BIOMEDICAL & VETERINARY SCIENCES

GRADUATE PROGRAM

ANNOUNCES

The Doctor of Philosophy Seminar and Examination of

Nicholas J. Catanzaro

“Molecular mechanisms of host responses to porcine reproductive and respiratory syndrome virus infection”

Monday, December 9th, 2019
9:00 am
ILSB, Rm 1040

Bio

Nick is from Lewiston, New York and earned his Bachelor of Science degree in Molecular Genetics from the State University of New York (SUNY) Fredonia. At SUNY Fredonia, Nick became involved in research, presenting his findings at the American Society of Microbiology national meeting. Nick participated in an NSF sponsored Research Experience of Undergraduates (REU) program in Microbiology program at Virginia Tech and eventually applied to the microbiology graduate program the year later. Nick officially joined Dr. X. J. Meng's lab the spring of 2014 and began studying the porcine virus PRRSV. During his graduate studies, Nick was awarded a pre-doctoral fellowship from the USDA to support his research of PRRSV. Nick will continue his research career as a post-doctoral research in the lab of Dr. Helen Lazear at University of North Carolina, Chapel Hill

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VMCVM Office of Research and Graduate Studies

Lay Language Abstract

Porcine reproductive and respiratory syndrome virus is one of the most economically devastating diseases affecting the global swine industry. Annually, PRRS is estimated to cause more than $600 million in economic losses. The causative agent of the disease is PRRS virus (PRRSV). Current vaccines against the virus are not effective due to the extreme heterogeneity of virus strains circulating in the field. PRRSV is also able to potently suppress several aspects of the host's immune response and therefore establish a persistent. The underlying mechanisms of PRRSV-mediated immune suppression are not very well understood. Therefore, in this dissertation we decided to investigate the molecular mechanisms of PRRSV replication and pathogenesis. In this study, we first examined the ability of the virus to stress granules (SGs). SGs are important intracellular regulatory components that modulate many aspects of the host's cellular processes, and have even been shown to play roles in regulating viral replication and controlling immune responses to viral infection. We show that PRRSV not only induces SGs, but that the PRRSV-induced SGs are closely associated with viral replication complexes (VRCs) within infected cells. The PRRSV-induced SGs were dispensable for viral replication.

We next investigated the PERK signaling pathway during PRRSV infection. Previously, PRRSV-induced SGs were shown to form in a PERK dependent manner. Therefore, in the second part of this dissertation research, we decided to investigate the PERK signaling pathway during PRRSV infection. PERK is an important sensor of ER stress and activator of the unfolded protein response (UPR). Our results showed that PRRSV potently induces ER stress and all three signaling branches of the UPR, including PERK. Further investigation revealed that PERK may play an important role in regulating the type I interferon response to PRRSV infection. The results from our studies will aid in the development of safer, more effective vaccines against this devastating swine pathogen.

Publications

Catanzaro N, Meng XJ. Induction of the unfolded protein response (UPR) suppresses porcine reproductive and respiratory syndrome virus (PRRSV) replication. *Virus Research*. 2019 Nov 16.

Catanzaro N, Meng XJ. Porcine reproductive and respiratory syndrome virus (PRRSV)-induced stress granules are associated with viral replication complexes and suppression of host translation. *Virus Research*. 2019 Feb 28; 265:47-56.

Zhang Z, He G, Han GS, Zhang J, **Catanzaro N**, Diaz A, Wu Z, Carman GM, Xie L, Wang X. Host Pah1p phosphatidate phosphatase limits viral replication by regulating phospholipid synthesis. *PLoS Pathogens*. 2018 Apr 12; 14(4):e1006988.

Cao QM, Ni YY, Cao D, Tian D, Yugo DM, Heffron CL, Overend C, Subramaniam S, Rogers AJ, **Catanzaro N**, LeRoith T, Roberts PC, Meng XJ. Recombinant Porcine Reproductive and Respiratory Syndrome Virus Expressing Membrane-Bound Interleukin-15 as an Immunomodulatory Adjuvant Enhances NK and γδ T Cell Responses and Confers Heterologous Protection. *Journal of Virology*. 2018 Jun 13; 92(13). pii: e00007-18.

