





PCV2: recent genotype evolution and update on vaccine implementation efficacy

**Eric Bousquet, DVM
Swine Medical Manager
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- **PCV-2 vaccination since 2006: amazing success**
- **Disease evolution from PMWS to subclinical infection**
- **PCVDs still present**
- **PCV-2 still evolves**
- **Peer reviewed update on virus genotyping and vaccination efficacy**

- **Virus features and evolution**
- **Vaccination efficacy**

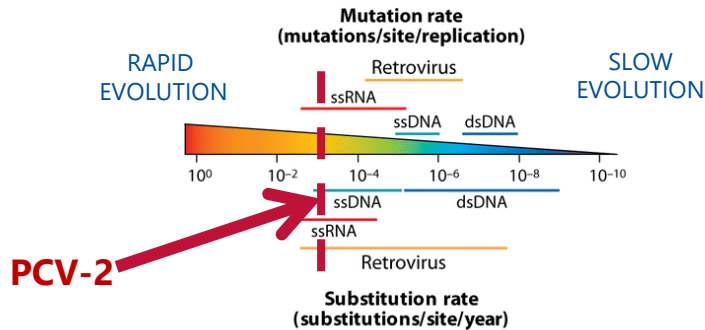
PCV-2: main features

- **Small icosahedral, non enveloped virus**
- **Circular single strand (ss) DNA**
- **Two major genes:**
 - **ORF1: replication**
 - **ORF2: capsid/immunogenicity/taxonomy (genotypes)**
- **High mutation rate**
- **Very resistant (low to high temperatures/disinfectants)**



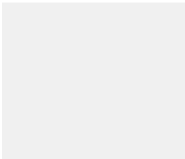
Mutation rates of RNA and DNA viruses

PCV-2: high mutation rate similar to RNA viruses



Holmes ED. 2009.

Annu. Rev. Ecol. Evol. Syst. 40:353–72



Global molecular genetic analysis of porcine circovirus type 2 (PCV2) sequences confirms the presence of four main PCV2 genotypes and reveals a rapid increase of PCV2d

Chao-Ting Xiao,¹ Patrick G. Halbur¹ and Tanja Opriessnig^{1,2}

- **PCV2a dominant worldwide till 2000**
- **Global genotype shift from PCV2a to PCV2b around 2003 simultaneously to an increase of PCV2 systemic disease outbreaks**
- **New genotype shift from PCV2b to PCV2d on going worldwide**
- **PCV2d type includes strains previously named as PCV2b-1C or mPCV2b isolated in EU, USA, Brazil, Asia**

Increase of prevalence of PCV2d from 38% (2012) to 72% (2016) in the USA

Veterinary Microbiology 197 (2016) 72–77



Contents lists available at ScienceDirect

Veterinary Microbiology

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



PCV2d-2 is the predominant type of PCV2 DNA in pig samples collected in the U.S. during 2014–2016



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Molecular Phylogenetics and Evolution

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



Phylogenetic analysis of porcine circovirus type 2 reveals global waves of emerging genotypes and the circulation of recombinant forms



Giovanni Franzo^{a,*}, Marti Cortey^{b,*}, Joaquim Segalés^b, Joseph Hughes^c, Michele Drigo^a

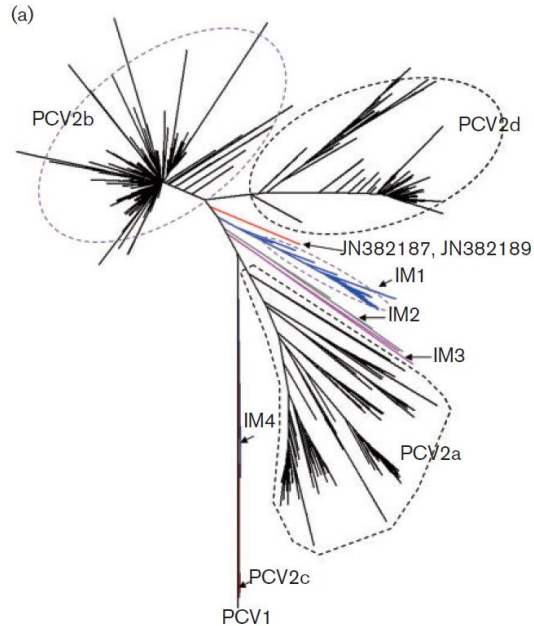
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^c MRC-University of Glasgow Centre for Virus Research, Glasgow, Scotland, United Kingdom

