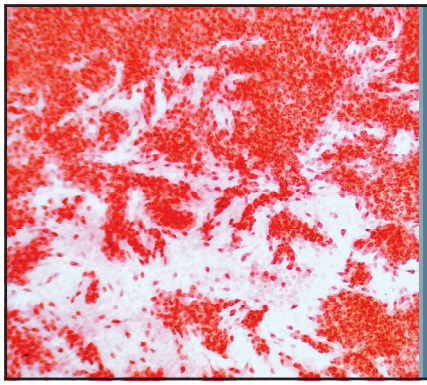


An Update on the World of Bovine Viral Diarrhea Virus

SHARI M. KENNEDY, THOMAS PASSLER, SHOLLIE M FALKENBERG, MANUEL F. CHAMORRO, CONSTANTINOS C. KYRIAKIS, PAUL H. WALZ, VIENNA R. BROWN, TIM LINDER.

1

Worldwide Antigen prevalence 2010-2021

(Su, Wang et al. 2022)

TABLE 2 Antigen prevalence of Bovine viral diarrhea virus of cattle in the word.

	No. studies	No. tested	No. positive	% (95% CI*)
Area*				
Asia	43	27,333	2,957	16.75% (11.27–23.04)
Europe	2	1,138	96	23.27% (0.00–89.41)
North America	1	7,544	24	0.32% (0.20–0.46)
South America	5	10,196	411	10.55% (2.63–22.82)
Sampling years				
Before 2017	30	26,608	1,625	17.18% (11.08–24.27)
After 2017	21	9,513	1,156	17.91% (10.33–26.99)

2

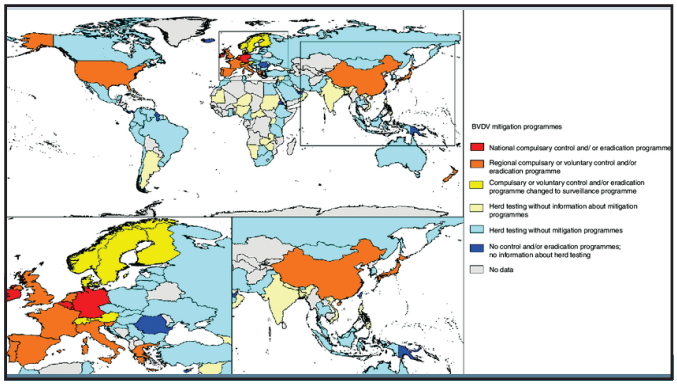
Worldwide Antibody prevalence 2010-2021

(Su, Wang et al. 2022)

TABLE 4 Antibody prevalence of Bovine viral diarrhea virus of cattle in the word.

	No. studies	No. tested	No. positive	% (95% CI*)
Area				
Asia	71	53,457	23,597	42.03% (35.99–48.18)
Europe	1	180	82	45.56% (38.32–52.88)
North America	1	385	184	47.79% (42.81–52.79)
South America	1	390	298	76.41% (72.06–80.50)
Africa	3	937	424	46.13% (26.82–66.06)
Sampling years				
Before 2017	55	33,177	15,345	43.63% (37.25–50.13)
After 2017	19	11,619	6,319	41.11% (27.05–55.95)

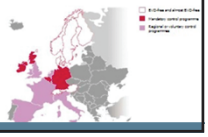
3



4

Implications of a resourceful virus

- The economic impact can be evaluated for BVDV by assessing differences in performance in the presence or absence of a PI animal
  - The average direct lossesper:
    - naïvedairy cow were**$199.50**
    - beef cow**$174.60**
    - animal in the feedlo**$93.52**
- Cost of testing
- Exposure of heterologous hosts
  - sheep, goats, deer, camels, alpaca, pigs, and a wide array of ungulate wildlife
  - Seroprevalence varied from 0-45% among herding districts for Reindeer in Norway
  - Feral swine seroprevalence ~6%
    - Individual state rangeD6.7%
    - CA, OK, TX highest seroprevalence
- Fetal bovine serum (500 ml bottles)
  - Super value - $446
  - Value FBS - $676
  - Premium - $800 US, $1656 New Zealand, $1608 Australia
  - Specialty - FBS call for pricing



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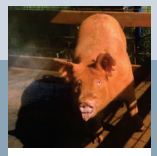
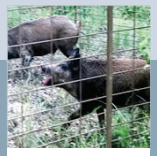
BVDV Heterologous hosts



