International Research Center for Infectious Diseases

Department of Infectious Disease Control
感染制御系

Professor	Yasushi Kawaguchi, D.V.M., Ph.D.	教　授	博士(獣医学)	川　口　　寧
Associate Professor	Akihisa Kato, Ph.D.	准教授	博士(医学)	加　藤　哲　久
Assistant Professor	Naoto Koyanagi, Ph.D.	助　教	博士(生命科学)	小　柳　直　人
Assistant Professor	Yuhei Maruzuru, Ph.D.	助　教	博士(生命科学)	丸　鶴　雄　平

Our special interest is focused upon searching for effective methods to protect or control viral infection by using accumulated knowledge based on molecular pathogenicity, and developing novel anti-viral drugs and attenuated strains for novel vaccines. The works have been conducted by close collaboration with Division of Molecular Virology, Department of Microbiology and Immunology.

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

Ayano Fukui, Yuhei Maruzuru, Shiho Ohno[1], Moeka Nobe, Shuji Iwata, Kosuke Takeshima, Naoto Koyanagi, Akihisa Kato, Shinobu Kitazume[2], Yoshiki Yamaguchi[1], Yasushi Kawaguchi: [1]Division of Structural Glycobiology, Institute of Molecular Biomembrane and Glycobiology, Tohoku Medical and Pharmaceutical University, Miyagi [2]Department of Clinical Laboratory Sciences, School of Health Sciences, Fukushima Medical University, Fukushima

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

Ayano Fukui, Yuhei Maruzuru, Kosuke Takeshima, Naoto Koyanagi, Akihisa Kato, Yasushi Kawaguchi

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 fusion. 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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