Title

Discrete Steps In The Entry Pathway And Disassembly Of SV40

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Date of Award

9-2011

Document Type

Campus Access

Degree Name

Doctor of Philosophy (PhD)

Degree Program

Microbiology

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Subject Categories

Microbiology | Virology

Abstract

Almost all DNA viruses must deliver their genomes to the nucleus in order to initiate infection. The route by which they accomplish that goal varies greatly and in many cases is not well characterized. SV40 is a non-enveloped virus and therefore does not have the option of fusing with cellular membranes in order to gain entry into a cell or its nucleus. It must solve the problem of having to cross at multiple cellular membranes before it can initiate infection. SV40 enters host cells via caveolae, and is then transported along the microtubules to the endoplasmic reticulum (ER). Within the lumen of the ER, the viral capsid undergoes structural modification followed by the translocation of the virus across the ER membrane and into the cytoplasm. In the final steps in the pathway to infection, the SV40 disassembly intermediate delivers the viral genome to the nuclear membrane where the DNA enters the nucleus and initiates an infection.

The research presented here investigates the state of the SV40 particles as well as attempts to clarify the route that the virus takes as it delivers its genome into the nucleus. We propose that the SV40 route to infection is a dynamic process in which the virus undergoes multiple disassembly steps while traversing through the host cell. The first disassembly event occurs within the ER which exposes the internal capsid proteins VP2, VP3 to detection by indirect immunofluorescence. Directly following the viral exit from the ER, the second capsid disassembly step takes place in the cytoplasm. The additional capsid modification within the cytoplasm allows for the detection of the viral genome by multiple detection methods. However, the DNA of the viral disassembly intermediates found within the cytoplasm retains a close association with VP2/3 and VP1 until the particles reach the nucleus. Upon reaching the nuclear membrane, the viral genome dissociates from the disassembly intermediate and the DNA enters the nucleus without VP2/3. In conclusion, this research adds to our current understanding of viral infection pathway, the nature of the viral particle during an infection, and finally investigates viral entry into the nucleus.

Recommended Citation