AP® EDITION

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# BIOLOGY

## Fourteenth Edition

**Sample Chapter**

**Student Edition**

Mc Graw Hill

Scientists are studying why bats harbor viruses yet do not get sick. Rosa Jay/Shutterstock

# 13

# Regulation of Gene Expression

Unlike humans and other mammals, bats can carry viruses but not get sick. Bats are the only order of mammals known that can remain healthy while harboring Ebola, influenza, SARS, and coronaviruses.

Researchers at the Duke-National University of Singapore analyzed the gene expression of key inflammatory genes in mammals. The authors found that bats have a lower expression of these genes. The genetic tolerance to viruses seems to be batspecific. This suggests that bats' immune systems have evolved to ignore these infections. Learning more about immune system gene expression in bats may lead to new ways of treating viral infections in humans.

Gene expression is the information in DNA transcribed and translated into a protein. Most cells within an organism contain the same set of genetic instructions, but the differential expression of specific genes determines metabolic pathways and cell specialization. In bacteria, two of the best studied regulatory systems are the inducible and repressible operons. In eukaryotes, gene expression is more complex. So, how does a cell know when to undergo gene expression? Gene expression needs to be controlled or regulated, and as you will see in this chapter, many mechanisms do this.

| AP Unit | AP Topics Covered | Chapter Section |
|---|---|---|
| **Unit 4: Cell Communication and Cell Cycle** | 4.2 Introduction to Signal Transduction | 13.1 |
| | 4.3 Signal Transduction | 13.1 |
| | 4.4 Changes in Signal Transduction Pathways | 13.1, 13.2, 13.3 |
| **Unit 6: Gene Expression and Regulation** | 6.5 Regulation of Gene Expression | 13.1, 13.2 |
| | 6.6 Gene Expression and Cell Specialization | 13.1, 13.2 |
| | 6.7 Mutation | 13.3 |

## AP Chapter Outline



## Before You Begin

Before beginning this chapter, take a few moments to review the following discussions.

**Figure 12.10** What is the central dogma of biology?

**Section 12.4** How is an mRNA transcript made?

**Section 12.5** What is the role of translation in gene expression?

UNIT 2

# Genetic Basis of Life

## Unit Outline



## Introduction

Genetic information provides for continuity of life. The storage and transfer of genetic information are critical for life to continue at the cell, organism, and species levels. This information passes to the subsequent generation via DNA. In the middle of the 20th century, scientists debated what type of molecule carries genetic information. A number of historical experiments that determined DNA is able to store information, replicate with high accuracy, and able to undergo changes, called mutations, that provide the genetic variability required for evolution. The structure of DNA supports these requirements for the molecule of heredity.

Most cells within an organism contain the same set of genetic instructions, but the differential expression of specific genes determines metabolic pathways and cell specialization. In bacteria, two of the best studied regulatory systems are the inducible and repressible operons. In eukaryotes, gene expression is more complex.

Humans can use biotechnology to manipulate the heritable information of DNA and alter gene expression. Advances in the field present opportunities to address human disease, but the use of these techniques raises ethical questions. For example, should society allow couples to produce “designer babies? Genetically modified crops are sold commercially, with the goal of increased yields and better nutrient content. Gene therapy can treat disorders and cure inborn errors of metabolism. CRISPR is a powerful tool that allows researchers to edit genomes by altering DNA sequences and modifying gene function.

As you have seen in the introduction to this AP Biology edition, the new AP Biology Curriculum Framework is based organized around eight Units. You will find information on the following AP Units in Unit 2: The Genetic Basis of Life:

| AP Unit | Key Topics | Chapter |
|---|---|---|
| **UNIT 1: Chemistry of Life** | An understanding of the chemistry of life is vital for every biology student. Life on Earth would not exist without the unique properties of the water molecule. The four main biological macromolecules: carbohydrates, lipids, proteins, and nucleic acids (DNA and RNA), form the building blocks of living systems | Chapter 12 |
| **UNIT 4: Cell Communication and Cell Cycle** | Cells communicate with each other in a variety of ways. Membrane proteins and modifications to cell membranes provide the structural basis for these communication functions. | Chapter 9, Chapter 13 |
| **UNIT 5: Heredity** | Genetic information provides for continuity of life and passes from parent to offspring via mitosis and meiosis. Mendel described a model of inheritance of traits; however, most traits result from interactions of many genes (and with their environment) and do not follow Mendelian patterns of inheritance. | Chapter 10, Chapter 11 |
| **UNIT 6: Gene Expression and Regulation** | Hereditary language stored in DNA’s double helix replicates during cell division and then is transcribed and translated into cell products that determine the metabolism and nature of the cell. Both internal and environmental signals regulate gene expression. | Chapter 12, Chapter 13, Chapter 14 |

# 13.1 Prokaryotic Regulation

**AP Learning Outcomes**

Upon completion of this section, you should be able to

1. Describe the structure and function of an operon in prokaryotic gene regulation.
2. Explain how the *trp* and *lac* operons of prokaryotes are regulated.
3. Distinguish between a repressible operon and an inducible operon.

Because their environment is ever changing, bacteria do not always need to express their entire complement of enzymes and proteins. In 1961, French microbiologists François Jacob and Jacques Monod showed that *Escherichia coli* is capable of regulating the expression of its genes. They observed that the genes in a metabolic pathway, called **structural genes,** are grouped on a chromosome and transcribed at the same time. Jacob and Monod, therefore, proposed the **operon** (L. *opera,* "works") model to explain gene regulation in prokaryotes. They were awarded a Nobel Prize in Physiology or Medicine in 1965 for their investigations.

An operon typically includes the following parts:

- **Regulator gene**—Normally located outside the operon, this codes for a DNA-binding protein that acts as a **repressor.** The repressor controls whether the operon is active or not.
- **Promoter**—A short sequence of DNA where RNA polymerase first attaches to begin transcription of the grouped genes. Basically, a promoter signals the start of the operon and the location where transcription begins.
- **Operator**—A short portion of DNA located before the structural genes. If a repressor is attached to the operator, then transcription cannot occur; conversely, if a repressor is not attached, then transcription can occur. In this way, the operator controls transcription of structural genes.
- **Structural genes**—These genes code for the enzymes and proteins involved in the metabolic pathway of the operon. The structural genes are transcribed as a unit.

Next, we will briefly review the findings of Jacob and Monod in their studies of two *E. coli* operons: the *trp* operon and the *lac* operon.

## The *trp* Operon

Tryptophan is an essential amino acid synthesized by the enzymes coded for in the *trp* operon. Many investigators, including Jacob and Monod, found that some operons in *E. coli* usually exist in the "on" rather than "off" condition. In the *trp* operon, the regulator codes for a repressor that ordinarily is unable to attach to the operator. Therefore, RNA polymerase can bind to the promoter, and the structural genes of the operon are ordinarily expressed (Fig. 13.1). Their products, five different enzymes, are part of an anabolic pathway for the synthesis of the amino acid tryptophan.

If tryptophan is already present in the medium, the cell does not need these enzymes, and the operon is turned off by the following method. Tryptophan binds to the repressor. A change in shape now allows the repressor to bind to the operator and prevent RNA polymerase from binding to the promoter, and the structural genes are not expressed. The enzymes are said to be repressible (can be turned "off"), and the entire unit is called a *repressible operon*. Tryptophan is called the **corepressor.** Repressible operons are usually involved in anabolic pathways that synthesize a substance needed by the cell.

## The *lac* Operon

Bacteria metabolism is remarkably efficient. If proteins or enzymes are needed for metabolism, then the structural genes are expressed. If no metabolism is necessary, then genes are not expressed. For example, if the milk sugar lactose is not present, there is no need to express genes for enzymes involved in lactose catabolism. But when only lactose is present, the cell immediately begins to make the three enzymes needed for lactose metabolism.

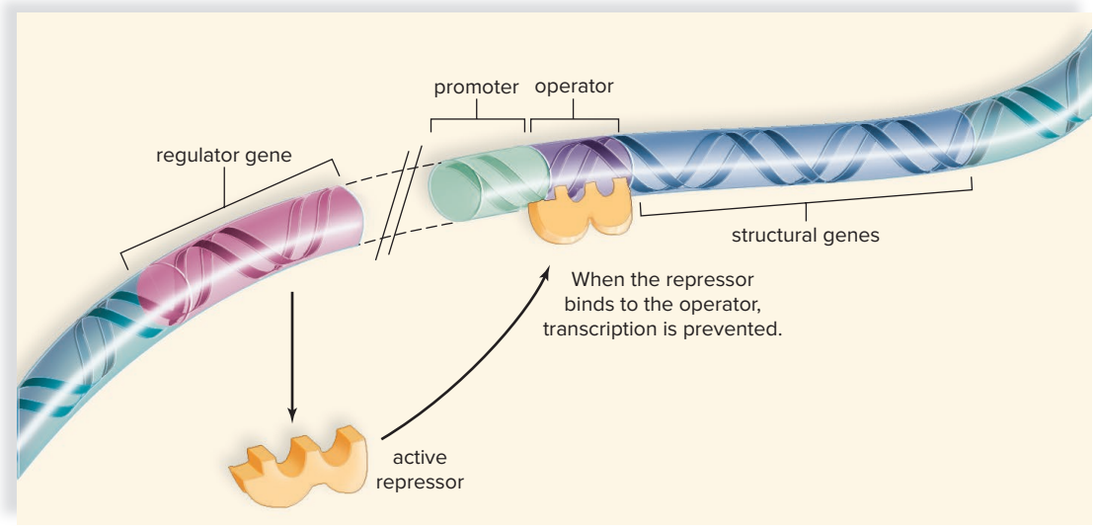
The enzymes that break down lactose are encoded by three genes (Fig. 13.2): One gene is for an enzyme called β-galactosidase, which breaks down the disaccharide lactose to glucose and galactose; a second gene codes for a permease that facilitates the entry of lactose into the cell; and a third gene codes for an enzyme called transacetylase, which has an accessory function in lactose metabolism.

The three structural genes are adjacent to one another on the chromosome and are under the control of a single promoter and a single operator. The regulator gene codes for a *lac* operon repressor that ordinarily binds to the operator and prevents transcription of the three genes. When only lactose (more correctly, allolactose, an isomer formed from lactose) is present, lactose binds to the repressor, and the repressor undergoes a change in shape that prevents it from binding to the operator. Because the repressor is unable to bind to the operator, RNA polymerase is better able to bind to the promoter. After RNA polymerase carries out transcription, the three enzymes of lactose metabolism are synthesized.

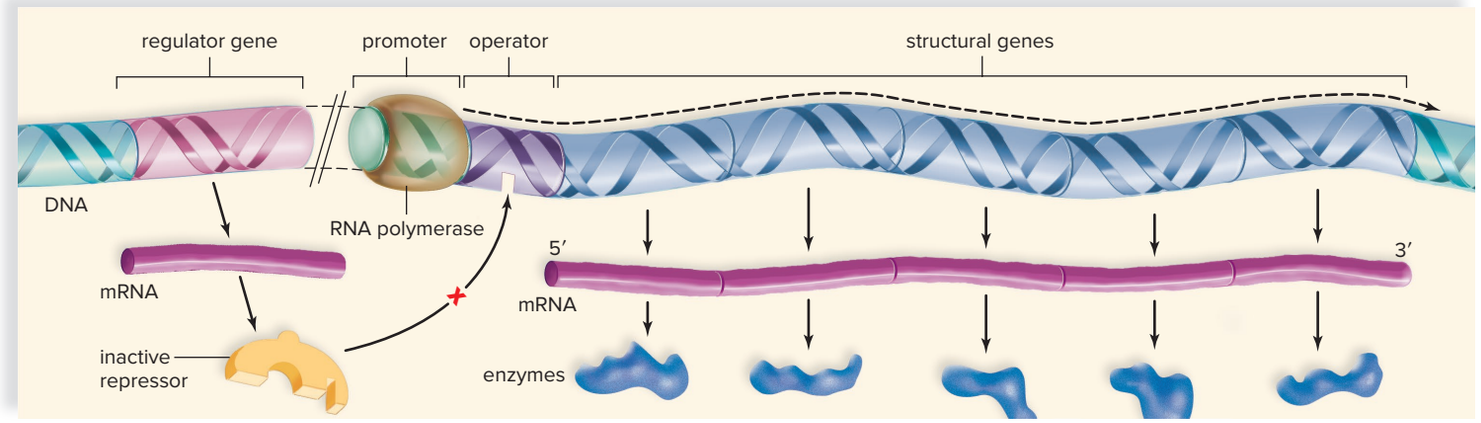
Because the presence of lactose brings about expression of genes, it is called an **inducer** of the *lac* operon: The enzymes are said to be inducible enzymes (can be turned "on"), and the entire unit is called an *inducible operon.* Inducible operons are usually found in catabolic pathways that break down a nutrient. Why is that beneficial? Because these enzymes need to be active only when the nutrient is present.

