Detection and Characterization of HIV Clusters Using HIV-TRACE among a Cohort of Persons Living with HIV in Washington, DC

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Background

- Washington, DC has a 2% HIV prevalence and approximately 400 incident cases annually.
- HIV phylodynamic analyses are being used to inform and direct public health prevention interventions to interrupt HIV transmission.
- Combining molecular sequence data with behavioral and clinical data may improve our ability to detect high priority clusters in a high prevalence city.

Objectives

- To characterize clusters and identify clinical and behavioral predictors of clustering that might lead to transmission among a large cohort of persons living with HIV (PLWH) in DC

Methods

DC COHORT MOLECULAR EPIDEMIOLOGY SUBSTUDY

Prospective Sequence and Behavioral Data Collection

- Participants were recruited from the DC Cohort study, an ongoing longitudinal observational cohort study of HIV-infected persons in care in Washington, DC at 14 participating clinical sites.
- Eligible participants were diagnosed with HIV within the prior 12 months or had longstanding infection and were viremic (i.e., viral load (VL) >1500 copies/ml).
- Collected behavioral data and plasma samples which were sequenced using Next-Gen® sequencing (n= 111 participants).

Retrospective Sequence Collection

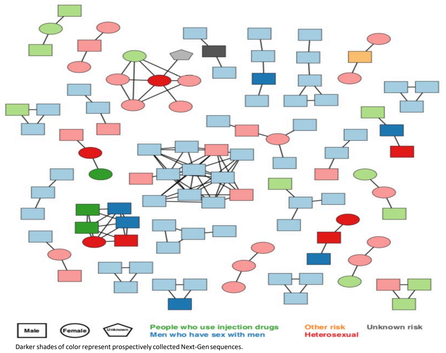
- Data were abstracted from DC Cohort participants' electronic medical records manually and through electronic exports.
- Molecular sequences collected by LabCorp® using Sanger sequencing from 2011–2017, among participants diagnosed from 1980–2017, were transferred to the DC Department of Health (DC DOH) (n= 3,132 participants).
- Per study protocol, matching was conducted with the DC DOH to identify sequences from Cohort participants.

ANALYSIS

- Demographic, clinical, and HIV sequence data were linked, as was self-reported behavioral data for those participants with prospective data.
- HIV-TRACE used to identify molecular transmission clusters using a pairwise genetic distance threshold ≤0.015 substitutions/site from the RT or PR/RT region.
- Conducted uni- and bivariate analyses comparing demographic characteristics and clinical outcomes by clustering.

Results

Figure 1. Retrospective and Prospective Clusters of Three or More Participants, N=28



Darker shades of color represent prospectively collected Next-Gen sequences.

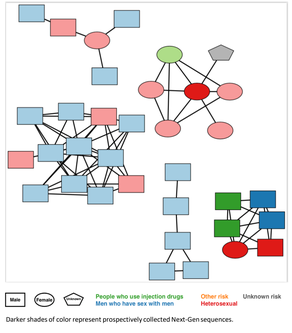
Table 1. Characteristics of Participants by Cluster Status (N=3,243)

	Total	In a Cluster of ≥ 3[1]	In a Cluster of ≤2[1]	P-value[2]
	N=3,243	N=107	N=3,136	
Participant Characteristic	**N (%)**	**N (%)**	**N (%)**	
Age (median, IQR)	44 (32, 53)	31 (24, 44)	44 (33, 53)	**<.0001**
Race/ethnicity				
NH Black	2,785 (86)	90 (85)	2,695 (86)	
NH White	255 (8)	9 (8)	246 (8)	.4137
Hispanic	146 (4)	7 (7)	139 (4)	
Other	51 (2)	0 (0)	51 (2)	
Sex at Birth				
Male	2,200 (68)	81 (76)	2,119 (68)	.0580
Female	1,037 (32)	25 (24)	1,012 (32)	
State of Residence				
DC	2,090 (90)	84 (91)	2,006 (90)	
MD	197 (8)	8 (9)	189 (8)	.6422
VA	35 (1)	0 (0)	35 (1)	
Other	5 (0.2)	0 (0)	5 (0.2)	
Mode of transmission (clinical data)				
MSM	1,549 (48)	61 (58)	1,488 (47)	
HRH	1,040 (32)	30 (28)	1,010 (32)	.0885
IDU	430 (13)	13 (12)	417 (13)	
Other	217 (7)	2 (2)	215 (7)	
Hx of STIs[3]	345 (15)	17 (18)	328 (15)	.3145
Hx of HBV	193 (8)	3 (3)	190 (8)	.0741
Hx of HCV	260 (11)	6 (6)	254 (11)	.1484
Years since HIV diagnosis	14 (8, 21)	9 (7, 12)	14 (9, 21)	**<.0001**
CD4 (cells/µl)	371 (186,560)	417 (258,598)	369 (186,559)	.1012
Viral Load (copies/ml)	10,470 (675, 50410)	12,955 (1340, 47750)	10,447 (670, 51000)	.3967
ARV history				
Experienced	18 (79)	68 (74)	1,763 (79)	
Naïve	13 (6)	8 (9)	127 (6)	.4272
Unknown	3 (15)	15 (16)	347 (15)	
Any ARV resistance	1,881 (81)	72 (78)	1,809 (81)	.5223

