PRRSV Prime - Boost Technical Paper

Cambridge Technologies

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Key Points:

1. PRRS remains a major problem to swine producers and due to rapid mutation and strain variation, vaccination with over the counter vaccines alone is difficult.
2. Recent research has shown success in using a combination of MLV and autogenous killed vaccines.
3. With Next Generation Sequencing, diagnosticians can identify and characterize any emerging viruses or viral variants present in a herd.
4. Multiple manufacturing options can offer a flexible approach to dealing with an ever changing disease.

Introduction

Porcine reproductive and respiratory syndrome virus (PRRSV) has been negatively impacting pork production around the world for nearly 30 years. Since it was first identified in the late 1980s, the virus has cost the industry billions of dollars, with estimated losses of $664 million just in the United States breeding and growing-pig herds[3]. In recent years, a highly pathogenic variant has emerged in China[6]. These strains cause disease similar to traditional PRRSV as well as neurological signs and erythematous blanching rash. The new variants have spread throughout Southeast Asia and can cause clinical disease and death in all ages of swine including adult pigs and pregnant sows[7].

Despite the nearly worldwide reach of the disease and its longevity, there is still much to be learned regarding vaccination protocols. The virus evolves and mutates quickly[5], making effective vaccination difficult. In recent years, a combination of commercial and autogenous vaccines has been found to boost humoral immunity in sows and to reduce viremia in weaned piglets[2].

Vaccination Protocol

Research showing how administration of a homologous, farm-specific vaccine can bring a positive response[1], has led to an increased belief that there is not a "one-size-fits-all" approach, and that in fact a unique approach to PRRSV versus other viruses may be warranted.

Inactivated vaccines including autogenous products are believed to be most effective when used in combination with a modified live vaccine, as the MLV "primes" the pigs in order to adequately respond to the second product. In a recent study conducted at Cambridge Technologies research facility, pigs vaccinated with experimental inactivated PRRS vaccines and had previously been vaccinated with a modified live PRRS vaccine were compared to those that did not receive any vaccine and those that received only modified live PRRS vaccine. The objective of this study was to evaluate the ability of the inactivated vaccine to bolster and broaden the neutralizing antibody response to pigs primed with a modified live virus vaccine.

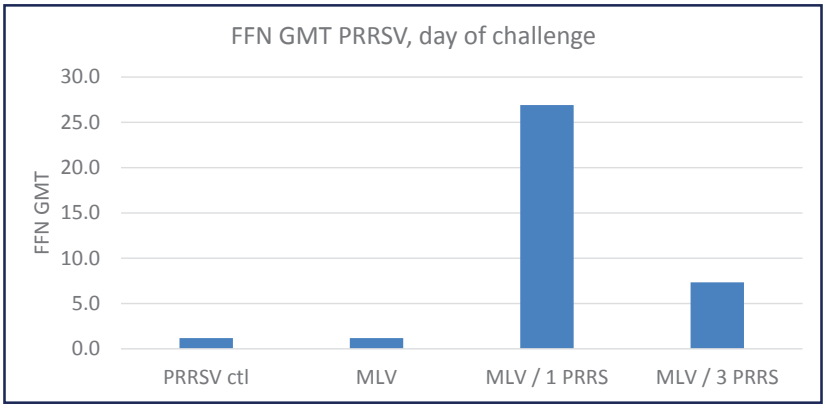
Four groups were included in the study as shown in Table 1.

Group	# of pigs	MLV PRRS Prime	Killed PPRS Vaccine	Vaccination Program
1	8	No	None	NA
2	8	Yes	None	NA
3	8	Yes	1 Strain killed	2 doses 4 wks apart
4	8	Yes	3 Strain killed	2 doses, 4 wks apart

Table 1

Group 3 was vaccinated with a one strain PRRS virus vaccine, RFLP type 1-4-4. Group 4 was vaccinated with a 3 strain PRRS virus vaccine, RFLP types 1-4-4, 2-6-2, and 1-4-2. All groups were challenged two weeks after the second dose of the killed vaccine with a PRRS RFLP type 1-4-4 which was homologous to the 1-4-4 in both autogenous vaccine groups. The results of this study were presented at the 2019 American Association of Swine Veterinarians annual meeting and are summarized here.

