Topic:

Post Translational Modifications

Contents:

Post Translational Modifications can be defined as:

Covalent or generally enzymatic modifications of proteins during or after the synthesis of the proteins.

Before understanding about it, first of all we must have information about the Translation.

Translation:

In Molecular Biology Translation refers to the formation of proteins from mRNA with the help of the ribosomes present in the cytoplasm of the cell in the case of prokaryotes while in eukaryotes translation is carried out at the membrane pf RER or in the cytosol. The mRNA decoded from DNA is migrated into the cytoplasm for the synthesis of proteins that then fold, acquire a tertiary conformation and perform their perspective functions.

Components required for Translation:

Amino Acids

tRNA

mRNA

Functionally components Ribosomes

Protein Factors

ATP and GTP required as energy sources.

Steps in Translation:

Initiation

Elongation

Termination

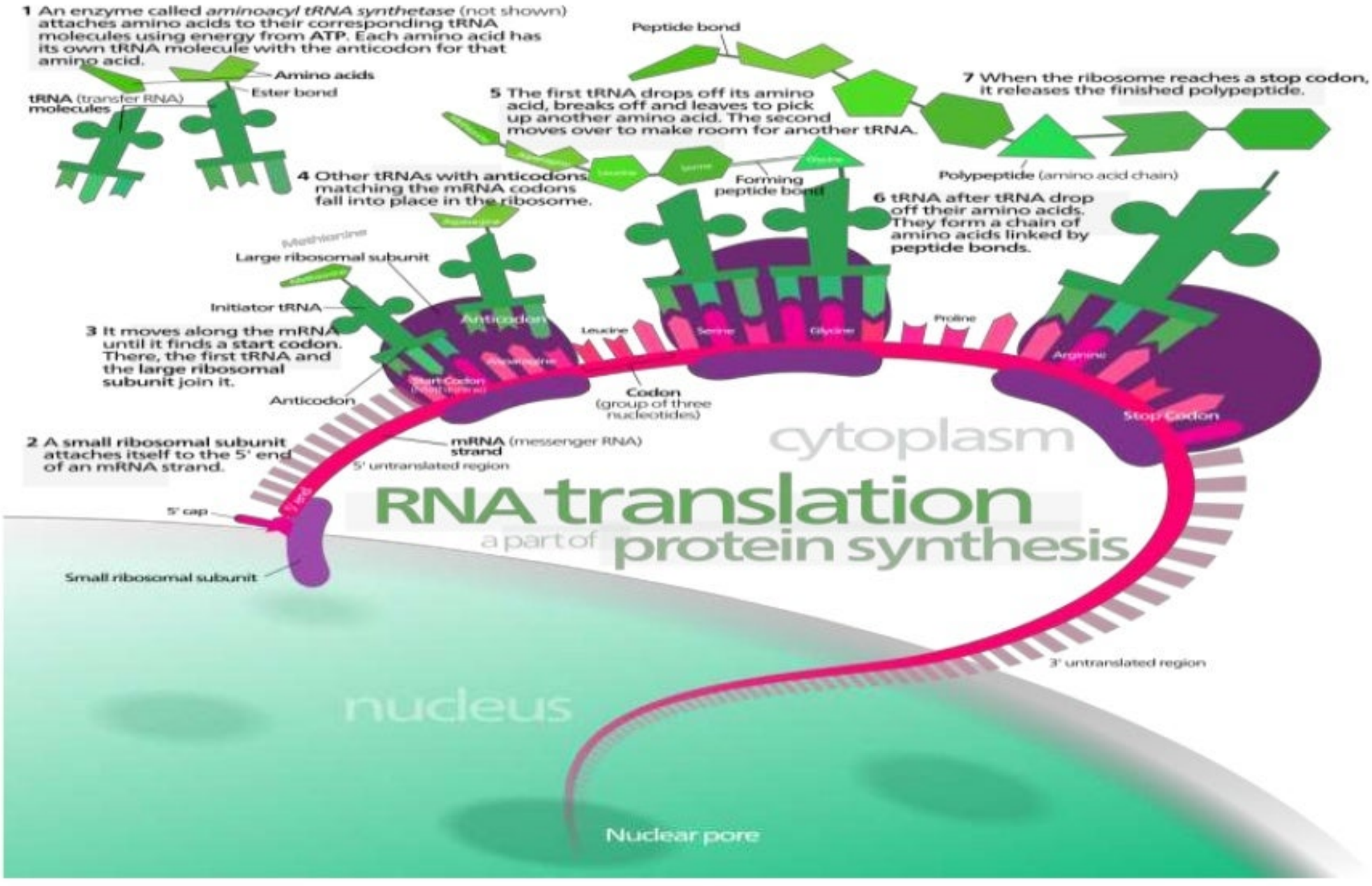


Fig showing the general mechanism of Translation:

Types Of Post Translational 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 modifiactions can be enzymatic or covalent.

In the human body these PTMs increases the diversity and accuracy of proteins.

