Inhibition of Host-Cell Endosomal Acidification by H1N1 Influenza

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This research investigated if and why specific proteins in H1N1 are able to inhibit the acidification of endosomes/lysosomes in order to mediate a host cell response favorable to viral replication. To do this, H1N1 viral-like particles (VLPs) containing only proteins necessary for early infection were produced. This allowed for the isolation of single protein effects by using the VLPs in conjunction with pH-sensitive fluorescing nano-probes to test for pH. A series of experiments were performed infecting cells with media containing both VLPs and pH-nanoprobes and a fluorescent microscope was used to image and track the cells over time. Based on these experiments, it was concluded that a viral protein M2 is able to directly inhibit endosomal acidification in cells, possibly leading to host cell protein activation favorable to viral replication. It was also found that H1N1 strains with a mutated M2 protein are less effective at both inhibition of endosomal acidification and activation of proteins favorable to viral replication. Together these observations support the idea that blocking endosomal acidification is a key process in the virus's ability to infect cells, opening the door for new drug discovery efforts.

Awards Won:

Fourth Award of $500