SCIENTIFIC CORRESPONDENCE

Herpes infection and AIDS

SIR-In individuals infected with the human immunodeficency virus (HIV), a prolonged period with no overt symptoms may be followed by the onset of AIDS (acquired immune deficency syndrome) of which the virus is the cause. The reasons for this prolonged latent period are unclear but are of major importance for the understanding and control of AIDS. In this regard the recent report by Mosca et al.1 that the promoter in the long terminal repeat (LTR) of HIV can be activated during infection with herpes simplex virus type 1 (HSV-1) is of obvious interest, especially as many AIDS patients exhibit opportunistic infections with HSV.

The fact, however, that the experiments were carried out using cell lines into which the HIV LTR (linked to a marker gene) had been stably introduced by transfection suggests that care must be taken in extrapolating these findings to cells latently infected with HIV itself. Thus, in similar experiments, a \beta-globin promoter introduced by transfection could be activated by subsequent HSV infection of the transfected cell line, although the endogenous β-globin gene was unaffected by such infection².

It seems therefore, that the chromatin structure of genes recently introduced by transfection may render them susceptible to a nonspecific induction by HSV infection, whereas the endogenous genes within the normal chromatin structure are unaffected. Although our laboratory has shown that a small number of endogenous cellular genes, with a normal chromatin structure, can be specifically activated during HSV infection^{3,4}, many more are nonspecifically activated.

The behaviour of an artificially introduced HIV promoter in response to HSV infection may not therefore be relevant to the regulation of the whole HIV genome in latently infected cells, particularly as transcription of other integrated viral genomes (for example those of polyoma and adenovirus) is known to be dramatically reduced when cells transformed with these viruses are infected with HSV5. Studies involving cells latently infected with HIV itself will be necessary to confirm the provocative suggestion of Mosca et al.¹ that infection with HSV could re-activate HIV and lead to the development of the symptoms associated with AIDS.

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Claws' claws

SIR-Kitchener's1 discussion of the possible habits of Baryony x^2 is intriguing, but needs three comments.

First, Baryonyx might well have had difficulty in dealing with tough skins¹, but this seems unlikely to have been true of typical theropods. Modern crocodiles have this problem because their teeth are more or less conical, and not adapted for slicing; but those of normal theropods were bilaterally compressed 'steak-knife' teeth, with serrated anterior and posterior edges, like those of various thecodontians and the sebecosuchid crocodiles. In this case, a better modern model for functional comparison would be the Komodo monitor, Varanus komodoensis, which has similar, though acrodont, teeth.

Second, adaptation of the claws for breaking into carcasses' would only be meaningful in terms of unbreached examples: most carcasses available to a scavenger that was not a primary predator would probably have been those of animals killed by typical theropods, and already broken into by them. It is doubtful that there could have been enough selection pressure to produce this adaptation.

Third, regarding weight^{1,2}, the large size of grizzly bears does not prevent them from catching salmon, despite their being fast swimmers, and even trout, when not swimming quickly, can be taken by 'tickling' as they swim across a hand held open under water. Lateral nares placed well back² would also allow a crouching fisher to wait motionless with the tip of the snout¹ under water.

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Sequence similarity

SIR-Several recent articles have described members of a rapidly growing family of proteins, each of which contain a similar domain of roughly 200 amino acids that is likely to be involved in nucleotide binding. The majority are bacterial proteins known to be ATP-binding components of periplasmic transport systems^{1,2}, and this family has recently been found to include the product of the mdr gene, a membrane glycoprotein (the P glycoprotein) responsible for multiple drug resistance in a variety of mammalian cell lines³⁻⁵. I would like to point out that the putative translation product of the gene white (w) in the fruit fly Drosophila melanogaster⁶ also fits very nicely into this group. The white locus is well studied genetically and molecularly because of the obvious and varied eye pigmentation phenotypes of its mutants, and is currently the focus of work on the molecular effects of transposable element insertions. Genetic evidence has suggested that the product of this locus functions in the deposition of pigment, but its precise biochemical role is unknown.

Homology between w and this family of proteins extends the unpublished observation of Gary Otto that w contains homology to a core of amino acids found in about a third of all proteins known to bind ATP. The homology involves amino acids 120-335 of white (five amino acids of the second exon and all but seven of the third6) and almost the entirety of bacterial proteins such as hisP and malK. The alignments of w with hisP and malK generated by the program DFASTP7 were assigned scores 13 standard deviations better than the mean score for proteins in the Protein Information Resource database. There is a comparable homology between w and other members of the family (pstB, oppD, hlyB or mdr). It is interesting that the region of homology is largely coincident with the third exon; perhaps the remainder of the white protein (the complete open reading frame contains 694 amino acids) carries out functions related to those of the other proteins of the homologous periplasmic transport systems.

This observation supports the notion that the w protein is involved in the active transport of pigments into pigment cells or pigment granules, an idea for which there is some experimental support⁸. There are two classes of pigment in the Drosophila eye, ommochromes (the brown pigments) and pteridines (the red pigments), and the question of how mutations in a single gene could eliminate the accumulation of both classes is longstanding. Here we see further similarity to the mdr locus, which confers resistance to a wide variety of compounds, and the histidine transport operon, which also functions in the transport of a variety of compounds, including histidine and basic amino acids. Although sequence homology does not provide a definitive biochemical explanation for the phenomenon of specific transport of multiple substrates, it does serve to make it less mysterious (see ref. 9 for a discussion of possibilities), and suggests that results obtained in any one of these transport systems should be of interest to those studying the other.

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