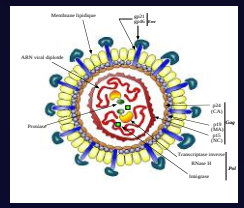
Epidemiological Aspects of HTLV-1 (Human T-Cell Leukemia virus type 1) with a Special Focus on Central Africa (the largest endemic HTLV-1 area)

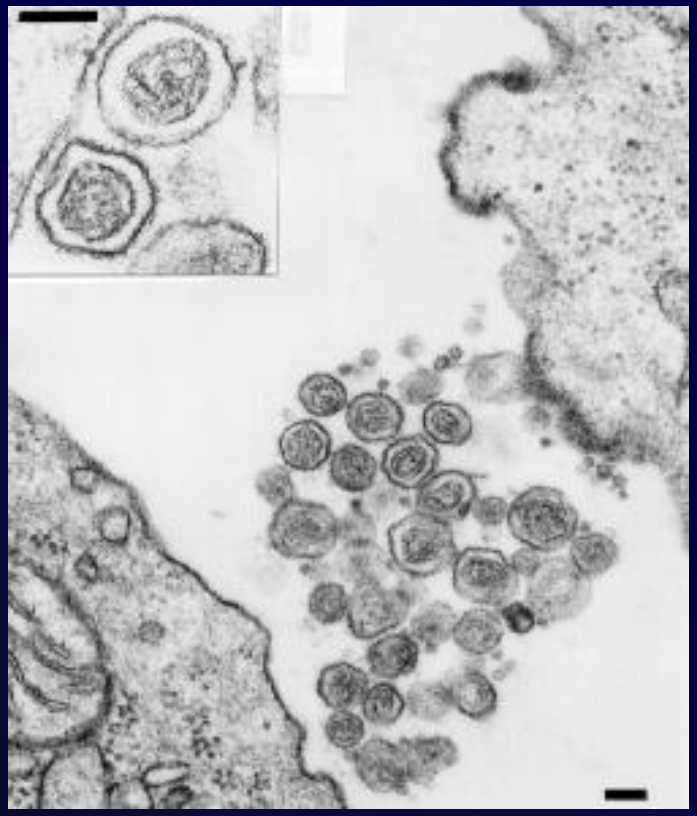
Antoine Gessain

Unité d'Epidémiologie et Physiopathologie des Virus Oncogènes

Institut Pasteur, CNRS UMR 3659

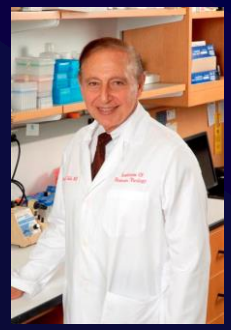
The First Human Onco-Retrovirus: HTLV-I





Extracellular Type C Retroviral particles produced by a T lymphoid cell line established from the culture of the PBMCs of a patient with a TSP/HAM. Gessain et al., 1989.

- Discovery: 1980 NIH USA, 1981 Japan
- *Retroviridae, Orthoretrovirinae, Deltaretrovirus*
- Several associated diseases (**hematological ATL**, **neurological TSP/HAM**, dermatological **ID**, muscular **Myositis**,…)
- Peculiar **epidemiology** (foci, high endemic areas, >5/10 millions of infected persons).
- *In vivo* tropism: mainly CD4+ and CD8 + lymphocytes
- Cellular receptor complex: HSPGs, GLUT-1 and NRP1

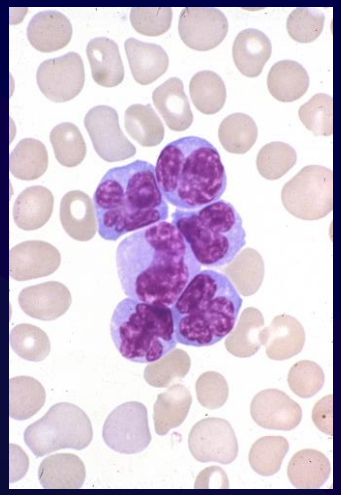


Isolation of HTLV-1 1980, USA

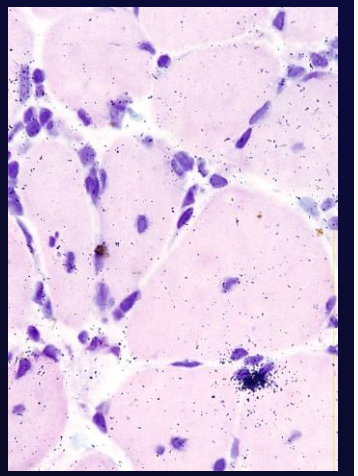
Description of ATL 1973-1977, Japan

Diseases associated with HTLV-1infection

ATL cells



Biopsy of a sIBM



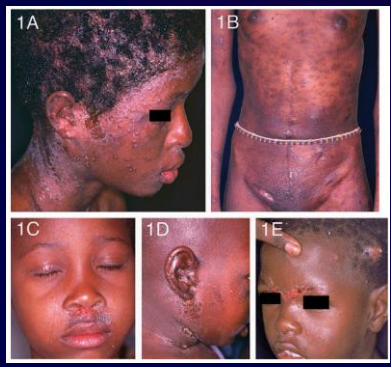
Diseases	Association
Adulthood	
• Adult T-cell leukaemia/lymphoma (ATLL)	++++
• Tropical spastic paraparesis/HTLV-1 associated myelopathy (TSP/HAM)	++++
• Infective dermatitis (very rare)	++++
• Intermediate uveitis (Japan/Caribbean)	+++
• Myositis (polymyositis and SIBM)	+++
• Bronchiectasis (Central Australia)	+++
• HTLV-1 associated arthritis (Japan)	++
Childhood	
• Infective dermatitis (Jamaica, Brazil, Africa)	++++
• TSP/HAM (very rare)	++++
• ATLL (very rare)	++++

The strength of association is based on epidemiological studies as well as molecular data, animal models and intervention trials. ++++ : proven association, +++ : probable association, ++ : likely association.
The geographical location corresponds to the regions where these diseases were most commonly reported.
SIBM : Sporadic Inclusion Body Myositis.

TSP/HAM patients

Gessain et al. Lancet 1985

Infective dermatitis patients



Some of the Main Remaining Unanswered Questions Concerning HTLV-1 Epidemiology

1) What is the current real geographical distribution of

HTLV-1 and

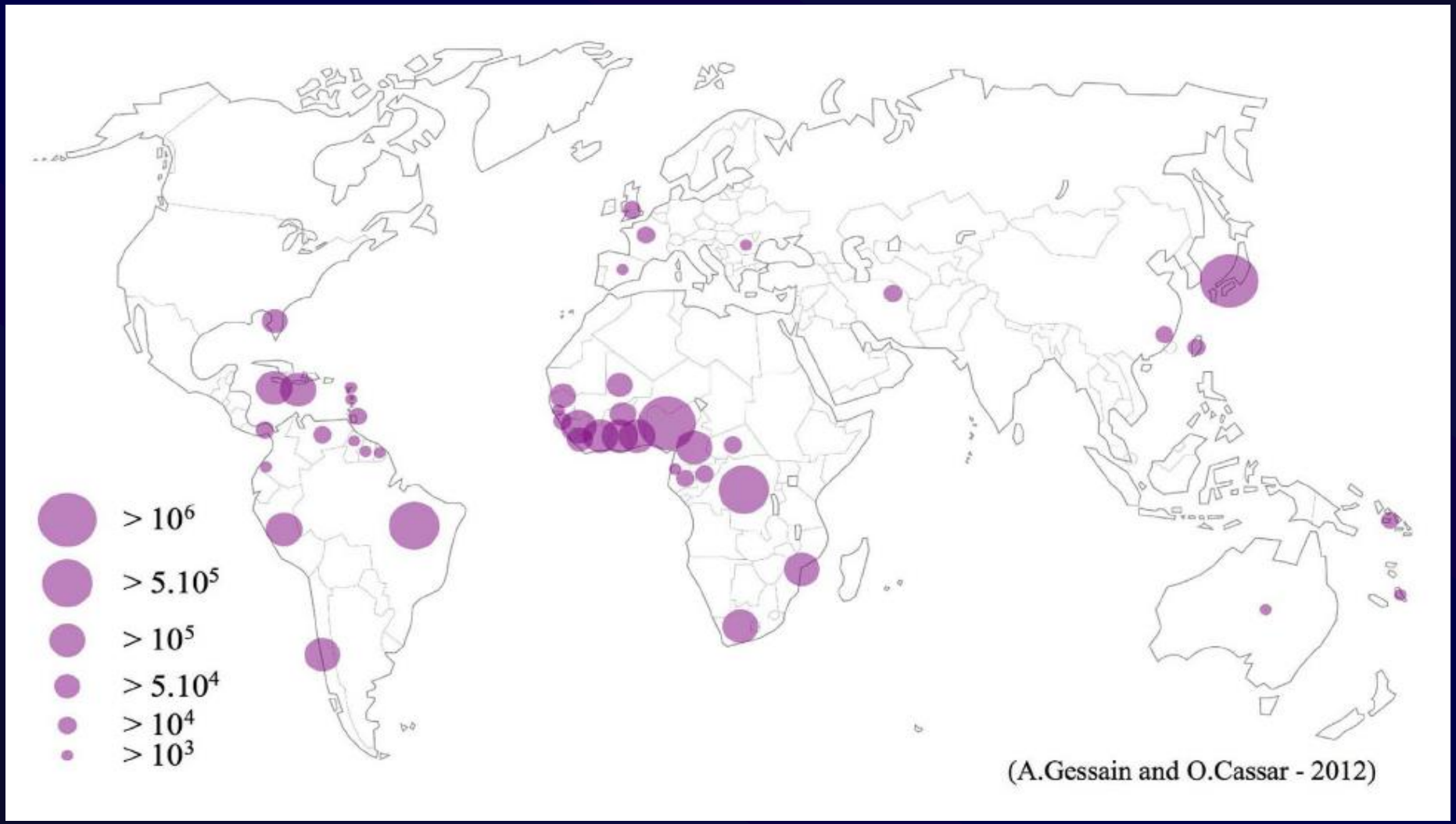
how many individuals are infected worldwide?

