Short Communication

Increased Risk for a Second Retroviral Infection (SIV or STLV Type I) for Wild African Green Monkeys Already Infected by One Retrovirus in Senegal (West Africa)

JEAN-PAUL DURAND,1 PHILIPPE TUPPIN,2 PATRICK MAISON,2 GÉRARD GALAT,3 ANH GALAT-LUONG,3 DOMINIQUE JEANNELE,3 and GUY DE THÉ2

The most widely distributed simian group in Africa, from Ethiopia to Senegal and from Sudan to South Africa, is Cercopithecus aethiops, with the subspecies in Senegal being C. a. sabaeus (commonly named green monkey [GM]). Simian immunodeficiency virus (SIV) seroprevalence is high in wild GMs from East Africa and in captive sooty mangabeys from West Africa.1-3 Natural infection of GMs and sooty mangabeys with their respective T cell lymphotropic virus type I (STLV-I) is high in several Old World species, which may exhibit spontaneous malignant lymphomas.4,5 The GM is known to be the Old World species with the highest SIV and STLV-I seroprevalence. Available literature on SIV or STLV-I mainly concerns captive monkeys, which could have been accidentally or artificially infected after capture. Reports on SIV/STLV-I dual infection are scarce, except for semi-free range colonies of sooty mangabeys and mandrills.5,6 However, to our knowledge, no survey has been carried out on the distribution of the two viruses in feral monkeys. Thus we compared seroprevalences of SIV and STLV-I in GM and analyzed determinants for double infection with the viruses.

The study areas were Kedougou in southeast Senegal, near the Guinean border, and Sine-Saloum in central Senegal near the Gambian border. While both areas are forested savannah, they are geographically separated by a distance of 600 km. The simian population for the study comprised 171 monkeys. One hundred and twenty were killed during yellow fever control in 1981 and 1982 in Kedougou; peripheral blood was obtained by cardiac puncture for SIV and STLV-I serology. The remaining 51 monkeys were trapped in 1989 and 1991 in Sine-Saloum, and blood samples were withdrawn under ketamine anesthesia from the femoral vein. All animals were examined by primatologists (G.G. and A.G.-L.). The monkeys were classified according to their body weight and sexual maturity. Green monkeys are semiterrestrial, living in multimale troops with multimale-multifemale mating behavior.

Sera from monkeys were stored at the Pasteur Institute in Dakar. They were tested for SIV by enzyme-linked immunosorbent assay (ELISA) (Elavir-Mixt 1-2; Diagnostics Pasteur, Marnes la Coquette, France) at the beginning of the study, and after the isolation of an SIV$\alpha$ strain from a GM living in Sine-Saloum, as reported elsewhere,10 sera were tested a second time by ELISA using this strain. All ELISA-positive sera were confirmed as SIV positive by Western blot using culture supernatants of cells infected with the isolated SIV$\alpha$ strain. Antibodies to STLV-I were detected by a commercially available ELISA kit (Du Pont de Nemours, Wilmington, DE) and by immunofluorescence assay. Positive sera were confirmed by HTLV-I Western blot (Du Pont de Nemours). The reliability of the human HTLV-I commercial test to detect STLV-I was good in view of the high sequence homology between these two viruses. Crude odds ratios (ORs) were calculated. The data were subjected to stepwise logistic regression analysis to select significant and independent determinants for SIV and/or STLV-I seropositivity. As shown in Table 1, the seroprevalence of SIV antibodies was high in GMs in both areas. The risk of SIV seropositivity in monkeys was significantly associated with sexual maturity (OR = 4.9, p < 0.0001) and STLV-I seropositivity (OR = 3.2, p < 0.0001). Increased risk of STLV-I seropositivity in GMs was significantly associated with two independent factors, i.e., SIV seropositivity (OR = 4.4, p < 0.0001) and geographic location in Kedougou (OR = 2.4, p < 0.05) (Table 1). These results disclosed that the two retroviruses might interact so as to increase the risk of double infection. The increased risk of SIV is associated with infection by STLV-I and vice versa.

