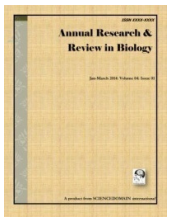

Annual Research & Review in Biology
5(1): 34-40, 2015, Article no.ARRB.2015.004
ISSN: 2347-565X

SCIENCEDOMAIN *international*
www.sciencedomain.org

Diversified Strains of Porcine Reproductive and Respiratory Syndrome Virus Circulating in China: A Mini-overview

Shao-Lun Zhai[1,2], Sheng-Nan Chen[3], Xiao-Hui Wen[1], Dian-Hong Lv[1], Zhong Huang[1], Man-Lin Luo[2*] and Wen-Kang Wei[1*]

[1]Institute of Animal Health, Guangdong Academy of Agricultural Sciences, Guangzhou 510640, China.
[2]College of Veterinary Medicine, South China Agricultural University,Guangzhou 510642, China.
[3]Guangdong Dahuanong Animal Health Products Co., Ltd., Xinxing 527400, China.

Authors' contributions

This work was carried out in collaboration between all authors. Authors SLZ and SNC read literatures, performed sequence alignment analysis and wrote the manuscript. Authors MLL, XHW, DHL, ZH and WKW reviewed and revised the manuscript. Authors SLZ and SNC should be listed as co-first authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/ARRB/2015/9371
Editor(s):
(1) George Perry, Dean and Professor of Biology, University of Texas at San Antonio, USA.
Reviewers:
(1) Alma Lilián Guerrero-Barrera, Centro de Ciencias Básicas, Universidad Autónoma de Aguascalientes, Aguascalientes, México.
(2) Sonia Navas-Martin, Department of Microbiology and Immunology, Drexel University College of Medicine, 245 North 15th Street, Philadelphia, PA 19102, USA.
(3) Anonymous, University of Thessaly, Greece.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=653&id=32&aid=6010

Mini Review Article

Received 5th February 2014
Accepted 13th March 2014
Published 9th September 2014

ABSTRACT

Porcine reproductive and respiratory syndrome virus (PRRSV) was considered as an important pathogen, which caused huge economic losses for the world swine industry annually. Until now, according to antigenic and genetic characteristics, two genotypes were identified, European (EU genotype, or type 1) genotype and North American genotype (NA genotype, or type 2), respectively. In China, both of them co-existed in swine herds, and even some novel viral strains emerged in the lastest years. The aim of the review was to describe genetic diversity of PRRSV based on non-structural protein 2 (Nsp2) in China, which could help us better understand molecular

**Corresponding author: Email: luoml@scau.edu.cn, wwk188@tom.com;*

epidemiology of PRRSV. Moreover, diversified strains of PRRSV circulating in Chinese swine herds might bring serious challenges to PRRS control for government, producers and veterinary practitioners.

Keywords: Porcine reproductive and respiratory syndrome virus; multiple viral strains; European genotype; North American genotype; genetic diversity; China.

1. INTRODUCTION

Porcine reproductive and respiratory syndrome virus (PRRSV) is an enveloped, single-stranded positive-sense RNA virus, which belongs to the family *Arteriviridae* of the order *Nidovirales* [1]. The PRRSV genome is approximately 15 kb in length. The genome possesses a 5'- capped and 3'- polyadenylated region, two untranslated regions (UTRs) at both the 5'- and 3'- ends, and at least nine ORFs [2-4]. ORFs 1a and 1b, close to the 5' UTR, cover most of the genome and encode the large ORF1ab replicase polyprotein whose proteolytic cleavage products relate to virus transcription and replication [5-13]. The remaining ORFs (2a–7) are located at the upstream of the 3' UTR and encode the structural proteins of the virion, including four glycoproteins (GP2a, GP3, GP4 and GP5), two unglycosylated envelope-associated proteins (E and M) and a nucleocapsid protein (N) [14-16].

