



FACULTY OF ENGINEERING & TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

- **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**

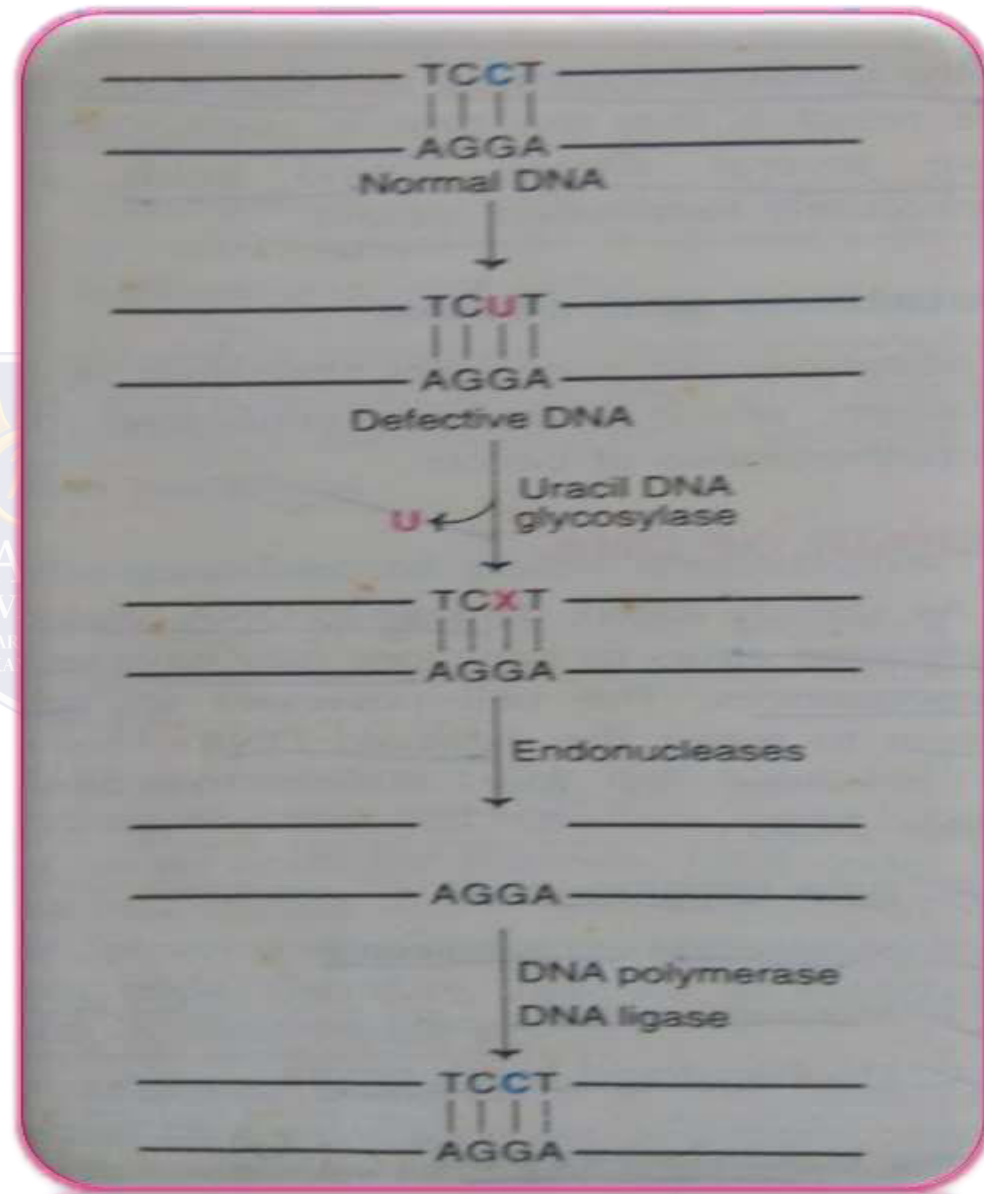


Base Excision Repair

