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HIV-1 Diversity in the Moscow Region, Russia: Phylodynamics of the Most Common Subtypes

Lebedev A.[1], Lebedeva N.[2], Moskaleychik F.[1], Pronin A.[2], Kazennova E.[1] and Bobkova M.[1]

1. N.F. Gamaleya National Research Center of Epidemiology and Microbiology; 2. Moscow Regional AIDS Center.

BACKGROUND

The Moscow region is the most densely populated subject of Russia with the HIV prevalence in the general population to be 0.7 %; the number of HIV-positive people reached 41,949 by 2018. Moscow is a highly developed transport hub, so the region is characterized by a high intensity of internal and external migration. This may be the cause of the wide range of HIV-1 subtypes in the region and contribute to the emergence of new recombinant forms of the virus. We present the results of the most extensive study in the Moscow region, devoted to diversity and temporal dynamic of the HIV-1 subtypes.

Table 1. Demographic characteristics of HIV-1-infected patients stratified by subtypes

	Total	HIV-1 subtypes				
		A6	B	URF_A6/B	CRF02_AG	Others†
	(*n*=896, 100.0%)	(*n*=763, 85.1%)	(*n*=68, 7.6%)	(*n*=38, 4.2%)	(*n*=11, 1.2%)	(*n*=16, 1.8%)
Age (years)						
< 30	170 (19.0)	143 (84.1)	15 (8.8)	7 (4.1)	1 (0.6)	4 (2.4)
30 – 35	332 (37.0)	289 (87.1)	21 (6.3)	13 (3.9)	5 (1.5)	4 (1.2)
> 35	394 (44.0)	331 (84.0)	32 (8.1)	18 (4.6)	5 (1.3)	8 (2.0)
Gender						
Male	524 (58.5)	424 (80.9)	61 (11.6)	23 (4.4)	4 (0.8)	12 (2.3)
Female	372 (41.5)	339 (91.1)	7 (1.9)	15 (4.0)	7 (1.9)	4 (1.1)
Risk group						
HSX	446 (49.8)	384 (86.1)	28 (6.3)	17 (3.8)	8 (1.8)	9 (2.0)
MSM	38 (4.2)	6 (15.8)	29 (76.3)	1 (2.6)	–	2 (5.3)
IDUs	357 (39.8)	323 (90.5)	11 (3.1)	17 (4.8)	3 (0.8)	3 (0.8)
MTCT	49 (5.5)	44 (89.8)	–	3 (6.1)	–	2 (4.1)
Unknown	6 (0.7)	6 (100.0)	–	–	–	–

HSX, heterosexuals; MSM, men who have sex with men; IDUs, intravenous drug users; MTCT, mother-to-child transmission.
† – HIV subtype A1, C, G, F1, CRF01_AE, CRF03_AB, CRF63_02A6 and nonA6/B URFs.

