

Supplementary methods

Details of timepoints Caió sequences were derived from:

HIV-2 *gag* (n = 86) – 16 sequences from 1996, 10 from 2003, 45 from 2006, 13 from 2007 and two from 2008.

HIV-2 *env* (n = 70) – 21 sequences from 2003, 43 from 2006, 5 from 2007 and one from 2008.

HIV-1 *env* (n = 56) - Four sequences were available from 1996, 27 from 2003, 11 from 2006 and 14 from 2007.

Description of Bayesian Skyline Plots:

The Bayesian skyline plot (BSP) is a coalescent-based method reconstructing the past demographic history of a population from the phylogeny of individuals randomly sampled from that population [1]. It allows the estimation of $N(t)$, a continuous function that represents the effective number of infections (N_e) at time t. That is the number of infections contributing to onward transmission at that time, rather than the number of actual infections. For infectious diseases, $N(t)$ is therefore directly related to the rate of transmission (i.e. the incidence) rather than the absolute number of infected individuals (i.e. the prevalence) [2], except during the exponential growth phase of an epidemic where there is a linear relationship between the transmission rate and the number of infected individuals [3].

Caveats:

(i) Under the coalescent theory, the population size is assumed to be homogeneous and under neutral evolution. Although these assumptions are often broken, neutral demographic processes (rather than selection) are the main driving force of HIV evolution at the population level [4]. This is illustrated, for instance, by the persistence of multiple viral lineages through time in the reconstructed Caió phylogenies. Moreover, selection is unlikely to play a major role when the number of infected individuals represents a small proportion of the total population size, as predicted by population genetics and evolutionary theories.

(ii) The effective population size may be lower than expected due to variability between individuals in infectiousness.

(iii) The phylodynamic patterns can also be affected by sampling. For instance, sampling a higher fraction of the infected individuals at a given time, or over-sampling of epidemiologically linked individuals, may result in more recent coalescent times, shorter terminal branches, and a different tree topology, which in turn may affect the population growth curve reconstructions.

The flattening of N_e in the most recent stage of the epidemic is a common feature of HIV BSPs [see for instance [4-7]]. This can be attributed to (i) partial sampling of recent transmission events, resulting in an overestimation of the time of the most recent coalescent event, and (ii) the accumulation of deleterious mutations, which haven't been purified out of the population yet and result in long terminal tree branches.

However, the fact that the HIV-1 and HIV-2 population growth curves reach equilibrium at the same level, but at different times, suggest that host demographic factors, such as the number of susceptible or infectious hosts, are decisive in these trends.

Choice of clock model for reconstruction of HIV-2 *gag* and *env* phylogenies and estimation of HIV-1 and HIV-2 effective population size:

Both strict and relaxed molecular clock models were tested independently and compared by computing a Bayes Factor (BF) [35]. The relaxed clock model provided a significantly better fit to the data, as indicated by a BF > 20, and was retained for the analysis. Tips of the dated phylogenies were calibrated with the sampling year of the sequences.

Bayesian Skyline Plot to estimate HIV-2 N_e :

A normal prior was set on the root height of the HIV-2 tree, with a mean of 67.86 years since the most recent tip (2007) and a standard deviation of 16, based on the time of origin of the HIV-2 epidemic estimated by Lemey *et al.*[13].

Details of Bayesian Markov Chain Monte Carlo (MCMC) searches:

The Bayesian MCMC searches were set to 65,000,000 (*gag* phylogeny), 100,000,000 (*env* phylogeny including 41 non-Caió sequences) or 50,000,000 iterations (Caió HIV-1 and HIV-2 *env* N_e estimations) with trees sampled every 1000th generations. A maximum clade credibility tree (MCCT) was selected from the sampled posterior distribution with the program TreeAnnotator version 1.5.2 (<http://beast.bio.ed.ac.uk>), after discarding trees corresponding to a 10% burnin. Bayesian skyline plots were generated, after discarding a 10% burnin, with the program Tracer v1.5 (<http://tree.bio.ed.ac.uk/software/tracer/>).

