Research projects available in the Daniel group 2015

Each of these 4 projects are envisioned as independent student projects (not team-based, but will involve interactions with other graduate students and collaborators of the Daniel Lab). Contact Prof. Daniel directly at sd386@cornell.edu. Please provide a resume and statement of interest.

Uncovering the fusion mechanism of enveloped viruses

Project 1:

In this project we are aiming to determine the key aspects of a newly-identified fusion peptide region in Coronavirus that may assist this virus in infecting new hosts. Coronavirus is a membrane-enveloped virus decorated with proteins called "Spike" that control the attachment and entry of the virus into host cells. Coronavirus has a larger animal reservoir and can occasionally jump into humans, as was the case with SARS in 2003 and MERS in 2012, making it a human health concern. Our collaborators in the Whittaker group in the Cornell Vet School have identified a novel cleavage site (S2') in the fusion peptide of Spike that could enable coronavirus to be "flexible" in the host species it chooses to infect. However it is difficult to study whole Spike, as there is not a crystal structure for it due to its large size, complex structure, and heavy glycosylation. However, a relevant short subsection of heptide repeats is known in the fusion peptide region. This subsection does not include the novel S2' section, so the goal of this project will be to extend out the known region to include this part of the peptide and figure out the local structure with all the fusion peptide relevant parts present. This project will require heavy use of molecular biology techniques, including cloning and expressing the new extension, and optimizing experimental conditions to maximize protein quantity and purification. We wish to also examine variants of the regions as well. Time permitting; the project can continue to crystallization and NMR studies of the amassed peptide material. This project will be carried out in collaboration with the Whittaker group at the Cornell Vet School.

Project 2:

Ebola virus enters cells via receptor-mediated endocytosis, and several recent studies have shown that Ebola virus infectivity is impacted by the presence of calcium ions. When cellular calcium stores are depleted, infectivity of cells is inhibited; however the mechanisms underlying this effect are poorly understood. We believe that the calcium may be binding near the fusion peptide of the Ebola virus glycoprotein, and altering its interaction with the host membrane. In this project, we plan to create various mutants of the Ebola virus glycoprotein, altering the predicted calcium-binding site and fusion peptide. We will examine relationships between calcium ions and these mutants, measuring infectivity using a pseudovirus system that is non-infectious to humans. Cell culture and luminescence assays will be used, followed by single particle fusion experiments if time permits to examine the role of the calcium directly on fusion, beyond basic infectivity screening. This project will be carried out in collaboration with the Whittaker group at the Cornell Vet School.