### *Further Control of the* lac *Operon*

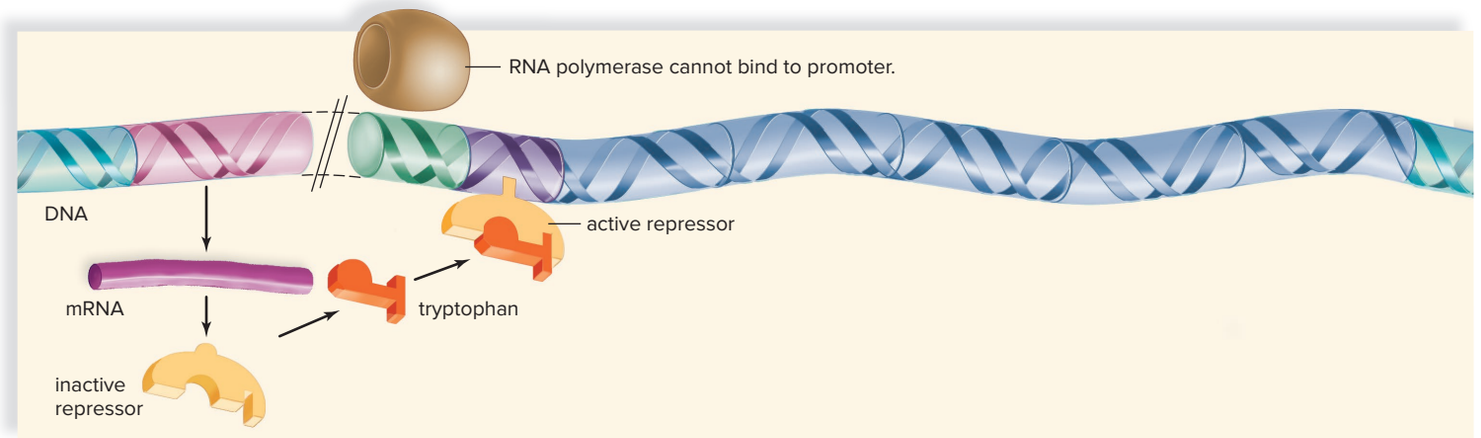
If both glucose and lactose are present, then *E. coli* preferentially breaks down glucose. The bacterium has a way to ensure that the lactose operon is fully turned on only when glucose is absent. A molecule called *cyclic AMP* (*cAMP*) accumulates when glucose is absent. Cyclic AMP, which is derived from




a. The *trp* operon is regulated by a gene that produces a repressor protein.

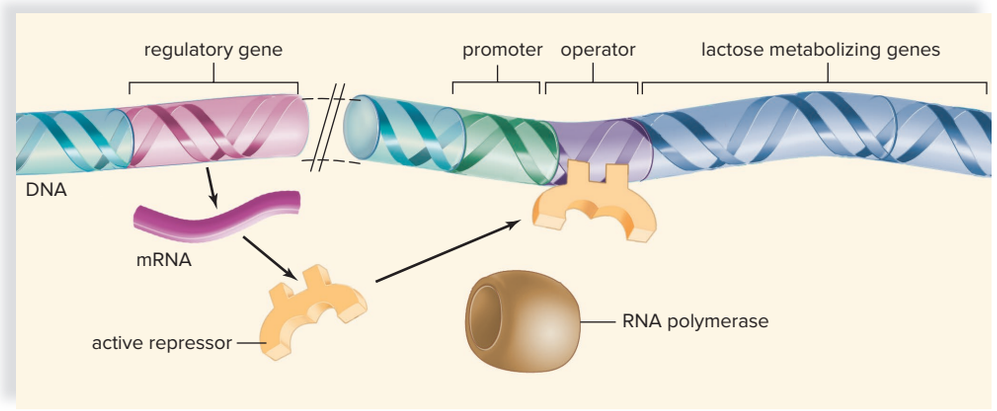



b. Tryptophan absent. Enzymes needed to synthesize tryptophan are produced.

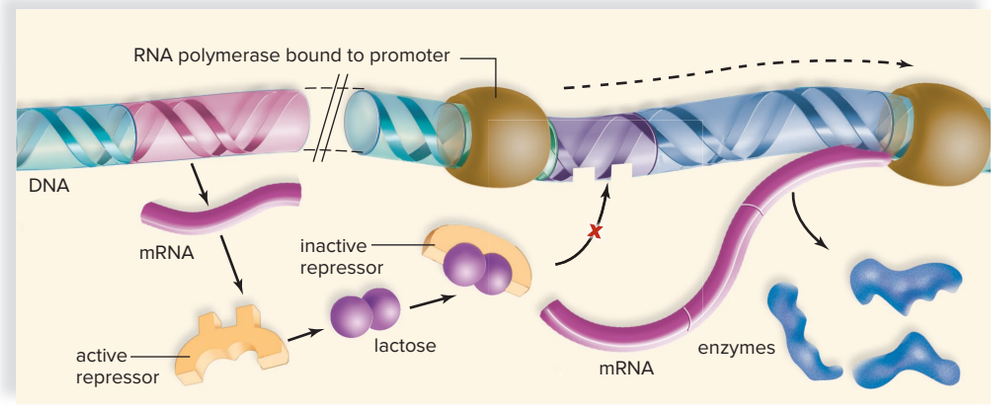



c. Tryptophan present. Presence of tryptophan prevents production of enzymes used to synthesize tryptophan.

**Figure 13.1 The *trp* operon.** **a.** The regulatory gene codes for a repressor protein that is normally inactive. **b.** When tryptophan is absent, the RNA polymerase attaches to the promoter, and the structural genes are expressed. **c.** When the nutrient tryptophan is present, it binds to the repressor, changing its shape. Now the repressor is active and can bind to the operator. RNA polymerase cannot attach to the promoter, and the structural genes are not expressed.



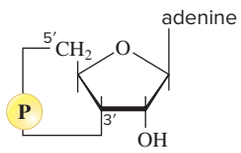

a. Operon when lactose is absent.




b. Operon when lactose is present.

**Figure 13.2 The *lac* operon.** **a.** The regulator gene codes for a repressor that is normally active. When it binds to the operator, RNA polymerase cannot attach to the promoter, and structural genes are not expressed. **b.** When lactose is present, it binds to the repressor, changing its shape, so it is inactive and cannot bind to the operator. Now RNA polymerase binds to the promoter, and the structural genes are expressed.

ATP, has only one phosphate group, which is attached to ribose at two locations:




**cyclic AMP**
(cAMP)

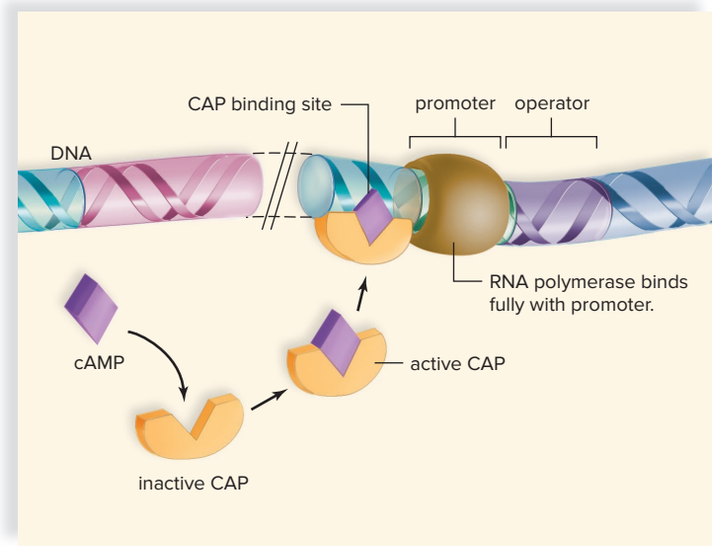
Cyclic AMP binds to a molecule called a *catabolite activator protein* (*CAP*), and the complex attaches to a CAP binding site next to the *lac* promoter. When CAP binds to DNA, DNA bends, exposing the promoter to RNA polymerase. RNA polymerase is now better able to bind to the promoter, so that the *lac* operon structural genes are transcribed, leading to their expression (Fig. 13.3).

When glucose is present, there is little cAMP in the cell; CAP is inactive, and the lactose operon does not function maximally. CAP affects other operons as well and takes its name for activating the catabolism of various other metabolites when glucose is absent. A cell's ability to encourage the metabolism of lactose and other metabolites when glucose is absent provides a backup system for survival when the preferred energy source, glucose, is absent.

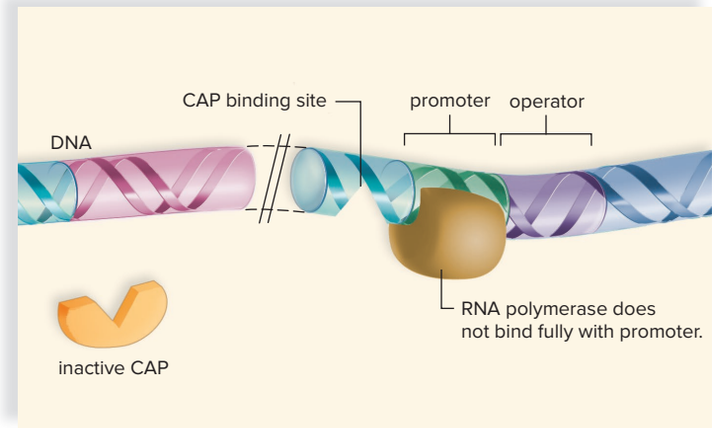
The CAP protein's regulation of the *lac* operon is an example of positive control. Why? When this molecule is active, it promotes the activity of an operon. The use of repressors, on the other hand, is an example of negative control, because when active they shut down an operon. A positive control mechanism allows the cell to fine-tune its response. In the case of the *lac* operon, the operon is only maximally active when glucose is absent and lactose is present. If both glucose and lactose are present, the cell preferentially metabolizes glucose.

## AP Check Your Progress 13.1

1. Explain the difference between the roles of the promoter and operator of an operon.
2. Summarize how gene expression differs in an inducible operon versus a repressible operon.
3. Describe the difference between positive control and negative control of gene expression.
4. Explain which operon discussed in this section is catabolic and which operon is anabolic.




a. Lactose present, glucose absent (cAMP level high)




b. Lactose present, glucose present (cAMP level low)

**Figure 13.3 Action of CAP.** When active CAP binds to its site on DNA, the RNA polymerase is better able to bind to the promoter, so that the structural genes of the *lac* operon are expressed. **a.** CAP becomes active in the presence of cAMP, a molecule that is prevalent when glucose is absent. Therefore, transcription of lactose enzymes increases, and lactose is metabolized. **b.** If glucose is present, CAP is inactive, and RNA polymerase does not completely bind to the promoter. Therefore, transcription of lactose enzymes decreases, and less metabolism of lactose occurs.

