Mutation

Mutation

- Sudden heritable change in genetic material or character of an organism is known as mutation
- Individuals showing these changes are known as **mutants**
- An individual showing an altered phenotype due to mutation are known as **variant**
- Factor or agents causing mutation are known as **mutagens**
- Mutation which causes changes in base sequence of a gene are known as gene mutation or point mutation

Mutagens

- **Factor or agents causing mutation are known as mutagens**

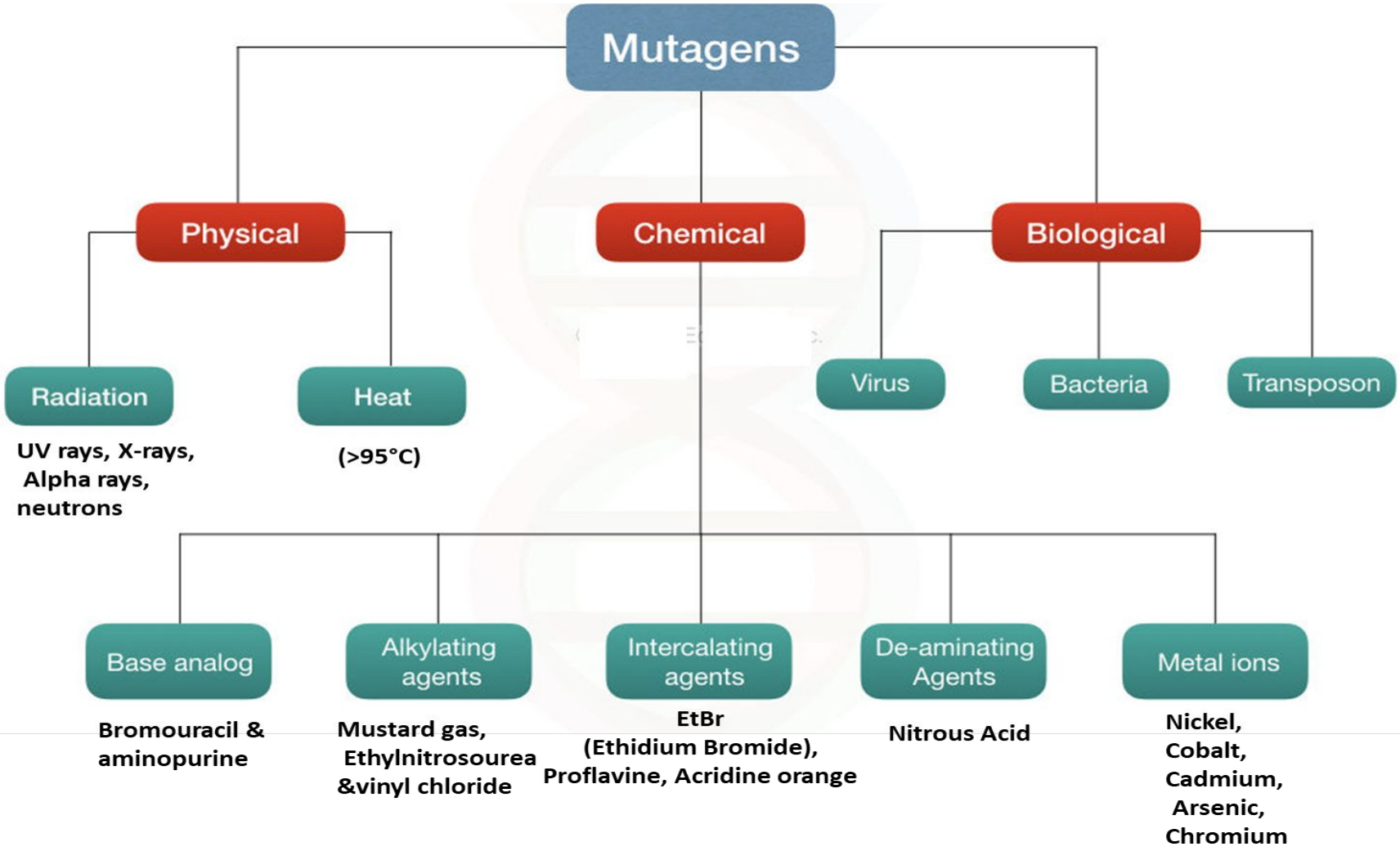
  Or

- **Mutagens are the known agents either physical, chemical or biological causes mutations by altering the genotype or gene expression which results in genetic abnormality."**

