NOT ALL CLUSTERS ARE EQUAL: STATEWIDE MOLECULAR HIV CLUSTER DYNAMICS IN RHODE ISLAND

30th CROI 2023 Conference on Retroviruses and Opportunistic Infections

854

Vlad Novitsky[1], Jon Steingrimsson[1], Mark Howison[2], Casey W. Dunn[3], Fizza S. Gillani[1], John Fulton[1], Thomas Bertrand[4], Katharine Howe[4], Lila Bhattarai[4], Guillermo Ronquillo[4], Meghan MacAskill[4], Utpala Bandy[4], Joseph Hogan[1], Rami Kantor[1]

[1] Brown University, Providence, RI, USA; [2] Research Improving People's Lives, Providence, RI, USA; [3] Yale University, New Haven, CT, USA; [4] Rhode Island Department of Health, Providence, RI, USA

BACKGROUND

Molecular HIV clusters are assumed to have uniform patterns over time. We hypothesized that assessment of cluster evolution may reveal distinct cluster patterns, improving molecular characterization of the local HIV epidemic and informing public health.

METHODS

Annual phylogenies were inferred by cumulative aggregation of partial pol sequences of all individuals with HIV-1 in Rhode Island (RI), diagnosed between 1990 and 2021. Molecular clusters were detected in annual phylogenies by strict and relaxed cluster definition criteria and the impact of annual newly-diagnosed cases to the structure and behavior of individual clusters were examined over time.

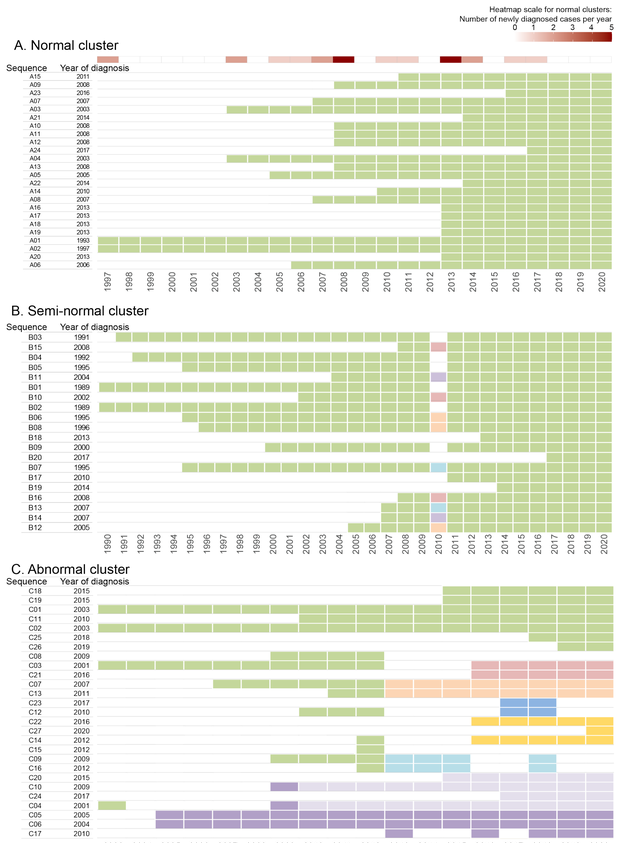

Figure 1. Types of clusters identified by cluster dynamics.

Comprehensive tracing of individual molecular HIV clusters over time in a statewide epidemic identified **distinct cluster types**. Knowledge that **not all clusters are equal** could improve methodology of molecular surveillance of HIV epidemics.

RESULTS

Of 2,370 individuals representing a statewide epidemic, 32% (strict criteria) to 48% (relaxed criteria) were found in clusters. Longitudinal tracking of individual clusters identified three cluster types: normal, semi-normal and abnormal (Figure 1, Table 1). Normal clusters (82%-87% of all identified clusters) showed predicted growing/plateauing dynamics, with ~3-fold higher growth rates in large (15%-16%) vs. small (~4%) clusters (Figure 2). Semi-normal clusters (1%-2% of all clusters) temporarily fluctuated in size and composition. Abnormal clusters (11%-17% of all clusters) demonstrated collapses and re-arrangements over time. Borderline values of cluster-defining parameters explained dynamics of non-normal clusters (Figure 3).

