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Sulfatide Is Required for Efficient Replication of Influenza A Virus

TADANOBU TAKAHASHI, KOUKI MURAKAMI, MOMOE NAGAKURA, HIDEYUKI KISHITA, SHINYA WATANABE, KAZUYA I. P. J. HIDARI, and TAKASHI SUZUKI,

Department of Biochemistry, Graduate School of Pharmaceutical Sciences

Sulfatide is abundantly expressed in various mammalian organs, including the intestine and trachea, in which influenza A viruses (IAVs) replicate. However, the function of sulfatide in IAV infection remains unknown. Sulfatide is synthesized by two transferases, ceramide galactosyltransferase (CGT) and cerebroside sulfotransferase (CST), and is degraded by arylsulfatase A (ASA).

In this study, we demonstrated that sulfatide enhanced IAV replication through efficient translocation of the newly synthesized IAV nucleoprotein (NP) from the nucleus to the cytoplasm, by using genetically produced cells in which sulfatide expression was down-regulated by RNA interference against CST mRNA or overexpression of ASA gene and in which sulfatide expression was up-regulated by overexpression of both CST and CGT genes. Treatment of IAV-infected cells with an anti-sulfatide monoclonal antibody (MAb) or an anti-hemagglutinin (HA) MAb, which blocks the binding of IAV and sulfatide, resulted in significant reduction in IAV replication and accumulation of the viral NP in the nucleus. Furthermore, anti-sulfatide MAb protected mice against lethal challenge with pathogenic influenza A/WSN/33 (H1N1) virus.

These results indicate that association of sulfatide with HA delivered to the cell surface induces translocation of the newly synthesized IAV ribonucleoprotein complexes from the nucleus to cytoplasm. Our findings provide new insights into IAV replication, and suggest new therapeutic strategies.

References

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