

CHAPTER 18

Molecular Genetics

Chapter Concepts

18.1 DNA Structure and Replication

- A molecule of DNA is made up of two long strands of nucleotides wound around each other in the shape of a double helix.
- During DNA replication, complementary base pairing ensures that each daughter molecule is identical to the original DNA molecule.

18.2 Protein Synthesis and Gene Expression

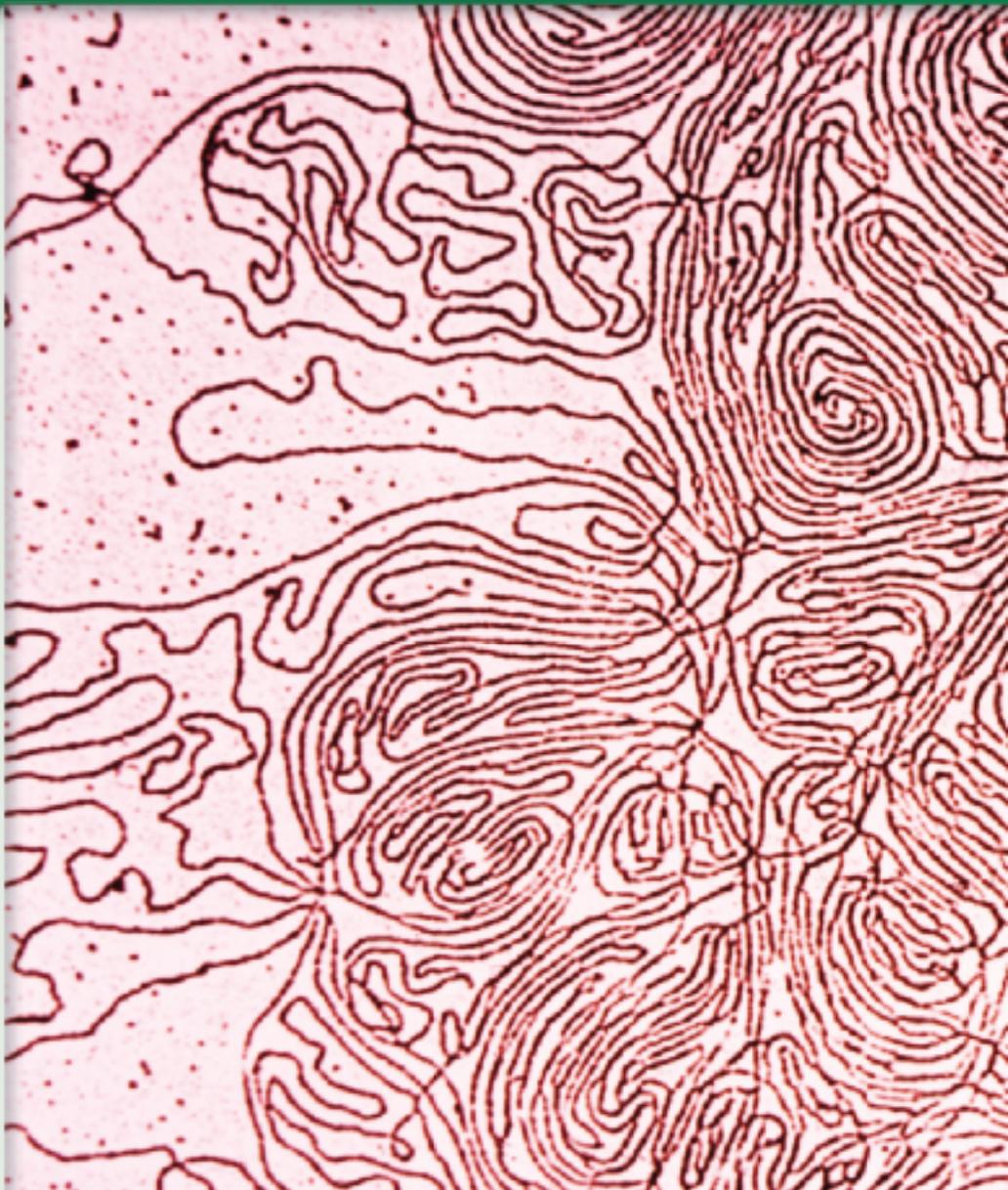
- Gene expression involves two basic steps: transcription of genetic information from DNA to RNA, then translation from RNA to protein.
- The genetic code is made up of nucleotide triplets called codons. Each codon corresponds to a specific amino acid.

18.3 Mutations and Genetic Recombination

- Permanent changes in DNA give rise to genetic variation and may also cause hereditary disorders or cancer.

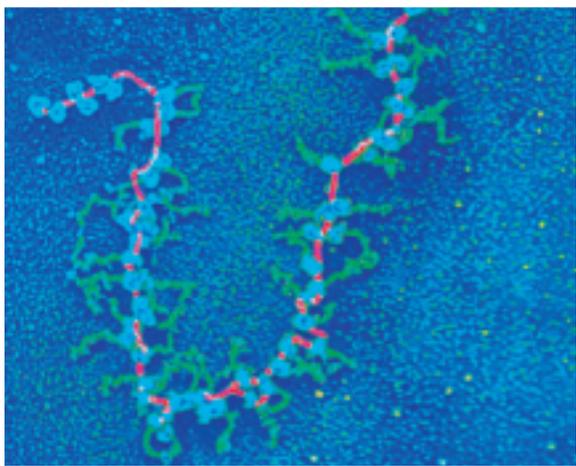
18.4 Genetics and Society

- Genetic technologies have many useful applications but can also give rise to challenging social and ethical questions.



The genetic information that is encoded in this DNA filament might define the colour of flower petals, the antibiotic resistance of a bacterial cell, the mating behaviour of a water bird, or even a child's chance of developing a deadly disorder. How does this kind of information find its way into—and out of—a series of biochemical reactions? Molecular genetics is the study of how DNA stores and transmits genetic information and how that information is expressed phenotypically in the world. This involves studying the unique molecular properties of DNA and the complex interactions between DNA and proteins. Increasingly, molecular genetics also involves confronting difficult moral and ethical questions and even questioning our definition of life itself.

Launch Lab



Within the cell, specialized structures called ribosomes (colourized blue) use genetic information (colourized pink) to construct proteins (green).

DNA Extraction

A powerful microscope is needed to observe the shape of a DNA molecule. What does DNA look like to the unaided eye?

Materials

- mortar and pestle
- graduated cylinder
- 250 mL beaker
- small piece of animal tissue
- 50 mL beakers (2)
- 0.9% NaCl solution
- glass stirring rod
- 10% detergent solution
- cheesecloth
- 95% ice-cold ethanol solution

Procedure

1. Place the sample of animal tissue in the mortar. Add 10 mL of the 0.9% NaCl solution, and grind thoroughly with the pestle for 2 to 5 min.
2. Strain the solution through three layers of cheesecloth. Collect the liquid in the 250 mL beaker.
3. Pour the liquid into a 50 mL beaker. Add 1.5 mL of the 10% detergent solution.
4. Estimate the volume of the fluid in the beaker. Then measure approximately twice as much of the ice-cold 95% ethanol into the other 50 mL beaker.
5. Slightly tilt the beaker holding the tissue extract. Gently add the ethanol by pouring ethanol down the inside of the beaker.
6. Gently stir the mixture with the stirring rod. When you see a precipitate form at the boundary of the two liquids, twirl the rod to wind the DNA sample onto the glass rod.

Analysis

1. Describe the DNA you extracted.
2. What kinds of studies and observations do you think researchers would have made as they worked from a description like yours to create a molecular model of DNA? List your ideas. Review and modify your ideas as you work through this chapter.

SECTION 18.1

DNA Structure and Replication

Section Outcomes

In this section, you will

- **summarize** the events and experiments that led to the discovery of the structure of DNA
- **explain** how the interaction between DNA and proteins results in the accurate replication of genetic information
- **design and construct** models to simulate the structure and replication of DNA

Key Terms

deoxyribonucleic acid (DNA)
ribonucleic acid (RNA)
transforming principle
nucleotides
Chargaff's rule
complementary base pairs
antiparallel
gene
genome
replication
semi-conservative
replication origin
helicases
replication bubble
replication fork
DNA polymerase
elongation
primer
leading strand
lagging strand
Okazaki fragments
DNA ligase
primase
replication machine
termination
DNA sequencing
Human Genome Project

In 1869, a young Swiss physician named Friedrich Miescher coined the term “nucleic acid” to describe a weakly acidic, phosphorus-containing substance that he had isolated from the nuclei of white blood cells. Miescher reported his findings only four years after Mendel had published his research on heredity in garden peas. Almost a century passed, however, before a series of studies and experiments—along with an occasional stroke of luck—led scientists to establish the connection between nucleic acid and Mendel's factors of inheritance.

Today, scientists know that **deoxyribonucleic acid (DNA)** is the nucleic acid molecule that governs the processes of heredity in all plant and animal cells. **Ribonucleic acid (RNA)**, a nucleic acid that plays a role in gene expression and protein synthesis, shares a similar structure with DNA. In the next few pages, you will examine some of the research that led to this knowledge and enabled scientists to deduce the molecular structure of DNA.

Isolating the Material of Heredity

In the early 1900s, a Russian-born American biochemist named Phoebus Levene isolated two types of nucleic acid. He called them *ribose nucleic acid (RNA)* and *deoxyribose nucleic acid (DNA)*. Levene went on to show that chromosomes are made up of a combination of DNA and proteins. Within a few years, Morgan and his team provided the first experimental evidence that genes are located on chromosomes. At this time, scientists did not know whether the DNA or the proteins in chromosomes served as the physical basis for genes. Research to determine the physical structure and function of genes began in earnest after Morgan's work. The first evidence that DNA played a role in heredity came by accident.

The Transforming Principle

In 1928, Frederick Griffith, an English medical officer, designed an experiment to study the pathogenic (disease-causing) bacteria that were responsible for a pneumonia epidemic in London. Griffith set up his experiment using dead *Streptococcus pneumoniae* bacteria as a control. To his surprise, he discovered that the dead pathogenic bacteria had somehow passed on their disease-causing properties to live, non-pathogenic bacteria (see Figure 18.1). Griffith called this phenomenon the **transforming principle**, because something from the heat-killed pathogenic bacteria must have transformed the living non-pathogenic bacteria to make them disease-causing.

Griffith died during World War II, but several scientists built on his work, attempting to identify the agent of transformation. In 1944, the team of Oswald Avery, Colin MacLeod, and Maclyn McCarty, at Rockefeller University in the United States, conducted a series of experiments and discovered the following:

- When they treated heat-killed pathogenic bacteria with a protein-destroying enzyme, transformation still occurred.
 - When they treated heat-killed pathogenic bacteria with a DNA-destroying enzyme, transformation did not occur.
- These results provided strong evidence for DNA's role in transformation. Even so, most scientists still were not prepared to view DNA as the likely source of hereditary material. Instead, they thought that DNA might activate gene-carrying proteins.

Hershey and Chase: Evidence in Favour of DNA as the Hereditary Material

Convincing evidence that DNA, not proteins, carried genetic information was finally provided in 1952. The American research team of Alfred Hershey and

Griffith's discovery of transformation

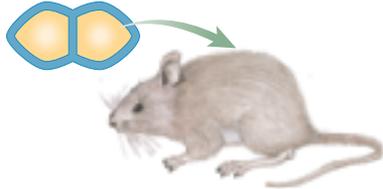
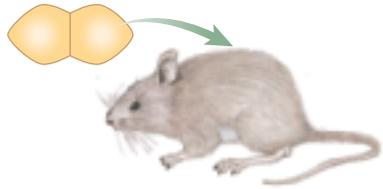
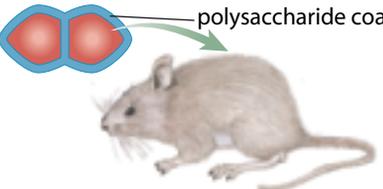
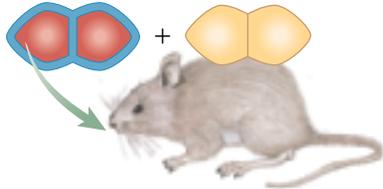
Injection of <i>Streptococcus pneumoniae</i>	Result
<p>Live pathenogenic strain of <i>S. pneumoniae</i></p> 	<p>Mice die</p> 
<p>Live non-pathenogenic strain of <i>S. pneumoniae</i></p> 	<p>Mice live</p> 
<p>Heat-killed pathenogenic strain of <i>S. pneumoniae</i></p> 	<p>Mice live</p> 
<p>Mixture of heat-killed pathenogenic and live non-pathenogenic strains of <i>S. pneumoniae</i></p> 	<p>Mice die. Their blood contains live pathenogenic <i>S. pneumoniae</i>.</p> 

Figure 18.1 Frederick Griffith found that hereditary information passed from dead bacterial cells to live bacterial cells. The live cells were transformed from a harmless form into a disease-causing form.

Martha Chase used a new technology, radioactive labelling, to show that genes are made of DNA. Their experiment is illustrated in Figure 18.2 on the next page.

Hershey and Chase used a strain of virus known as a T2 bacteriophage, which consists of a protein coat surrounding a length of DNA. This virus attaches to a bacterial cell and injects genetic information into the cell. The infected cell manufactures new viruses, and then it bursts. The newly released viruses go on to infect other cells. To determine whether viral protein or viral DNA was responsible for taking over the genetic machinery of the host cell, Hershey and Chase created two batches of the virus. In one batch, they labelled the protein coat using radioactive sulfur. In the other

batch, they labelled the DNA with radioactive phosphorus. The labelled viruses were allowed to infect bacterial cells. The cells were then agitated in a blender to separate the viral coats from the bacterial cells. Each medium was

- 1 What was Miescher's contribution to the study of hereditary material?
- 2 What conclusion did Avery, MacLeod, and McCarty draw from their study of the transforming principle?
- 3 What conclusion did Hershey and Chase draw from their study of the transforming principle?

tested for radioactivity. The results, shown in Figure 18.2, demonstrated that viral DNA, not viral protein, enters the bacterial cell.

The Structure of DNA

While some scientists were trying to identify the physical agent of heredity, other scientists were studying the structure of DNA. In the early 1900s, Phoebus Levene, a biochemist working at the newly established Rockefeller Institute in New York, contributed the first information about the molecular structure of DNA.

The Chemical Composition of DNA

After isolating DNA and RNA, Levene determined that both molecules are made up of long chains of individual units he called **nucleotides**. Both DNA and RNA contain a combination of four

different nucleotides. As shown in Figure 18.3, each DNA nucleotide is composed of a five-carbon sugar, a phosphate group, and one of five nitrogen-containing bases. The four bases that are found in DNA nucleotides are adenine (A), guanine (G), cytosine (C), and thymine (T). RNA has the base uracil (U) instead of thymine. Scientists often identify the nucleotides simply by referring to their bases: A, G, C, T (for DNA) and A, G, C, U (for RNA).

Levene also determined that nucleic acids are made up of long chains of nucleotides, strung together as shown in Figure 18.4. He concluded incorrectly, however, that the nucleotides were present in equal amounts and that they appeared in these chains in a constant and repeated sequence, such as ACTGACTGACTG. This was the main reason why most scientists looked to proteins, rather than DNA, as the hereditary material. Scientists assumed that the molecular structure of DNA was just too simple to provide the tremendous variation in inherited traits.

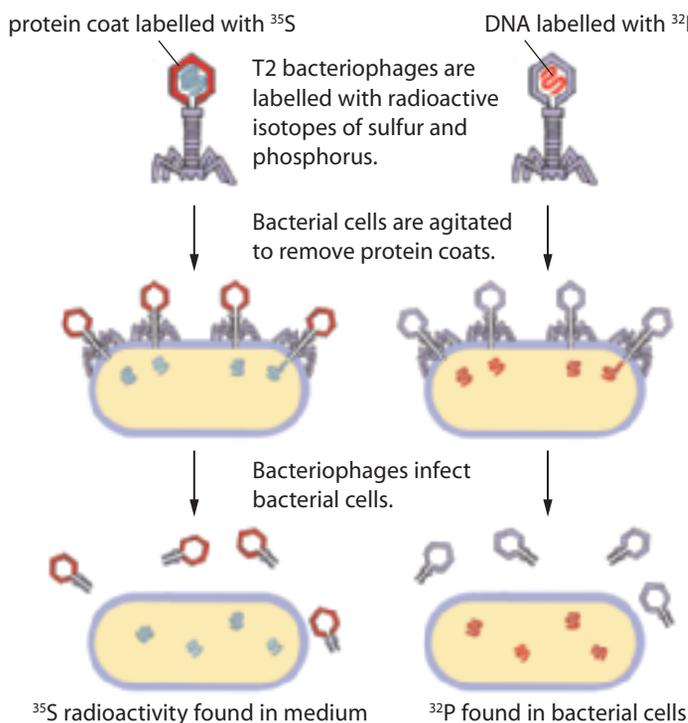


Figure 18.2 The Hershey-Chase experiment. The scientists knew that virtually all of the phosphorus present in the T2 virus is in its DNA, while sulfur is found only in its protein coat. Thus, they prepared two different samples of the T2 virus: one tagged with radioactive phosphorus (^{32}P) and the other tagged with radioactive sulfur (^{35}S). Bacterial cells that were infected by viruses with radioactive DNA were radioactive, indicating that the viral DNA entered the host cell. In contrast, bacterial cells that were infected by viruses with radioactive protein coats were not radioactive, indicating that no viral protein entered the host cell. Therefore, DNA must direct the cell to produce new viruses.

Chargaff's Rule

In the late 1940s, an important series of studies by Ukrainian-American biochemist Erwin Chargaff overturned Levene's incorrect conclusion about the

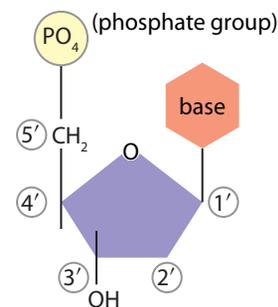


Figure 18.3 The general structure of a DNA nucleotide. An RNA nucleotide has an additional oxygen molecule in the five-carbon sugar ring. Notice the numbering of the carbon atoms on the sugar molecule. The five carbon atoms of the sugar of the nucleotide are numbered 1' to 5', and they proceed clockwise from the oxygen atom. The prime symbol (') indicates that the carbon belongs to the sugar rather than to the base.

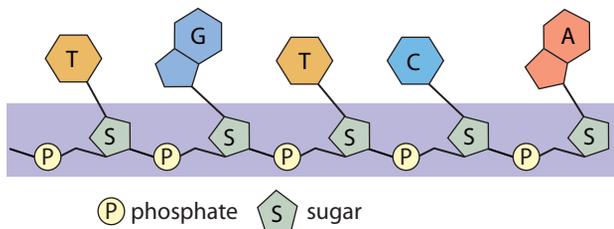


Figure 18.4 Nucleotides are joined together in a long chain. The “backbone” of the chain is made up of alternating sugar and phosphate groups that are joined by chemical bonds. The nitrogenous bases project out from the sugar-phosphate backbone.

four nucleotides in DNA. Chargaff found that the nucleotides are not present in equal amounts. Instead, the nucleotides are present in varying, but characteristic, proportions. Most significantly, as shown in Table 18.1, Chargaff found that the amount of adenine in any sample of DNA is always approximately equal to the amount of thymine, and the amount of cytosine is always approximately equal to the amount of guanine. This constant relationship became known as **Chargaff’s rule**.

The Three-Dimensional Structure of DNA

Early in the 1950s, British scientist Rosalind Franklin used X-ray photography to analyze the structure of DNA. Her observations provided crucial new information about the molecular structure of DNA.

One of Franklin’s images is shown in Figure 18.5. From images like this, she was able to conclude that DNA has a helical structure with two regularly repeating patterns—one recurring at intervals of 0.34 nm, and the other recurring at intervals of 3.4 nm.

As Franklin prepared her samples for photography, she observed how DNA

Table 18.1 Relative Proportions (Percent) of Bases in DNA of Several Organisms

Organism	A (Adenine)	T (Thymine)	G (Guanine)	C (Cytosine)
<i>Mycobacterium tuberculosis</i>	15.1	14.6	34.9	35.4
<i>Escherichia coli</i>	26.0	23.9	24.9	25.2
Yeast	31.3	32.9	18.7	17.1
Herring	27.8	27.5	22.2	22.6
Rat	28.6	28.4	21.4	21.5
Human	30.9	29.4	19.9	19.8

reacted with water. From her observations, she concluded that the nitrogenous bases were located on the inside of the helical structure, and the sugar-phosphate backbone was located on the outside, facing toward the watery nucleus of the cell. Franklin’s observations and her detailed X-ray work, along with the work done by Chargaff, proved to be important keys for understanding the structure of DNA.

