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Sequence Note

Identification of a Highly Divergent HIV Type 2 and Proposal for a Change in HIV Type 2 Classification

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ABSTRACT

We report the complete genome sequence of a highly divergent strain of human immunodeficiency virus type 2 (HIV-2), 96FR12034, identified in France from a patient of West African origin. This lineage, H, represents only the third definitive instance of a monkey-to-human transfer of SIVsm that has given rise to pathogenic HIV-2. As the different "subtypes" of HIV-2 are analogous to the different groups of HIV-1 we propose that HIV-2 subtypes henceforth by renamed groups in agreement with the HIV Nomenclature Committee. The single-strain lineages C to G and the 96FR12034 lineage identified here should be considered only as putative groups until related strains are identified that confirm circulation of these viruses in the human population.

INTRODUCTION

PHYLOGENETIC ANALYSIS has shown that human immunodeficiency virus type 2 (HIV-2) is closely related to simian immunodeficiency virus (SIVsm) isolated from the sooty mangabey (*Cercocebus torquatus atys*), a small monkey native to West Africa.[1] The several strains of SIVsm that have been reported so far show extensive genetic divergence. In fact, single troops of wild-living sooty mangabeys can harbor variants exhibiting levels of genetic distance that are comparable to those observed across the entire SIVsm/HIV-2 clade.[2] The range of the sooty mangabey closely matches HIV-2 endemicity in West Africa and to date seven different HIV-2 subtypes (A through G) have been reported,[3–5] each believed to represent a distinct cross-species transmission of the virus from its mangabey reservoir.[1,4,6] However, only two HIV-2 subtypes, A and B, show clear evidence of having established themselves as human epidemics.

The other subtypes (C through G) have not been identified in known symptomatic HIV-2-infected individuals. Some of these single-strain subtype viruses show close similarity to SIVsm recovered from wild-living or pet sooty mangabeys from the same local region,[2,6] highlighting the close links between phylogeny and geography in the SIVsm/HIV-2 radiation. The existence of these rare and unique HIV-2 strains has led to the suggestion that they may represent epidemiological "dead ends," lineages that have failed to establish a successful chain of infection after crossing into the human population from the monkey reservoir.[7]

Here we characterize a new and pathogenic HIV-2, 96FR12034, which forms a new lineage that we name H. As the different subtypes of HIV-2 are most likely to have arisen by independent cross-species transmission events, analogous to the different groups of HIV-1,[1] we propose to resolve this inconsistency in HIV nomenclature by renaming the HIV-2 subtypes as "groups."

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MATERIALS AND METHODS

Patient history

During a previous study on HIV-2 plasma RNA quantification, a partial sequence of a strain from a male patient originating from Ivory Coast (from a town near the Liberian border) indicated that the strain was highly divergent to other HIV-2 strains.[8] The patient, who arrived in France in mid-1995, was 31 years old when diagnosed with HIV in January 1996. He is presumed to have been infected through heterosexual contact. It is not known whether his present partner is also infected; she declined HIV testing. At the time of diagnosis, he had a CD4 cell count of 243×10^6/liter (18%) and was suffering from cerebral neurocystercosis. He received successive antiretroviral therapies from 1996 to 1997.[8] In 1997, a binucleotiside RT-inhibitor treatment was initiated, with protease inhibitors being introduced in 1999 (d4T/3TC/IDV/RTV). Cellular viremia and plasma viral load remained positive throughout bitherapy, and HIV-2 plasma viral load ranged between 10^3 and 10^4 copies/ml until the introduction of protease inhibitors.[8]

Virus amplification

To better characterize this HIV-2 strain (denoted "96FR-12034"), its complete genome was sequenced. Proviral DNA from fresh peripheral blood mononuclear cells (PBMC) collected at the initiation of treatment in 1996 was collected and extracted with phenol-chloroform, then precipitated with ethanol, and quantified spectrophotometrically. HIV-2 DNA was amplified by nested polymerase chain reaction (PCR) with first-round long (XL) PCR as previously described.[8] The following primer pairs were designed for use in the first amplification step: ENVF (5′)/GAGOG AS1 (3′), LTR1 (5′)/LTR2 (3′).[8] Details of the sequences of the primer pairs used for first-round and nested PCR are given in Table 1. The PCR products were purified using the Qiagen gel extraction kit (Chatsworth, CA). Sense and antisense DNA templates were then used as matrices for the corresponding primers in the Big-Dye Terminator kit (Applied Biosystems, Foster City, CA). Sequencing reactions were run on an automated DNA sequencer (Applied Biosystems 373A).

Phylogenetic analysis

The resulting full-length sequence was aligned against reference sequences from the LANL HIV Sequence Database[9] using the profile alignment option in CLUSTAL W[10] followed by some minor adjustments and removal of sites with gaps. Phylogenetic trees were reconstructed from the complete genome alignment (8643 sites), a partial *gag* alignment (760 sites from a region for which HIV-2 C, D, and E subtype sequences were available), a partial *pol* alignment (749 sites from a region for which HIV-2 C and D subtype sequences were available), and a partial *env* alignment (450 sites from a region for which HIV-2 C and D subtype sequences were available). All phylogenetic trees were reconstructed using PAUP* version 4.0[11] under a general time-reversible (GTR) model with gamma-distributed rate heterogeneity among sites and a proportion of invariant sites. For each alignment a neighbor-joining tree was inferred and used to estimate the parameters of the nucleotide substitution process. These parameters were then used in a maximum likelihood (ML) heuristic search using tree bisection-reconnection (TBR) branch-swapping. The parameters were then reestimated on the resulting tree. Bootstrapping was performed using 1000 neighbor-joining trees, with distances estimated using maximum likelihood.

