

**BIOMEDICAL & VETERINARY SCIENCES
GRADUATE PROGRAM**



ANNOUNCES

The Doctor of Philosophy Seminar
and Examination of

Danielle M. Yugo

"Pathogenesis and Cross-species Infection of Hepatitis E Virus"

Tuesday December 11, 2018

9:00 AM

ILSB 1040

Bio



Danielle M. Yugo, a PhD student in Dr. X.J. Meng's laboratory in the Department of Biomedical Sciences and Pathobiology, joined the Meng lab in 2012. Dr. Yugo completed her undergraduate Bachelor of Science degree in Biochemistry, Cellular, and Molecular Biology (BCMB) from the University of Tennessee, Knoxville in 2008. She completed her Doctorate in Veterinary Medicine and Masters in Veterinary Public Health from the University of Tennessee, Knoxville College of Veterinary Medicine in 2012. Dr. Yugo has also accepted a position as a Veterinary Medical Officer (VMO) working for the United States Department of Agriculture (USDA), Agricultural Select Agent Service (AgSAS) and she will continue to work at USDA upon graduation with her PhD. Her research has focused on understanding the mechanisms allowing for cross-species infection and pathogenesis of hepatitis E virus (HEV) in a variety of animal models. Specifically, she is interested in investigating additional animal models of HEV to better represent the infection seen in humans during acute and chronic infection. She hopes to pursue a career in infectious diseases and public health in the future. Dr. Yugo lives in Roanoke, VA with her daughter Vienna, yellow Labrador Howard, and Siamese cats Finn and Marley.

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Lay Language Abstract

Hepatitis E Virus (HEV), the causative agent of hepatitis E, is a zoonotic pathogen of worldwide significance. According to the World Health Organization, there are approximately 20 million HEV infections annually, which result in 3.3 million cases of acute hepatitis E and >44,000 HEV-related deaths. Hepatitis E is a self-limiting acute disease in general, but carries the ability to cause high mortality in pregnant women and chronic hepatitis in immunocompromised individuals. The underlying mechanisms of HEV host tropism and progression of disease to chronicity are poorly understood.

The dissertation research investigates a novel animal model for HEV, evaluates the possibility of an additional animal reservoir of HEV, and determines the mechanisms for host tropism and pathogenesis of the disease. The first project of the dissertation established an immunoglobulin (Ig) heavy chain knock-out JH (-/-) gnotobiotic piglet model that mimics the course of acute HEV infection observed in humans. The dynamics of acute HEV infection were determined in both the knock-out and wild-type gnotobiotic piglets with a genotype 3 human strain of HEV. We also investigated the role of immunoglobulin heavy-chain JH in HEV pathogenesis and virus infection. In the second project of the dissertation, we determined if cattle in the United States are infected with a bovine strain of HEV. We demonstrated serological evidence of an HEV-related agent in cattle with detection of antibodies recognizing and neutralizing HEV, but were unable to detect HEV-related sequence in cattle, suggesting that one should be cautious in interpreting the significance of HEV serological data in bovine and other species. The final project of the dissertation investigated the ability for chimeric viruses containing various genomic regions from zoonotic strains of HEV in the backbone of a human-exclusive genotype 1 HEV to infect a new host (pig) that normally is non-susceptible to infection by genotype 1 human HEV. We reported the construction and evaluation of these chimeric viruses and demonstrated that the swapped genomic regions within ORF1 were capable of conferring cross-species HEV infection. Collectively, the results from the dissertation research provide novel insights into the underlying mechanisms of HEV pathogenesis and cross-species infection.

Publications

Yugo, D.M., Cossaboom, C.M., Heffron, C.L., Huang, Y.W., Kenney, S.P., Woolums, A.R., Hurley, D.J., Opriessnig, T., Li, L., Delwart, E., Kanevsky, I., Meng, X.J., "Evidence for an Unknown Agent Antigenically Related to the Hepatitis E Virus in Dairy Cows in the United States." *Journal of Medical Virology*. 2018 Oct 14. doi: 10.1002/jmv.25339. [Epub ahead of print] PMID: 30318625.

Cao, D., Sooryanarain, H., **Yugo, D.M.**, Tian, D., Rogers, A.J., Heffron, C.L., Thimmasandra Narayanappa, A., LeRoith, T., Overend, C., Matzinger, S.R., Elankumaran, S., Hermann, J.R., Patterson, A.R., Meng, X.J., "Evaluation of the pathogenicity of mammalian orthoreovirus type 3 (MRV3) in germ-free gnotobiotic pigs and of the efficacy of an inactivated vaccine against MRV3 infection in neonatal conventional piglets." *Veterinary Microbiology*. 2018 Oct; 224: 23-30. doi: 10.1016/j.vetmic.2018.08.019. Epub 2018 Aug 22. PMID: 30269786.