The partnership between the American geneticist James Watson and the British physicist Francis Crick was the first to produce a structural model of DNA that could account for all the experimental evidence. In 1953, Watson and Crick published a two-page paper describing a double-helix model. This

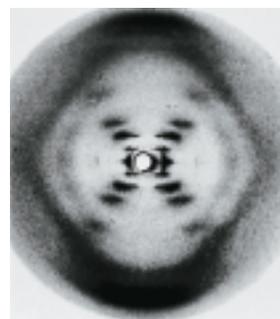


Figure 18.5 Rosalind Franklin’s work with X-ray diffraction images provided several important clues about the molecular structure of DNA.

Practice Problems

1. A sample of DNA contains A and C nucleotides in the following proportions: A = 34% and C = 16%. What are the proportions of G and T nucleotides in this sample? (Assume that the characteristic proportions are exactly equal.)
2. Use Chargaff’s rule to complete the following table. (Assume that the characteristic proportions are exactly equal.)

Nucleotide Composition of DNA in Sample X

Nucleotide	Proportion (%)
A	24
C	
G	
T	

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FYI

Watson attended a lecture by Rosalind Franklin in 1951. In this lecture, Franklin described her findings in some detail, including her inference about the helical shape of DNA. Watson did not take notes, however, and incorrectly remembered important points of the lecture. His inattention likely cost him and Crick two extra years of work.

model soon became accepted as the molecular structure of DNA.

The Double Helix Structure of DNA

DNA is a thread-like molecule, made up of two long strands of nucleotides that are bound together in a spiral shape called a *double helix*. If the helix were unwound, as shown in Figure 18.6, the DNA molecule would look something like a ladder. The “handrails” of the

ladder are the sugar-phosphate backbones of the two nucleotide strands. The “rungs” are the bases that protrude inward at regular intervals along each strand.

From Franklin’s images, Watson and Crick knew that the distance between the sugar-phosphate handrails remained constant over the length of the molecule. The nitrogenous bases are different sizes, however. Adenine and guanine are derived from the family of compounds known as purines, which have a double-ring structure. Thymine and cytosine are derived from pyrimidines, which have a single-ring structure. Using Chargaff’s rule, Watson and Crick hit upon the idea that an A nucleotide on one chain always sits across from a T nucleotide on the other chain, while a C nucleotide on one chain always sits across from a G nucleotide on the other chain. Thus, the two handrails maintain a constant total distance of three rings. The A-T and C-G pairs are called **complementary base pairs**. The complementary base pairs are held together by hydrogen bonds.

As you can see in Figure 18.6, the two strands of DNA that make up the double helix are not identical. They are complementary to each other. You can always deduce the base sequence on one strand from the base sequence on the other strand. The two strands are **antiparallel**, as well. That is, the phosphate bridges run in opposite directions in the two strands. Each end of a double-stranded DNA molecule contains the 5’ end of one strand and the 3’ end of the complementary strand. These two

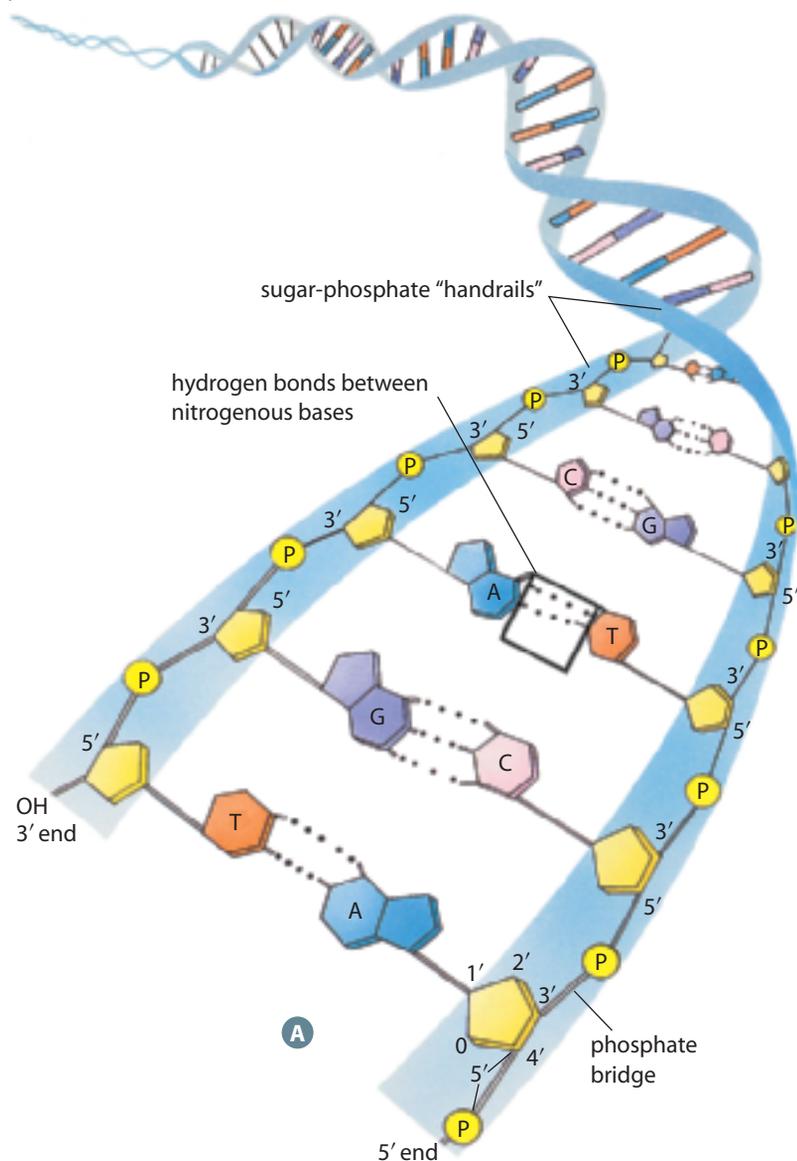
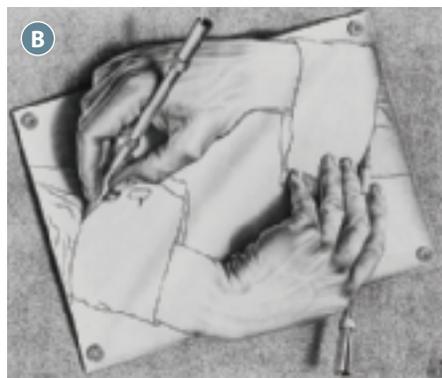


Figure 18.6 A DNA molecule is made up of two strands of nucleotides that are wound around each other (A). The two strands are held together by hydrogen bonds between complementary base pairs. C-G pairs are held together by three hydrogen bonds, and A-T pairs are held together by two hydrogen bonds. Notice that the chains are antiparallel—the 5’ to 3’ orientation runs in the opposite direction on each strand. Another example of antiparallelism is represented by M.C. Escher’s sketch, “Drawing Hands” (B).



M.C. Escher’s “Drawing Hands” ©2006 The M.C. Escher Company-Holland. All rights reserved.

properties have important implications for DNA replication and protein synthesis, as you will see later in this chapter.

4 What was the contribution of each of the following researchers to the study of DNA?

- a) Chargaff
- b) Franklin
- c) Watson and Crick

5 Explain how complementary base pairing maintains a constant width in a DNA molecule.

RNA

Like DNA, ribonucleic acid (RNA) is a nucleic acid. Both DNA and RNA are found in most bacteria and in the nuclei of most eukaryotic cells. The molecular structure of RNA is similar to the molecular structure of DNA, with three key differences:

- The sugar component of RNA is ribose rather than deoxyribose.

- RNA does not have the nucleotide thymine (T). In its place is the nucleotide uracil (U).
- RNA remains single-stranded, although the single strand can sometimes fold back on itself to produce regions of complementary base pairs.

The RNA molecule can assume different structures, which result in several different types of RNA, each serving a particular function. The specific structures and functions of some of these types of RNA are described in more detail later in this chapter.

Genes and the Genome

As scientists have learned more about the structure and function of DNA, they have developed new definitions to describe genetic material. For example, a gene was once described as an inheritable trait. Today, a **gene** is defined as a functional sub-unit of DNA that directs the production of one or more polypeptides (protein molecules).

The **genome** of an organism is the sum of all the DNA that is carried in each

Thought Lab 18.1 DNA Deductions

As you have seen, Edwin Chargaff discovered that the nucleotide composition of DNA varies from one species to another. The nucleotide composition always follows certain rules, however. You can use these rules to make deductions about the structure of a particular DNA molecule.

Procedure

1. Imagine that you are analyzing a DNA sample from the liver tissue of a newly discovered species of mouse. Use the information in the table below to complete the nucleotide composition of your sample.

Nucleotide	Presence in DNA sample (percent)
adenine	31
cytosine	
guanine	
thymine	

2. Draw a linear stretch of a double-stranded DNA molecule about 20 base pairs long, with a nucleotide composition that corresponds (as closely as you can)

to the nucleotide composition of your sample. Use solid lines to show chemical bonds and dotted lines to show hydrogen bonds.

Analysis

1. Explain what you would expect to find if you compared the nucleotide composition of your DNA sample with the nucleotide composition of a second DNA sample from the muscle tissue of the same mouse.
2. Would the nucleotide composition of your original DNA sample be different from the nucleotide composition of a tissue sample from the gametes of the same mouse? Explain your answer.
3. Would the nucleotide composition of your original DNA sample be different from the nucleotide composition of a tissue sample from the liver of a deer? Explain your answer.

Target Skills

Constructing a model of a portion of a DNA molecule

Analyzing data and **applying** a conceptual model to infer the structure of a DNA molecule

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Scientific exploration is not free from social and political values and biases. For example, Rosalind Franklin's role in the study of DNA was largely ignored during her lifetime, partly because of sexist attitudes toward women in science in the 1950s and because of an ongoing "feud" with Maurice Wilkins. Linus Pauling, who also was hot on the trail of the structure of DNA, missed a key scientific conference in London because the U.S. State Department refused to grant him a VISA due to his antiwar views. What part did personalities and politics play in the race to unlock the DNA code?

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cell of the organism. This DNA includes genes as well as regions of non-coding DNA, which may play various roles in gene expression. (You will learn more about gene expression later in this chapter.)

Genes are not spaced regularly along chromosomes. In humans, for example, chromosome 4 is about 200 000 000 bases long and has about 800 genes, while chromosome 19 is only 55 000 000 bases long but has almost 1500 genes. Similarly, there is no set relationship between the number of genes in an organism and the total size of its genome. The total human genome is about three billion base pairs, and it includes an estimated 20 000 to 25 000 genes. The single-celled protozoan *Amoeba dubai* has an enormous genome of over 650 billion bases but fewer than 7000 genes. The roundworm *Caenorhabditis elegans* (*C. elegans*), shown in Figure 18.7, has almost as many genes as a human, but its total genome is almost 30 times smaller.

6 Explain the difference between the terms gene and genome.

DNA Replication

Replication is the process of creating an exact copy of a molecule of DNA. As you know from Chapter 16, a cell replicates all of its DNA—its entire genome—once,



Magnification: 133 ×

Figure 18.7 *C. elegans* has been, and continues to be, an important organism in the study of genetics. Its genome is fairly small, and about one-third of *C. elegans* genes are very similar to those found in humans.

and only once, in the cell cycle, during S phase of interphase. A human cell can copy all of its DNA in a few hours, with an error rate of about one per one billion nucleotide pairs. As a comparison, imagine typing one letter for each base pair in the human genome. Working non-stop at a rate of one letter per second, this would take you close to 100 years to complete. To match the accuracy of a cell, you could make no more than a single one-letter error every 30 years. The speed and accuracy of the replication process relies on both the structural features of DNA and the action of a set of specialized proteins.

Semi-Conservative Replication

Watson and Crick's landmark paper on the structure of DNA concludes with this remark: "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material." Each strand of DNA serves as a template for the creation of its complementary strand. As illustrated in Figure 18.8, replication is **semi-conservative**—each new molecule of DNA contains one strand of the original complementary DNA molecule and one new parent strand. Thus, each new DNA molecule conserves half of the original molecule.

The main events of replication are described in the remainder of this section. They are presented as a sequence. In reality, however, all of these events take place simultaneously on the same molecule of DNA.

Initiation

Replication starts at a specific nucleotide sequence, called the **replication origin**. The small circular chromosome of a prokaryote contains a single replication origin, while the linear chromosome of a eukaryote may contain thousands of replication origins. A group of enzymes, called **helicases**, bind to the DNA at the replication origin. The helicases cleave and unravel a segment of the double

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When scientists first discovered non-coding DNA in the 1970s, it was often referred to as "junk DNA" because scientists hastily assumed that it had no function. Many "junk" sequences have since been shown to serve a variety of important developmental and regulatory functions. Approximately 90 percent of human DNA is "junk."

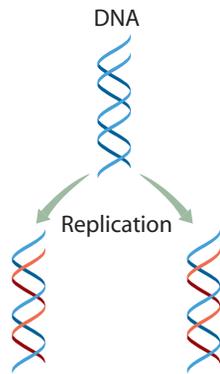


Figure 18.8 During DNA replication, two molecules of DNA are made from one. The original double helix unwinds. Two new strands of DNA are assembled using the original strands as templates. The resulting new molecules are identical to the original molecule. Each new molecule contains one original strand of DNA (shown here in blue) and one new strand (shown in red).

helix. This opening up of a region of DNA creates two Y-shaped areas at each end of the unwound area. The oval-shaped unwound area is called a **replication bubble**. Each Y-shaped area is called a **replication fork**. (See Figure 18.9.) The replication fork consists of two unwound DNA strands that branch out into unpaired (but complementary) single strands. These single strands serve as the templates for fashioning new strands of DNA. The molecule is now ready for replication to occur.

Elongation and Termination

An enzyme called **DNA polymerase** inserts into the replication bubble and begins to add nucleotides, one at a time, to create a strand of DNA that is complementary to the existing strand. The process of joining nucleotides to extend a new strand of DNA is called **elongation**, and it is the heart of replication. Elongation relies on the action of DNA polymerase. This enzyme attaches new nucleotides to the free 3' hydroxyl end of a pre-existing chain of nucleotides. There are two conditions for elongation. First, elongation can only take place in the 5' to 3' direction. Second, a short strand of RNA, known as a **primer**, must serve as a starting point for the attachment of new nucleotides.

The fact that DNA polymerase can only catalyze elongation in the 5' to 3' direction means that replication occurs in a slightly different way along each strand of the parent DNA. As shown in Figure 18.10 on the next page, one strand is replicated continuously in the 5' to 3' direction. This strand is known as the **leading strand**. The other strand, known as the **lagging strand**, is replicated in short segments. Nucleotides are still added in the 5' to 3' direction on the lagging strand, but the new DNA is synthesized in short

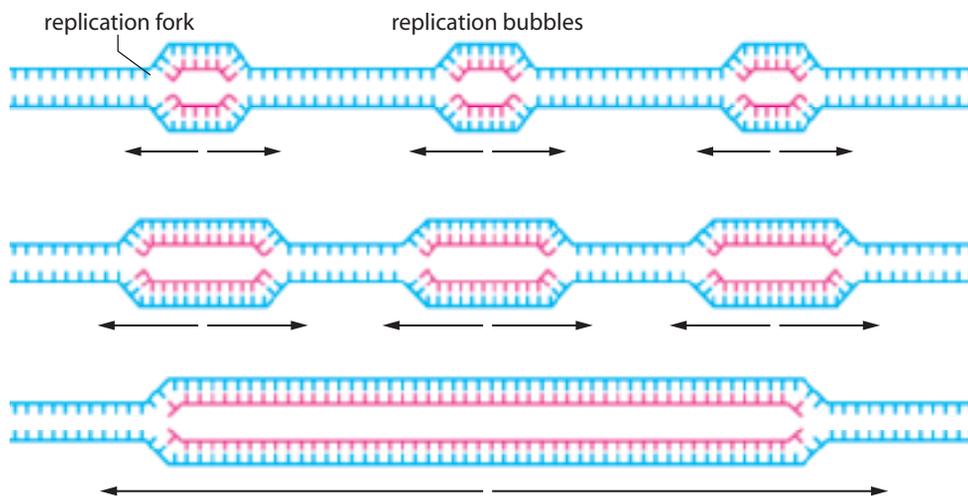


Figure 18.9 Replication takes place at several locations simultaneously. Each replication bubble represents two replication forks moving in opposite directions along the length of the chromosome. As replication proceeds along the strand, the bubbles grow until they meet. The parent strand of DNA is shown in blue. The new complementary strand is shown in red.

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Try This

Comparative genomics is the study of similarities and differences among the genomes of different organisms. For example, many human genes have counterparts in the pufferfish (*Fugu rubripes*). What could be some of the practical applications of comparing genomes?

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The semi-conservative model for DNA replication was one of three models proposed. The other two models are the conservative model and the dispersive model. How are these models different from the semi-conservative model? What experiments demonstrated that the semi-conservative model, not the conservative model or dispersive model, correctly illustrates how DNA replicates?



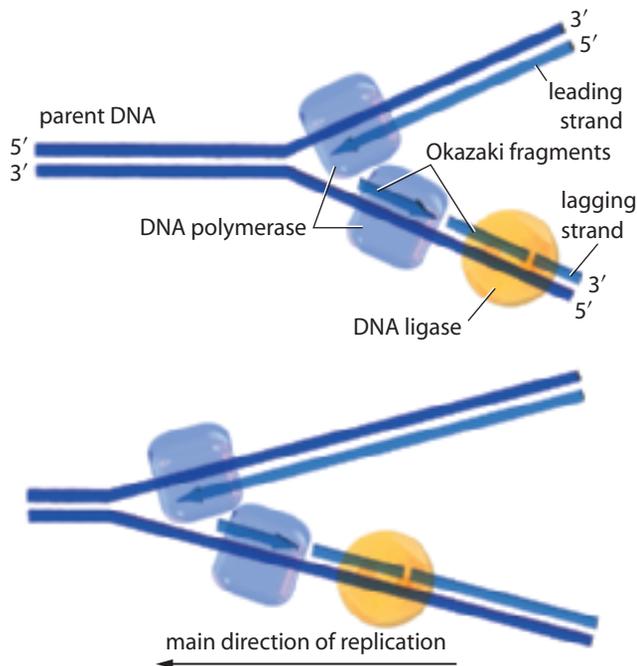


Figure 18.10 During DNA synthesis, the overall direction of elongation is the same along both strands, but elongation occurs differently. On the leading strand, DNA synthesis takes place along the DNA molecule in the same direction as the movement of the replication fork. On the lagging strand, DNA synthesis proceeds in the opposite direction to the movement of the replication fork. As well, the lagging strand is synthesized in short fragments.

segments called **Okazaki fragments**. The Okazaki fragments are then spliced together by an enzyme called **DNA ligase**.

Since DNA polymerase cannot synthesize new DNA fragments, an RNA primer serves as the starting point for the elongation of each new DNA strand. An enzyme called **primase** is required to construct the primer. Once the primer is in place, DNA polymerase extends each fragment by adding new nucleotides. Then DNA polymerase removes the RNA primer by eliminating the nucleotides in a 5' to 3' direction and fills in the space by extending the neighbouring DNA strand.

DNA polymerase has an important proofreading function, as well. After each nucleotide is added to a new DNA strand, DNA polymerase can recognize whether or not hydrogen bonding is taking place between the new base and its complement on the original strand. The absence of hydrogen bonding indicates a mismatch between the bases. When this occurs, DNA polymerase excises the

incorrect base from the new strand and adds the correct base using the parent strand as a template.

Along with polymerase, primase, ligase, and helicase, the coordinated activity of several other proteins and enzymes is required to accomplish DNA replication. These proteins and enzymes include enzymes that relieve torsion in the unwinding DNA helix and proteins that bind to exposed segments of single-stranded DNA to keep the unstable molecule from denaturing. Altogether, the complex of polypeptides and DNA that interact at the replication fork is known as the **replication machine**.

As the replication fork progresses along the replicating chromosome, only a very short region of DNA is found in a single-stranded form. As soon as the newly formed strands are complete, they rewind automatically into their chemically stable helix structure. Replication proceeds until the new strands are complete and the two new DNA molecules separate from one another. The completion of the new DNA strands and the dismantling of the replication machine is called **termination**.

Figure 18.11 shows the replication machine at work, and Table 18.2 summarizes the roles of the key enzymes. In Investigation 18.A, you will build a model to simulate DNA replication.

BiologyFile

FYI

Okazaki fragments are named in recognition of Japanese molecular biologist, Reiji Okazaki, who—aided by his colleagues, including his wife, Tsuneko Okazaki—demonstrated experimentally how DNA is replicated along each strand. Okazaki's death in 1975 resulted from leukemia brought on by his exposure to high levels of radiation; he was in Nagasaki when the second atomic bomb was dropped during World War II.

- 7 What is meant by the term “semi-conservative replication?”
- 8 Why does replication take place in a slightly different way on each DNA strand?
- 9 Explain how the leading and lagging strands of a DNA molecule are replicated.
- 10 Describe the components of the replication machine.

