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Circulation of Multiple Patterns of Unique Recombinant Forms B/CRF02_AG in France

Precursor Signs of the Emergence of an Upcoming Circulating Recombinant Form CRF_B/02_AG?



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AIDS 2011, in press



Travaux soutenus par l'Agence Nationale de Recherche contre le SIDA

BACKGROUND

HIV-1 group M is characterised by substantial genetic diversity, and includes nine subtypes, more than 45 CRFs, and numerous Unique Recombinant Forms (URFs).

In France, the epidemic is characterised by :

-predominance of subtype B strains,

- increasing prevalence of non-B subtypes (fig.1), CRF02_AG being the most prevalent,

- increasing at-risk behaviour in the MSM population.

The high prevalence and co-circulation of B and CRF02_AG strains in this population raise the possibility that recombinant forms might emerge and spread.

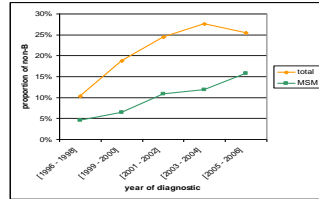


Fig.1: evolution of the proportion of non-B strains among primo-infections in France (adapted from Chaix et al, 2009)

METHODS

Screening for subtyping discordances in different regions of the genome

Near full length sequencing and pattern characterization

Searching for parental strains or minor recombinants using Single Genome Analysis

Analysis of the phylogenetic relationships between the B/CRF02 recombinants

RESULTS

Seven samples were selected from seven patients, of whom five are MSM (tab.1)

patient	sex	age (years)	origin	risk group	year of diagnosis of HIV infection	year of sampling	therapeutic status	CD4 (cells/mm ³)	RNA viral load Log copies/ml	URF ^a and size (bp)	nb of SGA sequences ^c
P1	M	67	France (caucasian)	homosexual	2008	2008	naive	490	5.8	URF1 : 8659	8
P2	F	46	France (caucasian)	IDU	2004	2009	naive	504	3.7	URF2 : 8891	11
P3	M	38	France (caucasian)	homosexual	2006	2009	treated	549	5	URF3 : 8295	8
P4	M	38	France (caucasian)	homosexual	2002	2002	naive	5.1	URF4 : 8424	10	
P5	M	25	France (caucasian)	homosexual	2010	2010	naive	159	5.1	URF5 : 8396	10
P6	M	39	France (caucasian)	homosexual	2006	2006	naive	391	5.2	URF6 : 9008	NA
P7	M	32	France (caucasian)	homosexual	2006	2006	naive	397	6.2	URF7 : 9158	NA

^a: not available

^b: URF identified in the patient

^c: number for a given URF of sequences obtained by SGA for breakpoint confirmation

NA: not applicable

Tab.1: Characteristics of the seven patients from whom the samples were selected, and of the corresponding URFs characterized

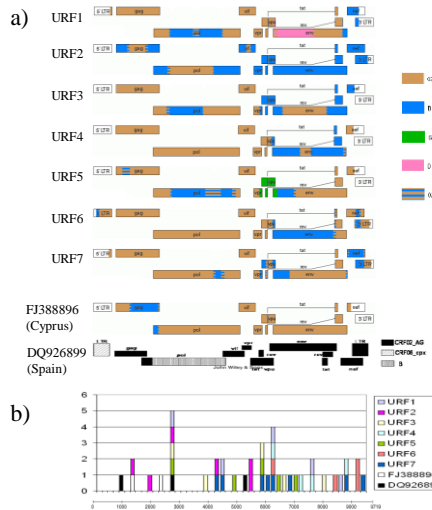


Fig.2: Recombination patterns of the 7 new URFs and the 2 previously described (a) and breakpoints distribution along the genome (b)

There was no evidence of parental or minor recombinant strains circulation, although polymorphism was observed for all the strains tested (fig. 3).

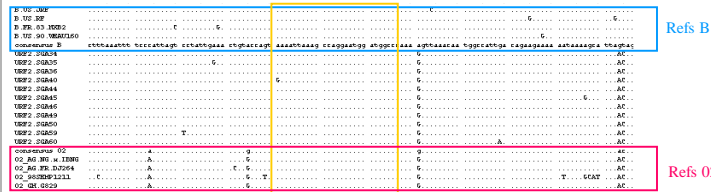
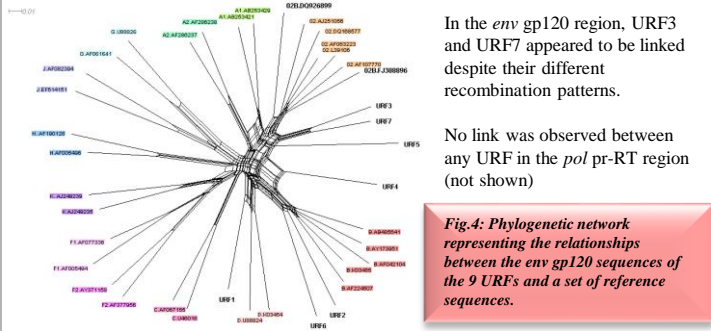


Fig.3: Example of SGA results for URF2. The 11 sequences obtained are aligned with a set of subtype B (blue box) and CRF02 (red box) reference sequences to determine their recombination patterns; the yellow box indicates the region where recombination occurred for these SGA sequences.



In the env gp120 region, URF3 and URF7 appeared to be linked despite their different recombination patterns.

No link was observed between any URF in the pol pr-RT region (not shown)

Fig.4: Phylogenetic network representing the relationships between the env gp120 sequences of the 9 URFs and a set of reference sequences.

CONCLUSIONS

The complexity of the molecular epidemiology is growing in France due to the raise of non-B strains prevalence and to subsequent recombinations. The predominant forms, subtype B and CRF02, are co-circulating in the MSM population and frequent co-infections led to local emergence of several URFs, one of those (URF7) being linked with a cluster of CRF02_AG sequences identified in the MSM population of Paris.

The absence of parental strains suggests direct transmission of these strains, indicating that they could spread in particular within this population. A surveillance is needed to determine if this dynamic could lead to the genesis of a new CRF_B/CRF02_AG in France.