N-Glycosylation Site Signatures in HIV Envelope of Post-Treatment Controllers

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Elmira Esmaeilzadeh[1], Behzad Etemad[1], Yijia Li[1], Christy Lavine[2], James Regan[1], Colline Wong[1], Elizabeth Connick[3], Paul Volberding[4], Michael Seaman[2], Jonathan Z. Li[1]

[1] Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA, [2] Beth Israel Deaconess Medical Center, Boston, MA, USA, [3] University of Arizona, Tucson, AZ, USA, [4] University of California, San Francisco, San Francisco, CA, USA

- **Post-treatment controllers have distinct patterns of envelope N-glycosylation when compared to non-controllers.**
- **This suggests the presence of distinct humoral immune responses in the setting of HIV remission.**

BACKGROUND

- HIV post-treatment controllers (PTCs) are individuals who can maintain viremia at low levels during treatment interruption.
- Viral evolution is frequently modulated by host immune pressures and comparing viral sequence changes in PTCs and post-treatment non-controllers (NCs) may provide insight on mechanisms behind HIV remission.
- N-glycosylation sites in HIV *env* play a critical role in viral evolution and immune escape against humoral immune responses.
- The link between the N-glycosylation and post-treatment control has not yet been established.

METHODS

- We performed single genome sequencing (SGS) PCR of *env* from plasma of 6 PTCs and 6 NCs for pre-ART, early (≤24 weeks), and late (>24 weeks) post-analytic treatment interruption (ATI) time points.
- N-glycosylated site dynamics were assessed at different time points using the GenSig tool of Los Alamos HIV sequence database.
- The R package "DESeq2" was used to evaluate differential N-glycosylation sites between PTCs and NCs groups in a comprehensive way and generalized estimating equation (GEE) to calculate between-group differences between PTCs and NCs at each time point.