RESULTS

96FR12034 most likely represents an independent cross-species transmission of HIV-2

The genomic organization of 96FR12034 was identical to previously described HIV-2s, with typical *vpx* and other regulatory genes. The genetic distance between 96FR12034 and several related viruses for which full genomic sequences were available was calculated across the genome with a diversity plot (Fig. 1). 96FR12034 was highly divergent across all genomic regions. Note that the full-length sequences from subtypes C–E were not available for this comparison.

The phylogenetic analyses (Figs. 2 and 3) confirmed the divergent nature of 96FR12034, but also revealed a significant relationship between 96FR12034 and the HIV-2 subtype C strain 2238, for which only three short *gag*, *pol*, and *env* sequence fragments were available for comparison. When these fragments were concatenated and analyzed, the resulting ML phylogeny indicated that although the split between them is very deep, 2238 and 96FR12034 form a monophyletic clade with strong (100%) bootstrap support (Fig. 3). Analyzed separately, the ML trees for the *gag* and *pol* fragments both strongly supported this clustering, while the *env* tree did not; however, the neighbor-joining tree for the *env* fragment did place 2238 and 96FR12034 together (data not shown).

DISCUSSION

Given the support for a 2238/96FR12034 grouping, a key question is whether the most recent common ancestor of these strains was a human virus or a monkey virus. In other words, is 96FR12034 a second "subtype C" virus, or did it enter the human population after an independent cross-species transmission event? Although it is impossible, given these data, to rule out the hypothesis that 2238 and 96FR12034 shared a common ancestor in humans, the fact that these strains are apparently extremely rare yet separated by considerable genetic divergence, relative to intrasubtype A or B comparisons (Fig. 3), argues in favor of separate origins. The uncorrected pairwise distance between 96FR12034 and 2238 from the concatenated *gag–pol–env* fragment alignment, at 15.5%, was outside the ranges of pairwise distances observed among the more numerous HIV-2 subtype A or B sequences (4.6–11.2% and 7.9–11.3%, for HIV-2 A and B, respectively). Assuming roughly equal evolutionary rates among different HIV-2s, a single cross-species transmission of the ancestor of 2238 and 96FR12034 would suggest that this hypothetical "subtype C" lineage had been evolving in humans considerably longer than either subtypes A or B, but had remained at a much lower prevalence than either, yet had exhibited greater genetic variation than HIV-2 A or B after a single comparison. Given that the most recent common ancestor of HIV-2 subtypes A and B has been estimated to have existed in 1940 ± 16 and 1945 ± 14, respectively,[12] it seems unlikely that a such rare and hypothetical "subtype C" lineage would have persisted for this length

TABLE 1. SEQUENCES OF THE PRIMERS USED FOR HIV-2/96FR12034 GENOME AMPLIFICATION

	Name		*Position*		*Reference*
XL PCR primers				1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4	
	LTR1	5′	624–646	T T C C C T G C T R G A C T C T C A C C A G	Damond *et al.* (1998)[a]
	LTR2	3′	9496–9515	A C A T C C C T T C C A G T C C C C C	Damond *et al.* (1998)[a]
	ENVF	5′	8818–8845	T A T A G G C C W G T T T T C T C T T C C C C Y C C C	Damond *et al.* (1998)[a]
	GAGOG AS1	3′	1619–1643	T T C A G G C A C T C T C A G A A G G C	Grankvist *et al.* (1992)[b]
Nested PCR and sequencing primers					
	EB0	5′	6865–6890	A T A C A G T G C T T R C C A G A C A A T G A T G	Damond *et al.* (1998)[a]
	EB6	3′	7501–7521	C C A T T R A A G C C A A A C C A W G T	Damond *et al.* (1998)[a]
	EB2	5′	7338–7360	T C A T G T G A Y A A R C A Y T A T T G G G	Damond *et al.* (1998)[a]
	EB5	3′	7861–7881	C T C C T C T G C A G T T A G T C C A C	Damond *et al.* (1998)[a]
	EB7	5′	7705–7722	C C Y A G G C A A G C A T G G T G	Damond *et al.* (1998)[a]
	ENVE	3′	8472–8492	G C A C A T C C C C A T G A A T T T A G	Damond *et al.* (1998)[a]
	ENVA	5′	8248–8281	G C T A G G G T T C T T G G G T T T T C T C G C R A C A G C A G G	Gao *et al.* (1994)[c]
	ENVB	3′	8969–8999	C A A G A G G C G T A T C A G C T G G C G G A T C A G G A A	Gao *et al.* (1994)[c]
	ENVF	5′	8818–8845	T A T A G G C C W G T T T T C T C T T C C C C Y C C C	Damond *et al.* (1998)[a]
	ENVG	3′	9119–9143	C T T C T T G G A T C C A C T C G C A C C C A T	Damond *et al.* (1998)[a]
	LTR9432	5′	491–513	A G G A G C T G G T G G G G A A C G C C C T	In house
	GAG OG S1 INV	3′	1095–1118	A G T T T C T C G C G C C C A T C T C C C A C	In house
	DR ENV1 5′	5′	7054–7069	T A A C A G G A A C A G C A A C A A C A A C A C C	In house
	GAG OG S1	5′	1095–1118	G T G G G A G A T G G G C G C G A G A A A C T	Grankvist *et al.* (1992)[b]
	GAG OG AS1	3′	1619–1643	G G A T T T C A G G C A C T C T C A G A A G G C	Grankvist *et al.* (1992)[b]
	GAGOG AS1 INV RAC	5′	1616–1640	C C A G G A T T T C A G G C A C T C T C A G A G	In house
	GAG B	3′	2137–2169	C C T A C T C C C T G A C A G G C C G T C A G C A T T T C T T C	In house
	GAG B DR	5′	2138–2156	G A A G A A A T G C T G A C G G C C T	In house
	RTC DR INV	3′	2862–2882	G A T T G G G G T G T C T C C T G T C A	In house

