The viroporin activity of VP2, VP3 and VP4 contribute to the SV40 viral life cycle

Kristina M Giorda, *University of Massachusetts Amherst*

Abstract

Viruses have evolved to exploit cellular pathways and machinery in order to deliver their genome to the cell, replicate, and produce viral progeny. Nonenveloped viruses must overcome membrane barriers to infect host cells and trigger lysis for virion release. The model nonenveloped virus, Simian Virus 40 (SV40), is bound at the cell surface and eventually delivered to the endoplasmic reticulum (ER) where penetration occurs resulting in delivery of the viral genome to the nucleus by an unknown mechanism. During the later stages of infection viral progeny are assembled in the nucleus and are liberated from the host cell through a cytolytic process. ^ SV40 appears to initiate cell lysis by expressing the late viral protein VP4 at the end of infection for virus release. Bacterially expressed and purified VP4 forms size selective pores in membranes. To investigate the role of VP4 in host cell lysis an inducible expression system was used to produce VP4 in mammalian cells. The viral protein was mainly localized along the nuclear envelope and correlated with the mislocalization of nuclear proteins and was associated with cell death. These results indicate that VP4 acts as a viroporin in the nuclear membrane to promote virus release. ^ Previous results indicated that the two minor structural proteins, VP2 and VP3, may act as membrane proteins during viral infection. Studies using purified proteins, bioinformatics, a cell-free membrane insertion assay and a thorough examination of viral propagation, assembly and infection processes have provided new insights into the role of the minor structural proteins during infection. Targeted disruption of the viroporin activity of VP2 and VP3 inhibited viral infection. Together, these results support that the late viral proteins VP2, VP3 and VP4 each act as viroporins and serve as critical triggers for the progression of the viral life cycle. This investigation provides new insight into how the viroporin activity of the late viral proteins is utilized in viral infection and release.^

Subject Area

Cellular biology|Biochemistry|Virology

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