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Dear Dr Maddox

Thank you for sending me a copy of Dr Gallo's 'over generous but effective reply'. I ca see why you, as an outsider of retrovirology, might feel that Dr Gallo's reply was effe tive. None of his claims are valid when one actually checks the published record. I gi just one example in this covering letter. He alleges (3rd paragraph) that his third pa (Schupbach, Sarngadharan & Gallo, Science, May 11, 1984) 'is clearly on HTLV-III not HTLV-I' and he goes on to say 'It is difficult to understand how he (Karpas) could mak such a mistake'. I therefore enclose a photocopy (enclosure 1) of their paper where yo can see for yourself that the term 'HTLV-III' was not mentioned, even once. The paper deals only with studies of HTLV-I in AIDS !! The term 'HTLV-I' can be found throughout the paper. You may also appreciate that at that time (1983) and up until May 1984, the use of the term 'HTLV' by Dr Gallo referred to HTLV-I. Likewise, all the references ar about the virus which is involved in adult T-cell leukaemia (ATLV/HTLV-I).

This example will illustrate to you that Dr Gallo still believes that in this day and of communication and science he can get away with not only saying, but even writing, t black is white and vice versa.

In the attached detailed reply to his letter I systematically answer all of Dr Gallo's allegations and show that none of his explanations are valid as far as they relate to published record. My reasons for being 'after him' are purely scientific. He has published an enormous number of misleading papers in the past 17 years and I, like others have found myself wasting a great deal of time trying to verify his data.

My letter 'AIDS Twists' summarizes an extraordinary and undoubtedly unique chapter in medical and scientific research. It relies exclusively on published information, none of which has been shown to be wrong in Dr Gallo's letter. Owing to the publication of misleading information, progress in AIDS research has been delayed. I therefore hope that Nature will redress the balance and publish my letter.

Yours sincerely

A Karpas ScD
Assistant Director of Research

cc Drs D Baltimore, H Temin, F Brown, H Varmus, L Montagnier.

Detailed Reply to Dr Gallo

Concerning the rest of Dr Gallo's 'effective reply' I am going to comment on the published record and in the order which appears in his reply.

1. Dr Gallo's 'essential reagents' which he provided to Dr Montagnier are responsible for the initial French mistaken belief that their AIDS virus isolate and the virus which is involved in adult T-cell leukaemia are related. Dr Gallo's monoclonal antibodies to p19, of HTLV-I reacts also with non-infected T-cells and therefore led also in the past to mistaken publications about the involvement of HTLV-I in other human diseases (see Leukaemia Research p511, 1985- enclosure 2) Dr Gallo's antibodies to p24 were polyclonal and appeared to have given non-specific misleading reactions. So much for his 'essential reagents'.

3. Dr Gallo's 'proposal' about HTLV-I involvement in AIDS as being 'by far the closest of all proposals and directly led to the solution...' is as valid as the recent paper he published in your journal about the involvement of HTLV-I and HTLV-III in multiple sclerosis (Nature 1985; 318: 154).

I trust that I need not remind you that an independent group from France and the USA, like ourselves, failed to detect any evidence of involvement of the adult T-cell leukaemia virus (ATLV/HTLV-I), nor of the AIDS virus (LAV/HTLV-III) in multiple scerlosis (Nature 1986; 322: 176, 177). I am probably right in assuming that Dr Gallo's rationale for publishing such claims is that should someone eventually determine the involvement of a retrovirus in multiple sclerosis, he could then claim priority.

4. Dr Gallo tried to convert his published record to the involvement of the virus that is causing adult T-cell leukaemia (ATLV/HTLV-I) into the AIDS virus which was discovered in France. In the French group's first paper they did not name their AIDS virus isolate but merely described it as a 'T-lymphotropic retrovirus' in the same way that the Epstein Barr virus is often described as a human B-lymphotropic virus.

The summary of the French group's first paper (Science 1983; May 20) also states that their isolate is '... clearly distinct from each previous isolate ..' (HTLV-I) and that '.. type-specific antisera to HTLV-I do not precipitate proteins of the new isolate ..' (enclosure 3).

The signatories of the 'Unanimous Agreement' naming the virus which was first established by Dr Y Hinuma as the causative agent of adult T-cell leukaemia (ATL) as HTLV, rather than its original designation of ATLV, represent Dr Gallo's guests to the meeting he organized in Cold Spring Harbor. It does not constitute or represent the International Committee on Taxonomy of viruses (ICTV). Dr F Brown FRS is chairman of ICTV but he is not a signatory of the 'Unaminous Agreement'. If one uses Dr Gallo's rigorous criteria for naming a newly discovered virus then the virus which is involved in the development of adult T-cell leukaemia should be called ATLV not HTLV and Dr Y Hinuma should be the only scientist to be credited with its discovery.

According to Montagnier's letter (Nature, 310, 1984 August 9 - enclosure 4) Dr Gallo received LAV on two occasions (July 17 1983 and September 23 1983) and his 'essential reagents' were HTLV-I 'which were useful to show that LAV was not related to HTLV-I'. Dr Gallo's third paper on the involvement of HTLV-I alone in AIDS was submitted on December 12 1983 (Science May 11 1984 - enclosure 1). His first paper about HTLV-III was submitted to Science on March 30 1984. This clearly indicates that he realised that LAV and not HTLV-I is involved in AIDS only in 1984 which also explains why the application for patent for the AIDS test was submitted in April 1984.

