I SEMESTER

PAPER – Cell Biology and Genetics

UNIT - IV

TOPIC – DNA Repair Mechanisms

SOURCE – INTERNET

NAME OF INSTRUCTOR – G.N.V. SATISH

DNA Repair mechanisms

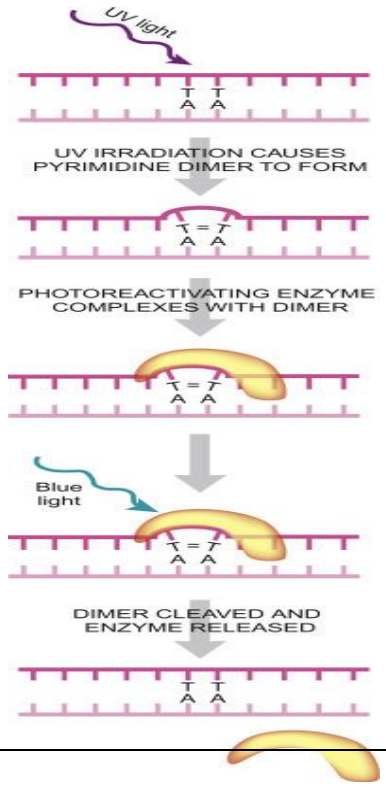
DNA repair is a collection of processes by which a cell identifies and corrects damages to the DNA molecules that encode its genome. The DNA repair processes are constantly active as it responds to damage to the DNA structure.

Most cells posses five different categories of DNA repair system:

- photoreactivation
- Alkylation
- Base excision repair
- Nucleotide excision repair
- Mismatch repair
- SOS Repair

photoreactivation

- The photoreactivation is common from the Direct repair.
- one common type of uv radiation mediated damages, are called as photoreactivation repair
- pyrimidine dimers, are repaired by a Light-dependent system called as "photoreactivation".
- In E.coli the process involves the enzyme called "DNA photolyase"
- when stimulated by light, the wavelength between 300 and 500 nm, the enzyme binds to pyrimidine dimers and converts them back to the original monomeric nucleotide.



Excision Repair

Base Excision Repair:-

1) Base Excision Repair involves removal of a damaged nucleotide base, by the excision of a short piece of the polynucleotide.

2) It is used to repair damages from the alkylation damage.

3) The enzyme is "DNA glycosylase" initiates the repair process in Base-Excision Repair.

4) An DNA glycosylase enzyme does not cleave phosphodiester bonds.

5) Instead cleave the N-glycosidic bond, liberating the altered base and generating apurinic (or) apyrimidinic site both called an "AP" site.

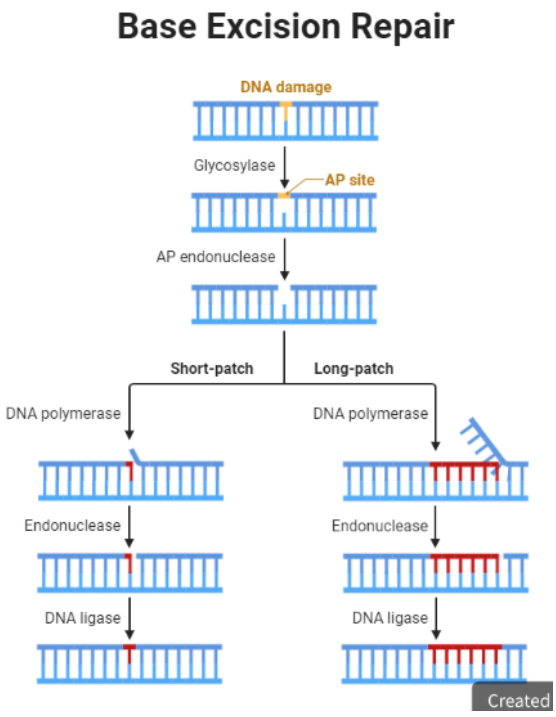
6) The AP site is repaired by an "Ap endonuclease".