Minimal estimation of 5-10 million HTLV-1 infected carriers based on available data for 1.5 billion persons originating from known endemic areas

Current number is probably much higher

World distribution major HTLV-1 endemic foci

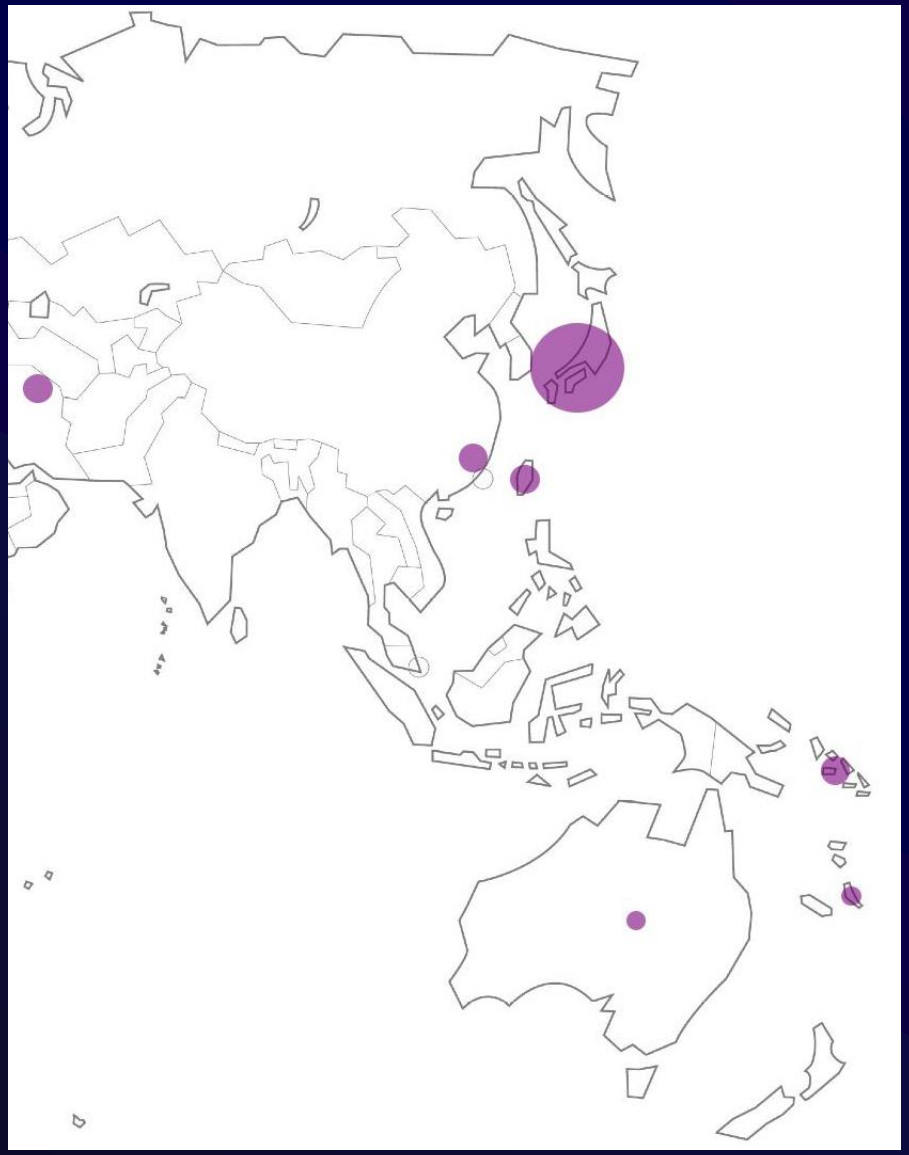
Prevalence can reach >>20/30% in adults > 50 years in some areas



Gessain and Cassar: Frontiers in Microbiology, 2012

Asia & Australo-Melanesia

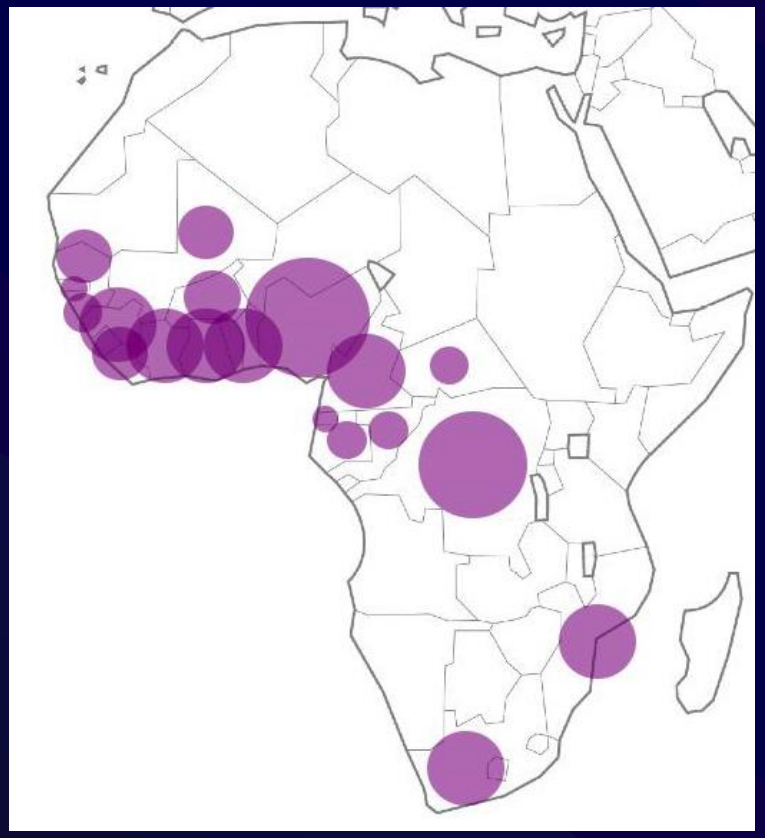
(>1.5 million)



Continent / Country	Population°	HTLV-1 range	
ASIA			
Fujian Province (China)	35 110 000	2 000	20 000
Japan*	127 368 088	1 080 000	1 300 000
Mashad area (Iran)	78 868 711	10 000	40 000
Taiwan	23 113 901	10 000	30 000
AUSTRALO-MELANESIA			
Australia (Aboriginal Australians)	463 900	2 500	5 000
Solomon Islands	584 578	3 000	6 000
Vanuatu	227 574	250	1 000

For nearly 3 billion persons (China, India,…), no reliable epidemiological data, despite the presence of several small series or sporadic reported cases of ATLL and TSP/HAM

Africa (>2.5-5.5 millions)



Continent / Country	Population°	HTLV-1 range	
AFRICA			
Senegal	12 969 606	30 000	105 000
Gambia	1 840 454	2 500	13 000
Guinea Bissau	1 628 603	12 000	28 000
Guinea	10 884 958	75 000	150 000
Sierra Leone/Liberia	5 485 998 / 3 887 886	50 000	100 000
Côte d'Ivoire	21 952 093	130 000	250 000
Ghana	25 241 998	125 000	375 000
Togo / Benin	6 961 049 / 9 598 787	80 000	160 000
Burkina Fasso	17 275 115	42 000	125 000
Mali	14 533 511	32 000	95 000
Nigeria	170 123 740	850 000	1 700 000
Cameroon	20 129 878	80 000	180 000
Equatorial Guinea	685 991	1 500	4 500
Gabon	1 608 321	16 000	30 000
Central African Republic	5 057 208	15 000	30 000
DRC	73 599 190	600 000	1 300 000
Republic of The Congo	4 366 266	12 000	36 000
Mozambique	23 515 934	120 000	360 000
South Africa	48 810 427	180 000	540 000

No reliable estimation for the highly populated areas of North and East Africa, around half of the african population.

Need large epidemiological surveys in Africa (Nigeria, South Africa) and in Asia (India).

2) Concerning Europe, what is the origin of HTLV-1 in

Romania and what is its real extend and importance?

