8.1 Identifying DNA as the Genetic Material

KEY CONCEPT DNA was identified as the genetic material through a series of experiments.

MAIN IDEAS

- Griffith finds a "transforming principle."
- Avery identifies DNA as the transforming principle.
- Hershey and Chase confirm that DNA is the genetic material.

VOCABULARY

bacteriophage, p. 228

Review

deoxyribonucleic acid (DNA), gene, enzyme

REVIEW AT CLASSZONE.COM

Connect Some people think a complicated answer is better than a simple one. If they have a head cold, for instance, they may use all sorts of pills, syrups, and sprays, when they simply need rest, water, and warm chicken soup. In the early 1900s, most scientists thought DNA's structure was too repetitive for it to be the genetic material. Proteins, which are more variable in structure, appeared to be a better candidate. Starting in the 1920s, experiments provided data that did not support this idea. By the 1950s, sufficient evidence showed that DNA—the same molecule that codes for GFP in the glowing mouse—carries genetic information.

MAIN IDEA

Griffith finds a "transforming principle."

In 1928 the British microbiologist Frederick Griffith was investigating two forms of the bacterium that causes pneumonia. One form is surrounded by a coating made of sugar molecules. Griffith called these bacteria the S form because colonies of them look smooth. The second form of bacteria do not have a smooth coating and are called the R, or rough, form. As you can see in **FIGURE 8.1**, when Griffith injected the two types of bacteria into mice, only the S type killed the mice. When the S bacteria were killed with heat, the mice were unaffected. Therefore, only live S bacteria would cause the mice to die.

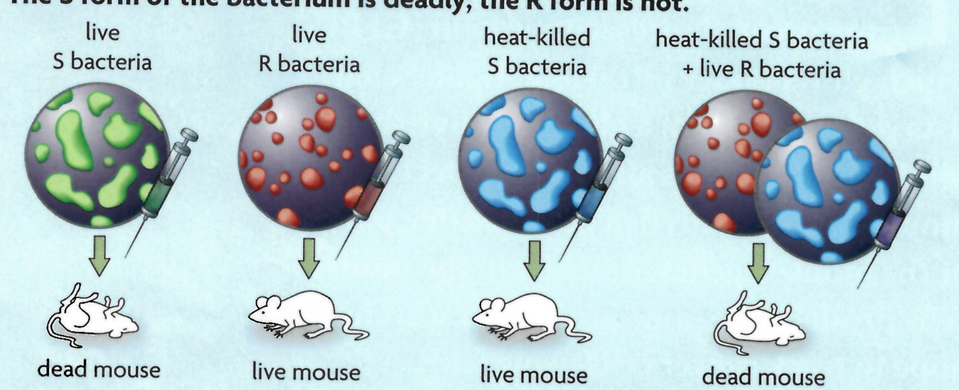
TAKING NOTES

Make a table to keep track of the experiments discussed in this section and how they contributed to our understanding of DNA.

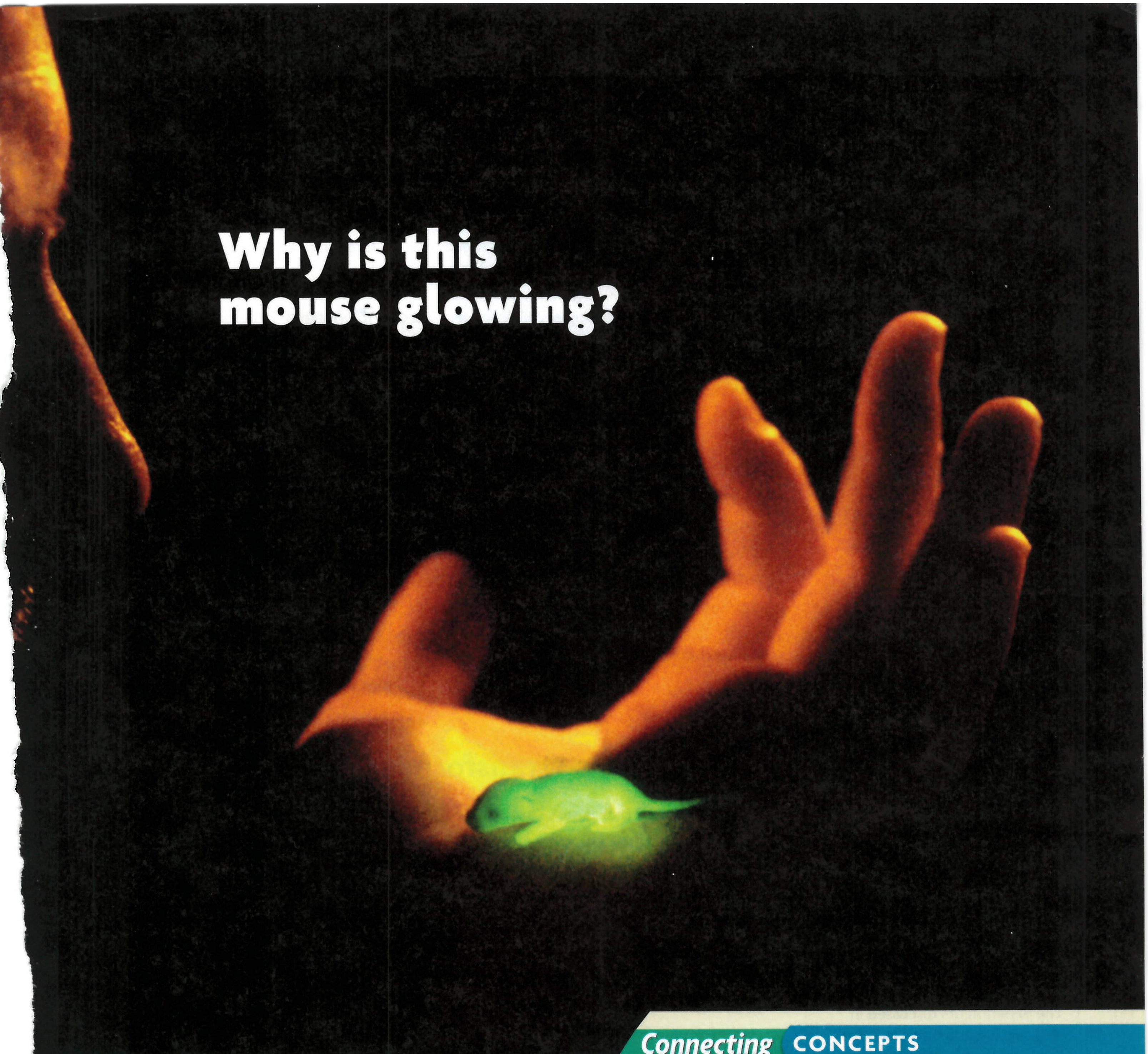
Experiment	*Results*
Griffith's mice	*A transferable material changed harmless bacteria into disease-causing bacteria.*

FIGURE 8.1 Griffith's Experiments

The S form of the bacterium is deadly; the R form is not.



Why is this mouse glowing?



This mouse's eerie green glow comes from green fluorescent protein (GFP), which glows under ultraviolet light. Scientists put a gene from a glowing jellyfish into a virus that was allowed to infect a mouse egg. The jellyfish gene became part of the mouse's genes. As a result, the mouse cells produce the same protein. Researchers hope to track cancer cells using GFP.

Connecting CONCEPTS

Translation This computer model of GFP shows the amino acids (purple) in the center of the protein that make the protein glow. The genetic code is universal, which means that a gene from one organism can be correctly translated into a protein in another organism. Although the gene for GFP comes from a jellyfish, GFP has been made in bacteria, yeast, slime mold, plants, fruit flies, zebrafish, and mammals.

Griffith next injected mice with a combination of heat-killed S bacteria and live R bacteria. To his surprise, the mice died. Even more surprising, he found live S bacteria in blood samples from the dead mice. Griffith concluded that some material must have been transferred from the heat-killed S bacteria to the live R bacteria. Whatever that material was, it contained information that changed harmless R bacteria into disease-causing S bacteria. Griffith called this mystery material the "transforming principle."

Infer What evidence suggested that there was a transforming principle?

Connecting CONCEPTS

Microbiology Much of our knowledge of the chemical basis of genetics has come from the study of bacteria. You will learn much more about bacteria in **Chapter 18.**

MAIN IDEA

Avery identifies DNA as the transforming principle.

What exactly is the transforming principle that Griffith discovered? That question puzzled Oswald Avery and his fellow biologists. They worked for more than ten years to find the answer. Avery's team began by combining living R bacteria with an extract made from S bacteria. This procedure allowed them to directly observe the transformation of R bacteria into S bacteria in a petri dish.

Avery's group next developed a process to purify their extract. They then performed a series of tests to find out if the transforming principle was DNA or protein.

- **Qualitative tests** Standard chemical tests showed that no protein was present. In contrast, tests revealed that DNA was present.
- **Chemical analysis** As you can see in **FIGURE 8.2**, the proportions of elements in the extract closely matched those found in DNA. Proteins contain almost no phosphorus.
- **Enzyme tests** When the team added to the extract enzymes known to break down proteins, the extract still transformed the R bacteria to the S form. Also, transformation occurred when researchers added an enzyme that breaks down RNA (another nucleic acid). Transformation failed to occur only when an enzyme was added to destroy DNA.

FIGURE 8.2 Avery's Discoveries

CHEMICAL ANALYSIS OF TRANSFORMING PRINCIPLE

	% Nitrogen (N)	% Phosphorus (P)	Ratio of N to P
Sample A	14.21	8.57	1.66
Sample B	15.93	9.09	1.75
Sample C	15.36	9.04	1.69
Sample D	13.40	8.45	1.58
Known value for DNA	15.32	9.05	1.69

Source: Avery, O. T. et al., *The Journal of Experimental Medicine* 79:2.

Analyze How do the data support the hypothesis that DNA, not protein, is the transforming principle?

Oswald Avery

In 1944 Avery and his group presented this and other evidence to support their conclusion that DNA must be the transforming principle, or genetic material. The results created great interest. However, some scientists questioned whether the genetic material in bacteria was the same as that in other organisms. Despite Avery's evidence, some scientists insisted that his extract must have contained protein.

Summarize List the key steps in the process that Avery's team used to identify the transforming principle.

MAIN IDEA

Hershey and Chase confirm that DNA is the genetic material.

FIGURE 8.3 This micrograph shows the protein coat of a bacteriophage (orange) after it has injected its DNA into an *E. coli* bacterium (blue). (colored TEM; magnification 115,000×)

Conclusive evidence for DNA as the genetic material came in 1952 from two American biologists, Alfred Hershey and Martha Chase. Hershey and Chase were studying viruses that infect bacteria. This type of virus, called a **bacteriophage** (bak-TEER-ee-uh-FAYJ), or "phage" for short, takes over a bacterium's genetic machinery and directs it to make more viruses.

Phages like the ones Hershey and Chase studied are relatively simple—little more than a DNA molecule surrounded by a protein coat. This two-part structure of phages offered a perfect opportunity to answer the question, Is the genetic material made of DNA or protein? By discovering which part of a phage (DNA or protein) actually entered a bacterium, as shown in **FIGURE 8.3**, they could answer this question once and for all.

Hershey and Chase thought up a clever procedure that made use of the chemical elements found in protein and DNA. Protein contains sulfur but very little phosphorus, while DNA contains phosphorus but no sulfur. The researchers grew phages in cultures that contained radioactive isotopes of sulfur or phosphorus. Hershey and Chase then used these radioactively tagged phages in two experiments.

- **Experiment 1** In the first experiment, bacteria were infected with phages that had radioactive sulfur atoms in their protein molecules. Hershey and Chase then used an ordinary kitchen blender to separate the bacteria from the parts of the phages that remained outside the bacteria. When they examined the bacteria, they found no significant radioactivity.
- **Experiment 2** Next, Hershey and Chase repeated the procedure with phages that had DNA tagged with radioactive phosphorus. This time, radioactivity was clearly present inside the bacteria.

From their results, Hershey and Chase concluded that the phages' DNA had entered the bacteria, but the protein had not. Their findings finally convinced scientists that the genetic material is DNA and not protein.

Apply **How did Hershey and Chase build upon Avery's chemical analysis results?**

8.1 ASSESSMENT

ONLINE QUIZ ClassZone.com

REVIEWING MAIN IDEAS

1. What was "transformed" in Griffith's experiment?
2. How did Avery and his group identify the transforming principle?
3. Summarize how Hershey and Chase confirmed that DNA is the genetic material.

CRITICAL THINKING

4. **Summarize** Why was the bacteriophage an excellent choice for research to determine whether genes are made of DNA or proteins?
5. **Analyze** Choose one experiment from this section and explain how the results support the conclusion.

Connecting CONCEPTS

6. **Mendelian Genetics** Describe how Mendel's studies relate to the experiments discussed in this section.

Extracting DNA

Oswald Avery wrote in a scientific article, "At a critical concentration . . . of alcohol the active material separates out in the form of fibrous strands that wind themselves around the stirring rod." In this lab, you can observe the same thing Avery observed as you extract DNA from wheat germ. This procedure is a simplified version of the one scientists commonly use to extract DNA today.

