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IPVS 2018 Digest:

Emerging porcine diseases – the drivers and the dogma

Trevor W Drew, OBE
Animal & Plant Health Agency, Weybridge, United Kingdom
In memory of Dr. T. J. L. Alexander

EIDAs
Center of Emerging and Re-emerging Infectious Diseases in Animals
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zoetis

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25th IPVS CONGRESS CHINA 2018 CHONGQING
Pig

Emerging porcine diseases! Trevor Drew

- Intensification of production
- Expansion of production to new areas
- Integrated animal production
- How to viruses adapt to environment change?
- The influence of mutant spectra in virus evolution

The influence of “mutant spectra” in virus evolution

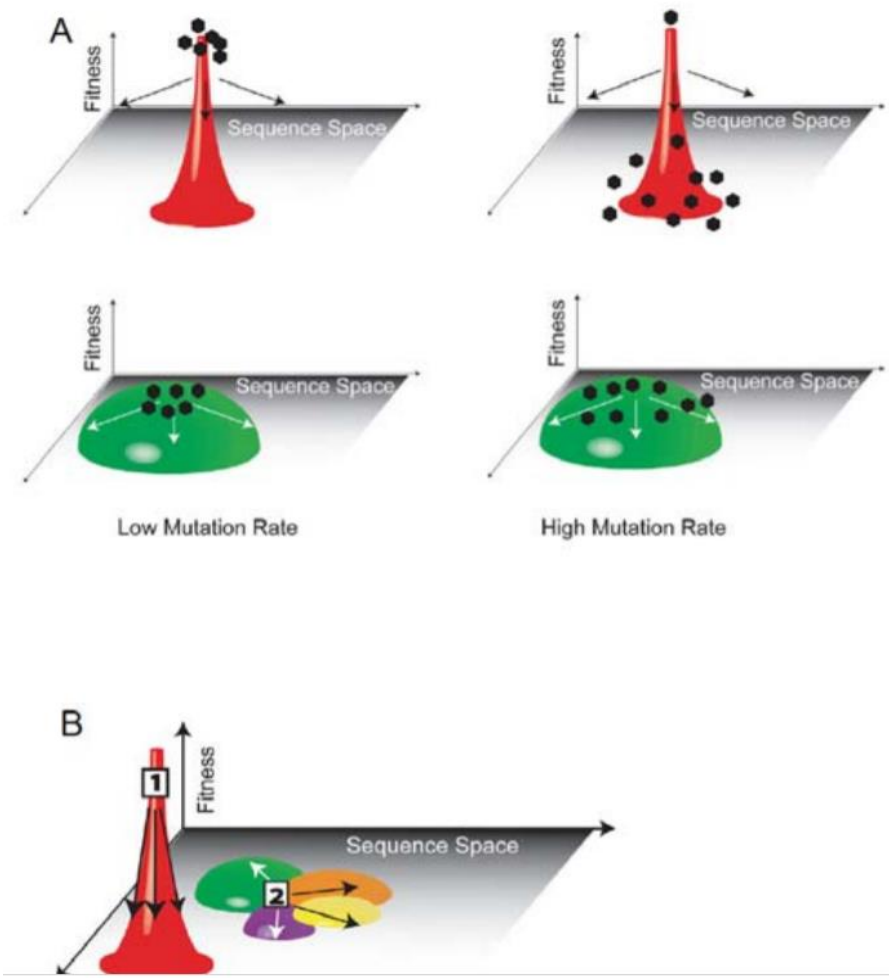


Figure 2. The fitness landscape and “survival of the flattest”.
(A) Virus populations can be of high or low relative fitness for the environment in which they exist and also exhibit high or low mutation rates. At low mutation rates (right), no matter what their fitness, variants will be genotypically stable and cluster at the top of the fitness peak. The variant with the highest fitness will easily outcompete all others. At high mutation rates (left), variants spread out over the corresponding peaks. Variants on the flatter peak (bottom right) remain near their fitness optimum and have a higher mean fitness than the population located on the steeper peak (top right). The flatter population will prevail.
(B) Population 1 has high fitness but is trapped in sequence space because any mutation leads to a dramatic loss of fitness. Population 2 is more mutationally robust because mutation leads only to minor relative fitness loss. This flatter population is ideally situated to move through sequence space and access other local peaks through neighbouring mutational networks. Such viruses are better able to adapt to environmental changes, or new environments. This gives them a greater ability to persist in the host, evade vaccinal immunity and evolve to infect new cell types – or even new hosts.