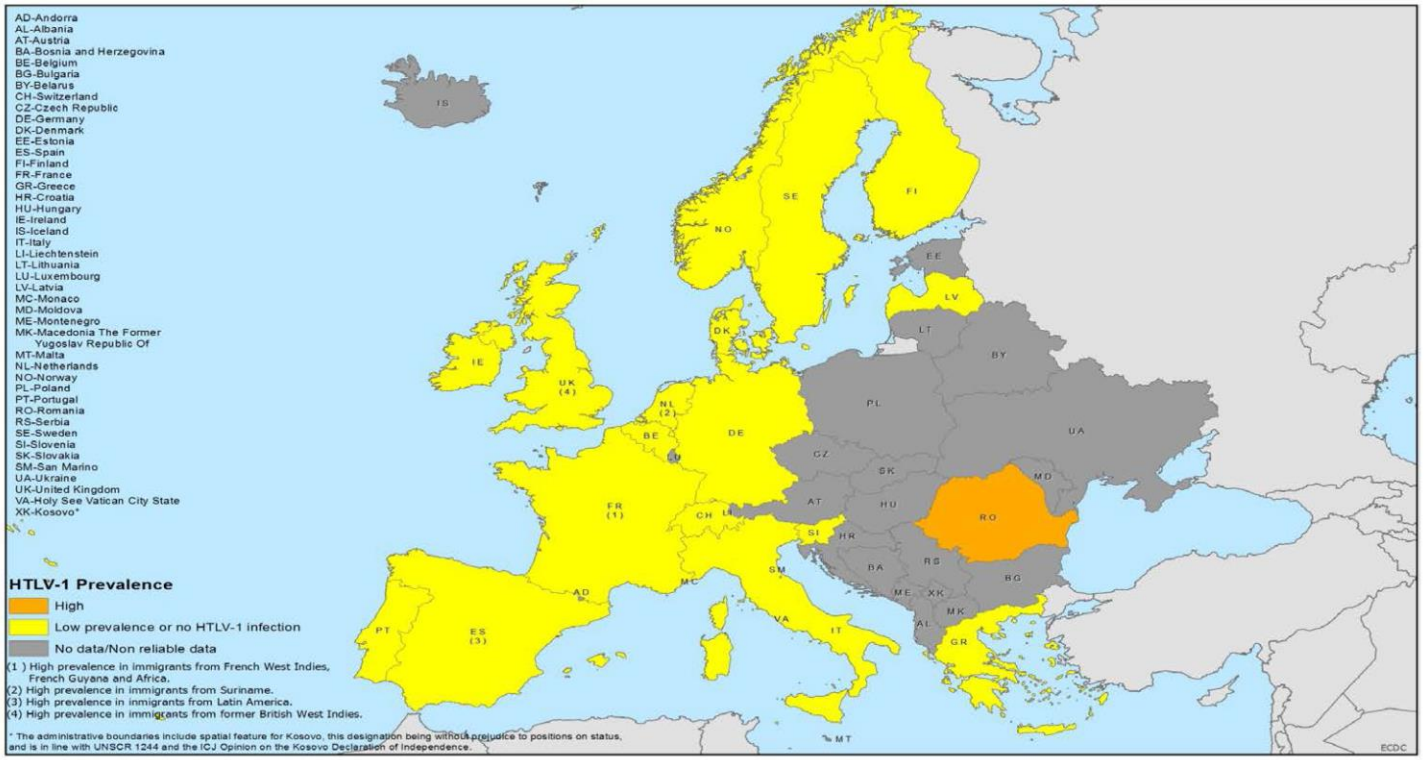
Europe (UK, France, Spain,..) Individuals originating from high HTLV-1 endemic areas (Caribbean area, South America and Africa,..), except Romania.

Continent / Country	Population°	HTLV-1 range	
EUROPE			
United kingdom**	63 047 162	20 000	30 000
France	65 630 692	15 000	25 000
Spain	47 042 984	1 000	8 000
Romania	21 848 504	3 000	15 000

In 2012, the EU Commission requested ECDC to construct a map indicating all the HTLV-1 high prevalence areas in the world. EPVO unit was asked to respond to a request for offer entitled : " *Systematic Review of Scientific Evidence on the Prevalence of HTLV-1 Infection*"

By analysing more than 1000 papers and hundreds of abstracts, we provided the first complete epidemiological data (maps and tables) for the 203 world's countries.

Figure 3. HTLV-1 prevalence in sovereign states and territories of Europe[3]



Ongoing collaborative studies (EPVO/Necker/Romania) combining:

1) Epidemiology
2) Genotyping of HTLV-1 strains (complete sequences)
3) Populations genetics

to try to decipher the origin of these strains and this HTLV-1 focus.

3) What is the situation in Australian Natives from Central Australia? Epidemiology and Genotype

The Guardian

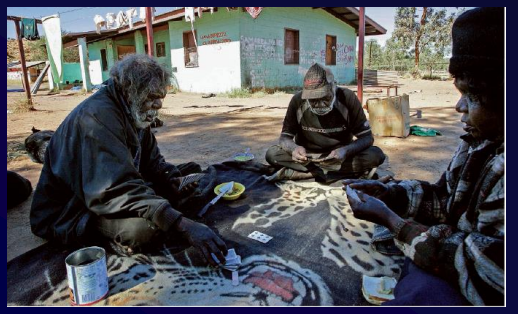
'People are scared': the fight against a deadly virus no one has heard of

HTLV-1 is endemic across central Australia. But testing takes six months and is not freely available

The Guardian

What is HTLV-1? The devastating health crisis afflicting central Australia

Between 5% and 10% of those with the virus will develop a rapidly fatal form of leukaemia



NEWS | IN DEPTH

INFECTIOUS DISEASES

A call to arms against the other retrovirus

HTLV-1, discovered just before HIV but almost forgotten, infects millions and causes cancer

844 25 MAY 2018 • VOL 360 ISSUE 6391 sciencemag.org SCIENCE

The Guardian

World experts call for Australia to act on devastating HTLV-1 virus

UK clinician says central Australia's 'shocking' 45% infection rate demands action

Correspondence

Time to eradicate HTLV-1: an open letter to WHO

*Fabiola Martin, Yutaka Tagaya, Robert Gallo
fabiola.martin@uq.edu.au

www.thelancet.com Vol 391 May 12, 2018

CNN Health » Doctors raise alarm about ancient HTLV-1 virus: 'Prevalence is off the charts' in Australia

Doctors raise alarm about ancient HTLV-1 virus: 'Prevalence is off the charts' in Australia

A) Indigenous Australians have one of the highest HTLV-1prevalence in the world

(long-term collaboration with Lloyd Einsiedel from Alice Springs)

Einsiedel *et al. BMC Public Health* (2016) 16:787
DOI 10.1186/s12889-016-3366-5

BMC Public Health

RESEARCH ARTICLE Open Access

Human T-Lymphotropic Virus type 1 infection in an Indigenous Australian population: epidemiological insights from a hospital-based cohort study

Lloyd Einsiedel[1,5*], Richard J. Woodman[1], Maria Flynn[1], Kim Wilson[2], Olivier Cassar[3,4] and Antoine Gessain[3,4]

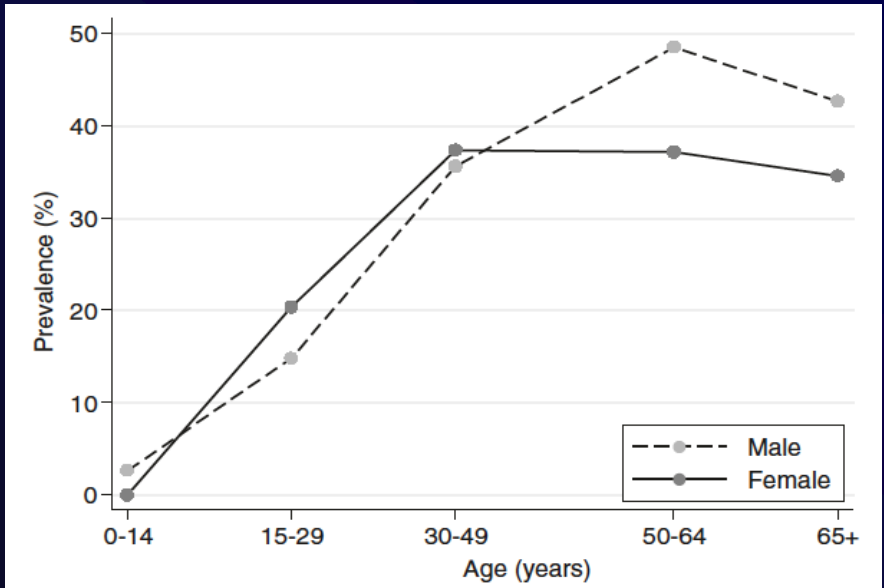


Fig. 3 Graph of HTLV-1 seropositivity rates for Indigenous males and females according to age among 1889 patients tested at Alice Springs Hospital

Variant Human T-cell Lymphotropic Virus Type 1c and Adult T-cell Leukemia, Australia

Lloyd Einsiedel,[1] Olivier Cassar,[1] Peter Bardy, Daniel Kearney, and Antoine Gessain

Human T-cell lymphotropic virus type 1 is endemic to central Australia among Indigenous Australians. However, virologic and clinical aspects of infection remain poorly understood. No attempt has been made to control transmission to indigenous children. We report 3 fatal cases of adult T-cell leukemia/lymphoma caused by human T-cell lymphotropic virus type 1 Australo-Melanesian subtype c.

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 19, No. 10, October 2013

Journal of Clinical Virology 57 (2013) 370–373

Contents lists available at SciVerse ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Case report

Human T-Lymphotropic Virus type 1 infective dermatitis in central Australia

Lloyd Einsiedel[a,*], Olivier Cassar[b,c], Lynne Gordon[d], Antoine Gessain[b,c]

[a] Northern Territory Rural Clinical School, Flinders University, 0870 Alice Springs, Northern Territory, Australia
[b] Unité d'Epidémiologie et Physiopathologie des Virus Oncogènes, Département de Virologie, Institut Pasteur, 28 rue du Dr. Roux, 75724 Paris Cedex 15, France
[c] CNRS, UMR 3569, F-75015 Paris, France
[d] Department of Dermatology, Flinders Medical Centre, Bedford Park, 5042 Adelaide, Australia

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PLOS | NEGLECTED TROPICAL DISEASES

Human T-Cell Lymphotropic Virus Type 1 Subtype C Molecular Variants among Indigenous Australians: New Insights into the Molecular Epidemiology of HTLV-1 in Australo-Melanesia

Olivier Cassar[1,2*], Lloyd Einsiedel[3*], Philippe V. Afonso[1,2], Antoine Gessain[1,2*]

1 Institut Pasteur, Unité d'Epidémiologie et Physiopathologie des Virus Oncogènes, Département de Virologie, Paris, France, 2 CNRS, UMR 3569, Paris, France, 3 Flinders University/Northern Territory Rural Clinical School, Alice Springs Hospital, Alice Springs, Northern Territory, Australia

MAJOR ARTICLE

Higher Human T-Lymphotropic Virus Type 1 Subtype C Proviral Loads Are Associated With Bronchiectasis in Indigenous Australians: Results of a Case-Control Study

Lloyd Einsiedel,[1,2] Olivier Cassar,[3,4] Emma Goeman,[5] Tim Spelman,[1] Virginia Au,[6] Saba Hatami,[6] Sheela Joseph,[1] and Antoine Gessain[3,4]

[1]Northern Territory Rural Clinical School/Flinders University, Northern Territory of Australia, Australia; [2]SA Pathology, Adelaide, South Australia, Australia; [3]Institut Pasteur, Unité EPVO, Département de Virologie, F-75015 Paris, France; [4]CNRS, UMR 3569, F-75015 Paris, France; [5]Department of Paediatrics, Alice Springs Hospital, Northern Territory of Australia, Australia; and [6]Department of Radiology, Flinders Medical Centre, Adelaide, South Australia, Australia

Such high prevalences have been already reported in some very high endemic areas for at least 20 to 40 years….

Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology
13(Suppl 1):S2–S7 © 1996 Lippincott–Raven Publishers, Philadelphia

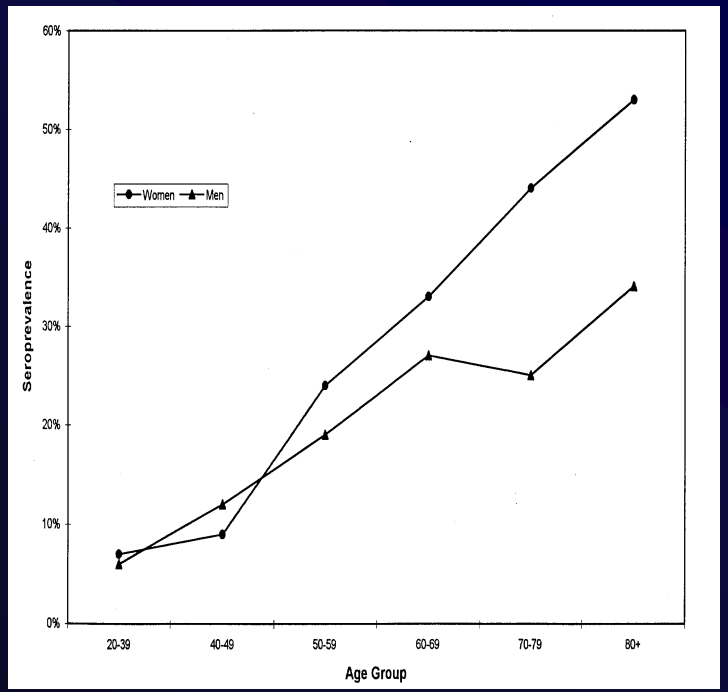
Findings from the Miyazaki Cohort Study

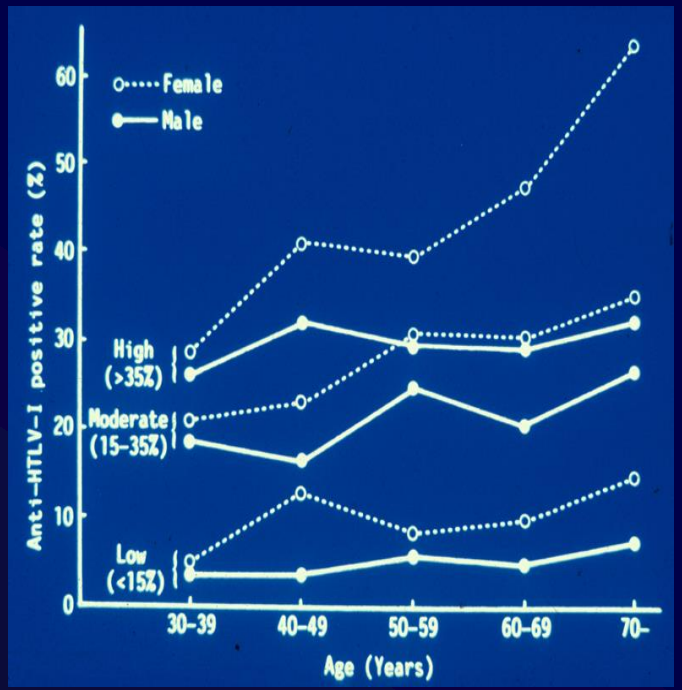
Nancy Mueller, *Akihiko Okayama, Sherri Stuver, and †Nobuyoshi Tachibana

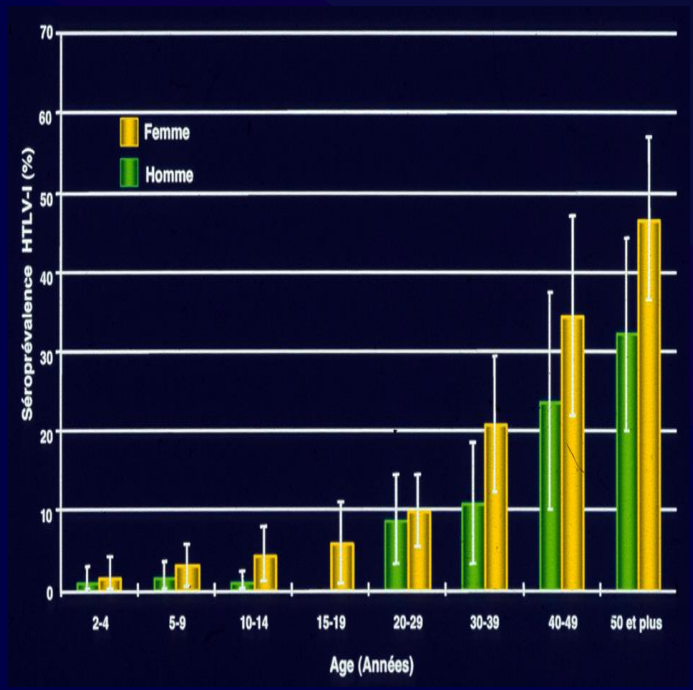
*Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, U.S.A., *Second Department of Internal Medicine, Miyazaki Medical School, Miyazaki, Japan, and †Oita Prefecture Institute for Health and Environment, Oita, Japan*

Villagers in South Japan

Noir-Marron
(population of African Origin)
in French Guyana







The origin of this puzzling geographical or often ethnic repartition, associated with a high prevalence is not well explained but is very probably linked to a founder effect in some groups, with a persistence of a high level of viral transmission rate

These modes of transmission could be different according to the situation

Pygmies, Indigenous Australians, South Japan,

Noir-Marron, Mashhad, Tumaco, Haut-Ogoué,....

B) HTLV-1c Genetic Variant is endemic in Indigenous people from Australo-Melanesia

(PNG, Solomon Islands, Vanuatu, Australia, …).

Proc. Natl. Acad. Sci. USA
Vol. 88, pp. 7694–7698, September 1991
Medical Sciences

Highly divergent molecular variants of human T-lymphotropic virus type I from isolated populations in Papua New Guinea and the Solomon Islands

(retrovirus/PCR/Melanesia/evolution)

ANTOINE GESSAIN*, RICHARD YANAGIHARA†‡, GENOVEFFA FRANCHINI*, RALPH M. GARRUTO†, CAROL L. JENKINS§, ANDREW B. ADUKIEWICZ¶, ROBERT C. GALLO*, AND D. CARLETON GAJDUSEK†

*Laboratory of Tumor Cell Biology, National Cancer Institute, and †Laboratory of Central Nervous System Studies, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892; ‡Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea; and ¶Ministry of Health and Medical Services, Central Hospital, Honiara, Solomon Islands

Contributed by D. Carleton Gajdusek, May 28, 1991

JOURNAL OF VIROLOGY, Feb. 1993, p. 1015–1023 Vol. 67, No. 2
0022-538X/93/021015-09$02.00/0

Complete Nucleotide Sequence of a Highly Divergent Human T-Cell Leukemia (Lymphotropic) Virus Type I (HTLV-I) Variant from Melanesia: Genetic and Phylogenetic Relationship to HTLV-I Strains from Other Geographical Regions

ANTOINE GESSAIN,[1]† ENZO BOERI,[1] RICHARD YANAGIHARA,[2] ROBERT C. GALLO,[1] AND GENOVEFFA FRANCHINI[1]*

Laboratory of Tumor Cell Biology, National Cancer Institute,[1] and Laboratory of Central Nervous System Studies, National Institute of Neurological Disorders and Stroke,[2] Bethesda, Maryland 20892

JOURNAL OF VIROLOGY, Nov. 1995, p. 6980–6993 Vol. 69, No. 11
0022-538X/95/$04.00+0

Isolation and Characterization of a New Simian T-Cell Leukemia Virus Type 1 from Naturally Infected Celebes Macaques (*Macaca tonkeana*): Complete Nucleotide Sequence and Phylogenetic Relationship with the Australo-Melanesian Human T-Cell Leukemia Virus Type 1

FERA IBRAHIM, GUY DE THÉ, AND ANTOINE GESSAIN*

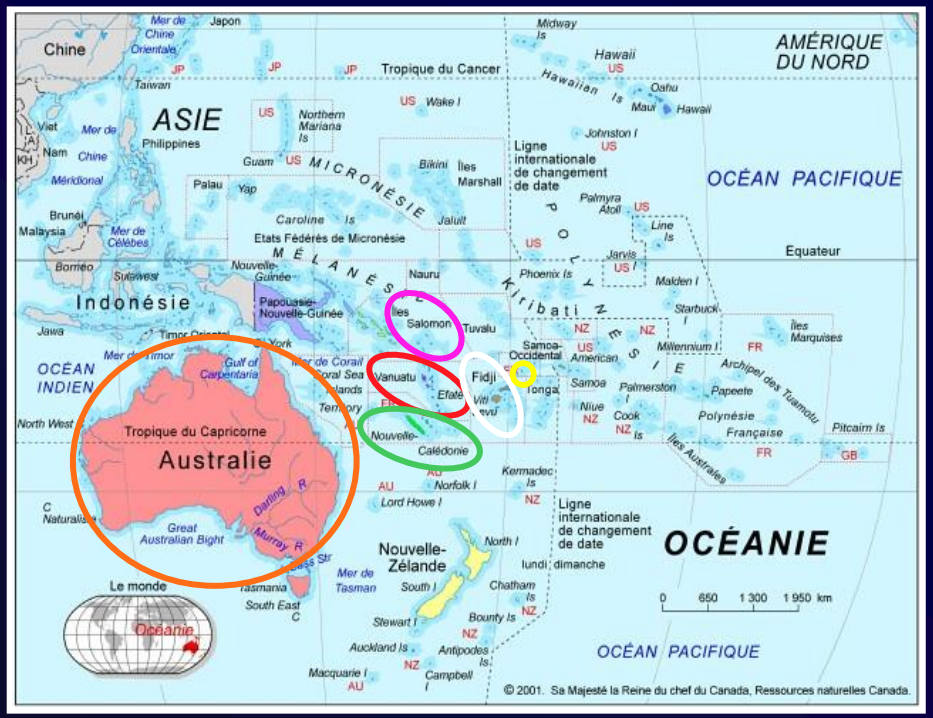
Unité d'Epidémiologie des Virus Oncogènes, Institut Pasteur, 75728 Paris Cedex 15, France

