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DDX21 Modulates HIV Replication and Latency

Abstract: HIV persistence and latency are major obstacles for curing viral infection. The virus stays dormant in infected cell reservoirs that are established early during infection despite antiretroviral therapy (ART). Understanding the molecular mechanisms that promote HIV latency and targeting the host factors that regulate HIV gene expression is crucial for developing new strategies for eradicating these hidden reservoirs. In a screen to identify host factors that regulate HIV gene expression, we identified DDX21 (DEAD-box helicase), as a potential factor involved in establishing HIV latency. DDX21 is part of a large family of evolutionarily conserved RNA helicases, responsible for transcription regulation, RNA processing, antiviral innate defense, RNA binding and folding. Previous results report show that DDX regulates HIV replication by facilitating the binding of the viral Rev protein to Rev Response Element (RRE) and by interacting with Rev in the nucleolus and nucleus. However, DDX21's role in HIV transcription and latency is poorly understood. Previous studies have shown that DDX21 knockout negatively regulates IFN-β production. Moreover, CPSF6 interacts directly with HIV capsid to promote nuclear entry of the pre-integration complex and its targeting for integration. In our study, we hypothesize that DDX21 could be crucial for maintaining viral integration via CPSF6 interaction and depletion of DDX21 could facilitate HIV replication by reducing the production of IFN-β. We utilized CRISPR-Cas9 to knock-out DDX21 in Jurkat T cells resulting in increased HIV replication. These findings suggest that DDX21 plays a complex role in regulating HIV latency and highlights its potential as a therapeutic target for eradicating latent HIV reservoirs.

Keywords: HIV latency, DDX21, Dead-box helicase, CPSF6 and HIV transcription.

Biography: Praveenkumar Murugavelu is a dedicated researcher currently pursuing his PhD at Department of Microbiology, Immunology and Genetics, Ben Gurion University, Israel. Born in India, Praveenkumar's academic journey and passion for virology research have taken him far from his homeland, leading to significant contributions in his field of study. His current research focuses on HIV transcriptional regulation and latency, aiming to uncover mechanisms that could lead to better therapeutic strategies for HIV. He has already made notable contributions to the field of virology, with two first-author and two co-author publications in reputed journals.

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