MAMMOTH

SCIENCE

Unit 11- Mutations & Gene Regulation

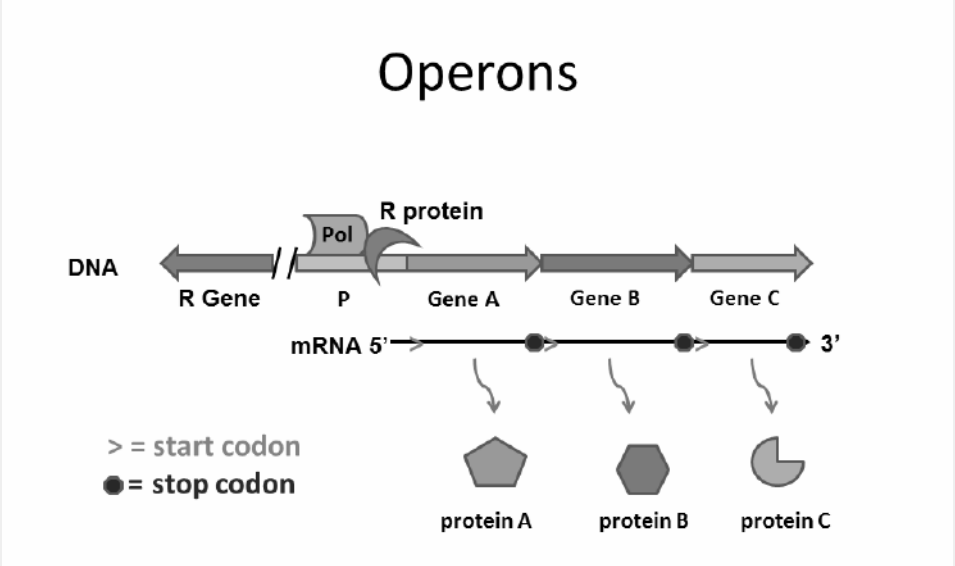
- *Compare and Contrast Gene expression and regulation in Prokaryotes vs Eukaryotes*
- *Identify and illustrate DNA mutations*
- *Gene rearrangement-an entire gene is moved to a new location.*
- *Identify and Describe Gene alterations*
- *Evaluate the significance of these mutations*

Menu

Gene Regulation - What is it?

Gene Regulation

- Gene Expression is regulated
- All cells have genes but not all genes are expressed all the time
- Constitutive genes are always expressed
- Some important genes are not always expressed.
- Gene expression is basically the synthesis of the polypeptide chain encoded by a particular gene. Therefore, we can say that the expression of the gene can be quantified in terms of the amount of protein synthesized by the genes.



Gene Expression - The Mechanisms

GENE EXPRESSION	GENE REGULATION
The process by which the instructions in our DNA are converted into a functional product, such as a protein	The number of mechanisms the process involved in turning genes on and off to ensure the appropriate expression of genes at the proper times
Two Steps: Transcription and Translation	Occurs either at the transcriptional, post-transcriptional, translational, and post-translational levels
Structural Elements: Introns and Exons	Structural Elements: Transcription initiation site, Promoter, Enhancers, and Silencers
Responsible for the synthesis of gene products	Responsible for controlling the amount and the type of gene products based on the requirements of the cell

Visit www.PEDIAA.com

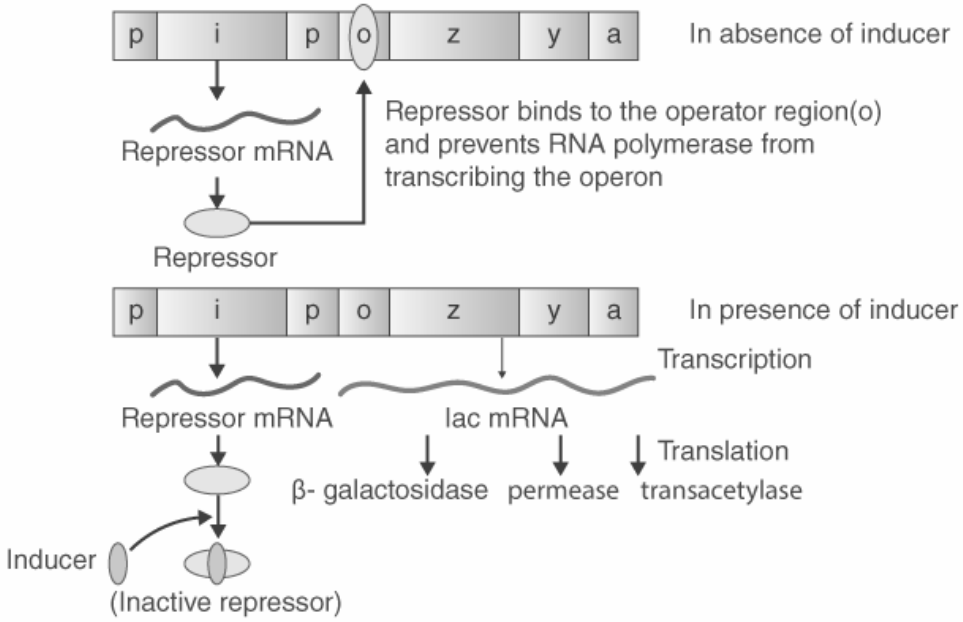
I. Regulation of Gene Expression the basics

- gene regulation can take place at various steps of gene expression which includes the following:
    2. **Replication level** – Any error in copying the DNA may result in an altered expression.
    3. **Transcriptional level** – During transcription, any error in the polymerization may again lead to a change in expression of the gene.
    4. **Post-transcriptional level** – During the post-transcriptional modification i.e., RNA splicing, there may be some changes.
    5. **Translational level** – During translation, if there is an error in the attachment of mRNA to the tRNA molecules, there may arise some changes.