Porcine reproductive and respiratory syndrome (PRRS) caused by PRRSV is a major negative economic disease on the swine industry worldwide, which emerged in North America in 1987 and in western Europe in 1990, and was isolated in the Netherlands in 1991 [17-18] and subsequently in the United States [19]. Even though the PRRSV isolates on the two continents emerged almost simultaneously, caused similar disease symptoms and shared the same virion morphology, there were lots of differences between European and North American strains antigenically and genetically [20-22]. Thus, two genotypes of PRRSV have been defined: the European (EU genotype, or type 1) and the North American (NA genotype, or type 2) strains [16,23]. Initially, EU PRRSV only existed in Europe, while NA PRRSV was restricted to North America and Asia. However, nowadays, the co-existence of the two genotypes has been identified in Europe, North America and Asia [22,24-29].

2. REVIEW

2.1 North American Type PRRSV (NA PRRSV) in China

2.1.1 Classic NA PRRSV

Since PRRS initial outbreak report in mainland China in 1996 [30], the first Chinese PRRSV isolate (CH-1a, GenBank No. AY032626) (Table 1) was identified, for its non-structural protein (NSP) region, Nsp2 had 86% nucleotide homology with VR-2332 isolate and only 45% nucleotide homology with Lelystad virus (LV) isolate [31]. And then, the first complete genome (15, 504 nt) of Chinese PRRSV strain (BJ-4) (Table 1) was obtained, it had high nucleotide homology (99.5%) with VR-2332 isolate [32]. Moreover, in 2004, the strains of HB-1(sh)/2002 and HB-2(sh)/2002 (Table 1) were also identified, their genomes in length were 15,411 and 15,373 nucleotides, respectively. Interestingly, HB-2(sh)/2002 had specific 12-amino acid (aa) deletion in Nsp2 between aa 471 and aa 482 (Supplementary file 1) in comparison with VR-2332, CH-1a and HB-1(sh)/2002 [33]. In the following, other classic PRRSV strains (such as HK4, HK12, HK13 [34], CH-1R, SD1-100, GM2 and QY2010) (Table 1) were descrided. Among them, in comparison with another classic strains, GM2 and QY2010 had significant differences (two continuous amino-acid deletions at aa 300-301 and 36-amino-acid insertions from aa 817 to aa 852) (Supplementary file 1) [35-36], meanwhile, experimental animal infection confirmed that QY2010 was a highly pathogenic PRRSV [35]. However, in Nsp2 region, both of them had highly nucleotide identity (about 90%) to the representative classic PRRSV strain (VR-2332), while, they had low nucleotide identity (about 88%) to the representative highly pathogenic PRRSV strain (JXA1) [35-36]. Phylogenetic analysis showed classic NA PRRSV strains were clustered together and divided into four subgenotypes (Fig. 1).

2.1.2 Emerging NA PRRSV

Since 2006, devastating large-scale outbreaks of PRRS, characterized by high fever and high morbidity and mortality, have overwhelmed almost all Chinese swine herds. The disease is caused by a highly pathogenic PRRSV (HP-PRRSV) containing a unique discontinuous deletion of 30 aa in Nsp2 [37]. Currently, PRRS has become one of the most significant problems for Chinese swine production, resulting in huge economic losses for pig farmers every year. However, between 2006 and 2011, almost all heretofore described PRRS viruses (including JXA1, HuN4, HZ-31, NJ-1106, NVDC-GD2-2011, NVDC-JS2-2011 and YD) (Table 1) are the HP-PRRSV isolates of the NA genotype in China [38-41]. Of these isolates, besides the two unique discontinuous deletions (1+29) of 30 aa in Nsp2, there were additional 30-, 13-, 19- and 22-aa deletion in the upstream of classic 29-amino acid (aa) deletion region for HZ-31 [42], NVDC-GD2-2011, NVDC-JS2-2011 [43] and YD [44], respectively (Supplementary file 1). Moreover, NJ-1106 had additional deletions of 144 aa (Supplementary file 1) in the downstream of classic 29-aa deletion region [45]. In the phylogenetic tree, those emerging NA PRRSV strains were divided into one separate branch (Fig. 1).