# 13.2 Eukaryotic Regulation

**AP Learning Outcomes**

Upon completion of this section, you should be able to

1. List the levels of control of gene expression in eukaryotes.
2. Summarize how chromatin structure may be involved in regulation of gene expression in eukaryotes.
3. Identify the mechanisms of transcriptional, posttranscriptional, and translational control of gene expression.

With a few minor exceptions, each cell of a multicellular eukaryote has a complete complement of genes; the differences in cell types are determined by the different genes that are actively expressed in each cell. For example, in muscle cells, a different set of genes is turned on in the nucleus and a different set of proteins is active in the cytoplasm, compared to nerve or liver cells.

Like prokaryotic cells, a variety of mechanisms regulate gene expression in eukaryotic cells. These mechanisms can be grouped under five primary levels of control; three of them pertain to the nucleus, and two pertain to the cytoplasm (Fig. 13.4). In other words, control of gene activity in eukaryotes extends from transcription to protein activity. The following types of control in eukaryotic cells can modify the amount of the gene product:

- *Chromatin structure:* Chromatin packing is used as a way to keep genes turned off. If genes are not accessible to RNA polymerase, they cannot be transcribed. Chromatin structure is one method of *epigenetic inheritance* (Gk. *epi,* "besides"), the transmission of genetic information outside the coding sequences of a gene.
- *Transcriptional control:* The degree to which a gene is transcribed into mRNA determines the amount of gene product. In the nucleus, transcription factors may promote or repress transcription, the first step in gene expression.
- *Posttranscriptional control:* Posttranscriptional control involves mRNA processing and how fast mRNA leaves the nucleus.
- *Translational control:* Translational control occurs in the cytoplasm and affects when translation begins and how long it continues. Small interfering RNA molecules (siRNA) are known to regulate translation. In addition, any condition that can cause the persistence of the 5′ cap and 3′ poly-A tail can affect the length of translation. Excised introns may also have effects on the life span of mRNA.
- *Posttranslational control:* Posttranslational control, which also takes place in the cytoplasm, occurs after protein synthesis. Only a functional protein is an active gene product.

We now explore each of these types of control in greater depth.

## Chromatin Structure

The DNA in eukaryotes is always associated with a variety of proteins, and together they make up a stringy material called **chromatin.** One of the more important types of these proteins is the histones. Histones play an important role in the compaction of the DNA (see Fig. 9.4), as well as in eukaryotic gene regulation. Without histones, the DNA would not fit inside the nucleus. Each human cell contains around 2 meters of DNA, yet the nucleus is only 5 to 8 micrometers (μm) in diameter.

The degree to which chromatin is compacted greatly affects the accessibility of the chromatin to the transcriptional machinery of the cell, and thus the expression levels of the genes. Active genes in eukaryotic cells are associated with more loosely packed chromatin called *euchromatin,* while the more tightly packed DNA, called *heterochromatin,* contains mostly inactive genes.

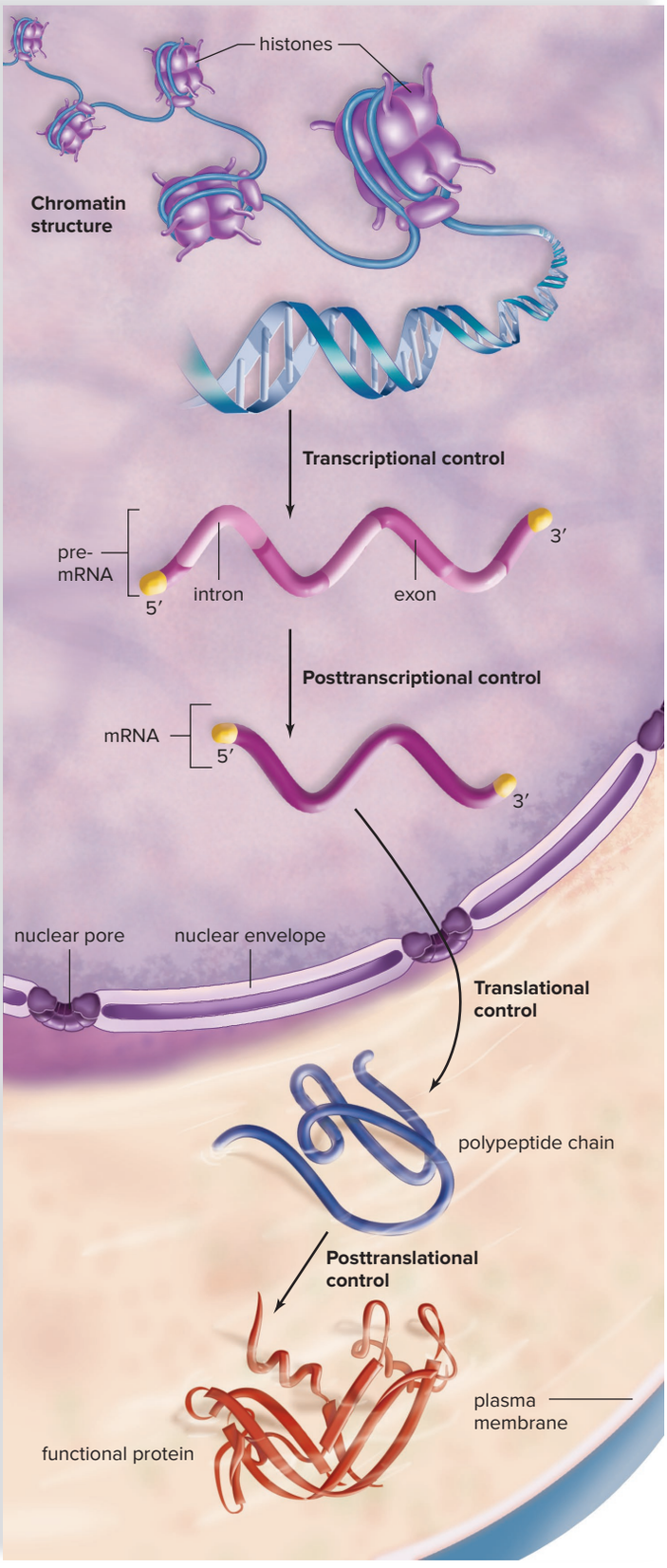



**Figure 13.4 Levels of gene expression control in eukaryotic cells.** The five levels of control are (1) chromatin structure, (2) transcriptional control, and (3) posttranscriptional control, which occur in the nucleus; (4) translational and (5) posttranslational control, which occur in the cytoplasm.

Under a microscope, the more densly compacted heterochromatin stains darker than euchromatin (Fig. 13.5*a*).

Whether the DNA exists as euchromatin or heterochromatin depends on how tightly the DNA is wrapped around DNA-histone complexes called nucleosomes (see Section 9.2). Histone molecules have *tails,* strings of amino acids that extend beyond the main portion of a nucleosome (Fig. 13.5*b*). In heterochromatin, the histone tails tend to bear methyl groups (—$CH_3$); in euchromatin, the histone tails tend to be acetylated and have attached acetyl groups (—$COCH_3$).

Histones regulate accessibility to DNA; euchromatin becomes genetically active when histones no longer block access to DNA. When DNA in euchromatin is transcribed, a group of proteins called the *chromatin remodeling complex* pushes aside, or *unpacks,* the histone portion of a nucleosome, so that access to DNA is not blocked and transcription can begin (Fig. 13.5*c*). After unpacking occurs, many decondensed loops radiate from the central axis of the chromosome. These chromosomes have been named lampbrush chromosomes, because their feathery appearance resembles the brushes that were once used to clean kerosene lamps.

In addition to physically moving nucleosomes aside to expose promoters, chromatin remodeling complexes may also affect gene expression by adding acetyl or methyl groups to histone tails.

## *Heterochromatin Is Not Transcribed*

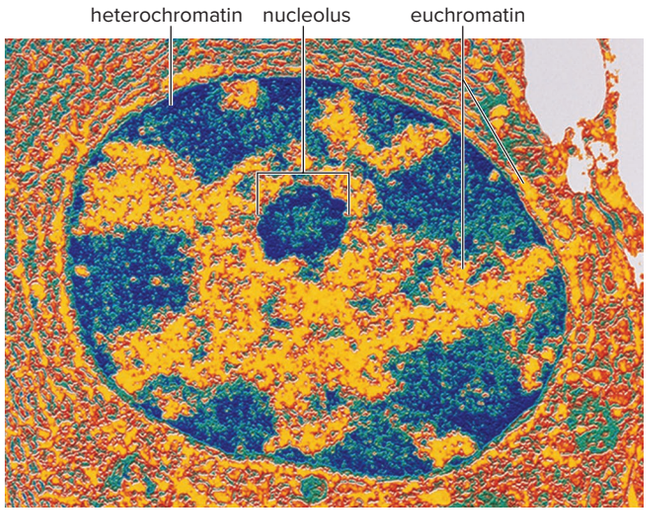
In general, highly condensed heterochromatin is inaccessible to RNA polymerase, and the genes contained within are seldom or never transcribed. A dramatic example of heterochromatin is the **Barr body** in mammalian females. This small, dark-staining mass of condensed chromatin adhering to the inner edge of the nuclear membrane is an inactive X chromosome. To compensate for the fact that female mammals have two X chromosomes (XX), whereas males have only one (XY), one of the X chromosomes in the cells of female embryos undergoes inactivation. The inactive X chromosome does not produce gene products, allowing both males and females to produce the same amount of gene product from a single X chromosome.

How do we know that Barr bodies are inactive X chromosomes that are not producing gene products? In a heterozygous female, 50% of the cells have one X chromosome active, and 50% have the other X chromosome active. The body of a heterozygous female is therefore a mosaic, with "patches" of genetically different cells. Investigators have discovered that human females who are heterozygous for an X-linked recessive form of ocular albinism have patches of pigmented and nonpigmented cells at the back of the eye.

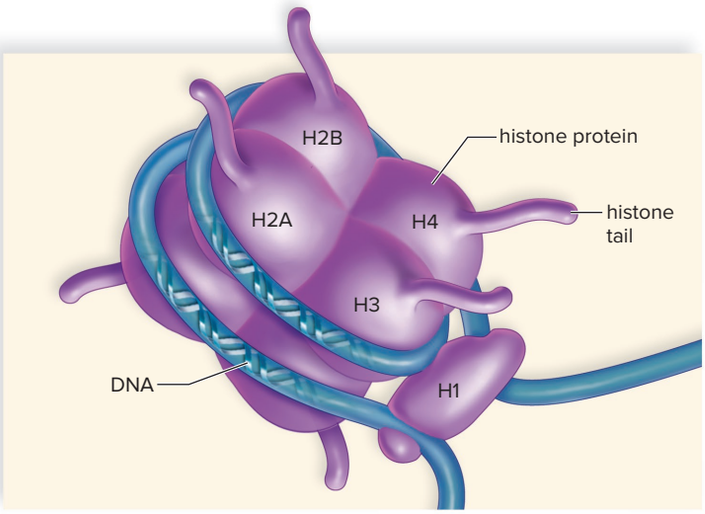
As other examples, women who are heterozygous for X-linked hereditary absence of sweat glands have patches of skin lacking sweat glands. And the female calico cat exhibits a difference in X-inactivation in its cells. In these cats, an allele for black coat color is on one X chromosome, and a corresponding allele for orange coat color is on the other. The patches of black and orange in the coat can be related to which X chromosome is in the Barr bodies of the cells found in the patches (Fig. 13.6).

