https://doi.org/10.29326/2304-196X-2025-14-2-114-122

Modern approaches to diagnosis and prevention of porcine reproductive and respiratory syndrome (review)

Yulia A. Nikolaeva
Federal Center for Toxicological, Radiation and Biological Safety, Nauchnyi gorodok-2, Kazan 420075, Republic of Tatarstan, Russia

ABSTRACT

Introduction. Porcine reproductive and respiratory syndrome (PRRS), caused by a virus from the family *Arteriviridae*, is one of the most economically significant porcine diseases in many countries. The disease is mainly manifested by reproductive disorders in sows, i.e. abortions in late pregnancy, early or delayed farrowing, birth of weak or non-viable piglets, irregular estrus; pathologies in early and middle pregnancy are less often reported. Piglets and fattening pigs have respiratory distress syndrome: coughing, sneezing, dyspnea and stunted growth. In addition, infection with PRRS virus undermines respiratory immunity, which makes the infected pigs more susceptible to secondary infections and increases mortality in the herd. This review provides up-to-date information on the current laboratory diagnostic tools and recent data on specific PRRS prevention and gives information on the promising biotechnological platforms that can be used to design new-generation vaccines.

Objective. To consider and summarize modern approaches to diagnosis and prevention of porcine reproductive and respiratory syndrome.

Materials and methods. Scientific publications of foreign and domestic authors served as the material for the research.

Results. The paper presents nosological characteristics of the disease, explores distinctive features of its clinical manifestations and epizootiology; analyzes structure of the pathogen's genome. This review describes and evaluates laboratory diagnostic techniques (both conventional and modern); currently available anti-PRRS vaccines and novel biotech platforms enabling to design safer and more effective next-generation vaccines. There are three major challenges in vaccine development at the current stage of PRRS pathogenesis research: insufficient understanding of immune protection mechanisms, the virus's ability to induce negative regulatory signals for the immune system, and the pathogen's high antigenic variability.

Conclusion. PRRS virus strains exhibit significant genetic and antigenic heterogeneity and frequently undergo recombination, which exacerbates the challenges of epizootiology, disease prevention, and control. Further in-depth study of host immune response characteristics, along with identification of T- and B-cell epitopes in the pathogen structure, will enable rational design of genetically engineered vaccines.

Keywords: review, porcine reproductive and respiratory syndrome, epizootiology, vaccination, diagnosis

Acknowledgements: The study was conducted as part of a state-funded research program of the Federal Center for Toxicological, Radiation and Biological Safety for 2025–2026 on topic 4.2.5 "Development of technological approaches for production of modern vaccines against viral and bacterial infections in animals".

For citation: Nikolaeva Yu. A. Modern approaches to diagnosis and prevention of porcine reproductive and respiratory syndrome (review). *Veterinary Science Today.* 2025; 14 (2): 114–122. https://doi.org/10.29326/2304-196X-2025-14-2-114-122

Conflict of interests: The author declares no conflict of interests.

For correspondence: Yulia A. Nikolaeva, Junior Researcher, Laboratory of Viral Anthropozoonoses, Federal Center for Toxicological, Radiation and Biological Safety, Nauchnyi gorodok-2, Kazan 420075, Republic of Tatarstan, Russia, *yulia.nikolaeva111@mail.ru*

УДК 619:616.98:578.833:636.4:616-076:616-085.371

Современные подходы к диагностике и профилактике репродуктивно-респираторного синдрома свиней (обзор)

Ю. А. Николаева
ФГБНУ «Федеральный центр токсикологической, радиационной и биологической безопасности» (ФГБНУ «ФЦТРБ-ВНИВИ»),
Научный городок-2, г. Казань, 420075, Республика Татарстан, Россия

РЕЗЮМЕ

Введение. Репродуктивно-респираторный синдром свиней (РРСС), вызываемый вирусом из семейства *Arteriviridae*, является одной из наиболее экономически значимых болезней свиней во многих странах мира. Основные проявления заболевания включают репродуктивную дисфункцию у свиноматок, которая проявляется абортами на поздних сроках беременности, ранними или отсроченными опоросами, рождением слабых или нежизнеспособных поросят, нерегулярным эструсом; реже сообщается о патологиях на ранних и средних сроках беременности. У поросят и откормочных свиней наблюдается респираторный дистресс-синдром: кашель, чихание, одышка, задержка роста. Кроме того, заражение вирусом РРСС приводит к снижению

респираторного иммунитета, что делает инфицированных свиней более восприимчивыми к вторичным инфекциям и повышает смертность среди поголовья. В настоящем обзоре представлена актуальная информация о текущем состоянии лабораторной диагностики и специфической профилактики РРСС, а также рассмотрены перспективные биотехнологические платформы для конструирования вакцин нового поколения.

Цель исследования. Рассмотреть и обобщить современные подходы к диагностике и профилактике репродуктивно-респираторного синдрома свиней.

Материалы и методы. Материалом для аналитического исследования послужили научные публикации зарубежных и отечественных авторов.

Результаты. Приведена нозологическая характеристика заболевания, рассмотрены особенности клинических проявлений, эпизоотологии, организации генома возбудителя. Описаны и обсуждены применяемые в ветеринарной практике классические и современные методы лабораторной диагностики, а также коммерчески доступные препараты для специфической профилактики РРСС и перспективные биотехнологические платформы для создания вакцин нового поколения, которые позволят достичь оптимального баланса между безопасностью и эффективностью. На текущем этапе изучения патогенеза РРСС существуют три основные проблемы в разработке вакцин: недостаточность сведений о механизмах иммунной защиты, способность вируса индуцировать негативные регуляторные сигналы для иммунной системы и значительная антигенная изменчивость возбудителя.

Заключение. Штаммы вируса РРСС демонстрируют значительную генетическую и антигенную гетерогенность и часто подвергаются рекомбинациям, что усугубляет проблемы эпизоотологии, профилактики и контроля заболевания. Дальнейшее углубленное изучение особенностей иммунного ответа организма-хозяина, а также идентификация Т- и В-клеточных эпитопов в структуре возбудителя позволит обеспечить рациональный дизайн генно-инженерных вакцин.