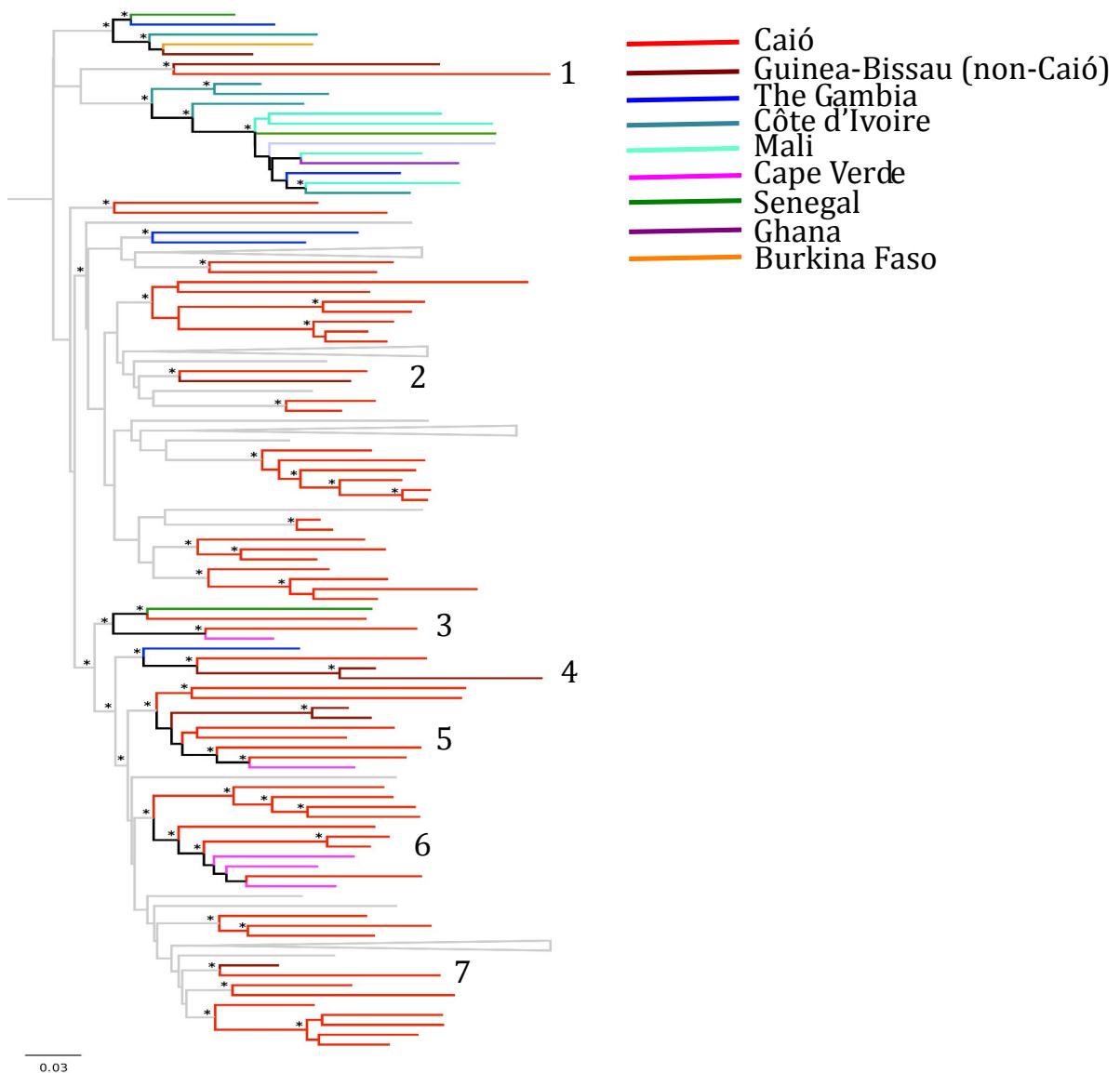
Analysis of HIV-2 population migration using the Slatkin-Maddison test:

Migration of the studied HIV-2 population was analysed using the Slatkin-Maddison test [8], as implemented in the package HyPhy [9].The test was performed on the HIV-2 *env* maximum likelihood phylogeny shown in Supplementary Figure 1. Sequences from Caió were grouped with other Guinea-Bissau sequences, resulting in 9 discrete geographical traits: Burkina Faso (1 sequence), Cameroon (1 sequence), Ivory Coast (9 sequences), Cape Verde (6 sequences), Ghana (2 sequences), the Gambia (6 sequences), Guinea-Bissau (83 sequences), Mali (5 sequences) and Senegal (3 sequences). Significance was assessed by comparing the observed number of migration events to a simulated distribution of migration events with 10,000 pseudo-replicates.

