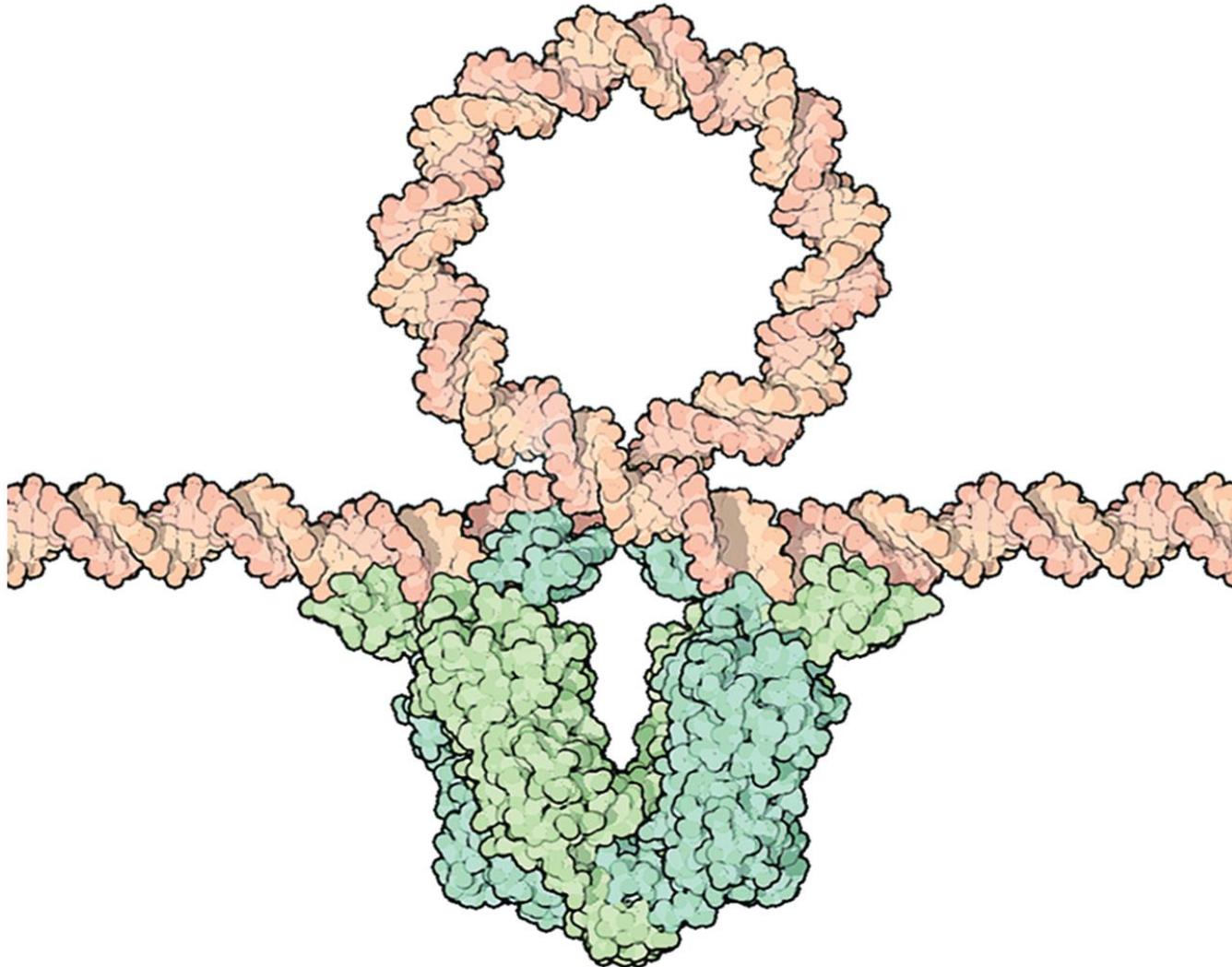


## Chapter 16 Gene regulation in bacteria



*A model showing the binding of a genetic regulatory protein to DNA, which results in a DNA loop. The model shown here involves the lac repressor protein found in E. coli binding to the operator site in the lac operon.*

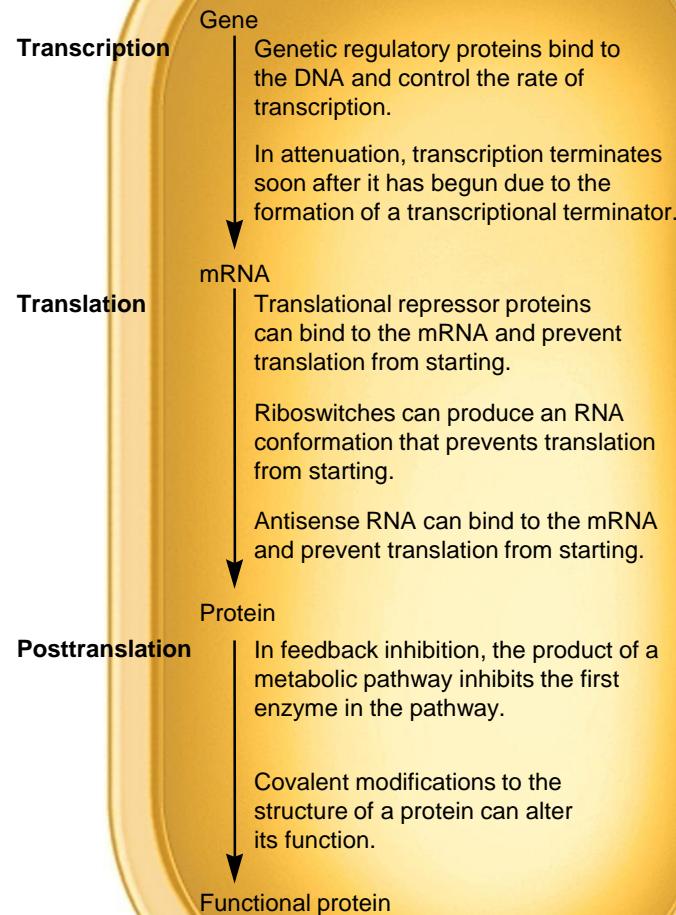
© Illustration by David S. Goodsell of The Scripps Research Institute



- Gene expression can be
  - Unregulated - **constitutive**
    - Essentially constant levels of expression
    - Frequently for proteins that are continuously necessary for the survival of the organism
  - **Regulated**
    - Expression may be increased or decreased according to the demand for the gene product
    - Encoded proteins will be produced only when required

- Gene regulation is important for cellular processes such as
  - Metabolism
  - Response to environmental stress
  - Cell division
- Regulation can occur at any of the points on the pathway to gene expression
  - Refer to Figure 16.1

## REGULATION OF GENE EXPRESSION



**Figure 16.1**

# 16.1 Overview of Transcriptional Regulation

- The function of activators and repressors
- How small effector molecules affect the function of activators and repressors

## Transcriptional Regulation

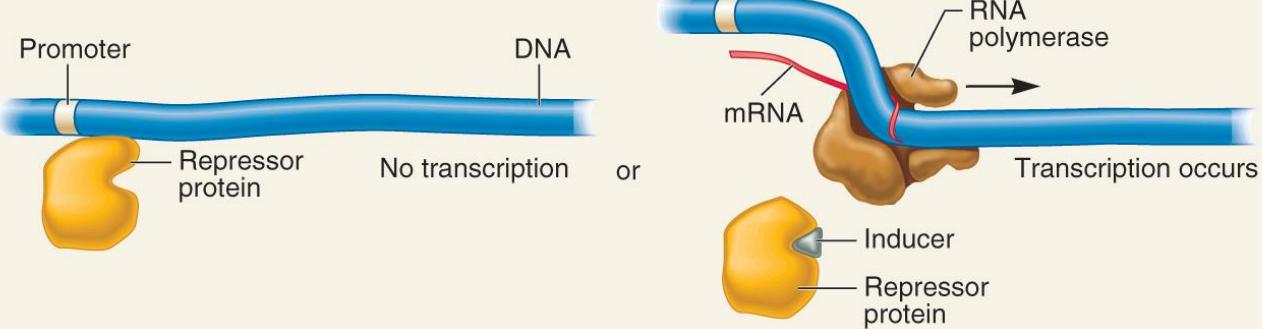
- The most common way to regulate gene expression in prokaryotes (and eukaryotes) is at the level of **transcription initiation**
  - The rate of RNA synthesis is increased or decreased
- Transcriptional regulation involves the actions of two main types of regulatory proteins
  - Negative control
    - **Repressors** - Inhibit transcription
  - Positive control
    - **Activators** - Increase transcription

- The activator and repressor proteins can be bound and affected by **small effector molecules**
- In some cases, the presence of a small effector molecule may increase transcription
  - These molecules are termed **inducers**
  - They function in two ways
    - Bind activators and cause them to bind to DNA
    - Bind repressors and prevent them from binding DNA
  - Genes that are regulated in this manner are termed **inducible**

- In other cases, the presence of a small effector molecule may inhibit transcription
  - **Corepressors** bind to repressors and cause them to bind to DNA
  - **Inhibitors** bind to activators and prevent them from binding to DNA
  - Genes that are regulated in this manner are called **repressible genes**
  - Refer to Figure 16.2

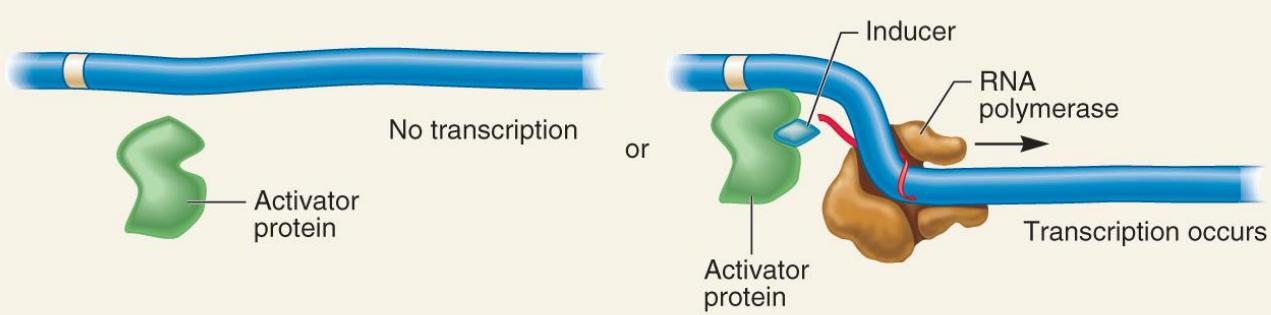
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In the absence of the inducer, this repressor protein blocks transcription. The presence of the inducer causes a conformational change that inhibits the ability of the repressor protein to bind to the DNA. Transcription proceeds.



(a) Repressor protein, inducer molecule, inducible gene

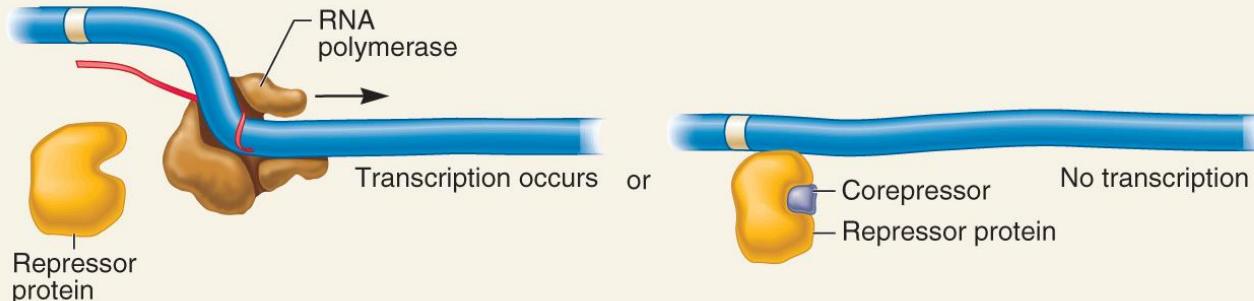
This activator protein cannot bind to the DNA unless an inducer is present. When the inducer is bound to the activator protein, this enables the activator protein to bind to the DNA and activate transcription.



(b) Activator protein, inducer molecule, inducible gene

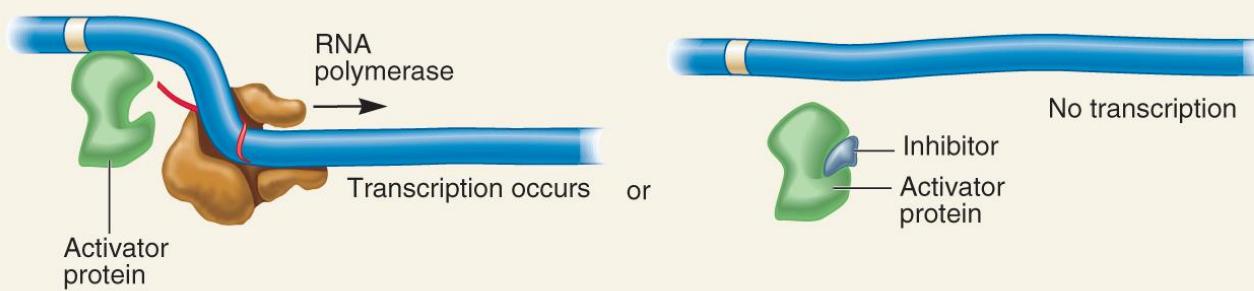
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In the absence of a corepressor, this repressor protein will not bind to the DNA. Therefore, transcription can occur. When the corepressor is bound to the repressor protein, a conformational change occurs that allows the repressor to bind to the DNA and inhibit transcription.



**(c) Repressor protein, corepressor molecule, repressible gene**

This activator protein will bind to the DNA without the aid of an effector molecule. The presence of an inhibitor causes a conformational change that inhibits the ability of the activator protein to bind to the DNA. This inhibits transcription.



