Types of Point Mutations

1. Silent Mutations:

Change the nucleotide but not the amino acid sequence (as it affect 3rd letter in codon) result in no change in protein.

AUG UAU CCA UAU CCA UAG

fMetTyr Pro Tyr Pro Term

AUG UAU CCU UAU CCA UAG

fMetTyr Pro Tyr Pro Term

2. **Missense Mutations**:

Change the nucleotide lead to changing one amino acid into another result in change in protein.

AUG UAU CCA UAU CCA UAG

fMetTyr Pro Tyr Pro Term

AUG UAU UCA UAU CCA UAG

fMetTyr Ser Tyr Pro Term

3. Nonsense Mutations:

Change the nucleotide to termination codon result in short protein.

AUG UAU CCA UAU CCA UAG

fMetTyr Pro Tyr Pro Term

AUG UAU CCA UAG CCA UAG

fMetTyr Pro Term ---- ----

3. Frame shift Mutations:

Insertion or deletion of nucleotides lead to change in frame read downstream to mutation result in incorrect protein.

For example, an insertion of an extra G between nucleotides 6 and 7 would give:

AUG UAU CCA UAU CCA UAG

fMetTyr Pro Tyr Pro Term

AUG UAU GCC AUA UCC AUA

fMetTyr Ala Ile Ser Ile

N.B: Silent mutation un noticed. Non sense & frame shift un noticed as abnormal or short protein is inactive. Mis sense change amino acid so change biological activity.

DNA Repair Mechanisms

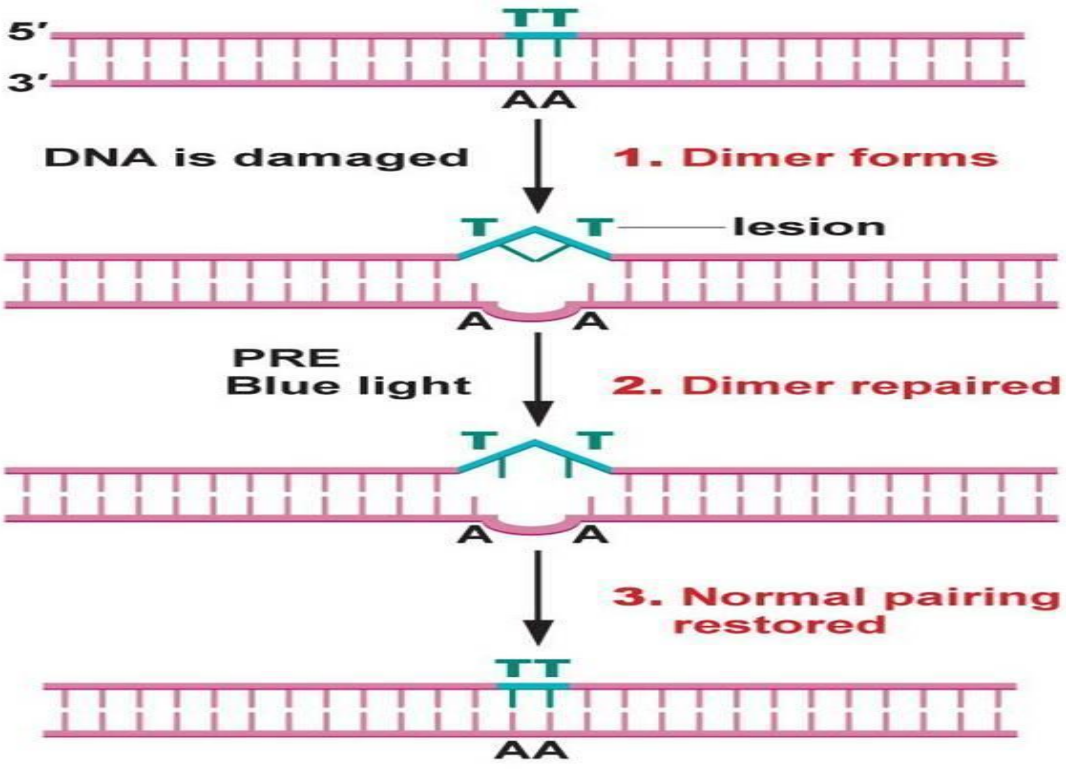
Cells exposed constantly to mutagen but rate of mutation in most species is low due to several repair mechanisms exist in cells which detect and repair damage to DNA.

A-Photo reactivation Repair (light repair):

UV-induced damaged to prokaryotes (e.g. E. coli) this effect may be partially reversed if, following irradiation, the cells exposed to visible light. The process of repair by an enzyme called the photo reactivation enzyme present in normal human cells.

Its mode of action is to cleave the bonds between the two thymine molecules in the thymine dimer, thus reversing the effect of UV light on DNA. The enzyme must absorb a photon of light (in the blue range of light spectrum) in order to cleave the dimer.

N.B: Xeroderma pigmentosum patients contain lower photo reactivation enzyme activity than normal cells.

