Evidence of Intra-Familial Transmission of an HIV-1 M/O Intergroup Recombinant Virus

Paul-Alain Ngoupo, Serge Alain Sadeuh Mba, Fabienne de Oliveira, V Ngono, L Ngono, Patrice Tchendjou, Véronique Penlap Beng, Thomas Mourez, Richard Njouom, Anfumbom Kfutwah, et al.

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Ngoupo PA[1,2,3], Sadeuh-Mba SA[1], De Oliveira F[3], Ngono V[1], Ngono L[1], Tchendjou P[1], Penlap Mbeng V[2], Mourez T[3], Njouom R[1], Kfutwah A[1] and Plantier JC[3]

[1] Centre Pasteur of Cameroon, Yaounde, Cameroon ; [2] University of Yaounde I, Yaounde, Cameroon ; [3] Rouen University Hospital, Rouen, France

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BACKGROUND

HIV-1 is divided into four groups: M (major), O (outlier), N (non-M- non O) and P. HIV-1 groups M and O co-circulate in Cameroon and dual infections as well as HIV-1 M/O intergroup recombinant viruses have been reported in some patients [1-3]. Recent data has described infection with HIV-1 M/O intergroup recombinant virus in the absence of dual infections thereby suggesting a direct transmission of the recombinant virus [4]. In this study, we described and characterized an HIV-1 M/O intergroup recombinant virus in the absence of dual infection in a couple living in Cameroon . We therefore provide for the first time evidence of a direct transmission of an HIV-1 M/O intergroup recombinant virus from one person to another.

METHODS

1- Patients: and samples:

- **REC003 (Husband)**: October 2012, March 2013 and September 2013.
- **REC024 (Wife):** April and September 2013

2- Serological and molecular characterization

- **HIV serotyping and Viral load**: Prior to viral load analysis, each sample was subjected to HIV serotyping using envelope (V3 and gp41) peptides. Viral loads were further determined using HIV-1 non specific, HV-1 /M and HIV-1/O specific techniques.
- **HIV-1 group M and O specific PCRs**: Presence of potential recombinant virus was investigated using HIV-1 M and HIV-1 O specific PCRs targeting the Protease (PROT), Reverse transcriptase (RT), Integrase (INT) and envelope (gp41) genes of HIV-1 groups M and O.
- **PCR for recombination break point**: The previously reported recombination hotspot in the vpr gene was investigated using RT-nested PCRs.
- **Complete genome analysis:** Near full length genome sequences of the viruses detected in both spouses were determined by amplification and sequencing of seven partially overlapping sub-genomic regions.
- **Phylogenetic and recombination profile** analyses were performed to investigate the genetic relatedness between viruses from both spouses

