GENE MUTATION

A gene mutation is defined as an alteration in the sequence of nucleotides in DNA. this change can affect a single nucleotide pair or larger gene segment of a chromosome. They are essential to the study of genetics and are useful in many other biological fields.

We can distinguish between two broad categories of mutations: somatic mutations and germ line mutations. Somatic mutations arise in somatic tissues, which do not produce gametes. These mutations are passed on to other cells through the process of mitosis, which leads to a population of genetically identical cells (a clone). The effect of these mutations depends on many factors, including the type of cell in which they occur and the developmental stage at which they arise. Many somatic mutations have no obvious effect on the phenotype of the organism, because the function of the mutant cell (even the cell itself) is replaced by that of normal cells.

However, cells with a somatic mutation that stimulates cell division can increase in number and spread; this type of mutation can give rise to cells with a selective advantage and is the basis for all cancers. Germ-line mutations arise in cells that ultimately produce gametes. These mutations can be passed to future generations, producing individual organisms that carry the mutation in all their somatic and germ-line cells.

MOLECULAR MECHANISM OF MUTATION

Mutations result from both internal and external factors. Those that are a result of natural changes in DNA structure are termed spontaneous mutations, whereas those that result from changes caused by environmental chemicals or radiation are induced mutations.

1. SPONTANEOUS MUTATION

Spontaneous mutation are those which arise naturally, not through the action of a mutagenic agent, they may arise through errors in DNA replication and Spontaneous alteration of a nucleotide within an existing DNA molecule.

1. Tautomerism- A base is changed by the repositioning of a hydrogen atom, altering the hydrogen bonding pattern of that bases, resulting in an incorrect base pairing replication.
2. Depurination- Loss of purine base (A or G) to form an apurinic site.

3. Deamination is removing the amino group from the amino acid and converting to ammonia. Since the bases cytosine, adenine and guanine have amino groups on them that can be deaminated .

2. INDUCED MUTATION

During its lifetime, an organism may be exposed to a variety of physical, chemical, and biological agents capable of causing damage to its genetic material

Physical mutagens

Radiation

a. Ionizing (e.g. X-ray, gamma ray, cosmic ray)

b. Non ionizing (e.g. UV ray)

