

Abstract

Functional and Structural Characterization of Novel Insect-Restricted Negev Viruses and Their Interaction with Host Cells [†]

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Abstract: Many viruses transmitted by blood-sucking arthropods have emerged worldwide and cause serious human and animal diseases. Arthropod-borne (arbo-)viruses possess a peculiar capacity to replicate in very different hosts, such as mosquitoes and mammals (e.g., dengue and chikungunya). However, the molecular mechanisms that enable arboviruses to enter and replicate in very different hosts—such as arthropods, mammals, and birds—remain highly enigmatic. Insect-restricted viruses provide a reference point regarding this issue, since they lack the strategies of infecting vertebrate hosts and are viewed as evolutionary precursors of arboviruses. Negev viruses comprise a recently discovered insect-restricted taxon exhibiting worldwide distribution among blood sucking arthropods. Negev viruses are enveloped, positive sense, nonsegmented RNA viruses. The virus genome is ca. 10 kb long and contains three ORFs, with the longest *ORF1* (7 kb) encoding putative replicative enzymes. *ORF2* (1.2 kb) and *ORF3* (0.7 kb) do not have any clear homologs and are predicted to encode membrane proteins. We explored the functional and structural aspects of Negev viruses and the role of their membrane glycoproteins during Negev virus entry into the mosquito cells. We employ biochemistry, structural biology, and microscopy to reveal mechanisms of Negev virion organization, and its entry into host cells followed by fusion with the host membranes to allow subsequent genome delivery and replication.

Keywords: Negev viruses; viral entry and fusion; viral envelope glycoproteins; Insect restricted viruses



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