Subject: Dissertation Defense - Carol Anderson, PHD Biosciences
Date: Tuesday, April 29, 2025 at 3:49:09 PM Eastern Daylight Time
From: SSB Faculty List on behalf of Diane St. Germain
To: SSB-FACULTY-LIST-L@LISTSERV.GMU.EDU

Dissertation Defense Announcement
To: The George Mason University Community

Candidate: Carol A. Anderson

Program: PhD in Biosciences

Date: Thursday May 15, 2025

Time: 1:00 p.m. (US and Canada)

Location:
In Person, Conference Room 1004
Institute for Advanced Biomedical Research (IABR)
10920 George Mason Cir, Manassas, VA 20109

And Virtual via Zoom
Join Zoom Meeting
https://gmu.zoom.us/j/95684289333?pwd=XmOOzHjU1R0p2Opl2YpDs9nMbqxvwh.1
Meeting ID: 956 8428 9333
Passcode: 956456

Committee Chair: Dr. Aarthi Narayanan

Committee members: Dr. Farhang Alem, Dr. Mariaelena Pierobon, Dr. Charles Chen

Title: Verteporfin, an FDA-Approved Small Molecule, Influences Host and Viral Events and Demonstrates Broad-Spectrum Efficacy Against Alphaviruses.

Abstract:
Alphaviruses, spread to humans through infected arthropod vectors, pose a serious threat to human health as they continue to emerge and re-emerge across the globe. In particular, the New World alphaviruses Venezuelan equine encephalitis (VEEV) and Eastern equine encephalitis viruses (EEEV) are classified as select agents under CDC regulations due to their ability to be aerosolized and potential use as biothreat agents. Symptoms typically manifest as fever and chills, and infection that can ultimately lead to encephalitic outcomes and febrile illness in humans. Western equine encephalitis virus (WEEV) is another New World alphavirus of concern as it has continued to spread in recent years. Of

additional interest are the Old World alphaviruses Sindbis (SINV) and Chikungunya virus (CHIKV) which cause fever, rash, and arthralgia that is sometimes persistent years after disease onset. CHIKV has spread from regions in which it was traditionally endemic to the Americas in 2005. No FDA-approved therapeutic or vaccines currently exist for any virus in this family and there is a pressing need to develop effective countermeasures. A protein-protein interaction inhibitor library of 409 small molecules was screened via a medium-throughput platform for assessment of antiviral efficacy against a luciferase tagged, BSL-2 VEEV TC-83 strain. Further assessment of down-selected candidates revealed 10 small molecules that are FDA approved for human use, including Verteporfin, which emerged as the lead candidate from this assessment. VP has previously been shown to effect levels of Yes associated protein (YAP), the final effector of the Hippo Signaling cascade in a light independent mechanism. Further work was conducted to identify host- and viral-based events contributing to infection and assess the protection garnered in central nervous system relevant cell lines. Work *in vitro* with Verteporfin (VP), assessed its selectivity index (SI), toxicity, and broad-spectrum anti-viral potential in the fully virulent strains of alphaviruses and other families of viruses. Additionally, Verteporfin's mechanism of action was evaluated via assessment of viral targets and previously undescribed host-targets, as well as modulation of key inflammatory and tight junction genes. *In vivo* toxicity and efficacy assessments took place in a lethal, VEEV TC-83 C3H/HeN mouse model, where VP conferred a modest survival advantage. Results from these studies identify novel host targets for therapeutic development as well as provide support for ongoing FDA Animal Rule approval efforts.

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