Structure and Dynamics of Glycans on a Viral Protein

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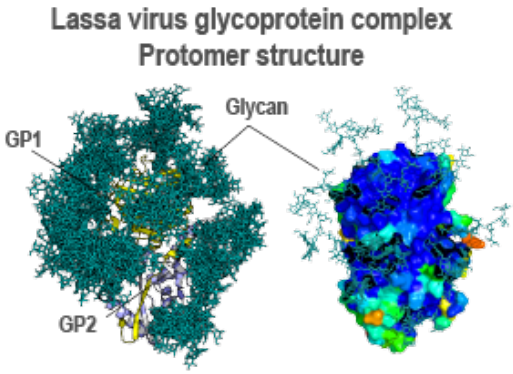
Glycosylation of proteins is one of essential biomolecular processes. It adds extra functions or modulates existing functions of proteins, affecting a range of cellular processes and diseases. Recent findings on the SARS-CoV-2 spike protein[1] emphasize that the glycans on a viral envelope protein can facilitate infection by either interfering with the antibody response or aiding interaction with host cell proteins. However, the investigation of functional roles of such glycans is hampered by the huge range of structures and interactions of glycans through their inherent complexity and flexibility, leaving their functional roles at the molecular level largely unknown.

Molecular dynamics (MD) simulations serve as a powerful tool to overcome this situation. The structure ensembles from the simulation can be used to characterize structures/motions of flexible biomolecules relevant to the function of glycans, which are difficult to obtain from experiments. Here, we built an atomistic model of a fully glycosylated envelope protein complex of the Lassa virus, which is small in size but has dense surface glycosylation. We performed MD simulations to characterize the variety of conformations and interactions of surface glycans. The results show that glycosylation non-uniformly shields the surface of the complex, and only marginally affects protein dynamics. The glycans gather in distinct clusters through interaction with protein residues, and only a few regions are left accessible by an antibody. We further successfully predicted the amino acid residues accessible to antibodies by integrating the simulation results with existing sequence- and structure-based epitope prediction methods. This work provides a molecular basis for integrating otherwise elusive structural properties of glycans into vaccine and neutralizing antibody developments.[2]



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