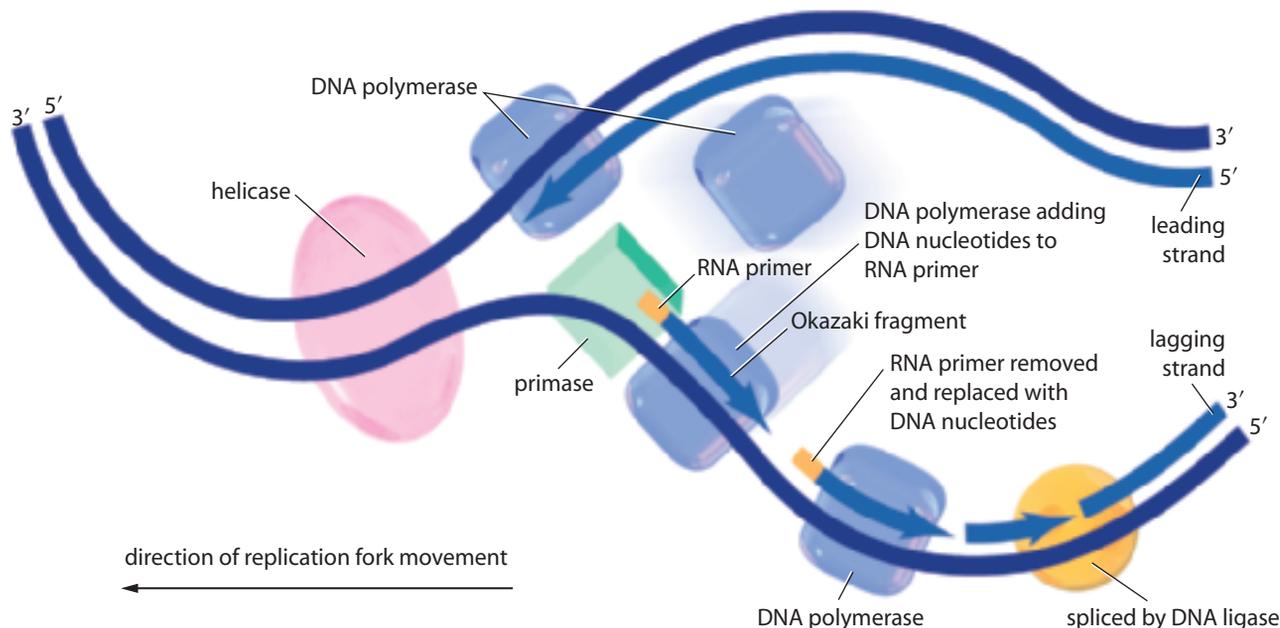


Figure 18.11 This simplified illustration of the replication machine shows how a loop in the lagging strand allows a single polymerase complex to replicate both DNA strands simultaneously.

Table 18.2 Key Enzymes in DNA Replication

Enzyme group	Function
helicase	cleaves and unwinds short sections of DNA ahead of the replication fork
primase	synthesizes an RNA primer to begin the elongation process
DNA polymerase	adds new nucleotides to the 3' OH group of an existing nucleotide strand; dismantles the RNA primer; proofreads base pairing
DNA ligase	splices together Okazaki fragments in the lagging strand

Sequencing Genomes

DNA sequencing is the process of identifying the precise nucleotide sequence of a DNA fragment. Researchers began sequencing DNA fragments more than 30 years ago. In 1977, the genome of the virus ϕ X174 became the first entire genome to be sequenced. At that time, the sheer size of eukaryotic genomes made it impossible for scientists to sequence these genomes using the same techniques. In the years since then, gene sequencing techniques have been refined and computer technology has advanced so that enormous databases of information can be quickly analyzed.

As a result, it is now routine for researchers to sequence genes, as well as the entire genomes of organisms.

In 2003, an international team of researchers completed the **Human Genome Project**, a monumental effort to sequence the entire human genome. The Human Genome Project is a landmark in the field of human genetics, and it has important applications in medicine and other sciences. Why? How does knowing the nucleotide sequence in a particular stretch of DNA contribute to our understanding of cell function? In the next section, you will examine how the information encoded in DNA molecules is expressed in living organisms.

Section 18.1 Summary

- Over a period of more than 50 years, various researchers conducted a series of experiments that identified DNA as the material of heredity and determined the properties of DNA.
- This research culminated in 1953, when Watson and Crick published a paper describing the molecular structure of DNA.
- DNA is made up of two strands of nucleotides, bound together to form a double helix.

BiologyFile

Try This

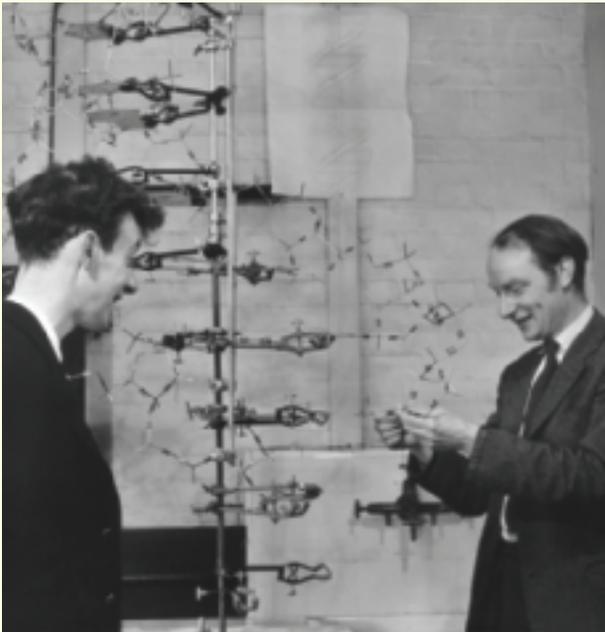
Many people confuse the terms “gene mapping” and “DNA sequencing.” Write two definitions or a single paragraph to clear up this confusion.

Target Skills

Constructing a model of DNA to demonstrate its structure and replication

Working cooperatively with team members to construct and assess a model

Modelling DNA Structure and Replication



Watson, Crick, and the model of DNA that they constructed

Watson and Crick did not conduct any experiments to determine the structure of DNA. Instead, they worked as synthesizers, examining and interpreting the research and discoveries made by other scientists. As well, Watson and Crick used a technique that was used previously by the chemist Linus Pauling to visualize and determine the helical structure of proteins by building physical models. Watson and Crick tried different arrangements until they created one model that could account for all the evidence. In this investigation, you will work in a group to design and build a model that can be used to simulate the structure and replication of DNA.

Question

How can you design a working model of a short strand of DNA (eight to ten base pairs) that can be used to simulate the molecular structure of DNA and the process of DNA replication?

Experimental Plan

1. Brainstorm ideas for designing and constructing a model.
2. Use your ideas to develop a plan. List the materials and equipment you will need.
3. When all the members of your group have approved the plan, write it down and review it with your teacher.
4. Create your model. Keep a written record of the steps you followed and any changes you made to your plan.

Data and Observations

5. Record the nucleotide sequences for each strand of DNA in your molecule, using the correct conventions.
6. Use your model to simulate the process of DNA replication. Keeping in mind the action of DNA polymerase, use your model to demonstrate
 - a) replication along the leading strand
 - b) replication along the lagging strand
 - c) the actions of primase, helicase, DNA polymerase, and DNA ligase

Analysis

1. In what ways is your model useful for explaining the structure and replication of DNA? What are the limitations of your model?
2. List the key replication enzymes in the order in which they are involved. For each enzyme, briefly describe what would happen if it were not present in the replication medium. (Assume the absence of any one enzyme does not affect the activity of others.)
3. In an early model tested by Watson and Crick, the sugar-phosphate handrails were on the inside of the helix and the nitrogenous bases protruded outward. How is this model inconsistent with experimental evidence about the structure of nucleic acids?

- Chemical bonds between sugar and phosphate molecules make up the backbone of each strand.
- Nitrogenous bases project out from the backbone.
- Hydrogen bonds between pairs of complementary bases hold the two strands together.
- Each DNA nucleotide carries one of four bases: adenine (A), guanine (G), cytosine (C), or thymine (T). A and T are complementary, and C and G are complementary.
- During DNA replication, the double helix opens. Each strand of the DNA molecule serves as a template for the creation of a complementary strand.
- DNA polymerase catalyzes the formation of new DNA molecules.
- Replication takes place in slightly different ways on the leading and lagging strands of the DNA molecule.
- The events of DNA replication show the close interaction of proteins and DNA in genetic processes.

Section 18.1 Review

- Describe one of the experiments that contributed to the study of DNA. How were the results of this experiment used by other researchers in subsequent work?
- For many years, scientists assumed that proteins rather than DNA made up the material of heredity.
 - What were some of the factors behind this assumption?
 - What experimental results provided strong evidence that genetic information was carried on DNA?
- Draw a single DNA nucleotide, and label its main parts.
- One strand in a stretch of DNA has the base sequence CCTGA. Draw this stretch of DNA, showing both strands. Label the sugar-phosphate backbone, the 5' and 3' ends of each strand, and the regions of hydrogen bonding.
- Lacking knowledge of Rosalind Franklin's X-ray analysis of the DNA molecule, Linus Pauling proposed a structure for DNA in which the phosphate groups were tightly packed on the inside of the molecule, thus leaving the nitrogenous bases projecting outward. If DNA replication occurred in this structure, how do you think it would differ from what you know is the actual process of DNA replication?
- Your research team is studying a virus that infects tomato plants. The genetic material of this virus is a single-stranded form of DNA. You extract two samples of DNA from an infected cell: one is the viral DNA and the other is the DNA of the plant cell. The table below shows the results of your analysis of the nucleotide composition of each sample. Which sample is the viral DNA? Explain.

Nucleotide	Presence in sample A (%)	Presence in sample B (%)
adenine	30.3	38.5
cytosine	19.7	10.7
thymine	30.3	13.3
guanine	19.7	37.5

- Create a table to show the similarities and differences between RNA and DNA.
- Explain what is meant by semi-conservative replication as it applies to DNA.
- Summarize the steps that are involved in the synthesis of the DNA molecule.
- What was the objective of the Human Genome Project?

SECTION 18.2

Protein Synthesis and Gene Expression

Section Outcomes

In this section, you will

- **explain** how genetic information is encoded in DNA molecules
- **describe** the processes through which genetic information is expressed in living cells
- **design** and **perform** a simulation to illustrate the steps of protein synthesis

Key Terms

amino acids
genetic code
gene expression
transcription
messenger RNA (mRNA)
transfer RNA (tRNA)
translation
codon
RNA polymerase
promoter
anticodon
ribosomal RNA (rRNA)
genomics
proteomics

In the same year that Watson and Crick published their model for the structure of DNA, in a laboratory at the same university, biochemist Frederick Sanger established that proteins consist of a sequence of molecules called **amino acids**. The specific sequence of amino acids determines the chemical properties of each protein. In turn, the specific proteins that are produced by a cell determine the structure, function, and development of the cell.

Once scientists understood that a given set of amino acids, arranged in a particular order, could produce the proteins that are responsible for inherited traits, they began to consider a new idea: Perhaps there was a connection between the sequence of nucleotides along a DNA molecule and the sequence of amino acids in a protein. Scientists soon showed that there is, in fact, a connection. The order of the base pairs in a DNA molecule makes up the **genetic code** of an organism. The genetic code determines how the amino acids are strung together and how the proteins are made. In other words, the order of the nucleotides in a gene provides the information, written in genetic code, that is necessary to build a protein.

Figure 18.12 summarizes the path of **gene expression**. The theory that genetic information flows from DNA to RNA to protein is often referred to as the “central dogma” of gene expression. During gene expression, DNA is copied into an RNA molecule in a process called **transcription**.

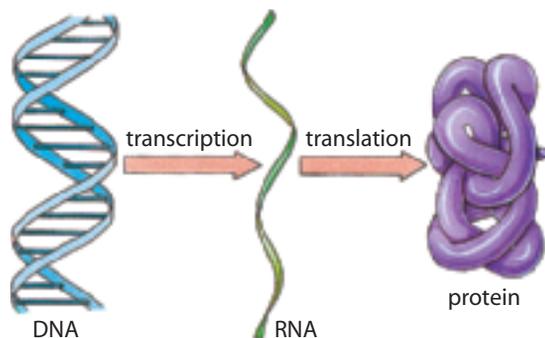


Figure 18.12

The path of gene expression. The “central dogma” proposes that genetic information passes (via transcription) from the genes (DNA) to an RNA copy of the gene, and the RNA copy directs the sequential assembly of a chain of amino acids to produce a protein (via translation).

In a eukaryotic cell, transcription takes place in the nucleus and involves a special type of RNA molecule called **messenger RNA (mRNA)**. The mRNA molecule moves into the cytoplasm of the cell, where the mRNA nucleotide sequence directs the synthesis of a polypeptide (a chain of amino acids) with the aid of another RNA molecule, **transfer RNA (tRNA)**. This process is known as **translation**. Over the next few pages, you will examine the genetic code and gene expression in more detail.

- 11 In what way is the structure of a protein related to the structure of DNA?
- 12 What are the two basic steps involved in gene expression?

The Genetic Code

In a gene, each set of three bases (for example, ACC or GAA) is known as a **codon**. By convention, the genetic code is always interpreted in terms of the mRNA codon rather than the nucleotide sequence of the original DNA strand. Table 18.3 lists all of the mRNA codons and their corresponding amino acids. To read the table, find the first letter of the mRNA codon in the column titled “First base.” Then read across the rows in the column titled “Second base” to find the second letter of the codon. This will take you to four possible amino acids. Finally, read down the column titled “Third base” to find the last letter of the codon. The last letter of the codon, combined with the previous two letters, identifies the amino acid that corresponds to the codon.

For example, the three nucleotides UAU code for the amino acid tyrosine. The first letter, U, is in the “First base” column. The second letter, A, is in the “Second base” column. The third letter,

Table 18.3 Messenger RNA Codons and Their Corresponding Amino Acids

First base	Second base				Third base
	U	C	A	G	
U	UUU phenylalanine	UCU serine	UAU tyrosine	UGU cysteine	U C A G
	UUC phenylalanine	UCC serine	UAC tyrosine	UGC cysteine	
	UUA leucine	UCA serine	UAA stop**	UGA stop**	
	UUG leucine	UCG serine	UAG stop**	UGG tryptophan	
C	CUU leucine	CCU proline	CAU histidine	CGU arginine	U C A G
	CUC leucine	CCC proline	CAC histidine	CGC arginine	
	CUA leucine	CCA proline	CAA glutamine	CGA arginine	
	CUG leucine	CCG proline	CAG glutamine	CGG arginine	
A	AUU isoleucine	ACU threonine	AAU asparagine	AGU serine	U C A G
	AUC isoleucine	ACC threonine	AAC asparagine	AGC serine	
	AUA isoleucine	ACA threonine	AAA lysine	AGA arginine	
	AUG methionine*	ACG threonine	AAG lysine	AGG arginine	
G	GUU valine	GCU alanine	GAU aspartate	GGU glycine	U C A G
	GUC valine	GCC alanine	GAC aspartate	GGC glycine	
	GUA valine	GCA alanine	GAA glutamate	GGA glycine	
	GUG valine	GCG alanine	GAG glutamate	GGG glycine	

* AUG is an initiator codon. It also codes for the amino acid methionine.
 ** UAA, UAG, and UGA are terminator codons.

U, is in the “Third base” column. Notice that the three nucleotides UAC also code for this same amino acid.

The genetic code has three important characteristics.

1. As you can see from Table 18.3, the genetic code is *redundant*—that is, more than one codon can code for the same amino acid. Only three codons do not code for any amino acid. As you will learn, these codons serve as “stop” signals to end protein synthesis.
2. The genetic code is *continuous*. That is, the genetic code reads as a series of three-letter codons without spaces, punctuation, or overlap. Knowing exactly where to start and stop translation is therefore essential. A shift of one or two nucleotides in either direction can alter the codon groupings and result in an incorrect amino acid sequence.
3. The genetic code is nearly *universal*. Almost all living organisms build

proteins with the genetic code shown in Table 18.3. As you will learn, this has important implications for gene technology, since a gene that is taken from one kind of organism and inserted into another kind of organism will produce the same protein.

- 13 How many bases make up each codon?
- 14 Describe each characteristic of the genetic code.
 - a) redundant
 - b) continuous
 - c) universal

Transcription

During transcription, the information in a segment of DNA is copied into messenger RNA (mRNA). Messenger RNA is a linear strand of RNA that carries

Practice Problems

3. Use Table 18.3 to find the amino acid that corresponds to each of the following codons.
 - a) CCA
 - b) AUG
 - c) GCA
4. What three RNA codons serve as “stop” signals?
5. Write three different codons that correspond to the amino acid arginine.

BiologyFile

FYI

The human genome contains fewer than 30 000 genes, but human cells produce more than 100 000 different proteins. A splicing process that takes place in eukaryotic cells enables a single gene to code for more than one protein.

information from DNA in the nucleus to the protein synthesis machinery in the cytoplasm of the cell. For each gene, only one strand of the double-stranded DNA molecule is transcribed. This strand is called the *sense strand*. The other strand, which is not transcribed, is called the *anti-sense strand*. In a single DNA molecule, either strand can serve as the sense strand for different genes.

The main enzymes that catalyze the synthesis of RNA are the **RNA polymerases**. (In eukaryotes, each RNA polymerase has a specific function.) A sequence of nucleotides on the DNA molecule serves as a **promoter** region that tells the RNA polymerase complex where to bind (Figure 18.13).

Once the RNA polymerase complex has bound to the sense strand of the DNA molecule, it opens a section of the double helix. The enzymes then work their way along the DNA molecule and synthesize a strand of mRNA that is complementary to the sense strand of DNA. In the mRNA strand, however, the base thymine is replaced with uracil. Like DNA polymerase, RNA polymerases work in the 5' to 3' direction, adding each

new nucleotide to the 3'-OH group of the previous nucleotide. RNA polymerases transcribe only one strand of the template DNA, however, so there is no need for Okazaki fragments.

A specific nucleotide sequence in the template DNA serves as a signal to stop transcription. When the RNA polymerases reach this signal, they detach from the DNA strand. The new mRNA strand is released from the transcription assembly, and the DNA double helix reforms.

Translation

For a cell to create the proteins it needs, it must translate the codons along a stretch of mRNA into amino acid sequences. This process requires both a chemical translator and a set of cellular protein synthesis equipment. Once the mRNA reaches the cytoplasm, the translator and protein synthesis equipment work together to assemble the proteins.

The molecule that links each mRNA codon to its specific amino acid is another form of RNA, called transfer RNA (tRNA). Transfer RNA is made up of a single strand of RNA that folds into the characteristic shape shown in Figure 18.14. One lobe

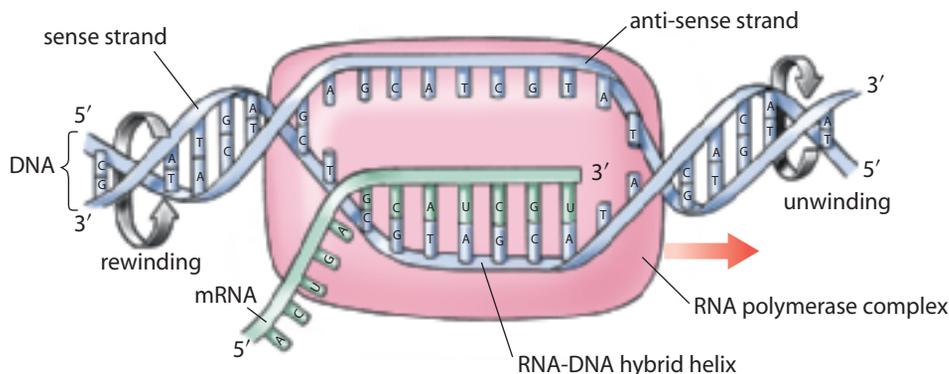


Figure 18.13 During transcription, a complex of RNA polymerases track along the DNA molecule, synthesizing a single-stranded mRNA molecule that is complementary to the sense strand of DNA. The DNA helix reforms behind the RNA polymerases complex.

Practice Problems

- An mRNA strand contains the following nucleotide sequence: AUGCCCACUACAUAAG. What amino acid sequence does this mRNA code for?
- A DNA strand contains the following nucleotide sequence: TACTGCCTCCCCATAAGAATT.
 - What is the nucleotide sequence of the mRNA strand that is transcribed from this DNA template?
 - What is the amino acid sequence of the polypeptide that is produced from this mRNA strand?

contains the **anticodon**, a stretch of three nucleotides that is complementary to the mRNA codon. At the opposite end of the molecule is a binding site for the amino acid that corresponds to the codon. The binding is accomplished by a specialized set of enzymes.

The main structures of the protein synthesis equipment are ribosomes. The ribosomes bring together the mRNA strand, the tRNA molecules carrying the amino acids, and the enzymes needed to build the polypeptides. The ribosomes also contain a third kind of RNA, known as **ribosomal RNA (rRNA)**. Ribosomal

RNA is a linear strand of RNA that remains associated with the ribosomes.

