DNA REPAIR MECHANISMS:

A. P. NAGRALE

DNA REPAIR

•One of the main objectives of biological system is to maintain base sequences of DNA from one generation to the other**.**

•DNA is relatively fragile, easily damaged molecule.

•The DNA of a cell is subjected to damage from a variety of environmental factors like radiations (X-rays, UV-rays), chemicals mutagens, physical factors etc.

•The survival of the cell depends on its ability to repair this damage.

•DNA damage is of two types – Monoadduct and Diadduct.

Monoadduct damage involves alterations in a single nitrogen base for example deamination reactions of chemical mutagen like HNO_2.

Diadduct damage are alterations involving more than one nitrogen base, for example Pyrimidine - Pyrimidine dimer produced by UV-radiations.

•There are three principal types of repair mechanisms.

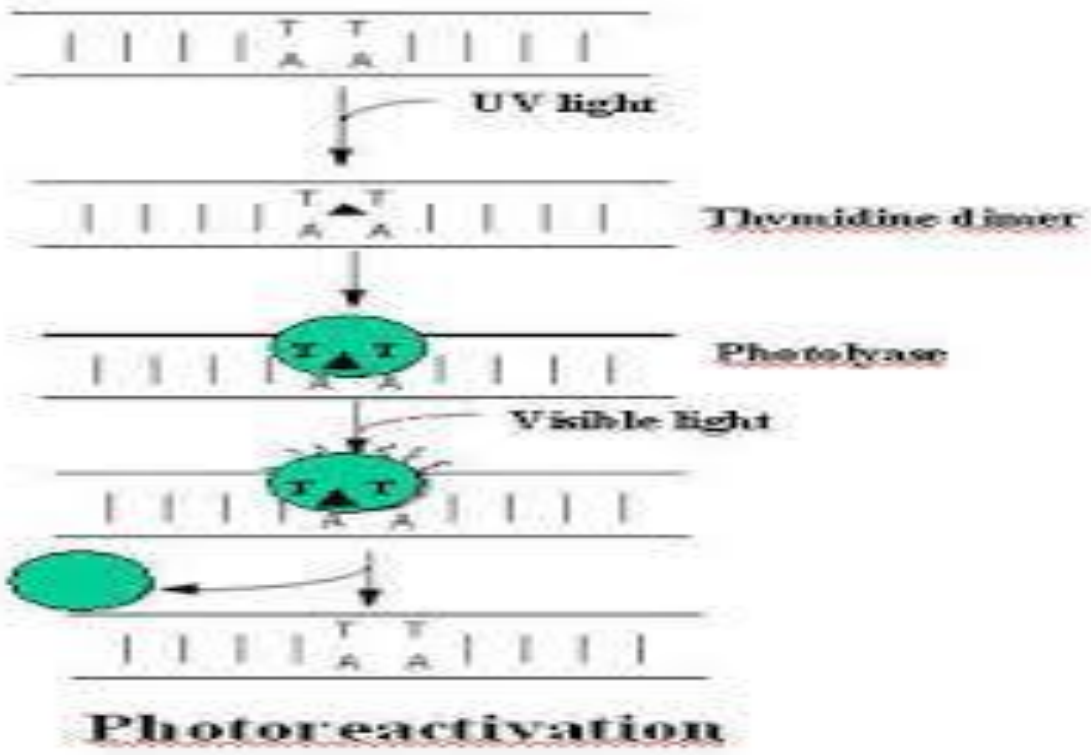
•Light Repair (Enzymatic Photoreacivation)

•Ultraviolet light causes the damage in DNA of bacteria and phages. UV-radiations (254 nm wavelength) cause the formation of covalent bond between adjacent pyrimidines to form dimer on the same strand of DNA (intrastrand bonding).

•The UV- light forms abnormal structure Thymine dimmer (T=T) in DNA. As a result, DNA replication cannot proceed and gene expression is also prevented.

•Damage to DNA caused by UV- light can be repaired after exposing the cells to visible light called photoreactivation or light repair.
•This photoreactivation requires a specific enzyme that binds to the defective site on the DNA.
•In this mechanism an enzyme *DNA photolyase* cleaves T=T dimmer and reverse to monomeric stage.

•This enzyme is activated only when exposed to visible light. This enzyme absorbs the light energy, binds of cyclobutane ring to defective site of DNA and absorbed energy promotes the cleavage of covalent bond between two thymine molecules. Finally, thymine residues are made free and UV induced DNA damage is repaired by visible light.



Photoreactivation

2. **Dark Repair (Excision Repair)** ----

Because visible light is not required for the action of these enzymes, this process is called dark repair.

• This repair is an enzymatic process. In this mechanism, the damaged portion is removed and replaced by new DNA. The second DNA strand acts as template for the synthesis of new DNA fragment.

• Excision repair systems are grouped into the following three classes based on length of DNA strand excised.

•Very short patch repair – this system deals with the repair of mismatches of a single base.

