

## Response to Ptashne

SIR — I am writing to comment on Dr Mark Ptashne's letter (*Nature* 352, 101; 1991) which discusses two papers on which I am a co-author<sup>1,2</sup>, and which relates these papers to the current controversy about the 1986 *Cell* paper by Weaver *et al.*<sup>3</sup>.

Ptashne's summary of the conclusions of our two papers is correct. However, it is not appropriate to infer that these conclusions fail to replicate the "central claim" of the 1985 *Cell* paper or that the papers support Dr Margot O'Toole's contentions regarding this "central claim".

First, the experiments that we performed were not designed to replicate the work of Weaver *et al.*, but instead to determine whether their results could be extended to a different antigen/idiotypic system which involves entirely different specificities. The fact that we did not find antibodies entirely derived from endogenous genes but carrying idiotypic determinants characteristic of our transgene implies only that the findings of Weaver *et al.* cannot be generalized to other lines of transgenic mice with different specificity. Different transgenic mice having different recombined antibody heavy chain transgenes have shown remarkable variability in their phenotypes; thus the differences between our results and those of Weaver *et al.* should not be overconstrued. On the other hand, Weaver *et al.* speculated that some of their results might be explained by transgene isotype switching; our subsequent work has demonstrated clearly that such isotype switching can, in fact, occur<sup>2,4</sup>. In this latter instance, con-

### Faux pas

SIR — John Maynard Smith's review of Robert Wesson's book *Beyond Natural selection* (*Nature* 352, 206; 1991) refers to the great French scientist "Jacob Monod".

I wonder whether this *coquille* derives from François Jacob and Jacques Monod being so often associated for their molecular biology work, or whether we must interpret it as an insidious attempt to decrease the number of French Nobel Prize recipients. Moreover, it would be unfair to reduce F. Jacob merely to J. Monod's first name.

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■ The error was made in the *Nature* office.  
— Editor, *Nature*.

sistency between results from two different strains of transgenic mice (rather than the lack of consistency) is more meaningful.

Finally, the "central claim" of Weaver *et al.* is most directly supported by their results, summarized in Table 3 of the 1986 *Cell* paper, with cloned idiotype-positive hybridomas<sup>3</sup>. About 50 per cent of these hybridomas produced IgG or IgA rather than IgM. It is correct that our more recent work has shown that, in some transgenic mice, some B-cells can produce two separate mu molecules, one encoded by the transgene (mu-a) and one encoded entirely by endogenous genes (mu-b), and that these B-cells can secrete IgM heterodimers of the mu-a/mu-b type<sup>2</sup>. However, as Dr Herman Eisen correctly indicates (*Nature* 352, 101; 1991), our observations of co-expression by IgM-producing cells are not relevant for the IgG-producing or IgA-producing hybridomas in Table 3 of Weaver *et al.*

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1. Durdik *et al. Proc. natn. Acad. Sci. U.S.A.* 86, 2345–2350 (1989).
2. Rath *et al. J. Immunol.* 143, 2074–2080 (1989).
3. Weaver *et al. Cell* 45, 247–259 (1986).
4. Gerstein *et al. Cell* 63, 537–548 (1990).

## More on psycho-darwinism

SIR — Regarding Christopher Badcock's suggestion<sup>1</sup> that I might be reluctant to recognize my "freudian proclivities", in fact, I take considerable pleasure the way in which psycho-darwinism<sup>2</sup> provides a means of tying Freud's idea of a death instinct back to the bedrock of evolutionary theory.

Some apparent difficulties are caused for psycho-darwinism by the phase in the human life cycle at which the onset of mental illness is most likely to occur, as M. S. Fazeli points out<sup>3</sup>. One possible explanation turns upon the exceptionally long period of nurturing that the human child requires. Because of this, in the natural state, the incapacity or elimination of a parent as a result of a mental disorder would, in almost all cases, seal the fate of the child, and genes common to both. Given that it is not always the most eligible partner who proves to be the most effective parent, there may be greater evolutionary stability in applying the relative success/failure test with greatest rigour well into the nurturing phase, rather than before reproduction.

Two other, mutually exclusive, possibilities are that: (1) it "pays" to rely

upon reproductive suppression, rather than mental illness and death, throughout the fertile period in case the individual eventually finds something it is relatively good at; or (2) in nature, natural selection operates on the incipient stages of mental illness, thus achieving elimination long before the mature phase we treat clinically.

Richard Dawkins' response<sup>4</sup> is particularly useful because it has led me to develop psycho-darwinism in a way which makes it fully compatible with neo-darwinism. As he points out, unless I could somehow insulate my heirs from his, the inevitable outcome would be a Dawkins/Waller amalgam which could in no sense be represented as a total triumph of my genes over his. However, this conclusion does at least serve to define what constitutes 'triumph' in this context: achieving unaltered replication, generation after generation.

In terms of both my parable and the real world, there is only one group that meets this criterion: those few genes that are actually responsible for the existence and operations of the comparator mechanism which is central to psycho-darwinism. While themselves remaining virtually unaltered, they, in effect, use all other genes as mere resources to be permuted and re-permuted, selected and rejected, simply to ensure that they, the omnipresent comparator genes, are always on the side that is winning. Individual 'survival machines' are mere sub-agents, to be 'turned-on' when doing relatively well, and 'turned-off' when not. And, most cunning of all, it is the individual's own brain that makes the judgements, and triggers the appropriate electrochemical responses.

I have two reasons for suggesting that this final twist to psycho-darwinism makes it fully compatible with neo-darwinism. First, the comparator mechanism meets the requirement of acting solely in the interests of a specific group of genes. Second, the whole process is remarkably close to the extended version of inclusive fitness known as the 'green-beard' hypothesis, a description of which is to be found on page 207 of *The Blind Watchmaker*<sup>5</sup>. The "label", equivalent to a green beard, to which the bearers of the comparator mechanism respond is "an individual whom I have identified as aspiring to fulfil the same role as I do within my species", that is, a member of a peer group.

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1. Badcock, C. *Nature* 351, 686 (1991).
2. Waller, M. J. C. *Nature* 351, 264 (1991).
3. Fazeli, M. S. *Nature* 351, 686 (1991).
4. Dawkins, R. *Nature* 351, 686 (1991).
5. Dawkins, R. *The Blind Watchmaker* (Penguin Books, London, 1988).