

# Polymerase patent problems

SIR — We are concerned about the broad scope of the European patent provisionally awarded to Hoffmann-La Roche for *Taq* DNA polymerase (see *Nature* 372, 212; 1994). Unlike its US counterpart, this patent does not claim DNA polymerase from *Thermus aquaticus* alone. Instead, it claims all thermostable nucleic acid polymerases, including DNA and RNA polymerases, with relative molecular masses of 86,000–90,000 that show high fidelity.

According to the European patent examiner involved in this case, Roche was able to demonstrate that, in contrast to the previously described *Taq* DNA polymerase<sup>1</sup>, its enzyme showed almost no activity in an amplification assay when one nucleotide was removed. This indicates a high fidelity or accuracy in DNA replication, even though the enzyme lacks a 3'–5' exonuclease activity and cannot therefore remove misincorporated bases. Indeed, because *Taq* lacks 3'–5' exonuclease activity, it has been thought unsuitable for applications requiring high fidelity. This has led to the introduction of alternative enzymes such as *U1Tma*, which is sold by Roche's PCR (polymerase chain reaction) partner Perkin-Elmer. It is the demonstration of high fidelity in *Taq* that appears to fulfil the novelty criterion.

The claims made in Roche's European patent cover every polymerase with these characteristics. These include three market competitors of *Taq*, *Vent* and *Deep Vent* (*Thermococcus litoralis*, New England Biolabs) and *Pfu* (*Pyrococcus furiosus*, Stratagene). Lundberg<sup>2</sup> demonstrated that *Pfu* has an 11–12 fold greater replication fidelity than *Taq*, with an average error rate of  $1.6 \times 10^{-6}$  for *Pfu* and  $2.0 \times 10^{-5}$  for *Taq*. Kong *et al.*<sup>3</sup> showed that *Vent* has a  $K_m$  of 0.07 nM compared to 1.4 nM for *Taq*. A low  $K_m$  value indicates an enhanced ability to replicate low DNA concentrations efficiently. Literature from New England Biolabs<sup>4</sup> indicates an error rate of  $57 \times 10^{-6}$  for *Vent* compared to  $285 \times 10^{-6}$  for *Taq*. In the case of *Vent*, *Deep Vent* and *Pfu* it has always been thought that the 3'–5' exonuclease activity is responsible for the low error rates, yet Roche has apparently managed to demonstrate sufficiently high fidelity of *Taq* for these enzymes to be covered in the patent claims. If the broad scope of Roche's European claims is upheld, these existing products will be in conflict with the new patent.

Our unease does not end here, as this patent could be used to prevent the sale of polymerases yet to be discovered. Because of this potential, the European patent examiner is expecting a large number of objections. Paradoxically, the latest

innovation in PCR (long-range PCR)<sup>5</sup> uses a combination of DNA polymerases, a technique that makes use of alternative enzymes developed by other companies in the absence of broad patent protection for nucleic acid polymerases. We have here another clear example<sup>6</sup> of an undesirably broad patent that provides the applicant with a monopoly which may inhibit the development of new and better products.

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## Opting for silence

SIR — John Funder finds it neither correct nor attractive to silence the 'p' when pronouncing words in which the Greek-derived 'pt' occurs in the middle of a composite word (*Nature* 371, 98; 1994). 'Helicopter' is, he believes, a convincing example. Undeniably, helicop-ter is the universally accepted pronunciation, but at the same time one has to realize that few people reflect upon the etymology of this word. However, in names of compounds such as aminopterin, an amino derivative of pterin, one must clearly opt for silencing the 'p' (as in apoptosis) in order to secure the understanding of the underlying chemistry.

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SIR — In writing about the etymology of the word apoptosis, Funder misses an important distinction between pronunciation and spelling. Indeed, using Funder's own examples, he shows when the 'p' is pronounced and when it is silent.

Apoptosis, as in pterydactyl, has a 'pt' at the beginning of a syllable. Unlike helicopter (or optic, option and so on), the 'p' is silent. Such a distinction is also made when a 'p' is followed by an 's', as in psychology. Even when the 'p' is preceded by an 'o', as in neuropsychology, the 'p' is silent.

An argument could be made that the

word is pronounced a 'pop'tosis, where the -pt would be in the middle of a syllable. However, that would be denying the etymology of the word on which Funder based his own argument. Because the term used to describe a particular type of cell death is derived from two greek words, *apo-* and *-ptosis*, the syllabic break is made between the two words when they are joined. Thus apo'(p)tosis is the correct pronunciation.

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## Nurture not nature

SIR — Although the alleged taking of a pink pigeon, now presumed dead, by a Mauritius kestrel is unfortunate, you go too far in describing the outlook for species preservation as "gloomy" (*Nature* 371, 544; 1994).

True, in the short term, greater protective measures will have to be taken; however, in the long term, the solution certainly lies in improved education. Perhaps, in the effort to re-establish native populations, insufficient attention has been paid to inculcating proper respect for species with divergent life-styles.

It is well to remember that the kestro-Mauritians (as they are properly termed) have, over the past century, suffered a devastating and nearly complete loss of their cultural as well as their genetic heritage at the hands of the very species who would now save them. Is it, then, surprising that these proud birds, who, after all, give the Ile aux Aigrettes its name, should strike out, in revenge, at the weak?

While it would be naive to suppose that this problem will disappear either quickly or completely, I am confident that it will, in time, yield substantially to the same sorts of efforts to which so many of our once-pressing social ills have proved susceptible: sympathetic counselling by both trained professionals and peer offenders, the establishment of support groups for those attempting to overcome their habituation to this form of violence, and, most importantly, exposure, from an early age, both in the nest and in the classroom, to the simple truth that, when all is said and done, "under the feathers, we are all birds."

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