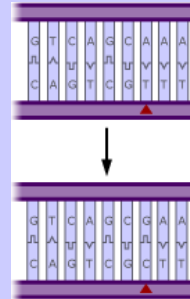




Dept. of Computer Science and Engineering
University of Rajshahi
www.ru.ac.bd

Dr. Shamim Ahmad

Mutation



Substitution

CTGGAG
CTGGCG

A substitution is a mutation that exchanges one base for another (i.e., a change in a single "chemical letter" such as switching an A to a G). Such a substitution could:

- **Change a codon to one that encodes a different amino acid**
- Small change in the protein produced
- Sickle cell anemia
- Substitution in the beta-hemoglobin gene
- Alters a single amino acid in the protein produced.

Substitution

change a codon to one that encodes the same amino acid

- No change in the protein produced
- Silent mutations.

change an amino-acid-coding codon to a single "stop" codon

- Incomplete protein
- Serious effects since the incomplete protein
- Probably won't function.

Insertion

CTGGAG
CTGG**T**GAG
Insertions are mutations in which **extra base pairs** are inserted into a new place in the DNA.

Deletion

CT**T**GAG
CTAG
Deletions are mutations in which a **section of DNA is lost, or deleted.**

Frameshift

~~X~~he fat cat sat
hef atc ats at
Insertions and **Deletions** can alter a gene

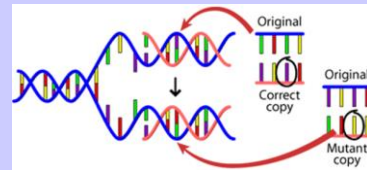
- Is message is no longer correctly parsed.
- These changes are called frameshifts.

The causes of mutations

DNA fails to copy accurately

Most of the mutations

- Matter to evolution
- "Naturally-occurring"
- The copy is not quite perfect.



The causes of mutations

External influences can create mutations

- Exposure to specific chemicals or radiation.
- These agents cause the DNA to break down.
- This is not necessarily unnatural
 - DNA breaks down
- Cell repairs the DNA
- It might not do a perfect job of the repair
- DNA slightly different than the original DNA



The effects of mutations

Somatic mutations

- Occurs in non-reproductive cells
- Won't be passed onto offspring.
- The golden color on half of this Red Delicious apple
- Its seeds will not carry the mutation
- mutations in our skin, muscle, or live



The effects of mutations

Germ line mutations

- The only mutations that matter to large-scale evolution
- Those that can be passed on to offspring
- These occur in reproductive cells

The effects of mutations

The effect of Germ line mutations

No change occurs in phenotype

- Mutation occurs in a stretch of DNA with no function
- Mutation occurs in a protein-coding region
 - Ends up not affecting the amino acid sequence of the protein.

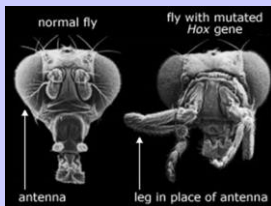
Small change occurs in phenotype

- A single mutation caused this cat's ears to curl backwards slightly

Big change occurs in phenotype

- DDT resistance in insects
- Mutations that cause the death of an organism

Mutations to control genes can transform one body part into another.



A case study of the effects of mutation

Sickle cell anemia

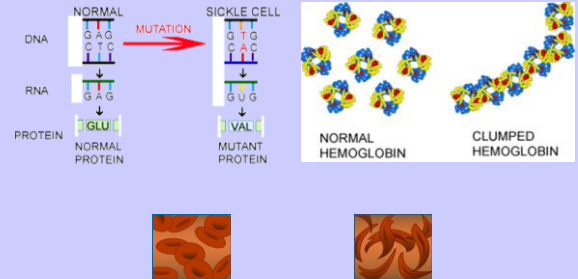
- Symptoms: Pain and anemia.
- Hemoglobin
 - Protein that carries oxygen in red blood cells.
- People with **two copies** of the sickle cell gene
 - Disease
- People with **only one copy** of the sickle cell gene
 - No disease
 - But may pass the gene on to their children.

A case study of the effects of mutation Sickle cell anemia

There are positive effects at the whole organism level

- Resistant to malaria
 - Parasites that cause this disease
 - Killed inside sickle-shaped blood cells.

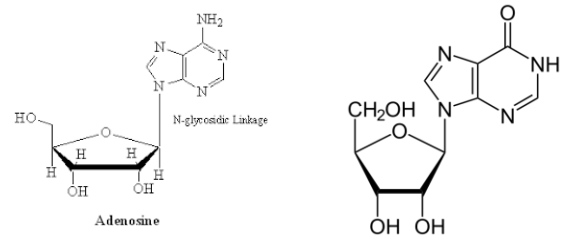
A case study of the effects of mutation: Sickle cell anemia.