**(d) Activator protein, inhibitor molecule, repressible gene**

**Figure 16.2**

# 16.2 Regulation of the *lac Operon*

## The Phenomenon of Enzyme Adaptation

- At the turn of the 20<sup>th</sup> century, scientists made the following observation
  - A particular enzyme appears in the cell only after the cell has been exposed to the enzyme's substrate
  - This observation became known as **enzyme adaptation**
- François Jacob and Jacques Monod at the Pasteur Institute in Paris were interested in this phenomenon
  - Their investigation of enzyme adaptation focused on **lactose metabolism in *E. coli***

# The *lac* Operon

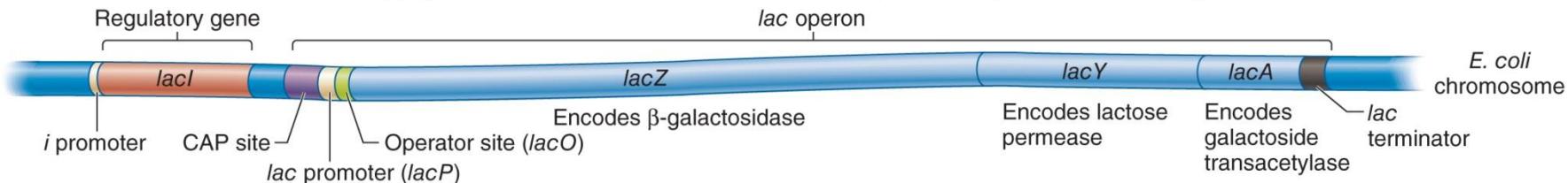
- An **operon** is a regulatory unit consisting of a few structural genes under the control of *one* promoter
  - It encodes a **polycistronic mRNA** that contains the coding sequence for two or more genes
  - This allows a bacterium to coordinately regulate a group of genes encoding proteins that are involved in a common process
    - Genes in the *lac* operon are involved in **lactose metabolism**

- The *lac* operon contains several different regions
  - **Promoter** – Binds RNA pol Holoenzyme
  - **CAP site** – Positive regulation-site for **catabolite activator protein** (CAP)
  - **Operator** – negative regulation when bound by repressor protein (the *lacI* gene product)
  - Protein-coding genes: ***lacZ***, ***lacY***, and ***lacA***
  - **Terminator**

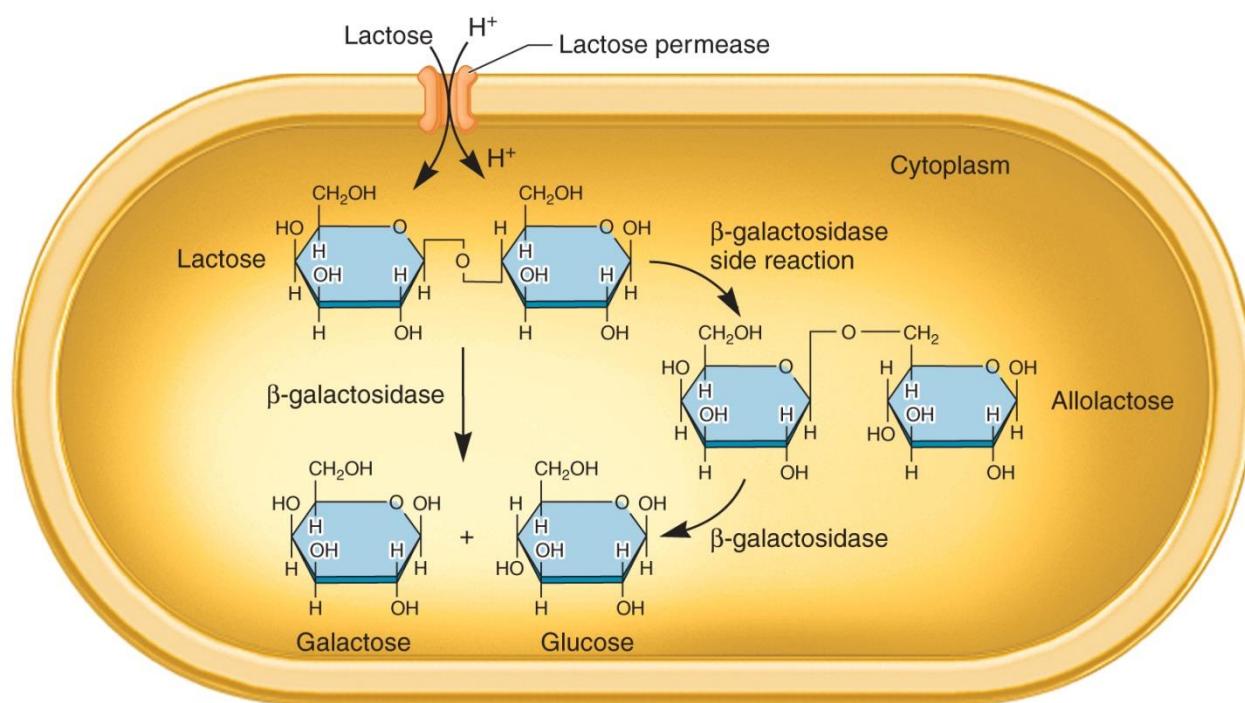
- Structural genes of the *lac* operon
  - ***lacZ*** - Encodes β-galactosidase
    - » Cleaves lactose and lactose analogues
    - » Also converts lactose into allolactose (an isomer)
  - ***lacY*** - Encodes lactose permease
    - » Membrane protein required for transport of lactose and analogues into the cell
  - ***lacA*** - Encodes transacetylase
    - » Covalently modifies lactose and analogues
    - » Its functional necessity remains unclear

Refer to Figure 16.3

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(a) Organization of DNA sequences in the *lac* region of the *E. coli* chromosome



(b) Functions of lactose permease and β-galactosidase

## Figure 16.3



# *lac* Operon Regulation

- Negative control mechanism
  - Uses *lac* repressor protein (*lacI* gene product)
  - Repressor binds to operator region
  - When bound to the operator region, it interferes with holoenzyme binding to promoter
  - Binding of allolactose, a catabolite of lactose, inactivates the repressor so that it can not bind to the operator
  - Refer to Figure 16.4

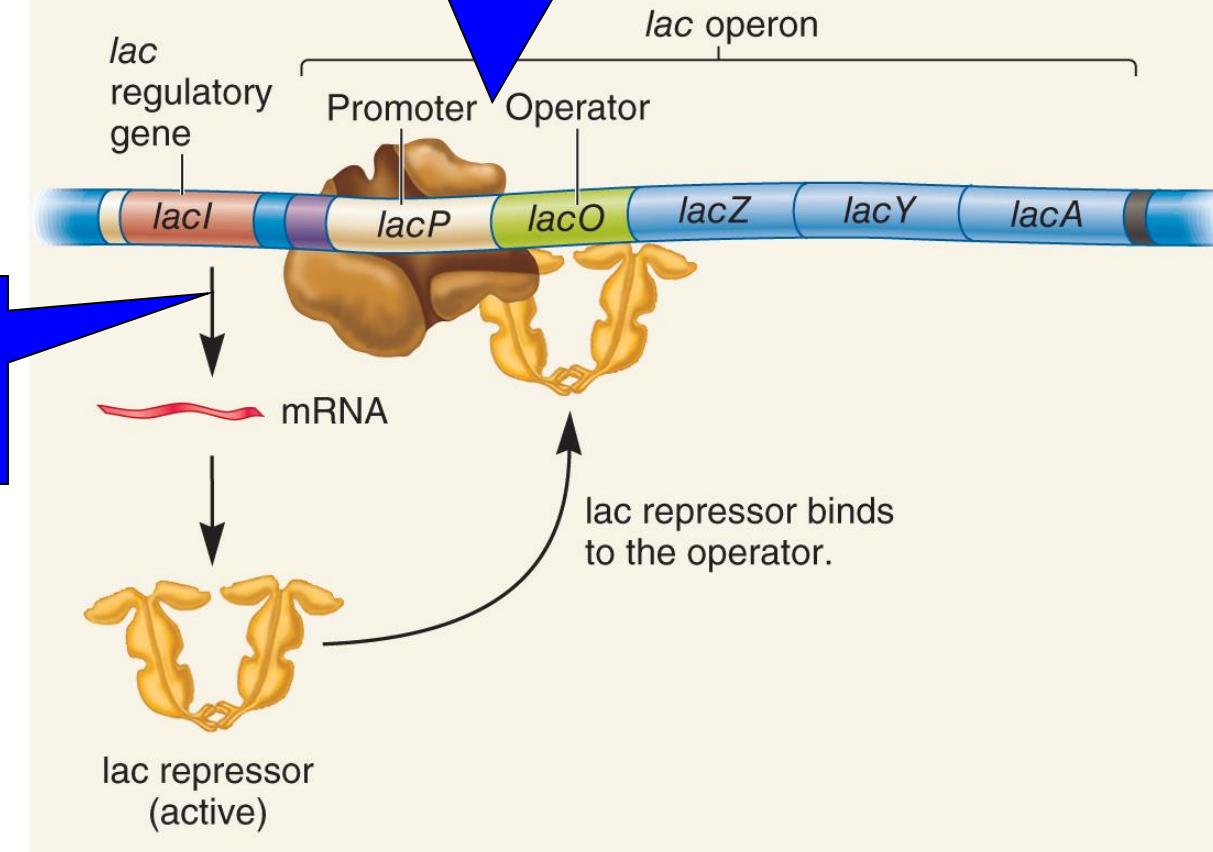
## RNA pol cannot access the promoter when repressor bound to operator

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the repressor protein is thereby inhibiting the ability of the operon.