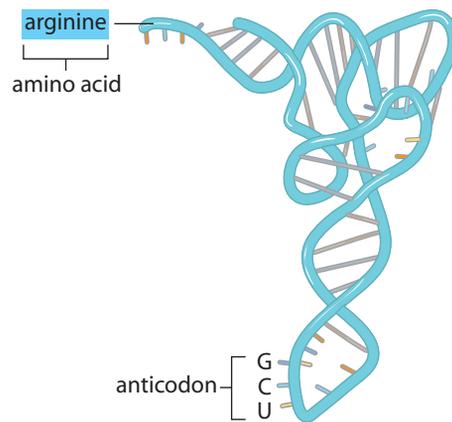


Figure 18.14 Each tRNA molecule is about 80 nucleotides long. The tRNA molecule shown here has the anticodon GCU, which pairs with the mRNA sequence CGA. This tRNA molecule carries the amino acid arginine.

Thought Lab 18.2 Transcription in Reverse

Target Skills

Constructing a model of a portion of a DNA molecule

Performing a simulation to demonstrate the transcription of a stretch of DNA

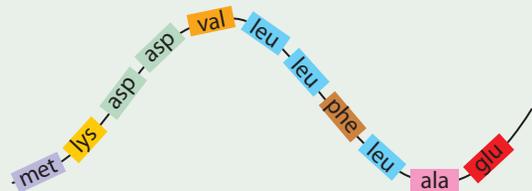
The analysis of DNA can help researchers determine which polypeptides are produced by particular genes. Similarly, but in reverse, the analysis of polypeptides can provide information about the genes that are associated with them. In this activity, you will work backward from a polypeptide chain to construct a stretch of DNA that might code for it.

Procedure

- The illustration shows an imaginary polypeptide produced by a bacterial cell. Using Table 18.3 (on page 633), and the table below, draw one possible nucleotide sequence for the DNA molecule that contains the gene for this polypeptide.
- Draw a labelled diagram to show the mRNA molecule being transcribed from the DNA strand.

Analysis

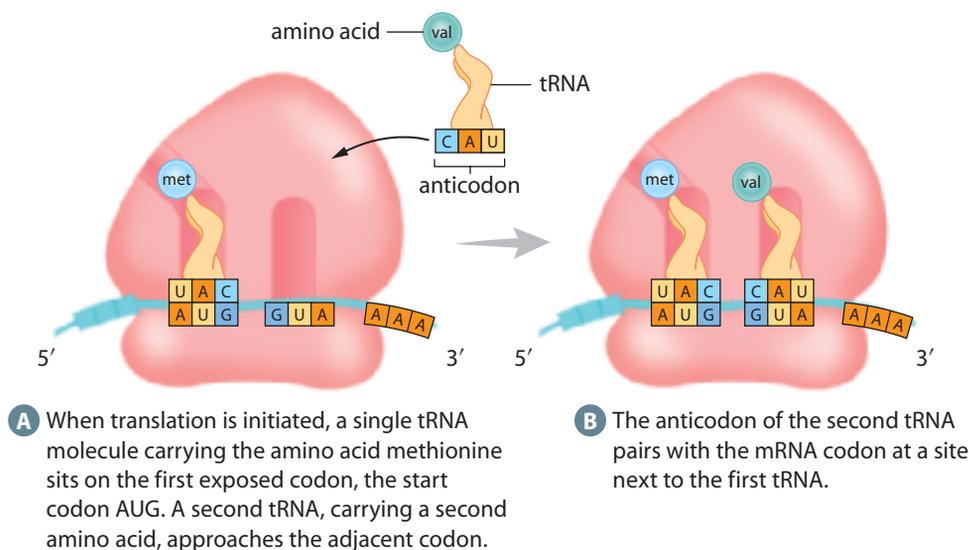
- Compare DNA molecules with your class. How many different sequences could code for the same polypeptide product? What advantage might this give a living cell?
- The processes of transcription and translation consume a great deal of cellular energy. Why do you think the cell does not simply translate proteins directly from DNA? Brainstorm some ideas, and discuss your ideas with your classmates.



Amino acid	Three-letter abbreviation
alanine	ala
arginine	arg
asparagine	asn
aspartate	asp
cysteine	cys
glutamate	glu
glutamine	gln
glycine	gly
histidine	his
isoleucine	ile

Amino acid	Three-letter abbreviation
leucine	leu
lysine	lys
methionine	met
phenylalanine	phe
proline	pro
serine	ser
threonine	thr
tryptophan	trp
tyrosine	tyr
valine	val

Figure 18.15 The translation cycle involves the base pairing of a new tRNA, the transfer of a growing polypeptide chain, and the movement of the ribosome along the mRNA molecule. The complete cycle occurs about 15 times per second in a prokaryotic cell.



Translation is activated when an mRNA molecule binds to an active ribosome complex. The mRNA binds in such a way that two adjacent codons are exposed. The first tRNA molecule carrying the amino acid methionine, base-pairs with the first exposed mRNA codon—the start codon, AUG. Once the tRNA and mRNA are in place, translation follows a cycle of three steps:

1. A second loaded tRNA molecule arrives at the codon adjacent to the first tRNA.
2. Enzymes catalyze the formation of a chemical bond that joins the amino acid carried by the first tRNA to the amino acid carried by the second tRNA. At the same time, the amino acid chain is transferred from the first tRNA to the second tRNA.
3. The ribosome moves a distance of one codon along the mRNA strand.

The first tRNA molecule detaches from the mRNA and picks up another amino acid. The second tRNA now holds a growing amino acid chain. A third tRNA molecule arrives at the newly-exposed codon next to the second tRNA, and the cycle repeats.

The translation cycle continues until a stop codon is reached. The completed polypeptide chain is then released, and the ribosome assembly comes apart. Figure 18.15 summarizes the steps in translation. Table 18.4 compares and contrasts the structures and functions of the different nucleic acids involved.

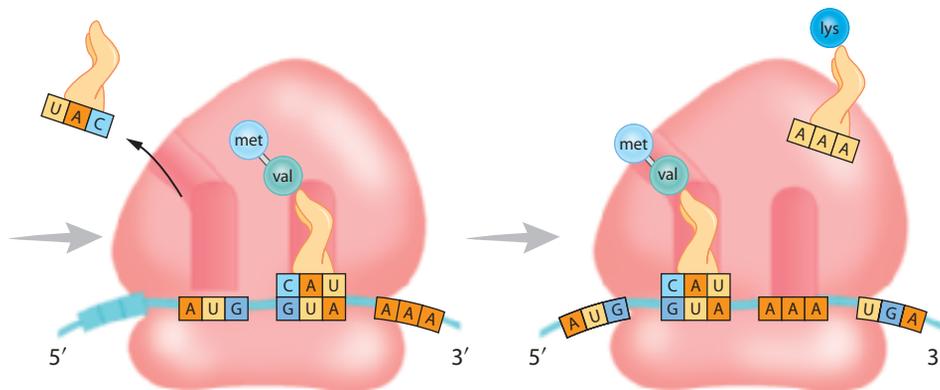
- 15 Describe the role of RNA polymerase complex in transcription.
- 16 What is the role of tRNA in translation?

Table 18.4 Nucleic Acids Involved in Gene Expression

Nucleic acid	Structure	Function
DNA	double helix	stores genetic information
messenger RNA (mRNA)	linear single strand	carries genetic information from DNA to the protein synthesis equipment; in eukaryotes, mRNA is processed before it moves to the cytoplasm for translation
transfer RNA (tRNA)	lobed shape	carries a particular amino acid to the correct codon site in the protein synthesis equipment
ribosomal RNA (rRNA)	linear single strand	combines with a complex of proteins to form a ribosome, the main structure of protein synthesis

Genomics and Proteomics

Since the late 1990s, progress in the field of genetics—the study of inheritance and the functions of genes—has opened up the field of genomics. **Genomics** is the study of entire genomes, including the interactions among multiple genes. Genomics is closely associated with **proteomics**, the study of all the proteins that are produced by a given genome.



C The first tRNA passes its amino acid to the second tRNA and leaves its binding site. A chemical bond is catalyzed between the two amino acids.

D The ribosome moves forward, exposing a new mRNA codon for a third tRNA. The cycle continues until the ribosome reaches the stop codon UGA. The polypeptide is released, and the assembly comes apart.

INVESTIGATION

18.B

Target Skills

Performing a simulation to demonstrate the replication of DNA and the transcription and translation of its information

Working cooperatively with team members to communicate information and ideas about DNA replication

Simulating Protein Synthesis

During the 1950s and 1960s, scientists developed several models to simulate and explain the steps in protein synthesis, even though they could not see most of the processes taking place at the cellular level. Today, researchers can use electron microscopes to observe and analyze molecular processes. Large-scale models, however, are still important tools in scientific research. In this investigation, you will work in a group to develop a model of protein synthesis.

Question

How can you use materials available in your home or classroom to simulate the processes of transcription and translation?

Experimental Plan

1. As a group, list the steps that are involved in transcription and translation. For each step, note the structures, molecules, and events involved.
2. Discuss how you might simulate transcription and translation in your classroom. Your simulation could take any form. For example, you could prepare an interactive computer program, write and perform a play, or construct a physical model.

3. Once you have agreed on a plan, list the materials and equipment you will need to carry out your simulation. Assign responsibilities to each member of your group. Then assemble your materials and prepare your simulation.

Data and Observations

4. Present your simulation to the class. Record any comments you receive from your classmates.

Analysis

1. Which parts of your presentation seemed to be the most effective at simulating protein synthesis? Now that you have seen what other groups did, how would you revise your own simulation?
2. Explain how a stop codon triggers the termination of the translation cycle. How does your simulation illustrate this?

Conclusion

3. What are some advantages and disadvantages of simulating molecular processes? What characteristics help to make a simulation effective?

Together, genomics and proteomics are influencing the research in many fields of biology, including medicine. For example, rather than targeting only the action of individual genes and proteins, scientists now study the interactions among genes and regulatory proteins that contribute to particular disorders. This, in turn, enables scientists to develop new treatments.

Key tools in these fields are computerized databases of the DNA sequences and associated proteins that are found in different organisms. Comparisons among different organisms are proving to be extremely valuable to scientists who are studying interactions between different genes, between genes and proteins, and between different proteins. You will learn more about the methods and applications of this research later in the chapter. In the next section, you will see how changes in genetic information can alter gene expression—and how such changes can be deliberately engineered.

Section 18.2 Summary

- In gene expression, the particular sequence of nucleotides in a stretch

of DNA directs the sequence of amino acids in a polypeptide.

- The “central dogma” of gene expression states that genetic information is first transcribed from DNA to RNA, and then translated from RNA to protein.
- During transcription, the sense strand of a gene is used as a template to synthesize a strand of messenger RNA (mRNA). (In eukaryotes, transcription takes place in the nucleus.) The mRNA transcript is then transported to the cytoplasm.
- During translation, the mRNA binds to a ribosome assembly. A tRNA carrying methionine binds with the start codon sequence exposed in the first binding site. Another tRNA molecule then recognizes the codon sequence at the next exposed binding site on the mRNA, and brings the corresponding amino acid to this site. Enzymes bind the amino acids held by adjacent tRNA molecules. As the ribosome progresses along the mRNA, the amino acid chain grows until a stop codon is reached and the new polypeptide is released.
- The processes of gene expression govern the development of living organisms.

Section 18.2 Review

1. What is the “central dogma” of gene expression?

Use the information in Table 18.3 to answer questions 2 and 3.

2. What amino acid corresponds to each of the following mRNA codons?

- a) UCC
- b) ACG
- c) GUG
- d) CAC

3. What codons could code for the amino acid serine?

4. Which characteristic of the genetic code provides evidence that all organisms have a common origin? Explain.

5. Use a labelled diagram to illustrate the process of transcription.

6. As you have learned, gene expression involves transcribing information from only one strand of the DNA molecule. What could be some of the biological advantages of double-stranded DNA?

7. What cellular structure provides the machinery for translation? Where is this structure located in a eukaryotic cell?

8. Use labelled diagrams to illustrate the three-step cycle in the elongation phase of translation.

9. Describe the structures and functions of the three main forms of RNA that are involved in gene expression.

10. In bacterial cells, transcription and translation can take place at the same time on the same strand of mRNA.

- a) Why is this not possible in a eukaryotic cell?
- b) In what ways could this have both advantages and disadvantages for bacterial cells?

Mutations and Genetic Recombination

Section Outcomes

In this section, you will

- **explain** some of the causes and effects of DNA mutations
- **describe** how random changes in nucleotide sequences provide a source of genetic variability
- **explain** how nucleotide sequences provide evidence that different species of organisms are related
- **design and perform** a simulation to illustrate the use of restriction enzymes and ligases to create recombinant DNA

Key Terms

mutation
somatic cell mutation
germ line mutation
point mutation
silent mutation
mis-sense mutation
nonsense mutation
frameshift mutation
mutagen
physical mutagen
chemical mutagen
carcinogenic
mitochondrial DNA (mtDNA)
genetic engineering
recombinant DNA
restriction enzyme
restriction endonuclease
restriction fragment
gel electrophoresis
DNA fingerprint

Much of what you have learned about genetics so far depicts hereditary information as relatively stable. You have seen, for example, how pedigrees trace the inheritance of a single trait through many generations. When Mendel first published his laws of inheritance, one of the objections was that these laws could not account for the newly emerging theory of evolution. If the factors of inheritance remain constant, how can species become adapted to new environments over time?

In fact, genomes are far from stable. In the dynamic environment of a cell, the structure of DNA is constantly changing. Some of these changes are quickly repaired by enzymes in the cell. Other changes are not. A permanent change in the genetic material of an organism is called a **mutation**. All mutations are inheritable. They are copied during DNA replication and passed on to daughter cells. Not all mutations are passed on to future generations, however. Only mutations that affect the genetic information in the gametes of an organism are passed on to the organism's offspring. Mutations that occur in the body cells are called **somatic cell mutations**. As you will learn later in this section, somatic cell mutations are a key cause of cancer. Mutations that occur in reproductive cells are called **germ line mutations**. These mutations are passed on from one generation to the next.

Types of Mutations

Most mutations involve small changes in nucleotide sequence. A chemical change that affects just one or a few nucleotides is called a **point mutation**. A point mutation may involve the *substitution* of one nucleotide for another, or the *insertion* or *deletion* of one or more nucleotides.

A point mutation that involves a nucleotide substitution may have a

relatively minor effect on the metabolism of the cell. One reason for this minor effect is the redundancy of the genetic code. A change in the coding sequence of a gene does not always result in a change to the polypeptide product of the gene. For example, a change in the DNA sense strand sequence from CCT to CCC will not alter the polypeptide produced, since the associated mRNA codons (GGA and GGG, respectively) both code for the same amino acid, glycine.

Even when a point mutation involves the substitution of one amino acid for another, this substitution may not have a significant effect on the final structure or function of the polypeptide produced. A mutation that has no effect on the cell's metabolism is called a **silent mutation**.

In comparison, other substitutions may lead to a slightly altered but still functional polypeptide. A mutation that results in an altered protein is called a **mis-sense mutation**. Mis-sense mutations can be harmful. For example, a change in a single amino acid in one of the polypeptides that makes up hemoglobin is responsible for the genetic blood disorder known as sickle cell disease, which you studied in Chapter 17. On the other hand, mis-sense mutations may help organisms develop new forms of proteins that can meet different requirements. For example, mis-sense mutations may play an important role in generating the enormous variety of antibodies that your body requires to fight new infections.

Unfortunately, some substitutions can have severe consequences. If a change in a gene's coding sequence deletes a start signal or results in a premature stop signal, the gene may be unable to produce a functional protein. Similarly, a nucleotide substitution that affects a *regulatory sequence* may result in the cell being unable to respond properly

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FYI

More than one trillion changes occurred in your DNA during the time it took you to read this sentence. Most—but not all—of these changes will be repaired before they are passed on to daughter cells. Some will remain as mutations in your DNA.

to metabolic signals. A mutation that renders the gene unable to code for a functional polypeptide is called a **nonsense mutation**. Figure 18.16 illustrates how a nucleotide substitution in a single coding sequence can result in a silent, mis-sense, or nonsense mutation.

Nucleotide substitutions do not affect neighbouring coding sequences. The insertion or deletion of one or two nucleotides, however, results in a **frameshift mutation**. A frameshift mutation causes the entire reading frame of the gene to be altered, as shown in Figure 18.17. A shift in the reading frame usually results in a nonsense mutation.

Chromosomal Mutations

Point mutations usually affect only one gene. Mutations that involve a rearrangement of genetic material may affect several genes, including genes

GUU–CAU–UUG–ACU–CCC–GAA–GAA
val – his – leu – thr – pro – glu – glu

A The normal coding sequence, with the codons in the top row and the resulting amino acids below them.

GUU–CAU–UUG–ACC–CCC–GAA–GAA
val – his – leu – thr – pro – glu – glu

B This mutation is silent, since the change in nucleotide sequence has no effect on the polypeptide product.

GUU–CAU–UUG–ACU–CCC–GUA–GAA
val – his – leu – thr – pro – val – glu

C This is a mis-sense mutation, since it causes the amino acid valine to be inserted in the place of glutamate within the polypeptide chain. The resulting protein is unable to transport oxygen effectively and produces a disorder known as sickle cell disease.

GUU–CAU–UAG
val – his – stop

D This substitution causes a nonsense mutation by changing the codon for the amino acid leucine (UUG) into a premature stop codon. No functional polypeptide will be produced from this gene.

Figure 18.16 A nucleotide substitution can have varied effects, as shown on this portion of the gene that codes for human beta-globulin, one of the two polypeptides in the blood protein hemoglobin.

17 What feature of the genetic code helps to protect a cell from the effects of nucleotide substitution?

18 What is a frameshift mutation?

19 Why is a mutation caused by an insertion or a deletion more likely to have serious consequences for a cell than one caused by a substitution?

located on different chromosomes. One example of a chromosomal mutation is crossing over. As you have seen, crossing over recombines genetic material from different chromosomes. Another example is the loss or duplication of portions of chromosomes during DNA replication. This can result in changes to structural or regulatory DNA sequences.

Causes of Mutations

Many mutations are caused by molecular interactions that take place naturally within cells. These mutations are known as *spontaneous mutations*. One source of spontaneous mutations is incorrect base

GUU–CAU–UUG–ACU–CCC–GAA–GAA
val – his – leu – thr – pro – glu – glu

A The normal coding sequence, with the codons in the top row and the resulting amino acids below them.

↓
GUU–CAU–GUU–GAC–UCC–CGA–AGA A
val – his – val – asp – ser – arg – arg

B The insertion of a single nucleotide, in this case guanine, results in a frameshift mutation.

↑
GUU–CAU–UUG–CUC–CCG–AAG–AA
val – his – leu – leu – pro – lys

C Similarly, a deletion of even a single nucleotide, in this case adenine, also results in a frameshift mutation.

Figure 18.17 Frameshift mutations are usually nonsense mutations.

pairing by DNA polymerase during the process of DNA replication. The rate of spontaneous mutations varies among organisms and even among different genes within a single cell.

While every cell undergoes spontaneous mutation, exposure to certain factors in the environment can increase the rate of mutation. Mutations that are caused by agents outside the cell are said to be *induced*. A substance or event that increases the rate of mutation in an organism is called a **mutagen**. Mutagens fall into two general categories: physical and chemical.

Physical Mutagens

Morgan studied the genetics of fruit flies for more than 20 years. During this time, he observed about 400 visible mutations in the tens of millions of fruit flies in his laboratory. In 1926, the American researcher Hermann Muller (one of Morgan's students) bombarded a population of fruit flies with X rays and produced several hundred mutants in a single day. X rays are a form of high-energy radiation. They tear through DNA molecules, causing random changes that range from point mutations to the loss of large portions of chromosomes. Because these mutagens cause physical changes in the structure of DNA, they are known as **physical mutagens**. High-energy radiation, such as that from X rays and gamma rays, is the most damaging form of mutagen known.

Ultraviolet (UV) radiation, which is present in sunlight, has a lower range of energy levels than X rays, but it is still a powerful mutagen. UV radiation can cause a chemical reaction between adjacent pyrimidine (C and T) bases. The result is a distortion in the DNA molecule that interferes with replication. Damage from UV radiation, as a result of exposure to sunlight, is a known cause of melanoma, a form of skin cancer. A single sunburn doubles a light-skinned person's chances of developing skin cancer.

Chemical Mutagens

A **chemical mutagen** is a molecule that can enter the nucleus of a cell and induce mutations by reacting chemically with the DNA. A chemical mutagen may act by inserting itself into the DNA molecule in a manner that causes a nucleotide substitution or a frameshift mutation. Other chemical mutagens have a structure that is similar to the structure of ordinary nucleotides but with different base-pairing properties. When these mutagens are incorporated into a DNA strand, they can cause incorrect nucleotides to be inserted during DNA replication. Examples of chemical mutagens include nitrites (which are sometimes used as a food preservative), gasoline fumes, and more than 50 different compounds found in cigarette smoke.

