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HTLV-2: an ancient infection among Indian people of Brazilian Amazon Region

HTLV-2: uma infecção antiga entre os povos indígenas da Amazônia brasileira

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Human T-cell lymphotropic viruses 1 and 2 (HTLV-1 and HTLV-2) were the first human retroviruses to be described causing diseases in humans; they were isolated in lymphocyte cultures and share numerous similarities in biological and molecular properties[1,2]. More recently, two new types, the human T-cell lymphotropic virus 3 (HTLV-3) and the human T-cell lymphotropic virus 4 (HTLV-4), were described in populations of the Republic of Cameroon, the former being associated with *Primate T-lymphotropic virus 3* (PTLV-3) and the latter showing no phylogenetic relationship to the HTLV and PTLV types known so far[3,4]. HTLV-3 and HTLV-4 are restricted to few cases among hunters, animal meat handlers and are still waiting for further evidences of human dissemination elsewhere.

Molecular studies revealed the existence of a genetic variant of HTLV-2 among the Kayapó group, called HTLV-2c[5], being distinct from the subtypes 2a and 2b described, until then, in other human populations[6]. The occurrence of subtype 2c has been confirmed in several villages of the Kayapó group, as well as among the Arara do Laranjal, Zo'é and Tiriyó tribes[5,7,8,9].

For many years, the endemic presence of HTLV-2 among indigenous communities in the Americas supported the theory of origin for this virus in the New World[10]. This hypothesis became attractive when Chen et al.[11] isolated the *Primate T-lymphotropic virus 2* (PTLV-2) in two species of New World monkeys, suggesting the transmission due to interspecific barrier crossing. However, new studies, conducted in primates from the Americas, were not successful in demonstrating evidences of PTLV-2 infection, ruling out the American origin hypothesis for HTLV-2.

The presence of HTLV-2b infection in Central African pygmy peoples[12] supports the hypothesis that the human infection with HTLV-2 is old and that it began on the African continent, followed by its spread to Europe and Asia through human migratory movements initiated some 100,000 years ago[13]. The finding of the new subtype HTLV-2d with high degree of genetic divergence in pygmies from the Democratic Republic of Congo has reinforced this hypothesis[14]. Likewise, the phylogenetic proximity between African and Amerindian HTLV-2a strains suggests that the evolution of HTLV-2a and HTLV-2b preceded the human migratory movement from Africa toward Europe and Asia. This is supported by the phylogenetic analysis which reveal that viral isolates in Africa are represented by all three subtypes (2a, 2b and 2d), showing the large heterogeneity of the virus in the continent.

The evidence of HTLV-2a in an isolated human community in Mongolia[15] suggested that the virus was disseminated following the human migratory movement towards Asia, a route that gave rise to Amerindian populations around 10,000 to 40,000 years. This hypothesis has also been strongly accepted to explain the endemic presence of HTLV-2b in several indigenous populations in the Americas[13].

The migratory waves towards the Americas have been reviewed and, according to archaeological, anthropological and genetic findings, the migrations of Amerindian ancestors occurred according to two or more independent routes[16]. Equally, the migratory movements towards South America had two possible routes: one towards the Amazon and the other down the Pacific coast, parallel to the Andes Cordillera[16,17]. This differential migratory flow of Amerindian ancestors to South America may have introduced HTLV-2c in the Amazon Region, characterizing a typical founder effect. On the other hand, as shown by the phylogenetic analysis, viral samples identified among Amerindian and urban groups (HTLV-2c) are distinct from those isolated from HTLV-2a found in North America[5,9]. Among other possible explanations for the origin of HTLV-2c in the Amazon, there is the possibility of an autochthonous origin, from a proto-HTLV-2a infecting an Ameridian ancestral who entered Brazil through the Amazon, and the new molecular subtype disseminated among the Indian peoples of Brazil as a result of the process of population expansion.

Many of the Indian populations of South America have been isolated, or establishing few interactions with other human groups (indigenous or not). This suggests that HTLV-2c infection is ancient, and probably existed in the present form or evolved during its migration together with their human ancestors to the New Continent. The genetic similarity of more than 99% among HTLV-2c strains, isolated from urban and indigenous areas, gives supports to the suggestions that the virus was actively transmitted to urban areas, increasing its geographic endemicity within the Amazon Region[9].

The major question still concerns about how and when HTLV-2c, usually found as an endemic infection among Indian communities[5], reached urban populations. Studies suggest that the virus was transmitted and disseminated among the colonizers through sexual contact with infected Indians and vertically, from mother to child, mainly through breastfeeding[8]. The extensive genetic mix that occurred during the initial settlement of the Amazonian people, most likely resulted in the introduction of HTLV-2c among urban communities in formation.

The hypothesis of the HTLV-2c transmission, through a process of miscegenation, is reinforced by the existence of socioeconomic activities, starting from the 18th century, which allowed the contact of previously isolated Indian populations with neo-Brazilian populations. Sexual intercourse, particularly among Indian men and non-Indian women, is a common practice, especially among some Kayapó communities, which are located close to small towns maintained by commercial activities, agriculture, and mining. The occurrence of HTLV-2c transmission through direct contact between Indian people isolated in the Amazon and drug users from large cities is an unlikely event.

