BIOCHEMISTRY SEMINAR SERIES

Midstream Presentation - Spring 2022

Alexander Stevens

Zhou Group

"Structural Characterization of Genome Management Strategies in Human Herpesviruses "

Human herpesviruses (HHVs) are a family of complex dsDNA viruses which infect most of the global populace and, as there are no cures and limited therapeutic interventions, represent a significant public health burden. Despite significant genetic variation between them, all HHVs share similar, highly regulated assembly strategies, in which their large genomes are packaged into proteinaceous shells, or capsids. These capsids are multifunctional containers that protect the genome during intercellular transport and ensure delivery to the nuclei of host cells where it can initiate viral replication. To carry out these roles the capsid must be dynamic enough to adopt unique conformations along assembly and infection pathways while remaining robust enough to cope with the force of the highly pressurized genome which can exceed 20 atmospheres. My work seeks to leverage high-resolution cryogenic electron microscopy to inform on the structures integral to HHV genome management strategies and identify targets along these assembly pathways to disrupt viral maturation. Specifically, we hope to determine which features of capsid architecture permit genome packaging and stabilize it against the pressure exerted by the genome. To do this we investigate byproducts of capsid assembly in the model alphaherpesvirus, herpes simplex virus 1, and the capsid stabilizing role of the large tegument protein pp150 against the exceptionally large genome of the human cytomegalovirus. Here I present our work on the structural characterization of herpesvirus assembly intermediates to shed light on the viral genome packaging and management strategies.

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3:30 pm

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