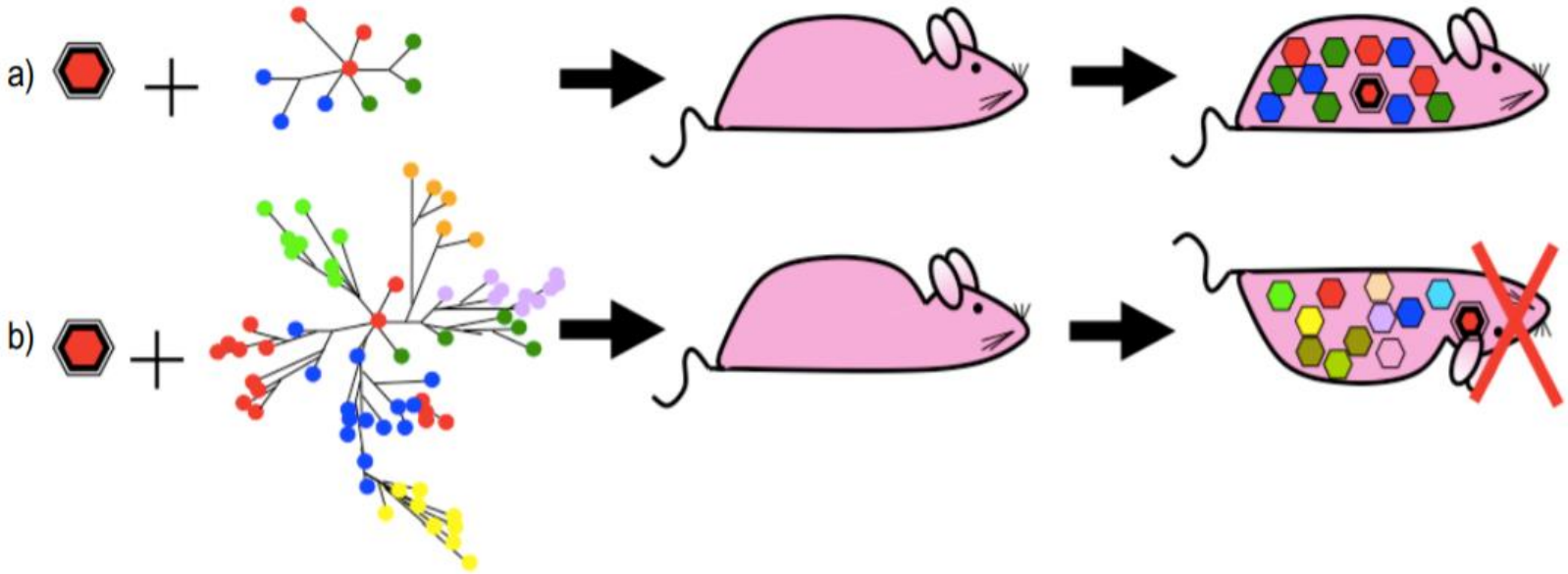
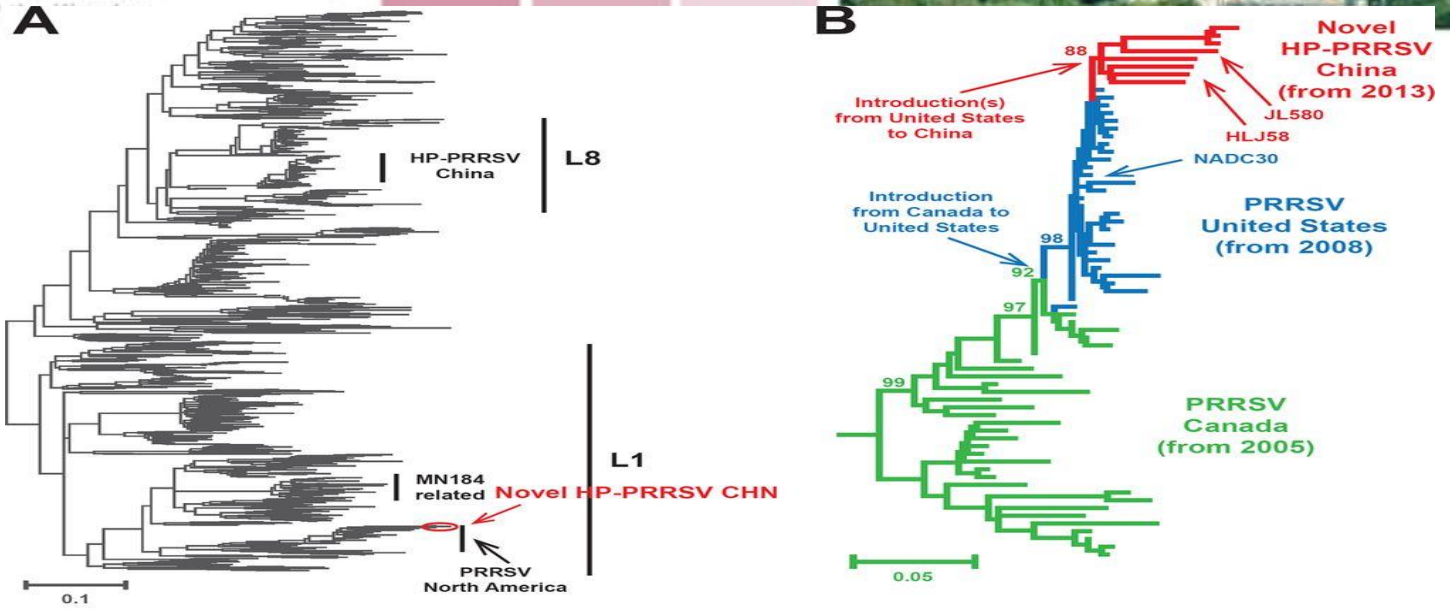
