Phylogeographic Study of HIV-2 Groups A and B Early Epidemics in Western Africa

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BACKGROUND

- To date ten distinct lineages of HIV-2 have been identified and appear to represent independent zoonotic transfers. These lineages have been termed groups A to I, but only groups A and B have spread in humans (Gao et al 1994, Damond et al. 2004).
- HIV-2 group A is mainly found in Western Africa and seems to have originally spread from Guinea-Bissau during the independence war (1963-1974) (Lemey et al. 2003).
- HIV-2 group B mainly predominates in Ivory Coast (Pieniazek et al. 1999)
- In France, HIV-2 represents 1 to 1.7% of all newly diagnosed HIV infections each year between 2009 and 2012 and more than 1101 HIV-2 infected patients have been included in the French ANRS CO5 HIV-2 cohort since 1994.
- Among patients identified in France, HIV-2 diversity is higher than in other Northern European countries with a higher prevalence of HIV-2 group B (35% of all identified viruses) and subtype A2 (25%). This is explained by a different immigration patterns with a strong representation of patients from Ivory-Coast, Mali, Burkina-Faso or Ghana (Damond et al. 2001, Visseaux et al 2016).

OBJECTIVES

- We explored the early spread of HIV-2 group B and subtype A2, recently described, in Western Africa using the unique French ANRS CO5 HIV-2 cohort dataset.

METHODS

- All HIV-2 *pol* sequences for which both the time of sampling and patient's country of birth was known were retrieved from public databases (n=49 and 8 for groups A and B, respectively) and the ANRS CO5 HIV-2 cohort (n=125 and 68 for groups A and B, respectively).
- All these sequences were sampled between 1986 and 2014.
- All potential recombinant sequences were identified and excluded using RDP 4.0.
- Bayesian MCMC phylogeographic reconstructions were performed for groups A and B under the best fitting combination of evolutionary, demographic and molecular clock models according to Bayes factor analysis using BEAST 1.8: GTR+G(4), Bayesian Skyline and a lognormal relaxed molecular clock model.
- The topology of the trees were consistent with maximum likelihood trees obtained using RAxML.
- Because of the large number of sequences sampled in France in the dataset, the patient's country of birth was used to model the geographical dispersion instead of the sampling country, under the assumption that infections were acquired in the home country of the patients (>85% of the patients included in the French ANRS CO5 cohort are born in West Africa).

RESULTS

- The Bayesian maximum clade credibility trees are shown in figure 1.
- The distribution of patients according to country of birth and HIV-2 clades is shown in Table 1.

- The estimated time of the most common ancestors (tMRCA) was 1945 [95% HPD 1935-53] and 1962 [1953-70] for groups A and B, respectively.

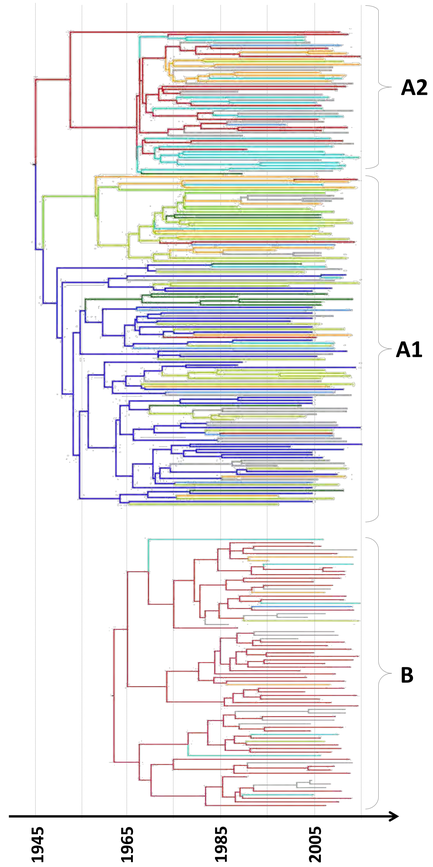

Figure 1. Phylogeographic trees obtained for HIV-2 A and B groups. These tree are time scaled and the colours of the branches depict the most probable location of the ancestors at this time, according to the colour code given in Figure 2. France is coloured in orange, all the other countries are coloured in gray.