Table 1. Reference sequences of PRRSV in this study

Genotype	GenBank no.	Strain name	Isolation time	Isolation Source	Complete genome (nt)	Nsp2 (nt)	Nsp2 (aa)
NA	AY150564	VR-2332*	1992	USA	15, 451	2, 940	980
	AF176348	PA8	1999	Canada	15, 483	2, 940	980
	AY032626	CH-1a*	1996	China	15, 432	2, 940	980
	AF331831	BJ-4	1997	China	15, 504	2, 937	979
	AY150312	HB-1(sh)/2002	2001	China	15, 447	2, 940	980
	AY262352	HB-2(sh)/2002	2001	China	15, 398	2, 940	980
	KF287134	HK4	2003	Hong Kong	15, 283	2, 940	980
	KF287139	HK12	2004	Hong Kong	15, 369	2, 940	980
	KF287140	HK13	2005	Hong Kong	15, 368	2, 940	980
	GQ914997	SD1-100	2009	China	15, 458	2, 940	980
	JN662424	GM2	2011	China	15, 559	3, 042	1014
	JQ743666	QY2010	2010	China	15, 526	3, 042	1014
	EU807840	CH-1R*	2007	China	15, 424	2, 937	979
	EF112445	JXA1*	2006	China	15, 347	2, 850	950
	EF635006	HuN4*	2007	China	15, 352	2, 850	950
	EF641008	JXwn06	2006	China	15, 374	2, 850	950
	EU097706	NX06	2006	China	15, 358	2, 850	950
	EU097707	BJsy06	2006	China	15, 357	2, 850	950
	JX880029	NJ-1106	2011	China	14, 915	2, 418	806
	KC445138	HZ-31	2012	China	15, 260	2, 763	921
	JQ715697	NVDC-GD2-2011	2011	China	15, 315	2, 814	938
	JQ715698	NVDC-JS2-2011	2011	China	15, 295	2, 793	931
	JF748717	YD	2009	China	15, 266	2, 784	928
	JF748718	DC	2010	China	15, 337	2, 847	949
EU	M96262	LV*	1991	Netherlands	15, 111	2, 583	861
	AY366525	EuroPRRSV*	2003	USA	15, 047	2, 532	844
	FJ349261	KNU-07	2007	Korea	15, 038	2, 523	841
	JF276434	Cresa3266	1996	Germany	14, 736	2, 583	861
	DQ864705	01CB1	2001	Thailand	14, 943	2, 583	861
	EU076704	HKEU16	2007	Hong Kong	15, 047	2, 583	861
	GU047344	BJEU06-1	2006	China	15, 059	2, 568	856
	GU047345	NMEU09-1	2009	China	15, 068	2, 577	859
	JX187609	NVDC-NM1-2011	2011	China	15, 081	2, 568	856

