MOLECULAR BASIS OF INHERITANCE
REGULATION OF GENE EXPRESSION

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Regulation of Gene Expression :

Regulation over the functioning of genes is called regulation of gene expression. It can be exerted at four levels.

(i) Transcriptional level during formation of primary transcript.

(ii) Processing like splicing, terminal additions or modifications.

(iii) Transport of RNAs from nucleus to cytoplasm.

(iv) Translation level.

Genes expression is of three types

(1) Inducible (2) constitutive (3) repressible.

(1) **Inducible :** In this types the Gene is switched on in response to the presence of substrate (Inducer).

(2) **Constitutive :** Genes and their enzymes remain operational throughout.

(3) **Repressible :** It is of two types

(a) **Positive Control :** The product of regulatory gene initiates expression of genes under of its control.

(b) **Negative control :** The product of a regulatory gene switches off the expression of genes under its control.

OPERON MODEL :

An operon is a segment of DNA that functions as single regulated unit comprising a regulator gene, a promoter gene, an operator gene, one or more structural genes, a repressor and an inducer or corepressor, these systems are common in prokaryotes.

First operon lac–Operon was discovered by **Jacob and Monod (1961) in E.coli**.

Operons involve two types.

(1) Inducible operon model **(2) Repressible operon model.**

Inducible Operon Model :

It is found in **catabolic pathway Ex: Lactose operon or Lac operon.** Lac operon consists of following components.

(i) **Structural genes :** They actually control the synthesis of m-RNA through transcription. They determine primary structure of polypeptide chain. In Lac operon three **structural gene z, y, a** take part in the formation of **polycistronic mRNA** that regulates the synthesis of **galactosidase, permease and transacetylase enzymes.** -galactosidase hydrolyses lactose in glucose & galactose. Permease allows the entry of Lactose in the cell. Transacetylase performs metabolism of toxic thiogalactosides.

(ii) **Operator gene :** It controls the activity of structural genes. When repressor of regulator gene binds to the operator gene. the latter becomes switched off.

(iii) **Promoter gene :** It acts as initiation signal. It bears **RNA polymerase enzyme**. When operator gene is functional, its RNA polymerase travels on structural gene and perform transcription.

(iv) **Regulator gene :** It regulates the synthesis of **repressor** . It is also called **inhibitor gene or i gene.**

(v) **Repressor :** It is proteinaceous substance formed by Regulator gene. It has two allosteric sites, one for the attachment of operator gene and other for the attachment of inducer.

(vi) Inducer : It is chemical substance (Hormone, enzyme etc). When inducer is present in the medium, inducer combines with repressor resulting some conformational changes occur in the repressor in such a way that it becomes unable to bind on operator gene. therefore the latter continuously operative. when inducer is completely consumed. Repressor is again activated. In lac-operon lactose acts as inducer **(Actual allolactose acts as inducer)** & substrate.

