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NON-NATURALLY OCCURRING PORCINE REPRODUCTIVE AND RESPIRATORY SYNDROME VIRUS (PRRSV) AND METHODS OF USING

Hiep Lai Xuan Vu

University of Nebraska-lincoln, hiepvu@unl.edu

Fernando Osorio

University of Nebraska - Lincoln, fosorio1@unl.edu

William W. Laegreid

Laramie, WY, wlaegrei@uwyo.edu

Asit K. Pattnaik

University of Nebraska - Lincoln, apattnaik2@unl.edu

Fangrui Ma

Lincoln, NE

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(54) **NON-NATURALLY OCCURRING PORCINE REPRODUCTIVE AND RESPIRATORY SYNDROME VIRUS (PRRSV) AND METHODS OF USING**

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(71) Applicant: **NUtech Ventures**, Lincoln, NE (US)
(72) Inventors: **Hiep Lai Xuan Vu**, Lincoln, NE (US);
Fernando Osorio, Lincoln, NE (US);
William W. Laegreid, Laramie, WY (US);
Asit K. Pattnaik, Lincoln, NE (US);
Fangrui Ma, Lincoln, NE (US)
(73) Assignees: **NUtech Ventures**, Lincoln, NE (US);
The Board of Trustees of the University of Illinois, Urbana, IL (US)

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

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A61K 39/12 (2006.01)
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A61K 39/00 (2006.01)
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(58) **Field of Classification Search**
None
See application file for complete search history.

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Primary Examiner — Shanon A. Foley
(74) *Attorney, Agent, or Firm* — Fish & Richardson P.C.

(57) **ABSTRACT**
A non-naturally occurring porcine reproductive and respiratory syndrome virus (PRRSV) is provided herein, and methods of making and using the non-naturally occurring PRRSV also are provided.

7 Claims, 5 Drawing Sheets
Specification includes a Sequence Listing.

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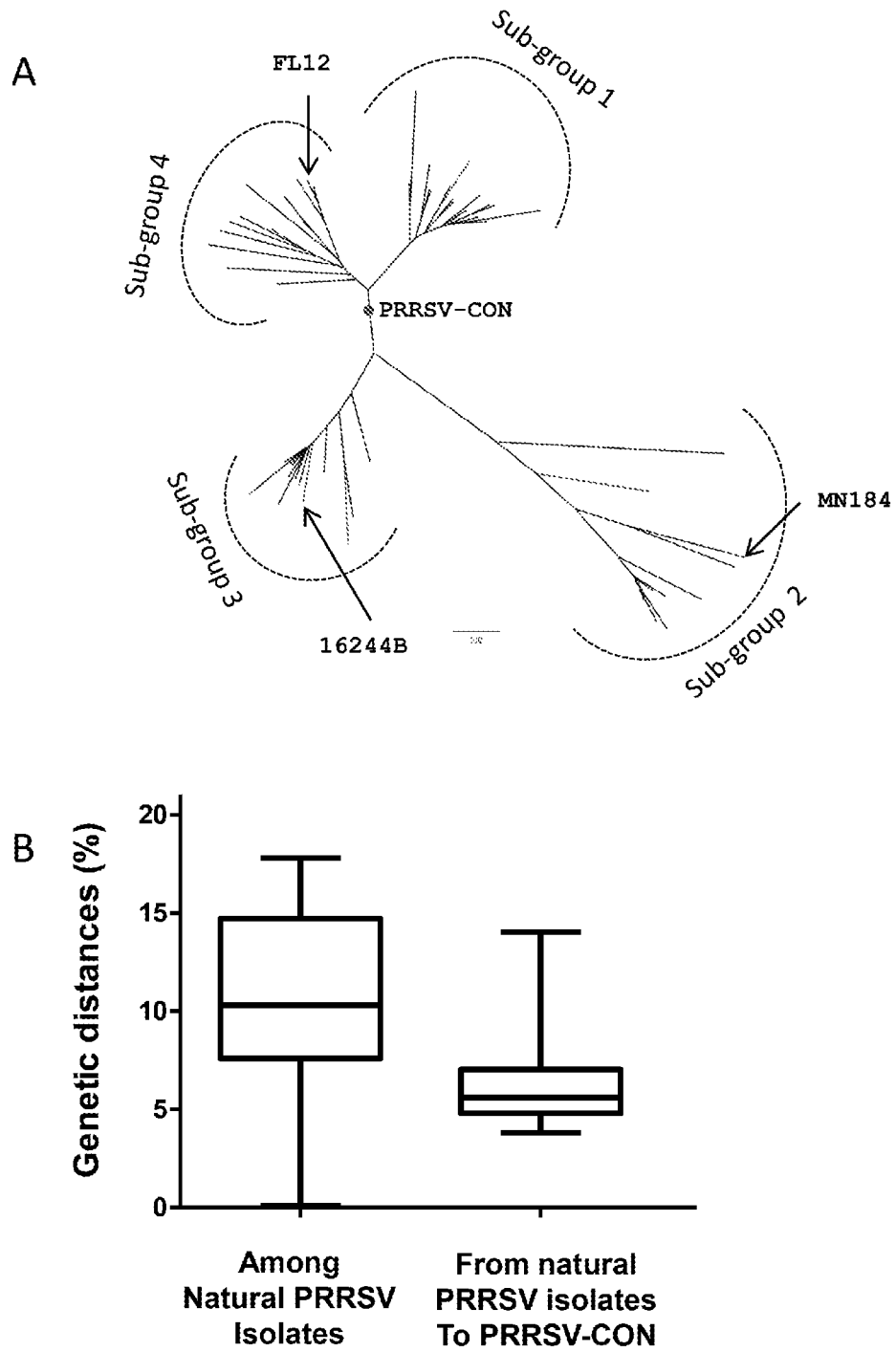


Figure 1

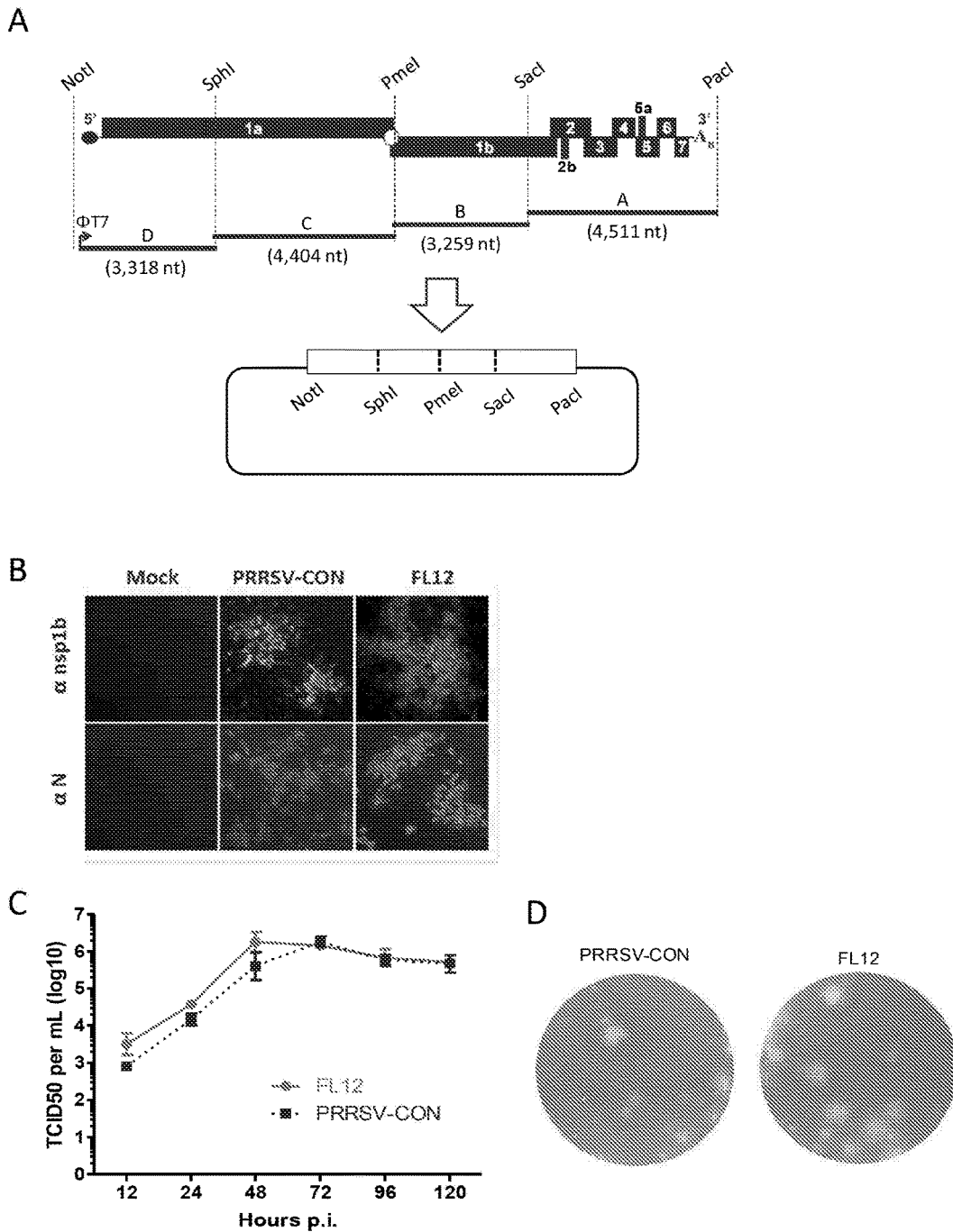
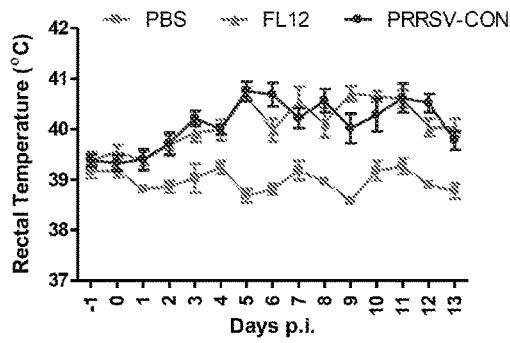
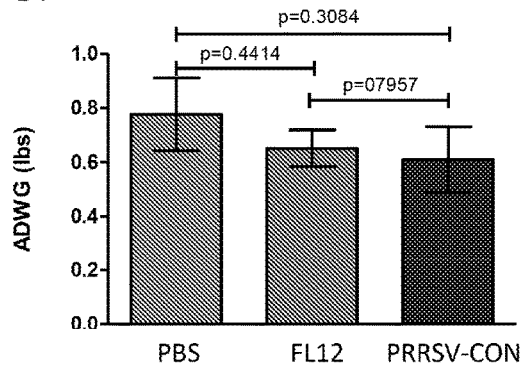


Figure 2

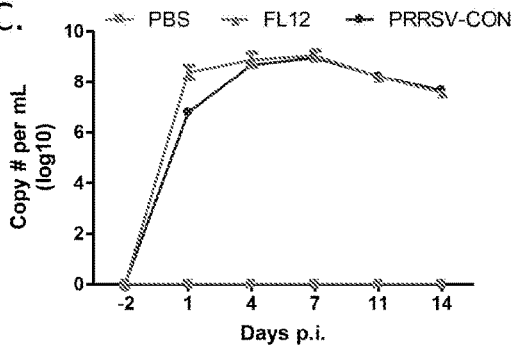
A.



B.



C.



D.

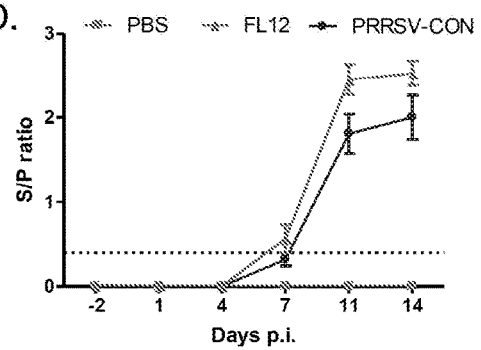


Figure 3

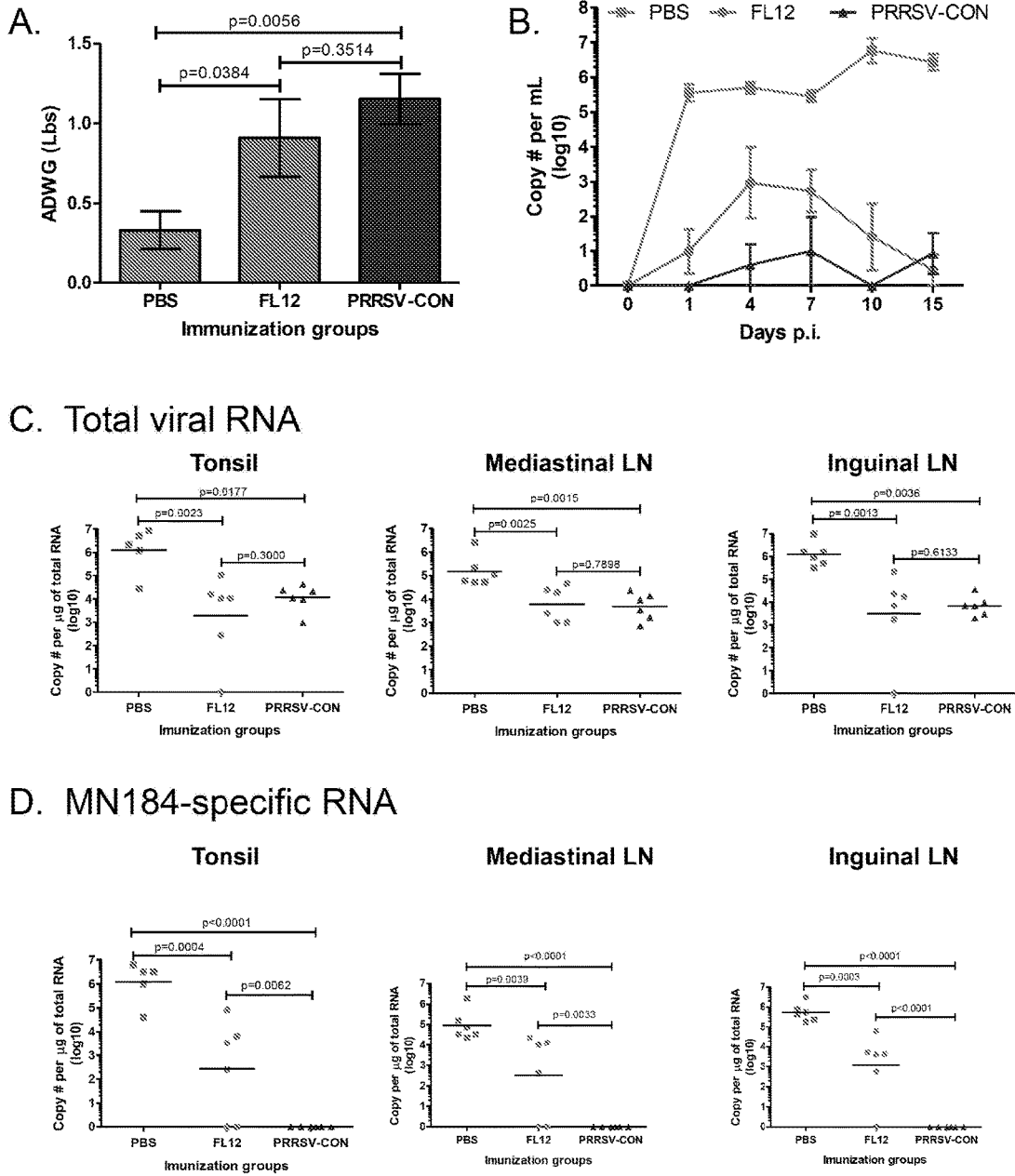


Figure 4

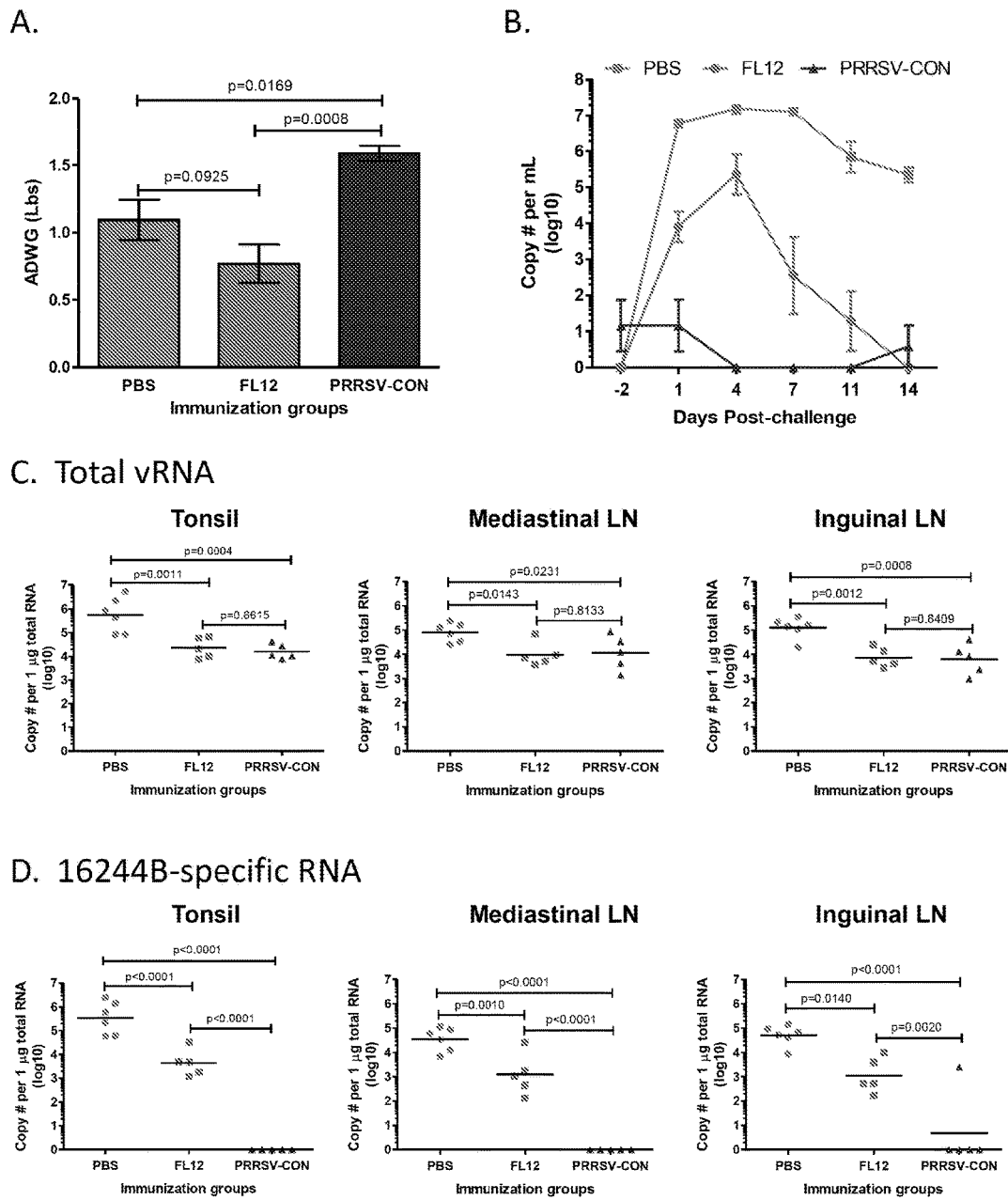


Figure 5

1

**NON-NATURALLY OCCURRING PORCINE
REPRODUCTIVE AND RESPIRATORY
SYNDROME VIRUS (PPRSV) AND
METHODS OF USING**

CROSS REFERENCE TO RELATED
APPLICATIONS

This application is a National Stage Application under 35 U.S.C. § 371 and claims the benefit of International Application No. PCT/IB2015/052214, filed Mar. 25, 2015, which claims the benefit of priority to U.S. Application No. 61/968,465, filed Mar. 21, 2014.