Gene Regulation - Prokaryotes

II. Gene Regulation in Prokaryotes

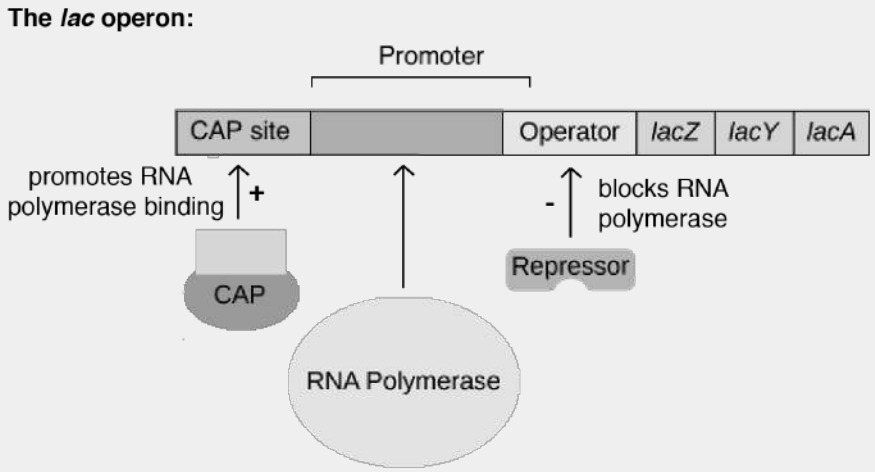
- **Gene regulation in prokaryotes is** most extensively observed at the initiation of transcription.
- **The gene expression during transcription** initiation is affected by regulation.
- **The regulation** usually takes place in the **expression of the RNA polymerase** at the **promoter site.**
- This **affects the accessory proteins** which **bind** to the **recognition sites.**
- These accessory proteins can regulate the promoter site in two ways:
    1. **Positive regulation** by **inducer**
    2. **Negative regulation** by **repressors**



Gene Regulation in Prokaryotes Continued

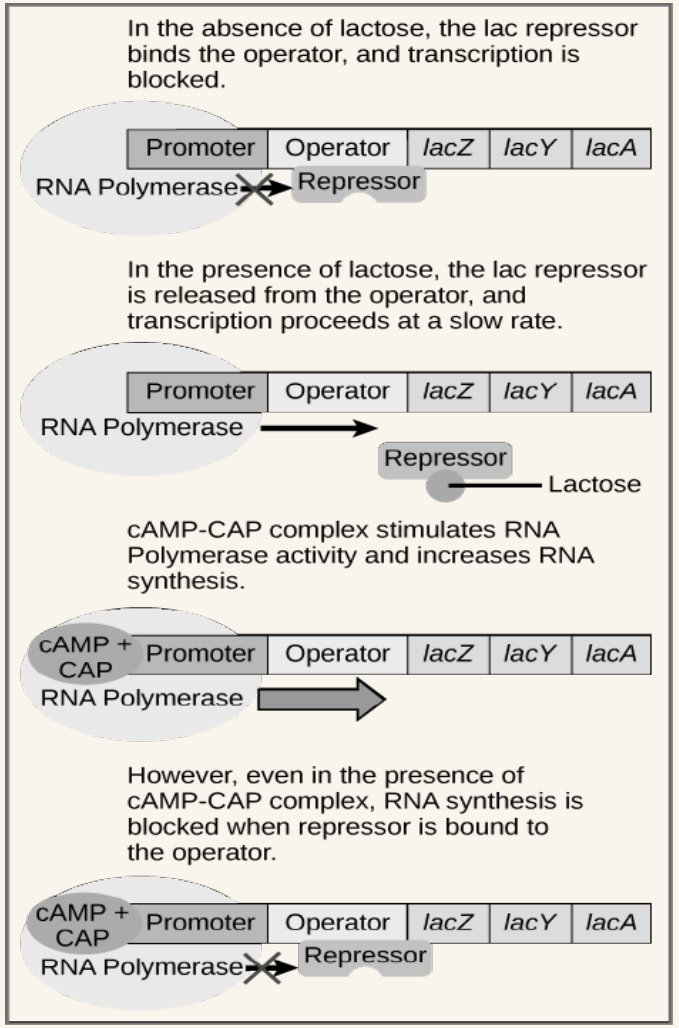
- In **Operons**, the **operator** is situated right next to the **promoter** where the **regulator binds** to **control** its entire functioning.
- **Lac Operon**

"Lac operon is an operon or a group of genes with a single promoter that encode genes for the transport and metabolism of lactose in E.coli and other bacteria."



Lac Operon

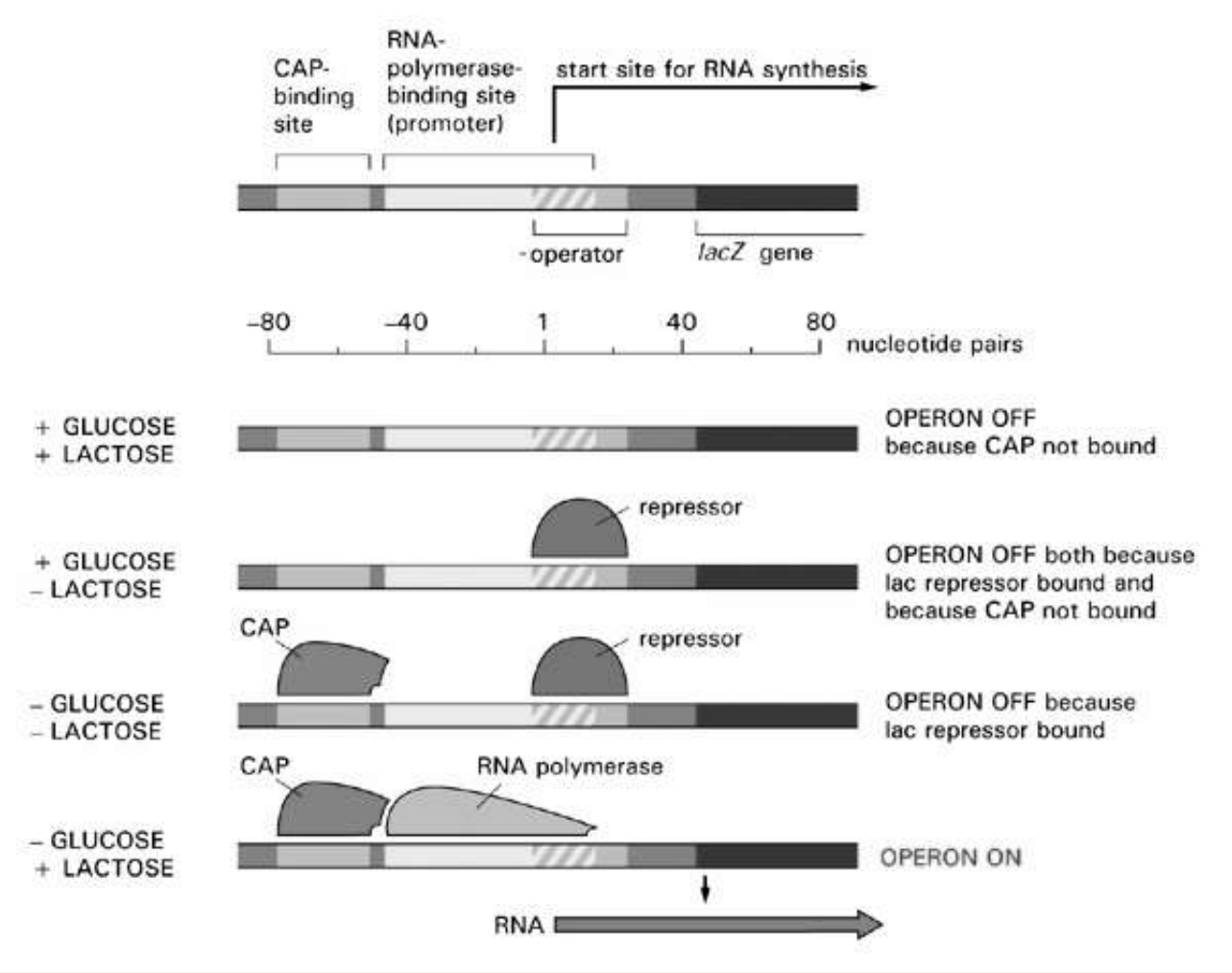
- **Lac Operon Concept**
  - **Gene regulation in prokaryotes** can be explained with the help of the **Lac Operon model.**
  - Here the **alteration** in **physiological** and **environmental** conditions can be observed leading to an alteration in expression in prokaryotes.
  - **The lac operon** consists of:
    a. **Regulatory gene i –** It codes for the repressor protein.
    b. **z gene –** It codes for beta-galactosidase which catalyzes the hydrolysis of lactose into glucose and galactose.
    c. **y gene –** It codes for permease which regulates the lactose permeability in the cell.
    d. **a gene –** It codes for transacetylase which assists the enzyme beta-galactosidase.