Cao D, Cao QM, Subramaniam S, Yugo DM, Heffron CL, Rogers AJ, Kenney SP, Tian D, Matzinger SR, Overend C, **Catanzaro N**, LeRoith T, Wang H, Piñeyro P, Lindstrom N, Clark- Deener S, Yuan L, Meng XJ. Pig model mimicking chronic hepatitis E virus infection in immunocompromised patients to assess immune correlates during chronicity. *Proceedings of the National Acaddemy of Sciences USA*. 2017 Jul 3; 114(27):6914-6923.

Subramaniam S, Cao D, Tian D, Cao QM, Overend C, Yugo DM, Matzinger SR, Rogers AJ, Heffron CL, **Catanzaro N**, Kenney SP, Opriessnig T, Huang YW, Labarque G, Wu SQ, Meng XJ. Efficient priming of CD4 T cells by Langerin-expressing dendritic cells targeted with porcine

epidemic diarrhea virus spike protein domains in pigs. *Virus Research*. 2017 Jan 2; 227:212-219.

Matzinger SR, Opriessnig T, Xiao CT, **Catanzaro N**, Beach NM, Slade DE, Nitzel GP, Meng XJ. A chimeric virus created by DNA shuffling of the capsid genes of different subtypes of porcine circovirus type 2 (PCV2) in the backbone of the non-pathogenic PCV1 induces protective immunity against the predominant PCV2b and the emerging PCV2d in pigs. *Virology*. 2016 Nov; 498:82-93.

Subramaniam S, Piñeyro P, Tian D, Overend C, Yugo DM, Matzinger SR, Rogers AJ, Haac ME, Cao Q, Heffron CL, **Catanzaro N**, Kenney SP, Huang YW, Opriessnig T, Meng XJ. In vivo targeting of porcine reproductive and respiratory syndrome virus antigen through porcine DC-SIGN to dendritic cells elicits antigen-specific CD4T cell immunity in pigs. *Vaccine*. 2014 Nov 28; 32(50):6768-75.

Presentations

Catanzaro N, Meng XJ. Integrated Life Sciences Building Seminar, oral presentation, "*Cellular stress responses to PRRSV infection*," Virginia Polytechnic Institute and State University, Blacksburg, Virginia (2019).

Catanzaro N, Meng XJ. International PRRSV – IPVS Symposium, oral presentation, *"PRRSV induced stress granules are closely associated with viral replication complexes and attenuation of host translation*" Chongqing, China (2018).

Catanzaro N, Meng XJ. Biomedical and Veterinary Sciences 28th Research Symposium, poster presentation, "*Induction of Stress Granules During PRRSV Infection,*" Virginia-Maryland College of Veterinary Medicine, Blacksburg, Virginia (2017).

Catanzaro N, Meng XJ. Biomedical and Veterinary Sciences 27th Research Symposium, poster presentation, "*Mechanisms of arterivirus immune evasion mediated by nonstructural proteins 1 and 2*" Virginia-Maryland College of Veterinary Medicine, Blacksburg, Virginia (2016).

Catanzaro N, Subramaniam S, Meng XJ. SUNY Fredonia Homecoming, oral presentation, "*Saving your bacon: a vaccine targeted to dendritic cells enhances protective immunity against a deadly pig virus*" SUNY Fredonia, Fredonia, New York (2015).

Catanzaro N, Lee T. American Society for Microbiology 113th General Meeting, poster presentation, "*Molecular characterization of a microbial community*" Denver, Colorado (2013).

Catanzaro N, Wallace R, Yang Z. Virginia Tech Undergraduate Research Symposium, oral presentation, *"Reverse genetics systems for M. xanthus"* Blacksburg, Virginia (2012).

Awards and Academic Achievements

Graduate Student Travel Fellowship Award, 2018
2018 International PRRSV Symposium and 2018 IPVS Congress
Chongqing, China

U.S. Department of Agriculture National Institute of Food and Agriculture Predoctoral Research Fellowship, 2017-2018 Award
Principal Investigator
Award Title: Elucidating the mechanism of PRRSV immune evasion by nonstructural proteins
Total Award Amount: $95,000

Examination Graduate Committee

Major Advisor/Chair:

Xiang-Jin Meng, MD, MS, PhD

University Distinguished Professor
Department of Biomedical Sciences & Pathobiology

Graduate Advising Committee Members:

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Liwu Li, PhD
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Lijuan Yuan, PhD
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