HETEROLOGOUS PRRS VACCINE PROTECTION

The protection provided by all commercially available modified-live virus PRRS vaccines is heterologous due to the high degree of variation among PRRSV field isolates.

PRRSV protection can't be predicted by a vaccine's lineage origin.

PRRSV protection can't be predicted by a vaccine's sequence similarities to field strains.

Ingelvac PRRS®

THE BASICS

Porcine reproductive and respiratory syndrome (PRRS) is a complex and costly disease, due in part to the high degree of genetic variation among PRRS field isolates. Throughout its 25-year history, Ingelvac PRRS® MLV, the number 1 PRRS vaccine on the market, has demonstrated its ability to provide heterologous protection against numerous wild-type PRRSV strains that differ from the vaccine strains in terms of nucleotide sequence and lineage.[2–4]

KEY TERMS

PRRSV PHYLOGENETIC CLASSIFICATION

Diverse PRRSV strains are classified by the nucleotide sequences in the Open Reading Frame 5 (ORF5) of viral DNA. Advanced software is used to further identify phylogenetic similarities between strains and provide a reference for future studies.

LINEAGE

Clusters of strains that appear to descend from a common genetic ancestor. The North American PRRSV strains are generally divided into nine lineages.

HOMOLOGOUS

When the nucleotide sequences between two strains vary by less than 2–3%.[5–8]

HETEROLOGOUS

When the nucleotide sequences between two strains vary by more than 2–3%.[5–8]

COMMERCIAL VACCINES PROVIDE HETEROLOGOUS PROTECTION

The protection provided by all commercially available modified-live virus PRRS vaccines is heterologous due to the high degree of variation among PRRSV field isolates.

A recent analysis of commercial PRRS vaccines found that none fall within the scientifically agreed-upon window to be considered homologous to lineage 1 field strains.[1]

See Table 1 below for more information.

Studies suggest that when there is a difference of more than 2–3% between two ORF5 sequences, they may not be closely related.[5–8] Homology tables, based on percent similarity of open reading frame 5 (ORF5) sequences, are commonly used to determine the relatedness of one virus to another.

None of the current commercial modified-live virus vaccines are close enough to the 2-3% threshold to be considered homologous to the recently isolated wild-type PRRSV lineage 1 strains shown in Table 1; therefore, they would be considered as heterologous to these wild-type PRRSV strains.[1]

TABLE 1. COMMERCIAL PRRSV VACCINES VS. CURRENT/WILD-TYPE LINEAGE 1 PRRSV ISOLATES[1]

ID	Prevacent® PRRS	Ingelvac PRRS® MLV	Ingelvac PRRS® ATP	Fostera® PRRS	Prime Pac® PRRS RR
B1-20190116...	COMPARED TO CONTEMPORARY WILD-TYPE PRRSV ISOLATES, ALL VACCINES LISTED DIFFER BY MORE THAN 10%[1]				
C1-20190104...					
D1-20190109...					
E1-20190124...					
F1-20171203...					
G1-20190110...					
H1-20180419...					
I1-20181227...					
J1-20180611...					
K1-20180720...					

CROSS-PROTECTION ACROSS LINEAGES

PRRSV protection can't be predicted by a vaccine's lineage origin.

Although it is sometimes assumed that vaccines with similar sequence or lineage origin to current field strains may provide more effective protection, studies have shown this isn't the case.[2–4] Ingelvac PRRS® MLV is classified as lineage 5.1, and challenge studies have shown that it provides heterologous protection against multiple lineage 1 PRRSV strains, including the common field strains 1-7-4[2] and 1-3-4,[3] in addition to 1-8-4 and 1-4-4.[4]

See Tables 2 and 3 below for more information.

INGELVAC PRRS MLV is classified as lineage 5.1. To confirm the vaccine provides effective cross-protection against current and virulent PRRSV strains of a different lineage, two challenge studies were conducted with PRRS 1-7-4 and 1-3-4 field isolates, both strains within lineage 1.[2,3] In both studies, pigs vaccinated with INGELVAC PRRS MLV showed significantly reduced lung lesions and significantly increased average daily weight gain (ADWG) compared with the placebo group.[2,3]

TABLE 2. EFFICACY OF INGELVAC PRRS MLV AGAINST PRRS 1-7-4 CHALLENGE: DAY 42 LUNG LESIONS (MEDIAN %) AND POST-CHALLENGE AVERAGE DAILY WEIGHT GAIN (ADWG)[2]

Treatment	Lung Lesions (Median %)	ADWG in lbs.
INGELVAC PRRS MLV	8.4[a]	0.61[a]
Competitive vaccine	12.9[a]	0.49[a]
Placebo	25.4[b]	0.24[b]

[a]Significantly different from the placebo at $P \leq 0.05$.

TABLE 3. EFFICACY OF INGELVAC PRRS MLV AGAINST PRRS 1-3-4 CHALLENGE: DAY 42 LUNG LESIONS (MEDIAN %) AND POST-CHALLENGE AVERAGE DAILY WEIGHT GAIN (ADWG)[3]

Treatment	Lung Lesions (Median %)	ADWG in lbs.
INGELVAC PRRS MLV	14.9[a]	0.317[a]
Competitive vaccine	27.4[a]	0.052[c]
Placebo	58.3[b]	-0.025[b]

Different letters indicate significant ($P \leq 0.05$) differences.

