

Clade diversity of HIV-1 subtype A *pol* gene in Côte d'Ivoire: evidence of underestimated rate of recombinant form

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Introduction

- Sub-Saharan Africa is more heavily affected by HIV and AIDS.
- An estimated 27.2 million people were living with HIV at the end of 2006 (UNAIDS, 2006).
- With an estimated rate of 4.7%, Côte d'Ivoire has the highest infection rate in West Africa.
- The group M represents the majority of HIV-1 viruses (McCutchan, 2000; Peeters & Sharp, 2000).
- This group has been divided into nine subtypes (A-D, F-H, J, and K).
- Subtype A has been subdivided into four sub-subtypes A1, A2, A3 and A4 (Gao *et al.*, 2001; Meloni *et al.*, 20004a, 20004b)

Introduction

- Reconstructions of ancestral HIV sequences or simple consensus sequence could be used to develop vaccine strains (Gaschen *et al.*, 2003; Nickle *et al.*, 2003).
- It is therefore crucial to continuously monitor the genetic diversity of HIV on the global perspective.
- The *Pol* gene is the most conserved region of HIV-1.
- This gene has been a target of antiretrovirals.
- Although most conserved, this gene allow phylogenetic classification (Hue *et al.*, 2004).

Introduction

- Since several years, HIV vaccine trial programs are on rise in Côte d'Ivoire.
- Many HIV-1 strains of this country have been sequenced.
- These sequences are composed of
 - 75% AG
 - 11% A
 - 10% (A1, A2, A3)
 - <5% others
- Many new subtype A sequences are not classified at the sub-subtype level.

Objectives

- Identify different lineage within the HIV-1 unclassified subtype A.
- Determine their phylogenetic relationship with the other sub-subtypes