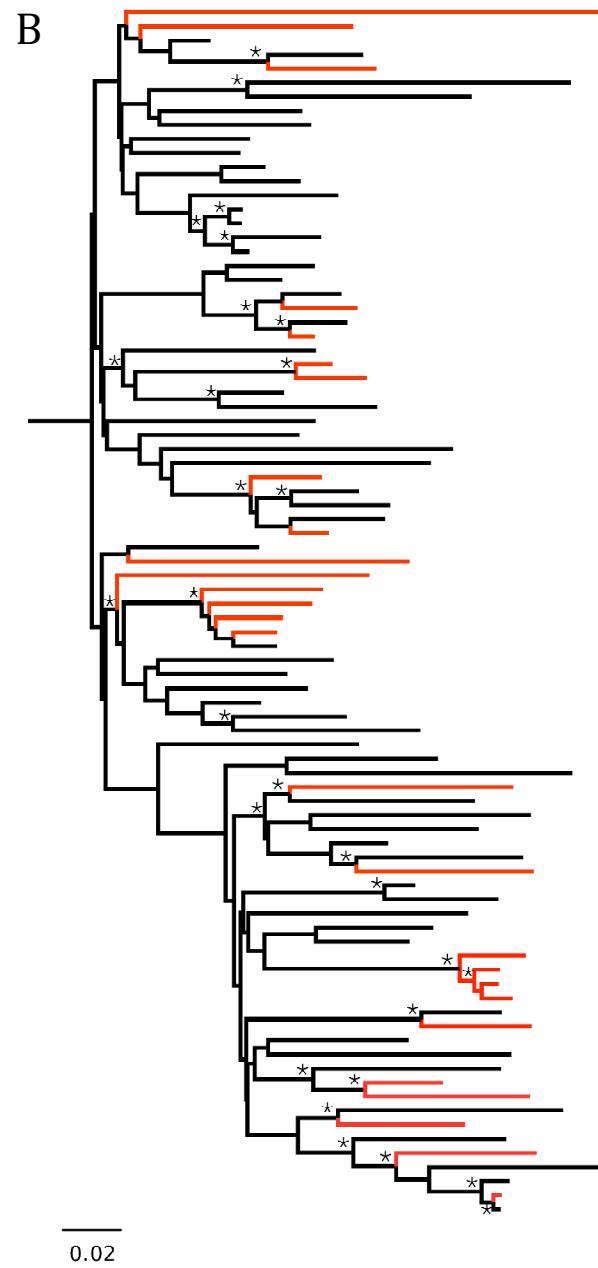
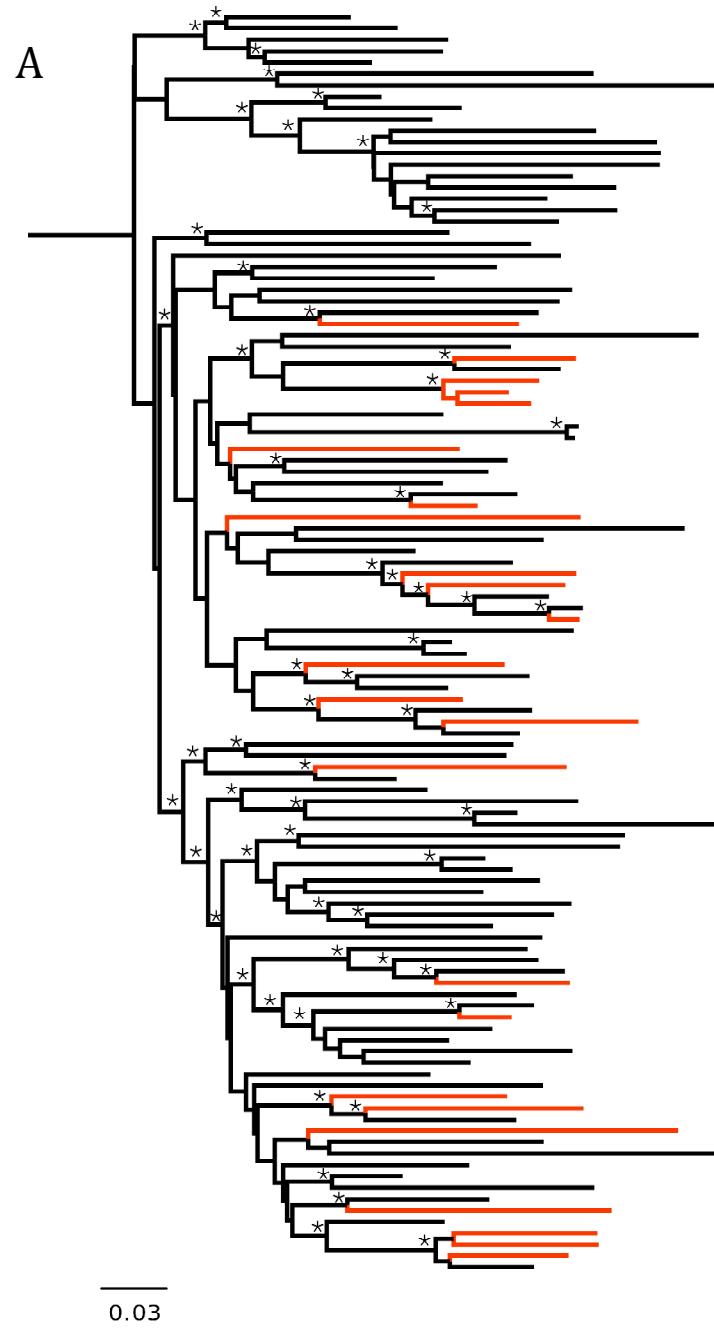
The observed number of migrations was significantly lower than that expected from a distribution of 10,000 simulations, rejecting the hypothesis of a random geographical distribution across the phylogeny ($p < 0.001$). A total of 24 observed migration events were identified, 6 of which (25%) were between Guinea-Bissau and Cape Verde. The second largest number of migration events was between Guinea-Bissau and the Gambia (3/24; 13%).