Types of Mutagens

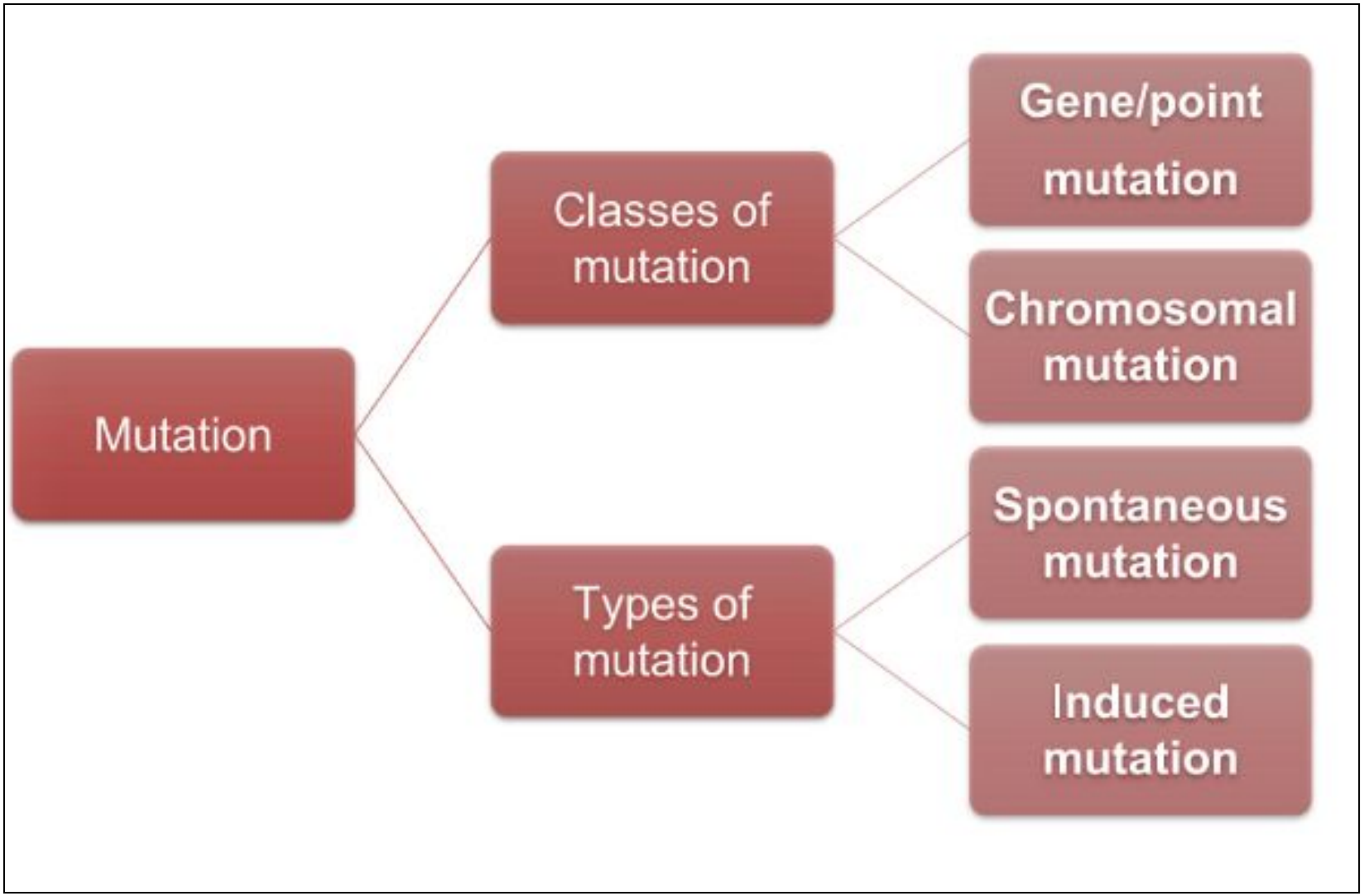
Three different types of common mutagens are observed in nature- physical and chemical mutagens agents and biological agents.

- **Physical Agents:** It includes high energy radiations such as gamma rays, X- rays and alpha particles and increase in temperature.
- **Chemical Agents:** They are of various types such as nitrous acid, alkylating agents, acridines, and base analogues.
- **Biological Agents:** It includes viruses, bacteria, and transposons.