tightly bound to the RNA polymerase to

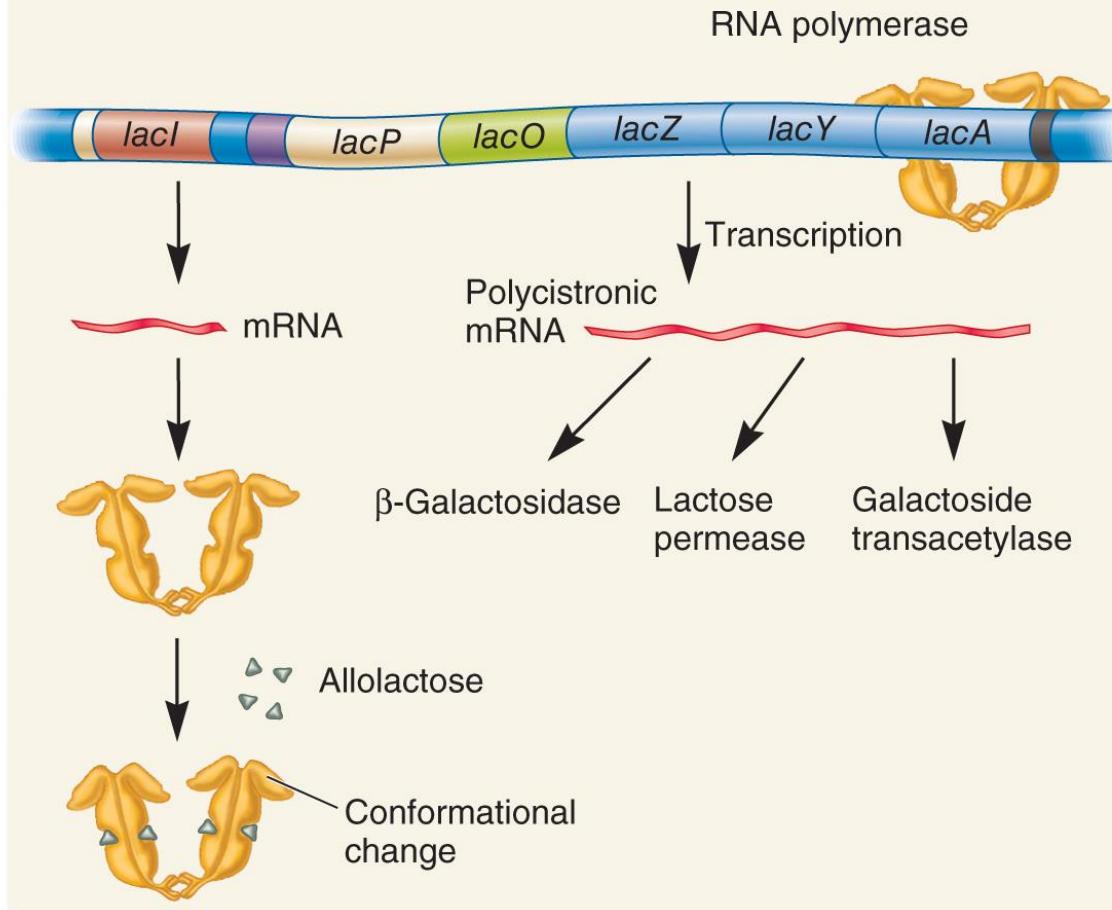
### Constitutive expression of lacI



(a) No lactose in the environment

Figure 16.4

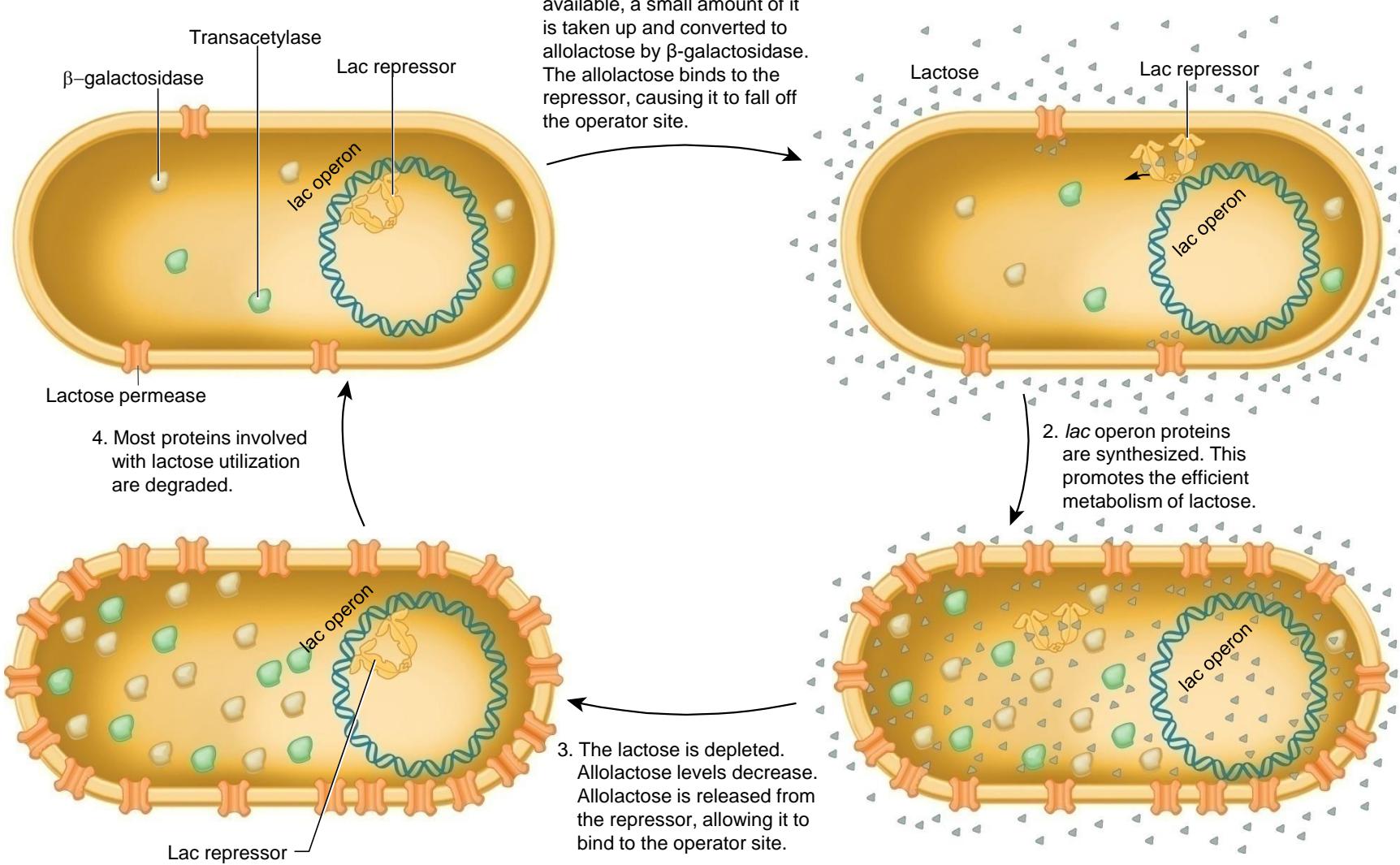
When allolactose is available, it binds to the repressor. This alters the conformation of the repressor protein, which prevents it from binding to the operator site. Therefore, RNA polymerase can transcribe the operon.



(b) Lactose present

Figure 16.4

- Presence of repressor protein does not completely inhibit transcription of *lac* operon
  - Low level of basal transcription
  - Produces enough  $\beta$ -galactosidase and permease to "sense" if lactose is in environment
  - Refer to Figure 16.5



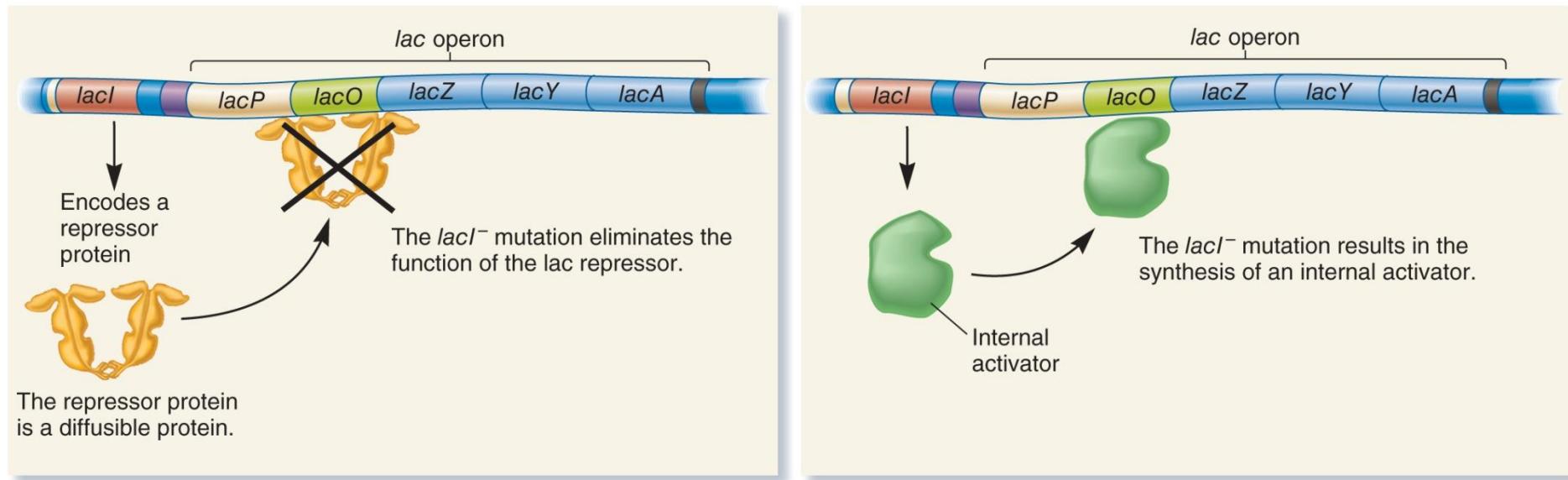
**Figure 16.5**

# Demonstration that the *lacI* Gene Encodes a Diffusible Repressor Protein

- In the 1950s, Jacob and Monod, and their colleague Arthur Pardee, identified a few rare mutant strains of bacteria with abnormal lactose adaptation
- One type of mutant involved a defect in the *lacI* gene
  - It was designated *lacI<sup>-</sup>*
  - It resulted in the **constitutive expression** of the *lac* operon even in the absence of lactose
  - The *lacI<sup>-</sup>* mutations mapped very close to the *lac* operon

- Jacob, Monod and Pardee proposed two different functions for the *lacI* gene
  - 1) Repressor
  - 2) Internal activator
- Jacob, Monod and Pardee applied a genetic approach to distinguish between the two hypotheses

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**Figure 16.6**

# The Hypothesis

The *lacI* mutation either

1. Results in the synthesis of an internal activator or
2. Eliminates the function of the *lac* repressor that can diffuse throughout the cell

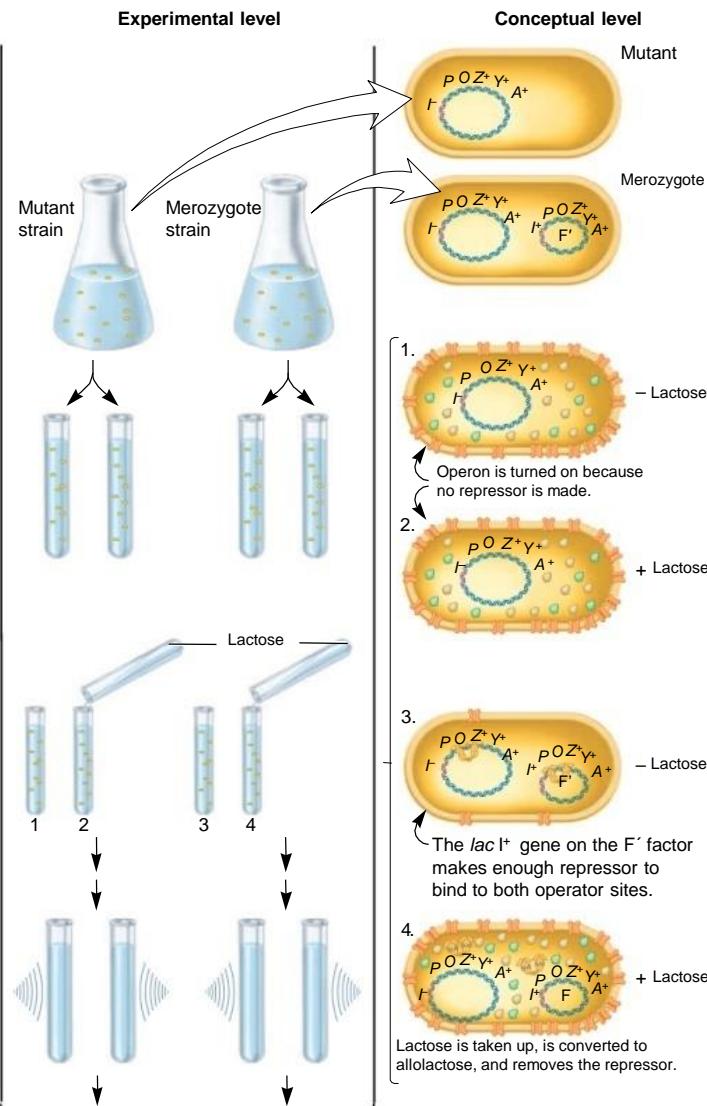
## Testing the Hypothesis

- Bacterial conjugation methods to introduce different portions of the *lac* operon into different strains
- They identified F' factors (plasmids) that carried portions of the *lac* operon
- For example: Consider an F' factor that carries the *lacI* gene
  - Bacteria that receive this will have two copies of the *lacI* gene
    - One on the chromosome and the other on the F' factor
  - These are called **merozygotes**, or partial diploids

- There are two key points
  - 1. The two *lacI* genes in a merozygote may be different alleles
    - *lacI<sup>-</sup>* on the chromosome
    - *lacI<sup>+</sup>* on the F' factor
  - 2. Genes on the F' factor are not physically connected to those on the bacterial chromosome
    - If hypothesis 1 is correct
      - The activator protein produced from the chromosome can diffuse and activate the *lac* operon on the F' factor
    - If hypothesis 2 is correct
      - The repressor from the F' factor can diffuse and turn off the *lac* operon on the bacterial chromosome

- Merozygotes tested for which genes were expressed from chromosome and the F' in the presence or absence of lactose
- Refer to Figure 16.7

1. Grow mutant strain and merozygote strain separately.



2. Divide each strain into two tubes.

3. In one of the two tubes, add lactose.

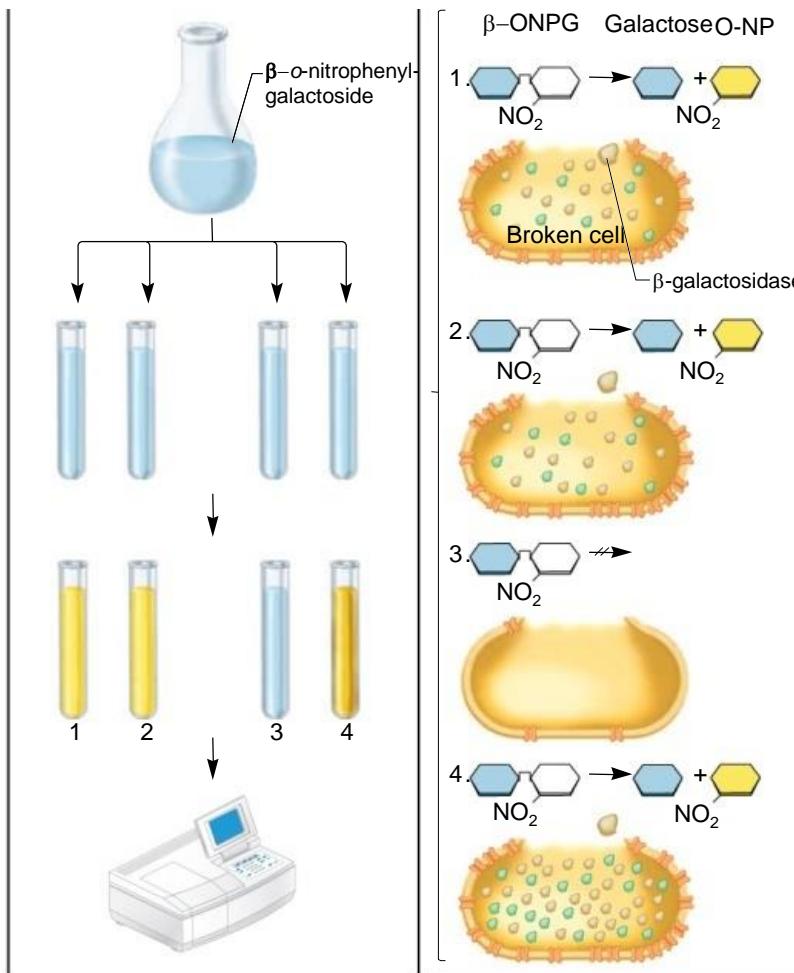
4. Incubate the cells long enough to allow lac operon induction.

5. Burst the cells with a sonicator. This allows β-galactosidase to escape from the cells.

6. Add  $\beta$ -D-nitrophenylgalactoside ( $\beta$ -ONPG). This is a colorless compound.  $\beta$ -galactosidase will cleave the compound to produce galactose and D-nitrophenol (D-NP). D-NP has a yellow color. The deeper the yellow color, the more  $\beta$ -galactosidase was produced.

7. Incubate the sonicated cells to allow  $\beta$ -galactosidase time to cleave  $\beta$ -ONPG.

8. Measure the yellow color produced with a spectrophotometer. (See the Appendix for a description of spectrophotometry.)



