AQC-321 (1+1)

Gene Regulation in Prokaryotes

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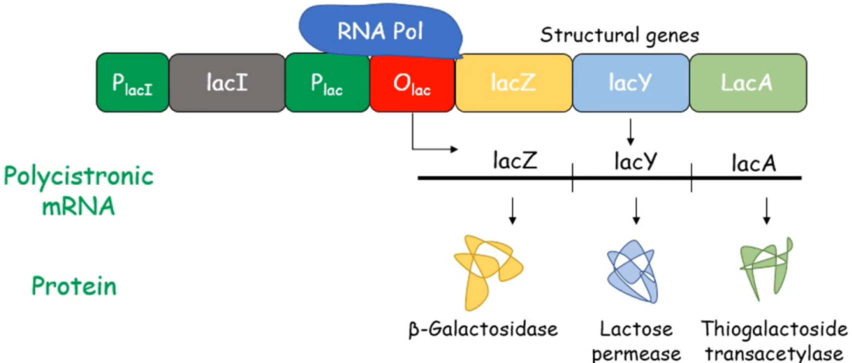
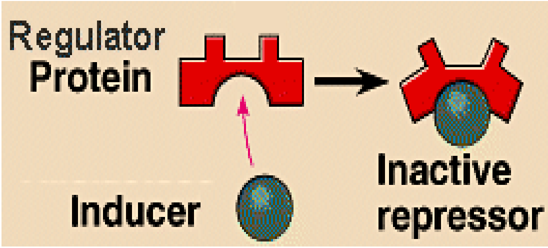
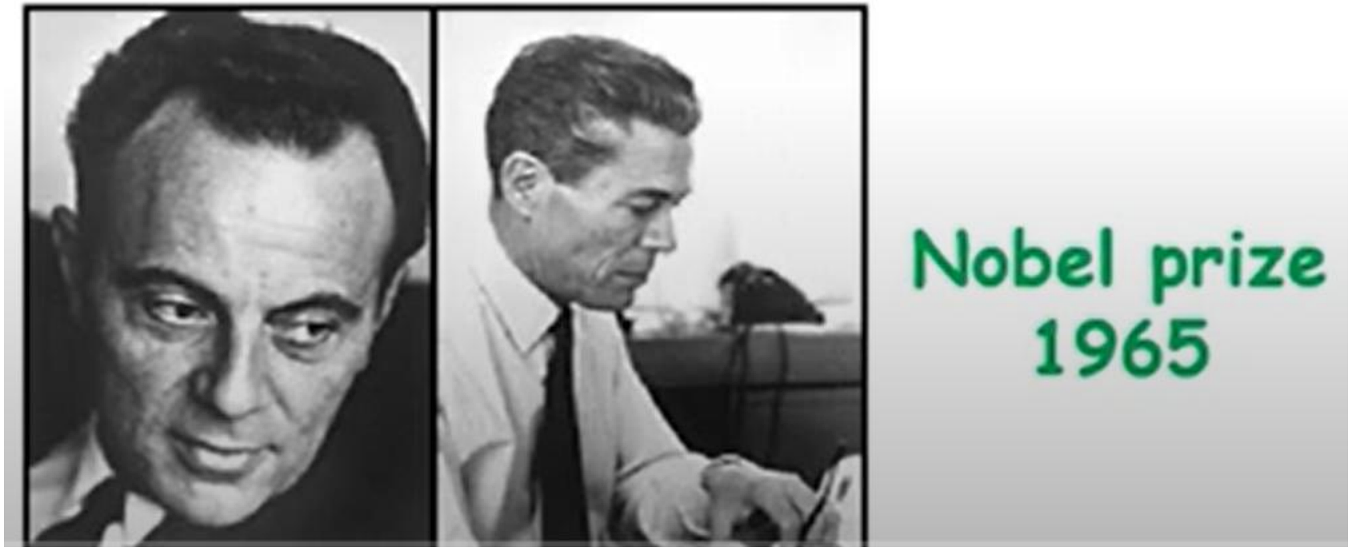