Ключевые слова: обзор, репродуктивно-респираторный синдром свиней, эпизоотология, вакцинация, диагностика

Благодарности: Исследование выполнено в рамках госзадания ФГБНУ «ФЦТРБ-ВНИВИ» на 2025–2026 гг. по теме 4.2.5 «Разработка технологических подходов к производству современных вакцин против вирусных и бактериальных инфекций животных».

Для цитирования: Николаева Ю. А. Современные подходы к диагностике и профилактике репродуктивно-респираторного синдрома свиней (обзор). *Ветеринария сегодня*. 2025; 14 (2): 114–122. https://doi.org/10.29326/2304-196X-2025-14-2-114-122

Конфликт интересов: Автор заявляет об отсутствии конфликта интересов.

Для корреспонденции: Николаева Юлия Александровна, младший научный сотрудник лаборатории вирусных антропозоонозов ФГБНУ «ФЦТРБ-ВНИВИ», Научный городок-2, г. Казань, 420075, Республика Татарстан, Россия, *yulia.nikolaeva111@mail.ru*

INTRODUCTION

Porcine reproductive and respiratory syndrome (PRRS) caused by the porcine reproductive and respiratory syndrome (PRRS) virus (*Betaarterivirus* types 1 and 2) is one of the most economically significant porcine diseases in many countries of the world: the global annual damage associated with this infection is estimated at more than 600 million US dollars. First outbreaks of the unknown disease were reported in the USA and Western Europe in the late 1980s and early 1990s, turning into a pandemic a few years later [1, 2]. Sows exhibited such reproductive failures as abortions, fetal mummification, stillbirths or birth of non-viable offspring, and growing piglets – respiratory manifestations (dyspnea, coughing and hyperthermia) [3] As it was established in the Netherlands in 1991, and later in the USA (in 1992), the disease was caused by the previously unknown RNA-containing virus. The disease came to be known as "porcine reproductive and respiratory syndrome" [4]. Retrospective research suggested that antibodies to PRRS pathogen had been detected before 1979 in Eastern Canada and in the mid-1980s in Iowa [5], but the viruses themselves were not identified. Presumably there were several critical epizootic milestones in the history of PRRS virus (PRRSV) dissimination, and therefore the origin of some strains, in particular from the cluster associated with MN184 strain [6], causing "acute PRRS" or "abortion storm" [7], and some highly pathogenic Chinese strains, remains unknown [8]. In Russia, the first PRRS outbreak was reported in 1991 following abortions in sows on the farms of the Kursk Oblast [9]. In 2007, during a PRRS outbreak in the Irkutsk Oblast, American genotype PRRSV-2 was isolated [10].

The causative agent is PRRSV, which is a small, enveloped positive-sense single-stranded RNA virus belonging to the genus *Betaarterivirus*, family *Arteriviridae*, order *Nidovirales* [11]. PRRSV strains are classified as PRRSV type 1 (European genotype – EU-like) and PRRSV type 2 (North American genotype – NA-like). The virus genome is characterized by high variability even if compared to other RNA viruses. Since the virus RNA-dependent RNA-polymerase lacks proofreading activity, the virus undergoes frequent mutations and recombination events resulting in occurrence of new virus isolates worldwide [12]. Having a length of about 14.9–15.5 kb, the viral genome contains at least 11 open reading frames (*ORFs*) with a 5' cap and 3' polyadenylated tail [13]. Non-structural proteins (nsp 1–12), which have the functions of protease, replicase, regulation of gene expression of the host cell and are responsible for the viral RNA synthesis, are encoded by *ORF1a* and *ORF1b,* which occupy approximately two thirds of the genome [14]. Structural proteins – capsid protein (N), membrane protein (M), glycoproteins GP2, GP3, GP4, GP5, and envelope protein (E) – are expressed by subgenomic RNA and encoded by *ORF2–7* [15]. Differences in nucleotide sequences of most conserved (*ORF7* gene encoding capsid protein N) and variable (*ORF5* gene encoding major glycoprotein GP5) form the basis of the current PRRSV genotyping system [16].

Despite multiple sequences deposited in databases, none of the existing classification systems covers diversity of the existing PRRSV variants [17]. Incomplete coverage of the available data and lack of reference sequences are the main shortcomings of the applied genotyping techniques [18]. In 2010, a phylogenetic lineage-based PRRSV

Table 1
PRRS virus genotypes and their known representatives [24, 25, 26, 27, 28]

Genotype	Known representatives, GenBank ID
PRRSV-1 (European genotype – EU-like)	
Subtype 1 (global)	strain Lelystad (NC_043487.1), Netherlands
Subtype 1 (Russian)	strain WestSib13 (KX668221.1), Russia
Subtype 2	strain Bor (JN651734.1), Belarus
Subtype 3	strain SU1-Bel (KP889243.1), Belarus
PRRSV-2 (North American genotype – NA-like)	
Lineage 1	strain NADC30 (MH500776.1), China
Lineage 3	strain QYYZ (JQ308798.1), China
Lineage 5	strain VR-2332 (AY150564.1), USA
Lineage 8	isolates JXA1 (AY032626.1), CH-1a (EF112445.1), China

typing system was proposed [19]. According to this system, PRRSV-1 strains are grouped into four subtypes (subtype 1 – global, subtype 1 – Russian, subtypes 2 and 3), and PRRSV-2 strains are grouped into nine lineages (lineage 1 – lineage 9) based on phylogenetic relationships in the *ORF5* region [20, 21]. Both genotypes, divided into clades, lineages, and sub-strains, exhibit high genetic diversity and possess approximately 60% nucleotide sequence identity [22, 23] (Table 1).

The objective of this analytical study was to review and summarize current approaches to the laboratory diagnosis and specific prevention of PRRS.

