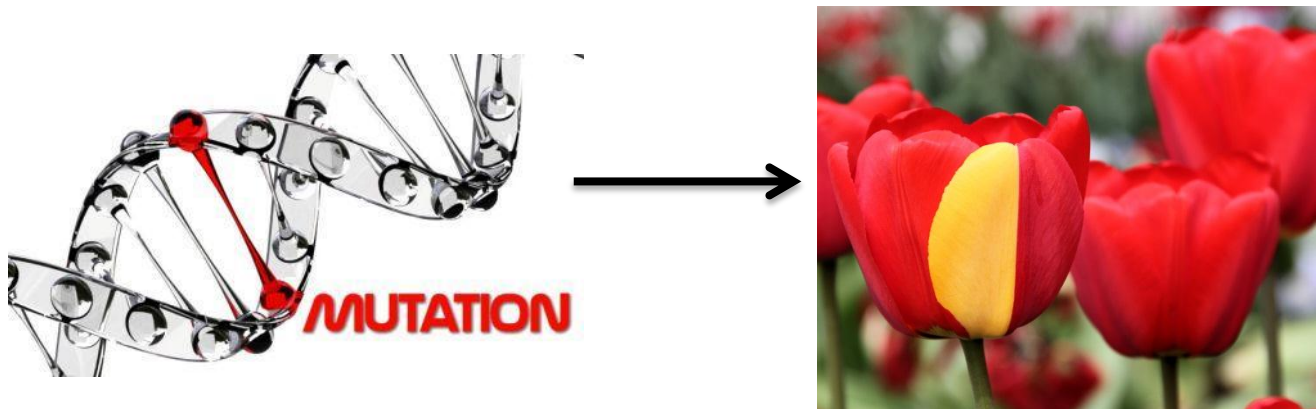


## Lecture 6

## 6.1. Mutation

**Mutation:** is the permanent alteration or change of the nucleotide sequence of the gene of an organism. Mutations can result from errors during DNA replication or other types of damage to DNA, Mutations may also result from insertion or deletion of segments of DNA due to mobile genetic elements.



**Mutagenesis:** is a process by which the genetic information of an organism is changed and cause a mutation. It may occur spontaneously in nature or non-spontaneously like exposure to mutagens.

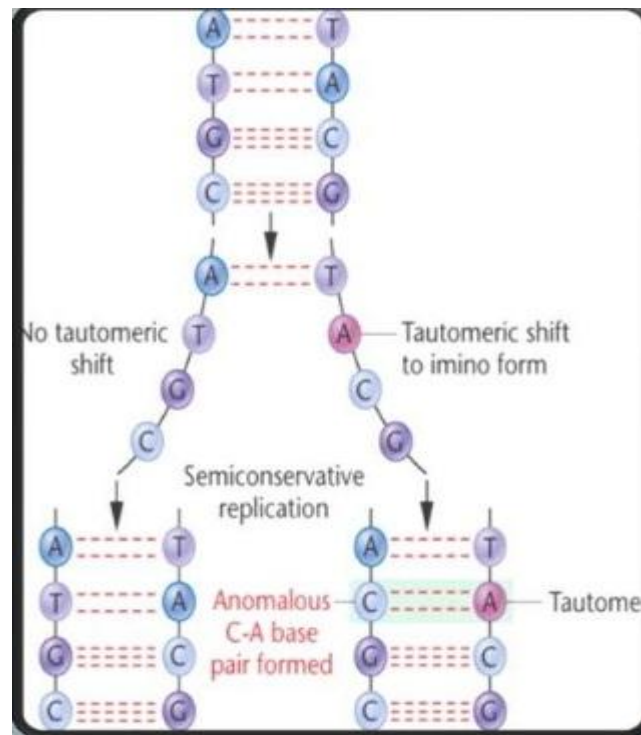
**Mutagen:** is a physical or chemical agent that causes mutagenesis in DNA of organism and increases the frequency of mutation.

## 6.2. Processes of Mutation:

(1) **Errors introduced during DNA repair.**

(2) **Spontaneous mutations** (Naturally):

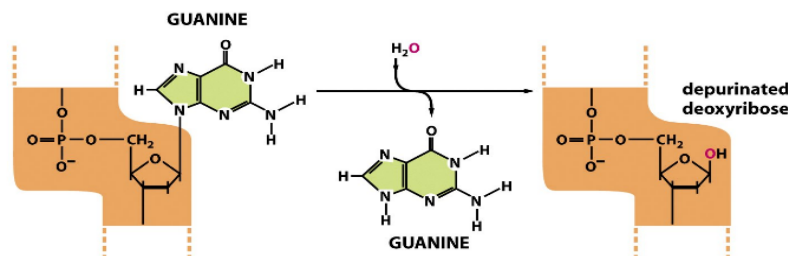
a) **Tautomerism:** one base is changed by the repositioning of a hydrogen atom, altering the hydrogen bonding pattern of that base, resulting in incorrect base pairing during replication.