MATERIALS

- balance
- 10 g raw wheat germ
- laboratory spatula
- test tube
- test tube rack
- 10 mL warm distilled water
- 2 eyedroppers
- 4 10-mL graduated cylinders
- 20 mL detergent solution
- 3 g meat tenderizer
- 20 mL salt solution
- 10 mL cold isopropyl alcohol
- glass stirring rod

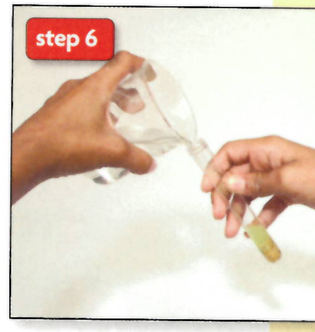
PROCESS SKILLS

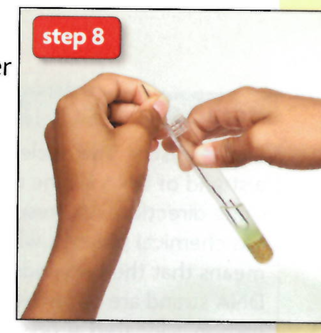
- Observing
- Analyzing

PROBLEM How do you extract the DNA from plant cells?

PROCEDURE

1. Place a small amount of wheat germ in a test tube. The wheat germ should be about 1 cm high in the test tube.
2. Add enough distilled water to wet and cover all of the wheat germ.
3. Add 25–30 drops of detergent solution to the test tube. For 3 minutes, gently swirl the test-tube contents. Avoid making bubbles.
4. Add 3 g of meat tenderizer.
5. Add 25–30 drops of salt solution to the test tube. Swirl for 1 minute.
6. Tilt the test tube at an angle as shown. Slowly add alcohol so that it runs down the inside of the test tube to form a separate layer on top of the mixture in the tube. Add enough alcohol to double the total volume in the tube. Let the test tube stand for 2 minutes.
7. Watch for stringy, cloudy material to rise from the bottom layer into the alcohol layer. This is the DNA.
8. Use the glass stirring rod to remove some DNA. Be careful to probe only the alcohol layer.
9. Draw in your lab report what the mixture and DNA looked like in steps 2–7. Be sure to include color, texture, and what happened after a new solution was added.





ANALYZE AND CONCLUDE

1. **Connect** Consider what you know about cell structure and the location of DNA. Suggest a reason for adding detergent solution to the test tube.
2. **Predict** What do you think might happen if the alcohol were added quickly and the two layers mixed?
3. **Infer** Meat tenderizer contains enzymes that break down proteins. What do you think is the purpose of adding meat tenderizer in this procedure?
4. **Connect** In what type of real-life situation would the extraction of DNA be useful?

EXTEND YOUR INVESTIGATION

Determine a method to calculate what percentage of the wheat germ consists of DNA.

8.2 Structure of DNA

KEY CONCEPT DNA structure is the same in all organisms.

MAIN IDEAS

- DNA is composed of four types of nucleotides.
- Watson and Crick developed an accurate model of DNA's three-dimensional structure.
- Nucleotides always pair in the same way.

VOCABULARY

nucleotide, p. 230
double helix, p. 232
base pairing rules, p. 232

Review
covalent bond, hydrogen bond

REVIEW AT CLASSZONE.COM

Connect The experiments of Hershey and Chase confirmed that DNA carries the genetic information, but they left other big questions unanswered: What exactly is this genetic information? How does DNA store this information? Scientists in the early 1950s still had a limited knowledge of the structure of DNA, but that was about to change dramatically.

MAIN IDEA

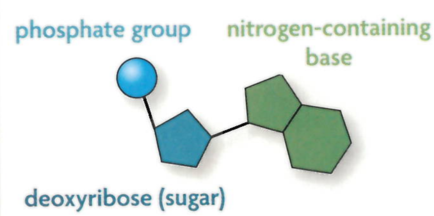
DNA is composed of four types of nucleotides.

Since the 1920s, scientists have known that the DNA molecule is a very long polymer, or chain of repeating units. The small units, or monomers, that make up DNA are called **nucleotides** (NOO-klee-oh-TYDZ). Each nucleotide has three parts.

- A phosphate group (one phosphorus with four oxygens)
- A ring-shaped sugar called deoxyribose
- A nitrogen-containing base (a single or double ring built around nitrogen and carbon atoms)

VISUAL VOCAB

The small units, or monomers, that make up a strand of DNA are called **nucleotides.** Nucleotides have three parts.



One molecule of human DNA contains billions of nucleotides, but there are only four types of nucleotides in DNA. These nucleotides differ only in their nitrogen-containing bases.

The four bases in DNA are shown in **FIGURE 8.4.** Notice that the bases cytosine (C) and thymine (T) have a single-ring structure. Adenine (A) and guanine (G) have a larger, double-ring structure. The letter abbreviations refer both to the bases and to the nucleotides that contain the bases.

For a long time, scientists hypothesized that DNA was made up of equal amounts of the four nucleotides, and so the DNA in all organisms was exactly the same. That hypothesis was a key reason that it was so hard to convince scientists that DNA was the genetic material. They reasoned that identical molecules could not carry different instructions across all organisms.

***Connecting* CONCEPTS**

Biochemistry The nucleotides in a strand of DNA all line up in the same direction. As a result, DNA has chemical polarity, which means that the two ends of the DNA strand are different. The 5′ carbon is located at one end of the DNA strand, and the 3′ carbon is located at the other end. When the two strands of DNA pair together, the 5′ end of one strand aligns with the 3′ end of the other strand.

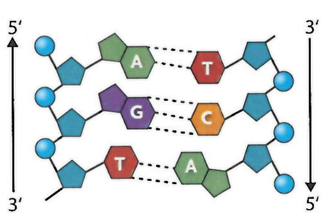
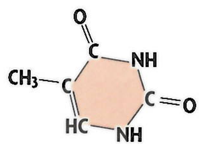
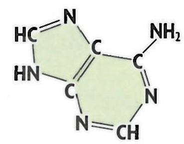
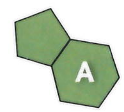
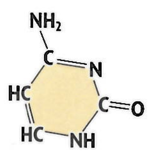
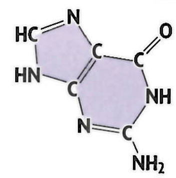
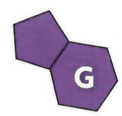


FIGURE 8.4 The Four Nitrogen-Containing Bases of DNA

PYRIMIDINES = SINGLE RING			PURINES = DOUBLE RING		
Name of Base	Structural Formula	Model	Name of Base	Structural Formula	Model
thymine			adenine		
cytosine			guanine		

Compare **Which base is most similar in structure to thymine?**

By 1950 Erwin Chargaff changed the thinking about DNA by analyzing the DNA of several different organisms. Chargaff found that the same four bases are found in the DNA of all organisms, but the proportion of the four bases differs somewhat from organism to organism. In the DNA of each organism, the amount of adenine approximately equals the amount of thymine. Similarly, the amount of cytosine roughly equals the amount of guanine. These A = T and C = G relationships became known as Chargaff's rules.

VOCABULARY

An amine is a molecule that contains nitrogen. Notice that the four DNA bases end in *-ine* and all contain nitrogen.

Summarize **What is the only difference among the four DNA nucleotides?**

MAIN IDEA

Watson and Crick developed an accurate model of DNA's three-dimensional structure.

The breakthrough in understanding the structure of DNA came in the early 1950s through the teamwork of American geneticist James Watson and British physicist Francis Crick. Watson and Crick were supposed to be studying the structure of proteins. Both men, however, were more fascinated by the challenge of figuring out DNA's structure. Their interest was sparked not only by the findings of Hershey, Chase, and Chargaff but also by the work of the biochemist Linus Pauling. Pauling had found that the structure of some proteins was a helix, or spiral. Watson and Crick hypothesized that DNA might also be a helix.

X-Ray Evidence

At the same time, Rosalind Franklin, shown in **FIGURE 8.5**, and Maurice Wilkins were studying DNA using a technique called x-ray crystallography. When DNA is bombarded with x-rays, the atoms in DNA diffract the x-rays in a pattern that can be captured on film. Franklin's x-ray photographs of DNA showed an X surrounded by a circle. Franklin's data gave Watson and Crick the clues they needed. The patterns and angle of the X suggested that DNA is a helix consisting of two strands that are a regular, consistent width apart.

FIGURE 8.5 Rosalind Franklin (above) produced x-ray photographs of DNA that indicated it was a helix. Her coworker, Maurice Wilkins, showed the data without Franklin's consent to Watson and Crick, which helped them discover DNA's structure.

FIGURE 8.6 James Watson (left) and Francis Crick (right) used a model to figure out DNA's structure. Their model was influenced by data from other researchers, including an x-ray image (far right) taken by Rosalind Franklin. When x-rays bounce off vertically suspended DNA, they form this characteristic x-shaped pattern.

James Watson and Francis Crick

The Double Helix

Back in their own laboratory, Watson and Crick made models of metal and wood to figure out the structure of DNA. Their models placed the sugar-phosphate backbones on the outside and the bases on the inside. At first, Watson reasoned that A might pair with A, T with T, and so on. But the bases A and G are about twice as wide as C and T, so this produced a helix that varied in width. Finally, Watson and Crick found that if they paired double-ringed nucleotides with single-ringed nucleotides, the bases fit like a puzzle.

In April 1953 Watson and Crick published their DNA model in a paper in the journal *Nature*. **FIGURE 8.6** shows their **double helix** (HEE-lihks) model, in which two strands of DNA wind around each other like a twisted ladder. The strands are complementary—they fit together and are the opposite of each other. That is, if one strand is ACACAC, the other strand is TGTGTG. The pairing of bases in their model finally explained Chargaff's rules.

Apply How did the Watson and Crick model explain Chargaff's rules?

MAIN IDEA

Nucleotides always pair in the same way.

Connecting CONCEPTS

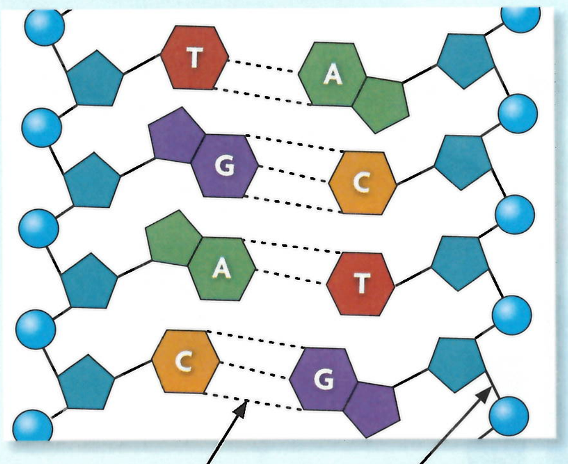
Chemical Bonds Recall from **Chapter 2** that a covalent bond is a strong bond in which two atoms share one or more pairs of electrons. Hydrogen bonds are much weaker than covalent bonds and can easily be broken.

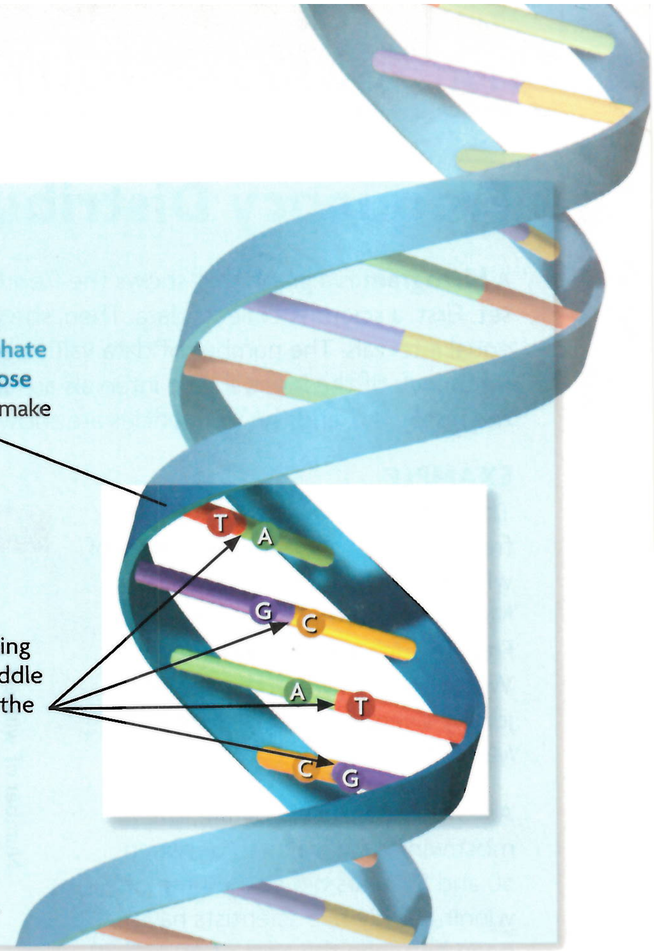
The DNA nucleotides of a single strand are joined together by covalent bonds that connect the sugar of one nucleotide to the phosphate of the next nucleotide. The alternating sugars and phosphates form the sides of a double helix, sort of like a twisted ladder. The DNA double helix is held together by hydrogen bonds between the bases in the middle. Individually, each hydrogen bond is weak, but together, they maintain DNA structure.

As shown in **FIGURE 8.7**, the bases of the two DNA strands always pair up in the same way. This is summarized in the **base pairing rules:** thymine (T) always pairs with adenine (A), and cytosine (C) always pairs with guanine (G). These pairings occur because of the sizes of the bases and the ability of the

FIGURE 8.7 Base Pairing Rules

The base pairing rules describe how nucleotides form pairs in DNA. T always pairs with A, and G always pairs with C.