Yugo, D.M., Heffron, C.L., Ryu, J., Uh, K., Subramaniam, S., Matzinger, S.R., Overend, C., Cao, D., Kenney, S.P., Sooryanarain, H., Cecere, T., LeRoith, T., Yuan, L., Jue, N., Clark-Deener, S., Lee, K., Meng, X.J., "Infection Dynamics of Hepatitis E Virus in Wild-Type and Immunoglobulin Heavy Chain Knockout JH -/- Gnotobiotic Piglets." *Journal of Virology*. 2018 Oct 12; 92(21). pii: e01208-18. doi: 10.1128/JVI.01208-18. Print 2018 Nov. 1. PMID: 30111571.

Cao, Q.M., Ni, Y.Y., Cao, D., Tian, D., **Yugo, D.M.**, Heffron, C.L., Overend, C., Subramaniam, S., Rogers, A.J., Catanzaro, N., LeRoith, T., Roberts, P.C., Meng, X.J., "Recombinant Porcine Reproductive and Respiratory Syndrome Virus Expressing Membrane-Bound Interleukin-15 as an Immunomodulatory Adjuvant Enhances NK and $\gamma\delta$ T Cell Responses and Confers Heterologous Protection." *Journal of Virology*. 2018 Jun 12; 92(13). pii. e00007-18. doi: 10.1128/JVI.00007-18. Print 2018 Jul 1. PMID: 2963245.

Subramaniam, S., Overend, C., **Yugo, D.M.**, Heffron, C.L., Matzinger, S.R., Rogers, A.J., Tian, D., Cao, Q.M., Kenney, S.P., Meng, X.J., "Isolation of Peripheral Blood CD8 T cells Specific to Porcine Reproductive and Respiratory Syndrome Virus Utilizing Porcine CD137 Activation Marker." *Viral Immunology*. 2018 May; 31(4): 333-337. doi: 10.1089/vim.2017.0189. Epub 2018 Feb 28. PMID: 29489438.

Subramaniam, S., **Yugo, D.M.**, Heffron, C.L., Rogers, A.J., Sooryanarain, H., LeRoith, T., Overend, C., Cao, D., Meng, X.J., "Vaccination of sows with a dendritic cell-targeted porcine epidemic diarrhea virus S1 protein-based candidate vaccine reduced viral shedding but exacerbated gross pathological lesions in suckling neonatal piglets." *Journal of General Virology*. 2018 January 4. doi: 10.1099/jgv.0.001001. [Epub ahead of print]. PMID: 29300158.

Cao, D., Cao, Q.M., Subramaniam, S., **Yugo, D.M.**, Heffron, C.L., Rogers, A.J., Kenney, S.P., Tian, D., Matzinger, S.R., Overend, C., Catanzaro, N., LeRoith, T., Wang, H., Pineyro, P., Lindstrom, N., Clark-Deener, S., Yuan, L., Meng, X.J. "Pig model mimicking chronic hepatitis E virus infection in immunocompromised patients to assess immune correlates during chronicity." *Proc. Natl. Acad. Sci. USA*. 2017 July 3. doi: 10.1073/pnas.1705446114. PMID: 28630341.

Tian, D., Cao, D., Heffron, C.L., **Yugo, D.M.**, Rogers, A.J., Overend, C., Matzinger, S.R., Subramaniam, S., Opriessnig, T., LeRoith, T., Meng, X.J., "Enhancing heterologous protection in pigs vaccinated with chimeric porcine reproductive and respiratory syndrome virus containing the full-length sequences of shuffled structural genes of multiple heterologous strains." *Vaccine*. 2017 April 25; 35(18): 2427-2434. PMID: 28343773

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Subramaniam, S., Cao, D., Tian, D., Cao, Q.M., Overend, C., **Yugo, D.M.**, Matzinger, S.R., Rogers, A.J., Heffron, C.L., Catanzaro, N., Kenney, S.P., Opriessnig, T., Huang, Y.W., Labarque, G., Wu, S.Q., Meng, X.J., "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 January 2; 227:212-219. doi:10.1016/j.virusres.2016.10.007. Epub 2016 Oct 23.

Yugo, D.M., Hauck, M.R., Shivaprasad, H.L., and Meng, X.J. "Hepatitis virus infections in poultry." *Avian Diseases*. 2016 September; 60(3): 576-588. PMID: 27610716.

Cossaboom, C.M., Heffron, C.L., Cao, D., **Yugo, D.M.**, Houk-Miles, A.E., Lindsay, D.S., Zajac, A.M., Bertke, A.S., Elvinger, F., and Meng, X.J. "Risk factors and sources of foodborne hepatitis E virus infection in the United States." *Journal of Medical Virology*. 2016 September; 88(9): 1641-1645. Epub 2016 Mar 17. PMID: 26889628.

