Mutations

Mutation is a permanent change in the DNA sequence that makes up a gene. Mutations range in size from one DNA base to a whole chromosome change.

Gene mutations occur in two ways:

- ❖ Inherited from a parent **(hereditary mutations or germline mutations)**
- ❖ Acquired during a person's lifetime and occur in the DNA of individual cells **(acquired or sporadic mutations).**

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 cannot be passed on to the next generation, but the germline mutations can do.

Types of Mutations:

Mutations may be gross (at the level of the chromosome) or point alterations (mutations not visible as cytological abnormalities), which can involve just a single nucleotide pair in DNA.

Point mutations: A point mutation is defined as an alteration in a single nucleotide pair in the DNA molecule and usually leads to a change in only one biochemical function. **(Point Mutations – changes in one or a few nucleotides)**

If a point Mutation occurs in a gamete or in a cell that gives rise to gametes, it may be transmitted to offspring and a succession of future generations, whereas, if a Mutation has a noticeably adverse effect on the phenotype, the mutant condition is referred to as a genetic disorder, or hereditary disease.

- **Substitution**
- THE FAT CAT ATE THE RAT
- THE FAT HAT ATE THE RAT

- **Insertion**
- THE FAT CAT ATE THE RAT ———THE FAT CAT XLW ATE THE RAT
- **Deletion**
- THE FAT CAT ATE THE RAT————THE FAT ATE THE RAT

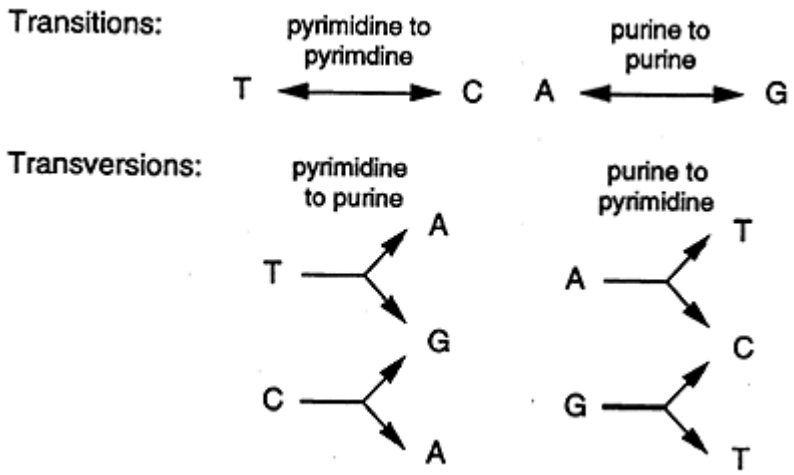
Point Mutation within a gene can be divided into many categories:

a. **Base- pair substitution.**
b. **Base –pair insertion or deletion.**
c. **Chromosome Mutations**

A- Base- pair substitution:

A type of mutation involving replacement or substitution of a single nucleotide base with another in DNA or RNA molecule. This type of mutation occurring in noncoding sequences often does not result in an altered amino acid sequence during translation. For example, this would occur when one nucleotide containing cytosine is accidentally substituted for one containing guanine. Point mutations are the most common type of mutation and there are two types.

1. **Transition:** this occurs when a purine is substituted with another purine or when a pyrimidine is substituted with another pyrimidine.
2. **Transversion:** when a purine is substituted for a pyrimidine or a pyrimidine replaces a purine.



Point mutations that occur in DNA sequences encoding proteins are either silent, missense or nonsense.

1. **Silent mutation**: A change in a base pair may transform one codon into other that translated into the same amino acid.
(Not resulting in a new amino acid in the protein sequence.) For example: If (UAC) is changed to (UAU), there is no noticeable effect, because both of these codons code for tyrosine.
2. **Nonsense mutation**: the base substitutions in a protein coding region may mutate an amino acid codon to a termination codon or vice versa. The former type, which results in a prematurely shortened protein, is referred to as

a nonsense mutation. For example, if (UAC) (tyrosine) is changed to (UAG) however, the result could be a drastic one because (UAG) is a stop codon.

3. **Missence mutation**: A base substitution could also result in an amino acid substitution. For example If (UAC)(tyrosine)is changed to(CAC) (histidine) then histidine is incorporated into the protein instead of tyrosine.

B. Base –pair insertion or deletion:

Insertion or deletions are additions or losses one or more nucleotide pairs in a gene. An insertion mutation occurs when an extra base pair is added to a sequence of bases. A deletion mutation is the opposite; it occurs when a base pair is deleted from a sequence. These two types of point mutations are grouped together because both of them can drastically affect the sequence of amino acids produced. With one or two bases added or deleted, all of the three-base codons change. This is called a frameshift mutation.

Frame shift Mutations – shifts the reading frame of the genetic message so that the protein may not be able to perform its functions. For example, if a sequence of codons in DNA is normally CCT ATG TTT and an extra A is added between the two cytosine bases, the sequence will instead read CAC TAT GTT T. This completely changes the amino acids that would be produced, which in turn changes the structure and function of the resulting protein and can render it useless. Similarly, if one base was deleted, the sequence would also shift.

- **Insertion**
  - **THE FAT CAT ATE THE RAT**
  - **THE FAT HCA TAT ETH ERA T**
- **Deletion**
  - **THE FAT CAT ATE THE RAT**
  - **TEF ATC ATA TET GER AT**

C. Chromosome Mutations:

Changes that affect entire chromosomes or segments of chromosomes can cause problems with growth, development, and function of the body's systems. These changes can affect many genes along the chromosome and alter the proteins made by those genes. Conditions caused by a change in the number or structure of chromosomes are known as chromosomal disorders. These changes can occur during the formation of reproductive cells or in early fetal development. Many cancer cells also have changes in their chromosome number or structure. These changes most often occur in somatic cells during a person’s lifetime.

Significance of Mutations:

- Most are neutral: e.g.: Eye color or Birth marks
- Some are harmful: e.g. Sickle Cell Anemia and Down Syndrome
- Some are beneficial: e.g. Sickle Cell Anemia to Malaria Immunity to HIV

Cause and repair of mutation:

Mutations are rare because DNA is a very stable molecule for several reasons:

- Because DNA is normally made of 2 complementary strands (double helix) repairs can be made when one side or the other is damaged, but not if both sides are damaged.
- All the potentially reactive side groups of the sugar molecules making up the backbone of each DNA strand are already covalently bonded
- The nucleotide bases lie protected inside the sugar-phosphate backbone, their potentially reactive side groups out of harm's way secured by hydrogen bonds.
- Finally, DNA's helix and Nucleosome coils provide a geometric tightness which deters most chemical reactions from taking place at normal temperatures.

There are two ways in which DNA can become mutated:

- Mutations can be inherited. e.g. Parent to child
- Mutations can be acquired.
  - Environmental damage
  - Mistakes when DNA is copied.

Mutagens: Any agent that causes a mutation is called a mutagen. Mutagens can be physical or chemical in nature. Typical mutagens are:

Physical:

- Gamma and X-rays
- Ultraviolet radiation
- Subatomic particles (high energy electrons)

Chemical:

- Cigarette smoke
- Free radicals and oxidizing agents
- Nucleotide look-a-like molecules