

DNA REPAIR MECHANISMS

Mod. 1st year 2023-2024

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DNA Repair Mechanisms

- DNA serves as the storage area for the genetic information in each living cell and its **integrity and stability** are of much greater consequence than other cellular components, such as RNA and proteins.
- DNA damage can interfere with essential cellular processes, such as **transcription or replication**, and also can harm the viability of the cell. that Specific DNA mutations can also induce the cause of cancer or other diseases as well as its role in the aging process.
- Since many Mutations or changes can occur in DNA either **spontaneously** or as a result of **exposure to chemicals or radiation** , So **DNA repair systems are very important to the survival of all organisms to maintain the integrity of their genomes.**

let's look at the DNA damage types:

the damage done to DNA by physical , chemical ,environmental agents and all this can be classified into 4 categories :

Categorie	Type example
1. Single base alterations	Depurination Deamination -- that changes of C to U Alkylation of base Insertion or deletion of nucleotide Base-analog incorporation
2. Two-base alterations	UV light-induced thymine-thymine (pyrimidine) dimer(T=T) or cytosines Dimers (C=C) in DNA via photochemical reactions.
3. Chain breaks	Ionizing radiation , Radioactive disintegration of backbone element , Oxidative free radical formation
4. Cross-linkages	Between bases in same or opposite strands Between DNA and protein molecules (eg, histones)

DNA Repair System

DNA repair is a collection of processes by which a cell identifies and corrects damage in the DNA molecules that encode its genome.

DNA repair process is a multi-step process:

- 1. damage in DNA structure is **detected**
- 2. The abnormal DNA is **removed**
- 3. Normal DNA is **synthesized**

DNA Repair types

The various DNA repair mechanisms are:

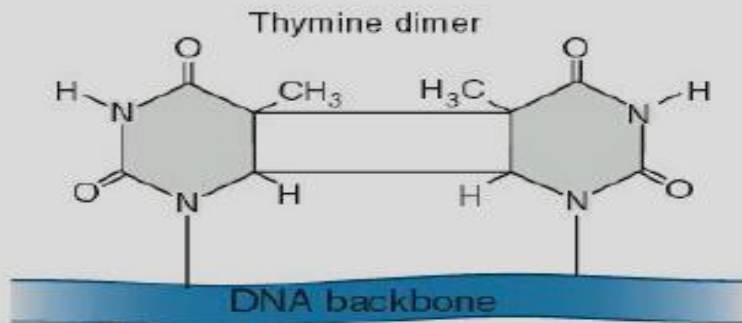
- 1. Direct Repair**
- 2. Excision Repair**
- 3. Mismatch Base Repair**
- 4. Recombination Repair System**
- 5. SOS Repair Mechanism.**

1/ Direct Repair

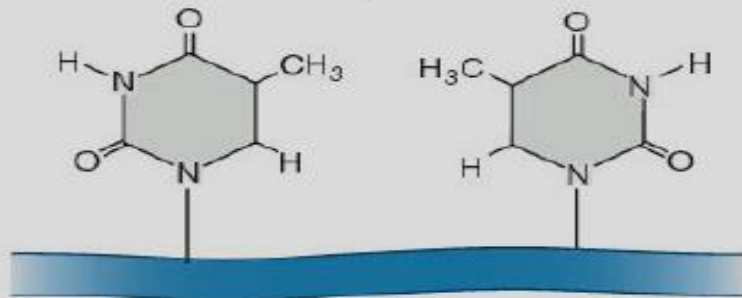
- defined as the elimination of DNA damage using **specific enzymes**, such as :
 - – **Photolyase** can repair thymine dimers induced by UV light.
 - – **alkyltransferase** repairs methylated or ethylated bases on the **DNA** bases.

