

## UNIT 3: Molecular Genetics

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### **Small-Scale Mutations**

*Point Mutation* – is a change in a single nucleotide within gene.

*Substitution* – is the replacement of one base pair in a DNA sequence by another base pair.

*Insertion* – is the addition of a base pair (small-scale mutation) or larger coding region (large-scale mutation) to a DNA sequence.

*Deletion* – is the removal of a base pair (small-scale mutation) or larger coding region (large-scale mutation) from a DNA sequence.

*Inversion* – is two adjacent bases trading places (small-scale mutation) or the reversal of a sequence of DNA (large-scale mutation).

*Single Nucleotide Polymorphism (SNP)* – is a difference in the DNA between individuals caused by point mutations.

*Missense Mutation* – is a mutation that changes a single amino acid in the coding sequence.

*Nonsense Mutation* – is a mutation that results in a premature stop codon.

*Silent Mutation* – is a mutation that does not alter the resulting sequence of amino acids.

*Frameshift Mutation* – is a shift in the reading frame resulting in multiple missense and/or nonsense effects.

Small scale mutations occur when one base pair or small groups of base pairs occurs. These types of mutations are called *point mutations*. There are several types of point mutations:

*Substitution*: replace one base for another.

*Insertion* and *deletion*: addition or removal of one base pair

*Inversion*: the removal and reinsertion of base pairs in reverse order.

Small scale mutations can be positive, neutral (no effect), or harmful. Small scale mutations are categorized into four groups: *missense*, *nonsense*, *silent*, and *frame shift*.

## Large-Scale Mutations

*Translocation* – is the movement of entire genes or sequences of DNA from one chromosome to another.

Large scale mutations may involve multiple nucleotide sequences, entire genes, or large regions of a chromosome. These mutations can affect the genome and the function of an organism.

Gene duplication (amplification) is the copying of genes or group of genes being copied to multiple regions of chromosomes. New genes can be formed with new functions which may be selected for.

Large scale deletion is the removal of large portions of DNA regions from a chromosome. This type of mutation can greatly affect the function of the cell.

Duchenne Muscular Dystrophy is caused by the deletion of all or part of the dystrophin gene; individuals may die by age 20.

Becker Muscular Dystrophy is caused if a small part of the dystrophin gene being deleted. Individuals may lead a normal life.

Translocation occurs when an entire gene or group of genes are moved to a new location on another chromosome. This may create new genes and polypeptide chain formation.

Transposable elements can move freely from chromosome to chromosome, throughout the genome. If inserted near genes they may enhance, disrupt, or modify the expression of the gene.

Inversion is the removal of a gene or genes and the reinsertion in the reverse order. This may not have a negative impact on the gene expression, but if it were cut in the middle of the gene sequence then it would be lost.

Trinucleotide repeats may occur, where nucleotide sequence is repeated a number of times. This is a normal occurrence. If the repeats expand uncontrollably, caused by a mutation, genetic disease may occur, such as; Huntington's disease.