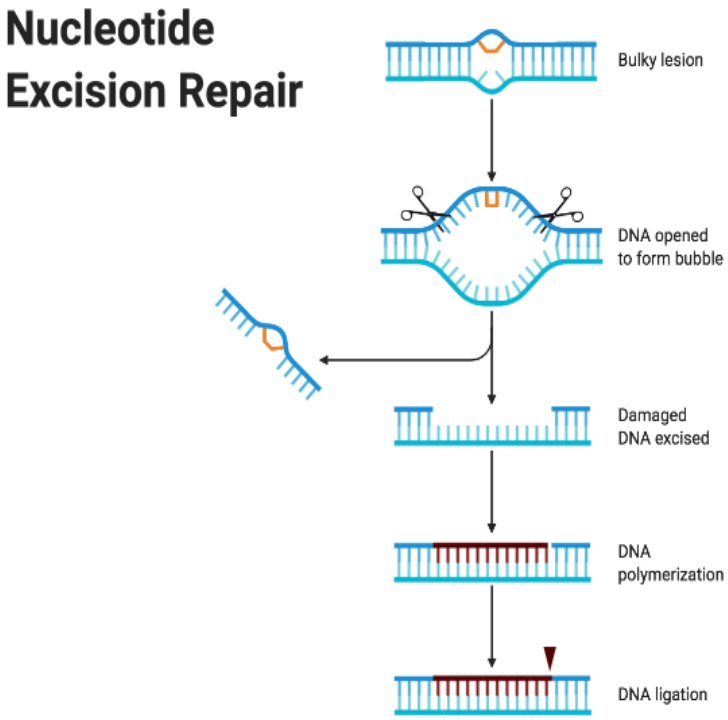
7) This bond cleavage initiates the bonds with help of three enzymes.

- Exonuclease
- DNA Polymerase I
- DNA ligase

Nucleotide excision repair:-

- This is similar to base - excision repair, but is not proceeded by the removal of damaged base and can act more substantially on damaged areas of DNA.
- This repair system includes the breaking of a phosphodiester bond on either side of lesion, on the same strand, resulting in the excision of an oligonucleotide.
- So the excision leaves a gap that is filled by repair systems, and a ligase seals the breaks.





Mismatch repair

DNA mismatch repair (MMR) recognizes and repairs erroneous insertion, deletion, and mis-incorporation of bases that can arise during DNA replication and recombination, and repair some forms of DNA damage. It plays an important role in maintaining genomic stability and cellular homeostasis. For example, MMR increases the accuracy of DNA replication by 20–400-fold in *Escherichia coli*.

The element of MMR system

Prokaryotic MMR system

The MMR system in *E. coli* is essentially composed of four identifiable proteins, MutS, MutL, MutH, and UVrs.

MutS

MutS is the pivotal protein of the MMR system that can detect mismatches in the double-stranded DNA. It initiates the MMR machinery by recognizing nonspecific interactions. It has two functional domains including a DNA-binding domain and an ATPase/dimerization domain.

MutL

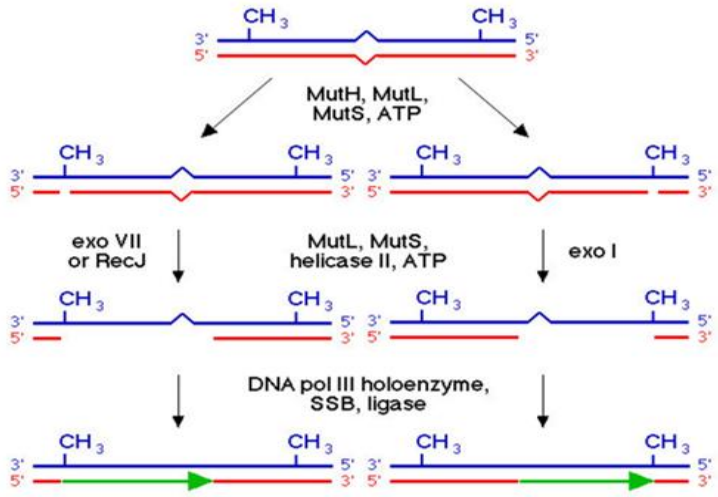
MutL protein acts as a mediator between the MutS and other protein complexes in the MMR systems. It creates a link between the MutS mismatch recognization and the excision of the mismatch bases by responsible proteins.