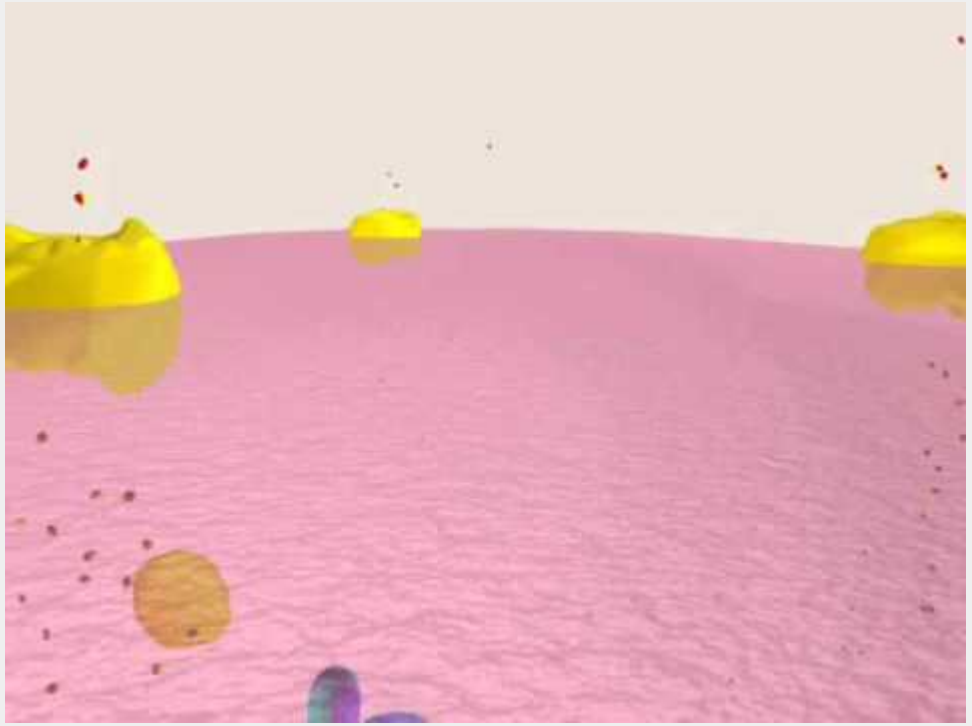


Lac Operon Continued

- **All these genes** help in **lactose metabolism.**
  1. **lactose** acts as an **inducer.**
     - **b) If lactose is provided** in the medium for the bacteria, the **regulatory gene** is **activated.**
     - c) The **inducer will bind** to the **repressor protein** and render it **inactive** which allows **transcription of the operon.**
     - d) The lac operon is **negatively regulated** in this case.
     - e) The **genes** are **expressed only** when **lactose** is **present** and **glucose** is **absent.**
     - f) The **operon** is **turned on and off** in response **to the glucose and lactose levels: catabolite activator protein and lac repressor.**
     - g) The **lac repressor blocks the transcription** of the operon**.** In the **presence of lactose,** it **stops acting** as a **repressor.**
     - **h) Catabolite activator protein activates** the **transcription** of the **operon, only** when **glucose levels are low.**