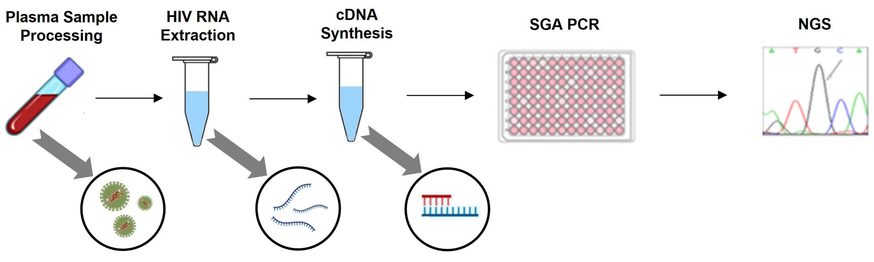


Figure 1- Heatmap of distinct glycosylated amino acids between PTCs and NCs

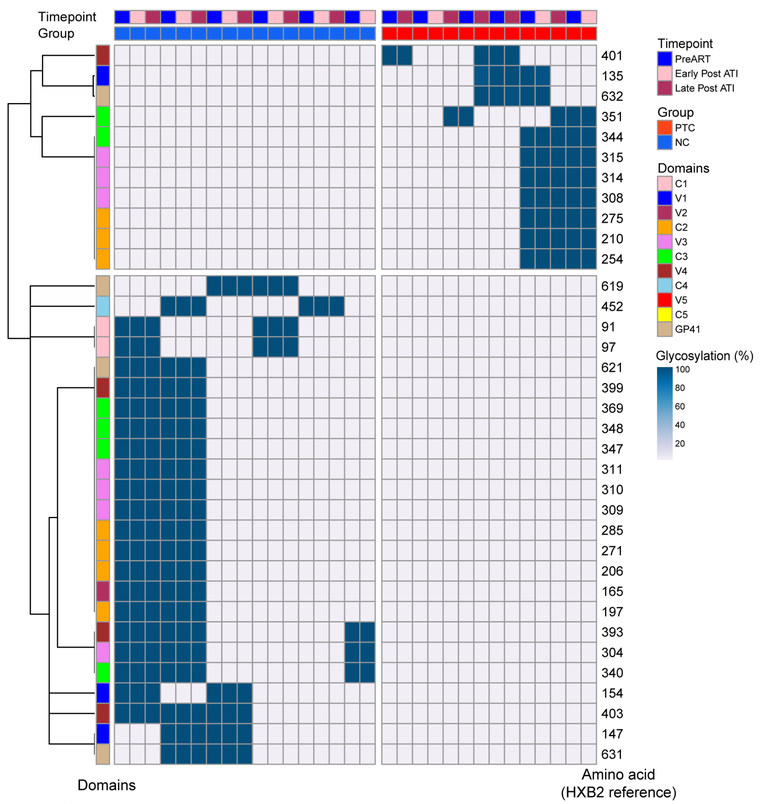


Figure 2- A principal component analysis glycosylated amino acids between PTCs and NCs

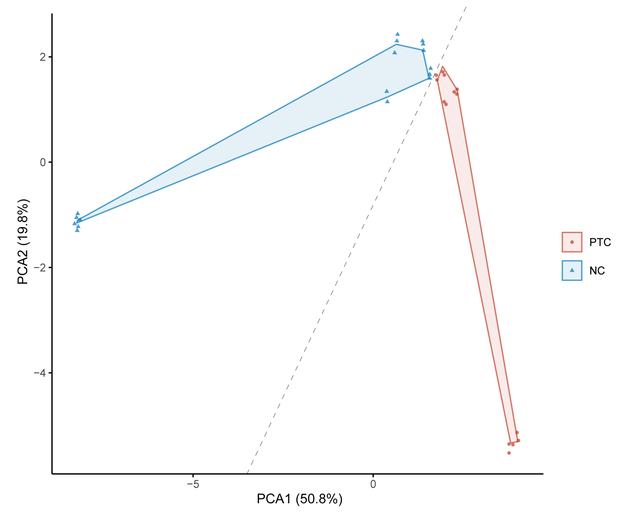
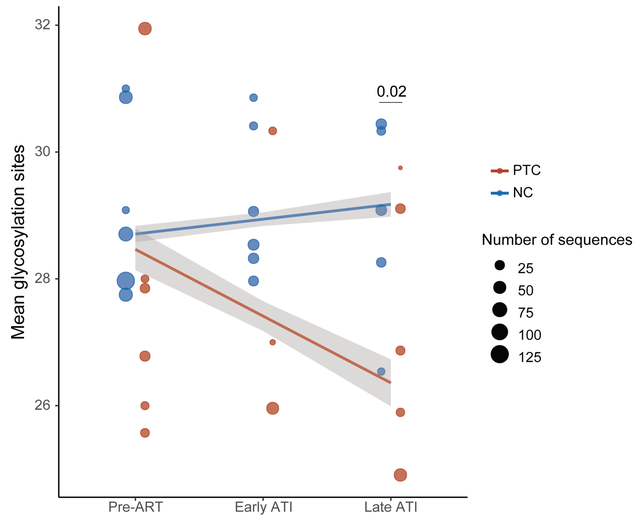


Figure 3-Number of N-glycosylation sites in PTCs vs NCs



RESULTS

- The median early and late post-ATI viral loads in PTCs were 174 and 153 copies/ml, respectively and 4383 and 5662 copies/ml for the NCs.
- There is a dynamic change in the pattern of N-glycosylated sites in HIV *env* between viruses over time in both PTCs and NCs. These changes were densely located in the gp120 domain of HIV *env,* specifically in V1 and V4 (median 32 for V1 and 26 for V4, P <0.01).
- PTCs and NCs demonstrated distinct sets of N-glycosylation sites (Figure 1, 2).
- There were differing trends in N-glycosylation site numbers between groups with N-glycosylation sites decreasing in PTCs and remaining stable in NCs. Late post-ATI, NCs had significantly higher number of N-glycosylation sites in *env* than PTCs (P=0.02, Figure 3).

CONCLUSIONS

- There are distinct patterns and dynamic changes in N-glycosylation sites between post-treatment controllers and non-controllers.
- Distinct humoral immune responses may be present in the setting of HIV remission.

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