INSTITUT PASTEUR

Human T Lymphotropic Virus Type 1 Subtype C Melanesian Genetic Variants of the Vanuatu Archipelago and Solomon Islands Share a Common Ancestor

Olivier Cassar,[1,2] Corinne Capuano,[3] Sylviane Bassot,[2] Françoise Charavay,[1] Renan Duprez,[2] Philippe V. Afonso,[2] Myriam Abel,[4] Helene Walter,[5] Woreka Mera,[5] Paul M. V. Martin,[1] Eliane Chungue,[1] and Antoine Gessain[2]

[1]Laboratoire d'Epidémiologie Moléculaire, Institut Pasteur de Nouvelle-Calédonie, Nouméa, and [2]Unité d'Epidémiologie et Physiopathologie des Virus Oncogènes, Département de Virologie, Institut Pasteur, Paris, France; [3]World Health Organization, [4]Ministry of Health of the Republic of Vanuatu, and [5]Vanuatu Family Health Association, Port Vila, Vanuatu



PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

A Novel Human T-lymphotropic Virus Type 1c Molecular Variant in an Indigenous Individual from New Caledonia, Melanesia

Olivier Cassar[1,2], Françoise Charavay[3], Frédéric Touzain[4], Patricia Jeannin[1,2], Jean-Paul Grangeon[5], Sylvie Laumond[5], Eliane Chungue[3], Paul M. V. Martin[3], Antoine Gessain[1,2]*

PLOS Neglected Tropical Diseases | DOI:10.1371/journal.pntd.0005278 January 6, 2017

OPEN ACCESS Freely available online

PLOS | NEGLECTED TROPICAL DISEASES

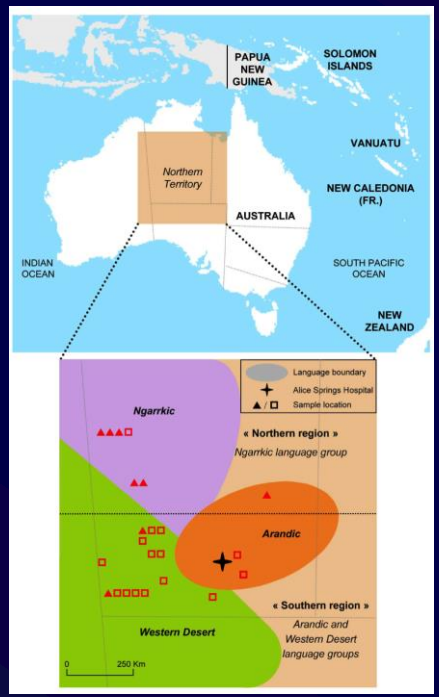
Human T-Cell Lymphotropic Virus Type 1 Subtype C Molecular Variants among Indigenous Australians: New Insights into the Molecular Epidemiology of HTLV-1 in Australo-Melanesia

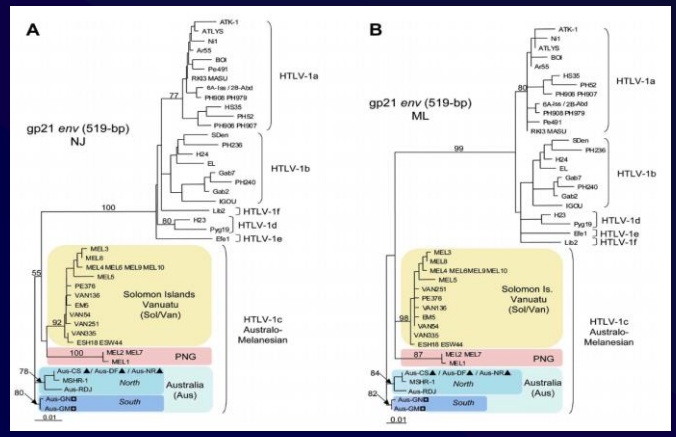
Olivier Cassar[1,2], Lloyd Einsiedel[3], Philippe V. Afonso[1,2], Antoine Gessain[1,2]*

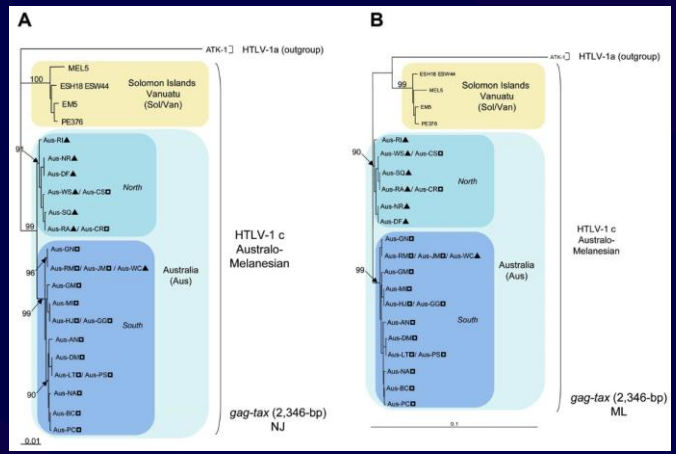
1 Institut Pasteur, Unité d'Epidémiologie et Physiopathologie des Virus Oncogènes, Département de Virologie, Paris, France, **2** CNRS, UMR 3569, Paris, France, **3** Flinders University/Northern Territory Rural Clinical School, Alice Springs Hospital, Alice Springs, Northern Territory, Australia

PLOS Neglected Tropical Diseases | www.plosntds.org 1 September 2013 | Volume 7 | Issue 9 | e2418

At least two different strains quite ancient >10.000 years







INSTITUT PASTEUR

4) What is the Simian Origin (STLV-1) of the Most Commonly World-Wide Spread Genotype (a Cosmopolitan) of HTLV-1?

HTLVs originate from STLVs found in Apes and Monkeys through interspecies transmission

