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Could Bovine Leukemia Virus Be a Possible Agent of Some Human Lymphatic Leukemias ?

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We are reproposing the hypothesis, not new in the international literature, that bovine leukemia virus (BLV) might be a cause or a contributing factor of human B-lymphatic leukemias. Epidemiological and virological data are now available, which, although not proving this hypothesis, might not be only coincidental.

In the USA a significantly higher incidence of acute and chronic lymphatic leukemias occurs in the agricultural states in the central area of the country, and the incidence of human lymphatic leukemias was higher in farmers living in counties where a higher rate of bovine leukemia was observed [1,2]. Similar evidence was obtained in the Soviet Union [3] and in Sweden [4]. On the other hand, the study of the epidemiological distribution of human chronic lymphatic leukemia (CLL) in different nations all over the world indicates that CLL is at least 10 times less frequent in India, Singapore and Japan than in Western countries [5]. CLL accounts for 25% of all leukemias in Western countries and for only 2% of all leukemias in the Far East; this latter incidence is in general characteristic of non-European populations [5]. The hypothesis that this might be due simply to the lack of susceptible aged subjects is certainly not valid for Japan where the average population survival is similar to that of Western countries. Then it is possible that this striking difference in the frequency of CLL in Europe and in populations mainly of European origine, compared to other populations of the world, could be due to different alimentary habits: in Western populations cow milk and particularly bovine meat have been for a long time and still are a food much more common than in the other world populations, mainly for economical reasons, or for religious attitudes (as in India), or for alimentary customs, as in Japan, where the main source of alimentary proteins is still fish, and where bovine meat was almost unknown until 50 years ago.

BLV infection is widespread in many bovine herds in Europe and in the USA. BLV determines in

affected animals B-lymphocytic leukemia, which is manifested by a persistent lymphocytosis or by a lymphosarcoma with lymph node enlargement. BLV is readily transmitted horizontally among susceptible cattle by direct contact or through milk [6]. It is infectious for sheep and goats and oncogenic for sheep [7]. Two of six infant chimpanzees fed unpasteurized milk from BLV-infected cows were reported to have developed an erythroleukemia [8]. Furthermore antibodies in the sera of human leukemia patients and BLV laboratory workers (but not in controls) to

antigens on the surface of lymphocytes from cattle infected with BLV were identified [9]. BLV can infect in vitro cells of human origin [10].

BLV is a retrovirus, similar to other animal retro-viruses. BLV provirus has been found to be integrated in cattle leukemic B-lymphocytes at multiple sites in tumor cell genome. It has been hypothesized that the provirus might act as a regional chromosomal activator: in this case the provirus itself might not be required for the maintenance of the tumor state. Search for viral RNA in bovine tumors has so far yielded negative results [11].

Studies on the BLV genome sequence have shown that its long terminal repeats (LTR), differently than LTR of the other animal leukemic viruses, are of the order of length of LTR of the HTL-ATL virus, the virus of human adult T-leukemia, which is the only virus causing human leukemia, so far demonstrated [11–14]. Furthermore it has been shown that strong stop c-DNA of BLV hybridizes significantly with the HTL-ATL virus LTR sequences under nonstringent conditions [12], and the virion proteins p24 of BLV and HTLV have similar aminoacid sequence [15]. This appears to suggest that BLV and HTL-ATLV derived from a common ancestor of retroviruses and are more strictly related than the other animal retro-viruses. BLV belongs to the class of chronic retroviruses [11], which induce neoplasia only after prolonged latent period and with low efficiency and do not contain oncogenes. Possible recombinational

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events of BLV might make it able to transform human B-lymphocytes in special circumstances. All these considerations do not prove, by themselves, a definite correlation between BLV and human chronic lymphatic and acute B-lymphatic leukaemias, but should stimulate at least to test the possibility of such a correlation.

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