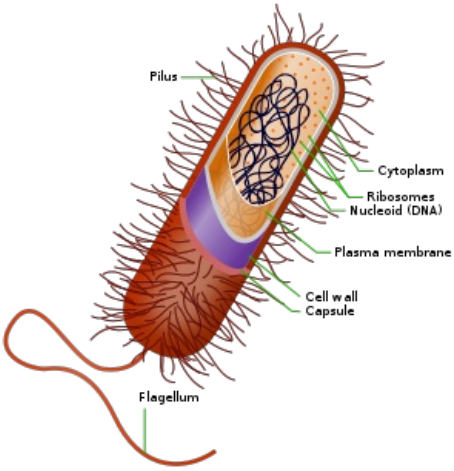
Regulation of gene expression in prokaryotes

Gene expression is regulated in prokaryotic cells by:

1. transcriptional regulation
2. mRNA stability
3. translation regulation
4. post-translational modification of polypeptides.

Regulation of transcription



Transcription in prokaryotes is fundamentally different from that in eukaryotic regulation . The basic difference is that in prokaryotes, one regulatory region may be common to multiple genes and the transcription of which is then affected together. However, In eukaryotes, there is always one promoter region per gene and vice versa. We refer to such bound genes as operons. The site where the RNA polymerase anneals is called the promoter and the site where the regulatory protein anneals is referred to as the operator.

The entire operon is then expressed as a single mRNA molecule .

We distinguish operons in two types: *catabolic* and *anabolic*. An example of a catabolic operon is the *Lac operon* - in the presence of lactose, which has an inductive effect on transcription, several genes responsible for lactose catabolism are transcribed at the same time. In contrast, the typical anabolic operon is the *Trp operon* - in the presence of tryptophan, the transcription of genes responsible for the anabolism of this amino acid is inhibited.

Transcription factors

We generally divide regulation into positive and negative. A number of proteinaceous transcription factors are involved in regulation, which must recognize a particular region on the DNA molecule - at sites in the deep groove of the DNA. Their DNA binding domains contain various conserved motifs (evolutionarily sparing sequences of proteins that are able to bind to DNA), with transcription factors for the operon system mostly containing β-sheets .

Other canned motifs are the following:

I. HTH (helix - turn - helix) and HLH (helix - loop - helix) = 2 α-helices connected by a short chain AMK → form a "turn";
II. HTH homeodomains - involved in ontogenesis;
III. Steroid receptors;
IV. Zinc - fingers = 1 α-helix and 1 β-ridge - held in a constant position by a Zn atom;
V. Leucine zippers = connect 2 α-helices by bonds between leucine molecules;
VI. β- sheets - operon system

Translation

To describe the regulation of translation, it is necessary to realize the fundamental differences in transcription and translation in prokaryotes compared to eukaryotes. Prokaryotic genes can be expressed together in a single operon as a single mRNA molecule, but at the same time transcription is not separated from translation due to the absence of a nuclear membrane. Thus, ribosomal subunits can anneal directly to the forming mRNA, which is therefore not subject to post-transcriptional modifications .

Post-translational adjustments

= removal of the first methionine from the N-terminus of the polypeptide, removal of the signal peptide from the N-terminus

Cascade control

- genes expressed in a certain order
- early transcription genes
- later late transcription genes
- genetically programmed cascade
- early transcription gene promoters have signal sequences to which the host cell's sigma-factor RNA polymerase binds
- initiates their transcription

Additional regulation

1. Among the early transcription genes is the gene for viral RNA polymerase, which specifically binds to the promoters of viral late transcription genes
2. Among the early transcription genes is a gene for a protein that replaces the host RNA polymerase σ-factor and ensures the specificity of bacterial binding to the promoters of late transcription genes

Positive and negative control of gene expression

Regulation of gene expression uses both positive and negative mechanisms of regulation. Both mechanisms work with regulatory genes whose products regulate the expression of other genes. In the case of a positive mechanism, the regulatory gene product induces the expression of structural genes; in the case of a negative mechanism, the regulatory gene stops the expression of other genes. Both mechanisms are used in the inductive and repressive system of regulation.