EPIDEMIOLOGY OF PRRS IN THE RUSSIAN FEDERATION

In the nomenclature of the World Organisation for Animal Health, PRRS is classified as a socially and economically significant disease [10]. According to the information provided, infection caused by PRRSV-2 is of greater epidemic importance, since viremia in animals infected with the strains of this genotype was more pronounced and prolonged than in those ones infected with PRRSV-1 [29]. PRRSV-1-1 isolates, including the so-called Russian group of viruses, PRRSV-1-2 and PRRSV-1-3 differ significantly in pathogenicity [3]. The phylogenetic analysis indicates that the European type of virus, mainly belonging to subtype 1 (Russian), is predominantly prevalent in Russia [29]. Most PRRSV-1 strains can be attributed to the Russian group; a small number of circulating strains homologous to Lelystad strain are probably associated with the use of attenuated vaccines based on PRRSV-1 [30]. However, during the PRRS outbreak in the Central Federal District in 2020, in addition to the viruses from the Russian group previously detected in these regions, Lelystad-like viruses were also detected [9, 31]. A virus phylogenetically closely related to this type was identified in Poland in 2010 [32]; this indicates that new PRRSV variants from Europe are still introduced into Russia. Until the mid-2000s, the North American PRRSV genotype had not been registered in Russia, but in 2007 an outbreak was recorded in the Irkutsk Oblast caused by high pathogenicity PRRSV-2, presumably brought in from China [33]. In addition, there is information about detection of PRRSV-2 in the Republic of Mordovia, Belgorod and Kemerovo Oblasts [3, 9, 34]. The origin of American strain introduction to the Russian territory has not been identified, but it is assumed that they could have been introduced, for example, from Denmark, where PRRSV-2 circulates and from where breeding animals are imported [9].

NOSOLOGICAL PROFILE OF PRRS

The disease is mainly manifested by reproductive disorders in sows, i.e. abortions in late pregnancy, early or delayed farrowing, birth of weak or non-viable piglets, irregular estrus; pathologies in early and middle pregnancy are less often reported [35, 36]. The primary cause of the reproductive disorders is virus-induced damage to the placenta and endometrium. Piglets and fattening pigs have respiratory distress syndrome: coughing, sneezing, dyspnea and stunted growth. In addition, PRRSV infection undermines respiratory immunity, which makes infected pigs more susceptible to secondary infections; as a result, bacterial pathogens manifest themselves in association with the viruses, thus, increasing livestock mortality [37]. The young animals are more susceptible to PRRSV than the adults are, while replacement boars and sows often suffer from subclinical infection [38].

LABORATORY DIAGNOSTICS

The main methods used for PRRS diagnostics are given in Table 2.

SPECIFIC PREVENTION

No ideal anti-PRRS vaccine has been developed so far. According to the modern requirements for a new generation of vaccines against PRRS, they shall demonstrate high efficacy, safety, and at the same time ensure cross-protection against different genotypes of the virus [44]. Due to the exceptional ability of PRRS to mutate and generate significant genetic variations, development of a broadly protective vaccine is particularly crucial for combating constantly emerging disease outbreaks [45].

The first commercially available modified live attenuated anti-PRRS vaccine (PRRSV-MLV) was released in the USA, in 1994. This event became a starting point for the vaccine large-scale safety and efficacy tests [46]. A significant

Table 2
Methods for diagnosing PRRS [3, 37]

Method	Principle of diagnosis	Peculiarities
Virus isolaton		
Culture method	Use of alveolar macrophage cell cultures.	Virus isolation may not be effective, since not all isolates (especially PRRSV-1) are capable of infecting MARC-145 and CL-2621 cells-clones derived from MA-104 monkey kidney cell line [39]
Serological methods		
Enzyme-linked immunosorbent assay (ELISA)	Based on detection of virus-specific antibodies using a diagnostic antigen. Most commonly used antibody detection method has been adapted to detect IgG, IgM, and IgA [40]	Commercial kits are available to determine serological status of pigs both in blood serum and in oral fluid used as a test object (test kits for detecting antibodies to PRRSV: "PRRS-SEROTEST", "PRRS-SEROTEST plus", Vetbiohim, Russia)
Immunofluorescence assay (IFA)	Based on detection of the viral antigen using specific antibodies labeled with a fluorescent dye. Specific fluorescence shall be observed in infected cells with the positive control serum. It is also designed to detect IgG, IgM and IgA [41]	IFA effectiveness depends on the quality of the labeled diagnostic antibodies and the test conditions. It is important to properly prepare samples and control tests that ensure reliability of the results
Virus neutralization test (VNT)	Based on the neutralization of the virus by antibodies of a specific serum. Used to detect functional antibodies related to the immune defense	According to the published sources, virus-neutralizing antibodies can be detected only on day 45 after infection, because antibody synthesis takes time. At early infection stages, antibody levels may be insufficient for detection. Thus, VNT may be ineffective at the initial stages of infection. The test has high specificity and sensitivity, which makes it one of the most reliable tests for detecting virus-neutralizing antibodies
Immunoperoxidase monolayer assay (IPMA)	Based on the use of fixed permissive line cells infected with the corresponding virus to detect specific antibodies. Used for detection of IgG isotype antibodies [42]	Can recognise a number of PRRSV variants, including field and vaccine strains; its sensitivity and specificity are comparable to those of RT-PCR. The most suitable method for early detection and monitoring of virus circulation
Molecular and genetic methods		
Real-time reverse transcription polymerase chain reaction (RT-PCR)	Based on detection of viral genome fragments. The advantages of RT-PCR are high sensitivity and specificity, as well as rapid assessment of the current infection status	This method does not differentiate inactivated virus from infectious virus. Available commercial test kits: "Test system 'PRRS' for detecting RNA and genotyping the porcine reproductive and respiratory syndrome virus (PRRSV) using polymerase chain reaction (PCR)" (developed by the Central Research Institute of Epidemiology, Rospotrebnadzor, Russia; "PCR-PRRS-FACTOR" (VET FACTOR, Russia); "AmpliPrime® PRRS" (NextBio, Russia)
ORF5 sequencing	Based on the molecular and genetic typing of PRRS virus isolates. Analysis of the *ORF5* fragment nucleotide sequences revealed significant genetic variability of the pathogen [43]. In 2010, a method for PRRSV typing based on phylogenetic relationships in the *ORF5* region was proposed [22], which later became conventional	No reliable data are available on correlation between the phylogenetic groups based on *ORF5* sequences and pathogenicity or cross-protection, therefore this approach is not suitable for assessing virulence of the virus strains
ORF7 sequencing	The *ORF7* sequence is widely used to determine genetic variations and phylogenetic relationships between different strains of PRRSV, which indicates the important role of *ORF7* in the pathogen evolution [23]	The reason for selecting *ORF7* as the sequencing region is the conserved nature of this gene. The method has several advantages: it can detect both genotypes of the virus, is fast, inexpensive, sensitive, and can detect new sublineages and subgenotypes. Thus, the method is a promising tool for diagnosis and epizootological surveillance
Morphological techniques		
Immunohistochemical method	Based on detection of specific antigens in formalin-fixed tissues. Allows visualization of the antigen alongside with histological lesions	This method enables virus identification at lesion sites; establishes cause and effect relationship, detects varying viral concentrations. It is less sensitive than PCR; there are certain requirements for sample preparation
Fluorescent *in situ* hybridization (FISH)	It is based on the use of DNA probes that bind to complementary targets in a sample. It is suitable for screening virus-infected tissues containing a relatively small number of affected cells	Although *in situ* hybridization is rarely used for diagnostic purposes, it is capable of detecting and differentiating PRRSV genotypes in formalin-fixed tissues. Sensitivity and specificity of this method for detecting PRRSV genome may be insufficient due to high genetic diversity of the virus, especially PRRSV-1. The method is useful for studying viral persistence and for routine diagnosis of PRRS