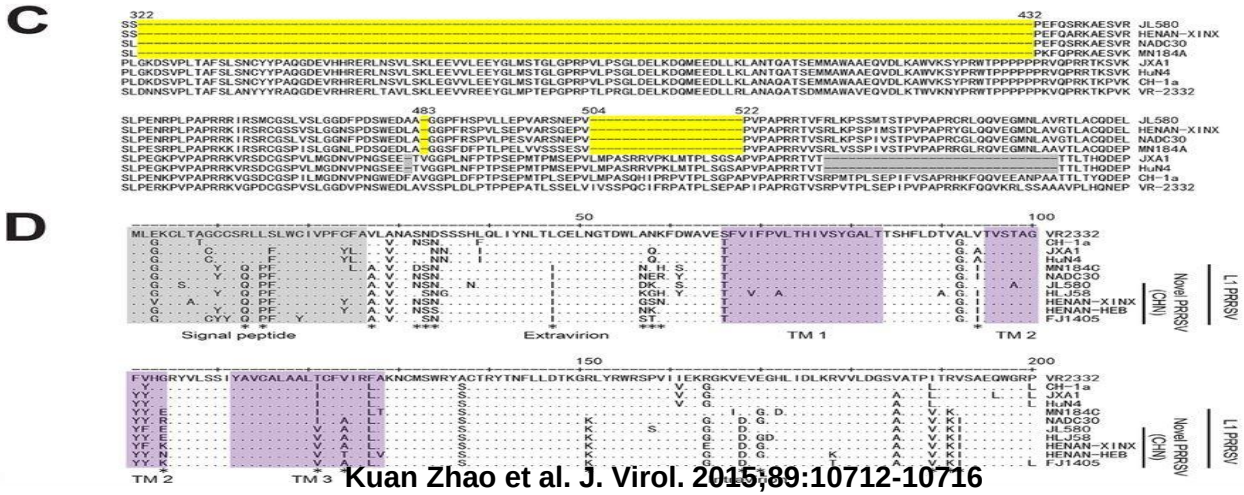