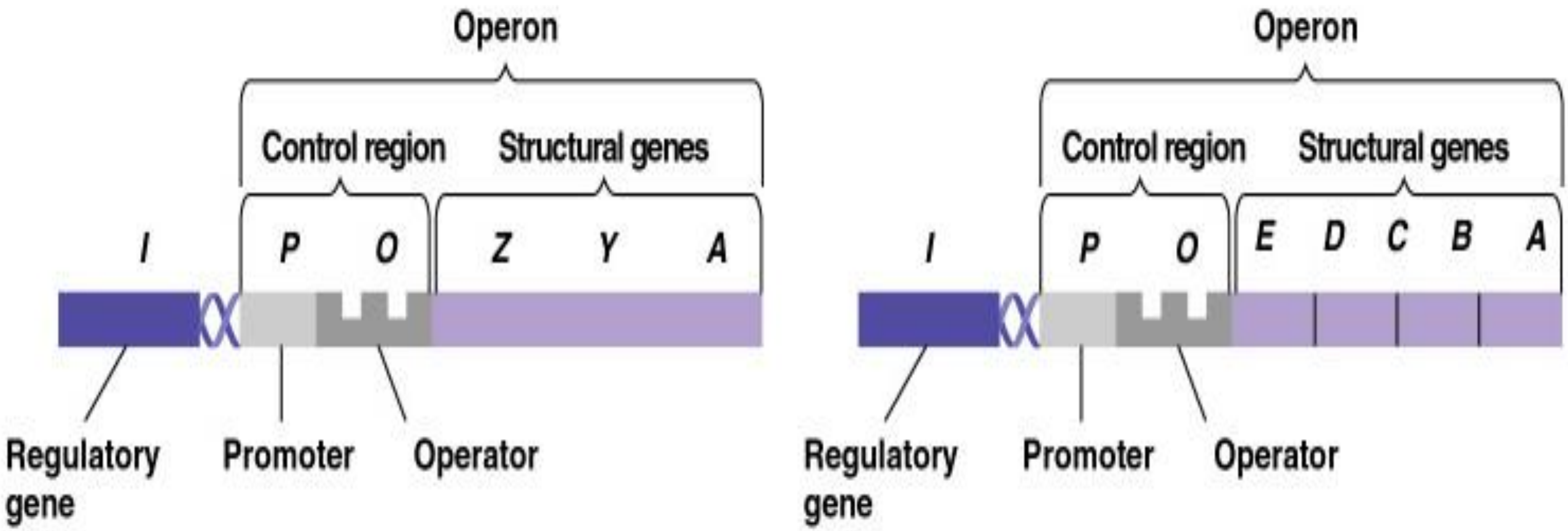
Operon Concept

- **Jacob & Monad in 1961** provided the concept of operon for prokaryotic gene regulation
- **Operon: Transcriptional unit in which several genes that encodes proteins with related functions are regulated together.**



F. Jacob J. Monod

General structure of an OPERON



Structure of the operon. The operon consists of the promoter (*P*), and operator (*O*) sites, and structural genes which code for the protein. The operon is regulated by the product of the regulatory gene (*I*).

Type of gene expression regulation in Prokaryotes

- The regulation of operon are done by specific regulatory proteins known as regulators. The regulatory proteins are coded by regulators gens of the concerned operon

1: Positive Regulation (Regulatory Proteins k/n as Activator)

2: Negative Regulation (Regulatory Proteins k/n as Repressor)

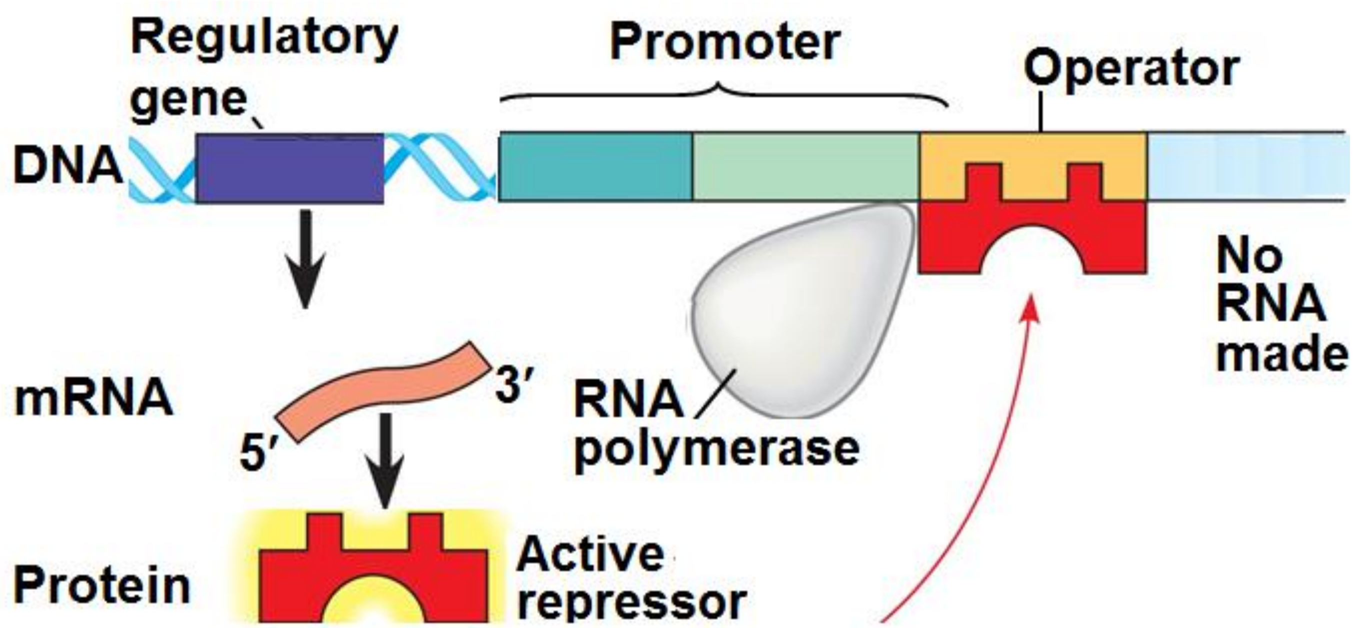
Positive vs. Negative Regulation

- **Positive:** Binding of regulator proteins to the operators is necessary for transcription to take place , such regulators are called **"activators".**

- **Negative:** Binding of regulator proteins to operator, prevents the transcription, such regulator proteins are called **"repressor".**

Regulatory Genes and Repressors

- Regulator gene- This gene produces a regulatory protein called a **repressor** that can inhibit the transcription of an operon by attaching to the operator.



Negative Regulation

- Operons showing negative control are divided into two types:

1: Inducible: Regulated by substrate of pathway (Metabolism of nutrients), eg: Lac Operon

2: Repressible: Regulated by end product of pathway (Biosynthetic pathway), eg: Tryptophan Operon

Inducible Operon

- In such operons, regulator gene produce active repressor (regulatory protein) that binds to the operator on their own and prevent the transcription.