FEDERALLY SPONSORED RESEARCH OR
DEVELOPMENT

This invention was made with Government support under 2013-31100-06031, 2012-31100-06031 and 2008-55620-19132 awarded by the United States Department of Agriculture National Institute of Food and Agriculture. The Government has certain rights in the invention.

TECHNICAL FIELD

This disclosure generally relates to a non-naturally occurring porcine reproductive and respiratory syndrome virus (PPRSV) and methods of using.

BACKGROUND

Current porcine reproductive and respiratory syndrome virus (PPRSV) vaccines are not adequately effective for control and eradication of porcine reproductive and respiratory syndrome (PPRS). The main limitation of the current PPRSV vaccines is their sub-optimal coverage against divergent PPRSV strains. Thus far, all commercial PPRSV vaccines are formulated using natural PPRSV strains, but the substantial genetic variation among the PPRSV strains is the biggest obstacle for the development of a broadly protective PPRSV vaccine.

SUMMARY

This disclosure provides a non-naturally occurring porcine reproductive and respiratory syndrome virus (PPRSV) and methods of making and using the non-naturally occurring PPRSV.

A PPRSV-CON nucleic acid is provided, where the nucleic acid has at least 50% sequence identity (e.g., at least 75%, at least 95%, or at least 99% sequence identity) to SEQ ID NO:1. In some embodiment, the nucleic acid has the sequence shown in SEQ ID NO:1. A virus particle comprising the PPRSV-CON nucleic acid described herein. A composition comprising the PPRSV-CON nucleic acid described herein and a pharmaceutically acceptable carrier. A composition comprising the virus particle described herein and a pharmaceutically acceptable carrier. The compositions described herein, further comprising an adjuvant.

A PPRSV-CON nucleic acid also is provided, where the nucleic acid has at least 95% (e.g., at least 99%) sequence identity to a sequence selected from the group consisting of SEQ ID NO:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, and 42. In some embodiments, the nucleic acid has a sequence selected from the group consisting of SEQ ID NO:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, and 42. In some

2

embodiments, the nucleic acid encodes, respectively, a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 and 43. A virus particle comprising the PPRSV-CON nucleic acid described herein. A composition comprising the nucleic acid described herein and a pharmaceutically acceptable carrier. A composition comprising the virus particle described herein and a pharmaceutically acceptable carrier. The composition described herein, further comprising an adjuvant.

A PPRSV-CON polypeptide is provided, where the polypeptide has at least 95% (e.g., at least 99%) sequence identity to a sequence selected from the group consisting of SEQ ID NO:3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 and 43. In some embodiments, the polypeptide has a sequence selected from the group consisting of SEQ ID NO:3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 and 43. In some embodiments, the polypeptide is encoded by a nucleic acid, respectively, having a sequence selected from the group consisting of SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, or 42. A virus particle comprising the PPRSV-CON polypeptide described herein. A composition comprising the polypeptide described herein and a pharmaceutically acceptable carrier. A composition comprising the virus particle described herein and a pharmaceutically acceptable carrier. The composition described herein, further comprising an adjuvant.

A method for eliciting an immune response to PPRSV in a porcine is provided. Such a method typically includes administering, to a porcine: (i) an effective amount of any of the nucleic acids described herein; (ii) an effective amount of any of the polypeptides described herein; (iii) an effective amount of any of the virus particles described herein; or (iv) an effective amount of any of the compositions described herein. Representative routes of administration include, without limitation, intramuscularly, intraperitoneally, and orally.

A method for treating or preventing PPRS in a porcine is provided. Such a method typically includes administering, to a porcine: (i) an effective amount of any of the nucleic acids described herein; (ii) an effective amount of any of the polypeptides described herein; (iii) an effective amount of any of the virus particles described herein; or (iv) an effective amount of any of the compositions described herein. Representative routes of administration include, without limitation, intramuscularly, intraperitoneally, and orally.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the methods and compositions of matter belong. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the methods and compositions of matter, suitable methods and materials are described below. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety.

DESCRIPTION OF DRAWINGS

FIG. 1, Panel (A) is a phylogenetic tree constructed from a set of 60 PPRSV full-genome sequences. These 60 PPRSV genomes are classified into 4 sub-groups. The locations of the viruses involved in the cross-protection

experiments are indicated by the arrows. FIG. 1, Panel (B) is a graph showing the genetic distances among natural PRRSV strains and the genetic distance from the PRRSV-CON described herein to the natural PRRSV strains. The lower and upper boundaries of the box indicate the 25th and 75th percentile respectively. The solid line within the box represents the median. Whiskers above and below the box indicate the minimum and maximum of the data.

FIG. 2 shows the generation and characterization of the PRRSV-CON virus. Panel (A) is a schematic showing the strategy to construct the PRRSV-CON full-genome cDNA clone. The upper half of Panel (A) depicts the schematic representation of the viral genome, together with the unique restriction enzyme sites used for cloning purposes. The horizontal black lines, with the letters A-D on top, represent the DNA fragments that were synthesized. The numbers inside the parenthesis below the lines indicate the length (in nucleotides) of each corresponding fragments. Φ T7 represents the T7 RNA polymerase promoter. Individual DNA fragments of the genome were sequentially inserted into the shuttle vector (shown in the lower half of Panel (A)) in the order of fragment A to fragment D. Panel (B) are photographs showing the reactivity of the indicated viruses with different PRRSV-specific monoclonal antibodies. MARC-145 cells were mock infected or infected with PRRSV-CON or PRRSV wild type strain, FL12. At 48 hours post-infection, the cells were stained with antibodies specific to the viral nucleocapsid protein (N protein; bottom row of photographs) or to the viral nonstructural protein 1 beta (nsp1b; top row of photographs). Panel (C) shows the plaque morphology of the viruses in MARC-145 cells. Panel (D) shows a multiple step growth curve. MARC-145 cells were infected with the indicated viruses at a multiplicity of infection (MOI) of 0.01. At different timepoints post-infection (p.i.), culture supernatant was collected and viral titer was determined by titration on MARC-145 cells.

FIG. 3 is data demonstrating replication of the PRRSV-CON in pigs. Panel (A) shows the rectal temperature measured daily from 1 day before infection to 13 days post-infection (days p.i.). Panel (B) shows the average daily weight gain (ADWG) within 14 days after inoculation. Panel (C) shows the viremia levels, determined by a commercial, universal RT-qPCR (Tetracore Inc., Rockville, Md.). Panel (D) shows the levels of antibody response after inoculation, determined by IDEXX ELISA; the horizontal dotted line indicates the cut-off of the assay.

FIG. 4 is data demonstrating cross-protection provided by the PRRSV-CON described herein against the PRRSV-strain, MN-184. Panel (A) shows the average daily weight gain (ADWG) within 15 days after challenge-infection. Panel (B) shows the viremia levels after challenge determined by a commercial, universal RT-qPCR (Tetracore Inc., Rockville, Md.). Panel (C) shows total viral RNA levels in different tissues collected at 15 days post-challenge as determined by a commercial, universal RT-qPCR (Tetracore Inc., Rockville, Md.). Panel (D) shows the MN-184-specific RNA levels as determined by a differential RT-qPCR developed in-house.

FIG. 5 is data demonstrating cross-protection against PRRSV strain, 16244B. Panel (A) shows the average daily weight gain (ADWG) within 15 days after challenge-infection. Panel (B) shows the viremia levels after challenge infection determined by a commercial, universal RT-qPCR (Tetracore Inc., Rockville, Md.). Panel (C) shows total viral RNA levels in different tissues collected at 15 days post-challenge as determined by a commercial, universal RT-qPCR (Tetracore Inc., Rockville, Md.). Panel (D) shows the

16244B-specific RNA levels as determined by a differential RT-qPCR developed in-house.

DETAILED DESCRIPTION

A non-naturally occurring porcine reproductive and respiratory syndrome virus (PRRSV) genome was designed using a large set of genomic sequences of PRRSV isolates, which represents the widest genetic diversity of PRRSV strains circulating in U.S. swine herds. The non-naturally occurring PRRSV genome was designed so that it has a high degree of genetic similarity to the PRRSV field-isolates studied when compared to any single, naturally occurring PRRSV strain.

Porcine reproductive and respiratory syndrome (PRRS) is one of the most economically important diseases in swine. Clinical signs of the disease include reproductive failure in pregnant sows and respiratory disorder in young pigs. The disease is more severe when animals are co-infected with other pathogens. The annual loss to the US swine industry was estimated to be about \$560 million in 2005 and about \$640 million in 2011.

The causative agent of PRRS is an RNA virus named PRRS virus (PRRSV). PRRSV is classified into two major genotypes: European (Type 1) and North American (Type 2). There is limited cross-protection between these two genotypes. Considerable genetic variation exists among PRRSV isolates within each of these genotypes. Importantly, genetic divergence has been shown to occur when a PRRSV strain is serially passed from pig to pig. This leads to co-circulation of multiple PRRSV variants within one herd or even within one animal that is persistently infected with PRRSV.

PRRSV vaccines have been in use since 1994. There are two types of PRRSV vaccines currently available in the market; modified-live and inactivated vaccines. In addition, several subunit vaccines against PRRSV are being tested in different laboratories worldwide, but none have been licensed for clinical application. Currently, PRRSV vaccines are prepared using naturally occurring PRRSV strains as the vaccine immunogens. The current PRRSV vaccines are not adequately effective for control and eradication of PRRS; they provide acceptable levels of homologous protection but they fail to provide consistent heterologous cross-protection. Extensive genetic diversity among PRRSV isolates is the main reason behind the sub-optimal heterologous protection of the current PRRSV vaccines.

The non-naturally occurring PRRSV-CON described herein confers superior cross-protective against different heterologous PRRSV strains, as compared to the PRRSV wild type strain FL12. Thus, the PRRSV-CON described herein can be used to formulate a universal PRRSV vaccine. In addition, the PRRSV-CON described herein provides an important tool to study the mechanism of heterologous protection against divergent PRRSV strains.

Nucleic Acids and Polypeptides

The PRRSV genome encodes at least 22 proteins; 14 non-structural proteins and 8 structural proteins. A nucleic acid is provided herein that encodes for a non-naturally occurring PRRSV. See SEQ ID NO:1 for the genomic sequence of PRRSV-CON. The non-naturally occurring PRRSV described herein possesses the highest degree of genetic identity with the naturally occurring PRRSV isolates. The PRRSV-CON genomic nucleic acid provided herein (i.e., SEQ ID NO:1) encodes for a number of different polypeptides. For example, the nucleic acid sequence shown in SEQ ID NO:2 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:3; the nucleic acid sequence shown in SEQ ID NO:4 encodes for

the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:5; the nucleic acid sequence shown in SEQ ID NO:6 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:7; the nucleic acid sequence shown in SEQ ID NO:8 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:9; the nucleic acid sequence shown in SEQ ID NO:10 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:11; the nucleic acid sequence shown in SEQ ID NO:12 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:13; the nucleic acid sequence shown in SEQ ID NO:14 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:15; the nucleic acid sequence shown in SEQ ID NO:16 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:17; the nucleic acid sequence shown in SEQ ID NO:18 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:19; the nucleic acid sequence shown in SEQ ID NO:20 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:21; the nucleic acid sequence shown in SEQ ID NO:22 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:23; the nucleic acid sequence shown in SEQ ID NO:24 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:25; the nucleic acid sequence shown in SEQ ID NO:26 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:27; the nucleic acid sequence shown in SEQ ID NO:28 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:29; the nucleic acid sequence shown in SEQ ID NO:30 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:31; the nucleic acid sequence shown in SEQ ID NO:32 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:33; the nucleic acid sequence shown in SEQ ID NO:34 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:35; the nucleic acid sequence shown in SEQ ID NO:36 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:37; the nucleic acid sequence shown in SEQ ID NO:38 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:39; the nucleic acid sequence shown in SEQ ID NO:40 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:41; and the nucleic acid sequence shown in SEQ ID NO:42 encodes for the polypeptide sequence having the amino acid sequence shown in SEQ ID NO:43.

As used herein, nucleic acids can include DNA and RNA, and includes nucleic acids that contain one or more nucleotide analogs or backbone modifications. A nucleic acid can be single stranded or double stranded, which usually depends upon its intended use. Nucleic acids and polypeptides that differ from SEQ ID NOs:1-43 also are provided. Nucleic acids that differ in sequence from SEQ ID NO:1 or any of SEQ ID NOs:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, or 42 can have at least 80% sequence identity (e.g., at least 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity) to SEQ ID NO:1 or any of SEQ ID NOs:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, or 42. Polypeptides that differ in sequence from any of SEQ ID NOs:3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 or

43, can have at least 80% sequence identity (e.g., at least 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity) to any of SEQ ID NOs:3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 or 43.

In calculating percent sequence identity, two sequences are aligned and the number of identical matches of nucleotides or amino acid residues between the two sequences is determined. The number of identical matches is divided by the length of the aligned region (i.e., the number of aligned nucleotides or amino acid residues) and multiplied by 100 to arrive at a percent sequence identity value. It will be appreciated that the length of the aligned region can be a portion of one or both sequences up to the full-length size of the shortest sequence. It also will be appreciated that a single sequence can align with more than one other sequence and hence, can have different percent sequence identity values over each aligned region.

The alignment of two or more sequences to determine percent sequence identity can be performed using the computer program ClustalW and default parameters, which allows alignments of nucleic acid or polypeptide sequences to be carried out across their entire length (global alignment). Chenna et al., 2003, *Nucleic Acids Res.*, 31(13): 3497-500. ClustalW calculates the best match between a query and one or more subject sequences, and aligns them so that identities, similarities and differences can be determined. Gaps of one or more residues can be inserted into a query sequence, a subject sequence, or both, to maximize sequence alignments. For fast pairwise alignment of nucleic acid sequences, the default parameters can be used (i.e., word size: 2; window size: 4; scoring method: percentage; number of top diagonals: 4; and gap penalty: 5); for an alignment of multiple nucleic acid sequences, the following parameters can be used: gap opening penalty: 10.0; gap extension penalty: 5.0; and weight transitions: yes. For fast pairwise alignment of polypeptide sequences, the following parameters can be used: word size: 1; window size: 5; scoring method: percentage; number of top diagonals: 5; and gap penalty: 3. For multiple alignment of polypeptide sequences, the following parameters can be used: weight matrix: blosum; gap opening penalty: 10.0; gap extension penalty: 0.05; hydrophilic gaps: on; hydrophilic residues: Gly, Pro, Ser, Asn, Asp, Gln, Glu, Arg, and Lys; and residue-specific gap penalties: on. ClustalW can be run, for example, at the Baylor College of Medicine Search Launcher website or at the European Bioinformatics Institute website on the World Wide Web.