Figure 1 shows the results of neutralizing antibody titers to the challenge virus from the four groups, two weeks after the second dose of the inactivated vaccines and prior to challenge. Both the single PRRS antigen and the three PRRS antigen vaccinated groups showed FFN titers above eight which is considered to be protective. MLV indicates the groups were previously exposed to the modified live virus vaccine.



The serum neutralizing antibody titers from the four groups was also compared to a bank of PRRS isolates of different RFLP types. Figure 2 shows that the monovalent autogenous PRRS vaccine group had serum neutralizing antibody titers above eight (considered to be protective) for 9 of the 10 PRRS virus strains tested. It also shows that the trivalent autogenous vaccine group had serum neutralizing antibody titers above eight for 5 of the 10 PRRS virus strains. The control group and the group previously exposed to the modified live virus vaccine did not show serum neutralizing titers above eight to any of the PRRS virus strains.

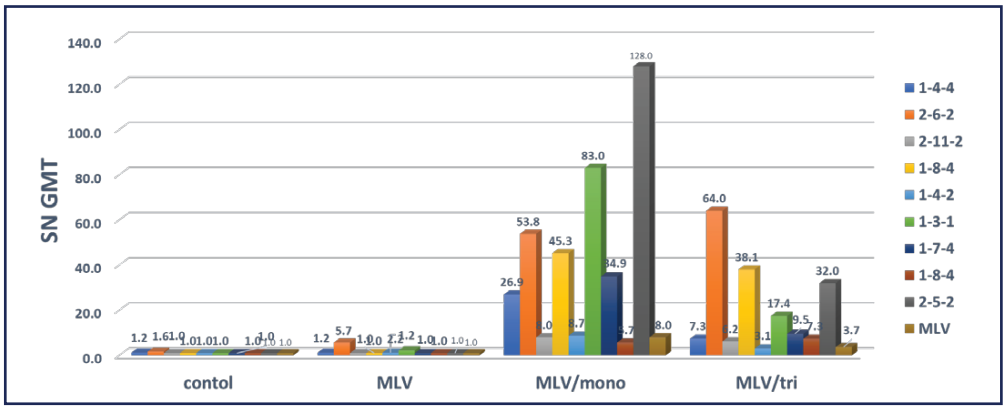


Figure 2

PRRS virus titers in the lungs and lung lesions were also measured post challenge. Figure 3 shows that the amount of virus in the lung was significantly reduced in both the monovalent autogenous vaccine group (MLV / 1PRRS) and the trivalent autogenous vaccine group (MLV / 3 PRRS) compared to the control group. The gross lung lesions showed a downward trend with lower scores in the monovalent and trivalent groups compared to the control group.

