DEPARTMENT OF HEALTH & HUMAN SERVICES

National Institutes of Health
National Cancer Institute

Memorandum

Date August 4, 1983

From Chief, Laboratory of Tumor Cell Biology, DTP, DCT, NCI

Subject Some Thoughts on the Possible Cause of AIDS by HTLV

To Director, National Cancer Institute

In the most simplistic terms possible, this is my view about the cause of AIDS, if HTLV is involved:

The HTLV genome can be represented at its left end by antigenically variant gag and polymerase genes which vary and which we use to classify the different isolates. We will call them I, II, III, etc., and we will continue in this pattern, as we have done, i.e., the various HTLV types, (I is by far the most common). At the 3' "half" are the locations of the env gene, and a possible coding region for unidentified small proteins called pX region, and the 3' LTR. I propose we call variants in any part of the genome A, B, C,..., etc., with the hypothesis that this area of the genome contains some special sequence which favors leukemogenicity, B contains some special sequence which favors immune suppression, and C is non-pathogenic. Further, I am speculating that HTLV arose in Africa, came to the Americas and Japan late, with slave trade in the former and via perhaps by the Portuguese in the latter. HTLV variants with B sequences never reached Japan. It is an "old" virus but formerly limited to central Africa. HTLV I can match with A, B, or C; similarly II can match with A, B, or C, etc. This general idea will be tested by the accumulation of various isolates of HTLV from leukemias, AIDS, and infected normal people (the latter appears to be very rare in Caucasians); molecular cloning of their genomes; and nucleotide sequencing. In addition, analysis of envelope proteins of various isolates will be attempted. These studies are now on-going and represent collaborative efforts from NIH and SKI clinicians with us; W. Haseltine, J. Mullins, and M. Essex at Harvard; S. Oroszlan and R. Gilden of FCRF; and D. Bolognesi and B. Haynes at Duke. Also, Haynes is attempting to test his idea that the pathogenesis of AIDS by thymus destruction mediated by an autoimmune mechanism which is a consequence of antibodies against HTLV proteins cross-reacting with some proteins present in normal thymus. He has data to suggest this as a possibility. I favor a specific genome 3' region (i.e., B-type) causing specific damage and release of T-cell suppressive molecules.

We are also attempting new prospective epidemiological studies and the development of animal models, (especially in primates).

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