Synthesize **Which base pairs do you think are held more tightly together? Why?**

bases to form hydrogen bonds with each other. Due to the arrangement of their molecules, A can form unique hydrogen bonds with T, and C with G. Notice that A and T form two hydrogen bonds, whereas C and G form three.

You can remember the rules of base pairing by noticing that the letters C and G have a similar shape. Once you know that C and G pair together, you know that A and T pair together by default. If a sequence of bases on one strand of DNA is CTGCTA, you know the other DNA strand will be GACGAT.

Apply **What sequence of bases would pair with the sequence TGACTA?**

8.2 ASSESSMENT

ONLINE QUIZ
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REVIEWING MAIN IDEAS

1. How many types of **nucleotides** are in DNA, and how do they differ?
2. How are the **base pairing rules** related to Chargaff's research on DNA?
3. Explain how the **double helix** model of DNA built on the research of Rosalind Franklin.

CRITICAL THINKING

4. **Infer** Which part of a DNA molecule carries the genetic instructions that are unique for each individual: the sugar-phosphate backbone or the nitrogen-containing bases? Explain.
5. **Predict** In a sample of yeast DNA, 31.5% of the bases are adenine (A). Predict the approximate percentages of C, G, and T. Explain.

Connecting CONCEPTS

6. **Evolution** The DNA of all organisms contains the same four bases (adenine, thymine, cytosine, and guanine). What might this similarity indicate about the origins of life on Earth?

DATA ANALYSIS
ClassZone.com

Frequency Distributions

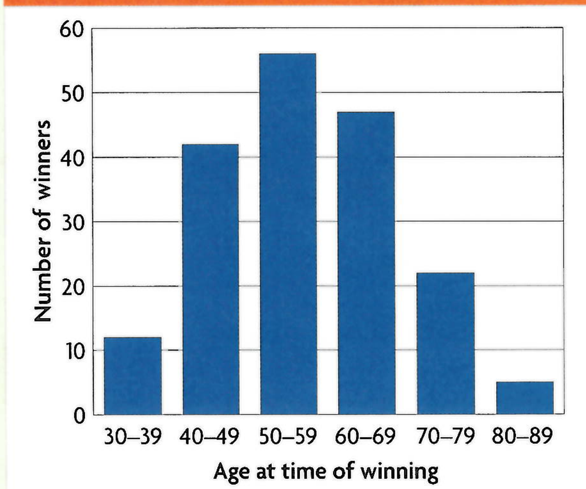
A **histogram** is a graph that shows the frequency distribution of a data set. First, a scientist collects data. Then, she groups the data values into equal intervals. The number of data values in each interval is the frequency of the interval. The intervals are shown along the *x*-axis of the histogram, and the frequencies are shown on the *y*-axis.

EXAMPLE

The histogram at right shows the frequency distribution of the ages of winners of the Nobel Prize in Medicine at the time of winning. Francis Crick was 46 and James Watson was 34 when they were jointly awarded a Nobel Prize in Medicine in 1962.

According to the histogram, the most winners have been between 50 and 59 years old at the time of winning. Only five scientists have been between the ages of 80 and 89 at the time of winning a Nobel Prize in Medicine.

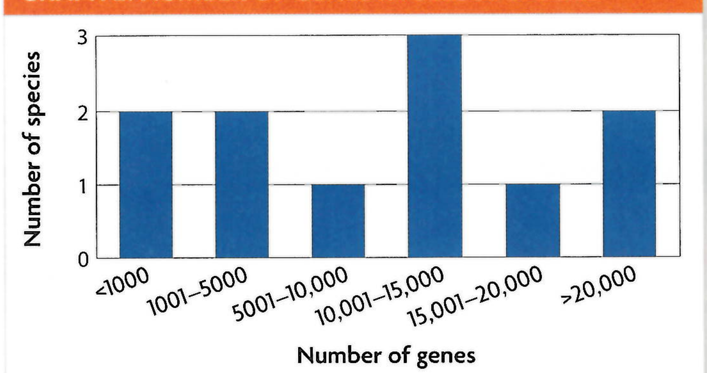
GRAPH 1. NOBEL PRIZE WINNERS BY AGE



ANALYZE A HISTOGRAM

The histogram below categorizes data collected based on the number of genes in 11 species.

GRAPH 2. NUMBER OF GENES IN SELECT SPECIES



1. **Identify** How many species had between 10,001 and 15,000 genes?
2. **Analyze** Are the data in graph 2 sufficient to reveal a trend in the number of genes per species? Explain your reasoning.

8.3 DNA Replication

KEY CONCEPT DNA replication copies the genetic information of a cell.

MAIN IDEAS

- Replication copies the genetic information.
- Proteins carry out the process of replication.
- Replication is fast and accurate.

VOCABULARY

replication, p. 235
DNA polymerase, p. 236

Review
base pairing rules, S phase

REVIEW AT CLASSZONE.COM

Connect Do you know that some of your cells are dying right now? You may live to the ripe old age of 100, but most of your cells will have been replaced thousands of times before you blow out the candles on that birthday cake. Every time that cells divide to produce new cells, DNA must first be copied in a remarkable process of unzipping and zipping by enzymes and other proteins. The next few pages will take you through that process.

MAIN IDEA

Replication copies the genetic information.

One of the powerful features of the Watson and Crick model was that it suggested a way that DNA could be copied. In fact, Watson and Crick ended the journal article announcing their discovery with this sentence: "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

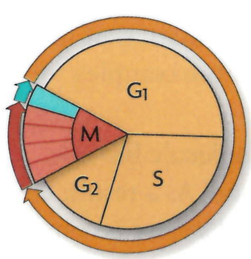
Recall that the bases that connect the strands of DNA will pair only in one way, according to the rules of base pairing. An A must bind with a T, and a C must bind with a G. If the base sequence of one strand of the DNA double helix is known, the sequence of the other strand is also known. Watson and Crick realized that a single DNA strand can serve as a template, or pattern, for a new strand. This process by which DNA is copied during the cell cycle is called **replication.**

Suppose all of your classmates took off their shoes, placed their left shoe in a line, and tossed their right shoe into a pile. You could easily pick out the right shoes from the pile and place them with the matching left shoes. The order of the shoes would be preserved. Similarly, a new strand of DNA can be synthesized when the other strand is a template to guide the process. Every time, the order of the bases is preserved, and DNA can be accurately replicated over and over again.

Replication assures that every cell has a complete set of identical genetic information. Recall that your DNA is divided into 46 chromosomes that are replicated during the S phase of the cell cycle. So your DNA is copied once in each round of the cell cycle. As a result, every cell has a complete set of DNA.

***Connecting* CONCEPTS**

Cell Biology In **Chapter 5** you learned that the cell cycle has four main stages. DNA is replicated during the S (synthesis) stage.



The fact that cells throughout the body have complete sets of DNA is very useful for forensic scientists. They can identify someone from nearly any cell in the body. A few cells from a drop of blood or from saliva on a cigarette butt are all detectives need to produce a DNA "fingerprint" of a criminal suspect.

Apply **How does replication ensure that cells have complete sets of DNA?**

MAIN IDEA

Proteins carry out the process of replication.

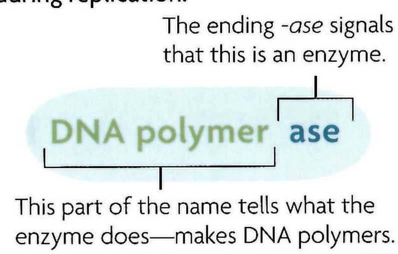
Connecting CONCEPTS

Biochemistry You read in **Chapter 2** that many proteins are enzymes that function as catalysts. Enzymes decrease the activation energy and increase the rate of chemical reactions. DNA polymerase catalyzes the reaction that bonds two nucleotides together.

Although people may say that DNA copies itself, the DNA itself does nothing more than store information. Enzymes and other proteins do the actual work of replication. For example, some enzymes start the process by unzipping the double helix to separate the strands of DNA. Other proteins hold the strands apart while the strands serve as templates. Nucleotides that are floating free in the nucleus can then pair up with the nucleotides of the existing DNA strands. A group of enzymes called **DNA polymerases** (PAHL-uh-muh-rays) bond the new nucleotides together. When the process is finished, the result is two complete molecules of DNA, each exactly like the original double strand.

VISUAL VOCAB

DNA polymerases are enzymes that form bonds between nucleotides during replication.



The Replication Process

The following information describes the process of DNA replication in eukaryotes, which is similar in prokaryotes. As you read, follow along with each step illustrated in **FIGURE 8.8.**

1. Enzymes begin to unzip the double helix at numerous places along the chromosome, called origins of replication. That is, the hydrogen bonds connecting base pairs are broken, the original molecule separates, and the bases on each strand are exposed. Unlike unzipping a jacket, this process proceeds in two directions at the same time.
2. Free-floating nucleotides pair, one by one, with the bases on the template strands as they are exposed. DNA polymerases bond the nucleotides together to form new strands that are complementary to each template strand. DNA replication occurs in a smooth, continuous way on one of the strands. Due to the chemical nature of DNA polymerase, replication of the other strand is more complex. It involves the formation of many small DNA segments that are joined together. This more complex process is not shown or described in detail here.
3. Two identical molecules of DNA result. Each new molecule has one strand from the original molecule and one new strand. As a result, DNA replication is called semiconservative because one old strand is conserved, and one complementary new strand is made.

Infer **How does step 3 of replication show that DNA acts as a template?**

TAKING NOTES

Use a cycle diagram to take notes about processes such as replication.

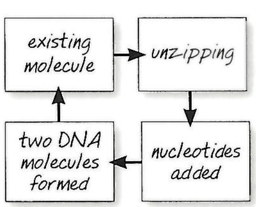
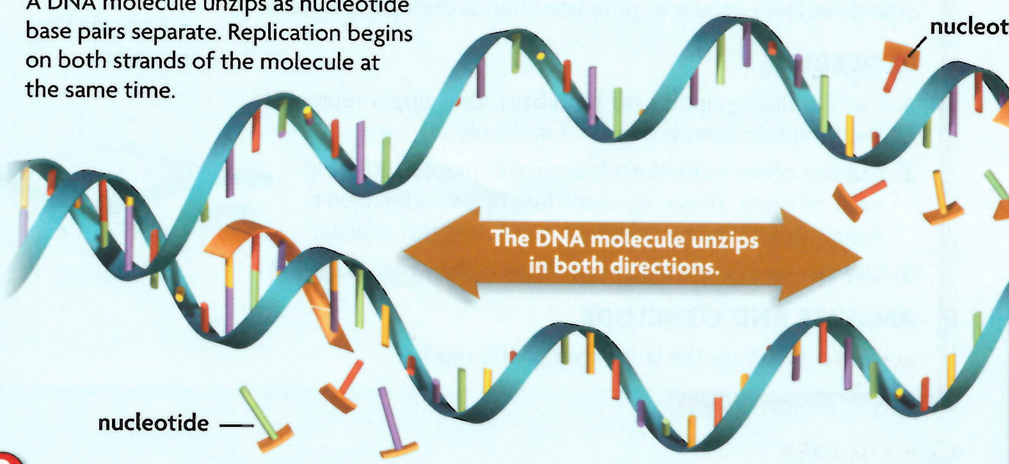


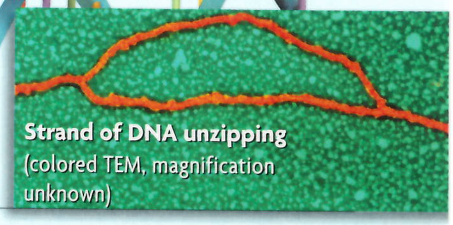
FIGURE 8.8 Replication

When a cell's DNA is copied, or replicated, two complete and identical sets of genetic information are produced. Then cell division can occur.

Animated BIOLOGY
See DNA replication in action at ClassZone.com.

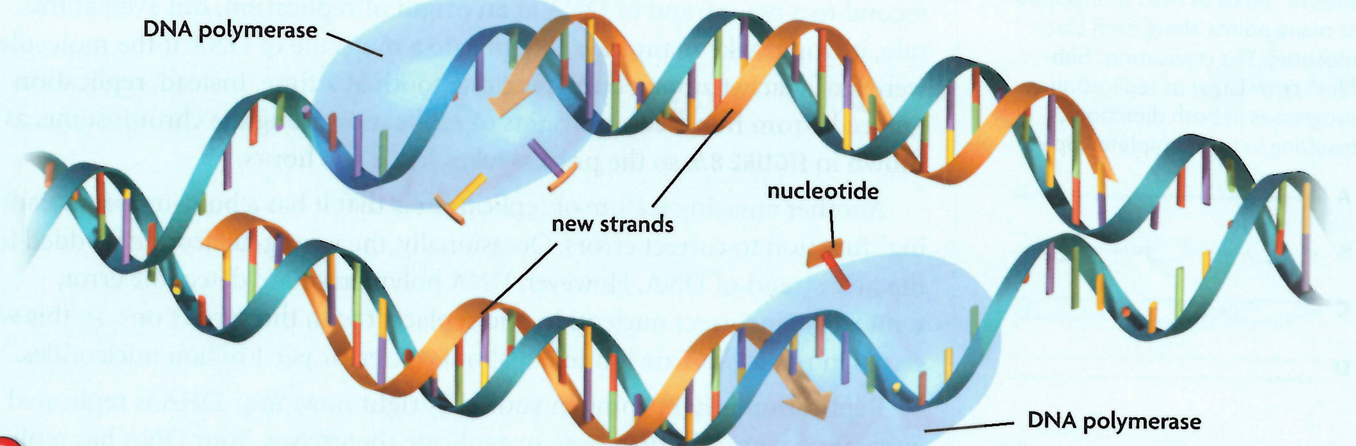
1 A DNA molecule unzips as nucleotide base pairs separate. Replication begins on both strands of the molecule at the same time.