- Repressor has two binding sites

1: **DNA Binding site**

2: **Effector (inducer or co-repressor) binding site**

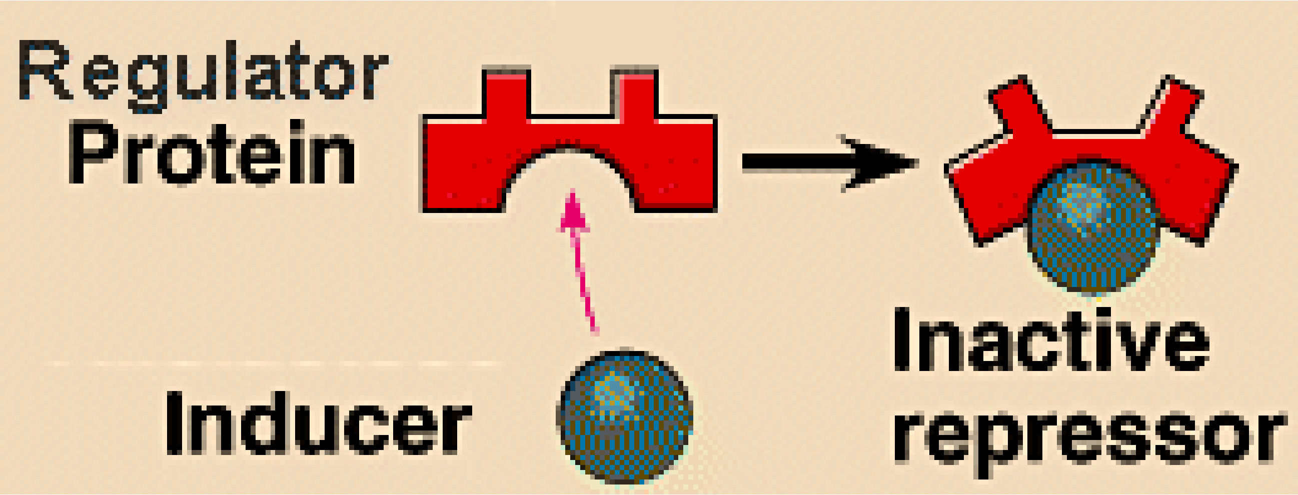
Effector or Inducer Molecule

- Inducer/Effector are usually small molecules that interact specifically with regulator proteins (repressor) in such as way that the DNA binding capacity of the regulator proteins are changed drastically.

- Binding of effector (inducer) at effector binding site change the conformation of DNA binding site of repressor molecular which cause the release of repressor from promoter that leads to transcription of downstream structural genes of operon by RNA Polymerase.

Interaction of Effector (Inducer) and Repressors

- Repressors have allosteric properties. Inducers can bind to the repressor at an allosteric site changing the conformation of the repressor, thereby deactivating the repressor. Usually the inducer is a product of the biochemical pathway.



Inducible Operon

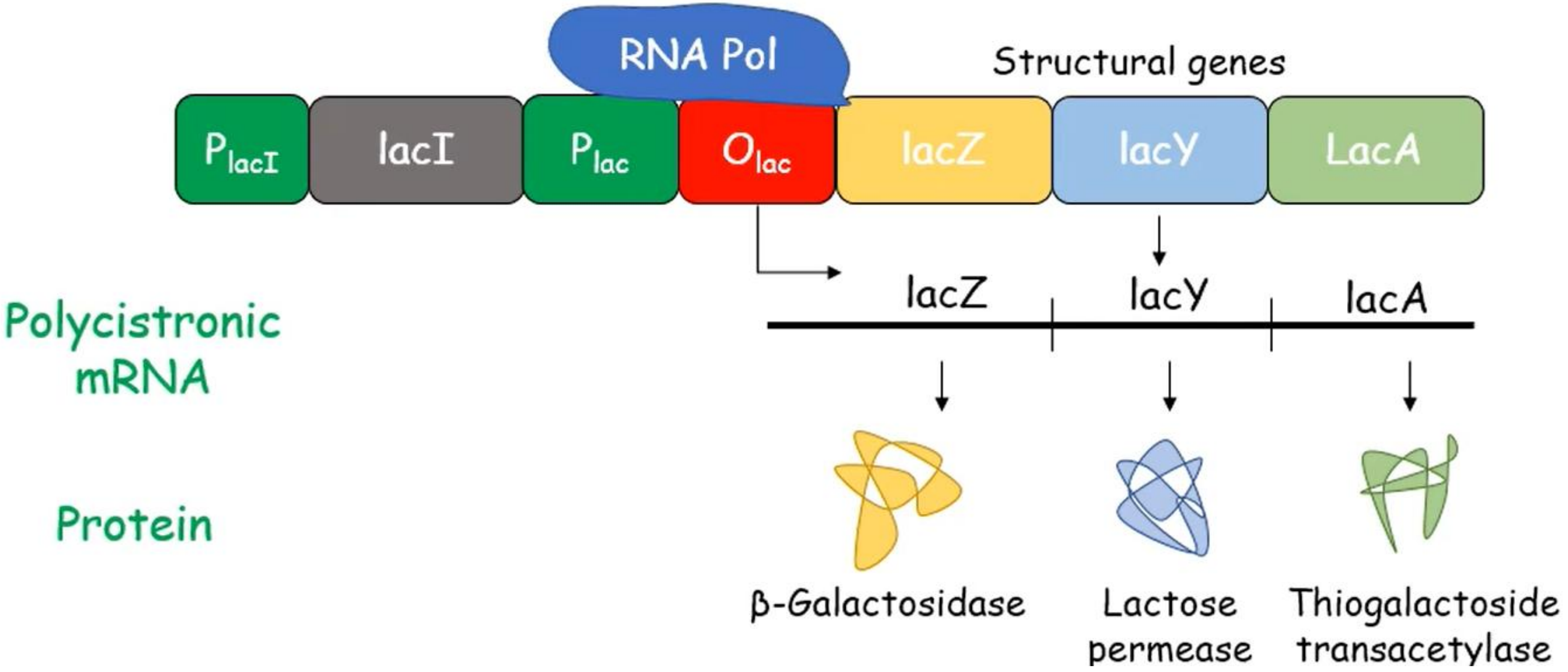
- Inducible Operon regulates the expression or production of those enzymes that are involved in substrate utilization or metabolism of nutrients. The substrate that is metabolized by the enzymes encoded by such an operon, serve as inducer for that operon. "**Inducible Operon is an operon that is induced, or turned on, by a particular inducer that inhibits the repressor. Inhibiting the repressor will allow for the transcription of the operon".**