References

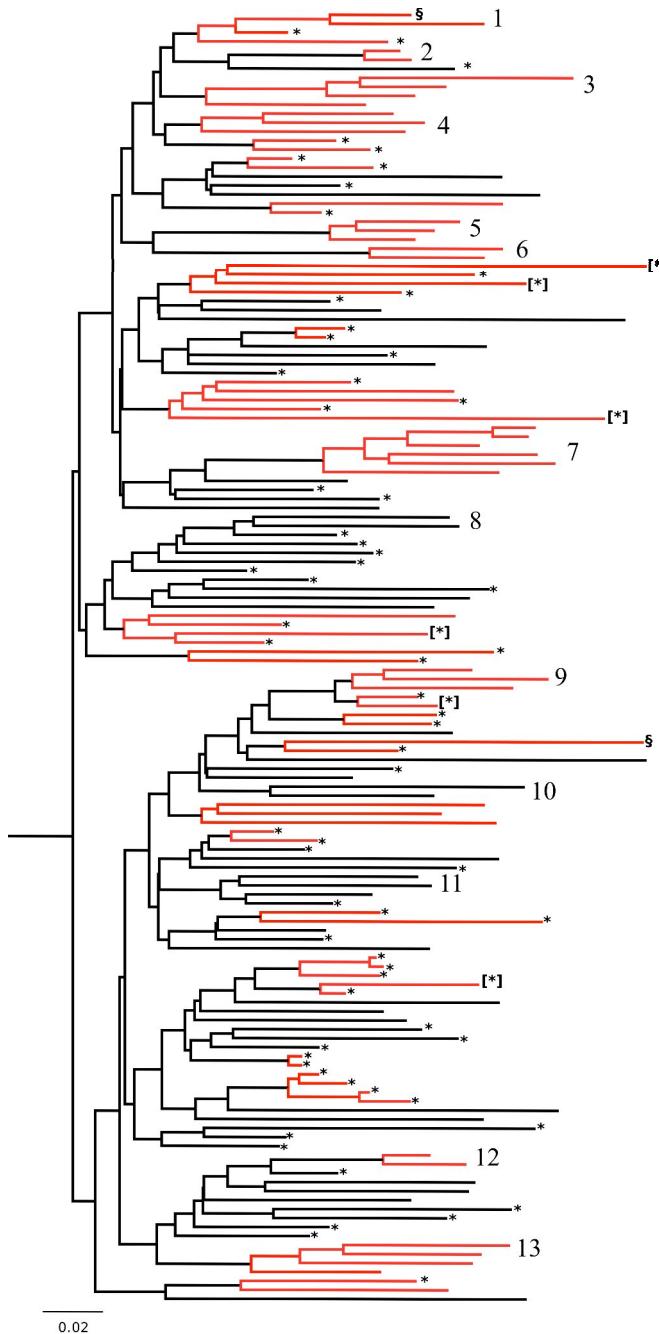
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Supplementary figure 1. HIV-2 *env* Maximum Clade Credibility Tree (MCCT) phylogeny demonstrating clustering of Caió sequences with external HIV-2 isolates. The tree is midpoint rooted. In bold are clusters with a Bayesian posterior probability of ≥ 0.95 and * indicates nodes with a posterior probability of >0.9 . Where possible, clades not supported by a posterior probability of >0.9 are collapsed. Scale bar indicates nucleotide substitutions per site. Clusters with a mix of both Caió and non-Caió isolates are numbered.