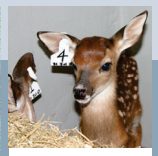
DOMESTIC SWINE

Genetic Changes PI vs CI



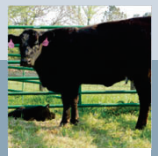
FERAL SWINE/WILD PIGS

Seroprevalence in US



WHITE-TAILED DEER

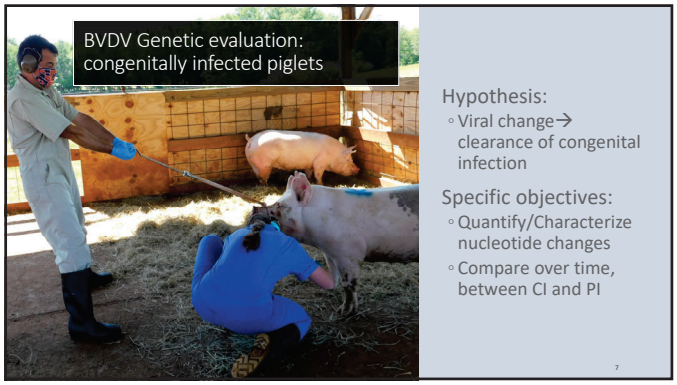
Commercial Test Comparisons



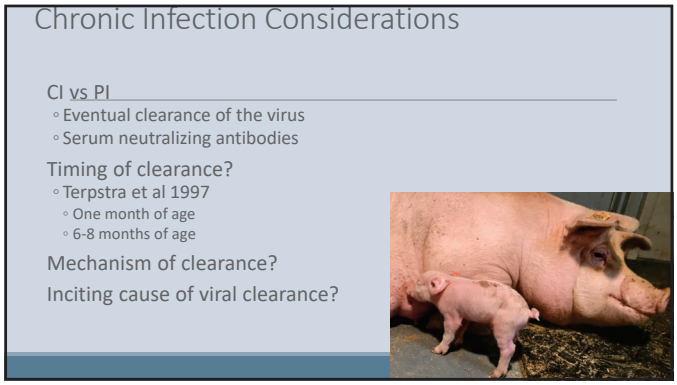
CATTLE

Swine vs Bovine BVDV PI Genetic

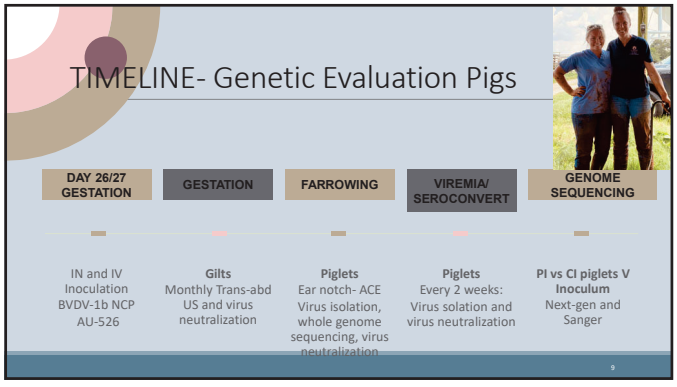
6


BVDV Genetic evaluation:
congenitally infected piglets
Hypothesis:
◦ Viral change→ clearance of congenital infection
Specific objectives:
◦ Quantify/Characterize nucleotide changes
◦ Compare over time, between CI and PI
7

7


Chronic Infection Considerations
CI vs PI
◦ Eventual clearance of the virus
◦ Serum neutralizing antibodies
Timing of clearance?
◦ Terpstra et al 1997
◦ One month of age
◦ 6-8 months of age
Mechanism of clearance?
Inciting cause of viral clearance?

8


TIMELINE- Genetic Evaluation Pigs
DAY 26/27 GESTATION
GESTATION
FARROWING
VIREMIA/ SEROCONVERT
GENOME SEQUENCING
IN and IV Inoculation BVDV-1b NCP AU-526
Gilts
Monthly Trans-abd US and virus neutralization
Piglets
Ear notch- ACE
Virus isolation, whole genome sequencing, virus neutralization
Piglets
Every 2 weeks:
Virus solation and virus neutralization
PI vs CI piglets V Inoculum
Next-gen and Sanger
9

9

Results

- 4 Litters- 2019
  - 26 live-born
  - 9 antigen positive at birth
    - Antigen Capture ELISA
    - PCR
  - 4D- chronically infected
    - Seroconverted ~5.5-6 months of age

10

Results: Repeat

- 3 Litters- 2020
  - 34 live-born piglets
  - 7 antigen positive at birth
    - Antigen Capture ELISA
  - 6 virus positive at birth
    - Virus isolation
  - 8H Chronic Infection
    - Seroconverted- ~6-8 weeks

