Efficient production of Rift Valley fever virus-like particles: The antiviral protein MxA can inhibit primary transcription of bunyaviruses

Nicola Penski, Valentina Wagner, Martin Spiegel, Anna K Overby, Georg Kochs, Juha T Huiskonen & Friedemann Weber

Rift Valley fever virus (RVFV) is a highly pathogenic member of the family Bunyaviridae that needs to be handled under biosafety level (BSL) 3 conditions. Here, we describe reverse genetics systems to measure RVFV polymerase activity in mammalian cells and to generate virus-like particles (VLPs). Recombinant polymerase (L) and nucleocapsid protein (N), expressed together with a minireplicon RNA, formed transcriptionally active nucleocapsids. These could be packaged into VLPs by additional expression of viral glycoproteins. The VLPs resembled authentic virus particles and were able to infect new cells. After infection, VLP-associated nucleocapsids autonomously performed primary transcription, and co-expression of L and N in VLP-infected cells allowed subsequent replication and secondary transcription. Bunyaviruses are potently inhibited by a human interferon-induced protein, MxA. However, the affected step in the infection cycle is not entirely characterized. Using the VLP system, we demonstrate that MxA inhibits both primary and secondary transcriptions of RVFV. A set of infection assays distinguishing between virus attachment, entry, and subsequent RNA synthesis confirmed that MxA is able to target immediate early RNA synthesis of incoming RVFV particles. Thus, our reverse genetics systems are useful for dissecting individual steps of RVFV infection under non-BSL3 conditions.

type: journal paper/review (English)
date of publishing: 15-3-2009
journal title: Virology (385/2)
ISSN electronic: 1096-0341
pages: 400-8