1/ Direct Repair

Direct repair of damaged bases in DNA

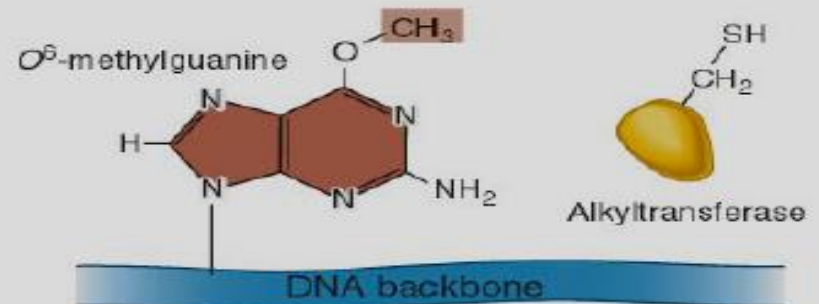


DNA photolyase cleaves the 2 bonds between the thymine dimer.

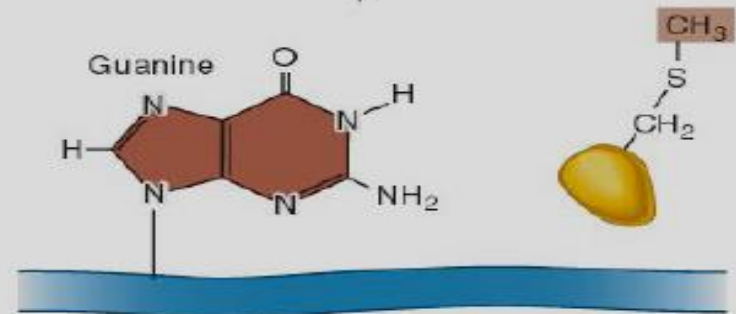


The normal structure of the 2 thymines is restored.

(a) Direct repair of a thymine dimer



Alkyltransferase catalyzes the removal of the methyl group onto itself.



The normal structure of guanine is restored.