Types Of PTMs:

PTMs can be catagorized as:

Trimming

Cavalent Attachments

Protein Folding

Protein Degradation

Trimming:

Insuline 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 insuline 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

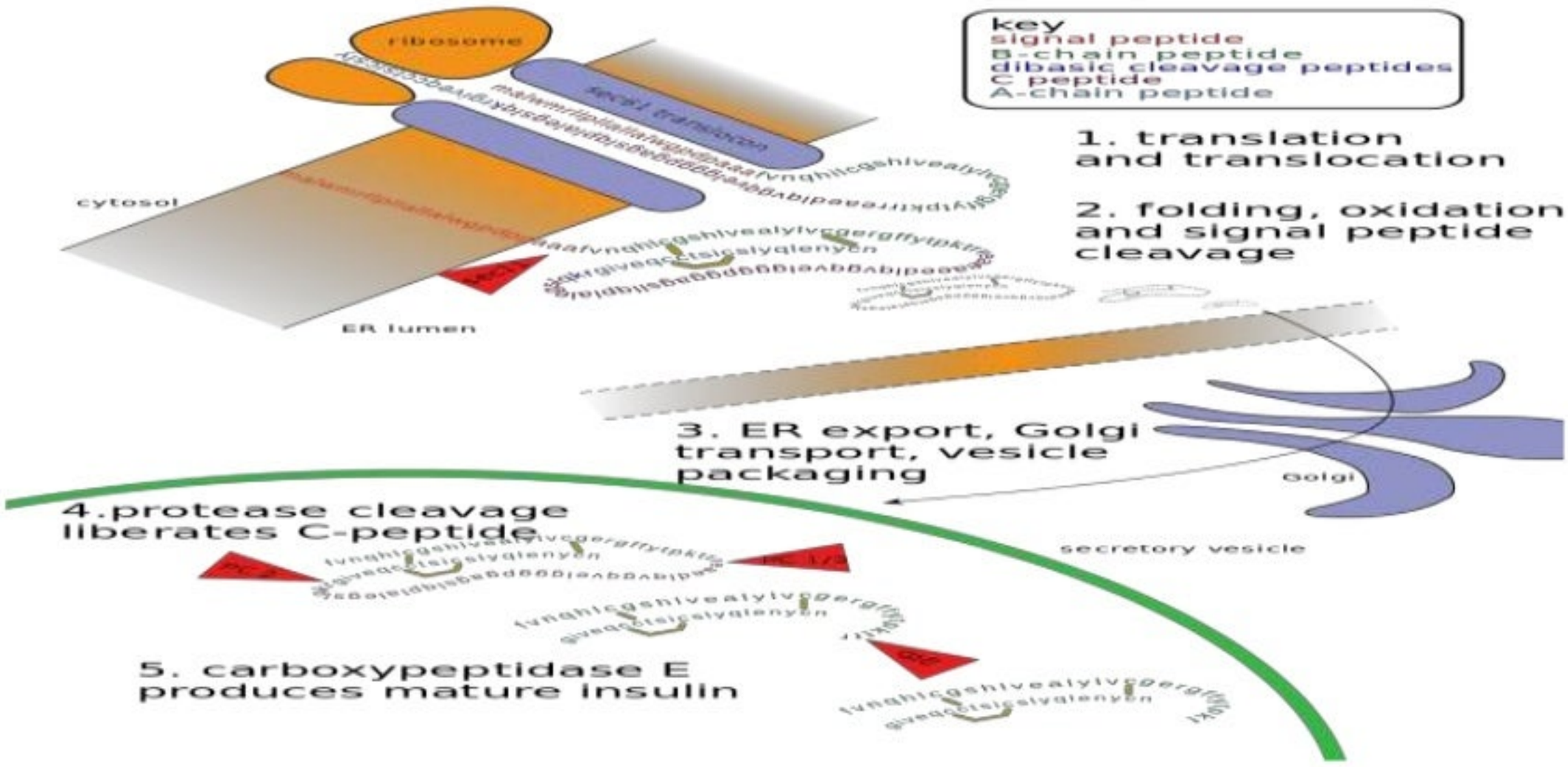


Fig showing the activation of insuline after PTM:

Covalent Attachments:

Covalent attachments 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

Phosphorylation:

Phosphoryalation 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. The vast majorirtis of phosphorylation occur as a mechanism to regulate the biological activity of a protein and as such are transient.

In animal cells Serine, tyrosine and thereonine are the amino acids that subjected to the phosphorylation.

Fig showing the phosphorylation of amino acids:

Glycosylation:

Glycosylation 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.