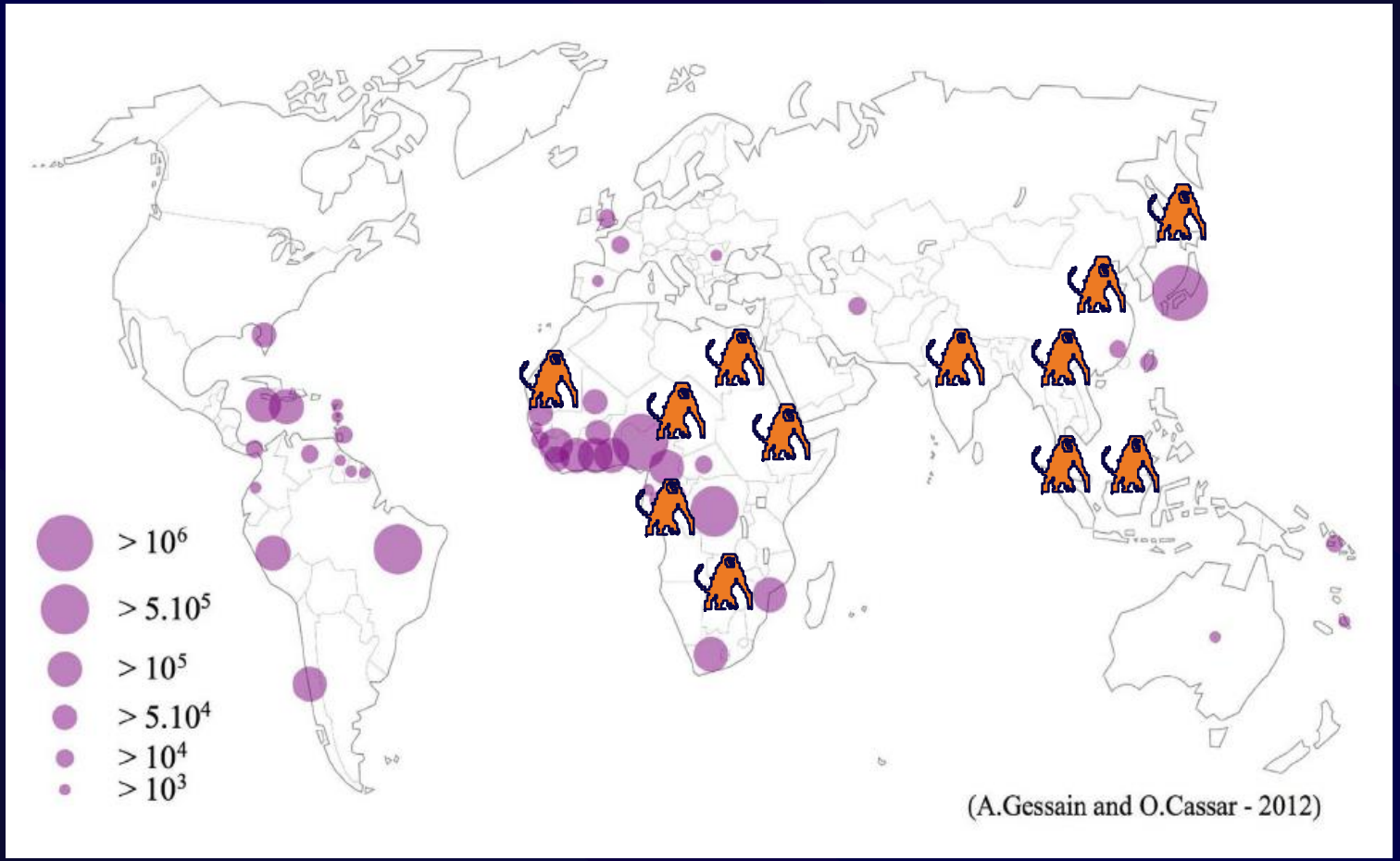
PTLV = Primate T-lymphotropic viruses

→ If found in **NHP = STLV**

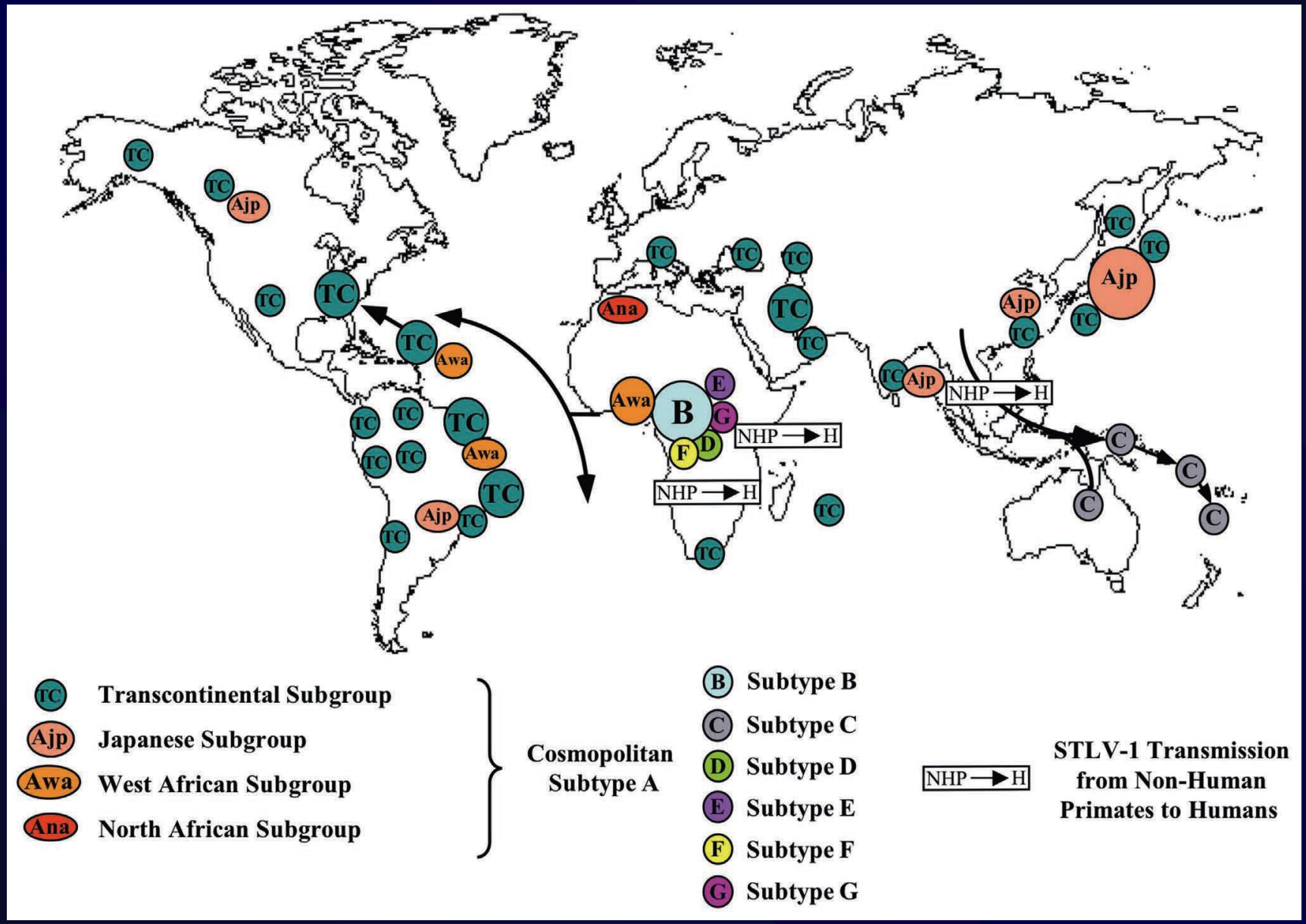
→ If found in **Human = HTLV**

1) Some of the infected monkeys develop a typical ATL with clonal integration of STLV-1 provirus in the tumor cells.

2) STLV-1 infection is widespread in Old World monkey and ape species (chimpanzee, gorilla, mandrill, AGM, macaques, Orang-utan).



Map of the geographical distribution of HTLV-1 subtypes (A–G), and the main modes of viral dissemination by movements of infected populations



Gessain and Cassar: Frontiers in Microbiology, 2012

Quid about interspecies transmission from STLV-1 monkeys to Human in Asia?

4) Several monkeys species are infected by STLV-1 in Asia (macaques ++), however there is no known human populations infected by such strains? This contrast with the situation in Central Africa where spill-over is still ongoing and also does not fit with the fact that other simian retroviruses, as the SFV, are still being transmitted from monkeys to humans in several Asian countries.

5) Are the different modes of transmission/acquisition of HTLV-1 similar on a quantitative point of view in the main high endemic areas?

Such data are crucial for public health actions aimed to decrease HTLV-1 infection.

HTLV-1 transmission

MTCT has been often considered as the most important mode of transmission in high endemic areas but solid data on such topic remain scarce. A recent paper in Japan demonstrated that sexual transmission between young adults is important with around 4,000 new infections/year>>MTCT.

The modes of acquisition of HTLV-1 in Central Africa, which is the largest HTLV-1 endemic area in the world

In Central Africa, at least five different modes of acquisition/transmission can occur:

Mother to child

Sexual

Transfusion

Scarification

Contact with fluids from NHPs

The relative contribution of each of the different transmission routes for HTLV-1/STLV-1 (between the different inter-humans modes and inter-humans *vs* inter-species/NHP-Humans) remains unknown

The first study was performed in Cameroon focused on the origin and interspecies transmission of different retroviruses from NHPs **living in the wild**

More than 5000 plasmas and buffy-coats of adults (mean age 50 years) were tested in a retrospective study in general rural population including Pygmees or Bantus living close to NHPs habitats and a prospective study focused on more than 300 individuals who reported direct contacts (bites, wounds,..) with animals, especially NHPs mainly during hunting activities.




Calattini et al., EID, 2007

STLV-3/HTLV-3

Retrovirology

BioMed Central

Short report

Open Access

Discovery of a new human T-cell lymphotropic virus (HTLV-3) in Central Africa

Sara Calattini†1, Sébastien Alain Chevalier†1, Renan Duprez1, Sylviane Bassot1, Alain Froment2, Renaud Mahieux†1 and Antoine Gessain*†1

New Strain of Human T Lymphotropic Virus (HTLV) Type 3 in a Pygmy from Cameroon with Peculiar HTLV Serologic Results

Sara Calattini,[1,a] Edouard Betsem,[1,3] Sylviane Bassot,[1] Sébastien Alain Chevalier,[1] Renaud Mahieux,[1,4] Alain Froment,[2] and Antoine Gessain[1]

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The Journal of Infectious Diseases 2009; 199:561–4

STLV-4/HTLV-4

Clinical Infectious Diseases

BRIEF REPORT

Zoonotic Transmission of Two New Strains of Human T-lymphotropic Virus Type 4 in Hunters Bitten by a Gorilla in Central Africa

Léa Richard,[1,2,3] Augustin Mouinga-Ondémé,[4] Edouard Betsem,[1,2,5,a] Claudia Filippone,[1,2,b] Eric Nerrienet,[5] Mirdad Kazanji,[4,c] and Antoine Gessain[1,2]

STLV-1/HTLV-1

Clinical Infectious Diseases Advance Access published April 1, 2015

MAJOR ARTICLE

A Severe Bite From a Nonhuman Primate is a Major Risk Factor for HTLV-1 Infection in Hunters From Central Africa

Claudia Filippone,[1,2] Edouard Betsem,[1,2,3] Patricia Tortevoye,[1,2] Olivier Cassar,[1,2] Sylviane Bassot,[1,2] Alain Froment,[4] Arnaud Fontanet,[5,6] and Antoine Gessain[1,2]

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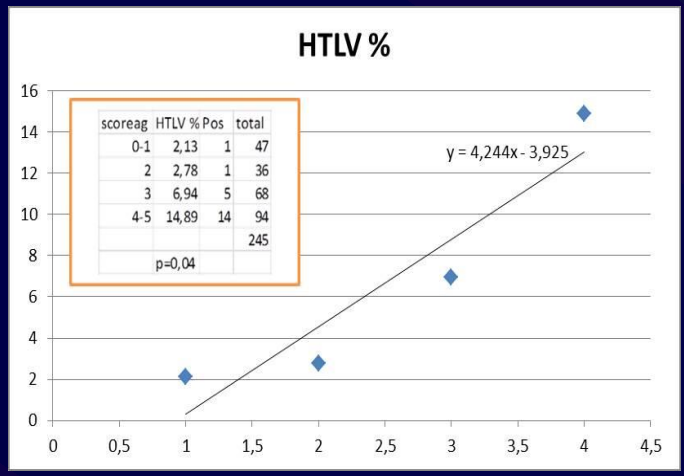

HTLV-1 infection was associated to the severity of the bite

Simian Foamy Viruses

OPEN ACCESS Freely available online PLoS PATHOGENS

Frequent and Recent Human Acquisition of Simian Foamy Viruses Through Apes' Bites in Central Africa

Edouard Betsem[1,2,3]*, Réjane Rua[1,2], Patricia Tortevoye[1,2], Alain Froment[4], Antoine Gessain[1,2]*

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Abstract

Human infection by simian foamy viruses (SFV) can be acquired by persons occupationally exposed to non-human primates (NHP) or in natural settings. This study aimed at getting better knowledge on SFV transmission dynamics, risk factors for such a zoonotic infection and, searching for intra-familial dissemination and the level of peripheral blood (pro)viral loads in infected individuals. We studied 1,321 people from the general adult population (mean age 49 yrs, 640 women and 681 men) and 198 individuals, mostly men, all of whom had encountered a NHP with a resulting bite or scratch. All of these, either Pygmies (436) or Bantus (1085) live in villages in South Cameroon. A specific SFV Western blot was used and two nested PCRs (*polymerase*, and LTR) were done on all the positive/borderline samples by serology. In the general population, 2/1,321 (0.2%) persons were found to be infected. In the second group, 37/198 (18.6%) persons were SFV positive. They were mostly infected by apes (37/39) FV (mainly gorilla). Infection by monkey FV was less frequent (2/39). The viral origin of the amplified sequences matched with the history reported by the hunters, most of which (83%) are aged 20 to 40 years and acquired the infection during the last twenty years. The (pro)viral load in 33 individuals infected by a gorilla FV was quite low (<1 to 145 copies per 10^5 cells) in the peripheral blood leucocytes. Of the 30 wives and 12 children from families of FV infected persons, only one woman was seropositive in WB without subsequent viral DNA amplification. We demonstrate a high level of recent transmission of SFVs to humans in natural settings specifically following severe gorilla bites during hunting activities. The virus was found to persist over several years, with low SFV loads in infected persons. Secondary transmission remains an open question.

