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Interactions of human cytomegalovirus with cellular membranes

V Cepeda, A Fraile-Ramos*

Spanish Research Council, Spain

As an enveloped virus, replication of human cytomegalovirus (HCMV), a member of the herpes virus family, is dependent on interaction with cellular membrane systems. HCMV has been shown to complete its final envelopment on cytoplasmic membranes prior to its secretion to the extra-cellular medium. However, the mechanisms underlying these processes are incompletely understood. We have recently reported that HCMV induces significant changes in the intracellular membranes systems and that acquires its final envelope from membranes with characteristics of both the trans-Golgi network (TGN) and endosomes [1]. We are now studying the cellular factors involved in HCMV envelopment and secretion to provide new insights into how HCMV and other herpes viruses undergo membrane envelopment. Interestingly, analysis of cellular gene expression in HCMV infected cells [2 and Vincent Emery, personal communication], showed that HCMV induces the expression of several Rab and SNARE proteins, which are involved in vesicle-mediated transport. Here we study the role of Rab27a, a small GTPase involved in the biogenesis and transport of lysosomes-related organelles (LRO), in HCMV production. Immunofluorescence staining indicated that HCMV induces the recruitment of Rab27a to virus factories - large accumulations of viral components and specific cell organelles in the perinuclear region where virus envelopment takes place. Depletion of Rab27a by short hairpin RNAs (shRNAs) in HCMV-infected cells reduced viral production. Furthermore, mouse cytomegalovirus production was also affected in melanocytes derived from Rab27a deficient mice. This study indicates that CMV and lysosome-related organelles biogenesis might share common molecular mechanisms.

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