Table 3
Commercial vaccines against PRRS

Vaccine name (developer)	Region where it is used	Genotype (strain)	Efficacy
Live vaccines [47, 48]			
Ingelvac® PRRS MLV (Boehringer Ingelheim, Germany)	Africa, Asia, Europe, North America, South America	PRRSV-2 (VR-2332)	Induces protection against homologous isolates, but limited cross-protection against heterologous strains. The efficacy of these vaccines is considered insufficient to eradicate the disease on farms: large-scale PRRS outbreaks were reported on farms where vaccination is practiced. Use of live modified anti-PRRS vaccines can be a problem, since the vaccine virus can be excreted for 2 weeks and may revert to a virulent form
Ingelvac® PRRS ATP (Boehringer Ingelheim, Germany)	Asia, Europe, North America	PRRSV-2 (JA-142)	
Fostera® PRRS (Zoetis, USA)	Africa, Asia, Europe, North America	PRRSV-2 (P129)	
Prime Pac® PRRS (MSD Animal Health, Netherlands)	Africa, Asia, Europe, North America	PRRSV-2 (Neb-1)	
Prevacent® PRRS (Elanco Animal Health Inc., USA)	Asia, Europe, North America	PRRSV-2 (RFLP 184)	
Unistrain® PRRS (Laboratorios Hipra, S.A., Spain)	Africa, Asia, Europe	PRRSV-1 (VP-046 BIS)	
ReproCyc® PRRS EU (Boehringer Ingelheim, Germany)	Africa, Asia, Europe	PRRSV-1 (94881)	
Pyrsvac-183® (Laboratorios Syva S.A., Spain)	Asia, Europe	PRRSV-1 (ALL-183)	
Suvaxyn® PRRS MLV (Zoetis, USA)	Europe	PRRSV-1 (96V198)	
ARRIAH-PRRS (Federal Centre for Animal Health, Russia)	Russia	PRRSV-2 (attenuated strain BD-DEP)	
ARRIAH-ResursVak (Federal Centre for Animal Health, Russia)	Russia	PRRSV-1 (attenuated strain Borz)	
Resvak (Shchelkovo biocombinat, Russia)	Russia	PRRSV-1 (strain PRRS-1SBC)	
Inactivated vaccines [49, 50]			
SUIPRAVAC® PRRS (Laboratorios Hipra, S.A., Spain)	Europe	PRRSV (VP-046 BIS)	Inactivated vaccines induce a weaker and shorter immune response and are often ineffective against heterologous strains, but they are more stable and less sensitive to storage conditions, and are safe for use in pregnant sows
PROGRESSIS® (Merial, France)	Europe	PRRSV-1 (P120)	
SUIVAC® PRRS-INe / SUIVAC® PRRS-IN (Dyntec, Czech Republic)	Europe	PRRSV-1 (VD-E1/VD-E2/VD-A1)	
Biosuis PRRS inact Eu+Am (Bioveta, Inc., Czech Republic)	Europe, Russia	PRRSV-1 (European strain MSV Bio-60, American strain MSV Bio-61)	
ARRIAH-PRRS Inact (Federal Centre for Animal Health, Russia)	Russia	PRRSV-1 (strain KPR-96)	
PRRS-FREE (Reber Genetics, Co. Ltd, China)	Asia, Russia	PRRSV-1, PRRSV-2 (antigens PE-PQAB-K13, PE-RSAB-K13, PE-DGD-K13, PE-M12-K13)	
VERRES-PRRS (Vetbiochim LLC, Russia)	Russia	PRRSV-1 (strain OB); recombinant proteins M and GP-5 PRRSV-1 (strain Tyu16)	
ARRIAH-RePovak (Federal Centre for Animal Health, Russia)	Russia	PRRSV-1 (strain KPR-96)	
ARRIAH-Aujeszky's+PRRS (Federal Centre for Animal Health, Russia)	Russia	PRRSV-1 (strain KPR-96)	