[1]Totals may not sum to N due to missing data; [2]Chi-square or Wilcoxon test; significant p-values <.05 bolded; [3]Chlamydia, gonorrhea, syphilis, trichomoniasis

Results

Figure 2. Five Largest Clusters, N= 35



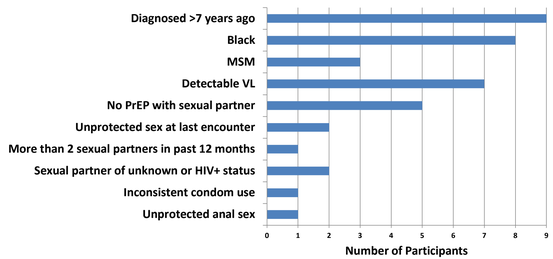
Darker shades of color represent prospectively collected Next-Gen sequences.

- The five largest clusters ranged in size from 5 to 12 participants.
- The largest cluster was comprised of all males whom reported mostly MSM risk.
- 3 of the 5 clusters included only PLWH who were retrospectively sequenced.
- One cluster included a prospectively sequenced PLWH who was diagnosed in 2012.

Table 2. Characteristics of Participants in Five Largest Clusters, N=35

	Cluster #				
Participant Characteristics	**1**	**2**	**3**	**4**	**5**
Cluster size	12	7	6	5	5
Retrospective vs. Prospective sequence	12 Retro	6 Retro, 1 Pro	6 Pro	5 Retro	5 Retro
No. of new diagnoses in cluster	0	0	0	0	0
Years since HIV diagnosis (Median, IQR)	9 (8,10)	7 (7,8)	22 (21,24)	8 (7,9)	12 (11,12)
Age at time of sequencing (Median, IQR)	25 (23,31)	28 (24,31)	49 (47,55)	32 (26,34)	28 (28,29)
Mode of transmission					
MSM	9 (75)	0 (0)	2 (33)	3 (60)	5 (100)
Het	3 (25)	5 (71)	2 (33)	2 (40)	0 (0)
IDU	0 (0)	1 (14)	2 (33)	0 (0)	0 (0)
On ARVs at time of sequencing	6 (50)	4 (57)	6 (100)	2 (40)	3 (60)
Median VL at time of sequencing (copies/ml) (IQR)	28,356 (5567,78902)	20,260 (8004,30872)	11,448 (4322,20315)	3,630 (2560,17320)	590 (411,2600)

Figure 3. Risk Behaviors of Participants in Prospective Only Clusters, N=9



Results (continued)

- Among 3,243 participants for whom we analyzed sequences, 86% were Black, 68% were male, the median age was 44 (IQR 32-53), and 48% were infected through male-to-male sexual contact (Table 1).
- HIV-TRACE found 207 genetic links connecting 267 individuals.
- HIV-TRACE identified 28 clusters of 3 or more sequences (size: 3-12) representing a total of 107 participants (Figure 1).
- Participants who clustered were significantly younger (median age 31 vs. 44, p<0.0001) and had been living with HIV a shorter period of time (median 9 vs. 14 years, p<0.0001) compared to those not clustering (Table 1).
- No significant differences were observed with respect to race/ethnicity, sex, HIV transmission risk, history of STIs, HBV or HCV, nor in VL or CD4 count among those PLWH in clusters vs. those not (Table 1).
- Among the 28 clusters, one cluster of 6 PLWH and one of 3 PLWH were comprised of only prospectively collected sequences.
- The prospective-only clusters included PLWH diagnosed between 1989 and 2008 of whom 8 were Black, and 3 each were MSM, PWID and heterosexually-infected (Table 2).
- Most members of these clusters (89%) self-reported being on antiretroviral therapy yet were viremic as of their most recent VL (median 12,810 copies/ml) (Table 2).
- Self-reported behaviors potentially associated with transmission in these clusters included lack of PrEP use among partners (n=5), unprotected sex at the last encounter (n=2), and a partner of unknown or HIV-positive status (n=2).

Conclusions

- Combining HIV-1 sequences, clinical, and behavioral data revealed risky behaviors and high levels of viremia among known PLWH that could potentially lead to ongoing transmission.
- While a number of relatively large clusters were identified, they did not include recently diagnosed PLWH, which might be more useful for cluster prioritization.
- Strengths of our analysis include the ability to triangulate data from multiple sources to comprehensively describe the behaviors and risks of cluster members.
- These analyses can complement active HIV surveillance efforts with the future goal of providing real-time HIV phylodynamic analyses to interrupt HIV transmission among defined populations and geographic areas.

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