Citation: Betsem E, Rua R, Tortevoye P, Froment A, Gessain A (2011) Frequent and Recent Human Acquisition of Simian Foamy Viruses Through Apes' Bites in Central Africa. PLoS Pathog 7(10): e1002306. doi:10.1371/journal.ppat.1002306

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Competing Interests: The authors have declared that no competing interests exist.

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Genetic Characterization of Simian Foamy Viruses Infecting Humans

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Viral Latency in Blood and Saliva of Simian Foamy Virus-Infected Humans

Rejane Rua[1,2,3], Edouard Betsem[1,2,4], Antoine Gessain[1,2]*

Case-control Study

Indicates the Presence of

Some Biological Differences

In Hunters Infected with SFV

from Gorilla

The Journal of Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association OXFORD

Clinical Signs and Blood Test Results Among Humans Infected With Zoonotic Simian Foamy Virus: A Case-Control Study

Florence Buseyne,[1,2] Edouard Betsem,[1,2,6] Thomas Montange,[1,2] Richard Njouom,[7] Chanceline Bilounga Ndongo,[8] Olivier Hermine,[3,4,5] and Antoine Gessain[1,2]

The second projet is currently developped in Gabon

We will try to quantify each of the different modes of transmission by conducting studies in specific populations including at least 12 000 persons:

1) General population of rural areas with a specific questionnaire for heterosexual transmission within couples, transfusion, hospitalisation, contact with monkeys, especially bites, and scarifications and other suspected risk factors. 2000 persons are already included. We plan to study 4 000 (both Bantus ++ and Pygmies).

2) Pregnant women (3000) and children (1500) to get insights into MTCT.
Children in such high endemic area can also be infected by transfusion.

3) Blood donors from the Libreville National Transfusion Centre. 3000 persons are already included.

Risk factors associated with HTLV-1 infection and corresponding

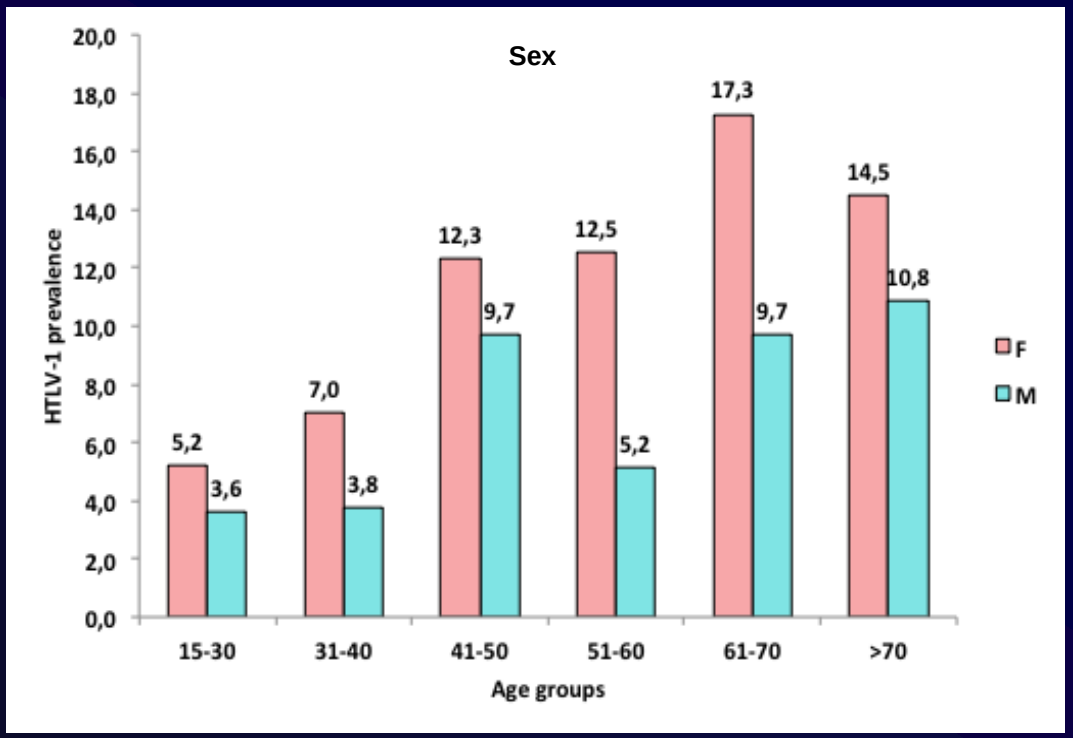
attribuable fractions will be identified using logistic regression models

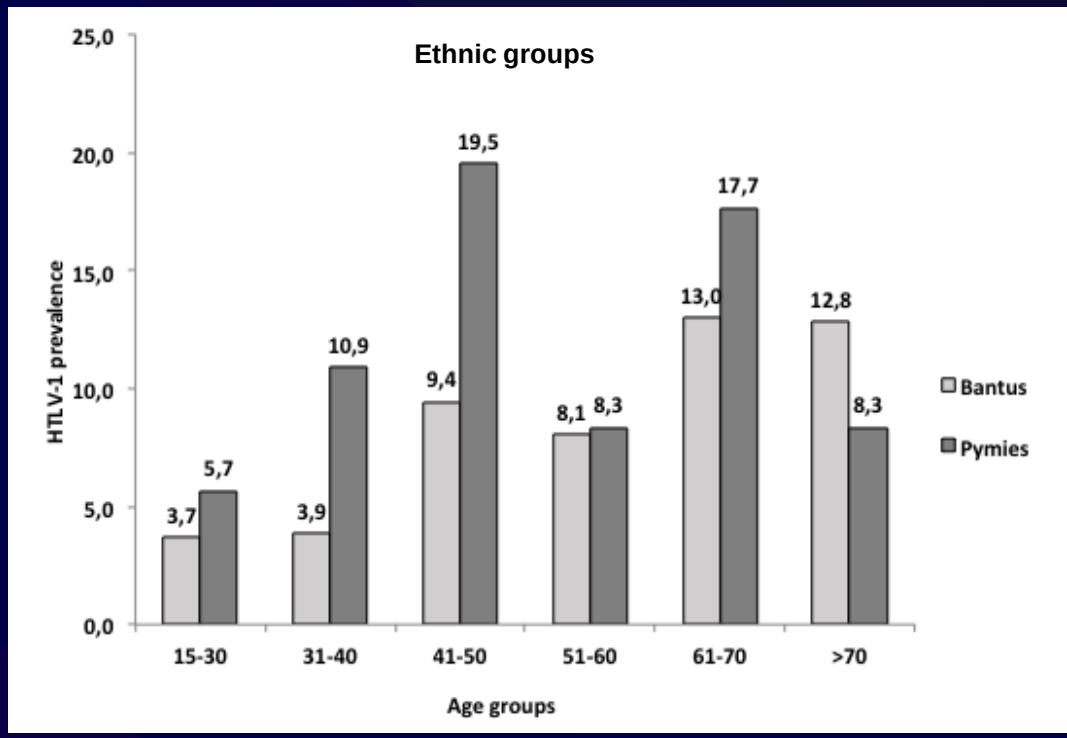
Preliminary data

2060 individuals from six different provinces

were included 1205 men and 855 women (mean age 49 years)

WB and PCR demonstrated that the prevalence rate is of 8.7%





Increase with age and higher in women and in Pygmies

D. D. Djuicy, PNTD 2018

The distribution of HTLV-1 infection is heterogeneous across the country

The overall prevalence (8.7%) appears to be higher than in neighboring countries (Cameroon CAR, ..) for similar populations

Risk factors for HTLV-1 infection

According to crude OR, HTLV-1 infection is associated with sex (women>> men), increased age, Pygmy groups, scarification, history of blood transfusion, multiple hospitalisations.

