tinsky reaction, are all associated with increases in entropy production as the driving force is increased.

I suspect Lavenda feels I am violating some deep-seated principle that nature is always seeking stability either in equilibria or in minimum dissipation. I do not think such a principle exists, and if '*die Entropie der Welt strebt einem Maximum zu*' then why should it not always strive to a maximum as fast as it possibly can?

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Superantigen function

SIR — Superantigens combine with class II molecules of the major histocompatibility locus to form ligands capable of inducing powerful proliferative responses in $CD4^+$ T cells that bear appropriate Vβ elements in their T-cell receptor. The prototype superantigens are encoded by the minor lymphocyte stimulatory (*Mls*) genes in mice and play an important role in selection of the T-cell repertoire during development by inducing clonal deletion of T cells expressing specific Vβ elements. No such elements have yet been identified in other species. Bacterial exotoxins are now recognized as acting as superantigens and this has stimulated further interest in the biological role of these proteins[1]. The product of the open reading frame in the 3′ long terminal repeat (LTR) of mouse mammary tumour virus (MTV) has recently been reported to encode the first identified viral superantigen[2]. Here we report that herpesvirus saimiri (HVS), a herpesvirus of primates, encodes a homologue of the product of the 3′ LTR open reading frame of MTV.

HVS establishes persistent asymptomatic infection of its natural host (*Saimiri sciureus*). But in other New World primates the virus induces rapidly progressive T-cell lymphomas. The pathology of these conditions varies between species, but is characterized by massive lymphocytic infiltration of many tissues. We have previously shown[3] that an abundant transcript of 1.3 kilobase pairs (kbp) present at immediate–early times of infection with HVS (strain 11 (onc)) has the potential to encode a polypeptide of 249 amino acids, which is similar to the product of the conserved open reading frame in the 3′ LTR of MTV, then of unknown function.

An alignment of the HVS protein with the putative superantigen reported by Choi *et al.*[2] and the homologous protein of a representative endogenous MTV is illustrated in the figure. Overall, the HVS and murine protein have an approximately 25 per cent identity and a 46 per cent similarity. Residues 161–218 of the HVS protein are 43 per cent identical and 60 per cent similar to both murine proteins and contain conserved acidic, basic and hydrophobic residues. In addition, all three proteins contain a single, highly hydrophobic region close to their predicted amino termini (see figure). Although correlations between the structure and function of viral superantigens have not yet been established, the similarities between the HVS and MTV proteins strongly suggest that they bear a significant evolutionary or functional relationship to each other. Superantigens encoded by bacteria do not share these structural features. No counterpart of this gene has been identified in other herpesviruses. HVS contains a number of genes that are likely to have been captured from the host cell (see refs 3 and 4). So the superantigen homologue could have been acquired from the natural host, implying the presence of *Mls*-like genes in the primate genome.

The mechanism by which HVS induces lymphoma is unknown, but is dependent on sequences from the 'left' end of the genome[4]. This region does not give rise to the 1.3-kbp transcript. In addition, most cell lines derived from HVS-induced lymphomas are of $CD8^+$ phenotype. So there is no simple link between the superantigen homologue and oncogenicity. The gene may, however, play an important role in mediating the massive, early lymphoproliferation characteristic of HVS infection in primates other than the natural host. The administration of exogenous superantigen to immunologically mature mice has recently been shown to induce a selective anergy[5] of $CD4^+$ cells bearing specific Vβ elements. Expression of a functional superantigen by HVS may therefore modulate the immune response to the virus and provide a novel mechanism of enhancing persistence in the natural host.

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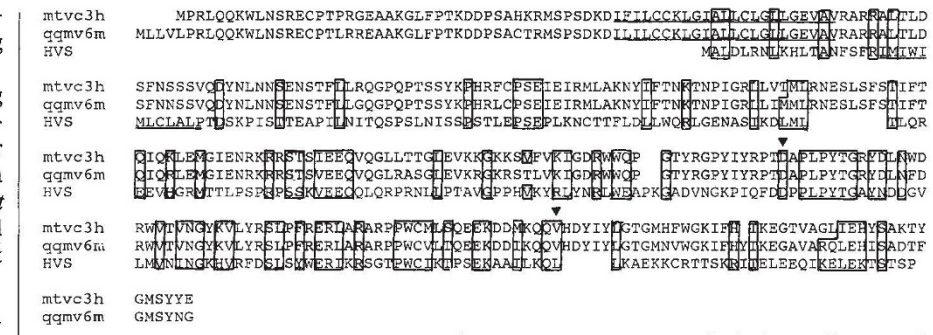

Alignment of the sequences of the predicted protein product of the 1.3 kbp immediate - early transcript of HVS, the putative superantigen reported by Choi *et al.*[2] (mtvc3h) (ref. 2) and the product of the major open reading frame in the 3′ LTR of an endogenous MTV (qqmv6m) (ref. 3). Identical and similar residues are boxed. Similar residues were members of the sets: L=I=V=M, R=K=H, F=Y=W, S=T, E=Q, D=N. Amino acids 161–218 of the HVS protein, indicated by solid triangles, share an approximately 43 per cent identity and 60 per cent similarity with both murine proteins. The single, highly hydrophobic region in all three proteins is underlined.

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Alzheimer's mutation

SIR — Goate *et al.* report[1] a mutation in the gene encoding the amyloid precursor protein in people with Alzheimer's disease in two unrelated families. The next step is to discover how commonly this mutation occurs in other cases of familial Alzheimer's disease.

We have screened an Italian and several French families that we have been studying[2,3]. Although we do not find the mutation reported by Goate *et al.* in our Italian family, we do find that it occurs in three individuals in one of the French families[4].

This result is particularly interesting in that one of these individuals has amyloid angiopathy. It is already known that a mutation reported by Levy *et al.*[5] in the amyloid-precursor-protein gene is also the site of the mutation leading to hereditary cerebral haemorrhage with Dutch-type amyloidosis.

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