Subject: Thesis Defense: Leykie I. Green, MS Biology
Date: Monday, April 1, 2024 at 10:56:17 AM Eastern Daylight Time
From: SSB Faculty List on behalf of Diane St. Germain
To: SSB-FACULTY-LIST-L@LISTSERV.GMU.EDU

Thesis Defense Announcement
To: The George Mason University Community

Candidate: Leykie I. Green

Program: M.S. in Biology

Date: Monday April 15, 2024

Time: 4:00 PM Eastern Time (US and Canada)

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Committee Chair: Dr. Aarthi Narayanan
Committee Members: Dr. Farhang Alem, Dr. Ancha Baranova

Title: “Inhibition of TC-83 Alphavirus by Small Molecule; Saracatinib and piscidin Peptide Candidates"

Abstract:
Venezuelan Equine Encephalitis Virus (VEEV) is an encephalitic alphavirus that is known to cause disease in the central nervous system (CNS). It is naturally transmitted by infected mosquitoes and causes disease in equines and humans on a regular basis in various parts of the world. VEEV also has the potential to be aerosolized, and when infection is acquired via the respiratory route, the chances of CNS penetration are higher, with increased incidences of morbidity and mortality. Even if infected individuals clear the infection, there is a potential for long term neurological sequelae in survivors, thus increasing the disease burden. There are currently no FDA-approved therapeutic intervention strategies

to treat the encephalitic manifestations of VEEV infection-induced disease. This thesis project focused on establishing early stage efficacy measurements for a candidate small molecule inhibitor, Saracatinib, which is already FDA-approved for the treatment of cancer. In addition, this project also involved screening a small library of synthetic antimicrobial peptides (AMPs) derived from a parent piscidin peptide. Piscidins are fish-derived, naturally occurring AMPs that have been demonstrated to have antibacterial and immunomodulatory properties. My project was based on the hypothesis that Saracatinib and synthetic piscidin-derived AMPs will demonstrate antiviral activities against VEEV. This project was performed using the attenuated TC-83 strain of VEEV, in the context of several human-derived cell lines of the blood brain barrier (BBB). Analysis of antiviral activities of Saracatinib in the nontoxic range demonstrated that endothelial cells were highly responsive to treatment and showed significant reduction in viral load in treated cells. Screening of the synthetic piscidin library has identified four candidates that showed statistically significant reduction in viral load in a human astrocyte cell line. Cumulatively, these data provide the foundation for further development of Saracatinib and prioritized synthetic piscidin AMPs as therapeutic intervention strategies against VEEV infection.

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