



Biomedical Engineering Seminar Series

Johns Hopkins School of Medicine and the Whiting School of Engineering



Dr. Gregory Melikian

Professor

Institute of Human Virology

University of Maryland, Baltimore

Monday, October 26, 2009 at 1:30

Talbot Room, Traylor 709

Host: Alexander Spector

Video-Teleconferenced to Homewood
Campus, Rome Room, Clark 110



Light lunch will be provided in Traylor 709

HIV-1 ENTRY: FUSION FROM WITHIN

Enveloped viruses enter cells by fusing with the host cell membrane, an event that is triggered by interactions with cognate receptors and/or by virus delivery into acidic endosomal compartments. Viruses undergoing pH-independent fusion, including HIV-1, are thought to fuse directly with the plasma membrane. In order to delineate the actual site of HIV-1 entry, we monitored the cytosolic delivery of the viral content using population-based and single virus imaging techniques. HIV-1 acquired resistance to a membrane-impermeant fusion inhibitor much earlier than to agents preventing fusion of both surface-accessible and intracellular viruses. This finding implies that HIV-1 fuses with intracellular compartments after undergoing receptor- and coreceptor-mediated endocytosis. Real-time single virus imaging showed that HIV-1 failed to undergo complete fusion with the plasma membrane, whereas endosomal fusion resulted in the viral content release into the cytosol. In spite of the failure to release its content at the cell surface, HIV-1 was able to transfer its membrane marker to the plasma membrane, demonstrating that fusion did not progress beyond the lipid mixing step. We found that dynasore, a small molecule dynamin inhibitor, blocked not only HIV-1 endocytosis, but, most importantly, the virus-endosome fusion step itself. Thus, HIV-1 fuses with endosomes in envelope glycoprotein- and dynamin-dependent manner. Together, these results show that HIV-1 infects cells via an endocytic pathway and suggest new strategies to prevent HIV infection.

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