11

Results- BVDV sequencing

WHOLE-GENOME/NEXT-GEN

98.8% Identical to AU526 460F6 inoculum

4s vs Inoculum
- 2 polymorphic sites E2

8s vs Inoculum
- 1 polymorphic site E^{RNS}
- 5 polymorphic sites in E2

SANGER

15 congenitally infected piglets
- Most of E1, E2, E^{RNS} Complete
- 1 polymorphic site E^{RNS}
- 5 polymorphic sites in E2

Compare to WGS/NGS- pending

M&M paper for lab tech

12

Phylogenic analysis

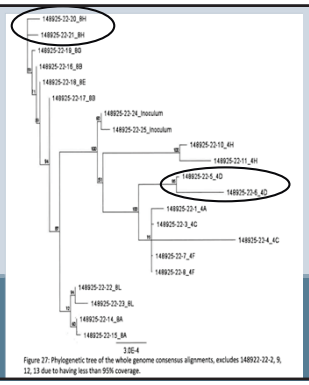


Figure 27: Phylogenetic tree of the whole genome consensus alignments, excludes 148922-22-2, 9, 12, 13 due to having less than 95% coverage.

13

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Feral Swine/wild pig seroprevalence

Manage the Damage
Stop Feral Swine

USDA Wildlife Services

Current US Feral Swine/Wild Pig BVDV knowledge:

- 0% Great Smokey Mountains National Park
- doi: 10.7589/0090-3558-30.1.103.

Seroprevalence rate for states with higher feral swine/wild pig or cattle population states

14

14

Feral Swine Seroprevalence

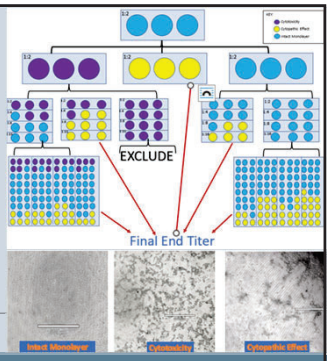
- Objective:
  - Determine BVDV seroprevalence in wild pigs in US
  - Determine if age, sex, or location associated with positive antibody titer

15

Methods

Approach:

- 945 serum convenience samples from 17 states collected by USDA-ARS NFSDM program and Auburn University College of Forestry, Wildlife and Environment
- Virus neutralization- 1:2 serial dilutions until final titer



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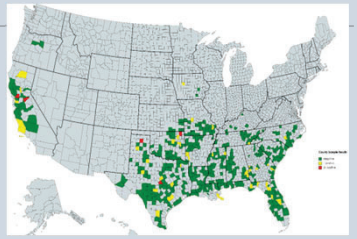
Feral swine BVDV seroprevalence: Results

- 67 samples excluded from cytotoxicity
- 878 samples analyzed
- Total BVDV seroprevalence= 5.8%
- BVDV-1b seroprevalence= 4.4%
- BVDV-2a seroprevalence= 3.6%
- Individual states 0-16.7%
- No difference in mean antibody titer BVDV-1b/2a by sex or age
- CA, OK, TX= greatest seroprevalence
  - Also, largest cattle and most established wild pig population states



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Review

Bovine viral diarrhea virus (BVDV) infections in pigs

ie Tao, Jinhu Liao, Yin Wang, Xinjun Zhang, Jianye Wang, Guoqiang Zhu *

ollege of Veterinary Medicine, Yangzhou University, China

Rev. sci. tech. Off. int. Epiz., 1990,

Ruminant pestivirus infection in pigs

Review

Bovine Viral Diarrhea Virus: Recent Findings about Its Occurrence in Pigs

Luís Guilherme de Oliveira [1,*], Marina L. Mechler-Dreibi [1], Henrique M. S. Almeida [1] and Igor R. H. Gatto [2]

[1] School of Agricultural and Veterinarian Sciences, São Paulo State University (Unesp), Jaboticabal. Via de Acesso Prof. Paulo Donato Castelanne s/n, Jaboticabal - SP 14884-900, Brazil; mlopesvet@gmail.com (M.L.M.-D.); henri_almeida2003@yahoo.com.br (H.M.S.A.)