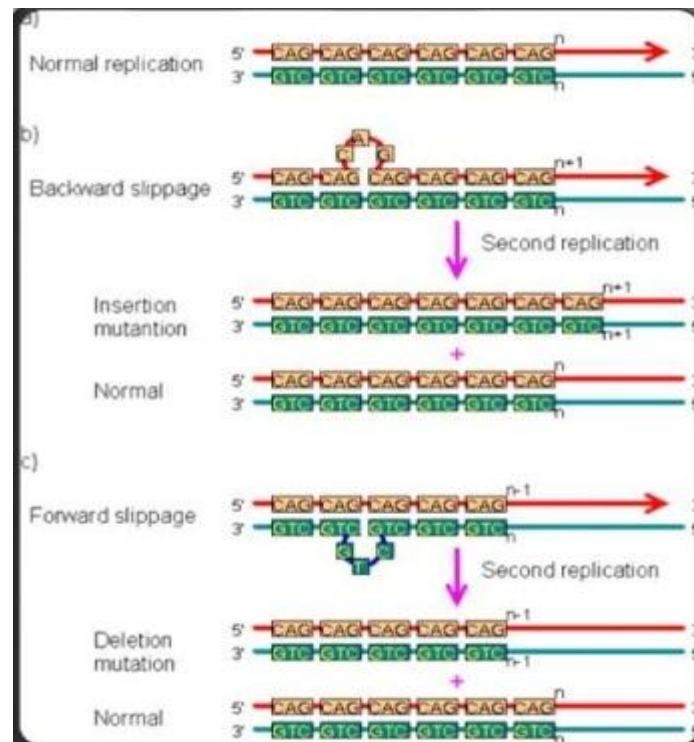
Tautomerism mutation

- b) **Depurination** : Loss of a purine base (A or G) to form an apurinic site.

## Depurination



- c) **Deamination – Hydrolysis**: changes a normal base to an atypical base  
 $C \rightarrow U$  and  $A \rightarrow HX$  (hypoxanthine).
- d) **Slipped strand miss-pairing**: Denaturation of the new strand from the template during replication, followed by renaturation in a different spot ("slipping"). This can lead to insertions or deletions.



Slipped strand miss-pairing mutation

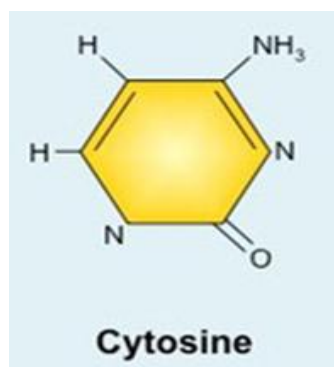
### (3) Induced mutations caused by mutagens.

Mutagen is any chemical or physical agent that causes mutation, mutagen can be classified:

#### I- Chemical agent

##### a) Hydroxylamine ( $\text{NH}_2\text{OH}$ )

It hydroxylates the Nitrogen (N) atom of Cytosine and converts it into a modified base (hydroxylamino cytosine) via a deamination process which causes base pairing.



**b) Base analogs**

Compounds are similar to one of four bases of DNA, they are able to replace the bases and cause stable mutation.

**Example**

- Bromodeoxyuridine which is an analogue to thymine and can replace thymine in DNA molecule.
- 2-aminopurin (1-AP) is purine analogue.

**c) Alkylating agents**

Addition an alkyl group such as (CH<sub>3</sub>) or (CH<sub>3</sub>-CH<sub>2</sub>) to amino group in nucleotides of DNA molecule.

**Example:**

- EMS (Ethyl methan sulphate) it is able to change the Guanine to Ethylguanine which is base pair with thymine.

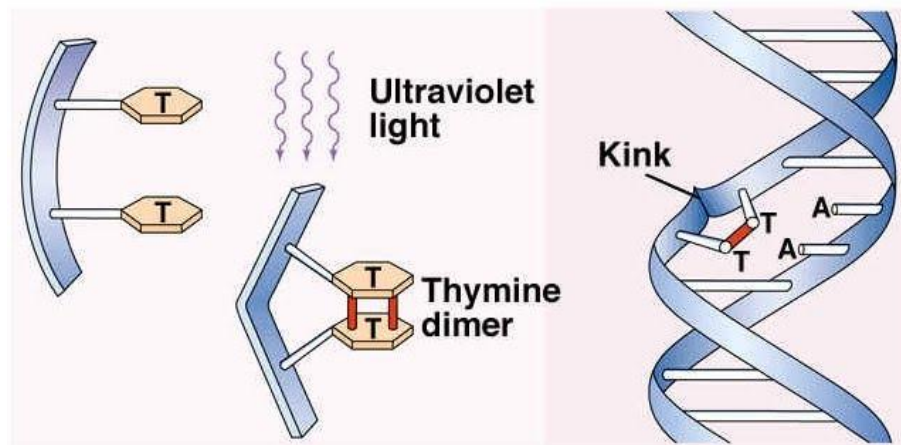
**d) DNA intercalating agents (ethidium bromide)****e) Oxidative damage**

f) **Nitrous acid (HNO<sub>3</sub>)** converts **amine groups** on (A) and (C) to **diazo** group, which leads to incorrect base pairing during replication.

