

APPENDIX D
SAES-422
Format for Multistate Research Activity
Accomplishments Report

Project/Activity Number: NC229

Project/Activity Title: PRRSV and other emerging viral diseases of swine

Period Covered: October 31, 2015 to September 1, 2016

Date of This Report:

Annual Meeting Date(s): December 4

Participants:

Eric Nelson South Dakota State U. (SDSU); eric.nelson@sdstate.edu

Osorio, Fernando A.; University of Nebraska-Lincoln (UNL); fosorio@unl.edu

Rowland, Raymond R.R.; Kansas State University (KSU); browland@vet.k-state.edu

Benfield, David, Ohio State University (OSU); benfield.2@osu.edu

Faaberg, Kay; National Animal Disease Center (NADC); kay.faaberg@ars.usda.gov

Gourapura, Renukaradhya J.; The Ohio State University (OSU); gourapura.1@osu.edu

Holland, Margo; USDA,CSREES; mholland@nifa.usda.gov

Johnson, Peter; USDA,CSREES; PJOHNSON@NIFA.USDA.GOV

Lunney, Joan; USDA-ARS, BARC, joan.lunney@ars.usda.gov

Mateu, E. CRESA Univ Autonoma de Barcelona, Spain; Enric.Mateu@uab.cat

Meng,X-J VPI (Virginia Tech); xjmeng@vt.edu

Murtaugh, Michael P; University of Minnesota (UMN); murta001@umn.edu

Prieto, Cinta; Universidad Complutense, Madrid, Spain; cprietas@vet.ucm.es

Pogranichniy Roman, Purdue University, rmp@purdue.edu

Ramamoorthy, S, North Dakota - North Dakota St Univ (ND) sheela.ramamoorthy@ndsu.edu

Zhang, Yanjin; University of Maryland; zhangyj@umd.edu

Zimmerman, Jeff; Iowa State University (ISU); jjzimm@iastate.edu

Zuckermann, Federico; University of Illinois at Urbana-Champaign (UIUC); fazaaa@illinois.edu

Yang, Hanchun; China Agricultural University; yanghanchun1@cau.edu.cn

Brief summary of minutes of annual meeting:

The 2016 NC229 meeting took place on December 4 2015, 8:00 am to 5:00 pm at Marriott Downtown Hotel in Chicago Illinois, as part of Pre-CRWAD satellite events and in a joint session with the North American PRRS Symposium. Both AM and PM sessions had an attendance that exceeded in both cases 150 persons. Stations represented are listed above. The Agenda for the meeting is shown in table 1. After the scientific sessions, future direction and funding opportunities were explored during the business meeting. In particular USDA NIFA staff provided an overview of NIFA funding opportunities for 2017. At 5:15 PM the meeting is adjourned.

