

Protein synthesis



The sequence of triplets of purine and pyrimidine nitrogen bases determines **the sequence** of aminoacids in chain and the same **secondary structure** and **biological** properties of proteins.

Appropriate „reading” of information and its realisation are crucial for the synthesis of physiological proteins.

Protein synthesis consists of two processes:

- ▶ Activation of aminoacids
- ▶ Translation – initiation, elongation, termination

The regulation of protein synthesis

- Energetic status of organism
- The presence of all aminoacids
- On the level of transcription (synthesis of mRNA)
- On the level of translation:
 - ▶ the changes in the content of ribosomes (anabolic status \uparrow , malnutrition \downarrow)
 - ▶ the content of mRNA
 - ▶ the formation of preinitiation complex (the status of phosphorylation of initiation factor IF-2)

Activation of aminoacids



Initiation

mRNA of eucariotic cells is monocistron – contains one coding fragment, one initiation codon (AUG) and one stop codon (UAA). One polypeptide chain is synthesised.

Indispensable are:

- ▶ Initiator (aminoacyl-tRNA with anticodon complementary to initiation codon)
- ▶ Both subunits of ribosome
- ▶ m RNA
- ▶ Initiation factors (only at the beginning)

Elongation

The sequence of similar reactions which are repeated several times. It requires GTP and cytoplasmic protein elongation factors.

- ▶ Binding of aminoacyl-tRNA to site A of ribosome
- ▶ Formation of peptide bond
- ▶ Translocation of peptydyl-tRNA from site A to P

Termination

It happens when nonsense codon will appear in site A. The liberation of peptide bond and the breakdown of ribosome takes place.

The energetics of protein synthesis

During the synthesis of one peptide bond 2 molecules of ATP and 2 GTP are used.

During the activation of aminoacids 2 bonds of ATP are used.

The reaction of aminoacyl-tRNA binding as well as translocation of peptydylo-tRNA use 2 bonds of GTP

Posttranslational protein modifications

Cover the proteolysis of signal sequence indicating the kind of protein. Moreover, the reactions leading to the formation of specific bonds and processes occur: the synthesis of disulfide bonds, hydroxylation, phosphorylation, carboxylation, glycosylation.

The regulation of topogenesis (intracellular transportation and translocation of proteins)

Signal sequence – carries the information about the need for the transportation of certain protein via cell membrane (few – several aminoacids)

Retain sequence – stops the translocation

The alterations in posttranslational modifications

Congenital defects in activity of enzymes that hydroxylate procollagen lead to alterations in the structure of collagen. Moreover, the alterations in the function of fibrous elements of connective tissue occur and lead to excessive expansibility, susceptibility to damage and changes in the shape.

The alterations in posttranslational modifications

- ▶ due to the error in transcription wrong proinsulin is formed (one of arginins is replaced by neutral aminoacid). Endoprotease is sensitive enough and recognises this modification - does not act on such protein. Split off is not possible – altered protein is secreted.
- ▶ due to the lack of appropriate endopeptidase appropriate proinsulin is not further modified and is secreted instead of insulin.
- ▶ alterations in the modifications of some apolipoproteins are known

The meaning of posttranslational modifications

- ▶ are additional source of biodiversity and specificity of proteins
- ▶ are essential stage of topogenesis (appropriate distribution of particular proteins in cells)
- ▶ as the result of posttranslational modifications signal sequence is detached and the protein becomes biologically active