Thesis Defense - Niloufar Boghdeh, MS Biology
April 19, 2021 4:00 - 6:00 PM
VIEW EVENT
All are invited to attend the defense. For more information please contact Graduate Coordinator at kharrism@gmu.edu.

Candidate: Niloufar Boghdeh

Program: Microbiology and Infectious Diseases, MS

Date: Monday, April 19, 2021

Time: 4:00 PM

Place: https://zoom.us/j/4687726629?pwd=YWhPeEdHbUduWHNvV1JiNTVyanA0dz09

Title: The Effect of Autophagy Inhibitors on RVFV production

Committee Chair: Dr. Kylene Kehn-Hall

Committee Members: Dr. Aarthi Narayanan, Dr. Yulia Dobrydneva, Dr. Ancha Baranova

ABSTRACT:

Rift Valley Fever Virus (RVFV) is an arbovirus that can infect ruminants and humans. It can cause many diseases including encephalitis, hemorrhagic fever, and ocular disease. A severe version of the disease is observed predominantly in pregnant and young livestock. While it is primarily transmitted by mosquitoes, most human cases are acquired through contact with blood or organs of an infected animal. Autophagy is an intracellular pathway that allows for the degradation of cytoplasmic organelles during cellular stress. The role of autophagy during viral infections is unclear. In some cases, it slows the progression of the infection, whereas, in many other cases the virus uses the autophagy system to enhance its replication. We hypothesized that inhibition of autophagy will cause RVFV titer reduction and provide evidence that the process of autophagy can be pro-viral to RVFV. To explore the impact of autophagy on RVFV replication, small molecule modulators of autophagy were utilized. CA- 5F, DC661, and ML240, which are all known autophagy inhibitors, were shown to b CA- 5F, DC661, and ML240, which are all known autophagy inhibitors, were shown to be capable of reducing RVFV infecSous Sters. CA-5F was selected for further studies due to it being one of the most potent and least toxic inhibitors. CA-5F is a late-stage autophagy inhibitor that funcSons by inhibiSng the autophagosome-lysosome fusion. Previous studies have shown CA-5F to have anS-tumor effects against lung cancer cells. HSEACs (Human Small Airway Epithelial Cells) were treated with non-toxic concentraSons of CA-5F and a significant decrease in viral producSon was observed. Furthermore, the greatest decrease in RVFV Sters was observed at 16 and 24 hours post-infecSon as compared to 8 hours post-infecSon. AddiSonally, extracellular, and intracellular RNA analysis showed that although CA-5F decreases RVFV infecSous Sters in a dose-dependent manner, it does not impact viral RNA producSon. This study provides evidence that the autophagy inhibitor, CA-5F, is capable of reducing RVFV producSon. Future studies will assess the importance of the viral protein NSs in CA-5F inhibiSon.