Subject: Thesis Defense: Hafsa Chaudhry, MS Biology
Date: Monday, July 14, 2025 at 8:15:07 AM Eastern Daylight Time
From: SSB Faculty List on behalf of Diane St. Germain
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Thesis Defense Announcement
To: The George Mason University Community

Candidate: Hafsa Chaudhry

Program: M.S. in Biology

Date: July 28, 2025

Time: 4:00 PM Eastern Time (US and Canada)

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Committee Chair: Dr. Fatah Kashanchi

Committee members: Dr. Ancha Baranova, Dr. Farhang Alem

Title: The Effect of 18BIOder on the Packaging Of GSK-3β Into EVs In HIV-1 Infected Cells

Abstract: Human Immunodeficiency virus type 1 (HIV-1) remains a global health challenge with an estimated 39.9 million people reported by WHO, living with HIV-1, as of 2023. Despite the success of combination antiretroviral therapy (cART), persistent low-level transcription and

translation of viral products continue, partly due to latent reservoirs and viral proteins that contribute to chronic inflammation and neurotoxicity. Latently infected cells harbor integrated but transcriptionally silent provirus that can sporadically reactivate, while residual viral proteins such as Tat can remain active even without full viral replication, sustaining inflammatory and neurotoxic signaling. Extracellular vesicles (EVs) are small, membrane-bound particles released by cells that mediate intercellular communication by transporting bioactive molecules—including host and viral proteins, transcripts, and regulatory RNAs—to recipient cells. In the context of HIV-1 infection, EVs can act as vehicles for spreading inflammatory signals and viral components, amplifying pathogenesis even in the absence of productive infection. Among the host factors packaged into EVs, glycogen synthase kinase-3 beta (GSK-3β) has emerged as a promising target due to its role in both viral replication and neurotoxicity. Packaging of GSK-3β into EVs can modulate downstream signaling in bystander cells, potentially enhancing HIV-1 transcriptional activity, promoting neuroinflammation, and disrupting cellular homeostasis. Inhibiting GSK-3β activity may therefore represent a dual therapeutic strategy to suppress viral persistence and reduce neurotoxic signaling. This thesis investigates the effects of 18BIOder, a second-generation derivative of 6BIO, on GSK-3β expression and its packaging into extracellular vesicles (EVs) in HIV-1-infected cells. Previous studies utilizing both 6BIO and 18BIOder demonstrated their inhibitory effects on HIV-1 replication and GSK-3β activity, and this work was directly influenced by those findings to further explore EV-associated GSK-3β as a mechanism of intercellular signaling. Monocytic cell lines were used in this study, including U937 and THP-1 (uninfected) alongside their HIV-1-infected counterparts, U1 and THP89GFP, and were treated with increasing concentrations of 18BIOder. EVs were isolated through differential ultracentrifugation, and western blotting was used to assess GSK-3β levels. Results suggest that 18BIOder modulates the presence of GSK-3β in distinct EV subpopulations, supporting the role of GSK-3β in intercellular signaling and offering insight into its therapeutic relevance in HIV-1 infection.

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