- **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.**



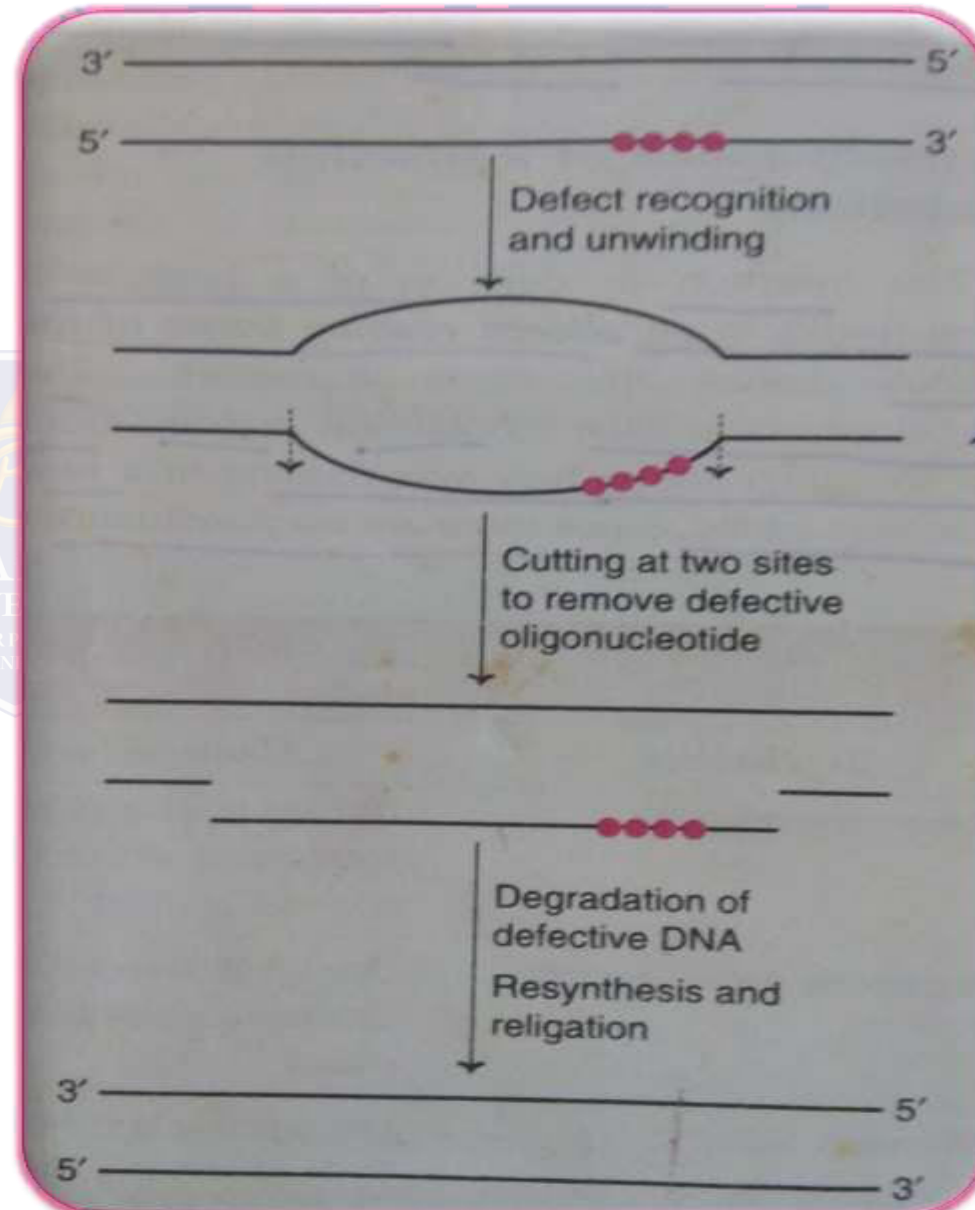
Base excision repair



- **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.**

- **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.**