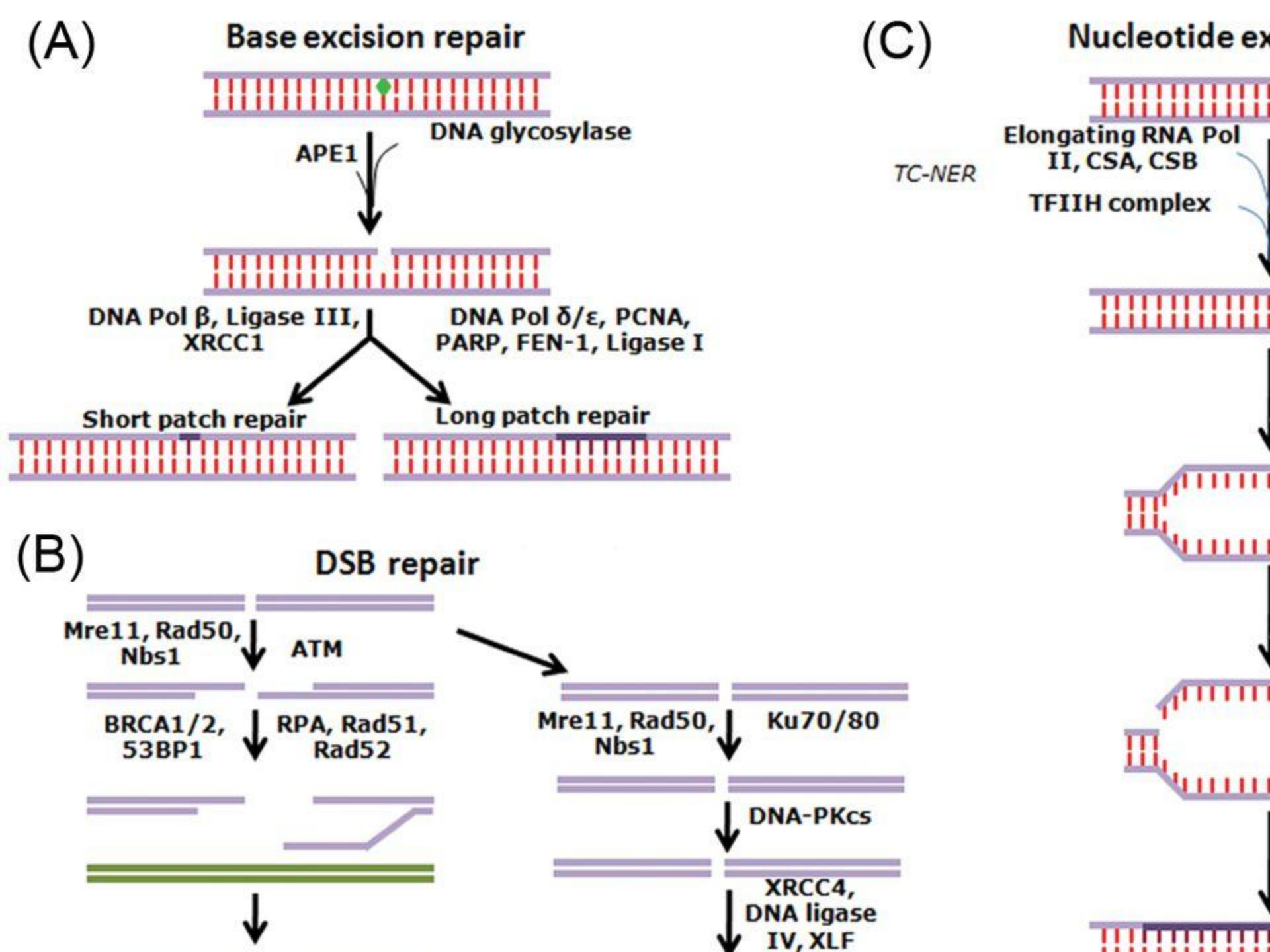
•Short patch repair - in this system about 20 bases long DNA strand is excised. This type of repair system accounts for about 99% of the excision repair activity in *E. coli*.

•Long patch repair – this system involves the excision of about 1500 bases long segment. It is much less common.

•The two principal excision repair systems are - **Base excision repair** and **Nucleotide excision repair.**

•In the base excision repair, an enzyme called a ***DNA glycosylase*** recognizes and removes the damaged base by hydrolyzing the glycosidic bond. *DNA glycosylases* are damage-specific (lesion-specific) and cells have several *DNA glycosylases* with different specificities.

•Unlike base excision repair, the nucleotide excision repair enzymes do not recognize any particular damage or lesion. This system recognizes the distortion in the shape of the double helix, caused due to damage and removes the short single-stranded segment (patch) that includes the lesion.


(A)
Base excision repair
DNA glycosylase
APE1
DNA Pol β, Ligase III, XRCC1
DNA Pol δ/ε, PCNA, PARP, FEN-1, Ligase I
Short patch repair
Long patch repair
(B)
DSB repair
Mre11, Rad50, Nbs1
ATM
BRCA1/2, 53BP1
RPA, Rad51, Rad52
Mre11, Rad50, Nbs1
Ku70/80
DNA-PKcs
XRCC4, DNA ligase IV, XLF
(C)
Nucleotide ex
TC-NER
Elongating RNA Pol II, CSA, CSB
TFIIH complex