

Department of Microbiology and Immunology

Division of Molecular Virology

ウイルス病態制御分野

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In our laboratory, we are promoting strategic fundamental research aimed at developing a novel method of viral infection control by elucidating the mechanism underlying viral proliferation/pathology. Moreover, using viruses as a biological probe, we are also challenging next-generation virology to reconsider viruses as a homeostasis factor and explore their significance, in addition to unraveling cells and physiological control mechanisms that cannot be elucidated by research on normal human hosts.

1. Dual impacts of a glycan shield on the envelope glycoprotein B of HSV-1: evasion from human antibodies in vivo and neurovirulence

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Identification of the mechanisms of viral evasion from human antibodies is crucial both for understanding viral pathogenesis and for designing effective vaccines. Here we show in cell cultures that an N-glycan shield on the herpes simplex virus 1 (HSV-1) envelope glycoprotein B (gB) mediated evasion from neutralization and antibody-dependent cellular cytotoxicity due to pooled γ -globulins derived from human blood. We also demonstrated that the presence of human γ -globulins in mice and immunity to HSV-1 induced by viral infection in mice significantly

reduced replication in their eyes of a mutant virus lacking the glycosylation site but had little effect on the replication of its repaired virus. These results suggest that an N-glycan shield on a specific site of HSV-1 envelope gB mediated evasion from human antibodies in vivo and from HSV-1 immunity induced by viral infection in vivo. Notably, we also found that an N-glycan shield on a specific site of HSV-1 gB was significant for HSV-1 neurovirulence and replication in the central nervous system of naïve mice. Thus, we have identified a critical N-glycan shield on HSV-1 gB that has dual impacts, namely evasion from human antibodies in vivo and viral neurovirulence.

2. Establishment of a system to quantify wild-type herpes simplex virus-induced cell-cell fusion reveals a role of N-glycosylation of HSV-1 envelope glycoprotein B in cell-cell fusion

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Wild-type herpes simplex virus (HSV) strains infrequently mediate cell-cell fusion in cell cultures and barely induce large multinucleated cells. In this study, we established a system to quantify infrequent cell-

cell fusion induced by wild-type HSV strains. The established system clarified that the HSV-1 envelope glycoprotein B and its N-glycosylation at asparagine at position 141 were required for efficient cell-cell fu-

sion. This study provides a link between cell-cell fusion induced by wild-type HSV-1 and viral pathogenesis in vivo.

Publications

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