X410	5′	2636–2657	C A C C T C A A T T C T C T C T T T G G A	In house
RT4	3′	4054–4084	T C C C C A A A T G A C T A G T G C T T C T T T T C C T A T	Gao *et al.* (1994)[c]
PFD INV	3′	5283–5304	C T G C C T T C T C T G A A A T A G A C C	In house
RT SEQ1	5′	3621–3642	G G A T G G G C T A T G A A C T A T G G C	In house
RT SEQ2	3′	4585–4605	G C C T A A T T C C C T G A C T C A C C	In house
POL OG 450	5′	5055–5078	G G A G T A G T A G A A G C A A T G A A T C A	Grankvist *et al.* (1992)[b]
DR POL2	3′	5453–5474	T C T C G G C A C C C T C C A A G T T G G	
POL OG 479	3′	5350–5373	C C T A C C T T G A C T A G G A C T G C T C C	Grankvist *et al.* (1992)[b]
POL OG 479 INV	5′	5350–5373	G G A G C A G T C C T A G T C A A G G T A G G	Grankvist *et al.* (1992)[b]
DR ENV1	3′	7054–7069	G G T G T T G T T G T T G C T G T T C C T G T T A	In house
DR POL3	5′	6002–6024	G C A G T G C A A C A T C T T C C C A G G G	In house
DR TAT1	3′	6471–6491	T T G A G T G C C G A C A T C C C C C T	In house
DR ENV0	5′	6798–6819	A T A C C T G C A T G G A G G A A C G C G	In house
DR ENV1	3′	7054–7069	G G T G T T G T T G T T G C T G T T C C T G T T A	In house
ENV4	5′	6945–6969	A G T A A C A G A G C A A G C A G T G G A A G A	In house
ENV3	3′	7376–7409	T A A C A G A G C A T A G C C T G G C G G T G	In house
SLTR5	3′	10100–10124	A C C T G C T A G T G C T G G A G A G A A C C T	In house
POL OG 479		5350–5373	C C T A C C T T G A C T A G G A C T G C T C C	Grankvist *et al.* (1992)[b]
DR ENV2	5′	9033–9053	A T T T G C C A G A G C C T C C A G C C	In house
LTR 2	3′	9496–9515		Damond *et al.* (1998)[a]
DR ENV2	5′	9033–9053	A T T T G C C A G A G C C T C C A G C C	In house
SLTR5	3′	10100–10124	A C C T G C T A G T G C T G G A G A G A A C C T	In house
DR NEF1	5′	9862–9888	G T C A G A G G A A G A G G T T A A G A G G A G G C	In house
LTR 9574	3′	626–645	T G G T G A G A G T C T A G C A G G G	Berry *et al* (1994)[e]

[a]Damond F, Loussert-Ajaka I, Apetrei C, *et al.*: Highly sensitive method for amplification of human immunodeficiency virus type 2 DNA. J Clin Microbiol 1998;36:809–811.

[b]Grankvist O, Bredbergraden U, Gustafsson A, *et al.*: Improved detection of HIV-2 DNA in clinical samples using a nested primer-based polymerase chain reaction. J Acquir Immun Def Synd 1992;5:286–293.

[c]Gao F, Yue L, Robertson DL, *et al.*: Genetic diversity of human immunodeficiency virus type 2: evidence for multiple sequence subtypes with differences in virus biology. J Virol 1994;68:7433–7477.

[d]Berry N, Aryoshi K, Jobe O, *et al.*: HIV type 2 proviral load measured by quantitative polymerase chain reaction correlates with $CD4^+$ lymphopenia in HIV type 2-infected individuals. AIDS Res. Hum Retroviruses 1994;10:1031–1037.