**Figure 16.7**

# Interpreting the Data

<i>Strain</i>	<i>Addition of lactose</i>	<i>Amount of <math>\beta</math>-galactosidase (percentage of parent strain)</i>
Mutant	No	100%

This is a negative control demonstrating that in the absence of lactose, expression occurs as expected

The strain lacks a functional repressor

<i>Strain</i>	<i>Addition of lactose</i>	<i>Amount of <math>\beta</math>-galactosidase (percentage of parent strain)</i>
Mutant	No	100%
Mutant	Yes	100%

Another control that demonstrates that the addition of lactose has no affect on the amount of enzyme produced

The result is as expected as there is no *lacI* product for the allolactose to bind

<i>Strain</i>	<i>Addition of lactose</i>	<i>Amount of <math>\beta</math>-galactosidase (percentage of parent strain)</i>
Mutant	No	100%
Mutant	Yes	100%
Merozygote	No	<1%

In the merozygote the F' carries a functional *lacI* gene

This gene interferes with expression from the host chromosomal *lac* operon as well as the F'

This data is consistent with hypothesis 2 (Eliminates the function of the *lac* repressor that can diffuse throughout the cell)

<i>Strain</i>	<i>Addition of lactose</i>	<i>Amount of <math>\beta</math>-galactosidase (percentage of parent strain)</i>
Mutant	No	100%
Mutant	Yes	100%
Merozygote	No	<1%
Merozygote	Yes	220%

Question: If the hypothesis I (internal inducer) was correct, what numbers you would get from this experiment?

Control demonstrating that the F' *lacI* can be regulated by lactose

Regulation of repression of expression of host *lac* operon behaves identically to *lacI* being on host chromosome

Expression occurs from both host chromosome and F'

This data is consistent with hypothesis 2

- Other strains of bacteria and different F's were tested to for *lac* operon expression to see the effect of different types of mutations within *lacI* or the *lac* operon
- Refer to Table 16.1

**TABLE 16.1**

**A Comparison of Loss-of-Function Mutations in the *lacI* Gene Versus the Operator Site**

Chromosome	F' factor	Expression of the <i>lac</i> Operon (%)	
		With Lactose	Without Lactose
Wild type	None	100	<1
<i>lacI</i> <sup>-</sup>	None	100	100
<i>lacO</i> <sup>-</sup>	None	100	100
<i>lacI</i> <sup>-</sup>	<i>lacI</i> <sup>+</sup> and a normal <i>lac</i> operon	200	<1
<i>lacO</i> <sup>-</sup>	<i>lacI</i> <sup>+</sup> and a normal <i>lac</i> operon	200	100

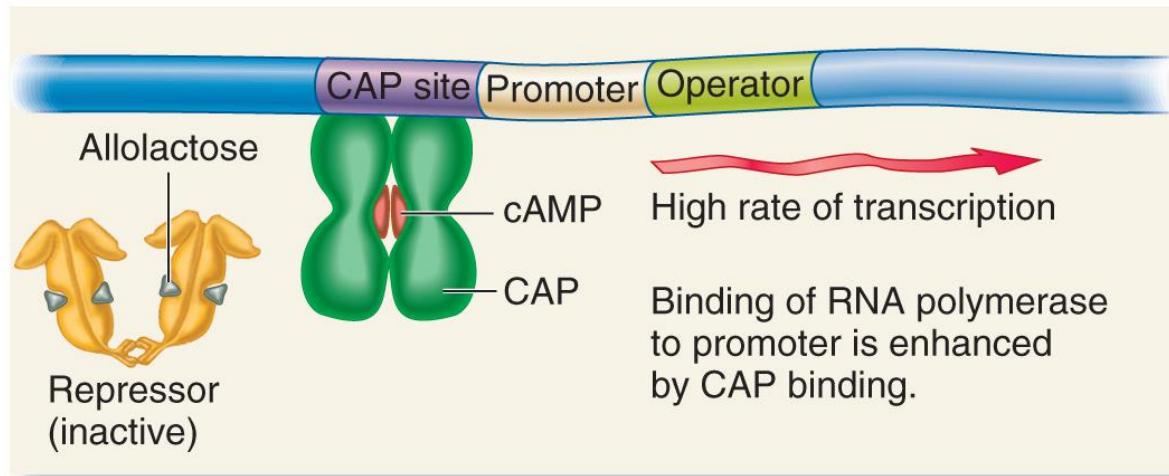
- The interaction between regulatory proteins and DNA sequences led to two definitions
  - 1. ***Trans*-effect** , or **trans-acting factor**
    - Genetic regulation that can occur even though DNA segments are not physically adjacent
    - Mediated by genes that encode regulatory proteins
    - Example: The action of the *lac* repressor on the *lac* operon
  - 2. ***Cis*-effect** or **cis-acting element**
    - A DNA sequence that must be adjacent to the gene(s) it regulates
    - Mediated by sequences that bind regulatory proteins
    - Example: The *lac* operator
  - A mutation in a *trans*-acting factor is complemented by the introduction of a second gene with normal function
  - However, a mutation in a *cis*-acting element is not

# The *lac* Operon Is Also Regulated by an Activator Protein

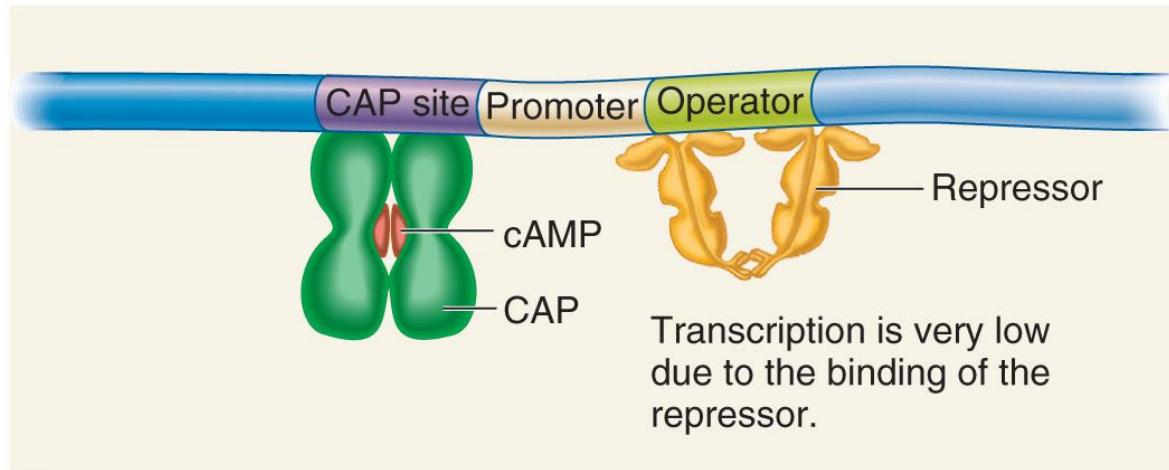
- The *lac* operon can be transcriptionally regulated in a second way, known as **catabolite repression**
- When exposed to both lactose and glucose
  - *E. coli* uses glucose first, and catabolite repression prevents the use of lactose
  - When glucose is depleted, catabolite repression is alleviated, and the *lac* operon is expressed
- The sequential use of two sugars by a bacterium is termed **diauxic growth**

- The small effector molecule in catabolite repression is not glucose
- It is the small molecule, **cyclic AMP** (cAMP)
  - It is produced from ATP via the enzyme adenylyl cyclase
  - cAMP binds an activator protein known as the Catabolite Activator Protein (CAP)

- The cAMP-CAP complex is an example of genetic regulation that is inducible and under positive control
  - The cAMP-CAP complex binds to the CAP site near the *lac* promoter and transcription rate increases
- In the presence of glucose, the enzyme adenylyl cyclase is inhibited
  - This decreases the levels of cAMP in the cell
    - Therefore, cAMP is no longer available to bind CAP and the transcription rate decreases
- Refer to Figure 16.8

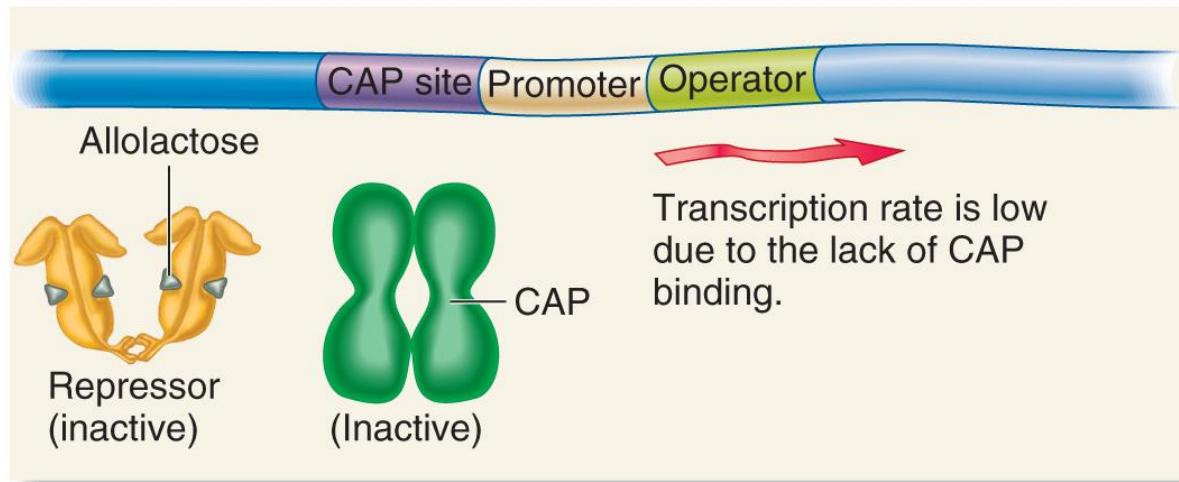


(a) Lactose, no glucose (high cAMP)

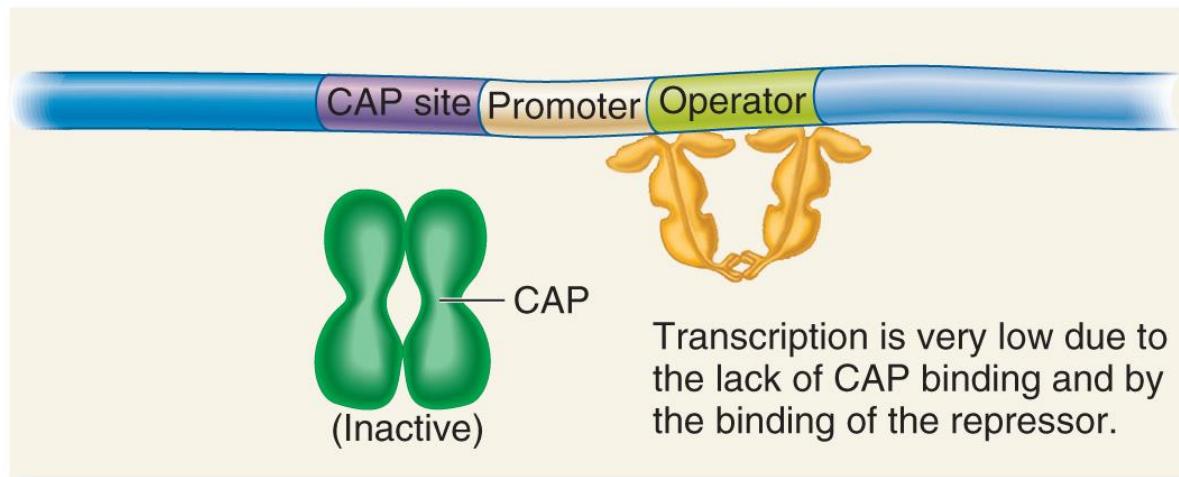


(b) No lactose or glucose (high cAMP)

Figure 16.8



(c) Lactose and glucose (low cAMP)



(d) Glucose, no lactose (low cAMP)

# The *lac* Operon Has Three Operator Sites for the *lac* Repressor

- Detailed genetic and crystallographic studies have shown that the binding of the *lac* repressor is more complex than originally thought
- In all, three operator sites have been discovered
  - $O_1$  – Slightly downstream from the promoter
  - $O_2$  - Downstream in the *lacZ* coding region
  - $O_3$  - Slightly upstream from the promoter
- The *lac* repressor must bind to two of the three operators to cause repression
  - It can bind to  $O_1$  and  $O_2$ , or to  $O_1$  and  $O_3$ 
    - But not  $O_2$  and  $O_3$
  - If either  $O_2$  or  $O_3$  is missing, maximal repression is not achieved
  - Refer to Figure 16.9