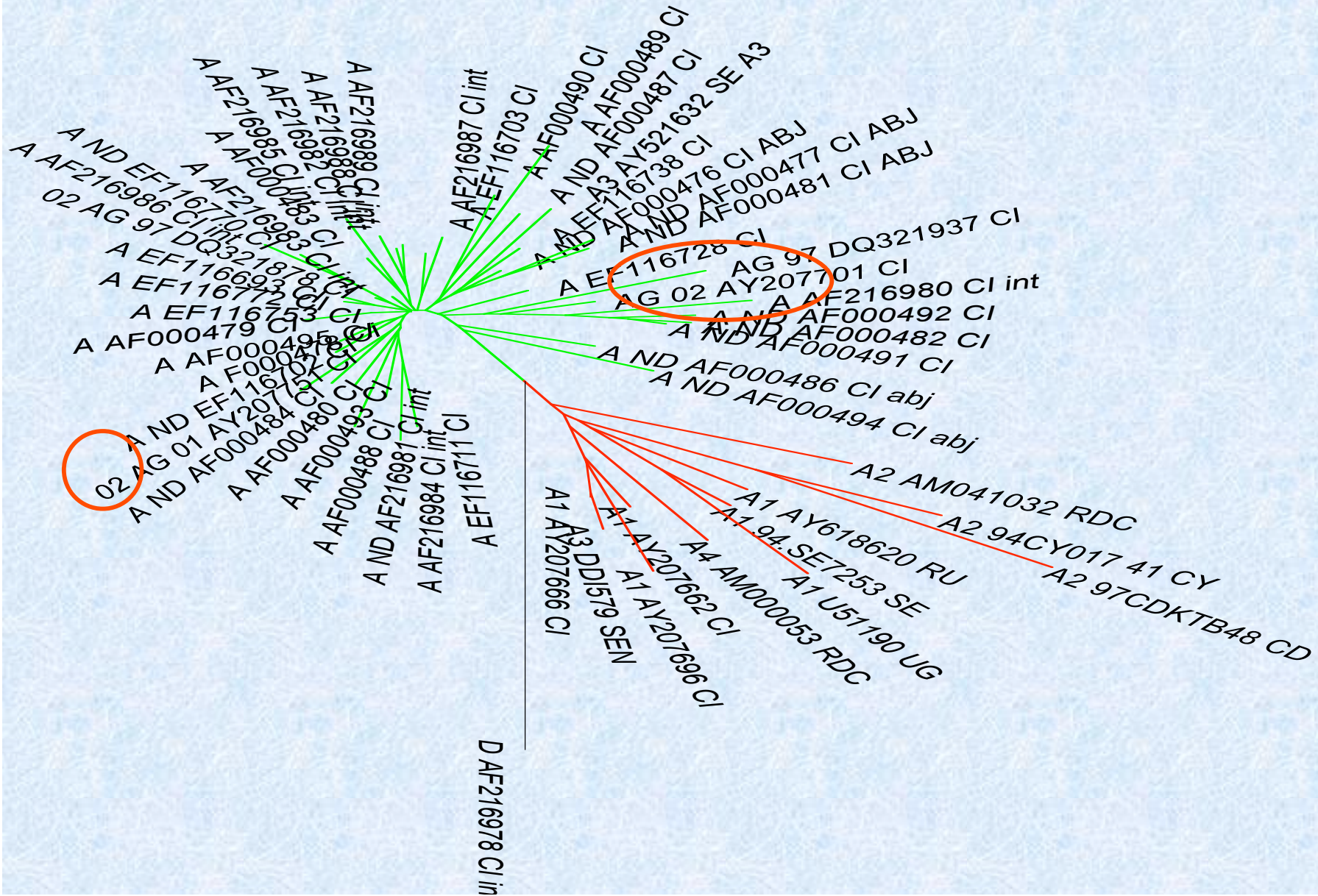
Methods

- Sequences of HIV-1 *pol* gene from Côte d'Ivoire were extracted from NCBI GenBank, and Los Alamos database.
- All these sequences were aligned using ClustalW program (Thompson *et al.*, 1994).
- Rega (de Oliveira *et al.*, 2005) was used for subtype identification.
- Simplot (Ray, 1999) was used for Bootscan analysis.

Methods

- A maximum-likelihood tree of *pol* gene sequences was produced by DNAML program in the PHYLIP.
- Pairwise genetic distances were calculated by using the DNADIST with F84 model of evolution
- Splitstree (Huson & Bryant, 2006) was used to draw phylogenetic network.

Results



Results

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1 A_AF000476																			
2 A_AF000477	0.017																		
3 A_AF000481	0.023	0.02																	
4 A_AF000490	0.031	0.045	0.045																
5 A_AF000488	0.031	0.041	0.034	0.045															
6 A_AF000494	0.038	0.049	0.049	0.052	0.056														
7 A_AF000489	0.038	0.048	0.041	0.041	0.056	0.056													
8 A_AF216981	0.035	0.045	0.045	0.024	0.031	0.052	0.059												
9 A_AF216984	0.031	0.042	0.042	0.052	0.035	0.056	0.056	0.024											
10 A_AF216989	0.024	0.034	0.035	0.038	0.042	0.042	0.049	0.028	0.038										
11 02_AG_02_A	0.024	0.035	0.035	0.031	0.035	0.043	0.049	0.028	0.039	0.024									
12 02_AG_DQ321880	0.021	0.031	0.024	0.027	0.024	0.035	0.045	0.024	0.035	0.021	0.01								
13 A_EF116772	0.031	0.041	0.042	0.038	0.034	0.038	0.056	0.027	0.038	0.031	0.014	0.014							
14 A_EF116728	0.028	0.038	0.031	0.041	0.045	0.038	0.052	0.035	0.042	0.024	0.017	0.021	0.017						
15 A_EF116703	0.031	0.041	0.042	0.041	0.042	0.056	0.052	0.037	0.042	0.034	0.024	0.027	0.017	0.034					
16 A1_AY618620	0.084	0.098	0.098	0.093	0.098	0.089	0.116	0.076	0.103	0.071	0.073	0.072	0.08	0.08	0.089				
17 A1_AY207698	0.082	0.093	0.093	0.082	0.078	0.094	0.109	0.067	0.09	0.07	0.064	0.067	0.071	0.071	0.082	0.058			
18 A2_AM04103	0.071	0.086	0.086	0.089	0.09	0.075	0.105	0.071	0.086	0.071	0.076	0.071	0.067	0.067	0.093	0.071	0.071		
19 A3_DDI579	0.078	0.089	0.089	0.085	0.089	0.09	0.105	0.071	0.093	0.067	0.061	0.063	0.067	0.067	0.071	0.05	0.031	0.067	
20 A4_AM00053	0.082	0.093	0.093	0.089	0.093	0.093	0.108	0.071	0.093	0.07	0.064	0.067	0.071	0.071	0.082	0.062	0.059	0.078	0.045

Discussion

- Toni *et al.* (2005) documented that the majority (80%) of the HIV-1 strains were CRF02_AG and about 11% could not be clearly assigned to a known sub-subtype or CRF.
- Our data suggest that all the unclassified subtypes A in Côte d'Ivoire are recombinant strains.
- The genetic distance between subtype A and the reference sequences is concordant with the data of Robertson *et al.* (1999)
- This study is particularly important, as precedent investigations have underestimate recombination forms in Côte d'Ivoire.

Discussion

- Rega and Simplot could not identify unclassified subtypes A, probably because of the short fragments used.
- It is likely that these sequences don't contain sufficient phylogenetic signals for subtype determination by these programs.

Conclusion

- Recombinant forms have been underestimated in Côte d'Ivoire.
- CRF are increasing in the population and may constitute >90% of HIV-1 viruses in Côte d'Ivoire.
- These results confirm the constant evolution of HIV-1 and indicate the relevance of a continuous molecular monitoring.
- It is important to explore the pattern of evolution of CRF in Côte d'Ivoire and other region of West Africa.

What's next?

- Understand why recombinant forms are so high in West Africa compared to other region of Africa.
- Understand why recombination often occur between subtypes A and G in West Africa.

Aknowledgement

- Centre Suisse de Recherches Scientifiques (CSRS) en Côte d'Ivoire
- Université d'Abidjan Cocody