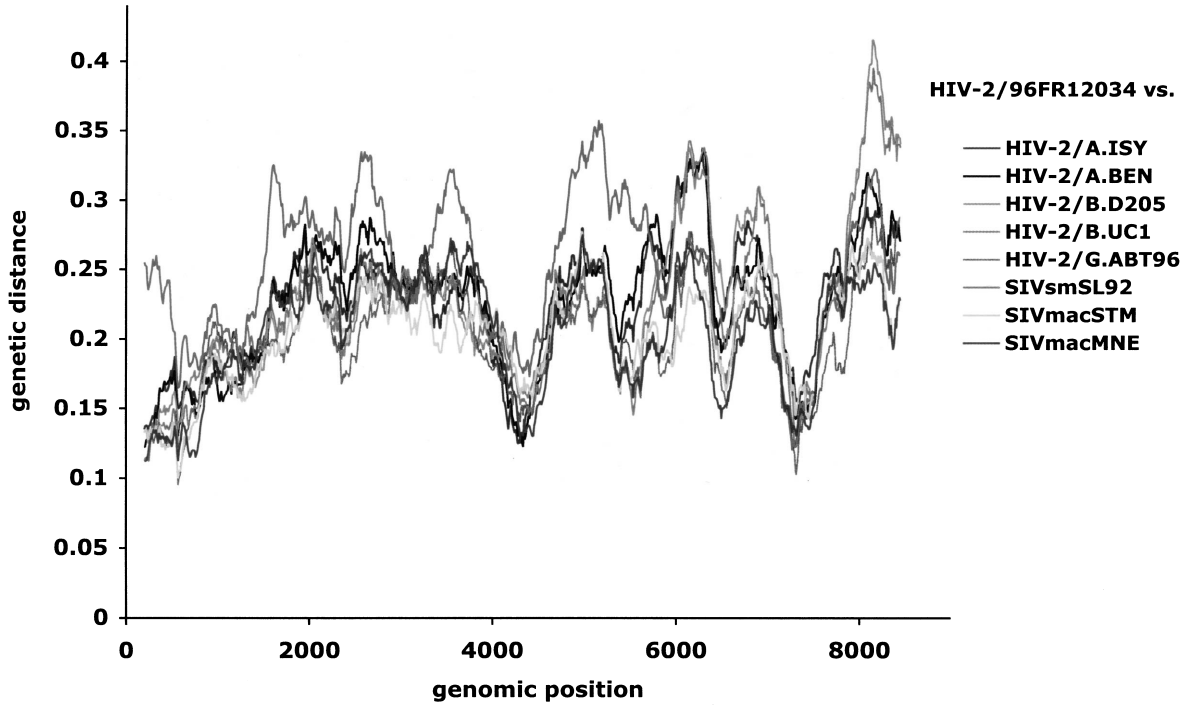

FIG. 1. Diversity plot comparing the genetic distance of the HIV-2 strain 96FR12034 to other SIVsm and HIV-2 complete genome sequences. Pairwise genetic distances were calculated for a window of 400 nucleotides moved in increments of 10 nucleotides. Genetic distance was plotted against the midpoint of each window for each comparison. Note that HIV-2 subtypes C, D, and E are not included since complete genomes were not available.

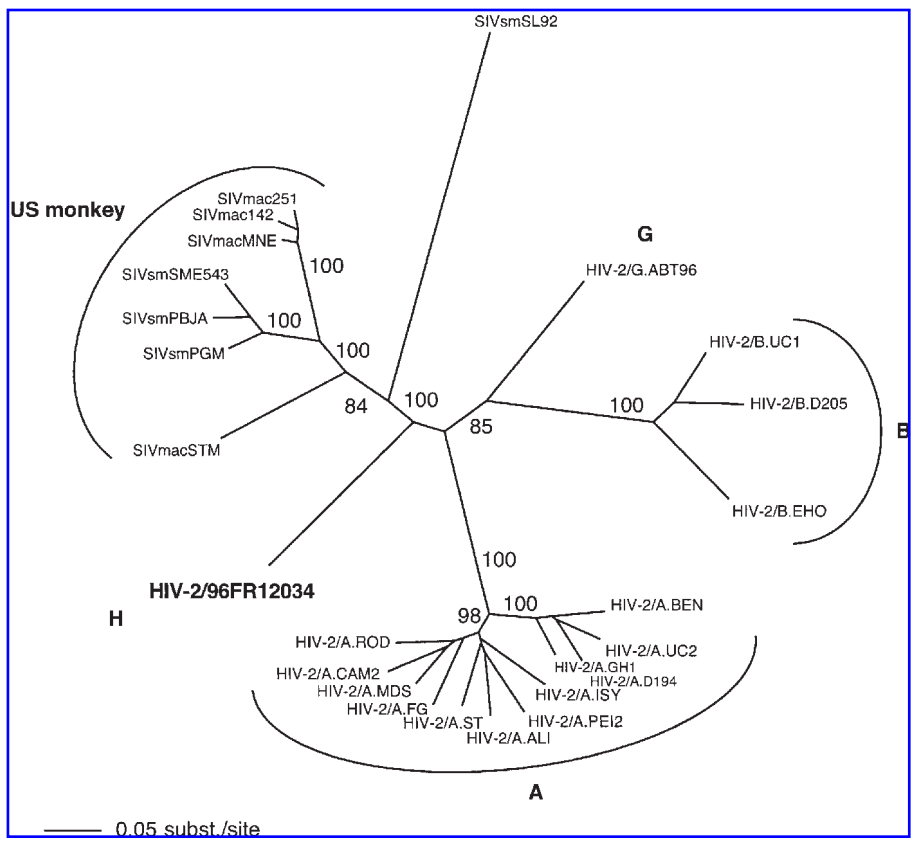

FIG. 2. Unrooted phylogenetic tree of the newly derived HIV-2 strain 96FR12034, and HIV-2 and SIVsm representatives inferred from the complete genome alignment by maximum likelihood. See text for further details. The numbers near nodes indicate the percentage of bootstrap replicates supporting a clade. Bootstrap values greater than 70% are shown. The scale indicates substitutions per site and refers to the branch lengths.

