Vaccination to induce cell-mediated immune response against PRRSV

PRRS virus (PRRSV) is an RNA virus of the Arterivirus genre (Nidovirus order). Currently, it is known that two distinct genotypes of the virus exist, the European (type 1) and the American (type 2), which differ by approximately 40% on a genomic level. Furthermore, the virus's genetic variability is high even within each genotype.

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The most representative signs of infection in breeders are reproductive failure characterised by mummified foetuses, late abortions, stillborn piglets and weak piglets at birth. In growing pigs, PRRSV causes disorders that can be clinical or subclinical, depending on the infective strain; and they are characterised by low growth rates and high susceptibility to secondary viral or bacterial infections. This virus is considered to be one of the main components of porcine respiratory complex.

Control of PRRS

Numerous effective strategies have been described to control PRRSV in individual farms. Successful control of the disease depends on a combination of the following strategies:

- Animal management (sow replacement, unidirectional animal flow, etc).
- Biosecurity (internal and external).
- Diagnosis (animals' immune status, monitoring, etc).
- Active immunisation.

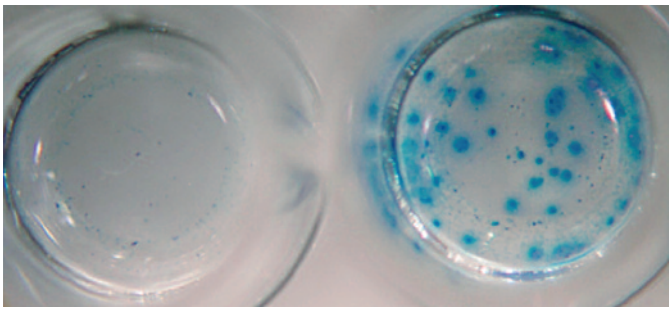
This article focuses on some of the key aspects of vaccination as a tool required for active animal immunisation. From an economic and practical perspective, vaccination is a feasible tool for all kinds of breeders when compared to other immunisation systems. In recent studies comparing active immunisation with modified live virus (MLV) vaccines and live virus inoculation (LVI), it was shown that when MLV vaccines are used to stabilise the breeder population after an outbreak, the mean time required to recover production levels and the impact on production are shorter and less severe than when LVI is used. Furthermore, the economic losses associated with an outbreak, quantified according to the piglets that are not bred, are greater with LVI than with MLV. Finally, the use of MLV ensures correct contact of all the animals with PRRSV; however, when LVI is used the quantity of administered virus cannot be ensured, and neither can correct immunisation of all the sows.

Vaccination

Although it is known not to prevent infection, vaccination is used in order to reduce the clinical onset of the disease and reduce viral excretion. Attenuated live vaccines effectively protect against reproductive and respiratory syndrome. When used in nulliparous sows there is a reduction in viraemia, dead piglets (before and after birth) and congenitally infected piglets. Moreover, live piglets show greater weight at birth and a higher survival rate than piglets from non-vaccinated nulliparous sows.

The use of MLV in multiparous sows infected with PRRSV effectively helps to reduce abortions and time to return to oestrus, increasing the birth rate and number of weaned piglets. In growing pigs in acute PRRS outbreaks or endemic infections, the use of attenuated live vaccines helps to reduce viral excretion and respiratory syndrome, also increasing the growth rate. The use of MLV in the field has been shown to be effective in controlling both reproductive and respiratory disease.

Currently, the greatest challenge related to the control of PRRSV is the heterologous protection provided by a given vaccine against the strains found in farms, as the virus presents high genetic and antigenic variability.



To calculate the frequency of PRRSV-specific IFN-γ-SC, the spot count obtained in the negative control wells were subtracted from the spot count obtained in the virus-stimulated wells.

Clinical heterologous protection can be defined as the clinical protection conferred by vaccine strains against the different field virus strains found in farms.

Immune response

It is very important to understand how immunity against PRRSV is developed in animals after vaccination in order to be able to design the best immunisation strategy.

In the development of immunity against the virus there is a considerable modulation of immune system cells from the onset of immune response, presenting unusual characteristics in both the humoral and cell component.

Innate response

Innate response is not specific and therefore generically recognises and responds to pathogens. PRRSV can act as an antagonist of the pig's defence mechanisms in this initial phase. It can also interfere in the correct presentation of the antigen and T-cell activation. PRRSV modulation of the immune system is variable and depends on each strain.

