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Viruses as pioneers in cell biology – molecular basis of a novel vesicular nucleo-cytoplasmic transport

The study of viruses has unraveled many basic biological features such as gene structure, RNA transcription and modification or signal transduction. In the last decade a novel mode of nucleo-cytoplasmic transport was detected and characterized in herpesviruses. During herpesvirus replication, nucleocapsids assembled in the nucleus have to cross the nuclear envelope (NE) to gain access to the cytosolic final maturation compartment. While nucleo-cytoplasmic transport usually occurs through nuclear pore complexes (NPC), the ca. 120nm capsids are too large to pass through NPC. Thus, herpesviruses use a novel vesicle-mediated nucleo-cytoplasmic transport by budding of nucleocapsids at the inner nuclear membrane thereby obtaining a primary envelope, which then fuses with the outer nuclear membrane to release the capsid into the cytosol. This nuclear egress is mediated by the heterodimeric viral nuclear egress complex (NEC) which alone is sufficient for membrane bending and scission in artificial membrane systems as well as authentic nuclear envelopes. Recently, the crystal structure of the NEC of several herpesviruses has been determined allowing targeted structure-function studies. Our data unravel basic principles of vesiculation from the INM including the formation of two hexagonal lattices composed of multiple copies of the NEC which induce bending of the INM resulting in the formation of vesicles of distinct size capable to accommodate the viral nucleocapsid for transport. Although this herpesvirus-induced vesicular transfer through the NE has been thought unique, it may actually also be used for transport through the NE of other large cellular cargo, e.g. nuclear RNP complexes.

Host: Dirk Görlich



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