Lac Operon - A Summary



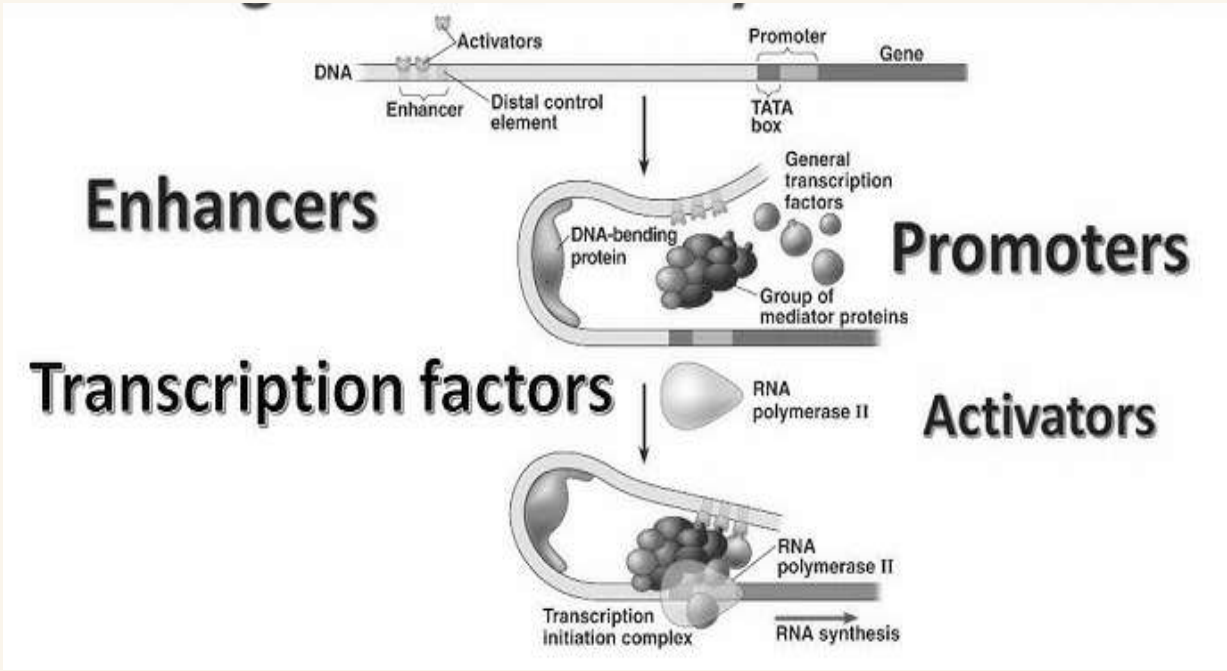


NDSU Virtual Cell Animations Project animation 'Lac Operon'

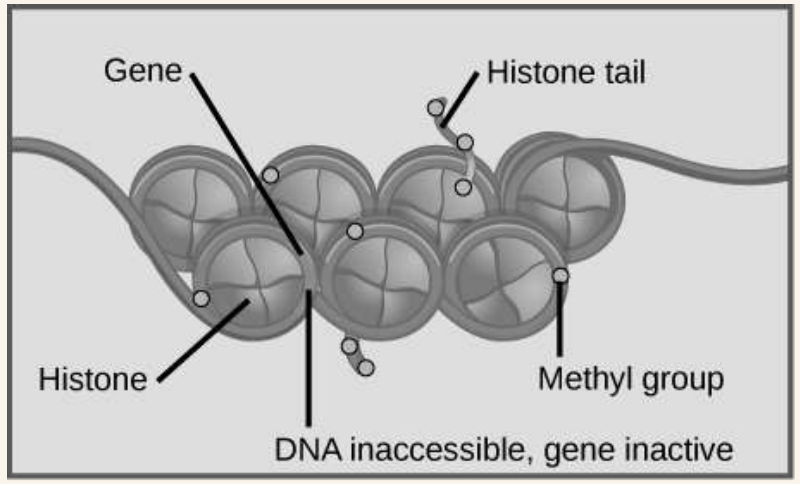
Gene Regulation in Eukaryotes

III. Gene Regulation in Eukaryotes

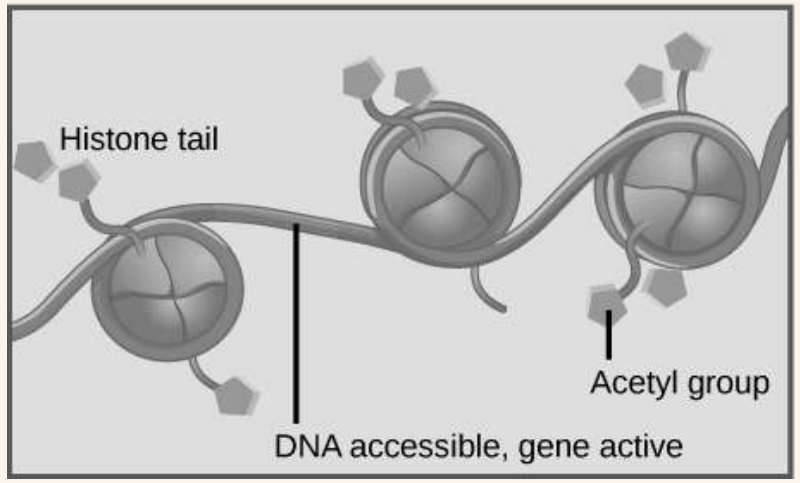
- Gene regulation in **eukaryotes** is **regulated** by transcriptional **inducers** and **repressors.**
- The **repressors bind** to specific DNA **sequences** and **inhibit transcription.**
- **In eukaryotes, transcription** involves several steps. It occurs in both **nucleus (transcription)** and **cytoplasm (translation).**
- **Eukaryotic cells also respond to environment**
  - ❑ **Multicellular:** allows for specialization and organization
  - ❑ Achieved through **differential gene expression**
  - ❑ Unlike in prokaryotes**, every level** is **regulated:**



Gene Regulation - The Mechanisms



Methylation of DNA and histones causes nucleosomes to pack tightly together. Transcription factors cannot bind the DNA, and genes are not expressed.



Histone acetylation results in loose packing of nucleo-somes. Transcription factors can bind the DNA and genes are expressed.

