Megan R. Culler’s Beckman Research Proposal

Paramyxoviridae, a family of negative-strand, enveloped, RNA viruses, includes several important human pathogens, including measles virus and human respiratory syncytial virus (RSV), as well as the newly emerged Hendra and Nipah viruses, making the study of these viruses quite pertinent to human health. In the life cycle of enveloped viruses, membrane fusion is necessary for the survival of the virus, allowing virus entry into the host cell and the release of the viral genome. The fusion of these viruses to the cell membrane is promoted by two surface glycoproteins, an attachment protein needed for primary receptor binding, and a fusion protein (F) which promotes fusion between the viral envelope and the cell membrane. Expression of fusion and attachment proteins at a cell surface is also sufficient to induce cell to cell fusion.

This membrane fusion event can be broken down into stages: mixing of the outer leaflets, the formation of a fusion pore, the enlargement of that pore, and the subsequent mixing of aqueous contents between the once separate cells. A mutant of the simian virus 5 (SV5) fusion protein lacking its cytoplasmic domain was found to promote mixing of lipids and the transfer of a small aqueous dye, but was defective in pore enlargement (Dutch et al., 2001). I hypothesize the SV5 F protein cytoplasmic tail interacts directly with cellular components which regulate the expansion of the fusion pore.

My project focuses on identification of novel interactions between cellular proteins and the cytoplasmic tail region of the fusion proteins from SV5 and Hendra virus, two distantly related viruses within the same family. Specifically, I intend to isolate cellular proteins which interact directly with the cytoplasmic tail of the fusion proteins, and then to test the role of these identified proteins in viral glycoprotein-mediated membrane fusion. After proteins which bind these cytoplasmic tail regions have been identified, I plan to study what specific part of the cytoplasmic tail sequence binds to that protein and also the effects that modified levels of identified cellular proteins have on membrane fusion events.

Megan’s Presentations:

- UK Molecular and Cellular Biochemistry Department Summer Conference 2006- Poster presentation
- Posters at the Capitol 2007- Oral Presentation
- AMSTEMM Class guest speaker NCUR 2007-poster Showcase of Undergraduate Scholars 2007-poster