Combined 3D-QSAR, Molecular Docking, and Molecular Dynamics Study to Identify Strong Inhibitors of *Trypanosoma cruzi* trans-sialidase

Trypanosoma cruzi is the protozoan responsible for Chagas' disease, a lethal disease that affects millions of people in Central and South America and is considered one of the fourteen neglected tropical diseases by the World Health Organization. *T. cruzi*'s trans-sialidase (TcTS), an enzyme vital to the life cycle of *T. cruzi*, catalyzes the transfer of sialic acids from mammalian host cells to parasitic cell surfaces in order to mask the infection from the host's immune system. Currently, there are no known strong inhibitors of TcTS. Schrodinger's Phase program is used to create three-dimensional quantitative structure—activity relationships (3D-QSAR) built using fragment compounds docked to TcTS using Schrodinger's Glide. The 3D-QSAR results create a pharmacophore hypothesis used to identify ideal ligand properties in potential inhibitors for binding to TcTS. Furthermore; the results suggest regions of the active site not previously targeted by researchers for drug design. Virtual screening for novel potential inhibitors will be performed using Glide SP while utilizing the pharmacophore model generated by Phase. Molecular dynamics combined with free energy calculations examine the dynamic interactions of the best screened drug candidates with TcTS and rank them more accurately in order to successfully identify strong potential inhibitors of this enzyme. The best potential *in silico* inhibitors will be obtained and assayed to determine their ability to prevent catalytic activity of TcTS *in vitro*.