FACULTY OF ENGINEERING &TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

DNA Repair

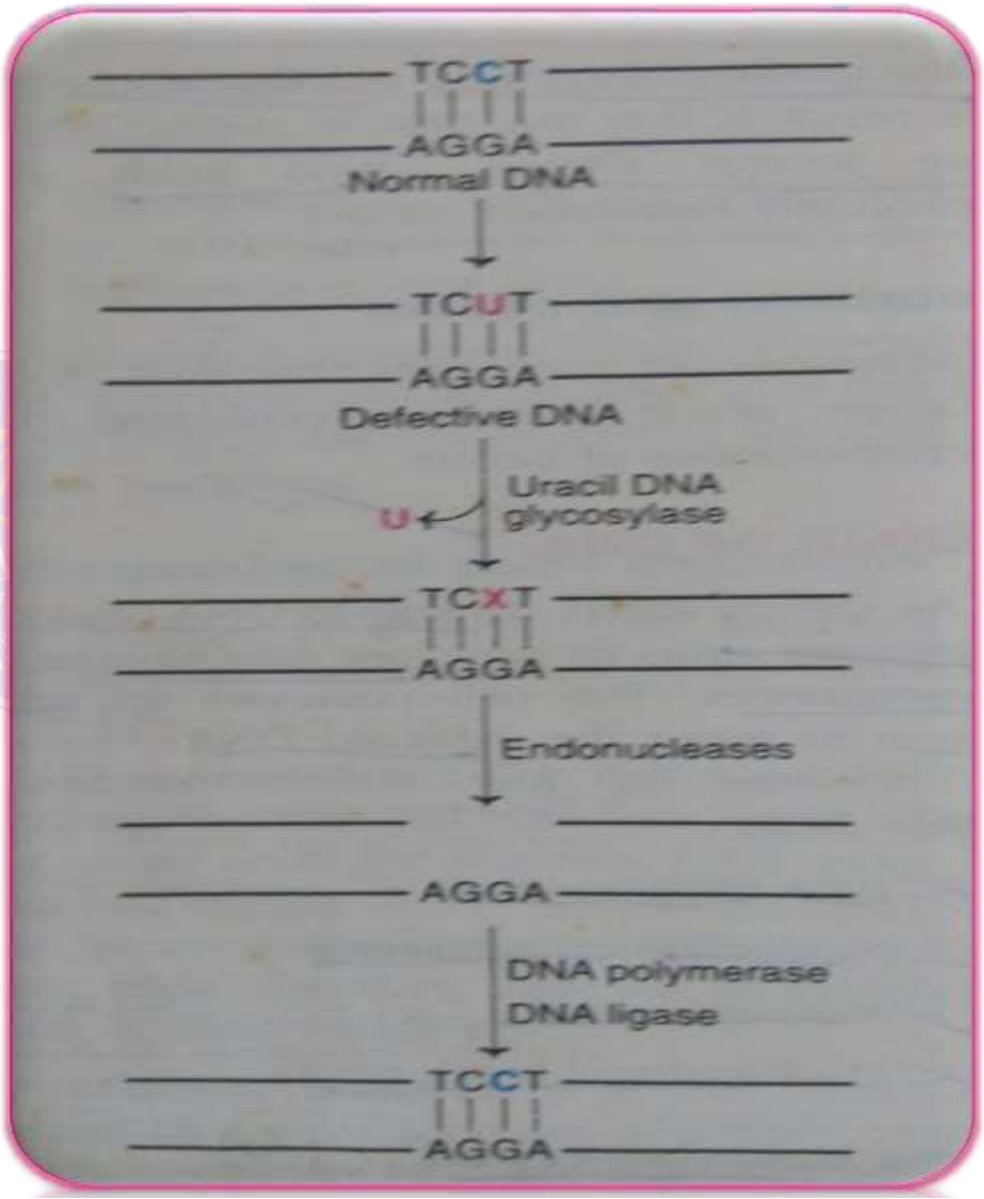
- The cell possesses an inbuilt system to repair the damaged DNA.

1. Base excision-repair
2. Nucleotide excision-repair
3. Mismatch repair
4. Double-strand break repair

Base Excision Repair

- The bases cytosine, adenine & guanine can undergo spontaneous depurination to respectively form uracil, hypoxanthine & xanthine.
- These altered bases do not exist in the normal DNA & therefore need to be removed.
- This is carried out by base excision repair.

