Aberrant cellular glycosylation may allow influenza virus to escape host immune responses

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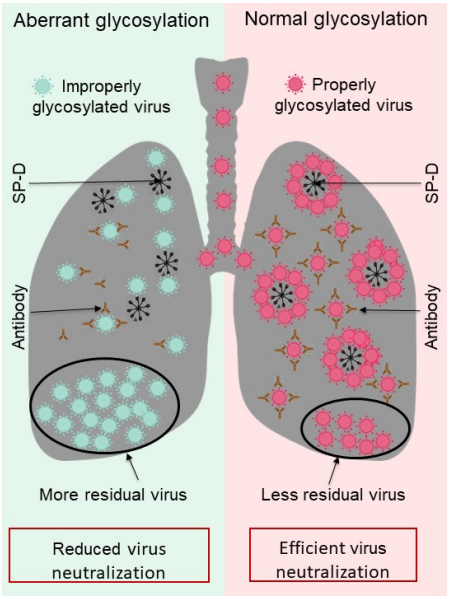
People with cancer, autoimmune disease, diabetes, or obesity often have metabolic dysregulation of cellular glycosylation, and also have tend to more severe influenza virus (IV) disease, with a poor immune response to the virus and low vaccine efficacy [1]. Host cells are responsible for glycosylation of the IV surface proteins, hemagglutinin (HA) and neuraminidase (NA), and glycosylation is important for interactions of these proteins with the immune system. To investigate the consequences of aberrant cellular glycosylation for the glycome, biology, and immune responses to IV, we moderately reduced N-linked glycosylation (NLG) in cultured cells with an oligosaccharyltransferase inhibitor, NGI-1. Treatment of cells with NGI-1 resulted in replication-competent virus with reduced NLG site occupancy of HA and NA. As with IV isolated from people with metabolic disorders, IV with an altered glycome did not show variations in genome and was able to efficiently infect cells that had normal glycosylation. However, glycome-altered IV required higher concentrations of the respiratory tract innate immune collectin surfactant protein D for virus neutralization than virus with normal glycan occupancy. It also generated lower total and protective antibody responses in mice than did IV with normal glycosylation. Thus, imbalanced cellular glycosylation can lead to sequence-neutral changes in the IV glycome, and these glycome-modified viruses may be less well recognized by the host innate and adaptive immune system resulting in more severe influenza disease and reduced IV vaccine efficacy.



Graphical abstract

Bibliographic references:

1. Mertz, D., Kim, T.H., Johnstone, J., Lam, P.P., Science, M., Kuster, S.P., Fadel, S.A., Tran, D., Fernandez, E., Bhatnagar, N., et al. (2013), BMJ (347), f5061.