Targeting viral glycans by synthetic carbohydrate receptors to stop viral infections – insights from MD simulations

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Abstract

The rapid emergence of viral diseases, such as the SARS-CoV-2 pandemic in 2020, Zika virus in 2016, and MERS-CoV in 2012, highlights the medical community's lack of a broad mechanism to mitigate the detrimental health effects of a wide range of viral threats and the urgent need for broad-spectrum antiviral (BSAs) strategies. One challenge present in developing BSAs is the absence of ubiquitous targets across viral families that could be exploited to design an effective drug.

Recently, glycans, which are common to the surfaces of enveloped viruses (EnV), have received increased attention as a potential target for BSAs. Viral glycans are known to shield potential antigens from the host and facilitate host-virus interactions. Disabling these properties allows for the potential of a development of new therapeutic strategies. In this work, we apply molecular dynamics (MD) simulations to investigate the binding of several synthetic carbohydrate receptors (SCRs), which showed antiviral activity against ZIKV in cell assays, towards biologically relevant carbohydrates. Our findings compare binding of SCRs towards glycans present on the Receptor Binding Domain (RBD) of SARS-CoV-2 spike protein using Saturation Transfer Difference NMR, displaying the chemical shift and intensity of specific binding interactions. We hypothesize that the SCRs interact with *N*-glycans on the surface of EnV, which leads to the inhibitions of the viral docking to a host cell.