Figure 3. Quasispecies interactions can contribute to pathogenesis [1]. A lethal, neurotropic strain of poliovirus with a polymerase gene with varying fidelity that could be altered *in vitro* was cultured to produce a) a very restricted and b) a very diverse mutant spectrum. When intravenously injected into mice at the same multiplicity of infection, the restricted clade a) was infectious, but did not kill the mice and no poliovirus was isolated from the brains. In contrast, mice infected with the diverse clade b) died and the neurotropic strain was isolated from the brains of the mice. This observation of cooperative interactions between different individuals within the quasispecies provides a rationale for the role of quasispecies diversity in infectivity and pathogenesis.

Genotyping of the HP-PRRSV strain that has newly emerged in China.





Kuan Zhao et al. J. Virol. 2015;89:10712-10716

Journal of Virology

10 yrs with Asf- Lessons learned

Kolbasov et al. (Russia)

- Economy & Human behavior
- Wild boar role (2-5 km/mth)
- No tick role in Eastern EU
- ASF can be controlled & eradicated without vaccine
- Biosecurity & farm structure

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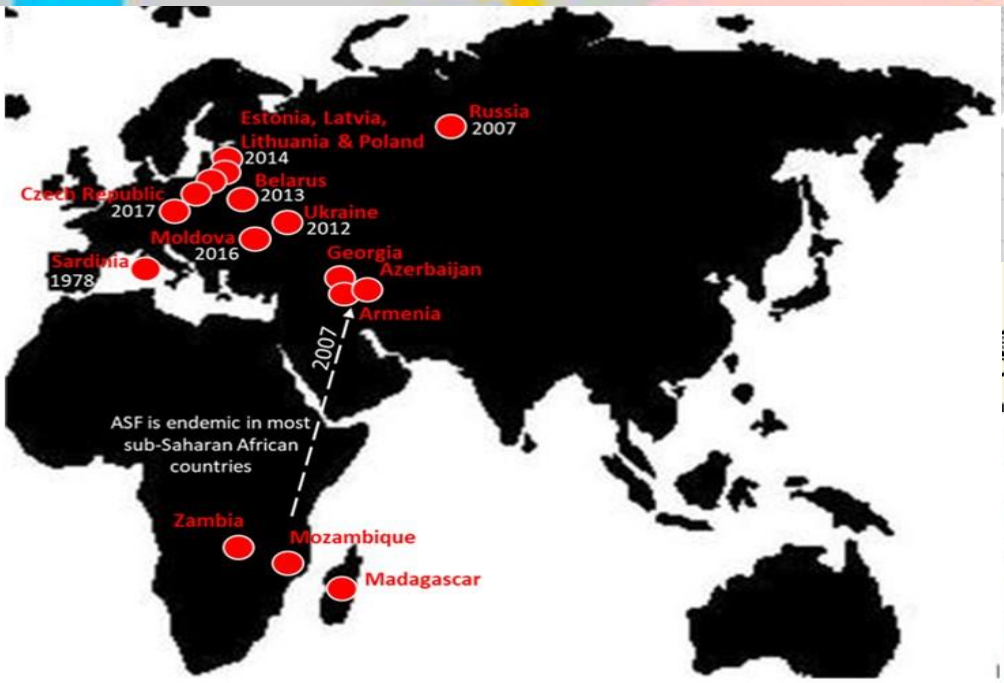
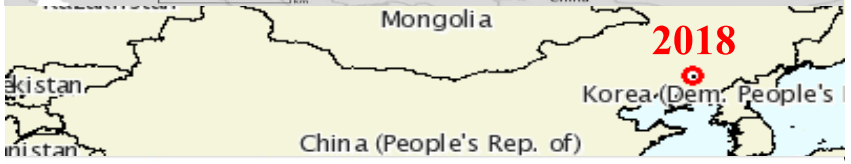


Countries that currently have ASF present in wild and/or domestic swine species. *Since the introductio ASF to Georgia in 2007, the virus has spread throughout Eastern and Central Europe with the most rece emergence in the Czech Republic (2017). Map is based upon the findings of Arias et al., 2017.*



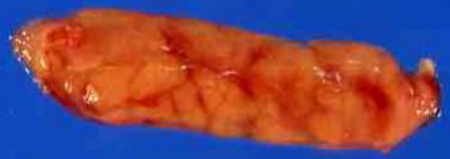
China culls 900 pigs after reports of first African swine fever outbreak in country

News of the infection will stoke concerns about possible spread to Japan and Korean peninsula

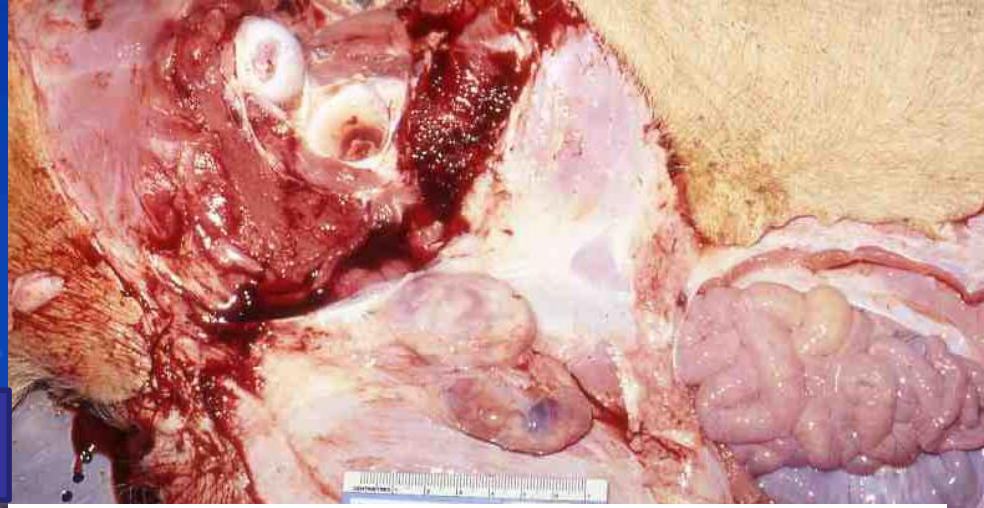
PUBLISHED : Friday, 03 August, 2018, 7:34pm
UPDATED : Friday, 03 August, 2018, 10:30pm