## *Epigenetic Inheritance*

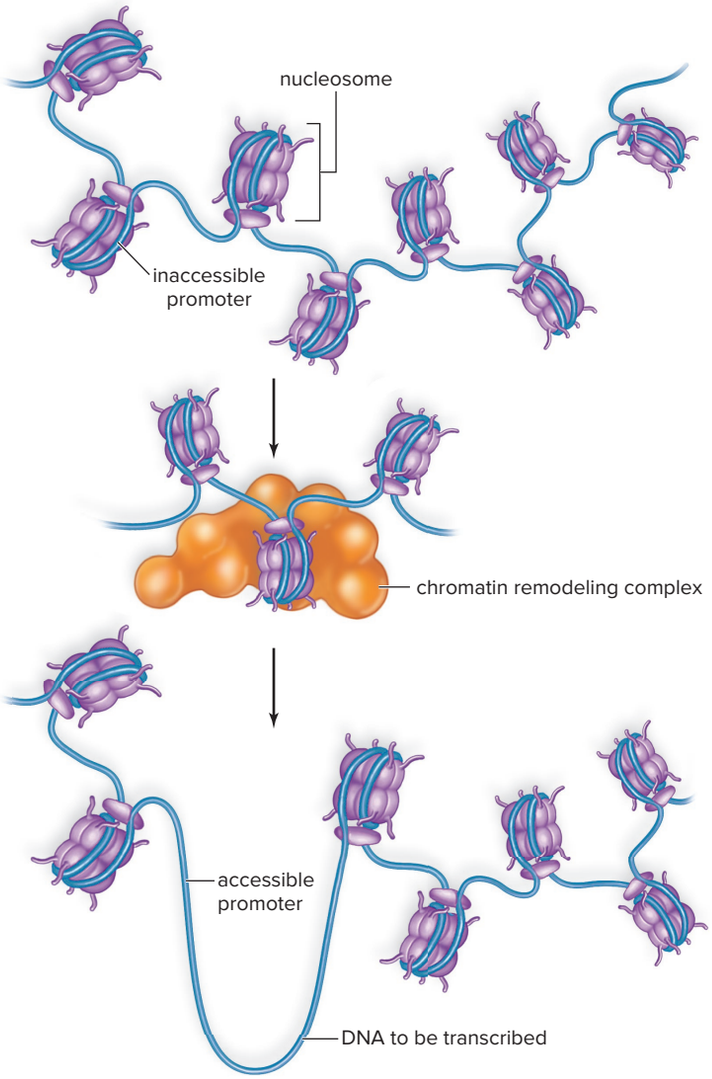
Histone modification is sometimes linked to a phenomenon termed **epigenetic inheritance,** in which variations in the pattern of inheritance are not due to changes in the sequence of the DNA




a. Darkly stained heterochromatin and lightly stained euchromatin




b. A nucleosome




c. DNA unpacking

**Figure 13.5 Chromatin structure regulates gene expression.** **a.** A eukaryotic nucleus contains highly condensed heterochromatin (darkly stained) and euchromatin (lightly stained), which is not as condensed. **b.** Nucleosomes ordinarily prevent access to DNA, so that transcription cannot take place. If histone tails are acetylated, access can be achieved; if the tails are methylated, access is more difficult. **c.** A chromatin remodeling complex works on euchromatin to make the DNA available, and thus the promoter accessible, for transcription. (a): Alfred Pasieka/Science Source

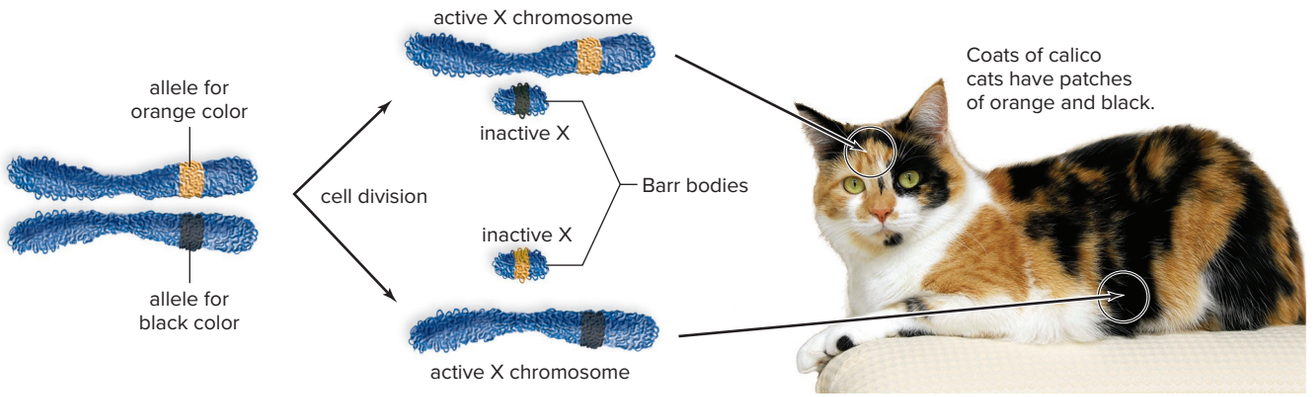



**Figure 13.6 X-inactivation in mammalian females.** In cats, the alleles for black or orange coat color are carried on the X chromosomes. Random X-inactivation occurs in females. Therefore, in heterozygous females, some of the cells express the allele for black coat color, while other cells express the allele for orange coat color. The white color on calico cats is provided by another gene. (photo): cgbaldauf/Getty Images

# BIG IDEA 3 Information Storage and Transmission

## Same but Not the Same—the Role of Epigenetics

Mia and Emma are identical twins in their early twenties. They both have a dimpled chin and blonde hair, and they wear the same-size clothes and shoes. As little girls, their parents emphasized their similarities by dressing them the same and giving them both the same opportunities to play piano and do gymnastics. As teenagers, things began to change. Their clothing styles were different—Mia preferred the current trends, whereas Emma loved black clothing. Mia was also more outgoing and popular; Emma was more reserved and thoughtful.

How is it possible that two people with the same genes and raised alike can be so different? Many scientists attribute a person's outcome to two factors: nature and nurture. Nature, your genes, gives you traits for eye color, hair color, and blood type. Nurture is based on your lifestyle and environment, including diet, rearing, and education. But is there a third force at work that can affect a person's overall health and well-being? Researchers working with identical twins believe there is a bridge between nature and nurture in the form of epigenetics.

The specific chemical reactions, or epigenetic "tags," can come in different forms but are often associated with DNA methylation, in which a methyl group attaches to the cytosine base of DNA (Fig. 13A). With a methyl group attached, transcription cannot occur. The methyl group interferes with transcription factors and other proteins in the transcription machinery, thereby silencing or weakening a gene. Over time, the differences in these tags accumulate, making twins increasingly different from each other (Fig. 13B).

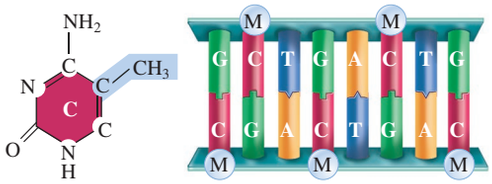



**Figure 13A DNA methylation.** DNA is methylated when a methyl group attaches to the cytosine nucleotide.

Epigenetics are heritable changes in gene expression without changing the DNA sequence. Chemical reactions due to environmental exposure influence how genes are turned off or on; how they are weakened or strengthened; how they change our immune systems; and how they build muscle, brains, and all other body parts. Identical twins present a unique opportunity to study epigenetics, because they are clones resulting from a split in a single fertilized egg (Fig. 13C). Assuming a similar upbringing, their gradual differences over time can therefore be attributed to their disparate control of genes.

Epigenetics has important implications for medicine. The appearance of tags on genes helps scientists discover the cause of some illnesses that cannot be explained by DNA or genetic mutations alone. Identical twins discordant (different) for autism, psychiatric disorders, and cancer have been shown to have different DNA methylation on certain genes.

In addition, the epigenetic changes are reversible. A study using rats showed that rat pups that are licked and nurtured by their mothers become calm adults. Rat pups that are not nurtured are anxious. Injecting a calm rat with a drug that adds methyl groups creates an anxious rat. Conversely, injecting an anxious rat with a different drug that removes methyl groups creates a calm rat. In drug development, epigenetic medicines could be used to correct or reverse the particular effect of a tag.

### Questions to Consider

1. How does epigenetics affect transcription and translation?
2. What lifestyle choices most likely negatively impact a person's epigenetics?

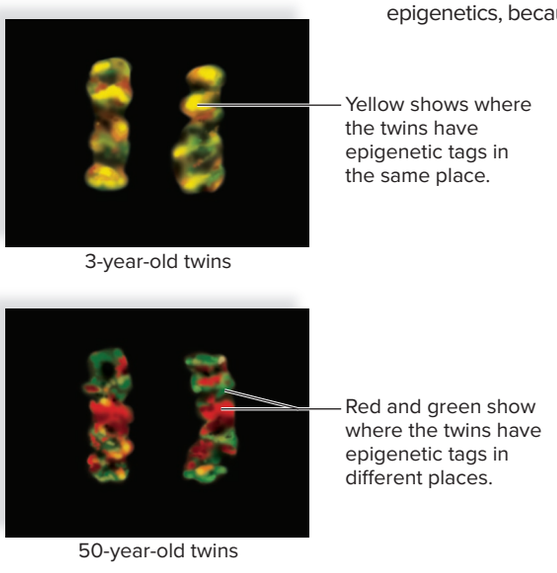



**Figure 13B Comparison of twins' chromosomes.** One of the twin's epigenetic tags are dyed green, and the other twin's tags are dyed red. An overlap in green and red shows up as yellow. The 50-year-old twins have more epigenetic tags in different places than do the 3-year-old twins.

**Figure 13C Identical twins.** Identical twins come from a single fertilized egg that splits in two. Their genes are the same. Hero/Corbis/Glow Images

nucleotides. The term is also used broadly to describe inheritance patterns that do not depend on the genes themselves. Epigenetic inheritance explains unusual inheritance patterns and may play an important role in growth, aging, and cancer.

One form of epigenetic inheritance involves the methylation of the DNA molecule. During *genomic imprinting,* either the mother's or the father's gene (but not both) is methylated during gamete formation. If an inherited allele is highly methylated, the gene is not expressed, even if it is a normal gene in every other respect. For traits that exhibit genomic imprinting, the expression of the gene depends on whether the unmethylated allele was inherited from the mother or the father. Twin studies, such as those described in the Big Idea 3 feature, "Same but Not the Same—the Role of Epigenetics," have allowed researchers to better understand the role of methylation in the inactivation of genes. It is hoped that this understanding will allow researchers to inactivate specific genes, such as those associated with diseases such as cancer.

## Transcriptional Control

Although eukaryotes have various levels of genetic control (see Fig. 13.4), **transcriptional control** remains the most critical of these levels. The first step toward transcription is availability of DNA, which involves chromatin structure. Transcriptional control also involves the participation of transcription factors, activators, and repressors.

### *Transcription Factors, Activators, and Repressors*

Although some operons like those of prokaryotic cells have been found in eukaryotic cells, transcription in eukaryotes is still controlled by DNA-binding proteins. Every cell contains many different types of **transcription factors,** proteins that help regulate transcription by assisting the binding of the RNA polymerase to the promoter. A cell has many different types of transcription factors, and a variety of transcription factors may be active at a single promoter. Thus, the absence of one can prevent transcription from occurring.

Even if all the transcription factors are present, transcription may not begin without the assistance of a DNA-binding protein called a **transcription activator.** These bind to regions of DNA called **enhancers,** which may be located some distance from the promoter. A hairpin loop in the DNA brings the transcription activators attached to the enhancer into contact with the transcription factor complex (Fig. 13.7). Likewise, the binding of repressors within the promoter may prohibit the transcription of certain genes. Most genes are subject to regulation by both activators and repressors.

