Regulation of Gene Expression

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Some Features of Prokaryotic Gene Expression Are Unique

- **Operon:** *genes involved in a metabolic pathway are often present in a linear array ,***ex:** the *lac operon.*
- ***Cistron*** *is the smallest unit of genetic expression.*
- One gene, one enzyme idea might more accurately be regarded as a ***one cistron, one subunit concept.***
- **A** single mRNA that encodes more than one separately translated protein is referred to as a ***polycistronic mRNA.***
- For example, *the polycistronic lac operon mRNA* is translated into three separate proteins.
- Operons and polycistronic mRNAs are common in bacteria but not in eukaryotes.

Some Features of Prokaryotic Gene Expression Are Unique

- An **inducible gene** is one whose expression increases in response to an inducer or activator, a specific positive regulatory signal.
- In general, inducible genes have relatively low basal rates of transcription.
- By contrast, genes with high basal rates of transcription are often subject to down-regulation by repressors (**repressible gene**).
- The expression of some genes is **constitutive,** meaning that they are expressed at a reasonably constant rate and not known to be subject to regulation. These are often referred to as **housekeeping genes.**

Analysis of Lactose Metabolism in *E coli* Led to the Operon Hypothesis

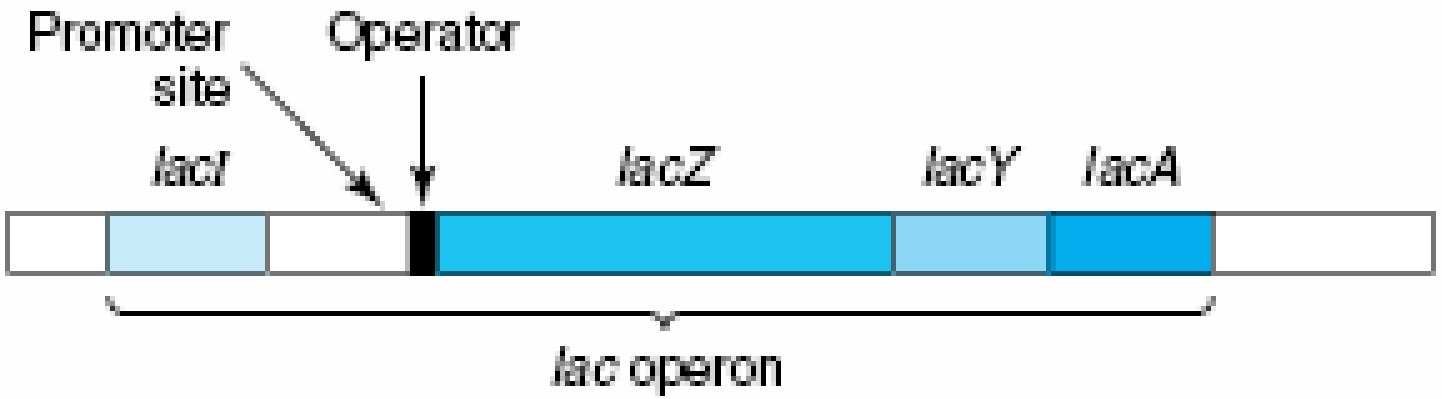


Figure 39–2. The positional relationships of the structural and regulatory genes of the *lac* operon. *lacZ* encodes β-galactosidase, *lacY* encodes a permease, and *lacA* encodes a thiogalactoside transacetylase. *lacI* encodes the *lac* operon repressor protein.