The results of the present study confirm what has recently been suggested by Xiao et al. (2015), namely the current occurrence of a second major “genotype shift”, characterized by the emergence and spread of PCV2d, which appears to be replacing PCV2b (Fig. 3).

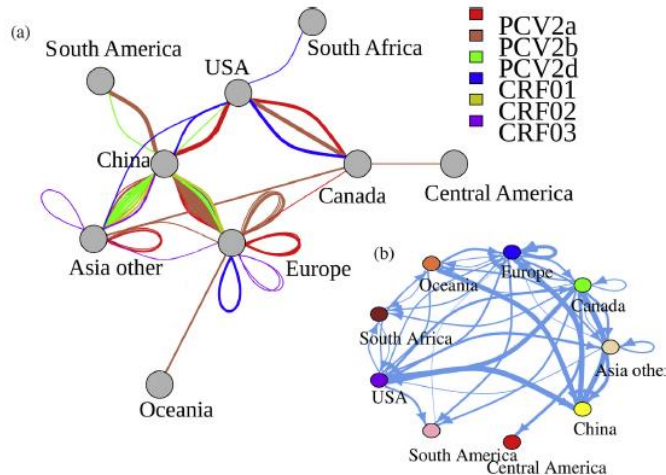
Phylogenetic tree based on 1680 PCV-2 ORF2 sequences



From Xiao *et al* 2015

Global pig trade and spreading of PCV2

G. Franzo et al. / Molecular Phylogenetics and Evolution 100 (2016) 269–280



China seems to be the major PCV2 source for other Asian countries

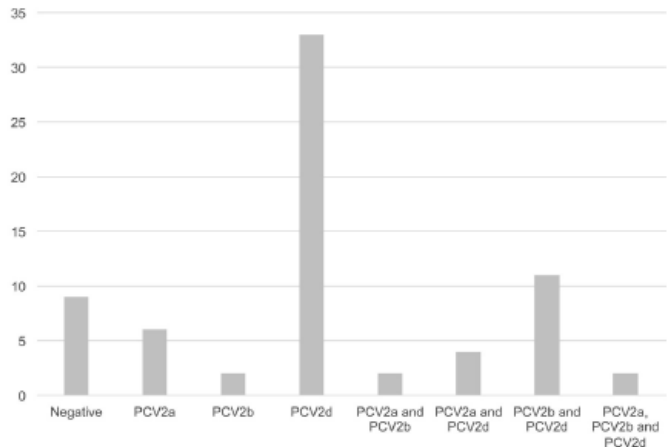


Genotypic diversity of porcine circovirus type 2 (PCV2) and genotype shift to PCV2d in Korean pig population



Taeyong Kwon, Dong-Uk Lee, Sung J. Yoo, Sang H. Je, Jeong Y. Shin, Young S. Lyoo*

College of Veterinary Medicine Konkuk University 120 Neungdong-ro Gwangjin-gu, Seoul 05029, South Korea



At farm level, 73% of PCV2 positive Korean farms host PCV2d alone or combined to other genotypes