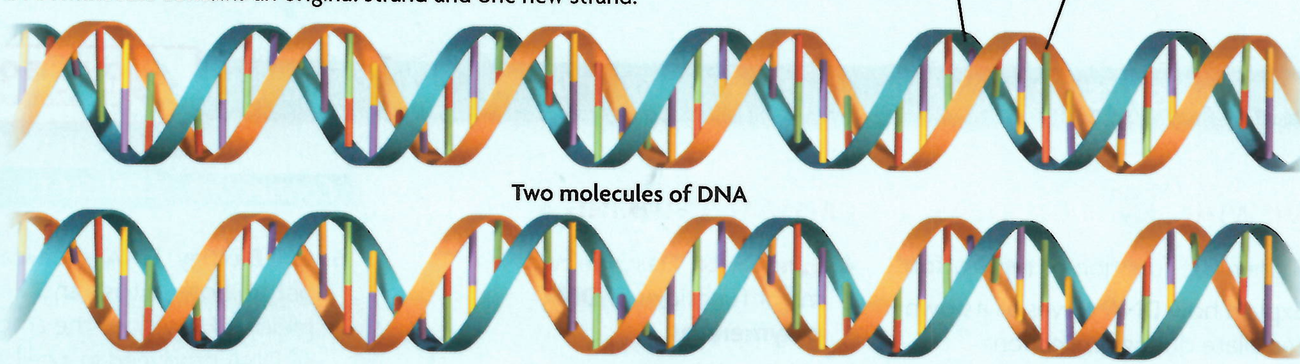


Strand of DNA unzipping (colored TEM, magnification unknown)

2 Each existing strand of the DNA molecule is a template for a new strand. Free-floating nucleotides pair up with the exposed bases on each template strand. DNA polymerases bond these nucleotides together to form the new strands. The arrows show the directions in which new strands form.



3 Two identical double-stranded DNA molecules result from replication. DNA replication is semiconservative. That is, each DNA molecule contains an original strand and one new strand.



CRITICAL VIEWING **How is each new molecule of DNA related to the original molecule?**

QUICK LAB **MODELING**

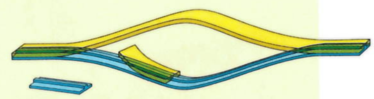
Replication

Use two zipping plastic bags to model how complementary strands of DNA attach to template strands during replication.

MATERIALS
- 2 zipping bags
- scissors

PROCEDURE

1. Cut the sliding zippers off both bags. One zipper represents the template strands of a DNA molecule.
2. Cut the other zipper into four smaller pieces and unzip each of them. These represent free nucleotides. Don't worry about which nucleotide is which in this activity.
3. Use the pieces to model replication as shown on page 237.



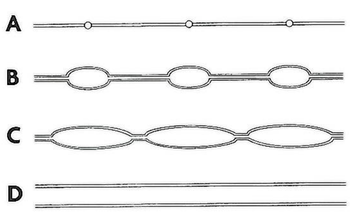
ANALYZE AND CONCLUDE

Evaluate What are the limitations of this model?

MAIN IDEA

Replication is fast and accurate.

FIGURE 8.9 Eukaryotic chromosomes have many origins of replication. The DNA helix is unzipped at many points along each chromosome. The replication "bubbles" grow larger as replication progresses in both directions, resulting in two complete copies.



In every living thing, DNA replication happens over and over again, and it happens remarkably fast. In human cells, about 50 nucleotides are added every second to a new strand of DNA at an origin of replication. But even at this rate, it would take many days to replicate a molecule of DNA if the molecule were like a jacket zipper, unzipping one tooth at a time. Instead, replication proceeds from hundreds of origins of replication along the chromosome, as shown in **FIGURE 8.9**, so the process takes just a few hours.

Another amazing feature of replication is that it has a built-in "proofreading" function to correct errors. Occasionally, the wrong nucleotide is added to the new strand of DNA. However, DNA polymerase can detect the error, remove the incorrect nucleotide, and replace it with the correct one. In this way, errors in replication are limited to about one error per 1 billion nucleotides.

Replication is happening in your cells right now. Your DNA is replicated every time your cells turn over, or replicate themselves. Your DNA has replicated trillions of times since you grew from a single cell.

Infer Why does a cell need to replicate its DNA quickly?

8.3 ASSESSMENT

ONLINE QUIZ ClassZone.com

REVIEWING MAIN IDEAS

1. Explain the function of **replication.**
2. Explain how DNA serves as its own template during replication.
3. How do cells help ensure that DNA replication is accurate?

CRITICAL THINKING

4. **Summarize** Describe two major functions of **DNA polymerases.**
5. **Infer** Why is it important that human chromosomes have many origins of replication?

Connecting CONCEPTS

6. **Cell Biology** DNA is replicated before both mitosis and meiosis. How does the amount of DNA produced in a cell during mitosis compare with that produced during meiosis?

8.4 Transcription

KEY CONCEPT Transcription converts a gene into a single-stranded RNA molecule.

MAIN IDEAS

- RNA carries DNA's instructions.
- Transcription makes three types of RNA.
- The transcription process is similar to replication.

VOCABULARY

central dogma, p. 239
RNA, p. 239
transcription, p. 240
RNA polymerase, p. 240
messenger RNA (mRNA), p. 240
ribosomal RNA (rRNA), p. 240
transfer RNA (tRNA), p. 240

REVIEW AT CLASSZONE.COM

Connect Suppose you want to play skeeball at a game center, but the skeeball lane only takes tokens. You only have quarters. Do you go home in defeat? Stand idly by as someone else becomes high scorer? No, you exchange your quarters for tokens and then proceed to show the other players how it's done. In a similar way, your cells cannot make proteins directly from DNA. They must convert the DNA into an intermediate molecule called RNA, or ribonucleic acid. That conversion process, called transcription, is the focus of this section.

MAIN IDEA

RNA carries DNA's instructions.

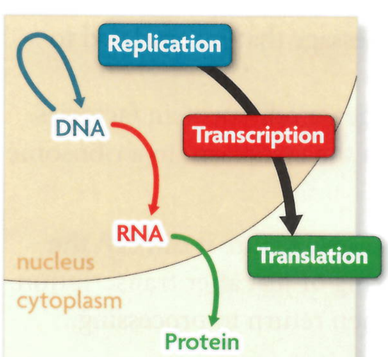
Soon after his discovery of DNA structure, Francis Crick defined the **central dogma** of molecular biology, which states that information flows in one direction, from DNA to RNA to proteins. The central dogma involves three processes, as shown in **FIGURE 8.10.**

- Replication, as you just learned, copies DNA (blue arrow).
- Transcription converts a DNA message into an intermediate molecule, called RNA (red arrow).
- Translation interprets an RNA message into a string of amino acids, called a polypeptide. Either a single polypeptide or many polypeptides working together make up a protein (green arrow).

In prokaryotic cells, replication, transcription, and translation all occur in the cytoplasm at approximately the same time. In eukaryotic cells, where DNA is located inside the nuclear membrane, these processes are separated both in location and time. Replication and transcription occur in the nucleus, while translation occurs in the cytoplasm. In addition, the RNA in eukaryotic cells goes through a processing step before it can be transported out of the nucleus. Unless otherwise stated, the rest of this chapter describes how these processes work in eukaryotic cells.

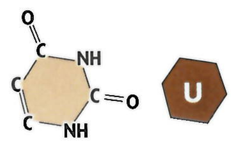
RNA acts as an intermediate link between DNA in the nucleus and protein synthesis in the cytoplasm. Like DNA, **RNA,** or ribonucleic acid, is a chain of nucleotides, each made of a sugar, a phosphate group, and a nitrogen-containing base. You can think of RNA as a temporary copy of DNA that is used and then destroyed.

FIGURE 8.10 The central dogma describes the flow of information from DNA to RNA to proteins. It involves three major processes, shown in a eukaryotic cell below.



Connecting CONCEPTS

DNA Structure As you learned in **Section 8.2**, nucleotides are made of a phosphate group, a sugar, and a nitrogen-containing base. In DNA, the four bases are adenine, cytosine, guanine, and thymine. In RNA, uracil (below) replaces thymine and pairs with adenine.



RNA differs from DNA in three significant ways. First, the sugar in RNA is ribose, which has one additional oxygen atom not present in DNA's sugar (deoxyribose). Second, RNA has the base uracil in place of thymine. Uracil, like thymine, forms base pairs with adenine. Third, RNA is a single strand of nucleotides, in contrast to the double-stranded structure of DNA. This single-stranded structure allows some types of RNA to form complex three-dimensional shapes. As a result, some RNA molecules can catalyze reactions much as enzymes do.

Contrast How do DNA and RNA differ?

MAIN IDEA

Transcription makes three types of RNA.

Transcription is the process of copying a sequence of DNA to produce a complementary strand of RNA. During the process of transcription, a gene—not an entire chromosome—is transferred into an RNA message. Just as replication is catalyzed by DNA polymerase, transcription is catalyzed by **RNA polymerases,** enzymes that bond nucleotides together in a chain to make a new RNA molecule. RNA polymerases are very large enzymes composed of many proteins that play a variety of roles in the transcription process. **FIGURE 8.11** shows the basic steps of transcription in eukaryotic cells.

1. With the help of other proteins and DNA sequences, RNA polymerase recognizes the transcription start site of a gene. A large transcription complex consisting of RNA polymerase and other proteins assembles on the DNA strand and begins to unwind a segment of the DNA molecule, until the two strands separate from each other.
2. RNA polymerase, using only one strand of DNA as a template, strings together a complementary strand of RNA nucleotides. RNA base pairing follows the same rules as DNA base pairing, except that uracil, not thymine, pairs with adenine. The growing RNA strand hangs freely as it is transcribed, and the DNA helix zips back together.
3. Once the entire gene has been transcribed, the RNA strand detaches completely from the DNA. Exactly how RNA polymerase recognizes the end of a transcription unit is complicated. It varies with the type of RNA.

VOCABULARY

The word *transcribe* means "to make a written copy of." *Transcription* is the process of transcribing. A *transcript* is the copy produced by transcription.

Transcription produces three major types of RNA molecules. Not all RNA molecules code for proteins, but most play a role in the translation process. Each type of RNA molecule has a unique function.

- **Messenger RNA (mRNA)** is an intermediate message that is translated to form a protein.
- **Ribosomal RNA (rRNA)** forms part of ribosomes, a cell's protein factories.
- **Transfer RNA (tRNA)** brings amino acids from the cytoplasm to a ribosome to help make the growing protein.

Remember that the RNA strand must be processed before it can exit the nucleus of a eukaryotic cell. This step occurs during or just after transcription. However, we will next examine translation and then return to processing.

Analyze Explain why transcription occurs in the nucleus of eukaryotes.

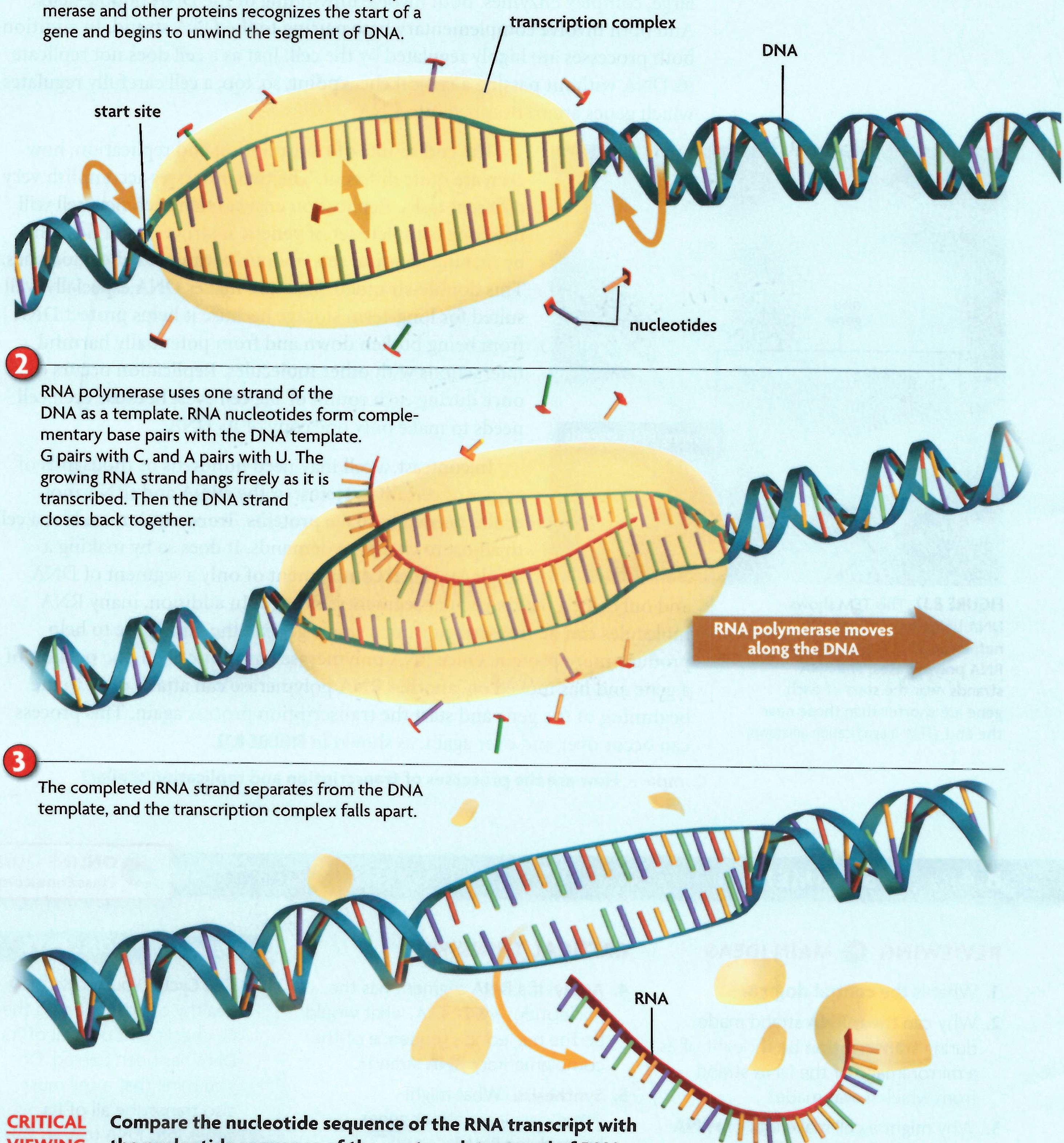
FIGURE 8.11 Transcription

Transcription produces an RNA molecule from a DNA template. Like DNA replication, this process takes place in the nucleus in eukaryotic cells and involves both DNA unwinding and nucleotide base pairing.

