Thesis Defense Announcement
To: The George Mason University Community

Candidate: **Naomi Jones**
Program: MS in Biology

Date: April 22, 2022

Time: 9:00 AM Eastern Time
Zoom Link: https://gmu.zoom.us/j/97246899303?pwd=bVF6OENpZjQzTXBlZThBU3JRWFZ5UT09

Title: **SARS-CoV-2 ORF3a Binds to and Modulates HMOX1 Expression and Function**

Committee Chair: Dr. Ancha Baranova

Committee Members: Dr. John Kehrl, Dr. Vikas Chandhoke

All are invited to attend the defense.

ABSTRACT:
This thesis describes the interaction between SARS-CoV-2 Open Reading Frame 3a (ORF3a) and the Heme Oxygenase 1 (HMOX1). SARS-CoV-2 is a novel coronavirus and the causative agent of COVID-19, the highly contagious infection behind the 2019 COVID-19 pandemic. SARS-CoV-2 ORF3a is a viroporin, a small virally encoded membrane protein that acts as an ion channel. Its expression causes cell apoptosis, necrosis, lysosomal damage, and disrupts host cell autophagy. It is also implicated in the egress of SARS-CoV-2 virions from infected cells. HMOX1 is an enzyme encoded by a human gene capable of modulating immune activity with an active role in suppressing viral infections and inflammatory pathways. In this thesis, we use confocal microscopy and a co-immunoprecipitation protocol to shed light on the interaction between SARS-CoV-2 ORF3a and HMOX1. Using this approach, we show that SARS-CoV-2 ORF3a and HMOX1 co-localize in the endoplasmic reticulum (ER). We also found that that ORF3a expression stabilizes HMOX1 protein levels within cells. These results suggest that ORF3a may affect ERC8, an important E3 ligase that help direct protein traffic through the ER and which is known to ubiquitinate HMOX1. These observations lay the foundation for additional studies aimed at studying the HMOX1/ ORF3a interaction. They also suggest that SARS-CoV-2 targets ERC8 and potentially other E3 ligases to redirect ER trafficking.