# Investigation of Sialic Acid Association Kinetics to H274Y Neuraminidase Using Molecular Dynamic Simulations

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Influenza is an extremely common and contagious respiratory illness that has the potential for epidemic and pandemic outbreaks. The major drug target for most influenza antivirals is neuraminidase, a homotetrameric viral capsid surface protein. The role of neuraminidase is to recognize and cleave terminal sialic acid moieties from cell surface receptors, allowing for nascent virus release. The purpose of our research is to understand how a mutant neuraminidase, H274Y, displays resistance to oseltamivir, currently one of the most-prescribed antivirals, but still binds to its natural substrate sialic acid even though the two molecules are very similar. To better understand H274Y ligand binding we investigated the pathways of sialic acid-protein complexation using multi-scale simulation methods. First, Brownian Dynamics (BD) was used to collect clusters representing the ligands' diffusional approach to neuraminidase, which allowed for the use of Molecular Dynamics (MD) to get detailed frame-by-frame trajectories as sialic acid approached the active and secondary binding sites. Data obtained from the MD simulations were analyzed using Molecular Mechanics/Generalized Born Surface Area (MM/GBSA) free energy calculations to highlight the favorable pathways and binding sites of the ligand.

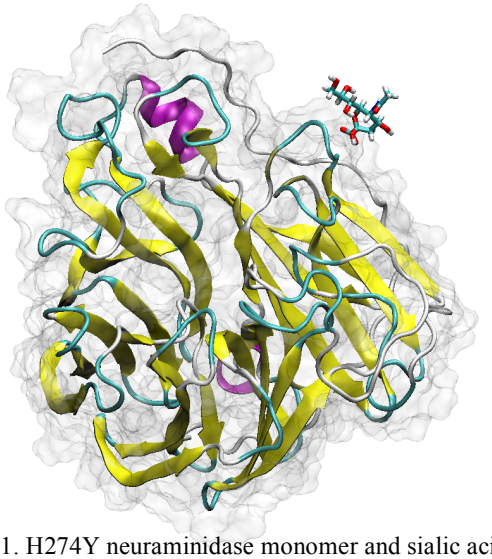

Figure 1. H274Y neuraminidase monomer and sialic acid