1 A large transcription complex made of RNA polymerase and other proteins recognizes the start of a gene and begins to unwind the segment of DNA.

2 RNA polymerase uses one strand of the DNA as a template. RNA nucleotides form complementary base pairs with the DNA template. G pairs with C, and A pairs with U. The growing RNA strand hangs freely as it is transcribed. Then the DNA strand closes back together.

3 The completed RNA strand separates from the DNA template, and the transcription complex falls apart.



CRITICAL VIEWING **Compare the nucleotide sequence of the RNA transcript with the nucleotide sequence of the nontemplate strand of DNA.**

MAIN IDEA

The transcription process is similar to replication.

The processes of transcription and replication share many similarities. Both processes occur within the nucleus of eukaryotic cells. Both are catalyzed by large, complex enzymes. Both involve unwinding of the DNA double helix. And both involve complementary base pairing to the DNA strand. In addition, both processes are highly regulated by the cell. Just as a cell does not replicate its DNA without passing a critical checkpoint, so, too, a cell carefully regulates which genes are transcribed into RNA.

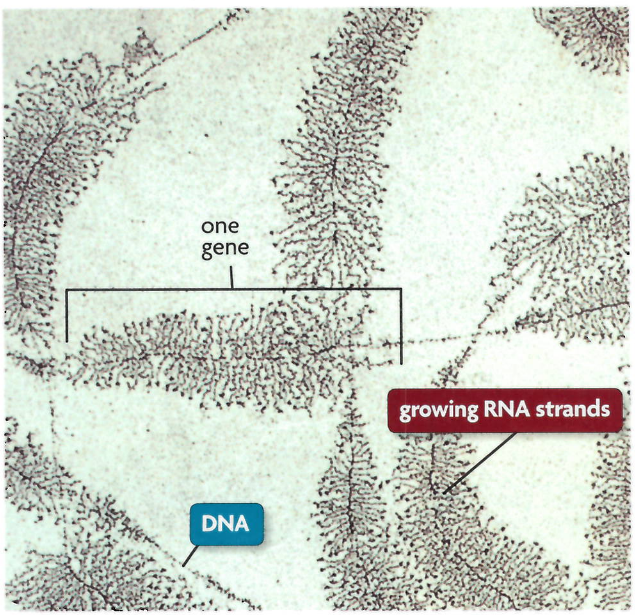


FIGURE 8.12 This TEM shows DNA being transcribed into numerous RNA strands by many RNA polymerases. The RNA strands near the start of each gene are shorter than those near the end. (TEM; magnification unknown)

The end results of transcription and replication, however, are quite different. The two processes accomplish very different tasks. Replication ensures that each new cell will have one complete set of genetic instructions. It does this by making identical sets of double-stranded chromosomes. This double-stranded structure makes DNA especially well suited for long-term storage because it helps protect DNA from being broken down and from potentially harmful interactions with other molecules. Replication occurs only once during each round of the cell cycle because each cell needs to make only one copy of its DNA.

In contrast, a cell may need hundreds or thousands of copies of certain proteins, or the rRNA and tRNA molecules needed to make proteins. Transcription enables a cell to adjust to changing demands. It does so by making a single-stranded complement of only a segment of DNA and only when that particular segment is needed. In addition, many RNA molecules can be transcribed from a single gene at the same time to help produce more protein. Once RNA polymerase has transcribed one portion of a gene and has moved on, another RNA polymerase can attach itself to the beginning of the gene and start the transcription process again. This process can occur over and over again, as shown in **FIGURE 8.12**.

Compare How are the processes of transcription and replication similar?

8.4 ASSESSMENT

ONLINE QUIZ
ClassZone.com

REVIEWING MAIN IDEAS

1. What is the **central dogma**?
2. Why can the **mRNA** strand made during **transcription** be thought of as a mirror image of the DNA strand from which it was made?
3. Why might a cell make lots of **rRNA** but only one copy of DNA?

CRITICAL THINKING

4. **Apply** If a DNA segment has the nucleotides AGCCTAA, what would be the nucleotide sequence of the complementary **RNA** strand?
5. **Synthesize** What might geneticists learn about genes by studying RNA?

Connecting CONCEPTS

6. **Cell Cycle** You know that a healthy cell cannot pass the G_2 checkpoint until all of its DNA has been copied. Do you think that a cell must also transcribe all of its genes into RNA to pass this checkpoint? Explain.

8.5 Translation

KEY CONCEPT Translation converts an mRNA message into a polypeptide, or protein.

MAIN IDEAS

- Amino acids are coded by mRNA base sequences.
- Amino acids are linked to become a protein.

VOCABULARY

translation, p. 243
codon, p. 243
stop codon, p. 244
start codon, p. 244
anticodon, p. 245

Review
peptide bond

REVIEW AT CLASSZONE.COM

Connect As you know, translation is a process that converts a message from one language into another. For example, English words can be translated into Spanish words, into Chinese characters, or into the hand shapes and gestures of sign language. Translation occurs in cells too. Cells translate an RNA message into amino acids, the building blocks of proteins. But unlike people who use many different languages, all cells use the same genetic code.

MAIN IDEA

Amino acids are coded by mRNA base sequences.

Translation is the process that converts, or translates, an mRNA message into a polypeptide. One or more polypeptides make up a protein. The "language" of nucleic acids uses four nucleotides—A, G, C, and T in DNA; or A, G, C, and U in RNA. The "language" of proteins, on the other hand, uses 20 amino acids. How can four nucleotides code for 20 amino acids? Just as letters are strung together in the English language to make words, nucleotides are strung together to code for amino acids.

***Connecting* CONCEPTS**

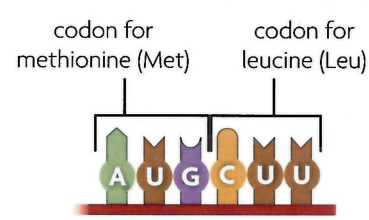
Biochemistry Recall from **Chapter 2** that amino acids are the building blocks of proteins. Although there are many types of amino acids, only the same 20 types make up the proteins of almost all organisms.

Triplet Code

Different words have different numbers of letters. In the genetic code, however, all of the "words," called codons, are made up of three letters. A **codon** is a three-nucleotide sequence that codes for an amino acid. Why is the genetic code read in units of three nucleotides? Well, we can't entirely answer that question, but consider the possibilities. If one nucleotide coded for one amino acid, RNA could code for only four amino acids. If two nucleotides coded for one amino acid, RNA could code for 16 (4^2) amino acids—still not enough. But if three nucleotides coded for one amino acid, RNA could code for 64 (4^3) amino acids, plenty to cover the 20 amino acids used to build proteins in the human body and most other organisms.

VISUAL VOCAB

A **codon** is a sequence of three nucleotides that codes for an amino acid.



Segment of mRNA

FIGURE 8.13 Genetic Code: mRNA Codons

The genetic code matches each mRNA codon with its amino acid or function.

Suppose you want to determine which amino acid is encoded by the CAU codon.

1. Find the first base, C, in the left column.
2. Find the second base, A, in the top row. Find the box where these two intersect.
3. Find the third base, U, in the right column. CAU codes for histidine, abbreviated as His.

First base	Second base: U		Second base: C		Second base: A		Second base: G		Third base
U	UUU	phenylalanine (Phe)	UCU	serine (Ser)	UAU	tyrosine (Tyr)	UGU	cysteine (Cys)	U
U	UUC	phenylalanine (Phe)	UCC	serine (Ser)	UAC	tyrosine (Tyr)	UGC	cysteine (Cys)	C
U	UUA	leucine (Leu)	UCA	serine (Ser)	UAA	STOP	UGA	STOP	A
U	UUG	leucine (Leu)	UCG	serine (Ser)	UAG	STOP	UGG	tryptophan (Trp)	G
C	CUU	leucine (Leu)	CCU	proline (Pro)	CAU	**histidine** (His)	CGU	arginine (Arg)	U
C	CUC	leucine (Leu)	CCC	proline (Pro)	CAC	histidine (His)	CGC	arginine (Arg)	C
C	CUA	leucine (Leu)	CCA	proline (Pro)	CAA	glutamine (Gln)	CGA	arginine (Arg)	A
C	CUG	leucine (Leu)	CCG	proline (Pro)	CAG	glutamine (Gln)	CGG	arginine (Arg)	G
A	AUU	isoleucine (Ile)	ACU	threonine (Thr)	AAU	asparagine (Asn)	AGU	serine (Ser)	U
A	AUC	isoleucine (Ile)	ACC	threonine (Thr)	AAC	asparagine (Asn)	AGC	serine (Ser)	C
A	AUA	isoleucine (Ile)	ACA	threonine (Thr)	AAA	lysine (Lys)	AGA	arginine (Arg)	A
A	AUG	methionine (Met)	ACG	threonine (Thr)	AAG	lysine (Lys)	AGG	arginine (Arg)	G
G	GUU	valine (Val)	GCU	alanine (Ala)	GAU	aspartic acid (Asp)	GGU	glycine (Gly)	U
G	GUC	valine (Val)	GCC	alanine (Ala)	GAC	aspartic acid (Asp)	GGC	glycine (Gly)	C
G	GUA	valine (Val)	GCA	alanine (Ala)	GAA	glutamic acid (Glu)	GGA	glycine (Gly)	A
G	GUG	valine (Val)	GCG	alanine (Ala)	GAG	glutamic acid (Glu)	GGG	glycine (Gly)	G

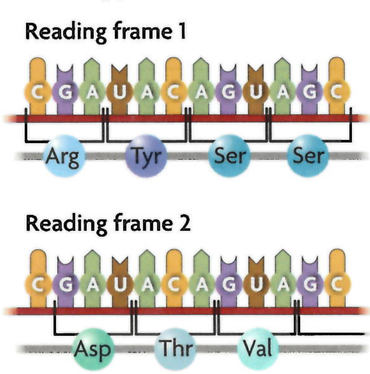
Apply **Which amino acid would be encoded by the mRNA codon CGA?**

As you can see in **FIGURE 8.13,** many amino acids are coded for by more than one codon. The amino acid leucine, for example, is represented by six different codons: CUU, CUC, CUA, CUG, UUA, and UUG. There is a pattern to the codons. In most cases, codons that represent the same amino acid share the same first two nucleotides. For example, the four codons that code for alanine each begin with the nucleotides GC. Therefore, the first two nucleotides are generally the most important in coding for an amino acid. As you will learn in Section 8.7, this feature makes DNA more tolerant of many point mutations.

In addition to codons that code for amino acids, three **stop codons** signal the end of the amino acid chain. There is also one **start codon,** which signals the start of translation and the amino acid methionine. This means that translation always begins with methionine. However, in many cases, this methionine is removed later in the process.

For the mRNA code to be translated correctly, codons must be read in the right order. Codons are read, without spaces, as a series of three nonoverlapping nucleotides. This order is called the reading frame. Changing the reading frame completely changes the resulting protein. It may even keep a protein from being made if a stop codon turns up early in the translation process. Therefore, punctuation—such as a clear start codon—plays an important role in the genetic code. **FIGURE 8.14** shows how a change in reading frame changes

FIGURE 8.14 Codons are read as a series of three nonoverlapping nucleotides. A change in the reading frame changes the resulting protein.



the resulting protein. When the mRNA strand is read starting from the first nucleotide, the resulting protein includes the amino acids arginine, tyrosine, and two serines. When the strand is read starting from the second nucleotide, the resulting protein includes aspartic acid, threonine, and valine.

