## BIOMEDICAL & VETERINARY SCIENCES

## GRADUATE PROGRAM

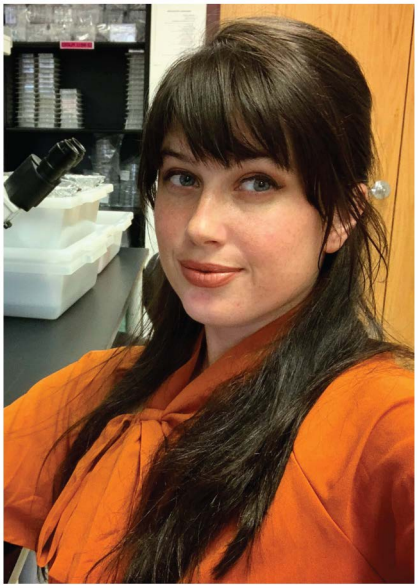
ANNOUNCES

The Doctor of Philosophy Seminar and Examination of

# Lauren Panny

"Utilizing proteomic techniques to discover host protein interactions with the E1 glycoprotein of Venezuelan equine encephalitis virus (VEEV) for anti-viral discovery"

**Friday, March 31st, 2023**
**1:00PM**
**VMCVM Classroom 100**



## Bio

Lauren Panny started her academic path in science when she obtained her B.S. in general biology at Louisiana State University in 2015. During her undergraduate experience, she worked as an NSF REU funded undergraduate researcher in Dr. David Donze's lab. During this time, Lauren explored the genetic implications of downregulating transcription factor tau 91 kDa subunit in Saccharomyces cerevisiae. Lauren then entered the science industry for 2 years, working for clinical research organizations performing ELISA analysis for some of the leading biopharmaceutical companies in the world. After reading Richard Preston's "Hot Zone" and the "Demon in the Freezer", Lauren was inspired to pursue a career researching high threat pathogens. She applied for acceptance at George Mason University and then transferred to Virginia Polytechnic University with her PI, Dr. Kylene Kehn-Hall. During her PhD, she has also simultaneously pursued a certificate in public health, believing that One Health approaches provide the best mediation strategies for combatting infectious diseases. Lauren hopes to apply her love of virology, her compassion for people and animals, and her adventurous spirit into a future career serving the U.S. government. Her passions outside of the lab include her dog, travelling, hiking, camping, volunteering at the animal shelter, and exploring national parks.


## Funded by

DTRA (Defense Threat Reduction Agency)
VMCVM Office of Research and Graduate Studies

# Lay Language Abstract

Venezuelan equine encephalitis virus (VEEV) causes disease in humans, as well as horses, donkeys and other closely related animal. In humans, the virus causes a flu-like disease and sometimes causes swelling of the brain. This can be associated with symptoms such as light sensitivity, confusion and sometimes coma. Prior to the Cold War, VEEV was researched by the US and previous Soviet Union's militaries in hopes to deploy the virus as a bioweapon. Current treaties prevent active production of such weapons, yet allows for defensive research to continue in preparation for a worst-case scenario. Currently no FDA approved medications or vaccines exist to combat the virus further exacerbating concerns. In order to protect laboratorians and prevent unintentional or intentional introduction of the virus into the community, the virus is only manipulated in highly secure facilities with barriers that separate the virus from personnel and the outside environment.

A component of the virus called E1, allows for the virus to be released from a structure, called an endosome, that transports the virus into the cell. Currently, E1 is mostly known for this function, yet our research found that E1 interacts with 486 protein components of the host cell, suggesting a more elaborate role of E1 than previously understood. This list of interactors provides numerous new targets for potential medications to combat VEEV and other closely related viruses. Discovered E1 interactors, protein disulfide isomerase family A member 6 (PDIA6) and valosin containing protein (VCP), were validated through extensive experimentation and their function in viral replication was further explored.

Protein disulfide isomerases (PDI), such as PDIA6, play an important role in folding proteins, which are cellular components made of organic building blocks called amino acids. PDIs do so by creating organic pillars, called disulfide bonds, between two cysteine amino acid residues. These disulfide bonds contribute to the 3D shape of the proteins they fold which are essential for the protein's function. E1 of VEEV has a total of eight disulfide bonds within its structure, highlighting that disulfide bonds are likely essential for the protein's structure, and therefore, function. We verified that E1 could not properly fold without PDI function by using two compounds that prevented PDI from forming or breaking disulfide bonds, specifically LOC14 and FDA approved drug nitazoxanide. Cells treated with one of either compound before and after infection with VEEV, were found to produce E1 protein with significantly less disulfide bonds therefore producing less viable virus. Further experiments also showed that the compounds also affected early stages in the virus production cycle. These two mechanisms explain the significant reduction in production of VEEV and related viruses when PDI is inhibited. These results provide a new VEEV drug target, PDIs, as well as two compounds that can potentially be used to combat VEEV and other related viruses that have no current treatment options.

Another host interactor, VCP, functions throughout the cell and is known for unfolding of numerous substrates, including proteins. It is involved in numerous cellular functions thus making this interactor a promising target for drug treatment. Cells with reduced VCP function were shown to produce less progeny VEEV. Cells treated with NMS-873, a compound that reduces VCP function was also shown to reduce VEEV production. NMS-863 inhibition of VCP was shown to effect early events in VEEV replication. These results further emphasize the E1 interactors discovered are invaluable novel targets for VEEV drug treatment.

