A typical starting point for learning about the immune response of pigs to PRRSV is the standard model of anti-viral immunity. Primary infection of a host cell triggers innate anti-viral responses. Innate defenses slow down initial replication and trigger adaptive humoral and T cell-mediated responses that eliminate the virus. Virus-specific memory in the form of antibody and T cells protects against future infection. However, the response to PRRSV appears to be defective or unusual at each of these stages, raising a series of questions whose answers provide clues to what we are missing about PRRS immunology.

What we know about the primary immune response to PRRSV

The innate response
The first, innate, response of animals to viral infection is the production of type I interferon (IFNα), often with inflammatory cytokines such as tumor necrosis factor (TNF) and interleukin-1 (IL-1). But the innate response to PRRSV at the site of infection is nil; production of IFNα and inflammatory cytokines is nil. PRRSV infection does not elicit type 1 interferon expression in vitro or in vivo\(^1\)–\(^3\). The lack of an IFNα response is significant, since IFNα-mediated events inhibit PRRSV replication in vitro\(^1\) and since elevation of IFNα in vivo by preinfection with PRCD substantially attenuates subsequent PRRSV replication\(^1\). Moreover, a weak innate immune response to PRRSV is consistent with a suboptimal stimulation of antigen-specific humoral and cell-mediated immunity. Influenza virus elicits potent inflammatory cytokine and interferon responses in the lung, and is rapidly cleared within one week of infection\(^4\), whereas PRRSV viremia has been observed for 6-7 weeks after infection\(^5\), and the virus can be reisolated months after initial infection\(^6\)–\(^9\).

PRRSV also blocks IFNα production after superinfection with swine transmissible gastroenteritis virus (TGEV), a strong inducer of IFNα by itself\(^2\). The down-regulation of IFNα production facilitates PRRSV replication since elevation of type I interferons by in vivo stimulation or exogenous administration substantially reduces viral growth and enhances humoral immune responses\(^8\)–\(^10\). In addition, suppression of innate anti-viral immune mechanisms may increase the risk of secondary infections.

Inflammatory cytokine expression is important in the initial response to a variety of viral respiratory infections\(^11\). However, PRRSV infection fails to elicit any significant cytokine expression\(^3\)–\(^12\). TNF and IL-1β are important activators of the nuclear transcription factor, NF-kB\(^13\)–\(^15\). NF-kB plays a central role in the innate response to infection by regulating the transcription of more than 100 genes, including inflammatory and immunoregulatory cytokines, antigen receptors, adhesion molecules, inhibitors of apoptosis, acute phase proteins, and innate effector molecules\(^16\). For these reasons, we speculate that the mild or subclinical respiratory involvement in PRRSV infection may be due to the lack of activation of NF-kB. Moreover, the lack of an acute inflammatory response and weak innate antiviral activity may also result in incomplete stimulation of antigen-specific immune responses, and allow for the establishment of persistent infection.

The humoral response
Antigen-specific humoral immunity first appears at about 7-10 days after infection. Antibodies directed against the nucleocapsid (N) protein encoded by open reading frame (ORF) 7 are most abundant and are relied on for serological testing, but are not neutralizing. Neutralizing antibodies appear in serum after about 14-28 days of infection. There are conflicting reports about the significance of antibodies in anti-PRRSV protection, especially with regard to the PRRSV-specific neutralization response which may not appear until 4 or more weeks after infection. The concurrent detection of neutralizing antibodies and infectious PRRSV in the blood of infected animals led to postulates that neutralizing antibodies do not play a role in protection against PRRSV infection. In addition, the observation that antibodies may enhance PRRSV replication in macrophages is an additional argument that PRRSV antibodies constitute a deleterious, non-protective response.

However, passive maternal immunity transferred to piglets in colostrum results in protection of piglets against development of clinical symptoms and curtailment of viremia. Moreover, protection disappears when colostral antibodies become undetectable. A full understanding of the role humoral immunity, and neutralizing antibodies in particular, in
protection is further complicated by lack of information about protective epitopes, and when effective levels of relevant antibodies are attained. Moreover, the broad genetic and antigenic variation in PRRSV, and the presence of multiple viral genotypes circulating in farms or production systems simultaneously, has an unknown effect on the efficacy of humoral and cell-mediated immune responses.

