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N. **Title:**

P8 EVALUATION OF HAZARA VIRUS INFECTION IN TICK CELL LINES AS A MODEL TO STUDY THE PERSISTENT INFECTION OF CRIMEAN-CONGO HAEMORRHAGIC FEVER VIRUS IN TICKS

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Abstract:

Background: Crimean-Congo haemorrhagic fever (CCHF) is a severe disease for humans caused by CCHF virus (CCHFV). Ticks of the genus Hyalomma are the principal vectors and they play an important role as natural reservoir. CCHFV establishes a persistent infection in ticks and they can transmit the virus to their hosts during blood feeding. To date, the mechanism allowing the persistent viral infection in ticks is mostly unknown. It has been shown that the presence of viral-derived DNA sequences (vDNA) is associated to a persistent infection in insects, down modulating the viral replication and promoting host survival and viral persistence. The aim of our study is to investigate the virus/vector interactions that allow the establishment of the persistent infection in ticks, in particular focusing on vDNA production, by adopting Hazara virus (HAZV) as a model. HAZV is an apathogenic virus closely related to CCHFV and can be handled in BSL2 instead of BSL4 containment that is required for CCHFV.

Methods: Two Hyalomma anatolicum-derived cell lines, Hae/CTVM8 and Hae/CTVM9, were infected with HAZV at MOI of 1 and 0.1 FFU/cell. At different time points post-infection, viral replication was evaluated by qPCR and viral particles titration. Furthermore, DNA was extracted from infected tick cells and analysed by PCR, using 9 pairs of primers mapping within the S segment of the HAZV ssRNA genome, to investigate the presence of vDNA.

Results and conclusions: Our preliminary results showed that HAZV persistently infected tick cells without any sign of cytopathic effect. vDNAs are detectable in infected tick cells already at 24 hours post-infection and independently from the employed MOI. Experiments with the retrotranscriptase inhibitor AZT suppressed the formation of vDNAs suggesting that their synthesis might be dependent on reverse transcriptase activity, likely codified by host-specific endogenous retrotransposons.

In conclusion, vDNA synthesis seems to represent a common strategy to control the replication of RNA viruses both in insect than in ticks.