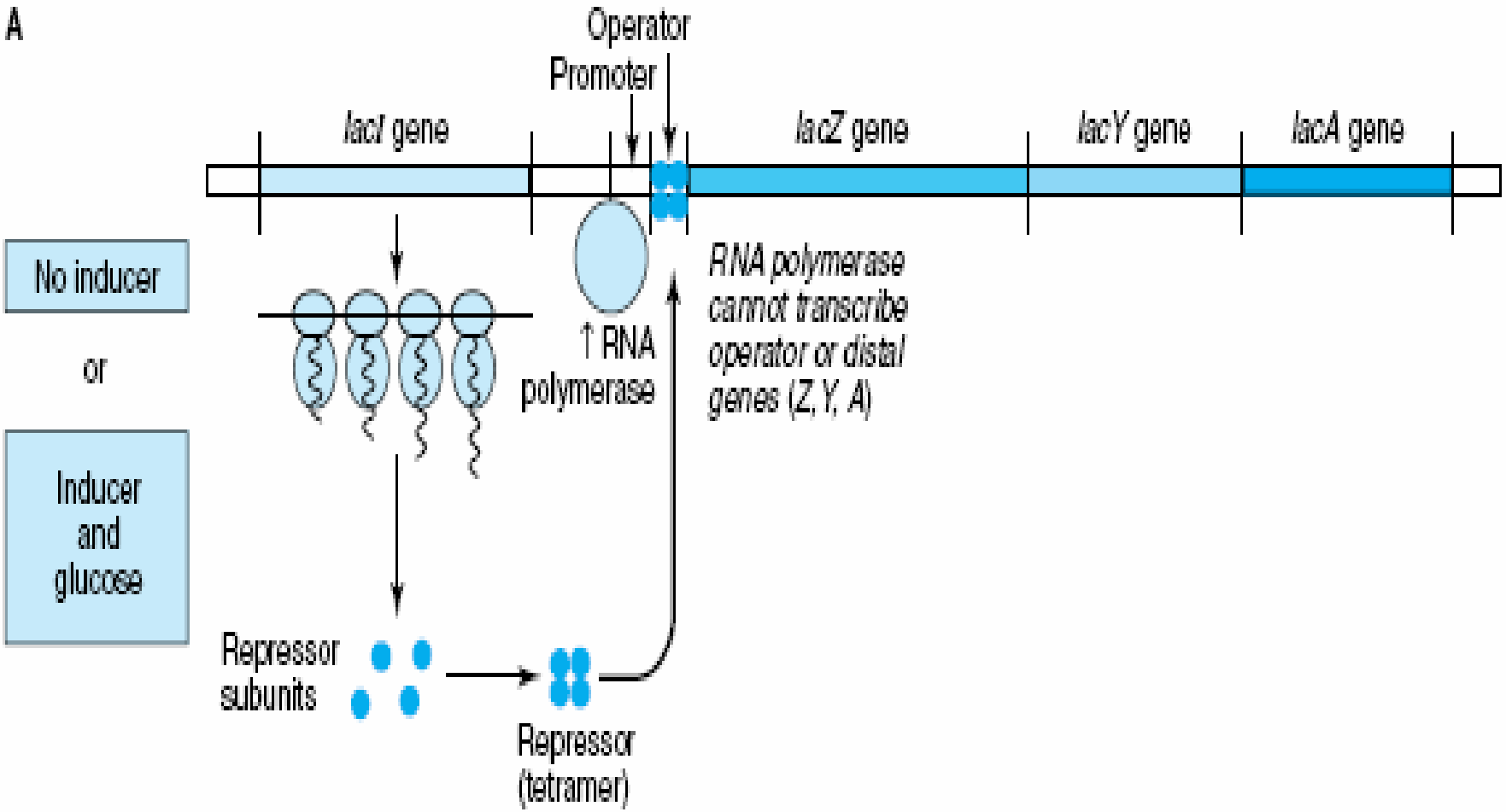
- Each gene is transcribed into one large mRNA molecule that contains multiple independent translation start (AUG) and stop (UAA) codons for each cistron. Thus, each protein is translated separately.
- This type of mRNA molecule is called a **polycistronic mRNA.**
- High concentrations of lactose, no or very low glucose in media; the expression of the activities of β-galactosidase, galactoside permease, and thiogalactoside transacetylase is increased 100-fold to 1000-fold*lac-specific mRN.*
- *As are* fully induced within 5–6 minutes after addition of lactose to a culture.

When *E coli is exposed to both lactose and glucose*

- The organisms first metabolize the glucose and then temporarily stop growing until the genes of the *lac operon become induced to provide the* ability to metabolize lactose as a usable energy source.
- It is now known that catabolite repression is in fact mediated by a **catabolite gene activator protein (CAP) in conjunction with cAMP.**
- Expression of the normal *lacI gene of the lac operon is* ***constitutive***

- The LacI repressor protein molecule, the product of *lacI*, has a high affinity for the operator locus.
- The **operator locus** is between the **promoter site**, at which the DNA-dependent RNA polymerase attaches to commence transcription, and the **transcription initiation site of the *lacZ gene, the structural*** gene for β-galactosidase.
- When attached to the operator locus, the LacI repressor molecule prevents transcription of the operator locus as well as of the distal structural genes, *lacZ, lacY, and lacA.*
- *Thus, the* LacI repressor molecule is a **negative regulator.**

Negative Regulation of Lac Operon



- Binding of the **inducer** to a **repressor** molecule attached to the operator locus induces a **conformational** change in the structure of the repressor and causes it to dissociate from the DNA.
- The polymerase generates a polycistronic mRNA whose 5′ terminal is complementary to the template strand of the operator.

- **An inducer derepresses the *lac* operon and allows transcription of the structural genes** for β-galactosidase, galactoside permease, and thiogalactoside transacetylase.

- Derepression of the *lac operon allows the cell to* synthesize the enzymes necessary to catabolize lactose as an energy source.

- There must also be present the **catabolite gene activator protein (CAP) to which** cAMP is bound.

- **In the presence of glucose**—or of glycerol in concentrations sufficient for growth—the bacteria will lack sufficient cAMP to bind to CAP because the glucose inhibits adenylyl cyclase.

- In **the presence of the CAP-cAMP complex**, which binds to DNA just upstream of the promoter site, transcription then occurs.

- Thus, the CAP-cAMP regulator is acting as a **positive regulator because its presence is required** for gene expression.

Positive Regulation of Lac Operon