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OC11 THE DEVD MOTIF OF CRIMEAN-CONGO HEMORRHAGIC FEVER VIRUS NUCLEOPROTEIN IS ESSENTIAL FOR VIRAL REPLICATION IN TICK CELLS

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Abstract:

Background: Crimean-Congo hemorrhagic fever (CCHF) is a zoonotic viral disease that is asymptomatic in infected animals, but a serious threat to humans who, following infection, develop a hemorrhagic syndrome with a high case fatality rate. CCHF virus (CCHFV) has been found in many species of ticks. In particular, members of the genus Hyalomma appear to be the principal vectors and both transstadial and transovarial transmission occur in this genus that represents the natural viral reservoir. In this study, we developed a model system for investigating CCHFV replication in its natural arthropod host cells.

Methods: Two Hyalomma anatolicum embryo-derived tick cell lines were infected with CCHFV at MOI of 0.1 and 1 FFU/cell under biosafety level 4 conditions. At different time points post-infection, viral replication was evaluated by qPCR, virus particles titration, and expression of viral nucleoprotein. Furthermore, a recombinant CCHFV containing a mutated DEVD motif (rCCHFVmut) and a CCHF transcriptionally-competent virus-like particle (tc-VLP) system were used to evaluate the role of the DEVD motif in viral replication.

Results: We found that CCHFV chronically infected H. anatolicum tick cell lines without causing cytopathic effects. The persistence of viral infection were confirmed by PCR until 282 days post-infection. Interestingly, we found that while rCCHFVwt was able to replicate in tick cells, rCCHFVmut showed a strong impairment in RNA replication and viral particle production. Our results suggested that the highly conserved proteolytic cleavage site in the nucleoprotein, the DEVD motif, is essential for virus replication in cells of its natural tick reservoir as opposed to human cells, where we observed only the reduction of the viral titer of roughly 1 log.

Conclusions: Our results support the applicability of tick cell lines to studying the biology of CCHFV in vector cells and virus/vector interaction. The virus/tick cell culture system reported here provides the basis for further studies to characterize the tick cellular response to CCHFV infections, and to determine the mechanism by which tick cells can tolerate persistent viral infections.