The promoter structure of eukaryotic genes is often very complex, and a large variety of regulatory proteins may interact with each other and with transcription factors to affect a gene's transcription level. Mediator proteins act as a bridge between transcription factors and transcription activators at the promoter. Now RNA polymerase can begin the transcription process (Fig. 13.7). Such protein-to-protein interactions are a hallmark of eukaryotic gene regulation. Together, these mechanisms can fine-tune a gene's transcription level in response to a large variety of conditions. For example, all the cells in a corn plant contain the gene for the pigment anthocyanin, but where and when anthocyanin is made is transcriptionally controlled. UV light induces anthocyanin production in the leaves where it is controlled by one set of transcription factors.

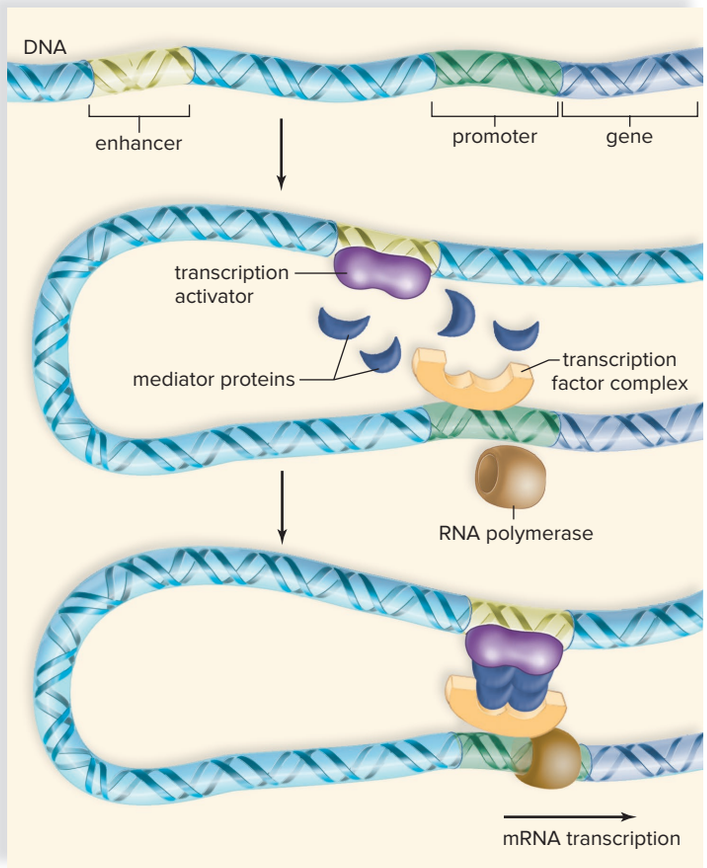



**Figure 13.7 Regulation of eukaryotic transcription.** Transcription in eukaryotic cells requires that transcription factors bind to the promoter, and transcription activators bind to an enhancer. The enhancer may be far from the promoter, but the DNA loops and mediator proteins act as a bridge joining activators to factors. Only then does transcription begin.

Later, organ development cues anthocyanin production in the kernels controlled by a different set of transcription factors.

## Posttranscriptional Control

**Posttranscriptional control** of gene expression occurs in the nucleus and includes alternative mRNA splicing and controlling the speed with which mRNA leaves the nucleus.

Recall that during pre-mRNA splicing, introns (noncoding regions) are excised, and exons (expressed regions) are joined together to form an mRNA (see Fig. 12.14). When introns are removed from pre-mRNA, differential splicing of exons can occur, and this affects gene expression. For example, an exon that is normally included in an mRNA transcript may be skipped, and it is excised along with the flanking introns (Fig. 13.8). The resulting mature mRNA has an altered sequence, and the protein it encodes is altered. Sometimes introns remain in an mRNA transcript. When this occurs, the protein-coding sequence is also changed.

Examples of alternative pre-mRNA splicing abound. Both the hypothalamus and the thyroid gland produce a protein hormone called calcitonin, but the mRNA that leaves the nucleus is not the same in both types of cells. This results in the thyroid's releasing a slightly different version of calcitonin than does the hypothalamus.

# BIG IDEA 3 Information Storage and Transmission

## Exercise and Gene Expression

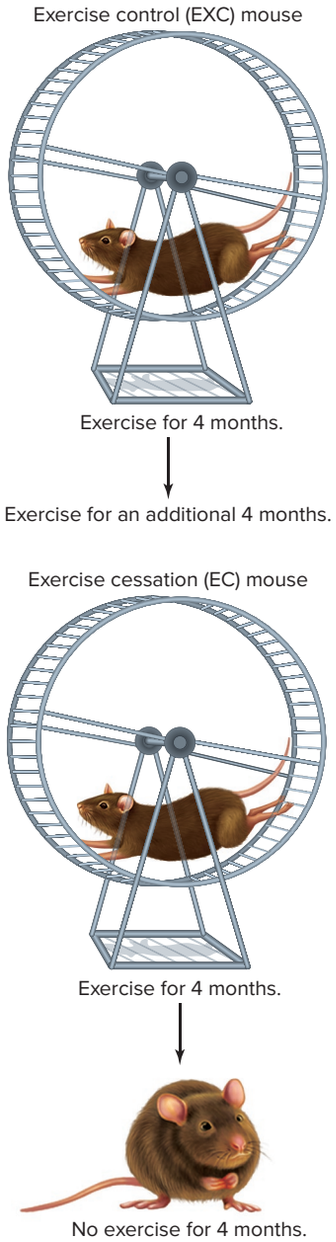



**Figure 13D Mice in two different exercise conditions.** The exercise control mice (EXCs) were allowed to run on their exercise wheel at any time. After 4 months, the exercise cessation mice (ECs) had their wheel taken away during daylight hours.

**Experiment: Stopping exercise can change how your genes are expressed.**

**Observation:** Studies have shown that humans who stop exercising exhibit anxiety, memory loss, and a decrease in cognitive abilities. Are the changes in mood and behavior the result of differential gene expression?

**Hypothesis:** Halting exercise changes the expression of genes responsible for mood, memory, and cognition.

**Experimental design:** Mice are model organisms. Studies conducted in mice can be used to predict similar outcomes in humans.

Two random groups of mice were used, one labeled EXC (exercise control) and one labeled EC (exercise cessation). Both sets of mice were allowed to use their exercise wheel at any time in a 24-hour period for 4 months. After 4 months, the wheel was removed during daylight hours for the EC group (Fig. 13D).

Two tests were used to measure memory and cognition. First, the Barnes maze trains a mouse to look through many holes until it reaches the hole that allows it to escape (Fig. 13E). The training takes several days and the mouse should improve over time. The longer it takes a mouse to escape, the weaker their memory and cognition.

Second, dissected brains were tested for gene expression of key genes located in the hippocampus. The hippocampus is the part of the brain responsible for emotion, memory, and the autonomic nervous system (Fig. 13F). One gene, *Gfap,* tested codes for cytoskeletal proteins in neurons called astrocytes. Astrocytes regulate the transmission of neural impulses in the brain and are linked to cognitive abilities.

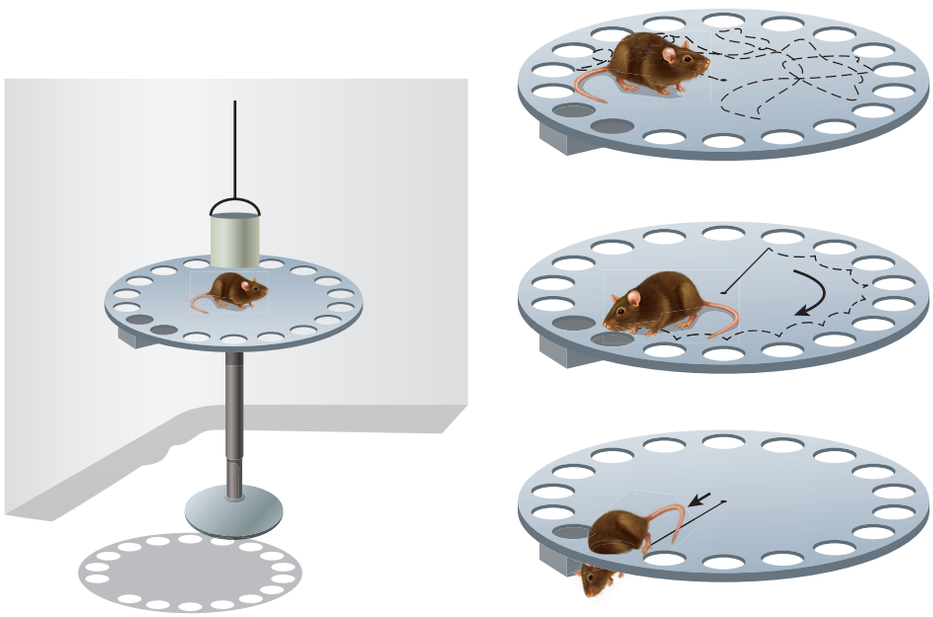


**Figure 13E The Barnes maze test.** This test is used to determine a mouse's memory and cognitive ability, because at the outset, a mouse takes a long time to reach the escape hole. After several days, the mouse remembers the fastest route to escape.

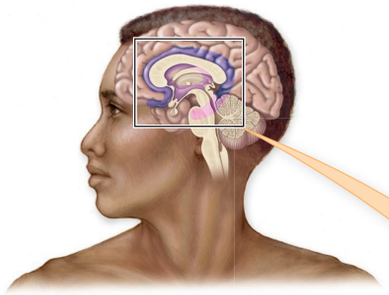
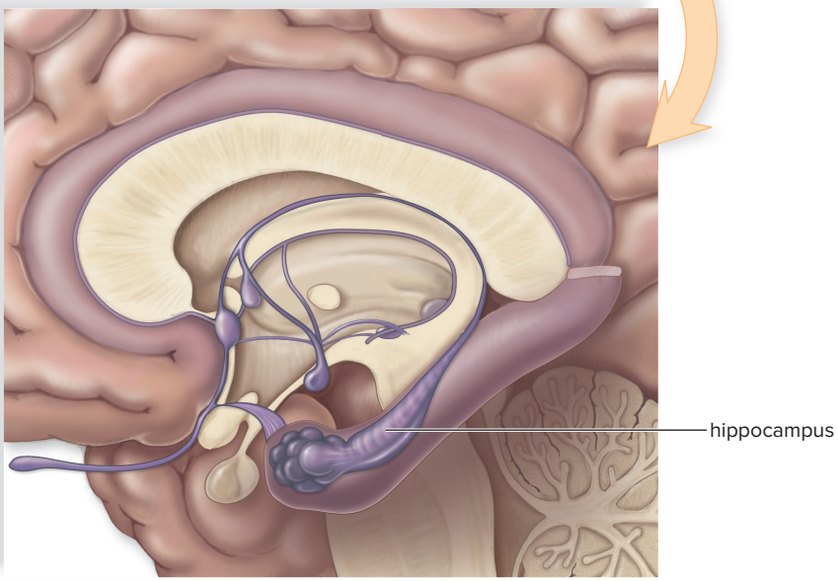


**Figure 13F The human hippocampus.** This shows the location of the hippocampus in the human brain.



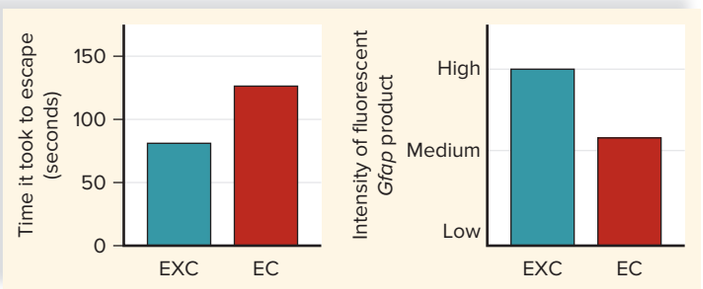

**Results:** Data show that EC mice have a decrease in memory and cognitive function and a decrease in gene expression of a gene known to be involved in memory and cognition (Fig. 13G).

