Virus Research 197 (2015) 35–47

Contents lists available at ScienceDirect

Virus Research

journal homepage: www.elsevier.com/locate/virusres

Review

Studying classical swine fever virus: Making the best of a bad virus

Wei Ji[a,*], Zhen Guo[b], Nai-zheng Ding[a], Cheng-qiang He[a,*]

[a] College of Life Science, Shandong Normal University, Jinan 250014, China
[b] Department of Computer and Information Science, Fordham University, Bronx, NY 10458, USA

ARTICLE INFO

Article history:
Received 30 September 2014
Received in revised form 2 December 2014
Accepted 4 December 2014
Available online 12 December 2014

Keywords:
Classical swine fever virus
Epidemiology
Reverse genetics
CSFV life cycle
Protein functions
Virulence

ABSTRACT

Classical swine fever (CSF) is a highly contagious and often fatal disease that affects domestic pigs and wild boars. Outbreak of CSF can cause heavy economic losses to the pig industry. The strategies to prevent, control and eradicate CSF disease are based on containing the disease through a systematic prophylactic vaccination policy and a non-vaccination stamping-out policy. The quest for prevention, control and eradication of CSF has moved research forward in academia and industry, and has produced noticeable advances in understanding fundamental aspects of the virus replication mechanisms, virulence, and led to the development of new vaccines. In this review we summarize recent progress in CSFV epidemiology, molecular features of the genome and proteome, the molecular basis of virulence, and the development of anti-virus technologies.

Contents

1. Patterns of CSF epidemics and vaccine strategies

Classical swine fever (CSF), formerly called hog cholera (HC), is an economically important, highly contagious disease of pigs, which is listed by the World Organization for Animal Health (OIE) Terrestrial Animal Health Code and must be reported to the OIE. CSF was first recognized in Tennessee, USA in 1810 (Agriculture, 2010; OIE, 2014), and then rapidly spread around the world (reviewedin Edwards et al., 2000). Although it had been successfully eradicated from Canada (1963), the United States (1978), Australia and New Zealand, it still exacts severe impacts in Asia, South America, eastern Europe and parts of the former Soviet Union (Fig. 1).

The etiological agent of CSF is classical swine fever virus (CSFV), which belongs to the genus *Pestivirus*, family *Flaviviridae*, together with bovine viral diarrhea virus (BVDV) and border disease virus (BDV) (Rice, 2001). Strategies to control CSFV mainly consist of a stamping out policy (non-vaccination) and a systematic prophylactic vaccination (see Edwards et al., 2000; Huang et al., 2014 for reviews). Under the non-vaccination policy, a CSFV outbreak always cause huge economic losses in areas with high-densities of pigs (see Dong and Chen, 2007 for a review). Therefore, many countries, except those in the European Union, use a systematic

* Corresponding authors at: Shandong Normal University, College of Life Science, Eastern Wenhua Road 88, Jinan 250014, China. Tel.: +86 0531 86188690.
E-mail addresses: jiwei.yunlong@126.com, 651444115@qq.com (W. Ji), hchqiang@126.com (C.-q. He).