- **i.e. inducible operons are "off" unless something turns them "on" – inducing them to act.**

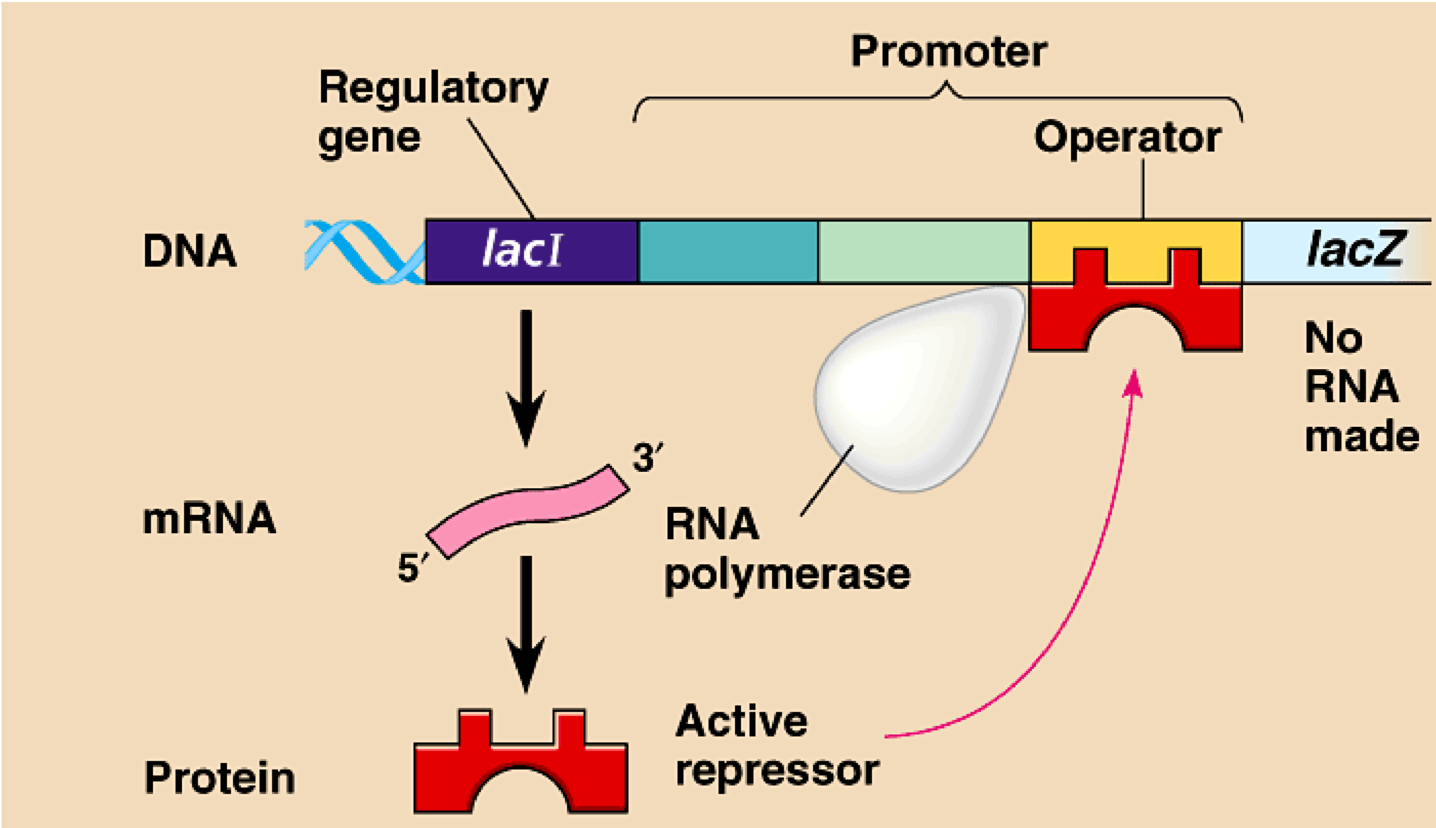
- **Example: Bacterial Lac Operon**

Inducible *lac* Operon

The *lac* operon has the ability to convert lactose into glucose and galactose. This involve three structural genes i.e. β-galactosidase, β-galactoside permease, β-galactoside transacetylase

