

BIOMEDICAL & VETERINARY SCIENCES

GRADUATE PROGRAM



ANNOUNCES

The Doctor of Philosophy Seminar and Examination of

Casey Hensley, LVT

**"Investigation of Novel Prophylactics Against Human
Rotavirus Using Gnotobiotic Pig Models"**

Tuesday, April 25th, 2023

2:00PM

Vet Med 121



Bio

Casey began her research career as a licensed veterinary technician at the University of Virginia, under the supervision of Dr. Sanford Feldman. Here, she helped establish a panel of TaqMan assays for defining the specific-pathogen free status of *Xenopus* species, as well as maintaining the murine sentinel program for the Center for Comparative Medicine. While working full-time at UVA, she simultaneously completed her B.S. in Leadership and Organizational Management at Eastern Mennonite University and applied to graduate school. Her PhD research in Dr. Lijuan Yuan's lab at Virginia Tech has only solidified her enthusiasm for research, particularly preclinical vaccine evaluation, and she hopes to continue her career in this field. Casey is currently a simultaneous Master of Public Health student with a concentration in infectious diseases and will complete this degree in Summer 2023. Casey plans to stay on as a postdoctoral associate in Dr. Yuan's lab while applying to veterinary school. In her spare time, she enjoys spending time with her husband and three sons, trail riding her Arabian horse, and working as a relief LVT at a small animal emergency veterinary hospital.

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Lay Language Abstract

Human rotavirus (HRV) is a major causative agent of acute gastroenteritis (AGE) in children under the age of five. Acute gastroenteritis is characterized by nausea, vomiting, and potentially deadly dehydrating diarrhea. There are two highly effective vaccines licensed for use in the United States; however, these vaccines are much less effective in low- and middle-income countries (LMICs), where HRV disease burden is the highest. There are several reasons thought to be responsible for the decrease in effectiveness seen in these areas, including chronic malnutrition and gut dysbiosis. Non-biological reasons for decreased efficacy may include the breakdown of cold-chain storage for these vaccines, which require constant low temperature storage that is often unavailable in LMICs. Thermostable vaccines are necessary for increasing vaccine distribution and efficacy in these areas. Because many of the biologic factors thought to interfere with the effectiveness of these vaccines appear to be confined to the gastrointestinal tract, development of next generation HRV vaccines have focused on the parenteral route of administration. The gnotobiotic (Gn) pig model is a highly relevant animal model that has been used for decades to evaluate novel HRV vaccine efficacy. Our first study evaluated a thermostable, dissolvable live oral vaccine administered as a dissolvable film in our Gn pig model. Two doses of this vaccine significantly reduced the severity of diarrhea and virus shedding in the stool. Our second study evaluated three mRNA-based intramuscular (IM) vaccines in the Gn pig model. Three doses of all mRNA candidates provided significant protection from virus shedding in the stool, as well as inducing the production of strong HRV-specific antibodies in the serum and high numbers of virus-specific T cells in the tissues. In our final study, we evaluated a nanoparticle-based vaccine as a two-dose IM regimen or as an IM booster preceded by an oral immunization using the commercially available Rotarix® vaccine. The prime-boost regimen significantly shortened the duration and severity of virus shedding in the stool. We also detected more cross-strain HRV-specific antibody-secreting cells in the tissues. All three vaccines evaluated in this dissertation offer differing novelty in the field of HRV vaccine development, and the Gn pig model has been instrumental in the evaluation of these vaccines.

Publications

Casey Hensley, Sandro Roier, Peng Zhou, Sofia Schnur, Charlotte Nyblade, Viviana Parreno, Annie Frazier, Maggie Frazier, Kelsey Kiley, Samantha O'Brien, Yu Liang, Benjamin Petsch, Susanne Rauch, Lijuan Yuan. mRNA-based rotavirus vaccine candidates are highly immunogenic and confer protection in the gnotobiotic pig model of human rotavirus infection and diarrhea. In preparation. 2023

Casey Hensley, Charlotte Nyblade, Peng Zhou, Viviana Parreno, Annie Frazier, Maggie Frazier, Ariana Fantasia-Davis, Sarah Garrison, Ruiqing Cai, Ming Xia, Ming Tan, Lijuan Yuan. Combined live oral priming and intramuscular boosting regimen with Rotarix and a nanoparticle-based multivalent rotavirus vaccine confers significant protection against both G4P[6] and G1P[8] human rotavirus infection in gnotobiotic pigs. *Vaccines*. Submitted for review. 2023.