Mutagens
Physical
Chemical
Biological
Radiation
Heat
Virus
Bacteria
Transposon
UV rays, X-rays, Alpha rays, neutrons
(>95°C)
Base analog
Alkylating agents
Intercalating agents
De-aminating Agents
Metal ions
Bromouracil & aminopurine
Mustard gas, Ethylnitrosourea &vinyl chloride
EtBr (Ethidium Bromide), Proflavine, Acridine orange
Nitrous Acid
Nickel, Cobalt, Cadmium, Arsenic, Chromium

Characteristics of Mutation

- Generally mutant alleles are **recessive** to their wild type or normal alleles
- Most mutations have **harmful effect**, but some mutations are beneficial
- **Spontaneous mutations occurs at very low rate**
- Some genes shows high rate of mutation such genes are called as **mutable gene**
- Highly mutable sites within a gene are known as **hot spots**.
- Mutation can occur in any tissue/cell (somatic or germinal) of an organism


Mutation
Classes of mutation
Gene/point mutation
Chromosomal mutation
Types of mutation
Spontaneous mutation
Induced mutation

Types of mutation

Spontaneous mutation	Induced mutation
• Occur spontaneously during DNA replication. • Eg. Nondisjunction	• Induced by mutagen. • Eg. Organism exposed to mutagen.

Classes of mutation

Gene/point mutation

- A change in a gene at a single nucleotide pair.
- Types :
- 1.Base substitution
- 2.Base insertions
- 3.Base deletions
- 4.Base inversion

Chromosomal mutation

- A change in a gene due to alteration of chromosome structure or number
- Types :
- 1. Chromosomal stucture (structural changes)
  - Deletion, Inversion, Translocation, Duplication
- 2. Chomosomal number
  - Aneuploidy, Polyploidy.

- **Based on causes of mutation**

1. Spontaneous mutation-

Spontaneous mutation occurs naturally without any cause. The rate of spontaneous mutation is very slow eg- Methylation followed by deamination of cytosine.

Rate of spontaneous mutation is higher in eukaryotes than prokaryotes.

Eg. UV light of sunlight causing mutation in bacteria

2. Induced Mutation-

Mutations produced due to treatment with either a chemical or physical agent are called induced mutation .

The agents capable of inducing such mutations are known as mutagen. use of induced mutation for crop improvement program is known as **mutation breeding.**