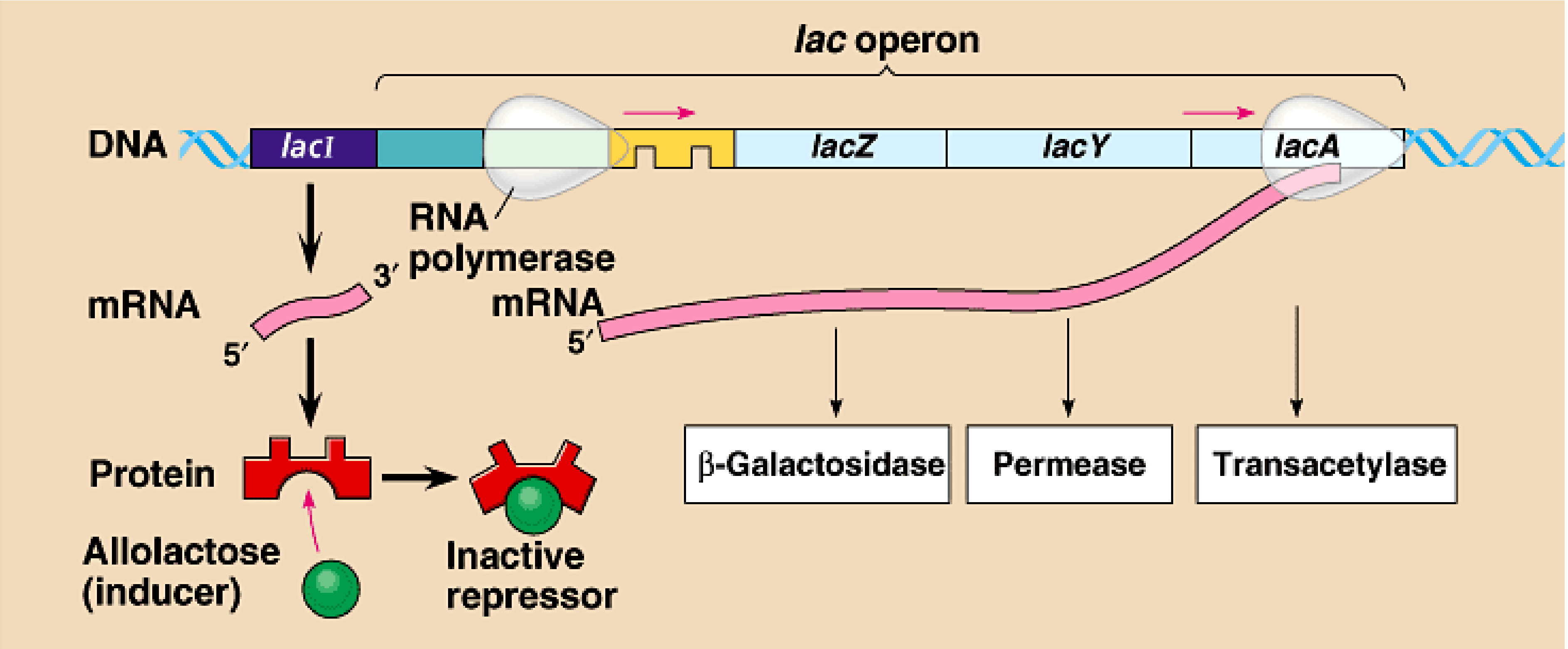


Absence of Lactose and the *lac* Operon



- If no lactose or allolactose is present, the repressor protein is active, binding to the operator site. This prohibits the RNA polymerase from transcribing the operon.

Presence of Allolactose and the *lac* Operon



(b) Lactose present, repressor inactive, operon on

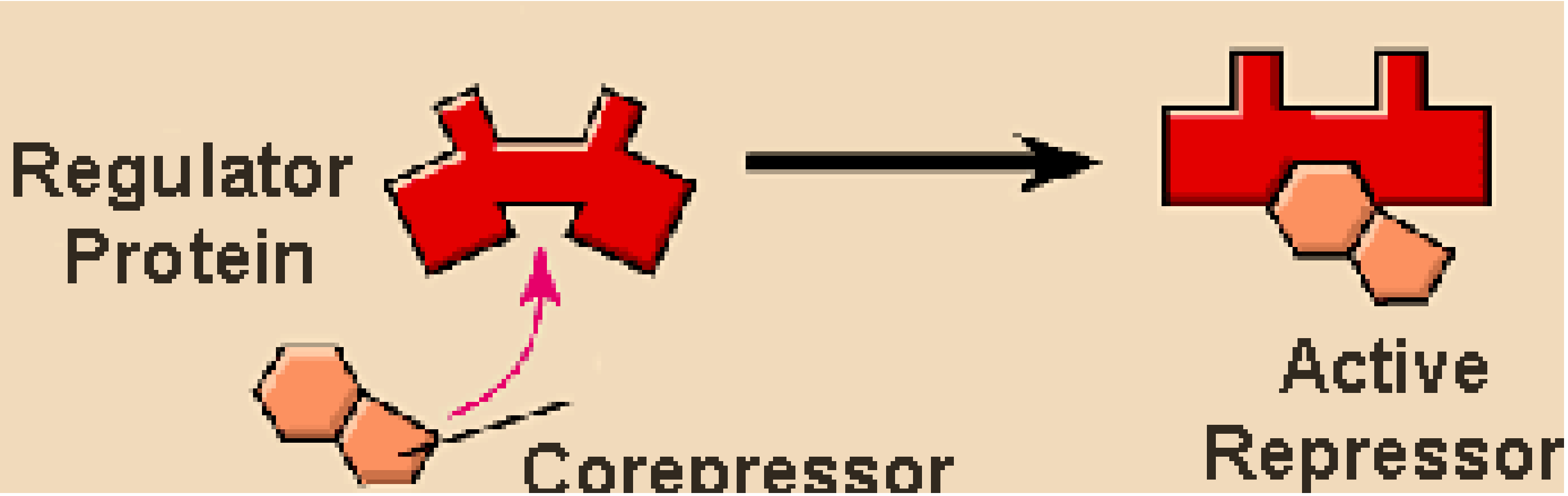
When cell encounter lactose, few lac enzyme take up the lactose and convert them into allolactose. Allolactose bind to lac repressor which cause the change in conformation of lac repressor and it get released from operator. The RNA polymerase is no longer blocked and expression of Lac ZYA occus.