CROSS-PROTECTION ACROSS SEQUENCES

> PRRSV protection can't be predicted by a vaccine's sequence similarities to field strains.

Another paper summarized **21 independent studies** conducted by Boehringer Ingelheim that evaluated the efficacy of Ingelvac PRRS® MLV and Ingelvac PRRS® ATP, following challenge with eight genetically diverse PRRSV isolates that varied by sequence similarities.[4] The paper found that INGELVAC PRRS MLV and INGELVAC PRRS ATP significantly reduced lung lesions in vaccinated pigs when compared to non-vaccinates.[4]

See Table 4 below and Table 5 on the following page for more information.

A paper summarized 21 independent studies evaluating the efficacy of INGELVAC PRRS MLV and INGELVAC PRRS ATP, following challenge with eight genetically diverse PRRSV isolates that varied by sequence similarities.[4]

TABLE 4. SUMMARY OF THE PERCENT NUCLEOTIDE SIMILARITY OF CHALLENGE ISOLATES TO INGELVAC PRRS MLV AND INGELVAC PRRS ATP, BASED ON ORF5 SEQUENCE[4]

Challenge Isolate	Lineage*	INGELVAC PRRS ATP	INGELVAC PRRS MLV
U66394 (NADC)	5.1	91%	94%
AF535152 (VR2332)	5.1	90%	100%
AY656993 (SDSU73)	8	90%	89%
Field isolate 1 (1-18-2)	1	87%	87%
Field isolate 2 (1-4-4)	1	86%	86%
Field isolate 3 (1-5-2)	NC**	87%	88%
17198-6 (1-4-2)	9	92%	90%
EF484031 (1-8-4)	1	86%	87%

*Lineage classification based on Shi M, Lam TT, Hon CC, et al. Phylogeny-based evolutionary, demographical and geographical dissection of North American Type 2 porcine reproductive and respiratory syndrome viruses. *J Virol* 2010;84(17):8700–8711.

**NC = not classified, based on analysis.

CROSS-PROTECTION ACROSS SEQUENCES

> PRRSV protection can't be predicted by a vaccine's sequence similarities to field strains.

The publication included 21 different challenge studies, using genetically diverse heterologous PRRS isolates, and found that pigs vaccinated with Ingelvac PRRS® MLV and Ingelvac PRRS® ATP had significantly reduced incidence of lung lesions when compared to non-vaccinates (Table 5).[4] These findings further demonstrate that sequence similarity between virus isolates is an unreliable way to predict cross-protective immunity.[9,10] In addition, the pig challenge model used in these studies is still the gold standard for evaluating the expected level of a vaccine's heterologous protection.

TABLE 5. LUNG LESIONS (%) IN VACCINATED AND UNVACCINATED PIGS CHALLENGED WITH PRRSV[4]

Study	Vaccinated	Non-vaccinated	Challenge isolate
1*	1.0	31.6	NADC
2*	10.0	37.5	VR2332
3‡	17.8	70.1	SDSU73
4‡	37.1	82.0	SDSU73
5‡	5.8	23.3	VR2332
6*	0.7	26.0	17198-6 (1-4-2)
7*	0.3	37.7	SDSU73
8*	0.6	14.8	17198-6 (1-4-2)
9*	12.0	39.9	MN 1-8-4
10*	10.4	36.2	MN 1-8-4
11c	8.7	62.5	MN 1-8-4
12*	8.0	47.0	SDSU73
13*	15.9	52.7	SDSU73
14*	29.8	36.0	MN 1-8-4
15‡	27.4	46.6	SDSU73
16*	4.5	32.9	MN 1-8-4
17‡	13.8	58.1	FI 1 1-18-2
18*	1.4	18.0	FI 3 (1-5-2)
19‡	0.7	18.0	FI 3 (1-5-2)
20*	37.4	52.9	FI 2 (1-4-4)
21*	2.4	17.6	MN 1-8-4

*INGELVAC PRRS MLV, ‡INGELVAC PRRS ATP, FI – Field isolate

ISOLATE LINEAGES

NADC – Lineage 5.1
VR2332 – Lineage 5.1
SDSU73 – Lineage 8
17198-6 (1-4-2) – Lineage 9
MN 1-8-4 – Lineage 1
FI 1 1-18-2 – Lineage 1
FI 3 (1-5-2) – Not Classified based on the analysis
FI 2 (1-4-4) – Lineage 1

TAKE NOTE

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[3] Patterson A, Fergen B, Hermann G, et al. Efficacy of Ingelvac PRRS® MLV against a heterologous PRRSV 1-3-4 RFLP challenge. In Proceedings. Allen D. Leman Swine Conf. 2017.

[4] Patterson A, Victoria J, Jordan D, et al. Modified-live PRRSV vaccination is efficacious following challenge with eight genetically diverse PRRSV isolates. In Proceedings. Allen D. Leman Swine Conf. 2013.

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[8] Christopher-Hennings J, Faaberg K, Murtaugh M, et al. Porcine reproductive and respiratory syndrome (PRRS) diagnostics: Interpretation and limitations. In J. Swine Health Prod. 2002:10(5):213-218.

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[10] Yeager M. NPB-funded research study. Iowa State University. 2014.

Boehringer Ingelheim