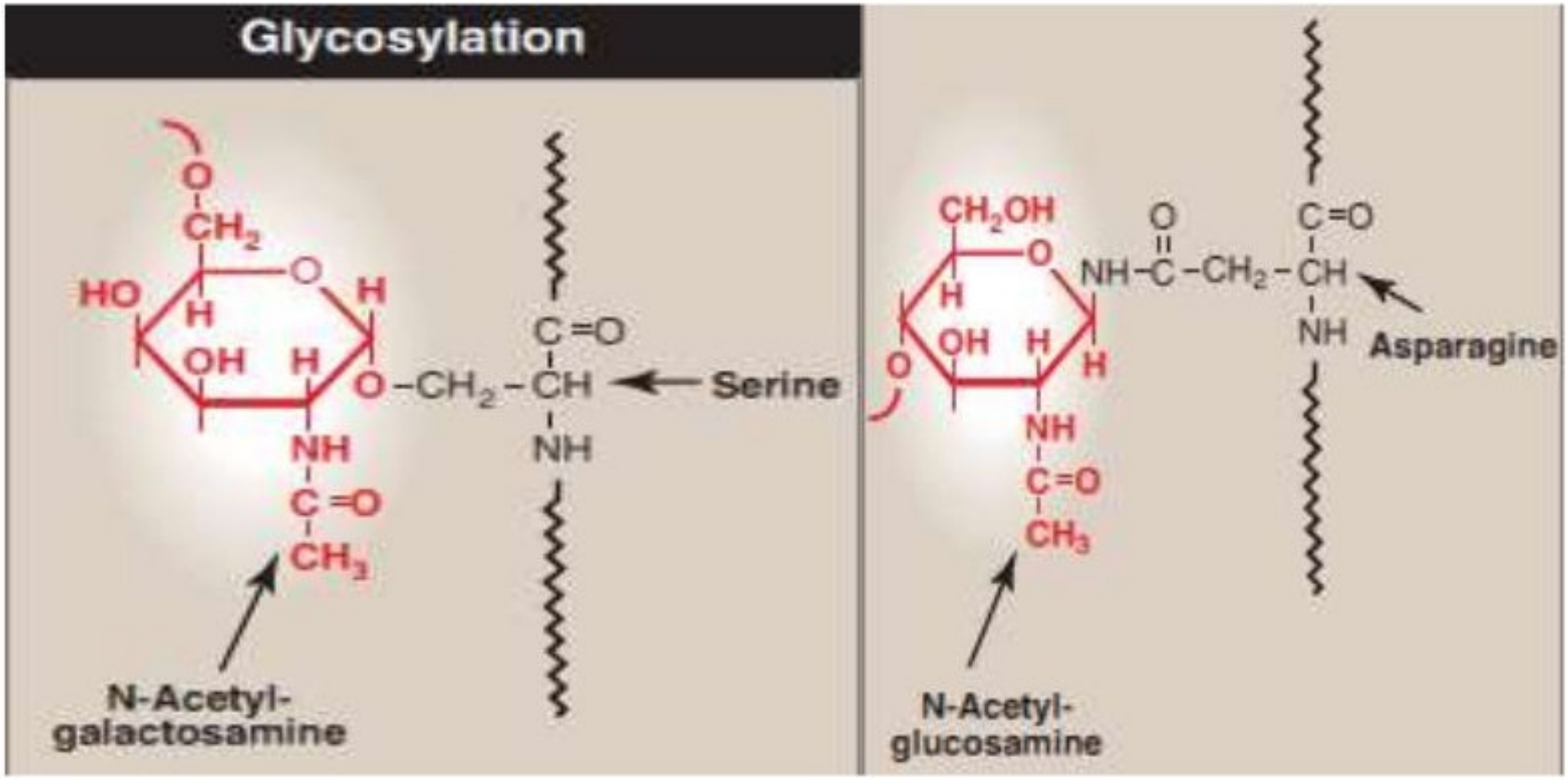


Fig showing the glycosylation of serine & Asparagin:

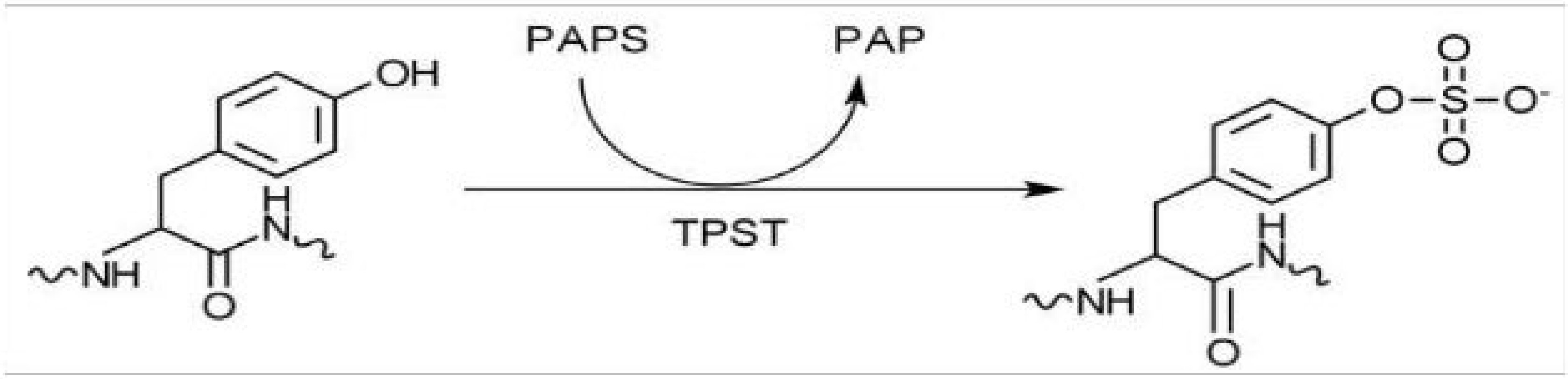
Sulfation:

Sulfate modidication 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

TPST-2

The universal phosphate donor is 3’-phosphoadenosyl-5’-phosphosulphate (PSPA).



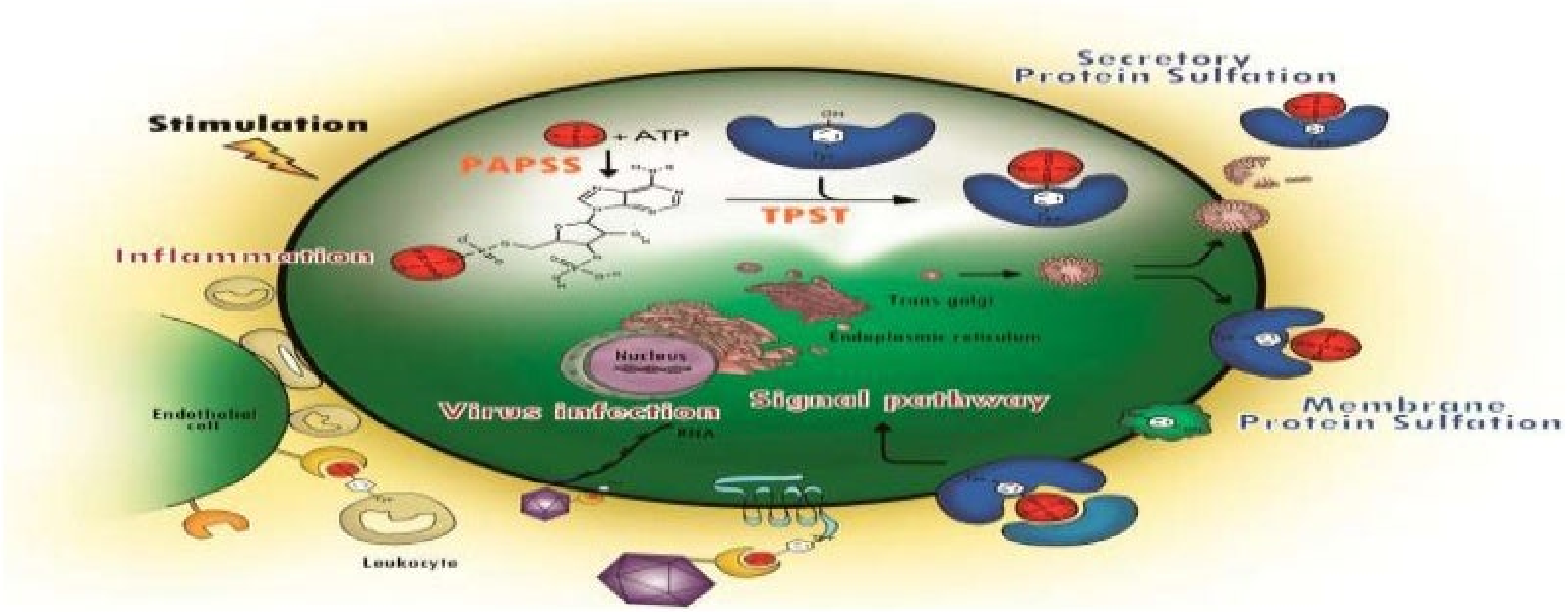


Fig showing the sulfation of tyrosine:

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.