Changes can be introduced into a nucleic acid molecule (e.g., SEQ ID NO:1 or any of SEQ ID NOs:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, or 42), thereby leading to changes in the amino acid sequence of the encoded polypeptide (e.g., SEQ ID NOs:3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 or 43). For example, changes can be introduced into nucleic acid coding sequences using mutagenesis (e.g., site-directed mutagenesis, PCR-mediated mutagenesis) or by chemically synthesizing a nucleic acid molecule having such changes. Such nucleic acid changes can lead to conservative and/or non-conservative amino acid substitutions at one or more amino acid residues. A "conservative amino acid substitution" is one in which one amino acid residue is replaced with a different amino acid residue having a similar side chain (see, for example, Dayhoff et al. (1978, in *Atlas of Protein Sequence and Structure*, 5(Suppl. 3):345-352), which provides frequency tables for amino acid substitutions), and a

non-conservative substitution is one in which an amino acid residue is replaced with an amino acid residue that does not have a similar side chain.

As used herein, an "isolated" nucleic acid molecule is a nucleic acid molecule that is free of sequences that naturally flank one or both ends of the nucleic acid in the genome of the organism from which the isolated nucleic acid molecule is derived (e.g., a cDNA or genomic DNA fragment produced by PCR or restriction endonuclease digestion). Such an isolated nucleic acid molecule is generally introduced into a vector (e.g., a cloning vector, or an expression vector) for convenience of manipulation or to generate a fusion nucleic acid molecule, discussed in more detail below. In addition, an isolated nucleic acid molecule can include an engineered nucleic acid molecule such as a recombinant or a synthetic nucleic acid molecule.

As used herein, a "purified" polypeptide is a polypeptide that has been separated or purified from cellular components that naturally accompany it. Typically, the polypeptide is considered "purified" when it is at least 70% (e.g., at least 75%, 80%, 85%, 90%, 95%, or 99%) by dry weight, free from the polypeptides and naturally occurring molecules with which it is naturally associated. Since a polypeptide that is chemically synthesized is, by nature, separated from the components that naturally accompany it, a synthetic polypeptide is "purified."

Nucleic acids can be isolated using techniques routine in the art. For example, nucleic acids can be isolated using any method including, without limitation, recombinant nucleic acid technology, and/or the polymerase chain reaction (PCR). General PCR techniques are described, for example in PCR Primer: A Laboratory Manual, Dieffenbach & Dveksler, Eds., Cold Spring Harbor Laboratory Press, 1995. Recombinant nucleic acid techniques include, for example, restriction enzyme digestion and ligation, which can be used to isolate a nucleic acid. Isolated nucleic acids also can be chemically synthesized, either as a single nucleic acid molecule or as a series of oligonucleotides.

Polypeptides can be purified from natural sources (e.g., a biological sample) by known methods such as DEAE ion exchange, gel filtration, and hydroxyapatite chromatography. A polypeptide also can be purified, for example, by expressing a nucleic acid in an expression vector. In addition, a purified polypeptide can be obtained by chemical synthesis. The extent of purity of a polypeptide can be measured using any appropriate method, e.g., column chromatography, polyacrylamide gel electrophoresis, or HPLC analysis.

A vector containing a nucleic acid (e.g., a nucleic acid that encodes a polypeptide) also is provided. Vectors, including expression vectors, are commercially available or can be produced by recombinant DNA techniques routine in the art. A vector containing a nucleic acid can have expression elements operably linked to such a nucleic acid, and further can include sequences such as those encoding a selectable marker (e.g., an antibiotic resistance gene). A vector containing a nucleic acid can encode a chimeric or fusion polypeptide (i.e., a polypeptide operatively linked to a heterologous polypeptide, which can be at either the N-terminus or C-terminus of the polypeptide). Representative heterologous polypeptides are those that can be used in purification of the encoded polypeptide (e.g., 6xHis tag, glutathione S-transferase (GST))

Expression elements include nucleic acid sequences that direct and regulate expression of nucleic acid coding sequences. One example of an expression element is a promoter sequence. Expression elements also can include

introns, enhancer sequences, response elements, or inducible elements that modulate expression of a nucleic acid. Expression elements can be of bacterial, yeast, insect, mammalian, or viral origin, and vectors can contain a combination of elements from different origins. As used herein, operably linked means that a promoter or other expression element(s) are positioned in a vector relative to a nucleic acid in such a way as to direct or regulate expression of the nucleic acid (e.g., in-frame). Many methods for introducing nucleic acids into host cells, both in vivo and in vitro, are well known to those skilled in the art and include, without limitation, electroporation, calcium phosphate precipitation, polyethylene glycol (PEG) transformation, heat shock, lipofection, microinjection, and viral-mediated nucleic acid transfer.

Vectors as described herein can be introduced into a host cell. As used herein, "host cell" refers to the particular cell into which the nucleic acid is introduced and also includes the progeny of such a cell that carry the vector. A host cell can be any prokaryotic or eukaryotic cell. For example, nucleic acids can be expressed in bacterial cells such as *E. coli*, or in insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Nucleic acids can be detected using any number of amplification techniques (see, e.g., PCR Primer: A Laboratory Manual, 1995, Dieffenbach & Dveksler, Eds., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.; and U.S. Pat. Nos. 4,683,195; 4,683,202; 4,800,159; and 4,965,188) with an appropriate pair of oligonucleotides (e.g., primers). A number of modifications to the original PCR have been developed and can be used to detect a nucleic acid.

Nucleic acids also can be detected using hybridization. Hybridization between nucleic acids is discussed in detail in Sambrook et al. (1989, Molecular Cloning: A Laboratory Manual, 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.; Sections 7.37-7.57, 9.47-9.57, 11.7-11.8, and 11.45-11.57). Sambrook et al. discloses suitable Southern blot conditions for oligonucleotide probes less than about 100 nucleotides (Sections 11.45-11.46). The T_m between a sequence that is less than 100 nucleotides in length and a second sequence can be calculated using the formula provided in Section 11.46. Sambrook et al. additionally discloses Southern blot conditions for oligonucleotide probes greater than about 100 nucleotides (see Sections 9.47-9.54). The T_m between a sequence greater than 100 nucleotides in length and a second sequence can be calculated using the formula provided in Sections 9.50-9.51 of Sambrook et al.

The conditions under which membranes containing nucleic acids are prehybridized and hybridized, as well as the conditions under which membranes containing nucleic acids are washed to remove excess and non-specifically bound probe, can play a significant role in the stringency of the hybridization. Such hybridizations and washes can be performed, where appropriate, under moderate or high stringency conditions. For example, washing conditions can be made more stringent by decreasing the salt concentration in the wash solutions and/or by increasing the temperature at which the washes are performed. Simply by way of example, high stringency conditions typically include a wash of the membranes in 0.2xSSC at 65° C.

In addition, interpreting the amount of hybridization can be affected, for example, by the specific activity of the labeled oligonucleotide probe, by the number of probe-binding sites on the template nucleic acid to which the probe has hybridized, and by the amount of exposure of an

autoradiograph or other detection medium. It will be readily appreciated by those of ordinary skill in the art that although any number of hybridization and washing conditions can be used to examine hybridization of a probe nucleic acid molecule to immobilized target nucleic acids, it is more important to examine hybridization of a probe to target nucleic acids under identical hybridization, washing, and exposure conditions. Preferably, the target nucleic acids are on the same membrane.

A nucleic acid molecule is deemed to hybridize to a nucleic acid but not to another nucleic acid if hybridization to a nucleic acid is at least 5-fold (e.g., at least 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 20-fold, 50-fold, or 100-fold) greater than hybridization to another nucleic acid. The amount of hybridization can be quantitated directly on a membrane or from an autoradiograph using, for example, a PhosphorImager or a Densitometer (Molecular Dynamics, Sunnyvale, Calif.).

Polypeptides can be detected using antibodies. Techniques for detecting polypeptides using antibodies include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. An antibody can be polyclonal or monoclonal. An antibody having specific binding affinity for a polypeptide can be generated using methods well known in the art. The antibody can be attached to a solid support such as a microtiter plate using methods known in the art. In the presence of a polypeptide, an antibody-polypeptide complex is formed.

Detection (e.g., of an amplification product, a hybridization complex, or a polypeptide) is usually accomplished using detectable labels. The term "label" is intended to encompass the use of direct labels as well as indirect labels. Detectable labels include enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Methods of Making and Using a PRRSV-CON Virus Particle

Methods of constructing a virus particle from a PRRSV-CON nucleic acid are known in the art and are described herein. As demonstrated herein, the PRRSV-CON described herein self-assembles into particles when appropriately expressed. The PRRSV-CON can be expressed *in vitro* or *in vivo*, for example, in a host cell. In some embodiments, a host cell can be transfected with the PRRSV-CON nucleic acid, or a host cell can be infected with a PRRSV-CON virus particle. Host cells can be, without limitation, porcine cells (e.g., porcine alveolar macrophage) or African green monkey kidney-derived cells (e.g., MARC-145). Virus particles can be isolated, for example, by ultracentrifugation.

The PRRSV-CON nucleic acids, polypeptides or virus particles described herein can be used to generate, enhance or modulate the immune response of a porcine. Such methods typically include administering a PRRSV-CON nucleic acid, polypeptide or virus particle described herein to a porcine in an amount sufficient to generate an immune response. As used herein, an "immune response" refers to the reaction elicited in an individual following administration of a PRRSV-CON nucleic acid, polypeptide or virus particle as described herein. Immune responses can include, for example, an antibody response or a cellular response (e.g., a cytotoxic T-cell response). A PRRSV-CON nucleic acid, polypeptide or virus particle can be used to prevent PRRS in porcine, e.g., as a prophylactic vaccine, or to establish or enhance immunity to PRRS in a healthy individual prior to exposure or contraction of PRRS, thus preventing the disease or reducing the severity of disease symptoms.

Methods for administering a PRRSV-CON nucleic acid, polypeptide or virus particle to a porcine include, without limitation, intramuscular (i.m.), subcutaneous (s.c.), or intrapulmonary routes. Methods for administering a PRRSV-CON nucleic acid, polypeptide or virus particle to a porcine also include, without limitation, intratracheal, transdermal, intraocular, intranasal, inhalation, intracavity, and intravenous (i.v.) administration.

Determining an effective amount of a PRRSV-CON nucleic acid, polypeptide or virus particle depends upon a number of factors including, for example, whether the antigen is being expressed or administered directly, the age and weight of the subject, the precise condition requiring treatment and its severity, and the route of administration. Based on the above factors, determining the amount and the dosing (e.g., the number of doses and the timing of doses) are within the level of skill of an ordinary artisan.

A composition can include a PRRSV-CON nucleic acid, polypeptide or virus particle as described herein and a pharmaceutically acceptable carrier. Pharmaceutically acceptable carriers are known in the art and include, for example, buffers (e.g., phosphate buffered saline (PBS), normal saline, Tris buffer, and sodium phosphate) or diluents. The compositions described herein can be formulated as an aqueous solution, or as an emulsion, gel, solution, suspension, or powder. See, for example, Remington's Pharmaceutical Sciences, 16th Ed., Osol, ed., Mack Publishing Co., Easton, Pa. (1980), and Remington's Pharmaceutical Sciences, 19th Ed., Gennaro, ed., Mack Publishing Co., Easton, Pa. (1995). In addition to a pharmaceutically acceptable carrier, the compositions described herein also can include binders, stabilizers, preservatives, salts, excipients, delivery vehicles and/or auxiliary agents.

In accordance with the present invention, there may be employed conventional molecular biology, microbiology, biochemical, and recombinant DNA techniques within the skill of the art. Such techniques are explained fully in the literature. The invention will be further described in the following examples, which do not limit the scope of the methods and compositions of matter described in the claims.

EXAMPLES

Example 1—Computational Design of the Artificial PRRSV-CON Genome

Full-genome sequences of 64 PRRSV isolates originating from the Midwestern states (Iowa, Nebraska and Illinois) of the U.S. were sequenced using the Roche 454-GS-FLX sequencing technology. In addition, more than 20 full-genome sequences of PRRSV isolates originating from the U.S. were collected from GenBank. After removing redundant sequences, a final set of 60 full-genome sequences of PRRSV was attained. The 60 PRRSV full-genome sequences were aligned using the MUSCLE program (Edgar R C, 2004, BMC Bioinform., 5:113). After that, a consensus genome sequence (PRRSV-CON) was generated by selecting the most common nucleotide found at each position of the viral genome, using the Jalview program. Phylogenetic analysis shows that the PRRSV-CON genome locates right at the center of the phylogenetic tree. See FIG. 1A. Consequently, the pairwise genetic distance from PRRSV-CON to the naturally occurring PRRSV strains is significantly shorter than the distance from any one naturally occurring PRRSV strains to each other ($p < 0.0001$). See FIG. 1B.

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Example 2—Generation of an Infectious PRRSV-CON Virus

It is generally difficult to accurately determine the sequence at 5' and 3' ends of a viral genome. Thus, we realized that the sequences at the 5' and 3' untranslated regions (UTRs) of the naturally occurring PRRSV genomes analyzed in Example 1 may not be accurate. To increase the change of recovering infectious virus, we replaced the 5' and 3'UTRs of the PRRSV-CON genome with the 5' and 3' UTRs of the infectious cDNA clone FL12 (Truong et al., 2004, *Virology*, 325:308-19). Four DNA fragments, designated A-D, encompassing the entire PRRSV-CON genome, were chemically synthesized by Genscript (Piscataway, N.J.). Each DNA fragment was flanked by a pair of restriction enzyme sites to facilitate the cloning purposes. The T7 RNA polymerase promoter sequence was incorporated into fragment D, preceding the viral 5' end, to facilitate the in vitro transcription of the viral genome. See FIG. 2A. Individual DNA fragments were sequentially cloned into the shuttle vector that carries the corresponding restriction enzyme site, following the order from fragment A to fragment D. Once the full-length PRRSV-CON cDNA clone was generated, standard reverse genetics techniques were applied to recover viable PRRSV-CON viruses.

Briefly, the plasmid containing full-length cDNA genome of PRRSV-CON was digested with AclI for linearization. The purified, linear DNA fragment was used as the template for an in vitro transcription reaction using the mMES-SAGEmMACHINE Ultra T7 kit (Ambion, Austin, Tex.) to generate full genome viral RNA transcripts. After that, about 5 µg of the full-genome RNA transcripts were transfected into MARC-145 cells cultured in a 6-well plate, using the TransIT®-mRNA Transfection Kit (Minis Bio, Madison, Wis.). Transfected cells were cultured in DMEM containing 10% FBS at 37° C., 5% CO₂ for up to 6 days. Typically, cytopathic effect (CPE) was observed between day 4 and day 6 after transfection. When clear CPE was observed, culture supernatant containing the rescued virus was collected and stored in 0.5 mL aliquots in a 80° C. freezer. See, Truong et al. (2004, *supra*)

Example 3—In Vitro Characterization of the PRRSV-CON Virus

To study the reactivity with different PRRSV-specific monoclonal antibodies, MARC-145 cells were mock infected or infected with the PRRSV-CON virus or the PRRSV strain FL12. At 48 hours post-infection (p.i.), the cells were immunostained with antibodies specific to the viral nucleocapsid (N) protein or the viral nonstructural protein 1 beta (nsp1b). To study the growth kinetics of the viruses in cell culture, MARC-145 cells were infected with the PRRSV-CON or FL12 at a multiplicity of infection (MOI) of 0.01. At different time-points p.i., culture supernatant was collected and viral titers were determined by titration in MARC-145 cells.

The PRRSV-CON virus displays typical in vitro characterizations of a naturally occurring PRRSV strain. It reacts with different PRRSV-specific monoclonal antibodies including antibodies against nsp1-beta and N protein (FIG. 2B). It replicates efficiently in cell culture (FIG. 2C), and it is able to form clear and distinct plaque morphology (FIG. 3D).

Example 4—the PRRSV-CON Virus can Infect Pigs as Efficiently as the Natural PRRSV Strain

A total of 18 PRRSV-seronegative, 3 week-old pigs were purchased from the University of Nebraska research farm.

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The pigs were randomly assigned into 3 experimental groups; each group was housed in a separate room in the Biosecurity Level-2 Animal Research Facilities at UNL, following the regulations established by the Institutional Animal Care and Use Committee. Pigs in group 1 were injected with PBS to act as the control. Pigs in groups 2 and 3 were inoculated intramuscularly with 10^{5.0} TCID₅₀ of PRRSV-CON and PRRSV strain FL12, respectively. The wild-type PRRSV strain, FL12, was included into this study for comparison purposes. The results are shown in FIG. 3. After infection, both of the PRRSV-CON and FL12-inoculated groups displayed significantly higher temperature than PBS-group (FIG. 3A), but there was no difference in temperature between PRRSV-CON-inoculated group and the FL12-inoculated group. Average daily weight gain (ADWG) was measured for each individual pig during the period of 14 days after infection. No statistical difference was observed among the three treatment groups, although pigs in the PRRSV-CON-inoculated group and the FL12-inoculated group tended to have lower ADWG than the PBS group (FIG. 3B). Viremia levels of the PRRSV-CON- and FL12-inoculated groups were almost identical (FIG. 3C). All pigs in the PRRSV-CON- and FL12-inoculated groups were seroconverted by 11 days p.i. The level of antibody response in the PRRSV-CON-inoculated group was slightly lower than that of the FL12-inoculated group (FIG. 3D). These results demonstrate that the PRRSV-CON can infect the natural host (i.e., pigs) as efficiently as the PRRSV strain, FL12.