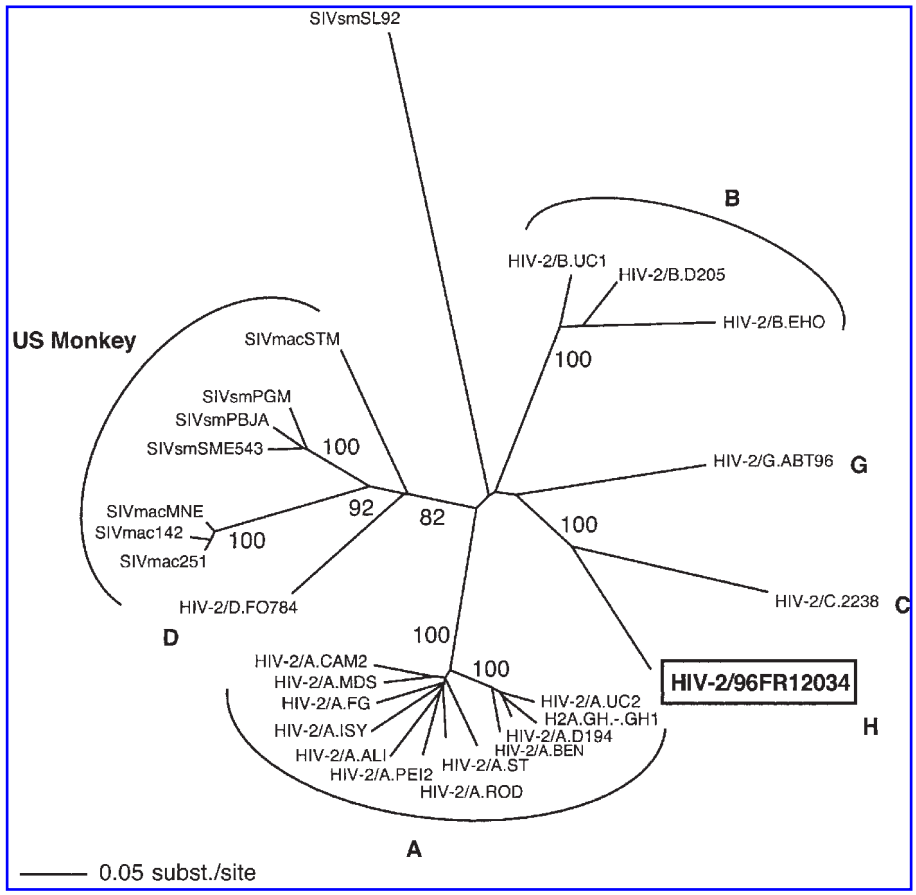

FIG. 3. Unrooted phylogenetic tree of the newly derived HIV-2 strain 96FR12034, and HIV-2 and SIVsm representatives inferred by maximum likelihood from the concatenated *gag-pol-env* fragments for which subtypes C, D, and E sequences were available. See text and Fig. 2 legend for further details.

of time in the human population. The fact that 96FR12034 was isolated from an individual who had lived near the border of Liberia—the same geographic area that 2238 originated from—links these HIV-2 strains geographically, making it plausible that the distant relationship between them indicates separate transmission events from the extensive pool of SIVsm variation known to exist in local populations of the HIV-2 reservoir.[6]

Assuming then that 96FR12034 did enter the human population after an independent transfer of SIVsm from sooty mangabeys, it represents the first example of an extremely rare HIV-2 lineage that is clearly pathogenic, and only the second such example—after HIV-1 group N[13,14]—among all HIV lineages. Given that the evidence that 96FR12034 arose from a distinct cross-species transmission event is about as compelling as that for other subtypes such as HIV-2 A and B, for which no closely related SIVsm sister subtype has yet been discovered, we propose that 96FR12034 be placed in a new HIV-2 subtype, which we designate H.

A proposal for a change in HIV-2 nomenclature

As the different "subtypes" of HIV-2 are analogous to the different "groups" of HIV-1 in that they are most likely to have arisen by independent cross-species transmission events,[1] we propose to resolve this inconsistency in HIV nomenclature. Although a strong argument could be made that the nomenclature used for HIV-2 (whereby the different strains nested within HIV type 2 are designated subtypes) is more rational than the HIV-1 convention (which nests "groups" within "type" and "subtypes" within "groups"), we think it is more practical to bring HIV-2 in line with HIV-1 than vice versa. This change in HIV classification is in agreement with the HIV nomenclature committee meeting that took place at AIDS Vaccine 2001, Philadelphia, and attended by D.L.R. and M.W. (see the LANL HIV Sequence Database website, hiv-web.lanl.gov, for further details). Therefore, we propose that HIV-2 "subtypes" be renamed as "groups."

Only the HIV-2 subtypes (A and B) that are known to be circulating in the human population should be considered as groups directly analogous to the HIV-1 groups. The former HIV-2 subtypes C to G, and the 96FR12034 lineage identified here, that apparently represent unique infections, we propose should be considered as putative groups until they are demonstrated definitively to be circulating in the human population. This natural partitioning of HIV-2 groups can either be considered implicitly when reference is made to the HIV-2 groups A to H, or, alternatively, we propose that HIV-2 groups be formally named as "groups" and "putative-groups." This latter proposal remains to be clarified by a meeting of the HIV Nomenclature Committee; the most up-to-date recommendations will be available from the LANL HIV Sequence Database website (hiv-web.lanl.gov).

This proposed "putative-group" nomenclature is not insignificant as it represents our knowledge that a unique HIV lineage (be it one of the single-strain HIV-2 lineages C–H or a hypothetical new single-strain HIV-1 lineage distinct from groups M, N, and O) is apparently not circulating in the human population and as such each lineage does not necessarily represent a cluster of human infections. Future reclassification of a putative-group as a group (if this nomenclature is adopted) would have to meet the same criteria as have been established for HIV-1[15]; representative strains must be identified in at least three individuals with no direct epidemiological linkage. Three near full-length genomic sequences are preferred, but two complete genomes in conjunction with partial sequences of a third strain are sufficient to designate a *bona fide* HIV-2 group.

