

National Institutes of Health National Cancer Institute Bethesda, Maryland 20892

Building 37 Room 6A09 (301) 496-6007

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Professor Andre Lwoff Director Emeritus Institut Pasteur 28, rue du Dr Roux 75724 Paris Cedex 15 France

Dear Dr. Lwoff:

I am most appreciative of your reply to my letter of July 7. Please be assured that I deeply value your opinions. My intentions in this letter are not to debate, nor to extend these problems, nor to add insults. Instead, I seek clarifications of certain key issues and to develop some common grounds. However, I must state from the onset that I feel you are getting a one-sided story. Additionally, some differences arise because of honest technical confusions and misunderstandings. However, I also believe that the malicious treatment given to me and the deception given to the public by the multiple commercial arms of the Pasteur Institute is unprecedented in contemporary scientific history. The use of base litigation lawyers and a propaganda ("public relations") firm from New York are designed to promote Montagnier and to hurt me in a way that is unprecedented in science and a bit disgusting. The last point in your letter states you have not gone public against my position because of your respect for my scientific contributions. Please allow me to mention another good reason: 1) you do not have all the facts; and 2) to join in the fracas in such a manner would minimize you as a person and as an objective scientist.

You raised four significant points in you letter. I will respond to each.

Point 1: You remind me that I said Montagnier sent us <u>very</u> little virus and I could not grow it, yet we had reverse transcriptase(RT) and EM results.

## My reply:

Montagnier himself brought an extremely small amount of virus to me in July 1983, which in fact was kept for awhile in a refrigerator in my home. However, NO virus was found by four independent workers (Dr. Prem Sarin, Dr. Flossie Wong-Staal, Dr. Mika Popovic, and Ms. Betsy Read) in my laboratory by two different techniques. We can prove this. The sample was certainly RT negative. However, a centrifuged pellet of the fluid was later shown to be positive by electron microscopy (EM) at Frederick, Maryland by a service contract. We never used this material any further. In any case, the point is moot. Chermann prepared another sample near the end of September (September 23, 1983), and indeed, we found the second sample positive and we were able to infect both cord blood cells and two permanent human leukemic T4 cell lines. We confirmed that they had a retrovirus, and this was orally communicated by my co-worker, Popovic, to Montagnier by telephone. He did not mention the approach used (EM or RT), but what else could be done? There was not a single reagent to the virus; none until we made the first ones in late 1983, but that we did these tests is obvious from our positive statement that we did indeed confirm that they had a retrovirus. We always said the second sample was positive, and quite frankly, I never knew the first sample was positive until very recently when I learned that an EM report came back positive. Once again, it is not a point of issue. We admit and always have that we asked for, received, and verified the second sample. If you will forgive me, I really fail to understand the issue, or why this point should be a problem.

Regarding "growing" the virus: I will repeat this again (I hope for almost the last time): we never continuously produced LAV1. We transiently transmitted it to human umbilical cord blood T-cells, but lost the cells due to cell killing by the virus just like the Pasteur group claimed always happened to them. We had transient success with a parental stock (of a very mixed cell population) of a T4 human leukemic cell line known as HUT 78. I can unequivocally prove this success was temporary. When I say we never "grew" the virus, we mean continuously or in mass. is very difficult to keep most isolates continually replicating. The virus kills the parental cell. Only some cloned cells are relatively resistant. If one goes back to the LAV stock of September, 1983, you will easily be able to confirm that just as Montagnier, et al., continuously claimed, LAV1 does not permanently go into a cell line. My laboratory is extremely open. Eighty percent of my co-workers are from Europe, including four from France. The early culture work was done by Mika Popovic, a Czech, and Elizabeth Read, an American. You also cannot forget when we succeeded in continuous mass production of the AIDS retrovirus for the first time, we did it with two isolates, HTLV-IIIB, which is close to LAV, (differs by 144 nucleotides) and HTLV-IIIRF which differs by over 1,000 nucleotides! Montagnier, Alizon, and some other co-workers of theirs conveniently and regularly forget about the RF strain of HTLV-III, referring only to HTLV-IIIB when they discuss an

HTLV-III comparison to LAV. If you have any additional question or problem on your mind regarding this, please let me know. Also, please note we signed the statement that we received LAV, and we had approval from them to do any and all experiments we desired. Note also, that when we sent LAV to collaborators who were paid as a service contract to do the electron microscopy (at the Frederick Cancer Research Facility), we labelled the virus "LAV from the French" (this facility is 40 miles from my lab). Does this sound like we were trying to take their virus? Please also note that after temporary transmission to the HUT 78 and Ti7.4 cell lines, Ti7.4/LAV was used later for comparison with HTLV-IIIB, a joint publication with Montagnier, et al., had been prepared. Unfortunately, this paper was never published.