Example 5—Evaluation of the Level of Cross-Protection Against PRRSV Strain MN-184

Materials and Methods

A total of 18 PRRSV-seronegative, 3 week-old pigs were purchased from the University of Nebraska research farm. The pigs were randomly assigned into 3 experimental groups; each group was housed in a separate room in the Biosecurity Level-2 Animal Research Facilities at UNL, following the regulations established by the Institutional Animal Care and Use Committee. Group 1 was injected with PBS and served as the non-immunization control. Group 2 was immunized by infection, intramuscularly, with PRRSV-CON at the dose of 10^{4.0} TCID₅₀ per pig. Group 3 was immunized by infection, intramuscularly, with the wild-type PRRSV strain, FL12, at the dose of 10^{4.0} TCID₅₀ per pig. See Table 1. At 53 days post-infection (p.i.), all control and immunized pigs were challenged, intramuscularly, with PRRSV strain MN-184 at a dose of 10^{5.0} TCID₅₀. Parameters used to evaluate protection by immunization with the PRRSV-CON virus included viremia and viral load in several different tissues as well as growth performance.

TABLE 1

Experimental Design to Evaluate Level of Cross-Protection Against PRRSV Strain MN-184		
Groups	Immunized with	Challenged with
1 (n = 6)	PBS	MN-184
2 (n = 6)	PRRSV-CON	(Sub-group 2)
3 (n = 6)	PRRSV strain FL12	

To measure growth performance, each pig was weighed right before challenge infection and 15 days post-challenge. Body weight was recorded in pounds. Average daily weight gain (ADWG) was calculated for the period of 15 days post-challenge.

To quantitate levels of viremia after challenge infection, blood samples were taken before challenge and at days 1, 4, 7, 10, and 15 post-challenge. Serum samples were extracted from each individual blood samples and stored in a -80° C. freezer. Viremia levels were quantitated by the Animal Disease Research and Diagnostic Laboratory, South Dakota State University, using the universal RT-qPCR kit (Tetracore Inc., Rockville, Md.). Results were reported as log₁₀ copy/mL. For statistical purposes, samples that had undetected level of viral RNA were assigned a value of 0 log₁₀ copy/mL.

To quantitate levels of viral load in tissues, pigs were humanely sacrificed and necropsied on day 15 post-challenge. Samples of tonsil, lung, mediastinal lymph node and inguinal lymph node were obtained and kept individually in Whirl-Pak® bags. The samples were snap-frozen in liquid nitrogen right after collection. After that, they were stored in a -80° C. freezer. To extract RNA, tissue samples were homogenized in Trizol reagent (Life Technologies, Carlsbad, Calif.) with a ratio of 300 mg tissue in 3 mL Trizol reagent. Total RNA was extracted using the RNeasy Mini Kit (Qiagen, Valencia, Calif.) following the manufacturer's instruction. RNA concentration was quantitated by the NanoDrop®ND-1000 (NanoDrop Technologies, Inc., Wilmington, Del.) and adjusted to a final concentration of 200 ng/ μ L.

It has been well characterized that PRRSV can colonize and persist in lymphoid tissues of infected pigs up to 150 days post-infection. In these experiments, the tissue viral load was evaluated at 15 days post-challenge, which corresponds to 67 days after the primary infection. At that time, it is likely that the pigs in the PRRSV-CON and FL12 groups still contained residual virus of the primary infection. Therefore, we used two different RT-PCR kits to quantify the viral RNA load in tissues: (i) the commercial RT-qPCR kit (Tetracore Inc., Rockville, Md.) that detects total viral RNA resulting from both the primary infection and the challenge infection, and (ii) the differential RT-PCR developed in-house that selectively detects only viral RNA from challenge infection. Five μ L of each RNA sample (equivalent to 1 μ g RNA) was used for each RT-qPCR reaction. Results were reported as log₁₀ copy/ μ g of total RNA. For statistical purposes, samples that had undetected viral RNA level were assigned a value of 0 log RNA copy/1 μ g of total RNA.

Results

The results of growth performance are presented in FIG. 4A. The mean ADWG of PBS-, PRRSV-CON- and FL12-immunized groups were 0.3 lbs (SD+/-0.3), 0.9 lbs (SD+/-0.6), and 1.2 lbs (SD+/-0.4), respectively. PRRSV-CON and FL12-immunized groups had greater ADWG than the PBS-immunized group. There was no statistical difference between the PRRSV-CON- and FL12-immunized groups.

The viremia levels after challenge infection are shown in FIG. 4B and Table 2. All pigs in the PBS-immunized group were viremic at all timepoints tested. The PRRSV-CON-immunized group only had 3 viremic pigs, of which 1 pig was viremic at 2 timepoints (pig #494 at 4 DPC and 7 DPC) and 2 pigs were viremic at only one timepoint (pigs #394 and 495 at 15 DPC). The remaining 3 pigs in this group (pigs #345, 410 and 459) were not viremic after challenge infection. By contrast, viremia was detected in 5 out of 6 pigs in the FL12-immunized group at two time-points or more after challenge infection. There was only 1 pig in this group (pig #440) that was not viremic at any time-point tested. Overall, the viremia level of PRRSV-CON-immunized pigs was significantly lower than that in the FL12-immunized group ($p < 0.05$) and the PBS-immunized group ($p < 0.0001$).

The results of total viral RNA quantitated by the universal RT-qPCR kit are shown in FIG. 4C. The PRRSV-CON- and FL12-immunized groups contained significantly lower levels of total viral RNA than the PBS-immunized group, regardless of the tissue types tested. However, there was no difference between the PRRSV-CON- and FL12-immunized groups in term of total viral RNA.

The results of MN-184 specific RNA quantitated by the differential RT-qPCR are shown in FIG. 4D. All pigs in PBS-immunized group carried MN-184 RNA in their tissues. Four pigs in the FL12-immunized group had MN-184 RNA in their tonsil and mediastinal lymph node, whereas 5 pigs in this group had MN-184 RNA in their inguinal lymph node. Remarkably, none of the pigs in the PRRSV-CON-immunized group had detectable level of MN-184 RNA in any of the tissue samples tested.

Taken together, these results clearly demonstrate that immunization of weaning pigs by infection with the non-naturally occurring PRRSV-CON resulted in significantly better cross-protection against challenge with PRRSV strain, MN-184, than did immunization with the PRRSV strain, FL12.

TABLE 2

Treatment	Pig ID	Viremia After Challenge Infection (log ₁₀ copy/mL)					
		Day post-challenge infection (DPC)					
		0 DPC	1 DPC	4 DPC	7 DPC	10 DPC	15 DPC
Group 1 (Injected ("immunized") with PBS)	365	0.00	4.94	5.43	5.45	6.79	6.32
	389	0.00	6.26	6.08	5.40	7.60	6.93
	407	0.00	4.91	6.00	5.86	7.56	6.75
	416	0.00	6.20	6.04	5.20	7.18	6.78
	417	0.00	5.18	5.59	4.86	5.90	6.45
	435	0.00	5.83	5.08	5.94	5.57	5.36
	Mean	0.00	5.55	5.70	5.45	6.77	6.43
	SD	0.00	0.62	0.40	0.40	0.86	0.57
Group 2 (Immunized by infection with PRRSV-CON)	345	0.00	0.00	0.00	0.00	0.00	0.00
	394	0.00	0.00	0.00	0.00	0.00	2.58
	410	0.00	0.00	0.00	0.00	0.00	0.00
	459	0.00	0.00	0.00	0.00	0.00	0.00
	494	0.00	0.00	3.58	5.98	0.00	0.00
	495	0.00	0.00	0.00	0.00	0.00	2.98
	Mean	0.00	0.00	0.60	1.00	0.00	0.93
SD	0.00	0.00	1.46	2.44	0.00	1.44	
Group 3 (Immunized by	349	0.00	0.00	2.81	2.92	0.00	0.00
	381	0.00	0.00	0.00	3.04	2.86	0.00

TABLE 2-continued

Viremia After Challenge Infection (log ₁₀ copy/mL)							
Treatment	Pig ID	Day post-challenge infection (DPC)					
		0 DPC	1 DPC	4 DPC	7 DPC	10 DPC	15 DPC
infection with FL12)	440	0.00	0.00	0.00	0.00	0.00	0.00
	455	0.00	0.00	4.18	4.34	0.00	0.00
	487	0.00	3.59	5.28	2.40	5.60	2.68
	507	0.00	2.32	5.56	3.70	0.00	0.00
	Mean	0.00	0.99	2.97	2.73	1.41	0.45
	SD	0.00	1.58	2.50	1.50	2.35	1.09

Example 6—Evaluation of the Level of Cross-Protection Against PRRSV Strain 16244B

Materials and Methods

The experimental design was the same as described above in Example 5. A total of 18 PRRSV-seronegative, 3 week-old pigs purchased from the UNL research farm were randomly assigned into 3 experimental groups. Each group was housed in a separate room at the Biosecurity Level-2 Animal Research Facilities at UNL, following the regulations established by the Institutional Animal Care and Use Committee. Group 1 was injected with PBS and acted as the control. Group 2 was immunized, intramuscularly, by infection with PRRSV-CON at the dose of 10^{4.0} TCID₅₀ per pig. Group 3 was immunized, intramuscularly, by infection with the wild type PRRSV, FL12, at the dose of 10^{4.0} TCID₅₀ per pig. See Table 3. One pig in group 3 (pig #543) and one pig in group 2 (pig #435) were removed from this study on 14 and 23 days after primary infection, respectively, due to lameness in their legs. At day 52 post-infection (p.i.), all pigs were challenged, intramuscularly, with PRRSV strain 16244B at the challenge dose of 10^{5.0} TCID₅₀. Parameters used to evaluate protection by immunization with the PRRSV-CON virus, including viremia and viral load in various tissues as well as growth performance, were measured as described above in Example 5.

TABLE 3

Experimental Design to Evaluate Level of Cross-Protection Against PRRSV Strain 16244B		
Groups	Immunized with	Challenged with
1 (n = 6)	PBS	16244B
2 (n = 6)	PRRSV-CON	(sub-group 3)
3 (n = 6)	PRRSV strain FL12	

Results

The results of growth performance are shown in FIG. 5A. Mean ADWG of PBS-, PRRSV-CON-, and FL12-immunized groups were 1.1 lbs (SD+/-0.3), 1.6 lbs (SD+/-0.1), and 0.8 lbs (SD+/-0.3), respectively. The PRRSV-CON-immunized group had greater ADWG than the PBS-immu-

nized group and the FL12-immunized group; whereas the FL12-immunized group was not statistically different from the PBS-immunized group.

The results of viremia levels after challenge infection are shown in FIG. 5B and Table 4. All pigs in the PBS-immunized group were viremic at all timepoints tested. Two out of 5 pigs in the PRRSV-CON-immunized group (pigs #442 and 445) did not resolve viremia at 52 days after primary infection as viral RNA was still detected in their serum samples collected at this timepoint. After challenge infection, 3 pigs in the PRRSV-CON-immunized group were viremic at only 1 timepoint. The remaining 2 pigs in this group (pigs #436 and 438) were not viremic throughout the period of 15 days post-challenge. By contrast, all pigs in the FL12-immunized group resolved viremia by 52 days post-primary infection. After challenge infection, all pigs in this group became viremic. Overall, the viremia level of the PRRSV-CON-immunized group was significantly lower than that of the FL12-immunized group (p<0.0001) or the PBS-immunized group (p<0.0001).

The results of total viral RNA quantitated by the commercial RT-qPCR kit (Tetracore Inc., Rockville, Md.) are shown in FIG. 5C. Both the PRRSV-CON- and FL12-immunized groups contained significantly lower levels of total viral RNA than the PBS-immunized group, regardless of the tissue types tested. However, there was no statistical difference between the PRRSV-CON-immunized group and the FL12-immunized group in terms of total viral RNA.

The results of 16244B-specific RNA quantitated by the differential RT-qPCR are shown in FIG. 5D. All pigs in the PBS- and FL12-immunized groups carried 16244B-specific RNA in their tissues, although the levels of 16244B RNA in the FL12-immunized group was lower than those in the PBS-immunized group. By contrast, only 1 pig in the PRRSV-CON-immunized group carried 16244B-specific RNA in its inguinal lymph node, while the remaining 4 pigs in this group did not carry 16244B-specific RNA.

All together, these results clearly demonstrate that immunization of weaning pigs by infection with the non-naturally occurring PRRSV-CON resulted in significantly better cross-protection against challenge with PRRSV strain, 16244B, than did immunization with the PRRSV strain, FL12.

TABLE 4

Level of Viremia After Challenge Infection (log ₁₀ copy/mL)							
Treatment	Pig ID	Day post-challenge					
		0 DPC	1 DPC	4 DPC	7 DPC	11 DPC	14 DPC
Group 1 (Injected)	440	0.00	6.62	6.99	6.79	6.15	4.67
	441	0.00	6.61	6.93	7.11	5.79	4.81

TABLE 4-continued

Level of Viremia After Challenge Infection (log ₁₀ copy/mL)							
Treatment	Pig ID	Day post-challenge					
		0 DPC	1 DPC	4 DPC	7 DPC	11 DPC	14 DPC
with PBS)	544	0.00	6.85	6.82	6.96	3.91	5.68
	545	0.00	7.11	7.41	7.11	6.81	5.93
	546	0.00	6.74	7.45	7.30	5.67	5.40
	547	0.00	6.77	7.51	7.36	6.73	5.52
	Mean	0.00	6.78	7.18	7.11	5.84	5.34
	SD	0.00	0.18	0.30	0.21	1.06	0.50
Group 2 (immunized by infection with PRRSV-CON)	435	Removed from experiment on day 23rd after primary infection					
	436	0.00	0.00	0.00	0.00	0.00	0.00
	437	0.00	2.48	0.00	0.00	0.00	0.00
	438	0.00	0.00	0.00	0.00	0.00	0.00
	442	2.81	0.00	0.00	0.00	0.00	2.93
	445	3.00	3.32	0.00	0.00	0.00	0.00
	Mean	1.16	1.16	0.00	0.00	0.00	0.59
SD	1.59	1.62	0.00	0.00	0.00	1.31	
Group 3 (immunized by infection with FL12)	439	0.00	4.34	6.78	3.54	2.48	0.00
	444	0.00	3.04	6.58	0.00	0.00	0.00
	446	0.00	5.26	4.84	0.00	0.00	0.00
	526	0.00	2.98	4.40	4.15	0.00	0.00
	540	0.00	3.90	4.18	5.08	3.95	0.00
	543	Removed from experiment on day 14th after primary infection					
	Mean	0.00	3.90	5.35	2.55	1.29	0.00
SD	0.00	0.95	1.23	2.39	1.84	0.00	

It is to be understood that, while the methods and compositions of matter have been described herein in conjunction with a number of different aspects, the foregoing description of the various aspects is intended to illustrate and not limit the scope of the methods and compositions of matter. Other aspects, advantages, and modifications are within the scope of the following claims.

Disclosed are methods and compositions that can be used for, can be used in conjunction with, can be used in preparation for, or are products of the disclosed methods and compositions. These and other materials are disclosed herein, and it is understood that combinations, subsets, interactions, groups, etc. of these methods and compositions

are disclosed. That is, while specific reference to each various individual and collective combinations and permutations of these compositions and methods may not be explicitly disclosed, each is specifically contemplated and described herein. For example, if a particular composition of matter or a particular method is disclosed and discussed and a number of compositions or methods are discussed, each and every combination and permutation of the compositions and the methods are specifically contemplated unless specifically indicated to the contrary. Likewise, any subset or combination of these is also specifically contemplated and disclosed.