Table 1: NC229 Annual Meeting Agenda of Activities

8:00am-8:15am	Opening remark
Session 1	Moderators: Ben Hause (Cambridge Technologies) & Luis Gimenez-Lirola (Iowa State University)
8:15am -10:00am	
Diego Diel South Dakota State University	Pathogenesis and infection dynamics of Senecavirus A in pigs, Abstract #42
Alexandra Buckley USDA	Senecavirus A infection in sows, neonates, and market weight gilts with subsequent protective immunity, Abstract #35
Steven Lawson South Dakota State University	Development of antibody reagents & assays for Senecavirus A serodiagnosis, Abstract #10
Fangfeng Yuan Kansas State University	Construction and characterization of a full-length cDNA infectious clone of emerging porcine Senecavirus A, Abstract #24
Rachel Palinski Kansas State University	A novel porcine circovirus distantly related to known circoviruses is associated with porcine dermatitis and nephropathy syndrome and reproductive failure, Abstract #18
Chantale Provost University of Montreal	Development of a new molecular method to discriminate Porcine Epidemic Diarrhea Virus infectious viral particles, from non-infectious ones, which are contaminating pig derived food additives, Abstract #21
Rolf Rauh Tetracore, Inc.	Evaluation of a portable real-time PCR platform (T-COR 8™) for ASF during outbreaks in an endemically infected population in Uganda, Abstract #11
10:00am-10:15am	Break
Session 2	Moderators: Ying Fang (Kansas State University) & Gustavo Delhon (University of Nebraska-Lincoln)
10:15am-12:00am	
Ignacio Correas University of Nebraska-Lincoln	Cross-reactivity of immune responses against Porcine Reproductive and Respiratory Syndrome virus, Abstract #38
Joseph Darbellay VIDEO-InterVac.	The progression to T cell immunity after infection with porcine reproductive and respiratory syndrome virus, Abstract #40
Junru Cui University of Connecticut	A GP5 Mosaic T-cell Vaccine for Porcine Reproductive and Respiratory Syndrome Virus Is Immunogenic, Induces Broad Cellular Responses to Diverse Strains and Confers Partial Protection to Pigs, Abstract #64
Kay Kimpston-Burkgren University of Nebraska-Lincoln	Contribution of PRRSV minor glycoproteins to a protective immune response in swine, Abstract #51
Tanja Opriessnig University of Edinburgh	Iowa State University, An interferon inducing PRRSV vaccine candidate protects against challenge with a heterologous virulent type 2 strain in a conventional pig model, Abstract #71
Volker Gerdts VIDEO-InterVac	Development of a Novel Vaccine for Porcine Epidemic Diarrhea Virus, Abstract #7
Jishu Shi Kansas State University	Pigs immunized with a novel E2 subunit vaccine are protected from subgenotype heterologous Classical Swine Fever Virus challenge, Abstract #76
12:00am – 1:30pm	Lunch On your own
Session 3	Moderators: Diego Diel (South Dakota State University) & Sheila Ramamoorthy (North Dakota State University)
1:30pm-3:00pm	

Marti Cortey IRTA-CReSA	Changes in the genetic composition of PRRSV quasispecies and its relationship with long and short viral infections, Abstract #39
Rui Guo Kansas State University	Porcine reproductive and respiratory syndrome virus takes advantage of host intercellular mitochondria transferring pathway for cell to cell spreading of the infection, Abstract #48
Ana Stoian Kansas State University	Identification of CD163 domain involved in the infection with Type II Porcine Reproductive and Respiratory viruses, Abstract #86
Hanzhong Ke University of Illinois	SAP domain in nsp1-beta of porcine reproductive and respiratory syndrome virus (PRRSV) correlates with interferon suppression in cells and pathogenesis in pigs, Abstract #50
Federico Zuckermann University of Illinois	The unfolded protein response induced by porcine reproductive and respiratory syndrome virus infection of alveolar macrophages is involved in immune dysregulation, Abstract #62
Pengcheng Shang Kansas State University	A novel mechanism of protein-stimulated trans-activation of ribosomal frameshifting in porcine reproductive and respiratory syndrome virus: implication in improved vaccine development, Abstract #85
3:00pm-3:15pm	Break
Session 4	Moderators: Dan Rock (University of Illinois) & KJ Yoon (Iowa State University)
3:15pm-4:30pm	
Susan Detmer University of Saskatchewan	Pathological findings at the maternal-fetal interface during the early type 2 PRRS virus infection of late gestation pregnant gilts, Abstract #41
Yanli Li UAB	Resolution of genotype 1 PRRSV attachment on bone marrow-derived dendritic cells, Abstract #53
Lei Zhou China Agricultural University	Attenuate Highly Pathogenic Porcine Reproductive and Respiratory Syndrome Virus by incorporating target site of hematopoietic-specific MicroRNA into viral genome, Abstract #82
Jenelle Dunkelberger Iowa State University	A major gene for host response under PRRS challenge is not negatively associated with overall performance in commercial pig lines under nonchallenged conditions, Abstract #44
Natasha Gaudreault Kansas State University	Genetically edited pigs lacking CD163 show no resistance following infection with the African Swine Fever Virus isolate, Georgia 2007/1, Abstract #47
4:30pm-5:00pm	NC229 business meeting

