

ImmunoTools *special* Award 2015



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Serologic and molecular investigation of HTLV-1/2 among pregnant women and lactating mothers living in the Oiapoque county, Amapa state in the border of French Guiana

The human T cell lymphotropic virus type 1 (HTLV-1) is a retrovirus etiologically involved in two main pathologies, the Adult T-cell leukemia/lymphoma (ATLL) and the Tropical Spastic Paraparesis (TSP) also known as HTLV-1 associated myelopathies (HAM). Comprising the Lentivirus genus, HTLV-1 can be transmitted by sexual intercourse and from infected lactating mother to breast feeding babies. Any other form of transmission can occur through HTLV-1 contaminated blood. Despite, a small percentage of HTLV-1 infected subjects develops any disease etiologically linked to the virus, its spread among populations, through familiar nucleus, certainly will increase the incidence of HTLV-1 related diseases. HTLV-1 detection among pregnant women and lactating mothers is an important tool to prevent virus spreading in the population as also, the utilization of preservatives during intercourse to prevent virus transmission in semen or genital fluids containing HTLV-1 infected lymphocytes. Serological surveys for HTLV-1, mainly among women, in the reproductive age, is mandatory, so measures to prevent transmission could be designed and applied, as substitution of breast milk of infected mothers by milk formulae, or during the birth, preventing mother infected blood to contaminate the newborn baby. ELISA assays coated with HTLV-1 antigens can be employed to detect antibodies against HTLV-1, and reactive serum/plasma samples can be confirmed by Western Blot test. Prevalence and incidence of virus infection is distinct in different geographical areas as also among ethnic groups, being most commonly found among Afro-descendants and Japanese subjects. For example, in Brazil, in the north and northeast areas there are the highest HTLV-1 prevalence, while in the south, in Santa Catarina state we have the lowest HTLV-1 virus incidence, due to the predominance of caucasian populations.

Presently, a serologic survey has been conducted in Oiapoque county, in the Amapa state, in the international border of French Guiana. It is known that French Guiana and Caribbean islands have predominance of Afro-descendants in their populations, therefore the HTLV-1 incidence is very high. In a short time, an international bridge

will be connecting French Guiana and Caribbean islands to Amapa state through Oiapoque, so the serological survey will show the HTLV-1 prevalence before the bridge opening and after the high traffic of tourists in both directions. The results of the current research work will provide data to support health planning and measures to avoid or diminish HTLV-1 spreading in the population. Besides prevention, until now there is not any effective drug to clear HTLV-1 infection and, the above mentioned diseases linked to HTLV-1 infection are incurable, being ATLL of rapid and fatal course, while TSP/HAM is of slow progression, debilitating and capable to incapacitate the patient. After disease progression, the patient and his/her family suffer and spend so much effort and money to have some kind of confort and treatment and also, the government spend so much financial and bureaucratic resources. Therefore, simple and rapid serological surveys can be better than after the occurrence of virus infection and disease progression, in terms of social, humane and economic aspects. Besides, these studies can support basic research to understand why some ethnic groups and people in some geographical areas are more prone to virus infection and disease progression than others. Also, natural products, abundant and diversified in the country, can be assayed for anti-HTLV-1 activity or, in indirect way to promote immune regulation with consequent viral silencing and/or clearance.

Literature consulted

Abad M, Dronda F, Dominguez E, Moreno S, Vallejo A. HTLV-2b among HIV type 1- coinfecting injecting drug users in Spain. *AIDS Res Hum Retroviruses*. 2011 May;27(5):579-83.

Barros Kanzaki LI, Casseb J. Unusual finding of HTLV-I infection among Amazonian Amerindians. *Arch Med Res*. 2007 Nov;38(8):897-900.

Brucato N, Cassar O, Tonasso L, Tortevoeye P, Migot-Nabias F, Plancoulaine S, Guitard E, Larrouy G, Gessain A, Dugoujon JM. The imprint of the Slave Trade in an African American population: mitochondrial DNA, Y chromosome and HTLV-1 analysis in the Noir Marron of French Guiana. *BMC Evol Biol*. 2010 Oct 19;10:314.

Carneiro-Proietti AB, Catalan-Soares BC, Castro-Costa CM, Murphy EL, Sabino EC, Hisada M, Galvão-Castro B, Alcantara LC, Remondegui C, Verdonck K, Proietti FA. HTLV in the Americas: challenges and perspectives. *Rev Panam Salud Publica*. 2006 Jan;19(1):44-53.

de Queiroz AT, Mota-Miranda AC, de Oliveira T, Moreau DR, Uripia Cde C, Carvalho CM, Galvão-Castro B, Alcantara LC. Re-mapping the molecular features of the human immunodeficiency virus type 1 and human T-cell lymphotropic virus type 1 Brazilian sequences using a bioinformatics unit established in Salvador, Bahia, Brazil, to give support to the viral epidemiology studies. *Mem Inst Oswaldo Cruz*. 2007 May;102(2):133-9.