Charlotte Nyblade, **Casey Hensley**, Viviana Parreno, Peng Zhou, Sofia Schnur, Vanessa Oakes, Maggie Frazier, Annie Frazier, Ashwin Ramesh, Shaohua Lei, Juan Ignacio Degiuseppe, Lijuan Yuan. Establishment of a gnotobiotic pig model of P[6] human rotavirus infection and disease. *Viruses*, 2022. 14(12): p. 2803

Charlotte Nyblade, Viviana Parreno, Peng Zhou, **Casey Hensley**, Vanessa Oakes, Hassan Mahsoub, Kelsey Kiley, Maggie Frazier, Annie Frazier, Yongrong Zhang, Hanping Feng, Lijuan Yuan. Establishment of a gnotobiotic pig model of *Clostridioides difficile* infection and disease. *Gut Pathogens*. 2022; 14:22

Casey Hensley, Peng Zhou, Sofia Schnur, Hassan M Mahsoub, Yu Liang, Min-Xuan Wang, Caroline Page, Lijuan Yuan, Victor Bronshtein. Thermostable, Dissolvable Buccal Film Rotavirus Vaccine Is Highly Effective in Neonatal Gnotobiotic Pig Challenge Model. *Vaccines*. 2021;9(5):437.

Lijuan Yuan, **Casey Hensley**, Hassan M Mahsoub, Ashwin Ramesh, Peng Zhou. Microbiota in Viral Infection in Humans and Farm Animals. In: *Progress in Molecular Biology and Translational Science*. Elsevier; 2020.

Casey Hensley, Katilin Bowes, Sanford Feldman. Defining the Specific Pathogen-Free State of *Xenopus* Using TaqMan Assays. *Cold Spring Harb Protoc*. 2020.

Presentations

Casey Hensley, Charlotte Nyblade, Peng Zhou, Viviana Parreno, Ashwin Ramesh, Annie Frazier, Maggie Frazier, Sarah Garrison, Ruiqing Cai, Ariana Fantasia-Davis, Peng-Wei Huang, Ming Xia, Ming Tan, Lijuan Yuan. Combined live oral priming and intramuscular boosting regimen with Rotarix and a nanoparticle-based trivalent rotavirus vaccine evaluated in gnotobiotic pig models of G4P[6] and G1P[8] human rotavirus infection. Abstract # 3896866. 42nd American Society for Virology Annual Meeting. June 24-28, 2023. Athens, GA. Oral Presentation.

Casey Hensley, Charlotte Nyblade, Peng Zhou, Viviana Parreno, Ashwin Ramesh, Annie Frazier, Maggie Frazier, Sarah Garrison, Ruiqing Cai, Ariana Fantasia-Davis, Peng-Wei Huang, Ming Xia, Ming Tan, Lijuan Yuan. Combined live oral priming and intramuscular boosting regimen with Rotarix and a nanoparticle-based trivalent rotavirus vaccine evaluated in gnotobiotic pig models of G4P[6] and G1P[8] human rotavirus infection. Biomedical and Veterinary Sciences Research in Progress Seminar. April 12, 2023. Blacksburg, VA. Oral Presentation.

Casey Hensley, Charlotte Nyblade, Peng Zhou, Viviana Parreno, Ashwin Ramesh, Annie Frazier, Maggie Frazier, Sarah Garrison, Ruiqing Cai, Ariana Fantasia-Davis, Peng-Wei Huang, Ming Xia, Ming Tan, Lijuan Yuan. Combined live oral priming and intramuscular boosting regimen with Rotarix and a nanoparticle-based trivalent rotavirus vaccine evaluated in gnotobiotic pig models of G4P[6] and G1P[8] human rotavirus infection. Interdisciplinary Graduate Education Program – Infectious Disease Recruiting Event. March 17, 2023. Blacksburg, VA. Poster Presentation.

Casey Hensley, Charlotte Nyblade, Peng Zhou, Viviana Parreno, Ashwin Ramesh, Annie Frazier, Maggie Frazier, Sarah Garrison, Ruiqing Cai, Ariana Fantasia-Davis, Peng-Wei Huang, Ming Xia, Ming Tan, Lijuan Yuan. Combined live oral priming and intramuscular boosting regimen with Rotarix and a nanoparticle-based trivalent rotavirus vaccine evaluated in gnotobiotic pig models of G4P[6] and G1P[8] human rotavirus infection. 32nd Annual Research Symposium. Virginia-Maryland College of Veterinary Medicine. March 14, 2023. Blacksburg, VA. Poster Presentation.

Casey Hensley, Charlotte Nyblade, Peng Zhou, Viviana Parreno, Ashwin Ramesh, Annie Frazier, Maggie Frazier, Sarah Garrison, Ruiqing Cai, Ariana Fantasia-Davis, Peng-Wei Huang, Ming Xia, Ming Tan, Lijuan Yuan. Combined live oral priming and intramuscular boosting regimen with Rotarix and a nanoparticle-based trivalent rotavirus vaccine evaluated in gnotobiotic pig models of G4P[6] and G1P[8] human rotavirus infection. 32nd Annual Research Symposium. Virginia-Maryland College of Veterinary Medicine. March 14, 2023. Blacksburg, VA. Flash Talk.