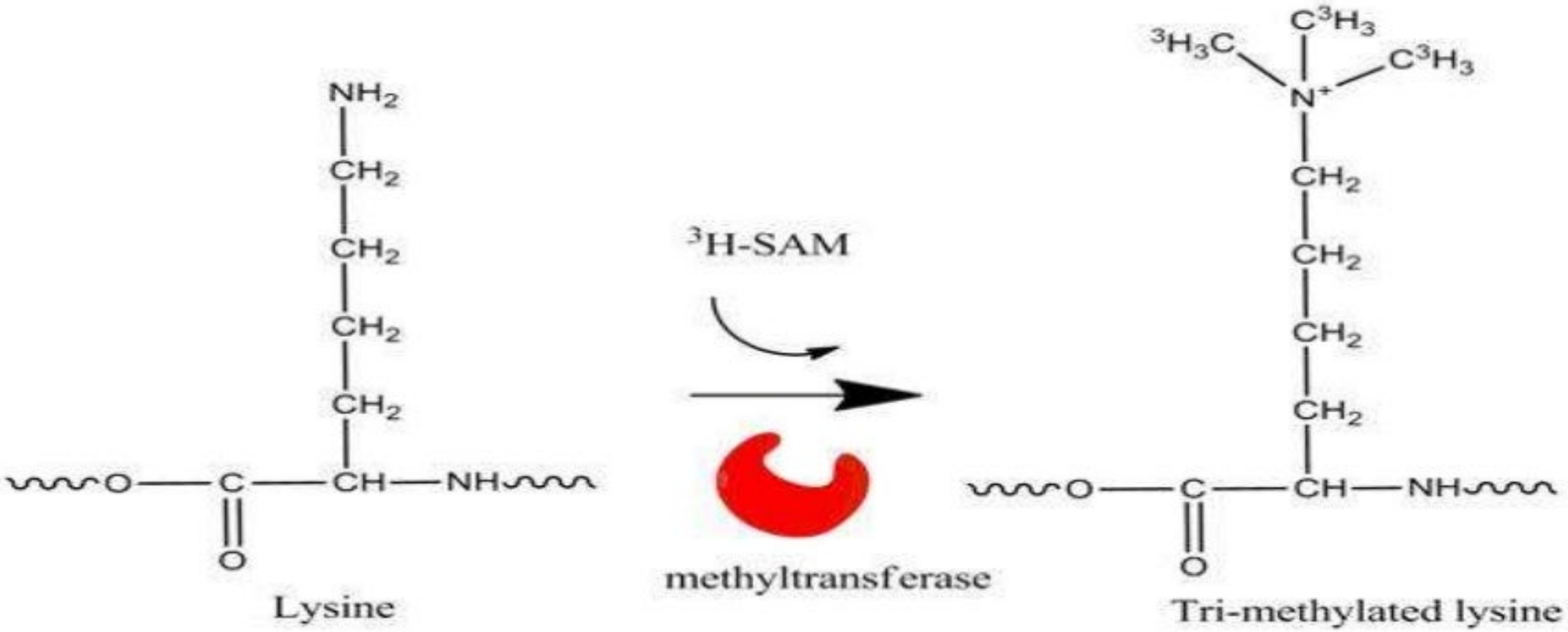


Fig showing methylation of lysine by SAM:

Hydroxylation:

The biological process of addition of a hydroxy group to a protein amino acid is called Hydroxylation. Protein hydroxylation is one type of PTM that involves the conversion of –CH group into –COH group and these hydroxylated amino acids are involved in the regulation of some important factors called transcription factors. Among 20, the two amino acids can be regulated these are proline and lysine.