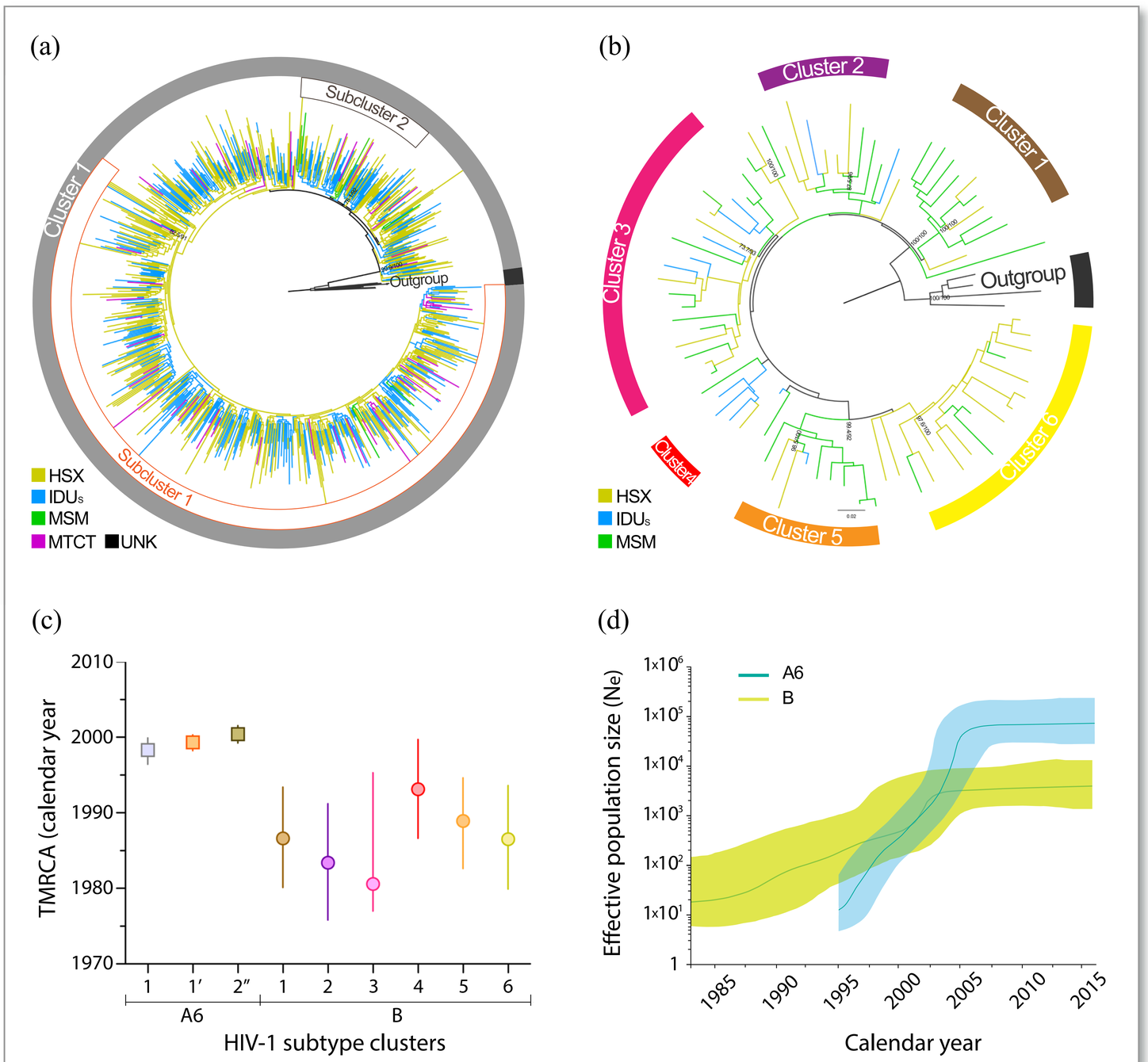

Figure 1. Maximum - likelihood phylogeny and phylodynamic analysis of the HIV-1 subtype A6 and B from Moscow region. **(a–b)** Major epidemic (sub-)clusters labeled in ML-tree. **(c)** The Times to the Most Recent Ancestor (TMRCA) for (sub-)clusters. **(d)** Bayesian plot showing effective number of infections through time Ne(t).

MATERIALS AND METHODS

We analyzed demographic and virologic data from 896 individuals diagnosed with HIV infection and received antiretroviral therapy (ART) between 2011 and 2016 at the Moscow regional AIDS Center (**Table 1**). Plasma samples were genotyped using the ViroSeq™ HIV-1. All codons associated with major drug-resistance mutations were removed from the final sequence alignment. The epidemiological clusters were identified using the maximum--likelihood phylogenetic analysis and SH–aLRT test. The phylodynamic analysis was performed using Bayesian coalescent-based methods. The temporal scale of evolutionary process was inferred from the sequences sampling dates using strict molecular clock model and Bayesian Skyline coalescent tree prior. New inter-subtype recombinant sequences were analyzed with jumping profile Hidden Markov Model algorithm.

RESULTS

Our analysis revealed a broad HIV-1 diversity in Moscow region (**Table 1**). We showed that the major HIV-1 subtype is A6, reaching 84.7 % in 2016, followed by 8.8 % for subtype B, the second dominant form. Noteworthy, we also observed a significant spread (4.2 %) of unique recombinants between two main subtypes. The study of the genetic relationships between HIV-1 A6-strains revealed that they all formed one cluster, including two subclusters (1'–2"), that arose approximately around 1998,3 (**Fig. 1a,c**). Within the subtype B, six major epidemic clusters (1–6) were identified. In contrast to sub-subtype A6, subtype B population to some extent showed genetic structuring depending on transmission route: each cluster contained strains associated with only one or two dominant transmission routes. Clusters 1–3, 5 and 6 (Pandemic subtype B) were responsible for 70.1 % of the sexually transmitted infections and played a dominant role in the B-epidemic in Moscow region among MSM and HSXs; Cluster 4 (FSU-B strain) was responsible for infections in IDUs. The emergence date of these clusters to be between 1980,6 and 1993,1 (**Fig. 1b,c**). Reconstruction of the demographic history of sub-subtype A6 and subtype B identified at least two epidemic growth phases. Both subtypes displayed the initial phase of rapid growth followed by a decline of growth rate in mid-2010s (**Fig. 1d**).

CONCLUSIONS

Our study points to the increasing genetic complexity of the HIV-1 epidemic in Moscow region, caused by the introduction of strain and clusters from other countries and the emergence of unique recombinant forms. The origin of clusters deserves further investigation, but we can already say with confidence that HIV-1 subtype B penetrated to the region much earlier than A6. The slowdown in the epidemic since the mid-2010s can be explained by the implementation of ART among all population groups. The study can contribute to a better understanding he HIV-1 temporal dynamics in one of the key regions for the HIV epidemic in Russia, as well as predicting of future trends of HIV infections.

Corresponding autor: Lebedev Aleksey, lebedevalesha236@gmail.com
123098, 18 Gamaleya str., Moscow, Russia. Tel/Fax: +7(499)190-30-63

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