(b) Direct repair of a methylated base

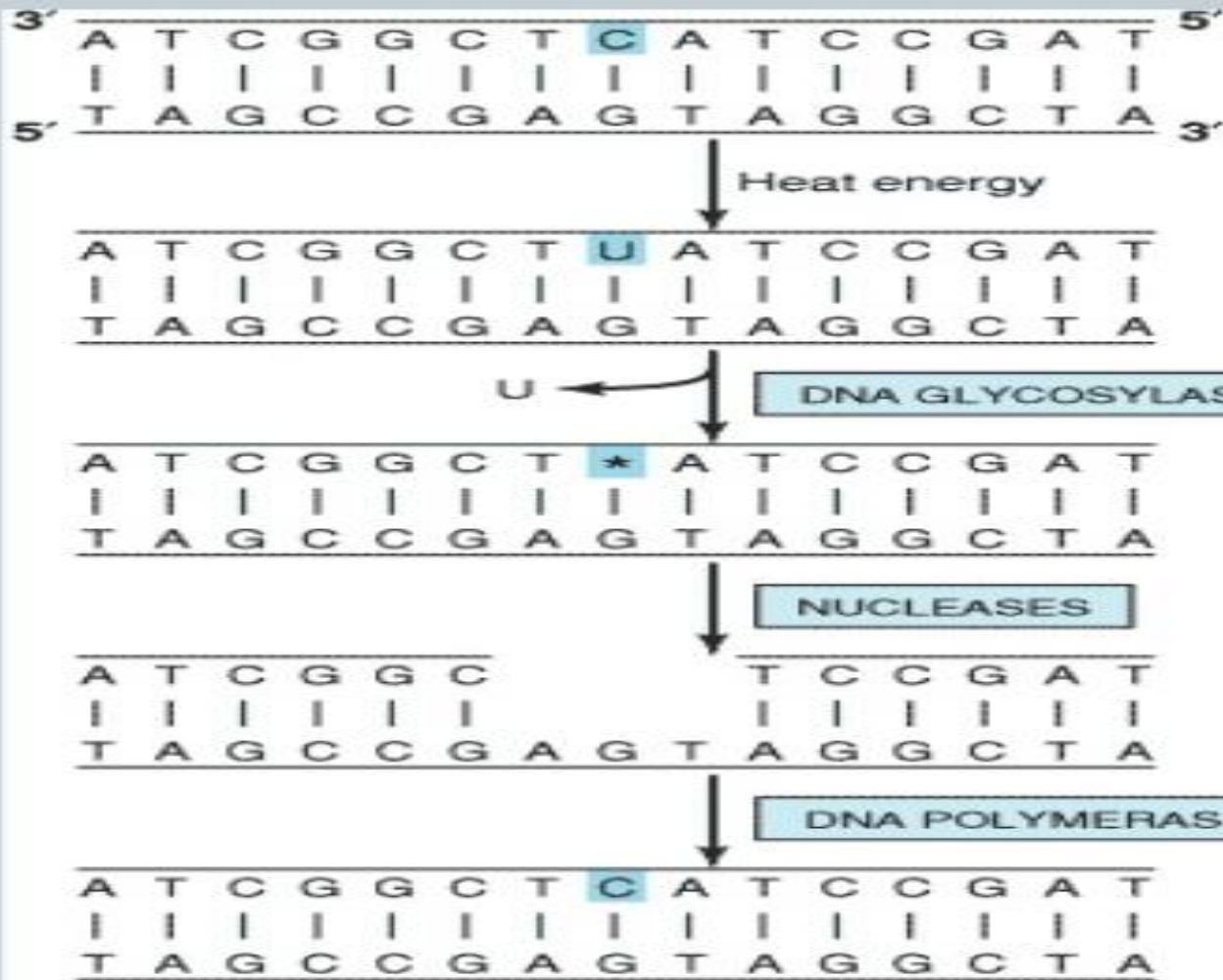
2/ Excision Repair

- Removal of the damaged bases followed by their replacement with newly synthesized DNA, where the damaged DNA is recognized and removed, either as free bases or as nucleotides. The resulting gap is then filled in by synthesis of a new DNA strand, using the undamaged complementary strand as a template.
- Three types of excision repair:
 - base-excision repair
 - nucleotide-excision repair
 - Double-Strand Break Repair

Base-excision repair(BER)

- involves an enzymes known as DNA glycosylases that can Removes a single damaged base and replaces it with new base, but excises few bases around it lead to a gap that filled by DNA polymerase with normal DNA, then ligase seals the region with correct base .

