INVITED SPEAKER

ALPHAVIRUS NSP1 CAPPING RINGS ARE FUNCTIONAL GATES OF MEMBRANOUS VIRAL FACTORIES

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Positive-sense single-stranded RNA viruses, such as coronaviruses, flaviviruses and alphaviruses, carry out transcription and replication inside virus-induced membranous organelles within host cells. The remodeling of the host-cell membranes for the formation of these organelles is coupled to the membrane association of viral replication complexes and to RNA synthesis. These viral niches allow for the concentration of metabolites and proteins for the synthesis of viral RNA, which prevents the detection of this RNA by the cellular innate immune system. I will present the cryo-electron microscopy structure of non-structural protein 1 (nsP1) of the alphavirus chikungunya virus, which is responsible for RNA capping and membrane binding of the viral replication machinery. The structure shows the enzyme in its active form, assembled in a monotopic membrane-associated dodecameric ring. The structure shows how the complex formation couples the membrane binding, oligomerization and allosteric activation of the capping enzyme. The stoichiometry—with 12 active sites in a single complex—redefines viral replication complexes as RNA synthesis reactors. The ring shape of the complex implies it has a role in controlling access to the viral organelle and ensuring the exit of properly capped viral RNA. Our results provide high-resolution information about the membrane association of the replication machinery of positive-sense single-stranded RNA viruses, and open up avenues for the further characterization of viral replication on cell membranes and the generation of antiviral agents.

Cryo-EM structure of Chikungunya capping pores