

**Dr Livio Heath** 

OIE Expert for African swine fever (Africa)

### Illegal use of ASF Vaccines

5.2.

Regional training course (Africa) Import risk analysis for African swine fever 9 November – 14 December 2021

Oie

Organisation Mondiale de la Santé Animale

World

Health

Organisation for Animal Organización Mundial de Sanidad Animal

# The Virus



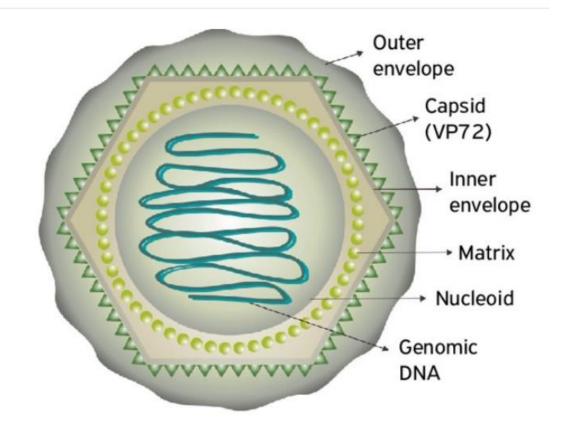
- ASFV virions have a complex multilayer structure
- More than 50 proteins are included in the virion
- Proteins on surface of virus particle are targets for antibody mediated protection
- Multi-Gene Families are involved in virulence and immune modulation

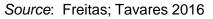
### Genome

Large double-stranded DNA virus

**Genes** Encodes about 151-167 genes

**Proteins of interest** P72, P54, P30, CD2V.





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Source: Karger et al., 2019

# Challenges to ASF vaccine developemnt

S.Z.

- Inactivated ASF virions do not induce protection
- Vaccines developed through serially passaged used in Portugal and Spain in 1960s caused postvaccination reactions in
- Complexity of virus (~160-175 genes encoded. Virus particles contain > 50 proteins in several concentric layers)
- Neutralising antibodies are not effective
- Genetic diversity complexity.
  - Many virus genotypes (24) have been defined by sequence of the gene encoding themajor capsid protein.
  - Lack of cross-protection between genotypes
  - Correlates of protection is not well understood.

# Types of Vaccines

- Live Attenuated Vaccines
  - Inactivation of immuno-modulating gene by recombination
- Recombinant subunit vaccines
  - Production various ASF proteins using viral vectors
- Replication deficient recombinant ASFV vaccine
  - Viral proteins expressed under control of a inducible promoter



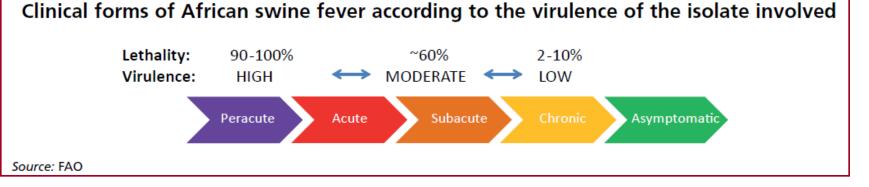




# Naturally Attenuated Viruses



- Acute cases of ASF can result in 100% Mortality
- Acutely infected animals often die before developing antibodies
- Some pigs develop subacute or chronic forms of the disease
- Surviving pigs are immune to re-infection



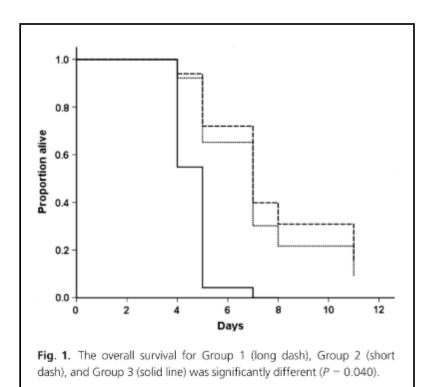
Otroin	Days post infection						
Strain	<b>Clinical Signs</b>	Viraemia	Sero-conversion		Death		
OURT 3/88	ND	ND	7 ø	14 <sup>øø</sup>			
MKUZE /78	7	18	<b>7</b> ø	14 <sup>øø</sup>	18*		
<b>BENIN 1/97</b>	2	3	7 ø		7		
MOZ 1/98	2	3			6		

ND not detected; \* Animals euthanized; <sup>ø</sup> one animal was positive; <sup>øø</sup> all pigs are sero-positive; samples collected

# Naturally Attenuated Viruses



- Surviving pigs are immune to re-infection with the same virus
- Pigs challenged with a different virus are not always protected against re-infection
- Vaccination does delays the onset of disease