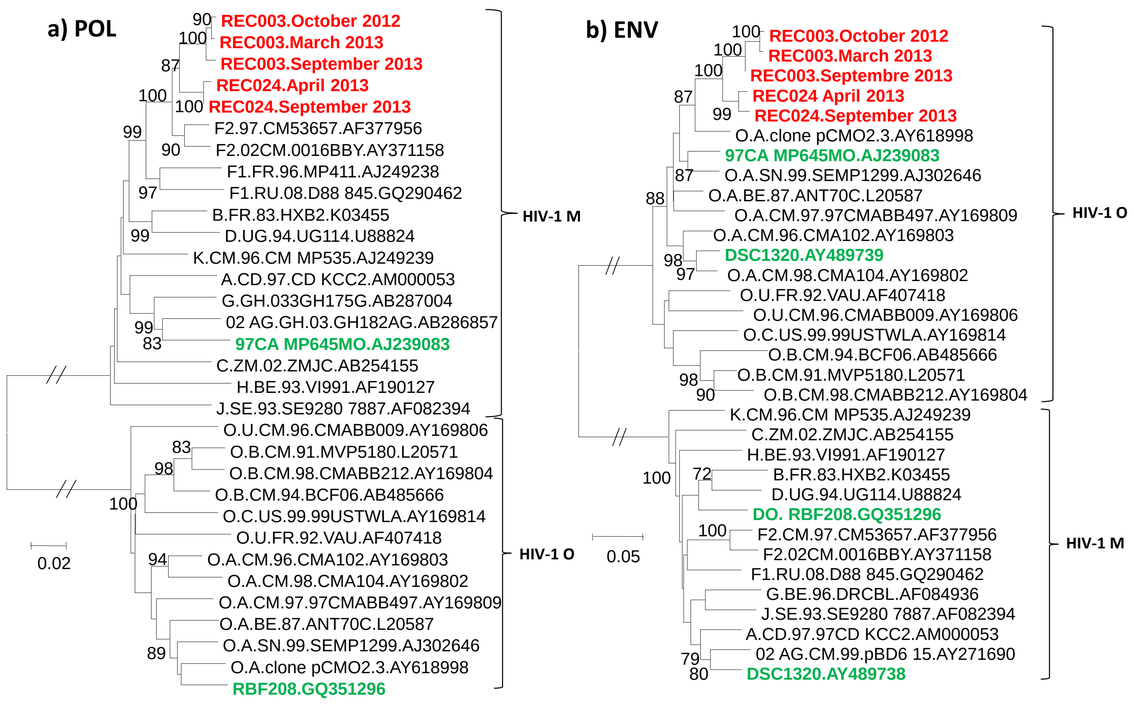
RESULTS

Table 1: Summary of HIV-1 serotyping, viral load and PCRs results

		REC003			REC024	
Sample collection date		October 2012	March 2013	September 2013	April 2013	September 2013
ART		None	3 months	9 months	None	None
Serotyping		HIV-1/ O	HIV-1/ O	HIV-1/ O	HIV-1/ O	HIV-1/ O
Abbott Real-time HIV-1		5.4 log	3.1 log	2.7 log	3.1 log	3.0 log
Group M specific PCR	PROT	+	+	+	+	+
	RT	+	+	+	+	+
	INT	+	+	+	+	+
	GP41	-	-	-	-	-
Group O specific PCR	PROT	-	-	-	-	-
	RT	-	-	-	-	-
	INT	-	-	-	-	-
	GP41	+	+	+	+	+
vpr PCR	MM	-	-	-	-	-
	OO	-	-	-	-	-
	MO	+	+	+	+	+
	OM	-	-	-	-	-

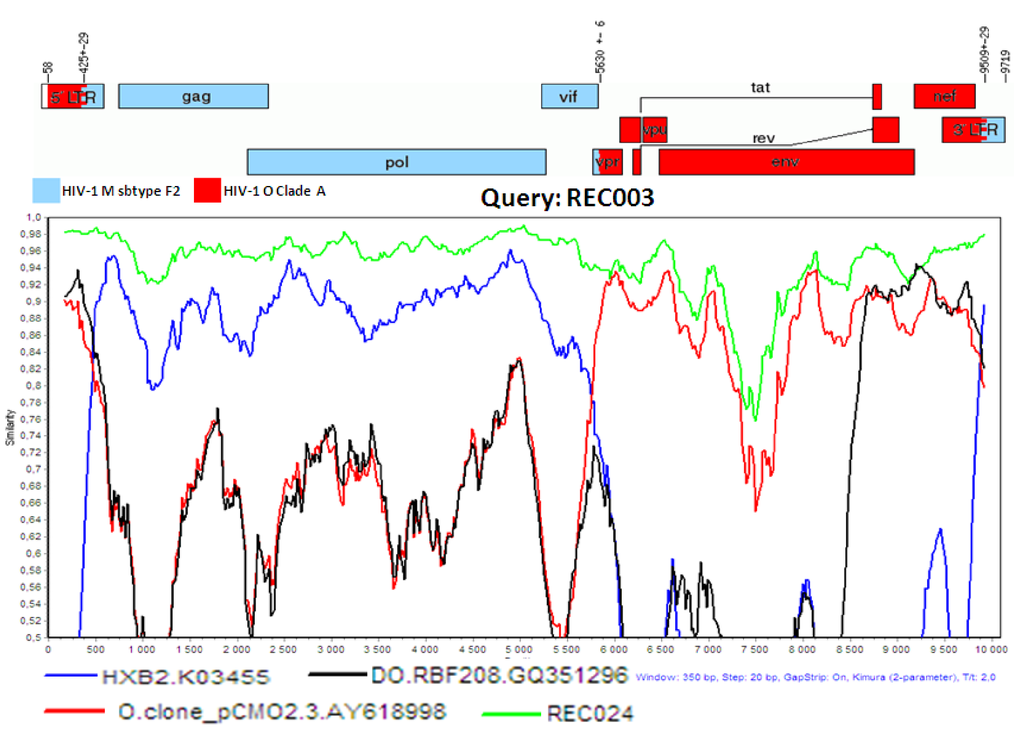
HIV serotyping (envelope peptides) indicated that both REC003 and REC024 were reactive with only peptides of HIV-1 group O.
Using group-specific RT-nested PCRs, we generated HIV-1 M amplicons in the POL (PROT, RT and INT) region from both REC003 and REC024 while HIV-1 O amplicons were obtained ENV (gp41) region. In vpr only the PCR using hetelogous primers MO yields a positive results. These results thus indicated the presence of a recombinant virus in both patients.

Phylograms of the POL and ENV derived sequences



POL and ENV derived sequences of both REC003 and REC024 viruses confirmed that the POL portion derived from HIV-1 M (subtype F2) and ENV portion from HIV-1 O (clade A) thus confirming the presence of an HIV-1 M/O recombinant virus in both patients. These sequences featured a close relationship to one another and therefore suggesting that they belong to a unique genetic lineage.

Simplot and genome map of the HIV-1 M/O recombinant



Both near complete genomes featured a close relatedness across the entire genome, with the least similarity in the Env region, and displayed the same breaking points located within the *vpr* gene and LTR region. The sequences of the virus genome of REC003 and REC024 displayed an M-O mosaic structure with the gag-Pol-Vif-5'vpr portion of the recombinant derived from HIV-1 group M and the 3'vpr-vpu-env-tat-nef potion from HIV-1 group O.

CONCLUSION

- health importance of transmitting these HIV-1 M/O recombinant virIn this study, we observed for the first time that HIV-1 M/O intergroup recombinant viruses could be transmitted from one person to another.
- This intergroup recombination could have important consequences in HIV diagnosis and follow-up. HIV-1 group O has been shown in a majority of cases to be naturally resistant to NNRTI and to present false negative results with some serological tests.
- The presence of HIV-1 M/O recombinant viruses in patients could also lead to false results with some viral load quantification techniques.
- The genetic diversity and public uses in such areas where both viruses (HIV-1 groups M and O) are endemic cannot be overemphasized.

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