Origin of Human T-Lymphotropic Virus Type 1 in Rural Côte d’Ivoire

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Simian T-lymphotropic virus type 1 (STLV-1) strains occasionally infect humans. However, the frequency of such infections is unknown. We show that direct transmission of STLV-1 from nonhuman primates to humans may be responsible for a substantial proportion of human T-lymphotropic virus type 1 infections in rural Côte d’Ivoire, where primate hunting is common.

Human T-lymphotropic virus type 1 (HTLV-1) can induce adult T-cell leukemia or lymphoma and HTLV-1–associated myelopathy or tropical spastic paraparesis. These pathologies are a serious threat to the several million persons infected with HTLV-1 (1).

Although HTLV-1 has spread globally, its geographic distribution is not uniform. Most infected persons live in areas where the virus is endemic and seroprevalence is comparatively high (>1%) (1), i.e., in Japan, Melanesia, South America, the Caribbean, and sub-Saharan Africa. Phylogenetic analyses demonstrate that the geographic distribution of HTLV-1 genetic diversity is also not uniform. The most genetic diversity is seen in sub-Saharan Africa, where 6 of the 7 human molecular subtypes (HTLV-1A, B, D, E, F, and G) are found. Of those 6 subtypes, 5 are mainly found in or endemic to central Africa: HTLV-1B, D, E, F, and G (1).

Molecular HTLV-1 subtypes from humans in central Africa belong to composite clades that comprise HTLV-1 strains and simian T-lymphotropic virus type 1 (STLV-1) strains derived from nonhuman primates (2). Nonhuman primates in Africa are considered to be the source of recurrent zoonotic transmissions of STLV-1 to local human populations; virus transmission is believed to occur during the collection and consumption of nonhuman primate bushmeat. This belief is supported by the fact that self-reported nonhuman primate hunters in Cameroon were infected with viruses closely related to STLV-1 strains circulating among local nonhuman primate prey (3). However, because intrafamilial transmission of HTLV-1B and -1D was also documented among hunters-gatherers in Cameroon (4), it is impossible to sort out cases of direct zoonotic transmission of STLV-1 from cases of consecutive human-to-human spread of virus (evolutionary rates for HTLV-1/STLV-1 are very slow) (5).

However, HTLV-1 and STLV-1 strains from western African segregate clearly in phylogenetic analyses; most humans are infected with HTLV-1A, the only human-restricted molecular subtype (6–9). Therefore, in western compared with central Africa, human infections with viruses closely related to local STLV-1 strains are much more likely to reflect direct zoonotic transmission. This situation enabled us to investigate the frequency of such direct zoonotic transmissions in a rural region of Côte d’Ivoire neighboring the Tai National Park (Figure 1).

The Study

During 2006–2007, blood samples were obtained from 776 volunteers living in 18 villages bordering Tai National Park. All participants signed informed consent forms and completed questionnaires aimed at determining their exposure to nonhuman primate bushmeat through activities such as hunting of nonhuman primates or consumption of nonhuman primate bushmeat.

To determine effective exposure to HTLV-1/STLV-1, we used an HTLV-1/2 ELISA to test serum samples for reactivity to HTLV-1/2 antigens (10). Of the 776 serum samples, 16 were positive according to the ELISA manufacturer’s criteria; an additional 15 samples had values just below the cutoff. We extracted DNA from all ELISA-reactive samples and performed a search for HTLV-1/STLV-1 by using an HTLV-1/2 ELISA to test serum samples (Table 1; online Technical Appendix, wwwnc.cdc.gov/EID/pdfs/11-1663-Techapp.pdf). To identify multiple infections with HTLV-1/STLV-1, this assay was applied on near endpoint dilutions of the 10 DNA extracts (2–6 starting template molecules per reaction; online Technical Appendix). For each person, 6–20 env and 2–20 LTR sequences (15–40 sequences per person) were determined by Sanger sequencing. No evidence of multiple infections was found.