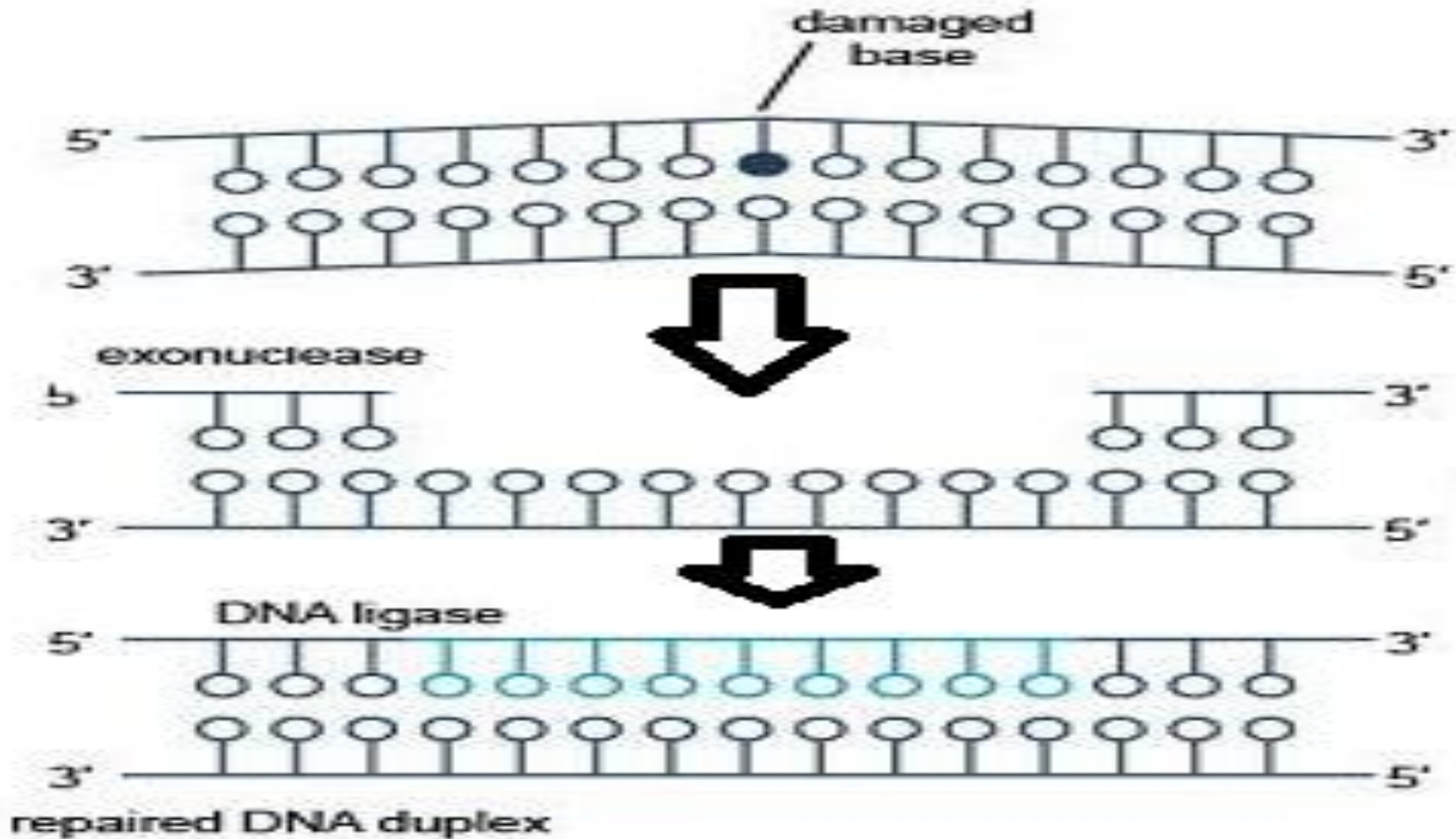
Base-excision repair(BER)



Nucleotide excision repair (NER)

