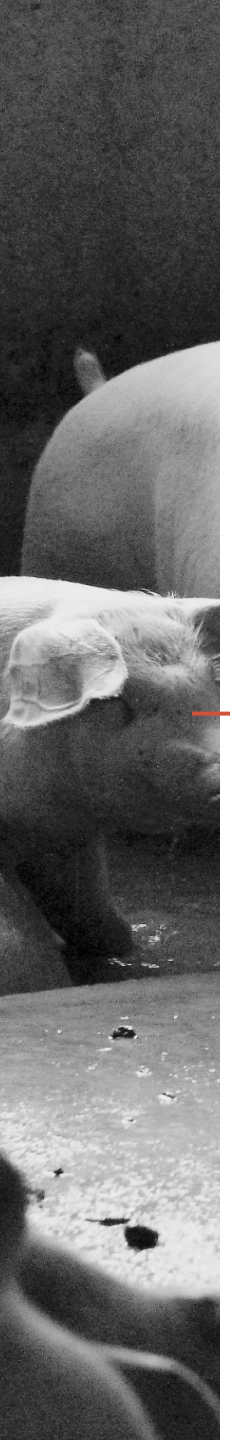


HOW PRRS AND INFLUENZA VIRUSES AFFECTS PIGLET'S MICROBIOTA AND INTESTINAL HEALTH

Alberto Morillo Alujas
PhD in Veterinary Science, Nutritionist & Diplomate in Statistics
Consultor of Tests and Trials

Sanitary challenges negatively affect feed intake and growth

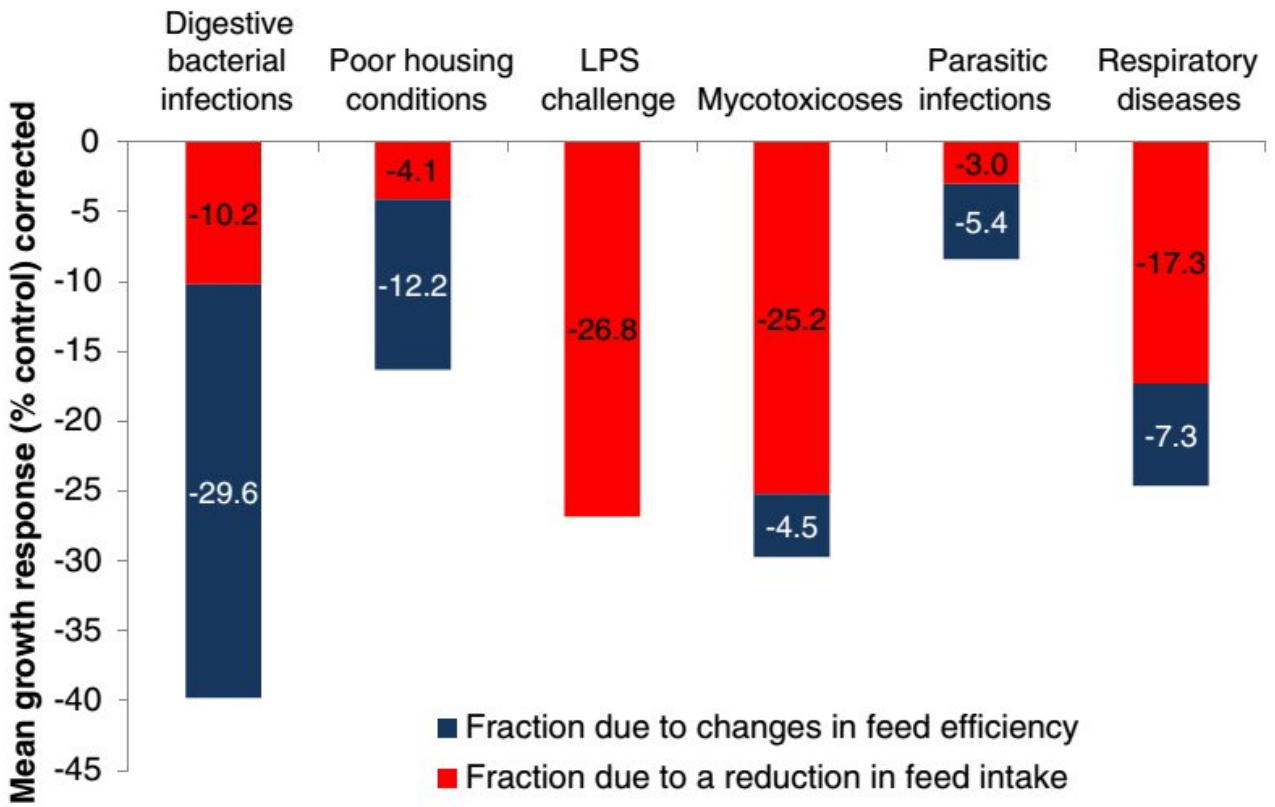
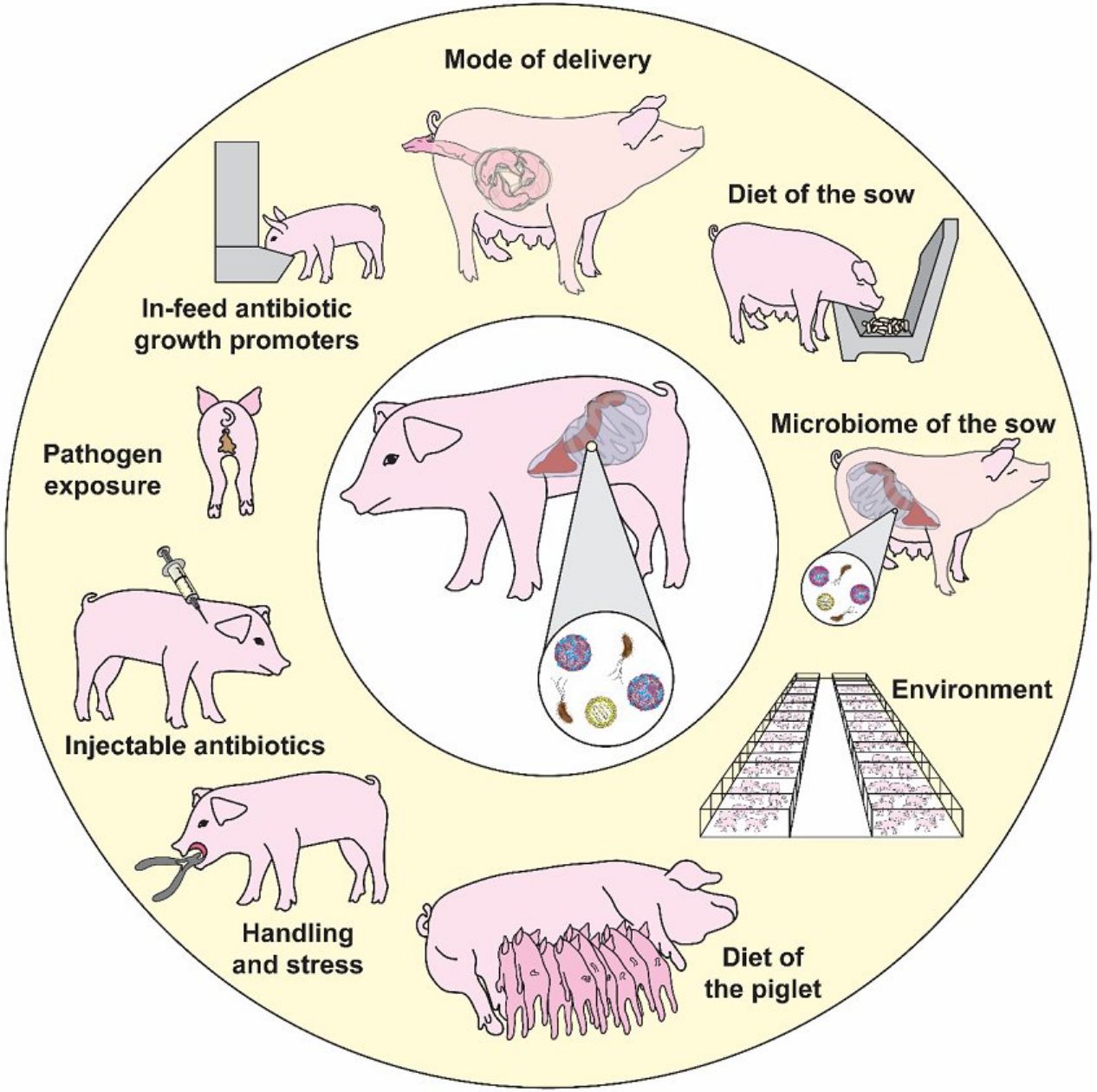


Figure 2 Metabolic consequences of an activated immune system. Partitioning the percentage decrease in average daily gain and feed efficiency as a result of different immune challenges (adapted from Pastorelli et al. [9]).

Pastorelli, H., Jet al., 2012. «Meta-Analysis of Feed Intake and Growth Responses of Growing Pigs after a Sanitary Challenge». *Animal* 6 (06): 952-61.



Factors affecting piglet's microbiota

Niederwerder, M.. 2017. «Role of the Microbiome in Swine Respiratory Disease». *Veterinary Microbiology* 209 (septiembre): 97-106.