Table 4
Candidate vaccines against PRRS

Name of the vaccine candidate	Method of preparation, protective characteristics
Deletion mutant vCSL1-GP5-N44S	Obtained by substituting the 44th amino acid in ectodomain of GP5 protein, serine-to-asparagine substitution. In an *in vivo* trial, no side effects were observed in piglets immunized with vCSL1-GP5-N44S; the vaccine induced high levels of neutralizing antibodies post infection [54]
Attenuated strain A2MC2-P90	Obtained after *in vitro* attenuation of PRRSV-A2MC2 after 90 serial passages in MARC-145 cells. The resulting strain A2MC2-P90 retained its ability to induce IFN in cell culture. A2MC2-P90 ensured 100% protection for vaccinated piglets against lethal infection with extremely virulent HP-BPCC-XJA1 strain, while non-vaccinated piglets demonstrated 100% mortality rate by day 21 post infection [55]
Chimeric virus vCSL1-GP5-N33D	Chimeric vaccine candidate based on PRRSV-2 expressing hypoglycosylated GP-5. It was used on PRRSV-affected farms; it induced neutralizing antibodies in high titers 8 weeks after the vaccination [56]
Chimeric virus VR2385-S3456	S3456 fragment contains full-length gene sequences encoding structural proteins (*ORF3-6*) embedded in PRSSV strain VR2385 genome. Induced a high level of neutralizing antibodies against two heterologous strains [57]
Chimeric virus K418DM1.1	A chimeric virus with genomic basis of FL12 infectious clone of highly virulent American PRRSV, containing genes of structural proteins of PRRSV-2 strain LMY. K418 was further modified by deglycosylation of GP5 and exhibited strong immunogenicity. No reversion to the virulent state was observed [58]
Chimeric virus rJS-ORF2-6-CON	The backbone consisted of a consensus sequence *ORF2-6* (ORF2-6-CON), encoding all enveloped proteins, developed on the basis of 30 currently circulating PRRSV Chinese isolates. Chimeric virus rJS-ORF2-6-CON was created using avirulent infection clone HP-PRRSV2 JSTZ1712-12. *In vivo* test results have shown that the virus is not pathogenic to piglets and provides cross-protection against heterologous strains [45]
Chimeric virus rTGEV-GP5-N46S-M	The backbone was the porcine transmissible gastroenteritis virus co-expressing GP5 proteins (except for the first glycosylation site) and M. After double immunization of piglets, virus neutralizing antibodies were found; the *in vivo* efficacy of the vaccine was also confirmed following challenge with the PRRSV/Olot91 strain. The disadvantage is instability of the recombinant virus: GP5 expression decreased during 8–10 passages [59]

number of conventional (live and inactivated) vaccines have been developed by now; their brief description is given in Table 3.

Studies demonstrating circulation and persistence of the vaccine virus, in turn, raise concerns about its safety: viremia implies potential transmission of the vaccine virus to non-infected animals. In addition, the vaccine virus can cross the placental barrier in pregnant sows and infect developing fetuses, resulting in the pathogen transmission to uninfected newborn piglets during lactation. It has also been shown that vaccine strains are able to recombine with field strains, creating potentially new genetically distinct variants of PRRSV on individual farms [51]. For these reasons, efficacy of live attenuated vaccines is somewhat controversial, and it is generally recognized that their safety needs to be improved. In this context, DIVA strategy (differentiation of infected from vaccinated animals) will be of great importance for control and possible eradication of PRRS [52, 53]. Epizootological and regulatory considerations indicate the need to develop anti-PRRS DIVA vaccine, which will be characterized by a negative marker (that is, a marker absent in the vaccine strain, but permanently present in wild-type strains). Similar candidate vaccines have been developed on the platform of large DNA viruses such as pseudorabies virus (PRV) and bovine herpesvirus type 1 (BHV-1) by deleting genes encoding some structural proteins. However, in case of a small RNA virus such as PRRSV, which encodes only a few proteins with basic functions, the creation of a mutant virus with a deletion of the immunodominant and conserved protein segments (or with a combination of deletions within a single protein or even in different proteins) seems to be a more difficult task. Nevertheless, this approach may become a promising alternative for development of a live attenuated marker vaccine against PRRS [8].

PROMISING BIOTECHNOLOGICAL PLATFORMS FOR CREATING CANDIDATE VACCINES

Table 4 provides main characteristics of some candidate vaccines against PRRS, developed on various biotechnological platforms.

CONCLUSION

Thus, at the current stage of PRRS pathogenesis study, three major challenges in developing more efficient next-generation vaccines can be identified: insufficient understanding of immune protection mechanisms, the virus's ability to induce negative regulatory signals for the immune system and its substantial antigenic variability [59]. In particular, the last factor is the reason behind poor efficacy of the existing vaccines against heterologous infection. Further in-depth analysis of the host's immune response, as well as the identification of T- and B-cell epitopes in PRRSV structure, will ensure rational design of genetically engineered vaccines and ultimately attaining the optimal safety-efficacy profile.

REFERENCES

1. Glazunova A. A., Korogodina E. V., Sevskikh T. A., Krasnova E. A., Kukushkin S. A., Blokhin A. A. Reproductive and respiratory syndrome of pigs in pig breeding enterprises (review). *Agricultural Science Euro-North-East*. 2022; 23 (5): 600–610. https://doi.org/10.30766/2072-9081.2022.23.5.600-610 (in Russ.)

2. Butler J. E., Lager K. M., Golde W., Faaberg K. S., Sinkora M., Loving C., Zhang Y. I. Porcine reproductive and respiratory syndrome (PRRS): an immune dysregulatory pandemic. *Immunologic Research.* 2014; 59: 81–108. https://doi.org/10.1007/s12026-014-8549-5

3. Raev S., Yuzhakov A., Bulgakov A., Kostina L., Gerasianinov A., Verkhovsky O., et al. An outbreak of a respiratory disorder at a Russian swine farm associated with the co-circulation of *PRRSV1* and *PRRSV2*. *Viruses.* 2020; 12 (10):1169. https://doi.org/10.3390/v12101169

4. Mananov M. Porcine reproductive and respiratory syndrome. *Animal Husbandry of Russia*. 2022; (1): 34–35. https://elibrary.ru/vcsowo (in Russ.)

5. Nan Y., Wu C., Gu G., Sun W., Zhang Y.-J., Zhou E.-M. Improved vaccine against PRRSV: current progress and future perspective. *Frontiers in Microbiology*. 2017; 8:1635. https://doi.org/10.3389/fmicb.2017.01635

6. Wang Y., Liang Y., Han J., Burkhart K. M., Vaughn E. M., Roof M. B., Faaberg *K. S.* Attenuation of porcine reproductive and respiratory syndrome virus strain MN184 using chimeric construction with vaccine sequence. *Virology*. 2008; 371 (2): 418–429. https://doi.org/10.1016/j.virol.2007.09.032

7. Snijder E. J., Kikkert M., Fang Y. Arterivirus molecular biology and pathogenesis. *Journal of General Virology*. 2013; 94 (10): 2141–2163. https://doi.org/10.1099/vir.0.056341-0

8. Fang K., Liu S., Li X., Chen H., Qian P. Epidemiological and genetic characteristics of porcine reproductive and respiratory syndrome virus in South China between 2017 and 2021. *Frontiers in Veterinary Science*. 2022; 9:853044. https://doi.org/10.3389/fvets.2022.853044

9. Yuzhakov A. G., Zhukova E. V., Aliper T. I., Gulyukin A. M. Porcine reproductive respiratory syndrome: situation in Russia. *Pigbreeding*. 2022; (5): 32–35. https://doi.org/10.37925/0039-713X-2022-5-32-35 (in Russ.)