Phylogenetic analyses were performed by using Bayesian and maximum likelihood methods on env and LTR datasets (online Technical Appendix). Both methods agreed on all essential features of the LTR tree topology.
Figure 1. Sampling zone in study of the origin of human T-lymphotropic virus type 1 in rural western Africa, 2006–2007. Tai National Park is indicated in white on the gray background of Côte d’Ivoire. The black rectangle overlapping Tai National Park defines a zone encompassing the 18 villages where study participants resided. Village names and the number of participants are as follows: Daobly (38), Djereoula (31), Djiboulay (40), Gahably (55), Gouléako (37), Goulégui-Béoué (55), Keibly (90), Pauléoula (20), Ponan (21), Port-Gentil (47), Sakré (75), Sioblooula (35), Taï (26), Tieleoula (40), Zagné (17), Zaïpobly (35), Taï (26), Gouléako (37), Goulégui-Béoué (55), Kéibly (90), Pauléoula (20), Ponan (21), Port-Gentil (47), Sakré (75), Sioblooula (35), Taï (26), Tieleoula (40), Zagné (17), Zaïpobly (35), Taï (26).

Conclusions

We investigated the frequency of direct zoonotic transmission of STLV-1 in a rural region of Côte d’Ivoire neighboring Tai National Park and found that only 2 of the STLV-1–related sequences would be compatible with a local human-to-human transmission (Gah050 and Kei005; Figure 2). Therefore, our data support the notion that direct zoonotic transmissions of STLV-1 represent a measurable proportion of HTLV-1 infections, at least in rural regions bordering nonhuman primate habitat. In addition, these results mirror observations made among adult chimpanzees from Tai National Park, which are often infected with retroviruses (i.e., simian foamy viruses and STLV-1) of their prey (Figure 2) (7,11).

Despite the high prevalence of STLV-1, simian foamy virus, and simian immunodeficiency virus infections among red colobus populations (8) and the fact that this nonhuman primate species is the one most frequently hunted by humans (4), most zoonotic transmissions of retroviruses in western Africa seem to originate from sooty mangabeys, as shown here for STLV-1 and previously described for simian immunodeficiency virus of sooty mangabeys, the precursor of HIV-2 (12). It remains to be determined whether these zoonotic transmissions from sooty mangabeys are favored as a result of molecular determinants (e.g., convergent

Table 1. Characteristics of persons positive for HTLV-1 or STLV-1 in a study of the origin of HTLV-1, rural western Africa, 2006–2007*

<table>
<thead>
<tr>
<th>Study participant†, sex</th>
<th>Infecting subtype</th>
<th>Minimum observed distance to any STLV-1, %</th>
<th>Type of contact and nonhuman primate contacted</th>
<th>Hunting</th>
<th>Dismembering</th>
<th>Preparation or cooking</th>
<th>Eating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>LTR</td>
<td>env</td>
<td>None</td>
<td>Monkeys</td>
<td>chimp</td>
<td>None</td>
</tr>
<tr>
<td>Gah050, M</td>
<td>STLV-1/SM</td>
<td>0.6</td>
<td>0.4</td>
<td>None</td>
<td>Monkeys</td>
<td>chimp</td>
<td>None</td>
</tr>
<tr>
<td>Guib014, F</td>
<td>HTLV-1A</td>
<td>3.2</td>
<td>2.9</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Monkeys</td>
</tr>
<tr>
<td>Kei005, F</td>
<td>STLV-1/SM</td>
<td>0.6</td>
<td>0.5</td>
<td>None</td>
<td>Monkeys</td>
<td>None</td>
<td>Monkeys</td>
</tr>
<tr>
<td>Kei025, M</td>
<td>STLV-1J</td>
<td>0.3</td>
<td>0.2</td>
<td>None</td>
<td>Monkeys</td>
<td>None</td>
<td>Monkeys</td>
</tr>
<tr>
<td>Pau002, F</td>
<td>HTLV-1A</td>
<td>3.0</td>
<td>3.0</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Monkeys</td>
</tr>
<tr>
<td>Pau009, M</td>
<td>STLV-1/SM</td>
<td>0.0</td>
<td>0.2</td>
<td>None</td>
<td>Monkeys</td>
<td>chimp</td>
<td>Monkeys</td>
</tr>
<tr>
<td>Pon002, F</td>
<td>HTLV-1A</td>
<td>4.2</td>
<td>2.8</td>
<td>None</td>
<td>Monkeys</td>
<td>None</td>
<td>Monkeys</td>
</tr>
<tr>
<td>Tie005, F</td>
<td>HTLV-1A</td>
<td>4.0</td>
<td>2.5</td>
<td>None</td>
<td>Monkeys</td>
<td>None</td>
<td>Monkeys</td>
</tr>
<tr>
<td>Tie011, F</td>
<td>HTLV-1A</td>
<td>4.5</td>
<td>2.4</td>
<td>None</td>
<td>Monkeys</td>
<td>None</td>
<td>Monkeys</td>
</tr>
</tbody>
</table>