COMMENTS: 3

Thymic atrophy



Classical swine fever

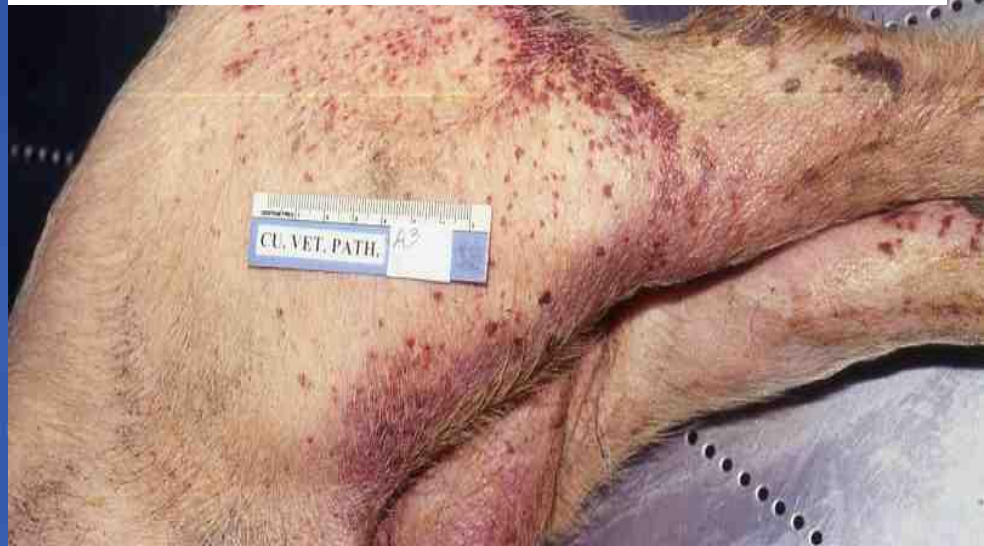


Other Pestiviruses (Paul Becher)

- **BVD, BDV, APPV,**

Bungowannah virus (Australia)

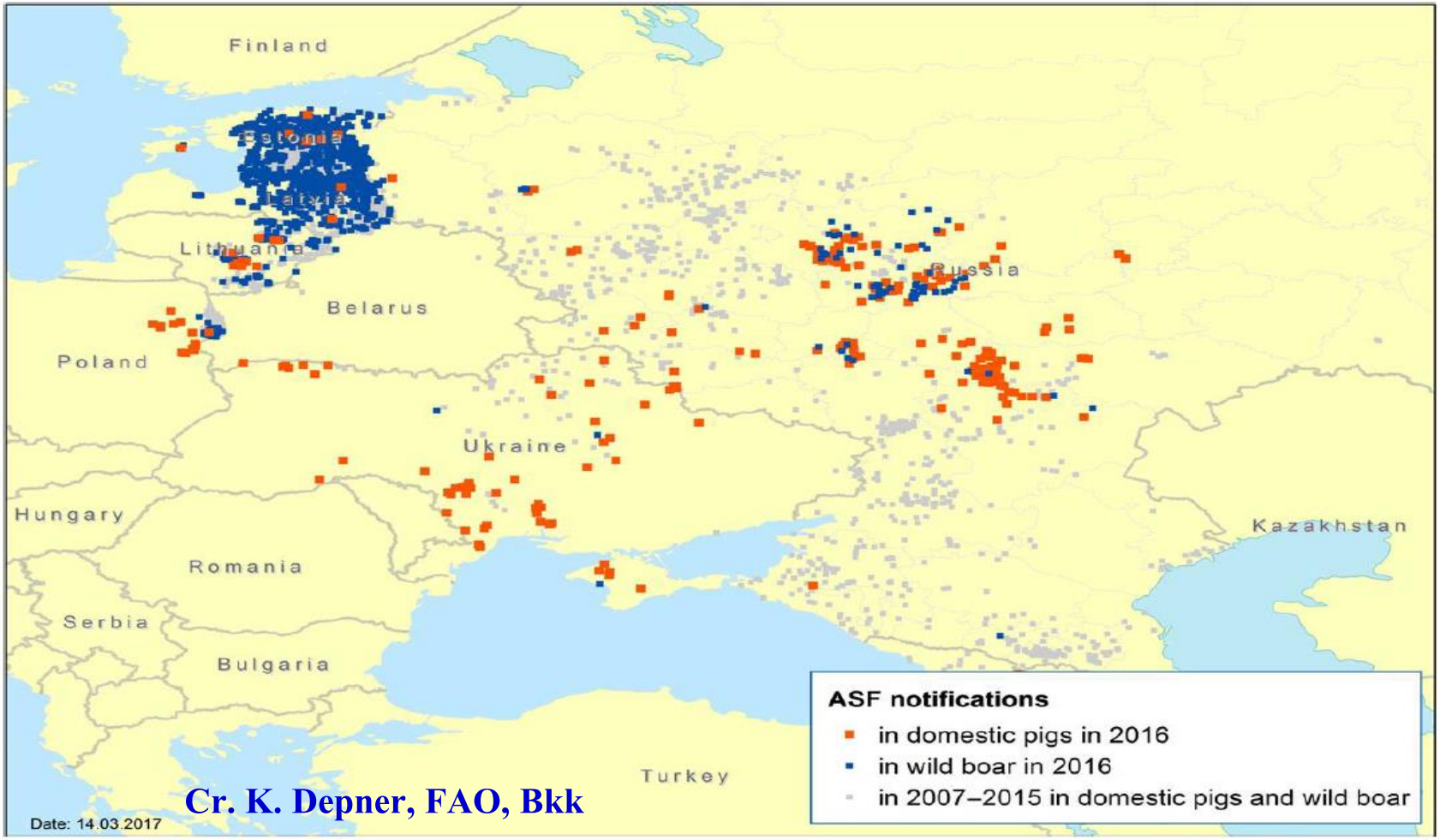
& Linda virus (Eastern EU)