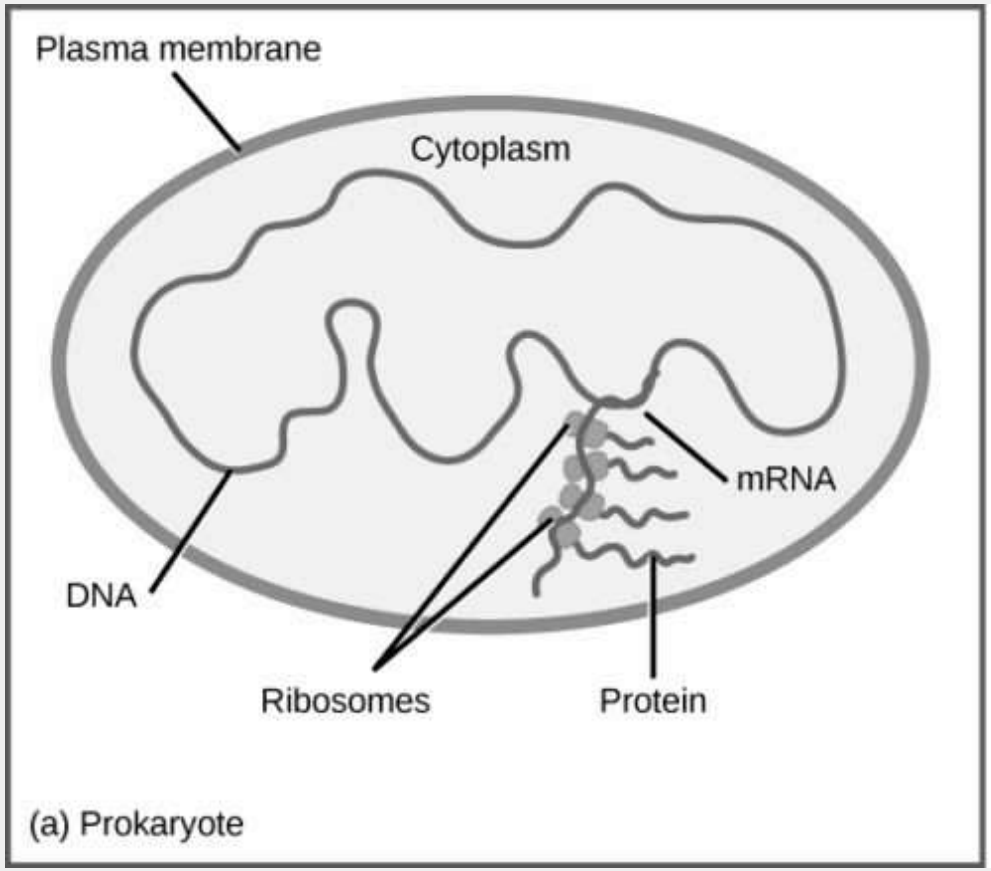
1. **Regulation of chromatin structure**
   - ➔ **Euchromatin**: loosely packed; genes can be active
   - ➔ **Heterochromatin**: densely packed; no gene expression
2. **Regulation of Transcription initiation**
   - ➔ Generally more complex than prokaryotes
   - ➔ Involves **DNA sequences** and **transcription factors-proteins that bind DNA**
   - ➔ **Promote** or **inhibit transcription** initiation
   - ➔ **Summary**:
     - **Dna packaging**: histone and/or DNA modification
     - DNA control elements

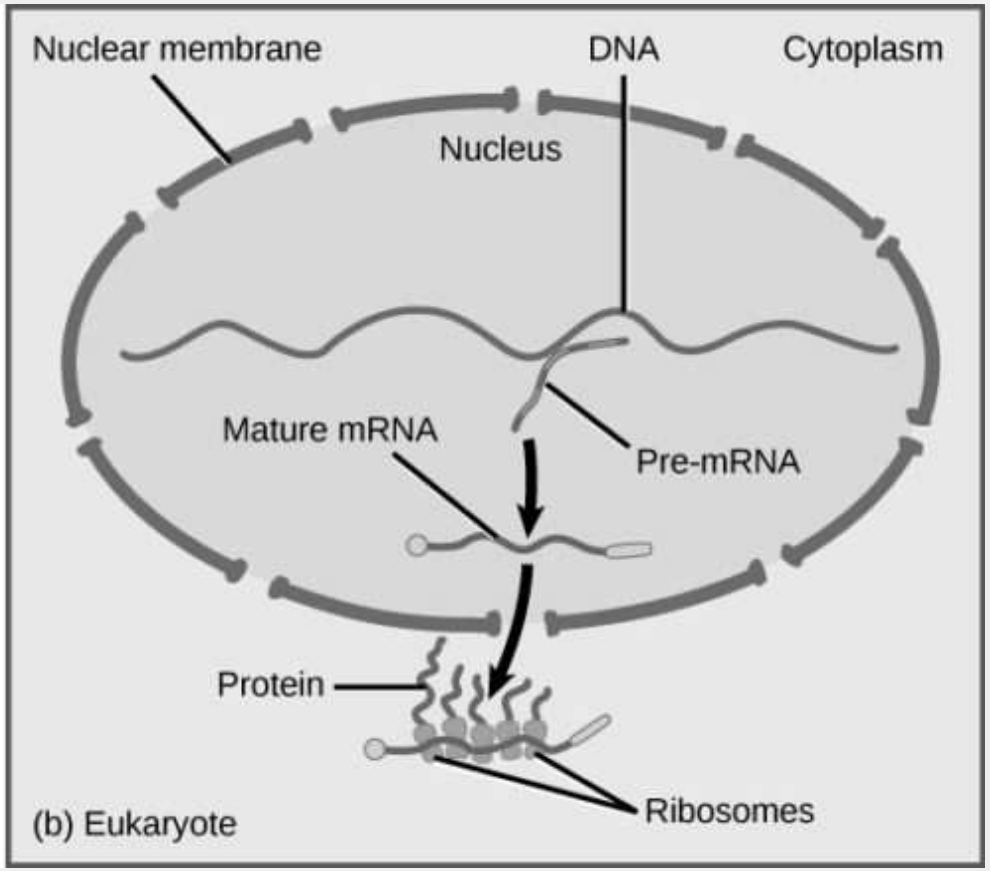
Mechanisms Continued

3. **Post-transcriptional regulation (manipulate RNA)**
    - ➔ **Length of poly-A tail** affects the level of expression
    - ➔ **Alternative splicing -** changes the way the exons are aligned
    - ➔ Different polypeptides from the same gene
4. **Post-translational regulation**
    - ➔ **Polypeptides** often processed -> final protein
    - ➔ Must be **folded correctly**
    - ➔ Often chemical modifications

- **Summary**
    - More complex than prokaryotes
    - Can involve: DNA packaging, transcription regulation, post-transcriptional regulation, post-translational regulation

Prokaryotic vs Eukaryotic Gene Regulation





Mutations - A Summary

III. Mutation:

- A gene mutation is a permanent change in the DNA sequence that makes up a gene.
- Mutations range in size from a single DNA building block (DNA base) to a large segment of a chromosome.
- Gene mutations occur in two ways:

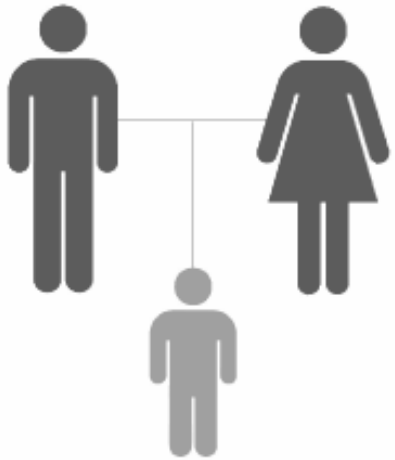
1. **Inherited from a parent**
    - ❏ **Mutations** that are **passed** from **parent** to **child** are called **hereditary mutations** or **germ-line mutations** (because they are **present in the egg and sperm cells**, which are also called **germ cells**).
    - ❏ This type of **mutation** is **present** throughout a **person's life** in **virtually** every **cell** in the body.
    - ❏ **Mutations** that occur **only** in an **egg** or **sperm** cell, or those that occur just after **fertilization**, are called new (**de novo**) mutations.
    - ❏ **De novo** mutations may explain **genetic disorders** in which an **affected** child has a **mutation** in every cell, but has **no family history of the disorder**.