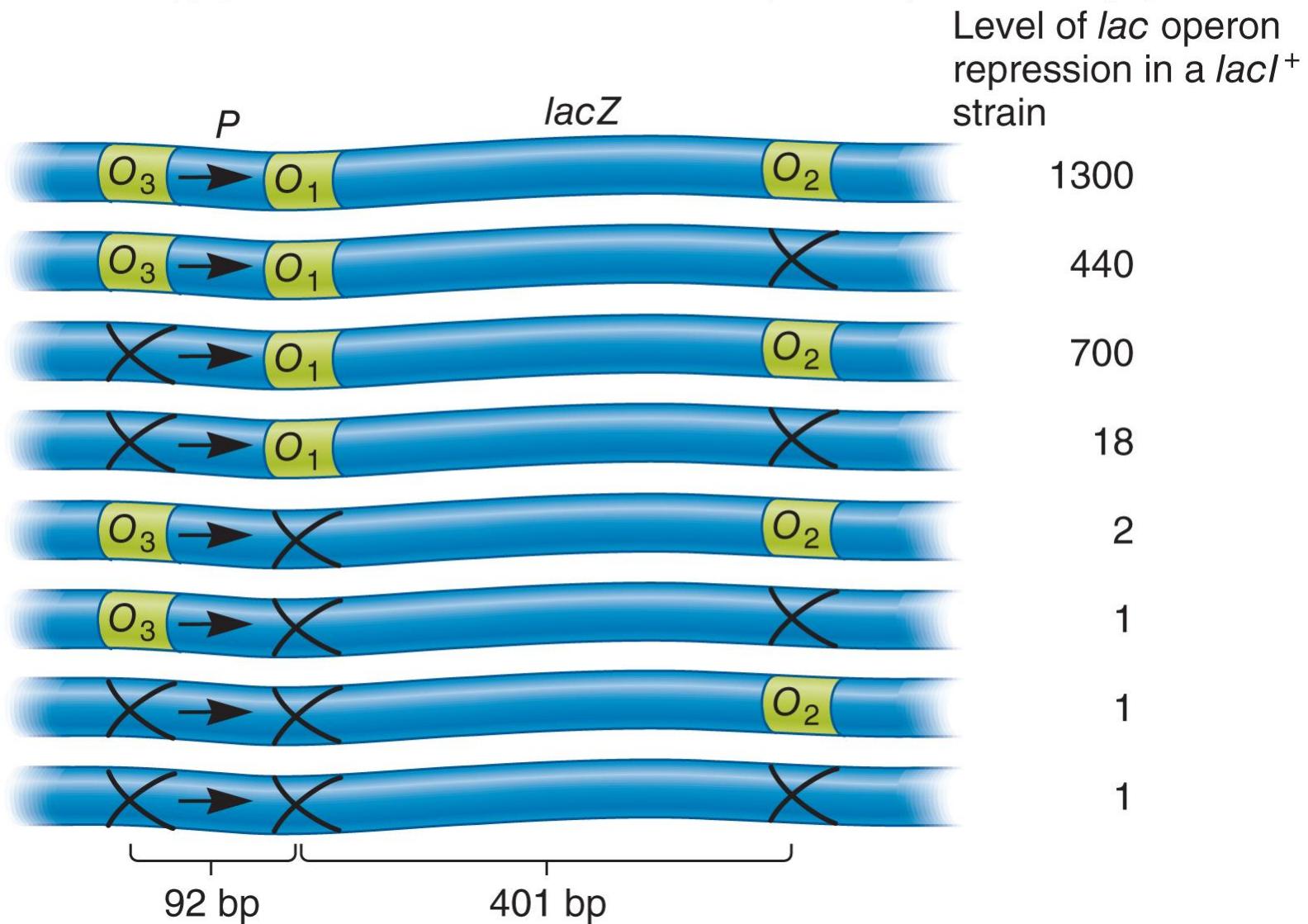
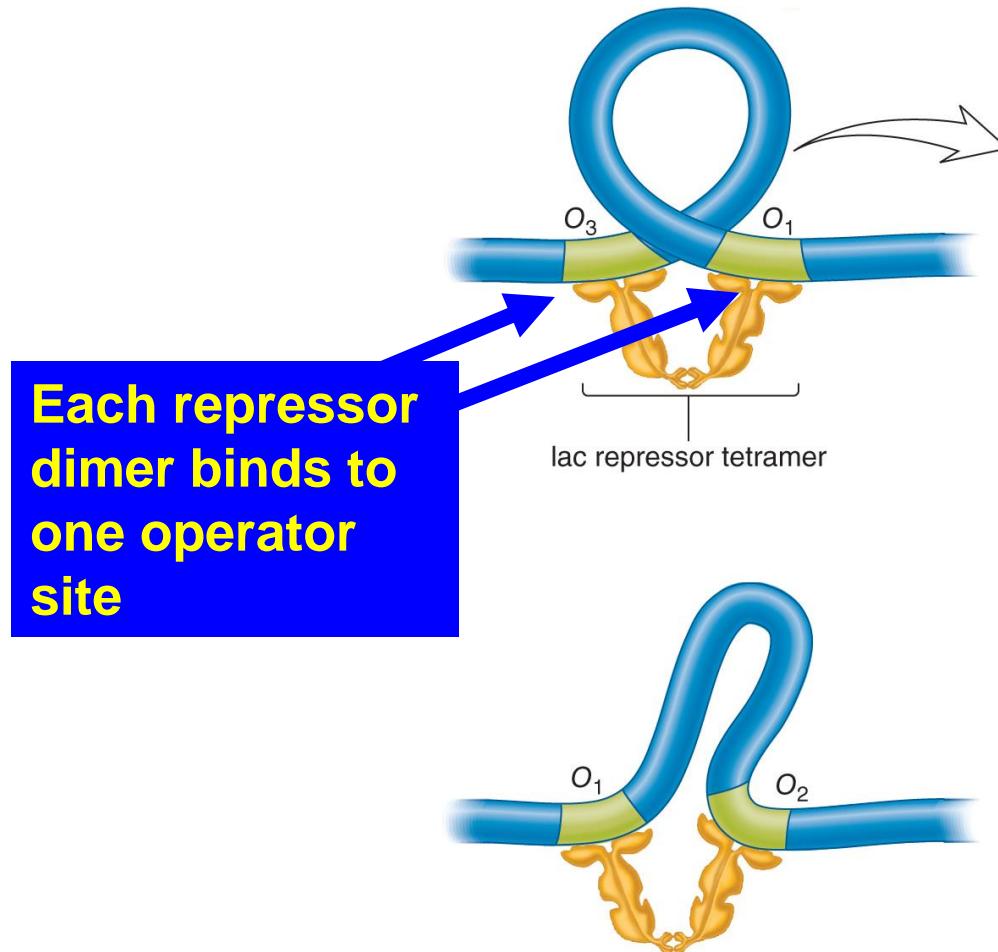


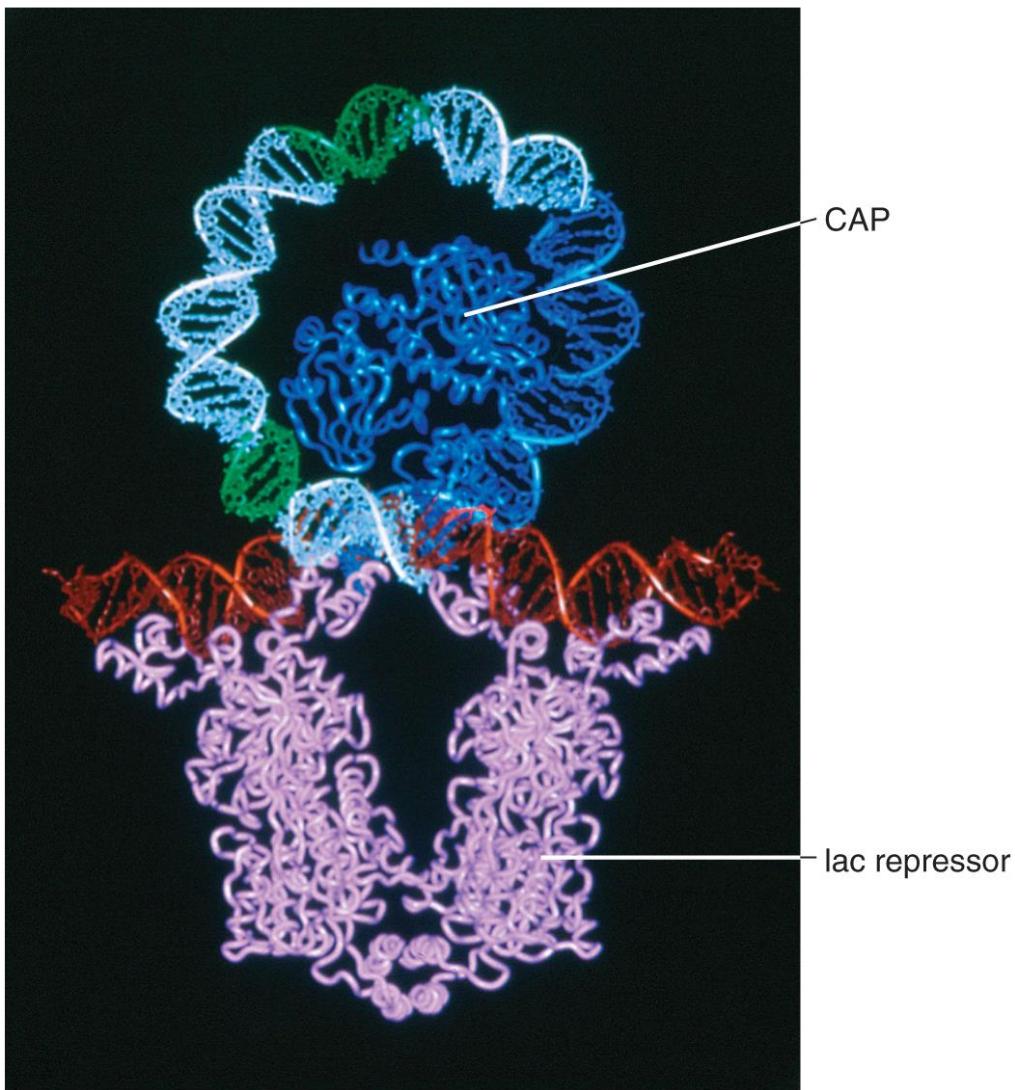
Figure 16.9

- Binding of the *lac* repressor to two operator sites requires that the DNA form a loop
  - A loop in the DNA brings the operator sites closer together
    - This facilitates the binding of the repressor protein



(a) DNA loops caused by the binding of the lac repressor

**Figure 16.10**



(b) Proposed model of the lac repressor binding to  $O_1$  and  $O_3$  based on crystallography

b: © SPL/Science Source

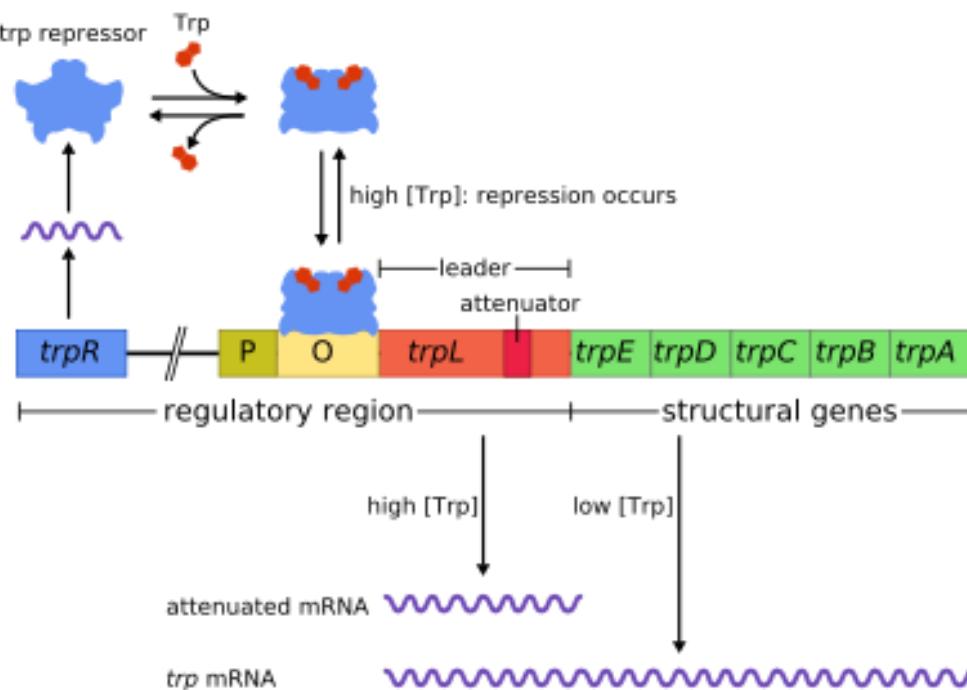
## Figure 16.10

# 16.3 Regulation of the *trp Operon*

- The organization of the *trp* operon
- How the *trp* operon is regulated by the *trp* repressor and by attenuation

## The *trp* Operon

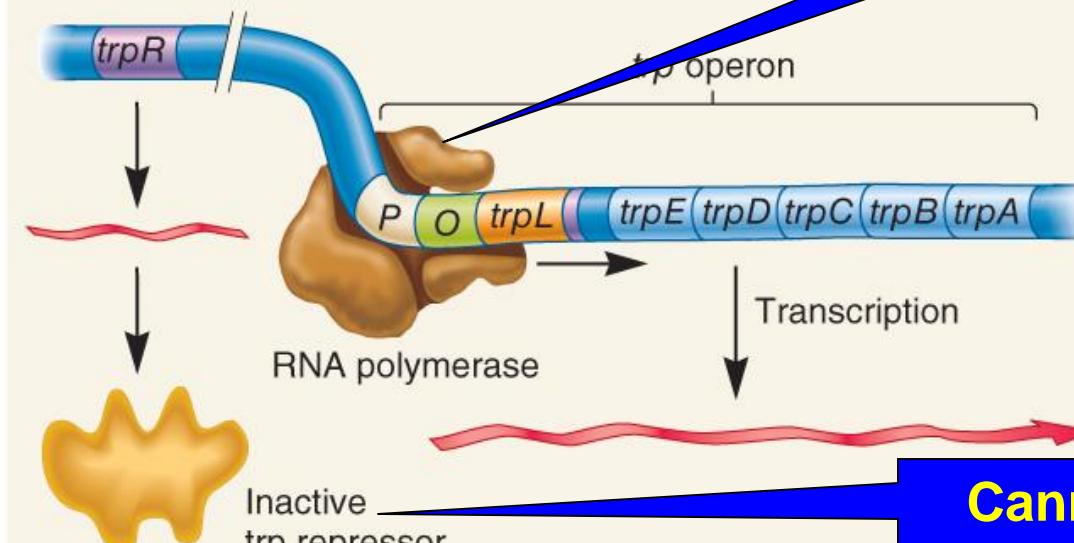
- The *trp* operon (pronounced “trip”) is involved in the biosynthesis of the amino acid tryptophan
- Structure of *trp* operon is similar to *lac* operon
  - Regulatory region
    - Operator
    - Promoter
  - Structural genes
    - The genes *trpE*, *trpD*, *trpC*, *trpB* and *trpA* encode enzymes involved in **tryptophan biosynthesis**



- *trpR* is a gene that encodes the **trp repressor** protein
  - Repression is achieved when the amino acid tryptophan binds to the repressor protein
  - Complex then binds to operator region to block transcription
  - Refer to Figure 16.11a and b

When tryptophan levels are low, tryptophan does not bind to the *trpR* repressor protein, which prevents the repressor protein from binding to the operator site. Under these conditions, RNA polymerase can transcribe the operon, which leads to the expression of the *trpE*, *trpD*, *trpC*, *trpB*, and *trpA* genes. These genes encode enzymes involved in tryptophan biosynthesis.