Montagnier has criticized us for not comparing the viruses and then showing they were the same. He forgets that a comparison was impossible until we succeeded in mass producing our virus. There were no reagents available. He, himself, in every publication re-named the isolate (LAV, RUB, IDAV, IDAV,...) because he could not know they were all the same virus. Once we could grow our virus, our primary goal was to protect the nation's blood supply. Our thoughts were not towards the academically interesting question of whether or not this was the same virus Montagnier had sent. When we had achieved this goal, we contacted Montagnier to collaborate on a comparison of the viruses. In May 1984, a member of my group took our producing cell line with him to Montagnier for the purpose of comparison. The enclosed sheet (Enclosure 1) in Montagnier's handwriting shows he did not believe they were the same virus.

Point 2: You state "did I not attack Montagnier rather fiercely during a 1984 symposium", and "no wonder bad feelings developed".

# My reply:

First, I think you mean a 1983 symposium. I do not remember "fiercely" attacking anyone in 1984. I assume you mean the September 1983 Cold Spring Harbor Symposium on HTLV or at the November 1983 Griffuel Prize of ARC in a symposium in Paris, also on HTLV. What I did was ask a series of questions. They were scientific and not personal. They were typical and normal for any Cold Spring Harbor meeting. Ironically, I was about the single only supporter of Chermann and Montagnier in the U.S. or Europe in early-mid 1983. I was the defender of their publication in Science in May 1983, and believe me the paper needed a lot of defending. What I tried to do in those symposia was to openly get answers to questions many people in the U.S. and in Europe (and perhaps particularly in France) were gossiping about in semi-private discussions. I felt that this was the scientific approach. You should also remember that in the September 1983 Cold Spring Harbor meeting and again during the

October 1983 meeting in Seilac, France, Montagnier emphasized that only 20% or less of AIDS patients had detectable serum antibodies to LAV. Also, major U.S. and French electron microscopists publicly and many times privately stated (and in writing) during 1983 that the Pasteur virus was not even a retrovirus but an irrelevant Arena virus. A few days after the Seilac meeting at the Paris Griffuel prize meeting organized by ARC, Montagnier changed his positive serology data from 20% (or less) to 38%. I commented that this was a big improvement in 3 days. He said it depended "where one drew the line". I commented "exactly". So with the very poor serology combined with the poor electron microscopy, it is no wonder that I became wary of this data. Nonetheless, to my way of thinking, I never fiercely attacked him.

## Point 3:

You state that what my group and Essex described in 1983 was the leukemia virus not the AIDS agent.

#### My reply:

Professor Lwoff, no one knew what the "AIDS Agent" was in May 1983. I never, ever stated that my May 1983 paper was an HTLV-III or LAV, later proven (mostly by my group) to be the cause of AIDS, and hence, the "AIDS Agent". Once it was clear to me that HTLV-III and LAV were the same virus genus, I always said that the first publication of this virus was by the Pasteur group. However, I disagree with you strongly on the history of what discovery of a cause of a disease means. In early mid-1982, we openly proposed the idea that AIDS was caused by a new human retrovirus. This stimulated the Pasteur group to work in this direction, and they openly admitted this on many occasions. did believe it would be a close relative of HTLV-I or II. However, the correct virus proved to be much more distant than we suspected. Clearly, we believed we might have had a variant of HTLV-I in our 1983 paper. Later we learned it was HTLV-I itself, not the cause of AIDS, and I said so. Thus, our hypothesis was not 100% accurate but far closer than anyone elses. However, I cannot understand how you or anyone can claim they had the AIDS agent all alone. They published a single case of lymphadenopathy (not AIDS). They stated for close to one year that 20% or less of AIDS patients had antibodies to the virus. There is no doubt they gave attention to this retrovirus, undoubtedly because it was something they could identify themselves with, but to believe they concluded it was the AIDS agent flies in the face of all facts. Please see the presentation by Montagnier in late September 1983 (Enclosure 2), in which he suggests LAV, HTLV (presumably I and II), other retroviruses yet to be found are probably all involved in the cause of AIDS. Please also note that in their only 1983 paper (the May Science paper) they call the virus: "a member of the HTLV Family". They conclude that it is immunologically related to HTLV and they state it is a type-C virus (see Enclosure 3). Later (July 1984), they concluded with CDC investigators that LAV was molecularly very close to HTLV-I