Heat

a. Break the N-glycosidic bond in DNA

b. Result from a purinic site or base less site

Chemical mutagens

a. Base analogs

b. Alkylating agent

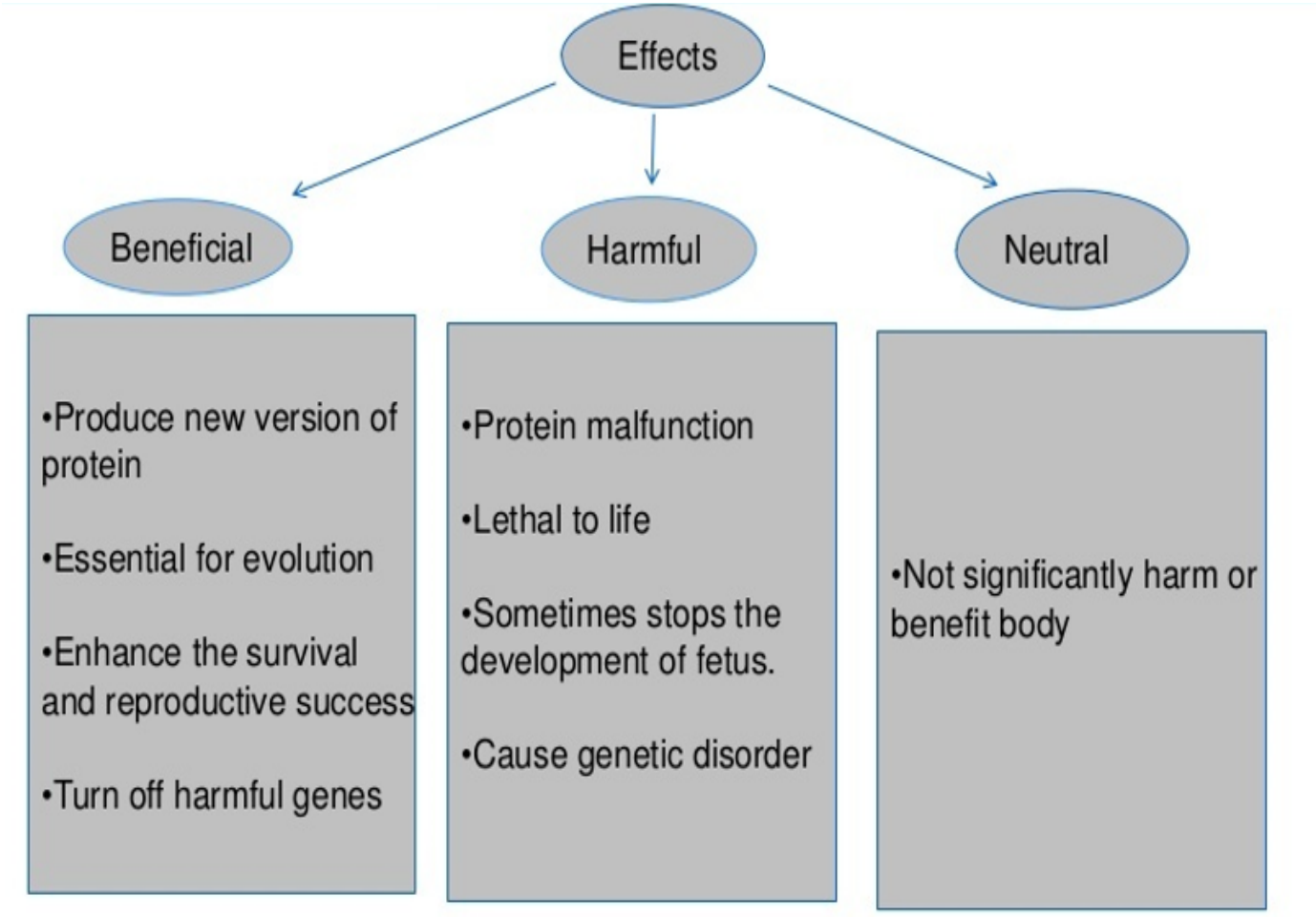
c. Intercalating agent

EFFECT OF GENE MUTATION

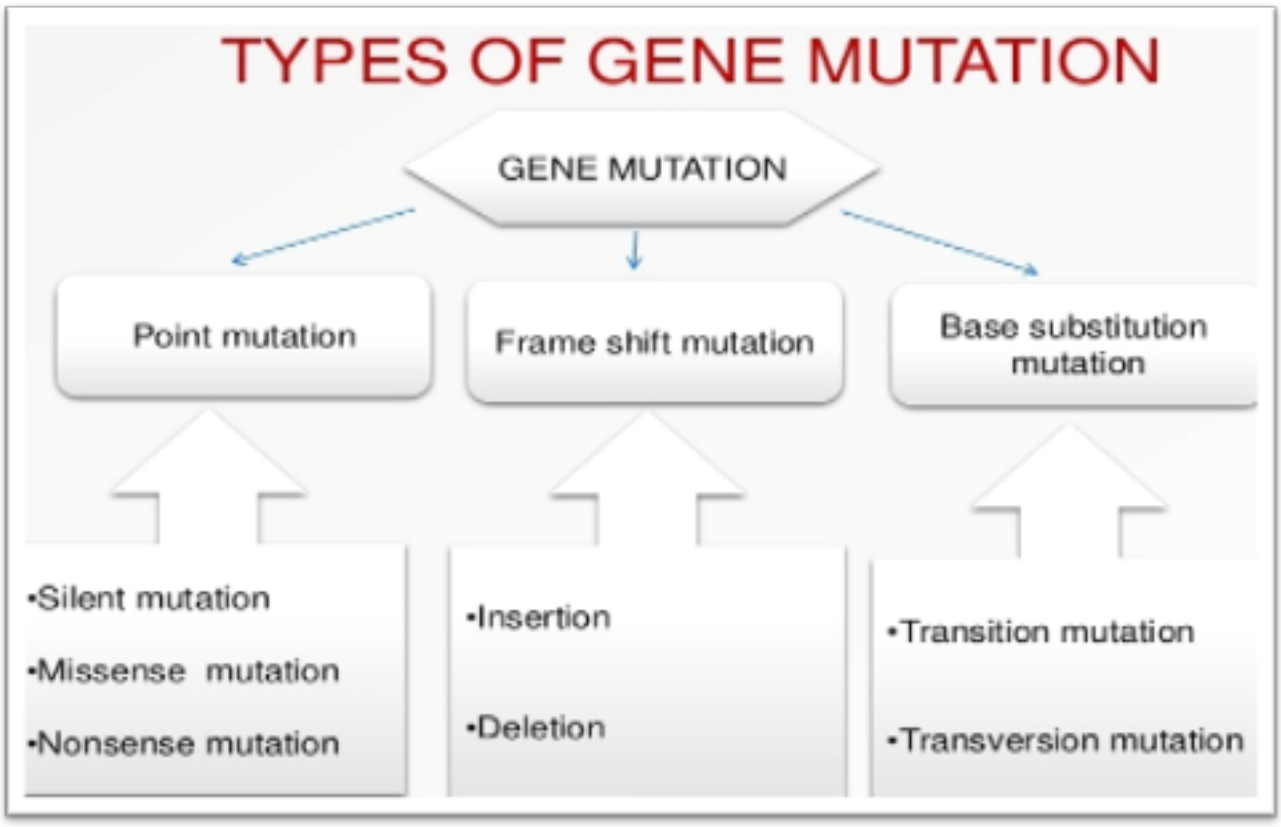
*A mutation may be neutral and have no effect. For example, the protein that a mutated gene produces may work just as well as the protein from the normal gene.

*A mutation may sometimes be beneficial. For example, people who are carriers (heterozygous) for the sickle