Humoural adaptive response

The adaptive response is specific to each antigen and characterised by immunological memory. Humoral response to PRRSV is characterised by the early appearance of largely non-neutralising antibodies.

Neutralising antibodies appear 2-4 weeks post-infection, but are occasionally not even detected.

Cell adaptive response

When cell-mediated response is evaluated using the ELISPOT assay (quantity of IFN-γ secreting cells (IFN-γ-SC)), it takes place 2-3 weeks post-infection. Its evolution is slow, erratic and of a low level compared to other porcine pathogens. The cell response generated against PRRSV appears to be a strain-dependent phenomenon.

In summary, adaptive cell response is weak and characterised by late, reduced production of neutralising antibodies and a poor cell-mediated response.

In an environment poor in neutralising antibodies, cell-mediated response can be used to evaluate immune response after vaccination and more or less effectively predict protection against the virus.

The objective of the following study was to evaluate the cell-mediated response generated in gilts vaccinated with Unistrain PRRS (Hipra) against different PRRSV strains isolated from clinical outbreaks in the field.

The study was conducted in six-month-old gilts, negative for PRRSV, coming from an historically disease-free farm. The animals were distributed in two groups: 75% were

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vaccinated intramuscularly with Unistrain PRRS (attenuated live vaccine, European genotype; strain VP-046 BIS) and the remaining 25% were administered 2ml of intramuscular PBS (control group).

Blood samples were collected from the animals to obtain peripheral blood mononuclear cells (PBMCs) on days 0, 7, 14, 28, 42 and 56 post-vaccination. The samples were sent to CReSA (Centre de Recerca en Sanitat Animal) to evaluate cell-mediated immune response by measuring IFN-γ-SC from the PBMCs (ELISPOT assay).

Heterologous cell response was evaluated using five genotype 1 PRRSV strains recovered from clinical outbreaks, which represent a wide range of strains that were isolated in different European countries in different years; their homology in the ORF5 relative to the vaccine strain presents high variability.

Results

PRRSV-specific IFN-γ-SC were first detected against all the strains 14 days post-vaccination (Fig. 1). In the strains isolated in Spain and the UK the response peak was found on day 14 post-vaccination; in the Spanish strain, the level found on day 14 was maintained until the end of the study (D56). In the strains isolated in Hungary, Slovak Republic and Italy, the response peak was found on day 28, after which it declined.

Conclusions

The genetic and antigen variability of PRRSV is considered to be the most important factor to explain the lack of cross reaction between strains, as heterologous protection is usually inconsistent and incomplete.

On the other hand, the percentage of similarity in the ORF5, or even the complete sequence of the strains, is not a useful parameter for predicting extent of protection provided by a vaccine against a given strain.

Although the immunity generated against PRRSV is not fully known, evaluation of neutralising antibodies and cell-mediated response is important and has to be taken into consideration if we want to know how a vaccine works. The role of cell-mediated immunity for viral elimination or for protecting against a challenge has been shown in several studies.

Therefore, in the absence of neutralising antibody production, which is common after the administration of a single dose of any attenuated commercial vaccine, the cell-mediated immunity generated after vaccination could play an important role in protection against the challenge.

The immunisation of all breeders, and especially the gilts, is a key point in the control of PRRS. The main objective in this phase is to obtain good immunisation of gilts, which is why this study was designed using six-month-old gilts. Despite the wide range of strains used, not only regarding ORF5 variability (88-98% similarity) but also year of isolation and origin, the results show that vaccination with Unistrain PRRS induces significant cell-mediated immune response against a wide range of PRRSV strains. ■

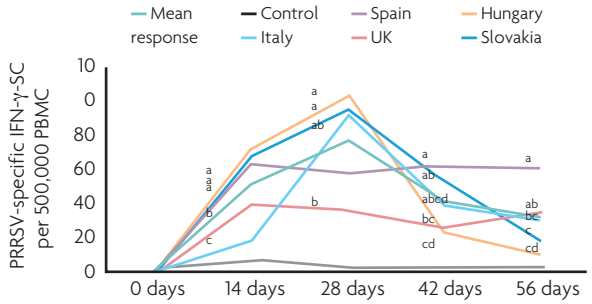

Fig. 1. PRRSV-specific IFN-γ-SC per 500,000 PBMC on days 0, 14, 28, 42 and 56 post-vaccination. Green line: mean response results against set of strains. The other lines are the mean values for each of the five strains. (*) Significant differences between the responses of the five strains on a given date (p<0.05).

References are available from the authors on request