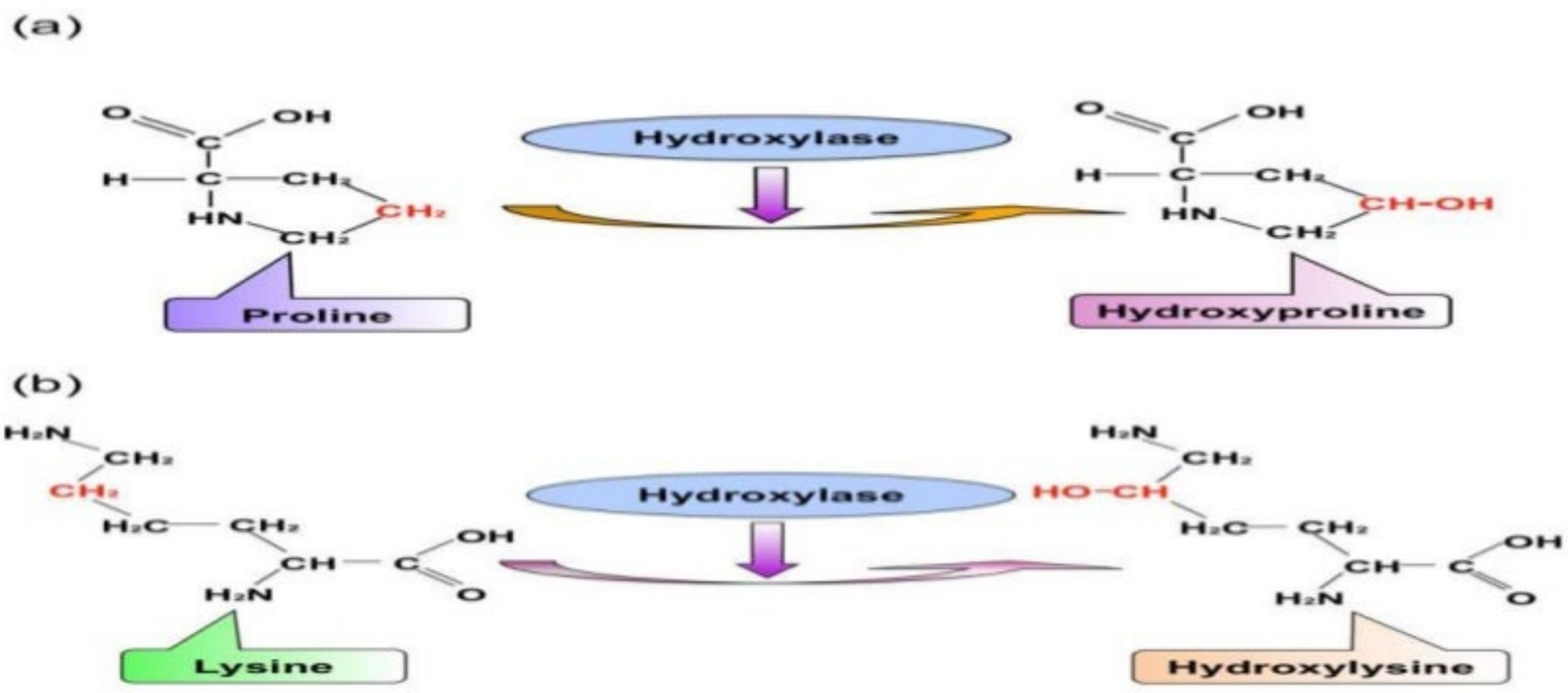


Fig: protein hydroxylation occuring at proline & lysine:

Other covalent Modifications:

Some other covalent modifications of the polypeptide chains involve the following processes.