PRRSv and microbiota

> J Vet Med Sci. 1998 May;60(5):555-61. doi: 10.1292/jvms.60.555

Dual infection with enterotoxigenic Escherichia coli and porcine reproductive and respiratory syndrome virus observed in weaning pigs that died suddenly

M Nakamine [?], Y Kono, S Abe, C Hoshino, J Shirai, T Ezaki

Affiliations + expand

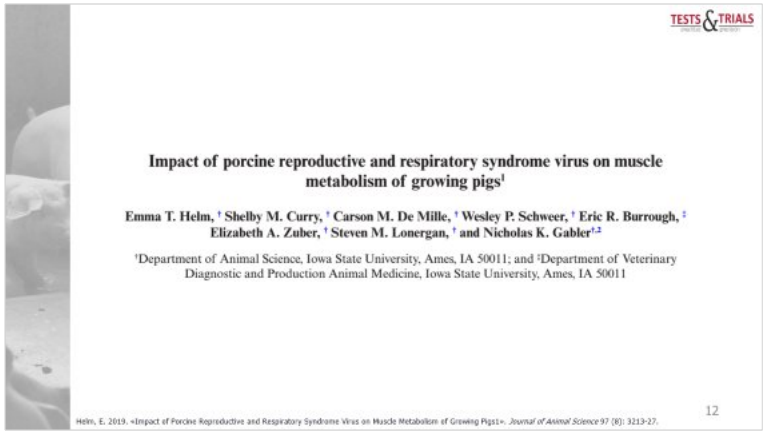
PMID: 9637287 DOI: 10.1292/jvms.60.555

Free article

Abstract

Diarrhea, sudden death after short duration of diarrhea and sudden death without apparent signs were observed in a herd of breeder pigs. Five pigs that died suddenly with diarrhea (SDD pigs) and 6 pigs that died suddenly without signs (SD pigs) were examined. The average age of the pigs was about 28 days. Twelve pigs of age 10 to 14 days old showing diarrhea (D pigs) were also examined. Eleven of them recovered. Large numbers of Escherichia coli were detected in all organs of every SDD and SD pig and in feces of D pigs. All of the isolates were identified as enterotoxigenic E. coli (ETEC) by the polymerase chain reaction (PCR). Porcine reproductive and respiratory syndrome (PRRS) virus cDNA was also detected from the lung of every SD and SDD pig by the RT-PCR. High and low titers of antibodies to PRRS virus were found in 10-day-old and 1-month-old pigs, respectively. In an experiment, 3 ETEC were isolated from 9 healthy weaning pigs during the quiescent stage in the herd. These data showed that growth of the ETEC was not active in healthy weaning pigs; however, following infection with PRRS virus ETEC infection became systemic and caused peracute death in the weaning pigs. It suggested also that infection with PRRS virus in 10-day-old pigs were protected by the colostral antibodies, and fatal infection by ETEC did not occur as a result.

Nakamine, M et al., 1998. «Dual Infection with Enterotoxigenic Escherichia Coli and Porcine Reproductive and Respiratory Syndrome Virus Observed in Weaning Pigs That Died Suddenly.» *Journal of Veterinary Medical Science* 60 (5): 555-61



Impact of porcine reproductive and respiratory syndrome virus on muscle metabolism of growing pigs[1]

Emma T. Helm, [†] Shelby M. Curry, [†] Carson M. De Mille, [†] Wesley P. Schweer, [†] Eric R. Burrough, [‡] Elizabeth A. Zuber, [†] Steven M. Lonergan, [†] and Nicholas K. Gabler[†,2]

[†]Department of Animal Science, Iowa State University, Ames, IA 50011; and [‡]Department of Veterinary Diagnostic and Production Animal Medicine, Iowa State University, Ames, IA 50011

Helm, E. 2019. «Impact of Porcine Reproductive and Respiratory Syndrome Virus on Muscle Metabolism of Growing Pigs1». *Journal of Animal Science* 97 (8): 3213-27.

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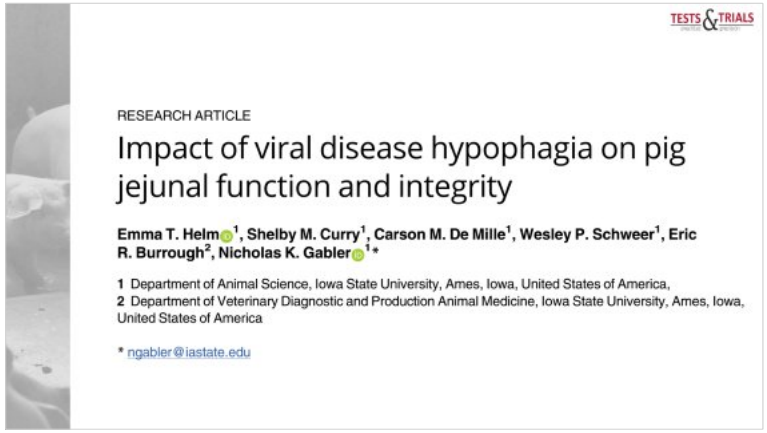


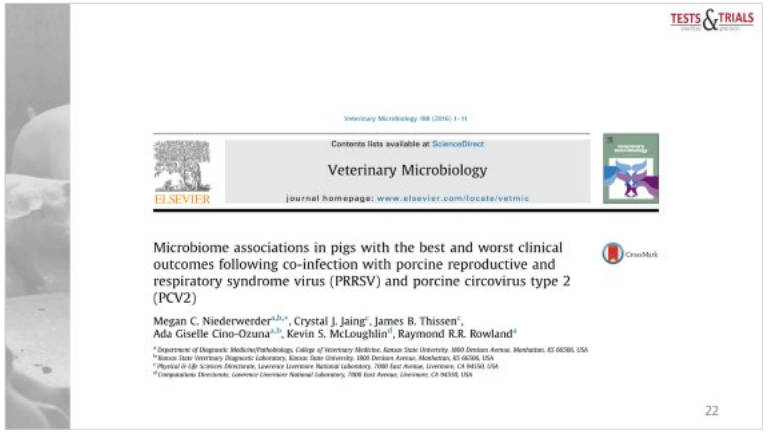
RESEARCH ARTICLE

Impact of viral disease hypophagia on pig jejunal function and integrity

Emma T. Helm[1], Shelby M. Curry[1], Carson M. De Mille[1], Wesley P. Schweer[1], Eric R. Burrough[2], Nicholas K. Gabler[1]*

1 Department of Animal Science, Iowa State University, Ames, Iowa, United States of America,
2 Department of Veterinary Diagnostic and Production Animal Medicine, Iowa State University, Ames, Iowa, United States of America

* ngabler@iastate.edu



Veterinary Microbiology 168 (2016) 1–11

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

Microbiome associations in pigs with the best and worst clinical outcomes following co-infection with porcine reproductive and respiratory syndrome virus (PRRSV) and porcine circovirus type 2 (PCV2)

Megan C. Niederwerder[a,b,*], Crystal J. Jaing[c], James B. Thissen[c], Ada Giselle Cino-Ozuna[a,b], Kevin S. McLoughlin[c], Raymond R.R. Rowland[a]

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J Vet Med Sci. 1998 May;60(5):555-61. doi: 10.1292/jvms.60.555.

Dual infection with enterotoxigenic Escherichia coli and porcine reproductive and respiratory syndrome virus observed in weaning pigs that died suddenly

M Nakamine [1], Y Kono, S Abe, C Hoshino, J Shirai, T Ezaki

Affiliations + expand

PMID: 9637287 DOI: 10.1292/jvms.60.555

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Diarrhea, sudden death after short duration of diarrhea and sudden death without apparent signs were observed in a herd of breeder pigs. Five pigs that died suddenly with diarrhea (SDD pigs) and 6 pigs that died suddenly without signs (SD pigs) were examined. The average age of the pigs was about 28 days. Twelve pigs of age 10 to 14 days old showing diarrhea (D pigs) were also examined. Eleven of them recovered. Large numbers of Escherichia coli were detected in all organs of every SDD and SD pig and in feces of D pigs. All of the isolates were identified as enterotoxigenic E. coli (ETEC) by the polymerase chain reaction (PCR). Porcine reproductive and respiratory syndrome (PRRS) virus cDNA was also detected from the lung of every SD and SDD pig by the RT-PCR. High and low titers of antibodies to PRRS virus were found in 10-day-old and 1-month-old pigs, respectively. In an experiment, 3 ETEC were isolated from 9 healthy weaning pigs during the quiescent stage in the herd. These data showed that growth of the ETEC was not active in healthy weaning pigs; however, following infection with PRRS virus ETEC infection became systemic and caused peracute death in the weaning pigs. It suggested also that infection with PRRS virus in 10-day-old pigs were protected by the colostral antibodies, and fatal infection by ETEC did not occur as a result.

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E. coli and PRRSv

- It seemed that sudden death in weaning pigs caused by ETEC septicemia was a result of concurrent infections with ETEC and PRRS virus, the both being activated following the decline of passive immunity to the agents.

- PRRS virus does have a distinct affinity for lung macrophages kills a high percent of these cells and impairs lung-level and systemic-level immune defenses.

- These effects might assist the “in vivo” invasion and replication of ETEC in the extraintestinal sites.

Nakamine, M.et al., 1998. «Dual Infection with Enterotoxigenic Escherichia Coli and Porcine Reproductive and Respiratory Syndrome Virus Observed in Weaning Pigs That Died Suddenly.» *Journal of Veterinary Medical Science* 60 (5): 555-61

E. coli and *PRRSv*

- Diseases outbreak occurred when the pigs were exposed to certain factors such as virus infection or stress which broke down the normal intestinal environments.

- PRRS virus infection may be one of the most important factors contributing to disease outbreak.

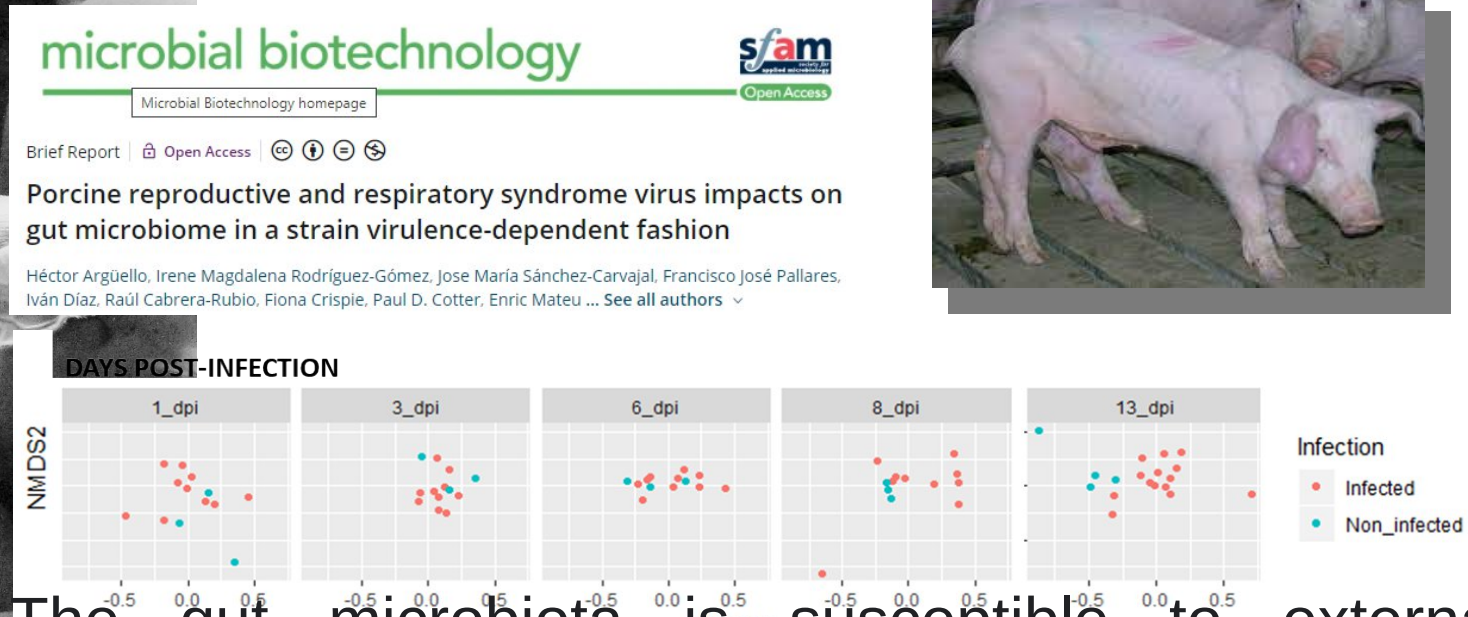
Nakamine, M.et al., 1998. «Dual Infection with Enterotoxigenic Escherichia Coli and Porcine Reproductive and Respiratory Syndrome Virus Observed in Weaning Pigs That Died Suddenly.» *Journal of Veterinary Medical Science* 60 (5): 555-61

