substitute pesticides were available. Most, if not all, of the potential substitutes for diclofenac are related drugs[11] that act in a similar way[12–14] and are also known to affect kidney function[8–10,14]. Settling on an acceptable substitute is very unlikely to happen before the birds are extinct in the wild; moreover, ways of implementing and enforcing a ban on the use of diclofenac as a veterinary medicine must be considered in any conservation strategy. India alone has an estimated 20,000 pharmaceutical companies and 500,000 pharmacists, who take "competition to a questionable extreme"[15].

The California condor, *Gymnogyps californianus*, also being poisoned by an environmental contaminant in the form of fragments of lead ammunition, was rescued from extinction by bringing all surviving birds into captivity. Such a programme, which would permit vultures to survive until they or their progeny might be reintroduced into the wild, is being discussed in India, and could yet be implemented in Pakistan. But talk has not resulted in action. In India, as occurred earlier in California, the argument is being made that 'nature' should be allowed to take its course. The immediate need to quarantine a sufficient number of each species to ensure their survival is ignored in discussions that focus on longer-term captive breeding and who would undertake it.

The surviving vultures are increasingly difficult to find, and because of the abundance of carcasses in the countryside, are increasingly difficult to trap. An effective conservation programme that might yet permit the survival of these birds in south Asia must emerge from the talking stage within the next several months. In demonstrating the cause of the mortalities, Oaks *et al.* also provide the impetus for the development of such a conservation programme; the timing of their paper is indeed propitious. ■

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This article was published online on 28 January 2004 (doi:10.1038/nature02365).

Molecular biology

Ensuring error-free DNA repair

Tomas Lindahl

Damaged DNA must be removed with the utmost precision, as mistakes are costly. The structure of a repair enzyme bound to its substrate provides a welcome clue to how this is achieved.

Certain forms of oxygen, known as reactive oxygen species, can be deleterious for living organisms. Although most cells can tolerate and even exploit them, these oxygen forms may contribute to cancer, tissue degeneration and ageing. In the nucleus of cells, active oxygen damages DNA, so it is important to repair an altered DNA base before it is copied during DNA replication. Failing this, the newly incorporated base opposite the original lesion may need to be removed and corrected.

One example of such repair kicks in after the conversion of guanine (G) — one of the four bases — to 8-hydroxyguanine (also known as 8-oxoguanine; oxoG) by active oxygen[1] and misincorporation of the normal base adenine (A) opposite the oxoG. A specific enzyme, called MutY in bacteria and MYH in higher organisms, breaks the link between such a misplaced adenine and the DNA sugar–phosphate backbone to initiate repair[2]. But the enzyme leaves well alone when oxoG is correctly paired with the base cytosine (C). On page 652, Fromme *et al.*[3] describe an ingenious way by which this specificity is achieved (see Fig. 1 of their paper for a scheme of the repair cycle).

The catalytic domain of the MutY protein had already been crystallized, so the three-dimensional structure of the protein was largely known[4]. But attempts failed to co-crystallize MutY and a short piece of double-stranded DNA containing an oxoG residue and its mismatched partner, adenine, apparently because the complex was unstable.

Fromme *et al.* have overcome this technical problem by trapping the protein and the DNA together by means of a covalent bond, a crosslink. The strategy used was to generate a short stretch of DNA that had a base containing a sulphur (thiol) residue located near the oxoG. This allowed a disulphide bond to form between the oligonucleotide and MutY. Ideas for where to position the thiol residue came from information gleaned from preliminary structural data and the conformation of the protein[4]. Fromme *et al.* show that MutY interacts at several sites within the A·oxoG pair. But it cannot 'flip out' the oxoG residue from the double-stranded DNA helix. Instead, the unmodified adenine is flipped out and excised by MutY.

MutY belongs to a group of enzymes known as DNA glycosylases, which recognize altered bases in DNA and help to remove them. Like other DNA glycosylases, it generates a sharp bend in the DNA at the site of the mismatch. The new structural data provide a suitable explanation for why — as is desired — MutY doesn't recognize and remove an adenine opposite its normal base partner, thymine (T): the extensive and precise contacts between MutY and an A·oxoG pair are entirely absent in a normal A·T pair. Similarly, the enzyme's active site does not accommodate a cytosine opposite an oxoG; for coding reasons, it is important that the oxidized base rather than the normal base is repaired in this partnership.

In humans, different forms (polymorphisms) of the *MYH* gene have been detected that result in the production of enzymes with a reduced ability to specifically and efficiently recognize these rare A·oxoG pairs. Given that reactive oxygen species are cancer-causing, and that mutations in *MYH* are risk factors for colorectal cancer[5,6], the results of Fromme *et al.*[3] will help in providing a detailed molecular picture of the consequences of such mutations[6,7]. Better relative risk estimates for the development of colorectal cancer associated with a malfunctioning MYH enzyme should also gradually become available for defects that affect different sites in the protein. ■

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Correction

In Karim Nader's News and Views article "Neuroscience: Re-recording human memories" (*Nature* **425,** 571–572; 2003) the citation of reference 6 was unclear. The reference concerned — Siegel, J. M. *Science* **294,** 1058–1063 (2001) — provides a critical review of the evidence for the role of sleep in memory consolidation. Contrary to an implication of the News and Views citation, however, the author of the review concludes that there is only tenuous evidence for a connection between sleep and memory consolidation.

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