Anti-PRRSV IgM antibodies appear in serum by 5-7 days post inoculation (PI) and then decline rapidly to undetectable levels after 2-3 weeks. Anti-PRRSV IgG antibodies are first detected 7-10 PI, peak at 2-4 weeks PI, remain constant for a period of months, and then decline to low levels by 300 days PI. Anti-PRRSV IgA can be detected in sera at 14 days PI, reaches a maximum at 25 days PI, and remains detectable until 35 days PI. The kinetics of anti-PRRSV antibody isotypes in bronchoalveolar lavage (BAL) fluid are similar to those in serum, indicating these antibodies extravasate from the vasculature. The antibodies in BAL may contribute to the clearance of PRRSV from the lung, but are unable to completely eliminate the virus.

Serum antibodies that neutralize viral infectivity (SN antibodies) appear at about 3 weeks of infection. SN antibodies are maintained for long periods, but at low levels. Substantial variation has been noted in the SN antibody responses of individual pigs, in both the kinetics of appearance and in titer values. Loemba et al. found that half of the PRRSV-inoculated pigs failed to develop detectable neutralizing antibodies, while other antibody types remained similar. Nelson et al. also reported animals that failed to seroconvert in the SN test. Anti-PRRSV immunoglobulins in serum after PRRSV infection are directed primarily against PRRSV N protein (encoded by ORF7) and M protein (encoded by ORF6). Antibodies against N protein can be detected within 7 days of infection, whereas antibodies against M protein appear by the end of the second week PI. GP5 (encoded by ORF5) specific antibodies may also appear by 7 days PI.

Neutralizing antibodies to PRRSV have been reported with specificities against GP5, GP4, and M. Murine monoclonal antibodies against GP5 are more effective in virus neutralization than are monoclonal antibodies to GP4. Moreover, SN titers were significantly correlated with anti-GP5 titers but not anti-GP4 titers. Antibodies against GP3 also may have a role in protection against PRRSV infection, though the data are less direct. A linear epitope on the ectodomain region of GP5 has been identified as the target of neutralizing antibodies by four laboratories, although the characteristics of the specific amino acid sequence involved in neutralization are not fully resolved.

The humoral immune response is presumed to play an important role in resistance to reinfection and in prevention or reduction of viral spread from animal to animal, since neutralizing antibodies have the potential to clear free virus from the circulation. Reproductive failure due to PRRSV infection also has been prevented by administration of serum containing a high titer of SN antibody. Nevertheless, the role of neutralizing antibodies in prevention of disease and in protection of pigs from infection under field conditions is not clear. Since viremia may occur in the presence of SN antibodies, the level of neutralizing antibodies normally generated against PRRSV may not be sufficient to control the replication of the virus. Selection of neutralization escape mutants has been proposed as one mechanism to account for inefficient neutralization, but neutralization escape mutants or genetic variation in the neutralization-sensitive ectodomain regions of GP5 have not been observed in experimental or field settings.

Moreover, all monoclonal antibodies bind both glycosylated and non-glycosylated forms of GP5, indicating that glycosylation is not associated with neutralizing epitopes of the protein (a complex to the Fc receptor, and thus facilitate viral binding and uptake through the macrophage PRRSV binding protein). Infection of alveolar macrophages by PRRSV is significantly enhanced in vitro in the presence of diluted anti-PRRSV antisera, and the mean level and duration of viremia are greater in pigs injected with SN antibodies prior to virus challenge than in pigs.
injected with normal IgG54,55. The prolonged duration of viremia and virus isolation from the tissues in piglets with low maternal antibodies also suggests ADE of PRRS57. Alternatively, Ostrowski et al.34 have proposed that immunodominant nonneutralizing epitopes on GP5 act as a decoy to delay the induction of antibody production directed against neutralizing epitopes of the protein.

Antibody responses are elicited to nonstructural proteins (nsp) of the replicase complex, particularly the nsp 2 polypeptide encoding a putative cysteine protease58,59. The antibodies recognize linear epitopes in nsp 2 and appear within 1–4 weeks of infection60. These antibodies are detected in boar semen and their presence is correlated with the duration of PRRSV excretion in semen. It is assumed that antibodies to nonstructural proteins do not have a role in protection since they must be released from dead and dying cells to interact with antibodies. However, these antibodies may have diagnostic value and the proteins may be important targets for T cell responses.