SEQUENCE LISTING

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ccccgggtga aaagcctcgt gttgggtggc agaaaagctg ttaaacaggg agtggtaaac 14880
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<210> SEQ ID NO 2

<211> LENGTH: 540

<212> TYPE: DNA

<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 2

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gttcttgagc tcgggggtgct gggcctatct tacaggcccg aagagccact ccggtggacg 180
ttgccacgtg cattccccac tgtcgagtgc tccccgcgg gggcctgctg gctttctgcg 240
atctttccaa ttgcacgaat gaccagtgga aacctgaact ttcaacaaag aatggtgctg 300
gtcgcagctg agctttacag agccggccag ctcaccctg cagtctttaa ggctctacaa 360
gtttatgaac ggggttgccg ctggtacccc attgttgac ctgtccctgg agtggccgtt 420
ttcgccaact ccctacatgt gagtgataaa cctttccgg gagcaactca tgtgttaacc 480
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<210> SEQ ID NO 3

<211> LENGTH: 180

<212> TYPE: PRT

<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 3

```

Met Ser Gly Ile Leu Asp Arg Cys Thr Cys Thr Pro Asn Ala Arg Val
1           5           10           15
Phe Met Ala Glu Gly Gln Val Tyr Cys Thr Arg Cys Leu Ser Ala Arg
20           25           30
Ser Leu Leu Pro Leu Asn Leu Gln Val Pro Glu Leu Gly Val Leu Gly
35           40           45
Leu Phe Tyr Arg Pro Glu Glu Pro Leu Arg Trp Thr Leu Pro Arg Ala
50           55           60
Phe Pro Thr Val Glu Cys Ser Pro Ala Gly Ala Cys Trp Leu Ser Ala
65           70           75           80
Ile Phe Pro Ile Ala Arg Met Thr Ser Gly Asn Leu Asn Phe Gln Gln
85           90           95
Arg Met Val Arg Val Ala Ala Glu Leu Tyr Arg Ala Gly Gln Leu Thr
100          105          110
Pro Ala Val Leu Lys Ala Leu Gln Val Tyr Glu Arg Gly Cys Arg Trp

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115	120	125
Tyr Pro Ile Val Gly Pro Val Pro Gly Val Ala Val Phe Ala Asn Ser		
130	135	140
Leu His Val Ser Asp Lys Pro Phe Pro Gly Ala Thr His Val Leu Thr		
145	150	155
Asn Leu Pro Leu Pro Gln Arg Pro Lys Pro Glu Asp Phe Cys Pro Phe		
	165	170
		175
Glu Cys Ala Met		
180		

<210> SEQ ID NO 4
 <211> LENGTH: 609
 <212> TYPE: DNA
 <213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 4

```

gctgacgtct atgacattgg tcatgacgcc gtcattgatg tggccgaagg gaaagtctcc    60
tgggcccctc gtggcgggga tgaagggaaa ttgaaactg tccccgagga gttgaagttg    120
attgcgaacc gactccacat ctctctcccg ccccaccacg cagtggacat gtctaagttt    180
gccttcatag cccttgggag tgggtgttcc atgcgggtcg agtgccaaca cggctgctc    240
cccgctgaca ctgtccctga aggcaactgc tgggtggcgt tgtttgactt gctcccactg    300
gaagttcaga acaagaagaat tcgccatgct aaccaatttg gctatcagac caagcatggt    360
gtcgtggca agtacctaca gcggaggctg caagttaatg gtctccgagc agtgactgac    420
ccaaatggac ctatcgtcgt acagtatttc tctgttaagg agagctggat ccgccactta    480
agactggcgg aagaacntag cctccctggg tttaggacc tcctcagaat aagggttgag    540
cccaacacgt cgccattggc tgacaaggat gagaaaatct tccggtttgg cagtcacaag    600
tggtacggt                                     609
    
```

<210> SEQ ID NO 5
 <211> LENGTH: 203
 <212> TYPE: PRT
 <213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 5

Ala Asp Val Tyr Asp Ile Gly His Asp Ala Val Met Tyr Val Ala Glu														
1			5				10						15	
Gly Lys Val Ser Trp Ala Pro Arg Gly Gly Asp Glu Gly Lys Phe Glu							25						30	
Thr Val Pro Glu Glu Leu Lys Leu Ile Ala Asn Arg Leu His Ile Ser							40						45	
Phe Pro Pro His His Ala Val Asp Met Ser Lys Phe Ala Phe Ile Ala							55						60	
Pro Gly Ser Gly Val Ser Met Arg Val Glu Cys Gln His Gly Cys Leu							70						75	80
Pro Ala Asp Thr Val Pro Glu Gly Asn Cys Trp Trp Arg Leu Phe Asp							85						90	95
Leu Leu Pro Leu Glu Val Gln Asn Lys Glu Ile Arg His Ala Asn Gln							100						105	110
Phe Gly Tyr Gln Thr Lys His Gly Val Ala Gly Lys Tyr Leu Gln Arg							115						120	125
Arg Leu Gln Val Asn Gly Leu Arg Ala Val Thr Asp Pro Asn Gly Pro							130						135	140

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Ile Val Val Gln Tyr Phe Ser Val Lys Glu Ser Trp Ile Arg His Leu
 145 150 155 160

Arg Leu Ala Glu Glu Pro Ser Leu Pro Gly Phe Glu Asp Leu Leu Arg
 165 170 175

Ile Arg Val Glu Pro Asn Thr Ser Pro Leu Ala Asp Lys Asp Glu Lys
 180 185 190

Ile Phe Arg Phe Gly Ser His Lys Trp Tyr Gly
 195 200

<210> SEQ ID NO 6
 <211> LENGTH: 3588
 <212> TYPE: DNA
 <213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 6

```

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gagcatctca agcactattc cccgcctgcc gacgggaact gtggttgga ctgcatttcc    180
gccatcgcca accggatggg gaattccaaa ttgaaacca cccttccga aagagtgaga    240
ccttcagatg actgggttac tgacgaggat cttgtgaata ccatccaaat cctcaggctc    300
cctgcggcct tggacaggaa cggtgcttgt gctagcgcca agtacgtgct taagctggaa    360
ggtgagcatt ggactgtctc tgtgacccct gggatgtccc cttctttgct ccccttgaa    420
tgtgttcagg gctgtttgta gcataagggc ggtcttggtt ccccagatgc ggtcgaagtt    480
tccggatttg accctgctg ccttgaccga ctggctgagg tgatgcactt gcctagcagt    540
gccatcccag ccgctctggc cgaatgtcc ggcgaccca atcgtccggc ttccccggtc    600
accactgtgt ggactgttcc gcagttcttt gcccgtcaca gaggaggaga gcaccctgat    660
caggtgtgct tagggaaaat catcagcctt tgtcaggtga ttgaggaatg ctgctgttcc    720
cagaacaaaa ccaaccgggt caccocggaa gaggtcgcgg caaagattga ccagtacctc    780
cgtggtgcaa caagtcttga agaatgcttg gccaggcttg agagggctcg cccgccgagc    840
gcaatggaca cctcctttga ttggaatggt gtgctccctg gggttgaggc ggcaactcag    900
acaaccaaac agccccatgt caaccagtgc cgcgctctgg tcctgtcgt gactcaagag    960
tctttggaca aagactcggg cctctgacc gccctctcgc tgtetaattg ctactaccct   1020
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gccaggcaaa cttcagaaat gatggcctgg gcagccgagc aggttgatct aaaagcttgg   1260
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acgaagtctg tcaagagctt gccagagaac aagcctgtcc ctgctccgcg caggaaggtc   1380
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<210> SEQ ID NO 7
<211> LENGTH: 1196
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

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<400> SEQUENCE: 7

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Ala Gly Lys Arg Ala Arg Lys Ala Arg Ser Gly Ala Thr Ala Thr Val
1           5           10           15
Ala His Arg Ala Leu Pro Ala Arg Glu Thr Gln Gln Ala Lys Lys His
20          25          30
Glu Val Ala Ser Ala Asn Lys Ala Glu His Leu Lys His Tyr Ser Pro
35          40          45
Pro Ala Asp Gly Asn Cys Gly Trp His Cys Ile Ser Ala Ile Ala Asn

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50					55					60					
Arg	Met	Val	Asn	Ser	Lys	Phe	Glu	Thr	Thr	Leu	Pro	Glu	Arg	Val	Arg
65					70					75					80
Pro	Ser	Asp	Asp	Trp	Ala	Thr	Asp	Glu	Asp	Leu	Val	Asn	Thr	Ile	Gln
				85					90					95	
Ile	Leu	Arg	Leu	Pro	Ala	Ala	Leu	Asp	Arg	Asn	Gly	Ala	Cys	Ala	Ser
			100					105					110		
Ala	Lys	Tyr	Val	Leu	Lys	Leu	Glu	Gly	Glu	His	Trp	Thr	Val	Ser	Val
		115					120						125		
Thr	Pro	Gly	Met	Ser	Pro	Ser	Leu	Leu	Pro	Leu	Glu	Cys	Val	Gln	Gly
	130					135					140				
Cys	Cys	Glu	His	Lys	Gly	Gly	Leu	Gly	Ser	Pro	Asp	Ala	Val	Glu	Val
145					150					155					160
Ser	Gly	Phe	Asp	Pro	Ala	Cys	Leu	Asp	Arg	Leu	Ala	Glu	Val	Met	His
				165					170						175
Leu	Pro	Ser	Ser	Ala	Ile	Pro	Ala	Ala	Leu	Ala	Glu	Met	Ser	Gly	Asp
			180					185						190	
Pro	Asn	Arg	Pro	Ala	Ser	Pro	Val	Thr	Thr	Val	Trp	Thr	Val	Ser	Gln
		195					200							205	
Phe	Phe	Ala	Arg	His	Arg	Gly	Gly	Glu	His	Pro	Asp	Gln	Val	Cys	Leu
210						215					220				
Gly	Lys	Ile	Ile	Ser	Leu	Cys	Gln	Val	Ile	Glu	Glu	Cys	Cys	Cys	Ser
225					230					235					240
Gln	Asn	Lys	Thr	Asn	Arg	Val	Thr	Pro	Glu	Glu	Val	Ala	Ala	Lys	Ile
				245					250						255
Asp	Gln	Tyr	Leu	Arg	Gly	Ala	Thr	Ser	Leu	Glu	Glu	Cys	Leu	Ala	Arg
			260					265						270	
Leu	Glu	Arg	Ala	Arg	Pro	Pro	Ser	Ala	Met	Asp	Thr	Ser	Phe	Asp	Trp
		275					280						285		
Asn	Val	Val	Leu	Pro	Gly	Val	Glu	Ala	Ala	Thr	Gln	Thr	Thr	Lys	Gln
290						295					300				
Pro	His	Val	Asn	Gln	Cys	Arg	Ala	Leu	Val	Pro	Val	Val	Thr	Gln	Glu
305					310					315					320
Ser	Leu	Asp	Lys	Asp	Ser	Val	Pro	Leu	Thr	Ala	Phe	Ser	Leu	Ser	Asn
				325					330						335
Cys	Tyr	Tyr	Pro	Ala	Gln	Gly	Asp	Glu	Val	Arg	His	Arg	Glu	Arg	Leu
			340					345						350	
Asn	Ser	Val	Leu	Ser	Lys	Leu	Glu	Glu	Val	Val	Arg	Glu	Glu	Tyr	Gly
		355					360						365		
Leu	Thr	Pro	Thr	Gly	Pro	Gly	Pro	Arg	Pro	Ala	Leu	Pro	Asn	Gly	Leu
						375						380			
Asp	Glu	Leu	Lys	Asp	Gln	Met	Glu	Glu	Asp	Leu	Leu	Lys	Leu	Val	Asn
385					390					395					400
Ala	Gln	Ala	Thr	Ser	Glu	Met	Met	Ala	Trp	Ala	Ala	Glu	Gln	Val	Asp
				405					410						415
Leu	Lys	Ala	Trp	Val	Lys	Asn	Tyr	Pro	Arg	Trp	Thr	Pro	Pro	Pro	Pro
			420						425					430	
Pro	Pro	Arg	Val	Gln	Pro	Arg	Lys	Thr	Lys	Ser	Val	Lys	Ser	Leu	Pro
			435					440						445	
Glu	Asn	Lys	Pro	Val	Pro	Ala	Pro	Arg	Arg	Lys	Val	Arg	Ser	Asp	Cys
			450				455					460			
Gly	Ser	Pro	Ile	Leu	Met	Gly	Asp	Asn	Val	Pro	Asn	Ser	Trp	Glu	Asp
465					470						475				480

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Ala Pro Leu Leu Gly Val Phe Ser Gly Ser Ser Arg Arg Val Arg Met
 900 905 910

Gly Val Phe Gly Cys Trp Leu Ala Phe Ala Val Gly Leu Phe Lys Pro
 915 920 925

Val Ser Asp Pro Val Gly Thr Ala Cys Glu Phe Asp Ser Pro Glu Cys
 930 935 940

Arg Asn Val Leu His Ser Phe Glu Leu Leu Lys Pro Trp Asp Pro Val
 945 950 955 960

Arg Ser Leu Val Val Gly Pro Val Gly Leu Gly Leu Ala Ile Leu Gly
 965 970 975

Arg Leu Leu Gly Gly Ala Arg Tyr Ile Trp His Phe Leu Leu Arg Leu
 980 985 990

Gly Ile Val Ala Asp Cys Ile Leu Ala Gly Ala Tyr Val Leu Ser Gln
 995 1000 1005

Gly Arg Cys Lys Lys Cys Trp Gly Ser Cys Ile Arg Thr Ala Pro
 1010 1015 1020

Asn Glu Ile Ala Phe Asn Val Phe Pro Phe Thr Arg Ala Thr Arg
 1025 1030 1035

Ser Ser Leu Ile Asp Leu Cys Asp Arg Phe Cys Ala Pro Lys Gly
 1040 1045 1050

Met Asp Pro Ile Phe Leu Ala Thr Gly Trp Arg Gly Cys Trp Thr
 1055 1060 1065

Gly Arg Ser Pro Ile Glu Gln Pro Ser Glu Lys Pro Ile Ala Phe
 1070 1075 1080

Ala Gln Leu Asp Glu Lys Lys Ile Thr Ala Arg Thr Val Val Ala
 1085 1090 1095

Gln Pro Tyr Asp Pro Asn Gln Ala Val Lys Cys Leu Arg Val Leu
 1100 1105 1110

Gln Ala Gly Gly Ala Met Val Ala Glu Ala Val Pro Lys Val Val
 1115 1120 1125

Lys Val Ser Ala Ile Pro Phe Arg Ala Pro Phe Phe Pro Thr Gly
 1130 1135 1140

Val Lys Val Asp Pro Glu Cys Arg Ile Val Val Asp Pro Asp Thr
 1145 1150 1155

Phe Thr Thr Ala Leu Arg Ser Gly Tyr Ser Thr Thr Asn Leu Val
 1160 1165 1170

Leu Gly Val Gly Asp Phe Ala Gln Leu Asn Gly Leu Lys Ile Arg
 1175 1180 1185

Gln Ile Ser Lys Pro Ser Gly Gly
 1190 1195

<210> SEQ ID NO 8
 <211> LENGTH: 690
 <212> TYPE: DNA
 <213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 8

```

ggccccacacc tcattgctgc cctgcatggt gctgctcoga tggcgttgca catgcttgct    60
gggatttatg taactgcagt ggggtcttgc ggtaccggca ccaacgatcc gtggtgcact    120
aacccgtttg ccgtccctgg ctaccggacct ggctctctct gcacgteccag attgtgcatc    180
tcccaacatg gccttaccct gcccttgaca gcacttgagg caggattcgg tcttcaggaa    240
attgccttgg ttgtttgat tttcgtttcc atcggaggca tggctcacag gttgagttgc    300
aaggctgata tgctgtgogt tttacttgca atcgccagct atgtttgggt accccttacc    360
    
```

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```

tgggtgcttt gtgtgtttcc ttgctgggtg cgctgggtct ctttgacccc cctcaccatc 420
ctatgggttg tgtttttctt gatttctgta aatatgcctt caggaatctt ggccgtgggtg 480
ttgttggttt ctctttggct tctaggtcgt tataactaatg ttgctgggtc tgtcaccccc 540
tatgacattc atcattacac cagtggcccc cgcggtgttg ccgccttggc tacgcacca 600
gatgggacct acttggccgc tgtccgccgc gctgcgttga ctggccgcac catgctgttt 660
accccgcttc agcttgggtc ccttcttgag 690

```

```

<210> SEQ ID NO 9
<211> LENGTH: 230
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

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```

<400> SEQUENCE: 9

```

```

Gly Pro His Leu Ile Ala Ala Leu His Val Ala Cys Ser Met Ala Leu
1           5           10          15
His Met Leu Ala Gly Ile Tyr Val Thr Ala Val Gly Ser Cys Gly Thr
20          25          30
Gly Thr Asn Asp Pro Trp Cys Thr Asn Pro Phe Ala Val Pro Gly Tyr
35          40          45
Gly Pro Gly Ser Leu Cys Thr Ser Arg Leu Cys Ile Ser Gln His Gly
50          55          60
Leu Thr Leu Pro Leu Thr Ala Leu Val Ala Gly Phe Gly Leu Gln Glu
65          70          75          80
Ile Ala Leu Val Val Leu Ile Phe Val Ser Ile Gly Gly Met Ala His
85          90          95
Arg Leu Ser Cys Lys Ala Asp Met Leu Cys Val Leu Leu Ala Ile Ala
100         105         110
Ser Tyr Val Trp Val Pro Leu Thr Trp Leu Leu Cys Val Phe Pro Cys
115        120        125
Trp Leu Arg Trp Phe Ser Leu His Pro Leu Thr Ile Leu Trp Leu Val
130        135        140
Phe Phe Leu Ile Ser Val Asn Met Pro Ser Gly Ile Leu Ala Val Val
145        150        155        160
Leu Leu Val Ser Leu Trp Leu Leu Gly Arg Tyr Thr Asn Val Ala Gly
165        170        175
Leu Val Thr Pro Tyr Asp Ile His His Tyr Thr Ser Gly Pro Arg Gly
180        185        190
Val Ala Ala Leu Ala Thr Ala Pro Asp Gly Thr Tyr Leu Ala Ala Val
195        200        205
Arg Arg Ala Ala Leu Thr Gly Arg Thr Met Leu Phe Thr Pro Ser Gln
210        215        220
Leu Gly Ser Leu Leu Glu
225        230

```

```

<210> SEQ ID NO 10
<211> LENGTH: 612
<212> TYPE: DNA
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 10

```

```

ggtgctttca gaactcaaaa gccctcactg aacaccgtca atgtggtcgg gtctccatg 60
ggctctggcg ggggtttcac catcgacggg aaaattaagt gcgtaactgc cgcacatgct 120
cttacgggta attcagctag ggtttccggg gtcggcttca atcaaatgct tgactttgat 180

```

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gtaaaagggg acttcgccaat agctgattgc ccgaattggc aaggggctgc tcccaagacc 240
caattctgca aggatggatg gactggccgt gcctattggc tgacatcctc tggcgtcgaa 300
cccgggtgca ttgggaatgg attcgccttc tgcttcaccg cgtgcggcga ttccgggtcc 360
ccagtgatca ccgaagccgg tgagcttgtc ggcgttcaca caggatcaaa caaacaagga 420
ggaggcattg tcacgcgccc ctcaggccag ttttgtaatg tggcaccat caagctgagc 480
gaattaagtg aattctttgc tggacctaag gtcccgtctg gtgatgtgaa ggttggcagc 540
cacataatta aagacataag cgagggtgct tcagatcttt gcgccttgct tgctgcaaaa 600
cccgaactgg aa 612

```

```

<210> SEQ ID NO 11
<211> LENGTH: 204
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 11

