The *lac* Operon

(BIOT 4006: Genetics and Molecular Biology)

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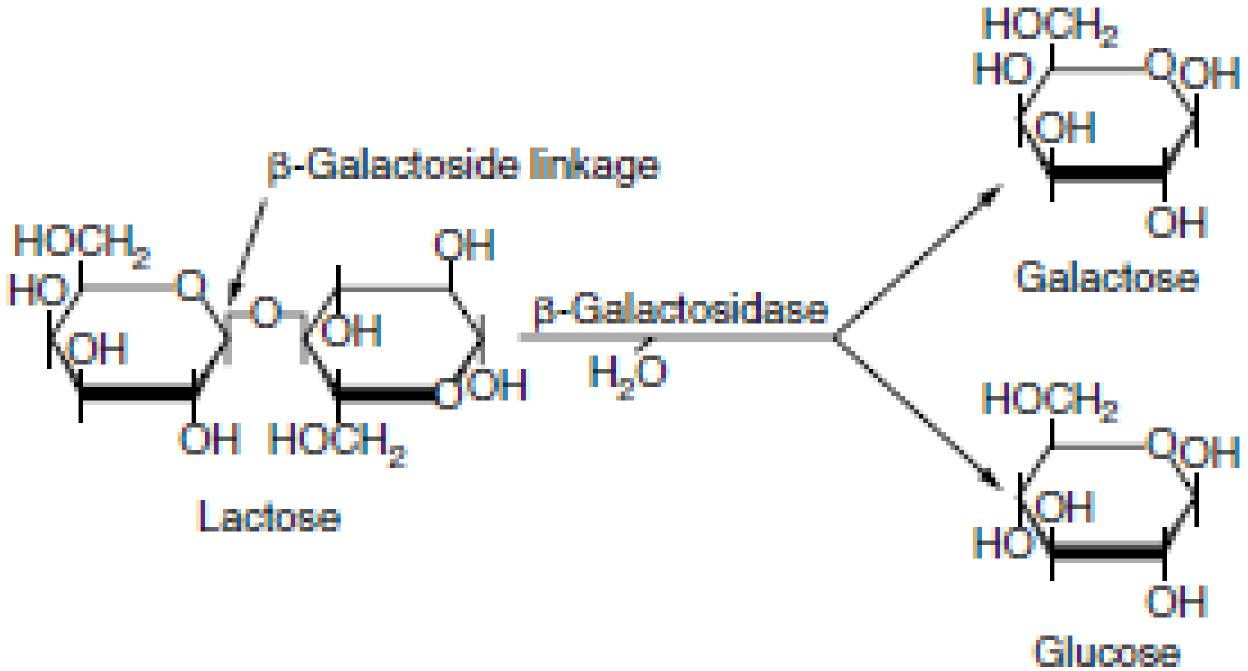
Structural genes of the *lac* operon

- Two enzymes have important role in lactose metabolism:

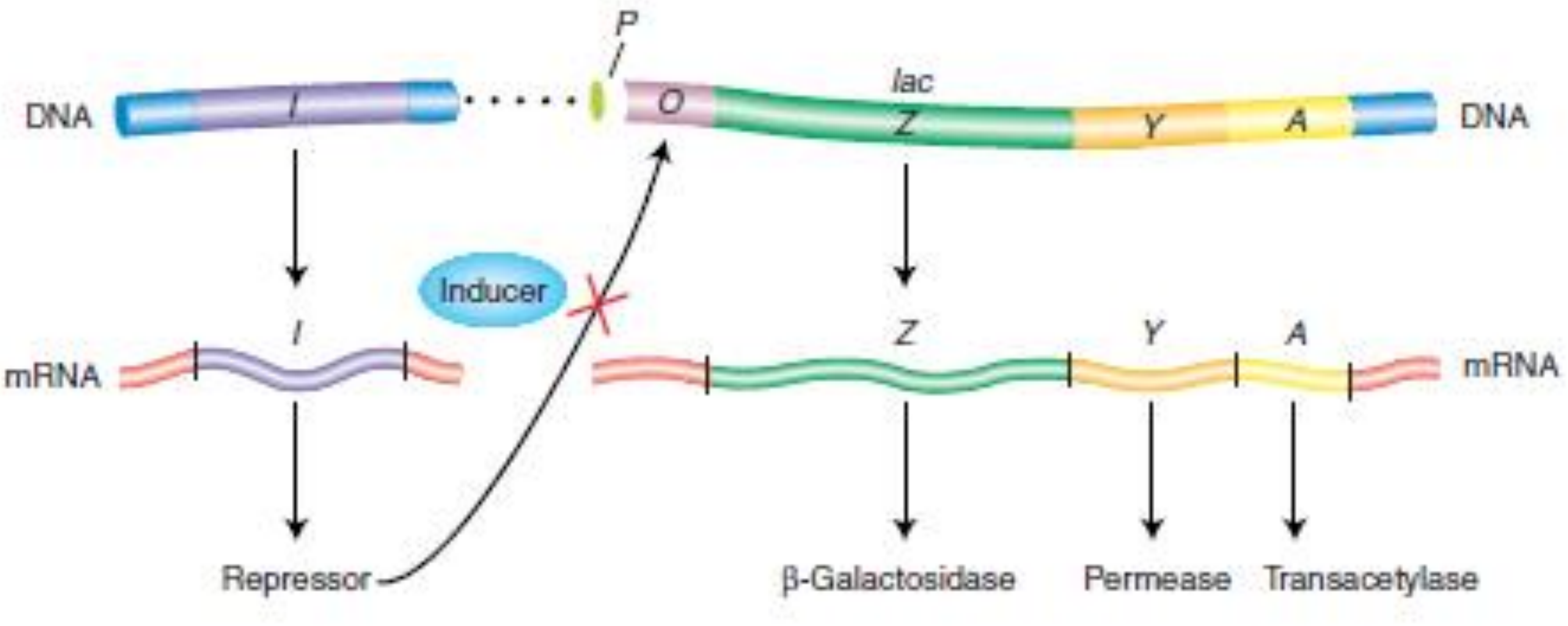
1. Permease: acts as a transporter for lactose intake.
2. β-galactosidase: breaks the lactose into glucose and galactose.



Lactose metabolism. Hydrolysis of the β-galactoside linkage present in lactose by β-galactosidase results in formation of galactose and glucose.

Reference: Introduction to Genetic Analysis, Ninth Edition, Anthony Griffiths et al., Chapter 10

- The adjacent genetic sequences Z and Y encode the β-galactosidase and permease proteins, respectively.
- The transacetylase enzyme (not needed in lactose metabolism) is encoded by the gene *A.* The genes *Z, Y* and *A* are called structural genes.
- All the three genes give a single mRNA after transcription however the products of Z and Y are important.
- The regulation of *lac* operon is done for synthesis of all the three enzymes simultaneously. That means, either the mRNA is synthesized or not synthesized.
- If the different proteins are transcribed by the genes acting as a single transcription unit, the regulation of their expression occurs coordinately.



A simple model of *lac* operon. The expression of the repressor protein by the *I* gene negatively controls the coordinated expression of the *Z, Y,* and *A* genes. Engagement of repressor by inducer results in expression of the structural genes.

Reference: Introduction to Genetic Analysis, Ninth Edition, Anthony Griffiths et al., Chapter 10

The *lac* regulatory components

- There are 3 Key regulatory components in the lac operon. One of them is a transcription regulatory protein and the other two are the docking sites for the regulatory protein and the RNA polymerase.

1. lac repressor coding gene. *I* gene codes for the Lac repressor protein (for blocking the expression of the Z, Y, and A genes). The *I* gene is located close to the structural genes (this closeness has no functional importance).

2. lac promoter site. The RNA polymerase binds to this site (P) for initiating transcription of the structural genes.

3. lac operator site. It is the binding site (O) for the lac repressor protein and is found between the promoter and *Z* gene close to transcription start site.