## Questions to Consider

1. What other controls not mentioned in the reading do you think were implemented for this experiment?
2. Why do you think that exercise improves memory and cognition?

Gene expression was tested using molecular techniques that use fluorescence to measure the concentration of the gene product of interest (*Gfap*).

**Data:**




a. b.

**Figure 13G Behavioral and genetic difference between EXC and EC mice.** **a.** Mice were timed in the Barnes maze. It took the EC mice longer to complete the maze than the EXC mice. **b.** Gene product *Gfap* was quantified using fluorescent intensity in astrocytes located in the hippocampus. The EXC mice had higher gene expression (because of the higher fluorescence) for *Gfap* than the EC mice.

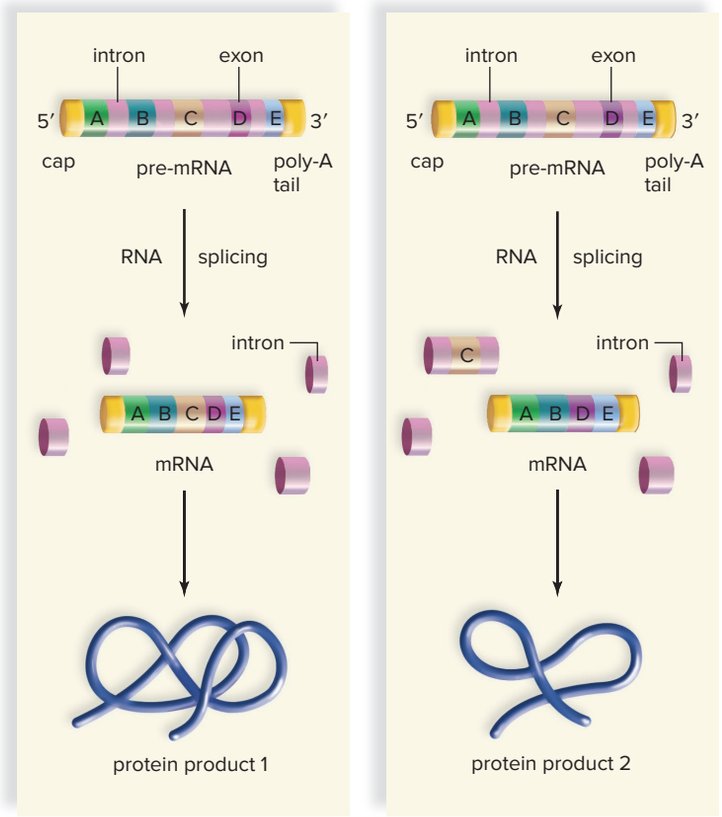



**Figure 13.8 Alternative processing of pre-mRNA.** Because the pre-mRNAs are processed differently in these two cells (**a** and **b**), distinct proteins result. This is a form of posttranscriptional control of gene expression.

Evidence of alternative mRNA splicing is found in other cells, such as those that produce neurotransmitters, muscle regulatory proteins, and antibodies.

Alternative pre-mRNA splicing allows humans and other complex organisms to recombine their genes in novel ways to create the great variety of proteins found in these organisms. Researchers are busy determining how small nuclear RNAs (snRNAs) affect the splicing of pre-mRNA. Alternative mRNA splicing can also result in the inclusion of an intron that brings about destruction of the mRNA before it leaves the nucleus.

Further posttranscriptional control of gene expression is achieved by modifying the speed of transport of mRNA from the nucleus into the cytoplasm. Evidence indicates there is a difference in the length of time it takes various mRNA molecules to pass through a nuclear pore, affecting the amount of gene product realized per unit of time following transcription.

## *Small RNA (sRNA) Molecules Regulate Gene Expression*

For a long time, scientists were faced with a mystery: A cell appeared to contain vastly more DNA than was needed to account for the number of expressed proteins. The DNA that was not expressed as proteins was initially termed "junk" DNA. Recently, however, scientists have begun to understand the role of this DNA in the cell. Although only about 1.5% of the transcribed DNA codes for protein, the remainder is used to form small RNA (sRNA) molecules. We now know that these sRNA molecules represent an important form of gene regulation that functions at multiple levels of gene expression.

Let's take a closer look at how these RNA molecules regulate gene expression (Fig. 13.9).

1. The transcribed RNA can form loops as hydrogen bonding occurs between its bases.

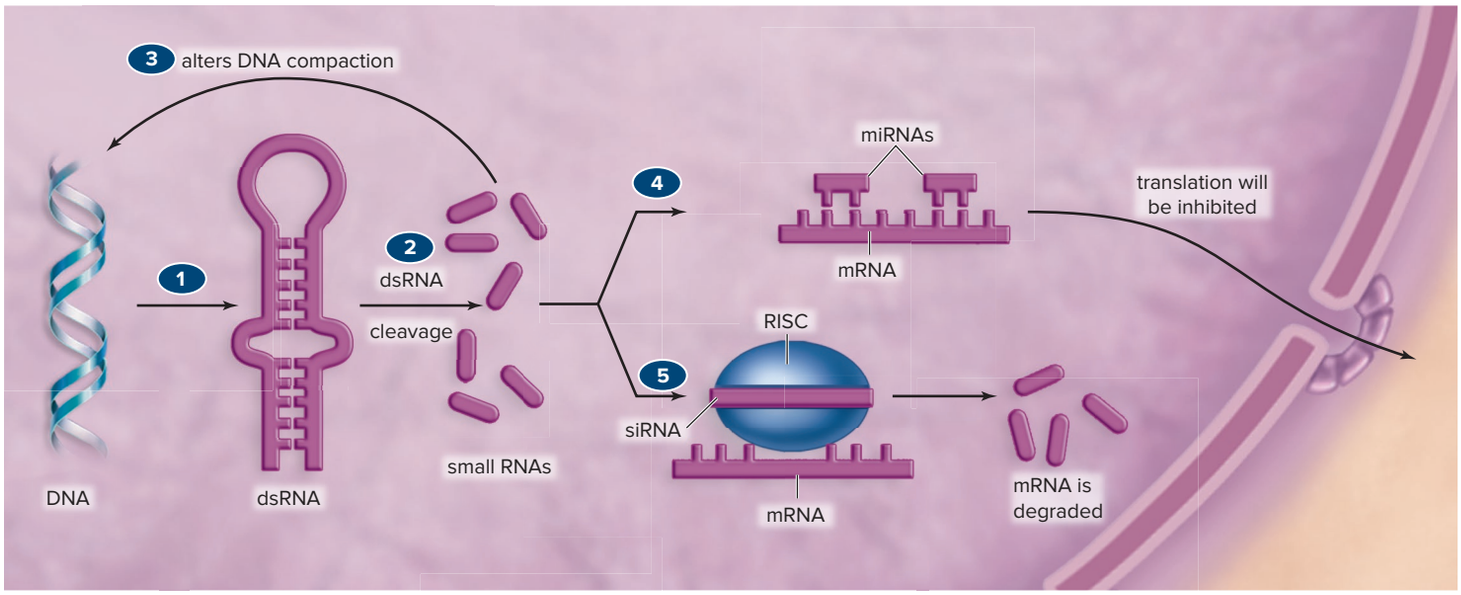



**Figure 13.9 Function of small RNA molecules.** Transcription of the DNA 1 may lead to looped and double-stranded RNA (dsRNA). The cleavage of the dsRNA 2 produces many small RNA (sRNA) molecules. 3 An sRNA can double back to increase DNA compaction, or it may become an miRNA or siRNA. 4 miRNA reduces translation by binding to complementary mRNA molecules. 5 siRNA forms a complex with RISC, which then degrades any mRNA with a sequence of bases that are complementary to the siRNA.

2. The double-stranded RNA (dsRNA) is diced up by enzymes in the cell to form sRNA molecules.
3. Some of these sRNA molecules regulate transcription, while others are involved in the regulation of translation. Various ways have been found by which sRNA may regulate gene expression. sRNA molecules have been known to alter the compaction of DNA, so that some genes are inaccessible to the transcription machinery of the cell.
4. Small RNAs are the source of *microRNAs* (*miRNAs*), small snippets of RNA that can bind to and disable the translation of mRNA in the cytoplasm.
5. Small RNAs are also the source of *small-interfering RNAs* (*siRNAs*) that join with an enzyme (an RNA-induced silencing complex, or RISC) to form an active silencing complex. This activated complex targets specific mRNAs in the cell for breakdown, preventing them from being expressed.

By using a combination of miRNA and siRNA molecules, a cell can fine-tune the amount of product being expressed from a gene, much as a dimmer switch on a light regulates the brightness of the room. Because both miRNA and siRNA molecules interfere with the normal gene expression pathways, the process is often referred to as **RNA interference.**

The first scientists to artificially construct miRNA and siRNA molecules to suppress the expression of a specific gene were Andrew Fire and Craig Mello. Following this discovery, medical scientists recognized that it may be possible to use sRNA molecules as therapeutic agents to suppress the expression of disease-causing genes. For their discovery, Fire and Mello received the 2006 Nobel Prize in Physiology or Medicine.

## Translational Control

**Translational control** begins when the processed mRNA molecule reaches the cytoplasm and before there is a protein product. Translational control involves the activity of mRNA for translation at the ribosome.

The presence or absence of the 5′ cap and the length of the poly-A (adenine nucleotide) tail at the 3′ end of a mature mRNA transcript can determine whether translation takes place and how long the mRNA is active. The long life of mRNAs that code for hemoglobin in mammalian red blood cells is attributed to the persistence of their 5′ end caps and their long 3′ poly-A tails. Therefore, any condition that affects the length of the poly-A tail or leads to removal of the cap may trigger the destruction of an mRNA.

## Posttranslational Control

**Posttranslational control** begins once a protein has been synthesized and has become active. Posttranslational control represents the last chance a cell has for influencing gene expression.

If all the proteins produced by a cell during its lifetime remained in the cell, serious problems would arise. Thus, proteins are continually being synthesized and then degraded.

Proteins needed only for a short time can be altered chemically, leaving them nonfunctional. Proteins may not be folded correctly or they may change shape over time, causing them to behave erratically or stick to one another and form aggregates. In fact, a number of neurodegenerative diseases, such as Alzheimer disease, Parkinson disease, and mad cow disease, are related to proteins that aggregate, forming plaques in the brain. Thus, in addition to normal turnover of proteins, cells need a way to get rid of old, unused, and incorrectly folded proteins.

Just how long a protein remains active in a cell is usually regulated by the use of **proteases,** enzymes that break down proteins. To protect the cell, proteases are typically confined to the lysosomes or special structures called **proteasomes.** For a protein to enter a proteasome, it has to be tagged with a signaling protein that is recognized by the proteasome cap (Fig. 13.10). When the cap recognizes the tag, it opens and allows the protein to enter the core of the structure, where it is digested to peptide fragments. Notice that proteasomes help regulate gene expression because they help control the amount of protein product in the cytoplasm.

### AP Check Your Progress 13.2

1. List the five levels of genetic control in eukaryotes.
2. Explain how chromatin structure influences gene expression.
3. Discuss how small RNA molecules and proteasomes regulate gene expression.

