

AHI detection among people who inject drugs in Russia reveals the HIV-1 transmission bottleneck

Elena Dukhovlinova[1], Alexey Masharsky[2,3], Sergei Verevochkin[3], Olga Toussova[3,4], Andrey Shevchenko[3,5], David Montefiori[6], Irving Hoffman[7], William Miller[7,8], Andrei Kozlov[2,3], Ronald Swanstrom[1,9]

1- CFAR and Lineberger CCC, University of North Carolina, Chapel Hill, NC, USA; 2- Saint Petersburg State University, Saint Petersburg, Russian Federation; 3- the Biomedical Center, Saint Petersburg, Russian Federation; 4- Pavlov State Medical University, Saint Petersburg, Russian Federation; 5- Theodosius Dobzhansky Center for Genome Bioinformatics, Saint Petersburg, Russian Federation; 6- Laboratory for AIDS Vaccine Research and Development, Duke University, Durham, NC, USA; 7- Center for Infectious Diseases, University of North Carolina, Chapel Hill, NC, USA; 8- Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, USA; 9- Department of Biochemistry and Biophysics, University of North Carolina, Chapel Hill, NC, USA

Abstract

Background: The expansion of the HIV-1 epidemic in Russia is mostly among people who inject drugs (PWID) due to unsafe injection practices with parenteral transmission. A pilot study to determine the feasibility of detecting acute HIV infection in PWID in St. Petersburg, Russia was conducted in 2011. Here we report the results of the molecular analysis of longitudinal blood samples obtained from the acutely HIV infected (AHI) PWID and their risk network partners.

Methods: We performed phylogenetic, Poisson Fitter and BEAST analysis of the SGA-derived full-length *env* genes of acutely infected PWIDs to estimate the multiplicity of HIV-1 infection. The AHI participants (n=7) were also followed for up to 12 months with the weekly blood draws in the first month post-infection. We included into the analysis single blood samples of the network members (n=8) to determine possible in-network transmission events. We analyzed the behavioral data provided by the subjects to suggest the parenteral over sexual risk of transmission for each AHI subject. A panel of pseudoviruses derived from the HIV-1 strains of AHI (n=13) and chronically infected (n=5) subjects was tested for the neutralization sensitivity. We compared our subtype A PWID neutralization data with the study of heterosexual transmission of subtype C viral strains.

Final conclusion on multiplicity of transmitted viruses in PWID was obtained by pooling together the data from 2011 and previously published 2008-09 cohorts (total n=19).

Table 1. Sample information, Poisson Fitter and BEAST data for all AHI subjects studied in 2011-13

Subject	Risk	Time point	Visit date	Days post neg visit	Fiebig stage	N seqs	POISSON FIT and APOBEC 3G correction (CI)			BEAST (Mut. rate 1.5E-5)		BEAST (Mut. rate 2.16e-5)	
							no APOBEC corr	w/APOBEC corr	StarPhy?	mean TMRH	MRCA 1.5 days	mean TMRH	MRCA 1.5d
O12	IDU	1	3/4/11	32	III/IV	28	29 (14, 43)	26 (11, 40)	y	87	58	62	41
		2	3/18/11	46	III/IV	16	52 (33, 71)	36 (27, 46)	y	58.5	39	40	27
		3	3/25/11	53	V	16	38 (25, 50)	34 (21, 46)	y	39	26	27	18
		4	4/4/11	63	V	29	63 (54, 73)	46 (39, 54)	y	57.5	38	40	27
O32	IDU	1	9/9/11	68 (31 post neg SGA)	III/IV	19	46 (33, 60)	44 (29, 59)	n	60	40	42	28
		2	9/16/11	75 (38 post neg SGA)	III/IV	18	43 (33, 52)	40 (29, 52)	n	48	32	33	22
		3	9/23/11	82 (45 post neg SGA)	V	8	70 (44, 96)	65 (36, 94)	n	65	43	45	30
O60	IDU > sex	1	1/21/11	n/a	I/II	11	15 (8, 23)	17 (9, 25)	y	17	11	11.5	8
		2	1/28/11	7 from 1st TP	III/IV	17	21 (13, 30)	24 (15, 33)	y	22	15	15	10
		3	2/4/11	14 from 1st TP	V	17	n/a (superinfection)	n/a (superinfection)	n/a	1730	1153	1202	801
		4	2/11/11	21 from 1st TP	V	19	n/a (superinfection)	n/a (superinfection)	n/a	1716	1144	1191	794
		5	2/18/11	28 from 1st TP	V	13	n/a (superinfection)	n/a (superinfection)	n/a	1159	773	804	536
		6	11/23/11	279 from 1st TP	VI	25	n/a (superinfection)	n/a (superinfection)	n/a	2614	1743	1815	1210
O67	IDU > sex	1	4/4/11	18	I/II	20	18 (12, 24)	15 (9, 21)	y	19	13	13	9
		2	4/14/11	28	III/IV	22	32 (22, 42)	25 (16, 35)	y	34	23	23	15
		3	5/18/11	67	V	16	44 (33, 55)	39 (29, 49)	y w/corr	40	27	27	18
		4	6/30/11	128	V	8	n/a	n/a	n/a	72	48	50	33
		5	10/28/11	246	VI	18	n/a	n/a	n/a	163	109	113	75
O87	IDU or sex	1	9/16/11	29	III/IV	28	33 (18, 48)	26 (11, 42)	y w/corr	112	75	78	52
		2	9/23/11	36	III/IV	39	48 (40, 56)	36 (29, 44)	y w/corr	46	31	32	21
		3	9/30/11	43	V	17	52 (42, 62)	39 (29, 48)	y w/corr	50	33	34	23
O111	IDU or sex	1	10/4/11	n/a	III/IV	41	52 (43, 61)	45 (39, 52)	n	61	41	42.5	28
		2	10/12/11	8 from 1st TP	III/IV	16	50 (38, 62)	52 (41, 64)	n w/corr	52	35	36	24
		3	10/19/11	15 from 1st TP	V	20	62 (51, 72)	61 (49, 73)	n	64.5	43	45	30
O162	IDU > sex	1	4/11/11	n/a	I/II	15	16 (7, 24)	13 (4, 21)	y	18	12	12	8
		2	4/19/11	7 from 1st TP	I/II	23	16 (9, 22)	15 (7, 22)	y	19	13	13.5	9