In conclusion, the newly identified strain 96FR12034 forms a new HIV-2 lineage, designated as H, and henceforth all HIV-2 subtypes should be referred to as groups. The pathogenic nature of the 96FR12034 virus serves as an important reminder that, for HIV, *pathogenic* potential (the capacity to induce immunosuppression symptoms in an infected individual) and *epidemic* potential (the capacity to establish a successful chain of human-to-human transmissions after an initial monkey-to-human transmission) are not necessarily linked. Some apparently "unsuccessful" HIV lineages (i.e., HIV-1 group N and HIV-2 lineages C–H) clearly include pathogenic strains, yet have been detected in only one or a handful of patients. Given that there are now three HIV-1 lineages (groups M, N, and O) and eight HIV-2 lineages (groups A–H) presumed to correspond to separate cross-species events, and they exhibit a variety of epidemic behaviours and histories, it is reasonable to speculate that HIV lineages—including ones with pathogenic potential—have been establishing themselves sporadically in human populations for as long as human beings have had contact with SIV-infected mangabeys and chimpanzees. Relatively recent changes in human ecology, such as rapid population growth and increased urbanization—perhaps even the widespread use of nonsterile needles—may have played an important role in the *spread* of HIV, but it does not necessarily follow that such factors were, or are, critical for newly emerging HIV strains to pass the milestone of initial human-to-human transmission, nor to become pathogenic.

SEQUENCE DATA

The 96FR12034 sequence was submitted to GenBank and has the accession number AY530889.

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REFERENCES

1. Hahn BH, Shaw GM, De Cock KM, and Sharp PM: AIDS as a zoonosis: Scientific and public health implications. Science 2000;287:607–614.
2. Chen Z, Telfer P, Gettie A, Reed P, Zhang L, Ho DD, and Marx PA: Genetic characterization of new West African simian immunodeficiency virus SIVsm: Geographic clustering of household-derived SIV strains with human immunodeficiency virus type 2 subtypes and genetically diverse viruses from a single feral sooty mangabey troop. J Virol 1996;70:3617–3627.
3. Chen Z, Luckay A, Sodora DL, Telfer P, Reed P, Gettie A, Kanu JM, Sadek RF, Yee J, Ho DD, Zhang L and Marx PA: Human immunodeficiency virus type 2 (HIV-2) seroprevalence and characterization of a distinct HIV-2 genetic subtype from the natural range of simian immunodeficiency virus-infected sooty mangabeys. J Virol 1997;71:3953–3960.
4. Gao, F, Yue L, Robertson DL, Hill SC, Hui H, Biggar RJ, Neequaye AE, Whelan TM, Ho DD, Shaw GM, Sharp PM, and Hahn BH: Genetic diversity of human immunodeficiency virus type 2: Evidence for multiple sequence subtypes with differences in virus biology. J Virol 1994;68:7433–7477.
5. Yamaguchi J, Devare SG, and Brennan CA: Identification of a new HIV-2 subtype based on phylogenetic analysis of full-length genomic sequence. AIDS Res Hum Retroviruses 2000;16:925–930.
6. Gao F, Yue L, White AT, Pappas PG, Barchue J, Hanson AP, Greene BM, Sharp PM, Shaw GM, and Hahn BH: Human infection by genetically diverse SIVsm-related HIV-2 in West Africa. Nature 1992;358:495–499.
7. Marx PA, Alcabes PG, and Drucker E: Serial human passage of simian immunodeficiency virus by unsterile injections and the emergence of epidemic human immunodeficiency virus in Africa. Phil Trans R Soc Lond B 2001;356:911–920.
8. Damond F, Gueudin M, Puyeo S, Farfara I, Robertson DL, Descamps D, Chène C, Matheron S, Campa P, Brun-Vézinet F, and Simon F: Plasma RNA viral load in HIV-2 subtype A and B infection. J Clin Microbiol 2002;40:3654–3659.
9. Kuiken CL, Foley B, Hahn BH, Korber B, Marx PA, McCutchan F, Mellors JW, and Wolinksy S, eds.: *HIV Sequence Compendium*. Theoretical Biology and Biophysics Research Group, Los Alamos National Laboratory, Los Alamos, NM, 2001.
10. Thompson JD, Higgins DG, and Gibson TJ. CLUSTAL W: Improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position-specific gap penalties and weight matrix choice. Nucleic Acids Res 1994;22:4673–4680.
11. Swofford, DL: *PAUP*: Phylogenetic Analysis Using Parsimony (* and Other Methods)*, Version 4.0b6. Sinauer Associates, Sunderland, MA, 2002.
12. Lemey, P, Pybus OG, Wang B, Saksena NK, Salemi M, and Vandamme A-M: Tracing the origin and history of the HIV-2 epidemic. J Virol 2003;100:6588–6592.
13. Ayouba A, Souquiere S, Njinku B, Martin P, Muller-Trutwin MC, Roques P, Barre-Sinoussi F, Mauclere P, Simon F, and Nerrienet E: HIV-1 group N among HIV-1 seropositive individuals in Cameroon. AIDS 2000;14:2623–2625.
14. Simon F, Mauclere P, Roques P, Loussert-Ajaka I, Muller-Trutwin MC, Saragosti S, Georges-Courbot MC, Barre-Sinoussi F, and Brun-Vezinet F: Identification of a new human immunodeficiency virus type 1 distinct from group M and group O. Nat Med 1998;4:1032–1037.
15. Robertson, DL, Anderson J, Bradac JA, Carr JK, Foley B, Funkhouser RK, Gao F, Hahn BH, Kalish M, Kuiken C, Learn GH, Leitner T, McCutchan F, Osmanov S, Peeters M, Pieniazek D, Salminen M, Sharp PM, Wolinsky S, and Korber B: HIV-1 nomenclature proposal. Science 2001;288:55–57.