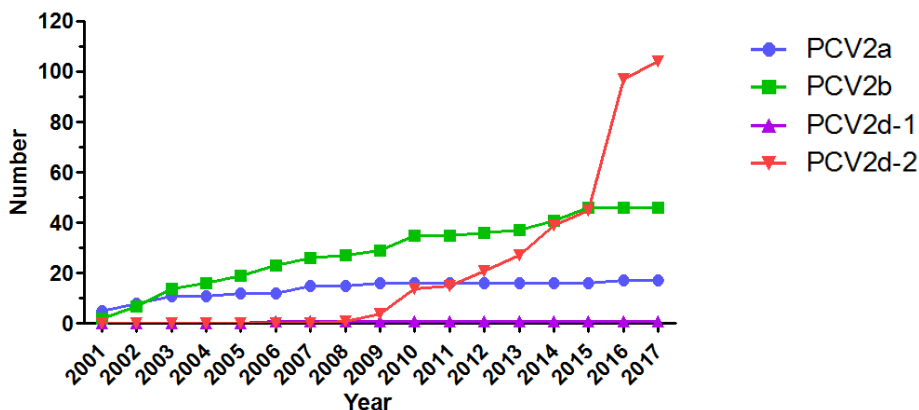
Genetic characterization of porcine circovirus type 2 from Taiwan reveals the emergence of PCV2d-2 since 2008

Guang-Ting Tsai¹, Chien-Ho Yu², Chao-Nan Lin¹, Ming-Tang Chiou¹,

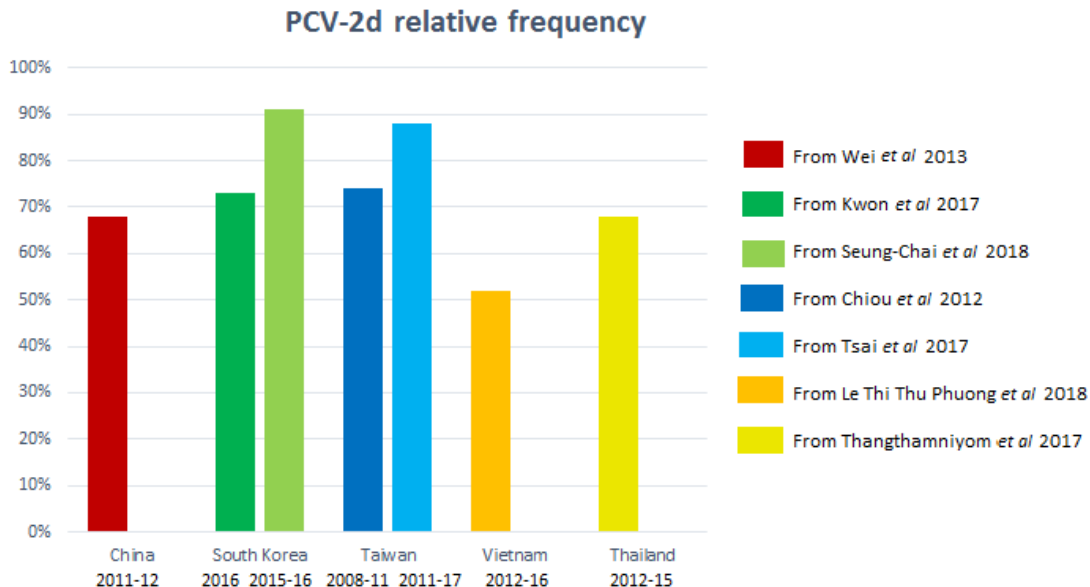
¹Department of Veterinary Medicine, National Pingtung University of Science and Technology

Time period (year)

²Ph D. Program of Agriculture Science, National Chiayi University



Litterature review on PCV-2d frequency in South East Asia



PCV-2 genotype evolution: conclusions

- 1. Current shift from PCV-2b to PCV-2d**
- 2. Vaccination pressure considered as playing a role in evolution**
 - 1. High level of PCV-2 vaccination**
 - 2. Pig herds density**
 - 3. Remaining PCV-2 circulation despite vaccination**
 - 4. High mutation rate of PCV-2**
- 3. The current use of PCV-2a vaccines may favor the emergence of new PCV-2 genotypes**

PCV-2 vaccines efficacy: facts and question marks

- **Most vaccines based on PCV-2a genotype**
- **Cross protection proven in experimental conditions (challenge models)**
- **Reports of *vaccination failure suspicions* in parallel to the emergence of PCV-2d genotype**



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Veterinary Microbiology

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Short communication

Emergence of a novel mutant PCV2b variant associated with clinical PCVAD in two vaccinated pig farms in the U.S. concurrently infected with PPV2