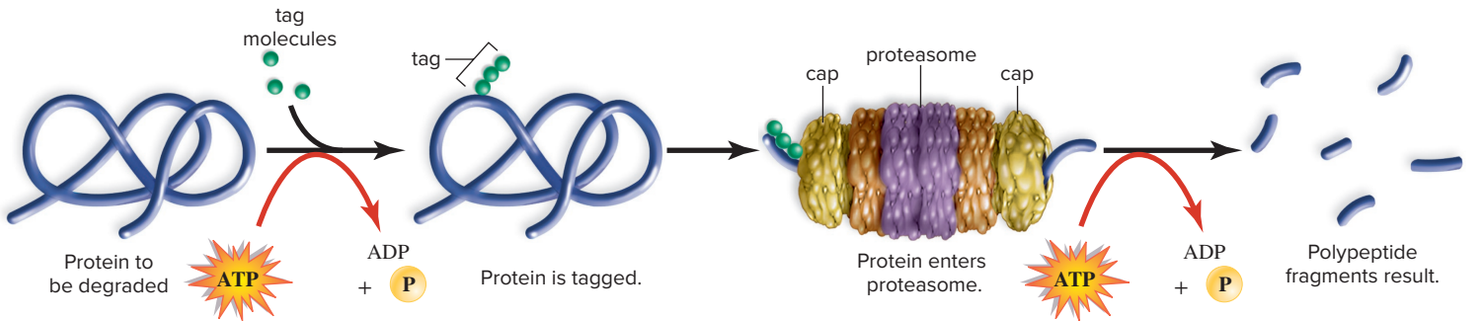



**Figure 13.10 Proteasomes and posttranslational control.** Proteins to be degraded are first tagged with a signaling molecule. They then enter the proteasome, where they are broken down into polypeptide fragments.

# 13.3 Gene Mutations

**AP Learning Outcomes**

Upon completion of this section, you should be able to

1. Distinguish between spontaneous and induced mutations.
2. Identify how mutations influence protein structure.
3. Summarize how mutations may cause cancer.

A **gene mutation** is a permanent change in the sequence of bases in DNA. The effect of a DNA base sequence change on protein activity can range from no effect to complete inactivity. Germ-line mutations are those that occur in sex cells and can be passed to subsequent generations. Somatic mutations occur in body cells and, therefore, may affect only a small number of cells in a tissue. Somatic mutations are not passed on to future generations, but they can lead to the development of cancer.

## Causes of Mutations

Some mutations are spontaneous—they happen for no apparent reason—whereas others are induced by environmental influences. In most cases, **spontaneous mutations** arise as a result of abnormalities in normal biological processes. **Induced mutations** may result from exposure to toxic chemicals or radiation, which induce (cause) changes in the base sequence of DNA.

### *Spontaneous Mutations*

Spontaneous mutations can be associated with any number of normal processes. For example, a movable piece of DNA, termed a *transposon,* may jump from one location to another, disrupting one or more genes and leading to an abnormal product (see Section 14.4). On rare occasions, a base in DNA can undergo a chemical change that leads to a mispairing during replication. A subsequent base-pair change may be carried forth in future generations. Spontaneous mutations due to DNA replication errors, however, are rare. DNA polymerase, the enzyme that carries out replication, proofreads the new strand against the old strand and detects any mismatched nucleotides, and each is usually replaced with a correct nucleotide. In the end, only about one mistake occurs for every 1 billion nucleotide pairs replicated.

### *Induced Mutations*

Induced mutations are caused by **mutagens,** environmental factors that can alter the base composition of DNA. Among the best-known mutagens are radiation and organic chemicals. Many mutagens are also **carcinogens** (cancer-causing mutagens).

Chemical mutagens are present in many sources, including some of the food we eat and many industrial chemicals. The mutagenic potential of AF-2, a food additive once widely used in Japan, and of safrole, a flavoring agent once used to flavor root beer, caused them to be banned. Surprisingly, many naturally occurring substances—like aflatoxin, produced in moldy grain and peanuts (and present in peanut butter at an average level of 2 parts per billion), and acrylamide, a natural product found in french fries—are also suspected mutagens.

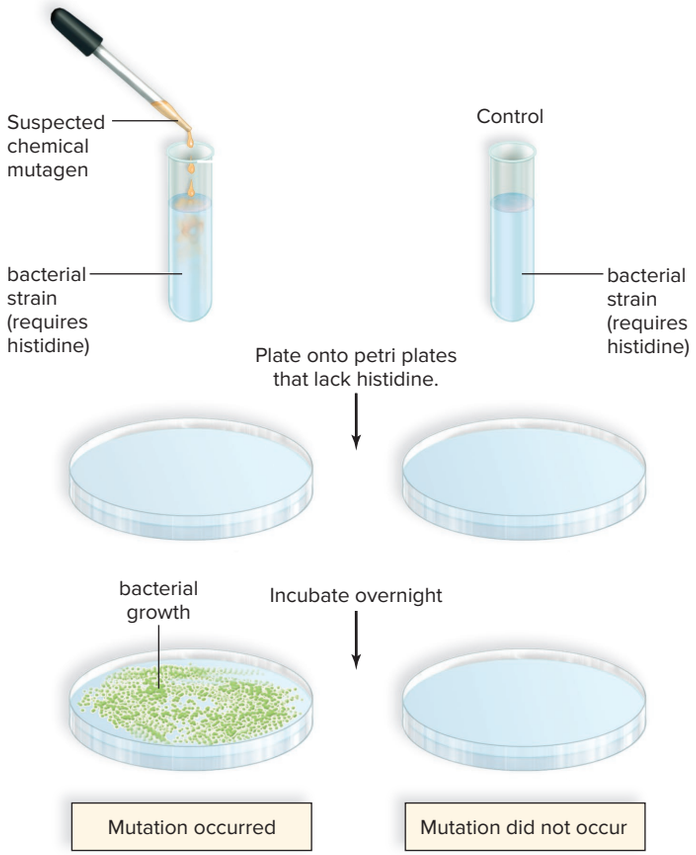



**Figure 13.11 The Ames test for mutagenicity.** A bacterial strain that requires histidine as a nutrient is exposed to a suspected chemical mutagen, but a control is not exposed. The bacteria are plated on a medium that lacks histidine; only the bacteria exposed to the chemical show growth. A mutation allowed the bacteria to grow; therefore, the chemical can be carcinogenic.

Tobacco smoke contains a number of organic chemicals that are known carcinogens, and it is estimated that one-third of all cancer deaths can be attributed to smoking. Lung cancer is the most frequent lethal cancer in the United States, and smoking is implicated in the development of cancers of the mouth, larynx, bladder, kidney, and pancreas. The greater the number of cigarettes smoked per day, the earlier the habit starts, and the higher the tar content, the greater is the possibility of these cancers. When smoking is combined with drinking alcohol, the risk of these cancers increases even more.

Scientists use the Ames test for mutagenicity to hypothesize that a chemical can be carcinogenic (Fig. 13.11). In the Ames test, a histidine-requiring strain of bacteria is exposed to a chemical. If the chemical is mutagenic, the bacteria can grow without histidine. A large number of chemicals used in agriculture and industry give a positive Ames test. Examples are ethylene dibromide (EDB), which is added to leaded gasoline (to vaporize lead deposits in the engine and send them out the exhaust), and ziram, which is used to prevent fungal disease on crops. Some drugs, such as isoniazid (used to prevent tuberculosis), are mutagenic according to the Ames test.

Aside from chemicals, certain forms of radiation, such as X-rays and gamma rays, are called ionizing radiation because they create free radicals, ionized atoms with unpaired electrons. Free

radicals react with and alter the structure of other molecules, including DNA. Ultraviolet (UV) radiation is easily absorbed by the pyrimidines in DNA. Wherever there are two thymine molecules next to one another, ultraviolet radiation may cause them to bond together, forming *thymine dimers.* A kink results in the DNA. Usually, these dimers are removed by **DNA repair enzymes,** which constantly monitor DNA and fix any irregularities. One enzyme excises a portion of DNA that contains the dimer, another makes a new section by using the other strand as a template, and still another seals the new section in place.

The importance of these repair enzymes is exemplified by individuals with the condition known as xeroderma pigmentosum. They lack some of the repair enzymes, and as a consequence, these individuals have a high incidence of skin cancer because of the large number of mutations that accumulate over time. Also, repair enzymes can fail, as when skin cancer develops because of excessive sunbathing or prolonged exposure to X-rays.

## Effect of Mutations on Protein Activity

**Point mutations** involve a change in a single DNA nucleotide. That change alters transcription and possibly changes the specific amino acid. One type of point mutation is a *base substitution,* resulting in one DNA nucleotide being replaced with another incorrect nucleotide. Notice the base difference in the second row of Figure 13.12*a* and how it changes the resultant amino acid sequence. Sometimes a base substitution has little or no effect on the final protein produced, but in some cases early stop codons can be introduced, or coding for the wrong amino acid can severely alter the protein shape. Such is the case with the genetic disorder sickle-cell disease (Fig. 13.12*b*). In this gene, there is a base substitution that alters the mRNA codon for glutamic acid. Instead, the codon for valine is present, altering the final shape of hemoglobin, the protein that carries oxygen in the blood. The abnormal hemoglobin molecules form semirigid rods, and the red blood cells become sickle-shaped, resulting in decreased blood flow through tiny blood vessels.

**Frameshift mutations** occur most often when one or more nucleotides are either added or deleted from DNA (Fig. 13.12*a*, bottom two lines). Because all the codons downstream of the mutation are now shifted, the result is a completely new sequence of codons, yielding a nonfunctional protein.

### *Nonfunctional Proteins*

A single nonfunctioning protein can have a dramatic effect on the phenotype, because enzymes are often a part of metabolic pathways. One metabolic pathway in cells is as follows:

$$\underset{\text{(phenylalanine)}}{\text{A}} \xrightarrow{E_A} \underset{\text{(tyrosine)}}{\text{B}} \xrightarrow{E_B} \underset{\text{(melanin)}}{\text{C}}$$

If a faulty code for enzyme $E_A$ is inherited, a person is unable to convert molecule A to B. Phenylalanine builds up in the system, and the excess causes an intellectual disability and other symptoms of the genetic disorder phenylketonuria (PKU). In the same pathway, if a person inherits a faulty code for enzyme $E_B$, then B cannot be converted to C, and the individual is an albino.

