PHYLOGENETICS AND HIV TRANSMISSION
P-Q10

ASSOCIATIONS BETWEEN PHYLOGENETIC TRANSMISSION CLUSTERS AND HLA PROFILES IN MEXICO

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Background

- Class I Human leukocyte antigen (HLA-I) is a major driver of HIV evolution, both at the individual and population level, promoting HIV adaptation to cellular immune responses.
- The extent to which HIV adaptation to HLA-I plays a role in transmission is not well understood.

Objective

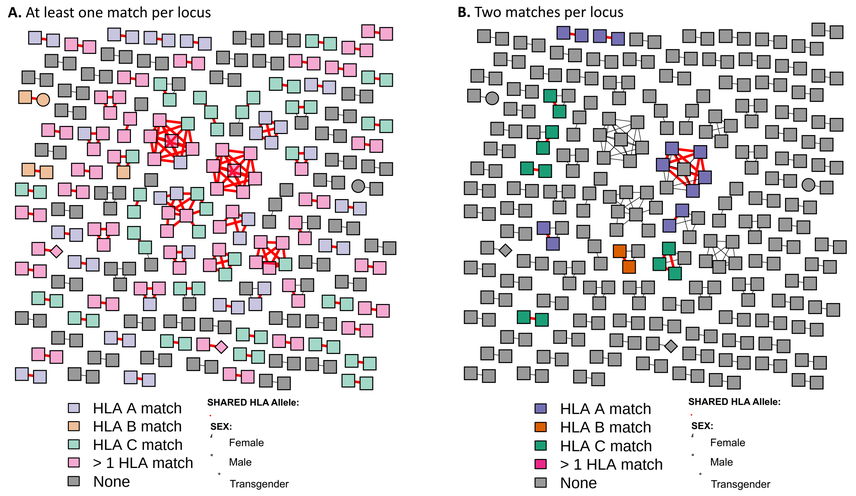
Determine the associations between HLA-I profiles and HIV transmission in the Mexico City HIV epidemic.

Methods

- **Study participants**. 1,049 HIV-1 subtype B *pol* sequences sampled between 2016 and 2018 from unique, HLA-I-typed persons with HIV (PWH) in Mexico City were analyzed. Participants were enrolled at the largest HIV care provider in Mexico City, the Condesa Clinic, with more than 14,000 active clients. All persons recently diagnosed with HIV were invited to participate in the study and donated a single blood sample after written informed consent.
- **HIV transmission network analyses.** Genetic distance-based network analyses were performed to infer putative relationships between HIV-1 partial pol sequences. We used HIV-TRACE software (HIV TRAnsmission Cluster Engine: www.hivtrace.org) to infer transmission links between sequences with a genetic distance ≤1.5%.
- **HLA profiling.** High-resolution HLA profiles were determined by next-generation sequencing, using a commercial kit (TruSight HLA; Illumina). HLA profiles were analyzed with Assign software (Illumina). HLA P groups were defined as HLA amino acid sequences having the same antigen binding domains based on exons 2 and 3 (hla.alleles.org).
- **Analyses.** Newman's assortativity coefficients for HLA-I molecules were estimated using igraph. Fisher's exact tests were used to determine whether there was enrichment of specific HLA alleles in the clustering vs. the non-clustering population. P-groups, known to bind similar peptides, were used for HLA-match analyses.

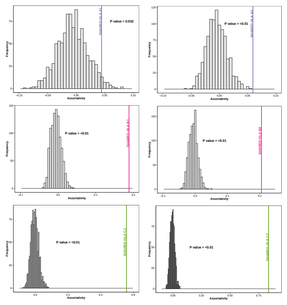
Results

Figure 1. Evidence of shared HLA profiles between individuals with genetically linked HIV.



All edges represent a genetic distance of ≤1.5%. Lines in bold red indicate individuals who shared any HLA-I P group. **A.** Nodes are colored according to locus of shared HLA alleles in persons with at least one match. **B.** Individuals with two HLA P group matches per locus A, B, or C are shown. >1 HLA match refers to matches at 2 different loci.

Figure 2. The network was assortative by all HLA-I loci.

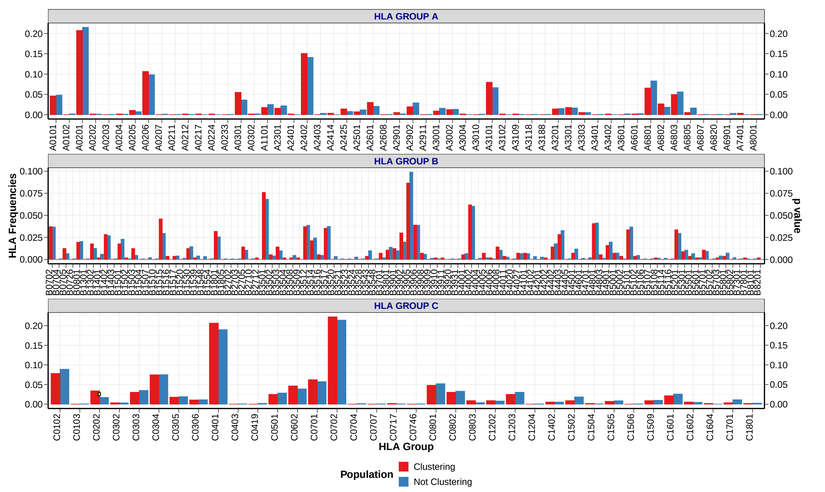


- 286/1,049 (27%) PWH were genetically linked with at least one other person, forming 120 clusters (size range: 2-8 PWH). All but 4 clustering PWH were male (2 female, 2 transgender). Clustering and non-clustering PWH did not differ by age, baseline CD4 or HIV RNA level.
- Overall, 65% (186/286) of clustering PWH shared at least one HLA-I P group in any of the three loci (Fig. 1A), and 26 had fully concordant (i.e. two matching alleles) HLA-A (13; 4.5%), HLA-B (2; 0.7%) or HLA-C (11; 3.8%) loci (Fig.1B).

Newman's assortativity coefficients for HLA loci were estimated using the R package igraph. Null distributions were obtained with the R sample function with 1000 iterations.

- The network was assortative by HLA-A, HLA-B, and HLA-C (Fig. 2).
- When comparing clustering and non-clustering PWH, we found enrichment of HLA-C*02:02 in the clustering population (p=0.02) (Fig. 3).
- Rates of HLA-I allelic concordance among clustering individuals were significantly higher than those expected by chance at all three loci (p<0.01).

Figure 3. HLA-C*02:02 was enriched in individuals in clusters.



Frequency of HLA alleles in clustering and non-clustering persons. Enrichment of HLA alleles in clustering vs. non-clustering individuals was assessed with Fisher's exact tests.

Conclusions

- HLA-I haplotypes were significantly more concordant than expected among clustering PWH in Mexico City.
- These findings suggest that viral adaptions may enhance transmissibility.
- Further work is needed to determine if this increased concordance is due to viral factors (i.e. adaptation) or sociodemographic factors (i.e. ancestry, racial assortativity).

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