Most chemical mutagens are **carcinogenic**—that is, they are associated with one or more forms of cancer. As you saw in Chapter 16, cancer is characterized by uncontrolled cell division in somatic cells. In molecular terms, cancer is the result of somatic cell mutations that disrupt the expression of genes involved in the regulation of the cell cycle. While carcinogens are present throughout the environment, personal choices can increase or decrease a person's risk of developing cancer. In Thought Lab 18.3 on the next page, you will examine the relationship between human activities, mutations, and cancer.

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FYI

Genetic material can be rearranged by the activity of transposable elements, also known as jumping genes or *transposons*. Transposable elements are short strands of DNA that are capable of moving from one chromosome to another.

20 Distinguish between the two terms in each pair of terms.

- a) induced mutation and spontaneous mutation
- b) chemical mutagen and physical mutagen

Mutations and Genetic Variation

A single mutation often has little or no effect on a living cell. Over time, however,

a series of spontaneous and induced mutations can add up to more serious damage in a cell. Most cancers are caused by combinations of mutations. Some of these mutations may be inherited, while others may occur as a result of exposure to mutagens in the environment. The fact that mutations accumulate within a cell helps to explain why exposure to carcinogenic factors does not always result in cancer, and why cancer can occur without exposure to any known carcinogens.

The accumulation of mutations over time also gives rise to the tremendous genetic variation among organisms. The study of DNA sequences extracted

from different organisms—including organisms that have been extinct for thousands of years—enables scientists to gather information and make hypotheses about the evolution of different species.

Tracing Ancestry Through Mitochondrial DNA

Earlier in this chapter, you read that almost all organisms have the same genetic code. A significant exception to this universality is the DNA of mitochondria and chloroplasts. These cellular organelles have their own DNA, and their genome is replicated, transcribed, and translated independently from the DNA in the nucleus of the cell in which

Thought Lab 18.3 Investigating Cancer Genes

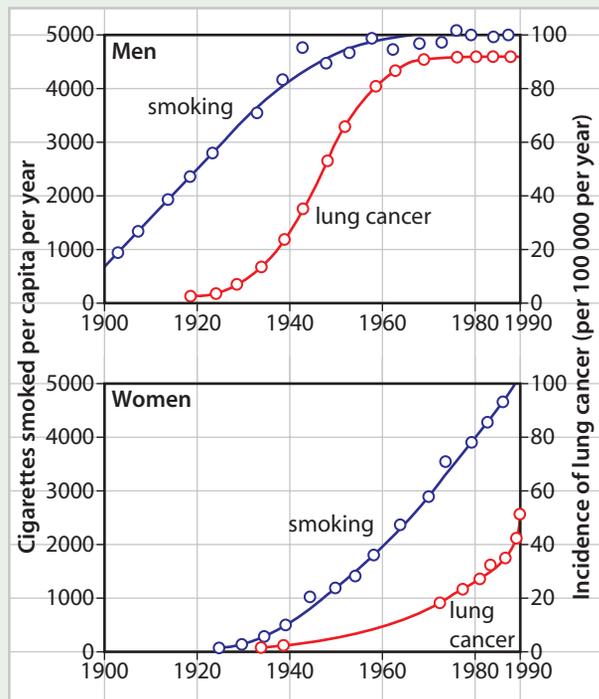
Target Skills

Analyzing relationships from published data between human activities and genetic changes that lead to inheritable mutations and cancer

Working cooperatively to investigate the relationship between human activities and mutations

Lung cancer is the most preventable of all cancers, and yet it is the leading cause of cancer deaths in Canada. In 2005, almost 20 000 Canadians died of lung cancer. Lung cancer is the result of somatic mutations in the cells of the lungs. What can the data indicate about the relationship between human activities and mutation rates?

The changing rates of lung cancer in men and women between 1900 and 1990



Procedure

1. Study the graphs. Write a brief summary of the relationships shown in the graph.
2. Record your ideas about the molecular reactions that may be occurring, based on what you have learned in this chapter.
3. Conduct research to describe one of the molecular reactions that might contribute to the relationship you see in the graph. You may find the following keywords helpful to guide your research:
 - oncogenes
 - stability genes
 - tumour-suppressor genes
 - p53 gene

Analysis

1. Write a brief report to describe how your personal choices can affect the chemical reactions that take place in your cells. How can these reactions in individual cells result in changes to your health and well-being?
2. Compare your research on the molecular reactions related to smoking with your classmates' research. How many different mutagens did your class find?
3. Suppose that you are a communications officer for the Canadian Lung Association. Your job is to help youth between the ages of 10 and 15 understand the risks of smoking. How would you reach this audience? What would your main messages be?

they are found. The expression of their DNA relies on a genetic code that is slightly different from the genetic code shown earlier in Table 18.3. The different genetic code of mitochondria and chloroplasts (along with evidence related to their structures and functions) supports the theory that these organelles were once independent prokaryotic cells. This theory, known as the *endosymbiont theory*, proposes that eukaryotic cells arose through a process in which one species of prokaryote was engulfed by another.

In addition to providing evidence about the origins of eukaryotic organisms, the study of **mitochondrial DNA (mtDNA)** is being used to gather information about the more recent history of individual species. Recall, from Chapter 16, that the cytoplasm in a zygote is donated by the ovum. The sperm cell contributes essentially no cytoplasm, and therefore no cytoplasmic organelles, to its offspring. While the DNA in the nuclei of your cells is made up of an equal combination of DNA from your mother and your father, your mtDNA is genetically identical to the mtDNA of your mother. Her mtDNA, in turn, is identical to the mtDNA of her own mother.

Over the countless generations of human history, mutations have arisen in mtDNA just as they have in nuclear DNA. Therefore, if two people have identical mtDNA sequences, they likely share a relatively recent maternal ancestor. By comparing the nucleotide sequences of the mtDNA of different living people, scientists can deduce lineage patterns that reveal prehistoric relationships among different human populations. Similarly, a comparison of the DNA of mitochondria and chloroplasts can provide information about the evolutionary path of animal and plant species.

Genetic Variation Within Species

The study of biological diversity and evolution usually involves examining genetic variations among different

species. DNA analysis allows scientists to study genetic variations among individuals of the same species, as well. This helps scientists develop an understanding of ancient ecosystems and track the evolution of a species through time.

A crucial tool in the study of biological diversity and evolution is the analysis of non-coding stretches of DNA. These non-coding stretches tend to have a higher mutation rate than the DNA within genes. The higher mutation rate leads to extensive genetic variations among individuals of the same species. These variations, in turn, can be interpreted to deduce patterns of mutations over time. Scientists can extract DNA from ancient plant and animal tissues that have been preserved in the soil. Comparing the DNA of ancient plants, animals, and even bacteria with the DNA of their modern counterparts (using computerized genome databases) can reveal such varied information as the ancestry of modern organisms, the movement of populations through time, the evolution of particular disease-causing bacteria, and the way that ecosystems respond to climate change.

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FYI

In 2005, scientists successfully sequenced the genome of a cave bear (*Ursus spelaeus*) that has been extinct for more than 10 000 years. This was the first sequencing of the DNA of a long-extinct organism.

21 Why is your mitochondrial DNA identical to the mitochondrial DNA of your mother, rather than father?

22 Give two examples of ways that the study of DNA sequences can help scientists learn about genetic relationships, genetic variations, or evolution.

Recombinant DNA

As you have seen, DNA mutations can arise spontaneously or be induced by a variety of environmental factors. Working in a laboratory, researchers can manipulate genetic material to alter genes and blend plant, animal, and bacterial DNA—a process known as **genetic engineering**. A molecule of DNA

that includes genetic material from different sources is called **recombinant DNA**. The pace of change in the field of genetic engineering is rapid. Even so, many of the enzymes and processes that were used in the 1970s still provide the basic tools for genetic engineering today.

Restriction Endonucleases

To defend themselves against infection by foreign DNA, most prokaryotic organisms manufacture one or more enzymes known as restriction enzymes. **Restriction enzymes** catalyze the cleavage of DNA at specific nucleotide sequences. Genetic engineers are especially interested in a specific group of these enzymes called

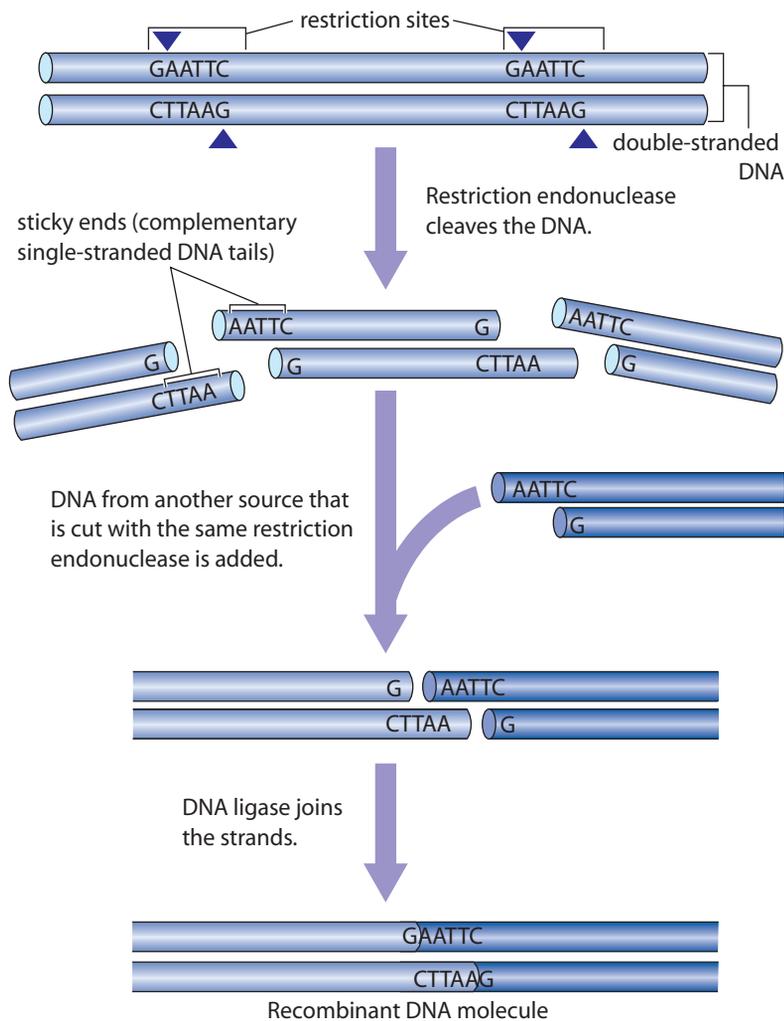


Figure 18.18 The target sequence of the restriction endonuclease known as EcoR1 is GAATTC. Wherever this sequence appears on one strand of a DNA molecule, the same sequence will appear running in the opposite direction on the complementary DNA strand. The result is a set of fragments with exposed complementary nucleotide sequences. These “sticky ends” may base-pair with one another. DNA ligase will then seal the break between them.

restriction endonucleases. The term endonuclease refers to a restriction enzyme that cuts within the interior of a DNA molecule, rather than at the ends.

Restriction endonucleases recognize a short sequence of nucleotides (called the *target sequence*) within a strand of DNA and cut the strand at a particular point within the sequence. This point is known as a *restriction site*. Many different endonucleases have been isolated, and each recognizes a different target sequence. For any given endonuclease, its target sequence will occur by chance in one or more locations in almost any fragment of DNA.

Figure 18.18 illustrates a typical restriction endonuclease reaction. Two characteristics of this reaction makes it useful to genetic researchers:

- **Specificity:** The cuts made by an endonuclease are specific and predictable. That is, the same enzyme will cut a particular strand of DNA the same way each time, producing an identical set of small DNA fragments. These small fragments are called **restriction fragments**.
- **Staggered cuts:** Most restriction endonucleases produce a staggered cut that leaves a few unpaired nucleotides on a single strand at each end of the restriction fragment. These short strands, often referred to as *sticky ends*, can then form base pairs with other short strands that have a complementary sequence. For example, they can base-pair with a restriction fragment produced by the action of the same restriction endonuclease on a different strand of DNA.

Once the sticky ends have formed base pairs with one another, the action of another enzyme, *DNA ligase*, splices them together. The result is a stable recombinant DNA molecule.

23 Explain why these characteristics of restriction endonucleases makes these enzymes useful to genetic engineers.

- a) specificity
- b) staggered cuts

Sorting and Analyzing DNA

Genetic researchers use many different tools to sort and analyze DNA samples. One of these tools is a process called **gel electrophoresis**. Gel electrophoresis is used to separate molecules according to their mass and charge. It can be used to separate fragments of DNA.

The process of gel electrophoresis is illustrated in Figure 18.19. To begin, a solution that contains DNA fragments is applied at one end of a gel. An electric current is then passed through the gel. This causes one end of the gel to develop a positive electric charge and the other end to develop a negative electric charge. Because DNA has a negative charge, the DNA fragments tend to move toward the gel's positive end. The smaller fragments move more quickly. After a period of time, the fragments separate into a pattern of bands. This pattern is called a **DNA fingerprint**.

Together, restriction enzymes and gel electrophoresis help researchers analyze and compare DNA samples. For

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FYI

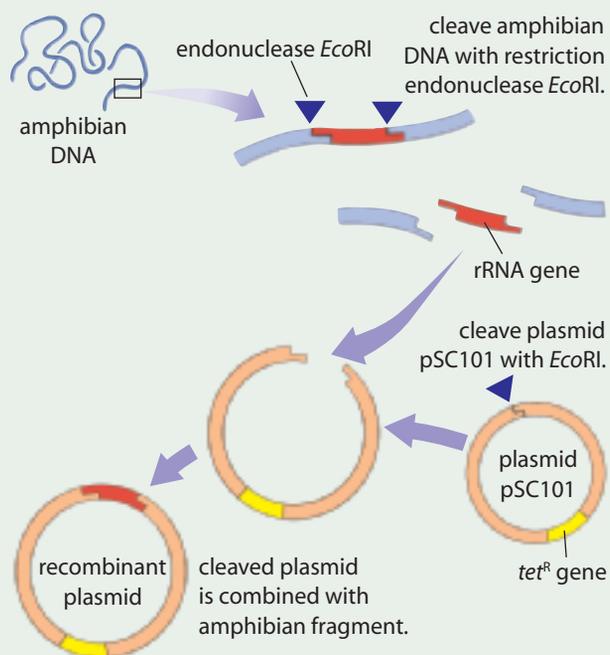
Before a small DNA sample can be analyzed, it must be *amplified*. That is, the DNA must be copied many times to produce a large number of identical DNA molecules. An automated process called the *polymerase chain reaction* can quickly generate billions of copies of a DNA sequence for analysis.

Thought Lab 18.4 Recreating the First Chimera

Target Skills

Performing a simulation to demonstrate the use of restriction endonucleases and DNA ligases

In genetic engineering, a chimera is a genetically engineered organism that contains DNA from unrelated species. The first chimera was created in 1973 by the American team of Stanley Cohen and Herbert Boyer. Bacteria were then exposed to the recombinant plasmid. Those bacteria that displayed tetracycline resistance had taken up the plasmid.



In Cohen and Boyer's experiment, the amphibian gene coded for the production of rRNA. The bacterial gene tet^R conferred resistance to the antibiotic tetracycline. They used the restriction endonuclease *EcoRI* and DNA ligase to splice (insert) a gene from a toad into a molecule of bacterial DNA plasmid pSC101.

Procedure

1. Study the illustration of the Cohen-Boyer experiment. Make a list of the materials that the researchers used.
2. Develop a plan to simulate the experiment. Show how you will use materials in your classroom to represent the materials that Cohen and Boyer used. Then perform your simulation.

Analysis

1. How did your simulation illustrate the action of an endonuclease and a ligase? In what ways was your simulation effective? What were its limitations?
2. The Cohen-Boyer experiment was important because it created a colony of bacterial cells that were resistant to the antibiotic tetracycline and produced amphibian rRNA. What other bacterial phenotypes would have resulted from this experiment? What would each phenotype indicate about events at the molecular level?
3. a) Give one example of how you might use this technology for a social or industrial purpose.
b) What environmental, social, or ethical issues would your experiment raise? Make a list of these issues, and discuss them with other students in your class.

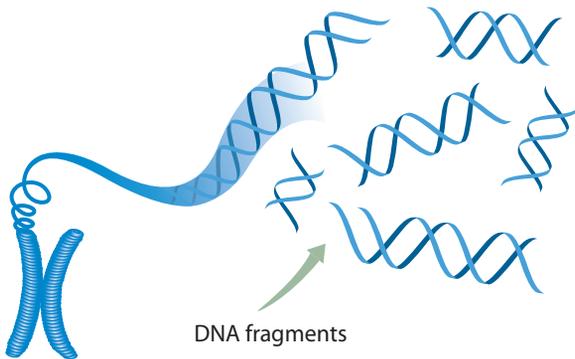
example, investigators at a crime scene might find a small sample of blood or skin tissue. The DNA from this sample can be cut with a restriction enzyme and run on a gel to create a DNA fingerprint. This can be compared with the DNA fingerprint of a suspect in the crime. Since no two people (other than identical

twins) have the same DNA fingerprint, a match is very strong evidence that the suspect was present at the crime scene.

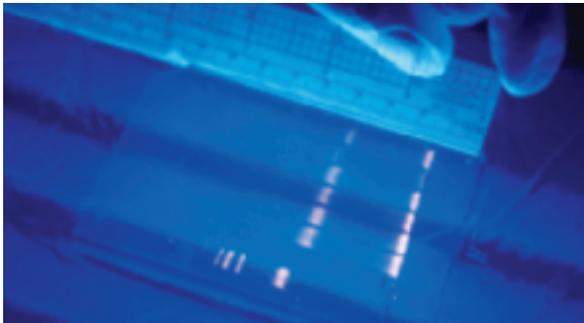
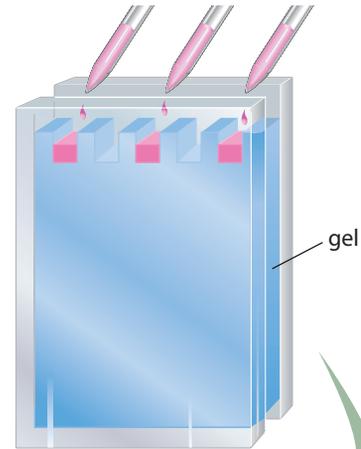
Similarly, DNA fingerprints can be used to solve disputes over parentage. Because DNA is inherited equally from both parents, a child's DNA fingerprint will show some matches with the DNA

Figure 18.19 Gel electrophoresis

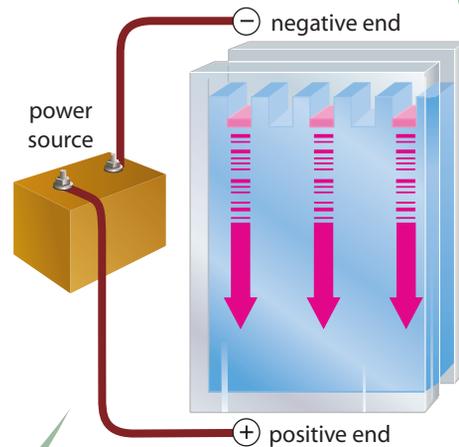
A Restriction enzymes Either one or several restriction enzymes are added to a sample of DNA. The enzymes cut the DNA into fragments.



B The gel A gel, with a consistency similar to gelatin, is formed so small wells are left at one end. Small amounts of the DNA sample are placed into these wells.

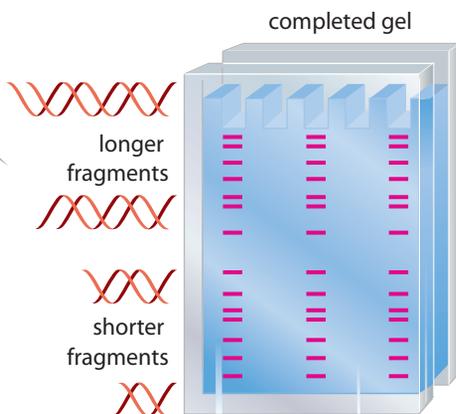


E Before the DNA fragments are added to the wells, they are treated with a dye that glows under ultraviolet light, allowing the bands to be studied.



C The electrical field The gel is placed in a solution, and an electrical field is set up so one end of the gel is positive and the other end is negative.

D The fragments move The negatively charged DNA fragments travel toward the positive end. The smaller the fragment, the faster it moves through the gel. Fragments that are the farthest from the well are the smallest.