Tian, D., Ni, Y-Y., Zhou, L., Opriessnig, T., Cao, D., Pineyro, P., **Yugo, D.M.**, Overend, C., Cao, Q., Heffron, C.L., Halbur, P.G., Pearce, D.S., Calvert, J.G., and Meng, X.J. "Chimeric porcine reproductive and respiratory syndrome virus containing shuffled multiple envelope genes confers cross-protection in pigs." *Virology*. 2014 November; 485: 402-413. PMID: 26342466.

Subramaniam, S., Pineyro, P., Tian, D., Overend, C., **Yugo, D.M.**, Matzinger, S.R., Rogers, A.J., Haac, M.E.R., Cao, Q., Heffron, C.L., Catanzaro, N., Kenney, S.P., Huang, Y-W., Opriessnig, T., and Meng, X.J. "In vivo targeting of porcine reproductive and respiratory syndrome virus antigen through porcine DC-SIGN to dendritic cells elicits antigen-specific CD4 T cell immunity in pigs." *Vaccine*. 2014 November 28; 32(50): 6788-6775. PMID: 25446829.

Yugo, D.M., Cossaboom, C.M., and Meng, X.J. "Naturally occurring animal models of human hepatitis E virus infection." *ILAR Journal*. 2014; 55(1): 187-199. PMID: 24936039

Yugo, D.M. and Meng, X.J. "Hepatitis E virus: foodborne, waterborne and zoonotic transmission." *International Journal of Environmental Research and Public Health*. 2013 September 25; 10(10): 4507-4533.

Presentations

Yugo, D.M., Kenney, S.P., and Meng, X.J. "Viral Genetic Determinants of Hepatitis E Virus Host Range, Update" VMCVM Research Symposium," Virginia Tech, Blacksburg, VA, 2018.

Yugo, D.M., Meng, X.J. "Hepatitis E Virus: An Emerging Foodborne Pathogen?" International Association for Food Protection Annual Meeting, Tampa, FL, July 9-12 2017.

Yugo, D.M., Kenney, S.P., and Meng, X.J. "Viral Genetic Determinants of Hepatitis E Virus Host Range, Update" VMCVM Research Symposium," Virginia Tech, Blacksburg, VA, 2017.

Cao, D., Heffron, C.L., **Yugo, D.M.**, Cao, Q.M., Rogers, A.J., Kenney, S.P., Tian, D., Matzinger, S.R., Overend, C., Subramaniam, S., Catanzaro, N., LeRoith, T., Wang, H., Pineyro, P., Lindstrom, N., Clark-Deener, S., Yuan, L., and Meng, X.J. "Establishment of a Pig Model for Chronic Hepatitis E Virus Infection". American Society for Virology 35th Annual Meeting, Blacksburg, VA, June 18-22, 2016.

Yugo, D.M., Kenney, S.P., and Meng, X.J. "Viral Genetic Determinants of Hepatitis E Virus Host Range, Update" VMCVM Research Symposium," Virginia Tech, Blacksburg, VA, 2016.

Yugo, D.M., Kenney, S.P. and Meng, X.J. "Viral Genetic Determinants of Hepatitis E Virus Host Range" VMCVM Research Symposium," Virginia Tech, Blacksburg, VA, 2015.

Cossaboom, C.M.; **Yugo, D.M.**; Heffron, C.L.; Kenney, S.P.; Pineyro, P.; Huang, Y.W.; Pierson, F.W.; Meng, X.J. "Construction of an Infectious cDNA clone of Rabbit Hepatitis E Virus Recovered from a Rabbit in the United States" Poster 33rd Annual Meeting of the American Society for Virology, Fort Collins, CO, June 21-25th, 2014.

Yugo, D.M.; Cossaboom, C.M.; Heffron, C.L.; Huang, Y.W.; Kenney, S.P.; Kanevsky, I; Kapoor, A; Meng, X.J. "Evidence for an Unknown Agent Serologically Related to the Hepatitis E Virus in Dairy Cows in the United States" Poster 33rd Annual Meeting of the American Society for Virology, Fort Collins, CO, June 21-25th, 2014.

Awards and Academic Achievements

2013 Recipient, American Society of Virology graduate student travel award

2012-2015 Recipient, NIH T32 Fellowship

Examination Graduate Committee

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Seminar title is:

**Antagonizing JAK/STAT Signaling by Porcine Reproductive and
Respiratory Syndrome Virus
Tuesday December 11th
2:00 pm VMIA classroom 220**



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