Repressible Operon

- In case of Repressible operon, the regulatory protein (repressor) encoded by the regulatory gene is unable to bind operator. Therefore, the operon is normally functional. But when repressor interacts with effector **(co-repressor),** it becomes active and bind operator and transcription stopped and operon becomes repressed.
- Repressible operons generally encode enzymes that catalyze biosynthetic pathways and the end-products of that biosynthetic pathways act as co-repressor for that operon.
- Example: **Tryptophan Operon**

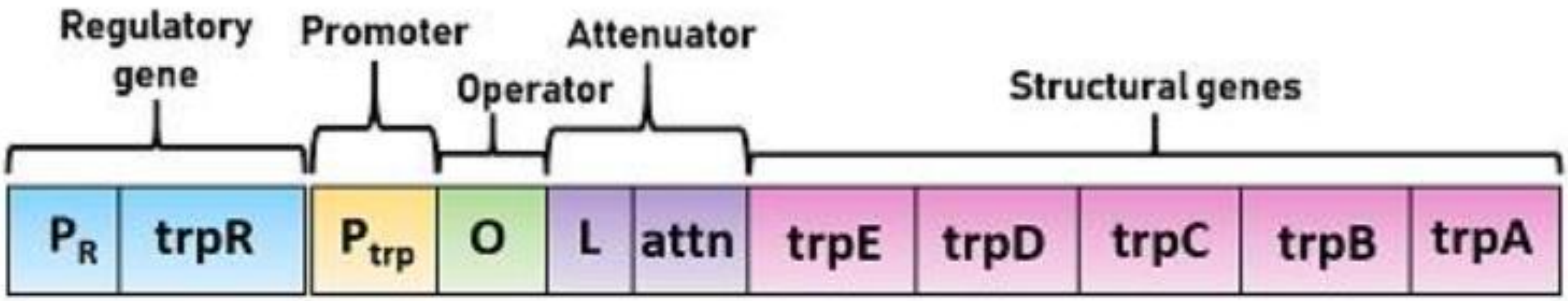
Interaction of Effector (Co-repressor) & Repressor

- Effector (Co-repressor) are usually the end-products of biosynthetic pathways of concerned operon. It interact specifically with regulator proteins (repressor) in such as way thatrepressor becomes active and bind the operator region which stopped the transcription.



Repressible Tryptophan Operon

- The purpose of the *trp* operon is to synthesize the amino acid tryptophan when needed. Repressible operons are "on" unless the presence of something actively turns them "off" – represses them to make them inactive. A scientist named **Charles Yanofsky** and co-workers have explicitly studied the role of regulatory and structural gene of the trp operon.



The structural genes encodes for the enzymes for the biosynthesis of tryptophan from chorismic acid

trpE encodes the enzyme Anthranilate synthase I.

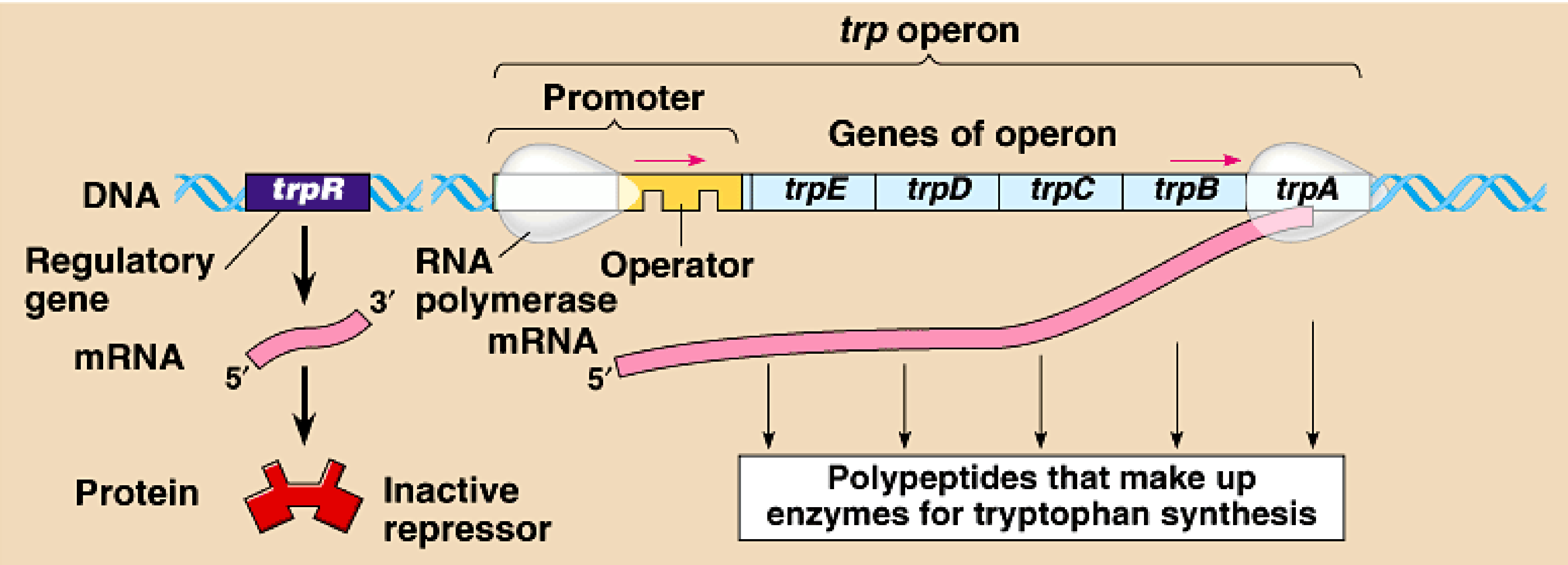
trpD encodes the enzyme Anthranilate synthase II.

trpC encodes the enzyme N-5'-Phosphoribosyl anthranilate isomerase & Indole-3-glycerolphosphate synthase.

trpB encodes the enzyme tryptophan synthase-B subunit.

