Mohona - Microbiology and Immunology

Abstract: As of December 5, 2022, the causative agent of the COVID-19 pandemic, SARS-CoV-2, has infected ~645 million people worldwide and claimed~6.64 million lives(source: WHO Coronavirus (COVID-19) Dashboard). Despite mass vaccination efforts and testing strategies, several SARS-CoV-2 variants are still actively circulating among us. Additionally, many survivors of SARS-CoV-2 infection exhibit persistent COVID-19 symptoms and suffer from related complications, which have been termed as long-COVID. It is not well understood why or how these patients show COVID-19 symptoms long after clearing the actual virus infection. Upon encountering its receptor on the host cells, viruses enter the cell and utilize essential host resources to successfully replicate. In general, the replication cycle of viruses can be divided into several distinct stages. Each stage is defined by unique virus-host interactions. My dissertation focuses on the “assembly” and “egress” stages of the SARS-CoV-2 life cycle, for their mechanisms have not yet been established. Using molecular approaches, we hope to determine the specific viral and host protein interactions required for successful virus assembly and egress. In addition to filling the information gap in the SARS-CoV-2 literature, my dissertation project will also have insights into the molecular determinants of long-COVID. It is very likely that during the acute infection phase, damage sustained by the host cell renders key host machineries and pathways nonfunctional. We are interested to know whether the host exocytic pathway is compromised during the assembly and egress processes of newly synthesized SARS-CoV-2 viruses. In an uninfected cell, the exocytic pathway is strictly regulated, so that only the cargo destined for extracellular space gets secreted. We hypothesize that following SARS-CoV-2 infection, the exocytic pathway of the host cell gets corrupted, which leads to the uncontrolled secretion of cellular “debris”. This putative uncontrolled secretion of cellular materials can explain the constant pro-inflammatory response in patients, which is a major hallmark of long-COVID.

Undergraduate Work: The goal of this project is to screen for host protein(s) involved in SARS-CoV-2 assembly and egress. To accomplish this goal, the undergraduate research student will assist the graduate student by testing pharmacological inhibitors on SARS-CoV-2 and MHV virus-like-particle (VLP) production. The work will take place in two phases –first the trainee will learn how to produce reporter protein expressing VLPs. Secondly, the trainee will work with the graduate student to test the putative inhibitors of VLP secretion. Inthe process of performing these experiments, the trainee will learn basic aseptic techniques required for mammalian cell culture. Additionally, the trainee will also learn the techniques required for protein expression in mammalian cells. Finally, the trainee will also develop necessary skills to perform a pharmacological inhibitor screening, which is a widely used method to identify and validate protein mediators of complex biological processes.