The cell-mediated response

PRRSV infection in the lung peaks at approximately day 9 after infection and foci of infection decline to near zero by day 20, although virus still may be isolated from lung fluids for extended periods8,61,62. During and subsequent to the decrease in PRRSV, lymphocyte numbers in the lung may either remain low and constant8 or increase substantially61. Samsom et al.61 identified a CD4+CD8+ T cell population that increased in the lung at later times. The lymphocytes were classified as cytotoxic T cells based on a cell marker phenotype of CD69,CD8+. Shimizu et al.63 also observed a substantial increase in CD8+ T cells that peaked at 25–35 days after infection. The antigen specificity of lymphocytes in the lungs in these reports was not studied.

PRRSV-specific T cell responses first appear in peripheral blood at approximately 4 weeks after infection45. An antigen-specific proliferative response was observed for 5 weeks, i.e. until 9 weeks after infection. The proliferative response was inhibited approximately 80% and 90% by anti-CD4 and anti-MHC II antibodies, respectively, and by 50% and 75% by anti-CD8 and anti-MHC I, respectively45. Challenge with the homologous virus restimulated a specific proliferative response in peripheral blood mononuclear cells which was detected for 3 weeks45. Lopez-Fuertes et al.64 also reported PRRSV-specific lymphocyte proliferation at 4 weeks PI. In this case, the responsive T cell type also was predominantly CD4+ and it was present for a period of 10 weeks after infection64. Stimulated cells expressed IFNγ and IL-2, but not IL-4 or IL-10, suggesting that the CD4+ T cells possessed a type I cytokine expression phenotype characteristic of cell-mediated immune responses to intracellular pathogens65. In vitro restimulation of PBMC with PRRSV antigen and IL-2 led to the surprising observation that the responding cells were primarily CD8+, and were either CD4+CD8+ double-positive cells, which are known to represent antigen-specific memory T-helper cells65, or were CD8+γδ+ cells with nonspecific constitutive natural killer activity66. T-cell proliferation is induced in response to individually purified structural proteins GP5, M, and N66. Expression of GP2, GP4, GP5, M and N individually in a vaccinia virus system revealed that the nonglycosylated M protein was the most potent inducer of proliferation, followed by GP5, GP3 and GP2, whereas N was the weakest inducer66.

IFNγ plays a key role in cell-mediated immune responses against a variety of cytopathic viral infections of animals67,68. IFNγ mRNA has been detected in the lymph nodes, lungs and peripheral blood mononuclear cells of PRRSV-infected pigs64,69. Moreover, IFNγ blocks PRRS virus replication in cultured cell67,69. The observation that PRRSV persists in lung and lymph nodes despite the presence of neutralizing antibodies in serum and bronchoalveolar lavage fluid6,8,43,70,71 argues that cell-mediated immunity is necessary for the complete elimination of the virus.

For this reason we have investigated the kinetics of PRRSV-specific IFNγ-secreting T cells in acute and persistent infection. In an experiment in young pigs, IFNγ-secreting T cells first appeared two–four weeks after PRRSV infection in low numbers (less than 100 per million PBMC). The response was highly variable, ranging from no significant change to a high response (over 400 cells per million PBMC), and transient. In all cases virus-specific T cells were less than 50 per million PBMC after 35 days of infection. All animals were nonviremic at this time. In 5–6 month-old gilts, a similar transient T cell response was observed, with the peak occurring at 50–70 days after infection, when all animals were nonviremic. PRRSV-specific T cells were enumerated in a variety of lymphoid tissues and compared to virus loads. The abundance of virus-specific T cells in both acutely (19 days after infection) and persistently (67 days after infection) infected animals was highly variable and showed no correlation to the amount of virus. No significant difference in antigen-specific T cell
abundance was observed in secondary lymphoid tissues in either acute or persistent infection except for tonsil, in which the number of responding cells was extremely low. CD4+ and CD8+ T cell frequencies did not change after PRRSV infection, though a decrease in γδ T cells was observed. We concluded that the slow but eventual resolution of PRRSV infection is not accomplished solely by the T cell response. Macrophages, the permissive cell type for PRRSV, were present in various levels in all tissue preparations and were not in proportion to local virus load. These findings indicate that a weak T cell response contributes to prolonged PRRSV infection and suggests that PRRSV suppresses T cell recognition of infected macrophages. Meier et al.72 also observed that the initial T cell response to PRRSV is weak and transient. They also reported that the T cell response increases over time such that the frequency of virus-specific T cells is greater than 1,000 per million at one to two years after infection.

