Host cell factors

HCF 4
The Mechanism of Herpes Simplex Virus 1 Entry into Different Cell Types

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HSV1 enters some cells by fusion of its envelope with the plasma membrane, whereas others are productively infected by endocytosis or phagocytosis. We compared the HSV1 entry into PtK2 cells, which we utilize for live cell imaging, with Vero and HeLa cells, which are models for entry via fusion at the plasma membrane and endocytosis, respectively. In Vero, PtK2 and HeLa cells, bafilomycin, which inhibits endosomal acidification, did neither reduce immediate-early viral gene expression nor nuclear capsid targeting. Class III phosphoinositide 3-kinases (PI3K) are involved in endosomal trafficking. The PI3K inhibitor wortmannin moderately inhibited nuclear targeting in HeLa cells, but had no effect in Vero or PtK2 cells. In all three cell lines, viral gene expression was not reduced. Electron microscopy of HSV1 infected PtK2 and HeLa cells at early time points showed viral fusion intermediates at the plasma membrane, and virions in vacuoles or invaginations. In contrast, Vero cells were mostly entered by fusion at the plasma membrane. PtK2 and HeLa cells additionally showed virions surrounded by plasma membrane extensions reminiscent of macropinocytosis or phagocytosis. Our electron microscopy results indicated that both, fusion at the plasma membrane and endocytosis may contribute to HSV1 cell entry into PtK2 and HeLa cells, while Vero cells were mostly entered by fusion at the plasma membrane. Since endosomal acidification and PI3K activity were not required for viral gene expression, fusion at the plasma membrane more likely leads to productive infection of PtK2 and HeLa cells.

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Host cell factors

HCF 5
Influenza Virus Polymerase Complex Plays a Crucial Role in Enhanced Tissue Tropism and Lymphocyte Depletion in Mice

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Previously, we have shown that adaptation of the highly pathogenic avian influenza virus (HPAIV) SC35 (H7N7) to mice is mediated by 7 mutations in the polymerase subunits and in the nucleoprotein.

Here, we have compared the pathology caused by infection with SC35 and its mouse-adapted variant SC35M (H7N7) in mice. The HPAIV SC35 causes a mild bronchiolitis resulting in low pathogenicity in mice. On the other hand, the highly mouse-pathogenic SC35M leads to severe hemorrhagic pneumonia accompanied by neurotropism. Further, mice infected with SC35M present high virus titers in their blood suggesting systemic infection while no virus could be detected in the blood of SC35 infected animals.

Comparison of the immune response upon low and high pathogenic infection revealed that SC35M causes severe lymphocyte depletion in mice. Furthermore, mice infected with SC35M mount a T-cell response while SC35M infected animals fail to induce an adequate T-cell response. Taken together, these data suggest that influenza virus polymerase plays a crucial role in enhanced tissue tropism and lymphocyte depletion in mice.

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