Protein Flexibility and Glycan Dynamics of the SARS-CoV-2 Spike

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Spike protein is crucial for SARS-CoV-2 entry into human cells and it is the main target of natural and induced immune response. Spike surface is covered with covalently attached complex sugars (glycans) which prevent antibody binding and complicate pharmacological interventions. Viral evolution leads to new variants, such as Omicron, that evade current vaccines. To understand the role of protein and glycan dynamics in these processes, we performed large-scale molecular dynamics simulations of glycosylated spikes. In collaboration with structural biology groups, we discovered surprising flexibility of the spike protein and predicted new antibody binding sites accessible through the dynamic glycan shield, which can be used for designing novel vaccines. We further show that majority of mutations in variants of concern occur within these accessible sites. Finally, we develop a simplified open-source method to rapidly predict glycan shielding with minimal computing power.