Mutations are random

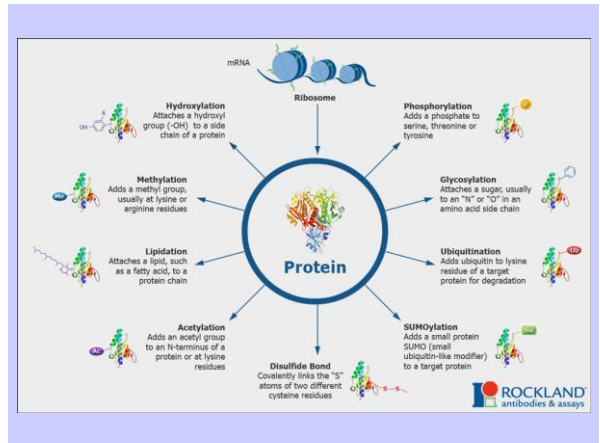
- Mutations can be beneficial, neutral, or harmful for the organism,
 - but mutations do not "try" to supply what the organism "needs."
- Factors in the environment may influence the rate of mutation
 - but are not generally thought to influence the direction of mutation.
- For example, exposure to harmful chemicals may increase the mutation rate,
 - but will not cause more mutations that make the organism resistant to those chemicals.

RAN editing: Inosine

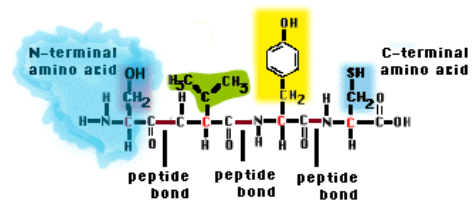
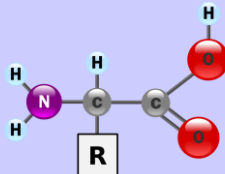
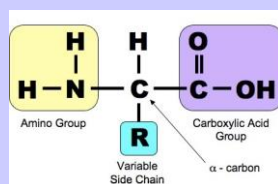


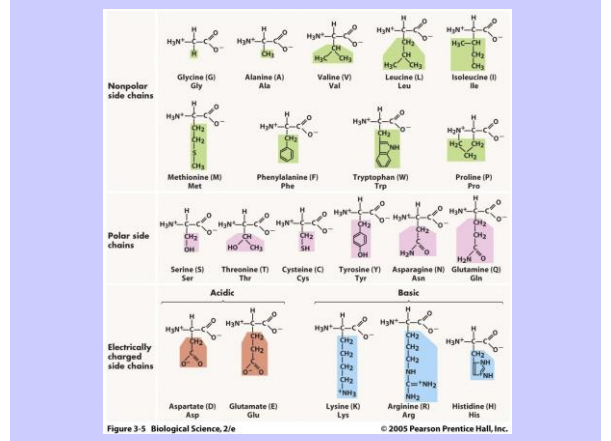
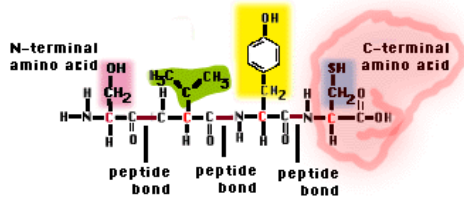
Post-translational modification (PTM)

- Refers to the covalent and generally enzymatic **modification of proteins**
- Post-translational modifications can occur on the **amino acid side chains** or at the **protein's C- or N- termini**.
- They can extend the chemical structure of the 20 standard **amino acids** by modifying an existing **functional group** or introducing a new one

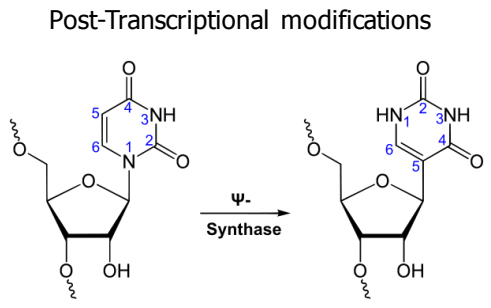


functional groups
Amine (-NH₂) and
Carboxyl (-COOH)

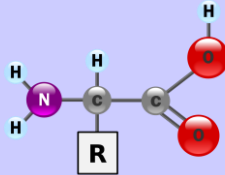
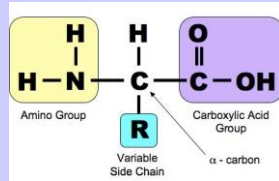




