# Structure-based design and optimization of ligands for novel antiviral strategies

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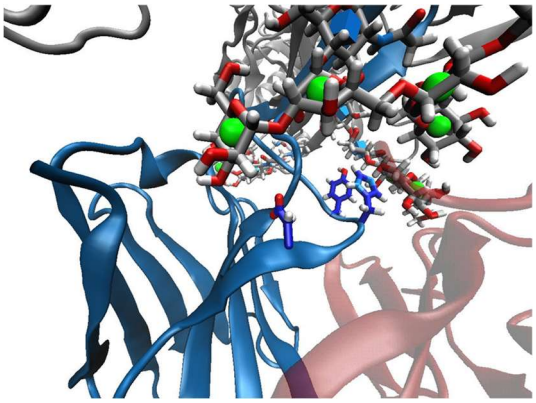
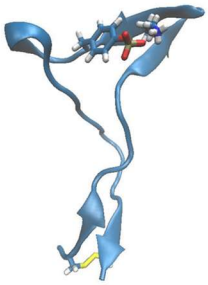
Broadly neutralizing antibodies that bind to viral fusion proteins represent a promising strategy for protection from viral infections. Such antibodies can be used for passive immunization and are currently tested in clinical trials, but they are expensive and difficult to produce. As an alternative, antibody-derived peptides may be used for this purpose. Suitable antibody sequences were identified using a newly developed computational pipeline that identifies interfaces in complexes of antibodies and viral fusion proteins. Application of this pipeline to 2050 interfaces of HIV-1 antibody-antigen complexes lead to several promising candidate peptides, which were investigated by molecular dynamics (MD) simulations.





The first peptides investigated by this MD-based optimization approach are from a sulfo-tyrosine containing broadly neutralizing antibody PG16. Optimization of the peptide length is based on the energetic analysis of the complex interface, which particularly focuses on the roles of glycans in the interaction. In addition, the effect of peptide cyclisation was assessed from microsecond MD-simulations of the free peptides. This approach resulted in a high-affinity peptide ligand that was experimentally demonstrated to exhibit a nanomolar affinity for the HIV-1 gp120 protein.