Common Language

The genetic code is shared by almost all organisms—and even viruses. That means, for example, that the codon UUU codes for phenylalanine when that codon occurs in an armadillo, a cactus, a yeast, or a human. With a few minor exceptions, almost all organisms follow this genetic code. As a result, the code is often called universal. The common nature of the genetic code suggests that almost all organisms arose from a common ancestor. It also means that scientists can insert a gene from one organism into another organism to make a functional protein.

Calculate Suppose an mRNA molecule in the cytoplasm had 300 nucleotides. How many amino acids would be in the resulting protein?

MAIN IDEA

Amino acids are linked to become a protein.

Let's take a step back to look at where we are in the process of making proteins. You know mRNA is a short-lived molecule that carries instructions from DNA in the nucleus to the cytoplasm. And you know that this mRNA message is read in sets of three nucleotides, or codons. But how does a cell actually translate a codon into an amino acid? It uses two important tools: ribosomes and tRNA molecules, as illustrated in **FIGURE 8.15.**

Recall from Chapter 3 that ribosomes are the site of protein synthesis. Ribosomes are made of a combination of rRNA and proteins, and they catalyze the reaction that forms the bonds between amino acids. Ribosomes have a large and small subunit that fit together and pull the mRNA strand through. The small subunit holds onto the mRNA strand, and the large subunit holds onto the growing protein.

The tRNA acts as a sort of adaptor between mRNA and amino acids. You would need an adaptor to plug an appliance with a three-prong plug into an outlet with only two-prong openings. Similarly, cells need tRNA to carry free-floating amino acids from the cytoplasm to the ribosome. The tRNA molecules fold up in a characteristic L shape. One end of the L is attached to a specific amino acid. The other end of the L, called the anticodon, recognizes a specific codon. An **anticodon** is a set of three nucleotides that is complementary to an mRNA codon. For example, the anticodon CCC pairs with the mRNA codon GGG.

FIGURE 8.15 TRANSLATION MACHINERY

Ribosomes The large and small ribosomal subunits pull mRNA through the ribosome, reading it one codon at a time.

tRNA In cells, tRNA forms a characteristic L shape. One end of the L has an anticodon that recognizes an mRNA codon. The other end is attached to an amino acid.

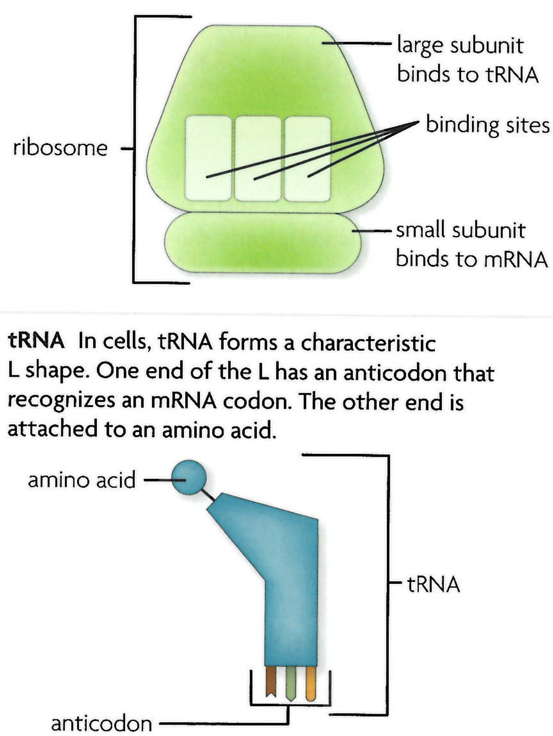
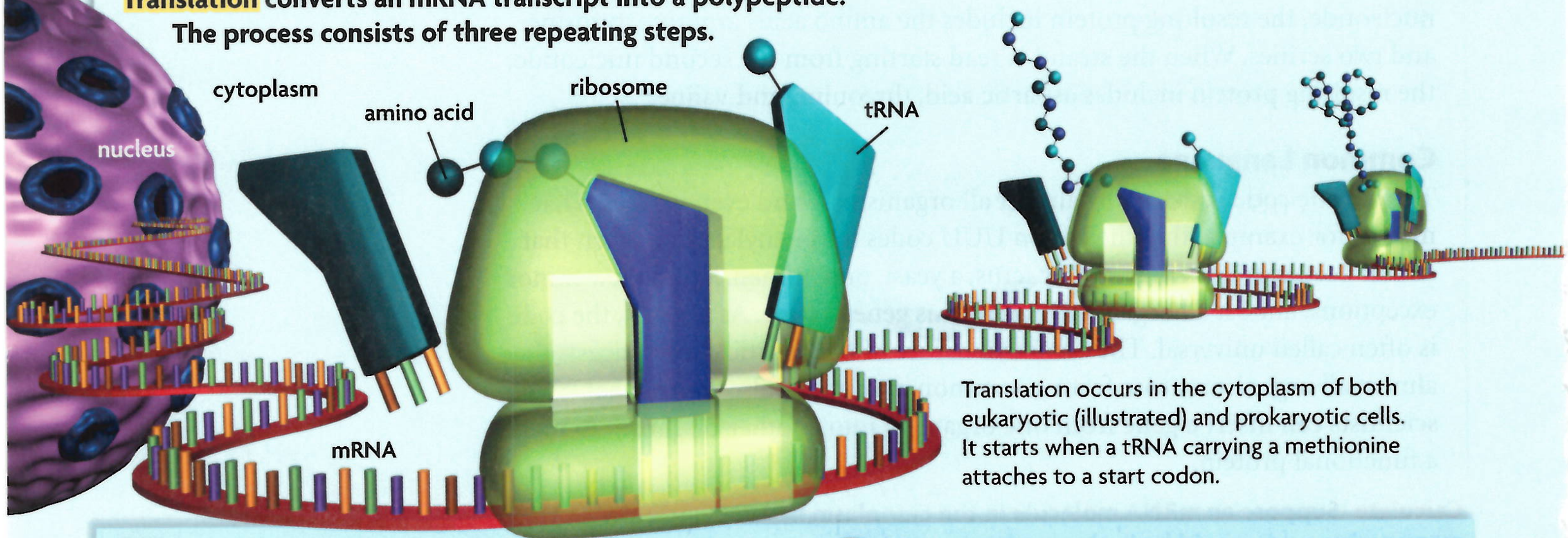


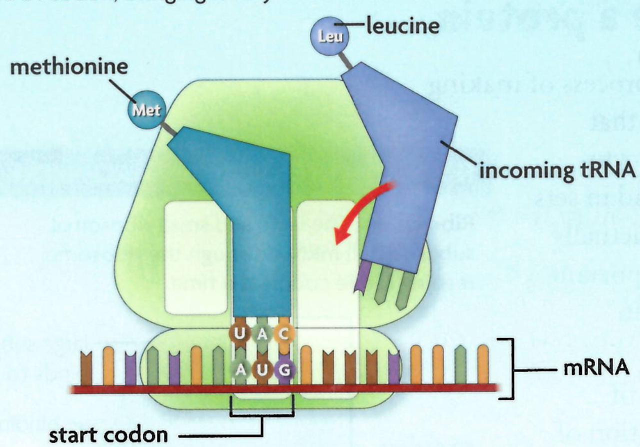
FIGURE 8.16 Translation

Translation converts an mRNA transcript into a polypeptide. The process consists of three repeating steps.

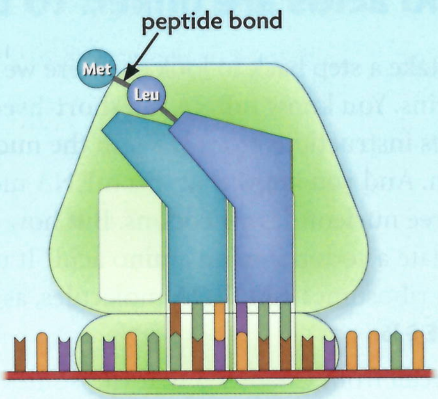


Translation occurs in the cytoplasm of both eukaryotic (illustrated) and prokaryotic cells. It starts when a tRNA carrying a methionine attaches to a start codon.

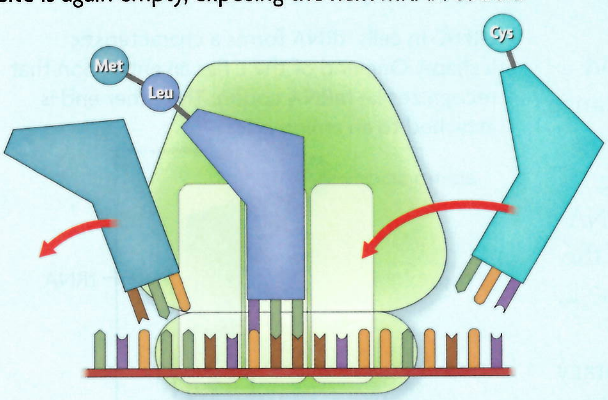
1 The exposed codon in the first site attracts a complementary tRNA bearing an amino acid. The tRNA anticodon pairs with the mRNA codon, bringing it very close to the other tRNA molecule.



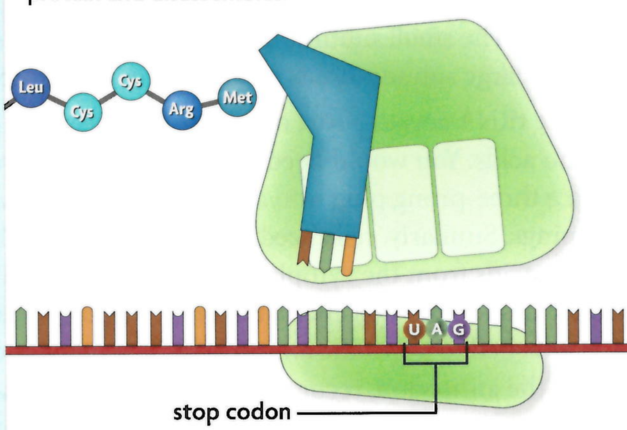
2 The ribosome forms a peptide bond between the two amino acids and breaks the bond between the first tRNA and its amino acid.



3 The ribosome pulls the mRNA strand the length of one codon. The first tRNA is shifted into the exit site, where it leaves the ribosome and returns to the cytoplasm to recharge. The first site is again empty, exposing the next mRNA codon.



The ribosome continues to translate the mRNA strand until it reaches a stop codon. Then it releases the new protein and disassembles.



CRITICAL VIEWING **The figure above shows how the first two amino acids are added to a growing protein. Draw a series of sketches to show how the next two amino acids are added.**

Translation, shown in **FIGURE 8.16,** has many steps and takes a lot of energy from a cell. It happens in the cytoplasm of both prokaryotic and eukaryotic cells. Before translation can begin, a small ribosomal subunit must bind to an mRNA strand in the cytoplasm. Next, a tRNA with methionine attached binds to the AUG start codon. This binding signals a large ribosomal subunit—which has three binding sites for tRNA molecules—to join. The ribosome pulls the mRNA strand through itself one codon at a time. As the strand moves, the start codon and its complementary tRNA molecule shift into the second site inside the large subunit. This shift leaves the first site empty, which exposes the next mRNA codon. The illustration shows the process in one ribosome, but in a cell many ribosomes may translate the same gene at the same time.

1. The exposed codon attracts a complementary tRNA molecule bearing an amino acid. The tRNA anticodon pairs with the mRNA codon. This action brings the new tRNA molecule very close to the tRNA molecule occupying the second site.
2. Next, the ribosome helps form a peptide bond between the two amino acids. The ribosome then breaks the bond between the tRNA molecule in the second site and its amino acid.
3. The ribosome pulls the mRNA strand the length of one codon. The tRNA molecule in the second site is shifted into the third site, which is the exit site. The tRNA leaves the ribosome and returns to the cytoplasm to be charged with another amino acid. The tRNA molecule that was in the first site shifts into the second site. The first site is again empty, exposing the next mRNA codon.

Another complementary tRNA molecule is attracted to the exposed mRNA codon, and the process continues. The ribosome moves down the mRNA strand, attaching new amino acids to the growing protein, until it reaches a stop codon. Then it lets go of the new protein and falls apart.

Summarize **Explain the different roles of the large and small ribosomal subunits.**

8.5 ASSESSMENT

REVIEWING MAIN IDEAS

1. Explain the connection between a **codon** and an amino acid.
2. Briefly describe how the process of **translation** is started.

CRITICAL THINKING

3. **Synthesize** Suppose a tRNA molecule had the **anticodon** AGU. What amino acid would it carry?
4. **Hypothesize** The DNA of eukaryotic cells has many copies of genes that code for rRNA molecules. Suggest a hypothesis to explain why a cell needs so many copies of these genes.

Connecting CONCEPTS

5. **Biochemical Reactions** Enzymes have shapes that allow them to bind to a substrate. Some types of RNA also form specific three-dimensional shapes. Why do you think RNA, but not DNA, catalyzes biochemical reactions?

8.6 Gene Expression and Regulation

KEY CONCEPT Gene expression is carefully regulated in both prokaryotic and eukaryotic cells.

MAIN IDEAS

- Prokaryotic cells turn genes on and off by controlling transcription.
- Eukaryotic cells regulate gene expression at many points.