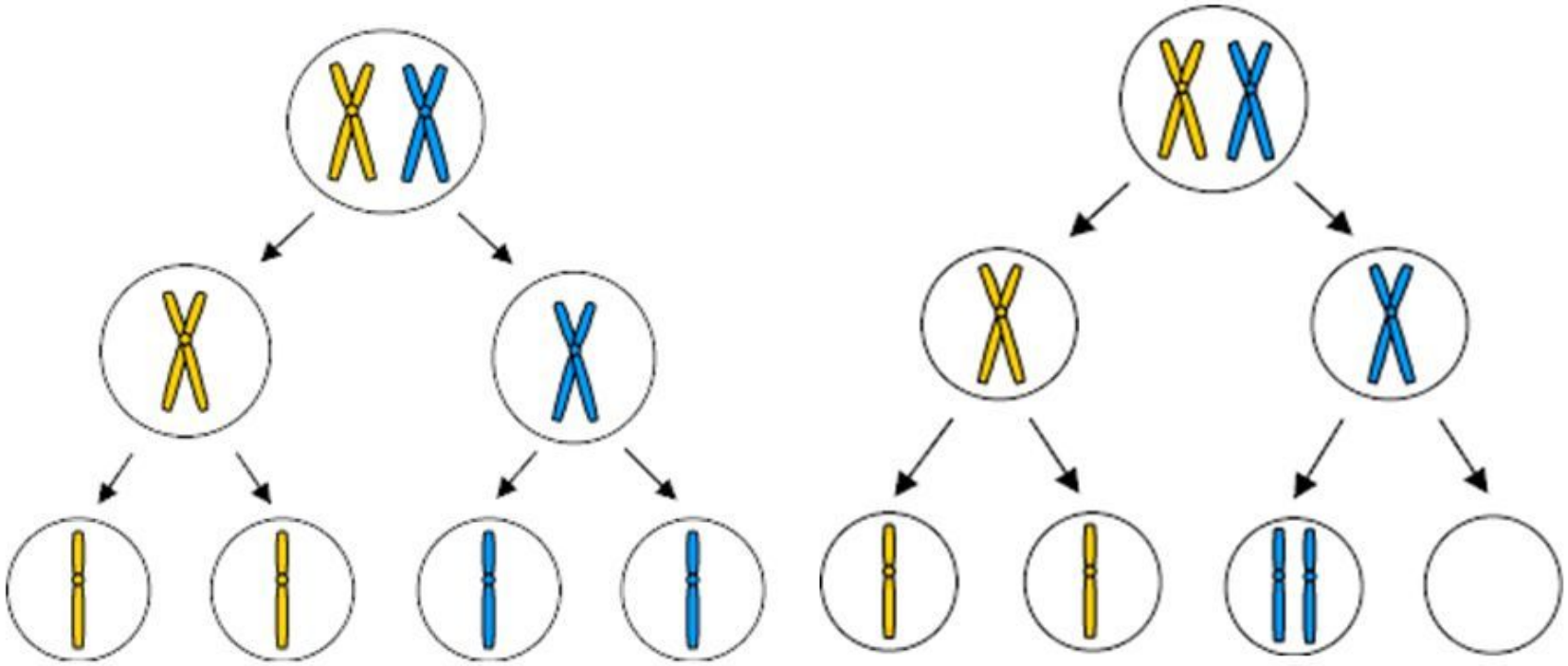
Eg. X- rays causing mutation in cereals

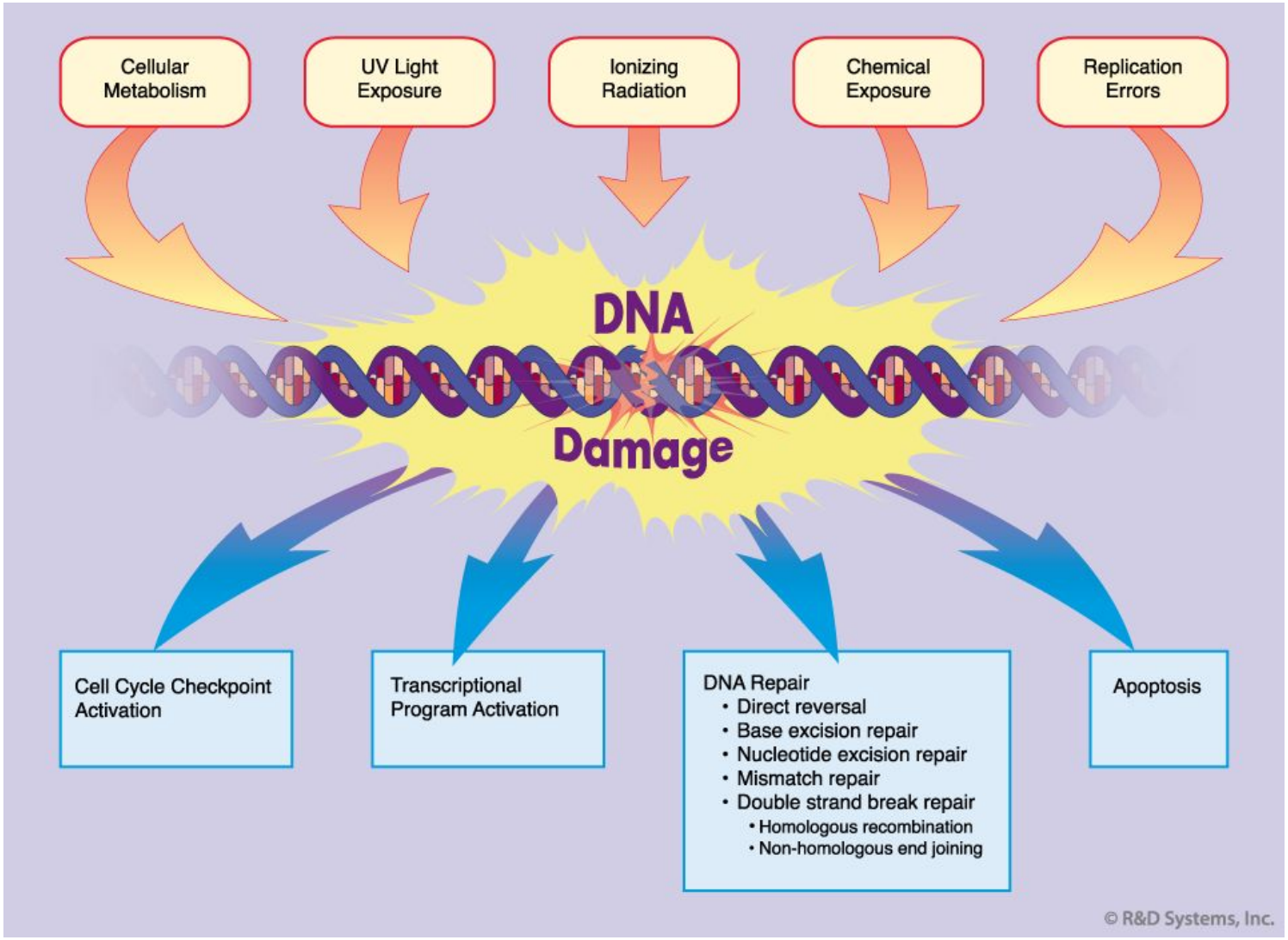
Nondisjunction

- The failure of homologous chromosomes to separate properly during meiosis.

What should happen

Nondisjunction




Cellular Metabolism
UV Light Exposure
Ionizing Radiation
Chemical Exposure
Replication Errors
DNA
Damage
Cell Cycle Checkpoint Activation
Transcriptional Program Activation
DNA Repair
• Direct reversal