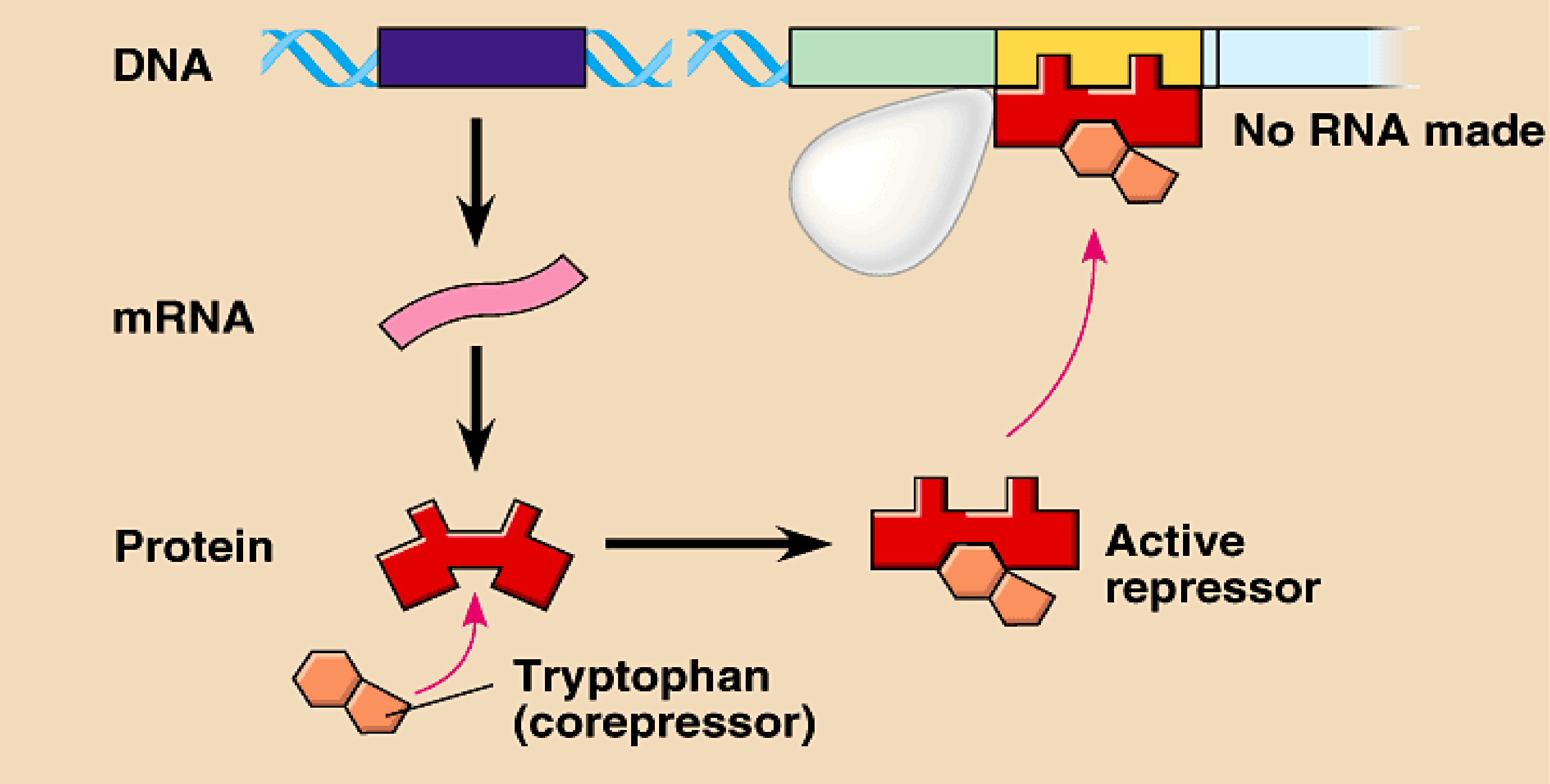
trpA encodes the enzyme tryptophan synthase-A subunit.

Repressible *trp* Operon



(a) Tryptophan absent, repressor inactive, operon on

Tryptophan Present and the Repressible *trp* Operon



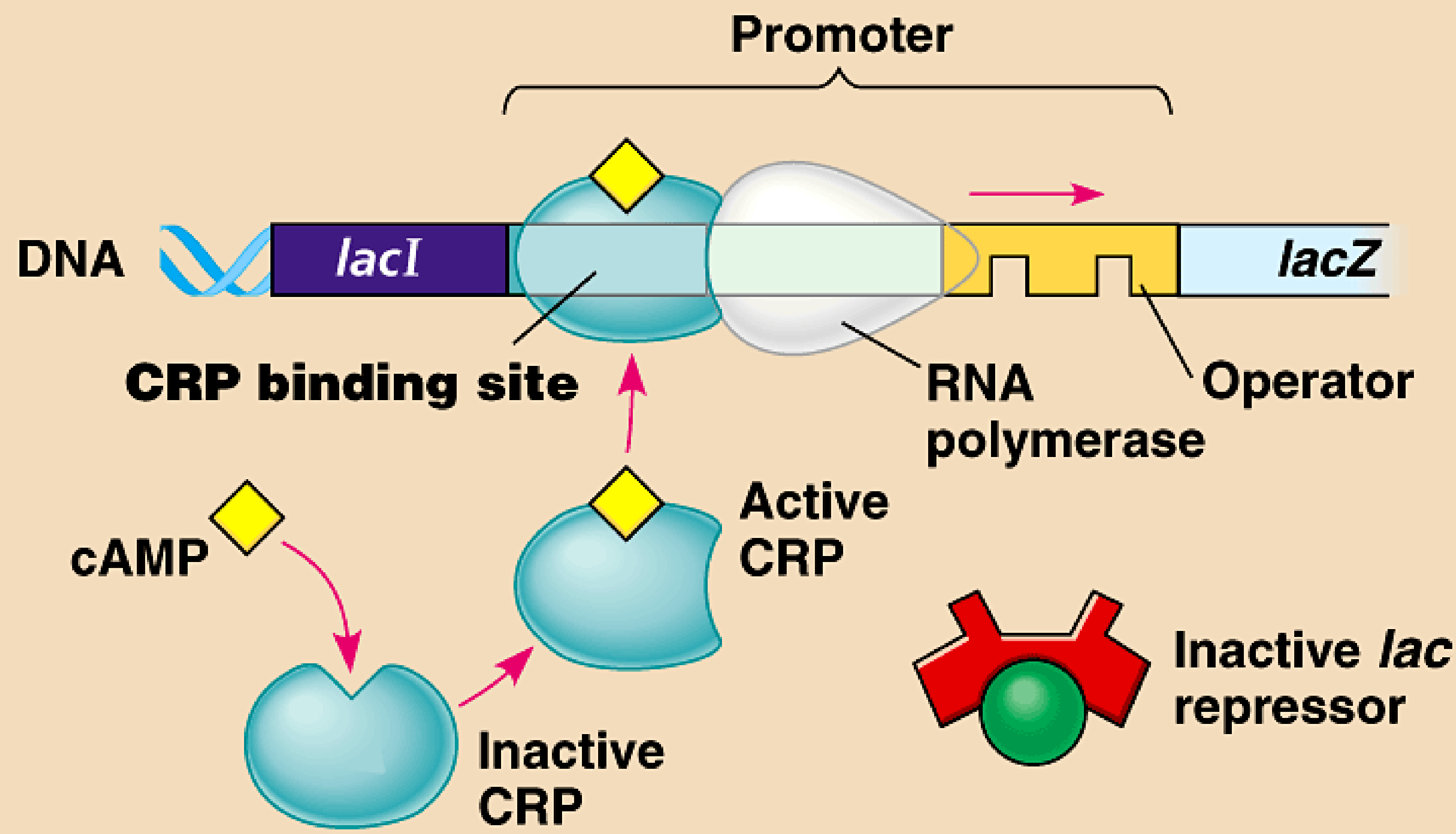
(b) Tryptophan present, repressor active, operon off