**RNA pol can bind to the promoter**

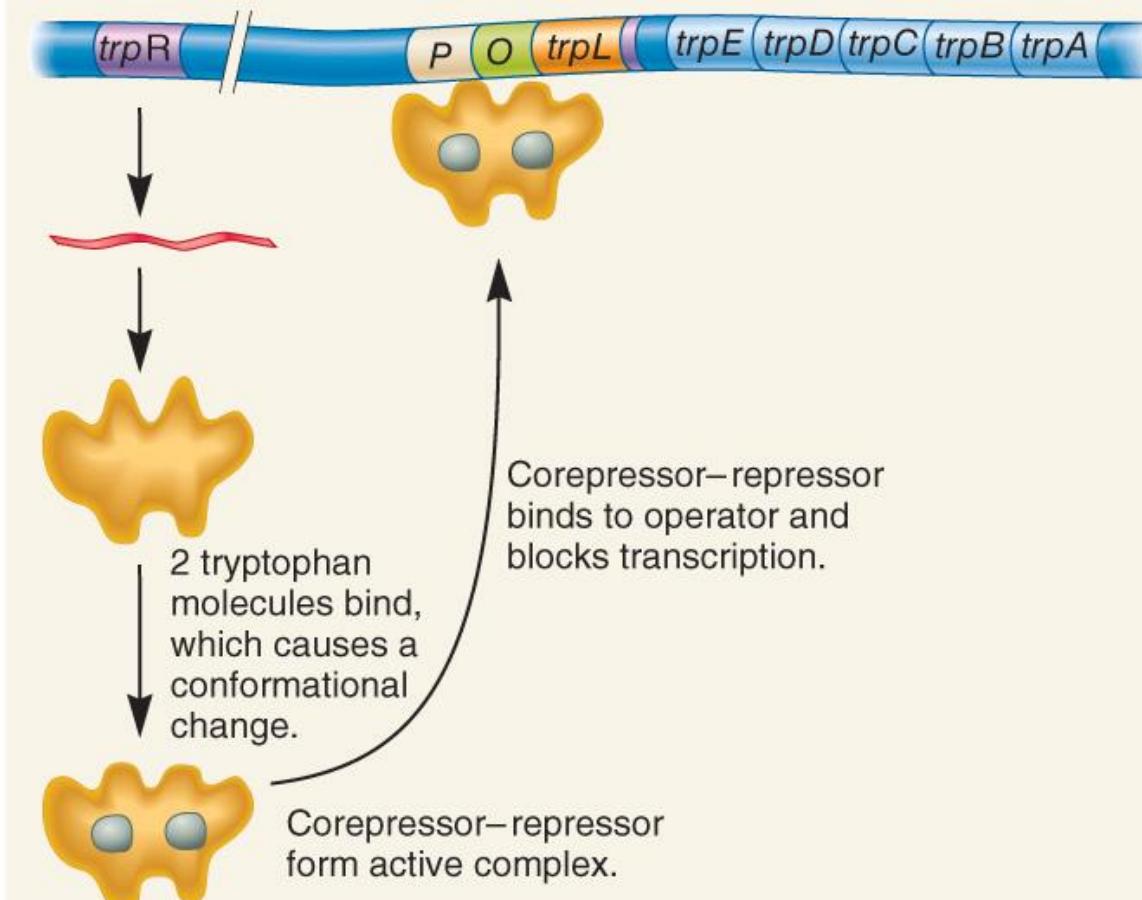


**Cannot bind to the operator site**

(a) Low tryptophan levels, transcription of the entire *trp* operon occurs

**Figure 16.11a**

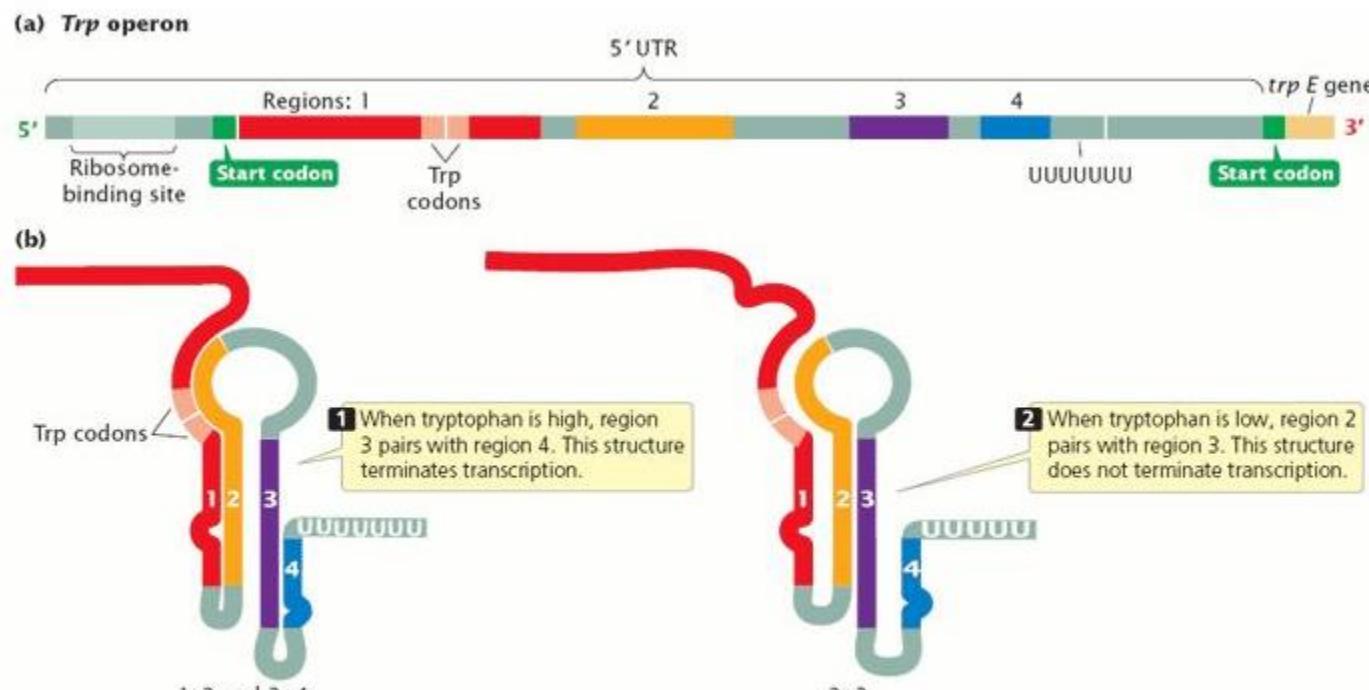
When tryptophan levels are high, tryptophan acts as a corepressor that binds to the trp repressor protein. The tryptophan-trp repressor complex then binds to the operator site to inhibit transcription.



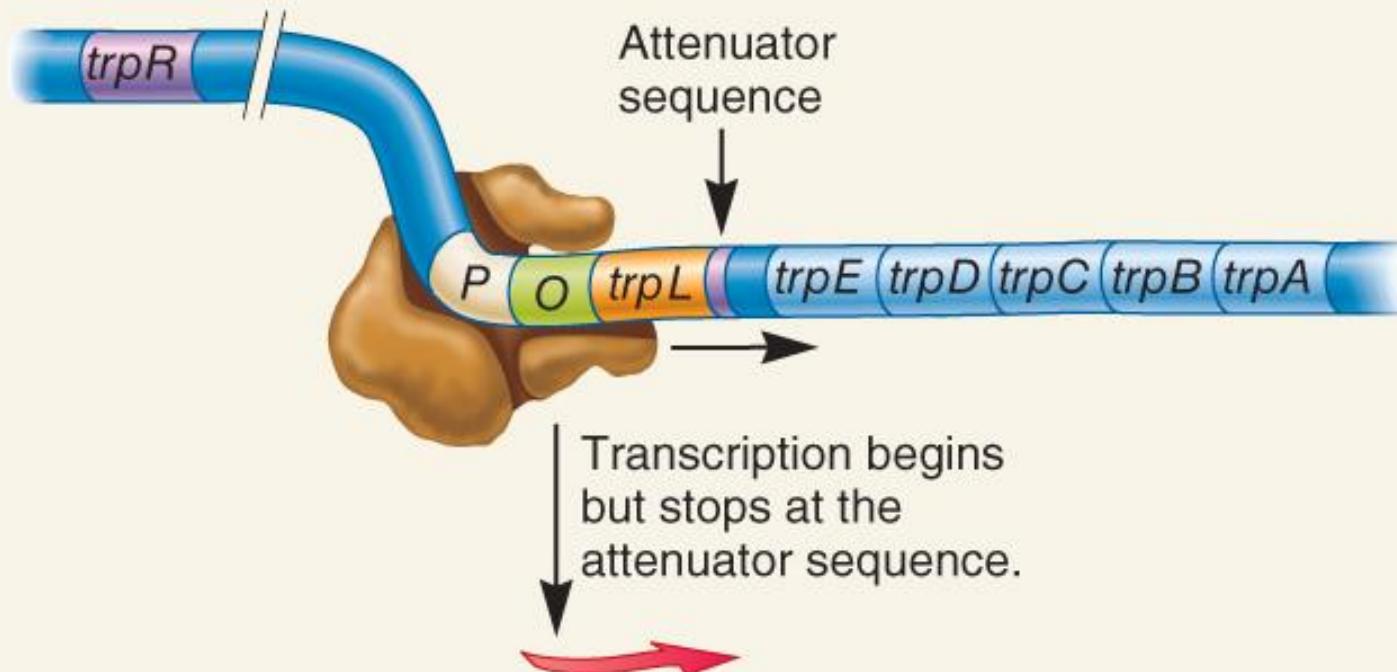
(b) High tryptophan levels, repression occurs

**Figure 16.11b**

- Another level of control exists with the *trp* operon
  - Also common in other operons involved in biosynthesis of amino acids
- **Attenuation**
  - Short transcript produced that is translated into a short peptide called the leader peptide
  - Leader peptide has several codons for the amino acid whose biosynthesis is the result of the expression of the operon
  - If enough of the amino acid is still present in the cell, rest of operon not expressed



Another mechanism of regulation is attenuation. When attenuation occurs, the RNA is transcribed only to the attenuator sequence, and then transcription is terminated.



(c) High tryptophan levels, attenuation occurs

**Figure 16.11c**

- Attenuation occurs in bacteria because of the coupling of transcription and translation
- During attenuation, transcription actually begins but it is terminated before the entire mRNA is made
  - A segment of DNA, termed the **attenuator sequence**, is important in facilitating this termination
  - In the case of the *trp* operon, transcription terminates shortly past the *trpL* region
  - Thus attenuation inhibits the further production of tryptophan

- The segment of *trp* operon immediately downstream from the operator site plays a critical role in attenuation
  - The first gene in the *trp* operon is *trpL*
    - It encodes a short peptide termed the *Leader peptide*
    - The RNA can form three different hairpin structures
    - Which structures form depends on how fast translation of the leader peptide occurs
    - Leader peptide transcript has several trp codons, how fast it is translated depends on how much trp is in the cell
    - Which hairpins form controls the transcription of the rest of the operon
  - Refer to Figure 16.12



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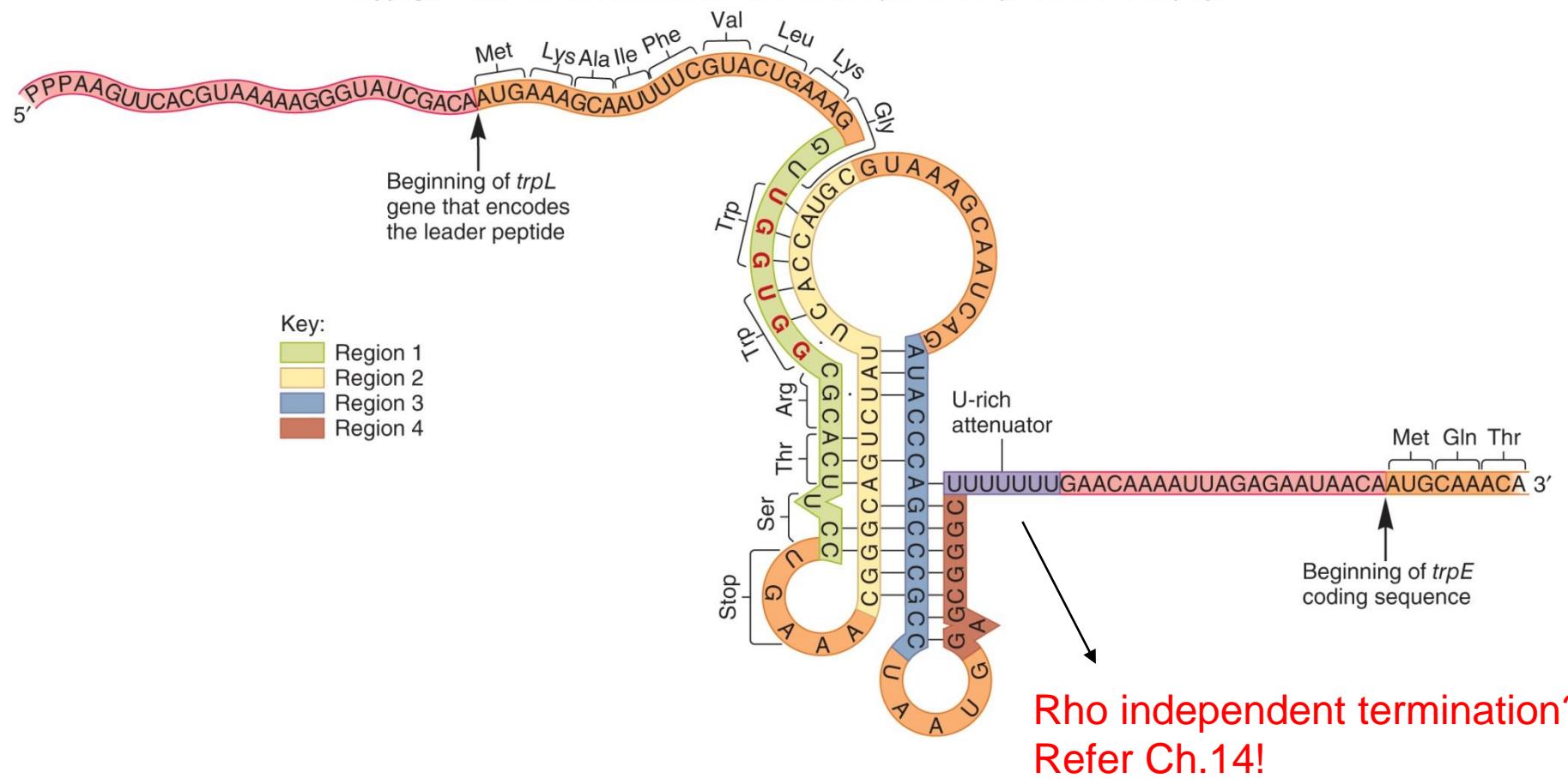