*Note: * Vaccine strain*

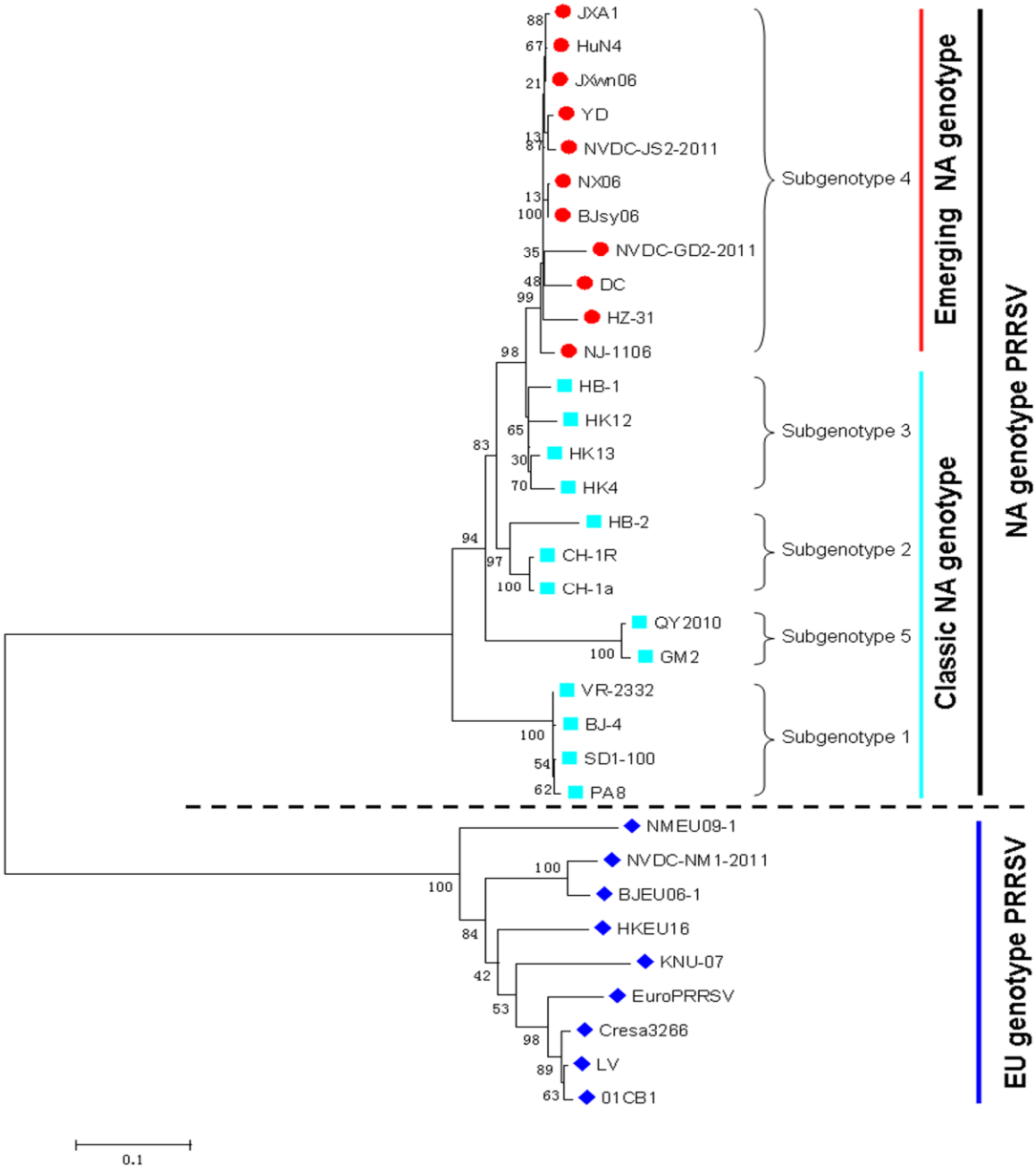

Fig. 1. Phylogenetic analysis of Nsp2 genes of NA-PRRSV and EU-PRRSV isolates. The Phylogenetic tree was constructed by using the neighbor-joining method with MEGA 5.1 software. The reliability of the different phylogenetic groupings was evaluated by using the bootstrap test (1000 bootstrap replications). Note: The isolates belonged to Classic NA PRRSV, emerging NA PRRSV and EU PRRSV were labelled by "■", "●" and "◆", respectively

2.2 European Type PRRSV (EU PRRSV) in China

Before 2011, although few partial sequences of European type PRRSV isolated in mainland China, such as B13, Ningbo42, FJ0603 and HKEU16 (GenBank nos. AY633973, EF473137, EF592535 and EU076704, respectively) have been submitted to GenBank, as yet European type PRRSV isolation and analysis have not been reported in the Chinese mainland. However, in 2011, Chen et al. firstly reported the evidence