http://dx.doi.org/10.1016/j.virusres.2014.12.006
0168-1702/

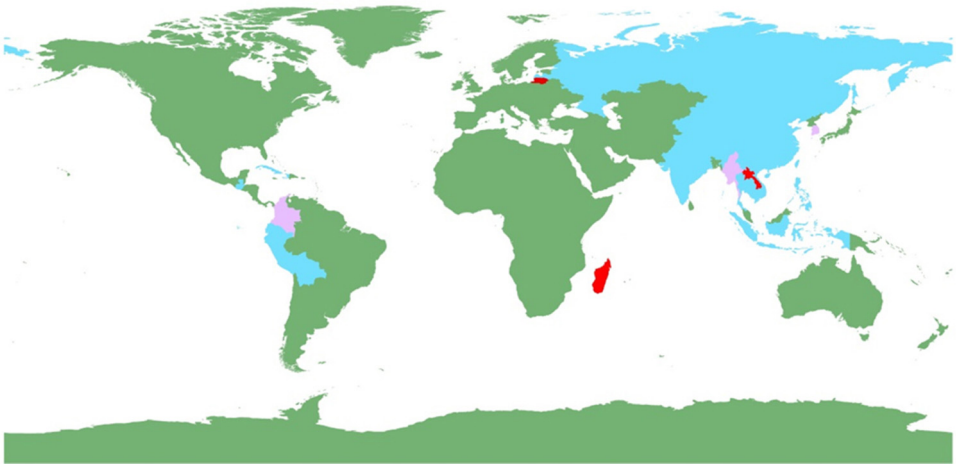

Fig. 1. Global distribution of CSF epidemics during 2011–2014 based on data from the OIE's new World Animal Health Information System (WAHIS). Four countries (red) reported CSF outbreaks in 2011–2012: Madagascar, Laos, Singapore and Lithuania. Three countries (lilac) reported CSF outbreaks in 2013–2014: Colombia, Myanmar and Rep. of Korea. Eighteen countries (blue) reported CSF outbreaks in both 2011–2012 and 2013–2014: Bolivia, Cuba, Ecuador, Guatemala, Haiti, Peru, Bhutan, Cambodia, China (People's Rep. of), India, Indonesia, Mongolia, Nepal, Philippines, Thailand, Vietnam, Latvia, and Russia. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

prophylactic vaccination to control or eradicate CSFV (see Van Oirschot, 2003 for a review). For instance, compulsory vaccination is the current policy in China, and vaccination coverage must be over 90% at any time in the year in the swine population (reviewed in Luo et al., in press). Many vaccines were developed after the pathogenic agent of CSF was shown to be a virus in 1904, (see Dong and Chen, 2007 for a review). Modified live vaccines (attenuated CSFV strains produced through serial passage in non-natural hosts; Table 1) have predominately been used and the most common vaccine is the commercial C-strain, because it is more effective and safer than other vaccines, such as the subunit differentiating infected from vaccinated (DIVA) individuals vaccine (see Huang et al., 2014 for a review). The C-strain vaccine up-regulates the antibody level and it also activates T-cell responses, while the subunit E2 vaccine only induces production of an antibody against CSFV (Huang et al., 2014).

Phylogenetic analysis of CSFV strains suggests there are three genotypes (Postel et al., 2012) that can be divided into high virulence, moderate virulence, and low to avirulent strains (the main vaccine strains) (Leifer et al., 2011). The highly virulent and modified live vaccine strains that have been identified belong to genotype 1, while the genotype 2 and 3 strains have moderate and low virulence (Dong and Chen, 2007; Leifer et al., 2011). Genotype 1 CSFV can accumulate many mutations in the field, as demonstrated by our research (Ji et al., 2014) and CSFV outbreaks caused by genotype 2 have been increasing in Europe and Asia (see Huang et al., 2014 for a review). This indicates that subunit E2 vaccines derived from genotype 1 strains may lose their effectiveness against virulent CSFV derived from genotype 2. The C-strain vaccine may continue to be effective for a longer time, due to T-cell responses. The GPE-strain vaccine can obtain pathogenicity by passaging it in pigs (Tamura et al., 2012), when there are mutations and selection

Table 1
The modified live vaccine were produced through serial passage in non-natural hosts.

Modified live vaccine	Country	Original strain	Adapted host	Reference
LPC	China, Taiwan	ROVAC	Rabbit	Lin et al. (1974), Lin et al. (1981)
HPLC	China, Mainland	Shimen	Rabbit	Tc (1980), Zhou (1980)
ROVAC	American		Rabbit	Koprowski et al. (1946)
SFA	British		Rabbit	Baker (1946)
GPE-	Japan	ALD	Swine testicle, bovine testicle and guinea-pig kidney cells, (29–30 °C)	Sasahara et al. (1969), Shimizu et al. (1970)
Thrivel	French	Alfort	Swine cell, Bovine cell (29–30 °C)	LunaisM (1972)
LOM/(Flc-LOM)	Japan	Miyagi(Japna)	Bovine kidney cells	Nishimura et al. (1964), Park et al. (2012)
Pestiffa	French	C-strain	Lamb kidney cells	Terpstra (1992)
SUVAC	Hungary	C-strain	Sheep	Olah (1985), Terpstra, (1992)
Cellpest	Poland	C-strain	PK-15A cell line	Pejsak et al. (1991)
Suiferin C	Former East Germany	C-strain		Dong and Chen (2007)
ЛК	former USSR	C-strain		Dong and Chen (2007)
VADIMUN	USA	C-strain		Dong and Chen (2007)
Riems	Germany	C-strain		Liess (1988)
Duvaxin	Germany			Björklund et al. (1998)
Norden	Mexico			Björklund et al. (1998)
Pestipan				Björklund et al. (1998)
Porcivac	Mexico			Björklund et al. (1998)
PS Poreo	Brazil			Björklund et al. (1998)
Tipest	Slovakia			Björklund et al. (1998)
TVM-1	Czech Republic			Björklund et al. (1998)
Russian LK	Russia			Björklund et al. (1998)

The strain of swine fever virus for the manufacture of a vaccine against classical swine fever, http://www.findpatent.ru/patent/205/2057805.html.