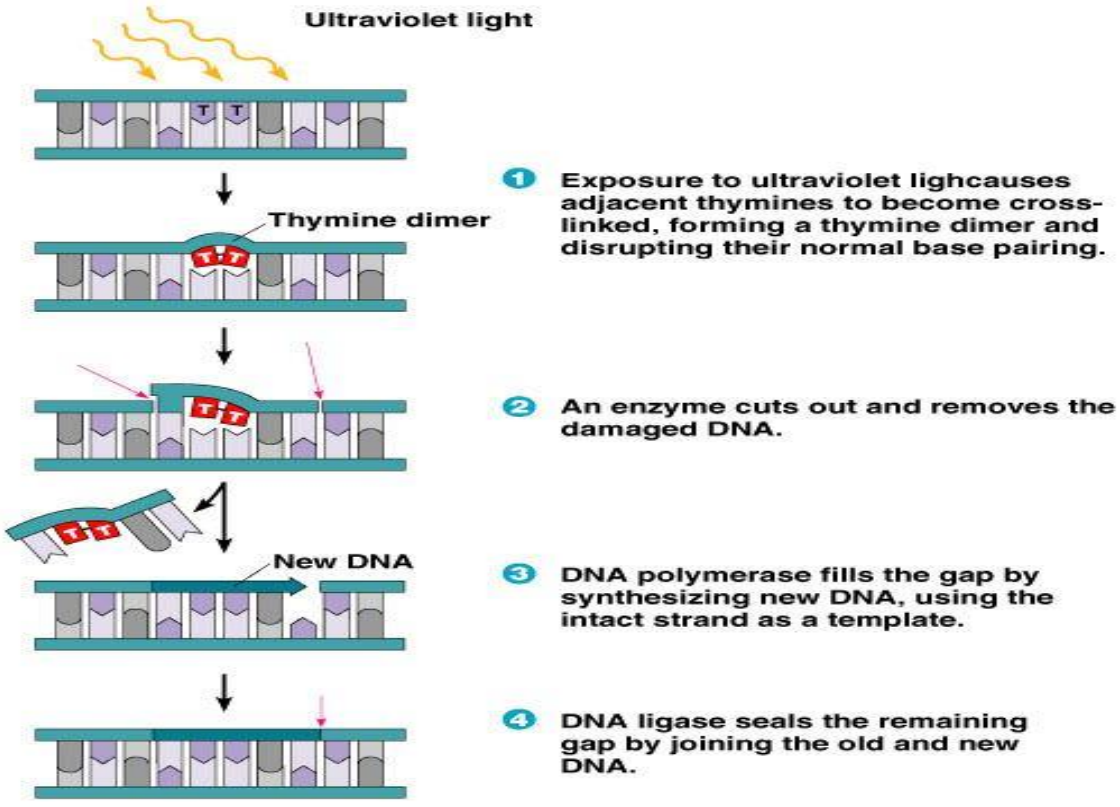


B. Excision Repair (dark repair):

UV-induced dimers removed by endonuclease activity of the DNA strand along with some nucleotides on either side. The gap is then filled in by repair synthesis (by DNA polymerase I).

Excised piece removed by an exonuclease activity then newly synthesized piece sealed by DNA ligase.

N.B: its dark repair not need light, most dimers removed by it.



C. SOS Repair (bypass system):

It allows DNA replication across damaged segments. Replication is carried out by synthesis of random (incorrect) nucleotides at the damaged site. This causes mutation so, SOS system is error-prone, and the replicated strands are often defective.

N.B: the principle of this system is survival with some loss of information is better than no survival at all

D. Proofreading repair:

By DNA polymerase III (have proofreading functions), during synthesis when an incorrect nucleotide is inserted the enzyme recognize the error and reverse it by cutting out the incorrect nucleotide and replacing it.

Mutation and Cancer

Cancer is a disease associated with changes in the genetic material that leads to the inability of the cell to control its reproduction, which leads to malignant tumors. In all cases studied, the tumor was found to originate from one cell, i.e. monoclonal.

Genetic material is the main target in mutagenicity and carcinogenicity; so many studies have thought to

establish the relation between these two processes. Mutation in gene which controls mitosis & cell division, it might loss its function, un controlled cell division & becomes a cancer cell.

A. Carcinogens

Certain factors change normal cells to malignant cells.

A.1. Chemical Carcinogens:

Chemical substance to be carcinogenic, it has to be mutagenic, i.e. its effect on DNA is direct. It includes asbestos, tar products, mustard gas, and polyvinylchloride.

A.2. Physical carcinogens:

These include mutagenic radiation:

UV cause skin cancer in humans affected with xeroderma pigmentosum. X-rays associated with leukemia (large percentage of ex-technicians working with X- rays die of leukemia more than unexposed people). Gamma rays produced by atomic fission are cancer producing.

N.B: increase degree of exposure to radiation increase incidence of cancer.

A.3. Biological carcinogens:

A.3.1. Oncogenic Viruses:

These are RNA viruses, and were first discovered in a cancer- causing virus in chicken called Rous Sarcoma Virus, Gross leukemia virus and Bittner mammary tumor in mice. The entrance of RNA viruses into normal cell transforms it to cancer cell as viral genome contain gene called oncogene transform normal cell to cancer cell.

A.3.2. Oncogenes:

An oncogene discovered in DNA from cells of human cancer of the urinary bladder similar in its nucleotide sequence to oncogene in oncogenic viruses. Normal human cells contain a similar oncogene but repressed called proto-oncogene activated under influence of carcinogens, as radiation, chemicals and viruses.