Accomplishments:

Objective 1. Control of PRRSV

In objective 1, the major areas of focus/achievements by the NC 229 group during 2016 included:

1.1 Innate immunity against PRRSV. Studies on the effect that different NSPs of PRRSV may have on innate immunity mechanisms, on apoptosis, or the capacity for modulating overall immune response by strains that cause stimulation of IFN rather than suppression. Also includes the effect of PRRSV of macrophages and cytokines modulation. The stations focusing in this area were: UCONN, UIUC, KSU, OSU, China Agr U, NE, NADC, SDSU and UMD

1.2 PRRSV immunity and vaccinology. Understanding correlates of immunity and mechanisms

to broaden protection, including neutralizing antibodies, developing of naturally occurring or synthetic strains of PRRSV inducing broader protection, alternative vectors for PRRSV antigens or epitopes, DIVA marker systems, mechanism of attenuation and immunogenic potential of NSPs etc. The stations that focused studies in this area were: UMN, UMD, VPI, NADC, UNL, UIUC, UWI, ISU, NE and KSU

1.3 Virulence of PRRSV. Understanding virulence factors/markers, some of these studies included co-infection with bacteria. The stations that focused studies on this area were: NADC and China Agr U

1.4 Genetic mapping of resistance to PRRSV infection (ISU, KSU, UMO, USDA), genetic modification of receptors (KSU)

1.5 Epidemiology of PRRSV transmission, which may include aerobiology, and virus evolution: UMN, ISU, VNIIIVViM Russia and UWI, Detection of PRRSV in populations (ISU)

1.6 Economic Impact of PRRSV control; UMN, ISU

Objective 2 Developing effective and efficient approaches for detection, prevention and control of pressing viral diseases of swine of recent emergence.

In objective 2, the major areas of focus/achievements by the NC 229 group during 2016 included:

2.1 ascertaining pathogenesis and transmission of and establishing diagnostics and reagents for **PEDV**: (ISU, UMN, OSU, KSU, SDSU, VNIIIVViM Russia, Purdue). Reverse genetics of PEDV (KSU). Studying the protective immune response to PEDV (OSU)

2.2 Genomics and replication of **PCV and novel ss DNA viruses** of swine (ISU, NADC)

2.3 Genetic and antigenic evolution of swine influenza virus (SIV) and epidemiology of transmission of SIV (NADC UMN, ISU, SDSU, CENSACuba) testing of SIV vaccines in vivo (NADC) and in vitro models (Purdue) testing of adjuvants for SIV inactivated immunogens (NADC)

2.4 Characterizing the ongoing outbreak of **Seneca valley virus**, development of diagnostic tools and characterization of pathogenesis, fulfillment of Koch's postulates: (ISU, NADC, UMN, KSU)

2.5 Characterization and diagnostic reagents for **Atypical Pestivirus of Swine** (KSU, ISU).

2.6 Classical swine fever pathogenesis & epidemiology (VNIIIVViM Russia, CENSACuba, UCON) and vaccinology (CENSACuba)

2.7 African Swine Fever Virus, epidemiology (VNIIIVViM Russia, UIUC) and protective immunity/vaccinology (VNIIIVViM Russia, UIUC, KSU, TX A&M) and diagnostics

2.8 Swine vesicular disease virus (VNIIIVViM Russia)

2.9 Population monitoring for various viral diseases (PRRSV, SIV, CSFV, FMDV, ASFV) utilizing oral fluids and body fluids (ISU, PIADC)

Impacts:

General impacts of the NC-229 program

- First, it should be mentioned that a very important verifiable impact has been the excellent reception (in respect to record attendance, and active interest of engaged audience) of the high quality scientific presentations that the NC-229 meeting featured this year jointly with the *North American PRRS and other Emerging Viruses Symposium*.
- A positive parameter that permits to anticipate important long term impacts for this current 5 year project is the number of publications submitted by the group during the year 2016 (third year of the project). As shown in the document attached (under “Publications”), the NC-229 group has published in 2016 a total of 135 refereed journal publications in the area of PRRSV, PCV2, influenza virus, swine enteric coronaviruses and senecavirus. The number would be higher if other publications are included.

A non-comprehensive list of impacts related to major swine viral pathogens, consisting only of some examples for 2015, follows:

Impacts in PRRSV Control:

- Possible role of IFN-positive PRRSV strain on vaccine improvement (UMD)
- Possible role of molecular attenuation in attaining better MLV vaccines (OHIO)
- Advances in understanding virulence of highly pathogenic PRRSV (CHINA Agr U)
- Patent (PCT132015/052214) for a synthetic PRRSV virus serving as seed vaccine candidate for broad protection against PRRSV type II. The invention received the “2015 Breakthrough of the Year Award” conferred by UNL (UNL/UIUC).Currently explored by industry
- Focus on broadly neutralizing antibodies and swine genetics may provide a bio-marker for broadly protective vaccine (KSU)
- Focus on DIVA marker candidates (NADC)

Impacts in PEDV and other endemic swine viruses research

- PEDV pathogenesis, and SVV pathogenesis and diagnostic tools (ISU, MN, SDSU, KSU)
- Elucidation of risk of feed transmission for PEDV (SDSU)
- Swine health monitoring program for studies on virus transmission (SIV) (MN)
- Strains and platforms to improve current SIV vaccines (NADC, ISU, MN)

Impacts in FAD :

- Vigorous emphasis for development of noninfectious diagnostic reagents (probes, microarrays, Elisas, Mabs) to be used in US labs (ISU, KSU, SDSU, MN)
- ASFV: international collaboration on ASFV virulence and protective immunity conducted in the field (VNIIIVViM Russia/UIUC)
- CSFV: Regional Surveillance of CSFV in the Caribbean area, and OIE twinning project for validation of CSF regional diagnostic tools (CENSACUBA/Hannover U. Germany)

Publications: See the attached

Authorization: Submission by an AES or CES director or administrative advisor through NIMSS constitutes signature authority for this information.

*Limited to three pages or less exclusive of publications, details may be appended.

Refereed publications by NC229 participants

PRRS virus:

1. Sun Y, Ke H, Han M, Chen N, Fang W, Yoo D. Nonstructural Protein 11 of Porcine Reproductive and Respiratory Syndrome Virus Suppresses Both MAVS and RIG-I Expression as One of the Mechanisms to Antagonize Type I Interferon Production. *PLoS One*. 2016 Dec 20;11(12):e0168314. doi: 10.1371/journal.pone.0168314.eCollection 2016. PubMed PMID: 27997564; PubMed Central PMCID: PMC5172586.
2. Piñeyro PE, Subramaniam S, Kenney SP, Heffron CL, Giménez-Lirola LG, Meng XJ. Modulation of Proinflammatory Cytokines in Monocyte-Derived Dendritic Cells by Porcine Reproductive and Respiratory Syndrome Virus Through Interaction with the Porcine Intercellular-Adhesion-Molecule-3-Grabbing Nonintegrin. *Viral Immunol*. 2016 Dec;29(10):546-556. Epub 2016 Sep 19. PubMed PMID: 27643915.
3. Sun H, Pattnaik AK, Osorio FA, Vu HLX. Identification of viral genes associated with the interferon-inducing phenotype of a synthetic porcine reproductive and respiratory syndrome virus strain. *Virology*. 2016 Dec;499:313-321. doi: 10.1016/j.virol.2016.09.018. Epub 2016 Oct 11. PubMed PMID: 27736706.
4. Evenson D, Gerber PF, Xiao CT, Halbur PG, Wang C, Tian D, Ni YY, Meng XJ, Opriessnig T. A porcine reproductive and respiratory syndrome virus candidate vaccine based on the synthetic attenuated virus engineering approach is attenuated and effective in protecting against homologous virus challenge. *Vaccine*. 2016 Nov 4;34(46):5546-5553. doi: 10.1016/j.vaccine.2016.09.049. Epub 2016 Oct 11. PubMed PMID: 27742217.
5. Ma Z, Yu Y, Xiao Y, Opriessnig T, Wang R, Yang L, Nan Y, Samal SK, Halbur PG, Zhang YJ. Sustaining Interferon Induction by a High-Passage Atypical Porcine Reproductive and Respiratory Syndrome Virus Strain. *Sci Rep*. 2016 Nov 2;6:36312. doi: 10.1038/srep36312. PubMed PMID: 27805024; PubMed Central PMCID: PMC5090871.
6. Chung CJ, Cha SH, Grimm AL, Chung G, Gibson KA, Yoon KJ, Parish SM, Ho CS, Lee SS. Recognition of Highly Diverse Type-1 and -2 Porcine Reproductive and Respiratory Syndrome Viruses (PRRSVs) by T-Lymphocytes Induced in Pigs after Experimental Infection with a Type-2 PRRSV Strain. *PLoS One*. 2016 Oct 31;11(10):e0165450. doi:

- 10.1371/journal.pone.0165450. eCollection 2016. PubMed PMID: 27798650; PubMed Central PMCID: PMC5087905.
7. Schlink SN, Lager KM, Brockmeier SL, Loving CL, Miller LC, Vorwald AC, Yang HC, Kehrli ME Jr, Faaberg KS. Enhancement of innate immunity with granulocyte colony-stimulating factor did not mitigate disease in pigs infected with a highly pathogenic Chinese PRRSV strain. *Vet Immunol Immunopathol*. 2016 Oct 15;179:70-6. doi: 10.1016/j.vetimm.2016.08.007. Epub 2016 Aug 10. PubMed PMID: 7590428.
 8. Yu Z, Huang C, Zhang Q, Feng WH. Porcine reproductive and respiratory syndrome virus (PRRSV) induces IL-12p40 production through JNK-AP-1 and NF-κB signaling pathways. *Virus Res*. 2016 Oct 2;225:73-81. doi: 10.1016/j.virusres.2016.09.009. Epub 2016 Sep 20. PubMed PMID: 27663131.
 9. Wang X, Yang X, Zhou R, Zhou L, Ge X, Guo X, Yang H. Genomic characterization and pathogenicity of a strain of type 1 porcine reproductive and respiratory syndrome virus. *Virus Res*. 2016 Oct 2;225:40-49. doi: 10.1016/j.virusres.2016.09.006. Epub 2016 Sep 13. PubMed PMID: 27619842.
 10. Du L, Liu Y, Du Y, Wang H, Zhang M, Du Y, Feng WH. Porcine reproductive and respiratory syndrome virus (PRRSV) up-regulates IL-15 through PKC β 1-TAK1-NF-κB signaling pathway. *Virology*. 2016 Sep;496:166-174. doi: 10.1016/j.virol.2016.06.007. Epub 2016 Jun 16. PubMed PMID: 27318153.
 11. Tabynov K, Sansyzbay A, Tulemissova Z, Tabynov K, Dhakal S, Samolyrova A, Renukaradhy GJ, Mambetaliyev M. Inactivated porcine reproductive and respiratory syndrome virus vaccine adjuvanted with Montanide™ Gel 01 ST elicits virus-specific cross-protective inter-genotypic response in piglets. *Vet Microbiol*. 2016 Aug 30;192:81-89. doi: 10.1016/j.vetmic.2016.06.014. Epub 2016 Jul 1. PubMed PMID: 27527768.
 12. Sun D, Khatun A, Kim WI, Cooper V, Cho YI, Wang C, Choi EJ, Yoon KJ. Attempts to enhance cross-protection against porcine reproductive and respiratory syndrome viruses using chimeric viruses containing structural genes from two antigenically distinct strains. *Vaccine*. 2016 Aug 5;34(36):4335-42. doi: 10.1016/j.vaccine.2016.06.069. Epub 2016 Jul 9. PubMed PMID: 27406935.
 13. Workman AM, Smith TP, Osorio FA, Vu HL. Complete Genome Sequence of Highly Virulent Porcine Reproductive and Respiratory Syndrome Virus Variants That Recently Emerged in the United States. *Genome Announc*. 2016 Aug 4;4(4). pii: e00772-16. doi: 10.1128/genomeA.00772-16. PubMed PMID: 27491998; PubMed Central PMCID: PMC4974319.
 14. Serão NV, Kemp RA, Mote BE, Willson P, Harding JC, Bishop SC, Plastow GS, Dekkers JC. Genetic and genomic basis of antibody response to porcine reproductive and respiratory syndrome (PRRS) in gilts and sows. *Genet Sel Evol*. 2016 Jul 14;48(1):51. doi: 10.1186/s12711-016-0230-0. PubMed PMID: 27417876; PubMed Central PMCID: PMC4944421.
 15. Li L, Zheng Q, Zhang Y, Li P, Fu Y, Hou J, Xiao X. Antiviral activity of recombinant porcine surfactant protein A against porcine reproductive and respiratory syndrome virus in vitro. *Arch Virol*. 2016 Jul;161(7):1883-90. doi: 10.1007/s00705-016-2838-3. Epub 2016 Apr 21. PubMed PMID: 27101074.
 16. Zhang L, Zhou L, Ge X, Guo X, Han J, Yang H. The Chinese highly pathogenic porcine reproductive and respiratory syndrome virus infection suppresses Th17 cells response in