Base excision repair

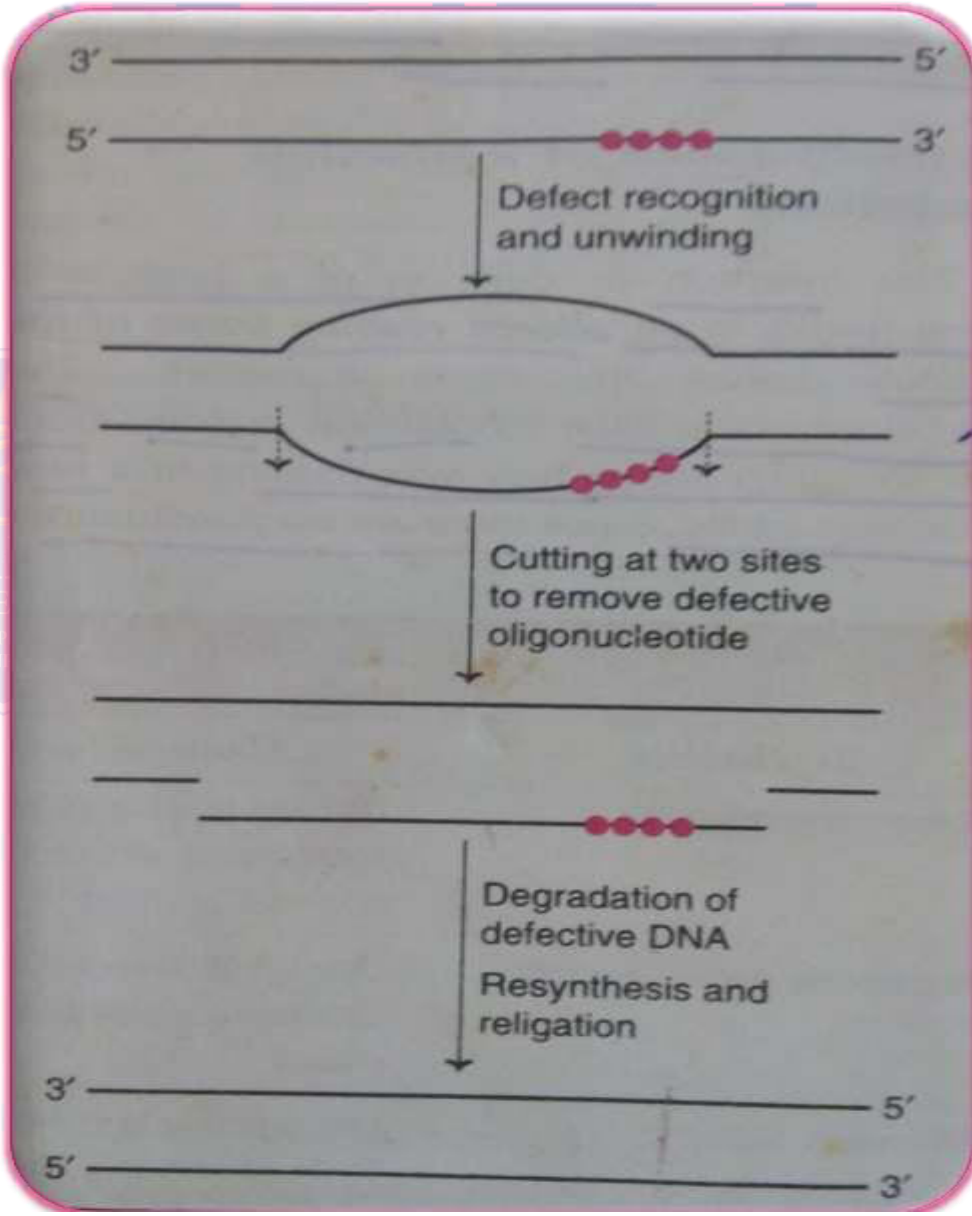


- A defective DNA in which cytosine is deaminated to uracil is acted upon by the enzyme uracil DNA glycosylase.
- This results in removal of defective base uracil
- An endonuclease cuts the back bone of DNA strand near the defect & removes a few bases.
- The gap is filled up by the action of repair DNA polymerase & DNA ligase.

Nucleotide Excision Repair

- The DNA damage due to ultraviolet light, ionizing radiation & other environmental factors results in modification of certain bases, strand breaks, cross-linkages.
- Nucleotide excision-repair is suited for large- scale defects in DNA.
- After the identification of the defective piece of the DNA.

Nucleotide excision repair



- The DNA double helix is unwound to expose the damaged part.
- An excision nuclease (exinuclease) cuts the DNA on either side (upstream & downstream) of the damaged DNA.
- This defective piece is degraded.
- The gap created by the nucleotide excision is filled up by DNA polymerase which gets ligated by DNA ligase.

