Mutation

A gene mutation is a permanent alteration in the DNA sequence that makes up a gene, such that the sequence differs from what is found in most people. Mutations range in size, they can affect anywhere from a single DNA building block (base pair) to a large segment of a chromosome that includes multiple genes.

Gene mutations can be classified in two major ways:

- **Hereditary mutations** are inherited from a parent and are present throughout a person's life in virtually every cell in the body. These mutations are also called germline mutations because they are present in the parent's egg or sperm cells, which are also called germ cells. When an egg and a sperm cell unite, the resulting fertilized egg cell receives DNA from both parents. If this DNA has a mutation, the child that grows from the fertilized egg will have the mutation in each of his or her cells.

- **Acquired (or somatic) mutations** occur at some time during a person's life and are present only in certain cells, not in every cell in the body. These changes can be caused by environmental factors such as ultraviolet radiation from the sun, or can occur if a mistake is made as DNA copies itself during cell division. Acquired mutations in somatic cells (cells other than sperm and egg cells) cannot be passed on to the next generation.
- **A genetic mutation** caused by one or more abnormalities in the genome. It can be caused by a mutation in a single gene (monogenic) or multiple genes (polygenic) or by a chromosomal abnormality**.**
- **Single gene disorder (monogenic disorder):** These disorders are the result of a single defective gene on the autosomes. They are inherited according to Mendel's Laws (Mendelian disorders). The mutation may be present on one or both chromosomes (one chromosome inherited from each parent). Examples of monogenic disorders are: sickle cell disease, cystic fibrosis, polycystic kidney disease.

Mechanism of gene mutation:

Most of gene mutation involve a change in only a single nucleotide or nitrogen base which called **point mutation,** or in more than one base pair which called **gross mutation**, gene mutation usually occur during replication of DNA which called **copy error mutation.**

Gene mutation occur by three methods:

1-Inversion 2-substitution (transition and transversion) 3-frameshift (insertion and deletion).

1- **Inversion:** a distortion of DNA by mutagen can change the base sequence, the result, new sequence have different codon.
2- **Substitution** (replacement): it mean a nitrogen base is replace with another, its two types:

A- **Transition**: a nitrogen base is replaced by another of its type, such as one purine is replaced by another purine.
B- **Trans-version:** a nitrogen base is replaced by another vice versa such as cytosine with guanine

3-**Frame-Shift mutation**: its two types

A- **Insertion:** in which, the reading of frame of base sequence shifts laterally in the forward direction due to insertion(addition) of one or more nucleotide.
B- **Deletion**: in which the reading of frame of base sequence shifts laterally in the backward direction due to the deletion of one or more nucleotide.

Mutation causes

DNA damage can be subdivided into two main types:

1. endogenous damage such as attack by reactive oxygen species produced from normal metabolic by products (spontaneous mutation), especially the process of oxidative deamination, also includes replication errors
2. exogenous damage caused by external agents such as
    1. hydrolysis or thermal disruption
    2. certain plant toxins
    3. Another causes such as:

- Physical factors: ultraviolet radiation from the sun and other radiation frequencies, including x-rays and gamma rays.
- Chemical factors: food contaminant, Alcohol , air pollution and smoking.
- Biological factors: Bacterial infection (*Helicobacter pylori*), viral infection (*Human papillomavirus* (HPV), Hepatitis B virus, Hepatitis C virus) and Parasitic infection (*Schistosoma spp).*

Due to the damaging effects that mutations can have on genes, organisms have mechanisms such as DNA repair to prevent or correct mutations by reverting the mutated sequence back to its original state**.**

DNA repair

Mechanism to correct errors during DNA replication and to repair DNA damage over the cells lifetime.. When normal repair processes fail, and when cellular apoptosis (programmed cell death) does not occur, irreparable DNA damage may occur, including

double-strand breaks and DNA cross linkages. This can eventually lead to malignant tumors, or cancer.