

# First isolation of HTLV-III

SIR—We wish to address several points raised in a recent commentary in *Nature*<sup>1</sup> regarding HTLV-III/LAV (human T-lymphotropic virus type III/lymphadenopathy-associated virus), the aetiological agent of acquired immune deficiency syndrome (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<sup>+</sup> permanent cell lines, including CCRF-CEM, was reported first by our laboratory<sup>2-4</sup>. The transmission of HTLV-III isolates into those T4<sup>+</sup> 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 biomedical, 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 re-

**Table 1** Summary of the chronological isolation of HTLV-III from patients with AIDS and ARC

No.	Patient samples	Date rec'd	Source	RT	EM	Immunological reactivities					
						HTLV-I p19	HTLV-I p24	AIDS sera	HTLV-III p19	HTLV-III p24	HTLV-III ND
1	G.W./AIDS	12/23/82	Gutterman, Houston, Texas	+	ND	-	-	ND	ND	ND	
2	C.C./AIDS*	2/15/83	Leibowitch, Paris	+	+	±	±	ND	ND	ND	
3	M.A./AIDS	2/15/83	Leibowitch, Paris	+	ND	-	-	ND	ND	ND	
4	B.U./AIDS	2/15/83	Leibowitch, Paris	+	ND	-	-	ND	ND	ND	
5	S.N./AIDS	9/23/83	Haynes, N. Carolina	+	ND	-	-	+	ND	ND	
6	R.F./AIDS	10/18/83	Hoxie, Philadelphia	+	+	-	-	+	ND	ND	
7	R.R./AIDS	2/4/84	Redfield, WRAIR, Washington, DC	+	+	-	-	+	+	+	
8	S.S./ARC	2/4/84	Redfield, WRAIR, Washington, DC	+	+	-	-	+	+	+	
9	K.E./ARC	2/4/84	Redfield, WRAIR, Washington, DC	+	+	-	-	+	+	+	
10	S.B./ARC	2/4/84	Redfield, WRAIR, Washington, DC	+	+	-	-	+	+	+	

Abbreviations used: G.W., C.C., M.A., etc., patients' initials; RT, reverse transcriptase; EM, electron microscopy; ND, not done.

\*Patient C.C. was infected with both HTLV-III and HTLV-I.

verse transcriptase assay and electron microscopic examination.

At the time we obtained LAV it was the contention of several experts on virus morphology that the particles shown in the electron micrograph published in *Science*<sup>5</sup> by Barre-Sinoussi *et al.* was an arena virus. Naturally we wanted to check the material received from Dr Montagnier by electron microscopy to check this contention. Before 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 electron microscopic examination showed the presence of virus particles with a cylindrical core, characteristic of HTLV-III (Table 1, Fig. 1). A chronological identification of some of these virus particles from cultures obtained from AIDS and ARC patients by our laboratory beginning in December 1982 is summarized in Table 1 and Fig. 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 aetiology of the disease, we decided first to obtain specific reagents against the new virus in order to publish definitive results concerning AIDS aetiology. The results presented in our four papers provided clearcut evidence that the aetiology of AIDS and ARC was the new lymphotropic retrovirus, HTLV-III<sup>2,3,6,7</sup>. 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.

ROBERT C. GALLO  
PREM S. SARIN  
BERNARD KRAMARSKY\*  
ZAKI SALAHUDDIN  
PHILIP MARKHAM†  
MIKULAS POPOVIC

Laboratory of Tumor Cell Biology,  
National Cancer Institute,  
Bethesda, Maryland 20892, USA

\*Electronucleonics, Inc.,  
Silver Spring, Maryland 20904, USA

†Bionetics Research, Inc.,  
1330-A Piccard Drive,  
Rockville, Maryland 20850-4373, USA

1. Beardsley, T. *Nature* **320**, 563 (1986).
2. Gallo, R.C. *et al.* *Science* **224**, 500-503 (1984).
3. Popovic, M. *et al.* *Science* **224**, 497-500 (1984).
4. Popovic, M., Read-Connole, E. & Gallo, R.C. *Lancet* **ii**, 1472-1473 (1984).
5. Barre-Sinoussi, F. *et al.* *Science* **220**, 868-870 (1983).
6. Shupbach, J. *et al.* *Science* **224**, 503-505 (1984).
7. Sarngadharan, M.G. *et al.* *Science* **224**, 506-508 (1984).

SIR—I wish to take issue with a comment by Tim Beardsley on the LAV/HTLV-III controversy<sup>1</sup>. Gilden *et al.* clearly state in their correction letter to *Science*<sup>2</sup> that I am not responsible for the erroneous mixing up of LAV and HTLV-III electron micrographs that appeared as part of a composite electron micrograph picture in my paper to *Science*<sup>3</sup>. Nevertheless, the first paragraph of Beardsley's comment evokes the impression that I am to be blamed for this embarrassing error. In fact, my work described in that *Science* paper dealt exclusively with serological and biochemical aspects of the new retrovirus. My drafts did not contain the controversial composite and neither R.V. Gilden nor M.A. Gonda were proposed as

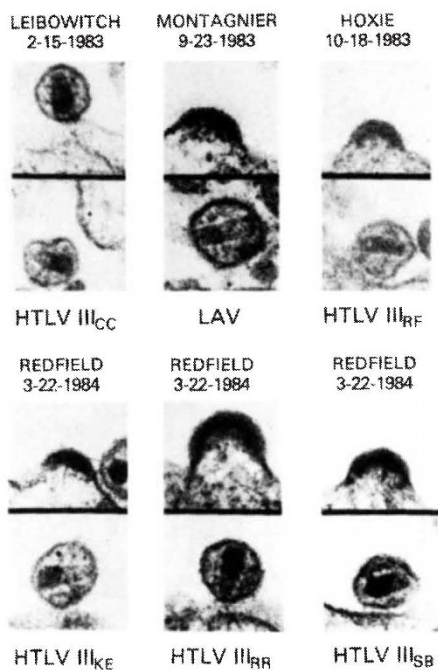


Fig. 1