cell allele are more resistant to malaria (a tropical disease) than people who do not have the mutated gene.

*Some mutations can be harmful. A change in the gene might produce a faulty or non-functioning protein, resulting in a genetic disease, such as cystic fibrosis.



TYPE OF GENE MUTATION

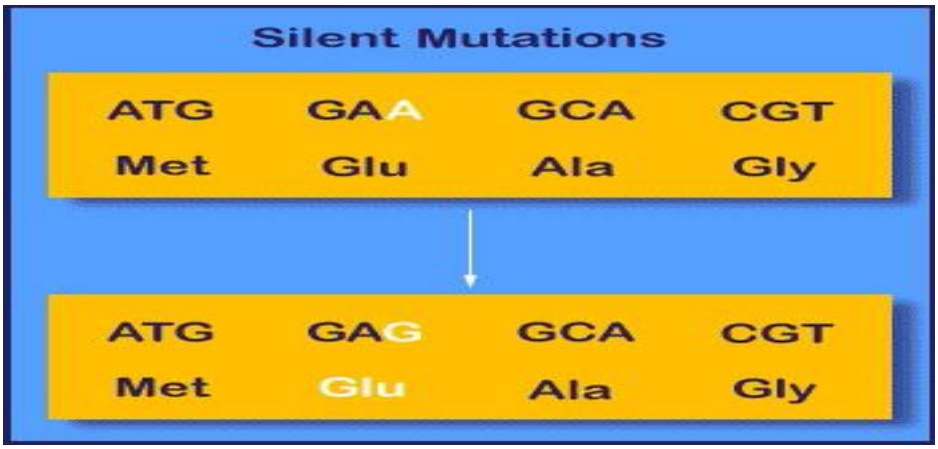


Point Mutation

Point mutations are the most common type of gene mutation. Also known as base pair substitution. Change in a single nucleotide base pair. Point mutation can be categorized into three types:

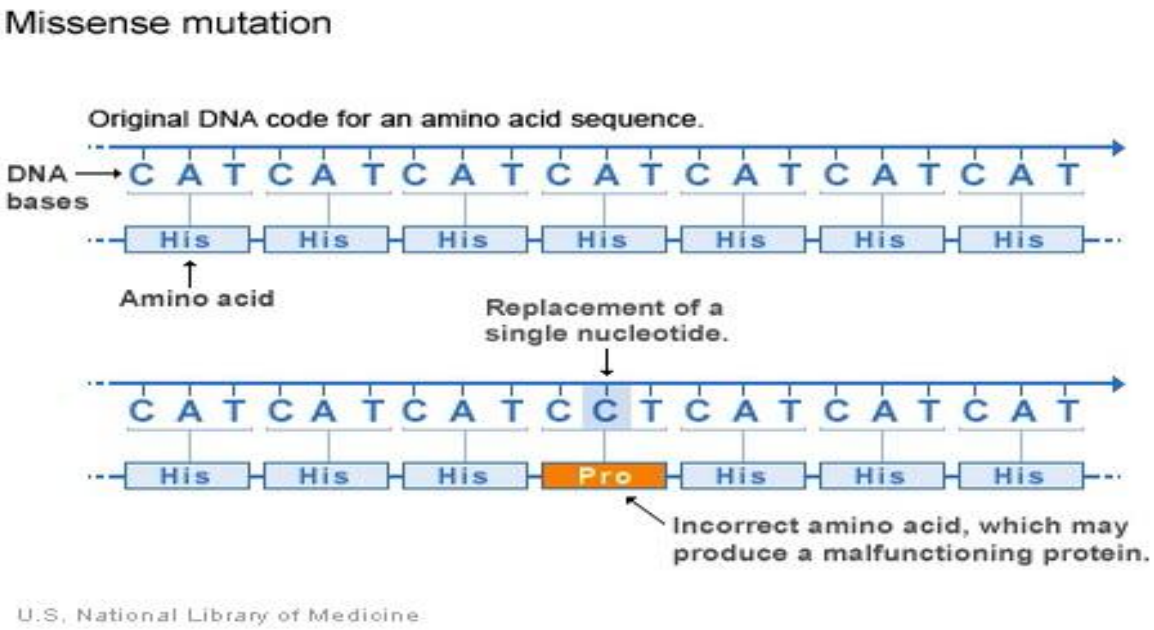
1. SILENT MUTATION

The change in one codon for an amino acid into another codon for that same amino acid . Silent mutations are also referred to as synonymous mutations.