Casey Hensley, Sandro Roier, Peng Zhou, Sofia Schnur, Charlotte Nyblade, Viviana Parreno, Annie Frazier, Maggie Frazier, Kelsey Kiley, Samantha O'Brien, Yu Liang, Benjamin Petsch, Susanne Rauch, Lijuan Yuan. mRNA-based rotavirus vaccine candidates are highly immunogenic and confer protection in the gnotobiotic pig model of human rotavirus infection and diarrhea. 14th International dsRNA Virus Symposium. October 10-14, 2022. Banff, Canada.

Casey Hensley, Charlotte Nyblade, Peng Zhou, Viviana Parreno, Annie Frazier, Maggie Frazier, Ariana Fantasia-Davis, Sarah Garrison, Ruiqing Cai, Ming Xia, Ming Tan, Lijuan Yuan. Combined live oral priming and intramuscular boosting regimen with Rotarix and a nanoparticle-based multivalent rotavirus vaccine confers significant protection against both G4P[6] and G1P[8] human rotavirus infection in gnotobiotic pigs. Center for Emerging, Zoonotic, and Arthropod-borne Pathogens Infectious Diseases Symposium. October 7, 2022. Blacksburg, VA. Poster Presentation.

Casey Hensley, Sandro Roier, Peng Zhou, Sofia Schnur, Charlotte Nyblade, Viviana Parreno, Annie Frazier, Maggie Frazier, Kelsey Kiley, Samantha O'Brien, Yu Liang, Benjamin Petsch, Susanne Rauch, Lijuan Yuan. mRNA-based rotavirus vaccine candidates are highly immunogenic and confer protection in the gnotobiotic pig model of human rotavirus infection and diarrhea. Biomedical and Veterinary Sciences Research in Progress Seminar. September 21, 2022. Blacksburg, VA. Oral Presentation.

Charlotte Nyblade, Viviana Parreno, Peng Zhou, **Casey Hensley**, Vanessa Oakes, Hassan Mahsoub, Kelsey Kiley, Maggie Frazier, Annie Frazier, Yongrong Zhang, Hanping Feng, Lijuan Yuan. National Association of Veterinary Scientists. 6th Annual Combined DVM/PhD Degree Colloquium Interdisciplinary Research & Collaboration, August 4th, 2022. St. Paul, MN.

Presentations continued

Casey Hensley, Sandro Roier, Peng Zhou, Sofia Schnur, Charlotte Nyblade, Viviana Parreno, Annie Frazier, Maggie Frazier, Kelsey Kiley, Samantha O'Brien, Yu Liang, Benjamin Petsch, Susanne Rauch, Lijuan Yuan. mRNA-based rotavirus vaccine candidates are highly immunogenic and confer protection in the gnotobiotic pig model of human rotavirus infection and diarrhea. Abstract # 3732718 W47. 41st American Society for Virology Annual Meeting. July 16-20, 2022. Madison, WI. Oral Presentation.

Casey Hensley, Peng Zhou, Sofia Schnur, Hassan M Mahsoub, Yu Liang, Min-Xuan Wang, Caroline Page, Lijuan Yuan, Victor Bronshtein. Abstract #3559841 W36-1. 40th American Society for Virology Annual Meeting. July 19-23, 2021. Virtual Oral Presentation.

Casey Hensley, Peng Zhou, Sofia Schnur, Hassan M Mahsoub, Yu Liang, Min-Xuan Wang, Caroline Page, Lijuan Yuan, Victor Bronshtein. 31st Annual Research Symposium. Virginia-Maryland College of Veterinary Medicine. March 25-26, 2021. Blacksburg, VA. Virtual Oral Presentation.

Awards and Academic Achievements

- 42nd American Society for Virology Annual Meeting Student Travel Award, 2023
- 42nd American Society for Virology Annual Meeting ASVCares Award, 2023
- 41st American Society for Virology Annual Meeting Student Travel Award, 2022
- 41st American Society for Virology Annual Meeting ASVCares Award, 2022
- 40th American Society for Virology Annual Meeting Student Registration Award, 2023

Examination Graduate Committee

Major Advisor/Chair:

Lijuan Yuan, PhD
Professor
Biomedical Sciences and Pathobiology

Graduate Advising Committee Members:

Xiang-Jin Meng, MD, MS, PhD
University Distinguished Professor
Biomedical Sciences and Pathobiology

Nisha Duggal, PhD
Assistant Professor
Biomedical Sciences and Pathobiology

Liwu Li, PhD
Professor
Biological Sciences



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