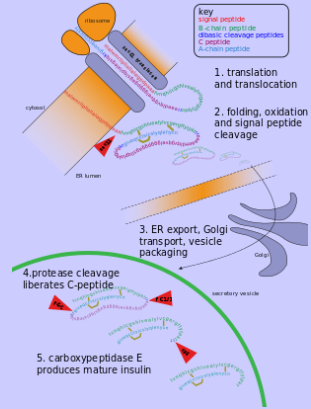
Post-Transcriptional modifications in RNA are not fully understood



functional groups Amine (-NH₂) and Carboxyl (-COOH)



Post-translational modification (PTM)



Definitions of the components:

1

2
3
4
5

1. **Post-translational modification (PTM):** The chemical modifications that take place at certain amino acid residues after the protein is synthesized by translation are known as post-translational modifications. These are essential for normal functioning of the protein. Some of the most commonly observed PTMs include:

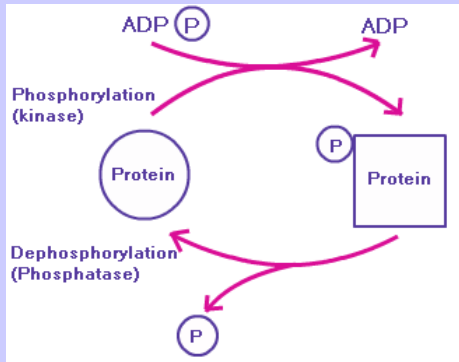
Definitions of the components:

1

2
3
4
5

Phosphorylation: The process by which a **phosphate group is attached to**

- **Certain amino** acid side chains in the protein
- Most commonly serine
- **Threonine and Tyrosine.**
- Addition of a phosphate group
- Convert a previously uncharged pocket of protein into a negatively charged
- Hydrophilic protein thereby inducing conformational changes in the protein



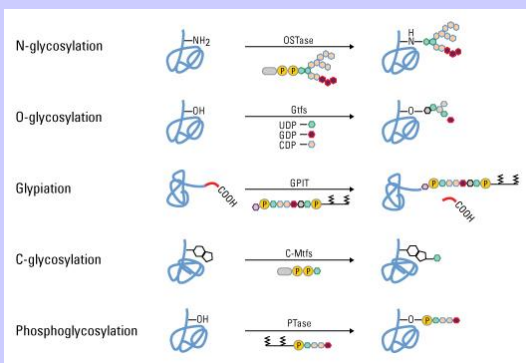
1 **Glycosylation:** The attachment of **sugar moieties** to **nitrogen or oxygen atoms** present in the side chains of amino acids like

- **Asparagine**
- **Serine**
- **Threonine.**

2 **N-linked glycosylation** occurs in the amide nitrogen of asparagine

3 **O-linked glycosylation** occurs on the oxygen atom of serine or threonine.

- 4**
- Critical roles in
 - Protein sorting
 - Immune recognition
 - Receptor binding
 - Inflammation
 - Pathogenicity.
- 5**



1 **Definitions of the components:**

2 **Acylation:** The process by which an **acyl group** is linked to the side chain of amino acids like

- **Asparagine**
- **Glutamine**
- **Lysine.**

3 **d) Alkylation:** Addition of **alkyl groups**, most commonly a **methyl group** to amino acids. Other longer chain alkyl groups may also be attached in some cases.

- 4**
- **Lysine**
 - **Arginine**
- 5**

1 Definitions of the components:

1

2

Acetylation: acetylation refers to addition of acetyl group in a protein. It is involved in several biological functions

- Protein stability
- Location
- Synthesis
- Apoptosis
- Cancer
- DNA stability

3

4

5

1 Definitions of the components:

1

2

Hydroxylation: This process adds a **hydroxyl group (-OH)** to the proteins.

- It is catalyzed by enzymes termed as 'hydroxylases'
- Aids in converting hydrophobic or lipophilic compounds into hydrophilic compounds

3

4

5

1 Definitions of the components:

1

2

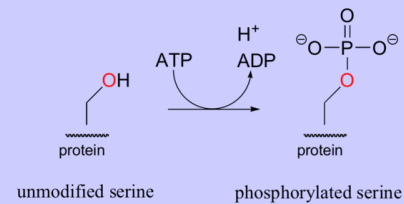
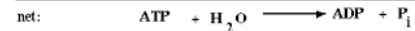
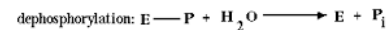
Methylation

Methylation refers to addition of a **methyl group** to

- Lysine
- Arginine residue
- Arginine can be methylated once or twice
- Lysine can be methylated once, twice, or thrice..
- Methylation can lead to **gene activation or repression** based on the residue that is methylated.

4

5



Carbonylation

- it is a type of protein oxidation
- Promoted by reactive oxygen species
- Lysine
- Arginine
- Proline
- Threonine



Prion

- properly **folded proteins** to convert into the **misfolded prion form**.
- In this way, the prion acts as a **template to guide the misfolding** of more proteins into prion form