Johns Hopkins Engineering

Molecular Biology 585.407

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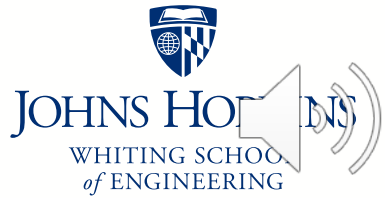
Module 12 / Lecture 1



The Regulation of Gene Expression

Gene regulation

Gene regulation is an important part of almost every process in nature.

Most genes are not expressed all the time.

Selective gene expression enables cells to synthesize only those gene products that are of immediate use.

Knowledge about the regulation of gene expression came from investigations of prokaryotes.

Bacteria are more amenable to the kinds of genetic and biochemical manipulations that marked the early studies of gene control mechanisms.

In prokaryotes, mechanisms of gene regulation operate mainly at the level of **transcription**.

Catabolic and anabolic pathways utilize different strategies for adaptive enzyme synthesis

Bacteria use two main strategies for regulating enzyme synthesis:

1. **catabolic** (degradative) or
2. **anabolic** (synthetic) pathway

The enzymes that catalyze such pathways are often **regulated coordinately** (ie, the synthesis of all the enzymes involved in a particular pathway is **turned on and off together**).

Catabolic pathways and substrate induction

Catabolic enzymes degrade specific substrates, often to obtain energy.

Figure 23-1 depicts the steps in the catabolic pathway that degrades disaccharide lactose into simple sugars that can then be metabolized by glycolysis.

The hydrolysis of lactose into the monosaccharides glucose and galactose is catalyzed by the enzyme β-galactosidase.

However, before lactose can be hydrolyzed, it must first be transported into the cell.

Galactoside permease is responsible for this transport, and it's synthesis is regulated coordinately with β-galactosidase.

