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Dr. Carlo Croce
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Dear Carlo:

I have just heard about your talk at the UCLA "onc" gene meeting. I have heard before from colleagues about your recent talks relating to HTLV-I and the 14 q 11.2, 1 translocation, but I neglected to comment believing there must be some misunderstanding or that you were misquoted. However, I was wrong.

Surely, if you are now aware enough to comment on HTLV-I disease you ought to do it with greater care. Obviously, you speak semantically when you say HTLV-I is an indirect cause of T-cell leukemia. This is the equivalent of saying mycobacterium tuberculosis is an indirect cause of TB (or increases the percent of peoply who get leukemia from HTLV-I). Your arguments would state that the granulomatous lesions which develop in some people infected with the mycobacterium are the cause of the TB if you believe the chromosomal change is the direct cause of the T-cell leukemia. What is most surprising to me is that your arguments sound straight out of a "Duesberg Performance," arguments when applied to your work you are quick to respond to. I was further astonished to see you write (based on your chromosomal arguments) that the situation is just like EBV and Burkitt lymphoma. Now I appreciate the similarities, but surely you are aware that there are about 4×10^9 people infected with EBV, and the incidence of Burkitt's with EBV is in the 10^3-10^4 range; i.e., whereas the number of people infected with HTLV-I who get leukemia (cumulative lifetime) are in the order of 1 in 10^2 to at most 1 in 10^3. Now if there are similarities to EBV as I agree, surely you understand and will agree that a $1:10^6$ (EBV) vs. a $1:10^{-2}$-10^3, i.e., a 10^4-fold greater leukemia rate, with HTLV-I is not the same. Whatever it does, it does it with orders of magnitude greater than EBV. Furthermore, Burkitt's lymphoma associated with EBV is amazingly limited in its geographic location as you well know. EBV is everywhere. BL is only in portions of Central Africa for all practical purposes. This is, of course, not the case with HTLV-I. Where you find the virus you find the disease and vice versa. Moreover, a baby born in the Caribbean infected with HTLV-I has the same risk for T-cell leukemia whether or not he or she remains in Jamaica or moves during infancy to England (as one example). This and numerous other studies clearly show that the virus is the key event and that if other factors are required they are as ubiquitous as oxygen. Contrast this with the holoendemic malaria story and BL. Malaria appears to be a virtual requirement for BL. No chemical, no other environmental factor has ever been implicated in HTLV-I disease.

Another point is the molecular biology. There is a clonal integration of HTLV-I in all cells of these T-cell leukemias. Is this the case with EBV and BL?

Regarding the chromosomal data itself: of course, I am ready to believe that a consistent chromosomal change may play a role in the development of these leukemias. In fact, it has been part of our thoughts from the very beginning of the HTLV-I discovery. How have your studies changed this? There are two issues here. First, even if proven, they do not detract from a primary direct causation of these leukemias by HTLV-I (unless one gets lost in semantics); but second, neither you nor anyone else has even shown this. Only 55% of these patients have the 14 q change. Although I do suspect this is significant, its inconsistency must merit some cautions in the interpretation. Moreover, HTLV-I in vitro transformed human T-cells produce malignant metastasizing lymphomas when put into hamsters (Miyoshi's data). These transformed human cells and the tumors produced in hamsters are normal diploid. You cannot just ignore this.

In short, Carlo, I was surprised by the rapidity and zest of making these conclusions. They appear self-serving and are not helpful to you or to the field.

Sincerely yours,

Bob

Robert C. Gallo, M.D.

RCG/bj

cc Dr. Bolognesi
Dr. Haseltine
Dr. Koprowski
Dr. Rovera