I did not comment on various unrecorded claims by Dr Gallo in the fourth paragraph (p2). As said earlier, I will relate only to the published record which was presented and published in the book he edited from the papers presented and submitted on September 15 1983 at his meeting on Human Leukaemia/Lymphoma Viruses. The French group's paper clearly states 'A further characterization of the virus, showing it to be an entity clearly distinct from human T-cell leukaemia virus (HTLV) isolates and to a certain extent analogous to the animal retrovirus equine infections anaemia virus ..' (which is a lentivirus). The French paper further states

'.. no homology between p24 of HTLV and p25 of our virus ..' and ' .. no homology between an ATLV DNA probe and DNA from LAV 1 infected cells ' (enclosure 5). It is important to re-emphasize that these data, together with an excellent electron micrograph of LAV were presented on September 15 1983 at Dr Gallo's own meeting. From the enclosed copy of his letter which was written 12 days later (September 27 1983) he states 'I never saw the virus that Luc Montagnier described ..' (enclosure 6).

5. As to Dr Gallo's hybridization data between ATLV/HTLV-I and LAV/HTLV-II, both the Science and Nature papers and message claim homology. The title of the Science paper (225; 927, 1984) is, 'Homology of genome of AIDS associated virus with genomes of human T-cell leukaemia viruses'. The Nature paper (312: 166, 1984) states in the summary 'We also demonstrate distinct nucleic acid homology between the cloned genome of HTLV-III and those of HTLV-I and HTLV-II ..'. The US group from California, who sequenced their independent AIDS retrovirus isolate (ARV2), stated in their summary (Science 1985; 227: 484) 'ARV2 was as closely related to murine and arian retroviruses as it was to human T-cell leukemia viruses (HTLV-I and HTLV-II)'. This conclusion also confirmed the French data, i.e. that there is no relationship between the AIDS virus and HTLV-I (see above).

In Cambridge we have also cloned both (our own) ATLV/HTLV-I and AIDS virus (HIV) isolates and, like others, could not find <u>any</u> molecular homology nor could we detect any immunological cross-reaction. Inspite of the fact that it is common knowledge by now that the AIDS virus is distinct (molecularly and immunologically), Dr Gallo still quotes his group's unreproducible data as proof of cross-hybridization and immunological cross-reaction.

As to Dr Gallo's claim that the French also showed homology between HTLV-I and LAV I (Science July 1984), I did not miss the July 1984 paper and the sentence which Dr Gallo quotes about 'Extensive homology between LAV and HTLV-II..' (Science 1984; 224: 321). The data, like the title of this paper, are about antibodies to LAV proteins and the above sentence is taken out of context. The paper does not document any homology between LAV and HTLV-I. Only in the discussion does it mention homology studies, referring to work in preparation by Dr Narayaman (Ref 13) (enclosure 7)

who is of CDC (not Paris) and it was written by the scientist from CDC, Atlanta (the first five authors). To the best of my knowledge Dr Narayaman of CDC, Atlanta never published his early mistaken data.

In conclusion there is no similarity, homology or cross-reactivity between the AIDS virus and the virus which causes adult T-cell leukaemia.

6. From the enclosed copies of Dr Rabson and Dr Martin's papers (Cell, March 1985: 477), and Science (enclosure 8), you can see that the first most incriminating evidence against Dr Gallo was produced by his next door colleagues in Bethesda when they analysed sequence data of the AIDS viruses and pointed to the genetic heterogeneity of independent AIDS virus isolates. Once again Dr Gallo claimed credit for other scientists' work when he stated 'I discovered the genomic heterogeneity of the AIDS retrovirus in late 1983 early 1984'. (While he was still submitting papers on the exclusive involvement of HTLV-I in AIDS (Science May 11 1984). Dr Gallo's 1984 claim of 48 independent isolates somehow turned out to have spoken French with a single voice before he naturalized them (enclosure 8).

I must emphasize again that the initial reports about the identity of LAV and HTLV-III (Cell, March 1985) came from NIH not from Cambridge or Paris!

7. I am pleased to note that Dr Gallo confirms that 'his' HT and H9 cell lines are indeed derived from Gazdar's original leukaemia HUT-78 cell line; since leukaemia is a clonal malignancy it is possible to trace the origin of cell lines even if their name was changed. Dr Gallo published numerous papers about HT and H9 cells but never acknowledged their origin nor their original name.

As to his claim to provide the essential help in establishing the cell lines, I would like to point out that 'sitting somewhere in Cambridge' I managed to establish numerous human leukaemia cell lines including T-cell lines. I have done this not only without Dr Gallo's help but also without ever using the T-cell growth factor (TCGF). Likewise, the Japanese who were first in establishing their virus (ATLV/HTLV-I) producing T-cells (MT-lines) have done so without Dr Gallo's T-cell growth factor (TCGF). So much

for his earlier claims (Nature 317, 315, 1985) to the important role of TCGF in the isolation ATLV/HTLV I.

He is also right when he says that by 'sitting somewhere in Cambridge' I know very little about life in Bethesda. This is the reason why my letter 'AIDS Twists' is based only on the published record which can be found even in the Cambridge library. However, it is interesting that the most incriminating evidence about Dr Gallo's plagiarism and dishonesty was provided first by scientists from Bethesda (Rabson and Martin - enclosure 8). Again Dr Gallo claims that between November/December 1983 he mass produced the AIDS virus while the record clearly shows that at least up to December 12 1983 he submitted papers (Science May 11, 1984 - enclosure 1) about HTLV-I alone being the cause of AIDS without mentioning HTLV-III. He also somehow forgot that on September 27 1983 he wrote 'I never saw the virus that Luc Montagnier described' (enclosure 6).

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