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In reply please quote:
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12 September 1983

Dr L Montagnier
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FRANCE

Dear Dr Montagnier

Your manuscript has now been seen by two referees whose comments are attached. In viewof their criticisms I am afraid we are unable to offer to publish your manuscript in Nature and I am therefore regretfully returning it. I hope you find our referees' comments useful.

Yours sincerely

Guil Winchester.

Guil Winchester
Assistant Editor

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Referee 1

This paper shows that a retrovirus under study in Paris transiently replicates (as judged by reverse transcriptase assays) in human OKT4$^+$ T-cells but not in OKT8$^+$ cells. This is of interest because the virus is claimed to be derived from an 'AIDS' patient deficient in OKT4$^+$ cells. This single result is of potential value as a short letter to Nature, but in this reviewer's opinion should not be published until the characterisation of the retrovirus has been made and is shown not to be a laboratory contaminant of an animal retrovirus.

The reason for this caveat is because many previous investigators have mistakenly identified animal retroviruses as being of human origin. In contrast to paragraph 3 of the present paper, it is clear from reference 7 that the retrovirus under study does not resemble HTLV. First, the core antigens are unrelated and the membrane cross-immunofluorescence may not be related to the virus at all, rather to autoantibodies to OKT4$^+$ cells. Second, the morphology of the particles in Figure 2 of ref 7 closely resemble MuLV, FeLV or GALV but look quite distinct from HTLV and BoLV. This reviewer would not be surprised if the putative human virus was really a thymotropic murine MCF-type virus. Gallo's laboratory spent almost 2 years carefully characterizing HTLV before they first ventured into print. Had the data been as rudimentary as for the Paris virus, no-one would have taken the findings seriously. The potential importance of an AIDS virus is too great to rush into print with one item papers.

Referee 2

The manuscript by Klatzmann et al. discusses the T-cell tropism of a new human retrovirus first identified in a patient "at risk" for AIDS. Their conclusion that OKT4$^+$ cells are selectively infected by cell-free virus would be of considerable importance; however, the manuscript provides insufficient data to support such a conclusion.

The authors might consider the following:

1. More thorough quantitative kinetics of virus infection should be performed. Virus production should be measured at earlier and more frequent intervals. Table 2 demonstrates significant reverse transcriptase activity at only one time point (9 days). OKT8$^+$ cells might show different kinetics.

2. As retroviruses are dependent upon cell replication for productive infection (see for example Temin: J Cell Physiol 69:53-64, 1967; Varmus et al.: Cell 11: 307-319, 1977), the properties of cells in infected populations should be monitored, in particular, the percentage of viable cells and the percentage of replicating cells at different times after infection.

3. The data for percentage of virus-positive cells determined by immunofluorescence should be presented to corroborate the reverse transcriptase data.

4. It would be advisable to perform the infections using purified virus since crude supernatants from cord blood cells are likely to contain lymphokines which may affect the viability and proliferation of the T-cell subpopulations differently.

5. The statement on page 4 that "All HTLV producing cell lines . . . express the OKT4$^+$ phenotype" is incorrect. For example, B lymphocytes may be infected (Yamamoto et al.: Nature 299:367-369, 1982).