Section Outcomes

In this section, you will

- **explain** how the insertion of new DNA sequences into cells can transform organisms
- **describe** some of the social, environmental, and ethical issues associated with genetic technologies

Key Terms

biotechnology
DNA microarray
copy DNA (cDNA)
transgenic
bioremediation
clone
ultrasound
amniocentesis
chorionic villi sampling
genetic marker
DNA probe
gene therapy
DNA vector
somatic gene therapy
germ-line therapy

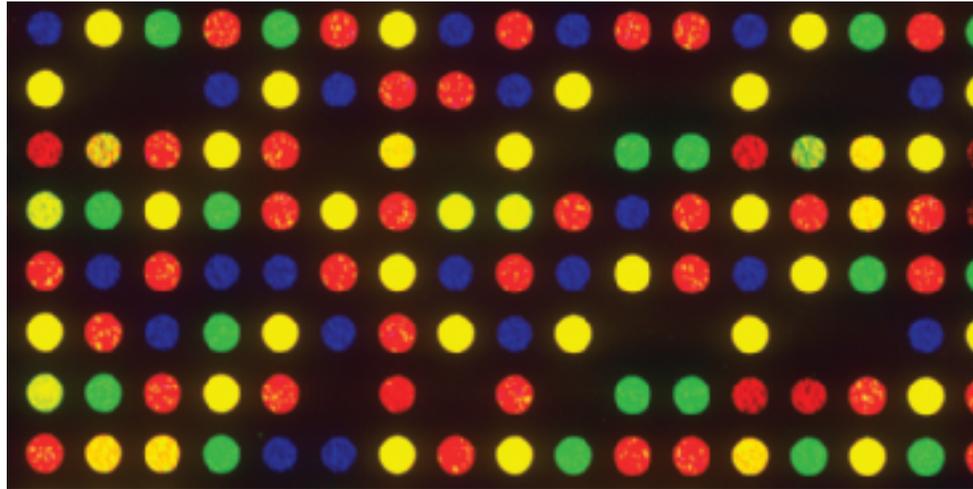


Figure 18.20 The results of a DNA microarray analysis comparing gene expression in two different cell samples. The red spots indicate genes that are expressed only by cells in the first sample, and the green spots indicate genes that are expressed only by cells in the second sample. The yellow spots indicate genes that are expressed by cells in both samples.

Biotechnology is the use of natural biological systems to create new technologies and products. Few sciences have as much potential as biotechnology to change the way we live—from the way we diagnose and treat diseases to the food we eat, the industries we work in, the air we breathe, and even the way we define life itself. Few technologies raise as broad a range of challenging social, ethical, and legal questions. Genetic engineering is one of the fastest-growing areas of biotechnology.

Gathering and Managing Genetic Information

As you have learned, one of the most important tools in the development of genetic engineering has been computers that are capable of handling the enormous amounts of information encoded in a eukaryotic genome. Genetics researchers use computerized gene banks and DNA libraries to store and organize genetic information.

Another important tool is a **DNA microarray**. A DNA microarray is a chip (usually a glass microscope slide or a polymer membrane) that contains a grid

of thousands of microscopic cells. Each cell contains a nucleic acid sequence that can bind with one of the mRNA molecules transcribed during gene expression. A typical microarray experiment includes the following steps:

1. mRNA is extracted from the cell or cells to be studied.
2. mRNA from each cell sample is used as a template to synthesize an artificial form of DNA, called **copy DNA (cDNA)**. The cDNA from each sample is marked by a fluorescent tag for later identification.
3. The labelled cDNA samples are incubated with the microarray. The cDNA binds to the microarray at locations that correspond to individual genes in the cell genome.
4. The microarray is scanned and analyzed to compare the patterns of gene expression in each cell sample.

The results of a typical microarray experiment are shown in Figure 18.20. A DNA microarray allows scientists to analyze the activity of thousands of genes at once. For example, a microarray can be used to compare the genes expressed

by the same cell in different environments, or to compare the genes expressed by healthy and cancerous cells. The results of a microarray allow scientists to pinpoint the genes that are responsible for particular functions or conditions, to study the interactions among genes, or to gather information about the relationship between environmental conditions and gene expression.

24 What is a DNA microarray, and for what purpose is it used?

Public Benefits of Genetic Research

Technologies such as DNA microarrays, and similar protein microarrays, enable scientists to analyze the enormous quantity of information that is gathered through studies such as the Human Genome Project. Some of the most important benefits of these technologies are in the area of human medicine. Studying the human genome, as a whole, offers the potential for developing drugs that are tailored not only to the expression of individual genes associated with particular disorders, but also to the unique genome of a patient. Studying the differences in gene expression among individuals can help medical researchers understand why certain drugs work better in some people than in others, and why certain people experience side effects from medications. The findings support the development of new techniques for predicting risks and diagnosing medical conditions.

All the research gathered through the Human Genome Project is publicly available. By making this a condition of the project, the scientists were able to share much of what they learned about human genetics. In other areas of genetic research, however, the relationship between public and private information is more complex.

25 What kind of information can a DNA microarray analysis provide?

26 How would medical researchers benefit from studying the human genome as a whole, rather than studying individual genes? Give an example.

Ownership of Genetic Information

In 2005, the National Geographic Society and the company IBM jointly launched the *Genographic Project*, a five-year venture to use DNA samples provided by volunteers around the world as a tool to learn more about the migrations of ancient peoples. Projects such as this can contribute valuable information to researchers in many fields. Who owns the genetic information, however? For example, should companies have the right to sell DNA information to other companies without the permission of the people who provided the samples? Should companies that use DNA in medical research be required to share the results of their work with the individuals or communities whose genetic information was used?

Many people argue that genetic information is a natural resource that belongs to everyone. Other people believe that an individual's genetic information belongs only to this individual. On the other hand, if companies cannot earn a profit from their research, there is little incentive for them to invest in genetic studies. In the world of genetics, where is the boundary between public and private property?

Patenting Organisms and Genes

When Saskatchewan farmer Percy Schmeizer met the international biotechnology corporation Monsanto in court, the case revolved around Monsanto's right to control how farmers use its products. Monsanto is the developer of

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Web Link

Different countries have developed different laws related to patenting genetic information. How do the laws in Canada compare with the laws in the United States, Europe, or Japan? Which country's laws do you think are more effective?



Roundup-Ready™ Canola, a genetically-engineered form of canola that is resistant to the herbicide Roundup™ (also produced by Monsanto).

This genetically modified plant has helped farmers increase their crop yields and save money on herbicide applications. Its use is also changing farming practices, however. Traditionally, farmers save seeds from one year's crop to plant the following year. Farmers also exchange seeds with one another. When plants appear by chance in a farmer's field—for example, as a result of seeds blown by the wind or dropped by passing birds—the farmer has had the opportunity to decide whether to keep or remove them. Farmers who buy seeds from Monsanto must agree not to save any seeds from their crop, but to buy fresh seeds every year. The farmers are not permitted to exchange Monsanto seeds with other farmers. If Roundup-Ready™ Canola appears by accident in their fields, they must remove and destroy the plants. These regulations provide a way for Monsanto to earn a profit from its work.

In the end, the Canadian courts upheld Monsanto's right to patent the Roundup-Ready™ gene and to control the use and distribution of its seeds. Many people remain skeptical about the growing role of global biotechnology companies in the production of crop plants. Some people are concerned about the loss of traditional ways of life and the increasing dependence of farmers on the corporations that patent seeds. Others are concerned about world food production becoming concentrated in the hands of private companies. These companies, however, play an important role in genetics research and in the development of gene technologies and products that have important public benefits. Gene patents offer a way to reward their investment and innovation.

The issue of gene patents extends to other fields, including medicine. For example, imagine that a company has identified the location and function

of a gene associated with breast cancer. Should the company be allowed to patent the gene? What if this means that the company then has control over all the treatments that affect the function of the gene? Governments, companies, and individuals around the world are grappling with the legal and ethical questions associated with the ownership of genetic information.

Biotechnology Products

Earlier in this chapter, you learned how genetic engineers insert foreign DNA into bacteria. Genetic engineers have also refined techniques for importing foreign DNA into plants and animals. The result of a procedure like this is a **transgenic** organism. A transgenic organism, such as the one shown in Figure 18.21, is an organism whose genetic material includes DNA from a different species. Below are just a few examples of some of the ways in which transgenic organisms are being used.

Medicinal Bacteria

In 1982, human insulin synthesized by transgenic bacteria was approved for

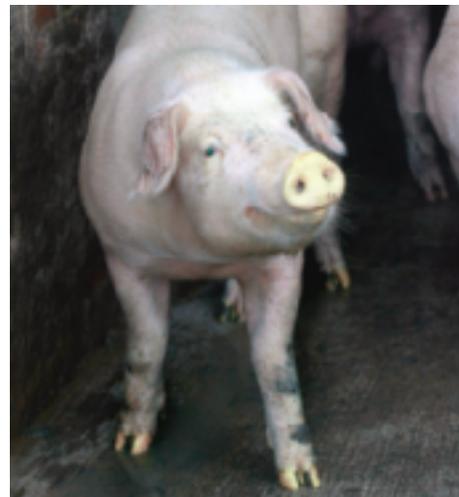


Figure 18.21 Pigs are often used as laboratory models in the study of human disorders and diseases. The embryos of these pigs, bred by Taiwanese researchers studying stem cells, were injected with green, fluorescent proteins from jellyfish. The pigs' internal organs are green, while external features such as eyes, mouths, and knuckles are a lighter, greenish tint.

medical use in the United States. This was the first example of a genetically engineered pharmaceutical product. Because bacteria can be cultured in large quantities at a relatively low cost, researchers are studying ways to use bacterial colonies to produce the polypeptides that form the basis for many medicines. This work can help to make medicines available at a lower cost.

Genetically-modified bacteria can support human health in other ways, as well. Some bacteria naturally degrade toxic substances, such as polychlorinated biphenyls (PCBs). Genetic engineering can enhance these metabolic functions, creating colonies of bacteria that can be used to clean up soils polluted with PCBs. The use of living cells for environmental remediation is known as **bioremediation**. Other examples of bioremediation include bacteria that have been designed to clean up oil spills, to filter air from factory smokestacks, or to remove heavy metals from water.

Transgenic Plants

Crop plants that contain recombinant DNA now account for over half the corn and canola produced in North America. Many of these plants have been modified to increase their resistance to herbicides, insect pests, or viruses. Genetic

engineering has made it possible for crops to be grown in new places, as well, by creating transgenic plants that are tolerant of drought or that can be grown in colder climates.

Some people argue that the real promise of plant genetic engineering is in the production of plants with increased nutrition value. Around the world, millions of people suffer from malnutrition because they lack access to sufficient food and balanced diets. In many developing countries, where rice is the main staple food, symptoms of iron and vitamin A deficiencies affect hundreds of thousands of people. In 2000, Swiss researchers developed a genetically modified strain of rice known as golden rice. As shown in Figure 18.22, this rice has been genetically engineered to increase its iron and vitamin A content. Golden rice is now available as a staple part of the food aid delivered to many developing countries.

Cloned and Transgenic Animals

Organisms that are genetically identical are said to be **clones** of one another. As you learned in Chapter 16, identical twins form when a single zygote develops into two fetuses. Identical twins are clones that arise naturally in animal populations. For many years, researchers

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Golden rice has wide-ranging humanitarian benefits, but it is not without controversy, both scientific and social. What concerns have been raised about this genetically modified food? How have those concerns been responded to, and what questions still remain?

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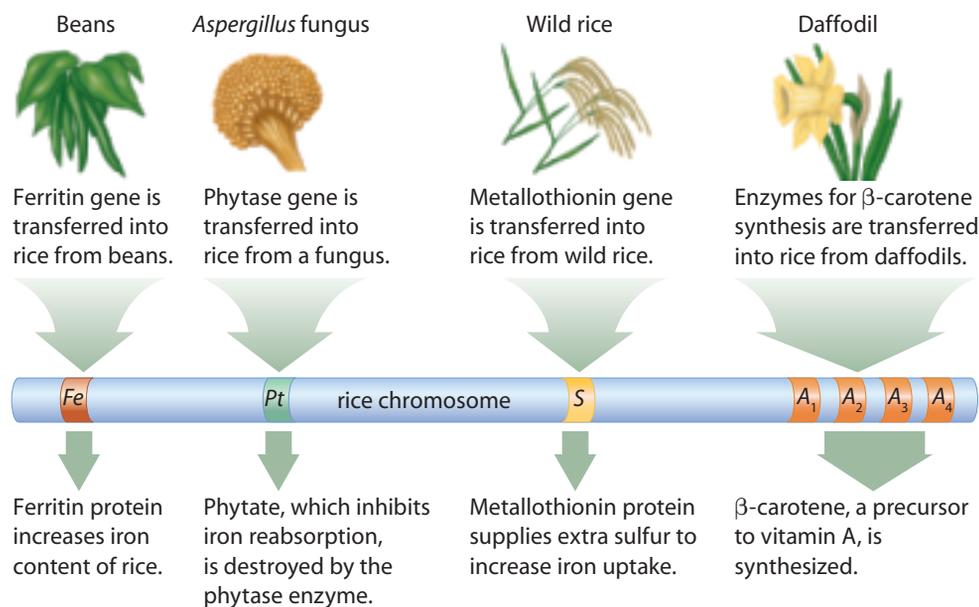


Figure 18.22 The transgenic product, golden rice, contains four different foreign genes. Three of these genes come from other plants, and one comes from a fungus.

believed that animals could not be cloned artificially. In the 1990s, however, researchers were successful in using the cells of mouse embryos to produce cloned mice. In 1997, the Scottish researcher Ian Wilmut and his team created the cloned sheep Dolly. They were the first scientists to clone a mammal successfully, using a cell from an adult donor. Figure 18.23 shows the basic steps in their cloning procedure.

Since the “invention” of Dolly, researchers have successfully used similar techniques to clone other mammals. Cloned offspring suffer from a high mortality rate, however, as well as a high incidence of disease. Many also show

signs of metabolic disorders, such as premature aging. Outcomes such as these reflect the need for ongoing research into the complexities of gene expression in animals.

Other forms of animal genetic engineering have been more successful. Researchers have been able to create new varieties of animals with useful traits. For example, transgenic milk-producing animals, such as goats, are being used to produce pharmaceutical products. Figure 18.24 shows the main steps in creating a herd of goats that are genetically modified to secrete a human polypeptide in their milk.

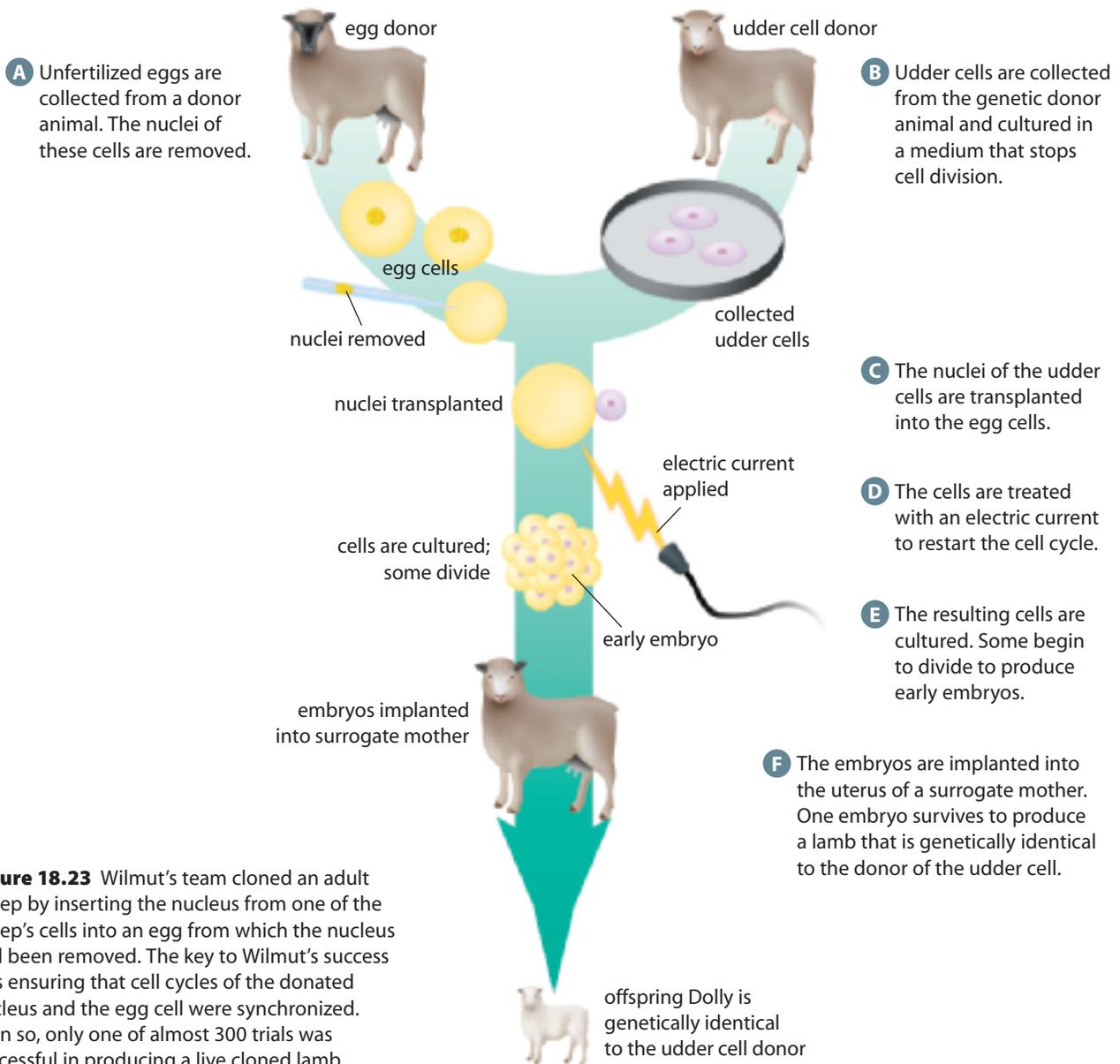


Figure 18.23 Wilmut’s team cloned an adult sheep by inserting the nucleus from one of the sheep’s cells into an egg from which the nucleus had been removed. The key to Wilmut’s success was ensuring that cell cycles of the donated nucleus and the egg cell were synchronized. Even so, only one of almost 300 trials was successful in producing a live cloned lamb.

Similar steps have been used by a Canadian research company to insert a spider gene into goats. The transgenic goats secrete spider silk in their milk. The silk can be extracted and spun into lightweight, strong fibres with many uses.

Another area of research involves developing transgenic animals that can serve as organ donors for humans. Usually, the transplantation of organs from animals, such as pigs, into human patients has very limited success because an antigen that is produced by the animal cells causes a serious immune response. Some genetic engineering research teams are conducting work to develop transgenic pigs that produce a human version of the antigen, or no antigen at all. These pigs could become a source of organs that are more compatible to the human body. Research such as this also raises some difficult issues, however. Some people are concerned about the risk of transferring diseases from pigs to humans. Other people ask whether it is ethical to create new kinds of animals purely for the purpose of harvesting their organs.

Assessing the Risks

In Canada, proposals for the development and use of transgenic products are reviewed by government agencies, such as Health Canada and the Canadian Food Inspection Agency. When deciding whether or not to approve a transgenic product for use in Canada, these agencies consider a number of criteria, including

- the potential social, economic, and environmental costs and benefits
- the process by which the product was made, including the source of the genetic material
- the biological characteristics of the transgenic product, compared with the characteristics of the natural variety
- the potential health effects, including the possibility that the product may contain toxins or allergens

Despite the review process, many organizations and citizen groups have opposed the use of transgenic organisms.

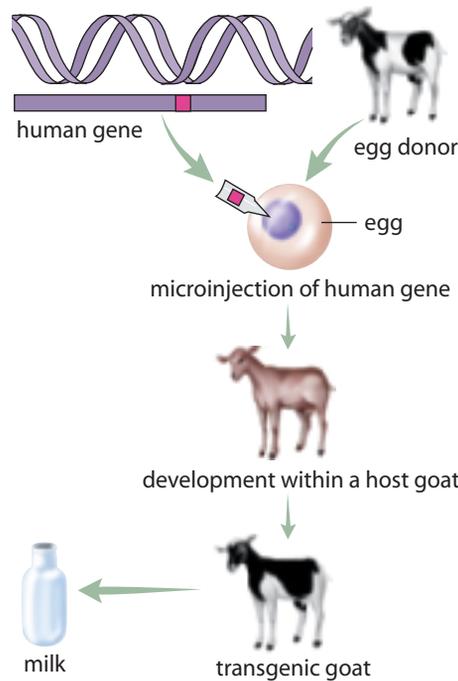


Figure 18.24 Genetic engineering can create transgenic mammals that secrete human proteins or other substances in their milk.

Below are some of the risks cited by these groups.

- **Environmental threats:** The use of herbicide-resistant plants could encourage farmers to use higher levels of herbicides. This, in turn, could lead to a buildup of herbicide chemicals in water supplies and neighbouring ecosystems. As well, there is evidence that engineered genes can be transferred to wild plants and other organisms, raising concerns about the emergence of “superweeds” and “superbugs.” More generally, ecosystems involve complex and delicate balances among many different organisms. The introduction of transgenic bacteria, plants, or animals could upset these balances, with unknown results.
- **Health effects:** Many consumer groups argue that not enough is known about the long-term effects of consuming transgenic products, including genetically modified foods and medicines. The complex processes of gene regulation are not well understood, so it is difficult to predict potential health risks.
- **Social and economic issues:** Advocates of genetically modified foods argue that these foods will help to improve

human health and alleviate world hunger. Their opponents argue that genetic research absorbs millions of dollars, which would be better spent directly helping people in need. In addition, as mentioned earlier, many people are concerned about the growing influence of private corporations over global food production. The treatment of plants and animals as commodities to be manipulated and patented also raises questions about our relationships with—and responsibilities to—other living organisms.