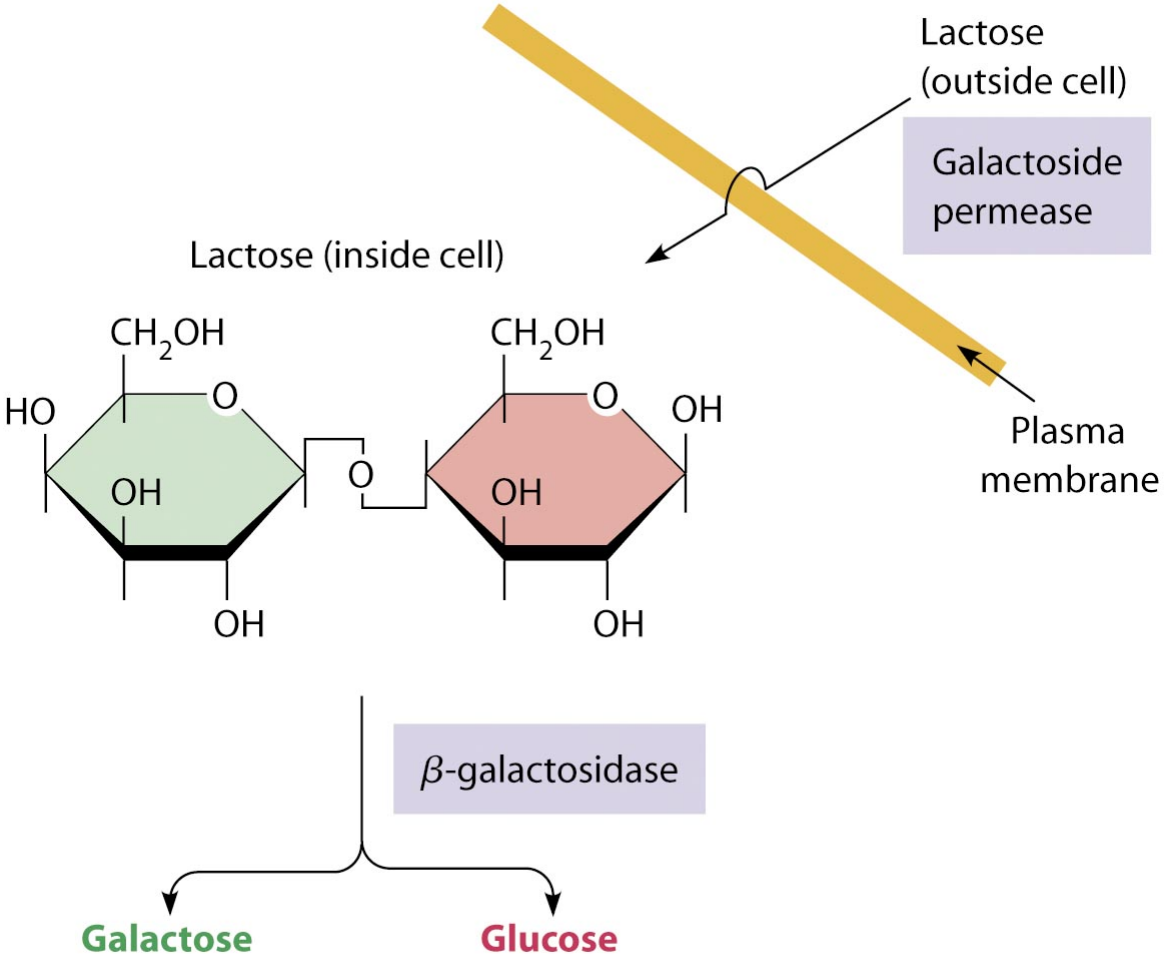


Figure 23-1

Anabolic pathways and end product repression

The regulation of **anabolic** pathways is the opposite of **catabolic** pathways.

Figure 23-2 summarizes the anabolic pathway for synthesizing the amino acid **tryptophan** from starting compound **chorismate**.

Enzymes that catalyze the six steps of this pathway are regulated coordinately at the genetic level.

For **anabolic** pathways, the amount of enzyme produced by a cell usually correlates with the intracellular concentration of the end-product of the pathway.

- **Tryptophan** is synthesized from the starting compound **chorismate**.
- **Chorismate**, is an important biochemical intermediate in plants and microorganisms.
- These reactions involve a set of enzymes (yellow boxes) whose synthesis is regulated in a coordinated way.

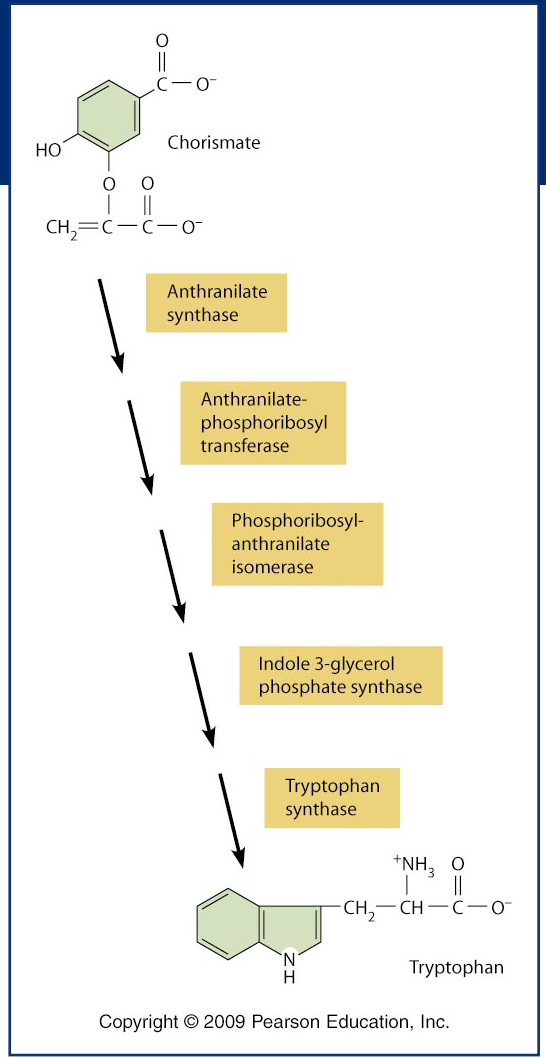


Figure 23-2

Anabolic pathways and end product repression

As the concentration of **tryptophan** rises, it is advantageous for the cell to economize on its metabolic resources by reducing its production of the enzymes involved in synthesizing tryptophan.

It is equally important that the cell be able to turn the production of these enzymes back on when the level of tryptophan decreases again.

This control is made possible by the ability of the **end-product** of an anabolic pathway. Tryptophan represses (reduces or stops) further production of the enzymes involved in its formation.

The reduction in the expression of the enzyme-coding genes is called end-product repression.

Most **biosynthetic** pathways in bacterial cells are regulated in this way.

Lac repressor is an allosteric protein whose binding to DNA is controlled by lactose

A key feature of the operon model is that genes with metabolically related functions are clustered together so their transcription can be regulated as a single unit.

For induction to occur, an additional gene must be present, a regulatory gene that they named *lacI* (for inducibility).

Whereas normal bacteria produce, β-galactosidase, galactoside permease and transacetylase only when an **inducer** is present, deletion of the *lacI* gene yielded cells that always produce these proteins, even when inducer is absent.

The *lac*I gene codes for a product that normally inhibits, and thereby regulates, expression of the lacZ, lacY, and lacA genes.