Factors that increase IFNγ expression might enhance anti-PRRSV cell-mediated responses. Foss et al.73 and Meier et al.72 show preliminary evidence that augmentation of PRRSV vaccination with IL-12 or IFNα, respectively, accelerates the development of a virus-specific IFNγ response. Thus, it is possible that the production of type 1 interferon or appropriately stimulatory cytokines during the innate immune response are a critical element that is missing from the anti-PRRSV response.

What does the immune response to PRRSV tell us about protection against PRRS?

All aspects of the innate and adaptive immune response to PRRSV indicate that pigs are essentially unaware that a serious infection has occurred. Innate immune surveillance mechanisms that signal viral infection, including inflammatory cytokines and, most importantly, IFNα, are not activated in the lung. Failure to elicit a robust IFN response leads to an ineffective activation of innate cellular anti-viral defenses that are the first line of defense against PRRSV infection. IFN and inflammatory cytokines also are important danger signals that mobilize adaptive immune responses75,74. Because PRRSV infection does not trigger innate danger signals, the development of adaptive immune responses is slow. PRRSV-specific T cells and neutralizing antibodies first appear 2-3 weeks after infection, when viral loads in the lung already are decreasing. These modest responses are in stark contrast to the course of influenza virus and foot-and-mouth disease virus infections, in which antibody and T cell responses are more rapid and robust, and the infection is cleared in about a week.

PRRSV replicates efficiently in vitro, lysing macrophages within 2-3 days. Therefore, it would not be surprising if PRRSV established a fulminating infection that destroyed lung macrophages, disrupted lung function, and was highly lethal. But this does not happen. Instead, the lung infection begins to subside before there is evidence of an effective adaptive immune response and more than 98% of macrophages do not become infected75. Pigs recover from the acute infection in nearly all cases but harbor infectious virus in lymphoid tissues for several more months until the infection is completely resolved in 120-150 days76.

In both acute and persistent infection the viral load is being reduced more efficiently than can be measured by categorical assessment of infection as positive or negative. Viral load in lungs peaks at 7-9 days after infection and declines thereafter, whereas the lung remains positive until 40 days after infection8. Our unpublished data show that PRRSV levels decrease up to 10,000-fold in lung and lymphoid tissue between 19 and 67 days after infection, but all animals are still positive in at least one lymphoid tissue. Recent studies using sensitive PCR methods to assess viral loads in lymphoid tissues show that pigs have PRRSV in lymphoid tissues 100 days after infection76,77. However, the levels are extremely low. These observations indicate that host responses are effective in reducing the viral load, albeit much less efficiently than the humoral and T cell responses in other porcine viral diseases that achieve sterilizing immunity in a matter of weeks.

Kinetic analyses of viral load and neutralizing antibody argue that antibody is not the primary factor in reducing viremia in acute infection, even though neutralizing antibody can prevent infection if administered passively in advance of viral infection40. The long-term persistence of virus in lymphoid tissues further indicates that neutralizing antibody is not effective in resolving PRRSV infections. T cell responses are likewise ineffective in eliminating the virus, since there is no correlation between the appearance or the frequency of PRRSV-specific T cells and the resolution of acute and persistent infection. The delayed increase in PRRSV-specific T cells reported by Meier et al.72 occurs after PRRSV has been cleared from the body76.

These observations suggest that protection against PRRSV is afforded primarily by something other than...
adapative immunity. One possibility is that there is a change in the permissiveness of macrophages to PRRSV. It is interesting that lactate dehydrogenase elevating virus (LDV), the arterivirus of mice, elicits ineffective neutralizing antibody and cytotoxic T cell responses, but is controlled primarily by a reduction in macrophages permissive for infection^{78}. Primary control of PRRSV infection by deletion of permissive macrophages would mean that neutralizing antibody and T cell responses are secondary and are more likely to play a role in the final elimination of virus than in bulk reduction of viral load. Strategies for immunological control that are based on enhancement of adaptive immune responses will need to address the relative importance of antibodies, both neutralizing and nonneutralizing, and of cytotoxic T cells, in control of infection in comparison to innate mechanisms such as natural killer cells and the abundance of permissive macrophages.

