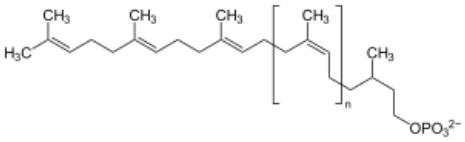
Post-translational glycosylation of proteins

After translocation into ER cisterns, many proteins are further modified. The signal peptide is cleaved, disulfide bonds are formed. Later, a certain section can be cleaved from the polypeptide chain proteolytically, and thus the protein is functionally activated (hormone, enzyme). The function of several proteins can be modified by phosphorylation, acetylation, or ADP-ribosylation (p.OOO). Many proteins acquire oligosaccharide residues in the ER and Golgi, making them **glycoproteins**. These changes in the finished peptide chain are called **post-translational modifications of proteins**, or also their covalent modifications. This structural and functional maturation of the protein is very important for the regulation of biochemical processes.

Oligosaccharides bind by either an N-glycoside bond to an asparagine residue or an O-glycoside bond to a serine or threonine residue of a protein. Oligosaccharide precursors are synthesized on an isoprene support – **dolichol phosphate**, contained in the ER membrane. If its phosphate group is on the cytosolic side of the membrane, two N-acetylglucosamines and five mannoses sequentially bind to it. The dolichol phosphate with this heptasaccharide is then oriented in the membrane so that the oligosaccharide is on the luminary side of the membrane, heading to the ER tank. Here, four more mannose and three glucose are transferred to it from another dolichol phosphate precursor (see figure).



Dolichol phosphate

The oligosaccharide thus activated is transferred to the Asn peptide, the phosphatase cleaves one of the dolichol pyrophosphate phosphates and the regenerated dolichol phosphate can re-enter the reaction cycle. The antibiotics **bacitracin** blocks this phosphatase. The attachment of Glc-NAc to dolichol phosphate is inhibited by the antibiotic **tunicamycin**.

In the ER, three glucose and one mannose are cleaved from the N-linked oligosaccharide. The protein is then transferred to the **Golgi apparatus (GA)**. In its vesicles, oligosaccharides also bind to the protein through an O-glycoside bond. The N-linked oligosaccharides are further modified. Six mannoses are sequentially cleaved and additional GlcNAc, galactose, fucose and finally **sialic acid (N-acetylneuraminic acid)** are added. These modifications in the Golgi apparatus are called **terminal glycosylations**, in contrast to the **basic glycosylations** (core glycosylations) already taking place in the ER. Lysosome-derived glycoprotein oligosaccharides are specifically phosphorylated.

During all processes after transfer of the protein to the ER tanks, the peptides in the membranes are oriented so that the oligosaccharide residues are on the luminal side of the membrane (in the tank, in the GA vesicles, in the transport vesicles). When the transport vesicles merge with the plasma membrane, the glycoprotein oligosaccharides reach the outer, extracellular side of the membrane. Some **asymmetry of the membranes** is maintained.

The glycoprotein part of the oligosaccharides have sometimes been shown as a signal or an *address*, to which proteins from the Golgi apparatus are sent to their proper function. There is **mucolipidosis** (I-cell disease), which is caused by a genetic error in the modification of oligosaccharide residues of lysosomal enzymes. In patients, instead of mannose-6-phosphate, there is only mannose. As a result of this variation, lysosomal enzymes are not transferred to lysosomes, but out of the cell and can be detected in blood plasma. In contrast, undecomposed glycosamines and glycolipids accumulate in lysosomes. The patient suffers from psychomotor retardation and skeletal deformities.

However, glycosylation of most proteins probably has a different function than providing the molecule with a targeting signal. Oligosaccharide residues of glycoproteins increase their solubility and help orient the protein molecule towards the aqueous phase. Another role of oligosaccharides is to protect the protein (e.g. immunoglobulin) from the proteases' activity. Carbohydrates are a marker for the uptake and subsequent degradation of plasma glycoproteins in the liver. Another significance is seen in the fact that the kinetics of glycoprotein modifications in ER and GA indicate a step in the passage of these proteins through cellular organelles, thus ensuring the time required for accurate sorting of synthesized proteins.

References

Related Articles

- Translation of membrane and secretory proteins (protein sorting, targeting)
- Translation, post-translational processing of proteins in eukaryotes
- Post-translational modifications and protein targeting

Source

- ŠTÍPEK, Stanislav. *Stručná biochemie : Uchování a exprese genetické informace.* 1. edition. Medprint, 1998. ISBN 80-902036-2-0.

References

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