D. D. Djuicy, PNTD 2018

		HTLV-1			Multivariate Analysis		
		+ (n=179)	- (n=1881)	%	OR	95% CI	P Value
Sex							
	Male	82	1 123	6,8	1		
	Female	97	758	11,4	1,61	[1,1-2,2]	0,004
Age							
	[15-30]	18	404	4,3	1		<0,001
	[31-40]	17	324	5,0	1,3	[0,6-2,5]	
	[41-50]	37	312	10,6	3,0	[1,7-5,5]	
	[51-60]	26	296	8,1	2,3	[1,2-4,3]	
	[61-70]	39	255	13,3	3,8	[2,0-7,0]	
	>70	42	290	12,7	3,5	[1,9-6,4]	
Number of hospitalizations							
	0	41	575	6,7	1		0,05
	1	43	537	7,4	1,03	[0,7-1,6]	
	2-5	64	547	10,5	1,4	[0,9-2,1]	
	>5	15	71	17,4	2,4	[1,2-6,4]	
Ethnic group							
	Bantus	153	1 644	8,5	1		
	Pygmies	26	235	10,0	1,93	[0,2-3,1]	0,008
	ND	0	2	-	-	-	-
PNH bite							
	No	171	1 824	8,5	1		
	Yes	8	45	10,0	1,9	[0,87-4,1]	0,06
	ND	0	12	-	-	-	-

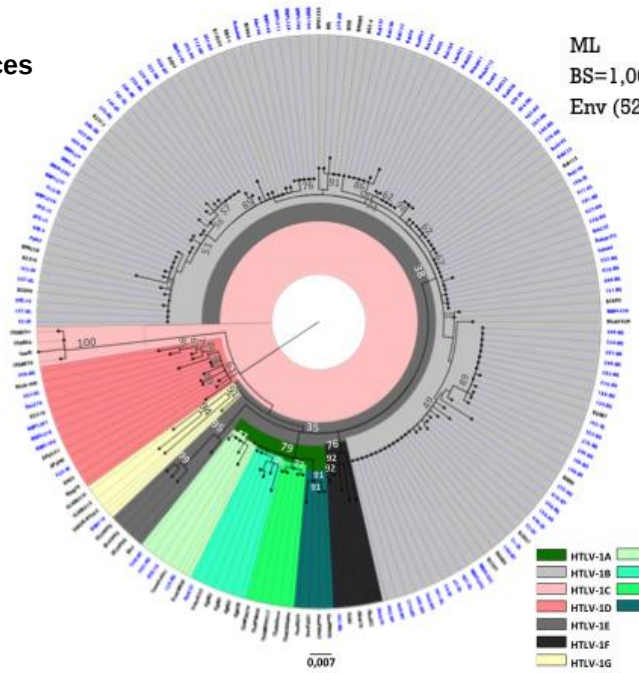
In the final multivariable analysis model, we found an increased independent risk of HTLV-1 in **women**, the **elderly**, persons having a **history of multiple hospitalizations** (more than 5 times) and **Pygmies**. In addition, a **NHP bite** appears to be marginally associated with a higher risk of HTLV-1.

Molecular Epidemiology of HTLV-1 in Central Africa

A total of 178 strains were partially characterized env and/or LTR.

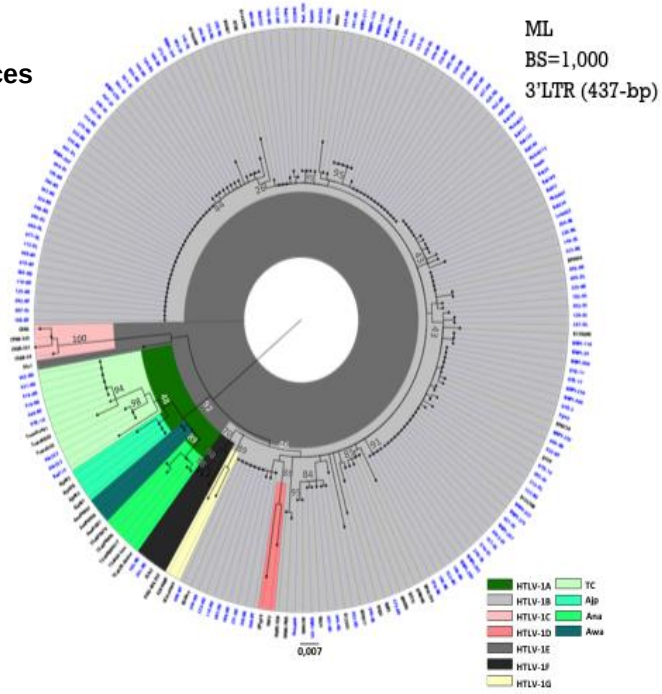
123 new Env sequences in blue color

- ✓ HTLV-1a → 5 (4,1%)
- ✓ HTLV-1b → 108 (87,8%)
- ✓ HTLV-1d → 6 (5,7%)
- ✓ HTLV-1f → 2 (1,6%)
- ✓ HTLV-1g → 1 (0,8%)



154 new 3'-LTR sequences in blue color

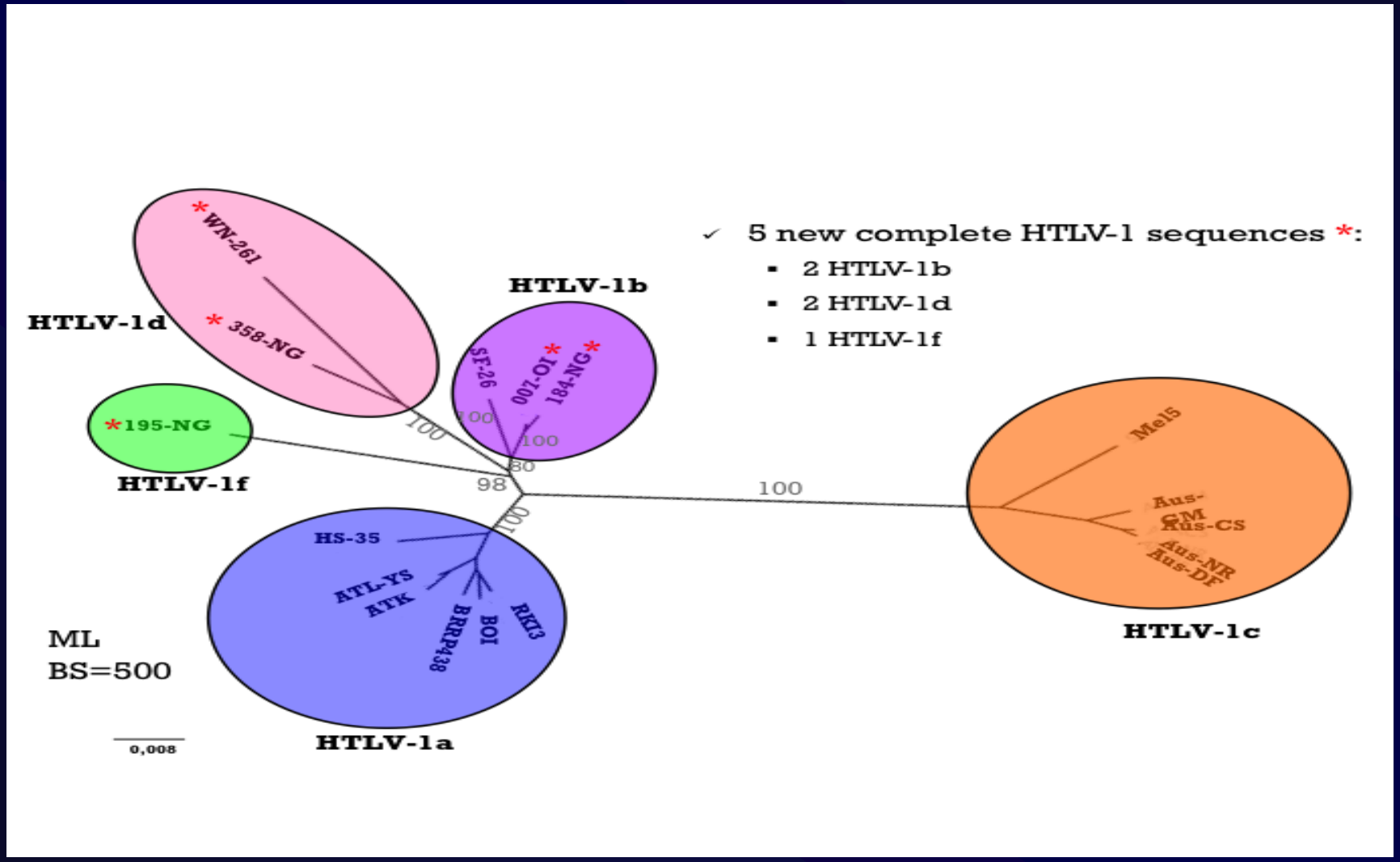
- ✓ HTLV-1a → 9 (5,8%)
- ✓ HTLV-1b→143 (92,9%)
- ✓ HTLV-1f→ 2 (1,3%)



The majority of the strains belong to the Central African molecular b-subtype (90.%).

However, there was a certain genetic diversity: 10 viral strains belong to the Cosmopolitan a subtype (TC subgroup) (3.8%), 6 strains to the d subtype (5.3%), while 3 strains are of the f-subtype (1.5%) and a single strain from Cameroon belongs to the rare g-subtype (0.6%).

First complete sequences of African HTLV-1 b, d and f genotypes



Take-Home Messages

1) The current real geographical distribution of HTLV-1 and the number of HTLV-1 infected individuals remain unknown: Need large epidemiological surveys in Africa and in Asia

2) In Africa, the largest HTLV-1 endemic area, the relative contribution of each of the different transmission routes remains unknown

3) Gabon is a very high HTLV-1 endemic foci and HTLV-1 can be acquired by different means: sexual, mother to child, during hospitalization, and through contact with NHPs.

4) In Central Africa there is some genetic diversity of HTLV-1 (b, d, e, f, g,) with subtype b being highly predominant.

What is the world burden of HTLV-1 associated diseases ?

Except in Japan where the situation is quite well known ar least for:

ATLL (around 800 -1000 cases/year) and TSP/HAM (at least 50 cases a year).

Situation in most of the other endemic areas in the world is not really known

This is linked to several factors:

- HTLV-1 and the associated diseases are not well known from the clinicians who thus do not diagnosed them.
- Tests for HTLV-1 infection are rarely available in many areas and countries.
- Hematologists and neurologists are rare in many countries endemic for HTLV-1 (Africa).
- No specific studies on large scale for a given country.

This leads to a huge under-reporting of such diseases and new studies are absolutely necessary

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Epidémiologie et Physiopathologie des Virus Oncogènes

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