**II- Physical Agent (Radiation)****a) non-ionizing radiation**

- Ultraviolet light (UV): Two nucleotide bases in DNA-cytosine (C) and thymine (T) are most sensitive to radiation that can change their properties. UV light can induce adjacent pyrimidine bases in a DNA strand to become covalently joined as a pyrimidine dimer.

## Pyrimidine Dimer



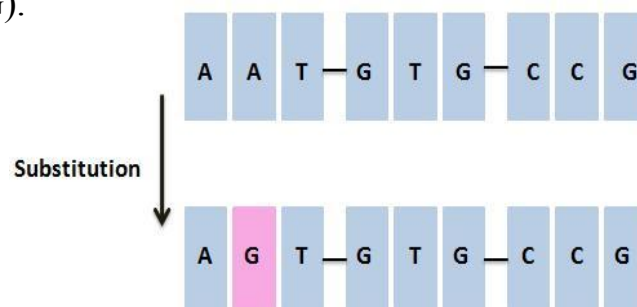
- **Ionizing radiation:**

Exposure to ionizing radiation, such as gamma radiation, can result in mutation, possibly resulting in cancer or death.

### 6.3. Classification of Mutation

#### I- Small-scale mutations

- a) **Substitution mutations:** caused by chemicals or malfunction of DNA replication. Include exchange a single nucleotide for another. These changes are classified as **transitions** or **transversions**. Most common is the transition that exchanges a purine for a purine ( $A \leftrightarrow G$ ) or a pyrimidine for a pyrimidine, ( $C \leftrightarrow T$ ). Less common is a transversion, which exchanges a purine for a pyrimidine or a pyrimidine for a purine ( $C/T \leftrightarrow A/G$ ).

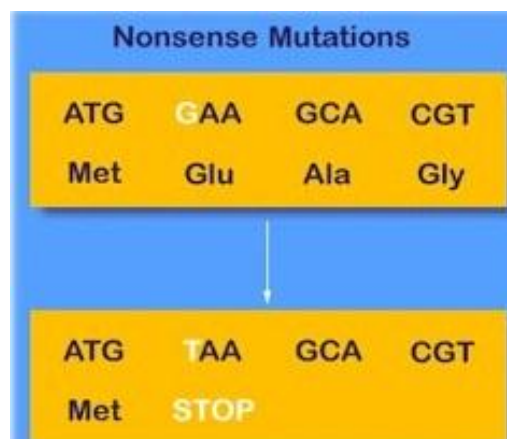


b) **Silent mutations:** results exchange in single base but it is code for the same amino acid.

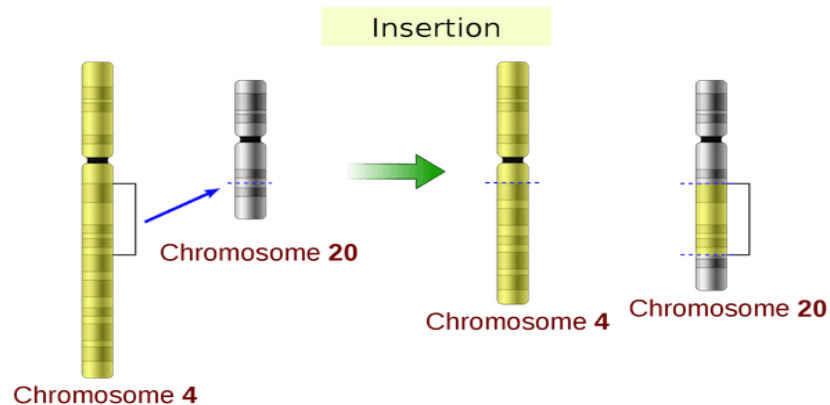
c) **Missense mutations:** which code for a different amino acid.



d) **Nonsense mutations:** which encode for a stop codon and can stop the protein synthesis.

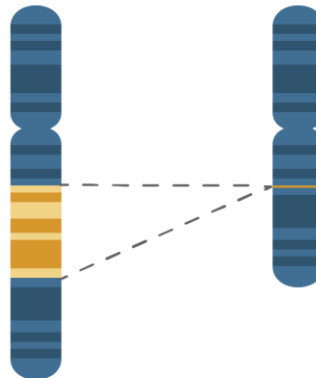


- e) **Insertion mutation:** add one or more extra nucleotides into the DNA. They are usually caused by transposable elements.



- f) **Deletions mutation:** remove one or more nucleotides from the DNA. Like insertions, these mutations can alter the reading frame of the gene.

### Deletion



## II- Large-scale mutations in chromosomal structure

- Amplifications** (or gene duplications) leading to multiple copies of all chromosomal regions, increasing the dosage of the genes located within chromosome.
- Deletions of large chromosomal regions**, leading to loss of the genes within those regions.
- Interstitial deletions:** an intra-chromosomal deletion that removes a segment of DNA from a single chromosome.

- d) **Chromosomal translocations:** interchange of genetic parts from nonhomologous chromosomes.
- e) **Chromosomal inversions:** reversing the orientation of a chromosomal segment.
- f) **Loss of heterozygosity:** loss of one allele, either by a deletion or a genetic recombination event, in an organism that previously had two different alleles.

