The SV40 late protein VP4 is a viroporin that forms pores to disrupt membranes for viral release

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Viruses exploit host cells for their propagation. Once an adequate number of viral particles have been assembled within the cell through the aid of cellular machinery of the host cell, the virus must be released from the cell for the virus to spread. For nonenveloped viruses or viruses that are solely encapsulated by a protein shell, this step most commonly involves the perforation of cellular membranes resulting in the lysis or death of the host cell. The mechanism for how this key terminal step in the viral life cycle is performed is poorly understood. We demonstrated that for the model nonenveloped virus SV40, the newly discovered virally encoded protein termed VP4 perforates membranes by forming pores with a diameter of ~3 nm in host cell membranes. While these pores are not of a sufficient size to provide a conduit that permits the movement of the virus through the membrane, they support membrane destabilization that leads to the disintegration of the membrane of the host cell and viral release. In host cells VP4 was localized along the nuclear envelope and caused aberrant localization of nuclear envelope proteins. This localization and phenotype was mitigated by mutation of VP4. These results suggest that VP4 is localized to the nuclear membrane to disrupt the host cell leading to lysis and virus release.

Our model for the timely localization of the late minor viral proteins to membranes during viral release. The major structural protein VP1 is synthesized (step 1) and oligomerizes into pentamers in the cytoplasm (step 2). VP2 and VP3 are synthesized 12 hr later and bind to waiting VP1 pentamers (step 3). These complexes are then imported into the nucleus for further capsid assembly around the viral minichromosome producing virions (step 4). Continued synthesis of VP2 and VP3 begin to saturate capsomers, which allows VP2 and VP3 to interact with nuclear membranes (step 5) along with newly produced VP4 (step 6). This triggers cytolysis of the host cell and release of the viral progeny (step 7).