10. Stafford V. V., Raev S. A., Alekseev K. P., Yushakov A. G., Aliper T. I., Zaberezhny A. D., et al. Immunohistochemistry method for the detection porcine reproductive and respiratory virus. *Veterinariya*. 2017; (2): 26–30. https://elibrary.ru/vmtbiz (in Russ.)

11. Du Y., Lu Y., Qi J., Wu J., Wang G., Wang J. Complete genome sequence of a moderately pathogenic porcine reproductive and respiratory syndrome virus variant strain. *Journal of Virology.* 2012; 86 (24): 13883–13884. https://doi.org/10.1128/JVI.02731-12

12. Sandri G. PRRSV sequencing and its use in practice. *Pig333.com: Professional Pig Community.* 5 March 2018. https://www.pig333.com/articles/prrsv-sequencing-and-its-use-in-practice_13422

13. Guo C., Liu X. Editorial: Porcine reproductive and respiratory syndrome virus – animal virology, immunology, and pathogenesis. *Frontiers in Immunology*. 2023; 14: 1194386. https://doi.org/10.3389/fimmu.2023.1194386

14. Zheng Y., Li G., Luo Q., Sha H., Zhang H., Wang R., et al. Research progress on the N protein of porcine reproductive and respiratory syndrome virus. *Frontiers in Microbiology*. 2024; 15:1391697. https://doi.org/10.3389/fmicb.2024.1391697

15. Brinton M. A., Gulyaeva A. A., Balasuriya U. B. R., Dunowska M., Faaberg K. S., Goldberg T., et al. ICTV Virus Taxonomy Profile: *Arteriviridae* 2021. *Journal of General Virology*. 2021; 102 (8):001632. https://doi.org/10.1099/jgv.0.001632

16. Thi Dieu Thuy N., Thi Thu N., Son N. G., Ha L. T. T., Hung V. K., Nguyen N. T., Khoa D. V. A. Genetic analysis of ORF5 porcine reproductive and respiratory syndrome virus isolated in Vietnam. *Microbiology and Immunology.* 2013; 57 (7): 518–526. https://doi.org/10.1111/1348-0421.12067

17. Yim-im W., Anderson T. K., Paploski I. A. D., VanderWaal K., Gauger P., Krueger K., et al. Refining PRRSV-2 genetic classification based on global ORF5 sequences and investigation of their geographic distributions and temporal changes. *Microbiology Spectrum*. 2023; 11 (6): e02916-23. https://doi.org/10.1128/spectrum.02916-23

18. Evans A. B., Loyd H., Dunkelberger J. R., van Tol S., Bolton M. J., Dorman K. S., et al. Antigenic and biological characterization of ORF2-6 variants at early times following PRRSV infection. *Viruses.* 2017; 9 (5):113. https://doi.org/10.3390/v9050113

19. Kappes M. A., Faaberg K. S. PRRSV structure, replication and recombination: origin of phenotype and genotype diversity. *Virology.* 2015; 479–480: 475–486. https://doi.org/10.1016/j.virol.2015.02.012

20. Zhang H., Xiang L., Xu H., Li C., Tang Y.-D., Gong B., et al. Lineage 1 porcine reproductive and respiratory syndrome virus attenuated live vaccine provides broad cross-protection against homologous and heterologous NADC30-like virus challenge in piglets. *Vaccines*. 2022; 10 (5):752. https://doi.org/10.3390/vaccines10050752

21. Shi M., Lam T. T.-Y., Hon C.-C., Hui R. K.-H., Faaberg K. S., Wennblom T., et al. Molecular epidemiology of PRRSV: a phylogenetic perspective. *Virus Research.* 2010; 154 (1–2): 7–17. https://doi.org/10.1016/j.virusres.2010.08.014

22. Pileri E., Mateu E. Review on the transmission porcine reproductive and respiratory syndrome virus between pigs and farms and impact on vaccination. *Veterinary Research.* 2016; 47 (1):108. https://doi.org/10.1186/s13567-016-0391-4

23. Scherbakov A. V., Timina A. M., Chelysheva M. V., Kanshina A. V. Phylogenetic characterization of the virus responsible for atypical reproductive and respiratory syndrome swine outbreak in the Irkutskaya Oblast of the Russian Federation. *Proceedings of the Federal Centre for Animal Health*. 2009; 7: 55–63. https://elibrary.ru/mouigt (in Russ.)

24. Shi M., Lemey P., Singh Brar M., Suchard M. A., Murtaugh M. P., Carman S., et al. The spread of type 2 porcine reproductive and respiratory syndrome virus (PRRSV) in North America: a phylogeographic approach. *Virology*. 2013; 447 (1–2); 146–154. https://doi.org/10.1016/j.virol.2013.08.028

25. Zhou L., Kang R., Zhang Y., Ding M., Xie B., Tian Y., et al. Whole genome analysis of two novel type 2 porcine reproductive and respiratory syndrome viruses with complex genome recombination between lineage 8, 3, and 1 strains identified in Southwestern China. *Viruses.* 2018; 10 (6):328. https://doi.org/10.3390/v10060328

26. Luo Q., Zheng Y., He Y., Li G., Zhang H., Sha H., et al. Genetic variation and recombination analysis of the *GP5* (*GP5a*) gene of PRRSV-2 strains in China from 1996 to 2022. *Frontiers in Microbiology.* 2023; 14:1238766. https://doi.org/10.3389/fmicb.2023.1238766

27. Fan Y.-F., Bai J., Jiang P. Analysis on *GP5* genetic variation of porcine reproductive and respiratory syndrome virus from Shandong Province. *Journal of Domestic Animal Ecology.* 2017; 38 (4): 63–67. http://jcst.magtech.com.cn/EN/Y2017/V38/I4/63 (in Chinese)

28. Murtaugh M. P., Stadejek T., Abrahante J. E., Lam T. T.-Y., Leung F. C.-C. The ever-expanding diversity of porcine reproductive and respiratory syndrome virus. *Virus Research*. 2010; 154 (1–2): 18–30. https://doi.org/10.1016/j.virusres.2010.08.015

29. Kukushkin S. A. Porcine reproductive and respiratory syndrome. Epidemiology and control in the world and in the Russian Federation. *Russian Journal of Veterinary Pathology*. 2006; (4): 89–95. https://elibrary.ru/oedrgf (in Russ.)

