Dissertation Defense - Gifty Mensah, PhD Biosciences

July 22, 2022 2:00 - 4:00 PM

All are invited to attend the defense. For more information please contact Graduate Coordinator at

dstgerma@gmu.edu

Candidate: Gifty Mensah
Program: PhD, Biosciences

Date: Friday July 29, 2022

Time: 1:00 PM

Meeting Location: https://gmu.zoom.us/j/98675482748?pwd=T2dyMXdLRTFoTnFBMlNObzcwdkFsQT09

Title: The Effects of Extracellular Vesicle-Associated Kinases on HIV-1 Pathogenesis

Committee Chair: Dr. Fatah Kashanchi

Committee Members: Dr. Lance Liotta, Dr. Ramin Hakami, Dr. Sergei Nekhai

ABSTRACT:
There are 37.7 million people living with Human Immunodeficiency Virus type 1 (HIV-1) as of 2020. Although great strides have been made in treatment options for HIV-1 and our understanding of the HIV-1 life cycle has vastly improved since the start of this global health crisis, a functional cure remains elusive. One of the main barriers to a cure is latency, which allows the virus to persist despite combined antiretroviral therapy (cART). Recently, we have found that extracellular vesicles (EVs), membrane-bound particles released by virtually all cell types and known to mediate intercellular communication, as being responsible for the increased transcription observed in HIV-1 latently infected cells. This study elucidates the molecular mechanism by which EVs derived from uninfected T-cells activate latent HIV-1. Our results show that kinases present in EVs such as c-Src initiate signal cascades that culminates in increased viral transcription via the PI3K/AKT/mTOR pathway. In addition, kinome profiling of EVs revealed that the kinases CDK10, GSK3β, and MAPK8 are differentially expressed in EVs from uninfected versus infected cells. These kinases were shown to be biologically active and capable of phosphorylating substrates, as well as modulate changes in the cell cycle dynamics of recipient cells. Overall, data from this study implicate EV-associated kinases as key contributors to HIV-1 pathogenesis - specifically at the transcriptional and cell cycle control levels. These findings are significant because they could serve as the basis for improving and supplementing the current antiretroviral treatment regimen.