and II (See Enclosure 4), and they also conclude then that it is a type-D retrovirus. Only still later do they conclude it belongs to the lenti-retrovirus subfamily (three changes in subclassification in one year). Whether Montagnier was or was not proving LAV was the cause of AIDS is debatable. clear is that when we decided to publish, we were first to publish the data that convinced the scientific community that we were sure about the cause of AIDS. This was done with publication of: 48 virus isolates, the first mass production of virus, the first specific reagents to the virus (allowing one to say for the first time that any two isolates were of the same virus type), the first workable and accurate blood test, and sero-epidemiology in hundreds of samples with 90% to 100% positive coded AIDS sera. We also established the chief technology used by the Pasteur group for LAV with our earlier work in HTLV-I and II. The next major new technology was mass production in certain T4 leukemic lines. This, too, the Pasteur group did following our example. The above facts combined with the following facts that: 1) they were following the idea developed by me that AIDS was likely caused by a retrovirus; 2) that Montagnier's main technician worked one year in my laboratory just before he got into human retroviruses; 3) that they received their original reagents allowing them to distinguish LAV from HTLV-I and II from me; 4) that they got our cell line producing HTLV-III in the spring of 1984 but to this day, I have never received a cell line producing LAV from them; 5) that we did the first molecular cloning, viral gene expression, discovery of the virus in the brain, and discovery of its heterogeneity. All of these I hope you will agree entitle us to be considered as a bit more than simply confirmatory of Montagnier. Finally, although we did not publish these findings, we nonetheless can (and will shortly) prove we had HTLV-III/LAV detected probably as early as December, 1982 and certainly by February, 1983. We elected to publish in the HTLV-I virus thinking, as I mentioned above, that it might be a variant and the cause of AIDS and not on the new virus because of difficulties at that time in the characterization of this new retrovirus.

Point 4: Your concern here is about the fairness of the patent and you wonder my position.

#### My reply:

- The patent business is a legal argument and perhaps a
  political one and not one for scientists. I am, in fact,
  amazed by the commercial interests.
- 2. I did <u>not</u> know Montagnier filed a patent. I was asked to do so to <u>save lives</u>. In all this mess, you and much of the Pasteur propaganda seem to have forgotten the key message; that we saved over 2,000 U.S. lives, prevented death in many other countries, and stopped the virus from a major infection

of the heterosexual population. We had an accurate sensitive test by January 1984. Pasteur's test was operational with any degree of accuracy or sensitivity only in late 1985. This, too, can be proven. I was told by U.S. officials that my name had to be used as inventor immediately to get virus to selected firms for mass blood screening.

- 3. My position is simple. The National Institutes of Health received no money from the patent. My co-workers and I received a token amount. We are not interested in the money. I hope the affair ends. I hope there is a settlement. However, the malicious sentiments and the attempts to mislead people, all with the purpose of minimizing me and my co-workers must first be resolved. I want the Pasteur Institute to come forward with a scientific history. I had this agreement in March 1986 with J.C. Chermann, who as you know is one of the leaders in AIDS research at the Pasteur. This agreement was made in the presence of Madame Claudine Escoffier-Lambiotte. However, this agreement was "killed" by Montagnier and/or Dedondor and their lawyers. I have never used this history agreement at the plea of Madame Escoffier-Lambiotte because it would harm Chermann.
- 4. I have been told that the U.S. Government has offered to put Montagnier's name on my patent and mine on his. They have also offered to disregard our next patent which covers growth of the virus in all cell lines today including CEM which, of course, we succeeded with and patented long ago. Also, they offered sharing the patent on cloning and expression of the viral gene for use of the proteins in a second generation blood test, although not royalty for the Pasteur. The Pasteur position now is also a request for some money. I do not know how to resolve this issue.

Finally, I wonder what your views are on the following: The U.S. highest award (the Lasker) will be given this year to both Montagnier and myself. As you may know, I received it before (in 1982) for opening the field of human retrovirology. The National Institutes of Health and the National Cancer Institute administrators greatly supported Montagnier's award as something fair. In stark contrast, I am informed: 1) that Montagnier alone received a 1 million dollar prize for "discovery of the AIDS virus"; 2) This year I received an honorary degree from Tel Aviv University and while I was in Israel, I was told by Israeli scientists that I would have received one from the Weizmann Institute but the Pasteur (presumably Jacob) intervened against me, and 3) At some TV extravaganza involving the Pasteur and its relationship with the Weizmann Institute (apparently you appeared on this program witnessed by 10 million people), Montagnier was singled out as the discover of the AIDS virus and also as

the winner of the major U.S. prize, the Lasker. I am told there was no mention of anyone else. I wonder what your views are on this?

Sincerely yours,

Robert C. Gallo, M.D.

Chief

Laboratory of Tumor Cell Biology

Enclosures

RCG/AHS/es