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A Large Double Stranded DNA Virus Life Cycle Is Strongly Dependent On Rab Proteins

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A Large Double Stranded DNA Virus Life Cycle Is Strongly Dependent On Rab Proteins

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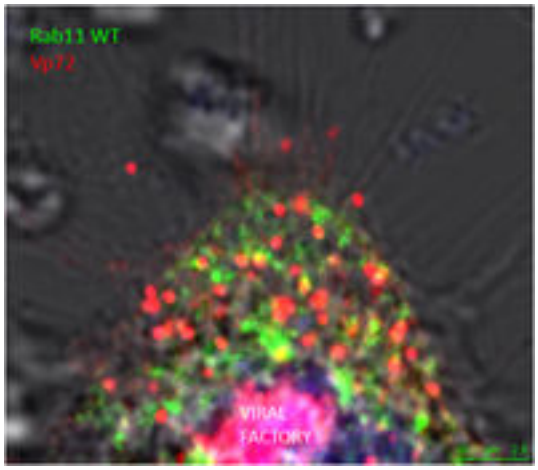
Introduction: Several DNA viruses enter the host cell by endocytosis but it is increasingly evident the crucial role of the endocytic pathway in the viral life cycle as it was found for other intracellular pathogens.

Methods: We used a large double stranded DNA virus as a model, African swine fever virus (ASFV), which enters the cell by a dynamin and clathrin dependent process (1) and depends on endosome acidification for infection. We studied its association with several proteins of the endocytic pathway, especially Rab GTPases 5, 7, their interacting proteins (EEA1) and lysosomal associated proteins (Lamp 1). We monitored these proteins association with virus particles by confocal microscopy throughout infection of Vero cells. Knock out function assays using drugs or dominant negative mutants of some of these proteins were analyzed for their impact on virus infection.

Results: The virus exploits the endocytic machinery for entry and the infection success is dependent on late endosome function. The virus recruited large amounts of Rab7 expressing membranes in the cytosol around the replication site in the centrosome. Multivesicular bodies and lysosomal proteins were involved in the formation of a secluded compartment or viral factory (2), where newly formed virions would assemble.

Discussion: In conclusion, several crucial steps of the ASFV life cycle were shown to be dependent on the endocytic pathway of the host cell. Specific Rab proteins were essential for the incoming virus to enter, be transported, maturate and settle at its replication site. Rab5 and its effectors, may play a role in virion internalization and initial intracellular transport, while Rab7 and lysosomal proteins are important during assemble and virus factory formation. Finally, we found that newly formed virions associate to Rab GTPases which regulate endocytic recycling pathway (Rab11) for virus egress and exocytosis.



Footnote: Vero cell after 24 h of infection with ASFV. Viral protein 72 and viral replication site "viral factory" (red), viral DNA (blue, ToPro) and Rab11WT- GFP (green)

References: (1) Hernáez B. and C Alonso. J Virol 84, 2100-2109, 2010

(2) Hernaez, B., J. M. Escribano, C. Alonso. Virology 350: 1-14, 2006

Keywords: Virus- cell interaction, Endocytic pathway, Recycling pathway, Rab GTPases