VOCABULARY

promoter, p. 248
operon, p. 248
exon, p. 251
intron, p. 251

REVIEW AT CLASSZONE.COM

Connect Ours is a world of marvels. So many, in fact, that we may overlook what seem like little ones, such as plumbing. The turn of a handle sends clean water to your sink or shower. One twist and the water trickles out; two twists and it gushes forth. Another turn of the handle and the water is off again. But think about the mess and waste that would result if you couldn't control its flow. In a similar way, your cells have ways to control gene expression. Depending on an organism's needs, a gene can make a lot of protein, a little protein, or none at all.

MAIN IDEA

Prokaryotic cells turn genes on and off by controlling transcription.

The regulation of gene expression allows prokaryotic cells, such as bacteria, to better respond to stimuli and to conserve energy and materials. In general, this regulation is simpler in prokaryotic cells than in eukaryotic cells, such as those that make up your body. DNA in a prokaryotic cell is in the cytoplasm. Transcription and translation can happen at the same time. As a result, gene expression in prokaryotic cells is mainly regulated at the start of transcription.

A gene includes more than just a protein-coding sequence. It may have many other nucleotide sequences that play a part in controlling its expression. The start of transcription is largely controlled by these sequences, including promoters and operators. A **promoter** is a DNA segment that allows a gene to be transcribed. It helps RNA polymerase find where a gene starts. An operator is a DNA segment that turns a gene "on" or "off." It interacts with proteins that increase the rate of transcription or block transcription from occurring.

VOCABULARY

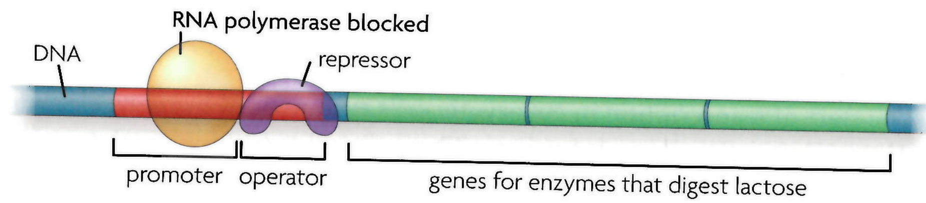
The word *promote* comes from the Latin prefix *pro-*, meaning "forward," and the Latin word *movere*, meaning "to move."

Bacteria have much less DNA than do eukaryotes, and their genes tend to be organized into operons. An **operon** is a region of DNA that includes a promoter, an operator, and one or more structural genes that code for all the proteins needed to do a specific task. Typically, operons are found only in prokaryotes and roundworms. The *lac* operon was one of the earliest examples of gene regulation discovered in bacteria. It will serve as our example. The *lac* operon has three genes, which all code for enzymes that play a role in breaking down the sugar lactose. These genes are transcribed as a single mRNA transcript and are all under the control of a single promoter and operator. This means that although we're dealing with several genes, they act together as a unit.

The *lac* operon is turned on and off like a switch. When lactose is absent from the environment, the *lac* operon is switched off to prevent transcription of the *lac* genes and save the cell's resources. When lactose is present, the *lac* operon is switched on to allow transcription. How does this happen?

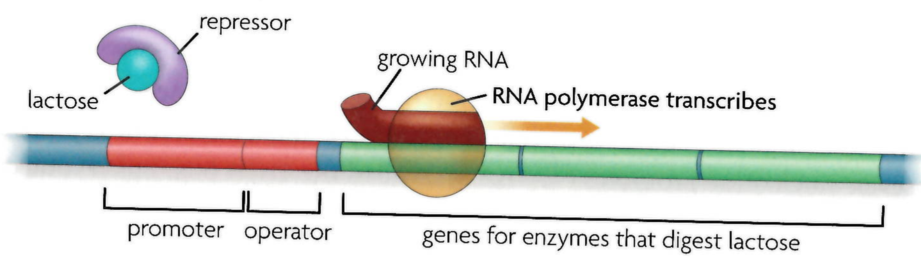
Bacteria have a protein that can bind specifically to the operator. When lactose is absent, this protein binds to the operator, which blocks RNA polymerase from transcribing the genes. Because the protein blocks—or represses—transcription, it is called a repressor protein.

Without lactose (switched off)



When lactose is present it binds to the repressor, which makes the repressor change shape and fall off the *lac* operon. RNA polymerase can then transcribe the genes in the *lac* operon. The resulting transcript is translated and forms three enzymes that work together to break down the lactose.

With lactose (switched on)



Analyze **Explain how the *lac* operon is turned on or off like a switch.**

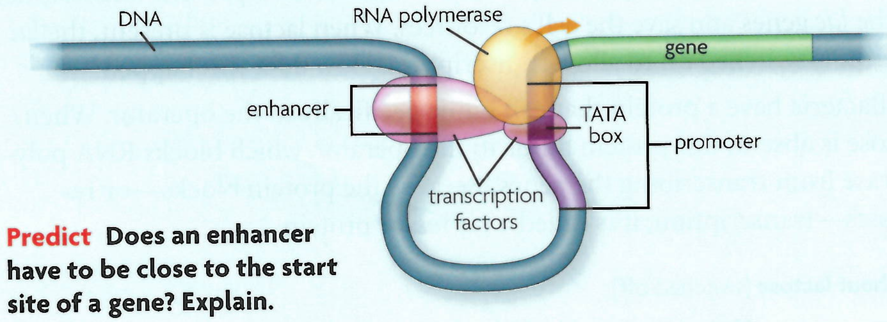
MAIN IDEA

Eukaryotic cells regulate gene expression at many points.

You have already learned that every body cell in an organism has the same set of DNA. But your cells are not all the same. Cells differ from each other because different sets of genes are expressed in different types of cells. Eukaryotic cells can control the process of gene expression at many different points because of their internal compartments and chromosomal organization. As in prokaryotic cells, however, one of the most highly regulated steps is the start of transcription. In both cell types, RNA processing is a part of the transcription process. In eukaryotic cells, however, RNA processing also includes the removal of extra nucleotide segments from an mRNA transcript.

FIGURE 8.17 Starting Transcription

Transcription factors that bind to promoters and other DNA sequences help RNA polymerase recognize the start of a gene in a eukaryotic cell.



Predict **Does an enhancer have to be close to the start site of a gene? Explain.**

Starting Transcription

The start of transcription in eukaryotic cells is controlled by many elements that work together in complex ways. These elements include regulatory DNA sequences and proteins called transcription factors, as shown in **FIGURE 8.17**. They occur in different combinations in different types of cells. The interplay between these elements results in specialized cells and cell responses.

Eukaryotes have many types of regulatory DNA sequences. These sequences are recognized by transcription factors that bind to the DNA strand and help RNA polymerase know where a gene starts. Some DNA sequences, such as promoters, are close to the start of a gene. Others are far away from the genes they affect. However, DNA can loop and bend, bringing these sequences with their transcription factors into close contact with the others.

Each gene has a unique combination of regulatory sequences. Some are found in almost all eukaryotic cells. For example, most eukaryotic cells have a seven-nucleotide promoter (TATAAAA) called the TATA box. Eukaryotic cells also have other types of promoters that are more specific to an individual gene. DNA sequences called enhancers and silencers also play a role by speeding up or slowing down, respectively, the rate of transcription of a gene.

Some genes control the expression of many other genes. Regulation of these genes is very important because they can have a large effect on development. One such gene codes for a protein called sonic hedgehog. This protein was first found in fruit flies, but many other organisms have very similar proteins that serve a similar function. Sonic hedgehog helps establish body pattern. When missing in fruit flies, the embryos are covered with little prickles and fail to form normal body segments.

mRNA Processing

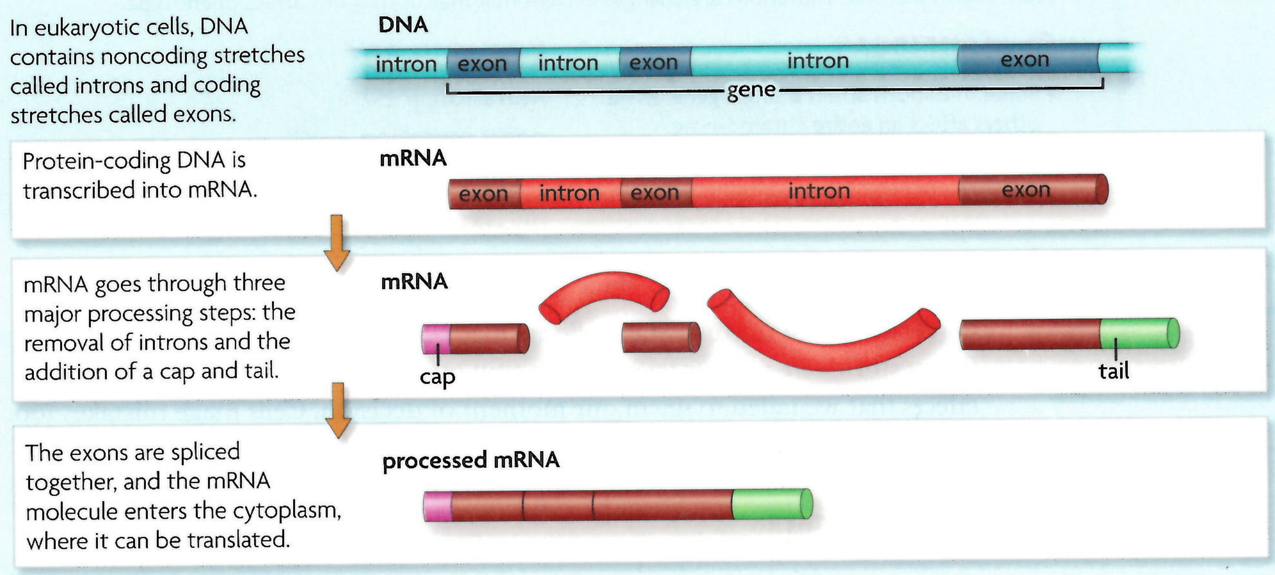
Another important part of gene regulation in eukaryotic cells is RNA processing, which is shown in **FIGURE 8.18**. The mRNA produced by transcription is similar to a rough cut of a film that needs a bit of editing. A specialized nucleotide is added to the beginning of each mRNA molecule, which forms a cap. It helps the mRNA strand bind to a ribosome and prevents the strand from being broken down too fast. The end of the mRNA molecule gets a string of A nucleotides, called the tail, that helps the mRNA molecule exit the nucleus.

Connecting CONCEPTS

Animals As you will learn in **Chapter 23**, most animals have homeobox genes. These genes are among the earliest that are expressed and play a key role in development. The illustration below shows the expression of homeobox genes in a fruitfly embryo.

FIGURE 8.18 mRNA Processing

An mRNA molecule typically undergoes processing during or immediately after DNA transcription.



Connect **Where does mRNA processing take place in a eukaryotic cell?**

The "extra footage" takes the form of nucleotide segments that are not included in the final protein. In eukaryotes, **exons** are nucleotide segments that code for parts of the protein. **Introns** are nucleotide segments that intervene, or occur, between exons. Almost no prokaryotes have introns. Introns are removed from mRNA before it leaves the nucleus. The cut ends of the exons are then joined together by a variety of molecular mechanisms.

The role of introns is not clear. They may regulate gene expression. Or they may protect DNA against harmful mutations. That is, if large regions of DNA are noncoding "junk," then mutations occurring in those regions will have no effect. Some mRNA strands can be cut at various points, resulting in different proteins. As a result, introns increase genetic diversity without increasing the size of the genome.

Apply **Which parts of a gene are expressed as protein: introns or exons?**

8.6 ASSESSMENT

ONLINE QUIZ ClassZone.com

REVIEWING MAIN IDEAS

1. What is a **promoter**?
2. In eukaryotic cells, genes each have a specific combination of regulatory DNA sequences. How do these combinations help cells carry out specialized jobs?

CRITICAL THINKING

3. **Predict** Suppose a bacterium had a mutated repressor protein that could not bind to the *lac* operator. How might this affect regulation of the **operon**?
4. **Summarize** What are the three major steps involved in mRNA processing?

Connecting CONCEPTS

5. **DNA** DNA is loosely organized in areas where RNA polymerase is transcribing genes. What might you infer about a region of DNA that was loosely organized in muscle cells but tightly coiled in lung cells?

8.7 Mutations

KEY CONCEPTS Mutations are changes in DNA that may or may not affect phenotype.

MAIN IDEAS

- Some mutations affect a single gene, while others affect an entire chromosome.
- Mutations may or may not affect phenotype.
- Mutations can be caused by several factors.

VOCABULARY

mutation, p. 252
point mutation, p. 252
frameshift mutation, p. 252
mutagen, p. 255

REVIEW AT CLASSZONE.COM

Connect We all make mistakes. Some may be a bit embarrassing. Others become funny stories we tell our friends later. Still others, however, have far-reaching effects that we failed to see in our moment of decision. Cells make mistakes too. These mistakes, like our own, can have a range of effects. When they occur in DNA, they are called mutations, and cells have evolved a variety of methods for dealing with them.

MAIN IDEA

Some mutations affect a single gene, while others affect an entire chromosome.

You may already know the term *mutation* from popular culture, but it has a specific meaning in biology. A **mutation** is a change in the an organism's DNA. Many types of mutations can occur, as shown in **FIGURE 8.20.** Typically, mutations that affect a single gene happen during replication, whereas mutations that affect a group of genes or an entire chromosome happen during meiosis.

FIGURE 8.19 Cystic fibrosis (CF) is a genetic disease that is most commonly caused by a specific deletion. It causes the overproduction of thick, sticky mucus. Although CF cannot be cured, it is treated in a number of ways, including oxygen therapy (above).

