



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

Memorandum

Date March 13, 1986
From Chief, Laboratory of Tumor Cell Biology, DTP, NCI
Subject Chronological Summary of Experiments Leading to the Isolation of HTLV-III
To The Record

Given below is the summary of events that took place between 1982 and 1984 leading to the isolation, characterization, and patenting of HTLV-III. The reverse transcriptase, and

1. August 1982: The idea to search for a retrovirus as the cause of AIDS was first proposed by Dr. Gallo and published in Medical News (August 16, 1982).
2. August 1982: First detection of HTLV-I in the cultures of an AIDS patient as evidenced by E.M., cell biology, immunological, and molecular biology studies.
3. December 1982: Detection of AIDS samples which were positive for reverse transcriptase but were negative for cross-reaction with HTLV-I p19 or p24. EM showed virus particles with morphology different from HTLV-I.
4. January 1983: Phone call to Dr. Gallo from Dr. Montagnier requesting HTLV-I antisera. Antiserum was sent.
5. February 1983: Letter from Dr. Montagnier requesting HTLV-I cloned DNA and antisera against HTLV-I antigens. The reagents were sent.
6. February 1983: Three AIDS samples obtained from Dr. Lebowitz were found to be positive for reverse transcriptase but negative for HTLV-I p19 and p24.
7. February 1983: Papers on the detection of HTLV in lymphocytes of two patients with AIDS submitted to Science by Gallo and co-workers.
8. March 1983: Sent HTLV-I DNA to Dr. Montagnier.
9. April 1983: Reviewed the paper by Montagnier and co-workers on the isolation of T-lymphotropic retrovirus from an AIDS patient and recommended its publication in Science.
10. April 1983: Requested the RUB cell line (AIDS patient) from Dr. Montagnier.
11. April 1983: Requested DNA from RUB cells from Dr. Montagnier for comparison with HTLV-I and HTLV-II. Twenty micrograms of DNA was received. Found to be mainly cellular and no viral sequences were detected.
12. January 1983-April 1983: Twenty-seven samples from AIDS and ARC patients were analysed. Three were found to be positive for reverse transcriptase.

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13. May 1983-September 1983: Eighty samples of AIDS and ARC patients were analysed for HTLV-III. Sixteen samples were found to be positive for reverse transcriptase.
14. July 1983: LAV supernatant was received from Dr. Montagnier. No virus was detectable by RT assay.
15. September 21-23, 1983: LAV supernatant was received from Dr. Montagnier. The sample had reverse transcriptase activity. It was transmitted to cord blood cells and cell lines (H9, HUT 78, T17.4). A transient production of virus RT was observed and the cells subsequently died. The cells were found to be negative for fluorescence with HTLV-I p19 p24 antibodies, suggesting that it was different from HTLV-I and HTLV-II. A stock of extracellular virus containing supernatant was stored in a freezer. A sample was sent to Dr. Honda, FCRI, for EM to verify the presence of virus.
16. October 1983-December 1983: Forty-two samples of AIDS and ARC patients were analysed for HTLV-III. Thirteen were found to be positive.
17. November 1983: HTLV-IIIg was transmitted to HT cell line.
18. December 1983: Specific reagents for HTLV-III were prepared. LAV was transmitted to a cell line T17.4 (obtained from M. D. Anderson Hospital). This cell line produced low levels of LAV. The HTLV-III and LAV were compared and found to be similar.
19. December 1983: Electron microscopic examination of "H9 variant" late called HTLV-III, showed virus particles containing cylindrical cores. This morphology was different to that seen with HTLV-I and HTLV-II.
20. January 1984-May 1984: One hundred and eighty-five samples were analysed for HTLV-III. Seventy-eight samples were found to be positive.
21. February 1984: HTLV-IIIg was transmitted to H9 clone.
22. February 1984: Attempts to transmit LAV to H9 cells were unsuccessful.
23. April 1984: Patent filed for large-scale production of HTLV-III and for the detection of HTLV-III antibodies in blood by Elisa.
24. May 1984: HTLV-III infected H9 cells sent to Dr. Montagnier.

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