ASF Transboundary movement

- A single introduction of contaminated pork or pork products (Sanchez-Vizcaino & Arias, 2012).
- A movement of free-ranging infected wild boar.
- Illegal movement of infected pigs or the use of contaminated pork products for feeding pigs (Vergne, Gogin, & Pfeiffer, 2015).

Epidemiological „screen shot“ ....



Cr. K. Depner, FAO, Bkk

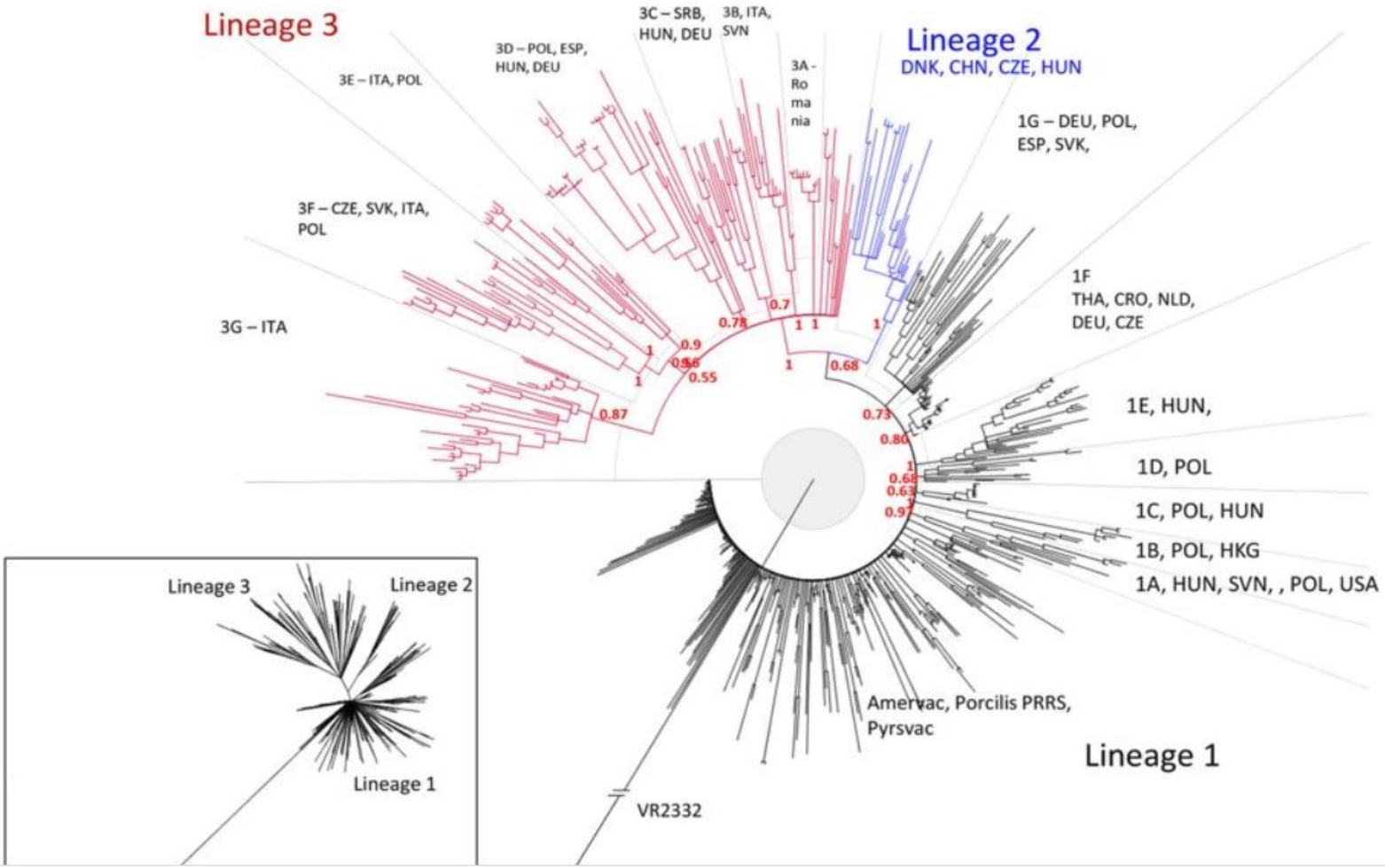
PRRSV Eric mateu

- Innate immunity may be the key!
- IFNα is partially inhibited by viral non-structural protein & vary by strains
- IL10 & TNFα response depending on the strains
- Phagocytic & Killing ability of neutrophils are reduced.

PRRSV Epidemiology: Emergence of new virus strains T. Stadejek

- Genotype 1 (1979) 10 yrs before seeing the disease
- Multiple sources of pigs are at high risk
- Rapid change in pig production in Central Eastern EU countries showing similar PRRSV genetic diversity to Western EU countries

From: Genetic diversity of PRRSV 1 in Central Eastern Europe in 1994–2014: origin and evolution of the virus in the region



Xie, Oh & Nauwynck (Ghent U)

