 hours prior to challenge. The third group received vaccine diluent as a placebo. H3-RP formulation and challenge material administration was the same as in Study 1. Clinical observation, blood collection, and qRT-PCR were conducted as in Study 1.

Results and Discussion

Study 1

All animals had detectable viral RNA in serum by three days post-challenge, indicating successful challenge. Compared to placebo, animals treated with H3-RP had significantly lower qRT-PCR titers at 10, 14, and 17 days post-challenge when compared to placebo.

Study 2

All animals became qRT-PCR positive by three days post-challenge, as in Study 1. Animals treated with H3-RP at 24 hours pre-challenge had a statistically significant reduction in qRT-PCR titers at 14 days post-challenge when compared to placebo. No other time points or treatments reached statistical significance in the qRT-PCR assay.

These results suggest that the immune response stimulated by H3-RP vaccination is effective at reducing PRRSV viremia in a young pig challenge model. This effect appears to be transient, and is likely due to the host response to the virus-like RP. Additional studies are needed to characterize the specific pathways involved in anti-PRRSV innate immune responses.

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