The early history of PRRS was marked by viral strains that caused mild respiratory disease in young pigs and moderate to severe late-term reproductive disease. More virulent strains appeared in the U.S. in the winter of 1996-1997 and again in 2001-2002 that caused significant sow mortality. It is not known if the increased virulence of these strains is due to changes in the effectiveness of innate immune responses, including macrophage permissiveness to infection, to a change in the adaptive immune response, or solely due to changes in the virus itself.

Protection afforded by vaccination

Attenuated, live vaccines have been effective in reducing disease severity, duration of viremia, virus shedding and the frequency of PRRSV infection^{22,41,79–84}. Neutralizing antibodies are presumed to play an important role in resistance to reinfection and in prevention or reduction of viral spread from animal to animal, since they have the potential to clear free virus from the circulation^{6,26,34,39}. Reproductive failure due to PRRSV infection also has been prevented by passive administration of serum containing a high titer of SN antibody^{40}. However, whether neutralizing antibodies or cytotoxic T cells are essential for protection or even play a key role under natural conditions of re-infection is not known.

The level of immunity against heterologous strains that is produced by vaccination with live, attenuated PRRSV is a vexing issue. Experimental studies commonly demonstrate a high level of protection for long periods of time, including the commercial lifetime of sows, against re-challenge with homologous strains of the immunizing virus. They also consistently demonstrate induction of recall responses with variable, though not total, protection, against challenge with heterologous strains. By contrast, field observations of chronic and endemic PRRS and of “vaccine failure” suggest that protective immunity may be a variable feature of the immune response to heterologous PRRSV isolates. The difficulties in achieving consistent and reliable control and prevention of PRRS with live, attenuated vaccines emphasizes our incomplete understanding of PRRS immunology. There are serious deficits in our knowledge of the events initiating immunity at the time of infection, of key immunologic targets for both antibody and cytotoxic T cell-directed protection, of the molecular and cellular mechanisms regulating induction and maturation of the immune response, of the consequences of genetic diversity in PRRSV on immune protection, and of the consequences of host genetic variation in pig populations on immune resistance to PRRSV. Thus, significant challenges remain in our efforts to develop better vaccines for prevention and control of PRRS.

Is immunity to vaccine different from field virus?

Vaccines for PRRS in the U.S. predominately are modified, live products which produce an acute infection with viremia followed by a state of persistence. Immunologically vaccine viruses are the same as virulent viruses because they interact equally with the immune system, expressing the same antigens in the same way. Vaccinated animals mount innate and adaptive immune responses that are the same as immune responses to field viruses. Vaccinated animals harbor virus persistently in lymphoid tissues and transmit the virus to other pigs, as evidenced by reisolation of vaccine strains from commercial herds. Vaccinated animals are resistant to reinfection, although the level of protection may not be complete. Immune vaccine protection against rechallenge with the homologous or parental viral strain is typically complete for infection and disease^{84} as also has been reported for field virus infection, followed by homologous challenge^{86, 87}. Nearly complete vaccine protection was achieved against severe respiratory infection caused by highly virulent heterologous strains (Pallares et al. manuscript submitted), but partial protection against heterologous strains in a reproductive disease model also was reported^{83}. A similar result of partial protection by field isolates against heterologous challenge was also reported^{86,87}. An interesting series of ex-
periments by Mengeling and colleagues showed that vaccination with various combinations of several attenuated strains exerted partial to high levels of protection against heterologous challenge with a single strain or a mixture of virulent isolates\textsuperscript{86–88}.

The reasons for variable levels of immune protection against challenge are not well understood. Dee and Batista (unpublished data) immunized pigs by infection with virulent virus and after 120 days challenged with the same virus or each of three other virulent isolates differing genetically in the orf 5 region by approximately 4-12%. Surprisingly, there was no significant difference in viremia or antibody response among the groups. In addition to antigenic differences among PRRSV isolates, reasons for variable levels of immune protection may include genetic and epigenetic differences in pigs in their immune response to PRRSV or in their susceptibility to the virus. Variability in the intensity of immune response to vaccine, including lack of seroconversion, is a feature of PRRSV that is not specific to vaccines. Substantial variation, including nonresponsiveness in the induction of neutralizing antibodies by virulent PRRSV, has been reported previously\textsuperscript{18,19,21,89}.

Immunity to PRRSV may be due to adaptive responses based on antibody or T cell effector mechanisms or to a reduction in permissive cells, which seems to be characteristic of arteriviruses. Regardless of the mechanisms by which it is obtained, it is clear that some type of immune memory exists to provide protection against reinfection and it is the same for attenuated and virulent forms of the virus.