Translation

1. **Acquired during a person's lifetime.**
   - ❑ **Acquired** (or **somatic**) mutations occur in the **DNA of individual cells** at some time during a person's life.
     - ➔ 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 **S-Phase of interphase** in cell division.
     - ➔ **Acquired** mutations in **somatic** cells (cells other than sperm and egg cells) **cannot** be passed on to the next generation.
2. **Mutations may also occur in a single cell within an early embryo**.
   - ❑ As all the **cells divide during growth and development**, the individual will have some cells **with** the **mutation** and some cells **without** the **genetic change**.
   - ❑ This situation is called **mosaicism**.
   - ❑ Some genetic changes are very rare; others **are common** in the population.
3. Genetic changes that occur in **more than 1 percent** of the population are called **polymorphisms**.
   - They are **common enough to be considered a normal** variation in the DNA.
   - **Polymorphisms** are responsible for many of the normal differences between people such as **eye color**, **hair color**, and **blood type**.
   - Although many **polymorphisms** have **no negative effects** on a person's health, some of these variations **may influence the risk of developing certain disorders**.

Inherited vs Acquired Mutations

GERMLINE MUTATION



- Inherited "germline" mutation
- ~10% of prostate cancer
- Genetic testing assesses one's risk for prostate cancer

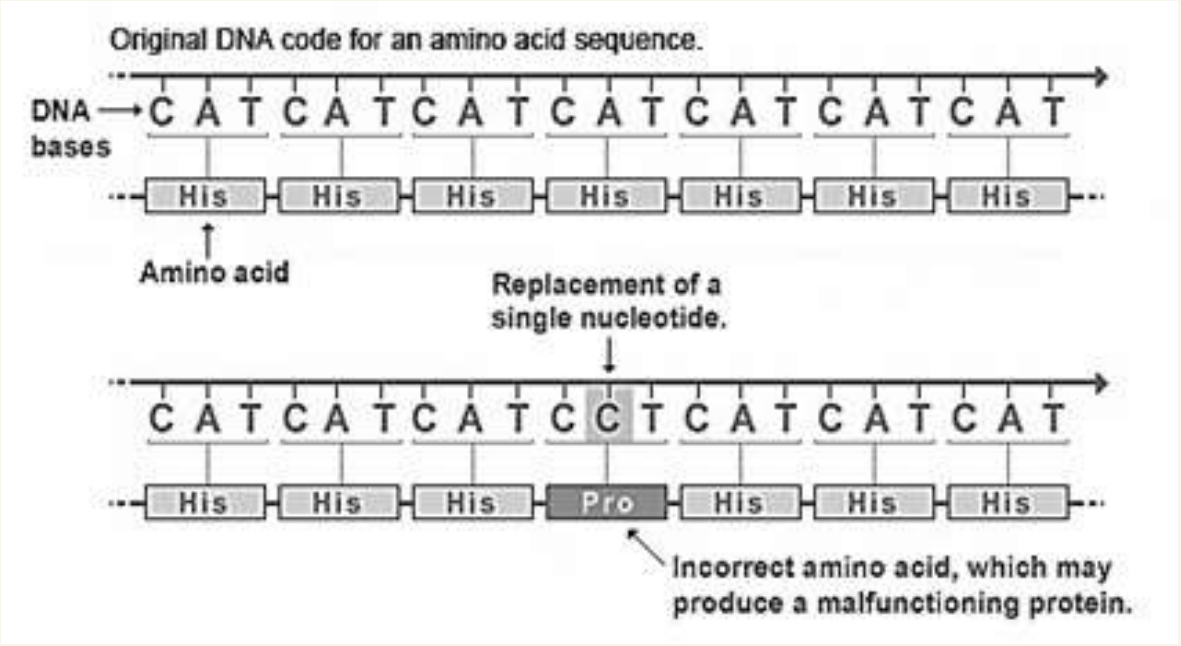
vs.

SOMATIC MUTATION

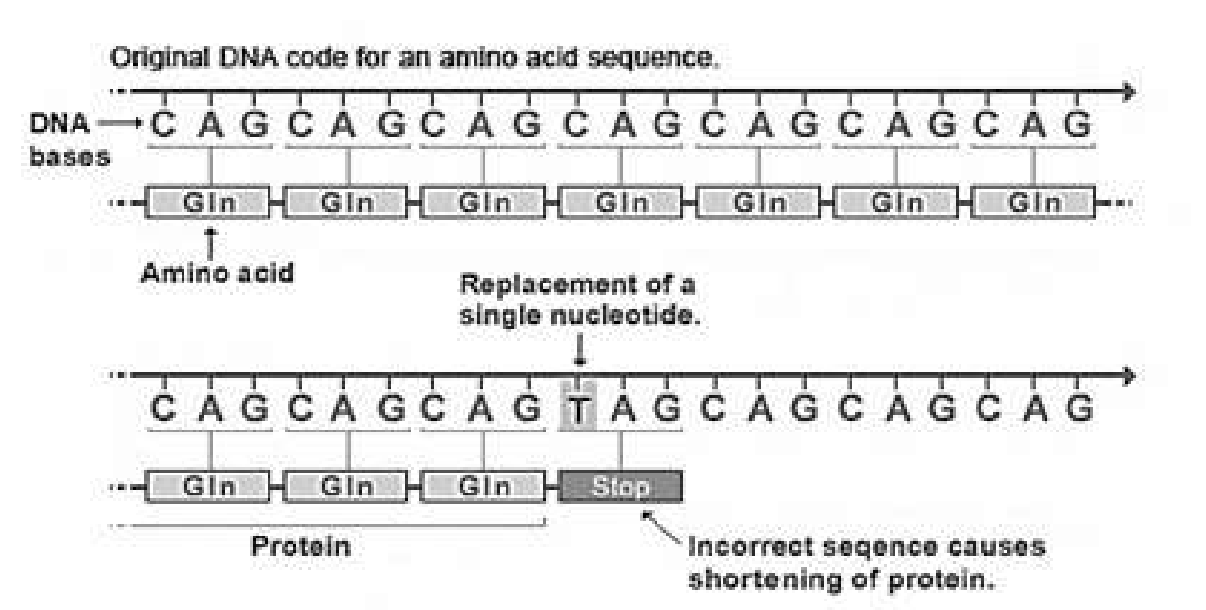
- DNA mutation not passed on to child
- ~90% of prostate cancer
- Genomic testing examines genes and helps predict prostate cancer behavior

Mutation Types - Substitution

- **Types of Mutations:**
  1. **Substitution (Missense) mutation**
     - ❑ This type of **mutation** is a **change** in **one DNA base pair** that results in the **substitution** of **one amino acid for another** in the **protein** made by a **gene**.



