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April 17, 1986 ✓

Dr. Tim Beardsley
Nature
1134 National Press Bldg.
Washington, DC 20045

Dear Tim:

As we discussed, I am enclosing our response to the recent commentary in Nature regarding the isolation of HTLV-III/LAV from patients with AIDS and ARC and the transmission of this virus to different cell lines. I think the enclosed information clearly shows that although we did not publish our results until we had reagents to fully characterize the virus, we had evidence for the presence of a retrovirus as early as December 1982 by identification of cultures showing reverse transcriptase activity with no cross-reaction with HTLV-I and HTLV-II reagents and by electron microscopy by February 1983. Thus, we had evidence of the presence of a retrovirus distinct from HTLV-I and HTLV-II in cells from AIDS patients long before we received any information about studies from the Pasteur group.

Sincerely yours,

Robert C. Gallo, M.D.

PSS/bj

Enclosure

*p.s. Tim, please tell me when
this is in press as soon
as possible.*

We wish to address several points raised in a recent commentary in Nature regarding HTLV-III/LAV, the etiological agent of AIDS. It was mentioned that the CEM cell line infected with HTLV-III/LAV may be a better source of antigen for testing HTLV-III/LAV in patients with AIDS and AIDS-related complex (ARC). The transmission of HTLV-III isolates in several T4+ permanent cell lines, including CCRF-CEM, was first reported by our laboratory(1-3). The transmission of HTLV-III isolates into those T4+ cell lines, including CEM, was the subject of a patent application made in early 1984 and now pending. The fact that we had in our possession electron microscopic pictures of transiently transmitted LAV in Hut-78 and Ti7.4 cell lines should not be surprising. The LAV sample was obtained as a tissue culture supernatant from Dr. Montagnier with the express understanding that it could be used for biochemical, biological and molecular biological studies. In accordance with this understanding, we had transiently transmitted LAV into the Hut-78 and Ti7.4 cell lines. Prior to the development of specific reagents for the detection of HTLV-III, the presence of retroviruses other than HTLV-I and HTLV-II could be detected in cultures from AIDS or ARC patients only by reverse transcriptase (RT) assay and EM examination. At the time we obtained LAV it was the contention of several experts on virus morphology that the particles shown in the EM published in the Barre-Sinoussi et al Science paper (4) was an arena virus. Naturally we wanted to check the material received from Dr. Montagnier by EM to check this contention. Prior to receipt of LAV, we had detected reverse transcriptase activity in a number of cultures from AIDS and ARC patients which showed no cross-reaction with HTLV-I or HTLV-II reagents, thus indicating the presence of a new retrovirus. In a number of cases EM examination showed the presence of virus particles with a cylindrical core, characteristic of HTLV-III (Table 1, Figure 1). A chronological identification of some of these virus particles from AIDS and ARC patients' cultures by our laboratory beginning December 1982 is summarized in Table 1 and Figure 1. The experimental results shown were obtained shortly after receipt of the samples, usually a matter of weeks.

We had evidence for the presence of a new retrovirus in AIDS and ARC patients long before the LAV particles were sent to us and even before the publication of the results by Barre-Sinoussi et al in 1983. Since we considered the mere detection of virus particles in cultures from AIDS and ARC patients to be insufficient to confirm scientifically our hypothesis that such particles were implicated in the etiology of the disease, we decided first to obtain specific reagents against the new virus in order to publish definitive results concerning the etiology of AIDS. The results presented in our four papers provided clear-cut evidence that the etiology of AIDS and ARC was the new lymphotropic retrovirus, HTLV-III (1,2,5,6). In addition, for the first time the virus was produced in large quantities, specific reagents to the virus were made, and a reliable blood test to protect the blood supply and prevent blood transfusion-associated AIDS was now available.

Sincerely,

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References:

1. R.C. Gallo et al. Science 224:500-503 (1984).
2. M. Popovic et al. Science 224:497-500 (1984).
3. M. Popovic, E. Read-Connole, and R.C. Gallo. Lancet 2:1472-1473 (1984).
4. F. Barre-Sinoussi et al. Science 220:868-870 (1983).
5. Shupbach et al. Science 224:503-505 (1984).
6. Sarngadharan et al. Science 224:506-508 (1984).

TABLE 1

SUMMARY OF THE CHRONOLOGICAL ISOLATION OF HTLV-III FROM PATIENTS WITH AIDS AND ARC¹

#	Patient Samples	Date Rec'd	Source	RT	EM	Immunological Reactivities				
						HTLV-I p19 p24	AIDS Sera	HTLV-III p19 p24		
1	GW/AIDS	12/23/82	Gutterman Houston, TX	+	ND	-	-	ND	ND	ND
2	CC/AIDS ²	2/15/83	Leibowitch Paris, FR	+	+	+	+	ND	ND	ND
3	MA/AIDS	2/15/83	Leibowitch Paris	+	ND	-	-	ND	ND	ND
4	BU/AIDS	2/15/83	Leibowitch Paris	+	ND	-	-	ND	ND	ND
5	SN/AIDS	9/23/83	Haynes N. Carolina	+	ND	-	-	+	ND	ND
6	RF/AIDS	10/18/83	Hoxie Philadelphia	+	+	-	-	+	ND	ND
7	RR/AIDS	2/4/84	Redfield WRAIR Wash, DC	+	+	-	-	+	+	+
8	SS/ARC	2/4/84	Redfield WRAIR Wash, DC	+	+	-	-	+	+	+
9	KE/ARC	2/4/84	Redfield WRAIR Wash, DC	+	+	-	-	+	+	+
10	SB/ARC	2/4/84	Redfield WRAIR Wash, DC	+	+	-	-	+	+	+

1. Abbreviations used are: AIDS=acquired immune deficiency syndrome; ARC=AIDS-related complex; GW, CC, MA, etc.=patients' initials; RT=reverse transcriptase; EM=electron microscopy; ND=not done

2. Patient CC was infected both with HTLV-III and HTLV-I.

LEIBOWITCH
2-15-1983



HTLV III_{CC}

MONTAGNIER
9-23-1983



LAV

HOXIE
10-18-1983



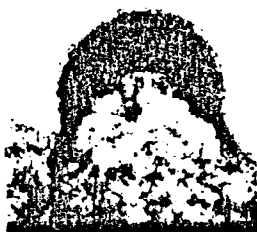
HTLV III_{RF}

REDFIELD
3-22-1984



HTLV III_{KE}

REDFIELD
3-22-1984



HTLV III_{RR}

REDFIELD
3-22-1984



HTLV III_{SB}