- Changing siglec-usage of PRRSV to enter macrophages, the basis of differences in PRRSV/pathogenicity and evolution?
- Siglec1+CD163+ (Lung & Repro),
- Siglec10+CD163+ (Nasal & CNS)
- Using PK15 as a model on viral titer

HP-PRRSV Pathogenesis Jun Han

- Expanded tissue tropism
- Enhanced ability to induce cell apoptosis
- Aberrant inflammatory cytokine responses
- Predisposition to bacterial infection
- Dysregulation of host immunity
- nsp9 & nsp10 mutation (Δ replication)

Vet Microbiol 209:30-47.

PRRSV

- Gene edited pigs are resistant to PRRSV infection (CD163) Burkard et al.
- Novel mechanisms of PRRSV infection: intercellular transmission & persistence Fang et al. (viral dsRNA persistence in the germinal center allowing the virus to escape)
- PRRSV control-the Danish way: Stable sow herd & management strategies Lar Larsen

Re-emerged pseudorabies virus: what has been changed?

- Genotype 1 : original strain
- Genotype 2 : Chinese isolate (Low efficacy to Bartha vaccine)
- Independent evolution

Article

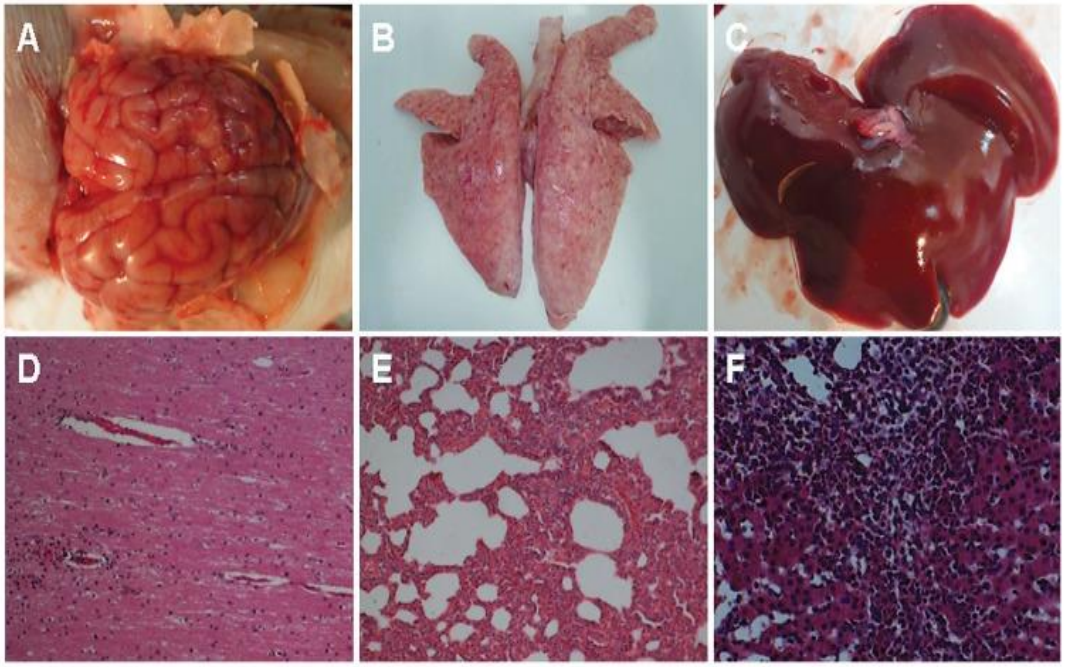
Emergence of highly virulent pseudorabies virus in southern China