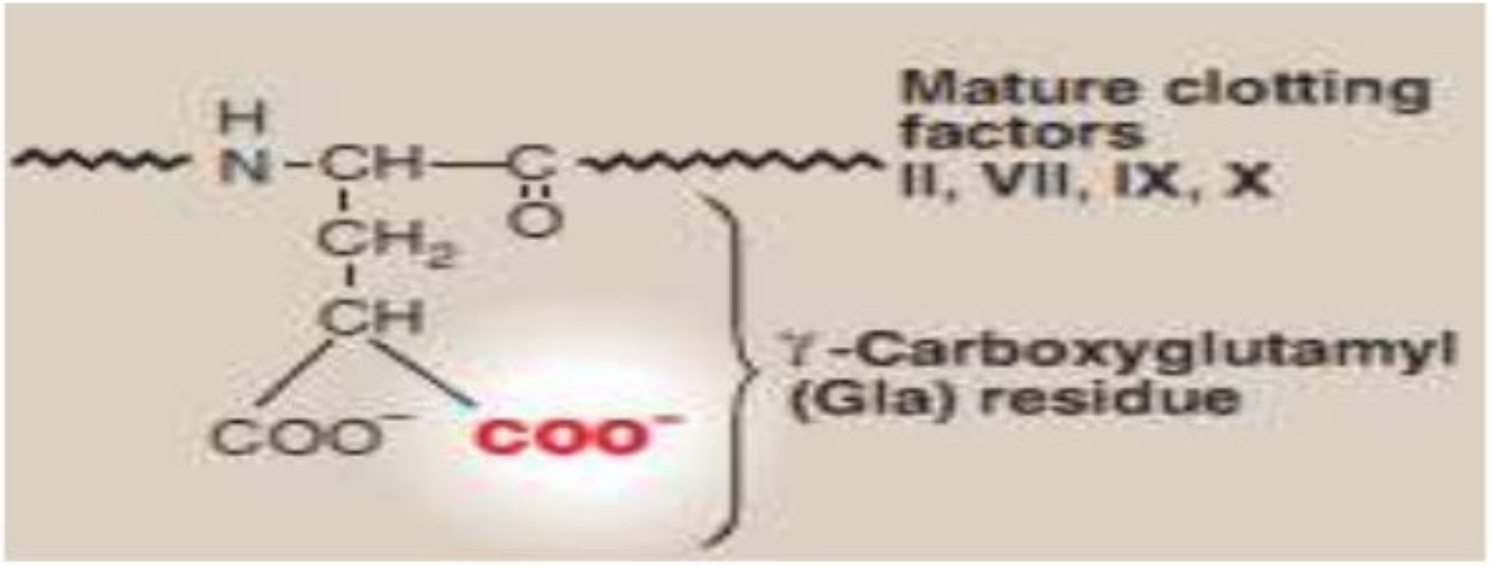
Carboxylation

Lipidation

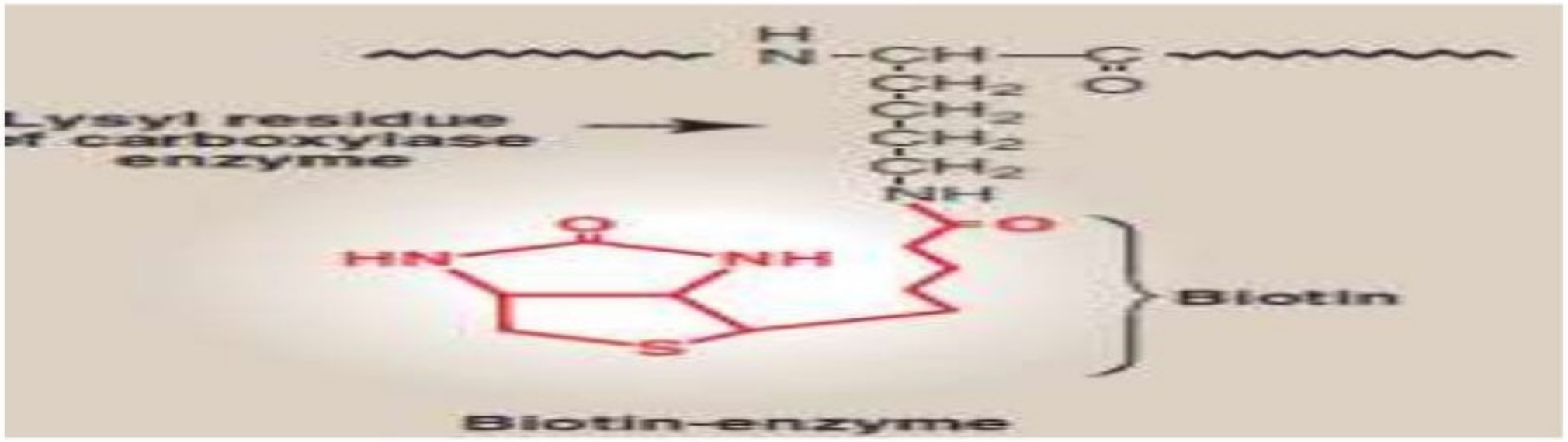
Biotinylation

Acetylation

Carboxylation:



Biotinylation:



Protein Degradation:

Proteins that are defective for example, misfolded or destined for rapid turnover are often marked for destruction by ubi ubiquitination-the attachment of chains of a small, highly conserved protein, called ubiquitin. Proteins marked in this way are rapidly degraded by a cellular component known as the proteasome, which is a macromolecular, ATP-dependent, proteolytic system located in the cytosol.

Protein Folding:

Proteins must fold to assume their functional state. Folding can be spontaneous or facilitated by proteins known as Cheperones.

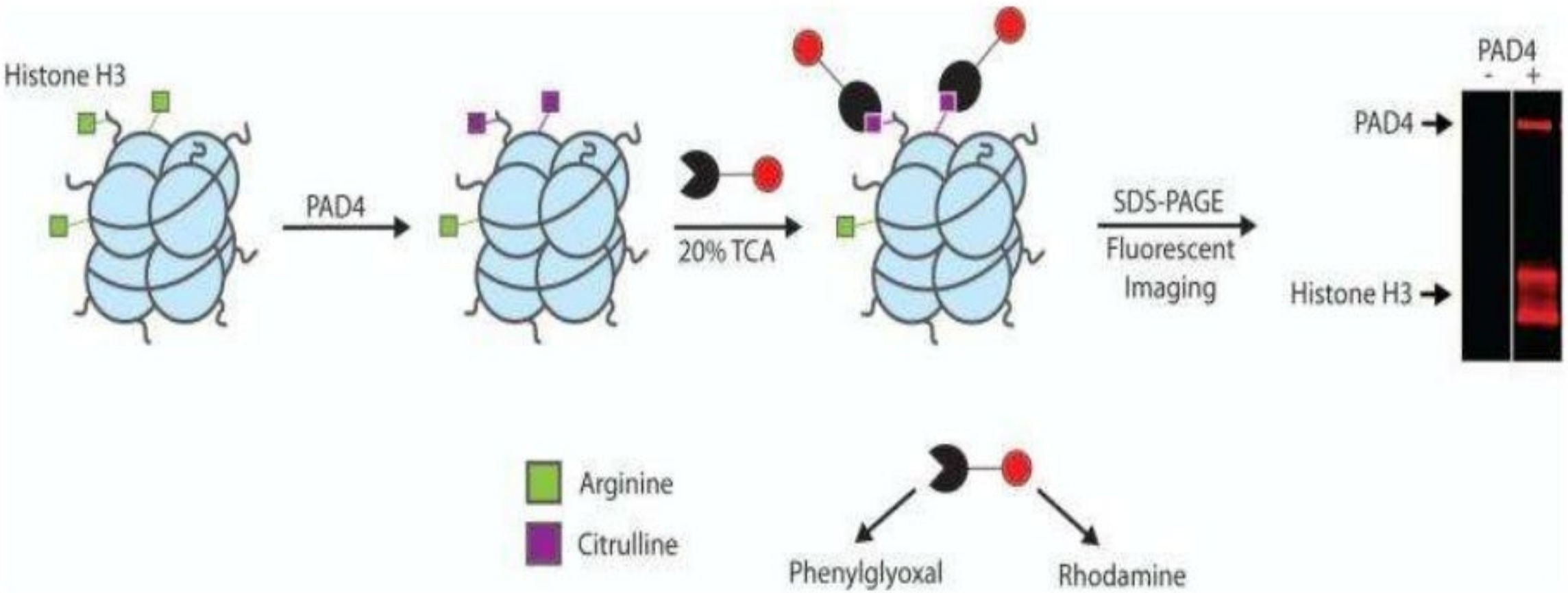
Detection of PTM:

There are several chemical and biological techniques for the detection of PTMs that whether the modification has occurred or completed in the protein or not. These methods are very helpful and advanced now a day for in vitro use too. The methods are:

- Mass Spectrometry
- Florescent staining of two dimensional gels
- Immune system activation
- By affinity binding DNA

There are some of the pictures that had shown the detection of post translational modifications of proteins by different methods.

Fig: showing detection of PTM by 2D page imaging:



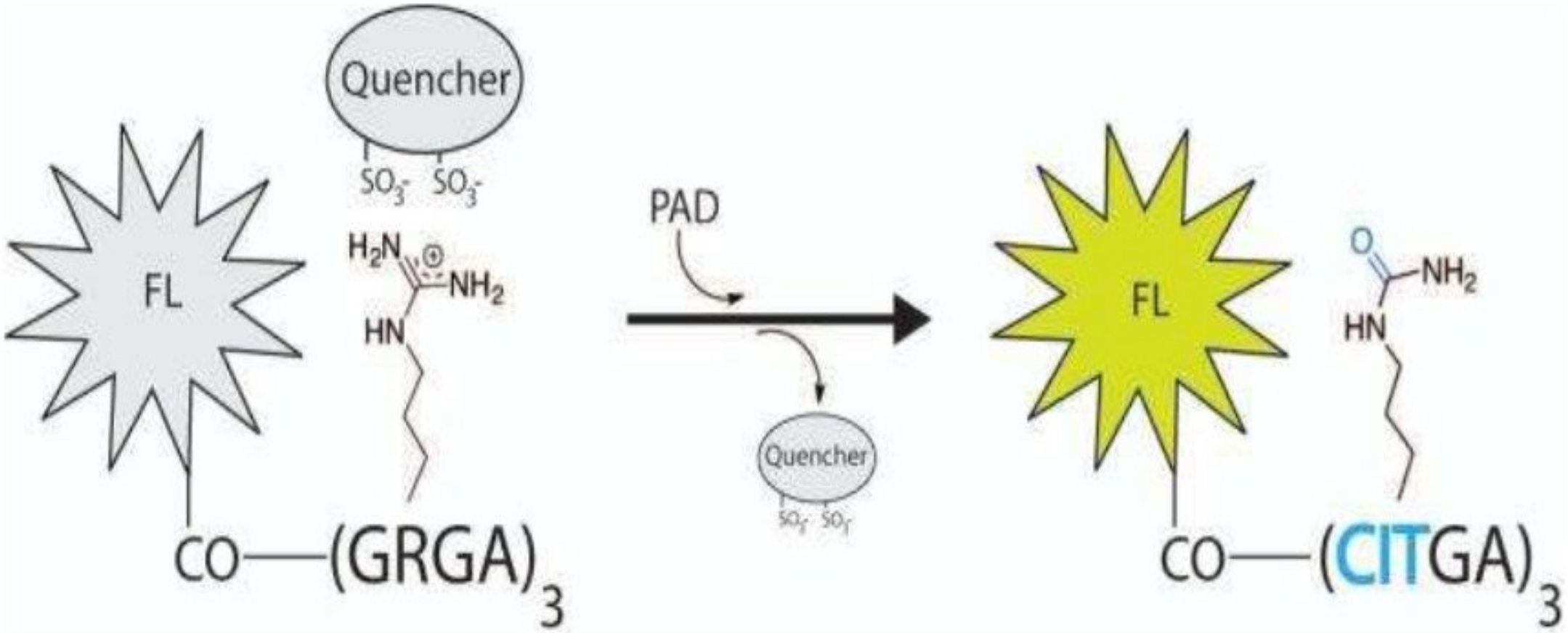


Fig: showing detection of PTMs via florescent assay:

Importance Of PTMs:

Post translational modifications are very important for the cells to live and progress. Some of the points related to the importance of the PTMs are listed below as:

- Post-translational modifications of proteins, which are not gene-template based, can regulate the protein functions, by causing changes in protein activity, their cellular locations and dynamic interactions with other proteins.
- Acetylation regulates many diverse functions, including DNA recognition, protein-protein interaction and protein stability
- Redox-dependent PTM of proteins is emerging as a key signaling system conserved through evolution, influences many aspects of cellular homeostasis

•Protein lipid-modifications including myristoylation, palmitoylation, farnesylation, and prenylation, known for a long time, have been shown to have a role in protein-membrane interactions, protein trafficking, and enzyme activity.

It is also evident that glycosylation plays a key role in immune regulation, e.g. in the development, survival and reactivity of T cells