```

```

Gly Ala Phe Arg Thr Gln Lys Pro Ser Leu Asn Thr Val Asn Val Val
1          5          10          15
Gly Ser Ser Met Gly Ser Gly Gly Val Phe Thr Ile Asp Gly Lys Ile
          20          25          30
Lys Cys Val Thr Ala Ala His Val Leu Thr Gly Asn Ser Ala Arg Val
          35          40          45
Ser Gly Val Gly Phe Asn Gln Met Leu Asp Phe Asp Val Lys Gly Asp
          50          55          60
Phe Ala Ile Ala Asp Cys Pro Asn Trp Gln Gly Ala Ala Pro Lys Thr
          65          70          75          80
Gln Phe Cys Lys Asp Gly Trp Thr Gly Arg Ala Tyr Trp Leu Thr Ser
          85          90          95
Ser Gly Val Glu Pro Gly Val Ile Gly Asn Gly Phe Ala Phe Cys Phe
          100          105          110
Thr Ala Cys Gly Asp Ser Gly Ser Pro Val Ile Thr Glu Ala Gly Glu
          115          120          125
Leu Val Gly Val His Thr Gly Ser Asn Lys Gln Gly Gly Gly Ile Val
          130          135          140
Thr Arg Pro Ser Gly Gln Phe Cys Asn Val Ala Pro Ile Lys Leu Ser
          145          150          155          160
Glu Leu Ser Glu Phe Phe Ala Gly Pro Lys Val Pro Leu Gly Asp Val
          165          170          175
Lys Val Gly Ser His Ile Ile Lys Asp Ile Ser Glu Val Pro Ser Asp
          180          185          190
Leu Cys Ala Leu Leu Ala Ala Lys Pro Glu Leu Glu
          195          200

```

```

<210> SEQ ID NO 12
<211> LENGTH: 510
<212> TYPE: DNA
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 12

```

```

ggaggcctct ccaccgtcca acttctgtgt gtgtttttcc tcctgtggag aatgatggga 60
catgectgga cgcccttggg tgctgtgggt ttttttatct tgaatgaggt tctcccagct 120
gtcctgttcc ggagtgtttt ctcccttggg atgtttgtgc tatcttggtc cacaccatgg 180
tctgcgcaag ttctgatgat caggcttcta acagcagctc ttaacaggaa cagatgttca 240

```


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cttgcctttt acagcctcgg tgcagtgacc ggttttgtcg cagatcttgc ggcaactcag   300
gggcatccgt tgcaggcagt gatgaattta agcacctatg ccttctctgcc tcggatgatg   360
gttgtgacct caccagtocc agtgattgcg tgtgggtgtg tgcacctcct tgccataatt   420
ttgtacttgt ttaagtaocg ttgcctgcac aatgtccttg ttggcgatgg agtgttctct   480
gcggtttctt tcttgcgata ctttgcgcgag                                     510

```

```

<210> SEQ ID NO 13
<211> LENGTH: 170
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 13

```

```

Gly Gly Leu Ser Thr Val Gln Leu Leu Cys Val Phe Phe Leu Leu Trp
 1          5          10          15
Arg Met Met Gly His Ala Trp Thr Pro Leu Val Ala Val Gly Phe Phe
          20          25          30
Ile Leu Asn Glu Val Leu Pro Ala Val Leu Val Arg Ser Val Phe Ser
          35          40          45
Phe Gly Met Phe Val Leu Ser Trp Leu Thr Pro Trp Ser Ala Gln Val
          50          55          60
Leu Met Ile Arg Leu Leu Thr Ala Ala Leu Asn Arg Asn Arg Trp Ser
          65          70          75          80
Leu Ala Phe Tyr Ser Leu Gly Ala Val Thr Gly Phe Val Ala Asp Leu
          85          90          95
Ala Ala Thr Gln Gly His Pro Leu Gln Ala Val Met Asn Leu Ser Thr
          100         105         110
Tyr Ala Phe Leu Pro Arg Met Met Val Val Thr Ser Pro Val Pro Val
          115         120         125
Ile Ala Cys Gly Val Val His Leu Leu Ala Ile Ile Leu Tyr Leu Phe
          130         135         140
Lys Tyr Arg Cys Leu His Asn Val Leu Val Gly Asp Gly Val Phe Ser
          145         150         155         160
Ala Ala Phe Phe Leu Arg Tyr Phe Ala Glu
          165         170

```

```

<210> SEQ ID NO 14
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 14

```

```

ggaaagtga ggaaggggt gtcgcaatcc tgccggatga atcatgag   48

```

```

<210> SEQ ID NO 15
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 15

```

```

Gly Lys Leu Arg Glu Gly Val Ser Gln Ser Cys Gly Met Asn His Glu
 1          5          10          15

```

```

<210> SEQ ID NO 16
<211> LENGTH: 777
<212> TYPE: DNA
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

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<400> SEQUENCE: 16

```

tcactgactg gtgccctgcg tatgagactc aatgacgagg acttggattt ccttacgaaa    60
tggactgatt ttaagtgctt tgtttctgcg tccaacatga ggaatgcagc gggccaattc    120
atcgaggctg cctatgctaa agcaacttaga gtagaacttg cccagttggt gcaggttgat    180
aaggttcgag gtactttggc caaacttgaa gcttttgctg ataccgtggc accccaactc    240
tcgcccggtg acattgttgt tgcctttggc cacacgcctg ttggcagtat cttcgacctc    300
aaggttggtg gcaccaagca taccctccaa gccattgaga ccagagtccct tgccgggtcc    360
aaaatgaccg tggcgcgctg cgttgaccca acccccacgc ccccaccgc acccgtgccc    420
atccccctcc caccgaaagt tetggagaat ggccccaacg cctgggggga tgaggaccgt    480
ttgaataaga agaagaggcg caggatgaa gccgtcggca tctttgttat gggcggaag    540
aagtaccaga aattttggga caagaattcc ggtgatgtgt tttatgagga ggtccatgat    600
aacacagatg cgtgggagtg cctcagagtt ggcgaccctg ccgactttga cctgagaag    660
ggaactctgt gtgggcatac caccattgaa gataaggctt acaatgtcta cgctcccaca    720
tctggcaaga agttcctggt ccccgcaaac ccagagagcg gaagagccca atgggaa    777

```

<210> SEQ ID NO 17

<211> LENGTH: 259

<212> TYPE: PRT

<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 17

```

Ser Leu Thr Gly Ala Leu Ala Met Arg Leu Asn Asp Glu Asp Leu Asp
1          5          10          15
Phe Leu Thr Lys Trp Thr Asp Phe Lys Cys Phe Val Ser Ala Ser Asn
20         25         30
Met Arg Asn Ala Ala Gly Gln Phe Ile Glu Ala Ala Tyr Ala Lys Ala
35         40         45
Leu Arg Val Glu Leu Ala Gln Leu Val Gln Val Asp Lys Val Arg Gly
50         55         60
Thr Leu Ala Lys Leu Glu Ala Phe Ala Asp Thr Val Ala Pro Gln Leu
65         70         75         80
Ser Pro Gly Asp Ile Val Val Ala Leu Gly His Thr Pro Val Gly Ser
85         90         95
Ile Phe Asp Leu Lys Val Gly Ser Thr Lys His Thr Leu Gln Ala Ile
100        105        110
Glu Thr Arg Val Leu Ala Gly Ser Lys Met Thr Val Ala Arg Val Val
115        120        125
Asp Pro Thr Pro Thr Pro Pro Pro Ala Pro Val Pro Ile Pro Leu Pro
130        135        140
Pro Lys Val Leu Glu Asn Gly Pro Asn Ala Trp Gly Asp Glu Asp Arg
145        150        155        160
Leu Asn Lys Lys Lys Arg Arg Arg Met Glu Ala Val Gly Ile Phe Val
165        170        175
Met Gly Gly Lys Lys Tyr Gln Lys Phe Trp Asp Lys Asn Ser Gly Asp
180        185        190
Val Phe Tyr Glu Glu Val His Asp Asn Thr Asp Ala Trp Glu Cys Leu
195        200        205
Arg Val Gly Asp Pro Ala Asp Phe Asp Pro Glu Lys Gly Thr Leu Cys
210        215        220
Gly His Thr Thr Ile Glu Asp Lys Ala Tyr Asn Val Tyr Ala Ser Pro

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225	230	235	240	
Ser Gly Lys Lys Phe Leu Val Pro Val Asn Pro Glu Ser Gly Arg Ala				
	245	250	255	
Gln Trp Glu				
<210> SEQ ID NO 18 <211> LENGTH: 138 <212> TYPE: DNA <213> ORGANISM: Porcine reproductive and respiratory syndrome virus <400> SEQUENCE: 18				
gctgcaaagc tttccgtgga gcaggccctt ggcatgatga atgtcgacgg tgaactgaca				60
gccaagaac tggagaaact gaaaagaata atgacaac tccagggcct gactaaggag				120
cagtgtttaa actgctag				138
<210> SEQ ID NO 19 <211> LENGTH: 45 <212> TYPE: PRT <213> ORGANISM: Porcine reproductive and respiratory syndrome virus <400> SEQUENCE: 19				
Ala Ala Lys Leu Ser Val Glu Gln Ala Leu Gly Met Met Asn Val Asp				
1	5	10	15	
Gly Glu Leu Thr Ala Lys Glu Leu Glu Lys Leu Lys Arg Ile Ile Asp				
	20	25	30	
Lys Leu Gln Gly Leu Thr Lys Glu Gln Cys Leu Asn Cys				
	35	40	45	
<210> SEQ ID NO 20 <211> LENGTH: 1917 <212> TYPE: DNA <213> ORGANISM: Porcine reproductive and respiratory syndrome virus <400> SEQUENCE: 20				
gccgccagcg gcttgaccgc ctgtggctgc ggcggcttgg ttgttactga gacagcggtg				60
aaaatagtca aatttcacaa ccggaccctc accctaggac ctgtgaattt aaaagtggcc				120
agtgaggttg agctaaaaga cgcggctgag cacaaccaac acccggttgc aagaccggtt				180
gatggtggtg ttgtgctcct gcgctccgca gttccttcgc ttatagacgt cttgatctcc				240
ggtgctgatg catctcccaa gttactgcc cgccacgggc cgggaaacac tgggatcgat				300
ggcacgcttt gggatthtga ggccgaagcc accaaagagg aaatcgact cagtgcgcaa				360
ataatacagg cttgtgacat taggcgcggc gacgcacctg aaattggtct cccttacaag				420
ctgtaccctg ttaggggcaa cctgagcgg gtaaaaggag ttttgacaga tacaaggttt				480
ggagacatac cttacaaaac ccccgatgac actggaagcc cagtgcacgc ggctgctcgc				540
ctcacgcccc atgccactcc ggtgactgat gggcgctccg tcttgccac gaccatgccc				600
tccggttttg agttgatgt accgaccatt ccagcgtctg tccttgatta tctgattct				660
aggcctgact gcccacaaca gttgacagag cacggctgtg aggatgccgc attgagagac				720
ctctccaagt atgacttgtc cacccaaggc tttgttttgc ctggagtctc tcgccttgtg				780
cgtaagtacc tgthtgccea tgtgggtaag tgcccgcctg tcatcggcc ttcacttac				840
cctgccaaga attctatggc tggaataaat gggaacaggt ttccaaccaa ggacattcag				900
agcgtccctg aaatcgactg tctgtgcgca caggccgtgc gagaaaactg gcaaactggt				960
accccttcta ccctcaagaa acagtattgc gggaagaaga agactaggac aatactggc				1020

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accaataact tcattgcgct ggcccaccgg gcagcgttga gtggtgtcac ccagggttc 1080
atgaaaaagg cgtttaactc gcccacgcc ctcgggaaaa acaaatttaa ggagctacag 1140
actccggtct tgggcaggtg ccttgaagct gatcttgcac cctgcgacgc atccacacct 1200
gcaattgtcc gctggtttgc cgccaatctt ctttatgaac ttgcctgtgc tgaagagcat 1260
ctaccgctgt acgtgctgaa ctgctgccac gacttactgg tcacgcagtc cggcgcagtg 1320
actaagagag gtggcctgtc gtctggcgac ccgatcactt ctgtgtccaa caccatttac 1380
agcttggtga tataatgcaca gcacatggtg ctcagttact ttaaaagtgg tcacccccat 1440
ggccttctgt ttctacaaga ccagctaaag tttgaggaca tgctcaaggt tcaaccctg 1500
atcgtctatt cggacgacct cgtgctgtat gccgagtctc ccacatgcc aaactaccac 1560
tggtggttg aacatctgaa cctgatgctg ggttttcaga cggaccctaaa gaagacagcc 1620
ataacagact cgccatcatt tctaggtgtg aggataataa atgggcgcca gctagtcccc 1680
aacctgaca ggattctcgc ggccctcggc taccacatga aggcgagcaa tgtttctgaa 1740
tactacgctt cggcggctgc aatactcatg gacagctgtg cttggttggg gtatgatcct 1800
gaatggtttg aagaacttgt ggttgaata gcgcagtgcg cccgcaagga cggctacagc 1860
tttcccgccc cgccgttctt cttgtccatg tgggaaaaac tcagggtccaa ttatgag 1917

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<210> SEQ ID NO 21
<211> LENGTH: 639
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

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<400> SEQUENCE: 21

```

Ala Ala Ser Gly Leu Thr Arg Cys Gly Arg Gly Gly Leu Val Val Thr
1          5          10          15
Glu Thr Ala Val Lys Ile Val Lys Phe His Asn Arg Thr Phe Thr Leu
20          25          30
Gly Pro Val Asn Leu Lys Val Ala Ser Glu Val Glu Leu Lys Asp Ala
35          40          45
Val Glu His Asn Gln His Pro Val Ala Arg Pro Val Asp Gly Gly Val
50          55          60
Val Leu Leu Arg Ser Ala Val Pro Ser Leu Ile Asp Val Leu Ile Ser
65          70          75          80
Gly Ala Asp Ala Ser Pro Lys Leu Leu Ala Arg His Gly Pro Gly Asn
85          90          95
Thr Gly Ile Asp Gly Thr Leu Trp Asp Phe Glu Ala Glu Ala Thr Lys
100         105         110
Glu Glu Ile Ala Leu Ser Ala Gln Ile Ile Gln Ala Cys Asp Ile Arg
115         120         125
Arg Gly Asp Ala Pro Glu Ile Gly Leu Pro Tyr Lys Leu Tyr Pro Val
130         135         140
Arg Gly Asn Pro Glu Arg Val Lys Gly Val Leu Gln Asn Thr Arg Phe
145         150         155         160
Gly Asp Ile Pro Tyr Lys Thr Pro Ser Asp Thr Gly Ser Pro Val His
165         170         175
Ala Ala Ala Cys Leu Thr Pro Asn Ala Thr Pro Val Thr Asp Gly Arg
180         185         190
Ser Val Leu Ala Thr Thr Met Pro Ser Gly Phe Glu Leu Tyr Val Pro
195         200         205
Thr Ile Pro Ala Ser Val Leu Asp Tyr Leu Asp Ser Arg Pro Asp Cys

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210					215					220					
Pro	Lys	Gln	Leu	Thr	Glu	His	Gly	Cys	Glu	Asp	Ala	Ala	Leu	Arg	Asp
225					230					235					240
Leu	Ser	Lys	Tyr	Asp	Leu	Ser	Thr	Gln	Gly	Phe	Val	Leu	Pro	Gly	Val
				245					250					255	
Leu	Arg	Leu	Val	Arg	Lys	Tyr	Leu	Phe	Ala	His	Val	Gly	Lys	Cys	Pro
			260					265					270		
Pro	Val	His	Arg	Pro	Ser	Thr	Tyr	Pro	Ala	Lys	Asn	Ser	Met	Ala	Gly
		275					280					285			
Ile	Asn	Gly	Asn	Arg	Phe	Pro	Thr	Lys	Asp	Ile	Gln	Ser	Val	Pro	Glu
290						295					300				
Ile	Asp	Val	Leu	Cys	Ala	Gln	Ala	Val	Arg	Glu	Asn	Trp	Gln	Thr	Val
305					310					315					320
Thr	Pro	Cys	Thr	Leu	Lys	Lys	Gln	Tyr	Cys	Gly	Lys	Lys	Lys	Thr	Arg
				325					330					335	
Thr	Ile	Leu	Gly	Thr	Asn	Asn	Phe	Ile	Ala	Leu	Ala	His	Arg	Ala	Ala
			340					345					350		
Leu	Ser	Gly	Val	Thr	Gln	Gly	Phe	Met	Lys	Lys	Ala	Phe	Asn	Ser	Pro
		355					360					365			
Ile	Ala	Leu	Gly	Lys	Asn	Lys	Phe	Lys	Glu	Leu	Gln	Thr	Pro	Val	Leu
370					375						380				
Gly	Arg	Cys	Leu	Glu	Ala	Asp	Leu	Ala	Ser	Cys	Asp	Arg	Ser	Thr	Pro
385					390					395					400
Ala	Ile	Val	Arg	Trp	Phe	Ala	Ala	Asn	Leu	Leu	Tyr	Glu	Leu	Ala	Cys
				405					410						415
Ala	Glu	Glu	His	Leu	Pro	Ser	Tyr	Val	Leu	Asn	Cys	Cys	His	Asp	Leu
			420					425					430		
Leu	Val	Thr	Gln	Ser	Gly	Ala	Val	Thr	Lys	Arg	Gly	Gly	Leu	Ser	Ser
		435					440					445			
Gly	Asp	Pro	Ile	Thr	Ser	Val	Ser	Asn	Thr	Ile	Tyr	Ser	Leu	Val	Ile
450						455					460				
Tyr	Ala	Gln	His	Met	Val	Leu	Ser	Tyr	Phe	Lys	Ser	Gly	His	Pro	His
465					470					475					480
Gly	Leu	Leu	Phe	Leu	Gln	Asp	Gln	Leu	Lys	Phe	Glu	Asp	Met	Leu	Lys
				485					490					495	
Val	Gln	Pro	Leu	Ile	Val	Tyr	Ser	Asp	Asp	Leu	Val	Leu	Tyr	Ala	Glu
			500					505					510		
Ser	Pro	Thr	Met	Pro	Asn	Tyr	His	Trp	Trp	Val	Glu	His	Leu	Asn	Leu
		515					520					525			
Met	Leu	Gly	Phe	Gln	Thr	Asp	Pro	Lys	Lys	Thr	Ala	Ile	Thr	Asp	Ser
530						535					540				
Pro	Ser	Phe	Leu	Gly	Cys	Arg	Ile	Ile	Asn	Gly	Arg	Gln	Leu	Val	Pro
545					550					555					560
Asn	Arg	Asp	Arg	Ile	Leu	Ala	Ala	Leu	Ala	Tyr	His	Met	Lys	Ala	Ser
				565					570					575	
Asn	Val	Ser	Glu	Tyr	Tyr	Ala	Ser	Ala	Ala	Ala	Ile	Leu	Met	Asp	Ser
			580					585					590		
Cys	Ala	Cys	Leu	Glu	Tyr	Asp	Pro	Glu	Trp	Phe	Glu	Glu	Leu	Val	Val
			595				600					605			
Gly	Ile	Ala	Gln	Cys	Ala	Arg	Lys	Asp	Gly	Tyr	Ser	Phe	Pro	Gly	Pro
610						615					620				
Pro	Phe	Phe	Leu	Ser	Met	Trp	Glu	Lys	Leu	Arg	Ser	Asn	Tyr	Glu	
625					630						635				