Gene Mutations

A **point mutation** is a mutation in which one nucleotide is substituted for another. That is, an incorrect nucleotide is put in the place of the correct nucleotide. Very often, such a mistake is caught and fixed by DNA polymerase. If it is not, the substitution may permanently change an organism's DNA.

A **frameshift mutation** involves the insertion or deletion of a nucleotide in the DNA sequence. It usually affects a polypeptide much more than does a substitution. Frameshift mutations are so named because they shift the entire sequence following them by one or more nucleotides. To understand how this affects an mRNA strand, imagine a short sentence of three-letter "codons":

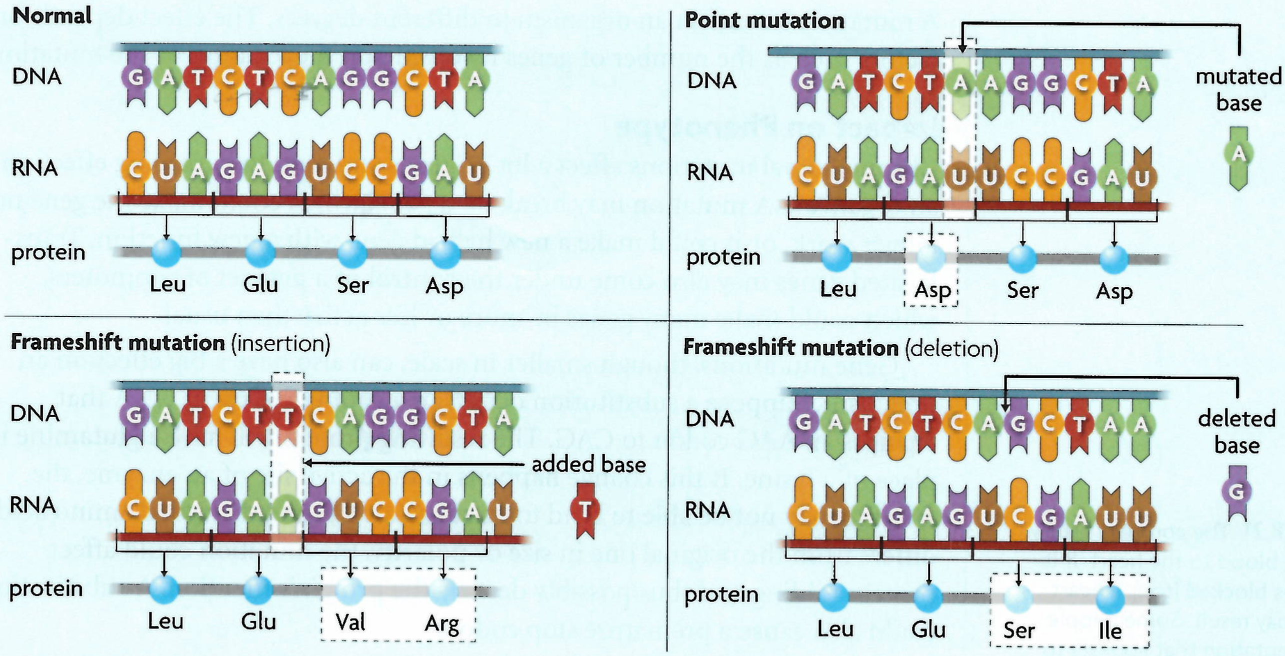
THE CAT ATE THE RAT

If the letter *E* is removed, or deleted, from the first "THE," all the letters that follow shift to the left. The sentence now reads:

THC ATA TET HER AT . . .

FIGURE 8.20 Types of Mutations

A mutation is a change in an organism's DNA.



Evaluate **Explain which mutation you think would have the greatest effect.**

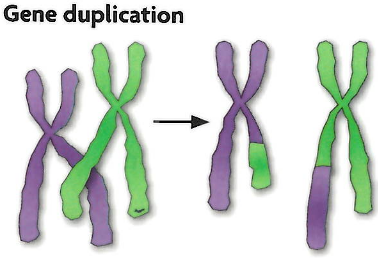
The sentence no longer makes sense. The same would be true if a nucleotide was added, or inserted, and all the letters shifted to the right. In the same way, a nucleotide sequence loses its meaning when an insertion or deletion shifts all the codons by one nucleotide. This change throws off the reading frame, which results in codons that code for different amino acids.

Chromosomal Mutations

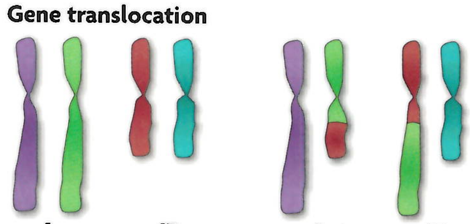
Recall that during meiosis, homologous chromosomes exchange DNA segments through crossing over. If the chromosomes do not align with each other, these segments may be different in size. As a result, one chromosome may have two copies of a gene or genes, called gene duplication. The other chromosome may have no copy of the gene or genes. Gene duplication has happened again and again throughout eukaryotic evolution.

Translocation is another type of chromosomal mutation. In translocation, a piece of one chromosome moves to a nonhomologous chromosome. Translocations are often reciprocal, which means that the two nonhomologous chromosomes exchange segments with each other.

Gene duplication



Gene translocation



Explain **How does a frameshift mutation affect reading frame?**

MAIN IDEA

Mutations may or may not affect phenotype.

A mutation can affect an organism to different degrees. The effect depends on factors such as the number of genes involved and the location of the mutation.

Impact on Phenotype

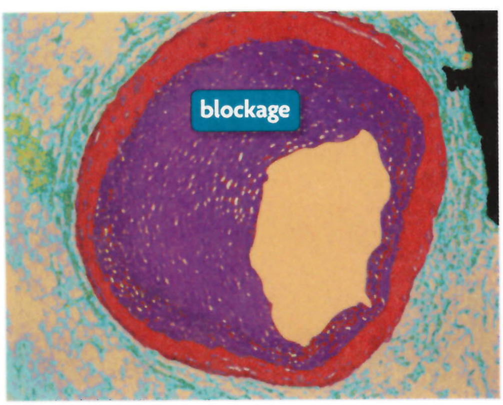
Chromosomal mutations affect a lot of genes and tend to have a big effect on an organism. A mutation may break up a gene, which could make the gene no longer work, or it could make a new hybrid gene with a new function. Translocated genes may also come under the control of a new set of promoters, which could make many genes be more or less active than usual.

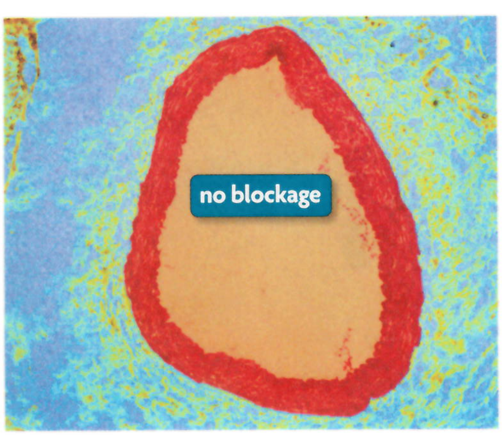
Gene mutations, though smaller in scale, can also have a big effect on an organism. Suppose a substitution occurs in a coding region of DNA that changes an AAG codon to CAG. The resulting protein will have a glutamine in place of a lysine. If this change happens in the active site of an enzyme, the enzyme may not be able to bind to its substrate. If the substituted amino acid differs from the original one in size or polarity, the mutation could affect protein folding and thus possibly destroy the protein's function. A substitution could also cause a premature stop codon.

Even a mutation that occurs in a noncoding region can cause problems. For example, such a mutation could disrupt an mRNA splice site and prevent an intron from being removed. A mutation in a noncoding region could also interfere with the regulation of gene expression, keeping a protein from being produced or causing it to be produced all the time.

Many gene mutations, however, do not affect an organism's phenotype. Remember that many codons code for the same amino acid. Therefore, some substitutions have no effect, especially those occurring in the third nucleotide of a codon. If AAG changes to AAA, the resulting protein still has the correct amino acid, lysine. A mutation that does not affect the resulting protein is called silent. Similarly, an incorrect amino acid might have little effect on a protein if it has about the same size or polarity as the original amino acid or if it is far from an active site. If a mutation occurs in a noncoding region, such as an intron, it may not affect the encoded protein at all.

FIGURE 8.21 The coronary artery supplies blood to the heart. If it becomes blocked (top), a heart attack may result. Some people have a mutation that appears to help protect against coronary artery disease (bottom) by increasing their "good" cholesterol levels and decreasing their triglyceride levels. (colored LMs; magnifications: 15×)





Impact on Offspring

Mutations happen both in body cells and in germ cells. Mutations in body cells affect only the organism in which they occur. In contrast, mutations in germ cells may be passed to offspring. They are the underlying source of genetic variation, which is the basis of natural selection. Mutations in the germ line affect the phenotype of offspring. Often, this effect is so harmful that offspring do not develop properly or die before they can reproduce. Other mutations, though less severe, still result in less adaptive phenotypes. In such cases, natural selection removes these mutant alleles from the population. More rarely, a mutation results in a more beneficial phenotype. These mutations are favored by natural selection and increase in a population.

Apply **Why aren't mutations in body cells passed on to offspring?**

MAIN IDEA

Mutations can be caused by several factors.

Mutations are not uncommon, and organisms have many tools to repair them. However, events and substances can make mutations happen faster than the body's repair system can handle.

Replication Errors

As you have learned, DNA polymerase has a built-in proofreading function. Nevertheless, a small number of replication errors are not fixed. They build up over time, and eventually affect how the cell works. For example, many studies suggest that mutations are a significant cause of aging.

Mutagens

Mutagens are agents in the environment that can change DNA. They speed up the rate of replication errors and, in some cases, even break DNA strands. Some mutagens occur naturally, such as ultraviolet (UV) rays in sunshine. Many others are industrial chemicals. Ecologists such as Rachel Carson, shown in **FIGURE 8.22**, warned the public about mutagens.

The human body has DNA repair enzymes that help find and fix mutations. For instance, UV light can cause neighboring thymine nucleotides to break their hydrogen bonds to adenine and bond with each other instead. Typically, one enzyme removes the bonded thymines, another replaces the damaged section, and a third bonds the new segment in place. Sometimes, these enzymes do not work. If these mistakes interfere with regulatory sites and control mechanisms, they may result in cancer. In rare cases, people inherit mutations that make their DNA repair systems less active, which makes these people very vulnerable to the damaging effects of sunlight.

Some cancer drugs take advantage of mutagenic properties by causing similar damage to cancer cells. One type wedges its way between nucleotides, causing so many mutations that cancer cells can no longer function.

FIGURE 8.22 Rachel Carson was one of the first ecologists to warn against the widespread use of pesticides and other potential mutagens and toxins.

Summarize **Explain why mutagens can damage DNA in spite of repair enzymes.**

8.7 ASSESSMENT

ONLINE QUIZ
ClassZone.com

REVIEWING MAIN IDEAS

1. Explain why **frameshift mutations** have a greater effect than do **point mutations.**
2. If GUA is changed to GUU, will the resulting protein be affected? Explain.
3. Explain how **mutagens** can cause genetic **mutations** in spite of your body's DNA repair enzymes.

CRITICAL THINKING

4. **Connect** Some genetic mutations are associated with increased risk for a particular disease. Tests exist for some of these genes. What might be the advantages and disadvantages of being tested?
5. **Infer** How could a mutated gene produce a shorter protein than that produced by the normal gene?

Connecting CONCEPTS

6. **Ecology** How might the presence of a chemical mutagen in the environment affect the genetic makeup and size of a population over time?

Use these inquiry-based labs and online activities to deepen your understanding of DNA.

DESIGN YOUR OWN INVESTIGATION

UV Light and Skin Cancer

Exposure to the ultraviolet (UV) radiation in sunlight can lead to skin cancer caused by mutations in the DNA of skin cells. The most common type of damage from UV light is the formation of thymine dimers, or pairs of thymine bases bonded together. These mutations interfere with both replication and transcription. Sunscreens receive ratings based on the amount of protection from UV radiation they provide. The higher the sun protection factor (SPF), the more radiation the lotion blocks.

MATERIALS
- 3 different kinds of sunscreen
- sunlight or UV light box
- 12 UV beads

SKILLS Collecting Data, Defining Operational Variables

PROBLEM Which sunscreen blocks more UV rays?

PROCEDURE

1. Choose either three different brands of sunscreen or three samples of the same brand with different SPFs.
2. Design an experiment using the UV beads to test the effectiveness of each of the sunscreens. Remember to include a control group and multiple trials.
3. Identify the independent and dependent variables and any constants in your procedure.
4. Once your teacher has approved your experimental design, carry out your procedure. Record your results in a data table.

ANALYZE AND CONCLUDE

1. **Analyze** What can you conclude about the effectiveness of the sunscreens?
2. **Apply** Identify the operational definition of your variable in this experiment.
3. **Evaluate** What was the importance of having a control in this procedure?
4. **Experimental Design** Identify sources of unavoidable error and reasons for inconsistent results.

EXTEND YOUR INVESTIGATION

Exposure to high levels of UV radiation during the teenage years is a major risk factor for skin cancer, but the cancer itself generally does not develop until many years later. Use what you have learned about mutations to propose a reasonable explanation for why skin cancer usually appears later in life.