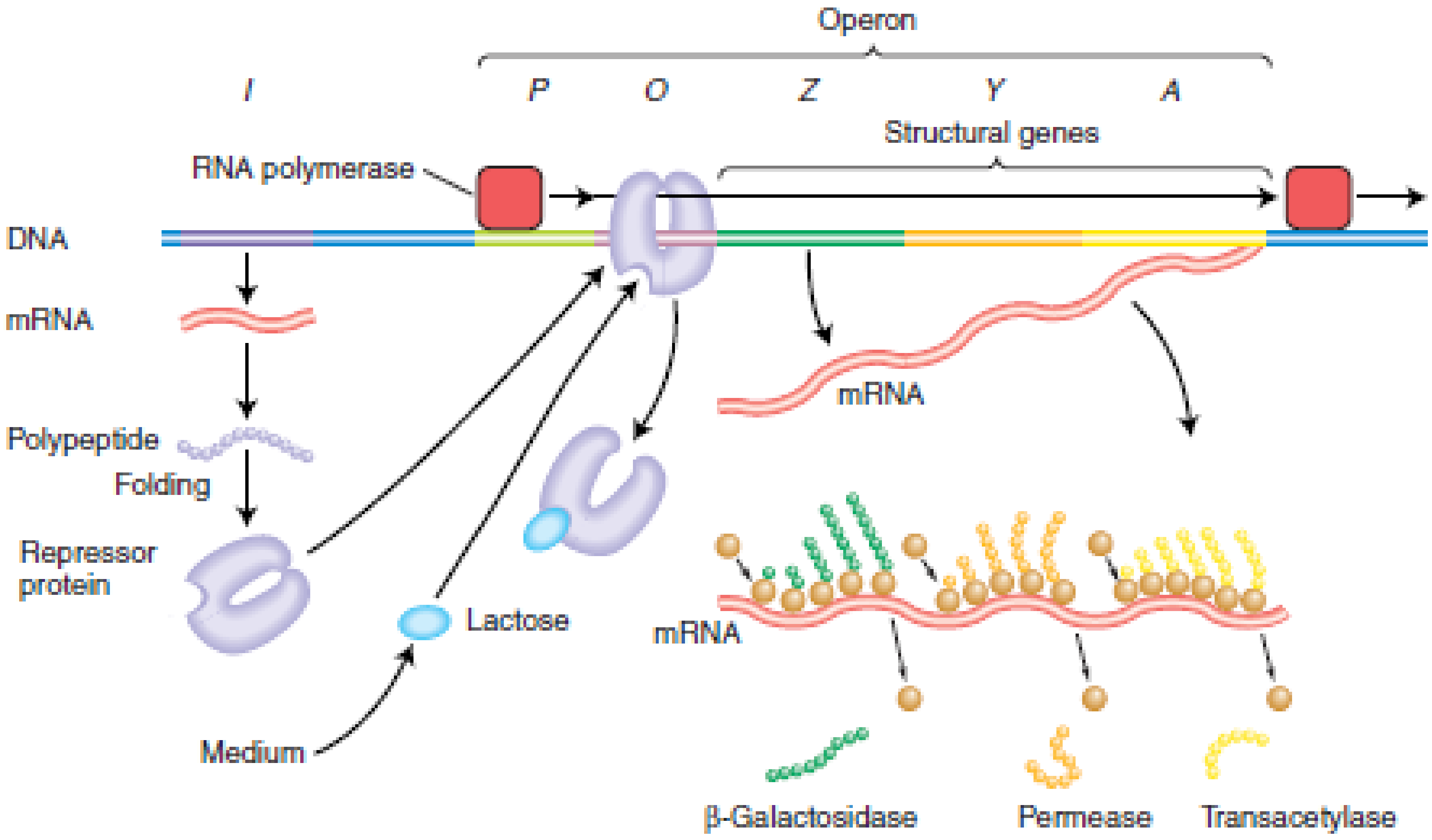
lac operon induction

- The lac operon is constituted by the P, O, Z, Y, and A segments. So a lac operon can be defined as a functional unit of DNA coding for the structural genes as well as the common promoter & regulatory region.

- The *lacI* gene is excluded from the lac operon defining region. However it has important role in transcriptional regulation in the form of interaction between repressor, operator and inducer.

- The lac repressor has one DNA binding domain for operator binding and an allosteric site for binding to inducer.

- The DNA binding domain on repressor is selective only for the region present adjacent to the genes that are controlled by it.



How *lac* operon is regulated? There is a constant expression of *I* gene, so repressor is always present. Transcription of structural genes is blocked by repressor binding to operator in absence of inducer (lactose). When lactose is present, it attaches with repressor and changes the latter's shape in such a manner that it looses its capacity to bind with operator. An unbound operator results in transcription of the structural genes and so production of respective enzymes.

Reference: Introduction to Genetic Analysis, Ninth Edition, Anthony Griffiths et al., Chapter 10

- Even if RNA polymerase is bound with the sequences adjacent to promoter, it can’t start transcription in presence of repressor bound with the operator.
- To prevent repressor’s halting of RNA polymerase, the former needs to be made unable to bind with the operator. This is done by lactose or its analogs that bind with repressor’s allosteric domain and change its DNA binding domain’s shape.
- The altered DNA binding domain (so the repressor) looses its affinity for operator and repressor falls off the DNA.
- The control system thus acts in a manner that the presence of lactose/analogs of lactose acts as a stimulant for transcription.
- In this way suppression of transcription is relieved by presence of lactose/analogs of lactose. They result in allosteric inactivation of the suppressor.
- Lactose/analogs of lactose are also called inducers as they cause induction of the transcription of structural genes.