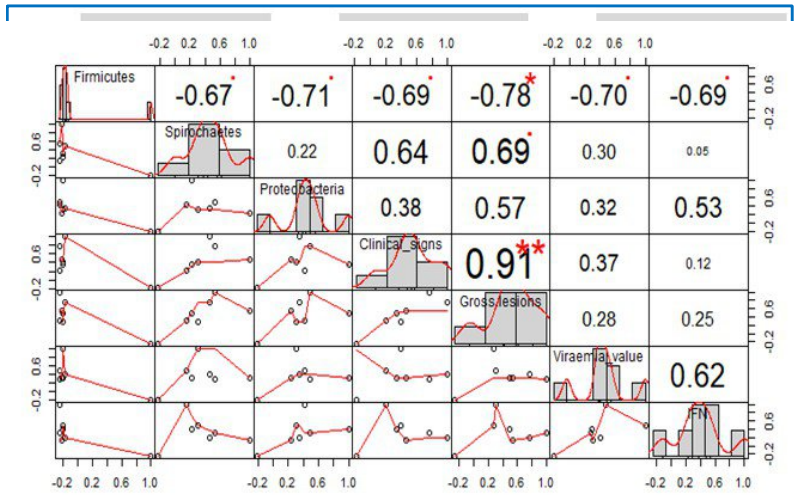
E. coli and *PRRSv*

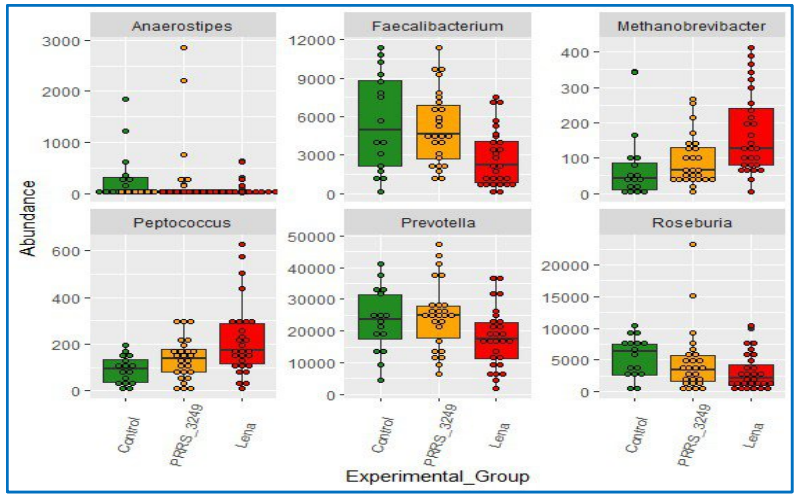
- It was therefore hypothesized that sudden death in weaning pigs was caused by a combination of at least 3 factors:
  - first, an age factor relating to decline of passive immunity;
  - second, infection by PRRS virus which reduces the resistance to bacterial infections;
  - third, “in vivo” replication of ETEC which leads the host to death.

Nakamine, M.et al., 1998. «Dual Infection with Enterotoxigenic Escherichia Coli and Porcine Reproductive and Respiratory Syndrome Virus Observed in Weaning Pigs That Died Suddenly.» *Journal of Veterinary Medical Science* 60 (5): 555-61

Microbiota and systemic diseases: PRRSv & microbiota







The gut microbiota is susceptible to external challenges, including those that hamper local and systemic immune responses. PRRSV infection alters the composition of the gut microbiome in a strain-virulence-dependent manner and is associated with selected immune markers.

Argüello, H. et al. 2021. «Porcine reproductive and respiratory syndrome virus impacts on gut microbiome in a strain virulence-dependent fashion». *Microbial Biotechnology* 15 (3): 1007-18.

Reduction of beneficial bacterial families

as *Prevotella*, *Ruminococcaceae*, *Streptococcaceae*, *Lactobacillus*, *Veillonellaceae*.

Veterinary Microbiology
Volume 188, 30 May 2016, Pages 1-11

Microbiome associations in pigs with the best and worst clinical outcomes following co-infection with porcine reproductive and respiratory syndrome virus (PRRSV) and porcine circovirus type 2 (PCV2)

Megan C. Niederwerder [a, b], Crystal J. Jaing [c], James B. Thissen [c], Ada Giselle Cino-Ozuna [a, b], Kevin S. McLoughlin [d], Raymond R.R. Rowland [a]

Veterinary Microbiology
Volume 208, September 2017, Pages 203-211

Increased microbiome diversity at the time of infection is associated with improved growth rates of pigs after co-infection with porcine reproductive and respiratory syndrome virus (PRRSV) and porcine circovirus type 2 (PCV2)

Rebecca A. Ober [a], James B. Thissen [c], Crystal J. Jaing [c], Ada G. Cino-Ozuna [a, b], Raymond R.R. [illegible] Megan C. Niederwerder [a, b]

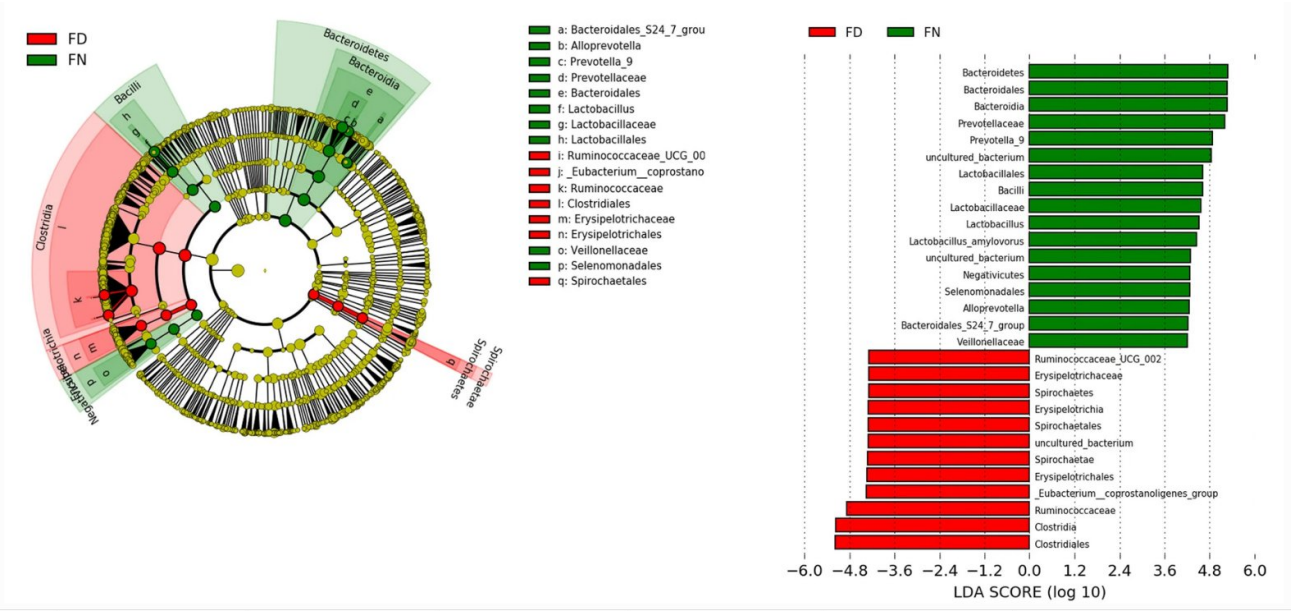
Curr Microbiol. 2019 Feb;76(2):222-230. doi: 10.1007/s00284-018-1613-y. Epub 2018 Dec 15.

Illumina MiSeq Sequencing Investigation of Microbiota in Bronchoalveolar Lavage Fluid and Cecum of the Swine Infected with PRRSV

Nan Jiang [1], Huan Liu [1], Peng Wang [1], Jing Huang [1], Hui Han [1], Qinfu Wang [2]

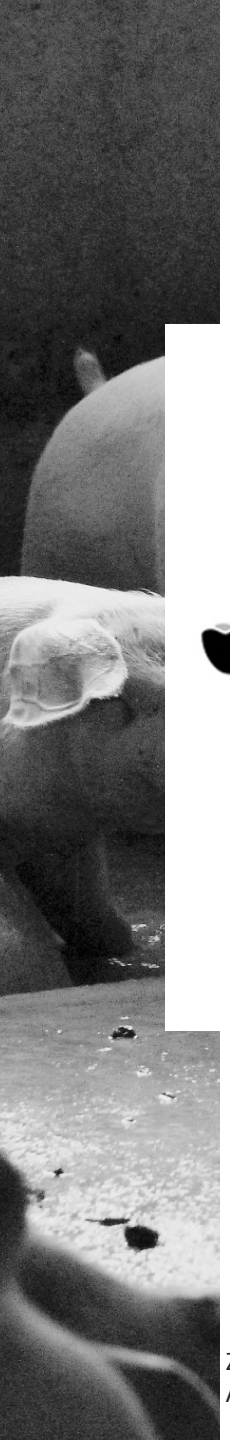
Affiliations + expand

PMID: 30554323 DOI: 10.1007/s00284-018-1613-y



Jiang, N. et al., 2019. «Illumina MiSeq Sequencing Investigation of Microbiota in Bronchoalveolar Lavage Fluid and Cecum of the Swine Infected with PRRSV». *Current Microbiology* 76 (2): 222-30.