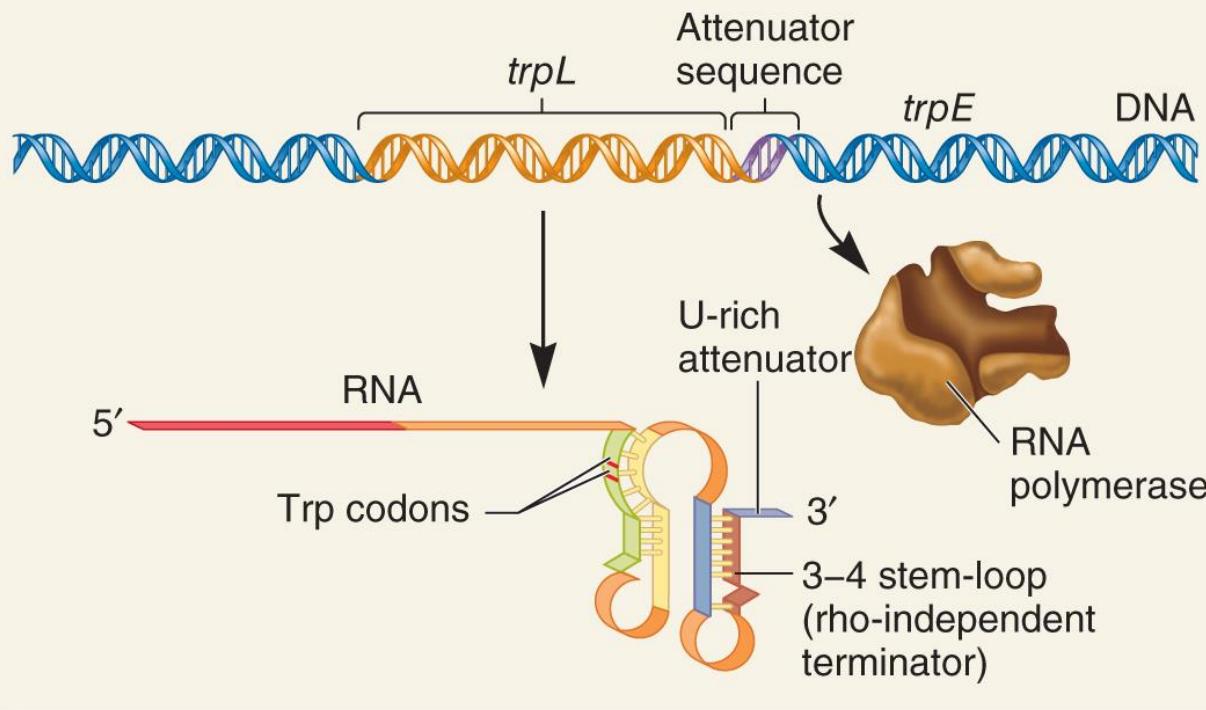
Figure 16.12

- Therefore, the formation of the 3-4 stem-loop causes RNA pol to terminate transcription at the end of the *trpL* gene
- Conditions that favor the formation of the 3-4 stem-loop rely on the translation of the *trpL* mRNA
- There are three possible scenarios
  1. No translation
  2. Low levels of tryptophan
  3. High levels of tryptophan

- The possible hairpin structures are
  - Region 1 and region 2
  - Region 3 and region 4
  - Region 2 and region 3
- Possible hairpin combinations:
  - If Region 1 binds to region 2, then region 3 can bind to region 4
  - If region 1 does not bind to region 2, then region 2 can bind to region 3 and region 4 can not bind to region 3

- Which of these form depends on how much trp is in the cell
  - Low trp
    - Region 2 and region 3 form
  - High trp
    - Region 1 and region 2 form
    - Region 3 and region 4 also form – acts as a rho independent transcriptional terminator
- If ribosome can pass over trp codons relatively quickly, it will cover up region 1 and force the formation of a hairpin between region 2 and 3
- Refer to Figure 16.13a, b, and c

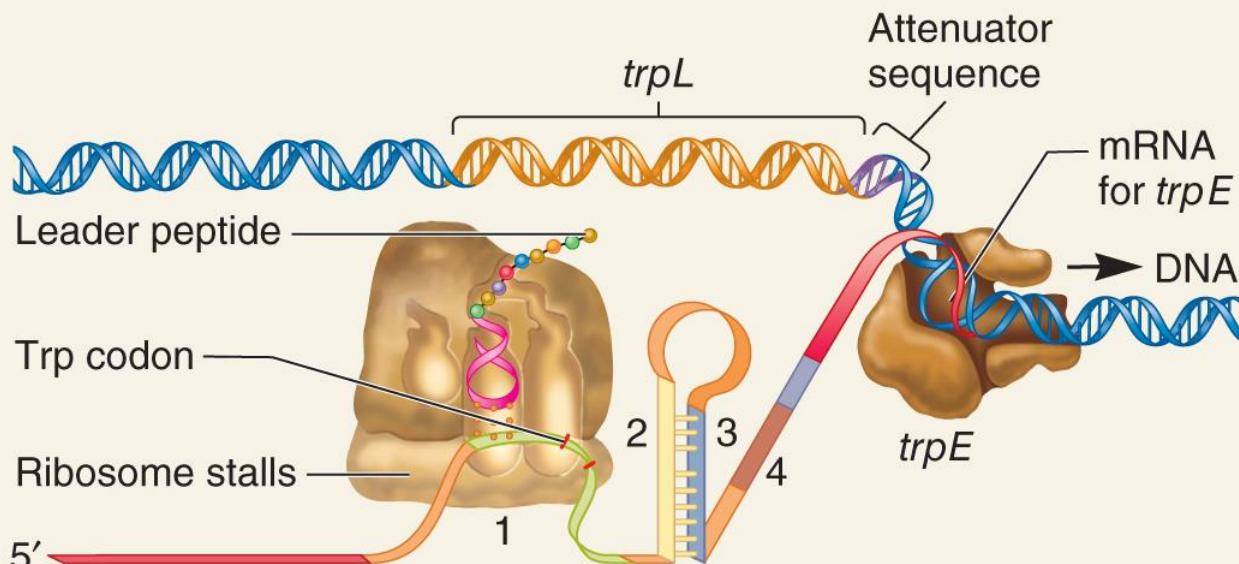
When translation is not coupled with transcription, region 1 hydrogen bonds to region 2 and region 3 hydrogen bonds to region 4. Because a 3–4 terminator stem-loop forms, transcription will be terminated at the U-rich attenuator.



(a) No translation, 1–2 and 3–4 stem-loops form

## Figure 16.13a

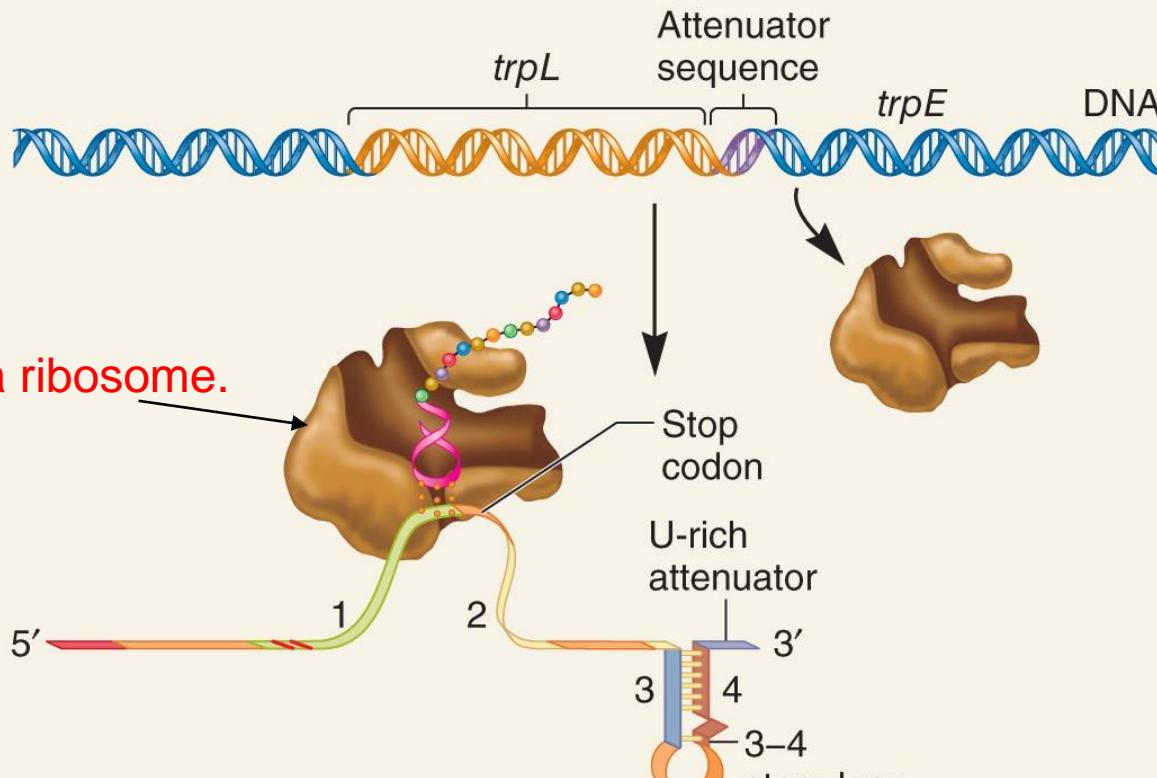
Coupled transcription and translation occur under conditions in which the tryptophan concentration is very low. The ribosome pauses at the Trp codons in the *trpL* gene because insufficient amounts of charged tRNA<sup>Trp</sup> are present. This pause blocks region 1 of the mRNA, so region 2 can hydrogen bond only with region 3. When this happens, the 3–4 stem-loop structure cannot form. Attenuation does not occur, and RNA polymerase transcribes the rest of the operon.



(b) Low tryptophan levels, 2–3 stem-loop forms

## Figure 16.13b

Coupled transcription and translation occur under conditions in which a sufficient amount of tryptophan is present in the cell. Translation of the *trpL* gene progresses to its stop codon, where the ribosome pauses. This blocks region 2 from hydrogen bonding with any region and thereby enables region 3 to hydrogen bond with region 4. This terminates transcription at the U-rich attenuator.



(c) High tryptophan levels, 3–4 stem-loop forms

**Figure 16.13c**

# Inducible vs. Repressible Regulation

- The study of many operons revealed a general trend concerning inducible versus repressible regulation
  - Operons involved in catabolism (i.e., breakdown of a substance) are typically inducible
    - The substance to be broken down (or a related compound) acts as the inducer
  - Operons involved in anabolism (i.e., biosynthesis of a substance) are typically repressible
    - The inhibitor or corepressor is the small molecule that is the product of the operon

# 16.4 Translational and Posttranslational Regulation

- How translational regulatory proteins and antisense RNAs regulate translation
- How feedback inhibition and posttranslational modifications regulate protein function

## Translational and Posttranslational Regulation

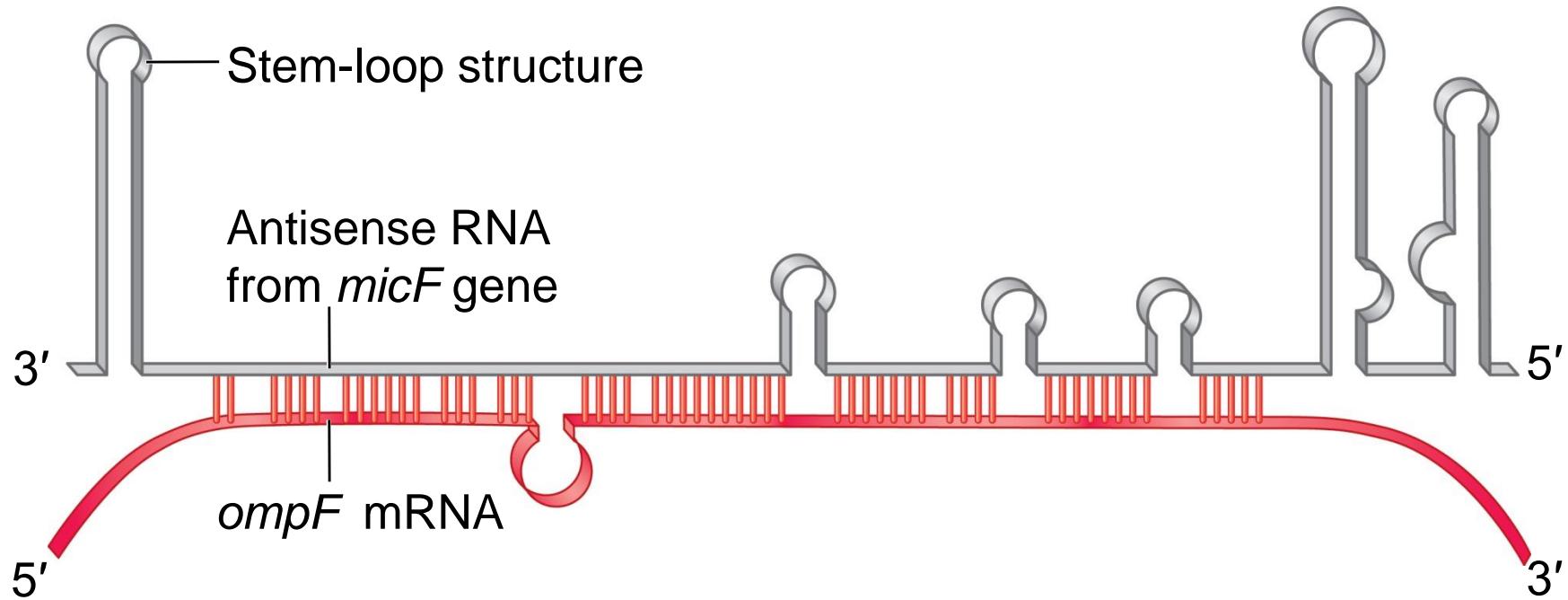
- Genetic regulation in bacteria is exercised predominantly at the level of transcription
  - However, there are many examples of regulation that occurs at a later stage in gene expression
- For example, regulation of gene expression can be
  - Translational
  - Posttranslational