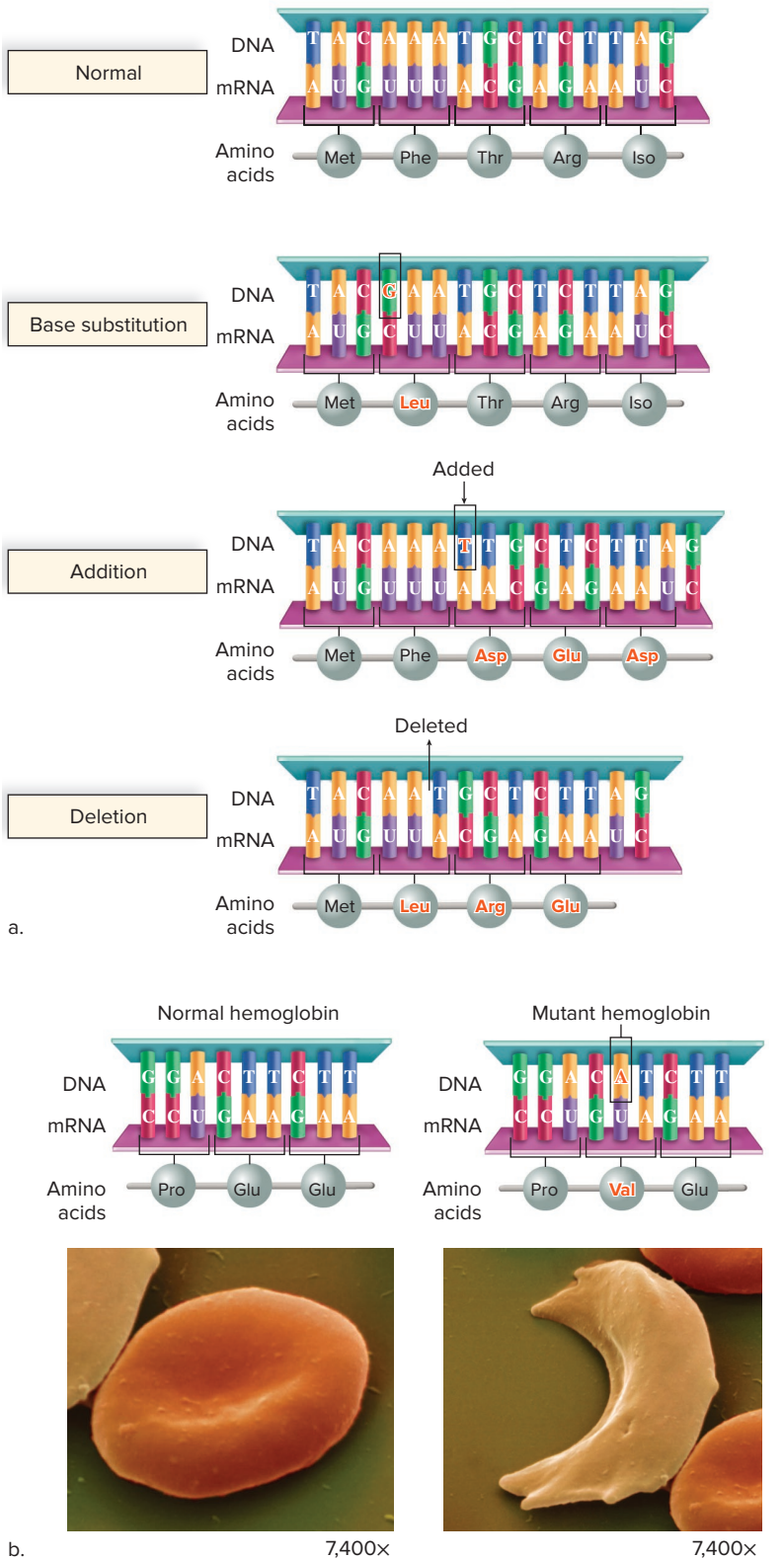



**Figure 13.12 Point mutations.** The effect of a point mutation can vary. **a.** Starting at the *top:* Normal sequence of bases results in a normal sequence of amino acids. Next, a base substitution can result in the wrong amino acid. In the final two rows, an addition or deletion can result in a frameshift mutation, altering all the codons downstream of the point mutation. **b.** Due to a base substitution in the hemoglobin gene, the DNA now codes for valine instead of glutamic acid, and the result is that normal red blood cells become sickle-shaped. (b, both): Eye of Science/Science Source

A rare condition called androgen insensitivity is due to a faulty receptor for androgens, which are male sex hormones, such as testosterone. In a male with this condition, plenty of testosterone is present in the blood, but the cells are unable to respond to it. Female instead of male external genitals form, and female instead of male secondary sex characteristics occur at puberty. The individual, who appears to be a normal female, may be prompted to seek medical advice when menstruation never occurs. The karyotype is that of a male rather than a female, and the individual does not have the internal sexual organs of a female.

## Mutations Can Cause Cancer

It is estimated that one in three people will develop cancer at some time in their lives. Of these affected individuals, one-third of the females and one-fourth of the males will die due to cancer. In the United States, the three deadliest forms of cancer are lung cancer, colon and rectal cancer, and breast cancer.

The development of cancer involves a series of accumulating mutations that can be different for each type of cancer. As discussed in Section 9.4, tumor suppressor genes ordinarily act as brakes on cell division, especially when it begins to occur abnormally. Proto-oncogenes stimulate cell division but are usually turned off in fully differentiated, nondividing cells. When proto-oncogenes mutate, they become oncogenes that are active all the time (see Fig. 9.11). Carcinogenesis begins with the loss of tumor suppressor gene activity and/or the gain of oncogene activity. When tumor suppressor genes are inactive and oncogenes are active, cell division occurs uncontrollably, because a cell signaling pathway that reaches from the plasma membrane to the nucleus no longer functions as it should (see Fig. 9.12).

It often happens that tumor suppressor genes and proto-oncogenes code for transcription factors or proteins that control transcription factors. As we have seen, transcription factors are a part of the rich and diverse types of mechanisms that control gene expression in cells. They are of fundamental importance to DNA replication and repair, cell growth and division, control of apoptosis, and cellular differentiation. Therefore, it is not surprising that inherited or acquired defects in transcription factor structure and function contribute to the development of cancer.

For example, the tumor suppressor gene called *p53* is more frequently mutated in human cancers than is any other known gene. It has been found that the p53 protein acts as a transcription factor, and as such it is involved in turning on the expression of genes whose products are cell cycle inhibitors (see Section 9.1). *p53* also promotes apoptosis (programmed cell death) when it is needed. The retinoblastoma protein (RB) controls the activity of a transcription factor for cyclin D and other genes whose products promote entry into the S stage of the cell cycle. When the tumor suppressor gene *p16* mutates, the RB protein is always available, and the result is too much active cyclin D in the cell.

Mutations in many other genes also contribute to the development of cancer. Several proto-oncogenes code for ras proteins, which are needed for cells to grow, to make new DNA, and to not grow out of control. A point mutation is sufficient to turn a normally functioning *ras* proto-oncogene into an oncogene, and abnormal growth results.

### AP Check Your Progress 13.3

1. List some common causes of spontaneous and induced mutations.
2. Explain how a frameshift mutation may disrupt a gene's function.
3. Discuss how a mutation in a tumor suppressor gene and in proto-oncogenes disrupts the cell cycle.

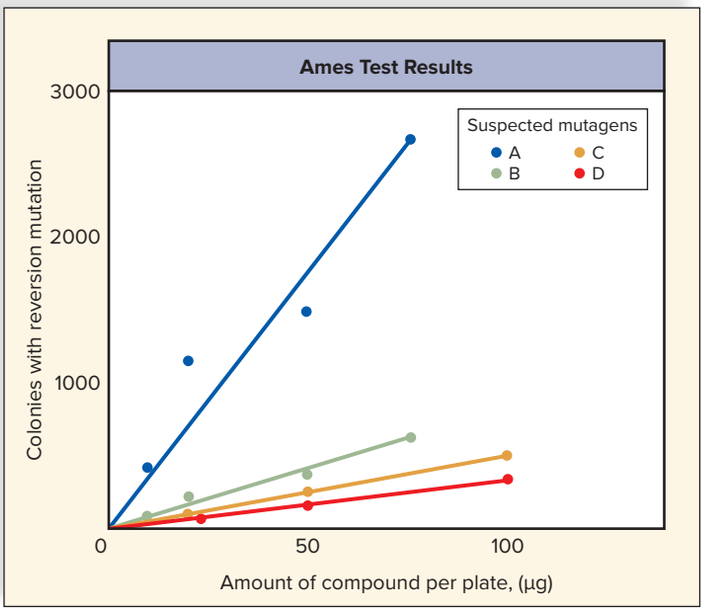
# AP Chapter 13 Review and Assessment

| Chapter 13 | AP Topics Covered |
|---|---|
| **Unit 4: Cell Communication and Cell Cycle** | **4.2 Introduction to Signal Transduction (13.1)**<br>• Signal transduction is how cells link signal reception with response, and begins when a chemical messenger is recognized by a receptor on a target cell.<br>• Prokaryotic regulation of gene expression is a good example of signal transduction.<br>– The lac operon is activated (cellular response) when lactose (a ligand) binds to the repressor (receptor).<br>– This makes the repressor unable to bind to the operator, allowing transcription to proceed.<br>**4.3 Signal Transduction (13.1)**<br>• Signal transduction pathways influence how cells respond to the environment and express genes.<br>• Both prokaryotic and eukaryotic gene expression depends on particular signal transduction pathways activating.<br>**4.4 Changes in Signal Transduction Pathways (13.1, 13.2, 13.3)**<br>• Chemicals in a cell may interfere with signal transduction, eg. lactose interfering with the repression of the *lac* operon.<br>• Mutations can also affect signal transduction pathways. |
| **Unit 6: Gene Expression and Regulation** | **6.5 Regulation of Gene Expression (13.1, 13.2)**<br>• All cells contain the same DNA, but not all cells express all the genes coded in that DNA.<br>• Regulatory sequences control the transcription of specific genes.<br>• Some genes are regulated together.<br>– In prokaryotes, these are called operons, and are transcribed together as a single mRNA transcript.<br>– In eukaryotes, the same transcription factors may influence a group of genes. |

| Chapter 13 | AP Topics Covered |
|---|---|
| **Unit 6: Gene Expression and Regulation** | **6.6 Gene Expression and Cell Specialization (13.1, 13.2)**<br>• Promotors are areas of DNA which bind to transcription factors to initiate the transcription of specific genes.<br>• These promoters can be blocked by inhibitory molecules.<br><br>**6.7 Mutation (13.3)**<br>• A mutation is a change in the nucleotide sequence which makes up a gene.<br>• A point mutation happens when a single nucleotide is changed, resulting in a different codon.<br>• A frameshift mutation happens when bases are added or deleted, thus changing the reading frame of the codons. |

## AP Assessment

1. Regulatory proteins control the expression of genes in both prokaryotes and eukaryotes through transcriptional control. At what stage in the gene expression process would regulatory proteins have their effect?
   a. They modulate the binding of RNA polymerase to the DNA promoter.
   b. They control RNA editing and processing.
   c. They moderate the rate at which tRNAs assemble at the ribosome.
   d. They interfere with the joining of amino acids to tRNAs.
2. Your classmate is lactose intolerant, and therefore consumes no lactose-containing foods. Consider the population of *E. coli* living in your classmate's gut. Which statement best describes these bacteria?
   a. Their *lac* operon must operate at high speed to manufacture enough lactose.
   b. Their *lac* operon will be deactivated and removed from the bacterial chromosome, due to the permanent lack of lactose.
   c. Their *lac* operon is always turned on, utilizing other disaccharides to interact with their *lac* repressor.
   d. Their *lac* operon is always turned off, without lactose to interact with their *lac* repressor.
3. Posttranscriptional control provides another avenue for gene regulation in eukaryotic cells. One such control mechanisms involves small RNA's. What is the most common effect of microRNAs(miRNAs)?
   a. amplification of gene expression by copying genes
   b. increasing rate of RNA processing in the nucleus
   c. silencing genes by inhibiting the translation of their mRNA
   d. inhibiting gene expression by blocking transcription
4. The term mutation refers to any change in the nucleotide sequence of a gene. Of the types of mutations listed below, predict which would likely cause the least change in the gene.
   a. point mutation
   b. frameshift mutation
   c. transposon
   d. nondisjunction
5. Unit 6 Use the figure below to answer question 5.




Data obtained from: Ames. B.N. 1979. Identifying environmental chemicals causing mutations and cancer. Science. 204: 587–593.

A mutagen is chemical that can cause DNA to mutate. It is very important, then, for scientists to determine if compounds are mutagens or not. The Ames test is used to identify mutagens. The test uses a strain of bacteria that cannot make the amino acid histidine. The bacteria are exposed to a suspected mutagen and grow on a medium without histidine. The bacteria that grow have a mutation called a reversion because they reverted to the natural condition of making histidine. The compounds in the graph were Ames tested.
   a. **Describe** the relationship between the amount of the compound and the mutation.
   b. **Analyze** which compound is the strongest mutagenic compound.
6. Unit 4 Unit 6 Eukaryotes have evolved a variety of regulatory mechanisms that allow them to fine-tune gene expression and produce a large number of proteins from a relatively small number of genes. Explain how three regulatory mechanisms of gene expression support efficient cell function.

**For further AP exam practice, access the additional questions available in your online course.**