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<210> SEQ ID NO 22
 <211> LENGTH: 1323
 <212> TYPE: DNA
 <213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 22

```

gggaagaagt ccagagtgtg cgggtactgc ggggccccgg ccccgtagc cactgcctgt    60
ggcctogaag tctgtattta ccacaccac ttccaccagc attgtccagt cataatctgg    120
tgtggccatc cagcgggttc tggttcttgt agtgagtgca aacccccct agggaaaggc    180
acaagccctc tagatgaggt gttggaacaa gtcccgtata agcctccacg gaccgtaatc    240
atgcatgtgg agcagggtct caccctctt gaccaggca gataccagac tcgccgcgga    300
ttagtctcgg ttaggcgtgg catcagggga aatgaagttg acctaccaga cggtgattat    360
gctagcacog ccttgctccc cacttgtaaa gagatcaaca tggtcgctgt cgcttctaata    420
gtggtgca gcaagggtcat catcgggtcca cccggtgctg ggaaaacata ctggctcctt    480
caacagggtcc aggatgtgga tgtcatttac acaccaactc atcagaccat gcttgacatg    540
attaaggctt tggggacgtg ccggttcaac gtcccggcag gcacaacgct gcaattccct    600
gccccctccc gtaccggccc gtgggttcgc atcctggccg gcggttggtg tcctggcaag    660
aatcctctcc tggatgaagc agcgtattgt aatcaccttg atgtcttgag gcttcttagc    720
aaaactacc tcacctgtct gggagacttc aaacaactcc acccagtggg tttgattct    780
cattgctatg tttttgacat catgcctcag actcaactga agaccatctg gaggtttgga    840
cagaatatct gtgatgccat tcagccagat tacagggaca aacttggtgc catggtcaac    900
acaaccctgt taacctacgt ggaaaaacct gtcaagtatg ggcaagtcc cacccttac    960
cacagggacc gagaggacgg cgccatcaca attgactcca gtcaaggcgc cacatttgat    1020
gtggttacat tgcatttgc cactaaagat tcaactcaaca ggcaagagc ccttgttgct    1080
atcaccaggg caagacatgc tatctttgtg tatgaccac acaggcaact gcagagcatg    1140
tttgatcttc ctgcaaaagg cacaccctgc aacctgcgctg tgcaccgtga cgagcagctg    1200
atcgtgctag atagaaataa caaagaatgc acggttgctc aggctctagg caatggggat    1260
aaattcaggg ccacagacaa gcgcgttgta gattctctcc gcgccatttg tgcagatcta    1320
gaa                                                                    1323
    
```

<210> SEQ ID NO 23
 <211> LENGTH: 441
 <212> TYPE: PRT
 <213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 23

```

Gly Lys Lys Ser Arg Val Cys Gly Tyr Cys Gly Ala Pro Ala Pro Tyr
1           5           10           15
Ala Thr Ala Cys Gly Leu Asp Val Cys Ile Tyr His Thr His Phe His
20           25           30
Gln His Cys Pro Val Ile Ile Trp Cys Gly His Pro Ala Gly Ser Gly
35           40           45
Ser Cys Ser Glu Cys Lys Pro Pro Leu Gly Lys Gly Thr Ser Pro Leu
50           55           60
Asp Glu Val Leu Glu Gln Val Pro Tyr Lys Pro Pro Arg Thr Val Ile
65           70           75           80
Met His Val Glu Gln Gly Leu Thr Pro Leu Asp Pro Gly Arg Tyr Gln
    
```

-continued

85				90				95							
Thr	Arg	Arg	Gly	Leu	Val	Ser	Val	Arg	Arg	Gly	Ile	Arg	Gly	Asn	Glu
			100							105				110	
Val	Asp	Leu	Pro	Asp	Gly	Asp	Tyr	Ala	Ser	Thr	Ala	Leu	Leu	Pro	Thr
		115					120							125	
Cys	Lys	Glu	Ile	Asn	Met	Val	Ala	Val	Ala	Ser	Asn	Val	Leu	Arg	Ser
		130				135					140				
Arg	Phe	Ile	Ile	Gly	Pro	Pro	Gly	Ala	Gly	Lys	Thr	Tyr	Trp	Leu	Leu
					150						155				160
Gln	Gln	Val	Gln	Asp	Gly	Asp	Val	Ile	Tyr	Thr	Pro	Thr	His	Gln	Thr
					165					170					175
Met	Leu	Asp	Met	Ile	Lys	Ala	Leu	Gly	Thr	Cys	Arg	Phe	Asn	Val	Pro
			180							185				190	
Ala	Gly	Thr	Thr	Leu	Gln	Phe	Pro	Ala	Pro	Ser	Arg	Thr	Gly	Pro	Trp
			195				200							205	
Val	Arg	Ile	Leu	Ala	Gly	Gly	Trp	Cys	Pro	Gly	Lys	Asn	Ser	Phe	Leu
			210			215					220				
Asp	Glu	Ala	Ala	Tyr	Cys	Asn	His	Leu	Asp	Val	Leu	Arg	Leu	Leu	Ser
						230				235					240
Lys	Thr	Thr	Leu	Thr	Cys	Leu	Gly	Asp	Phe	Lys	Gln	Leu	His	Pro	Val
					245					250					255
Gly	Phe	Asp	Ser	His	Cys	Tyr	Val	Phe	Asp	Ile	Met	Pro	Gln	Thr	Gln
			260							265					270
Leu	Lys	Thr	Ile	Trp	Arg	Phe	Gly	Gln	Asn	Ile	Cys	Asp	Ala	Ile	Gln
			275				280							285	
Pro	Asp	Tyr	Arg	Asp	Lys	Leu	Val	Ser	Met	Val	Asn	Thr	Thr	Arg	Val
			290			295					300				
Thr	Tyr	Val	Glu	Lys	Pro	Val	Lys	Tyr	Gly	Gln	Val	Leu	Thr	Pro	Tyr
					310						315				320
His	Arg	Asp	Arg	Glu	Asp	Gly	Ala	Ile	Thr	Ile	Asp	Ser	Ser	Gln	Gly
					325					330					335
Ala	Thr	Phe	Asp	Val	Val	Thr	Leu	His	Leu	Pro	Thr	Lys	Asp	Ser	Leu
			340							345				350	
Asn	Arg	Gln	Arg	Ala	Leu	Val	Ala	Ile	Thr	Arg	Ala	Arg	His	Ala	Ile
			355				360							365	
Phe	Val	Tyr	Asp	Pro	His	Arg	Gln	Leu	Gln	Ser	Met	Phe	Asp	Leu	Pro
			370			375					380				
Ala	Lys	Gly	Thr	Pro	Val	Asn	Leu	Ala	Val	His	Arg	Asp	Glu	Gln	Leu
					390						395				400
Ile	Val	Leu	Asp	Arg	Asn	Asn	Lys	Glu	Cys	Thr	Val	Ala	Gln	Ala	Leu
					405					410					415
Gly	Asn	Gly	Asp	Lys	Phe	Arg	Ala	Thr	Asp	Lys	Arg	Val	Val	Asp	Ser
			420							425				430	
Leu	Arg	Ala	Ile	Cys	Ala	Asp	Leu	Glu							
			435				440								

<210> SEQ ID NO 24
 <211> LENGTH: 669
 <212> TYPE: DNA
 <213> ORGANISM: Porcine reproductive and respiratory syndrome virus
 <400> SEQUENCE: 24

gggtcgagct ctccgctccc caaggtcgca cacaacttgg gattttattt ctcacctgat 60
 ttgacacagt ttgctaaact cccggtagaa cttgcacccc actggcccggt ggtgacaacc 120

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```

cagaacaatg aaaagtggcc agaccggctg gttgccagcc ttegccctat ccataaatat 180
agccgcgcgt gcatcgggtg cggetatatg gtgggccctt cgggtgttct aggcaccctt 240
ggggttgtgt catactatct cacaaaattt gttaagggcg aggctcaagt gcttccggag 300
acagtcttca gcaccggcgc aattgaggta gattgccggg agtatcttga tgatcgggag 360
cgagaagttg ctgagtcctt cccacatgcc ttcattggcg acgtcaaagg cactaccggt 420
ggaggatgtc accatgtcac ctccaaatac cttccgcgct tccttcccaa ggaatcagtt 480
gcggtagtcg gggtttcaag ccccgggaaa gccgcaaaag cagtttgac attaacagat 540
gtgtacctcc cagacctga agcttaoctc caccagaga cccagtccaa gtgctggaaa 600
atgatgttgg acttcaagga agttcgactg atggtctgga aagacaaaac ggctatattt 660
caacttgaa 669

```

```

<210> SEQ ID NO 25
<211> LENGTH: 223
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 25

```

```

Gly Ser Ser Ser Pro Leu Pro Lys Val Ala His Asn Leu Gly Phe Tyr
1      5      10      15
Phe Ser Pro Asp Leu Thr Gln Phe Ala Lys Leu Pro Val Glu Leu Ala
20     25     30
Pro His Trp Pro Val Val Thr Thr Gln Asn Asn Glu Lys Trp Pro Asp
35     40     45
Arg Leu Val Ala Ser Leu Arg Pro Ile His Lys Tyr Ser Arg Ala Cys
50     55     60
Ile Gly Ala Gly Tyr Met Val Gly Pro Ser Val Phe Leu Gly Thr Pro
65     70     75     80
Gly Val Val Ser Tyr Tyr Leu Thr Lys Phe Val Lys Gly Glu Ala Gln
85     90     95
Val Leu Pro Glu Thr Val Phe Ser Thr Gly Arg Ile Glu Val Asp Cys
100    105    110
Arg Glu Tyr Leu Asp Asp Arg Glu Arg Glu Val Ala Glu Ser Leu Pro
115    120    125
His Ala Phe Ile Gly Asp Val Lys Gly Thr Thr Val Gly Gly Cys His
130    135    140
His Val Thr Ser Lys Tyr Leu Pro Arg Phe Leu Pro Lys Glu Ser Val
145    150    155    160
Ala Val Val Gly Val Ser Ser Pro Gly Lys Ala Ala Lys Ala Val Cys
165    170    175
Thr Leu Thr Asp Val Tyr Leu Pro Asp Leu Glu Ala Tyr Leu His Pro
180    185    190
Glu Thr Gln Ser Lys Cys Trp Lys Met Met Leu Asp Phe Lys Glu Val
195    200    205
Arg Leu Met Val Trp Lys Asp Lys Thr Ala Tyr Phe Gln Leu Glu
210    215    220

```

```

<210> SEQ ID NO 26
<211> LENGTH: 462
<212> TYPE: DNA
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 26

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```

ggccgccatt tcacctgga tcagcttgca agctatgcct cgtacatccg agttcctggt    60
aactctacgg tgtatttga ccctgcacg gccctgccc tttgcaacag aagagttgtc    120
gggtccactc attggggggc tgacctgca gtcacccctt atgattatgg tgccaaaatc    180
attctgtcta gtgcatacca tggtgaaatg cctcctgggt acaaaatcct ggcgtgcgcg    240
gagttctcgc ttgacgatcc agtgaggtag aaacacacct gggggtttga atcgataca    300
gcgtatctgt acgagttcac cggaaacggt gaggactggg aggattacaa tgatgcggtt    360
cgtgcgcgcc agaaagggaa aatttataag gccactgcca ccagcatgag gtttcatttt    420
cccccgggcc ctgtcattga accaactttg gcctgaatt ga                        462

```

```

<210> SEQ ID NO 27
<211> LENGTH: 153
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 27

```

```

Gly Arg His Phe Thr Trp Tyr Gln Leu Ala Ser Tyr Ala Ser Tyr Ile
1          5          10          15
Arg Val Pro Val Asn Ser Thr Val Tyr Leu Asp Pro Cys Met Gly Pro
20         25         30
Ala Leu Cys Asn Arg Arg Val Val Gly Ser Thr His Trp Gly Ala Asp
35         40         45
Leu Ala Val Thr Pro Tyr Asp Tyr Gly Ala Lys Ile Ile Leu Ser Ser
50         55         60
Ala Tyr His Gly Glu Met Pro Pro Gly Tyr Lys Ile Leu Ala Cys Ala
65         70         75         80
Glu Phe Ser Leu Asp Asp Pro Val Arg Tyr Lys His Thr Trp Gly Phe
85         90         95
Glu Ser Asp Thr Ala Tyr Leu Tyr Glu Phe Thr Gly Asn Gly Glu Asp
100        105        110
Trp Glu Asp Tyr Asn Asp Ala Phe Arg Ala Arg Gln Lys Gly Lys Ile
115        120        125
Tyr Lys Ala Thr Ala Thr Ser Met Arg Phe His Phe Pro Pro Gly Pro
130        135        140
Val Ile Glu Pro Thr Leu Gly Leu Asn
145        150

```

```

<210> SEQ ID NO 28
<211> LENGTH: 771
<212> TYPE: DNA
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 28

```

```

atgaaatggg ggctatgcaa agcctttttg acaaaattgg ccaacttttt gtggatgctt    60
tcacggaatt tttggtgtcc attggtgata tcatcatatt tttggccatt ttgtttgget    120
tcaccatcgc cggttggctg gtggtctttt gcatcagatt ggtttgetcc gcggtactcc    180
gtgcgcgccc taccattcac cctgagcaat tacagaagat cctatgaggc ctttctttct    240
cagtgccggg tggacattcc cacctgggga actaaacatc ccttggggat gctttggcac    300
cataaggtgt caaccctgat tgatgaaatg gtgtcgcgtc gaatgtaccg catcatggaa    360
aaagcaggac aggetgectg gaaacaggtg gtgagcgagg ctacgctgtc tcgcattagt    420
ggtttgatg tggtggtcca ttttcagcat cttgccgcca ttgaagccga gacctgtaaa    480
tatttggcct ctcggctgcc catgctacac aacctgcgca tgacagggtc aaatgtaacc    540

```

-continued

```

atagtgtata atagtacttt gaatcagggtg tttgctatatt ttccaacccc tggttcccgg      600
ccaaagcttc atgattttca gcaatgggta atagctgtgc attcctccat attttcctct      660
gttgacgctt cttgtactct ttttgtgtg ctgtgggtgc ggattccaat gctacgtact      720
gtttttggtt tccactgggt aggggcaatt ttctcttcca actcacagtg a                771

```

```

<210> SEQ ID NO 29
<211> LENGTH: 256
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 29

```

```

Met Lys Trp Gly Leu Cys Lys Ala Phe Leu Thr Lys Leu Ala Asn Phe
1           5           10          15
Leu Trp Met Leu Ser Arg Asn Phe Trp Cys Pro Leu Leu Ile Ser Ser
20          25          30
Tyr Phe Trp Pro Phe Cys Leu Ala Ser Pro Ser Pro Val Gly Trp Trp
35          40          45
Ser Phe Ala Ser Asp Trp Phe Ala Pro Arg Tyr Ser Val Arg Ala Leu
50          55          60
Pro Phe Thr Leu Ser Asn Tyr Arg Arg Ser Tyr Glu Ala Phe Leu Ser
65          70          75          80
Gln Cys Arg Val Asp Ile Pro Thr Trp Gly Thr Lys His Pro Leu Gly
85          90          95
Met Leu Trp His His Lys Val Ser Thr Leu Ile Asp Glu Met Val Ser
100         105        110
Arg Arg Met Tyr Arg Ile Met Glu Lys Ala Gly Gln Ala Ala Trp Lys
115        120        125
Gln Val Val Ser Glu Ala Thr Leu Ser Arg Ile Ser Gly Leu Asp Val
130        135        140
Val Ala His Phe Gln His Leu Ala Ala Ile Glu Ala Glu Thr Cys Lys
145        150        155        160
Tyr Leu Ala Ser Arg Leu Pro Met Leu His Asn Leu Arg Met Thr Gly
165        170        175
Ser Asn Val Thr Ile Val Tyr Asn Ser Thr Leu Asn Gln Val Phe Ala
180        185        190
Ile Phe Pro Thr Pro Gly Ser Arg Pro Lys Leu His Asp Phe Gln Gln
195        200        205
Trp Leu Ile Ala Val His Ser Ser Ile Phe Ser Ser Val Ala Ala Ser
210        215        220
Cys Thr Leu Phe Val Val Leu Trp Leu Arg Ile Pro Met Leu Arg Thr
225        230        235        240
Val Phe Gly Phe His Trp Leu Gly Ala Ile Phe Pro Ser Asn Ser Gln
245        250        255

```