### Does animal age matter in the immune response to PRRSV?

Reviews of PRRS immunology often do not consider that the disease occurs in three different developmental stages, fetus, young and growing pig, and adult gilts and sows. The immune system of pigs is developing in the fetus and does not become fully competent until 4-8 weeks after birth. Pigs that are infected in utero and born alive are weak, frequently die before weaning, and are persistent carriers. Pigs infected early in life suffer respiratory disease, whereas gilts or sows are severely affected with reproductive disease if infected late-term, but do not appear to have significant disease if infected when nonpregnant or early in pregnancy. These observations would suggest that the immune response improves with age, and is less effective in more severely affected animals. However, the few prospective studies that have been performed do not provide a clear answer. Infection of fetuses elicits PRRSV-specific antibody production, contrary to the expectation that antigens presented in utero might be perceived as self\textsuperscript{90}. Furthermore, no differences were observed in respiratory disease or immune response in pigs infected at 1-week, 4-weeks or 10-weeks of age\textsuperscript{42}. At this point we do not know if animal age or state of development contributes significantly to the induction of anti-PRRSV immunity. Even if it does, the tremendous genetic and antigenic variation in PRRSV in the field may mask a smaller effect of animal age or developmental stage. However, the question remains relevant for vaccine protection against PRRS. Since there is no significant antigenic variation in the vaccine strain of virus and protection must be produced against heterologous viruses, differences in host animals that affect the potency of vaccinal immunity may be important.

### How useful are immunodiagnostics?

Screening of serum for antibodies to PRRSV by ELISA, neutralization, and immunofluorescence is valuable in assessing the exposure status of pigs and herds. The assays used now, however, cannot discriminate vaccine from field virus exposure and they provide no information on antigenic variation in field isolates. Extensive amino acid sequence information of viral proteins is available, and methods of protein expression are widely available. Therefore it is a reasonable expectation that scientists will identify antigenic proteins relevant to humoral and T cell immunity that also assist in discriminating among types of viruses, especially vaccine-related and field isolates. Assays that measure PRRSV-specific IFN\(\gamma\) production by T cells are now used for research applications but their value for diagnostic use has not yet been validated.

### What are we missing?

PRRSV interacts with pigs differently than do other pathogens. In contrast to nearly all other pathogens, it surreptitiously infects pigs of all ages without engaging innate immune defenses. The minimal anti-viral response to the primary infection enables the virus to become firmly established in the lung and lymphoid tissues. It also fails to stimulate T and B cell responses so that effective antibody and cytotoxic T cells responses are slow to develop and ineffective. As a result PRRSV is maintained in pigs for a period of months. We lack the knowledge needed to stimulate a more effective innate
immune response that might reduce the extended period of viremia as well as limit or abolish persistent infection. Research is being performed to determine if innate danger signals, including IFNα and cholera toxin, can increase the level of immunity and protection afforded by vaccines. One would expect that a stronger innate danger signal at the time of infection would increase the level and quality of the adaptive, PRRSV-specific response.

The surprising observation that neither antibody nor T cell responses satisfactorily accounts for the decline and eventual resolution of PRRSV infection indicates that we do not yet have a sufficient theoretical basis to enhance anti-PRRS immunity. In order to develop targeted approaches for more effective induction of cross-protective immunity and discriminating diagnostics, we need critical information about the role of individual viral proteins in induction and maintenance of immunity, the mechanisms of immune induction that will reduce acute and persistent infection, and the role of antibodies and cytotoxic T cells in PRRSV-specific immunity. The problem of inadequate immunity to PRRSV is particularly acute since antigenic variation in PRRSV is highly conserved epitopes may provide effective cross-diagnostics directed toward the same regions might be variable epitopes may be an ineffective strategy, whereas particularly acute since antigenic variation in PRRSV is inadequate immunity to PRRSV is extraordinarily large. Immunity directed toward highly variable epitopes may be an ineffective strategy, whereas diagnostics directed toward the same regions might be advantageous. Conversely, immunity directed toward highly conserved epitopes may provide effective cross-protection and control of PRRS. Success in this endeavor will require specific knowledge of conserved sequences that are important in the viral life cycle and amenable to immunological recognition and attack.

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References