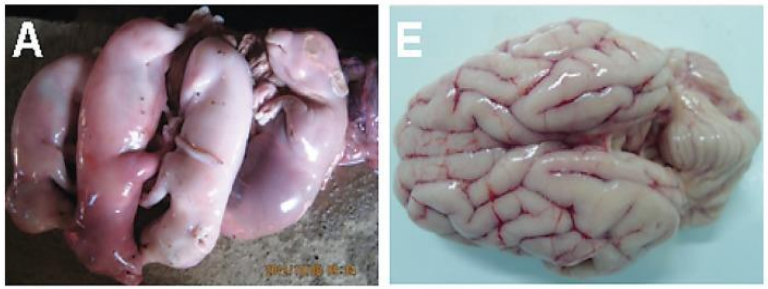
Zhenqing Gu, Chengcai Hou, Haifeng Sun, Wenping Yang, Jing Dong, Juan Bai, Ping Jiang

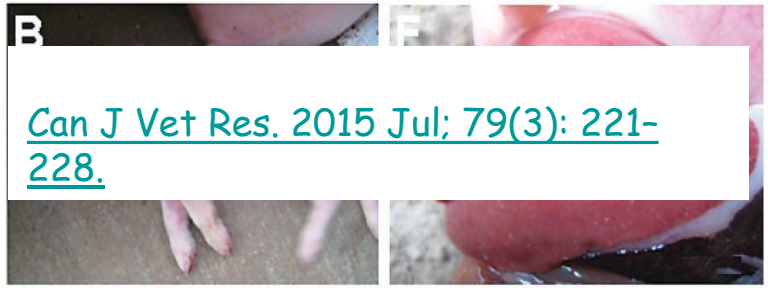
Abstract

Pseudorabies has been controlled efficiently in China for many years by vaccination. However, it suddenly broke out in many pig farms in 2012–2013 in southern China. In this study, a systematic investigation that included virus isolation, genetic and pathological studies, and immunogenicity analysis was carried out with the aim of understanding the pathogenetic and antigenic features of novel isolates of pseudorabies virus (PRV). Of 38 tissue samples collected from pigs with clinical signs of pseudorabies on 13 farms in 4 provinces in southern China in 2012–2013, 29 showed wild-type PRV infection by polymerase chain reaction. Sequence analysis of 5 isolates from the 4 provinces showed that they belonged to a relatively independent cluster that shared 2 insertions of a single amino acid in the *gE* gene and 1 insertion of 7 amino acids in the *gC* gene. In experiments, isolate ZJ01 caused death in 100% of pigs that were either 14 or 80 days old. The serum antibodies to the commercial PRV vaccines had significantly lower neutralizing activity against the ZJ01 isolate than against the vaccine strains. The antigenic relatedness between ZJ01 and the vaccine strains was 0.378 to 0.455. These findings indicated that a novel, highly virulent PRV strain with antigenic variance had spread widely in southern China.

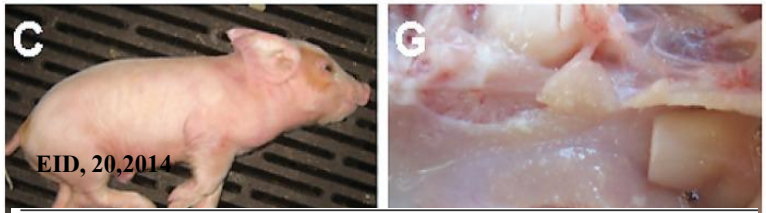
Genotype 2







Can J Vet Res. 2015 Jul; 79(3): 221-228.



EID, 20,2014

DISPATCHES

Pathogenic Pseudorabies Virus, China, 2012

Xiuling Yu,[1] Zhi Zhou,[1] Dongmei Hu,[1] Qian Zhang,[1] Tao Han, Xiaoxia Li, Xiaoxue Gu, Lin Yuan, Shuo Zhang, Baoyue Wang, Ping Qu, Jinhua Liu, Xinyan Zhai, and Kegong Tian

In 2012, an unprecedented large-scale outbreak of disease in pigs in China caused great economic losses to the swine industry. Isolates from pseudorabies virus epidemics in swine herds were characterized. Evidence confirmed that the pathogenic pseudorabies virus was the etiologic agent of this epidemic.

Getah virus from Chinese pigs

- GETV, Alphavirus, a mosquito-borne enveloped RNA virus found in horses & pigs in Korea, Japan
- Malaysia, Mongolia & Russia are primitive strain
- Public health concern

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