```

<210> SEQ ID NO 30
<211> LENGTH: 765
<212> TYPE: DNA
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 30

```

```

atggctaata gctgtgcatt cctccatatt ttctctgtt gcagcttctt gtactctttt      60
tgtttgtgctg tggttgcgga ttccaatgct acgtactggt tttggtttcc actggtttagg      120
ggcaattttt ccttccaact cacagtgaat tacacgggtg gtccaccttg cctcaaccgg      180

```

-continued

```

caagcagccg ctgagatcta cgaaccggc aggtctcttt ggtgcaggat agggcatgac 240
cgatgtaggg aggacgatca tgacgaacta gggttcatgg ttccgcctgg cctctccagc 300
gaaggccact tgaccagtgt ttacgcctgg ttggcgttcc tgtccttcag ctacacggcc 360
cagttccatc ccgagatatt tgggataggg aatgtgagtc aagtttatgt tgacatcaag 420
caccaattca tctgcgcca acatgacggg cagaacgcca ccttgcctcg ccatgacaac 480
atctcagccg tgtttcagac ctactaccaa catcaggctg acggcggcaa ttggtttcac 540
ctagaatggc tgcgcccctt cttttcctct tggttggttt taaatgtttc gtggtttctc 600
aggcgttcgc ctgcaagcca tgtttcagtt cgagtctttc agacatcaag accaacacca 660
ccgcagcagc aagctttggt gtctctcaag acatcagctg ccttaggcat ggcgactcgt 720
cctctgaggc gattcgcaaa agctctcagt gccgcacggc gatag 765

```

<210> SEQ ID NO 31

<211> LENGTH: 254

<212> TYPE: PRT

<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 31

```

Met Ala Asn Ser Cys Ala Phe Leu His Ile Phe Leu Cys Cys Ser Phe
 1          5          10          15
Leu Tyr Ser Phe Cys Cys Ala Val Val Ala Asp Ser Asn Ala Thr Tyr
          20          25          30
Cys Phe Trp Phe Pro Leu Val Arg Gly Asn Phe Ser Phe Glu Leu Thr
          35          40          45
Val Asn Tyr Thr Val Cys Pro Pro Cys Leu Thr Arg Gln Ala Ala Ala
          50          55          60
Glu Ile Tyr Glu Pro Gly Arg Ser Leu Trp Cys Arg Ile Gly His Asp
65          70          75          80
Arg Cys Arg Glu Asp Asp His Asp Glu Leu Gly Phe Met Val Pro Pro
          85          90          95
Gly Leu Ser Ser Glu Gly His Leu Thr Ser Val Tyr Ala Trp Leu Ala
          100          105          110
Phe Leu Ser Phe Ser Tyr Thr Ala Gln Phe His Pro Glu Ile Phe Gly
          115          120          125
Ile Gly Asn Val Ser Gln Val Tyr Val Asp Ile Lys His Gln Phe Ile
          130          135          140
Cys Ala Glu His Asp Gly Gln Asn Ala Thr Leu Pro Arg His Asp Asn
145          150          155          160
Ile Ser Ala Val Phe Gln Thr Tyr Tyr Gln His Gln Val Asp Gly Gly
          165          170          175
Asn Trp Phe His Leu Glu Trp Leu Arg Pro Phe Phe Ser Ser Trp Leu
          180          185          190
Val Leu Asn Val Ser Trp Phe Leu Arg Arg Ser Pro Ala Ser His Val
          195          200          205
Ser Val Arg Val Phe Gln Thr Ser Arg Pro Thr Pro Pro Gln Gln Gln
          210          215          220
Ala Leu Leu Ser Ser Lys Thr Ser Ala Ala Leu Gly Met Ala Thr Arg
225          230          235          240
Pro Leu Arg Arg Phe Ala Lys Ala Leu Ser Ala Ala Arg Arg
          245          250

```

<210> SEQ ID NO 32

<211> LENGTH: 537

-continued

<212> TYPE: DNA

<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 32

```

atggctgcgc cccttctttt cctcttggtt ggttttaaat gtttcgtggt ttctcaggcg      60
ttcgctgca agccatgttt cagttcgagt ctttcagaca tcaagaccaa caccacgcga      120
gcagcaagct ttgttgcctt ccaagacatc agctgcctta ggcattggca ctcgtcctct      180
gaggcgattc gcaaaagctc tcagtgcgcg acggcgatag ggacaccctg gtacatcacc      240
atcacagcca atgtgacaga tgagaattat ttacattctt ctgatctcct catgctttct      300
tcttgctttt tctatgcttc tgagatgagt gaaaagggat tcaagtggtt atttggaat      360
gtgtcaggca tcgtggctgt gtgtgtcaac tttaccagct acgtccaaca tgtcaaggag      420
tttacccaac gctccttggt ggtcgacctt gtgcggctgc ttcatttcat gacacctgag      480
accatgaggt gggcaaccgt ttagcctgtt ctttttgcca ttctggtggc aatttga      537

```

<210> SEQ ID NO 33

<211> LENGTH: 178

<212> TYPE: PRT

<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 33

```

Met Ala Ala Pro Leu Leu Phe Leu Leu Val Gly Phe Lys Cys Phe Val
 1          5          10         15
Val Ser Gln Ala Phe Ala Cys Lys Pro Cys Phe Ser Ser Ser Leu Ser
          20          25          30
Asp Ile Lys Thr Asn Thr Thr Ala Ala Ala Ser Phe Val Val Leu Gln
          35          40          45
Asp Ile Ser Cys Leu Arg His Gly Asp Ser Ser Ser Glu Ala Ile Arg
          50          55          60
Lys Ser Ser Gln Cys Arg Thr Ala Ile Gly Thr Pro Val Tyr Ile Thr
 65          70          75          80
Ile Thr Ala Asn Val Thr Asp Glu Asn Tyr Leu His Ser Ser Asp Leu
          85          90          95
Leu Met Leu Ser Ser Cys Leu Phe Tyr Ala Ser Glu Met Ser Glu Lys
          100         105         110
Gly Phe Lys Val Val Phe Gly Asn Val Ser Gly Ile Val Ala Val Cys
          115         120         125
Val Asn Phe Thr Ser Tyr Val Gln His Val Lys Glu Phe Thr Gln Arg
          130         135         140
Ser Leu Val Val Asp His Val Arg Leu Leu His Phe Met Thr Pro Glu
          145         150         155         160
Thr Met Arg Trp Ala Thr Val Leu Ala Cys Leu Phe Ala Ile Leu Leu
          165         170         175
Ala Ile

```

<210> SEQ ID NO 34

<211> LENGTH: 603

<212> TYPE: DNA

<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 34

```

atgttgggga aatgcttgac cgcgggctgt tgctcgcat tgcctttttt gtgggtgata      60
gtgccgttct gttttgctgc gctcgtcaac gccaacagca acagcagctc ccatttacag      120
ttgatttata acttgacgct atgtgagctg aatggcacag attggtggc taacaaattt      180

```

-continued

```

gattgggcag tggagacttt tgtcatcttt cccgtgttga ctcacattgt ctctatggt 240
gccctcacca ccagccattt ccttgacaca gtcggtctgg tcaactgtgtc taccgccggg 300
ttttatcaag ggcggatagt cttgagtagc atctacgcgg tctgtgccct ggctgcggtg 360
atgtgcttgc tcattaggtt tgcgaagaac tgcattgtct ggcgctactc atgtaccaga 420
tataccaact ttcttctgga cactaagggc agactctatc gttggcggtc gcccgtcac 480
atagagaaaa ggggtaaagt tgaggtcgaa ggtcatctga tcgacctcaa aagagttgtg 540
cttgatggtt ccgtggcaac cctttaacc agagtttcag cggaacaatg gggctgtcct 600
tag 603

```

```

<210> SEQ ID NO 35
<211> LENGTH: 200
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 35

```

```

Met Leu Gly Lys Cys Leu Thr Ala Gly Cys Cys Ser Arg Leu Leu Ser
1           5           10          15
Leu Trp Cys Ile Val Pro Phe Cys Phe Ala Ala Leu Val Asn Ala Asn
20          25          30
Ser Asn Ser Ser Ser His Leu Gln Leu Ile Tyr Asn Leu Thr Leu Cys
35          40          45
Glu Leu Asn Gly Thr Asp Trp Leu Ala Asn Lys Phe Asp Trp Ala Val
50          55          60
Glu Thr Phe Val Ile Phe Pro Val Leu Thr His Ile Val Ser Tyr Gly
65          70          75          80
Ala Leu Thr Thr Ser His Phe Leu Asp Thr Val Gly Leu Val Thr Val
85          90          95
Ser Thr Ala Gly Phe Tyr His Gly Arg Tyr Val Leu Ser Ser Ile Tyr
100         105         110
Ala Val Cys Ala Leu Ala Ala Leu Ile Cys Phe Val Ile Arg Phe Ala
115         120         125
Lys Asn Cys Met Ser Trp Arg Tyr Ser Cys Thr Arg Tyr Thr Asn Phe
130         135         140
Leu Leu Asp Thr Lys Gly Arg Leu Tyr Arg Trp Arg Ser Pro Val Ile
145         150         155         160
Ile Glu Lys Arg Gly Lys Val Glu Val Glu Gly His Leu Ile Asp Leu
165         170         175
Lys Arg Val Val Leu Asp Gly Ser Val Ala Thr Pro Leu Thr Arg Val
180         185         190
Ser Ala Glu Gln Trp Gly Arg Pro
195         200

```

```

<210> SEQ ID NO 36
<211> LENGTH: 525
<212> TYPE: DNA
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 36

```

```

atggggctcgt ccttagacga cttctgccat gatagcacgg ctccacaaaa ggtgcttttg 60
gcgtttteta ttacctacac gccagtgatg atatatgccc taaaggtaag tcgcggccga 120
ctgctagggc ttctgcacct tttgattttt ctgaattgtg ctttcacctt cgggtacatg 180
acattcgcgc actttcagag cacaaataag gtcgcgctca ctatgggagc agtagttgca 240

```

-continued

```

ctcctttggg ggggtgactc agccatagaa acctggaaat tcatcacctc cagatgccgt   300
ttgtgcttgc taggccgcaa gtacattctg gccctgccc accacgttga aagtgccgca   360
ggctttcatc cgattgccc aaatgataac cacgcatttg tcgtccggcg tcccggctcc   420
actacgggtca acggcacatt ggtgccggg ttgaaaagcc tcgtgttggg tggcagaaaa   480
gctgttaaac agggagtggg aaacctgtc aaatatgcca aataa                       525

```

```

<210> SEQ ID NO 37
<211> LENGTH: 174
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 37

```

```

Met Gly Ser Ser Leu Asp Asp Phe Cys His Asp Ser Thr Ala Pro Gln
 1                               5          10          15
Lys Val Leu Leu Ala Phe Ser Ile Thr Tyr Thr Pro Val Met Ile Tyr
                               20          25          30
Ala Leu Lys Val Ser Arg Gly Arg Leu Leu Gly Leu Leu His Leu Leu
   35          40          45
Ile Phe Leu Asn Cys Ala Phe Thr Phe Gly Tyr Met Thr Phe Ala His
   50          55          60
Phe Gln Ser Thr Asn Lys Val Ala Leu Thr Met Gly Ala Val Val Ala
 65          70          75          80
Leu Leu Trp Gly Val Tyr Ser Ala Ile Glu Thr Trp Lys Phe Ile Thr
   85          90          95
Ser Arg Cys Arg Leu Cys Leu Leu Gly Arg Lys Tyr Ile Leu Ala Pro
 100          105          110
Ala His His Val Glu Ser Ala Ala Gly Phe His Pro Ile Ala Ala Asn
 115          120          125
Asp Asn His Ala Phe Val Val Arg Arg Pro Gly Ser Thr Thr Val Asn
 130          135          140
Gly Thr Leu Val Pro Gly Leu Lys Ser Leu Val Leu Gly Gly Arg Lys
 145          150          155          160
Ala Val Lys Gln Gly Val Val Asn Leu Val Lys Tyr Ala Lys
 165          170

```

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<210> SEQ ID NO 38
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

```

```

<400> SEQUENCE: 38

```

```

atgccaaata acaacggcaa gcagcagaag aaaaagaagg gggatggcca gccagtcaat   60
cagctgtgcc agatgctggg taagatcadc gccagcaaa accagtccag aggcaagggg   120
ccgggaaaga aaaataagaa gaaaaacccg gagaagcccc attttcctct agcgactgaa   180
gatgacgtca gacatcaact taccctagt gagcggcaat tgtgtctgtc gtcaatccag   240
actgccttta atcaaggcgc tggaacttgt accctgtcag attcaggagg gataagttac   300
actgtggagt ttagtgtgcc gacgcatcat actgtgcgcc tgatccgct cacagcatca   360
ccctcagcat ga                                                         372

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<210> SEQ ID NO 39
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

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-continued

<400> SEQUENCE: 39

Met Pro Asn Asn Asn Gly Lys Gln Gln Lys Lys Lys Lys Gly Asp Gly
 1 5 10 15
 Gln Pro Val Asn Gln Leu Cys Gln Met Leu Gly Lys Ile Ile Ala Gln
 20 25 30
 Gln Asn Gln Ser Arg Gly Lys Gly Pro Gly Lys Lys Asn Lys Lys Lys
 35 40 45
 Asn Pro Glu Lys Pro His Phe Pro Leu Ala Thr Glu Asp Asp Val Arg
 50 55 60
 His His Phe Thr Pro Ser Glu Arg Gln Leu Cys Leu Ser Ser Ile Gln
 65 70 75 80
 Thr Ala Phe Asn Gln Gly Ala Gly Thr Cys Thr Leu Ser Asp Ser Gly
 85 90 95
 Arg Ile Ser Tyr Thr Val Glu Phe Ser Leu Pro Thr His His Thr Val
 100 105 110
 Arg Leu Ile Arg Val Thr Ala Ser Pro Ser Ala
 115 120

<210> SEQ ID NO 40

<211> LENGTH: 156

<212> TYPE: DNA

<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 40

atgttcaagt atgttgggga aatgcttgac cgcgggctgt tgctcgcgat tgctttcttt 60
 gtggtgtatc gtgccgttct gttttgctgc gctcgtcaac gccaacagca acagcagctc 120
 ccatttacag ttgatttaca acttgacgct atgtga 156

<210> SEQ ID NO 41

<211> LENGTH: 51

<212> TYPE: PRT

<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 41

Met Phe Lys Tyr Val Gly Glu Met Leu Asp Arg Gly Leu Leu Leu Ala
 1 5 10 15
 Ile Ala Phe Phe Val Val Tyr Arg Ala Val Leu Phe Cys Cys Ala Arg
 20 25 30
 Gln Arg Gln Gln Gln Gln Leu Pro Phe Thr Val Asp Leu Gln Leu
 35 40 45
 Asp Ala Met
 50

<210> SEQ ID NO 42

<211> LENGTH: 222

<212> TYPE: DNA

<213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 42

atgggggcta tgcaaagcct ttttgacaaa attggccaac tttttgtgga tgctttcacg 60
 gaatttttgg tgtccattgt tgatatcadc atatttttgg ccattttgtt tggettccacc 120
 atcgcgggtt ggctgggtgt cttttgcadc agattggttt gctccgcggt actccgtgcg 180
 cgccctacca ttcaccctga gcaattacag aagatcctat ga 222

<210> SEQ ID NO 43

-continued

<211> LENGTH: 73
 <212> TYPE: PRT
 <213> ORGANISM: Porcine reproductive and respiratory syndrome virus

<400> SEQUENCE: 43

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Met Gly Ala Met Gln Ser Leu Phe Asp Lys Ile Gly Gln Leu Phe Val
1           5           10          15
Asp Ala Phe Thr Glu Phe Leu Val Ser Ile Val Asp Ile Ile Ile Phe
20          25          30
Leu Ala Ile Leu Phe Gly Phe Thr Ile Ala Gly Trp Leu Val Val Phe
35          40          45
Cys Ile Arg Leu Val Cys Ser Ala Val Leu Arg Ala Arg Pro Thr Ile
50          55          60
His Pro Glu Gln Leu Gln Lys Ile Leu
65          70
    
```

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What is claimed is:

1. A porcine reproductive and respiratory syndrome virus (PPRSV)-CON nucleic acid having the sequence shown in SEQ ID NO: 1.
2. A composition comprising the nucleic acid of claim 1 and a pharmaceutically acceptable carrier.
3. The composition of claim 2, further comprising an adjuvant.
4. A virus particle comprising the PPRSV-CON nucleic acid of claim 1.

5. A composition comprising the virus particle of claim 4 and a pharmaceutically acceptable carrier.

25 6. A method for imparting heterologous cross-protection against porcine reproductive and respiratory syndrome (PPRS) Type 2 strains in a porcine, comprising administering, to a porcine, an effective amount of the virus particle of claim 4.

30 7. The method of claim 6, wherein the administration is selected from the group consisting of intramuscularly, intraperitoneally, and orally.

* * * * *