DEPARTMENT OF HEALTH & HUMAN SERVICES

National Institutes of Health
National Cancer Institute

Memorandum

Date August 19, 1985

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

Subject Science Article May 1983

To Associate Director, NCI

Recollection of contacts leading to Science article May 1983. These are confirmed with letters to Dr. Kulstad, Science, and Dr. Chermann (our correspondence).

Dr. Chermann called reporting that the group at Pasteur was looking for a retrovirus they had detected R.T. in one case of AIDS. Dr. Gallo related data from Dr. Essex and LTCB being prepared for publication. Dr. Gallo encouraged the group to publish their findings, even though both he and the Pasteur group felt the results were preliminary. Dr. Gallo made Ruth Kulstad, Science Editor, aware of the French work and encouraged publication of all submitted papers together, although this meant holding up Dr. Gallo's and Dr. Essex's articles for several weeks. Dr. Gallo, Dr. Sarin, and Dr. Popovic acted as referees for the French paper and strongly supported publication (copy enclosed).

At this time (February 1983) reagents for HTLV(I) were sent promptly to Dr. Montagnier to enable him to prepare a paper for publication. TCGF had been sent to their lab on a previous occasion (1980) although they report using another source for this project. Molecular probes for HTLV-I were sent (March 1983) and further cell lines sent in May 1983. Dr. Chermann has publicly recognized this.

The idea to search for a retrovirus as the cause of AIDS was first proposed at Cold Spring Harbor in February 1982 by Dr. Gallo. The background for this proposal is well known:

1. Findings that HTLV(I) could be somewhat immune suppressive.

2. Animal retrovirus were known to be associated with immune deficiency.

3. Modes of transmission of the known retrovirus HTLV-I (sexual, blood products) were similar.

4. Likely African origin of AIDS and the HTLV's.

5. The target cell in ATL and AIDS is the same. The working hypothesis was that a variant of HTLV (HTLVII had recently been isolated and described) could induce immune deficiency with lymphoma. The laboratory tested patient material and found evidence of retrovirus (R.T.) with negative IF for known retrovirus antigens (p19 p24) as early as December 1982. In addition, HTLV-I was isolated for two patients and reported along with Dr. Essex's paper. This work seemed to focus attention on an infectious human T-lymphotropic retrovirus in the immune deficiency syndrome.

Dr. Chermann publicly stated in a September 1984 virus meeting in Leriche, Italy, that they initiated their experiments in January 1983 and got the idea from Dr. Gallo to look for a retrovirus.

A group of experiments was also begun in June '83 that quickly showed evidence of R.T. activity with negative IF for HTLV-I and is summarized. Virus was co-cultured but could not be maintained in culture for isolation and characterization. It would have been impossible to relate each isolate without the ability to clone virus and develop immunologic reagents. In no case of material in December 1982 or in any period in 1983-1984 did an AIDS RT positive sample give immortalized T-cells--additional evidence that it was not HTLV-I or II.

In fact, the French paper came under extensive criticism after publication for this reason. It should be noted that four electron microscopists felt that this was probably not even a retrovirus, much less, a distinct variant. Dr. John Moloney (former Director of the Virus Cancer Program) called Dr. Gallo directly to relate his and Dr. John Dalton's (U.S. Leading Electron Microscopist on Retroviruses) feelings to that effect. Dr. Francoise Hagneau conveyed the same impression to me and openly at the Selliac meeting November 1983. Dr. Hagneau is the leading electron microscopist for retroviruses in France. Finally Dr. Siegel, at Roswell Park, submitted a letter to Science suggesting the EM's looked more like arena viruses. Dr. Gallo strongly encouraged the Science editors not to publish this letter because he believed that the French were going in the right direction and should be given a chance. This action was in spirit 180° opposite from the deceptive and vicious manner in which it has been presented to you. I feel all parties will document this.

It was Dr. Gallo's scientific opinion that they did have a retrovirus, subsequently called LAV, and so Dr. Gallo encouraged publication, provided reagents, and defended their preliminary work against attack. Over the course of this work we are responding to a public health crisis and the need to develop useful assays such as the ELISA screening assay. We do not intend to keep records of legal standing and they are often incomplete. In contrast to this rather normal behavior is the meticulous and apparently premeditated documentation of others interested, it seems, more in patents and notoriety.

Receipt of LAV. 20 micrograms of DNA was received in April 1983. A few blots were done without results and was apparently all cellular DNA; i.e., no viral DNA.

After repeated requests to extend this work on a mutually agreeable collaborative basis, we received supernatant in July 1983 which did not contain detectable virus (Popovic). Again, in September 1983 we received supernatant from which Dr. Popovic reports he was able to detect R.T. in these supernatants (see memo from Popovic for details).

(5)
Pool

Numerous isolates from AIDS patients' material were obtained in our laboratory prior to receiving any LAV and prior to receiving viable LAV (Markham-Salahuddin summary). It should be noted that this laboratory is not physically connected with Dr. Popovic's, did not receive any of the French materials, and did not receive them or share material with Dr. Popovic. These isolates showed R.T. activity, were co-cultured, and were negative for p24 and p19 of HTLV-I. We felt EM would not be more informative at this stage. Witness the quality of electromicroscopy in the first French paper.

Material placed into the permanent cell line H9 and published in May 1984 to develop reagents and molecular clones was pooled from several patients who showed high R.T. activity in primary culture. These were separate isolations entirely distinct from the LAV samples received.

The primary clone reported, BH10, differs from the LAV isolate reported by 1-2% for a total of 144 nucleotides and 58 aminoacids. It is not identical to LAV but probably represents the similarity within the known range of variation of viruses isolated from different patients at different times. This is supported by data from Marv Reitz, George Shaw, and Flossie Wong-Staal. In addition, we have evidence that shows that virus does not change in culture over a prolonged period of time. Thus, these changes were not accumulated in culture.

We have numerous other isolates that have been put into permanent cell lines at the same time. These are clearly distinct from LAV and the BH10 clone. These isolates were made at different times and different sources from the LAV and also the distinct BH10 clone. It is possible that material that has been viably preserved and frozen isolated from June 1983 and on could be put into permanent cell line. We would predict that some of these would be similar to and some distinct from the BH10 clone.

RC

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Enclosures