# Publications


Panny, L., Akrhymuk, I., Bracci, N., Woodson, C., Flor, R., Zhou, W., Narayanan, A., Campbell, C., & Kehn-Hall, K. (2023). Venezuelan equine encephalitis virus E1 protein interacts with PDIA6 and PDI inhibition reduces alphavirus production. Antiviral research, 105560. Advance online publication. https://doi.org/10.1016/j.antiviral.2023.105560

Vesuna, F., Akhrymuk, I., Smith, A., Winnard, P. T., Jr, Lin, S. C., Panny, L., Scharpf, R., Kehn-Hall, K., & Raman, V. (2022). RK-33, a small molecule inhibitor of host RNA helicase DDX3, suppresses multiple variants of SARS-CoV-2. Frontiers in microbiology, 13, 959577. https://doi.org/10.3389/fmicb.2022.959577

Dahal, B., Lehman, C. W., Akhrymuk, I., Bracci, N. R., Panny, L., Barrera, M. D., Bhalla, N., Jacobs, J. L., Dinman, J. D., & Kehn-Hall, K. (2021). PERK Is Critical for Alphavirus Nonstructural Protein Translation. Viruses, 13(5), 892. https://doi.org/10.3390/v13050892

Lin, S. C., Lehman, C. W., Stewart, A. K., Panny, L., Bracci, N., Wright, J., Paige, M., Strangman, W. K., & Kehn-Hall, K. (2021). Homoseongomycin, a compound isolated from marine actinomycete bacteria K3-1, is a potent inhibitor of encephalitic alphaviruses. Antiviral research, 191, 105087. https://doi.org/10.1016/j.antiviral.2021.105087

Lehman, C. W., Kehn-Hall, K., Aggarwal, M., Bracci, N. R., Pan, H. C., Panny, L., Lamb, R. A., & Lin, S. C. (2021). Resveratrol Inhibits Venezuelan Equine Encephalitis Virus Infection by Interfering with the AKT/GSK Pathway. Plants (Basel, Switzerland), 10(2), 346. https://doi.org/10.3390/plants10020346

Preprint: Haymond, A., Mueller, C., Steinberg, H., Hodge, K. A., Lehman, C. W., Lin, S. C., Collini, L., Branscome, H., Nguyen, T. V., Rucker, S., Panny, L., Flor, R., Guirguis, R., Hoefer, R., Lorenzin, G., Petricoin, E., Kashanchi, F., Kehn-Hall, K., Lanzafame, P., Liotta, L., … Luchini, A. (2020). Clinical Utility of a Highly Sensitive Lateral Flow Immunoassay as determined by Titer Analysis for the Detection of anti-SARS-CoV-2 Antibodies at the Point-of-Care. medRxiv : the preprint server for health sciences, 2020.07.30.20163824. https://doi.org/10.1101/2020.07.30.20163824

Preprint: Zinn, A. A., Izadjoo, M., Kim, H., Kehn-Hall, K., Woodson, C., Brody, R. L., Roth, R. R., Vega, A., Nguyen, K. K., Ngo, N. T., Zinn, H. T., Panny, L., Flor, R., Antonopoulos, N., & Stoltenberg, R. M.. (2020). Rapidly self-sterilizing PPE capable of 99.9% SARS-CoV-2 deactivation in 30 seconds. https://doi.org/10.1101/2020.11.16.384040

# Presentations

**Discovering Antiviral Treatments for Alphaviruses Through Proteomic Analysis of the VEEV E1 Glycoprotein**
Poster and Flash Talk, Virginia Polytechnic University
Blacksburg, Va, 2023

**Inhibition of Protein Disulfide Isomerases as a Broad-Spectrum Antiviral Target**
Poster Presentation, Chemical and Biological Defense Science & Technology
San Francisco, CA, 2022

**Host Interactors of the E1 Glycoprotein of Venezuelan Equine Encephalitis Virus as Potential Antiviral Targets**
Oral Presentation, Center for Emerging, Zoonotic and Arthropod-borne Pathogens Symposium
Blacksburg, VA, 2022

**Delineating Alphavirus E1 and Host PDIA6 Interaction**
Speed Talk Presentation, American Society of Virology Conference
Madison, WI, 2022

**Inhibition of Alphaviruses through Disruption of E1 and PDIA6 Interaction**
Oral Presentation, American Society of Virology Conference
Virtual, 2021

**Discovering Antivirals Targeting E1 Protein of Venezuelan Equine Encephalitic Virus Utilizing Interactome Analysis**
Oral Presentation, American Society of Virology Conference
Virtual, 2020

**Discovering Antivirals Targeting E1 Protein of Venezuelan Equine Encephalitic Virus Utilizing Interactome Analysis**
Poster Presentation, School of Systems Biology Fall 2019 Student Research Day
Manassas, VA, 2019

## Awards and Academic Achievements

- Chemical and Biological Defense Science and Technology Student Travel Award, 2022
- 2022 American Society of Virology Student Travel Award, 2022
- 2020 American Society of Virology Student Travel Award, 2020
- One Health Case Study Competition, Second Place, 2020
- Outstanding Poster Presentation Award, George Mason Student Research Day, 2019

## Examination Graduate Committee

### Major Advisor/Chair:

Kylene Kehn-Hall, MS, PhD
Professor
Department of Biomedical Sciences and Pathobiology

### Graduate Advising Committee Members:

Nisha Duggal, PhD
Assistant Professor
Department of Biomedical Sciences and Pathobiology VA-MD College of Veterinary Medicine

XJ Meng, MD, MS, PhD
University Distinguished Professor of Molecular Virology, VMCVM
Professor of Internal Medicine, VTC School of Medicine
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