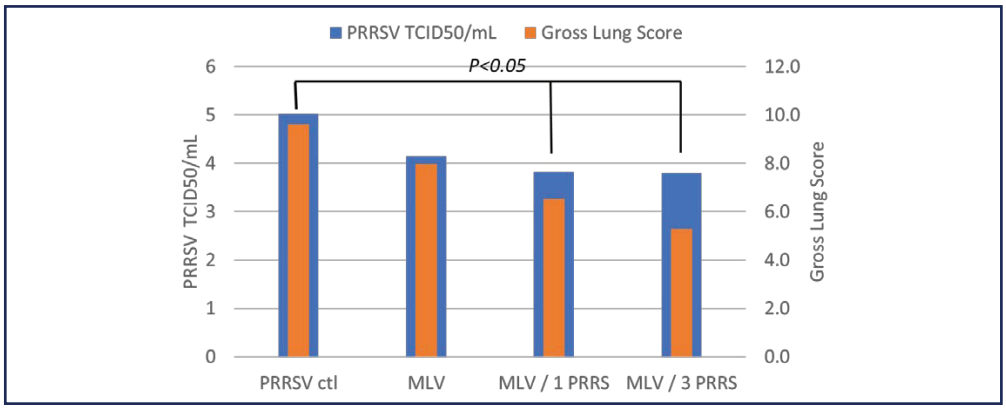


Figure 3

Based on this information, it would be beneficial for a PRRSV vaccination protocol to include administration of an autogenous vaccine to pigs whose immune system is primed against the PRRS virus. The autogenous product can expose the animal to farm-specific viral proteins increasing the breadth of antibodies targeted at that virus. The results of this study indicate that the broad antibody response generated through this prime boost vaccination program could provide neutralizing antibodies to a broad array of PRRS virus RFLP types.

Cambridge Technologies works with veterinarians and producers using Precision Vaccinology®, which includes our next-generation diagnostics and quality custom manufacturing processes, to produce an autogenous vaccine that will fit a herd specific prime boost vaccination program.

Diagnostic Methods

As the initial step in the Precision Vaccinology® process, Cambridge Technologies uses next-generation sequencing processes such as metagenomics for both detection of the virus and strain identification/selection. This enables diagnosticians to identify and fully sequence any novel or emerging viruses or variants, such as is common with PRRSV. In cases where there is a complex interaction between multiple bacteria and viruses, such as respiratory disease caused by PRRSV interacting with PCV2, metagenomic sequencing can be used to identify all of the viruses potentially associated with the condition while also producing a complete genome sequence of them. If needed, qPCR can be used to quantify the identified viruses.

Metagenomics can help to answer questions about potential virus transmission with the ability to profile animals coming from multiple sources, points of comingling and concentration, and transport vehicles moving in and out. Longitudinal metagenomic profiling can be used to see what viral and bacterial changes take place in a herd over time. Veterinarians and producers can compare what is present in healthy animals to what is present when there is disease, in order to establish a clearer picture of what challenges the animals are facing, and when.

Evaluation for and of virulence factors is necessary as potential selection criteria for final choice of isolates used in the vaccine. In Precision Vaccinology®, Cambridge Technologies uses a next generation sequencing technique known as Multi Locus Sequence Typing to characterize and compare isolates from a herd to select those that are most relevant for use in a vaccine.

Vaccine Manufacturing

When manufacturing autogenous killed PRRSV vaccine it is important to maintain the integrity of the viral protein structure, which generates immune response when introduced to the pig's immune system. A key part of the Precision Vaccinology® process is our proprietary manufacturing process that protects this structure, keeping it as close as possible to the originally isolated virus.

Another important component of Precision Vaccinology® is optimization of virulence factors during the manufacturing process. Toxins, proteins, etc., that have been identified as being part of the selected isolate(s) should be included in an inactivated vaccine in order to selectively target the pathogen[4].

Certain adjuvants can enhance the immune response and/or aid in the administration of the antigen. There are multiple options to choose from when deciding on a route of administration as well. Our autogenous vaccines can be developed for intranasal, intramuscular, intradermal, or subcutaneous administration. The technical staff at Cambridge Technologies works throughout the Precision Vaccinology® process with the herd veterinarian to select the most appropriate adjuvant and route of administration.

Conclusion

Forward-thinking manufacturers such as Cambridge Technologies continue to work toward identifying the most effective protocols for PRRSV vaccination. Researchers have found success in using a combination of commercial and autogenous MLV and killed products. Our Precision Vaccinology® has raised the bar in both PRRSV diagnosis and vaccine formulation, including our use of metagenomic diagnostics and a proprietary vaccine manufacturing process. In the face of continually emerging PRRSV variants, pork producers and veterinarians who partner with Cambridge Technologies can be confident that they are on the leading edge of combatting the disease.

Sources

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