

Role of Gp120 Glycosylation in Sexual Transmission of HIV

Background:

In chronic HIV patients, the viral populations are genetically diverse due to mutations introduced by the viral reverse transcriptase during HIV replication. However, more than 80% new infections result from single transmission founder (TF) viruses; therefore, targeting the TFs is key to control AIDS worldwide.

Gp120 is a glycosylated envelope protein required for HIV infection, propagation, and transmission. Glycans on gp120 influence HIV infectivity through their interactions with lectins, the carbohydrate-binding immune proteins in the host mucosa. To transmit sexually, viruses must overcome the lectin traps to access more target T cells.

Hypothesis:

TF viruses are less likely to be trapped by host lectins due to their reduced gp120 glycosylation, thus more infectious.

Methods:

We aim to characterize and compare the gp120 glycosylation signatures in TF and chronic HIV strains, B4 and Q0 respectively, using mass spectrometry (MS), surface plasmon resonance (SPR), and capillary electrophoresis (CE).

To date, we have established a work flow to purify gp120 glycoproteins, perform MS using ETHcD methods, and analyze raw MS data using the GlycoPAT software. We are currently analyzing MS data for three replicates of B4 and the first replicate of Q0. Then we will compare the glycosylation patterns between the two strains. CE and SPR will be performed to test the glycan enrichment and functional interactions between gp120 and lectins, respectively.

Discussion:

Our results will provide qualitative and quantitative details about gp120 glycosylation underlying the strong infectivity of TF viruses, shedding light on new strategies to develop HIV vaccines.