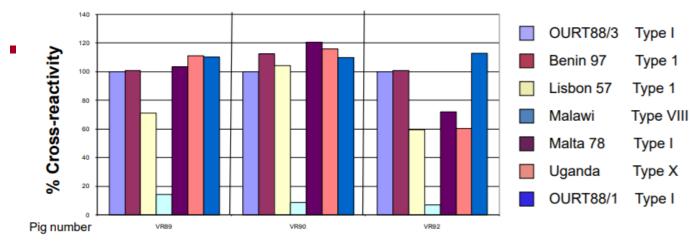
Source: Souto et al. 2014

Table 2.	Characteristics of disease in pigs vaccinated with a live attenu-
ated strai	n (OURT 3/88) and challenged with virulent MOZ 1/98

		Days post-challenge (dpc)					
Groups	No. of pigs	Fever	Clinical Signs	Viraemia*	End point		
Group 1 (vaccinated twice)	6	2	3	3	5–9		
Group 2 (vaccinated once)	6	1–4	3–4	3	5–11		
Group 3 (control group)	3	2	3	3	4–5		

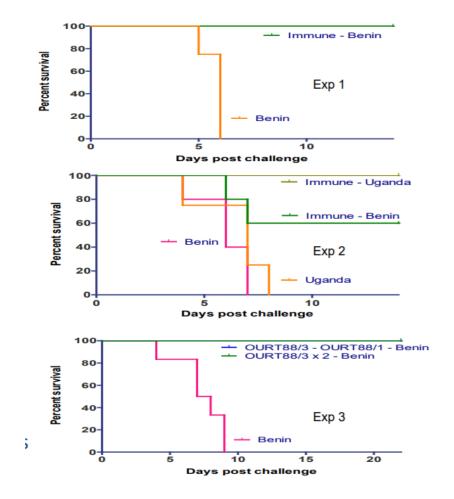
### Live Attenuated Vaccines

- LAV are developed by deleting one or more immune modulating genes
- Pigs challenged with a different virus are not always protected against re-infection



Cross-reactivity of vaccinated pigs

Source: L Dixon et al., 2012





# Sub-unit vaccines



### Recombinant protein vaccines

- Induced antibodies responses
- Partial protection achieved with recombinant proteins expressed in baculovirus:
  - a mixture of proteins p30 and p54 does not fully protect vaccinated pigs
  - CD2-like protein (or haemmaglutinin)
- Delay in onset of disease signs and viraemia, some pigs recover from infection and clear virus

### Viral vector vaccines

- Viral vectors expressing selected ASF proteins *in vivo*
- Induces CTL-responses
- Protects vaccinated pigs from challenges.
- Reduced safety concerns.

### Low-virulent ASF in China



- Surveillance of 22
   ASFVs reveled two non-HAD isolates with lower virulence
- Both viruses were highly transmissible
- Infections resulted in non-lethal chronic disease, and persistence

### Low-virulent Genotype II

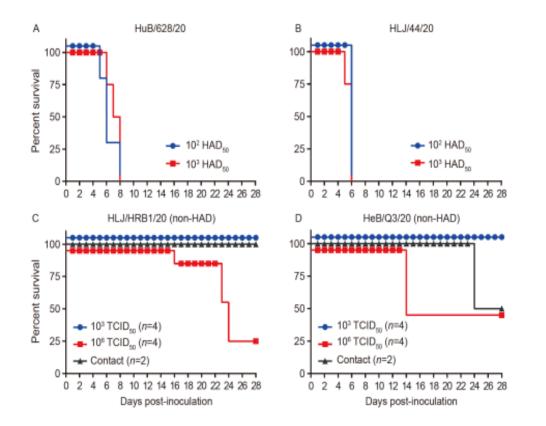
#### Research Paper | Published: 26 February 2021

Emergence and prevalence of naturally occurring lower virulent African swine fever viruses in domestic pigs in China in 2020

Encheng Sun, Zhenjiang Zhang, Zilong Wang, Xijun He, Xianfeng Zhang, Lulu Wang, Wenqing Wang, Lianyu Huang, Fei Xi, Haoyue Huangfu, Ghebremedhin Tsegay, Hong Huo, Jianhong Sun, Zhijun Tian, Wei Xia, Xuewu Yu, Fang Li, Renqiang Liu, Yuntao Guan, Dongming Zhao 🖾 & Zhigao Bu

<u>Science China Life Sciences</u> 64, 752–765 (2021) | <u>Cite this article</u> 660 Accesses | 11 Citations | 15 Altmetric | Metrics

- The viruses contained natural mutations or deletion in the EP402R gene
- Similar approaches have been used to generate LAVs



#### Source: Sun et al. (2021)

# Illegal use of vaccine





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HOG PRODUCTION

New China African Swine Fever Strains Point to Unlicensed Vaccines



Use of Illegal ASF Vaccines in China Causing Worldwide Concern

February 11, 2021







By Ann Reus | April 1, 2021





"Illegal vaccines endanger the eradication of African swine fever in Asia" DATE March 3rd, 2021 CATEGORY