ASF resistance could be driven by pig microbiota

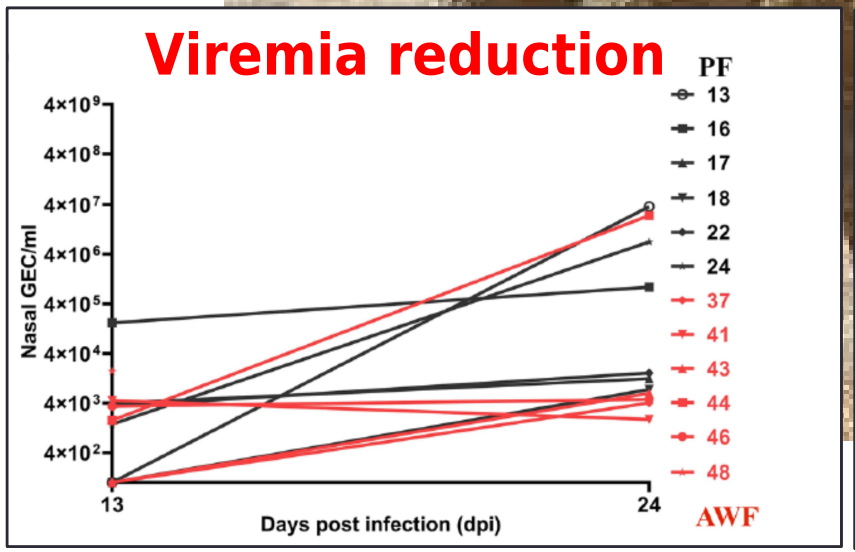


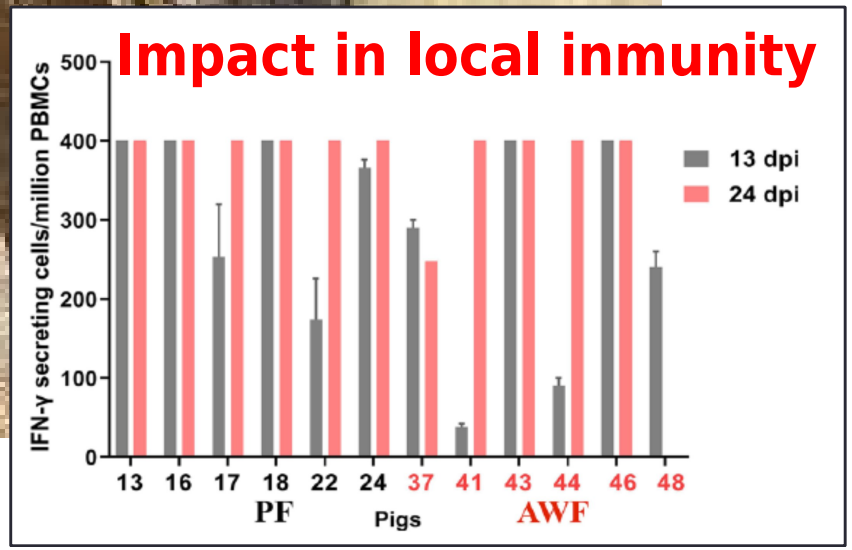
scientific reports

OPEN

Fecal microbiota transplantation from warthog to pig confirms the influence of the gut microbiota on African swine fever susceptibility

Jinya Zhang[1,2], Fernando Rodríguez[1,2✉], Maria Jesus Navas[1,2], Mar Costa-Hurtado[1,2], Vanessa Almagro[3], Laia Bosch-Camós[1,2], Elisabeth López[1,2], Raul Cuadrado[1], Francesc Accensi[1,2,4], Sonia Pina-Pedrero[1,2], Jorge Martínez[1,2,4,5] & Florencia Correa-Fiz[1,2,5✉]





Zhang, Jinya, F. Rodríguez, MJ Navas, M Costa-Hurtado, V, Laia Bosch-Camós, E López, et al. 2020. «Fecal Microbiota Transplantation from Warthog to Pig Confirms the Influence of the Gut Microbiota on African Swine Fever Susceptibility». *Scientific Reports* 10 (1): 17605.

Impact of porcine reproductive and respiratory syndrome virus on muscle metabolism of growing pigs[1]

Emma T. Helm, [†] Shelby M. Curry, [†] Carson M. De Mille, [†] Wesley P. Schweer, [†] Eric R. Burrough, [‡] Elizabeth A. Zuber, [†] Steven M. Lonergan, [†] and Nicholas K. Gabler[†,2]

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Helm, E. 2019. «Impact of Porcine Reproductive and Respiratory Syndrome Virus on Muscle Metabolism of Growing Pigs1». *Journal of Animal Science* 97 (8): 3213-27.

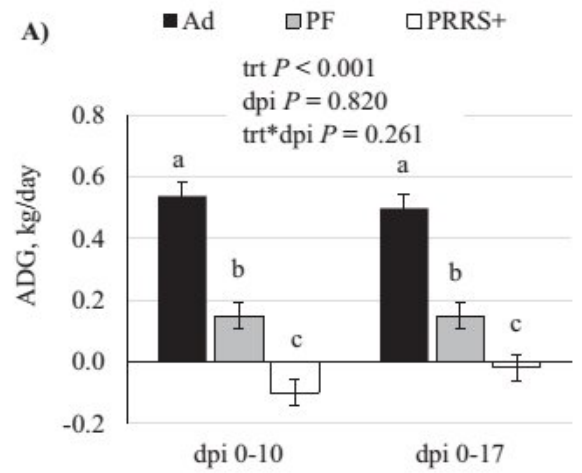
Impact of PRRSv on muscle metabolism

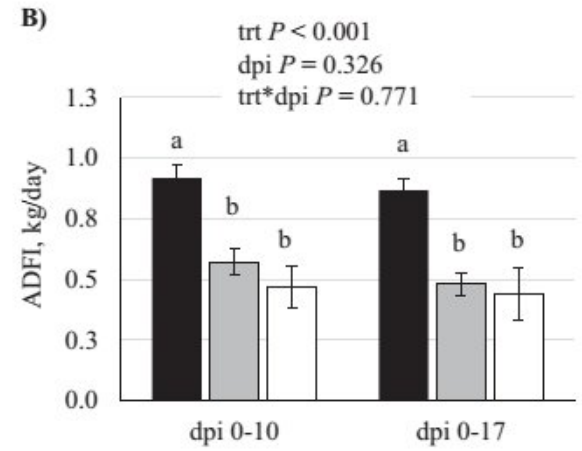
PRRS virus challenge is often accompanied by reduced feed intake, making it difficult to discern which effects are virus vs. feed intake driven.

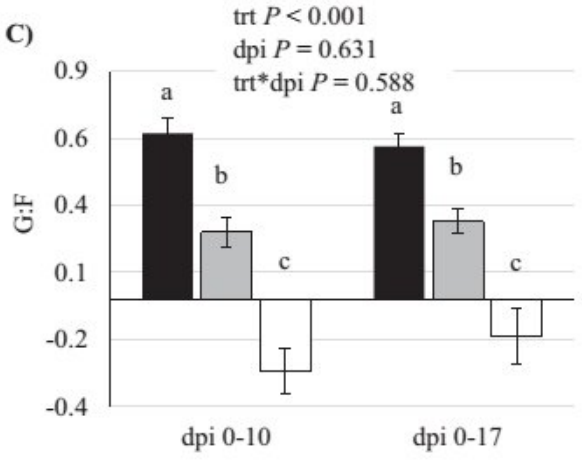
1. PRRS naïve, ad libitum fed (Ad)
2. PRRS-inoculated, ad libitum fed (PRRS+)
3. PRRS naïve, pair-fed to the PRRS-inoculated pigs' daily feed intake (PF)

- proteolysis (LM only)
- protein synthesis (LM only),
- oxidative stress (LM only),
- gluconeogenesis (liver),
- glycogen concentrations (LM and liver)

Helm, E. 2019. «Impact of Porcine Reproductive and Respiratory Syndrome Virus on Muscle Metabolism of Growing Pigs1». *Journal of Animal Science* 97 (8): 3213-27.







Pig performance selected for necropsy at either days post inoculation (dpi) 10 or dpi 17.

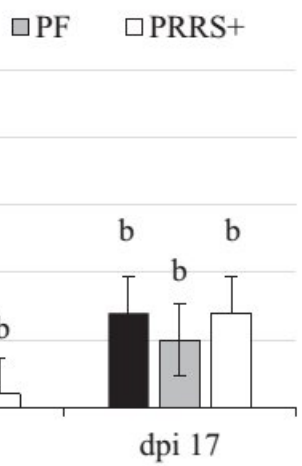
(A) Average daily gain (ADG),
(B) Average daily feed intake (ADFI), and
(C) eed efficiency (G:F)

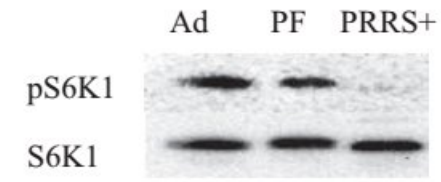
in pigs challenged with virus (PRRS+),

1. PRRS naïve, ad libitum fed (Ad)
2. PRRS-inoculated, ad libitum fed (PRRS+)
3. PRRS naïve, pair-fed to the PRRS-inoculated pigs' daily feed intake (PF)

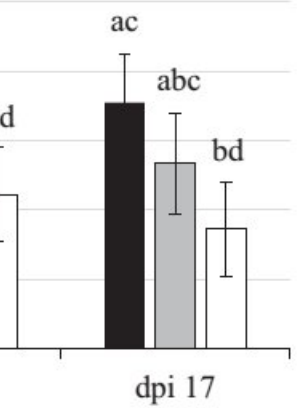
Differing letters a,b, and c represent $P < 0.05$. n = 8 pigs per treatment per dpi.

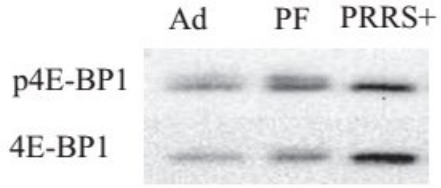
Relative LM protein abundance of phosphorylated to total at either days post inoculation (dpi) 10 or dpi 17.