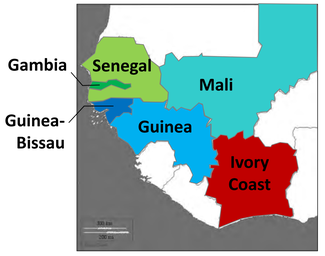

Figure 2. Colour code used in the tree for Western Africa countries.

Country	A1	A2	B	*Total*
Ivory Coast	5	11	47	*63*
Senegal	32	1	2	*35*
Guinea-Bissau	29	0	0	*29*
Mali	5	15	6	*26*
France	12	7	5	*23*
Gambia	11	1	0	*12*
Guinea	7	2	2	*11*
Cap Verde	8	0	0	*8*
Portugal	6	0	0	*6*
Cameroun	0	3	2	*5*
Ghana	1	2	2	*5*
Others	6	9	10	*25*

Table 1. Number of patients included in the final dataset according to their country of birth and HIV-2 group or subtype.

HIV-2 subtype A1

- The divergence between subtypes A1 and A2 occurred at the very beginning of the epidemic in 1947 [1937-58].
- Subtype A1, mainly present in patient born in Senegal, Gambia, Guinea-Bissau and Guinea, experienced an early diversification since 1947 [1937-58] with two distinct sub-epidemics: the main one emerging in Guinea-Bissau and a second one in Senegal, suggesting that the virus was already present in Senegal before the Guinea-Bissau independence war. Several subsequent transmission events from Guinea-Bissau to Senegal were also observed during the time scale of this war.
- The HIV-2 A1 sub-epidemic in Guinea Bissau presented a regular expected growth phase after its emergence. On the contrary, most of the nodes observed in the Senegalese sub-epidemic are mainly observed after 1963 [1956-71].

HIV-2 subtype A2

- Subtype A2, mainly present in patients born in Ivory Coast and Mali, presented a similar topology than the A1 Senegalese sub-epidemic with tMRCA in 1955 [1947-63] and most of the spreading occurring latter, after 1962 [1951-69].
- Subtype A2 initially spread in Ivory Coast (posterior probability >67%), in consistency with the location of the *Sooty mangabey* colonies at the origin of the epidemic. The introduction of this subtype in Mali was observed in 1965 [1961-70].

HIV-2 group B

- HIV-2 group B is mostly restricted to Ivory Coast and all deep nodes of the tree are located in this country (posterior probability >99%). All the other countries are dispersed across the whole group B tree and no single transmission event can be identified from Ivory Coast to any other country.

DISCUSSION

- This phylogeographic study is the first to reconstruct the early subtype A2 and group B dispersal and allows a better understanding of the HIV-2 early epidemics spreading pattern in West Africa.
- The tMRCA observed for HIV-2 group A, 1945 [1935-53], is concordant with previous estimations done by Faria et al. (1938[1928-45]) or Lemey et al. (1940 [1924-56]) on *env* and *gag* genes.
- The mean tMRCA observed for HIV-2 group B, 1961 [1952-70] overlap with the previous calculation done by Lemey et al. but is slightly more recent (1945 [1931-59]).
- Both A2 and B clades firstly emerged in Ivory Coast and diversified latter than subtype A1 suggesting that local historical or socio-demographic events may have triggered the dispersal of these viral strains.
- An early fonder effect was identified in Senegal and occurred before the Guinea-Bissau independence war. This suggest that HIV-2 group A was already circulating in these two countries before the independence war of Guinea Bissau that greatly contributed to further dispersal of HIV-2 within and outside West Africa (Lemey et al 2003).
- All these observations need to be confirmed by the *env* gene analysis within the French ANRS CO5 cohort dataset. This new dataset will be helpful as more *env* sequences are publicly available contrary to *pol* gene, especially for Ghana where the group B is highly represented, and as *env* is well known to exhibit more temporal signal than *pol*.

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