*Gray shading indicates infections with STLV-1–like HTLV-1 (as determined through phylogenetic analyses). Minimum distances were calculated by using the same datasets as for phylogenetic analyses (see online Technical Appendix, wwwnc.cdc.gov/EID/pdfs/11-1663-Techapp.pdf). HTLV-1, human T-lymphotropic virus type 1; STLV-1, simian T-lymphotropic virus type 1; LTR, long terminal repeat; chimp, chimpanzee(s).
†First 3 letters refer to the persons’ village of residence.
evolution of retroviral receptors) or behavioral determinants (e.g., increased aggressiveness).

Considering the human exposure to nonhuman primate bushmeat in this region (as illustrated by ≥150,000 kg sold per year in markets) (13) and given the high prevalence of STLV-1 among local nonhuman primates (7,8), the observation that zoonotic transmission events are, in absolute terms, exceedingly rare is striking. Yet, the accumulation of genetically distinct HTLV-1/STLV-1 over restricted geographic areas remains possible, as illustrated by the finding of 1 person infected with HTLV-1A and 2 persons infected with putative STLV-1 in a single village, Kéibly (Table 1; Figure 1). Such local accumulations add to the threat represented by direct transmissions of STLV-1 because they can provide an opportunity for recombinant viruses to emerge, even though HTLV-1/STLV-1 biology may be unfavorable to recombination (14).

The analysis of behavioral data reveals generalized exposure of local populations to cooked nonhuman primate bushmeat (Table 2). Exposure to fresh tissues, which can be expected to be more risky in terms of retroviral transmission, is less common (Table 2). Along a gradient of bushmeat freshness, going from hunting to preparation and cooking, a clear reversal of sex-related skew can be observed: only men are hunters, men and women are equally involved in dismembering, and women predominantly prepare and cook nonhuman primate bushmeat (Table 2). Hence, men likely constitute a population at risk. In our study, 75% of persons who were identified as infected with viruses closely related to STLV-1 were men, whereas all HTLV-1A–infected persons were women. Increased surveillance for zoonotic transmission of STLV-1 to humans in areas where such transmission is more likely and increased surveillance of nonhuman primate species with high transmission potential (like sooty mangabeys) will contribute to a better understanding of risk factors.

Acknowledgments

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Table 2. Type of nonhuman primate contact by participants in a study of the origin of HTLV-1 in rural western Africa, 2006–2007*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Activity resulting in contact</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hunting</td>
</tr>
<tr>
<td>Women, n = 402</td>
<td>0%</td>
</tr>
<tr>
<td>Men, n = 371</td>
<td>11.6%</td>
</tr>
<tr>
<td>Relative exposure, men vs. women</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Sex assignation was lost for 3 persons; thus, the total sampling size was 773 rather than 776, the total number included in the study. HTLV-1, human T-lymphotropic virus type 1; NA, not applicable.
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Dr Calvignac-Spencer is a researcher at the Robert Koch-Institut. His research interest is in the patterns of viral transmission in the wild between and within primate species.

References


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