[2] Ourofino Animal Health Ltda. Rodovia Anhanguera SP 330, Km 298. Distrito Industrial, Cravinhos – SP 14140-000, Brazil; igatto_10@hotmail.com

* Correspondence: luis.guilherme@unesp.br

isociated with the detection of BVDV
erds

rreia Lima Linhares [2] · Henrique Meiroz de Souza Almeida [1] · nos de Medeiros [1] · Zvonimir Poljak [3] · Samir Issa Samara [1] ·

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Seroprevalence and risk factors for the presence of ruminant pestiviruses in the Dutch swine population

W.L.A. Loeffen [a,*], A. van Beuningen [a,1], S. Quak [a], A.R.W. Elbers [a,b]

[a] Department of Virology, Central Veterinary Institute of Wageningen UR (CVI-Lelystad), P.O. Box 65, 8200AB Lelystad, The Netherlands
[b] Department of Swine Health, Animal Health Service, P.O. Box 9, 7400AA Deventer, The Netherlands

'2, China

transmission and full protection against
ission in pigs experimentally infected
iduces 'DV type 1b
ay highly , S. Quak, W.L.A. Loeffen

'IDC-Lelystad), P.O. Box 2004, 8203AA Lelystad, The Netherlands

evised form 12 June 2006; accepted 16 June 2006

18

Comparative BVDV COMMERCIAL TESTS

Commercially available and validated for Cattle

- RealPCR BVDV RNA Mix
- IDEXX SNAP BVDV Antigen Test ★
- IDEXX BVDV PI X2 Test
- IDEXX BVDV Total Ab Test
- IDEXX BVDV Ag/Serum Plus Test
- IDEXX BVDV p80 Ab Test
- IDEXX BVDV Ag Point-of-Care Test ★

Hypothesis:

- Heterologous hosts would have an elevated false-positive ACE results

★ Could easily be used by producers and veterinarians

https://www.idexx.com/en/livestock/livestock-tests/ruminant-tests/idexx-bvdv-pi-x2-test/

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Appropriate testing?- DR. PASSLER

Year	acELISA*	Immunohistochemistry	RT-nPCR
2006/07 440 deer	22 Positive		
2007/08 577 deer	7 Positive, 13 Suspect	5 Positive, 4 Suspect	2 Positive
2008/09 590 deer	4 Suspect, 3 Positive	Pending	0 Positive

*S/P ratios : Suspect 0.2 – 0.39, Positive: > 0.39

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21

21

Comparative test conclusion

Reliably detect negative or non-viremic animals.

High specificity between IDEXX BVDV PI X2 Antigen-capture ELISA with PCR

Unknown sensitivity- likely high false positives in previous studies?

22

22

Swine vs Bovine BVDV isolate PI infection

Evaluate antigenic changes during immune recognition of pregnant cattle and creation of PI

- BVDV propagated in heterologous hosts
- BVDV propagated in cattle hosts

23

23

Swine Isolate

460f6

Pre-colostrum viremia PI calf

Acute Infection Heifer

Inoculum

VS

Bovine Isolate

AU-526

Pre-colostrum viremia PI calf

Acute Infection Heifer

Inoculum

Swine vs Cattle BVDV PI Genetics

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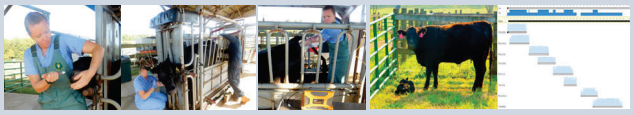
24

Research timeline- swine vs cattle

DAY 75 GESTATION | ACUTE INFECTION | GESTATION | PARTURITION | SEQUENCING



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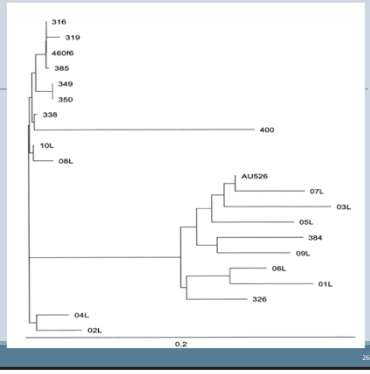
Swine vs Cattle Genetics Results



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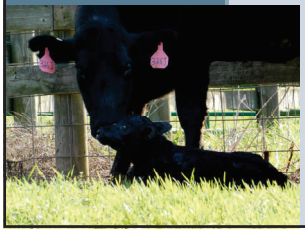
Cell-mediated immunity during pregnancy recognition with a PI fetus



Does pregnancy with a PI fetus alter the cell mediated immunity and the ability for the adaptive immune system to respond to both specific and non-specific challenges?