The question arises as to whether the fact that mature monkeys are more prone to be captured or hunted than immature ones has created biased results. Samples from animals in Sine-Saloum should be representative of the population because the troops were trapped, then released. Also, the age structure of the Sine-Saloum monkeys used in our study did not differ from that reported.11 In Kedougou, the STLV-I seroprevalence was similar to that found in 1984–1985 in the same region12 (40.8 vs. 41%, respectively). In our care to avoid possible biases, we...
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Prevalence</th>
<th>Area</th>
<th>Sex</th>
<th>Age</th>
<th>STLV</th>
<th>SIV and STLV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>n+</td>
<td>%</td>
<td>OR^a</td>
<td>p</td>
<td>OR^b</td>
</tr>
<tr>
<td>Prevalence</td>
<td>171</td>
<td>66</td>
<td>38.6</td>
<td>35.7</td>
<td>0.05</td>
<td>37</td>
</tr>
<tr>
<td>Area</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STLV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

^aCrude OR.

^bOR obtained by a stepwise logistic regression including age, sex, area, and presence of antibodies to the second retrovirus. For SIV/STLV only age, sex, and area were included.
grouped the monkeys according to their sexual maturity prior to analysis. Because SIV- or STLV-positive monkeys generally do not present pathologies associated with the viruses, biases due to hunting more easily infected monkeys than noninfected ones remain unlikely.

We calculated the expected numbers of coinfected monkeys, assuming that the two viruses are independently distributed. However, significant differences between the expected and observed numbers of coinfections implied a dependence in the distribution of the two viruses. To compare our results post hoc with those already published for other species with different behaviors, we calculated the expected and observed numbers from two studies reporting SIV–STLV coinfections: mandrills in a semifree-range colony in Gabon and sooty mangabeys in a breeding colony in the United States. The results disclosed a significant excess of both HTLV-I and HTLV-II infections in African Americans compared with that of whites or Hispanics.

Preinfection with HTLV-I/II may also increase the susceptibility to HIV infections as well. In populations with predominantly heterosexual transmission of HIV and HTLV, an association between the two viruses has been reported in Haiti (HIV-I/HTLV-I) and Guinea-Bissau (HIV-2/HTLV-I)\textsuperscript{10}. The results from our survey on endemic simian retroviruses and retrospective analysis of published data indicate that dual infection occurs more frequently than expected in several species with different mating behaviors. Thus, one retroviral infection may induce an enhanced susceptibility of the host to a second retrovirus. It could be further investigated in several species of monkeys for whom the immunosuppression linked to SIV infection is not present and could not facilitate infection by STLV.

Potential disease manifestations of dual infection have been described in green monkeys. A study of wild-caught monkeys points out a high level of \( T \) lymphocytes and a low hemoglobin level in coinfected monkeys compared with monkeys seronegative for both viruses, but no comparisons were done between coinfected monkeys and monkeys infected by only one of the viruses.\textsuperscript{20} A lymphoproliferative disease and immuno-deficiency were reported for a monkey dually infected, suggesting an alternative reciprocal activation of SIV by STLV-I, which could have resulted in immunosuppression and compromised immune surveillance, thereby promoting unchecked proliferation of rare STLV-transformed cells.\textsuperscript{8} The similarity found