- vivo. *Vet Microbiol.* 2016 Jun 30;189:75-85. doi: 10.1016/j.vetmic.2016.05.001. Epub 2016 May 3. PubMed PMID: 27259830.
- 17. Huang C, Du Y, Yu Z, Zhang Q, Liu Y, Tang J, Shi J, Feng WH. Highly Pathogenic Porcine Reproductive and Respiratory Syndrome Virus Nsp4 Cleaves VISA to Impair Antiviral Responses Mediated by RIG-I-like Receptors. *Sci Rep.* 2016 Jun 22;6:28497. doi: 10.1038/srep28497. PubMed PMID: 27329948; PubMed Central PMCID: PMC4916416.
 - 18. Hess AS, Islam Z, Hess MK, Rowland RR, Lunney JK, Doeschl-Wilson A, Plastow GS, Dekkers JC. Comparison of host genetic factors influencing pig response to infection with two North American isolates of porcine reproductive and respiratory syndrome virus. *Genet Sel Evol.* 2016 Jun 20;48(1):43. doi: 10.1186/s12711-016-0222-0. PubMed PMID: 27324857; PubMed Central PMCID: PMC4915112.
 - 19. Yuan S, Zhang N, Xu L, Zhou L, Ge X, Guo X, Yang H. Induction of Apoptosis by the Nonstructural Protein 4 and 10 of Porcine Reproductive and Respiratory Syndrome Virus. *PLoS One.* 2016 Jun 16;11(6):e0156518. doi: 10.1371/journal.pone.0156518. eCollection 2016. PubMed PMID: 27310256; PubMed Central PMCID: PMC4911139.
 - 20. Binjawadagi B, Lakshmanappa YS, Longchao Z, Dhakal S, Hiremath J, Ouyang K, Shyu DL, Arcos J, Pengcheng S, Gilbertie A, Zuckermann F, Torrelles JB, Jackwood D, Fang Y, Renukaradhya GJ. Development of a porcine reproductive and respiratory syndrome virus-like-particle-based vaccine and evaluation of its immunogenicity in pigs. *Arch Virol.* 2016 Jun;161(6):1579-89. doi: 10.1007/s00705-016-2812-0. Epub 2016 Mar 23. PubMed PMID: 27008569.
 - 21. Chen N, Trible BR, Kerrigan MA, Tian K, Rowland RR. ORF5 of porcine reproductive and respiratory syndrome virus (PRRSV) is a target of diversifying selection as infection progresses from acute infection to virus rebound. *Infect Genet Evol.* 2016 Jun;40:167-75. doi: 10.1016/j.meegid.2016.03.002. Epub 2016 Mar 4. PubMed PMID: 26961593.
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 - 23. Wilkinson JM, Bao H, Ladinig A, Hong L, Stothard P, Lunney JK, Plastow GS, Harding JC. Genome-wide analysis of the transcriptional response to porcine reproductive and respiratory syndrome virus infection at the maternal/fetal interface and in the fetus. *BMC Genomics.* 2016 May 20;17:383. doi: 10.1186/s12864-016-2720-4. PubMed PMID: 27207143; PubMed Central PMCID: PMC4875603.
 - 24. Zhang L, Cui Z, Zhou L, Kang Y, Li L, Li J, Dai Y, Yu S, Li N. Developing a Triple Transgenic Cell Line for High-Efficiency Porcine Reproductive and Respiratory Syndrome Virus Infection. *PLoS One.* 2016 May 16;11(5):e0154238. doi: 10.1371/journal.pone.0154238. eCollection 2016. Erratum in: *PLoS One.* 2016 Jul 26;11(7):e0160325. PubMed PMID: 27182980; PubMed Central PMCID: PMC4868347.
 - 25. Xiao Y, Ma Z, Wang R, Yang L, Nan Y, Zhang YJ. Downregulation of protein kinase PKR activation by porcine reproductive and respiratory syndrome virus at its early stage infection. *Vet Microbiol.* 2016 May 1;187:1-7. doi: 10.1016/j.vetmic.2016.03.004. Epub 2016 Mar 7. PubMed PMID: 27066702.

