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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)

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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 SIV strain is not associated with overt immunosuppressive disease. On the other hand, the seroprevalence of simian T cell lymphotropic virus type I (STLV-I) is high in several Old World species, which may exhibit spontaneous malignant lymphomas.[4–8] 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 semifree range colonies of sooty mangabeys and mandrills.[3,9] 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 The remaining 51 monkeys were trapped in 1989 and 1991 in Sine-Saloum, and blood samples were withdrawn under ketamine anesthesia from the femoral vein.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) (Elavia-Mixt 1-2; Diagnostics Pasteur, Marnes la Coquette, France) at the beginning of the study, and after the isolation of an SIV_{agm} 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_{agm} 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 seropositivity to STLV-I (OR = 3.2, $p < 0.001$). 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 region[12] (40.8 vs. 41%, respectively). In our care to avoid possible biases, we

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TABLE 1. GREEN MONKEYS: ODDS RATIO FOR PRESENCE OF SIV, STLV, SIV AND STLV ANTIBODIES BY AREA, SEX, AND AGE

		SIV						*STLV*						*SIV and STLV*					
Parameter	*N*	*n+*	%	*OR*[a]	p	*OR*[b]	p	*n+*	%	*OR*[a]	p	*OR*[b]	p	*n+*	%	*OR*[a]	p	*OR*[b]	p
Prevalence	171	66	38.6					61	35.7					37	21.6				
Area																			
Kedougou	120	47	39.2	1.1				49	40.8	2.2	<0.05	2.4	<0.05	31	25.8	2.6	<0.05		
Sine-Saloum	51	19	37.3	1				12	37.2	1		1		6	11.8	1			
Sex																			
Male	103	33	32.0	0.5	<0.05			38	36.9	1.1				21	20.4	0.8			
Female	68	33	48.5	1				23	33.8	1				16	23.5	1			
Age																			
Young	79	14	17.7	1		1		17	21.5	1				5	6.3	1		1	
Adult	92	52	56.5	6.0	<0.0001	4.9	<0.0001	44	47.8	3.3	<0.001			32	34.8	7.9	<0.0001	7.9	<0.001
STLV																			
Negative	110	29	26.4	1		1													
Positive	61	37	60.7	4.3	<0.0001	3.2	<0.001												
SIV																			
Negative	105							24	22.8	1		1							
Positive	66							37	56.1	4.3	<0.0001	4.4	<0.0001						

[a]Crude OR.

[b]OR 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[9] and sooty mangabeys in a breeding colony in the United States.[3] The results disclosed a significant excess of coinfected animals (Table 2). We also compared HIV-1/2 and HTLV-I/II coinfections in different geographic areas and risk groups within which both viruses were present. In the 1980s, intravenous drug users (IVDUs) had a significant excess of both HIV-1 and HTLV-I/II infections in the northeastern United States, that is, New Jersey, Baltimore, Manhattan, and Brooklyn[13–17] (Table 2). The findings could be due to the high proportion of blacks in the study samples, because African Americans are known to have a higher HTLV-I/II seroprevalence 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-1/HTLV-I) and Guinea-Bissau (HIV-2/HTLV-I).[18,19]

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.[20] A lymphoproliferative disease and immunodeficiency 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.[8] The similarity found

TABLE 2. DEPENDENCE OF RETROVIRAL INFECTIONS IN MONKEYS AND HUMANS

Sample (ref.)	N	*SIV (%)*	*STLV (%)*	*SIV/STLV (% observed)*	*SIV/STLV (% expected)*	p
Monkeys						
C. aethiops[a]	171	38.6	35.7	21.6	13.8	<0.01
Sooty mangabey (3)	138	57.0	33.0	27.0	18.8	<0.05
Mandrill (9)	40	12.5	12.5	7.5	1.6	<0.01
		HIV (%)	*HTLV (%)*	*HIV/HTLV (% observed)*	*HIV/HTLV (% expected)*	
Humans						
IVDA, 1985–1987 (13)						
Total	1160	39.1	12.2	5.8	4.8	NS
Manhatan	139	39.6	23.7	15.1	9.4	<0.05
Brooklyn	666	48.5	8.3	5.1	4.0	NS
New Jersey	175	34.9	8.6	5.7	3.0	<0.05
IVDA, 1987–1988 (16)						
Total	1800	21.2	11.5	2.7	2.4	NS
New Jersey	284	24.3	2.8	1.9	0.7	<0.05
IVDA, 1987–1989 (17)						
Total	387	7.8	16.8	2.3	1.3	NS
Black people	228	3.9	24.6	7.9	1.0	<0.05
IVDA, 1991 (14)						
Baltimore	356	6.5	1.4	1.1	0.1	<0.0001
Baltimore	575	4.2	2.3	1.6	0.1	<0.0001
Haiti, 1988–1989 (18)						
Hospitalized	628	49.8	11.5	8.9	5.7	<0.001
Guinea-Bissau, 1991 (19)						
Hospitalized	987	19.6	6.7	2.9	1.3	<0.0001
Policemen	512	13.7	3.7	3.5	0.5	<0.0001

[a]This study.

