Virus Receptors and Entry

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Structure-based function analyses of pseudorabies virus glycoprotein H

S. Böhm[1], M. Backovic[2], E. Eckroth[1], W. Fuchs[1], B. G. Klupp[1], F. A. Rey[2], T. C. Mettenleiter[1]

[1]Friedrich-Loeffler-Institut, Molecular Biology, Greifswald, Insel Riems, Germany
[2]Institut Pasteur, Unité de Virologie Structurale, Paris, France

Membrane fusions are crucial events in pro- and eukaryotic organisms, e.g. during cell division, autophagy, endo- and exocytosis. Viruses also utilize fusion for entry into and release from host cells. In herpesviruses three conserved envelope glycoproteins are essential for penetration, cell-to-cell spread and induction of syncytia: the core fusion protein gB, and a heterodimer formed by gH and gL. Recently crystal structures of three gH homologues including the pseudorabies virus (PrV) protein have been uncovered, which revealed four highly conserved domains. The N-terminal domain I is required for gL-binding, whereas domain IV which includes a flap region covering a hydrophobic patch, is relevant for fusion activity. Domain II contains a planar β-sheet (fence), and a syntaxin-like bundle of α-helices (SLB), similar to those found in eukaryotic fusion proteins. These structures of PrV gH were altered by targeted mutations leading to helix disruption, or prevention of structural changes during fusion by introduction of cysteine pairs within or between fence, SLB, and domain III. Processing and transport of mutated gH was tested by Western blot and immunofluorescence analyses. Fusion assays in cells cotransfected with expression plasmids for PrV glycoproteins, and replication studies of PrV mutants are currently performed to determine the effects of the introduced mutations on gH function.

Corresponding author:
Sebastian Böhm
sebastian.boehm@fli.bund.de