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Intracellular localization of the Pseudorabies Virus large tegument protein pUL36

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Homologs of the essential large tegument protein pUL36 of Pseudorabies Virus (PrV) are conserved throughout the Herpesviridae, form a complex with pUL37, and constitute part of the capsid-associated 'inner' tegument. pUL36 is crucial for transport of the incoming capsid to and docking at the nuclear pore as well as for virion maturation in the cytoplasm. Deletion analyses revealed several nonessential regions in PrV pUL36, while the C-terminal 62 amino acids are essential for virus replication. Our previous studies showed that PrV pUL36 enters the nucleus when expressed in isolation, presumably mediated by the N-terminal nuclear localization signals (NLS). Substitution of the NLS1 or only of a single amino acid in the motif abrogated nuclear localization of transiently expressed pUL36, and pUL36 function in virus replication. In contrast, during PrV infection pUL36 is not detectable in the nucleus and absent from primary enveloped virions in the perinuclear cleft suggesting that pUL36 is retained in the cytoplasm by interaction with other viral proteins. To identify possible interaction partners which may interfere with nuclear localization of pUL36, immunofluorescence studies after transient cotransfection of PrV pUL36 with pUL19, pUL25, pUL37 and pUL48 and after infection with respective mutant viruses were performed. Random transposon-mediated mutagenesis delineated further functional domains in pUL36 including a centrally located region essential for pUL36 function.