---

**Table 2. Dependence of Retroviral Infections in Monkeys and Humans**

<table>
<thead>
<tr>
<th>Sample (ref.)</th>
<th>N</th>
<th>SIV (%)</th>
<th>STLV (%)</th>
<th>SIV/STLV (% observed)</th>
<th>SIV/STLV (% expected)</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monkeys</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. aethiops\textsuperscript{9}</td>
<td>171</td>
<td>38.6</td>
<td>35.7</td>
<td>21.6</td>
<td>13.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sooty mangabey (3)</td>
<td>138</td>
<td>57.0</td>
<td>33.0</td>
<td>27.0</td>
<td>18.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mandrill (9)</td>
<td>40</td>
<td>12.5</td>
<td>12.5</td>
<td>7.5</td>
<td>1.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Humans</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>1160</td>
<td>39.1</td>
<td>12.2</td>
<td>5.8</td>
<td>4.8</td>
<td>NS</td>
</tr>
<tr>
<td>New Jersey</td>
<td>139</td>
<td>39.6</td>
<td>23.7</td>
<td>15.1</td>
<td>9.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Brooklyn</td>
<td>666</td>
<td>48.5</td>
<td>8.3</td>
<td>5.1</td>
<td>4.0</td>
<td>NS</td>
</tr>
<tr>
<td>total</td>
<td>175</td>
<td>34.9</td>
<td>8.6</td>
<td>5.7</td>
<td>3.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>total</td>
<td>1800</td>
<td>21.2</td>
<td>11.5</td>
<td>2.7</td>
<td>2.4</td>
<td>NS</td>
</tr>
<tr>
<td>New Jersey</td>
<td>284</td>
<td>24.3</td>
<td>2.8</td>
<td>1.9</td>
<td>0.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>total</td>
<td>387</td>
<td>7.8</td>
<td>16.8</td>
<td>2.3</td>
<td>1.3</td>
<td>NS</td>
</tr>
<tr>
<td>total</td>
<td>228</td>
<td>3.9</td>
<td>24.6</td>
<td>7.9</td>
<td>1.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>total</td>
<td>356</td>
<td>6.5</td>
<td>1.4</td>
<td>1.1</td>
<td>0.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>total</td>
<td>575</td>
<td>4.2</td>
<td>2.3</td>
<td>1.6</td>
<td>0.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>total</td>
<td>628</td>
<td>49.8</td>
<td>11.5</td>
<td>8.9</td>
<td>5.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>total</td>
<td>987</td>
<td>19.6</td>
<td>6.7</td>
<td>2.9</td>
<td>1.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>total</td>
<td>512</td>
<td>13.7</td>
<td>3.7</td>
<td>3.5</td>
<td>0.5</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

---

*Abbreviation: IVDA, Intravenous drug abuser; NS, not significant.*

---

9. This study.
between the results of our survey and post hoc analysis of hu-
mam populations suggests the possibility that the findings in
mam might be extended to humans. The susceptibility to an
fection by a second retrovirus should be explored by a fol-
low-up of two groups of monkeys or humans infected, or not
fected, by STLV or HTLV to compare the incidence of SIV or HIV
fection in both groups, taking into account behavioral
patterns, to disclose different levels of exposure to SIV or HIV
in these groups.

ACKNOWLEDGMENTS

This study was supported by the Agence Nationale de la
Recherche sur le SIDA (ANRS) and the Pasteur Institute of
Dakar. P. Tippin was the recipient of a fellowship from the
Caisse Nationale d'Assurance Maladie and Pasteur Institute.
Thanks to L. Ferrara, R. Chateau, and F. Legros at ORSTOM
for their help in hunting the monkeys and Dr. R. Bomford and
T. Suzuki for their assistance in the preparation of this manu-
script.