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1. Pedro Borrego, Rita Calado, José M. Marcelino, Patrícia Pereira, Alexandre Quintas, Helena Barroso, Nuno Taveira. 2013. An ancestral HIV-2/simian immunodeficiency virus peptide with potent HIV-1 and HIV-2 fusion inhibitor activity. *AIDS* **27**:7, 1081-1090. [CrossRef]
2. Ming Chang, Geoffrey S. Gottlieb, Joan A. Dragavon, Stephen L. Cherne, Donna L. Kenney, Stephen E. Hawes, Robert A. Smith, Nancy B. Kiviat, Papa Salif Sow, Robert W. Coombs. 2012. Validation for clinical use of a novel HIV-2 plasma RNA viral load assay using the Abbott m2000 platform. *Journal of Clinical Virology* **55**:2, 128-133. [CrossRef]
3. Parviz Soleimani, Abolfazl Barzegar, Ali Movafeghi. 2012. Phylogenetic study of SIVcpz MT145 virus based on proteome and genome analysis. *Journal of Biomolecular Structure and Dynamics* **30**:3, 328-337. [CrossRef]
4. Vânia Oliveira, Inês Bártolo, Pedro Borrego, Cheila Rocha, Emília Valadas, Jorge Barreto, Elsa Almeida, Francisco Antunes, Nuno Taveira. 2012. Genetic Diversity and Drug Resistance Profiles in HIV Type 1- and HIV Type 2-Infected Patients from Cape Verde Islands. *AIDS Research and Human Retroviruses* **28**:5, 510-522. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
5. Ivona Pandrea, Alan L. LandayImplications for Therapy 81-132. [CrossRef]
6. Antoinette C van der Kuyl, Ben Berkhout. 2012. The biased nucleotide composition of the HIV genome: a constant factor in a highly variable virus. *Retrovirology* **9**:1, 92. [CrossRef]
7. Sabrina Locatelli, Martine Peeters. 2012. Cross-species transmission of simian retroviruses. *AIDS* 1. [CrossRef]
8. Jan Münch, Frank KirchhoffNatural SIV Infection 3-45. [CrossRef]
9. Michael Worobey, Guan-Zhu HanThe origins and diversification of HIV 15-24. [CrossRef]
10. N. R. Faria, I. Hodges-Mameletzis, J. C. Silva, B. Rodes, S. Erasmus, S. Paolucci, J. Ruelle, D. Pieniazek, N. Taveira, A. Trevino, M. F. Goncalves, S. Jallow, L. Xu, R. J. Camacho, V. Soriano, P. Goubau, J. D. Sousa, A.-M. Vandamme, M. A. Suchard, P. Lemey. 2011. The phylogeographic footprint of colonial history in the global dispersal of HIV-2 group A. *Journal of General Virology* . [CrossRef]
11. Shiro Ibe, Wataru Sugiura. 2011. Clinical significance of HIV reverse-transcriptase inhibitor-resistance mutations. *Future Microbiology* **6**:3, 295-315. [CrossRef]
12. Kevin Peterson, Sabelle Jallow, Sarah L. Rowland-Jones, Thushan I. de Silva. 2011. Antiretroviral Therapy for HIV-2 Infection: Recommendations for Management in Low-Resource Settings. *AIDS Research and Treatment* **2011**, 1-11. [CrossRef]
13. Lucie Etienne, Eric Delaporte, Martine PeetersOrigin and Emergence of HIV/AIDS 689-710. [CrossRef]
14. P. M. Sharp, B. H. Hahn. 2010. The evolution of HIV-1 and the origin of AIDS. *Philosophical Transactions of the Royal Society B: Biological Sciences* **365**:1552, 2487-2494. [CrossRef]
15. Pavol Prokop, Jana Fančovičová, Peter Fedor. 2010. Health Is Associated With Antiparasite Behavior and Fear of Disease-Relevant Animals in Humans. *Ecological Psychology* **22**:3, 222-237. [CrossRef]
16. Shiro Ibe, Yoshiyuki Yokomaku, Teiichiro Shiino, Rie Tanaka, Junko Hattori, Seiichiro Fujisaki, Yasumasa Iwatani, Naoto Mamiya, Makoto Utsumi, Shingo Kato, Motohiro Hamaguchi, Wataru Sugiura. 2010. HIV-2 CRF01_AB: First Circulating Recombinant Form of HIV-2. *JAIDS Journal of Acquired Immune Deficiency Syndromes* **54**:3, 241-247. [CrossRef]
17. Susmita R Gurjar, A Mangaiarkarasi, V Ravi, Udaykumar Ranga, Anita Desai. 2009. Molecular Characterization of a Full-Length Genome of a HIV-2 Isolate From India. *JAIDS Journal of Acquired Immune Deficiency Syndromes* **52**:3, 329-335. [CrossRef]
18. R. Behrendt, U. Fiebig, S. Norley, L. Gürtler, R. Kurth, J. Denner. 2009. A neutralization assay for HIV-2 based on measurement of provirus integration by duplex real-time PCR. *Journal of Virological Methods* **159**:1, 40-46. [CrossRef]
19. R. Susmita Gurjar, V. Ravi, Anita Desai. 2009. Molecular Epidemiology of HIV Type 2 Infections in South India. *AIDS Research and Human Retroviruses* **25**:3, 363-372. [Abstract] [Full Text PDF] [Full Text PDF with Links]
20. Sushama Jadhav, Srikanth Tripathy, Smita Kulkarni, Kalpana Agnihotri, Arun Risbud, Ramesh Paranjape. 2009. Molecular Phylogenetics of Nearly Full-Length HIV Type 2 envelope Gene Sequences from West India. *AIDS Research and Human Retroviruses* **25**:1, 115-121. [Abstract] [Full Text PDF] [Full Text PDF with Links]
21. Thushan I. de Silva, Matthew Cotten, Sarah L. Rowland-Jones. 2008. HIV-2: the forgotten AIDS virus. *Trends in Microbiology* **16**:12, 588-595. [CrossRef]
22. Silvia Baroncelli, Donatella RM Negri, Zuleika Michelini, Andrea Cara. 2008. Macaca mulatta , fascicularis and nemestrina in AIDS vaccine development. *Expert Review of Vaccines* **7**:9, 1419-1434. [CrossRef]
23. Myron S. Cohen, Nick Hellmann, Jay A. Levy, Kevin DeCock, Joep Lange. 2008. The spread, treatment, and prevention of HIV-1: evolution of a global pandemic. *Journal of Clinical Investigation* **118**:4, 1244-1254. [CrossRef]