Tanja Opriessnig^{*}, Chao-Ting Xiao, Priscilla F. Gerber, Patrick G. Halbur

Department of Veterinary Diagnostic and Production Animal Medicine, College of Veterinary Medicine, Iowa State University, Ames, IA, USA

Arch Virol (2014) 159:3107–3111

DOI 10.1007/s00705-014-2164-6

BRIEF REPORT

Veterinary Microbiology 176 (2015) 337–343



Contents lists available at ScienceDirect

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



Genetic and antigenic characterization of a newly emerging porcine circovirus type 2b mutant first isolated in cases of vaccine failure in Korea

Hwi Won Seo · Changhoon Park · Ikjae Kang ·
Kyuhung Choi · Jiwoon Jeong · Su-Jin Park ·
Chanhee Chae



Short Communication

Detection of a new cluster of porcine circovirus type 2b strains in domestic pigs in Germany

M. Eddicks^{a,*}, R. Fux^b, F. Szikora^a, L. Eddicks^c, M. Majzoub-Altweck^c,
W. Hermanns^c, G. Sutter^b, A. Palzer^a, E. Banholzer^d, M. Ritzmann^a

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^d Zentis GmbH, Schellingstraße 1, 10785 Berlin, Germany

Three peer-review published field cases of perceived vaccination failure with PCV-2d isolation

Country	Herds	Vaccination	Findings
USA (Opriessnig <i>et al</i> 2013)	2 wean-to-finish farms (associated to 4000-6000 sow breed-to-farrow farms)	Piglets: 3 weeks of age	PCVAD outbreak mPCV2* isolation PPV2 isolation
Korea (Seo <i>et al</i> 2014)	Farm A: 350-sow herd Farm B: 550-sow herd	Pregnant sows + Piglets (Farm A) Piglets (Farm B) (3 weeks)	A: epizootic diarrhea B: PMWS-like symptoms mPCV2* isolation Vaccination failure
Germany (Eddicks <i>et al</i> 2015)	7 farms	Routine PCV2 vaccination	PCVAD PCV2b-1C* isolation Vaccination failure? (lack of data on vaccination compliance)

***mPCV-2 = PCV2b-1C = PCV-2d**

Vaccination failures suspicions: conclusions

- **Field cases reported in various regions in parallel to PCV-2b mutation towards PCV-2d**
- **No definitive conclusion on the cause of failure**
 - **Vaccine?**
 - **Vaccination process?**
 - **Co-infections?**
- **Some question marks**

Genotype evolution of PCV-2: some questions

- **Regarding PCV-2 strains:**
 - **Possible difference of virulence between genotypes?**
- **Regarding PCV-2 vaccines:**
 - **Is protection improved by homologous genotype vaccine?**