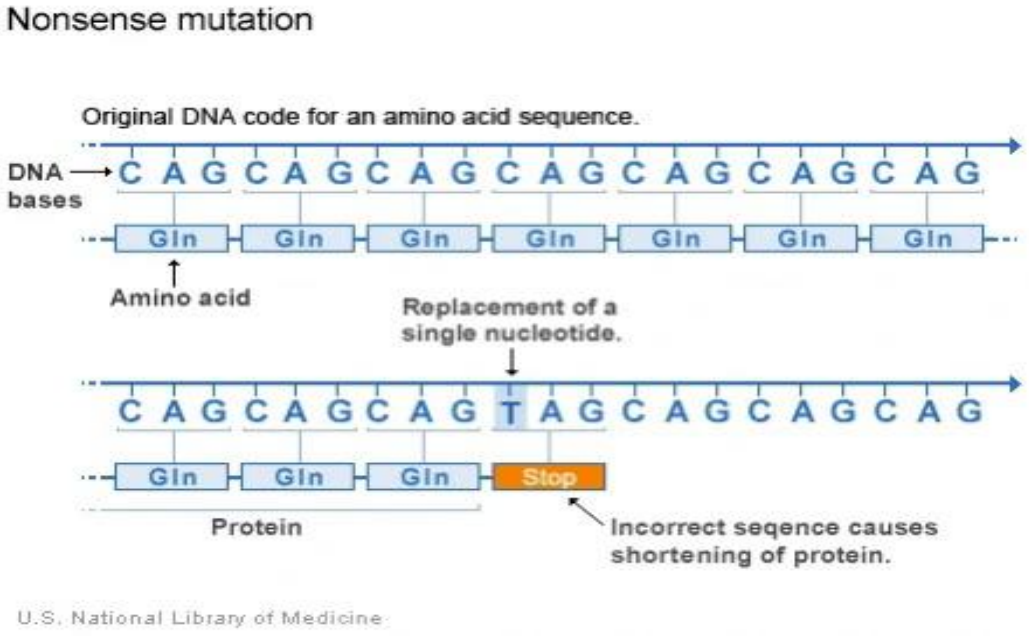
2. MISSENSE MUTATION

The codon for one amino acid in mRNA is changed into a codon for another amino acid. Missense mutations are sometimes referred to as non-synonymous mutations.



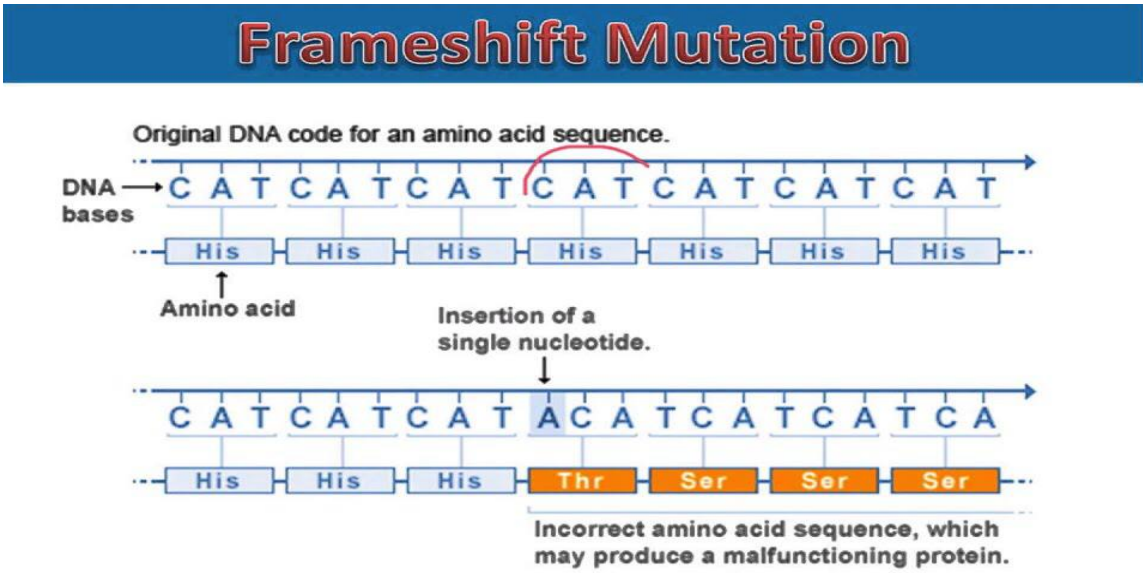
3. NONSENSE MUTATION

changes a sense codon (one that specifies an amino acid) into a nonsense codon (one that terminates translation). If a nonsense mutation occurs early in the mRNA sequence, the protein will be greatly shortened and will usually be nonfunctional.