Supplementary Figure 2. *env* (a) and *gag* (b) Maximum Clade Credibility Tree (MCCT) phylogenies of the HIV-2 subtype A. Trees are midpoint rooted. Branches in red indicate incident HIV-2 cases, which are distributed throughout the phylogeny. * indicates nodes with a posterior probability of >0.9. Scale bar indicates nucleotide substitutions per site.



Supplementary Figure 3. Maximum Clade Credibility Tree (MCCT) in nucleotide substitutions per site reconstructed using only Caió *env* sequences and inclusion of additional individuals sampled in 1991. Significant clusters (posterior probability of 0.99 or higher at relevant nodes) are highlighted in red. The additional 68 sequences included from individual samples in 1991 are denoted by a *. Caió Transmission clusters identified in the previous *env* phylogeny are denoted by numbers 1 – 13. The additional ($n = 68$) pre1989 sequences almost exclusively form new clusters with each other, or cluster with other pre1989 sequences included in the prior analysis (denoted by [*]; other than on two occasions where they form mixed clusters with incident cases (\$)).

Supplementary Table 1. Details of all sequences used in the study

Sample ID	Country ¹	Year of sampling	Virus Region	Accession Number
CA5625	GWc	2007	HIV-2 p26	JX570546
CA6417	GWc	2007	HIV-2 p26	JX570547
CA6666	GWc	2007	HIV-2 p26	JX570541
CA6936	GWc	2007	HIV-2 p26	JX570542
CA7164	GWc	2007	HIV-2 p26	JX570548
CA7205	GWc	2007	HIV-2 p26	JX570549
CA7235	GWc	2007	HIV-2 p26	JX570550
CA7253	GWc	2007	HIV-2 p26	JX570551
CA7284	GWc	2007	HIV-2 p26	JX570552
CA7340	GWc	2007	HIV-2 p26	JX570543
CA8036	GWc	2008	HIV-2 p26	JX570544
N00009	GWc	1996	HIV-2 p26	JX570554
N00038	GWc	1996	HIV-2 p26	JX570570
N00054	GWc	1996	HIV-2 p26	JX570571
N00076	GWc	1996	HIV-2 p26	JX570572
N00096	GWc	1996	HIV-2 p26	JX570568
N00115	GWc	1996	HIV-2 p26	JX570559
N00125	GWc	1996	HIV-2 p26	JX570558
N00126	GWc	1996	HIV-2 p26	JX570563
N00129	GWc	1996	HIV-2 p26	JX570556
N00135	GWc	1996	HIV-2 p26	JX570557
N00154	GWc	1996	HIV-2 p26	JX570564