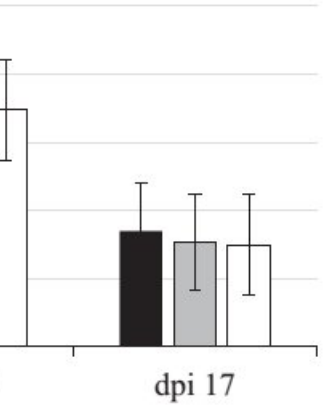


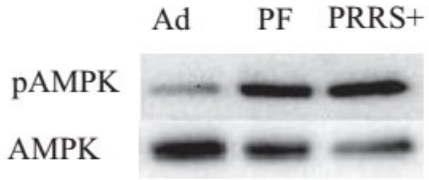
trt $P = 0.004$
dpi $P = 0.550$
trt*dpi $P = 0.006$





trt $P = 0.017$
dpi $P = 0.807$
trt*dpi $P = 0.057$





trt $P = 0.317$
dpi $P = 0.224$
trt*dpi $P = 0.255$

(A) S6K1
(B) 4E-BP1 and
(C) AMPK(G:F)

in pigs challenged with virus (PRRS+),

1. PRRS naïve, ad libitum fed (Ad)
2. PRRS-inoculated, ad libitum fed (PRRS+)
3. PRRS naïve, pair-fed to the PRRS-inoculated pigs' daily feed intake (PF)

Differing letters a,b, and c represent $P < 0.05$. n = 8 pigs per treatment per dpi.

TESTS & TRIALS
exactitud precisión

RESEARCH ARTICLE

Impact of viral disease hypophagia on pig jejunal function and integrity

Emma T. Helm[1], Shelby M. Curry[1], Carson M. De Mille[1], Wesley P. Schweer[1], Eric R. Burrough[2], Nicholas K. Gabler[1]*

1 Department of Animal Science, Iowa State University, Ames, Iowa, United States of America,
2 Department of Veterinary Diagnostic and Production Animal Medicine, Iowa State University, Ames, Iowa, United States of America

* ngabler@iastate.edu

Jejunum integrity, digestive enzyme activity, and

	Treatment				P-value	
	Ad	PF	PRRS+	SEM	Ad vs others	PF vs PRRS*
TER[2]	96.38	55.64	59.80	7.083	<0.001	0.679
FD4flux[3]	26.18	39.49	42.49	8.031	0.114	0.783
Glucose, µA[4]	19.18	41.25	76.06	10.28	0.003	0.014
Glutamine, µA[4]	1.59	9.091	14.83	3.171	0.002	0.069
Na+-K+ ATPase[5]	1.93	0.95	1.28	0.334	0.048	0.479
Lactase[6]	7.34	11.12	5.01	1.657	0.678	0.006
Sucrase[6]	19.84	24.94	15.67	2.485	0.819	0.001
Maltase[6]	56.01	66.07	46.27	5.847	0.975	0.006
Aminopeptidase[7]	4351	4737	4087	452.3	0.914	0.321

Pigs were either challenged with porcine respiratory and reproductive syndrome virus (PRRSV), PRRSV naïve and fed ad libitum (Ad), or PRRSV naïve and pair fed to PRRS+ pigs intake (PF). Pigs were euthanized at days post inoculation (dpi) 17.
2 TER =transepithelial resistance, Ω×cm^2
3 Macromolecule (FD4) permeability, ug/mL/min/cm^2
4 Active absorption calculated by subtracting µA before substrate (glucose or glutamine) from µA after substrate addition
5 µmol liberated inorganic P/h/mg protein
6 µM liberated 4-nitroaniline/min/mg protein
7 µmol liberated glucose/min/g protein

Helm, E.. 2020. «Impact of Viral Disease Hypophagia on Pig Jejunal Function and Integrity». Edited by David L. Harmon. *PLOS ONE* 15 (1): e0227265.

Jejunum morphology and globet cell counts[1]

	• Treatment				• P-value	
	• Ad	• PF	• PRRS+	• SEM	• Ad vs others	• PF vs PRRS*
• Morphology, µm						
• Villus height	• 481	• 411	• 324	• 27.3	• 0.003	• 0.036
• Crypt depth	• 293	• 228	• 243	• 19.2	• 0.017	• 0.588
• V:C[2]	• 1.72	• 1.89	• 1.37	• 0.122	• 0.369	• <0.001
• Globet cells/10,000 µm^2	• 6.73	• 7.04	• 7.46	• 0.499	• 0.155	• 0.294

1 Pigs were either challengedwith porcine respiratory and reproductive syndrome virus (PRRS+),PRRSV naïve and fed ad libitum (Ad), or PRRSV naïve and pair-fed to PRRS+ pigs intake (PF). Pigs were euthanized at days post inoculation (dpi) 17.
2 V:C =Villus height:Crypt depth

Helm, E.. 2020. «Impact of Viral Disease Hypophagia on Pig Jejunal Function and Integrity». Edited by David L. Harmon. *PLOS ONE* 15 (1): e0227265.

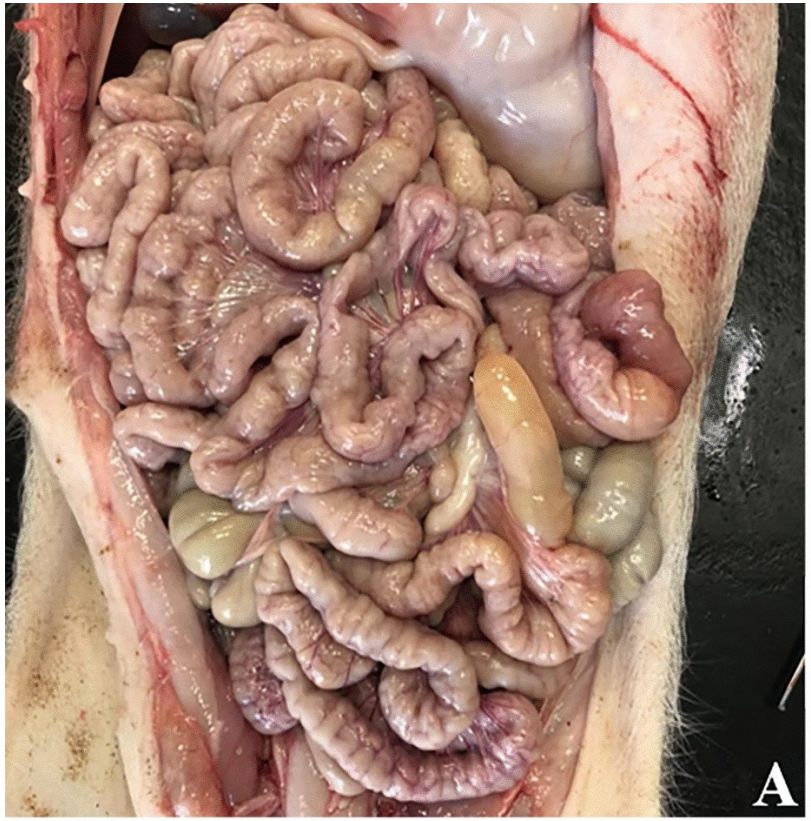
Jejunum mRNA abundance as measured via PCR[1]

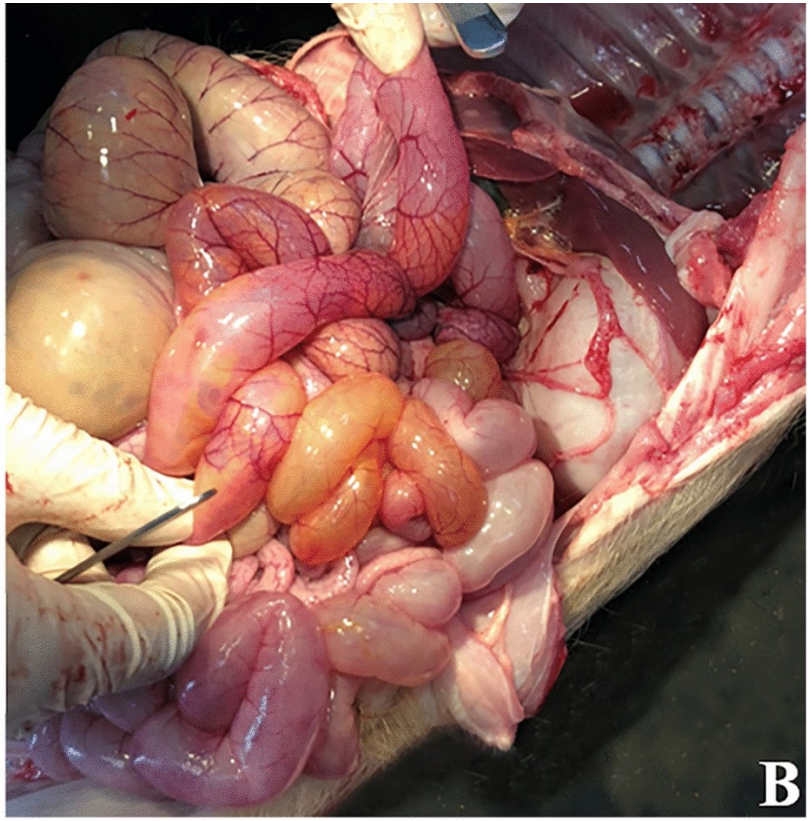
	0.94Treatment				P-value	
	Ad	PF	PRRS+	SEM	Ad vs others	PF vs PRRS*
Claudin 2	1.45	1.34	0.69	0.209	0.094	0.025
Claudin 3	1.05	0.72	0.54	0.114	0.006	0.273
Claudin 4	0.91	1.21	0.76	0.223	0.778	0.133
Ocludin	0.75	0.84	0.64	0.165	0.936	0.310
ZO-1	1.09	1.10	0.48	0.196	0.194	0.026
Glucose transporter 2	0.89	1.01	0.63	0.131	0.681	0.046
SGLT1	0.89	0.83	0.83	0.197	0.771	0.996
AMPK	0.94	0.94	0.38	0.336	0.204	0.474

1 Pigs were either challengedwith porcine respiratory and reproductive syndrome virus (PRRS+),PRRSV naïve and fed ad libitum (Ad), or PRRSV naïve and pair-fed to PRRS+ pigs intake (PF). Pigs were euthanized at days post inoculation (dpi) 17.
2 Gene abundances expressedas fold changes from Ad average (2-ΔΔCt)

Helm, E.. 2020. «Impact of Viral Disease Hypophagia on Pig Jejunal Function and Integrity». Edited by David L. Harmon. *PLOS ONE* 15 (1): e0227265.