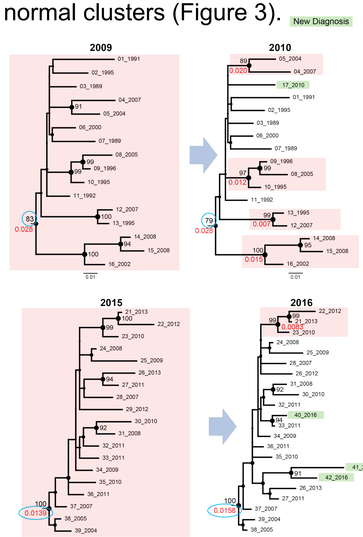

Figure 3. Dynamics of *abnormal* clusters

Table 1. **Types of molecular HIV clusters identified by relaxed and strict definition criteria.**

	Cluster definition criteria			
Cluster types	Relaxed: bootstrap ≥ 80%; mean pwd ≤ 0.045 substitutions/site		Strict: bootstrap ≥ 90%; mean pwd ≤ 0.015 substitutions/site	
	Cluster type, number (%*)	People in cluster types, number (% of all clustered[§]; % of all sequences[#])	Cluster type, number (%*)	People in cluster types, number (% of all clustered[§]; % of all sequences[#])
Normal clusters	**249 (87%)**	**1126 (88%; 48%)**	**197 (82%)**	**769 (81%; 32%)**
Semi-Normal clusters	**7 (2%)**	**50 (4%; 2%)**	**2 (1%)**	**12 (1.3%; 0.5%)**
Abnormal clusters	**32 (11%)**	**104 (8%; 4%)**	**40 (17%)**	**174 (18%; 7%)**

* The denominators for the calculations of cluster type proportions was the total number of identified clusters per the cluster definition criteria; n=288 at relaxed and n=239 at strict cluster definition criteria.

[§] The denominators for the calculations of proportions of individuals in the different cluster types out of all individuals who clustered were n=1,280 at relaxed and n=955 at strict cluster definition criteria;

[#] The denominators for the calculations of proportions of individuals in the different cluster types out of all the total number of sequences was n=2,370.

pwd: TN93 pairwise distances.

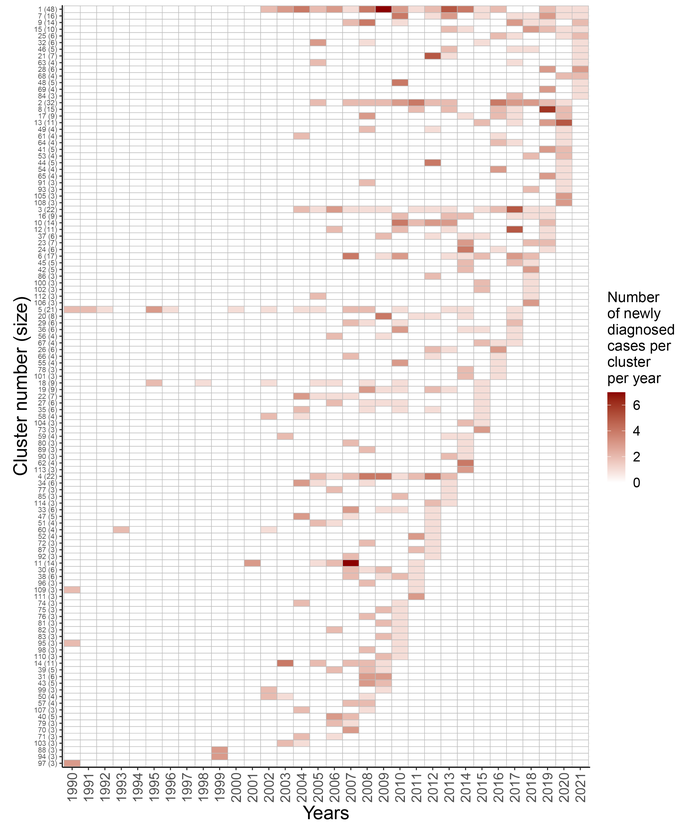

Figure 2. Annual activity of *normal* clusters with ≥3 members

CONCLUSIONS

We identified 3 cluster types - normal, semi-normal and abnormal, which might better inform understanding of the local HIV epidemic dynamics and help prioritize public health interventions. Our findings challenge the dominating perceptions that clusters demonstrate consistent behavior and that cross-sectional characterization of HIV epidemics is precise; and promote longitudinal evaluation of individual clusters. We show that while all RI clusters start as normal, not all maintain continuous growth and/or plateau over time. In fact, some collapse or have their sequences re-arranged, a phenomenon that should be considered for more accurate estimation of cluster dynamics over time and characterization of local HIV epidemics.