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

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

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REFERENCES

1. Hendry RM, Wells MA, Phelan MA, Schneider AL, Epstein JS, and Quinnan GV: Antibodies to simian immunodeficiency virus in African green monkeys in Africa in 1957–62. Lancet 1986;ii:485.
2. Otha 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 virus in various nonhuman primates. Int J Cancer 1988;41:115–122.
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 monkeys. AIDS 1990;4:619–625.
4. Hayami M, Komuro A, Nozawa K, Shotake T, Ishikawa K, Yamamoto K, Ishida T, Honjo S, and Hinuma Y: Prevalence of antibody to adult T-cell Leukemia virus associated antigens (ATLA) in Japanese monkeys and other non-human primates. Int J Cancer 1984;33:179–183.
5. Ishikawa K, Fukasawa M, Tsujimoto H, Else J, Isahakia M, Ubhi N, Ishida T, Takenaka O, Kawamoto Y, Shotake T, Ohsawa H, Ivanoff B, Cooper R, Frost E, Grant F, Spriatna Y, Sutarman, Abe K, Yamamoto K, and Hayami M: Serological survey and virus isolation of simian T-cell leukemia/T-lymphotropic virus type I (STLV-I) in non-human primates in their native countries. Int J Cancer 1987;38:233–239.
6. Saksena NK, Herve V, Durand JP, Le Guenno B, Diop O, Digoutte JP, Mathiot 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 phylogenetic analyses of simian T-cell leukemia viruses (STLV-I) from various naturally infected monkeys species from Central and Western Africa. Virology 1994;198:297–310.
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-lymphotropic virus (STLV). J Med Primatol 1986;15:311–318.
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.
9. Estaquier J, Peeters M, Bedjabaga L, Honoré C, Bussi P, Dixson A, and Delaporte E: Prevalence and transmission of simian immunodeficiency 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, Saksena NK, Nerrienet E, Chappey C, Herve V, Durand JP, Legal-Campodonico P, Lang MC, Digoutte JP, Georges A, Georges-Courbot MC, Sonigo P, and Barré-Sinoussi F: Simian immunodeficiency viruses from Central and Western Africa: Evidence for a new species specific lentivirus in tantalus monkeys. J Virol 1993;67:1227–1235.
11. Galat-Luong A, Galat G, Bibollet-Ruche F, Durand JP, Diop O, Pourrut X, Sarni-Manchado P, Senzani M, and Pichon G: Social structure and prevalence of SIVagm in two troops of green monkeys, *Cercopithecus aethiops sabaeus*, in Senegal. Proceedings of the XIVth Congress of the International Primatology Society, Strasbourg, 1994.
12. Coursaget P, Barres JL, Yvonnet B, Chiron JP, Cornet M, Ferrara L, and Eyraud M: Antibodies to human T-cell leukemia virus (HTLV-I) in non human primates from Senegal. Biomed Pharmacother 1985;39:198–199.
13. Lee HH, Weiss SH, Brown LS, Mildvan D, Shorty V, Saravolatz L, Chu A, Ginzburg HM, Markowitz N, Des Jarlais DC, Blattner WA, and Allain JP: Patterns of HIV-1 and HTLV-I/II in intravenous drug abusers from the middle atlantic and central regions of the USA. J Infect Dis 1990;162:347–352.
14. Constantine NT, Bansal J, and Marsiglia VC: HIV-1 and HTLV-I/II coinfection in Baltimore. J Acquir Immune Defic Syndr 1992;5:535.
15. Brown LS Jr, Lee H, Cerney M, Allain JP, Chu A, and Foster K: HTLV-I and HIV-1 infection in intravenous drug abusers (IVDAs). 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 Battjes RJ. HTLV-I/II seroprevalence and HIV/HTLV coinfection among U.S. intravenous drug users. J Acquir Immune Defic Syndr 1991;4:460–467.
17. Lentino JR, Pachuki CT, Schaaff DM, Schaefer MR, Holzer TJ, Heynen C, Dawson G, and Dorus W: Seroprevalence of HTLV-I/II and HIV-1 infection among male intravenous drug abusers in Chicago. J Acquir Immune Defic Syndr 1991;4:901–909.
18. Allain JP, Hodges W, Einstein MH, Geisler J, Neilly C, Delaney 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.
19. Naucler A, Andersson S, Albino P, Paolo da Silva A, Andreasson PA, and Biberfeld G: Association between HTLV-I and HIV-2 infections in Bissau, Guinea-Bissau. AIDS 1992;6:510–511.
20. Fincham JE, Van Der Riet F, Steytler JG, *et al.*: Increased peripheral lymphocytes, lymphoid, hepatitis and anaemia in African vervet monkeys seropositive to retroviruses. J Comp Pathol 1989;101:53–68.

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