Structure of a Lipid-bound Viral Membrane Assembly Protein Reveals a Novel Modality for Interacting with Lipid Bilayer

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Abstract

Cellular membranes are maintained as closed compartments, only broken up transiently during membrane reorganization or lipid transportation. However, open-ended membranes, likely derived from scissions of the endoplasmic reticulum (ER), persist in vaccinia virus-infected cells during the assembly of the viral envelope. A group of viral membrane assembly proteins (VMAPs) were identified as essential for this process. Here, we report the crystal structure of the largest VMAP, named A6, which is a soluble protein with two alpha-helical domains. The larger C-terminal domain forms a unique cage that encloses multiple glycerophospholipids with a lipid bilayer-like configuration. The smaller N-terminal domain does not bind lipid but negatively affects lipid-binding by A6. Mutations of key hydrophobic residues lining the lipid-binding cage disrupt lipid-binding and abolish viral replication. Our results reveal a novel protein modality for interacting with lipid-bilayer and provide the molecular insight on a viral machinery involved in generating and/or stabilizing open-ended membranes.