PRRSV infection causes pathological injury of the lungs and intestine

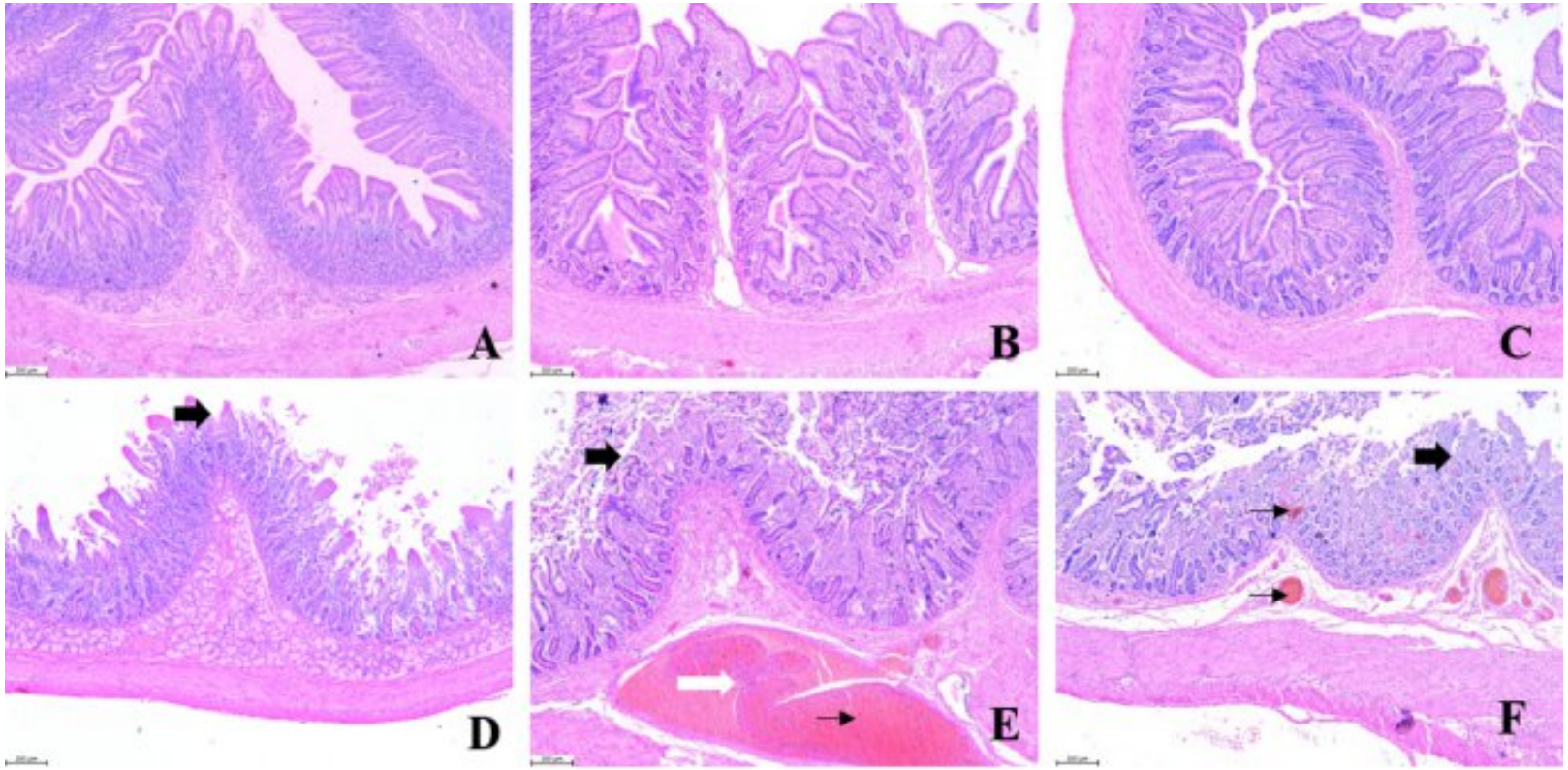




Representative images of the intestine in the experimental pigs.
A control group. B PRRSV-infected group.

Zhao, Jin, et al. 2021. «Damage to intestinal barrier integrity in piglets caused by porcine reproductive and respiratory syndrome virus infection». *Veterinary Research* 52 (1): 93.

Histopathological changes in the intestine



Microscopy magnification: 50 × . Scale bar: 200 μm.
A–C Duodenum, jejunum and ileum samples collected from control pigs.
D–F Duodenum, jejunum, and ileum samples collected from

Zhao, Jin, et al. 2021. «Damage to intestinal barrier integrity in piglets caused by porcine reproductive and respiratory syndrome virus infection». *Veterinary Research* 52 (1): 93.

Veterinary Microbiology 188 (2016) 1–11

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

Microbiome associations in pigs with the best and worst clinical outcomes following co-infection with porcine reproductive and respiratory syndrome virus (PRRSV) and porcine circovirus type 2 (PCV2)

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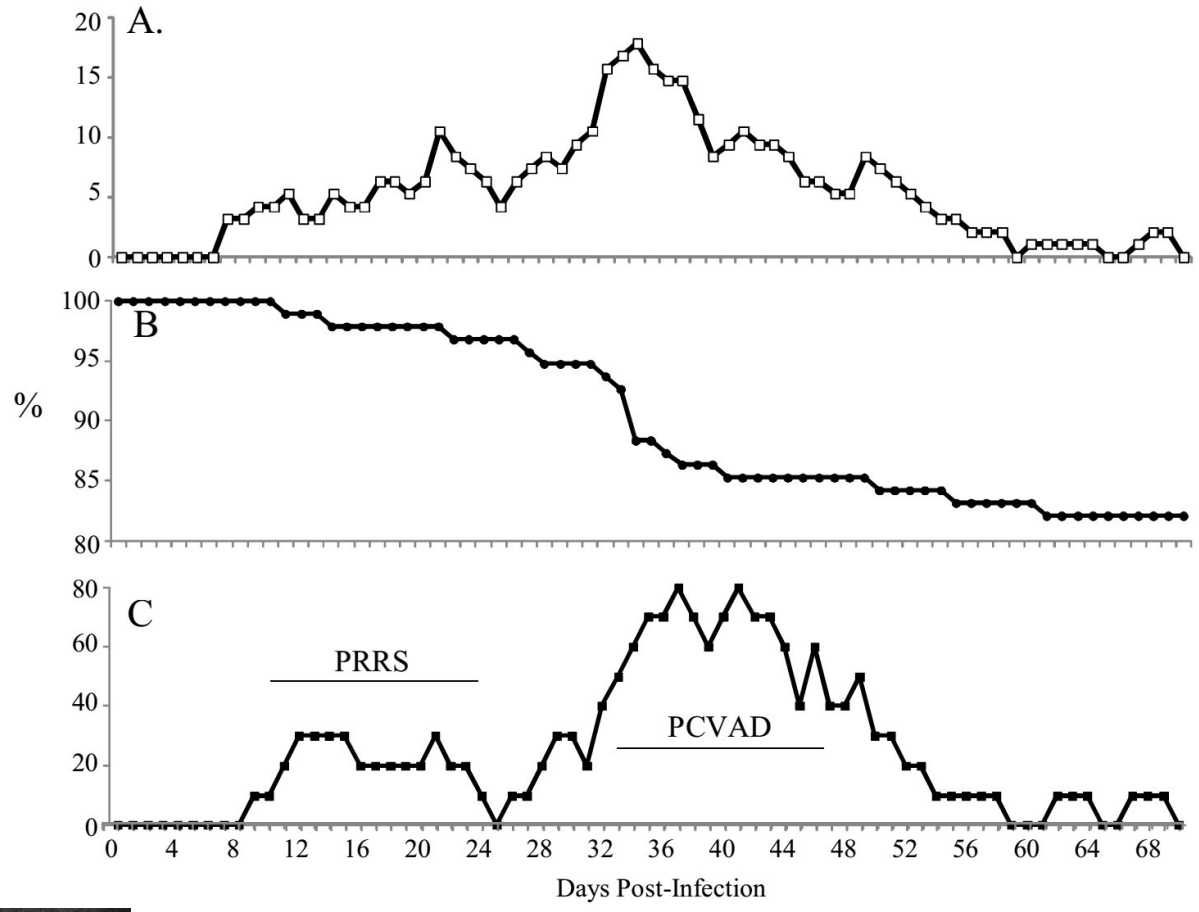
Clinical disease following co-infection with PRRSV and PCV2



a) Percent of pigs receiving treatment as a result of clinical signs (n = 95)
b) Percent survival over time (n = 95)
c) Percent of worst outcome pigs receiving treatment as a result of

Niederwerder, M.. 2016. «Microbiome Associations in Pigs with the Best and Worst Clinical Outcomes Following Co-Infection with Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) and Porcine Circovirus Type 2 (PCV2)». *Veterinary Microbiology* 188 (mayo): 1-11.

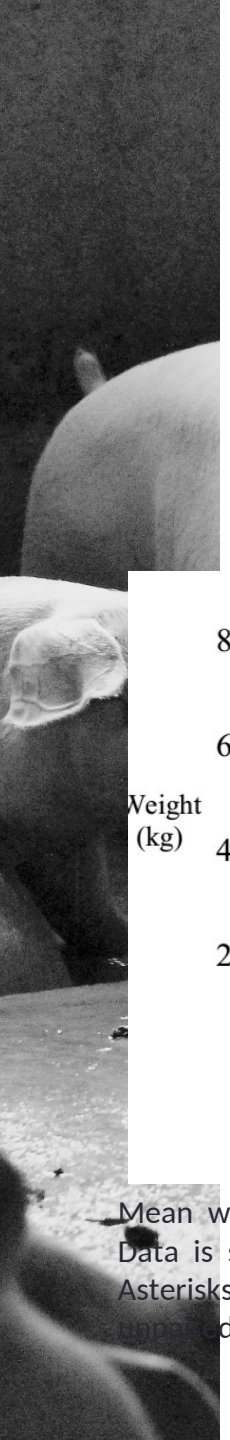
Niederwerder, M.. 2016. «Microbiome Associations in Pigs with the Best and Worst Clinical Outcomes Following Co-Infection with Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) and Porcine Circovirus Type 2 (PCV2)». *Veterinary Microbiology* 188 (mayo): 1-11.