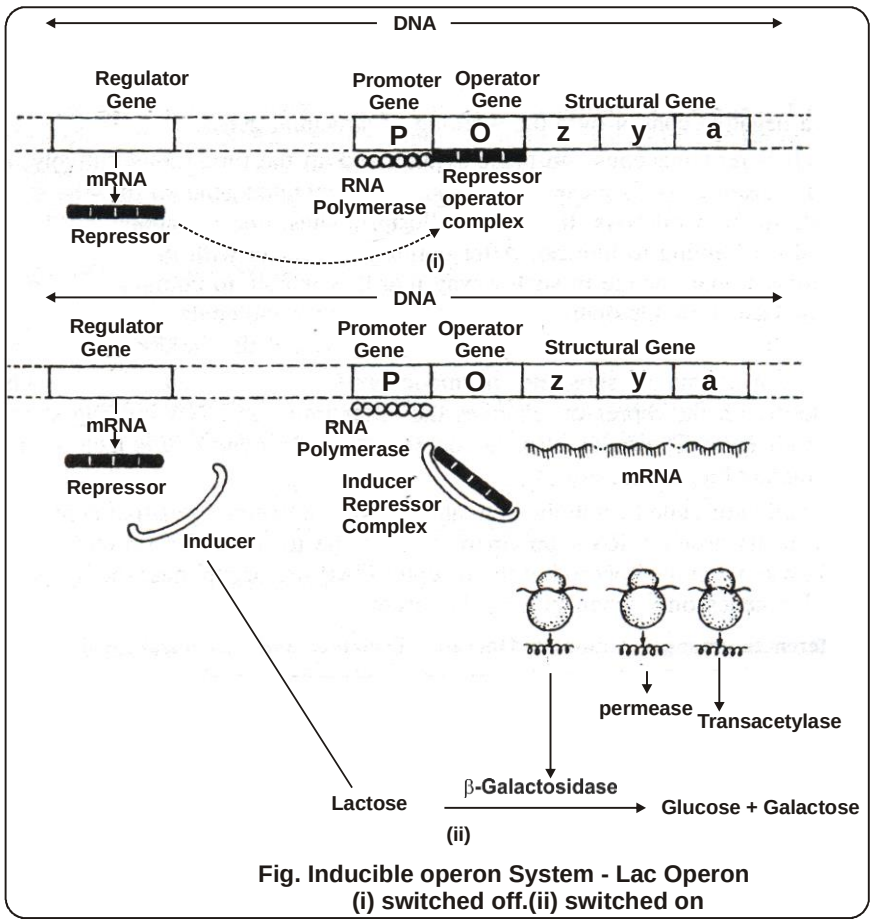

Fig. Inducible operon System - Lac Operon
(i) switched off.(ii) switched on

(vii) CAP (catoabolic Activator Protein) : It exerts positive control on Lac operon but in its absence RNA polymerase is unable to recognize Promoter gene.

REPRESSIBLE OPERON MODEL :

Repressible operon System is found in **anabolic pathways. Ex:Tryptophan or trp operon of E.coli**

Trp operon consists of the following components.

(i) **Structural Genes :** The genes are connected to transcription of mRNAs. Tryptophan operon has **five structural genes trp E, D, C, B, A.** They form enzymes for five steps of tryptophan synthesis.

(ii) **Operator Gene :** It regulates the activity of structural genes usually. Aporepressor produced by regulator gene is unable to completely block operator gene.

(iii) **Promoter Gene :** It acts as initiation signal. It bears **RNA polymerase enzyme**. When operator gene is functional, its RNA polymerase travels on structural gene and perform transcription.

(iv) **Other Regulatory Components :** It involves two components that lie between **operator gene** and **structural gene E.**

(a) **Leader sequence (L) :** It is controller of attenuator.

(b) **Attenuator (A) :** It helps in reducing tryptophan synthesis when it is available in sufficient amount without switching off the operon.