REFERENCES

1. Hendry RM, Wells MA, Phelan MA, Schneider AL, Epstein JS,
and Quinman GV: Antibodies to simian immunodeficiency virus in
2. Ohta Y, Masuda T, Tsujimoto H, Ishikawa K, Kodama T,
Morikawa S, Nakai M, Honjo S, and Hayami M: Isolation of SIV
from African green monkeys and seroepidemiologic survey of the
3. Fultz PN, Gordon TP, Anderson DC, and McClure HM: Prevalence
of natural infection with simian immunodeficiency virus and simian
T-cell leukemia virus type I in a breeding colony of sooty mangabey
Yamamoto K, Ishida T, Honjo S, and Hinuma Y: Prevalence of
antibody to adult T-cell leukemia virus associated antigens (ATLA)
N, Ishida T, Takenaka O, Kawamoto Y, Shotake T, Ohsawa H,
Ivanoff B, Cooper R, Frost E, Grant F, Spriata Y, Sutarmar, Abe
K, Yamamoto K, and Hayami M: Serological survey and virus iso-
lation of simian T-cell leukemia/T-lymphotropic virus type I
JP, Mathieu C, Muller MC, Love JL, Dube S, Sherman MP, Benz
PM, Erensoy S, Galat-Luong A, Galat G, Paul B, Dube DK, Barre-
Sinoussi F, and Poiesz BJ: Seroepidemiologic, molecular and phy-
genetic analyses of simian T-cell leukemia viruses (STLV-I) from
various naturally infected monkeys species from Central and
7. Sakakibara I, Sugimoto Y, Sasagawa A, Honjo S, Tsujimoto H,
Nakamura H, and Hayami M: Spontaneous malignant lymphoma in
an African green monkey naturally infected with simian T-lym-
8. Traina-Dorge V, Blanchard J, Martin L, and Murphey-Corb M:
Immunodeficiency and lymphoproliferative diseases in an African
green monkey infected with SIV and STLV-I. AIDS Res Hum
Retroviruses 1992;8:97-100.
A, and Delaporte E: Prevalence and transmission of simian immu-
nodeficiency virus and simian T-cell leukemia virus in semi-
free-range breeding colony of mandrills in Gabon. AIDS 1991;5:1385-1386.
10. Muller MC, Sakaiena NK, Nerrinien C, Chappey C, Herve V,
Durand JP, Legal-Campodanico P, Lang MC, Digne JP, Georges
A, Georges-Courbot MC, Sonigo P, and Barre-Sinoussi F: Simian
immunodeficiency viruses from Central and Western Africa:
Evidence for a new species specific lentivirus in tamarus monkeys.
structure and prevalence of SIVagm in two troops of green mon-
keys, Cercopithecus aethiops sabaeus, in Senegal. Proceedings of
the XIlth Congress of the International Primatology Society,
L, and Eyraud M: Antibodies to human T-cell leukemia virus
(HTLV-I) in non human primates from Senegal. Biomed
L, Chu A, Ginzburg HM, Markowits N, Des Jarlais DC, Blattner
WA, and Allain JP: Patterns of HIV-1 and HTLV-I in intra-
venous drug abusers from the middle atlantic and central regions
14. Constantine NT, Bansal J, and Marigilga VC: HIV-1 and HTLV-
I/II coinfection in Baltimore. J Acquir Immune Defic Syndr
HTLV-I and HIV-1 infection in intravenous drug abusers (IVDA).
Fourth international conference on AIDS, book II, June 12-16,
1988, Stockholm, Sweden, IV;190. [Abstract 4514].
16. Cantor KP, Weiss SH, Goedert JJ, and Batjus RJ. HTLV-I/II
seroconversion and HIV/HTLV coinfection among U.S. intravenous
17. Lentino JR, Pachuki CT, Schaaff DM, Schaefer MR, Holzer TJ,
Heynen C, Dawson G, and Douris W: Seroprevalence of HTLV-
I/II and HIV-1 infection among male intravenous drug abusers in
S, Hodges B, and Lee H: Antibody to HIV-1, HTLV-I, and HCV
in three populations of rural haitians. J Acquir Immune Defic Syndr
1992;5:1230-1236.
PA, and Biberfeld G: Association between HTLV-I and HIV-2 in
20. Fincham JE, Van der Riet F, Steyler JG, et al: Increased periph-
eral lymphocytes, lymphoid, hepatitis and anemia in African
vervet monkeys seropositive to retroviruses. J Comp Pathol
1989;101:53-68.

Address reprints requests to:
Philippe Tippin

Unité d’Épidémiologie des Virus Oncogènes
Institut Pasteur

28, rue du Dr. Roux
75015 Paris, France