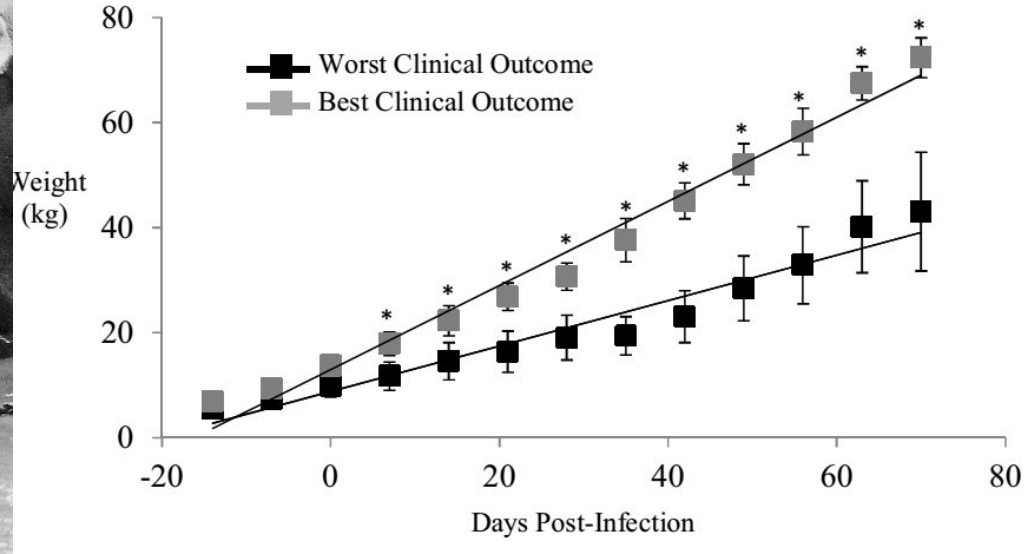
Average daily gain between 0 and 70 dpi

• Worst Performing		• Best Performing	
• Pig	• ADG (g)	• Pig	• ADG (g)
• 12	• 149	• 30	• 779
• 50	• 280	• 55	• 797
• 3	• 492	• 43	• 805
• 47	• 493	• 98	• 808
• 61	• 495	• 29	• 827
• 16	• 506	• 15	• 831
• 1	• 537	• 62	• 848
• 28	• 542	• 6	• 883
• 24	• 555	• 63	• 889
• 88	• 698	• 54	• 903
• **Mean[1]**	• **475**	• **Mean[1]**	• **837**
• **SD**	• **153**	• **SD**	• **42**

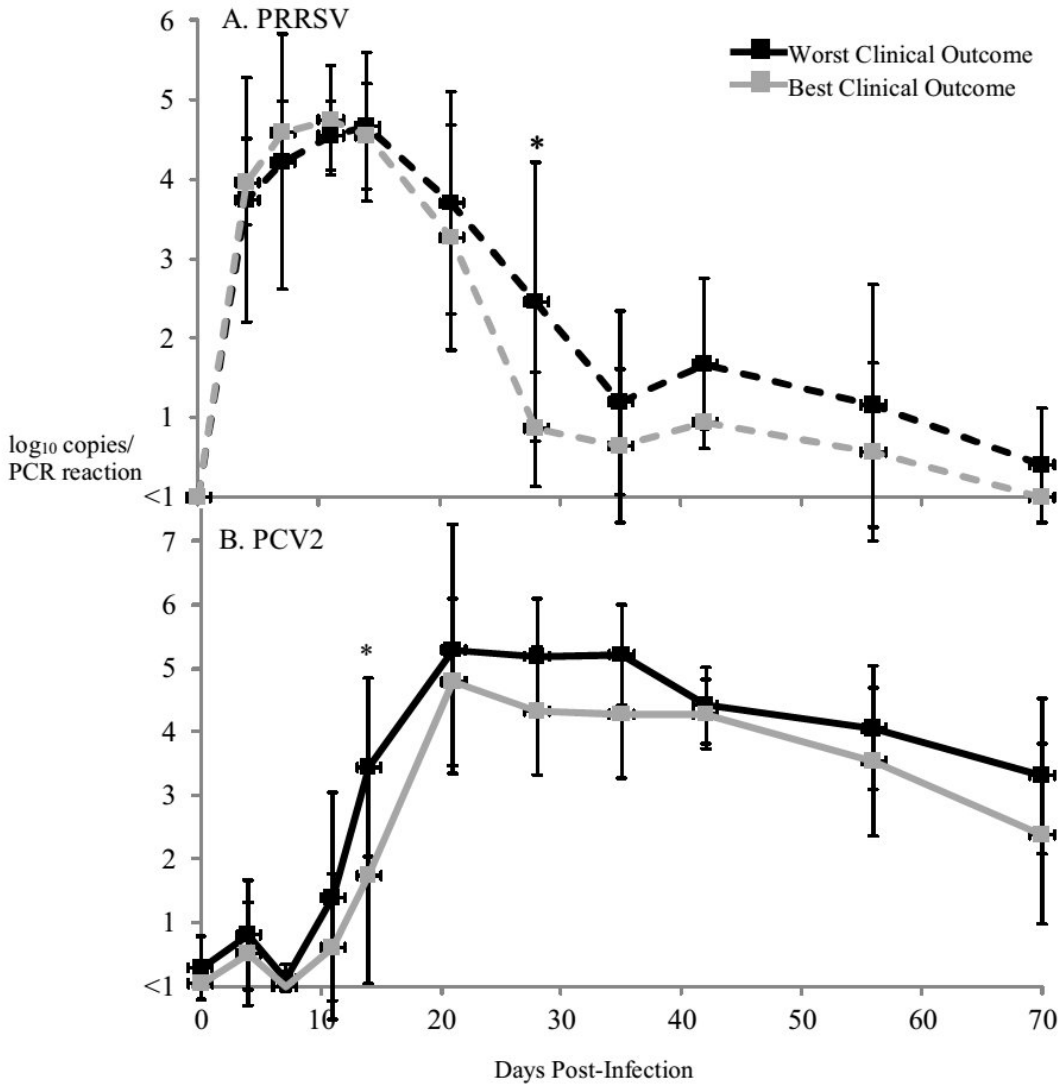
*Significant difference between means, $p < 0.0001$, unpaired t-test.

Outcomes over time for pigs with the best and worst clinical





Mean weights over time for pigs with the best and worst clinical outcomes. Data is shown as mean weight one standard deviation with regression lines. Asterisks identify statistically significant differences between groups ($p < 0.005$, unpaired t-test using repeated measures analysis).

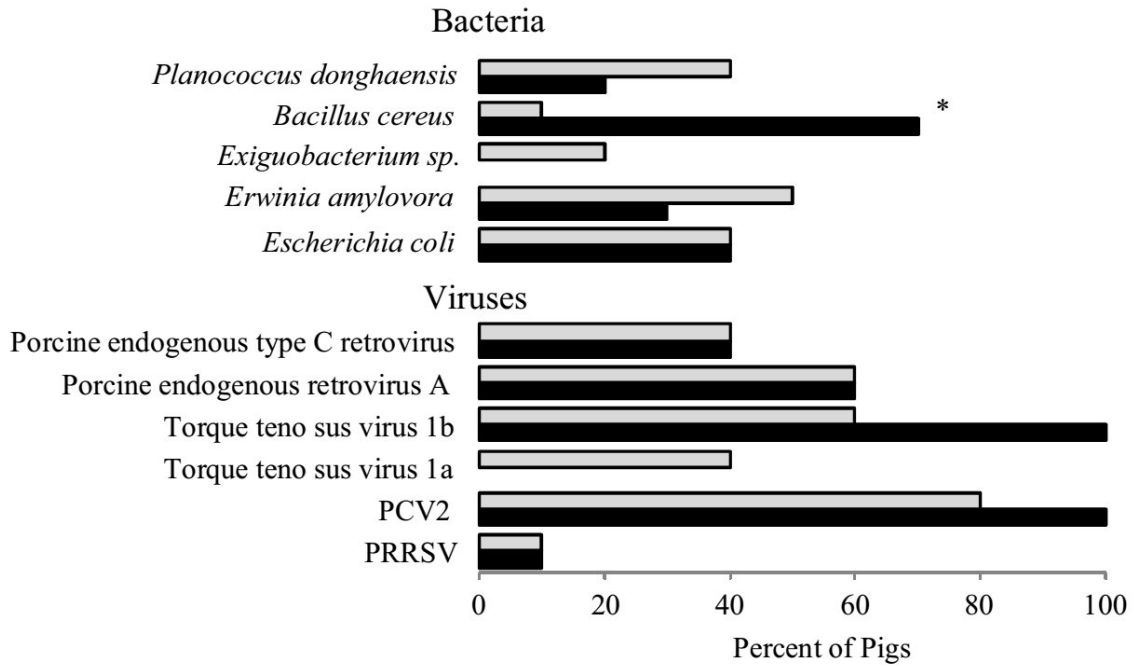


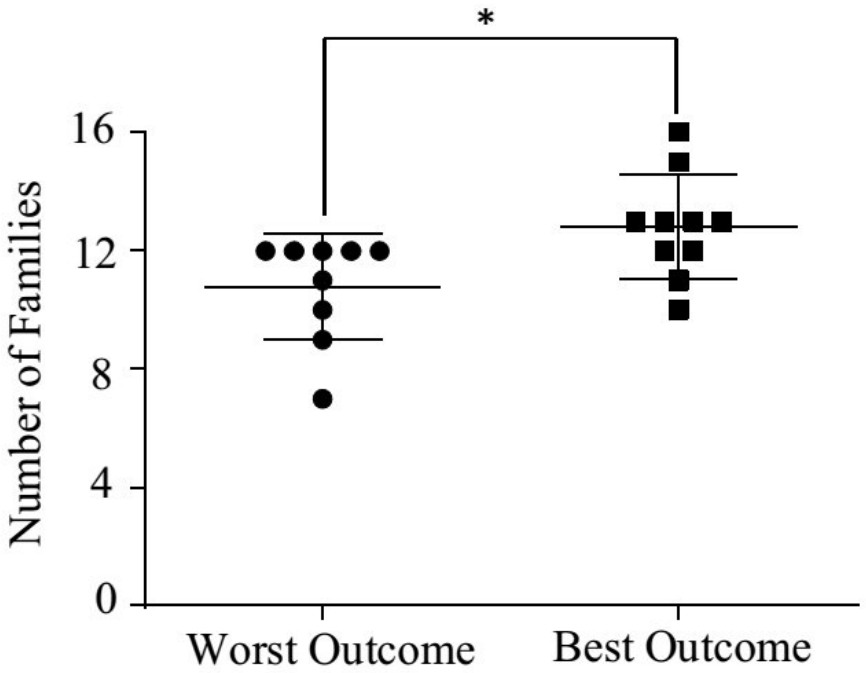
PRRSV and PCV2 viremia in pigs with best and worst clinical outcomes. The figure shows mean PCR values 1 standard deviation after challenge with PRRSV and PCV2. Asterisks identify statistically significant differences between groups ($p < 0.05$, unpaired t-test)

Niederwerder, M.. 2016. «Microbiome Associations in Pigs with the Best and Worst Clinical Outcomes Following Co-Infection with Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) and Porcine Circovirus Type 2 (PCV2)». *Veterinary Microbiology* 188 (mayo): 1-11.