PCV-2 virulence diversity

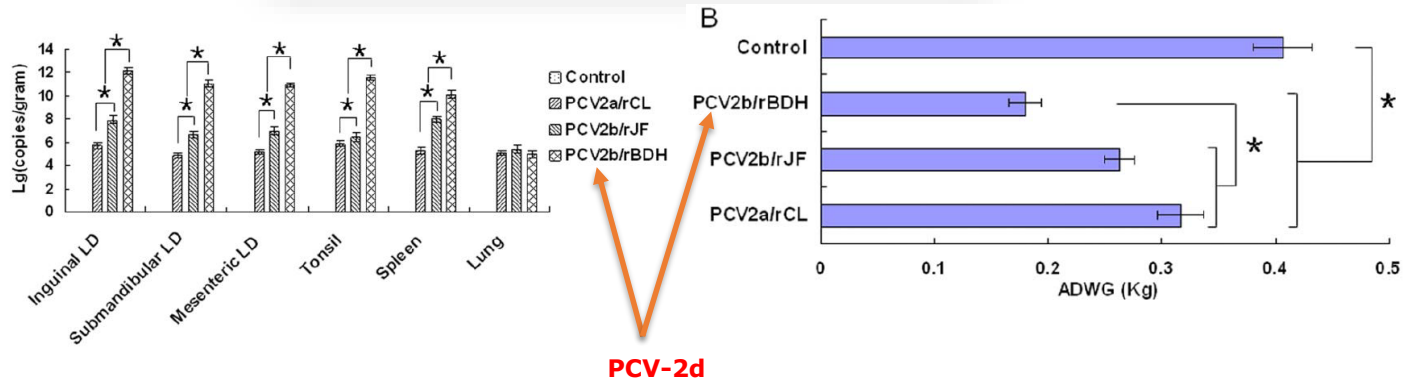
OPEN ACCESS Freely available online



A Porcine Circovirus Type 2 (PCV2) Mutant with 234 Amino Acids in Capsid Protein Showed More Virulence *In Vivo*, Compared with Classical PCV2a/b Strain

Longjun Guo, Yujie Fu, Yiping Wang, Yuehua Lu, Yanwu Wei, Qinghai Tang, Peihu Fan, Jianbo Liu, Long Zhang, Feiyan Zhang, Liping Huang, Dan Liu, Shengbin Li, Hongli Wu, Changming Liu*

Division of Swine Infectious Diseases, State Key Laboratory of Veterinary Biotechnology, Harbin Veterinary Research Institute, Chinese Academy of Agricultural Sciences, Harbin, China

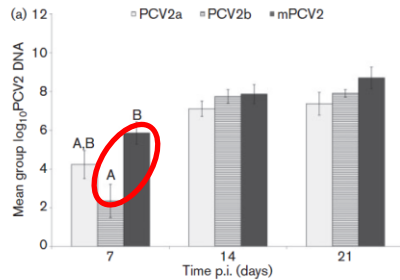


PCV-2 virulence diversity

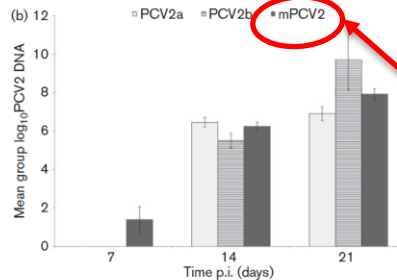
Journal of General Virology (2014), 95, 2495–2503

DOI 10.1099/vir.0.066423-0

Serum



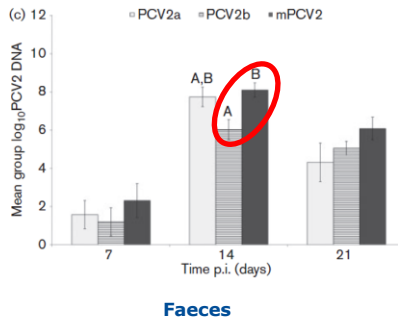
Nasal swabs



Mutant USA strain of porcine circovirus type 2 (mPCV2) exhibits similar virulence to the classical PCV2a and PCV2b strains in caesarean-derived, colostrum-deprived pigs

Tanja Opriessnig,^{1,2} Chao-Ting Xiao,² Priscilla F. Gerber,² Patrick G. Halbur,² Shannon R. Matzinger³ and Xiang-Jin Meng³

PCV-2d



Faeces

Similar lesions induced by the different genotypes

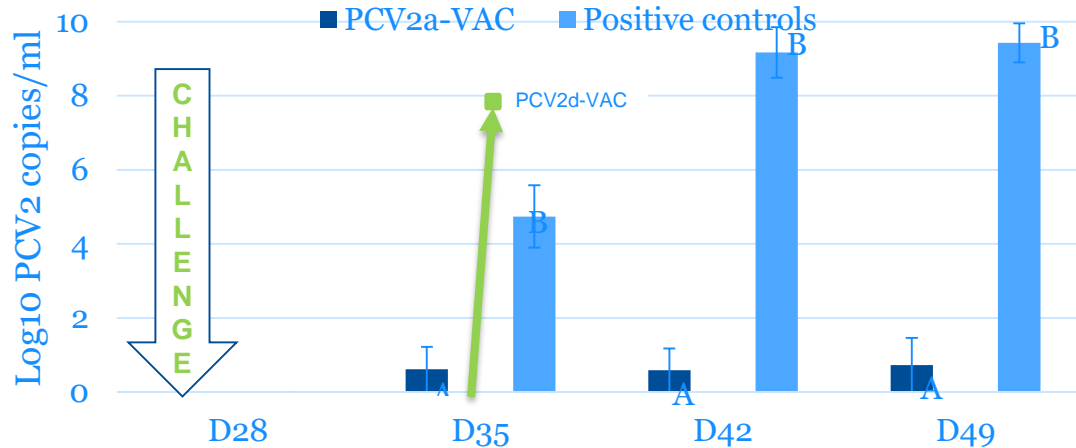
Some differences on viremia and virus shedding between genotypes

