diseases as atherosclerosis and certain neurological conditions. The steps by which damaged DNA generates permanently altered nucleotide sequences are, however, obscure in mammalian cells. The question is probably closest to resolution in bacteria where there seems to be an intriguing interaction between DNA damage and the fidelity of DNA polymerases.

Ultraviolet light is commonly used as an experimental DNA damaging agent and initiates mutagenesis through constitutive or inducible pathways depending on the circumstances. The existence of this inducible pathway, proposed and termed 'SOS' repair by Miroslav Radman, is best illustrated by the fact that UV-irradiation of bacteriophages λ or ØX174 leads to the production of mutations only if the phages are plated on bacteria that have themselves been UV irradiated or given some other 'inducing' treatment.

A mechanism for the action of DNA polymerases in ultraviolet mutagenesis has now been proposed by Radman's group (Villani *et al. Proc. natn. Acad. Sci. U.S.A.* **75**, 3037; 1978) who have shown that photoproducts produced in the DNA of ØX174 by ultraviolet constitute a block to DNA replication by cell-free extracts of *E. coli* operating either through DNA polymerase I or III. (Recent studies have pointed towards the role of DNA polymerase III in bacteria as the mutagenic enzyme, particularly in the inducible pathway (see Bridges & Mottershead *Molec. gen. Genet.* **162**, 35; 1978)). In experiments with purified DNA polymerase I (large fragment) they further showed that DNA synthesis on an irradiated ØX174 primed template was accompanied by a large turnover of nucleoside triphosphates into monophosphates, in contrast to synthesis on an unirradiated template.

DNA polymerase I large fragment lacks 5′ to 3′ exonuclease activity but retains both polymerising and 3′ to 5′ exonuclease activities. The latter is believed to act as a 'proof-reader', excising newly incorporated terminal bases which are not paired correctly with the template base. Villani *et al.* suggest that ultraviolet photoproducts in the template strand do not prevent incorporation by the polymerase function but that the bases incorporated opposite photoproducts are registered as mismatched and are immediately excised by the proof-reading exonuclease. The net result is that nucleoside triphosphates are converted to monophosphates with no DNA chain elongation, a condition termed polymerase 'idling'. They further suggest that newly-incorporated mismatched bases could persist and be seen as mutations if SOS induction involved the inhibition of the proof-reading function so that chain elongation could proceed beyond the photoproduct and its potentially mismatched partner. In support of this they give evidence that AMV reverse transcriptase, an error-prone DNA polymerase devoid of any exonuclease activity, is both highly prone to insert wrong bases and replicates UV-irradiated ØX174 DNA far above the level of *E. coli* DNA polymerase I.

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The findings of Villani *et al.* suggest a possible signalling mechanism for triggering the SOS inducible pathway. SOS mutagenesis in *E. coli* is dependent on the *recA*$^+$ gene and it has been thought to be similar in its operation to other *recA*$^+$-dependent phenomena such as prophage induction. The *recA*$^+$ protein is produced in substantial amounts after ultraviolet irradiation and seems to act in prophage induction by carrying out proteolytic cleavage of the λ repressor. Villani *et al.* suggest that the nucleoside monophosphates produced by idling polymerases may well be the initial inducing signal leading to enhanced production of *recA*$^+$ protein and thus to the cleavage of λ and other SOS repressors.

Another, simpler possibility is apparent, however, if we consider the recent work of Byrnes *et al.* (*Biochemistry* **16**, 3740; 1977) who have shown that nucleoside 5′-monophosphates inhibit specifically the 3′ to 5′ exonuclease but not the polymerase function of DNA polymerase I, and of Que, Downey and So (*Biochemistry* **17**, 1603; 1978) who have further produced evidence that the nucleoside 5′-monophosphates bind at the primer terminus site for the 3′ to 5′ exonuclease activity. On the basis of their observations one might argue that SOS mutagenesis induction might be more simply explained as follows. Arrival of a photoproduct at the replication fork causes polymerase III idling and accumulation of nucleoside monophosphates. These in turn directly inhibit the 3′ to 5′ exonuclease function ('induction') and allow chain elongation to continue with any mismatched bases (both opposite the photoproduct and elsewhere) persisting as mutations. Return to high fidelity replication would occur after normalisation of the nucleoside monophosphate pool. The elementary hypothesis of direct control by nucleoside monophosphate levels suggested here does not, however, have any obvious requirement for repressor cleavage by the *recA*$^+$ protein. Although it may seem heretical, perhaps the possibility should be considered that the *recA*$^+$ protein does not act proteolytically in ultraviolet mutagenesis but rather interacts directly at the DNA level to 'stabilise' the photoproduct-primer terminus configuration so as to allow polymerase idling. Consequent elevation of nucleoside monophosphate levels would then result in direct inhibition of the 3′ to 5′ exonuclease function and this in turn would lead to mutagenesis and survival. Certainly a constitutive level of the *recA*$^+$ protein exists and the protein is known to bind to single-stranded DNA. Furthermore the γ-irradiation resistance conferred by the *recA*$^+$ gene seems to be independent of protein synthesis and does not involve inducibility. Could this also be true for ultraviolet mutagenesis? Such an explanation, while based on slender experimental evidence, would seem to merit consideration, if only because of its simplicity. One would still have to find a role on either hypothesis for other genes (*lexA, lexC, umuC,* and *recB uvrD,* for example) which affect ultraviolet mutagenesis.

Whether or not the postulated inhibition of the proof-reading exonuclease function by nucleoside monophosphates is direct or indirect will doubtless become clear in the not too distant future. The concept of polymerase idling proposed by Radman's group is, however, very plausible and should stimulate the necessary experiments, particularly those designed to reveal whether it occurs *in vivo* as well as with the purified enzyme fragment. Also to be resolved is the question of whether DNA polymerase III behaves *in vivo* the way the polymerase I fragment behaves *in vitro,* and the question of constitutive mutagenic repair should this, as seems likely, also be mediated by polymerase III. Does this also involve inhibition of the proof-reading function and if so, how?

A hundred years ago

CAPTAIN PATTERSON, Superintendent of the U.S. Coast Survey, has lately initiated a very important undertaking in connection with the work of the Survey, namely, in determining the extent and position of the oyster beds of the Chesapeake Bay, primarily with reference to the formation of oyster reefs, and their interference with navigation, but broad enough in its scope to serve as the basis of a critical investigation of the whole subject of the oyster fisheries and oyster culture in the United States. The work is being prosecuted in the Chesapeake Bay by the Coast Survey Steamer *Palinurus,* Mr. H. J. Rice, formerly of Johns Hopkins University, looking more particularly after the natural history features, such as the embryology and development of the oyster, &c.
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