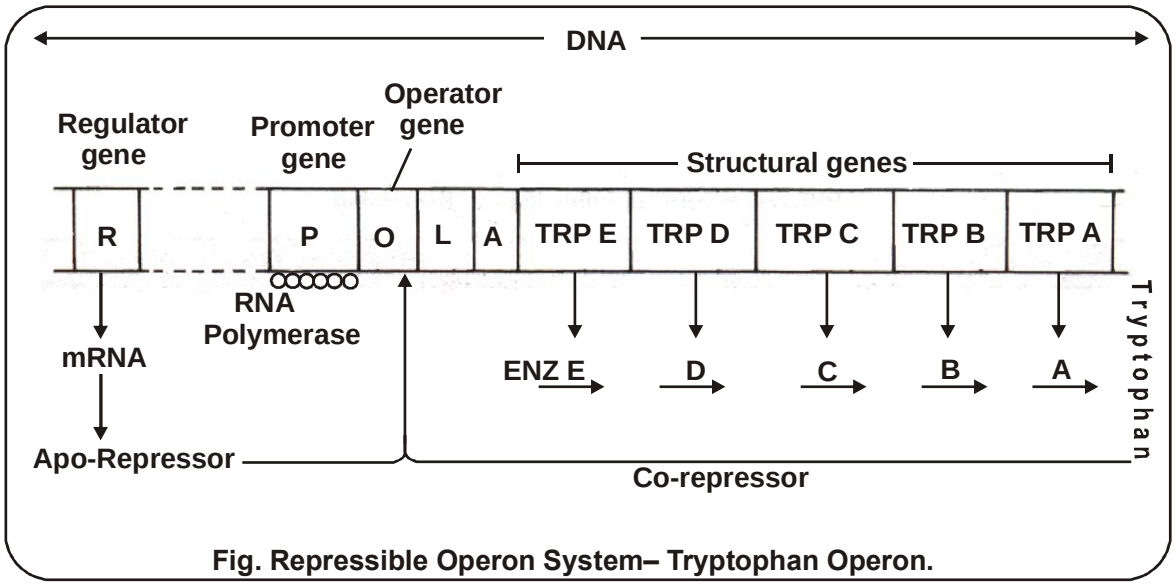

Fig. Repressible Operon System– Tryptophan Operon.

(v) **Regulator Gene :** It produces proteinaceous component (such as Aporepressor) for possible blocking the activity of operator gene.

(vi) **Aporepressor :** It is a proteinaceous substance formed by regulator gene. Independently it is unable to block the activity of operator gene. for this purpose It requires a corepressor.

(vii) **Corepressor :** It is a nonproteinaceous component of repressor that may be an end product of reactions. In trp operon, when end product Tryptophan is accumulated in sufficient amount its some molecules act as corepressor. the latter combines with aporepressor. and forms repressor that block the operator gene resulting structural genes become switched off. The phenomenon is called **feed-back repression** that exerts a negative control.

GENE EXPRESSION IN EUKARYOTES :

In eukaryotes, functionally related genes may not be clusered together constituting an operon. The most popular model is **'Gene battery model'** proposed by **Britten and Davidson** in 1969. A set of **structural genes** is controlled by **one sensor site** that is termed as **battery**.

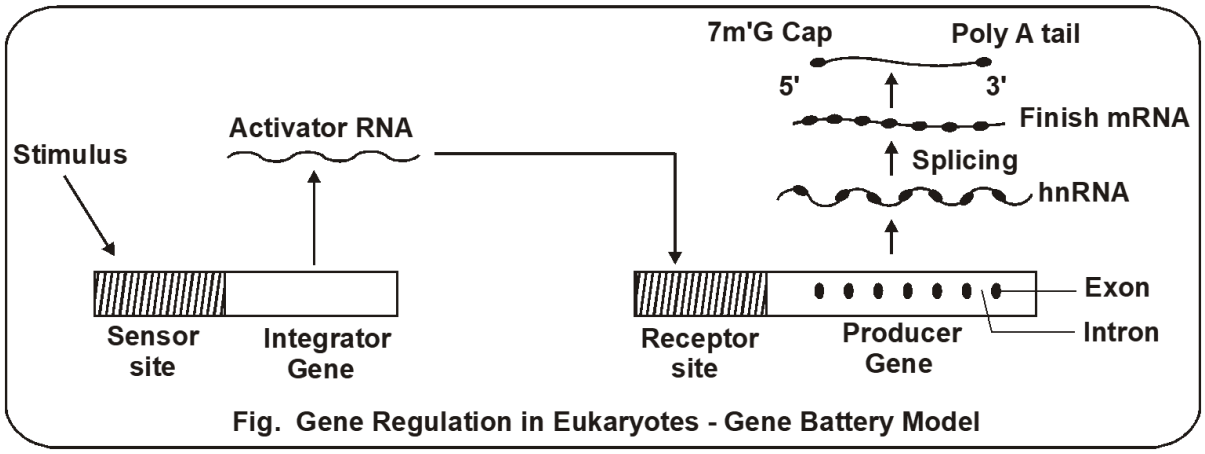

Fig. Gene Regulation in Eukaryotes - Gene Battery Model

Eukaryotes seem to have specific genes that enhance or slow down the expression of certain genes. They

According to Gene-battery model there are four classes of sequences.

(i) **Producer gene :** It is comparable to structural gene of prokaryotic operon.

(ii) **Receptor site :** It is comparable to operater gene of bacterial operon and one such receptor site is assumed to be present adjacent to each producer gene.

(iii)Integrator gene : Integrator gene is comparable to regulator gene and is responsible for synthesis of an activator or RNA. It activates the receptor site.

(iv) Sensor site : A sensor site regulates the activity to integrator gene. Activator gene can be transcribed only when the sensor site is activated. These are called enhancer genes and silencer genes respectively.