30. Stadejek T., Oleksiewicz M. B., Scherbakov A. V., Timina A. M., Krabbe J. S., Chabros K., Potapchuk D. Definition of subtypes in the European genotype of porcine reproductive and respiratory syndrome virus: nucleocapsid characteristics and geographical distribution in Europe. *Archives of Virology*. 2008; 153 (8): 1479–1488. https://doi.org/10.1007/s00705-008-0146-2

31. Frydas I. S., Verbeeck M., Cao J., Nauwynck H. J. Replication characteristics of porcine reproductive and respiratory syndrome virus (PRRSV) European subtype 1 (Lelystad) and subtype 3 (Lena) strains in nasal mucosa and cells of the monocytic lineage: indications for the use of new receptors of PRRSV (Lena). *Veterinary Research*. 2013; 44 (1):73. https://doi.org/10.1186/1297-9716-44-73

32. Balka G., Podgórska K., Brar M. S., Bálint Á., Cadar D., Celer V., et al. Genetic diversity of PRRSV 1 in Central Eastern Europe in 1994–2014: origin and evolution of the virus in the region. *Scientific Reports*. 2018; 8 (1):7811. https://doi.org/10.1038/s41598-018-26036-w

33. Orlyankin B. G., Aliper T. I., Mishin A. M. Infektsionnye respiratornye bolezni svinei: ehtiologiya, diagnostika i profilaktika = Infectious respiratory porcine diseases: etiology, diagnosis and prevention. *Pigbreeding*. 2010; (3): 67–69. https://elibrary.ru/oxoynv (in Russ.)

34. Grechukhin A. N., Zelenukha E. A. Analiz protivoepizooticheskikh meropriyatii pri reproduktivno-respiratornom sindrome svinei (RRRS) na krupnom svinokomplekse = Analysis of antiepizootic measures taken to control porcine reproductive and respiratory syndrome (PRRS) on a large commercial pig farm. *Pigbreeding*. 2011; (4): 54–55. https://elibrary.ru/nvxjej (in Russ.)

35. Lunney J. K., Fang Y., Ladinig A., Chen N., Li Y., Rowland B., Renukaradhya G. J. Porcine reproductive and respiratory syndrome virus (PRRSV): pathogenesis and interaction with the immune system. *Annual Review of Animal Biosciences*. 2016; 4: 129–154. https://doi.org/10.1146/annurev-animal-022114-111025

36. Fiers J., Maes D., Cay A.-B., Vandenbussche F., Mostin L., Parys A., Tignon M. PRRSV-vaccinated, seronegative sows and maternally derived antibodies (II): impact on PRRSV-1 vaccine effectiveness and challenge outcomes in piglets. *Vaccines*. 2024; 12 (3):257. https://doi.org/10.3390/vaccines12030257

37. Rowland R. R. R., Lawson S., Rossow K., Benfield D. A. Lymphoid tissue tropism of porcine reproductive and respiratory syndrome virus replication during persistent infection of pigs originally exposed to virus *in utero*. *Veterinary Microbiology*. 2003; 96 (3): 219–235. https://doi.org/10.1016/j.vetmic.2003.07.006

38. Zimmerman J., Benfield D., Christopher-Hennings J., Dee S., Stevenson G. Porcine reproductive and respiratory syndrome (PRRS). *Hogs, Pigs, and Pork*. August 28, 2019. https://swine.extension.org/porcine-reproductive-and-respiratory-syndrome-prrs

39. Rodríguez-Gómez I. M., Käser T., Gómez-Laguna J., Lamp B., Sinn L., Rümenapf T., et al. PRRSV-infected monocyte-derived dendritic cells express high levels of SLA-DR and CD80/86 but do not stimulate PRRSV-naïve regulatory T cells to proliferate. *Veterinary Research*. 2015; 46 (1):54. https://doi.org/10.1186/s13567-015-0186-z

40. Kanshina A. V., Scherbakov A. V. Serological diagnosis of PRRS: results of participation in international comparative trials. *Veterinary Science Today*. 2012; (2): 26–29. https://elibrary.ru/svjqlj

41. Teifke J. P., Dauber M., Fichtner D., Lenk M., Polster U., Weiland E., Beyer J. Detection of European porcine reproductive and respiratory syndrome virus in porcine alveolar macrophages by two-colour immunofluorescence and in-situ hybridization-immunohistochemistry double labelling. *Journal of Comparative Pathology*. 2001; 124 (4): 238–245. https://doi.org/10.1053/jcpa.2000.0458

42. Pan J., Zeng M., Zhao M., Huang L. Research progress on the detection methods of porcine reproductive and respiratory syndrome virus. *Frontiers in Microbiology*. 2023; 14:1097905. https://doi.org/10.3389/fmicb.2023.1097905

43. Montaner-Tarbes S., del Portillo H. A., Montoya M., Fraile L. Key gaps in the knowledge of the porcine respiratory reproductive syndrome virus (PRRSV). *Frontiers in Veterinary Science*. 2019; 6:38. https://doi.org/10.3389/fvets.2019.00038

44. Park C., Choi K., Jeong J., Chae C. Cross-protection of a new type 2 porcine reproductive and respiratory syndrome virus (PRRSV) modified live vaccine (Fostera PRRS) against heterologous type 1 PRRSV challenge in growing pigs. *Veterinary Microbiology*. 2015; 177 (1–2): 87–94. https://doi.org/10.1016/j.vetmic.2015.02.020

45. Chen N., Li S., Tian Y., Li X., Li S., Li J., et al. Chimeric HP-BPPCC2 containing an *ORF2-6* consensus sequence induces antibodies with broadly neutralizing activity and confers cross protection against virulent NADC30-like isolate. *Veterinary Research*. 2021; 52 (1):74. https://doi.org/10.1186/s13567-021-00944-8