for the presence of EU PRRSV in mainland China [46]. Complete genome sequences were determined for BJEU06-1 and NMEU09-1 isolates, they had 15, 059- and 15, 068-nt genome in length, respectively (Table 1). And then, the strain of NVDC-NM1-2011 (15, 081-nt genome) (Table 1) was also reported in 2013 [47]. Compared with EU PRRSV prototypic strain Lelystad virus (LV), among the above three isolates, BJEU06-1 and NVDC-NM1-2011 had the same size of Nsp2 (2, 568 nt, 856 aa) (Table 1). Interestingly, there were two unique discontinuous deletions (4+1) of 5 aa in Nsp2 of BJEU06-1 and NVDC-NM1-2011 (Supplementary file 2), meanwhile, they had high nt identity (95.1%) and aa identity (92.5%) for Nsp2 region. However, NMEU09-1 with 2 aa deletion (Supplementary file 2) had low nt identity (77.9%-78.9%) and aa identity (72.7%-72.9%) with them for Nsp2 region. Phylogenetic analysis results also showed that EU PRRSV strains were clustered together (Fig. 1).

3. CONCLUSION

In this overview, we selected Nsp2 region (one of variable region) as a study object. The results suggested that lots of diversified strains of PRRSV circulated in Chinese swine herds. Overally, they were not only isolated from NA PRRSV but EU PRRSV. Notably, those strains from NA PRRSV were divided into at least five subgenotypes, subgenotype 1 to subgenotype 5, respectively. Based on these evidences, a series of NA PRRSV vaccines (attenuated vaccine and inactivated vaccine) were developed and used in Chinese swine herds, such as VR-2332, CH-1a, CH-1R, R98, JXA1, HuN4, TJM-F92. There was no doubt that vaccination could help us reduce the occurrence of PRRS and improve sow longevity and semen quality [48-51], meanwhile, under vaccination pressure, it might lead to more and more emerging PRRS viral strains [35,36,42-44]. In the recent years, EU PRRS also emerged in China, however, the commercial vaccines were not available in the market. For the control of PRRS, at least in China, we still face serious challenges.

ACKNOWLEDGEMENTS

This review is part of the work supported by grants (No. 2011B050700007, No. 2012A061100006, No. 2012A020601010, No. 2012224-26 and No. 2013GB2E000352) funded by Guangdong Provincial Department of Science and Technology, Guangzhou Science and Technology and Information Bureau, and Ministry of Science and Technology of the People´s Republic of China, respectively.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Cavanagh D. Nidovirales: A new order comprising *Coronaviridae* and *Arteriviridae*. Arch Virol. 1997;142(3):629–33.
2. Conzelmann KK, et al. Molecular characterization of porcine reproductive and respiratory syndrome virus, a member of the Arterivirus group. Virology. 1993;193(1):329–39.
3. Meulenberg JJ, et al. Lelystad virus, the causative agent of porcine epidemic abortion and respiratory syndrome (PEARS), is related to LDV and EAV. Virology. 1993;192(1):62–72.
4. Snijder EJ, Meulenberg JJ. The molecular biology of arteriviruses. J Gen Virol. 1998;79(Pt 5): 961–79.
5. Snijder EJ, et al. The arterivirus Nsp2 protease. An unusual cysteine protease with primary structure similarities to both papain-like and chymotrypsin- like proteases. J Biol Chem. 1995; 270(28):16671–6.
6. Snijder EJ, et al. The arterivirus Nsp4 protease is the prototype of a novel group of chymotrypsin-like enzymes, the 3C-like serine proteases. J Biol Chem. 1996;271(9):4864–71.
7. van Dinten LC, et al. Processing of the equine arteritis virus replicase ORF1b protein: Identification of cleavage products containing the putative viral polymerase and helicase domains. J Virol. 1996;70(10):6625–33.
8. Wassenaar AL et al. Alternative proteolytic processing of the arterivirus replicase ORF1a polyprotein: Evidence that NSP2 acts as a cofactor for the NSP4 serine protease. J Virol. 1997;71(12):9313–22.
9. Snijder EJ. The arterivirus replicase. The road from RNA to protein(s), and back again. Adv Exp Med Biol. 1998;440:97–108.

