



Conserved regions in the 5'-non-coding regions in homoeobox-containing genes. The initiator AUG is at the right-hand end of the figure. Vertical lines between pairs of sequences indicate identical nucleotides. Regions of high conservation are boxed. A short region conserved in the *Drosophila* gene *Deformed* is indicated. *Fushi tarazu* has a small stretch of nucleotides (TCTGATTTTGCTATATAT, approximately -100 upstream of the AUG) similar to the second and third boxed regions of X1Hbox 2 and HHO.c1 (not shown).

Most interestingly, we unexpectedly found extensive nucleotide conservations in the 5'-non-coding regions immediately preceding the initiator AUG, as shown in the figure. The conservation is maximal among the four genes mentioned above. For X1Hbox 2 (ref. 3) and HHO.c1 (ref. 9) it is 91% (over 99 nucleotides), for Xhox-36 (ref. 2) and Hox 1.1 (ref. 7) it is 77% (over 102 nucleotides), and for Hox 1.1 and X1Hbox 2 it is 77% (over 100 nucleotides). Sequence conservations in this region occur in other genes: mouse Hox 2.1 (ref. 5) and Hox 1.3 (ref. 6) are 63% conserved over 114 nucleotides.

Why are non-coding nucleotides conserved in many genes from such diverse organisms? Perhaps this merely reflects the common evolutionary origin of homoeobox genes. Alternatively, the sequences may have remained invariant because of strong evolutionary pressure to preserve a common function. The best argument in favour of this is provided by the homologues X1Hbox 2 and HHO.c1 (ref. 9). These two genes have been evolving for at least 350 million years, since the separation of amphibians and the mammalian ancestors. Their 5'-non-coding regions next to the AUG are 91% conserved, but the 3'-non-coding regions show no sequence conservation.

In the coding region between the amino terminus and the homoeobox there is very little nucleotide similarity and even in the homoeobox regions, where the protein reading frame is under strong pressure to remain invariant, the conservation is only 81%. We think the 5'-non-coding region is the most conserved not only because of a common evolutionary origin but because it carries an important biological function.

The conservations shown in the figure are not due to a translational reading frame, because in all sequences there are stop codons in all reading frames and frequent insertions that would produce frameshifts. As the 5'-leader conservations are closely associated with the initiation codon, an attractive hypothesis is that these sequences are involved in translational control. Translational control has been implicated in the expression of homoeobox genes in *Drosophila*: the best

example being the maternal gene *caudal* whose mRNA, although uniformly distributed in the egg, is translated only in the posterior of the embryo^{11,12}. The possibility of translational regulation has been shown for the frog gene X1Hbox 2 in an experiment in which deletion of most of the 5'-leader of a cDNA clone, leaving only 26 nucleotides in front of the AUG, stimulated *in vitro* translation of SP6 messenger RNAs over 20-fold by both reticulocyte and wheat-germ systems⁴. The proteins translated from both constructs were of the same size⁴, providing direct evidence that the 5'-conserved region is not translated.

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AIDS incubation period in male haemophiliacs

SIR—Ekert¹ concludes that there is no adequate explanation for the tenfold lower rate of conversion of infection with the human immunodeficiency virus (HIV) to clinical AIDS (acquired immune deficiency syndrome) in male haemophiliacs compared with other groups of HIV carriers. A possible explanation is that, unlike heterosexual male haemophiliacs, other groups of HIV carriers are exposed during sexual intercourse to the immunosuppressant effects of seminal plasma.

Human seminal plasma contains various immunosuppressive agents². In par-

ticular, seminal plasma may inhibit the normal immune response to a viral infection³. Prostaglandin E₂, a constituent of seminal plasma, has been shown *in vitro* to facilitate HIV replication⁴. Clinically, both the transmission⁵ and the neoplastic complications⁶ of HIV are associated with receptive anal intercourse. We have recently suggested that following sexual intercourse the suppression of the immune response to HIV by seminal plasma may be important in patients who are already HIV carriers³. Such an effect could hasten the development of clinical AIDS in HIV carriers and is consistent with the higher incidence of Kaposi's sarcoma⁶ and lymphomas⁷ in male homosexual HIV carriers compared with other HIV carriers, including haemophiliacs.

Thus, a longer incubation period and a lower incidence of clinical AIDS in haemophiliacs following HIV infection may be more apparent than real because of the shorter incubation period in other HIV carriers.

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HIV vaccination and blood transfusion

SIR—With the increasing attention being given to the possibility of vaccination against human immunodeficiency virus (HIV)¹⁻³, we wish to raise the question of the impact of vaccination on blood donor screening.

Vaccination would produce seropositive individuals whose blood is reactive with HIV-antibody screening tests currently in use for blood donor screening. As even confirmatory tests could not establish whether a positive test was the result of