Regulation of Gene Expression

Gene expression regulation encompasses a vast array of processes that can occur at multiple levels. Since gene expression ultimately leads to the synthesis of a polypeptide, regulation can take place at various stages.

In eukaryotes, gene expression can be controlled at four primary levels:

(i) Transcriptional Level: This involves the initiation and regulation of transcription, leading to the formation of the primary transcript.

(ii) Processing Level: Regulation occurs during post-transcriptional processing, particularly in the splicing of introns and exons.

(iii) mRNA Transport: This level focuses on the transportation of mature mRNA molecules from the nucleus to the cytoplasm, where translation takes place.

(iv) Translational Level: Regulation occurs during the translation process, where mRNA is translated into a polypeptide chain.

Genes within a cell are expressed to fulfill specific functions. In eukaryotes, functionally related genes are not organized into operons but are dispersed across different chromosomal sites. These structural genes, known as split genes, consist of both exons and introns, resulting in discontinuous base triplet-to-amino acid matching. During RNA splicing, the non-coding intronic regions are removed, and the exonic coding regions are fused together. A significant portion, approximately 50-90%, of the primary transcribed RNA is discarded during this processing.

The coordinated regulation of gene expression is essential for the development and differentiation of embryos into adult organisms.

Gene expression can be influenced by metabolic, physiological, or environmental conditions, which act as regulatory factors.

Operon Concept

Francois Jacob, a geneticist, and Jacques Monod, a biochemist, introduced a model of gene regulation in bacteria known as the operon model. An operon refers to a coordinated cluster of genes, including the structural gene, operator gene, promoter gene, and regulator gene, which collaborate to regulate a metabolic pathway as a unified entity. Examples of operons include the lac operon, trap operon, area operon, his operon, and Val operon.

(i) Regulator gene: This gene is responsible for synthesizing a biochemical or regulatory protein that can function both positively as an activator and negatively as a repressor. It regulates the activity of the operator gene.

(ii) Operator gene: Acting as a receiver of the product from the regulator gene, the operator gene permits the operation of the operon when it is not obstructed by the biochemical produced by the regulator gene.

(iii) Promoter gene: Serving as the attachment site for RNA polymerase, the promoter gene initiates the transcription process.

(iv) Structural gene: This gene transcribes mRNA required for the synthesis of polypeptides.

The Lac operon

The lac operon, named after lactose, comprises several components: one regulatory gene (or inhibitor gene), one promoter gene, one operator gene, and three structural genes. This operon governs the breakdown of lactose in Escherichia coli. The structural genes are transcribed together as a polycistronic unit, regulated by a shared promoter and regulatory gene.

In E. coli, the breakdown of lactose necessitates the action of three enzymes. These enzymes are synthesized in a coordinated manner by the lac operon, which serves as a functional DNA unit. Notably, the addition of lactose itself prompts the production of these required enzymes, rendering the lac operon an inducible system.

Lac Operon Genes

1. **Structural genes**

   The lac operon encompasses three structural genes:

   (i) lac z: Encodes for ß-galactosidase, the enzyme primarily responsible for catalyzing the hydrolysis of lactose into its constituent monosaccharides, galactose, and glucose.

   (ii) lac y: Encodes for permease, a protein that enhances the cell's permeability to ß-galactosidase.

   (iii) lac a: Encodes for transacetylase, an enzyme capable of transferring acetyl groups to ß-galactosidase.

2. **Operator gene**

   This gene interacts with a protein molecule or a regulatory molecule, which in turn prevents the transcription of the structural genes.

3. **Promoter gene**

   This gene contains the site where RNA polymerase attaches to initiate transcription.

4. **Regulator gene (i)**

   This gene codes for a protein called the repressor protein, which is continually synthesized from the i-gene. Hence, it is a constitutive gene, functional at all times.

   The operon is switched off when the repressor protein, produced by the regulatory or inhibitor gene, binds to the operator gene. This binding event blocks RNA polymerase, halting transcription.

   The presence of the repressor protein interacting with the operator gene results in the operon being deactivated.

   The regulation of the lac operon by the repressor protein is known as negative control or regulation.

   When lactose is present in the bacterial growth medium, it is transported into the cells with the help of permease. It is crucial to maintain a basal level of lac operon expression within the cell at all times, even in the absence of lactose, to ensure that lactose can enter the cells effectively.

   In the presence of an inducer, such as lactose or allolactose, the repressor protein is rendered inactive through interaction with the inducer molecule. This deactivation of the repressor allows RNA polymerase to bind to the promoter region of the lac operon, thereby enabling the initiation of transcription.

   The presence of the repressor protein along with the operator gene leads to the operon being activated.

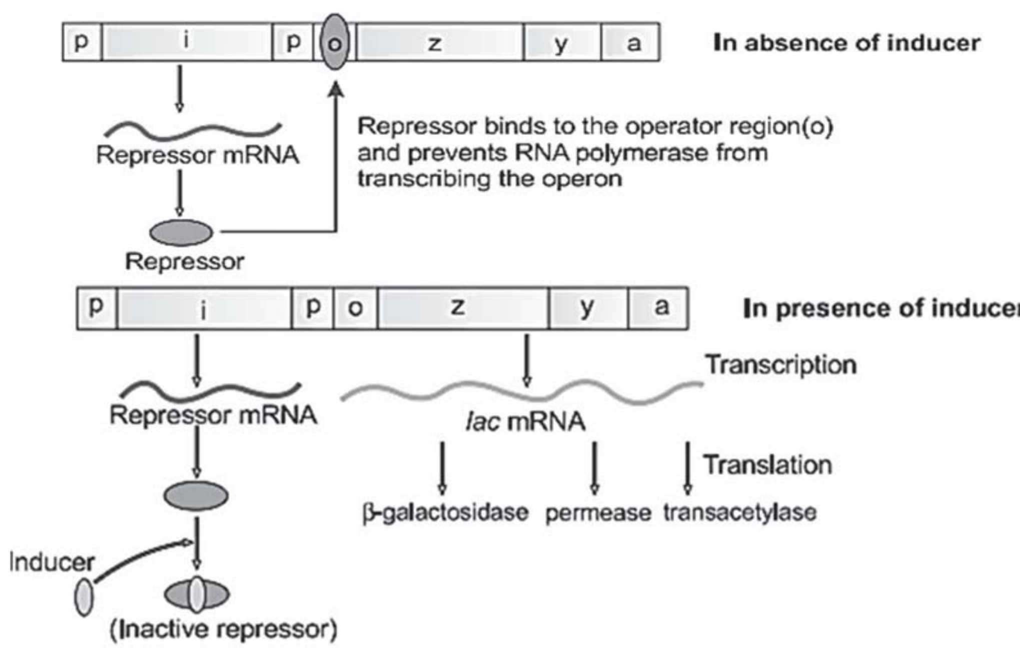

Fig. : The *lac* Operon