10. Allende R et al. North American and European porcine reproductive and respiratory syndrome viruses differ in nonstructural protein coding regions. J Gen Virol. 1999;80(Pt 2):307–15.
11. Wootton S, Yoo D, Rogan D. Full-length sequence of a Canadian porcine reproductive and respiratory syndrome virus (PRRSV) isolate. Arch Virol. 2000;145(11):2297–323.
12. Ziebuhr J, Snijder EJ, Gorbalenya AE. Virus-encoded proteinases and proteolytic processing in the Nidovirales. J Gen Virol. 2000;81(Pt 4):853–79.
13. Fang Y, Snijder EJ. The PRRSV replicase: Exploring the multifunctionality of an intriguing set of nonstructural proteins. Virus Res. 2010;154(1–2):61–76.
14. Meulenberg JJ, et al. Characterization of proteins encoded by ORFs 2 to 7 of Lelystad virus. Virology. 1995;206(1):155–63.
15. Murtaugh MP, Elam MR, Kakach LT. Comparison of the structural protein coding sequences of the VR-2332 and Lelystad virus strains of the PRRS virus. Arch Virol. 1995;140(8):1451–60.
16. Nelsen CJ, Murtaugh MP, Faaberg KS. Porcine reproductive and respiratory syndrome virus comparison: Divergent evolution on two continents. J Virol. 1999;73(1):270–80.
17. Keffaber KK. Reproductive failure of unknown etiology. Am Assoc Swine Prac News. 1989:1(2): 1–10.
18. Wensvoort G, et al. Mystery swine disease in The Netherlands: The isolation of Lelystad virus. Vet Q. 1991;13(3):121–30.
19. Collins JE et al. Isolation of swine infertility and respiratory syndrome virus (isolate ATCC VR-2332) in North America and experimental reproduction of the disease in gnotobiotic pigs. J Vet Diag Invest. 1992;4(2):117–26.
20. Rossow KD. Porcine reproductive and respiratory syndrome. Vet Pathol. 1998;35(1):1–20.
21. Forsberg R, et al. The genetic diversity of European type PRRSV is similar to that of the North American type but is geographically skewed within Europe. Virology. 2002;299(1): 38–47.
22. Ropp SL et al. Characterization of emerging European-like porcine reproductive and respiratory syndrome virus isolates in the United States. J Virol. 2004;78(7):3684–703.
23. Meng XJ, et al. Phylogenetic analyses of the putative M (ORF 6) and N (ORF 7) genes of porcine reproductive and respiratory syndrome virus (PRRSV): implication for the existence of two genotypes of PRRSV in the U.S.A. and Europe. Arch Virol. 1995;140(4): 745–55.
24. Dewey C, et al. Lelystad-like strain of porcine reproductive and respiratory syndrome virus (PRRSV) identified in Canadian swine. Can Vet J. 2000;41(6):493–4.
25. Fang Y, et al. Diversity and evolution of a newly emerged North American type 1 porcine arterivirus: Analysis of isolates collected between 1999 and 2004. Arch Virol. 2007;152(5):1009–17.
26. Balka G, et al. Genetic diversity of porcine reproductive and respiratory syndrome virus strains circulating in Hungarian swine herds. Vet Microbiol. 2008;127(1–2):128–35.
27. Amonsin A, et al. Comparative analysis of complete nucleotide sequence of porcine reproductive and respiratory syndrome virus (PRRSV) isolates in Thailand (US and EU genotypes). Virol J. 2009; 6(1):143.
28. Cha SH, et al. Molecular characterization of recent Korean porcine reproductive and respiratory syndrome (PRRS) viruses and comparison to other Asian PRRS viruses. Vet Microbiol. 2006;117(2–4):248–57.
29. Kim HK, et al. Genetic analysis of ORF5 of recent Korean porcine reproductive and respiratory syndrome viruses (PRRSVs) in viremic sera collected from MLV-vaccinating or non-vaccinating farms. J Vet Sci. 2009;10(2):121–30.
30. Guo BQ, et al. Isolation of PRRSV from aborted fetus with typical clinical PRRS manifestations. Chin J Prev Vet Med. 1996;2:1–5. (in Chinese).
31. Liu GQ, et al. Molecular cloning and genetic characteristics of non-structural genes of CH-1a strain of Porcine reproductive and respiratory syndrome virus (PRRSV). Chin J Prev Vet Med. 2000;S1:78. (in Chinese).
32. Yang HC, et al. Sequencing of Genome of Porcine reproductive and respiratory syndrome virus (PRRSV) isolate BJ-4. J Agricul Biotechnol. 2001;9(3):212–18. (in Chinese)
33. Gao ZQ, Guo X, Yang HC. Genomic