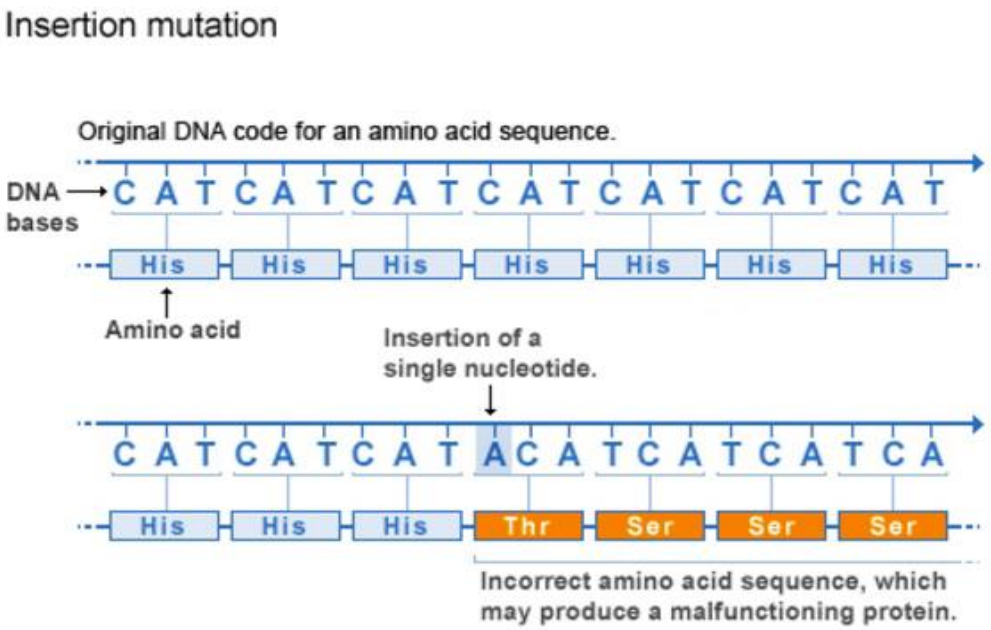
FRAME SHIFT MUTATIONS

This type of mutation occurs when the addition or loss of DNA bases changes a gene' s reading frame. A reading frame consists of 3 bases, each code for one amino acid. A frame shift mutation shifts the grouping of these bases and changes the code for amino acids.The resulting protein is usually nonfunctional. Insertions and deletion can all be frame shift mutations.



١.INSERTION

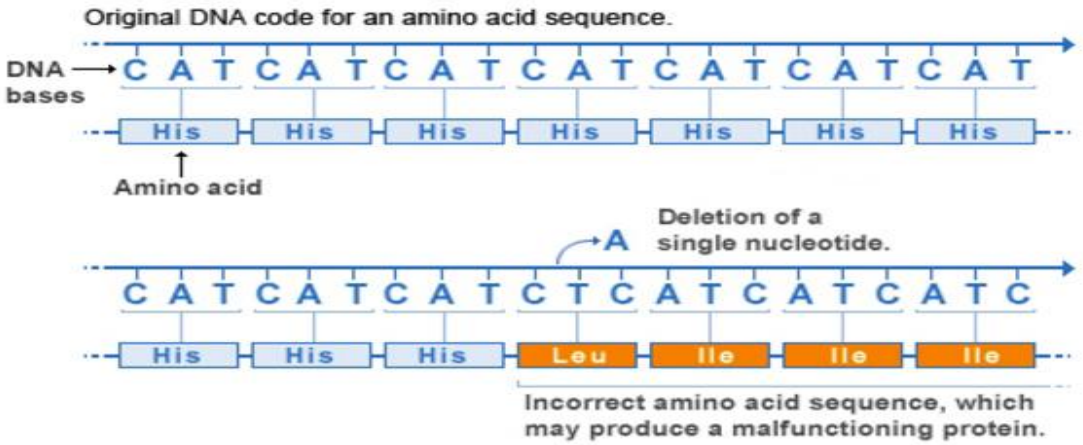
An insertion changes the number of DNA bases in a gene by adding a piece of DNA. As a result, the protein coded by the gene may not function properly.



2. DELETION

A deletion changes the number of DNA bases by removing a piece of DNA. Small deletion may remove one or few base pairs within a gene . Larger deletions can remove one entire gene or several neighboring genes. The deleted DNA may alter the function of the resulting protein.

Deletion mutation



Base substitution mutation

mutation in which one base pair is replaced by another. Base substitutions can be divide into two subtype

1. TRANSITION MUTATION

A transition is the replacement of a base by the other base of the same chemical.

2. TRANSVERSION MUTATION

A transversion is the opposite the replacement of a base of one chemical category by a base of the other.