Mutation Types - Termination

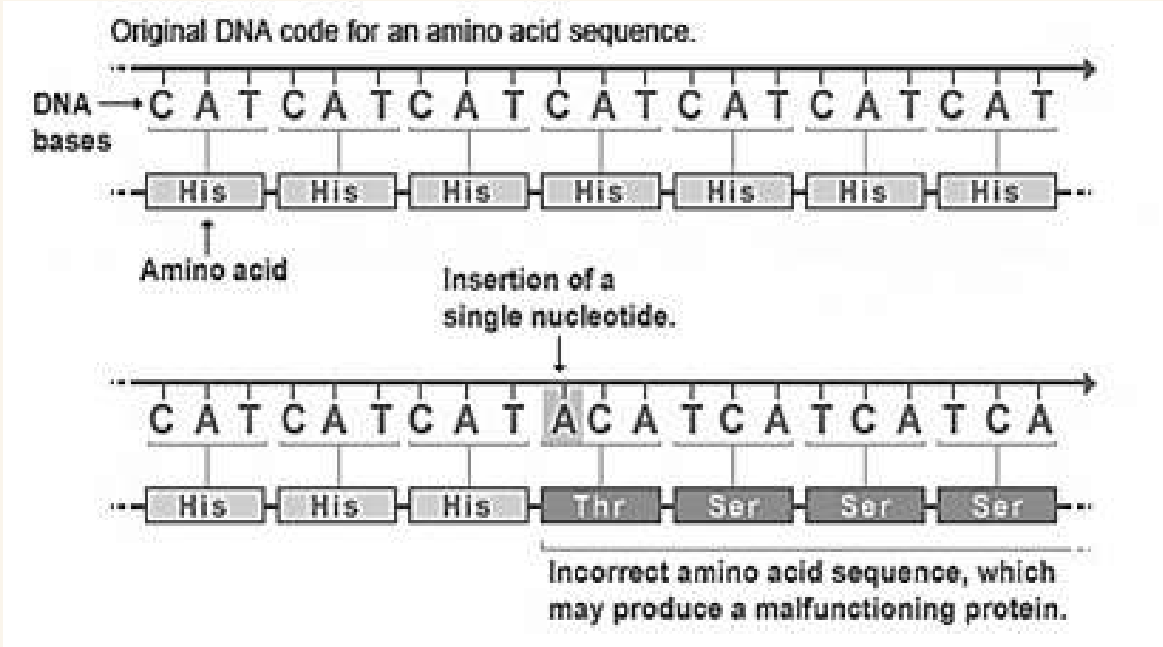


2. Termination (Nonsense) mutation

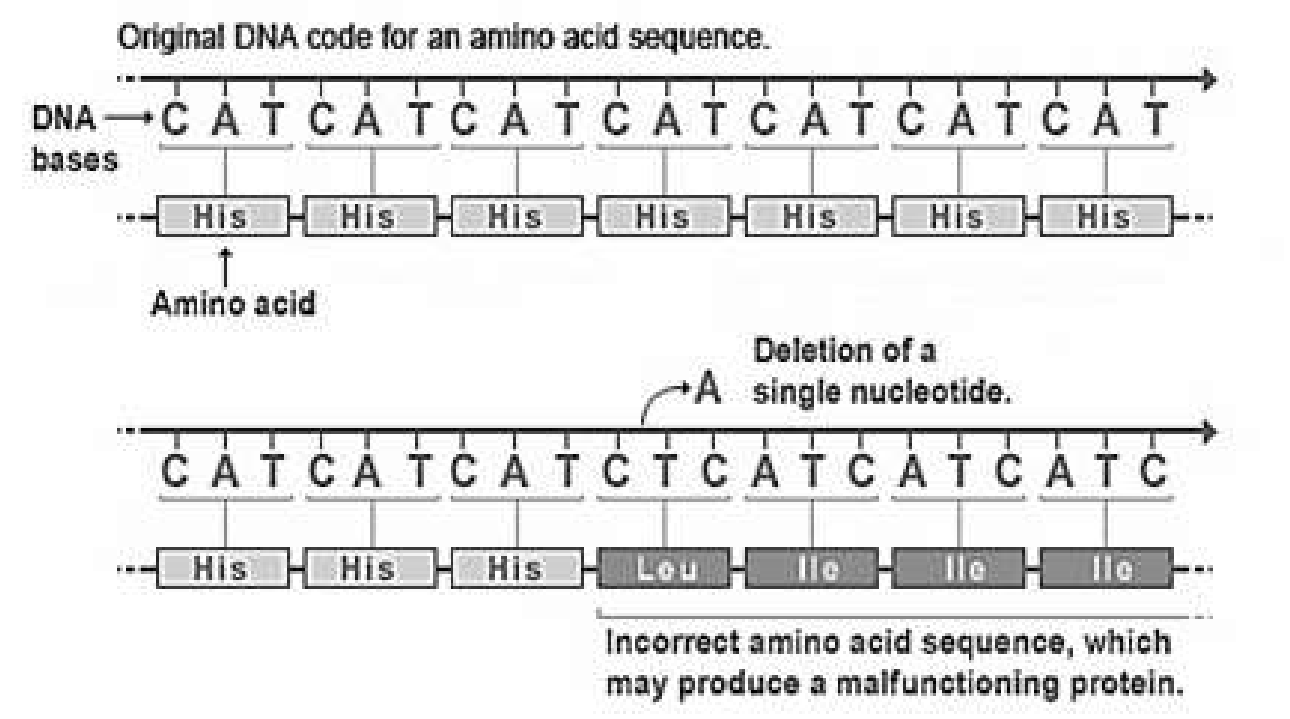
- A **nonsense mutation** is also a **change** in **one DNA base pair.**
- Instead of substituting one amino acid for another, however, the altered DNA sequence **prematurely signals the cell to stop** building (making a stop codon) a protein.
- This type of mutation results in a **shortened protein that may function improperly or not at all**.

