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

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BACKGROUND

The Human Immunodeficiency Virus type 1 (HIV-1) genetic diversity includes 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. Here we 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

Consecutive samples were obtained from a couple identified during routine HIV viral load analysis. The blood collection dates were as follows:

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

- 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: These samples were subsequently screened for the presence of potential recombinant virus 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

1. HIV-1 serotyping and viral load

	REC003			REC024	
Sample collection date	October 2012	March 2013	September 2013	April 2013	September 2013
HAART	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 (Integrase gene)	5.4 log	3.1 log	2.7 log	3.1 log	3.0 log
Generic HIV viral load (LTR gene)	ND	3.5 log	2.8 log	3.5 log	3.3 log
"In house " group O viral load (Integrase gene)	ND	<1.6 log	<1.6 log	<1.6 log	<1.6 log

HIV serotyping (envelope peptides) indicated that both REC003 and REC024 were reactive with only peptides of HIV-1 group O.
Viral load was undetectable with HIV-1 O specific technique ("In house " group O viral load) but detectable viral loads were obtained with HIV-1 M specific (Generic HIV Viral load) or HIV-1 non specific (Abbot Real-time HIV-1)) techniques.

2. Molecular characterization

		REC003			REC024	
Sample collection date		October 2012	March 2013	September 2013	April 2013	September 2013
Serotyping		HIV-1 O	HIV-1 O	HIV-1 O	HIV-1 O	HIV-1 O
Group M specific PCR	**PROT**	+	+	+	+	+
	RT	+	+	+	+	+
	INT	+	+	+	+	+
	GP41	-	-	-	-	-
Group O specific PCR	PROT	-	-	-	-	-
	RT	-	-	-	-	-
	INT	-	-	-	-	-
	GP41	+	+	+	+	+
vpr PCR	MM	-	-	-	-	-
	OO	-	-	-	-	-
	MO	+	+	+	+	+
	OM	-	-	-	-	-

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.

3. Phylogenetic analysis

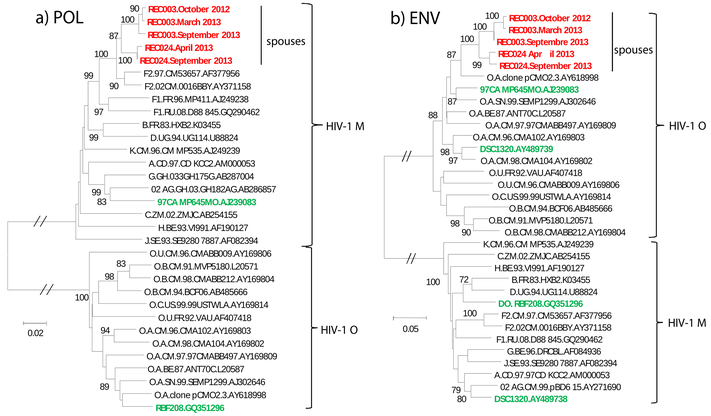


Figure 1: Pylogenetic trees of POL and ENV derived sequences

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.

4. Recombination profile of the HIV-1 M/O Recombinant

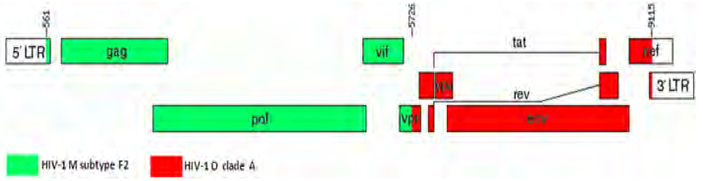


Figure 2: Schematic representation of the genomic structure of the recombinant virus found in the spouses (REC003 and REC024)

The near complete sequences of the virus genome of REC003 and REC024 displayed an M-O mosaic structure with the same break point located within the vpr gene.

CONCLUSION

- In 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 health importance of transmitting these HIV-1 M/O recombinant viruses in such areas where both viruses (HIV-1 groups M and O) are endemic cannot be overemphasized.

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