24. Julie Yamaguchi, Ana Vallari, Nicaise Ndembi, Ruthie Coffey, Charlotte Ngansop, Dora Mbanya, Lazare Kaptué, Lutz G. Gürtler, Sushil G. Devare, Catherine A. Brennan. 2008. HIV Type 2 Intergroup Recombinant Identified in Cameroon. *AIDS Research and Human Retroviruses* **24**:1, 86-91. [Abstract] [Full Text PDF] [Full Text PDF with Links]
25. Maarten F. Schim van der LoeffEpidemiology, Natural History and Treatment of HIV-2 Infections 637-647. [CrossRef]
26. Yutaka Takebe, Rie Uenishi, Xiaojie LiGlobal Molecular Epidemiology of HIV: Understanding the Genesis of AIDS Pandemic **56**, 1-25. [CrossRef]
27. Xiao-Jie Li, Rie Uenishi, Saiki Hase, Huanan Liao, Tee Kok Keng, Shigeru Kusagawa, Yutaka Takebe. 2007. HIV/AIDS in Asia: The shape of epidemics and their molecular epidemiology. *Virologica Sinica* **22**:6, 426-433. [CrossRef]
28. Fran Van Heuverswyn, Yingying Li, Elizabeth Bailes, Cecile Neel, Benedicte Lafay, Brandon F. Keele, Katharina S. Shaw, Jun Takehisa, Matthias H. Kraus, Severin Loul, Christelle Butel, Florian Liegeois, Bienvenue Yangda, Paul M. Sharp, Eitel Mpoudi-Ngole, Eric Delaporte, Beatrice H. Hahn, Martine Peeters. 2007. Genetic diversity and phylogeographic clustering of SIVcpzPtt in wild chimpanzees in Cameroon. *Virology* **368**:1, 155-171. [CrossRef]
29. Fran Heuverswyn, Martine Peeters. 2007. The origins of HIV and implications for the global epidemic. *Current Infectious Disease Reports* **9**:4, 338-346. [CrossRef]
30. Rajeev Gautam, Anders Chase Carter, Nathalia Katz, Isolde F. Butler, Mary Barnes, Atsuhiko Hasegawa, Marion Ratterree, Guido Silvestri, Preston A. Marx, Vanessa M. Hirsch, Ivona Pandrea, Cristian Apetrei. 2007. In vitro characterization of primary SIVsmm isolates belonging to different lineages. In vitro growth on rhesus macaque cells is not predictive for in vivo replication in rhesus macaques. *Virology* **362**:2, 257-270. [CrossRef]
31. Jaime R. Torres, Maria A. Torres-Viera, Jorg Schupbach, Hector R. Rangel, Flor H. Pujol. 2007. Non-immune thrombocytopenia responsive to antiretroviral therapy and HIV-2 infection. *Journal of Infection* **54**:1, e21-e24. [CrossRef]
32. M VANREGENMORTEL. 2007. Virus species and virus identification: Past and current controversies. *Infection, Genetics and Evolution* **7**:1, 133-144. [CrossRef]
33. Eric Delwart, Mary C. Kuhns, Michael P. Busch. 2006. Surveillance of the genetic variation in incident HIV, HCV, and HBV infections in blood and plasma donors: Implications for blood safety, diagnostics, treatment, and molecular epidemiology. *Journal of Medical Virology* **78**:S1, S30-S35. [CrossRef]
34. Berta Rodes, Carlos Toro, Victoria Jimenez, Vincent Soriano. 2005. Viral Response to Antiretroviral Therapy in a Patient Coinfected with HIV Type 1 and Type 2. *Clinical Infectious Diseases* **41**:2, e19-e21. [CrossRef]
35. Diane Descamps, Florence Damond, Sophie Matheron, Gilles Collin, Pauline Campa, Severine Delarue, Sophie Pueyo, Genevieve Ch#ne, Francoise Brun-V#zinet. 2004. High frequency of selection of K65R and Q151M mutations in HIV-2 infected patients receiving nucleoside reverse transcriptase inhibitors containing regimen. *Journal of Medical Virology* **74**:2, 197-201. [CrossRef]
36. Michael WorobeyThe Origins and Diversification of HIV 13-21. [CrossRef]