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27. Wilkinson JM, Ladinig A, Bao H, Kommadath A, Stothard P, Lunney JK, Harding JC, Plastow GS. Differences in Whole Blood Gene Expression Associated with Infection Time-Course and Extent of Fetal Mortality in a Reproductive Model of Type 2 Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) Infection. *PLoS One.* 2016 Apr 19;11(4):e0153615. doi: 10.1371/journal.pone.0153615. eCollection 2016. PubMed PMID: 27093427; PubMed Central PMCID: PMC4836665.\
28. Khatun A, Shabir N, Seo BJ, Kim BS, Yoon KJ, Kim WI. The Attenuation Phenotype of a Ribavirin-Resistant Porcine Reproductive and Respiratory Syndrome Virus Is Maintained during Sequential Passages in Pigs. *J Virol.* 2016 Apr 14;90(9):4454-68. doi: 10.1128/JVI.02836-15. Print 2016 May. PubMed PMID: 26889041; PubMed Central PMCID: PMC4836337.
29. Hu Y, Cong X, Chen L, Qi J, Wu X, Zhou M, Yoo D, Li F, Sun W, Wu J, Zhao X, Chen Z, Yu J, Du Y, Wang J. Synergy of TLR3 and 7 ligands significantly enhances function of DCs to present inactivated PRRSV antigen through TRIF/MyD88-NF- κ B signaling pathway. *Sci Rep.* 2016 Apr 5;6:23977. doi: 10.1038/srep23977. PubMed PMID: 27046485; PubMed Central PMCID: PMC4820752.
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