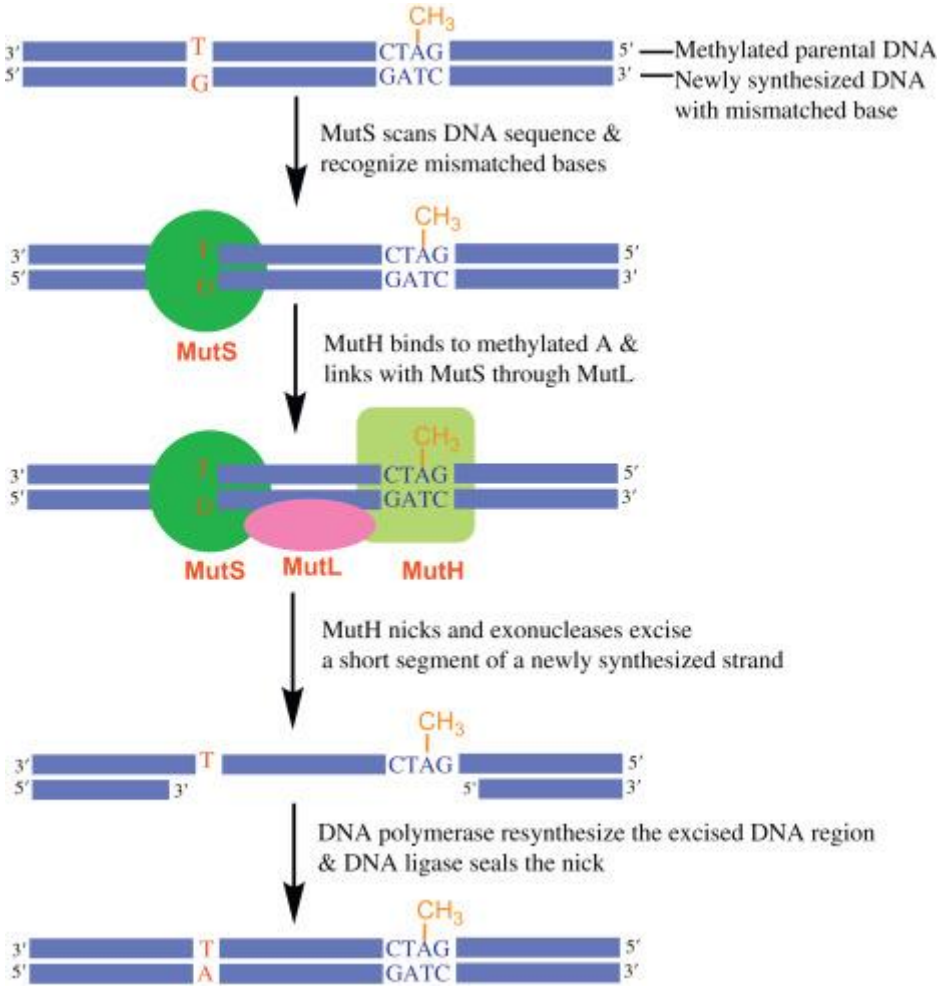
MutH

MutH is a member of the type II family of restriction endonucleases. It cleaves the mismatch-containing DNA single strand specifically at hemimethylated GATC sites. MutH nicking activity is stimulated by the MMR complex consisting of MutS, MutL, and ATP. The C-terminal helix of MutH protein acts as a molecular attache′ through which MutS and MutL communicate and activate MutH.

UvrD

UvrD is a DNA helicase II that unwinds DNA starting from the nick generated by MutH. It is loaded onto MutL at the DNA duplex lesion site, which increases its intrinsic helicase activity. The nick generated by MutH serves as a point of entry for single stranded DNA-binding protein and UvrD/helicase II. The loading of UvrD/helicase II at the nick is facilitated through protein–protein interactions with MutL.




CH3
3′
T
CTAG
5′
5′
G
GATC
3′
Methylated parental DNA
Newly synthesized DNA with mismatched base
MutS scans DNA sequence & recognize mismatched bases
MutS
MutH binds to methylated A & links with MutS through MutL
MutS
MutL
MutH
MutH nicks and exonucleases excise a short segment of a newly synthesized strand
DNA polymerase resynthesize the excised DNA region & DNA ligase seals the nick
A