N00157	GWc	1996	HIV-2 p26	JX570555
N00186	GWc	1996	HIV-2 p26	JX570569
N00203	GWc	1996	HIV-2 p26	JX570561
N00255	GWc	1996	HIV-2 p26	JX570565
N04066	GWc	2003	HIV-2 p26	JX570579
N04083	GWc	2003	HIV-2 p26	JX570580
N04189	GWc	2003	HIV-2 p26	JX570574
N04265	GWc	2003	HIV-2 p26	JX570577
N04269	GWc	2003	HIV-2 p26	JX570581
N04276	GWc	2003	HIV-2 p26	JX570578
N04280	GWc	2003	HIV-2 p26	JX570575
N04388	GWc	2003	HIV-2 p26	JX570582
N04405	GWc	2003	HIV-2 p26	JX570576
N04426	GWc	2003	HIV-2 p26	JX570573
N04722	GWc	2008	HIV-2 p26	JX570545
N62522	GWc	1996	HIV-2 p26	JX570566
N65309	GWc	2006	HIV-2 p26	GQ485448
N65310	GWc	2006	HIV-2 p26	GQ485449
N65313	GWc	2006	HIV-2 p26	GQ485450
N65330	GWc	2006	HIV-2 p26	GQ485457
N65331	GWc	2006	HIV-2 p26	GQ485458
N65333	GWc	2006	HIV-2 p26	GQ485460
N65336	GWc	2006	HIV-2 p26	GQ485461
N65341	GWc	2006	HIV-2 p26	GQ485465
N65347	GWc	2006	HIV-2 p26	GQ485467
N65349	GWc	2006	HIV-2 p26	GQ485468

N65350	GWc	2006	HIV-2 p26	GQ485469
N65354	GWc	2006	HIV-2 p26	GQ485472
N65358	GWc	2006	HIV-2 p26	GQ485475
N65361	GWc	2006	HIV-2 p26	GQ485476
N65363	GWc	2006	HIV-2 p26	GQ485477
N65367	GWc	2006	HIV-2 p26	GQ485478
N65369	GWc	2006	HIV-2 p26	GQ485479
N65370	GWc	2006	HIV-2 p26	GQ485480
N65382	GWc	2006	HIV-2 p26	GQ485482
N65384	GWc	2006	HIV-2 p26	GQ485483
N65386	GWc	2006	HIV-2 p26	GQ485484
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N65392	GWc	2006	HIV-2 p26	GQ485488
N65394	GWc	2006	HIV-2 p26	GQ485489
N65398	GWc	2006	HIV-2 p26	GQ485490
N65403	GWc	2006	HIV-2 p26	GQ485491
N65406	GWc	2006	HIV-2 p26	GQ485492
N65410	GWc	2006	HIV-2 p26	GQ485495
N65415	GWc	2006	HIV-2 p26	GQ485496
N65418	GWc	2006	HIV-2 p26	GQ485497
N65424	GWc	2006	HIV-2 p26	GQ485498
N65426	GWc	2006	HIV-2 p26	GQ485499
N65435	GWc	2006	HIV-2 p26	GQ485500
N65436	GWc	2006	HIV-2 p26	GQ485501
N65494	GWc	2006	HIV-2 p26	GQ485504
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N65552	GWc	2006	HIV-2 p26	GQ485506
N65555	GWc	2006	HIV-2 p26	GQ485507
N65575	GWc	2006	HIV-2 p26	GQ485509
N65600	GWc	2006	HIV-2 p26	JX570562
N65601	GWc	2006	HIV-2 p26	GQ485511
N65605	GWc	2006	HIV-2 p26	GQ485512
N65611	GWc	2006	HIV-2 p26	GQ485513
N65612	GWc	2006	HIV-2 p26	GQ485514
N65613	GWc	2006	HIV-2 p26	GQ485515
N65666	GWc	2007	HIV-2 p26	JX570553
N65667	GWc	2007	HIV-2 p26	JX570567
N65668	GWc	2007	HIV-2 p26	JX570560
9649	ML	1995	HIV-2 env	AF170039
96150	CV	1996	HIV-2 env	AF170041
96151	ML	1996	HIV-2 env	AF170034
96199	CV	1995	HIV-2 env	AF170043
96202	BF	1995	HIV-2 env	AF170040
96203	CV	1995	HIV-2 env	AF170049
96205	GH	1996	HIV-2 env	AF170031
96206	SN	1994	HIV-2 env	AF170048
96308	CV	1994	HIV-2 env	AF170042
96310	SN	1996	HIV-2 env	AF170036
96323	CI	1994	HIV-2 env	AF170032
96324	GW	1996	HIV-2 env	AF170046
96326	ML	1994	HIV-2 env	AF170038
96327	CV	1996	HIV-2 env	AF170044