Mutation and description	Illustration
No mutation: This is the normal condition.	<p><b>DNA</b> 5'...CAAATGACCGGTTTCATGCTTA...3' 3'...GTTTACTGGCCAAGTACGAAT...5'</p> <p><b>mRNA</b> 5'...CAA AUG ACC GGUUCAUGCUUA...3'</p> <p><b>polypeptide</b> -- Met Thr Gly Ser Cys Leu --</p>
A <b>missense mutation</b> occurs when a change of a single base pair or group of base pairs results in the code for a different amino acid. The protein that is synthesized will have a different sequence and structure, and it may be non-functional or function differently. A missense mutation can be beneficial if it creates a new, desirable effect.	<p><b>DNA</b> 5'...CAAATGACCGGT<b>C</b>CATGCTTA...3' 3'...GTTTACTGGCCA<b>G</b>GTACGAAT...5'</p> <p>mutated base pair from in normal DNA</p> <p><b>mRNA</b> 5'...CAA AUG ACC GGU<b>C</b>AUGCUUA...3'</p> <p>altered sense codon</p> <p><b>polypeptide</b> -- Met Thr Gly <b>Pro</b> Cys Leu --</p> <p>altered amino acid</p>
A <b>nonsense mutation</b> occurs when the change of a single base pair or group of base pairs results in a premature stop code in the gene. The polypeptide is cut short and, most likely, will be unable to function.	<p><b>DNA</b> 5'...CAAATGACCGGTTTCATG<b>A</b>TTA...3' 3'...GTTTACTGGCCAAGTAC<b>T</b>AAT...5'</p> <p>mutated base pair from in normal DNA</p> <p><b>mRNA</b> 5'...CAA AUG ACC GGUUCA<b>U</b>GAUUA...3'</p> <p>codon changed to stop</p> <p><b>polypeptide</b> -- Met Thr Gly Ser -- premature termination of polypeptide</p>
A <b>silent mutation</b> occurs when the change in one or more base pairs does not affect the functioning of the gene. The mutated DNA sequence codes for the same amino acid as the non-mutated sequence, and the resulting protein is not altered.	<p><b>DNA</b> 5'...CAAATGACCG<b>G</b>CTCATGCTTA...3' 3'...GTTTACTGG<b>C</b>GAGTACGAAT...5'</p> <p>mutated base pair from in normal DNA</p> <p><b>mRNA</b> 5'...CAA AUG ACC <b>G</b>GUUCAUGCUUA...3'</p> <p>codon changed for another for same amino acid</p> <p><b>polypeptide</b> -- Met Thr Gly Ser Cys Leu --</p> <p>no change in amino acid</p>
A <b>frameshift mutation</b> occurs when one or more nucleotides are inserted into or deleted from a DNA sequence, causing the reading frame of codons to shift in one direction or the other. This results in multiple missense and/or nonsense effects. The frameshift mutation "shifts" the reading frame by one or more steps, and every amino acid coded for after this mutation is affected. Any deletion or insertion of base pairs in multiples of three does not cause frameshifts because the reading frame is unaltered. Tay Sachs disease is a result of the insertion of four base pairs.	<p><b>DNA</b> 5'...CAAATGACCG<b>A</b>GCTCATGCTTA...3' 3'...GTTTACTGG<b>C</b>T<b>C</b>GAGTACGAAT...5'</p> <p>insertion of a base pair</p> <p><b>mRNA</b> 5'...CAA AUG ACC <b>G</b>A<b>G</b>CUCAUGCUUA...3'</p> <p>reading frame off by one from here on</p> <p><b>polypeptide</b> -- Met Thr <b>Glu Leu Met Leu</b> --</p> <p>amino acids altered due to frameshift</p>

**Figure 2:** Types of mutations in a DNA sequence and how they affect the mRNA and Protein sequences.

## Causes of Genetic Mutations

**Spontaneous Mutation** – is a mutation that is caused by an error in DNA replication.

**Induced Mutation** – is a mutation that is caused by an environmental agent.

**Mutagen** – is an environmental agent that directly alters the DNA within a cell.

Mutations are group into two categories; *spontaneous* or *induced*. Spontaneous occurs during DNA replication, where inaccuracies occur in the nucleotide sequence. Induced mutations are caused by environmental factors, known as *mutagens*. Mutagens can be in the form of chemicals and radiation. Spontaneous and induced mutations can be either small or large scale.

### Chemical Mutagens

Any chemical agent may enter the nucleus and alter the structure of the DNA molecule. Some agents can change the nucleotide structure to resemble other base pairs resulting in replication errors.

Other chemical mutagens can mimic a DNA nucleotide and alter the shape of the DNA molecule affecting replication, such as; benzene and ethidium bromide.

### Radiation

Electromagnetic radiation can also cause mutations; low energy radiation (ultraviolet B) causes extra bonds to form between nucleotides, forming kinks in the backbones of the DNA molecule complicating DNA replication and transcription. These types of mutations may lead to skin cancer.

High energy radiations (x-ray, gamma, radioactive decay) may strip molecules of electrons breaking bonds within the DNA molecule. Rearrangement or deletion of large portions of a chromosome may occur.

## **Mutations: Positive or Negative?**

*(Beneficial, Neutral, or Harmful)*

Mutation that gives an advantage to an individual, who experiences a greater survival and reproductive success and can be passed onto successive generations, is beneficial.

Most mutations are neutral or silent mutations. They occur in non-coding regions of the chromosome, therefore will have no impact on gene expression.

Mutations are only harmful to individuals; it does not harm groups or species of organisms. A mutation will render an individual weaker than other individuals; within the group and is selected against by nature.

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