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PHYLOGEOGRAPHIC ANALYSIS SUGGESTS GRAVITY MODEL OF HIV TRANSMISSION IN MEXICO

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Background

- As the largest nation in Mesoamerica, the phylodynamics of the Mexican HIV epidemic are complex. Regional epidemics exist throughout the country, but they are also linked together.
- Although Mexico has been highly successful in providing free ART for all HIV infected individuals, HIV detection and prevention could be improved.

Objective

Understanding the transmission dynamics of HIV across Mexico to improve identification of infected individuals and targeting of HIV prevention efforts.

Methods

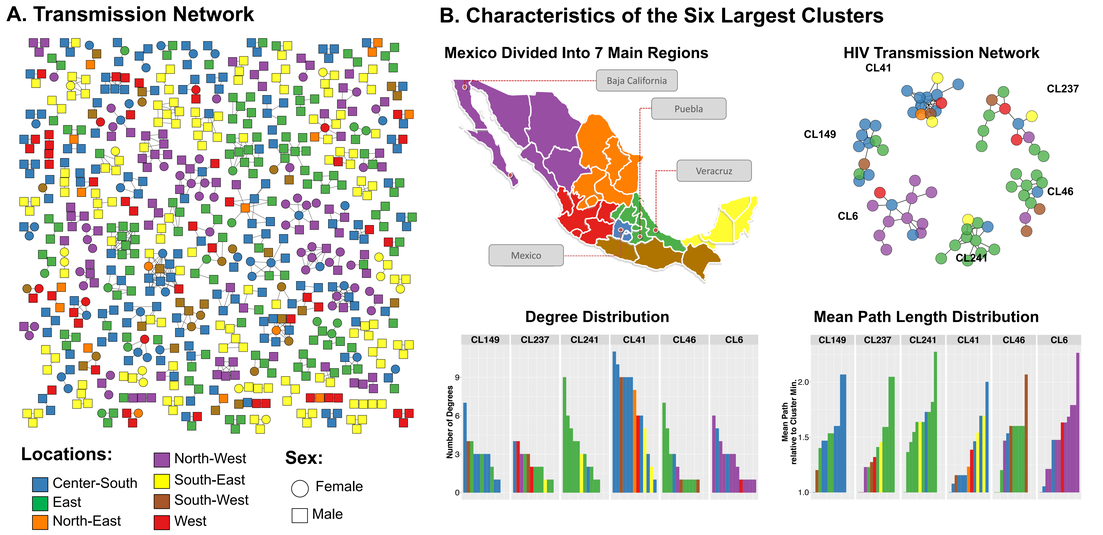
- Population: 4,192 HIV-1 subtype B *pol* sequences sampled from unique individuals from 23 states across Mexico between 2001-2016 were analyzed.
- Network inferences: HIV TRAnsmission Cluster Engine (www.hivtrace.org) was used to infer transmission links between sequences with a genetic distance ≤1.5%.
- Geospatial dispersal: The diffusion of the epidemic across previously defined socio-economic regions of Mexico was inferred using a Slatkin-Maddison approach on 1,000 iterations of random subsets of equal number of sequences per region.

Results

- 1,389/4,192 (33.1%) sequences had a putative linkage with at least one other sequence forming 510 clusters (range: 2-13 individuals).
- Clustering individuals were significantly younger (p<0.0001), but MSM were not more likely to cluster (p=0.61).
- Of the 1,260 putative links, 942 (74.8%) were between individuals residing in the same state and 116 (9.2%) were between individuals from states with a shared border.
- 43.3% (221/510) of the clusters spanned multiple states, and two-thirds (147/221, 66.5%) included individuals from the Center-South region, which includes Mexico City (**Figure 1A**).

Results

Figure 1. Phylogenetic and network analyses highlight the regional nature of HIV transmission in Mexico.



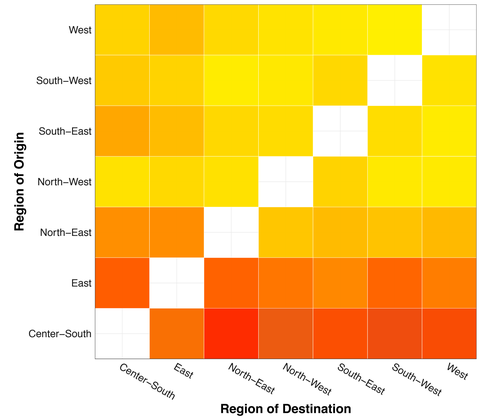
Legend. A. Transmission network across Mexico 2001-2016. All edges represent a genetic distance of ≤1.5% separating nodes. Color indicates the Region of sampling; shape denotes gender (ellipse: female; square: male). Only non-dyad clusters are shown. **B. Characteristics of the six largest clusters.** The map (*top left*) represents the 7 main regions in Mexico. Sequences from individuals originating from the Center-South region (blue) are central in all but one cluster (*top right*). Degree distribution (*bottom left*) and mean path length relative to cluster min (*bottom right*) for the 6 largest clusters.

- Six large clusters (size range 11-13) were identified. Compared to sequences from other regions, sequences from the Center South Region (which includes Mexico City) had higher connectivity and shorter path length (**Figure 1B**).

Conclusions

- Viral migration patterns highlight the local and regional nature of transmission in the Mexican HIV epidemic, and also demonstrate that the major metropolitan areas of Mexico City, Puebla and Veracruz were important hubs in interstate transmission.
- Together, these results are consistent with a gravity model of transmission, and suggest that focusing prevention resources on major metropolitan hubs may have an enhanced effect on reducing new HIV transmissions.

Figure 2. Viral migration analyses suggest the Center-South and East Regions are major sources of viral migration within Mexico.



Legend. Viral Migration across Mexico 2001-2016. Viral migration patterns were inferred using the Slatkin-Maddison approach on 1,000 iterations of random subsets of equal number of sequences per location.

- Sampled sequences from the border states of Baja California (including the city of Tijuana) and Quintana Roo (including Cancun), and the state of Puebla (previously shown to have strong migrational links to New York City), were significantly more likely to cluster (OR: 1.57, 1,73 and 1.87 respectively (p<0.001).
- The median distance between linked individuals from different states was 445 km (IQR 160-834), suggesting regional transmission patterns.
- Two thirds (98/147) of the non-dyad clusters included sequences from the Center-South and East Regions, including 84 of the 221 cross-state clusters.
- Viral migration analysis revealed that the Center-South and East regions were main hubs of the epidemic, as significantly more inferred transmissions originated from these regions to the rest of the country (**Figure 2**).

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