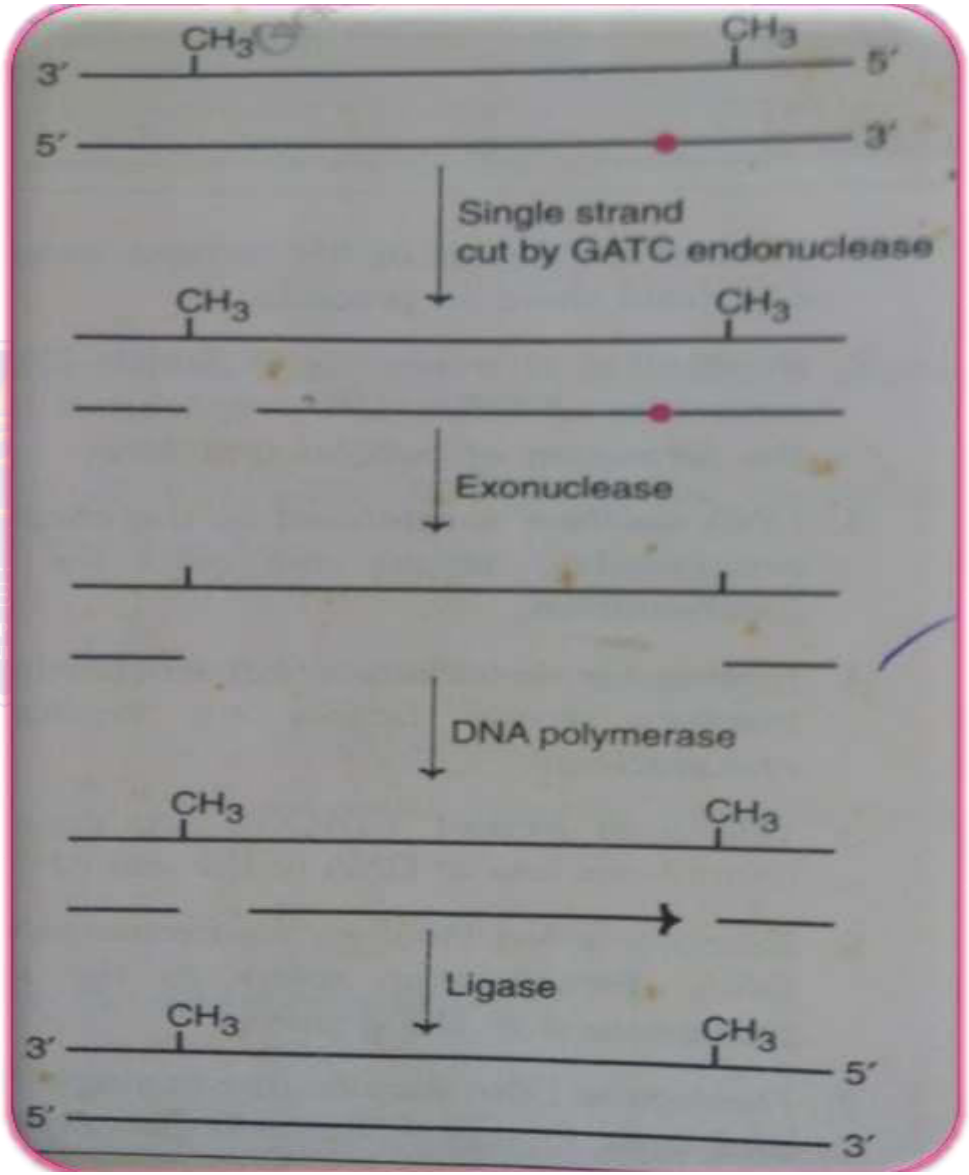
Xeroderma pigmentosum (XP)

- Xeroderma pigmentosum (XP) is a rare autosomal recessive disease.
- The affected patients are photosensitive & susceptible to skin cancers.
- It is now recognized that XP is due to a defect in the nucleotide excision repair of the damaged DNA.

Mismatch Repair

- Despite high accuracy in replication, defects do occur when the DNA is copied.
- For instance, cytosine (instead of thymine) could be incorporated opposite to adenine.
- Mismatch repair corrects a single mismatch base pair e.g. C to A, instead of T to A.

Mismatch repair



- The template strand of the DNA exists in a methylated form, while the newly synthesized strand is not methylated.
- This difference allows the recognition of the new strands.
- The enzyme GATC endonuclease cuts the strand at an adjacent methylated GATC sequence.

- This is followed by an exonuclease digestion of the defective strand & its removal.
- A new DNA strand is now synthesized to replace the damaged one.
- Hereditary nonpolyposis colon cancer (HNPCC) is one of the most common inherited cancers.
- This cancer is now linked with faulty mismatch repair of defective DNA.

Double Strand break repair

- Double-strand breaks (DSBs) are dangerous.
- They result in genetic recombination which may lead to chromosomal translocation, broken chromosomes & finally cell death.
- DSBs can be repaired by homologous recombination or non-homologous end joining.
- Homologous recombination occurs in yeasts while in mammals, non-homologous & joining dominates.

DNA Repair Mechanism

Mechanism	Damage to DNA	DNA Repair
Base excision repair	Damage to a single base due to spontaneous alteration or by chemical or radiation means	Removal of the base by N-glycosylase; abasic sugar removal, replacement
Nucleotide excision-repair	Damage to a segment of DNA by spontaneous chemical or radiation means	Removal of the DNA fragment (- 30 mt length)& replacement
Mismatch repair	Damage due to copying errors (1-5 base unpaired loops).	Removal of the strand (by exonuclease digestion) & replacement
Double-strand break repair	Damage caused by ionizing radiations, free radicals, chemotherapy.	unwinding, alignment & ligation