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Ultrastructural Analysis of Virion Formation and Intraaxonal Transport of Herpes Simplex Virus Type 1 in Primary Rat Neurons

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The mode of anterograde intraaxonal transport of neuroinvasive alphaherpesviruses is still a subject of debate, and two different models have been developed. Whereas the "subassembly model" assumes separate axonal transport of nucleocapids and envelope precursors, the "married model" entails anterograde transport of complete virus particles within vesicles. High resolution transmission electron microscopy of primary neuronal cultures from embryonic rat superior cervical ganglia infected by the porcine alphaherpesvirus pseudorabies virus (PrV) strongly supported the "married model" (Maresch et al. 2010, J Virol 84:5528-39). We now performed similar analyses with four different strains of herpes simplex virus type 1 (HSV-1). In general, the number of HSV-1 particles in axons was significantly less (ca. 5- to 10-fold) than observed after PrV infection. In neurons infected by HSV-1 strains HFEM, 17+ or SC16, most virus particles observed intraaxonally or in growth cones late after infection constituted enveloped virions within vesicles. These amounted to approx. 75% of virus particles, whereas approx. 25% presented as naked capsids. In neurons infected with HSV-1 strain KOS, which exhibits a defect in the expression of the US9 protein considered to be relevant for anterograde transport, the ratio was reversed with approx. 70% naked nucleocapsids and only approx. 30% enveloped virions within vesicles. In conclusion, our data support the "married model" of anterograde axonal transport also for HSV-1. The different results obtained with HSV-1 strain KOS correlate with the proposed functional relevance of the US9 protein for this specific mode of virus spread.