

## When evolution cannot go into reverse

SIR—P.L. Williams (*Nature* 328, 21–22; 1987) incorrectly refers to “ambiguity” in our article on irreversible evolution (*Nature* 326, 128; 1987). For the purpose of our discussion, the process was defined as involving “evolutionary routes that, once taken, preclude return”, and illustrated with an example taken from hymenopteran wasps in which both biology and theory are understood. In none of the cases cited by Williams is there any reason to believe that a strict retracing of evolution could not occur if all ancestral environments were retraced. In the peppered moth example, the complications cited by Williams do not prevent reversible evolution. The whole point of our article was that, on occasion, there are good reasons why an evolutionary route would not be retraced even given the ancestral intermediate environments.

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## Function of a new globin gene

SIR—Recently a new gene ( $\theta 1$ ) has been identified at the 3' end of the  $\alpha$ -globin cluster in several species<sup>1–3</sup> including man. It has been suggested that this gene may be functional in higher primates because in the orang-utan and olive baboon it has all of the structural features necessary for expression and in man it has given rise to a processed pseudogene elsewhere in the genome<sup>4</sup>. Further evidence for its functional status comes from comparisons of the silent versus replacement site substitutions in two primate  $\theta 1$  genes which indicate that it has been evolving under selective constraints<sup>2</sup>. Speculation about the function of  $\theta 1$  has centred on its possible role as an embryonic globin involved in placentation<sup>1,2</sup>.

At present no protein or messenger RNA corresponding to the  $\theta 1$  gene has been reported. In the past, the function of various globin genes has been established by identifying haemoglobins corresponding to their gene products and observing

the effect of naturally occurring mutants of globin synthesis (thalassaemias) on the phenotype of affected individuals. As far as we know, however, there are no unassigned human globins and therefore no candidate gene products for  $\theta 1$ . Interestingly, analysis of the predicted amino-acid sequence of the  $\theta 1$  counterpart in horse suggests that it may not encode a viable globin-like protein at all (see page 465 of this issue<sup>5</sup>) but as it has clearly been conserved throughout evolution, may subserve some other function.

In man, the  $\theta 1$  gene lies at the 3' end of the  $\alpha$ -globin complex which includes an embryonic gene ( $\zeta$ ), two adult  $\alpha$  genes ( $\alpha 2$  and  $\alpha 1$ ) and three pseudogenes ( $\psi\zeta 1$ ,  $\psi\alpha 1$  and  $\psi\alpha 2$ ) (see figure). We have recently shown that a determinant for  $\alpha$  thalassaemia in South-East Asia results from a deletion that removes both  $\alpha$  genes ( $\alpha 2$  and  $\alpha 1$ ) and the  $\theta 1$  gene (see figure)<sup>6</sup>. Heterozygotes for this determinant have a mild anaemia but are otherwise normal. Homozygotes survive *in utero* until 28–32 weeks of gestation but, with rare exceptions<sup>9</sup>, die in the perinatal period due to the effects of prolonged intrauterine hypoxia; this condition is known as the Hb Bart's hydrops fetalis syndrome. The fact that such infants can survive at all until this late stage in development makes it very unlikely that the  $\theta 1$  gene encodes a critical embryonic globin.

Observations on homozygotes for this deletion may also be instructive in evaluating other possible roles for the  $\theta 1$  gene. Although infants with the Hb Bart's hydrops fetalis syndrome have a relatively high incidence of congenital malformations, there is no consistently abnormal developmental pattern and it is likely that such abnormalities are secondary to chronic intrauterine hypoxia. We have re-evaluated the genotype of a child with this syndrome who has been intensively treated and kept alive by blood transfusions<sup>9</sup>. We find this child to be homozygous for the South-East Asian  $\alpha$ -thalassaemia determinant, both  $\theta 1$  genes are deleted (see figure), and yet the child appears to have developed normally, indicating that  $\theta 1$  does not encode any other critical protein that cannot be replaced by regular blood transfusion.

It is possible that  $\theta 1$  is only one member of a family of  $\theta$ -like genes<sup>1</sup> and that deletion of a single member ( $\theta 1$ ) is of little or no consequence. However, the observations reported here raise some doubts as to whether  $\theta 1$  is expressed as a

protein; it is unlikely to be a part of a viable haemoglobin molecule<sup>7</sup> and probably does not encode a critical protein, although it may represent a non-essential facultative protein. If this is the case, it raises the interesting question of why the  $\theta 1$  gene has been so well conserved throughout mammalian evolution.

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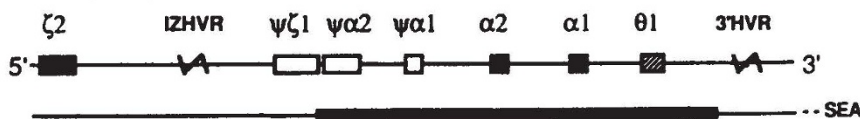
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## Th/Nd abundance ratio in the surfaces of G-dwarfs

SIR—In a stimulating recent article, Butcher<sup>1</sup> makes wide-ranging conclusions about the age of the Galaxy from his observations of the essential constancy of the Th/Nd abundance ratio in the surfaces of G-dwarfs of varying age. He argues that in the simplest model of chemical evolution for the Galaxy, one in which the nucleosynthesis rate per unit mass of interstellar medium is constant so that stable-element gas concentrations rise linearly in time, the ratio of the concentration of Th to that of a coproduced stable element observed today in a G-dwarf that had formed at time  $T$  rises as  $(e^{sT}-1)/\lambda T \approx 1 + 0.025T$ . Accordingly, in terms of the age of the star (galactic age  $-T$ ) the surface concentrations today decrease with increasing age. His data, reproduced in the figure, do not decline with age, leading to Butcher's powerful conclusions.

I write in admiring caution to argue that, from a purely theoretical point of view, the simplest model expectation is of opposite sign and matches the data well (the curve in the figure). In the astrophysically simplest model, the  $r$ -process abundances are primary and indeed grow linearly in time, but the  $s$ -process abundances are secondary, being proportional to the initial stellar metallicity, so that they grow quadratically in time. Because Th/Nd observed today measures  $\text{Th}/(\text{Nd} + \text{Nd}_s)$  at time  $T$ , the ratio expressed above should, in terms of the time dependence of this simple model, be



The normal human  $\alpha$ -globin complex. The heavy black rectangle below depicts the extent of the South-East Asian deletion.