Fig.1 Highlighter plots of single *env* genes show homogeneous viral population in 6 out of 7 AHI subjects studied

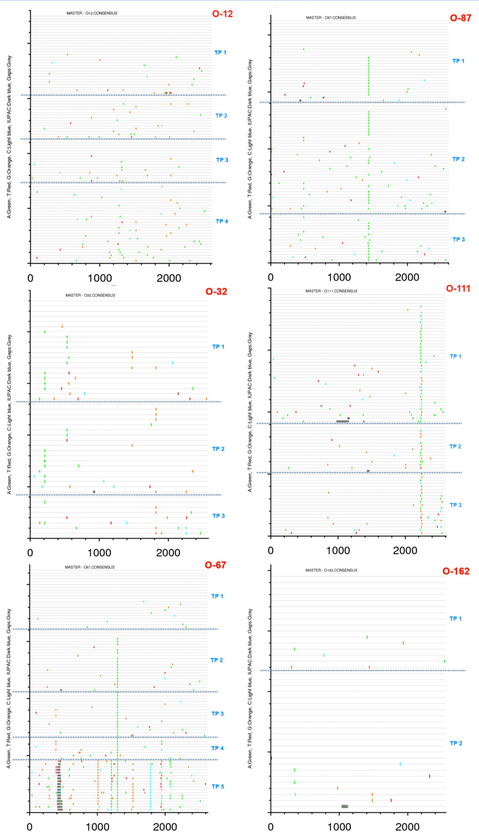


Fig.2 In the blood of AHI O60 at TP3-6 we saw additional viral variants distinct from the founder strain of two potential donors

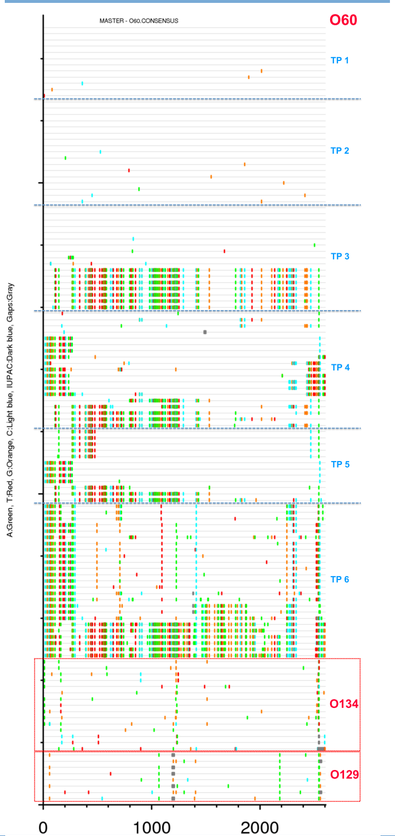
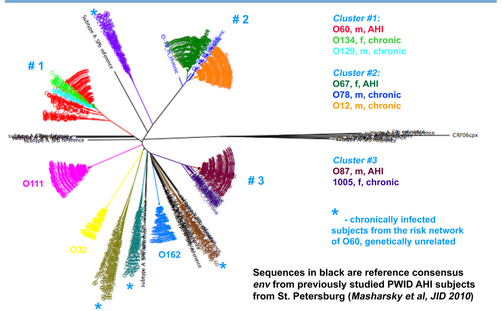


Fig.3 Phylogenetic tree of all AHI and chronic subjects studied reveal 3 transmission clusters, one of them (#2) involving a possible AHI-to-AHI transmission


1
2
3
O111
O32
O162
C.BR.92BR020.AB023804
C.ZM.96.96ZM651.AF110392
C.ZA.97.97ZA012.AF286227
C.BW.00.00BW07621.AF443088
C.ZA.97.97ZA003.AF286225