• Base excision repair
• Nucleotide excision repair
• Mismatch repair
• Double strand break repair
• Homologous recombination
• Non-homologous end joining
Apoptosis
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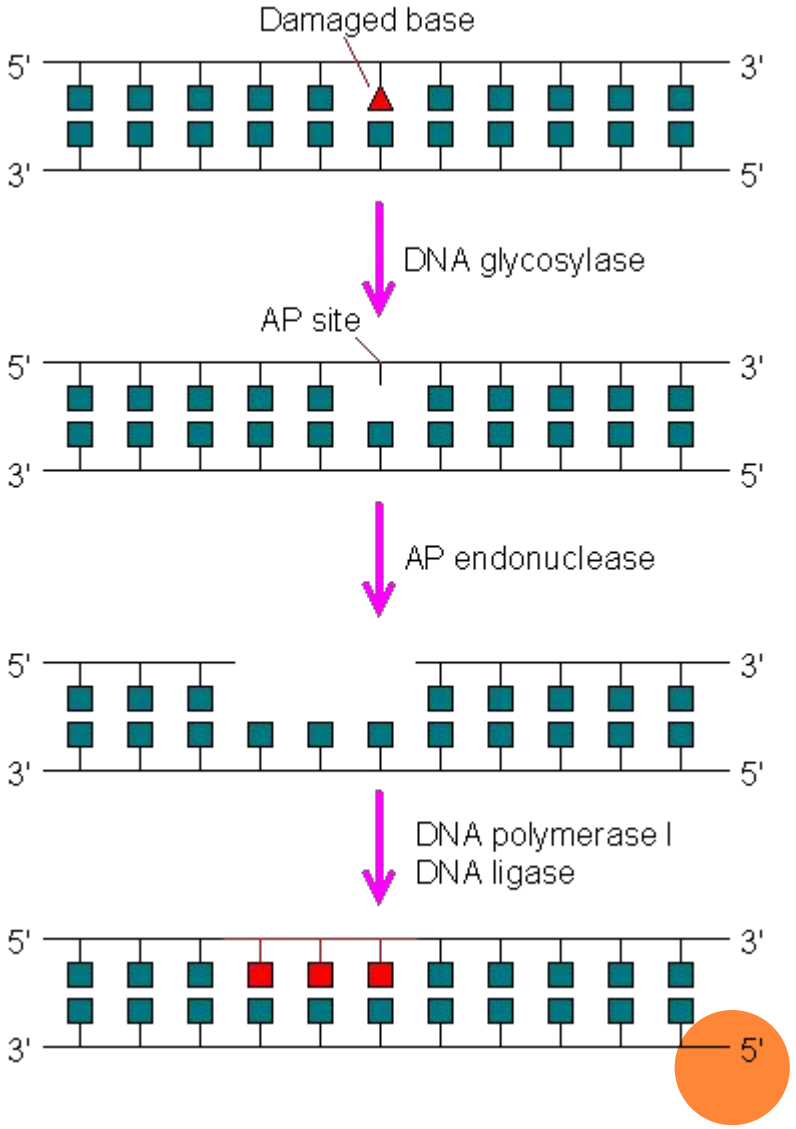
Base Excision Repair

Base Excision Repair (BER) is a repair mechanism that corrects damaged DNA by identifying damaged bases and replacing damaged bases with the correct nucleotide.