Operon model of transcriptional regulation

The mechanism of transcriptional regulation in prokaryotes was described by F. Jacob and J. Monod in 1961. They found that the expression of a gene or group of contiguous structural genes of a metabolic pathway is controlled by two transcriptional regulatory elements: (i) a regulator gene the repressor, and (ii) the operator to which the repressor is linked. The unit of regulation of gene function, consisting of the operator, promoter and structural genes, was called the operon. They obtained their findings by studying lac operon mutations in E. coli. In addition to the promoter and operator, this operon comprises three structural genes that allow the bacterium to metabolize lactose: gene Z (encodes beta-galactosidase), gene Y (encodes beta-galactoside permease) and gene A (encodes beta-galactoside transacetylase).

a) Inductive operon system

The inductive operon system is typical for regulating the transcription of genes encoding catabolic reaction enzymes.

The regulatory gene is transcribed constitutively (permanently). His product, the repressor, is tied to the operator of the operon. An operator is a segment of DNA that is part of the promoter of structural genes. Binding of a repressor to an operator prevents RNA polymerase from binding to the promoter and initiating transcription of structural genes. Under these conditions, the cell produces only about 1% of the maximum possible amount of protein (enzyme) encoded by the structural genes.

When there is a substance in the environment that these enzymes can metabolize, this substance acts as an inducer. Inductors change the allosteric configuration of the repressor and thus prevent its connection to the operator. RNA polymerase can bind to the released promoter and initiate transcription of structural genes. In the case of the lac operon, the inducer is lactose. When lactose is present, it binds to the lac operon receptor and the bacteria produce enzymes that allow the use of lactose as an energy source. After depletion of lactose resources, lactose is also released from binding to the repressor.

The free (active) repressor binds to the operon and transcription of the lac operon genes is repressed.

b) Repressive operon system

The repressive operon system is typical of genes encoding enzymes of anabolic reactions. The regulatory gene in this system produces an inactive repressor, i. that the repressor does not have the ability to bind to the operator. The repressor is activated by binding the repressor. A corepressor is usually a product of a metabolic chain, the synthesis of which is catalyzed by enzymes encoded by operon genes. The repress operon model is the trp operon, which encodes enzymes for tryptophan amino acid synthesis.

The E. coli trp operon comprises 6 structural genes (trpL, trpE, trpD, trpC, trpB, trpA), the products of which catalyze metabolic steps from chorismic acid to tryptophan. If the bacterium has enough tryptophan for protein synthesis, transcription of the trp operon is blocked by binding of the repressor + compressor (tryptophan) complex to the operator. After depletion of tryptophan stocks in the cytoplasm, tryptophan bound to the repressor is released. Thus, the repressor is inactivated, does not bind to the operator, and RNA polymerase initiates transcription of the structural genes of the trp operon.

Catabolite repression

In a study of the lac operon, Jacob and Monod found that lactose did not induce transcription of the lac operon in the presence of glucose. Glucose prevented the induction of the production of other enzymes involved in the metabolism of other sugars. This phenomenon is called catabolite repression or the glucose effect.

In the case of the trp operon, there is a second level of regulation of enzyme synthesis, which is independent of repression or derepression of the operon and which is related to the presence of a nucleotide sequence in the trpL region (determines the leader sequence of the polypeptide). The phenomenon was studied in detail and explained as attenuation, and the section of DNA in trpL that controls this phenomenon was called the attenuator.

TRANSLATION REGULATION

In prokaryotes, multigenic mRNA is transcribed to encode multiple proteins (enzymes), usually one metabolic chain. Detailed studies have shown that although these genes are expressed simultaneously as part of a single operon, different amounts of individual proteins (enzymes) are formed during translation.

This is made possible by the following mechanisms:

a) Uneven translational initiation efficiency of different operon genes, different rates of ribosome movement in mRNA intergene regions, and mRNA hairpin formation that affect the rate at which ribosomes move across mRNA and different rates of mRNA degradation.

b) Post-translational regulatory mechanisms

In addition to the described regulation of transcription and translation, regulations on the level of enzyme activity are described in prokaryotes. Sufficient end product of a particular metabolic pathway can inhibit the activity of the first enzyme of that pathway. This mechanism is called feedback inhibition or enzyme inhibition by end products. Enzymes capable of this reaction have, in addition to the substrate binding site, binding site (s) for the final product of the metabolic chain.

Upon binding of the final product, the allosteric configuration of the enzyme molecule changes, thereby reducing its affinity for the substrate. These proteins are called allosteric proteins.

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