Programme : **Bachelor of Science (Second Year)**
Subject : **Microbiology**
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Course Title : **Molecular Biology**
Unit 4 : **Translation**
Module Name : **Post Translational Processing and Modification: Part 1**

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Notes

Introduction of Post Translational Processing and Modification (PTMs)

It refer to any alteration in the amino acid sequence of the protein after its synthesis. It may involve the modification of the amino acid side chain, terminal amino or carboxyl group by means of covalent or enzymatic means following protein biosynthesis. Generally, these modifications influence the structure, stability, activity, cellular localization or substrate specificity of the protein. Post translational modification provides complexity to proteome for diverse function with limited number of genes. Post Translational Modifications can be defined as: Covalent or generally enzymatic modifications of proteins during or after the synthesis of the proteins.

Location of Post Translational Processing

Post-translational modifications (PTMs) mainly occur in the endoplasmic reticulum of the cell but sometimes continue in the Golgi bodies as well.

Why PTM is necessary???

Stability of Protein, Biochemical Activity (Activity Regulation), Protein Targeting (Protein Localization), Protein Signalling (Protein-Protein Interaction cascade amplification).

Types Of Post Translational Processing and Modifications

Post translational modifications or PTMs are involved in modifying the protein structure after they have been translated according to information on the mRNA. The post translational modifications can be enzymatic or covalent. In the human body these PTMs increases the diversity and accuracy of proteins.

PTMs can be categorized as:

- ❑ **Trimming Covalent Attachments Protein Folding Protein Degradation**
- Trimming: Insulin is synthesized in the cells and it is in inactive form that it is can't perform it's function.
- For the proper functioning of insulin its post translational modifications occurs that have involve the removal of the part of protein to convert it into a three dimensional and fully active form
- ❑ **Covalent Attachments**
- It refers to the addition or the transfer of the polypeptide chain that acts as an acceptor region.
- In this way, proteins are modified for the diversity of function.
- It includes: Phosphorylation Glycosylation Sulfation Methylation Hydroxylation

Post Translational Processing and Modification

- ✓ After synthesis is completed, proteins can be modified by various methods such as
- ❑ Proteolysis
- ❑ Phosphorylation
- ❑ Glycosylation
- ❑ Sulfation
- ❑ Methylation
- ❑ ADP ribosylation

- ❑ Hydroxylation
- ❑ Addition of other groups
- ❑ SUMOylation
- ❑ Disulfide bond formation
- ❑ Lipidylation
- ❑ Acetylation
- ❑ Prenylation etc.

Proteolysis

As the newly synthesized protein is released in the lumen of the ER, signal peptidases cleave peptide sequence. Apart from signal peptide, some polypeptide sequence of the protein is also cleaved resulting in the final sequence. Proteolytic cleavage of polypeptide chains after synthesis is common occurrence with every class of proteins. Proteolytic enzymes in digestive tract produced are in inactive forms known as zymogens. After selective Proteolysis , these enzymes are converted into active forms.

Example: Proteolytic cleavage is the conversion of preproinsulin into insulin. 1st, removal of the signal peptide from the newly synthesized peptide preproinsulin generates the proinsulin precusor molecule. Finally removal of C- peptide moiety of proinsulin gives insulin. Post translational modifications ensure proper function which involves the removal of the part of protein to convert it into a three dimensional and fully active form.

Phosphoryalation

It is the addition of one or more phosphate groups to the protein. Post Translational Phosphorylation is one of the most common protein modifications that occur in animal cells.Majority of phosphorylation occurs as a mechanism to regulate the biological activity of a protein. In animal cells Serine, tyrosine and thereonine are the amino acids that subjected to the phosphorylation.

Glycosylation

It is the addition of carbohydrate molecules to the polypeptide chain and modifying it into glycoproteins. Many of the proteins that are destined to become a part of plasma membrane or to be secreted from the cell, have carbohydrate chains attached to the amide nitrogen of asparagine(N linked) or the hydroxyl groups of serine, threonine(O linked). N glycosylation occurs in ER and O glycosylation occurs in the golgi complex.

Sulfation

Sulfate modification takes place by the addition of sulphate molecules and these modifications of proteins occurs at tyrosine residues. Tyrosine sulfation accomplished via the activity of tyrosylproteinsulfotransferases (TPST) which are membrane associated enzymes of trans-Golgi network. There are two known TPSTs. TPST-1 and TPST-2. The universal phosphate donor is 3'-phosphoadenosyl- 5'-phosphosulphate (PSPA).

Methylation

The transfer of one-carbon methyl groups to nitrogen or oxygen to amino acid side chains increases the hydrophobicity of the protein and can neutralize a negative amino acid charge when bound to carboxylic acids. Methylation is mediated by methyltransferases and S-adenosyl methionine (SAM) is the primary methyl group donor.