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Partial functional complementation of a PrV UL25 deletion mutant by pUL25 of HSV-1 parallels binding of either protein to pUL19 and pUL34 of PrV

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Homologs of the UL25 gene product of herpes simplex virus (HSV) have been identified in all three subfamilies of the Herpesviridae. The highly conserved capsid-associated pUL25 is essential for virus replication, but its exact function is still unknown. Although it was originally speculated that pUL25 may be involved in cleavage of newly replicated concatemeric DNA into unit length genomes and/or encapsidation current evidence suggests that it plays a role in triggering primary envelopment of DNA-containing mature capsids at the inner nuclear membrane. To assess whether the high sequence homology corresponds to functional homology, we analysed the ability of HSV-1 pUL25 to complement a pseudorabies virus (PrV) UL25 deletion mutant and vice versa. Whereas a HSV-1 pUL25 expressing cell line partially complemented the lethal defect in a PrV UL25 deletion mutant reciprocal complementation of a HSV-1 UL25 deletion mutant by PrV pUL25 was not observed. In addition, an interaction between PrV pUL25 and the major capsid protein pUL19 which required the presence of the triplex proteins pUL18/pUL38 by glutathione S-transferase (GST) pull-down assay was identified. Moreover, GST pull-down assays showed an interaction between pUL25 and pUL34, a predicted type II membrane protein required for nuclear egress. These results indicate that pUL25 plays a role in capsid egress from the nucleus, by linking DNA-filled mature capsids with the future primary envelope. Correlating with the complementation data HSV-1 pUL25 was also able to bind to PrV pUL19 and pUL34, suggesting that this interaction is conserved among the alphaherpesviruses.

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