Replication Cycles and Anayses of Viral Factories of Giant Viruses

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With a particle size of ~800 nm and a DNA genome of 1.2M base-pairs, the recently discovered amoeba-infecting virus Mimivirus is the largest virus heretofore identified, blurring the established division between viruses and single-cell organisms. Such unusual parameters raise fundamental questions related to various aspects of the Mimivirus infection cycle. These include the mechanisms that promote entry of the huge Mimivirus genome into host cells and its trafficking within the highly crowded host cytoplasm, virion assembly, membrane biogenesis and genome packaging. Our studies indicate that, in contrast to all other DNA viruses, the Mimivirus releases its genome into the host cytoplasm in a single step that is promoted by a large-scale conformational change of the viral capsid. This process is followed by the assembly of a large and highly elaborate viral factory in the host cytoplasm, within which multiple viral progeny are rapidly generated in a pathway that is independent of the host nucleus. The transactions that occur in the viral factory, including replication, transcription, translation, as well as membrane and capsid assembly are well coordinated in time and space, thus providing an unusual and exciting case study in self-assembly. Moreover, the transactions that lead to the generation of viral factories raise the intriguing notion that such factories might have acted as precursors to eukaryotic nuclei. The implications of these findings on the evolution of viruses and the role viruses might have played in the emergence of eukaryotic cells will be discussed.