PCV-2 virulence diversity: conclusions

- **Virulence vary among PCV-2 strains (according to challenge models)**
- **No definitive answer on increase of virulence with the emergence of PCV-2d genotype**
- **Virulence varies also within genotype**

Is protection improved by homologous genotype vaccine?

Post challenge viremia reduction by homologous or heterologous genotype vaccine



PCV2a-VAC: commercial vaccine
PCV2d-VAC: experimental vaccine

Opriessnig et al., Vaccine 2014 32:230-237

PCV2d viremia reduction:

- 100% for the PCV2d vaccine
- 92.2% for the PCV2a vaccine



Review

Porcine Circovirus Type 2 (PCV2) Vaccines in the Context of Current Molecular Epidemiology

Anbu K. Karuppannan¹ and Tanja Opriessnig^{1,2,*}

- **PCV-2a-based vaccines confer cross-protection against challenge with PCV-2a, PCV-2b or PCV-2d genotypes**
- Possible *leaky vaccine situation?*
 - **-Decrease the transmission and infection rate in a vaccine trial or in the presence of good biosecurity**
 - **-Limited protection under conditions of repeated exposure with other cofactors**

Limitations of challenge tests to assess vaccines efficacy

- **The virus**
 - **PCV-2 inoculation alone does not reproduce the full picture of PCVADs (clinical, histopathological)**
 - **Single PCV-2 challenge vs co-infecting agents (PRRS...)**
- **The animal**
 - **SPF pigs vs naturally infected and immunized**
 - **Breed and genetic susceptibility?**
- **The environment**
 - **Temperature, stocking density**
 - **Biosecurity**

PCV-2 vaccination perceived failure: assessment

- **Diagnosis: laboratory confirmation (histopathology, detection of PCV-2 in tissular lesions)**
- **Vaccination implementation**
 - **Reception and storage of vaccines (cold chain, shelf life, leftovers)**
 - **Compliance (all targeted pigs, recommended dose(s))**
 - ***Age at vaccination?***
- **Intercurrent infections: PRRS, PPV...**
- **Vaccine efficacy?**

Interference of MDI (maternally derived immunity) with PCV-2 vaccination

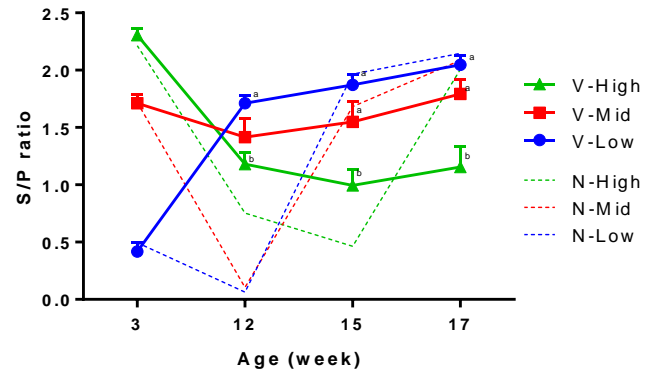
- **Interference of MDI with seroconversion after vaccination widely demonstrated**
 - **Consequences regarding piglets protection?**
 - **Impact on pigs performance?**

Immune response of piglets with low and high maternal antibody after PCV2 vaccination (W.C. Lee, personal communication)

Basic information of sera from PCV2 vaccinated pigs

MDA	S/P ratio	ELISA titer	N
High	> 2.0	>4922	15
Mid	1.0 – 2.0	2296-4922	13
Low	< 1.0	<2296	17

Biochek PCV2 Ab ELISA



- Different alphabet indicates statistical significance ($p < 0.05$) between groups.