27 How can transgenic organisms help to achieve social, economic, or environmental goals? Give one example of a transgenic bacterium, transgenic plant, and transgenic animal designed for one of these goals.

28 Give two examples of social, legal, or moral issues that are associated with the development of transgenic organisms.

The Diagnosis and Treatment of Genetic Disorders

Geneticists have identified the genes associated with more than 2000 human disorders, ranging from prostate cancer to insomnia. In some cases, a single defective gene is responsible for a particular disorder. In other cases, a certain gene may put an individual at a higher risk for developing a disorder. A number of technologies offer different ways to diagnose and treat genetic conditions.

Prenatal Diagnosis and Genetic Screening

In Chapter 17, you learned how to predict the chance that a child might inherit a particular genetic condition from his or her parents. If a woman has already conceived, several tests can be done to find out whether the fetus has an

inherited disorder. Figure 18.25 shows an **ultrasound** image of a developing fetus. During an ultrasound procedure, sound waves beyond the limit of human hearing are sent through the amniotic fluid. The sound waves bounce off the developing fetus and are used to create a cross-sectional image of the fetus. This image can reveal physical abnormalities, such as a missing limb, malformed heart, or cleft palate. Many other genetic conditions, however, can be identified only by analyzing a tissue sample from the fetus.

In Chapter 17, you also learned how a karyotype can be used to identify chromosomal disorders, such as Down syndrome. The risk of having a baby with Down syndrome increases if the mother is over 40 years old. To find out whether her developing fetus is affected, a woman may choose to have an **amniocentesis**. As shown in Figure 18.26, in an amniocentesis, a needle is used to withdraw a small sample of amniotic fluid from the uterus. The extracted fluid is placed in a special nutrient-rich medium and the cells are allowed to multiply. When the cell sample is large enough, researchers can prepare a karyotype or another genetic analysis.

Due to the risk of injuring the fetus, an amniocentesis cannot be done before the fourteenth week of pregnancy. After that, weeks may pass before the results



Figure 18.25 An ultrasound image like this one can provide information about genetic conditions that have visible effects.

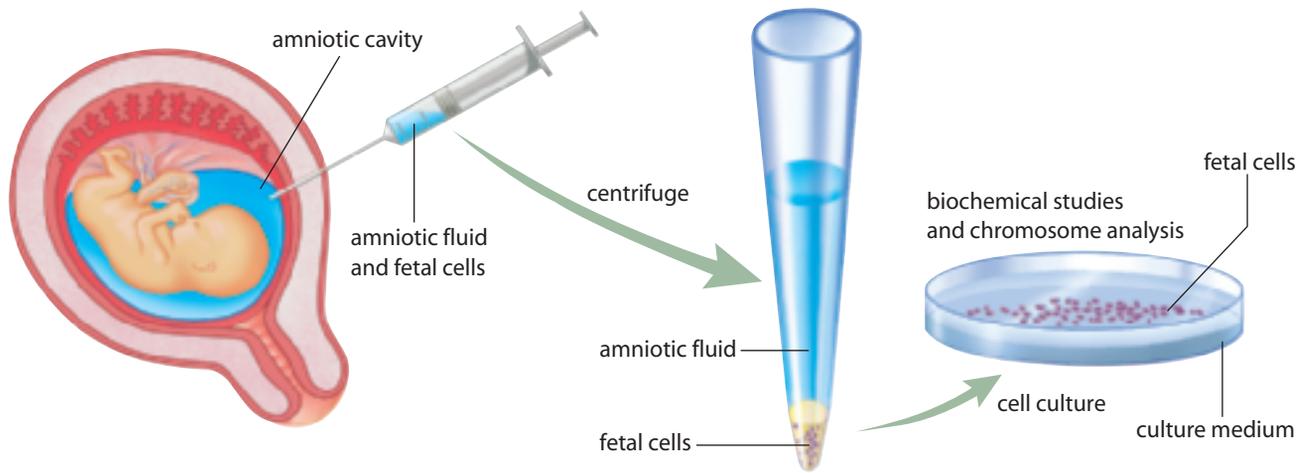


Figure 18.26

Amniocentesis enables analysts to perform about 40 tests for different genetic problems. Because few cells are available in the amniotic fluid, up to four weeks may be needed to wait for sufficient numbers to develop in the culture medium.

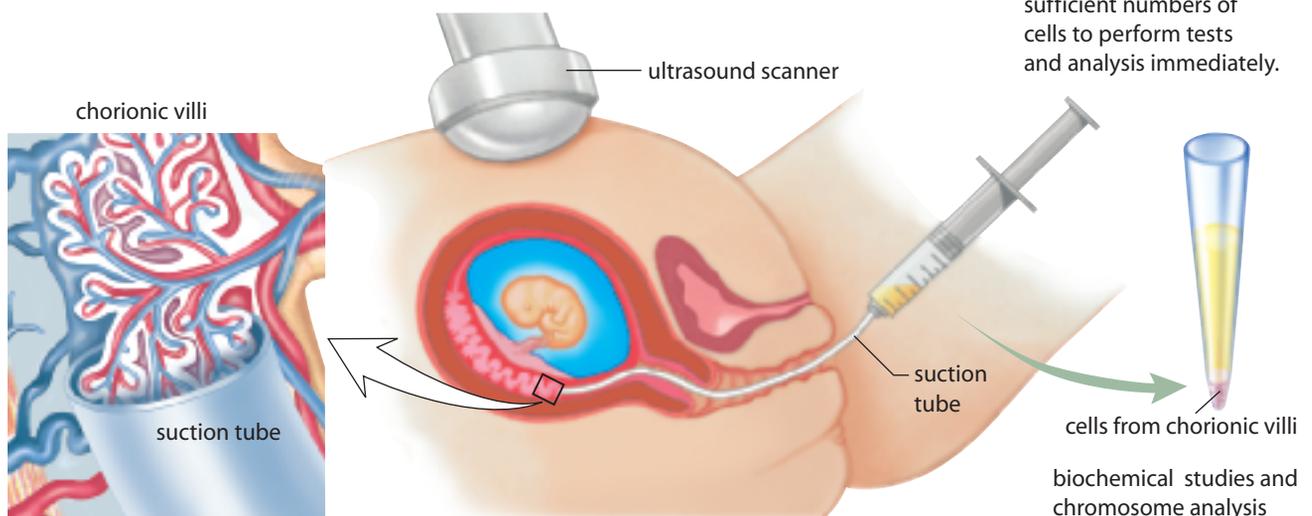
are available. A woman who is interested in obtaining results sooner may opt for a procedure called **chorionic villi sampling** (see Figure 18.27). Around the ninth week of pregnancy, cells can be removed from the chorion, a tissue that surrounds the amniotic sac. The chorion is one of the tissues that make up the placenta. The chorionic cells are fetal cells, and therefore they carry the same genetic information as the developing fetus. A sample of chorionic cells can be used to prepare a karyotype.

Genetic material from a fetal tissue sample—or from a child or adult—can also be screened for specific **genetic markers**. A genetic marker is a characteristic that provides information about the genotype of an individual. Think about Mendel’s pea plants, for example. The white flowers were a genetic marker

indicating the homozygous recessive genotype *rr*. Genetic markers for many human genetic disorders have also been identified at the molecular level. For example, a genetic marker may be a nucleotide sequence that is known to be associated with, or even part of, the gene of interest.

A genetic marker can be found using a **DNA probe**. A DNA probe consists of a molecule of DNA with a nucleic acid sequence that is complementary to the marker sequence, “marked” with a radioactive or fluorescent chemical tag. DNA from the tissue sample is placed in a suspension with the DNA probe. If the DNA sample contains the gene of interest, the probe will bind to the marker sequence. Using the tag, researchers can verify the presence of the gene of interest.

Figure 18.27 Chorionic villi sampling provides sufficient numbers of cells to perform tests and analysis immediately.



29 What kind of genetic information can be obtained from each of the following procedures?

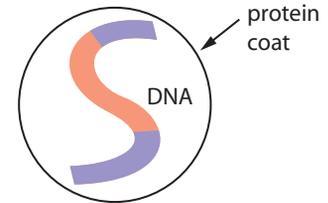
- a) ultrasound
- b) amniocentesis
- c) DNA probe

Treating Human Genetic Disorders

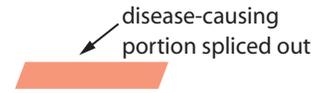
Since the 1990s, researchers have been exploring ways to treat genetic conditions by correcting the functions of the defective genes. The process of changing the function of a gene in order to treat or prevent a genetic disorder is called **gene therapy**. The results of gene therapy trials show that some disorders, such as diabetes and Parkinson's disease, can be combated by targeting their genetic causes, rather than simply treating their symptoms.

In gene therapy, a molecule called a **DNA vector** carries foreign DNA into target cells in the patient. One type of DNA vector commonly used in gene therapy trials is a modified form of virus. Viruses are well-suited to gene therapy because most have the ability to target certain types of living cells and to insert their DNA into the genomes of these cells. Using restriction endonucleases, viruses can be genetically altered to carry a desired gene. Figure 18.28 shows the basic steps in creating a viral vector.

The benefits of using viruses in gene therapy are countered by some risks. Even though disease-causing genes are first spliced out of the viral genome, the remaining viral protein coat can trigger an immune response, including high fever and organ failure. Several deaths in clinical trials have been attributed to an immune response. As well, some researchers are concerned that a disarmed virus in the body might be able to regain its pathogenic properties if it comes in contact with other viruses. Because of the risks associated with viral vectors, researchers are exploring other forms of vectors, including artificial chromosomes.



A The intact virus is made up of a protein coat containing a strand of DNA.



B The viral DNA is isolated and the disease-causing portion of the viral genome (red) is spliced out. Genes coding for the enzymes that allow the virus to insert its DNA into the genome (blue) of its host cell are left intact.



C A working human gene (green) is inserted into the viral genome. The modified viruses are then cultured with human cells. Some of the viruses will transfer the new gene into the cells' genome.

Figure 18.28 Viruses can be modified and used as vectors to carry new genes into a human cell. The human immunodeficiency virus (HIV)—one of the deadliest viruses known—has the potential to be a very powerful viral vector. The viruses that cause common colds are also useful vectors.

As researchers strive to make gene therapy an effective medical tool, some individuals and organizations are raising concerns about the ethical and moral aspects of manipulating the human genome. So far, all gene therapy trials in humans have focused on **somatic gene therapy**—that is, therapy aimed at correcting genetic disorders in somatic cells. While somatic gene therapy can improve the health of a patient, it does not prevent the disorder from being passed on to the patient's children.

One of the most controversial types of gene therapy is **germ-line therapy** gene therapy used to modify the genetic information carried in egg and sperm cells. In theory, this kind of therapy could eliminate inherited genetic

disorders. In reality, however, it could have many unforeseen effects on future generations. Human germ-line therapy research is currently banned in Canada and in many other countries.

Like other genetic technologies, genetic screening and gene therapy research raise difficult ethical issues. For example, what genetic conditions should be considered “disorders” that deserve treatment? How much control should parents have over the “design” of their babies? The potential benefits of all biotechnologies must constantly be balanced by public interests and beliefs. Governments, companies, communities, and individuals all play a role in the lively debate that is helping to chart the future course of genetic research.

Section 18.4 Summary

- Tools such as DNA microarrays enable researchers to examine the expression and interaction of thousands of genes at once. This provides a way to study the genetic processes that underlie many diseases and offers the possibility of developing individually tailored treatments.

- The development of transgenic organisms that contain recombinant DNA is changing agriculture, industries, and society.
- Many people have concerns about the risks associated with genetic research. Among the concerns are the potential environmental, health, social, and ethical impacts of creating new organisms and releasing them into the world.
- Gene therapy experiments and clinical trials in humans have had some success, but they also carry some risks.
- Gene therapy involves inserting new genes into human cells.
- Geneticists distinguish between somatic gene therapy (which changes the genetic information in somatic cells) and germ-line therapy (which alters the genetic information carried in reproductive cells, and therefore influences the genetic make-up of future generations).
- Although gene therapy is likely to become a powerful treatment for disorders such as cancer, its applications raise difficult social and ethical issues.

Section 18.4 Review

1. Describe two of the potential applications of the genetic research conducted through the Human Genome Project.
2. What is a DNA microarray? Why is it a useful tool for genetic research?
3. Imagine that you have been hired as an advisor to an international body that establishes conventions for genetic research. Your job is to develop a policy on the collection and ownership of genetic information.
 - a) What are some of the issues you will consider?
 - b) Briefly summarize how your policy will balance public and private interests.
4. A private company has developed a transgenic carrot that secretes its own pesticide. This carrot is therefore resistant to the insects and worms that often damage root crops.
 - a) What are some of the risks and benefits that the Canadian government will consider when deciding whether to approve this plant for agricultural use?
 - b) If approved, what advantages will this transgenic carrot offer to farmers? What are some potential drawbacks for farmers?
 - c) Do you believe that foods produced with genetically modified ingredients (such as this carrot) should be labelled for consumers? List your arguments. Then list some of the arguments you could make to support the other side.
5. Briefly describe how each of the following procedures can contribute to the diagnosis of genetic conditions.
 - a) ultrasound
 - b) chorionic villi sampling
6. What is a DNA probe? How is it used to screen for genetic conditions?
7. Describe the difference between somatic gene therapy and germ-line therapy. How could each be used in the treatment of cancer?

Biotechnology: Assessing Unintended Consequences

Would you approve of a new technology that could lead to the death of hundreds of thousands of people every year and drastically alter the environment around the world? If not, you would not have welcomed the automobile.

We are living during the early years of a developing biotechnology industry. Like the automobile industry, biotechnology is certain to have a widespread impact on society. Few people in the 1920s foresaw how vehicle exhausts would eventually contribute to air pollution and global warming. Similarly, the long-term effects of biotechnology are unpredictable. How can society balance the benefits and risks of new technologies when some of their outcomes are uncertain?

Predicting Complex Systems

Is genetically modified (GM) food harmful or beneficial? Research data supports both sides. To understand why, consider the following characteristics of any complex system, such as food production:

- A complex system has many components, which are interconnected.
- The components of a complex system are dynamic. That is, they can change independently of control by a central agent.
- Some components are not easily observed or measured, but nevertheless affect the operation of the system.
- Our ideas and models of systems may be incorrect due to lack of knowledge and incorrect hypotheses.

These four characteristics mean that we can never be certain about the results of altering a complex system. The results that we intend by adding something new to a system may not be the results that actually occur.

Speed of Change

Another difficulty of controlling the impact of biotechnology is the speed with which new technologies spread. Genetic engineering passed from laboratories to farms and hospitals before governments fully studied its implications. GM foods were on store shelves while people still debated issues of safety, regulation, and labelling.

The Precautionary Principle

In Europe, in the 1960s and 1970s, groups concerned about the potential impacts of new technologies developed an idea called the *precautionary principle*. Various versions of this idea have since been included in many international treaties. A key point of the precautionary principle is that governments should act in advance, as a precaution, to prevent potential harm from new technologies. Furthermore, governments should act even when neither danger nor the effectiveness of the preventive measures have been demonstrated scientifically.

Although the precautionary principle appears to be a reasonable approach to reducing unknown risks, it has also had unintended consequences. For example, during 2002, millions of people in southern Africa were at risk of famine as a result of severe droughts that had reduced crop yields in several countries. The United States offered corn and soybean products to these countries, but the aid was initially rejected because of concerns that the food included GM plants. These countries had to choose between certain widespread starvation or uncertain, unproven, and even undefined future risks from GM crops.

Making an Analysis

The difficulty of predicting the effects of a new technology does not mean that we must reject the technology or give up the effort to control or reduce its risks. Consider automobiles, for example. Over time, governments have developed regulations governing speed limits, emission controls, fuel efficiency, safety design, and seat-belt use to reduce the harm from automobiles.

•••

1. Do you think government regulations are the best way to protect people from the potential risks of biotechnology? Explain why or why not.
2. Do the risks and benefits of a new technology affect everybody in society equally? Do you think they should? What is your opinion?

Research to determine the physical basis of heredity and the molecular structure of DNA involved many different teams over several decades. Watson and Crick were the first scientists to prepare a physical model of DNA that could account for all the experimental evidence.

DNA is made up of two strands of nucleotides. These two strands wind around one another to form a double helix. The two strands of the double helix are complementary and antiparallel. The base-pairing properties of DNA provide a mechanism for accurate replication.

The nucleotides along a strand of DNA make up three-letter codons in the genetic code. Each codon corresponds to one amino acid. The genetic code is nearly universal among living organisms.

The path of gene expression involves two processes: the transcription of DNA into RNA, and the translation of RNA

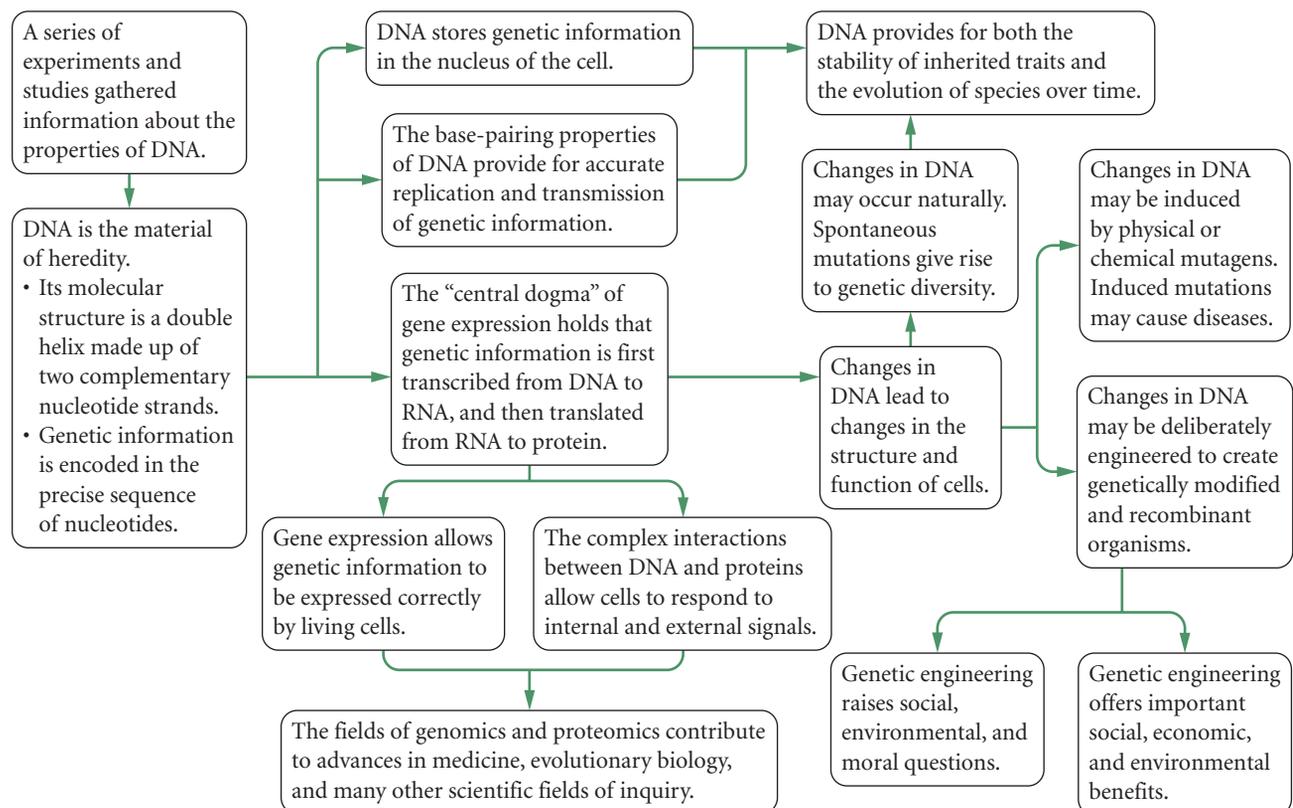
into protein. These processes involve several types of RNA, as well as enzymes.

A mutation is a permanent change in the DNA sequence in a cell. Mutations that affect genetic material in gametes can contribute to genetic variation within species. Mutations can be spontaneous or induced. Several factors contribute to the severity of a mutation.

Using restriction endonucleases and DNA ligase, genetic engineers can splice genes from one organism into the genome of another. The development of this technology has led to the development of transgenic organisms which have benefits and costs for humans and the environment.