- Damaged bases are first identified and removal of the mutated base from the DNA helix by an enzyme known as **DNA glycosylase**.
- The damaged base is often called the "**Abasic Site**" or "**AP site**".
  - **AP** (apurinic/apyrimidinic) **endonuclease** makes an incision at the abasic site, creating a break, or nick, in the strand of DNA.
- With the removal of damaged bases, **DNA polymerase** synthesize the correct nucleotide to fill the region.
- Lastly, **DNA ligase** helps to close and seal the bond..

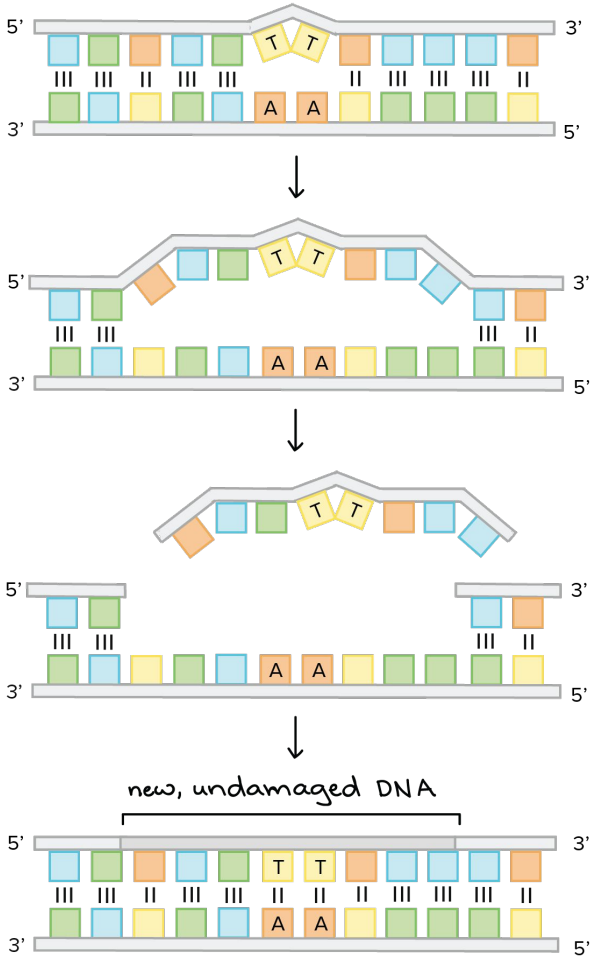


Nucleotide Excision Repair

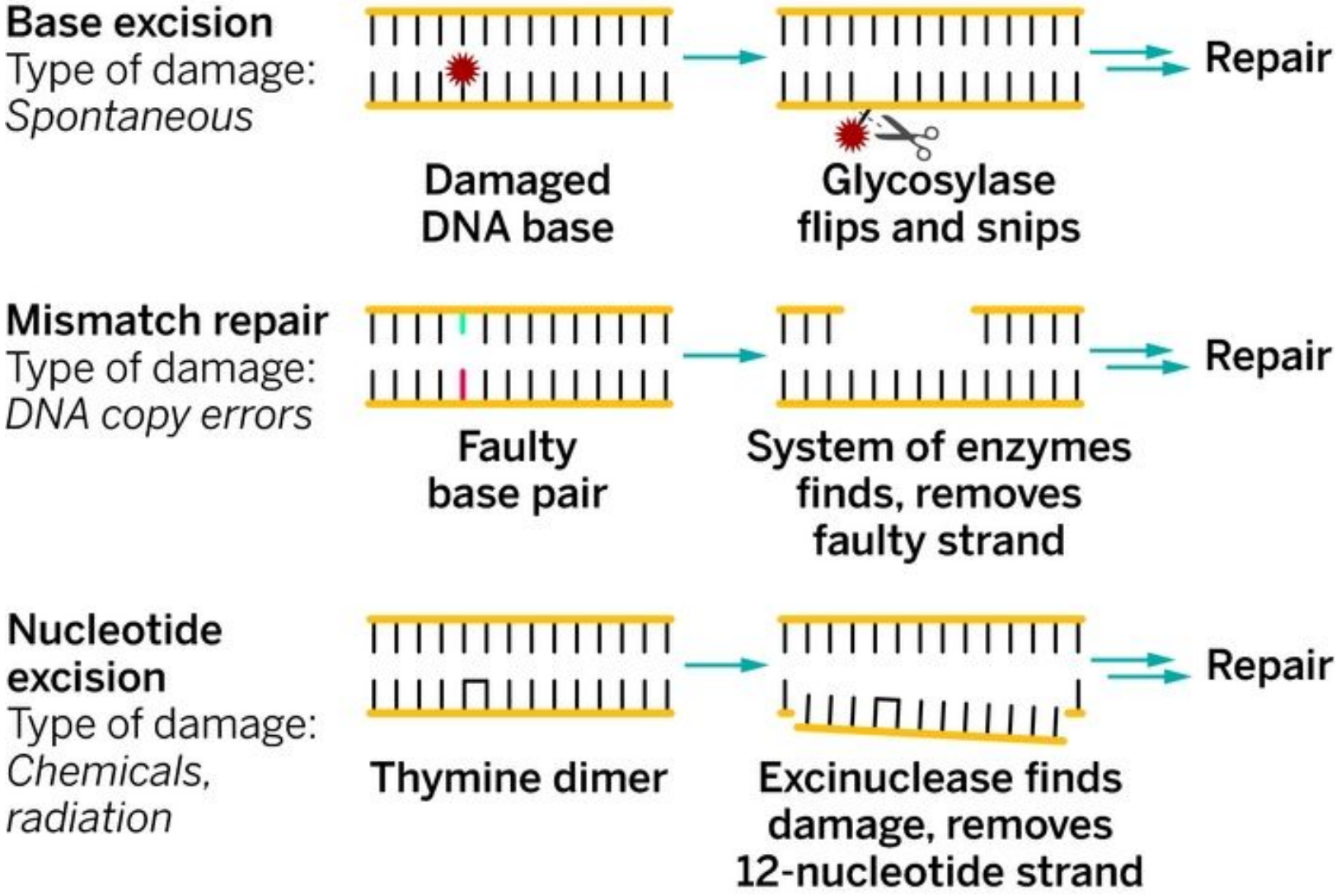
Nucleotide excision repair (NER) is a particularly important excision mechanism that removes DNA damage induced by ultraviolet light (UV). UV DNA damage results in bulky DNA adducts.