96329	GW	1994	HIV-2 env	AF170045
97223	CI	1997	HIV-2 env	AF170033
03CM510	CM	2003	HIV-2 env	EU028345
7312A	CI	1990	HIV-2 env	L36874
ALI	GW	1989	HIV-2 env	AF082339
B1002	GWc	1991	HIV-2 env	AJ008283
B1010	GWc	1991	HIV-2 env	AJ008284
B1011	GWc	1991	HIV-2 env	AJ011223
B1014	GWc	1991	HIV-2 env	AJ011250
B1015	GWc	1991	HIV-2 env	AJ008285
B1022	GWc	1991	HIV-2 env	AJ008286
B1024	GWc	1991	HIV-2 env	AJ011224
B1025	GWc	1991	HIV-2 env	AJ011225
B1027	GWc	1991	HIV-2 env	AJ011226
B1028	GWc	1991	HIV-2 env	AJ008288
B1033	GWc	1991	HIV-2 env	AJ008289
B1036	GWc	1991	HIV-2 env	AJ011227
B1041	GWc	1991	HIV-2 env	AJ008290
B1042	GWc	1991	HIV-2 env	AJ011228
B1046	GWc	1991	HIV-2 env	AJ008291
B1048	GWc	1991	HIV-2 env	AJ008292
B1049	GWc	1991	HIV-2 env	AJ008293
B1053	GWc	1991	HIV-2 env	AJ011251
B1054	GWc	1991	HIV-2 env	AJ011231
B1058	GWc	1991	HIV-2 env	AJ008294
B1068	GWc	1991	HIV-2 env	AJ008295

B1079	GWc	1991	HIV-2 env	AJ008297
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B1089	GWc	1991	HIV-2 env	AJ011255
B1095	GWc	1991	HIV-2 env	AJ008298
B1100	GWc	1991	HIV-2 env	AJ011233
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B1127	GWc	1991	HIV-2 env	AJ011234
B1128	GWc	1991	HIV-2 env	AJ011235
B1129	GWc	1991	HIV-2 env	AJ008300
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B1207	GWc	1991	HIV-2 env	AJ011243
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B1231	GWc	1991	HIV-2 env	AJ008307
B1233	GWc	1991	HIV-2 env	AJ011268
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B1297	GWc	1991	HIV-2 env	AJ008314
B1301	GWc	1991	HIV-2 env	AJ011272
B1302	GWc	1991	HIV-2 env	AJ008315
B1303	GWc	1991	HIV-2 env	AJ008316
BEN	ML	1987	HIV-2 env	M30502
CA6417	GWc	2007	HIV-2 env	JN863883
CA7164	GWc	2007	HIV-2 env	JN863884
CA7205	GWc	2007	HIV-2 env	JN863897
CA7253	GWc	2007	HIV-2 env	JN863898

CA7340	GWc	2007	HIV-2 env	JN863882
CAM1	GW	1987	HIV-2 env	U05359
CAM2	GW	1987	HIV-2 env	D00835
CAM3	GW	1987	HIV-2 env	U05355
CAM4	GW	1987	HIV-2 env	U05356
CAM5	GW	1987	HIV-2 env	U05357
CAM6	GW	1987	HIV-2 env	U05358
CBL21	GM	1988	HIV-2 env	U05350
CBL22	GM	1988	HIV-2 env	U05351
CBL23	GM	1988	HIV-2 env	AY509259
CBL24	GM	1988	HIV-2 env	AJ238999
D194	GM	1987	HIV-2 env	J04542
FGNIHZ	GW	1986	HIV-2 env	J03654
GH1	CI	1986	HIV-2 env	M30895
ISYSBL6669	GM	1985	HIV-2 env	J04498
MIC97	GW	1997	HIV-2 env	AY168925
MJC97	GW	1997	HIV-2 env	EU021092
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N65320	GWc	2006	HIV-2 env	JN863869
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N65332	GWc	2006	HIV-2 env	GQ485522
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N65411	GWc	2006	HIV-2 env	JN863879
N65415	GWc	2006	HIV-2 env	GQ485544
N65418	GWc	2006	HIV-2 env	GQ485545
N65426	GWc	2006	HIV-2 env	GQ485546
N65494	GWc	2006	HIV-2 env	GQ485547
N65552	GWc	2006	HIV-2 env	JN863880