It is reasonable to suggest that the presence of this viral variant, among the native Indians of Brazil, was sequentially disseminated to urban populations through interethnic contact, and the current maintenance of the virus in urban areas through sexual contact, breastfeeding and injecting drug use.

REFERENCES

1 Poiesz BJ, Ruscetti FW, Reitz MS, Kalyanaraman VS, Gallo RC. Isolation of a new type C retrovirus (HTLV) in primary uncultured cells of a patient with Sézary T-cell leukaemia. Nature. 1981 Nov 19;294(5838): 268-71.

2 Kalyanaraman VS, Sarngadharan MG, Nakao Y, Ito Y, Aoki T, Gallo RC. Natural antibodies to the structural core protein (p24) of the human T-cell leukemia (lymphoma) retrovirus found in sera of leukemia patients in Japan. Proc Natl Acad Sci U S A. 1982 Mar;79(5):1653-7.

3 Calattini S, Chevalier SA, Duprez R, Bassot S, Froment A, Mahieux R, et al. Discovery of a new human T-cell lymphotropic virus (HTLV-3) in Central Africa. Retrovirology. 2005 May;2:30.

4 Wolfe ND, Heneine W, Carr JK, Garcia AD, Shanmugam V, Tamoufe U, et al. Emergence of unique primate T-lymphotropic viruses among central African bushmeat hunters. Proc Natl Acad Sci U S A. 2005 May;102(22):7994-9.

5 Ishak R, Harrington WJ Jr, Azevedo VN, Eiraku N, Ishak MO, Guerreiro JF, et al. Identification of human T-cell lymphotropic virus type IIa infection in the Kayapo, an Indigenous population of Brazil. AIDS Res Hum Retroviruses. 1995 Jul;11(7):813-21.

6 Hall WW, Takahashi H, Liu C, Kaplan MH, Scheewind O, Ijichi S, et al. Multiple isolates and characteristics of human T-cell leukemia virus type II. J Virol. 1992 Apr;66(4):2456-63.

7 Hall WW, Ishak R, Zhu SW, Novoa P, Eiraku N, Takahashi H, et al. Human T-lymphotropic virus type II (HTLV-II): epidemiology, molecular properties, and clinical features of infection. J Acquir Immune Defic Syndr Hum Retrovirol. 1996;13 Suppl 1:S204-14.

8 Ishak R, Vallinoto ACR, Azevedo VN, Lewis M, Hall WW, Ishak MOG. Molecular evidence of mother-to-child transmission of HTLV-IIc in the Kararao Village (Kayapo) in the Amazon Region of Brazil. Rev Soc Bras Med Trop. 2001 Nov-Dec;34(6):519-25.

9 Vallinoto ACR, Ishak MOG, Azevedo VN, Vicente ACP, Otsuki K, Hall WW, et al. Molecular epidemiology of human T-lymphotropic virus type II infection in Amerindian and urban populations of the Amazon region of Brazil. Hum Biol. 2002 Oct;74(5):633-44.

10 Gessain A, Thé G. What is the situation of human T-cell lymphotropic virus type II (HTLV-II) in Africa? Origin and dissemination of genomic subtypes. J Acquir Immune Defic Syndr Hum Retrovirol. 1996;13 Suppl 1:S228-35.

11 Chen YM, Jang YJ, Kanki PJ, Yu QC, Wang JJ, Montali RJ, et al. Isolation and characterization of simian T-cell leukemia virus type II from New World monkeys. J Virol. 1994 Feb;68(2):1149-57.

12 Gessain A, Mauclère P, Froment A, Biglione M, Le Hesran JY, Tekaia F, et al. Isolation and molecular characterization of a human T-cell lymphotropic virus type II (HTLV-II), subtype B, from a healthy Pygmy living in a remote area of Cameroon: an ancient origin for HTLV-II in Africa. Proc Natl Acad Sci U S A. 1995 Apr;92(9):4041-5.

13 Biggar RJ, Taylor ME, Neel JV, Hjelle B, Levine PH, Black FL, et al. Genetic variants of T-lymphotropic virus type II in American Indian Groups. Virology. 1996 Feb;216(1):165-73.

14 Vandamme AM, Salemi M, Van Brussel M, Liu HF, Van Laethem K, Van Ranst M, et al. African origin of human T-lymphotropic virus type 2 (HTLV-2) supported by a potential new HTLV-2d subtype in Congolese Bambuti Efe Pygmies. J Virol. 1998 May;72(5):4327-40.

15 Hall WW, Zhu SW, Horal P, Furuta Y, Zagaany G, Vahlne A. HTLV-II infection in Mongolia. AIDS Res Hum Retrov. 1994;10:443.

16 Nemecek S. Who were the first Americans? Sci Am. 2000 Sep;283(3):80-7.

17 Rothhammer F, Silva C. Peopling of Andean South America. Am J Phys Anthropol. 1989 Mar;78(3):403-10.