Positive Regulation of Lac Operon

- While most prokaryotic gene regulation is negative, there are some examples of positive gene regulation. The *lac operon* has both a negative and a positive way to regulate the gene. It is an additional regulatory mechanism which allow lac operon to sense the presence of glucose. In presence of glucose, cell switch off lac operon by the mechanism called **catabolite repression.**

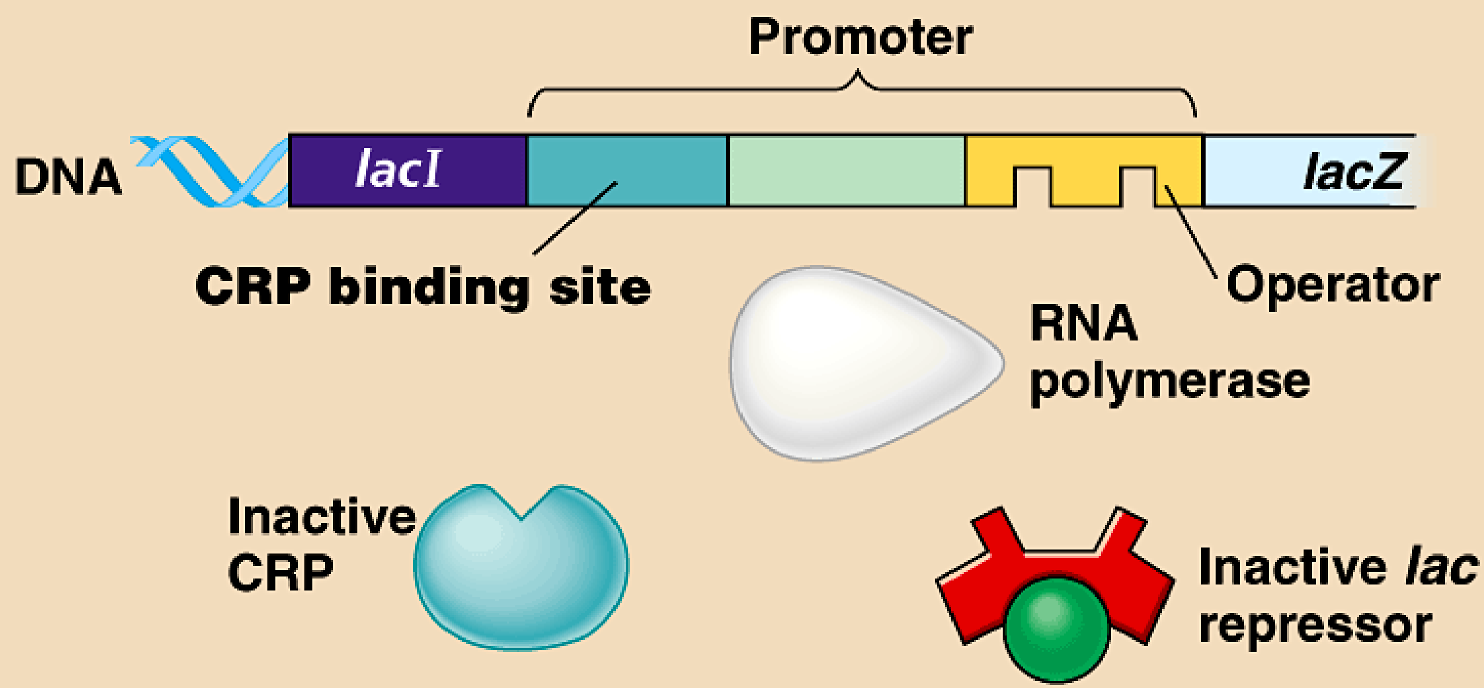
- Catabolite "activator" protein (CAP) in presence of effector (co-activator) increase the rate of transcription of lac operon in absence of glucose in cell.

CAP is positive regulator of Lac Opron



(a) Lactose present, glucose scarce (cAMP level high): abundant *lac* mRNA synthesized

Both Lactose and Glucose Present



(b) Lactose present, glucose present (cAMP level low): little *lac* mRNA synthesized

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