Relationship of AIDS to other retroviruses

SIR — Lymphadenopathy-associated virus (LAV)[1] is now considered to be the probable causative agent of acquired immune deficiency syndrome (AIDS). Other LAV-like viruses (the human T-cell leukaemia/lymphoma virus type III[2] and AIDS-associated retrovirus, ARV[3]) have been isolated and assumed, as some nomenclature would imply, to be a member of the HTLV superfamily of retrovirus which includes HTLV-I, HTLV-II and bovine leukaemia virus (BLV). Whether or not the AIDS virus indeed belongs to this 'superfamily' has become the subject of intense speculation.

The nucleotide sequences of both LAV[4] and HTLV-III[5,6], as well as that of ARV[7], allow definite comparisons with those of the HTLV/BLV group. First, the LAV and HTLV-III nucleotide sequences differ by less than 1% overall, whereas LAV and ARV differ by about 5% overall. The greatest sequence variation, both point mutations and insertion/deletions map to the *env* gene. Nevertheless, their deduced genetic organizations are identical, and differ from that of HTLV-I (Fig.1). Thus there is only a single AIDS retrovirus, and LAV, HTLV-III and ARV represent different isolates of the same virus. A hallmark of this virus is the presence, apart from the statutory *gag*, *pol* and *env* genes of a replication competent retrovirus, of two other open reading frames (ORF) which were called Q and F for LAV. The location of ORF Q is unprecedented, it overlaps with the end of *pol* and is followed by an apparently noncoding region, since hitherto the *pol* and *env* genes were contiguous. Directly 3′ to *env* is ORF F which is half-encoded by the U3 element of the long terminal repeat.

We have also compared the deduced amino-acid sequences of LAV proteins with those of HTLV-I and other retroviruses and find no significant homology, except for domains *pol* and *gag* which are generally conserved among retroviruses. These regions probably correspond to the core structures of essential viral proteins.

Only the protein sequence of *pol* is conserved enough to allow computation of retroviral taxonomy. This we have done for the LAV *pol* sequence corresponding to the conserved regions of the endonuclease, as has already been reported elsewhere for a number of other retroviruses. The phylogeny of the LAV endonuclease sequence (Fig.2) is that of a distant relative of all other endonuclease sequences so far established. The HTLV/BLV superfamily is most closely related to RSM, MMTV and SMRV subgroup (see Fig.2 legend). It is clear that at least the endonuclease domains of LAV and HTLV-I have been independently evolving for some considerable period of time. LAV cannot be amalgamated with the HTLV/BLV superfamily without taking a number of other retroviruses with it.

It is possible that LAV is in fact a member of the lentivirus family of retroviruses, as exemplified by visna virus[8]. We have previously noted their comparable genome sizes (9.2 kilobases including one LTR), and unusually large glycoproteins[4,9]. Their base compositions are virtually identical (LAV : U = 22.2%, C = 17.8%, A = 35.8% and G = 24.2%; visna : U = 22%, C = 16%, A = 36% and G = 26%)[4,10]. Using Southern blotting under non-stringent conditions ($T_m = 55°C$), we observed no DNA hybridization between cloned visna and LAV probes.

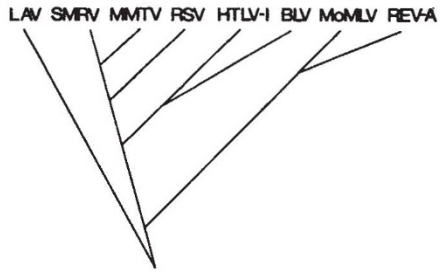

Fig.2 Phylogenetic tree of retroviral endonuclease amino-acid sequences. The tree was constructed using a partition analysis program, written by Drs William Saurin and Philippe Marliere at Institut Pasteur. The distances between branch points have no meaning. All subtrees generated by permutations of seven sequences were the same as that shown in the figure. In addition, trees constructed from segments of the eight sequences also produced identical trees. Our data are in perfect agreement with those of Sagata *et al.*[11] who, using an unweighted pair-group cluster method, produced the same tree as shown above for the SMRV, MMTV, RSV, HTLV-I, BLV and MoMLV sequences. The sequences corresponding to the conserved endonuclease sequence are, respectively, SMRV (squirrel monkey retrovirus 1-540, ref. 12), MMTV (mouse mammary tumour virus 1-540, ref. 12), RSV (Rous sarcoma virus 4,213-4,746, ref. 13), LAV (lymphadenopathy/AIDS virus 3,767-4,288, ref. 14), BLV (bovine leukaemia virus 3,982-4,530, ref. 11), MoMLV (Moloney-murine leukaemia virus 4,767-5,327, ref. 15) and REV-A (reticuloendotheliosis virus A 4,969-9,526, ref. 16). The numbering of RSV, HTLV and MoMLV is as in EMBL data bank. Others correspond to those cited by the original authors.

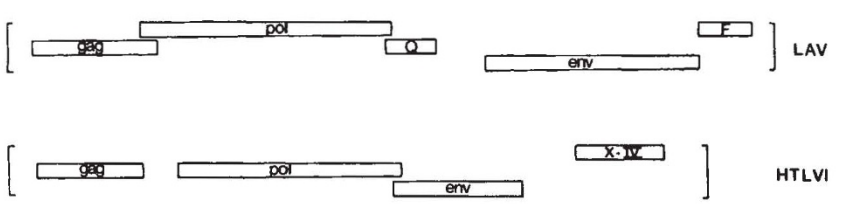

Fig.1 Organization of the viral genome of LAV and HTLV-I. Boxes represent open reading frames. Limits of the genome are indicated by brackets.

The absence of a close relationship between LAV and other retroviruses reinforces questions as to the origin of this virus and the cause of the recent emergence of AIDS.

SIMON WAIN-HOBSON
Unité de Recombinaison et Expression Génétique,
Institut Pasteur,
MARC ALIZON
LUC MONTAGNIER
Unité d'Oncologie Virale,
Institut Pasteur, 25 rue du Dr. Roux,
75724 Paris Cédex 15, France

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Microtubule assembly as a phase transition

SIR — In a *News and Views* item[1], J.R. McIntosh discusses two articles on microtubule assembly and disassembly[2]. I would like to discuss a point of McIntosh's presentation where he refers to the famous condensation-polymerization model of Oosawa-Kasaï (Oosawa later wrote a book on the same subject[3]): "... but unlike most phase transitions, the number of polymers formed increases rather slowly with increasing concentrations of subunits...".

If the effects of biological regulation such as GTP binding and hydrolysis are neglected, the autoassembly of biological fibres such as actin filaments, microtubules and microfilaments is one example of a general phenomenon called equilibrium polymerization where linear structures are formed in thermodynamic equilibrium. Other examples of equilibrium polymerization are found in several other areas of chemistry and physics: for instance, in liquid sulphur, long chains of sulphur atoms polymerize in equilibrium out of small S_8 rings[4,5]; the viscosity of liquid sulphur rises suddenly around 167°C in a fully reversible manner. Certain ionic surfactants together with water and salt can