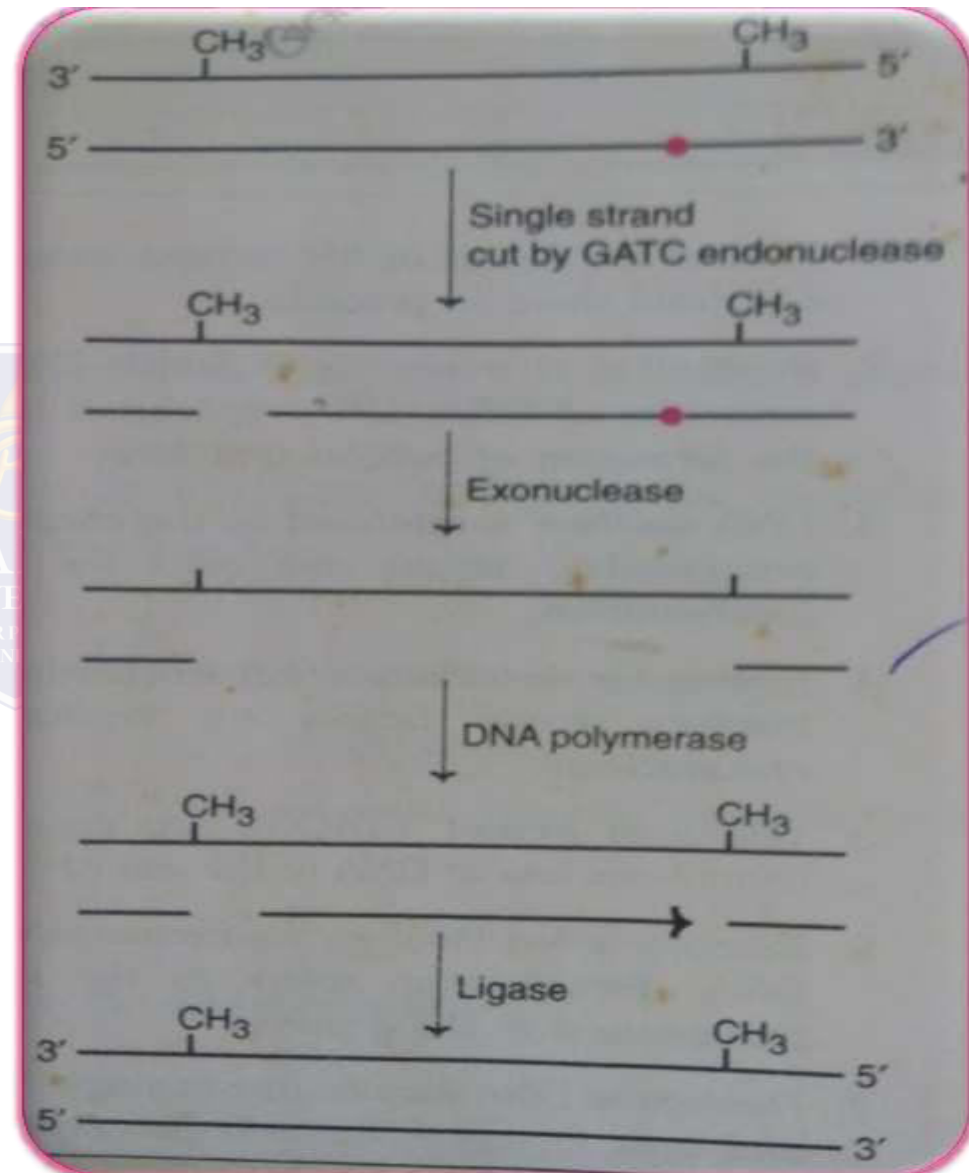
Xeroderma pigmentosum (XP)

- **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.**

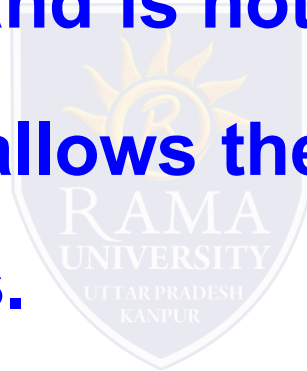
Mismatch Repair

- **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