characterization of two Chinese isolates of porcine respiratory and reproductive syndrome virus. Arch Virol. 2004;149(7):1341–51.
34. Shi M, et al. Recombination is associated with an outbreak of novel highly pathogenic porcine reproductive and respiratory syndrome viruses in China. J Virol. 2013;87(19):10904-7.
35. Deng Y, et al. Complete genome sequence of porcine reproductive and respiratory syndrome virus strain QY2010 reveals a novel subgroup emerging in China. J Virol. 2012; 86(14):7719-20.
36. Lu W, et al. Complete genome sequence of a novel variant porcine reproductive and respiratory syndrome virus (PRRSV) strain: Evidence for recombination between vaccine and wild-type PRRSV strains. J Virol. 2012;86(17):9543.
37. Tian K, et al. Emergence of fatal PRRSV variants: Unparalleled outbreaks of atypical PRRS in China and molecular dissection of the unique hallmark. PLoS One. 2007;2(6):e526.
38. Li Y, et al. Genetic variation analysis of porcine reproductive and respiratory syndrome virus isolated in China from 2002 to 2007 based on ORF5. Vet Microbiol. 2009;138(1–2):150–5.
39. Zhou L, et al. Molecular variation analysis of porcine reproductive and respiratory syndrome virus in China. Virus Res. 2009;145(1):97–105.
40. Zhou YJ, et al. Genetic diversity of the ORF5 gene of porcine reproductive and respiratory syndrome virus isolates in China from 2006 to 2008. Virus Res. 2009;144(1–2):136–44.
41. Zhou L, Yang H. Porcine reproductive and respiratory syndrome in China. Virus Res. 2010;154(1–2):31–7.
42. Shen J et al. Complete genome sequence of a novel deletion porcine reproductive and respiratory syndrome virus strain. Genome Announc. 2013;1(4):e00486-13.
43. Zhou Z, et al. Complete genome sequence of two novel Chinese virulent porcine reproductive and respiratory syndrome virus variants. J Virol. 2012;86(11):6373–4.
44. Zhang G, et al. Complete genome sequence of two variant porcine reproductive and respiratory syndrome viruses isolated from vaccinated piglets. J Virol. 2012;86(20):11396–7.
45. Du Y, et al. Complete genome sequence of a moderately pathogenic porcine reproductive and respiratory syndrome virus variant strain. J Virol. 2012;86(24):13883–4.
46. Chen N, et al. Emergence of novel European genotype porcine reproductive and respiratory syndrome virus in mainland China. J Gen Virol. 2011;92(Pt 4):880–92.
47. Zhou Z, et al. Complete genome sequence of a European genotype porcine reproductive and respiratory syndrome virus in China. Genome Announc. 2013;1(3):e00175-13.
48. Papatsiros VG, et al. Long-term administration of a commercial porcine reproductive and respiratory syndrome virus (PRRSV)-inactivated vaccine in PRRSV-endemically infected sows. J Vet Med B Infect Dis Vet Public Health. 2006;53(6):266-72.
49. Papatsiros VG, et al. Impact of a porcine reproductive and respiratory syndrome inactivated vaccine on the health and semen traits of boars. J Hell Vet Med Soc, 2011; 62(3):221-28.
50. Papatsiros VG. Impact of a killed PRRSV vaccine on sow longevity in a PRRSV infected swine herd. J App Anim Res. 2012;40(4):297-304.
51. Papatsiros VG. Porcine herd health management practices for the control of PRRSV infection. In: A Bird's-Eye View of Veterinary Medicine, Perez-Marin CC. (Ed.). 2012;281-300. ISBN: 978-953-51-0031-7.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=653&id=32&aid=6010