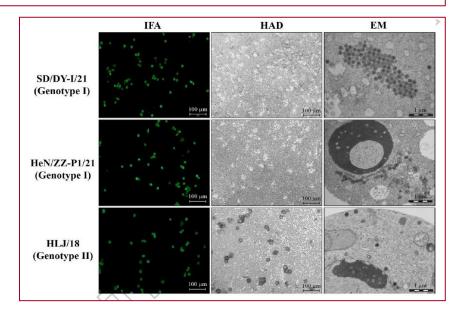
# Illegal use of vaccine

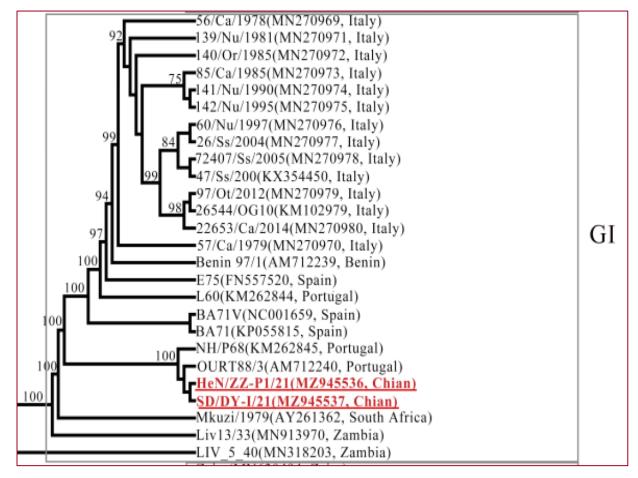


### Low-virulent Genotype I

#### Genotype I African swine fever viruses emerged in domestic pigs in China and caused chronic infection

Emergence of genotype I ASFVs in China.



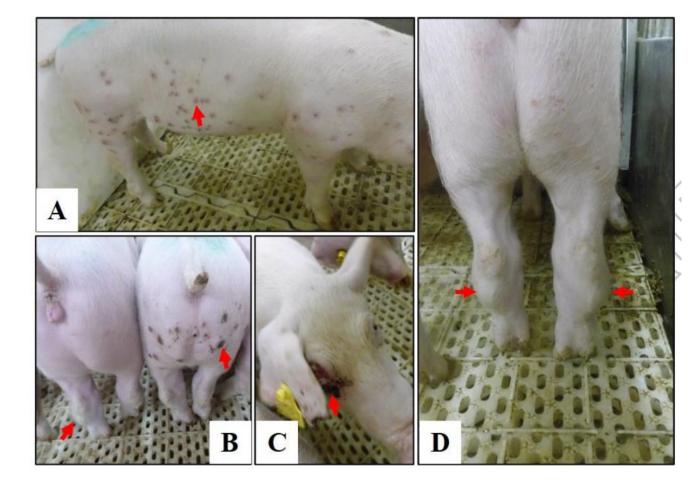


Source: Sun et al. (2021b)

# Chronic African swine fever



- Disease signs in pigs infected with the genotype I isolate SD/DY-I/21
- Clinical signs include papules on the flank and rear
- Cutaneous necrosis
- Arthroncus of hind legs



Source: Sun et al. (2021b)

# Monitoring African Swine Fever Variant Strains

S.Z.

- Triple fluorescent PCR method targeting p72/CD2v/MGF
- A protocol for an I177L gene-specific real time PCR should be included to address potential LAVderived isolates that may be transmitted and circulate
  - EDTA blood or nasal swabs to be collected from live pig.
  - Samples should be tested using real-time PCR protocols to detect LAVs
  - PCR tests should be confirmed by convectional or Whole Genome Sequencing

	Test results				
Comprehensive decision result	P72-FAM	CD2v-VIC	MGF-Cy5		
ASFV epidemic strain positive	+	+	+		
ASFV CD2v gene deletion strain positive	+	-	+		
ASFV MGF gene deletion strain positive	+	+	-		
ASFV CD2v and MGF gene double deletion strain positive	+	-	-		
ASFV negetive	-	-	-		

Source: Dr Zhiliang Wang

### International initiatives

# S.Z.

### Food and Agriculture Organization

 Laboratory diagnosis and surveillance of African swine fever virus: addressing novel emergent variants

### World Organisation for Animal Health

- OIE Reference Laboratory Network for African swine fever
- Open Access Information Sharing Platform for the dissemination African swine fever epidemiological and Genomic information
- Technical support by OIE Reference Laboratories

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United Nations



# Thank you for your attention! f 🖻 🕑 🕞 😶



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World Organisation for Animal Health

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