Mechanism of induced mutagenesis by ultraviolet light in Escherichia coli

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Mechanism of Induced Mutagenesis by Ultraviolet Light in *Escherichia coli*

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1 Background and Perspective

The genetic prosperity of organisms is dependent on the preservation of their genome. To that aim living cells require a reliable mechanism of replication. Thus, it is not surprising that error frequencies of replication are generally only 10^{-9} to 10^{-10} per replicated nucleotide (for a review, see Echols and Goodman 1991). On the other hand, many physical and chemical agents in our environment can jeopardize the genetic information by the formation of lesions in the DNA that may block DNA replication or cause changes in its sequence (mutations). Nevertheless, organisms have developed an important diversity in enzymatic pathways for the removal or tolerance of DNA damage (for a comprehensive review, see Friedberg 1985; Sedgwick 1986). In some instances when error-free repair is not possible or fails, the mechanisms of tolerance may allow sequence changes, leading to mutations that generate variability, thus making evolution possible. Without versatile mechanisms that permit mutations to occur, organisms might never have existed as we know them today, or might have become extinct a long time ago due to the inability to cope with certain forms of strong selective pressure.

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G. Obe (ed.), *Advances in Mutagenesis Research*

Although mutations are a fundamental source of genetic variation, most newly arising mutations are thought to be harmful to the organisms, some may be selectively neutral, and only a very few may be favorable. Taking these facts into account, i.e. both the preservation of the genome and the evolutionary requirement of genetic change, it is not unlikely that an equilibrium between these two phenomena occurs. In fact, both the low spontaneous mutation rate and the numerous and elaborated mechanisms of DNA repair and tolerance present in living cells are believed to have evolved as a compromise, producing a mutation rate high enough to generate the favorable mutations required by species in order to evolve, but not so high that the species suffer extensive genetic damage from the majority of harmful mutations.

The mechanisms that lead to mutations are believed to be hazardous. In 1943 Luria and Delbrück demonstrated the spontaneous induction of mutations. In this sense only the mutations that are neutral or show a selective advantage for the organism are kept in the gene pool of the population, whereas the deleterious ones are eliminated. Although these ideas have been generally accepted since the 1940s, it has been recently suggested that certain forms of mutagenesis may direct the mutations towards selective advantages for organisms under conditions of extreme starvation; this means that advantageous mutations might arise in some way directed by an unknown mechanism towards the right genes (Cairns et al. 1988; Hall 1988). On the other hand, certain forms of mutagenesis, such as SOS induction in *Escherichia coli*, have been considered as a mechanism that allows genetic variation in stressed cells, increasing the probability of generating a successful individual adapted to survive environmental stress (Echols 1982; Echols and Goodman 1990).

Another important implication of mutagenesis is related to human populations. A causal relationship between DNA damage and carcinogenesis has been recognized for several years (see Nagao et al. 1978). The idea of DNA alteration as a critical step in the initiation of carcinogenesis is supported by several types of evidence, including: (1) the observation that many chemical and physical agents which induce cancer in mammals also induce mutations in bacterial and other suitable test systems (see ICPEMC 1982) and (2) the demonstration that oncogenes involved in the development of human neoplasias can be activated during the initiation of carcinogenesis as a direct consequence of the mutagenic action of the carcinogens (Barbacid 1986).

The clarification of the origin of mutations and other aspects in relation to the accurate estimation of the potential hazard of many mutagenic agents requires a better understanding of the mechanisms of mutagenesis. Unfortunately, these remain intriguingly elusive in many cases. Our knowledge of such mechanisms has increased remarkably over the last few years, but the exact way in which many mutagens cause mutations is not yet known.

The induction of mutations by ultraviolet light (UV) has been studied as a model system for mutagenesis for more than 40 years. Some aspects of mutagenesis mechanisms mediated by some lesions produced by UV are now better understood. This chapter summarizes current knowledge on the mechanism of