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Glycomics characterization of influenza hemagglutinin glycoprotein antigens

Influenza hemagglutinin (HA) recognizes host cell surface sialyl N-glycans to facilitate virus invasion of the host cell. It is also the major antigen present in seasonal influenza vaccine. HA glycosylation can impact the host immune response in several ways including: 1) Alteration of its receptor site specificity; 2) masking antigenic sites and; 3) impacting interactions with the lectin based host innate immune system elements, thus, influencing the response. In the vaccine context, HA glycosylation can vary with the cell substrate used to generate virus or subunit protein for vaccine production. Differences in glycosylation can impact vaccine efficacy and safety. To investigate glycosylation dependent structure-function relationships, we have developed a glycomics workflow, which includes: 1) Analysis of released and permethylated-glycans; 2) glycopeptide analysis by nano-LC/MSE; 3) percent site occupancy determination and 4) molecular modeling of glycosylation at the HA surface to investigate interactions with antigenic sites and with host lectin based immune factors. We have also developed in-house glycoinformatics tools to aid in our analyses. This work-flow will be discussed as well as our major findings regarding structure function relationship involving HA glycosylation in H3N2, H1N1 and H1N7 derived HA glycoproteins. Specific examples will describe how: Increasing the number of N-glycosylation sites impact interaction with lung surfactant SP-D; changes in glycan subclass effect interactions with DC-SIGN; differences in HA peptide structure may alter N-glycan subclass and therefore interaction with host immune response.

Biography

John F Cipollo completed his PhD work at the State University of New York at Albany. He performed Post-doctoral studies at Boston University School of Medicine where he was the first to report the glycome of the model organism *Caenorhabditis elegans*, discovered phosphorylcholinyl oligosaccharides and demonstrated their synthesis in this organism. These compounds are host immune response modulators in parasitic nematodes. He was a Professor of Biochemistry at Boston University until recruited in 2007 to Center for Biologics Evaluation and Research at the US Food and Drug Administration where he has made meaningful contributions to the understanding of vaccine antigen glycosylation. He has published over 30 papers in reputed journals. He has also written guidance documents for the World Health Organization and United States Pharmacopeial Convention.

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