In nucleotide excision repair, the damaged nucleotide(s) are removed along with a surrounding patch of DNA.

- In this process, a **helicase** (DNA-opening enzyme) cranks open the DNA to form a bubble, and DNA-cutting enzymes chop out the damaged part of the bubble.
- A **DNA polymerase** replaces the missing DNA, and a **DNA ligase** seals the gap in the backbone of the strand^9

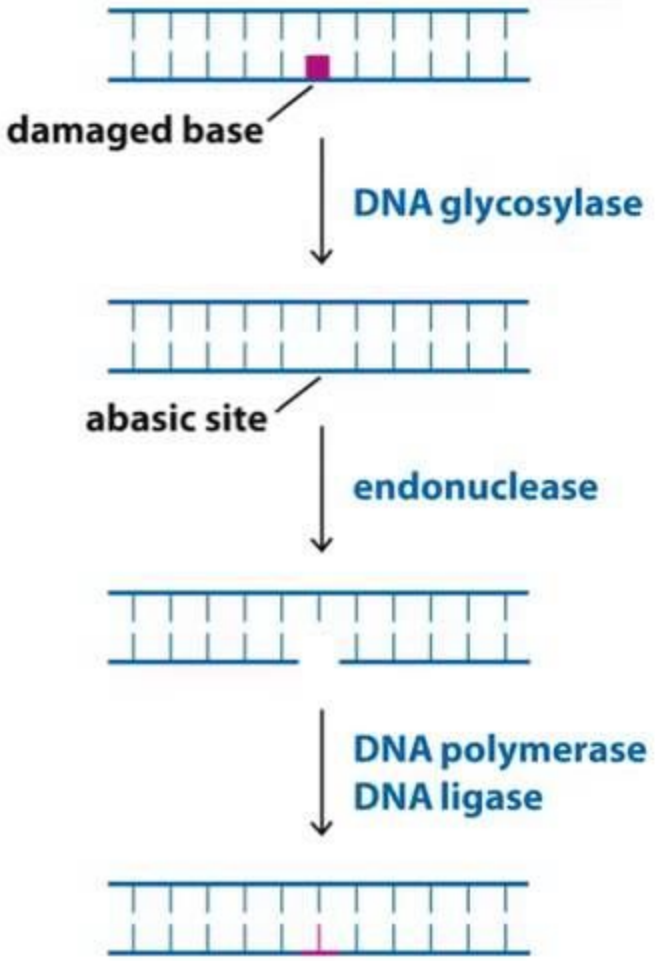


Deficiencies in NER are associated with the extremely skin cancer-prone **inherited disorder xeroderma pigmentosum**.

