Similarities among retrovirus proteins

SIR — In recent correspondence to *Nature*, Cianciolo *et al.*[1] reported a region of similarity between the transmembrane protein p15E of murine and feline leukaemia viruses and gp21 of the human T-cell leukaemia viruses types I and II (HTLV-I and -II). We agree that these proteins are indeed similar and draw attention to additional sequence similarities and structural features common to the transmembrane proteins. The transmembrane proteins of Rous sarcoma virus (RSV), bovine leukaemia virus (BLV) and mouse mammary tumour virus (MMTV) are included in the analysis.

Figure 1 shows a schematic comparison of the transmembrane proteins and Fig. 2 depicts three regions of amino acid sequence similarity (regions IA, IB and IC). The following features are present in all of the transmembrane proteins considered:

The amino-terminal domain of the transmembrane proteins has a hydrophobic character and contains region IA. This domain is followed by a strong polar region. The position of the hydrophobic region at the amino terminus of the transmembrane protein is reminiscent of the fusion sequence of other viral transmembrane proteins such as the Sendai and influenza viruses (see ref. 2 for review). For this reason, we speculate that this region of the HTLV envelope may be responsible for the fusion activity observed for HTLV virus[3]. The spacing of cysteine residues located near the middle of the transmembrane proteins is also conserved. Moreover, these residues occur in a highly conserved amino acid sequence context (region IB). We postulate that this region is in direct contact with the exterior glycoprotein, and that disulphide bonds are formed between these two cysteine residues and the similarly spaced and conserved cysteine residues close to the middle of the external glycoproteins. Conservation of sequence in this region might be dictated by structural constraints required for protein–protein contact. Potential glycosylation sites are located near the carboxyl end of region IB in most of the viruses considered. Glycosylation can occur at these sites, as the transmembrane proteins of HTLV-I, HTLV-II, BLV and MMTV are glycoproteins.

There is a hydrophobic region near the carboxyl terminus which includes a highly conserved sequence (region IC). This region has the correct length and position to traverse the cellular membrane. An α-helix is the most favoured configuration of this portion of the transmembrane region[4,5]. Moreover, this hydrophobic domain terminates with a positively charged amino acid located three residues (except in RSV) carboxyl terminal to a conserved cysteine residue.

A small, highly variable region is coded for by the extreme carboxyl terminus of the envelope gene precursor of retroviruses. This region, designated R, is cleaved from the envelope gene precursor late in maturation in murine viruses[6].

At present, there is no experimental evidence to discard the involvement of any of the regions of similarity or structural features reported in the immunosuppressive activity demonstrated for murine and feline p15E.

A more extensive analysis of similarities among the p15E as well as other retrovirus proteins is contained in our review of HTLV-I structure[3].

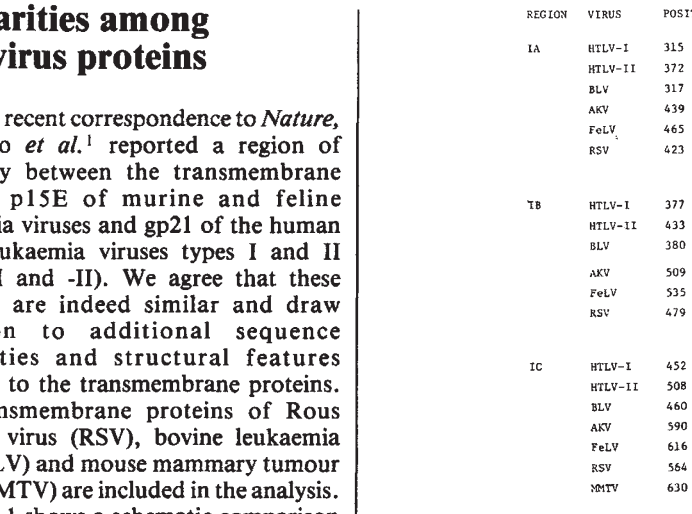

Fig. 2 Alignment of three regions of sequence similarity among the transmembrane proteins of the retroviruses mentioned in Fig. 1. Conserved positions are boxed and conservative substitutions underlined. Although MMTV does not show significant similarity in regions IA and IB, it was included because the general structural features described in the text also apply.

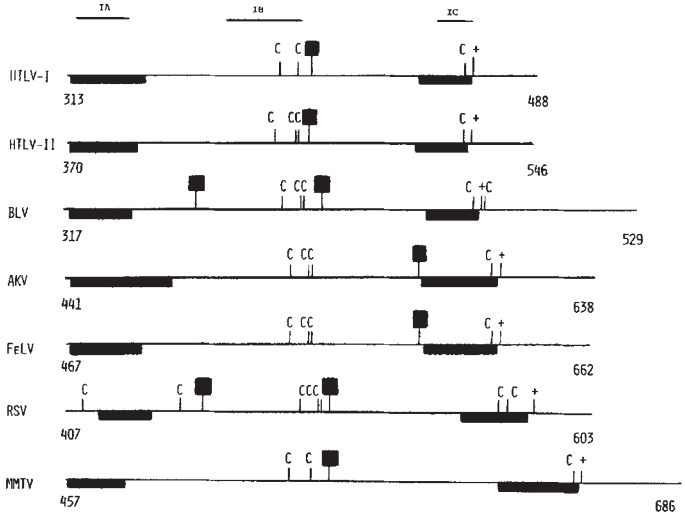

Fig. 1 Schematic comparison of the transmembrane proteins of: human T-cell leukaemia virus types I (ref. 7) and II (ref. 8) (HTLV-I and -II), bovine leukaemia virus[9] (BLV), AKV[4], feline leukaemia virus[10] (FeLV), Rous sarcoma virus[11] (RSV) and mouse mammary tumour virus[12] (MMTV). The hydrophilicity pattern was obtained using the Intelligenetics PEP program. The hydrophobic regions discussed in the text are indicated by a thick bar beneath the line. Potential glycosylation sites are indicated by a square, cysteine residues by a C and the position of a positively charged amino acid 3′ to the transmembrane region is depicted by +. The position of regions IA, IB and IC from Fig. 2 is also shown for HTLV-I.

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