Effect of kinase inhibitor treatment on Rift Valley Fever Virus replication

Brandon B. Verkinderen, David A. Meekins, and Juergen A. Richt

Department of Diagnostic Medicine/Pathobiology, College of Veterinary Medicine, Kansas State University, Manhattan, Kansas

Rift Valley fever virus (RVFV) is a mosquito-borne pathogen that can cause significant disease in humans and livestock species. It is at high risk for transboundary spread due to widespread vector competence and increased travel/trade among endemic and non-endemic countries. There are no commercially available vaccines or therapeutics to prevent or treat RVFV infection in humans. The severity of RVFV is attributed to the activity of its nonstructural protein, NSs, which is a major virulence factor responsible for inhibition of host antiviral immune responses. Previous studies show NSs is phosphorylated by casein kinase 2 (CK2), and evidence suggests that this may be necessary for NSs-interaction with specific E3-ubiquitin ligases that results in shutdown of the host cell's interferon response. The purpose of this study was to test whether inhibition of NSs phosphorylation could be used as a treatment strategy to limit RVFV replication *in vitro*. Human A549 cells were treated with the drug CX4945, a potent and specific CK2 inhibitor. The effect of CX4945 on RVFV replication over 24 hours was determined via plaque assay using the RVFV MP-12 vaccine strain on treated cells compared to non-treated cells at differing MOI. Analysis of MP-12 viral replication in the presence of CX4945 show ~25-45% decrease in viral titers at 24 hours post infection. These data suggest that CK2 inhibition does affect RVFV replication, but the effect is not statistically significant. Further investigations are necessary to determine the effect of kinase inhibitors on RVFV replication and to fully elucidate the role of NSs phosphorylation in RVFV virulence in order to develop novel treatment strategies for RVFV infections in humans.

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