Outcomes over time for pigs with the best and worst clinical

Niederwerder, M.. 2016. «Microbiome Associations in Pigs with the Best and Worst Clinical Outcomes Following Co-Infection with Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) and Porcine Circovirus Type 2 (PCV2)». *Veterinary Microbiology* 188 (mayo): 1-11.





Microarray detection of microbes in serum 70 days after co-infection with PCV2 and PRRSV. Percent of best clinical outcome pigs (n = 10, open bars) and worst clinical outcome pigs (n = 10, black bars) are shown for each microbe detected on the array. Asterisks identify statistically significant differences between groups (p = 0.02, Fisher's exact test).

Fecal microbiome diversity in pigs with the best and worst clinical outcomes. Data is shown as the total number of microbial families detected by DNA microarray 70 days after co-infection with PRRSV and PCV2. Group means and standard deviations are represented by horizontal lines. The number of microbial families detected in feces were significantly different between the best and worst outcome groups (*p = 0.017, Mann-Whitney U test).

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Virus Research

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Short communication

Pathogenesis and inflammatory responses of swine H1N2 influenza viruses in pigs

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Received 12 March 2007; received in revised form 2 May 2007; accepted 3 May 2007
Available online 14 June 2007

Cytokines

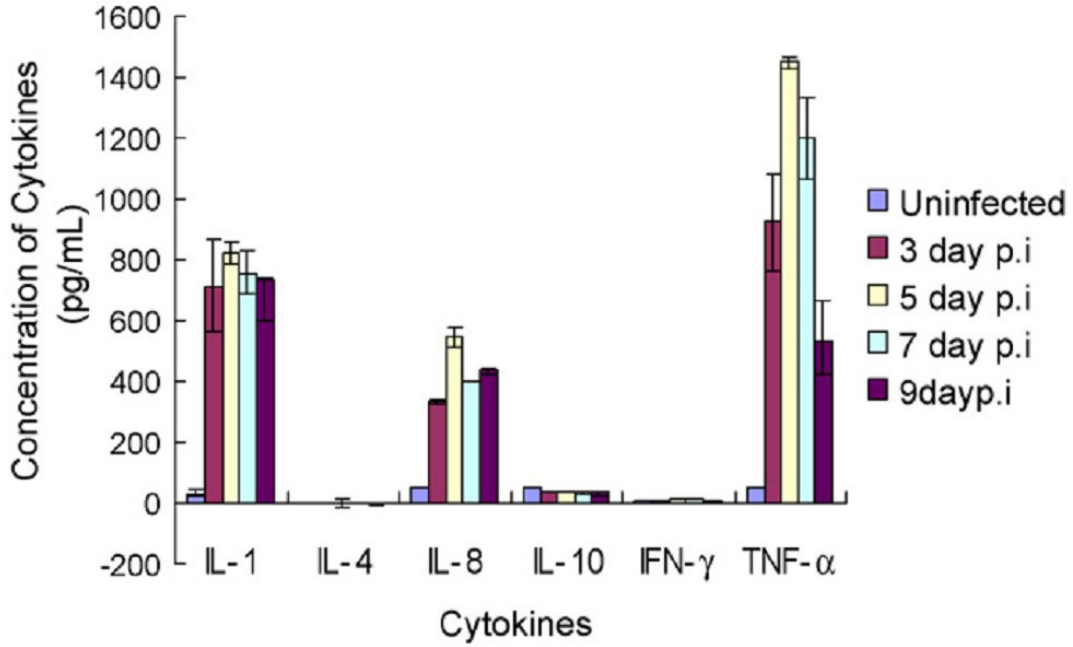
- Pro-inflammatory:
  - TNF-α: Tumor Necrosis Factor Alfa
  - IL-1: Interleukin 1
  - IL-8: Interleukin 8
- Anti-Inflammatory:
  - IL-4: Interleukin 4
  - IL-10: Interleukin 10

Diarrhea also is present in Influenza outbreaks

• Clinical signs	• Infected pigs • (showing clinical signs/total pigs)	• Uninfected pigs (showing clinical signs/total pigs)
• Coughing	• 5/5	• 0/5
• Labored breathing	• 4/5	• 0/5
• Dyspnea	4/5	• 0/5
• Nasal discharge	• 5/5	• 0/5
• Facial edema	• 5/5	• 0/5
• Anorexia	• 3/5	• 0/5
• Diarrhea	• 3/5	• 0/5

Jo, Su Kyoung, 2007. «Pathogenesis and Inflammatory Responses of Swine H1N2 Influenza Viruses in Pigs». *Virus Research* 129 (1): 64-70.

The inflammatory cytokine inductions in lungs of infected pigs.



Pigs were i.n. infected with 10^4 $TCID_{50}$/ml (1 ml) of A/Swine/Korea/S5/05 (H1N2) influenza viruses, and tissues were collected at 3, 5, 7, and 9 days p.i. and homogenized in 1 ml of PBS (pH 7.4) before cytokines were detected with cytokine ELISA kit specific for porcine cytokines. The results are the mean of five pigs ± standard errors. Five uninfected pigs were used as a control.

Jo, Su Kyoung, 2007. «Pathogenesis and Inflammatory Responses of Swine H1N2 Influenza Viruses in Pigs». *Virus Research* 129 (1): 64-70.

Associations between the gastrointestinal microbiome and outcome in infectious respiratory disease

Table 1. Associations between the gastrointestinal microbiome and outcome in infectious respiratory disease

Pathogen or disease	Species	Beneficial microbiome characteristic(s)	Outcome	Reference
PRRSV and PCV2 co-infection	Pig	Increased microbial diversity, *Escherichia coli*	Decreased virus replication, reduced clinical disease, increased weight gain, reduced lung pathology	(Niederwerder et al., 2016)
Mycoplasma hyopneumoniae	Pig	Fecal microbiota transplant†, increased microbial diversity	Earlier seroconversion, decreased coughing, reduced gross lung pathology	(Schachtschneider et al., 2013)
Rhodococcus equi	Horse	None detected	Compared foals with clinical and subclinical pneumonia to healthy foals	(Whitfield-Cargile et al., 2015)
Respiratory syncytial virus	Mice	*Lactobacillus johnsonii*†	Decreased airway inflammation, reduced IL-4, IL-5, IL-13 and IL-17 expression, decreased lung pathology	(Fujimura et al., 2014)
Influenza virus	Mice	*Lactobacillus brevis*†	Decreased weight loss, improved overall condition, increased IgA antibody production, increased IFN-α	(Waki et al., 2014b)
Influenza virus	Mice	*Lactobacillus acidophilus*†	Reduced virus titers in lung, reduced lung pathology, increased IFN-α	(Goto et al., 2013)
Influenza virus	Mice	*Bifidobacterium longum*†	Decreased weight loss and clinical disease, reduced viral replication, lower histopathological lung scores	(Iwabuchi et al., 2011)
Influenza virus	Mice	Endogenous microbiota, neomycin-sensitive bacteria	Increased antibody titer and CD4 T-cell response, increased cytokine expression and cytotoxic T-cell activity, reduced virus in lung	(Ichinohe et al., 2011)
Influenza virus	Mice	Endogenous microbiota, neomycin-sensitive bacteria	Reduced lung pathology, increased IFN-γ and IL-17 expression	(Wu et al., 2013)
Burkholderia thailandensis	Mice	*Escherichia coli*†	Reduced wasting of skeletal muscle and fat, decreased weight loss	(Schieber et al., 2015)
Streptococcus pneumoniae	Mice	Endogenous microflora, fecal microbiota transplant†, increased microbial diversity	Reduced bacteria in lung, decreased lung pathology, decreased mortality, increased alveolar macrophage function	(Schuijt et al., 2016)
Methicillin-resistant *Staphylococcus aureus*	Mice	Segmented filamentous bacteria	Decreased bacteria in lung, decreased bacterial dissemination, less severe pneumonia, decreased mortality, increased IL-22 in lung	(Gauguet et al., 2015)
Mycobacterium tuberculosis	Mice	Lack of *Helicobacter hepaticus*	Reduced IL-10 expression, decreased bacterial load in lung, reduced lung pathology	(Arnold et al., 2015)
Klebsiella pneumoniae	Mice	Endogenous microbiota, Fecal microbiota transplant†	Decreased mortality, decreased systemic pathogen dissemination, increased TNF-α and CXCL-1	(Fagundes et al., 2012)
Escherichia coli	Mice	Endogenous microbiota	Decreased bacterial dissemination, reduced mortality, decreased bacteria in lung, enhanced alveolar macrophage activity, increased neutrophil activity, decreased lung pathology	(Chen et al., 2011)
Pseudomonas aeruginosa	Mice	Endogenous microbiota	Decreased mortality, increased TNF and IL-1β in lung,	(Fox et al., 2012)

Nieder[illegible] 2017. «Role of the Microbiome in [illegible]ine Respiratory Disease». *Veterinary [illegible]biology* 209 (septiembre): 97-

Differences in taxonomic abundance between the modulated and control group upper respiratory microbiome

• Phylum	• Control Upper Respiratory	• Modulated Upper Respiratory	• P-value
• Actinobacteria	• 5.17 %	• 3.91 %	• 0.003
• Bacteroidetes	• 38.30 %	• 46.45 %	• 0.001
• Firmicutes	• 51.80 %	• 44.88 %	• 0.002
• Synergistetes	• 0.14 %	• 0.62 %	• 0.0015

Schachtschneider, K.M.,et al.. 2013. «Modulation of Systemic Immune Responses through Commensal Gastrointestinal Microbiota». Edited by Sarah K. Highlander. *PLoS ONE* 8 (1): e53969

Conclusions

- The former microbiota status can affect the development of new diseases in piglets weaned
- Also, viral and bacterial diseases change the microbiota of the piglet
- Controlling not only intestinal diseases but respiratory diseases can succeed in the production improvement variables in pig business