46. Renukaradhya G. J., Meng X.-J., Calvert J. G., Roof M., Lager K. M. Live porcine reproductive and respiratory syndrome virus vaccines: current status and future direction. *Vaccine*. 2015; 33 (33): 4069–4080. https://doi.org/10.1016/j.vaccine.2015.06.092

47. Li J., Miller L. C., Sang Y. Current status of vaccines for porcine reproductive and respiratory syndrome: interferon response, immunological overview, and future prospects. *Vaccines*. 2024; 12 (6):606. https://doi.org/10.3390/vaccines12060606

48. Bajbikov T. Z., Gusev A. A., Dudnikova N. S., Dudnikov S. A., Gavrilova V. L., Kurman I. Ja., et al. Swine reproductive-respiratory syndrome virus strain "BD" for preparing diagnostic and vaccine preparations. Patent No. 2220202 C1 Russian Federation, Int. Cl. C12N 7/00, A61K 39/12. All-Russian Research Institute for Animal Health. No. 2002110976/13. Date of filing: 25.04.2002. Date of publication: 27.12.2003.

49. Bajbikov T. Z., Kukushkin S. A., Baborenko E. P., Dolganova E. K., Gavrilova V. L., Teterin I. A. Inactivated emulsion vaccine against swine's reproductive-respiratory syndrome. Patent No. 2316346 C2 Russian Federation, Int. Cl. A61K 39/12, A61P 31/12, C12N 7/00. All-Russian Research Institute for Animal Health. No. 2006105369/13. Date of filing: 20.02.2006. Date of publication: 10.02.2008. Bull. No. 4.

50. Baborenko Ye. P., Dolganova Ye. K., Gruzdev K. N. Testing of combined vaccines against Aujezsky's disease, porcine reproductive and respiratory syndrome and porcine parvovirus infection for their antigenicity. *Veterinary Science Today*. 2018; (2): 13–17. https://doi.org/10.29326/2304-196X-2018-2-25-13-17

51. Madapong A., Saeng-chuto K., Tantituvanont A., Nilubol D. Safety of PRRSV-2 MLV vaccines administrated via the intramuscular or intradermal route and evaluation of PRRSV transmission upon needle-free and needle delivery. *Scientific Reports.* 2021; 11 (1):23107. https://doi.org/10.1038/s41598-021-02444-3

52. Galeeva A. G., Usoltcev K. V., Khammadov N. I., Nasyrov Sh. M. Design of antigenic composition based on partial E2 glycoprotein of classical swine fever virus. *Veterinarian*. 2024; (1): 28–33. https://elibrary.ru/rdihub (in Russ.)

53. Ahunova A. A., Nasyrov Sh. M., Galeeva A. G., Arutyunyan G. S., Efimova M. A., Gulyukin M. I. Application of direct fluorescent antibodies test in process control of classical swine fever virus master seeds. *Veterinarian*. 2024; (3): 27–33. https://elibrary.ru/mnswgm (in Russ.)

54. Choi J.-C., Kim M.-S., Choi H.-Y., Kang Y.-L., Choi I.-Y., Jung S.-W., et al. Porcine reproductive and respiratory syndrome virus engineered by serine substitution on the 44th amino acid of *GP5* resulted in a potential vaccine candidate with the ability to produce high levels of neutralizing antibody. *Veterinary Sciences.* 2023; 10 (3):191. https://doi.org/10.3390/vetsci10030191

55. Li Y., Li J., He S., Zhang W., Cao J., Pan X., et al. Interferon inducing porcine reproductive and respiratory syndrome virus vaccine candidate protected piglets from HP-PRRSV challenge and evoke a higher level of neutralizing antibodies response. *Vaccines.* 2020; 8 (3):490. https://doi.org/10.3390/vaccines8030490

56. Choi H.-Y., Kim M.-S., Kang Y.-L., Choi J.-C., Choi I.-Y., Jung S.-W., et al. Development of a chimeric porcine reproductive and respiratory syndrome virus (PRRSV)-2 vaccine candidate expressing hypo-glycosylated glycoprotein-5 ectodomain of Korean lineage-1 strain. *Veterinary Sciences.* 2022: 9 (4):165. https://doi.org/10.3390/vetsci9040165

57. Tian D., Cao D., Lynn Heffron C., Yugo D. M., Rogers A. J., Overend C., et al. Enhancing heterologous protection in pigs vaccinated with chimeric porcine reproductive and respiratory syndrome virus containing the full-length sequences of shuffled structural genes of multiple heterologous strains. *Vaccine.* 2017; 35 (18): 2427–2434. https://doi.org/10.1016/j.vaccine.2017.03.046

58. Choi H.-Y., Lee S.-H., Ahn S.-H., Choi J.-C., Jeong J.-Y., Lee B.-J., et al. A chimeric porcine reproductive and respiratory syndrome virus (PRRSV)-2 vaccine is safe under international guidelines and effective both in experimental and field conditions. *Research in Veterinary Science.* 2021; 135: 143–152. https://doi.org/10.1016/j.rvsc.2021.01.012

59. Cruz J. L. G., Zúñiga S., Bécares M., Sola I., Ceriani J. E., Juanola S., et al. Vectored vaccines to protect against PRRSV. *Virus Research*. 2010; 154 (1–2): 150–160. https://doi.org/10.1016/j.virusres.2010.06.017

Received 17.01.2025
Revised 18.02.2025
Accepted 25.03.2025

INFORMATION ABOUT THE AUTHOR / ИНФОРМАЦИЯ ОБ АВТОРЕ

Yulia A. Nikolaeva, Junior Researcher, Laboratory of Viral Anthropozoonoses, Federal Center for Toxicological, Radiation and Biological Safety, Kazan, Republic of Tatarstan, Russia;
https://orcid.org/0009-0007-0105-7171, yulia.nikolaeva111@mail.ru

Николаева Юлия Александровна, младший научный сотрудник лаборатории вирусных антропозоонозов ФГБНУ «ФЦТРБ-ВНИВИ», г. Казань, Республика Татарстан, Россия;
https://orcid.org/0009-0007-0105-7171, yulia.nikolaeva111@mail.ru

Contribution of the author: Nikolaeva Yu. A. – conducting search and analytical work, preparing and writing the review article.

Вклад автора: Николаева Ю. А. – проведение поисково-аналитической работы, подготовка и написание статьи.