Subject: Dissertation Defense - Yuriy Kim, PhD Biosciences
Date: Friday, April 5, 2024 at 11:15:10 AM Eastern Daylight Time
From: SSB Faculty List on behalf of Diane St. Germain
To: SSB-FACULTY-LIST-L@LISTSERV.GMU.EDU

Dissertation Defense Announcement
To: The George Mason University Community

Candidate: Yuriy Kim

Program: PhD Biosciences

Date: Friday April 19, 2024

Time: 12:00 PM Eastern Time (US and Canada)

Location: Via Zoom

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Committee chair: Dr. Fatah Kashanchi
Committee members: Dr. Ramin Hakami, Dr. Lance Liotta, Dr. Sergey Iordanskiy
Title: "The Characterization of Early and Late Extracellular Vesicles Released from HIV-1-infected Cells and Their Effect on the Recipient Cells"

Abstract:

Human immunodeficiency virus type 1 (HIV-1) is a causative agent of acquired immunodeficiency syndrome (AIDS) and, since its discovery in 1981, it has caused approximately 40.1 million deaths worldwide. The implementation of combination antiretroviral therapy (cART) has drastically reduced morbidity and mortality in HIV-1 patients. Modern cART drugs effectively target stages of HIV-1 cycle such as viral entry, reverse transcription, integration, protease cleavage of viral polyproteins, and virion maturation. However, life-long adherence to a cART is required to suppress viral replication to the safe level. We have recently shown that Extracellular Vesicles (EVs) from HIV-1-infected cells play major role

in viral pathogenesis and can facilitate viral spread. First, we have attempted to address the timing of EVs and virions release from HIV-1-infected cells. Uninfected, HIV-1- and HTLV-1-infected cells were synchronized in G0 of cell cycle and then released into normal cell cycle. The supernatants and cell samples were collected at different time points and tested for the markers of EVs, autophagy and for viral proteins and RNAs. As a result, HIV-1 supernatant from 6-hour sample (early EVs) was found not to be infectious, however, the virus from 24-hour sample (late EVs) was able to start productive infection in the recipient cells. Next, we analyzed biochemical and functional properties of large EVs from HIV-1-infected T-cells. After differential ultracentrifugation large EVs were further purified by size-exclusion chromatography and EV-rich fractions showed the presence of viral proteins, RNAs and amphisome markers. Overall, our data shows that EVs with virus-related cargo are released before the virus from infected cells, thereby implicating a potentially significant effect on uninfected recipient cells prior to subsequent viral infection. Moreover, large EVs from HIV-1-infected T-cells, produced at 24hrs post-release, contain infectious material and have amphisome markers on their surface.

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