Investigating the Binding pathway of Peramivir to Neuraminidase Through Molecular Dynamics Simulations and MM/GBSA Analysis

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Influenza is a common viral infection that attacks the respiratory system. Neuraminidase (NA) is a viral capsid enzyme that facilitates proliferation of the virus by cleaving sialic acid moieties found on host cell surface receptors. Oseltamivir (Tamiflu) has been used as an antiviral treatment because of its ability to inhibit NA activity. However, with the increased usage of oseltamivir, resistant strains of influenza have emerged. Peramivir (PER) is also a NA competitive inhibitor and has been demonstrated to be an effective agent against the influenza virus. To fully understand how PER interacts with NA, we simulated its full binding trajectory using a multi-scale computational approach. Brownian dynamics (BD) was first used to analyze the diffusional movement of PER towards the NA. After taking some representative clusters from the BD simulation, molecular dynamics was used to simulate PER's close range interaction with NA. Molecular mechanics/generalized Born surface area (MM/GBSA) free energy calculations were used to identify the specific favorable binding pathways.

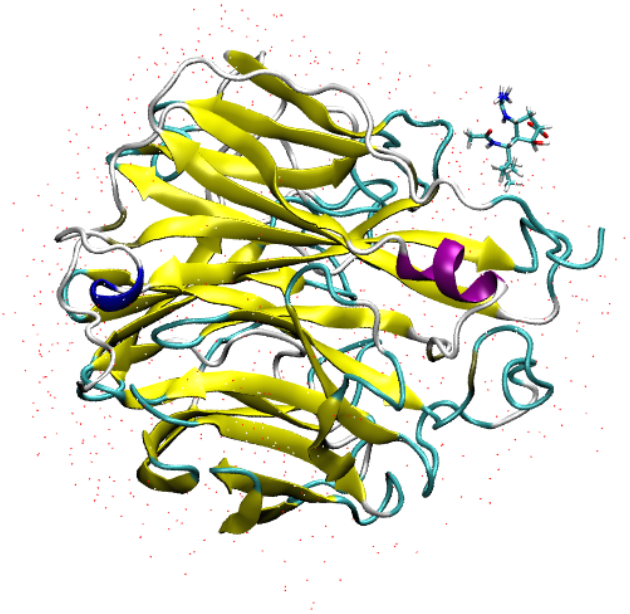

Figure 1. Neuraminidase monomer with peramivir ligand