RESEARCH ARTICLE

Open Access



Impact of maternally derived immunity on piglets' immune response and protection against porcine circovirus type 2 (PCV2) after vaccination against PCV2 at different age

Paolo Martelli^{1*}, Roberta Saleri¹, Giulia Ferrarini¹, Elena De Angelis¹, Valeria Cavalli¹, Michele Benetti¹, Luca Ferrari¹, Elena Canelli¹, Paolo Bonilauri², Elena Arioli³, Antonio Caleffi³, Heiko Nathues⁴ and Paolo Borghetti¹

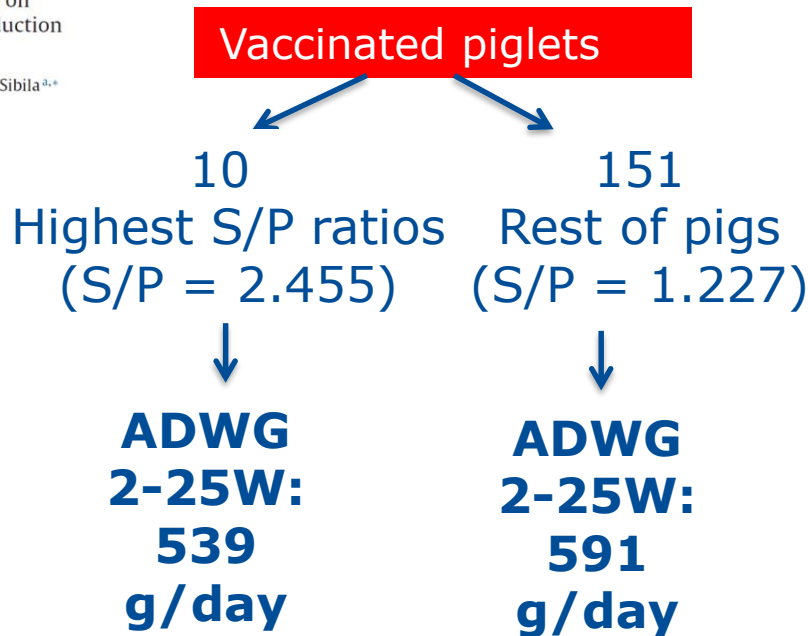
- Sows vaccinated at mating
- Piglets vaccinated at different ages
- Significantly lower morbidity rate (%) from weaning to finishing in 1st and 3rd parity when vaccination at 6W

Vaccination age	4 W	6 W	8 W	NV
1st parity	6.2 ^a	5.4 ^a	14.7 ^b	18.9 ^b
2 nd parity	22.7 ^a	20.7 ^a	21.3 ^a	22.4 ^a
3rd parity	10.3 ^a	0 ^b	8.3 ^a	18.2 ^a

High viremia

Effect of high and low levels of maternally derived antibodies on porcine circovirus type 2 (PCV2) infection dynamics and production parameters in PCV2 vaccinated pigs under field conditions

Hua Feng^{a,1}, Joaquim Segalés^{b,c}, Lorenzo Fraile^d, Sergio López-Soria^a, Marina Sibila^{a,*}



Difference of 52 g/day

P>0.05

Conclusions

- **Amazing success of PCV-2 vaccination**
 - **Decrease of mortality**
 - **Increase of ADG**
- **Successive PCV-2 genotype shifts**
 - **Follow up of vaccines efficacy required**
 - **Risk of escape mutants?**
 - **Evolution of vaccines design**
- **Global approach required from vaccine to vaccination process**

A photograph of several pigs in a barn. In the foreground, a pink pig lies on a dark, ribbed metal floor, looking towards the camera. In the background, several other pigs are resting on the same floor. The lighting is warm and slightly dim, typical of an indoor farm setting.

THANK YOU!

INNOVATION

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