N65601	GWc	2006	HIV-2 env	GQ485548
N65605	GWc	2006	HIV-2 env	GQ485549
N65613	GWc	2006	HIV-2 env	GQ485550
N65614	GWc	2006	HIV-2 env	JN863881
PEI2	ML	1987	HIV-2 env	U22047
ROD	CV	1985	HIV-2 env	M15390
ST	SN	1987	HIV-2 env	M31113
UC2	CI	1988	HIV-2 env	U38293
vcp	GW	1986	HIV-2 env	EU580099
E134	GWc	1996	HIV-1 env	JN863732
E159	GWc	1996	HIV-1 env	JN863733
E197	GWc	1996	HIV-1 env	JN863734
E246	GWc	1996	HIV-1 env	JN863735
E4005	GWc	2003	HIV-1 env	JN863773
E4006	GWc	2003	HIV-1 env	JN863772
E4015	GWc	2003	HIV-1 env	JN863774
E4037	GWc	2003	HIV-1 env	JN863775
E4048	GWc	2003	HIV-1 env	JN863776
E4078	GWc	2003	HIV-1 env	JN863777
E4080	GWc	2003	HIV-1 env	JN863778
E4084	GWc	2003	HIV-1 env	JN863771
E4101	GWc	2003	HIV-1 env	JN863779
E4106	GWc	2003	HIV-1 env	JN863781
E4107	GWc	2003	HIV-1 env	JN863780
E4128	GWc	2003	HIV-1 env	JN863782
E4129	GWc	2003	HIV-1 env	JN863770

E4163	GWc	2003	HIV-1 env	JN863769
E4171	GWc	2003	HIV-1 env	JN863783
E4174	GWc	2003	HIV-1 env	JN863784
E4197	GWc	2003	HIV-1 env	JN863768
E4212	GWc	2003	HIV-1 env	JN863785
E4233	GWc	2003	HIV-1 env	JN863767
E4285	GWc	2003	HIV-1 env	JN863786
E4301	GWc	2003	HIV-1 env	JN863766
E4366	GWc	2003	HIV-1 env	JN863765
E4385	GWc	2003	HIV-1 env	JN863736
E4394	GWc	2003	HIV-1 env	JN863787
E4418	GWc	2003	HIV-1 env	JN863764
E4424	GWc	2003	HIV-1 env	JN863763
E4425	GWc	2003	HIV-1 env	JN863762
E5006	GWc	2006	HIV-1 env	JN863737
E5050	GWc	2006	HIV-1 env	JN863738
E5380	GWc	2006	HIV-1 env	JN863739
E5535	GWc	2006	HIV-1 env	JN863740
E5539	GWc	2006	HIV-1 env	JN863741
E5657	GWc	2006	HIV-1 env	JN863742
E6006	GWc	2006	HIV-1 env	JN863743
E6403	GWc	2006	HIV-1 env	JN863744
E6482	GWc	2007	HIV-1 env	JN863745
E6498	GWc	2007	HIV-1 env	JN863746
E6591	GWc	2007	HIV-1 env	JN863747
E6865	GWc	2007	HIV-1 env	JN863748

E6922	GWc	2007	HIV-1 env	JN863749
E6952	GWc	2007	HIV-1 env	JN863750
E6958	GWc	2007	HIV-1 env	JN863751
E7019	GWc	2006	HIV-1 env	JN863752
E7114	GWc	2006	HIV-1 env	JN863753
E7165	GWc	2006	HIV-1 env	JN863754
E7367	GWc	2007	HIV-1 env	JN863755
E7424	GWc	2007	HIV-1 env	JN863756
E7467	GWc	2007	HIV-1 env	JN863757
E7582	GWc	2007	HIV-1 env	JN863758
E7635	GWc	2007	HIV-1 env	JN863759
E7650	GWc	2007	HIV-1 env	JN863760
E7743	GWc	2007	HIV-1 env	JN863761

¹ County code: BF: Burkina Faso, CI: Cote d'Ivoire, GH: Ghana, GM: Gambia, CV: Cape Verde, GW: Guinea Bissau, GWc: Guinea Bissau, Caio, ML: Mali, SN: Senegal, CM: Cameroon.