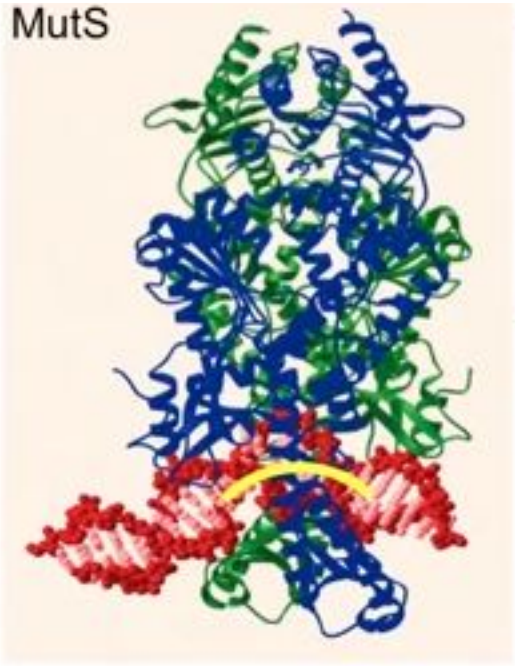

Base excision
Type of damage:
Spontaneous
Damaged
DNA base
Glycosylase
flips and snips
Repair
Mismatch repair
Type of damage:
DNA copy errors
Faulty
base pair
System of enzymes
finds, removes
faulty strand
Repair
Nucleotide
excision
Type of damage:
Chemicals,
radiation
Thymine dimer
Excinuclease finds
damage, removes
12-nucleotide strand
Repair

Base Excision Repair

- Base excision repair mechanism
  - Removal and replacement of modified bases
  - DNA glycosylase binds DNA and removes damaged base
  - AP endonuclease nicks the backbone
    - "AP": apurinic/apyrimidinic
  - DNA polymerase fills in the gap; ligase seals the nick

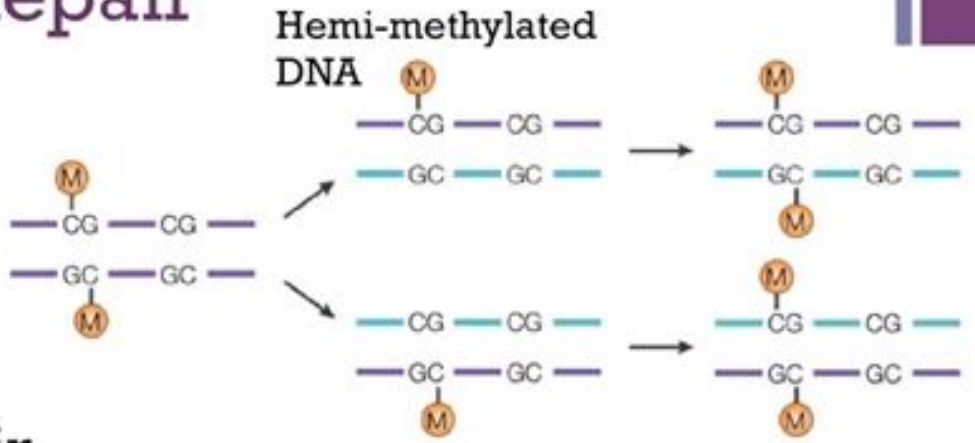


Mismatch Repair



- Mismatch repair
  - Repairs mispairings of nucleotides shortly after replication
  - Bacterial **MutS** protein binds mis-matched pair and causes **DNA** to bend
  - This induces an endonuclease to cleave the strand with the wrong nucleotide

Mismatch Repair



- Mismatch repair
  - This induces endonuclease to cleave the strand with the wrong nucleotide
    - How does it know which one is wrong?
    - Mature DNA is methylated at distinct sites; newer DNA not yet methylated
    - Newer strand assumed to be in error
  - DNA polymerase fills in the gap and ligase seals the nick

☺ EXCISION REPAIR

- Base excision repair
  - **Repair of modified bases**
  - **Glycosylase removes base, leaves backbone intact**
  - **AP endonuclease cut backbone, AP lyase removes sugar**
- Nucleotide excision repair
  - **Repair of adducts and large distortions in DNA double helix**
  - **Double excision removes damage as an oligonucleotide (12-13 nt in *E. Coli*, 27-29 nt in humans)**

DNA polymerase fills gap
DNA ligase seals nick