POSTTRANSLATIONAL MODIFICATION OF POLYPEPTIDE CHAINS

Many polypeptide chains are covalently modified, either while they are still attached to the ribosome or after their synthesis has been completed. Because the modifications occur after the translation is initiated, they are called posttranslational modifications. These modifications may include the removal of a part of the translated sequence or the covalent addition of one or more chemical groups required for protein activity. Some types of posttranslational modifications are listed below

A. Trimming

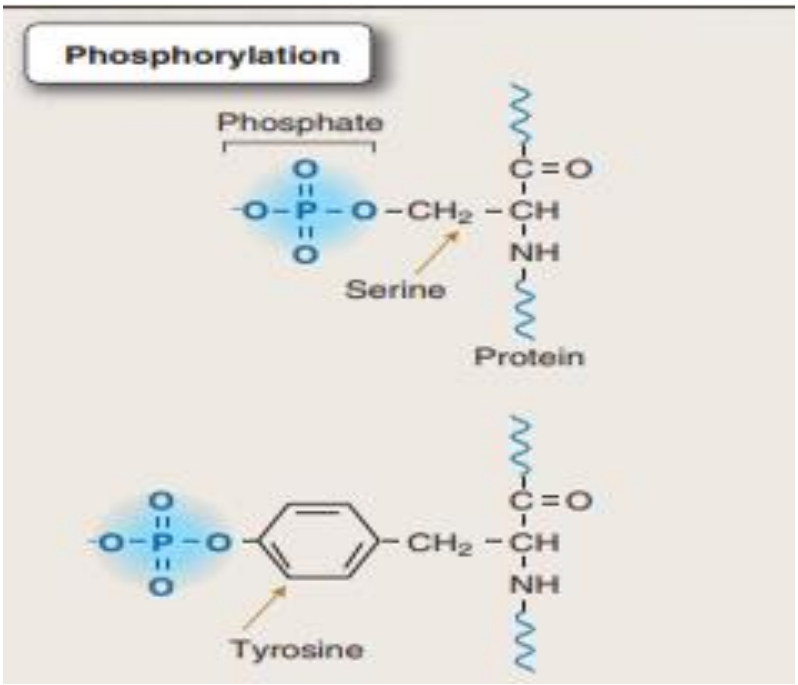
Many proteins destined for secretion from the cell are initially made as large, precursor molecules that are not functionally active. Portions of the protein chain must be removed by specialized endoproteases, resulting in the release of an active molecule. The cellular site of the cleavage reaction depends on the protein to be modified. For example, some precursor proteins are cleaved in the endoplasmic reticulum or the Golgi apparatus, others are cleaved in developing secretory vesicles, and still others, such as collagen, are cleaved after secretion. Zymogens are inactive precursors of secreted enzymes (including the proteases required for digestion). They become activated through cleavage when they reach their proper sites of action. For example, the pancreatic zymogen, trypsinogen, becomes activated to trypsin in the small intestine.

B. Covalent alterations

Proteins, both enzymatic and structural, may be activated or inactivated by the covalent attachment of a variety of chemical groups

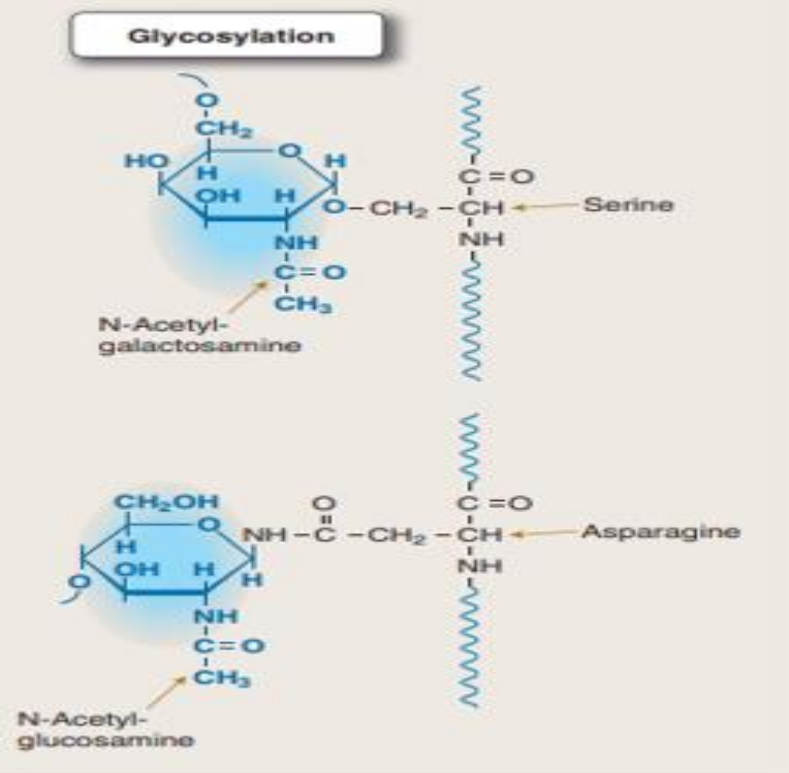
1. Phosphorylation:

Phosphorylation occurs on the hydroxyl groups of serine, threonine, or, less frequently, tyrosine residues in a protein. This phosphorylation is catalyzed by one of a family of protein kinases and may be reversed by the action of cellular protein phosphatases. The phosphorylation may increase or decrease the functional activity of the protein.



2.Glycosylation:

Many of the proteins that are destined to become part of a plasma membrane or lysosome, or to be secreted from the cell, have carbohydrate chains attached to serine or threonine hydroxyl groups (O-linked) or the amide nitrogen of asparagine (N-linked). The addition of sugars occurs in the endoplasmic reticulum and the Golgi apparatus



3. Hydroxylation:

Proline and lysine residues of the α chains of collagen are extensively hydroxylated in the endoplasmic reticulum.

4. Other covalent modifications:

These may be required for the functional activity of a protein. For example, additional carboxyl groups can be added to glutamate residues by vitamin K-dependent carboxylation. The resulting γ-carboxyglutamate residues are essential for the activity of several of the blood clotting proteins.