Gallo RC. Research and discovery of the first human cancer virus, HTLV-1. *Best Pract Res Clin Haematol*. 2011 Dec;24(4):559-65.

Gessain A, Gallo R C, Franchini G. Low degree of human T-cell leukemia/lymphoma virus type I genetic drift in vivo as a means of monitoring viral transmission and movement of ancient human populations. *J Virol*. 1992 April; 66(4): 2288–2295.

Gessain A. Human retrovirus HTLV-1: descriptive and molecular epidemiology, origin, evolution, diagnosis and associated diseases. *Bull Soc Pathol Exot*. 2011 Aug;104(3):167-80.

Gonçalves DU, Proietti FA, Ribas JG, Araújo MG, Pinheiro SR, Guedes AC, Carneiro-Proietti AB. Epidemiology, treatment, and prevention of human T-cell leukemia virus type 1-associated diseases. *Clin Microbiol Rev*. 2010 Jul;23(3):577- 89.

Kanzaki L I B. Epidemiologia del HTLV en la Amazonia brasileña: seroprevalencia e identificación del virus circulante. Monterrey, Nuevo Leon, 1995. <http://cdigital.dgb.uanl.mx/te/1020112164.PDF>

Kanzaki LIB, Casseb J. Human T-Lymphotropic Viruses Evolution Possibly Explained by Primate Deltaretrovirus Geographical Segregation. *Retrovirology: Research and Treatment* 2008:1 15-20.

Mahieux R, Gessain A. HTLV-3/STLV-3 and HTLV-4 viruses: discovery, epidemiology, serology and molecular aspects. *Viruses*. 2011 Jul;3(7):1074-90.

Pillat MM, Bauer ME, de Oliveira AC, Ulrich H, Casseb J. HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP): still an obscure disease. *Cent Nerv Syst Agents Med Chem*. 2011 Dec 1;11(4):239-45.

Posada-Vergara MP, Montanheiro P, Fukumori LM, Bonasser F, Duarte AJ, Penalva de Oliveira AC, Casseb J. Clinical and epidemiological aspects of HTLV-II infection in São Paulo, Brazil: presence of tropical spastic paraparesis/HTLV-associated myelopathy (TSP/HAM) simile diagnosis in HIV-1-co-infected subjects. *Rev Inst Med Trop Sao Paulo*. 2006 Jul-Aug;48(4):207-10.

Song KJ, Nerurkar VR, Saitou N, Lazo A, Blakeslee JR, Miyoshi I, Yanagihara R. Genetic analysis and molecular phylogeny of simian T-cell lymphotropic virus type I: evidence for independent virus evolution in Asia and Africa. *Virology*. 1994 Feb 15;199(1):56-66.

Switzer WM, Black FL, Pieniazek D, Biggar RJ, Lal RB, Heneine W. Endemicity and phylogeny of the human T cell lymphotropic virus type II subtype A from the Kayapo Indians of Brazil: evidence for limited regional dissemination. *AIDS Res Hum Retroviruses*. 1996 May 1;12(7):635-40.

Vandamme AM, Bertazzoni U, Salemi M. Evolutionary strategies of human T-cell lymphotropic virus type II. *Gene*. 2000 Dec 30;261(1):171-80. -Yamashita M, Ishida T, Ohkura S, Miura T, Hayami M. Phylogenetic characterization of a new HTLV type 1 from the Ainu in Japan. *AIDS Res Hum Retroviruses*. 2001 May 20;17(8):783-7.

Screening of antiretroviral activity among natural products utilizing SIV as a model

Amazonian medicinal plant extracts and synthetic peptides of animal venoms will be assayed for antiretroviral activity utilizing established human lymphoblastic cell lines infected with Simian Immunodeficiency Virus (SIV), as a model for HIV infection. Human lymphoblastic cell lines likewise 174XCEM, HUT-78 and MOLT-4, will be treated with plant extracts and animal venoms and, in different treatment periods, cells will be infected with SIVmac, and periodically, SIVp27 viral peptide will be quantified in cell supernatant utilizing an ELISA assay. In order to test the cytotoxicity of plant extracts and animal venoms, cells will be checked by flow cytometry for viability by the CD4⁺ cell membrane markers targeted with monoclonal antibodies and fluorescent conjugate to count live cells, after treatment with plant extracts and animal venoms. Aiming to evaluate the behaviour of the human established lymphoblastic cell lines, previously and after treatment with plant extracts and animal venoms, it will be determined the cytokine profile of those cell lines by ELISA assays. Also, the same lymphoblastic cell lines will have the cytokine profile determined after infection by SIV and when treated by plant extract and animals venom and challenged by SIV infection.

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includes 22 reagents

FITC - conjugated anti-human CD4, Annexin V,

PE - conjugated anti-human CD4, Annexin V,

human ELISA-set for 96 wells, human IFN-gamma, human IL-4, human IL-6, human IL-8, human IL-10 and human TNF-a (each 3 reagents) [DETAILS](#) more [AWARDS](#)