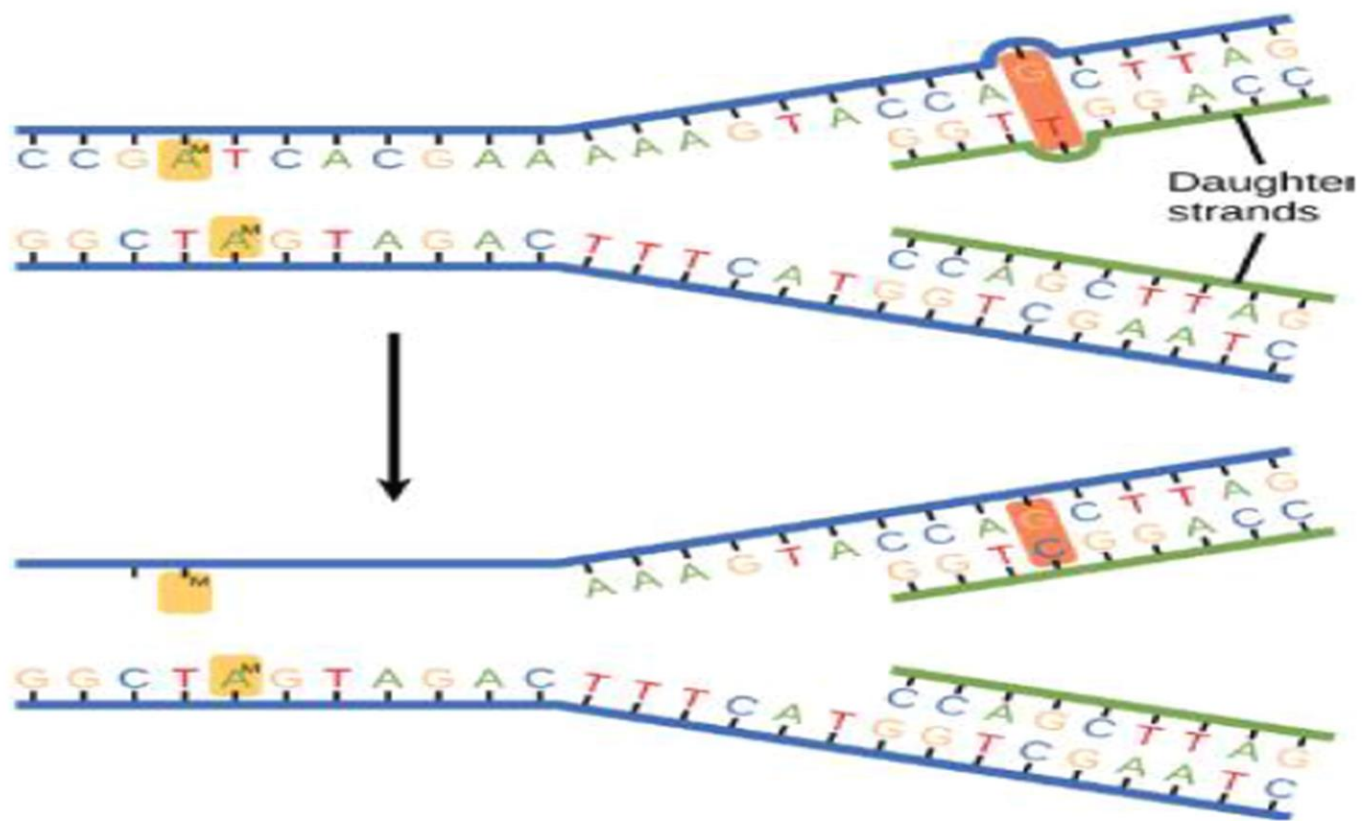
- a type of system repair can repaired many types of DNA damage, including Thymine dimers and chemically modified bases by a **mechanisms** similar to that found in BER with some exception such as the DNA glycosylases uses and the damaged DNA pieces recognized and removed.

Nucleotide excision repair (NER)



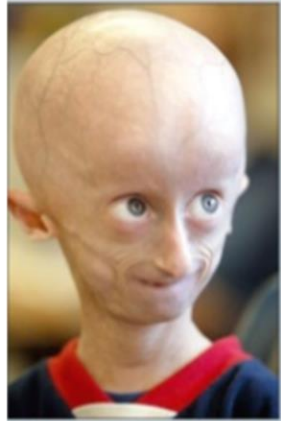
3/Mismatch Base repair (MMR)

- is a system for recognizing and repairing wrong insertion, deletion and miss-pairing of bases that can arise during DNA replication and recombination, as well as repairing some forms of DNA damage by aid of Proofreading,
- enzymes represented by DNA polymerase that has 3' → 5' exonuclease activity which recognizes mismatched bases and excises them and corrects them.



DNA Repair system disorder

- Several human diseases with inherited defects in genes involved DNA Repair system such as :Progeria (Progeria syndrome), Xeroderma pigmentosum.
- **Xeroderma pigmentosum (XP)** is a rare autosomal recessive disease, The affected patients that characteristic by an increased sensitivity to sunlight& susceptible to skin cancers. It is now recognized that XP is due to a **defect in the nucleotide excision repair of the damaged DNA.**
- **Progeria (Progeria Syndrome)** is an extremely rare genetic disorder that causes the affected individual to undergo advanced aging at an early age. • The symptoms closely resemble aging and include wrinkles, hair loss, and delayed growth.



Progeria



**Xeroderma
pigmentosum (XP)**