Mutation Types - Insertion

3. **Insertion**
   - ❑ An **insertion changes the number of DNA bases** in a gene by **adding a piece of DNA**. As a result, the protein made by the **gene may not function properly**.



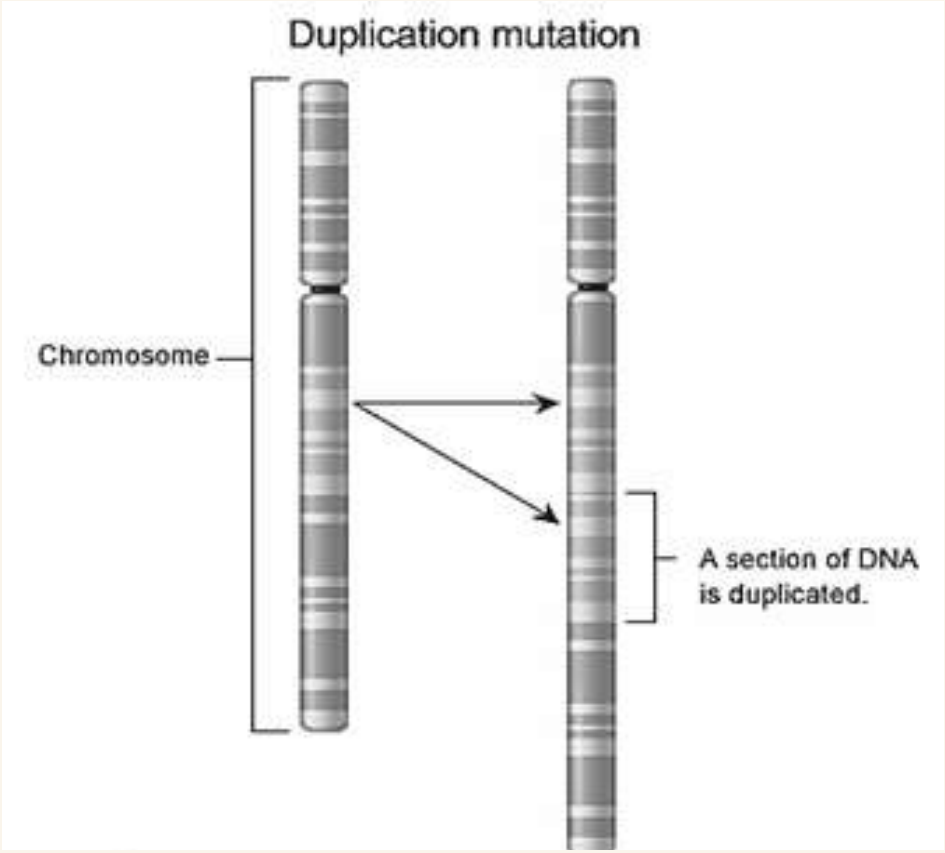
Mutation Types - Deletion



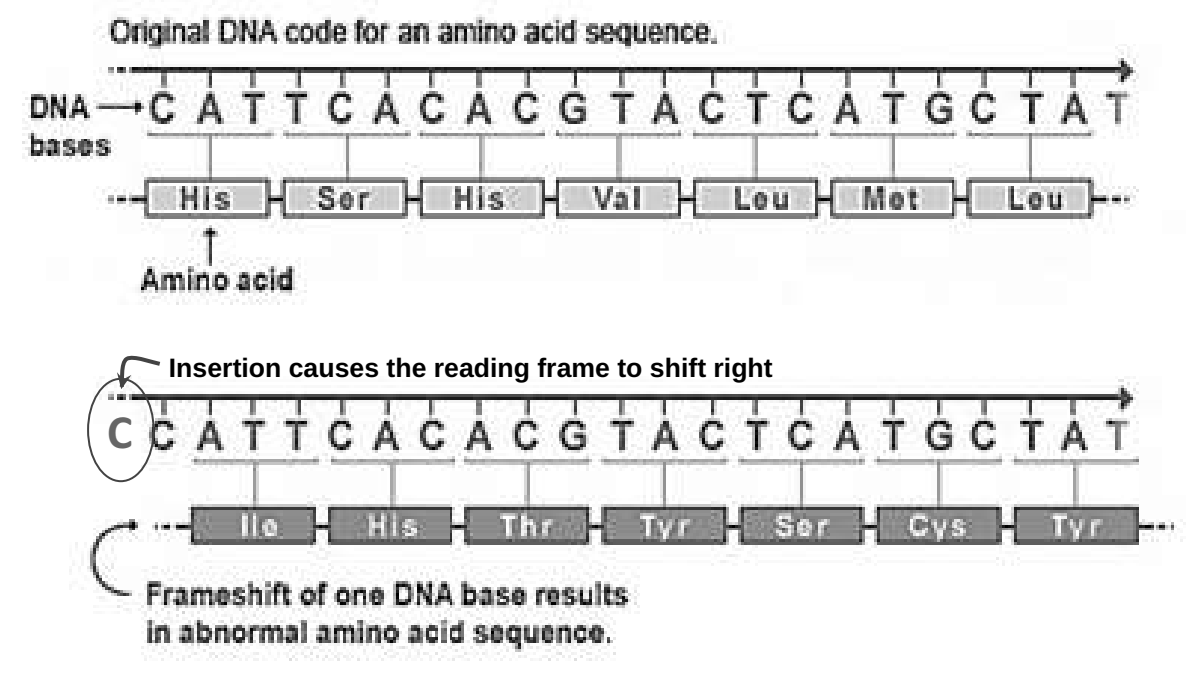
4. **Deletion**
   - A **deletion** changes the number of DNA bases by **removing** a **piece of DNA**. Small deletions may **remove one or a few base pairs** within a gene, while **larger deletions can remove an entire gene** or several neighboring genes. The **deleted DNA may alter the function of the resulting protein**(s).

Mutation Types - Duplication

5. **Duplication**
   - A **duplication** consists of a **piece of DNA that is abnormally copied one or more times**. This type of mutation **may alter the function** of the resulting protein.



Mutation Types - Frame Shift



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

Thank you!

Do you have any questions?

instructor@email.com
xxx-xxx-xxxx