## Translational Regulation

- For some bacterial genes, the translation of mRNA is regulated by the binding of proteins
- A **translational regulatory protein** recognizes sequences within the mRNA
- In most cases, these proteins act to inhibit translation
  - These are known as **translational repressors**
- Translational repressors inhibit translation in two ways
  1. Binding next to the Shine-Dalgarno sequence and/or the start codon
    - **Blocking the ribosome** from initiating translation
  2. Binding outside the Shine-Dalgarno/start codon region
    - **Stabilizing an mRNA secondary structure** that prevents initiation

- Another way to regulate translation is via the synthesis of **antisense RNA**
  - An RNA strand that is complementary to mRNA
- Example: **Osmoregulation** - the ability to control the amount of water inside the cell
  - The protein *ompF* in *E. coli* is important in osmoregulation
    - *ompF* protein is preferentially produced at low osmolarity
      - At high osmolarity its synthesis is decreased
    - The *micF* transcript is antisense to the *ompF* transcript
      - Binds to and inhibits translation of *ompF*
    - Refer to Figure 16.14

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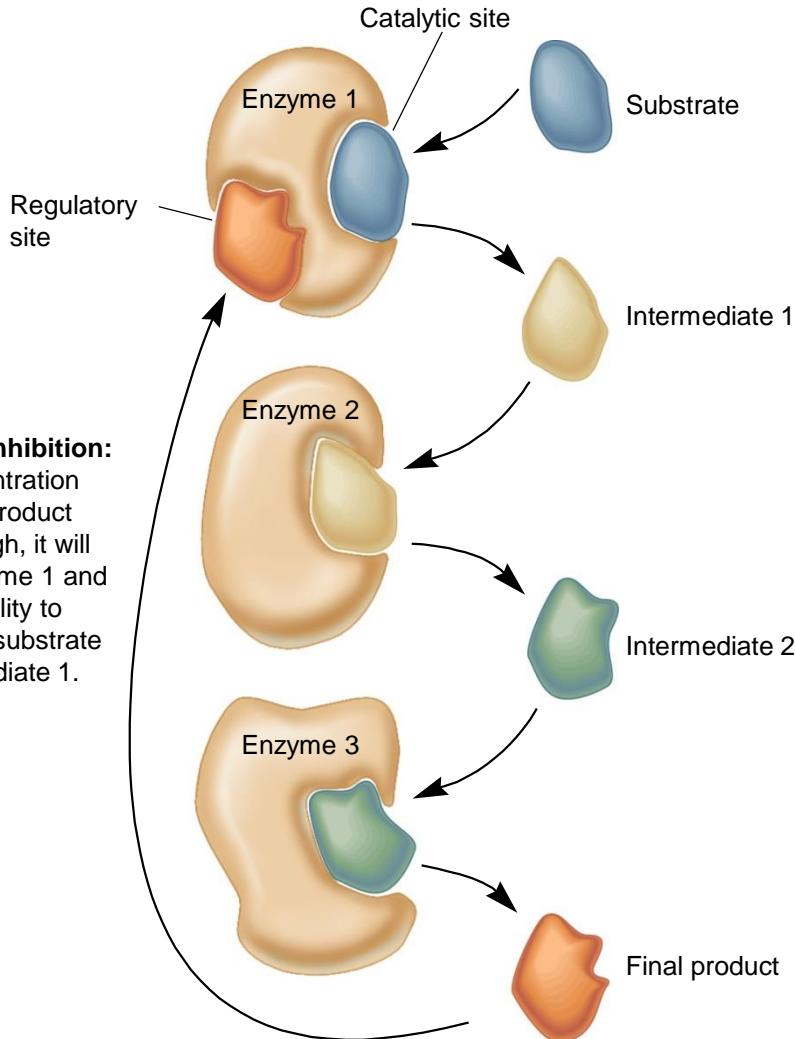


**Figure 16.14**

# Posttranslational Regulation

- Control of protein function can occur by
  - Feedback inhibition, or
  - Covalent modification of amino acids in the protein
- **Feedback inhibition** is a common mechanism to regulate the activity of metabolic enzymes
  - The final product in a pathway often can inhibit the enzyme that acts early in the pathway
  - Refer to Figure 16.15

**Feedback inhibition:**  
If the concentration of the final product becomes high, it will bind to enzyme 1 and inhibit its ability to convert the substrate into intermediate 1.



**Figure 16.15**

- **Enzyme 1 is an allosteric enzyme, which means it contains two different binding sites**
  - **Catalytic site → binds substrate**
  - **Regulatory site → binds final product of the pathway**

**When the concentration of the final product becomes high it will bind to enzyme 1, inhibiting enzyme 1**

- The **covalent modification** of amino acids can change the protein's confirmation
- Some modifications are irreversible
  - Proteolytic processing
  - Attachment of prosthetic groups, sugars, or lipids
- Other modifications are reversible and transiently affect protein function
  - Phosphorylation ( $-PO_4$ )
  - Acetylation ( $-COCH_3$ )
  - Methylation ( $-CH_3$ )

# 16.5 Riboswitches

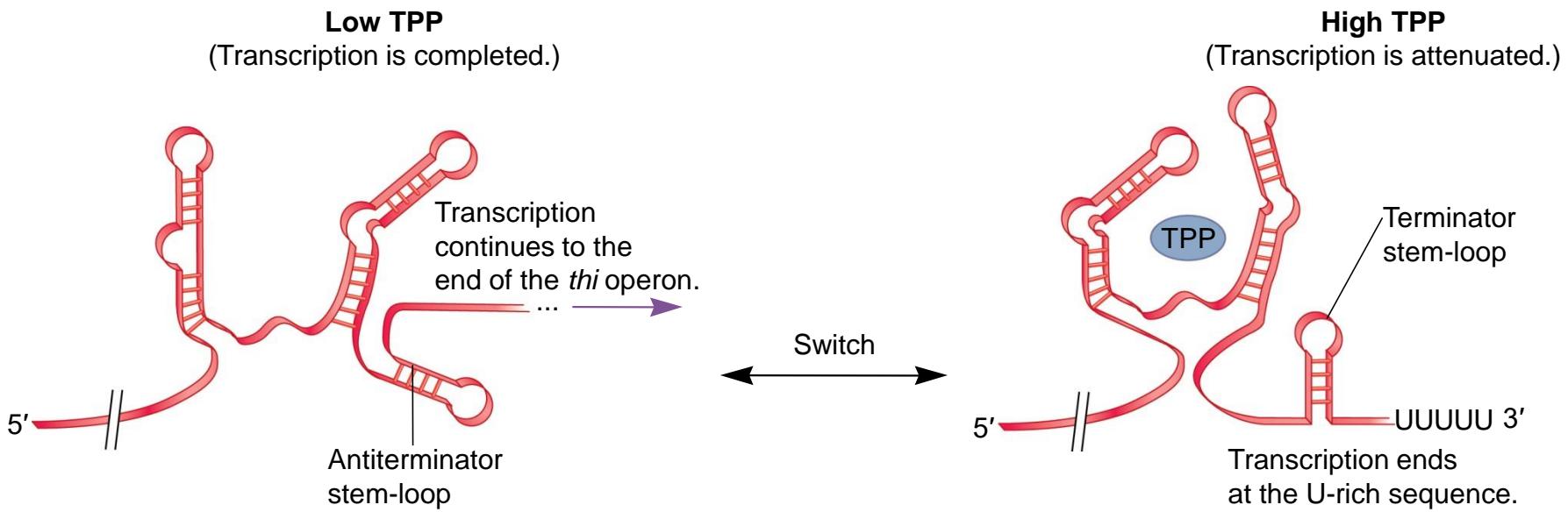
- How riboswitches can regulate transcription and translation
- Type of regulation found in prokaryotes and eukaryotes
- Discovered in 2001 and 2002 in several labs
- In this type of regulation
  - RNA can exist in **two different confirmations**
    - One confirmation is active
    - One confirmation is inactive
  - Switch from one confirmation to the other relies on a small molecule
- Riboswitches can be a form of control for
  - Transcription
  - Translation
  - RNA stability
  - Splicing

**TABLE 16.2****Types of Riboswitches**

Type of Regulation	Description
Transcription	The 5' region of an mRNA may exist in one conformation that forms a ρ-independent terminator, which causes attenuation of transcription. The other conformation does not form an early terminator and is completely transcribed.
Translation	The 5' region of an mRNA may exist in one conformation in which the Shine-Dalgarno sequence cannot be recognized by the ribosome, whereas the other conformation has an accessible Shine-Dalgarno sequence that allows the mRNA to be translated.
RNA stability	One mRNA conformation may be stable, whereas the other conformation acts as a ribozyme that causes self-degradation.
Splicing	In eukaryotes, one pre-mRNA conformation may be spliced in one way, whereas another conformation is spliced in a different way.

# A Riboswitch Can Regulate Transcription

- Example: **Thiamin pyrophosphate (TPP) in *B. subtilis***
  - Important vitamin – essential coenzyme for the citric acid cycle
- When TPP levels are low, a stem-loop forms called the **antiterminator**
  - Allows the cell to make more TPP
- When TPP is high, it binds to the RNA, causing a change in the secondary structure
  - Stops transcription, inhibiting production of enzymes to make more TPP

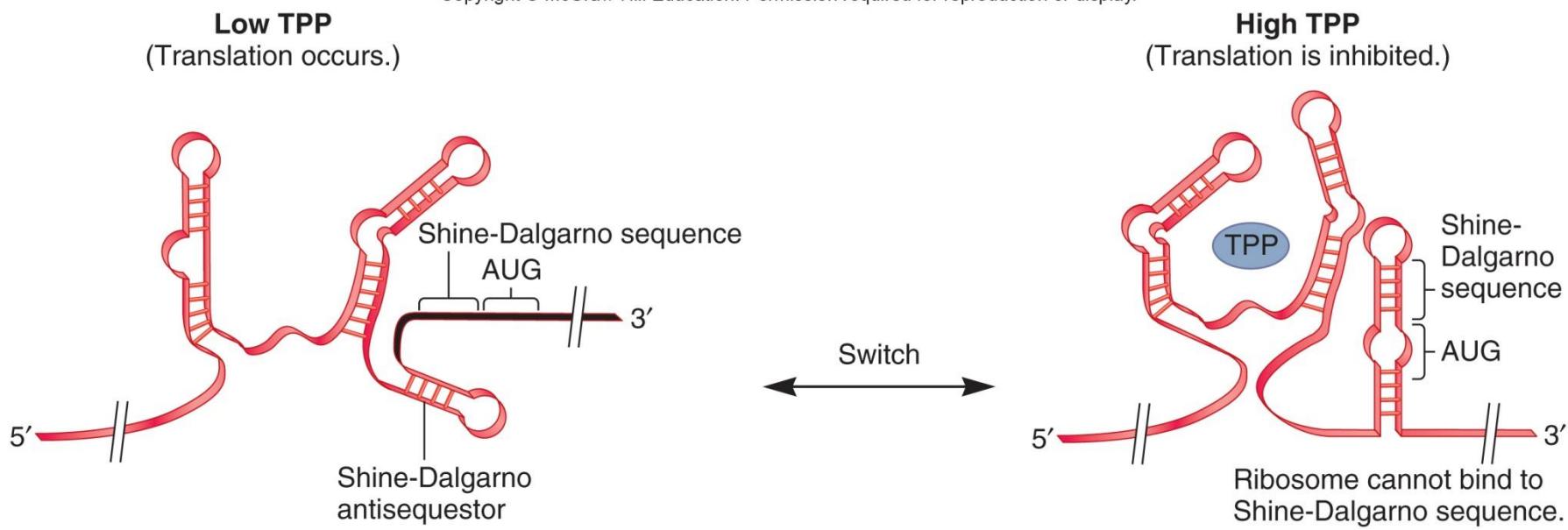


**Figure 16.16**

# A Riboswitch Can Regulate Translation

- Example: **Thiamin pyrophosphate (TPP) in *E. coli***
  - **thiMD operon** encodes 2 enzymes for TPP biosynthesis
  - When TPP levels are low, the 5' end of the mRNA folds into a stem-loop called the **Shine-Dalgarno anti-sequestor**
    - Makes the Shine-Dalgarno accessible, so translation occurs for more TPP enzymes
  - When TPP levels are high, TPP binds the RNA, changing its structure to sequester the Shine-Dalgarno
    - Blocking translation

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**Figure 16.17**