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CMI Assay Heifers

Materials and Methods

Measuring CMI responses using the PrimeFlow RNA assay: A new method of evaluating BVDV vaccination response in cattle

Shollie M. Falkenberg[a,*], Rohana P. Dassanayake[a], John D. Neill[a], Paul H. Walz[b], Eduardo Casas[a], Julia F. Ridpath[a], James Roth[c]

[a] Ruminant Disease and Immunology Research Unit, National Animal Disease Center, USDA, Agricultural Research Service, Ames, IA, 50010, United States
[b] Department of Pathobiology, College of Veterinary Medicine, 129 Sugg Laboratory, Auburn University, AL, 36849, United States
[c] Department of Veterinary Microbiology and Preventive Medicine, College of Veterinary Medicine, Iowa State University, IA, United States

- 76: Prior to Challenge; Early gestation
- 130: Early gestation; 50 days post challenge
- 190: Mid-gestation; 110 days post challenge
- 240: Late-gestation; 160 days post challenge

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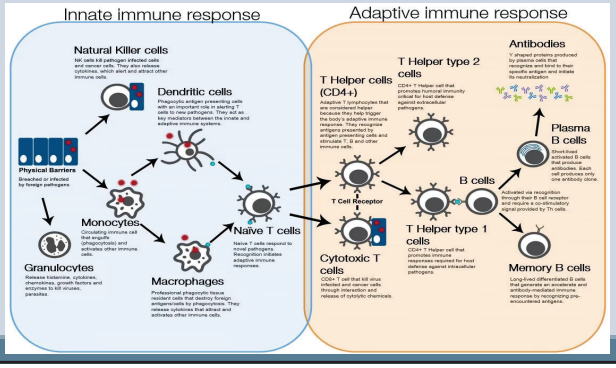

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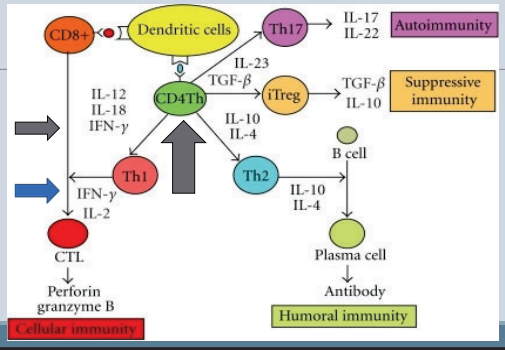

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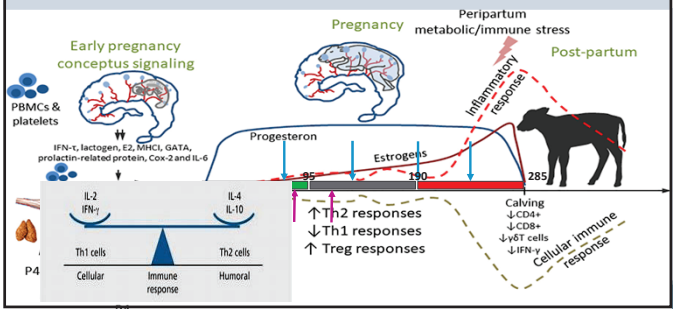
Immune response during pregnancy



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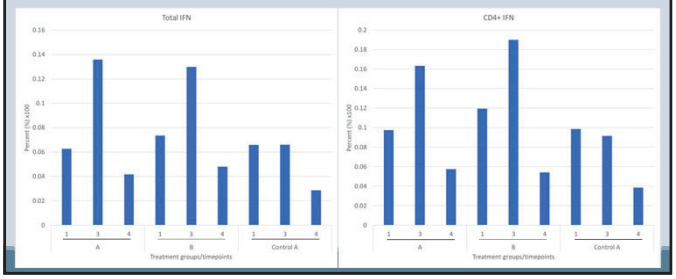
Heifers with PI and non-PI fetuses
Mitogen stim- Total IFN and CD4s



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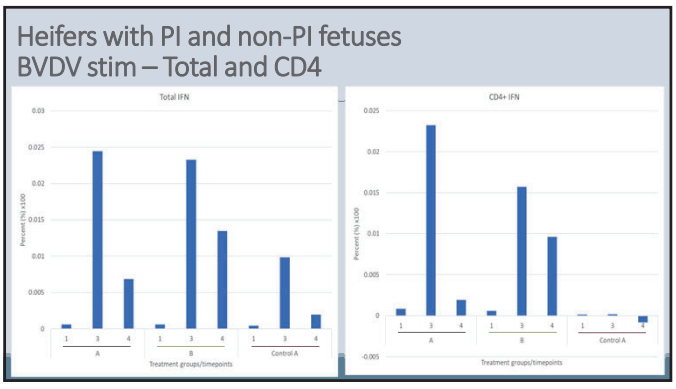
Heifers with PI and non-PI fetuses
BVDV stim – Total and CD4



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Thank you

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