PHYLODYNAMIC FEATURES OF ACTIVE LARGE CLUSTERS FUELING THE MSM HIV EPIDEMIC IN QUEBEC

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Background

An understanding of the dynamics of primary transmission and optimization of long-term prevention strategies to control epidemics among men having sex with men (MSM). Our studies used whole genome sequences taken from the male subtype B infections excluding mixed gender and IDU/HTN cluster.

Methods

Our data comprise 4051 time-stamped HIV Pol sequences taken from the male subtype B infections excluding mixed gender and IDU/HTN clusters. Expanding on previous work, 24 large clusters, having 20+ distinct members were identified, having high bootstrap support (>90) and sufficient genetic similarity (<0.05 maximum pairwise genetic distances). We applied a birth-death SIR (BSIR) model available in the phylodynamic add-on for BEAST2 version 2.4.3 and Richard's five parameter asymmetric dose response curves to model growth trajectories. Genotyping across the viral integration and V3 loop was performed on representative infections within clusters. Epidemiological and demographic data from the genotyping and Montreal primary HIV cohort revealed clustered risk correlates implicated in clustering.

Results

Phylogenetics revealed two patterns of HIV-1 spread among MSM. While half of the HIV epidemic was ascribed to small self-limiting clusters (size 1-4), thirty-two viral strains contributed to micro-epidemics (cluster size 20-145) disproportionately rising from 13%, 23%, and 42% of new diagnoses in 2004-2007, 2008-2011, and 2012-2015, respectively. BSIR plots deduced early, active and dying phases of expansion for individual clusters. Ten to twenty 20+ clusters fueled spread of HIV in each quarterly period. Epidemiological and virological data deduced factors contributing to the expansion of the ten active strains from 2012-2016.

Clusters were concentrated in the Montreal area with cluster 678 reflecting a second-wave epidemic in Quebec City. Belonging to 20+ clusters was associated with primary/recent infection and being under 30 years of age (odds ratio 3.7 and 3.3, respectively). Clusters over the 2012-2015 quademnial period arose in significantly younger populations. The heightened transmissibility of strains belonging to distinct 20+ clusters were related to increased viral replicative fitness and/or dual tropism.

Risk factors associated with transmission clustering

Cluster group (transmissions per cluster) 0 2-4 5-9 10-19 20-145 (n=1359) Test statistic

| Age | 0-24 | 25-39 | 40-59 | 60-79 | 80+
|-----|------|------|------|------|------
| Median (IQ) | 43 (36-40) | 40 (32-48) | 40 (31-45) | 41 (33-49) | 34 (28-43)
| % group under 30 | 14.2 | 21.0 | 22.4 | 29.1 | 35.1
| Odds ratio | 1 | 1.6 | 1.8 | 1.6 | 1.6

Clinical indication of primary infection (0-6 months) at first genotyping

% cluster group | 25.0 | 37.8 | 44.6 | 47.0 | 48.3
| Odds-ratio | 1 | 1.9 | 2.4 | 2.7 | 2.8

Recent infection (0-0.4% mixed base calls)

% cluster group | 29.0 | 44.7 | 38.5 | 55.5 | 57.4
| Odds ratio | 1 | 2.2 | 2.5 | 2.7 | 3.7

Sexual contacts in 3 months prior to primary infection

| % partners | 20.7 | 21.7 | 23.0 | 20.0 | 26.4
| % cluster group | 20.7 | 21.7 | 23.0 | 20.0 | 26.4

Table 1. Bayesian parameter estimates and 95% HPD intervals (in parentheses) from the BSIR analysis on the 16 well defined MSM clusters within the infected HIV-1 type B population in Quebec:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate (95% HPD)</th>
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<tbody>
<tr>
<td>β</td>
<td>0.12 (0.05, 0.21)</td>
</tr>
<tr>
<td>τ</td>
<td>0.61 (0.36, 0.93)</td>
</tr>
<tr>
<td>K</td>
<td>3.20 (1.54, 5.62)</td>
</tr>
<tr>
<td>μ</td>
<td>0.92 (0.50, 1.70)</td>
</tr>
</tbody>
</table>

Acknowledgments

The authors thank all participants of the Montreal PHI cohort, Marie Legault, coordinator of the cohort and all participating physicians.

Conclusion

HIV-1 continues to spread among MSM with an alarming shift towards large cluster outbreaks, emphasizing the need for improved prevention paradigms.