The regulatory gene product that inhibits expression of other genes is called a **repress**

Genetic repression (notes)

True genetic repression always has an effect on protein synthesis.

The end products of biosynthetic pathways often have an inhibitory effect on enzyme activity.

Feedback inhibition differs from repression in both mechanism and result:

- feedback inhibition, molecules of enzyme are still present, but their catalytic activity is inhibited.
- end product repression, the enzyme molecules are never made.

Effector molecules

One feature common to both induction and repression of enzyme synthesis is that control is exerted at the gene level in both cases.

Control is triggered by small organic molecules called **effectors** present within the cell or the cell's surroundings.

Effectors induce shape changes in allosteric proteins that control gene expression.

For **catabolic pathways**, effectors are almost always **substrates** (lactose example) - they function as inducers of gene expression and enzyme synthesis.

For **anabolic pathways**, effectors are usually **end products** (example – tryptophan) - they usually lead to the repression of gene expression and repression of enzyme synthesis.

Genes involved in lactose catabolism are organized into an inducible operon

Classic example of an inducible enzyme system occurs in the bacterium Escherichia coli.

It involves a group of enzymes involved in lactose catabolism - the enzymes that catalyze the steps shown in **Figure 23-3**.

Much of what we know about the regulation of gene expression in bacteria, including the vocabulary used to express that knowledge is based on the pioneering studies of this system carried out by French molecular geneticists Franyois Jacob and Jacques Monod.

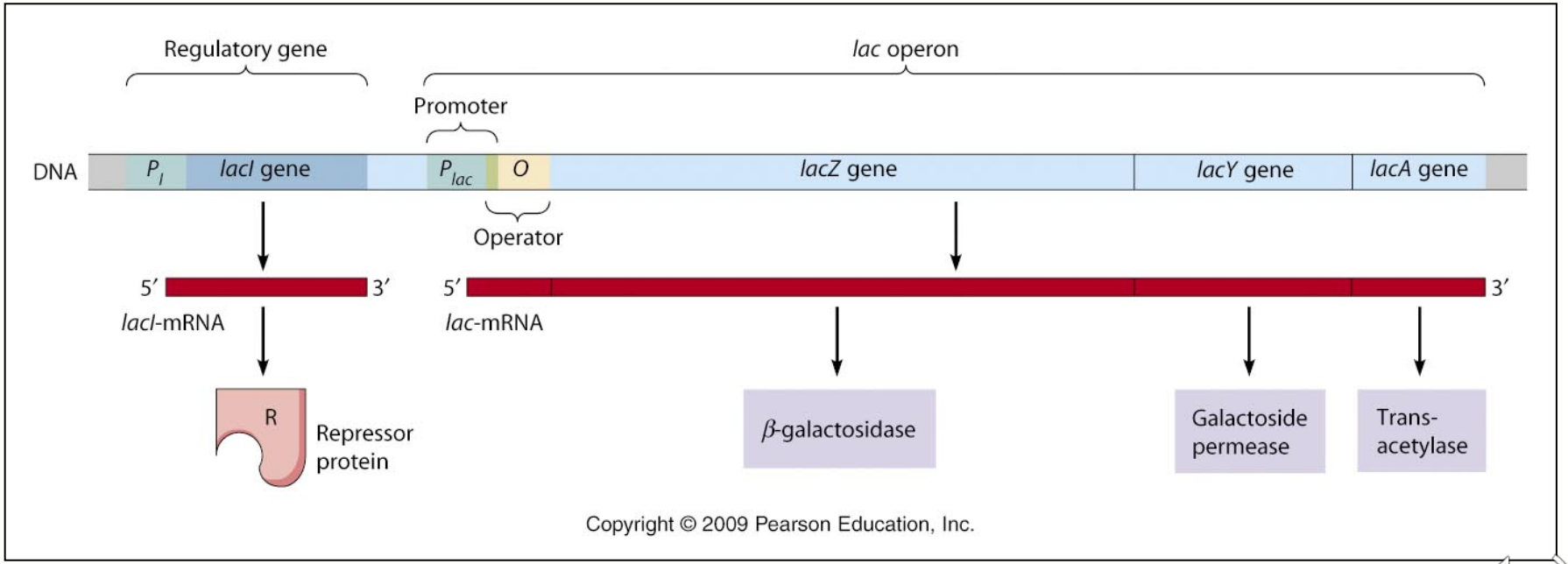

Regulatory gene
lac operon
Promoter
DNA
P_I
lacI gene
P_{lac}
O
lacZ gene
lacY gene
lacA gene
Operator
5′
3′
lacI-mRNA
5′
3′
lac-mRNA
R
Repressor protein
β-galactosidase
Galactoside permease
Trans-acetylase
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Figure 23-3