Researchers can use a variety of techniques to diagnose and screen for genetic conditions, both before and after birth. Gene therapy offers an avenue for the treatment of many disorders, but it raises some difficult moral and ethical questions.

Chapter 18 Graphic Organizer



Understanding Concepts

- Describe the main steps in the 1952 experiment by Alfred Hershey and Martha Chase. What was the significance of their experiment?
- Define Chargaff's rule. How did Chargaff's findings overturn earlier beliefs about DNA?
- Using symbols to represent the different nucleotides, illustrate the molecular structure of a portion of a double-stranded DNA molecule.
- What is the base sequence of a DNA strand that is complementary to a strand with the sequence TTCGAATCGA?
- DNA can only be synthesized in one direction. The replication of DNA strands, however, proceeds in two directions at once. Use a labelled diagram to show how this is possible.
- Arrange the following events in the order in which they occur during the replication of a single portion of a DNA molecule:
 - Primase synthesizes a new RNA strand.
 - Helicases cleave DNA.
 - Ligase binds nucleotides together.
 - DNA polymerase adds nucleotides to a fragment of DNA.
- How does the base-pairing property of DNA contribute to the proofreading function of DNA polymerase?
- Name three characteristics of the genetic code, and explain why they are significant.
- Define the following terms, and explain their significance with respect to gene expression.
 - codon
 - anticodon
 - ribosome
- Create a table that compares the various types of RNA and their roles in gene expression.
- Using examples, explain the difference between a physical mutagen and a chemical mutagen.
- Explain what a restriction endonuclease does. What two features of this action are particularly useful for genetic engineers?
- Would restriction endonucleases still be of use in genetic engineering if DNA ligase were not available? Explain.
- Three different adult sheep were involved in the cloning process that led to the birth of the lamb Dolly.
 - What were their roles?
 - Which one was Dolly's clone?
- Briefly explain how each of the following procedures could be used to diagnose or treat a genetic condition.
 - ultrasound
 - fetoscopy
 - chorionic villi sampling
 - amniocentesis

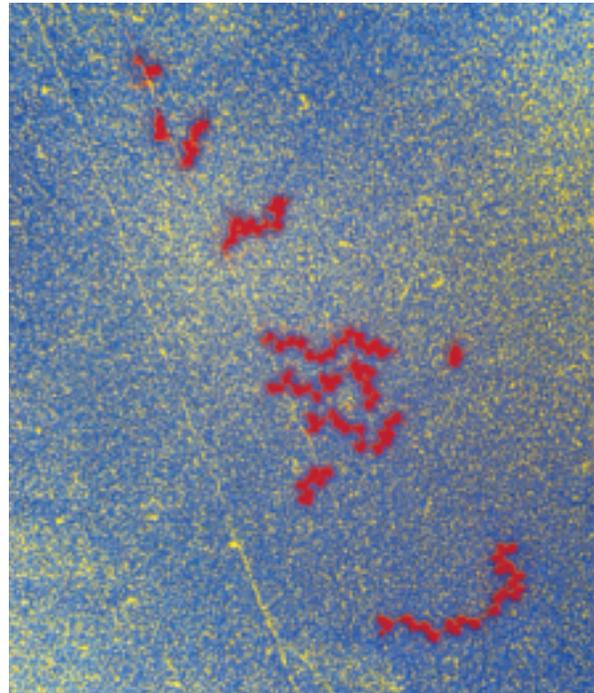
Applying Concepts

- Imagine that you have isolated the genetic material of a particular strain of virus. Your analysis of the genetic material indicates the following base composition:

Nucleotide	Presence in (%)
A	36
C	24
G	18
U	22
T	0

Is the genetic material of this virus likely to be made up of RNA or DNA? Explain your reasoning.

- In the following image, the pale linear strand is a molecule of DNA. The red bodies are ribosomes.



- What processes are occurring?
- Are these processes occurring in a prokaryotic or eukaryotic cell? Explain.

- 18.** A dog breeder wants to develop a breed of dog with fur colour that changes according to the season. She establishes a partnership with a furrier who breeds stoats (animals with a coat that is white in winter and brown in summer).
- Develop an experimental plan that would enable the two researchers to develop a breed of transgenic dog.
 - Briefly describe one social or ethical issue the researchers should consider before they begin their experiment.
- 19.** Suppose that you have samples of DNA from two different plants. You want to find out whether these plants are clones. Your laboratory is equipped with DNA ligase, restriction enzymes, and gel electrophoresis equipment.
- Outline the steps you would take to analyze the DNA samples.
 - Use a labelled diagram to show the results you would expect if the plants are clones.
- 20.** You are working in a lab that is trying to find a gene associated with stunted growth in mice. You know that the gene contains the sequence GGCATTATCCG on one strand of DNA. Explain how you could use a DNA probe to determine which chromosome carries this gene.
- Making Connections**
- 21.** A certain species of invertebrate has a genome that is 6000 times larger than the genome of a particular yeast cell.
- What conclusions, if any, could you make about the relative complexities of the two organisms?
 - What practical applications could result from a study that compared the genomes of the two organisms?
- 22.** A given organism has many different tissues, but its cells all carry the same genetic information. Explain how this is possible.
- 23.** DNA is sometimes said to be like a language. Explain whether you think this comparison is valid.
- 24.** Working with a partner, debate the following statement: “Human cloning should never be permitted.” Then list what you think are the best arguments on each side of the debate.
- 25.** At a school career fair, you tell a career counsellor that you plan to become a molecular geneticist and study viral genomes. The career counsellor asks, “Don’t you think it would be more useful to study human genetics?” What points would you make in your response?
- 26.** Many nitrites are known to be mutagenic, yet they are still commonly used as preservatives in processed foods. Describe some of the costs and benefits to society of permitting the use of mutagens in industry and food production.
- 27.** An aquaculture research corporation based in Prince Edward Island has created a variety of transgenic salmon that grows ten times faster than normal salmon.
- What are the potential advantages of this transgenic fish?
 - What are the potential risks associated with this fish?
 - What regulations would you recommend to govern the use of this fish in commercial fish-farming operations?
- 28.** Using examples, briefly describe two ethical dilemmas that arise from our ability to detect genetic disorders before or after birth.

Career Focus: Ask a Cancer Geneticist



Motivation comes naturally to Dr. Juliet Daniel. As an internationally recognized biology professor, she teaches students about cell development at McMaster University in Ontario, and she conducts research on proteins that are involved in normal cell growth and the spread of cancer in the body—a process called metastasis. She hopes that her research will lead to life-saving cancer treatments.

Q What made you want to study cancer genetics?

I wanted to study cancer. While I was an undergraduate student, the first discoveries were made regarding *oncogenes* and the role they played in promoting cancer. My instructor was pretty excited about the whole thing, and her enthusiasm got to most of us. With this discovery the general feeling was that now we might actually make some progress in understanding cancer, and hopefully develop treatments for it. In fact, the majority of treatments have come from those kinds of studies.

Q What have we learned about cancer and how to treat it since Terry Fox started his Marathon of Hope in 1980?

Many of the oncogene discoveries were being made around that time. Since then, we've advanced quite a lot. For example, the success rate for treating childhood leukemia is about 80 percent. For some of the other cancers, such as breast cancer, there's still a lot of work to be done. There are now some therapies that are working, and they're a result of our understanding of oncogenes, as well. We also understand more about how proteins work and what processes they regulate in the cell. This has given us more and more insight into how the body works normally. And that's going to help us understand how to treat not just cancer, but many other diseases.

Q How do genes and the proteins they encode play a role in cancer?

Basically most proteins that are linked to cancer all have normal functions in the cell, but can contribute to cancer in one of two main ways: Either they are

over-expressed, and then they're what we call tumour-promoting, or *oncoproteins*. Or, if they're under-expressed, absent, or non-functional, they are considered tumour-suppressors. That means their normal role was to prevent tumour progression by keeping the cell in check.

Q You discovered a protein called Kaiso. What does this protein do?

Kaiso is a transcription factor. Transcription factors are proteins that regulate the expression of *other* proteins. Transcription factors are usually localized in the nucleus, and they bind to the DNA. As you know, the DNA contains the gene, and the gene encodes the protein, and it's the protein that performs the function. So the transcription factor regulates genes, and therefore ultimately regulates the expression of other proteins that have roles in cells.

Q Is Kaiso an oncoprotein or a tumour suppresser protein?

This is what we're working on right now. Some proteins can play both roles, depending on the situation. We know that Kaiso is over-expressed in some breast, colon, and skin cancers, and under-expressed in other breast, colon, and skin cancers. Basically, it's misregulated.

Q Where does the name "Kaiso" come from?

It's a Caribbean word for a type of music, called calypso. I'm from Barbados originally, and when I identified the gene I had a chance to name it, so I wanted to name it something to reflect my heritage. And also, when my colleagues and I were doing the experiments we listened to lots and lots of calypso music!

Other Careers Related to Genetics

Animal Breeder Breeders specialize in raising livestock (such as poultry or cattle), working animals (such as police dogs), or pets. Livestock breeders can acquire the skills they need through work experience, a two-year diploma in livestock production or agriculture technology, or a bachelor's degree in agriculture, biology, or genetics. People who breed fish, birds, cats, dogs, and other companion animals have informal training or a combination of on-the-job training and post-secondary education in animal care. Breeders associated with kennel clubs or similar organizations must abide by a code of practice and ethics.

Bioethicist Some geneticists and social scientists study the implications of genetic testing on society and individuals, or the societal perceptions of genetic engineering, mammalian cloning, or other genetics-related issues. These bioethicists may require graduate training. Lawyers may specialize in bioethics, as well, to address issues such as genetic testing in the workplace or to help form policies about the use of transgenic organisms.

Biotechnologist Biotechnology is the study of making useful products from living organisms, such as using bacteria to make insulin. Biotechnologists often use genetic engineering to develop micro-organisms that will produce tailor-made antibiotics, vitamins, food additives, bleaching agents, and other products. Biotechnologists take various educational routes. In general, a bachelor's degree in a relevant science is required for work in an industrial setting.

Forensic Laboratory Analyst Analysts work with police services to examine evidence from crime or accident scenes. Forensic technologists have a diploma in biological or chemical science technologies, and forensic scientists have a bachelor's degree in forensic science or related disciplines. Some analysts work specifically in biology. Their job includes analyzing blood and other samples, and producing genetic fingerprints.

Genetic Counsellor Genetic counsellors have a nursing degree or a master's degree in genetic counselling. They help families and other health professionals understand genetic tests, disorders, and possible treatments. For example, a genetic counsellor may meet with a family to discuss appropriate treatments for a child's genetic condition or to explain the significance of test results. In addition to having a solid understanding of genetics, a genetic counsellor must be able to communicate and interact well with people.

Microbial Geneticist Some microbial geneticists specialize in comparing rRNA sequences among micro-organisms to establish their evolutionary relationships. Others identify gene sequences or functions, or study how microbial genes are regulated in specific situations, such as when bacteria cause a disease. To work at research institutions, most microbial geneticists have a doctorate degree and post-doctoral training.

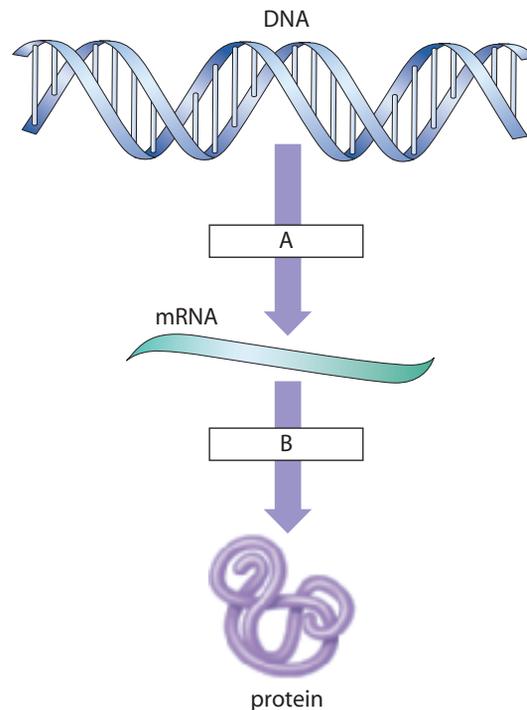
Go Further...

1. *Proto-oncogenes* are normal genes that code for proteins that stimulate cell division. Mutated proto-oncogenes can become oncogenes. List and describe three types of mutations that could convert a proto-oncogene into an oncogene.
2. Some tumour suppressor genes regulate apoptosis (programmed cell death) in unhealthy cells. What might trigger the apoptosis of a cell?
3. Certain viruses can cause proto-oncogenes to become oncogenes. Hypothesize how this might occur. Research this topic to confirm your hypothesis.



Understanding Concepts

- Explain what is meant by the term “cell cycle.”
 - Arrange the following events into the order in which they take place during mitosis: anaphase; metaphase; prophase; telophase.
 - A diploid plant cell contains 54 chromosomes ($2n = 54$). Describe the number and arrangement of chromosomes in each of the following:
 - a leaf cell immediately following cytokinesis
 - a gametophyte cell at the conclusion of the S phase of mitosis
 - a sporophyte cell at the conclusion of anaphase I
 - Explain how Mendel’s laws derive from events that take place during meiosis.
 - Distinguish between the following:
 - genotype and phenotype
 - homozygote and heterozygote
 - recessive and dominant
 - Assume that no crossing over takes place. What is the possibility that a woman’s egg cell contains only chromosomes that the woman inherited from her father? Explain the significance of your answer.
 - Nondisjunction and crossing over are two events that may take place in a reproducing cell.
 - Use labelled diagrams to illustrate each event.
 - Which event is more likely to result in non-viable daughter cells? Explain.
 - Compare and contrast the life cycles of humans and ferns. What reproductive advantages does each life cycle offer?
 - For each of Mendel’s laws of heredity, provide
 - an explanation in terms of classical (Mendelian) genetics
 - an explanation in terms of molecular genetics
- Use the following information to answer questions 10 to 13.
- In a particular breed of fly, black eyes (B) are dominant to grey eyes (b); normal wings (W) are dominant to short wings (w); and hairy legs (H) are dominant to smooth legs (h).
- What ratio of phenotypes would you expect to find in
 - the F_1 generation of a cross between a true-breeding normal-winged fly (WW) and a true-breeding short-winged fly (ww)?
 - the F_2 generation of the cross in (a)?
 - Describe a procedure you could use to find out the genotype of a black-eyed fly.
 - A cross between a normal-winged fly and a short-winged fly resulted in the following F_1 offspring: 489 normal-winged; 511 short-winged. What can you infer about the genotypes of the P_1 generation?
 - You cross two flies that are both heterozygous for both traits. Assume that the genes are not linked. Of 1000 offspring, how many would you expect to have
 - normal wings?
 - black eyes and short wings?
 - grey eyes and short wings?
 - A couple has three children, two of whom have hemophilia. What is the probability that their next child will have hemophilia? Use a Punnett square to explain your reasoning.
 - Examine the following figure.
 - What process does A represent?
 - What process does B represent?

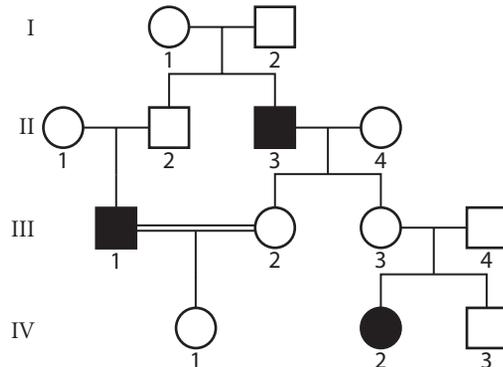


- The coding strand of a segment of DNA in a bacterial chromosome has the following base sequence: 5'-TACACATGCATC-3'. Refer to Table 18.3 to answer these questions.
 - Draw a section of the double-stranded DNA molecule that includes this segment.

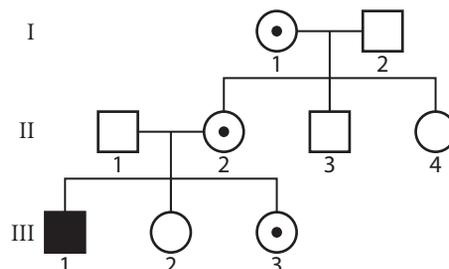
- b) Which end of the segment has a free –OH group?
 c) What is the amino acid sequence of the polypeptide product of this gene?
 d) Show how a nucleotide substitution could result in a silent mutation of this gene.
17. Describe the function(s) of each of the following enzymes:
 a) DNA polymerase
 b) DNA ligase
 c) RNA primase
 d) RNA polymerase
 e) helicase
18. Identify three different types of RNA and describe their roles in gene expression.
19. For each of the following terms, provide a brief definition and a description of its significance in the field of genetic engineering:
 a) restriction endonuclease
 b) DNA microarray
 c) DNA vector
 d) recombinant DNA
20. A species of grass has four chromosomes. In this grass, the gene for bunched seeds (*S*) is dominant to the gene for loose seeds (*s*). Use a labelled diagram to show how these genes assort independently in the gametes of a heterozygote plant.
21. “In an organism that reproduces asexually, there is no difference between a somatic cell mutation and a germ line mutation.” Is this statement true? Explain.
22. Describe two features that are characteristic of the action of restriction endonucleases. How do these features make restriction endonucleases useful to genetic engineers?
23. Explain why DNA fragments migrate in a gel electrophoresis. Which fragments migrate farthest: large or small?

Applying Concepts

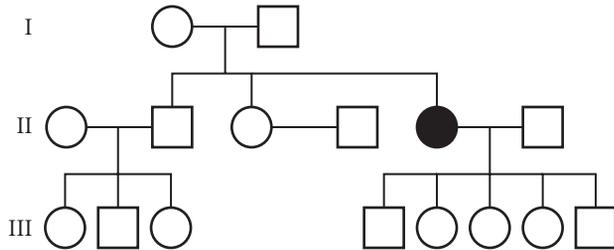
24. “Every cell is haploid for at least part of its life cycle.” Explain whether or not this statement is true.
25. Explain why a karyotype is a useful research tool, and describe how you would prepare a karyotype.
26. A researcher in your lab has created a chemical that prevents microtubules from attaching to centromeres. “We can use this to stop the spread of cancerous tumours,” the researcher claims. Is the researcher right? Why or why not?
27. A scientist creates a substance that denatures the enzyme DNA ligase. What impact will this substance have on the cell cycle? Explain.
28. Familial Mediterranean Fever (FMF) results in short but reoccurring episode of fever, as well as pain in the chest, joints, and abdomen. The disease occurs most frequently in individuals of Mediterranean descent. The gene responsible for FMF was discovered on chromosome 16 in 1997. The following pedigree shows the occurrence of this disorder in one family. How is FMF inherited? Provide the phenotypes and genotypes of all the individuals in the pedigree. Whose genotype can you not be sure of?



29. Lesch-Nyhan syndrome is an X-linked recessive disorder caused by a deficiency of a certain enzyme known as HPRT. Lack of HPRT leads to a build up of uric acid in the body, resulting in moderate mental retardation, poor muscle control, and the formation of crystals in the joints, kidneys, and nervous system. The following pedigree shows the occurrence of this disorder in a family. Provide the phenotypes and genotypes of all the individuals in the pedigree.



- 30.** In humans, the allele for normal hearing (H) is dominant over the allele for a particular form of congenital deafness (h). The trait is not sex-linked. Interpret the pedigree shown here in order to answer the following questions.



- a)** Explain how it is possible for individual II 5 to be congenitally deaf if neither parent has the condition.
- b)** Individual II 5 has five children, none of whom are congenitally deaf. What can you infer about the genotype of individual II 6? Can you be certain of this conclusion? Explain why or why not.
- c)** You are a genetic counselor. One of II 5's children comes to see you. She and her husband, whose sister is congenitally deaf, are planning to start a family. Using a Punnett square, explain what you will tell this couple about the likely phenotypes and genotypes of their children.
- 31.** Frieda breeds her black rooster with Elsie's white hen. The offspring are all evenly speckled black and white. Elsie keeps all the chicks and adds them to her flock of white chickens. "I want to breed chickens that look like Dalmation dogs: mostly white, but with some black speckles," says Elsie. Will Elsie be able to do this? Use Punnett squares to explain your answer.
- 32.** An attendant in a hospital accidentally mixes up the name tags on the four babies in the nursery. "Don't worry," says her partner. "We can use the blood type charts to match the babies to their parents." The blood type information is summarized below. Which baby belongs to which parents?
- Baby A: blood type A
 Baby B: blood type B
 Baby C: blood type AB
 Baby D: blood type O
 Parents 1: blood types A and B
 Parents 2: blood types O and O
 Parents 3: blood types AB and O
 Parents 4: blood types B and B
- 33.** A farmer wishes to create a variety of lemon that will grow in Alberta and starts by collecting seeds from varieties of lemon trees that grow naturally in cooler climates.
- a)** How might the farmer use artificial selection to create the new variety of lemon?
- b)** How might the farmer use genetic engineering to create the new variety of lemon?
- c)** What is one advantage and one disadvantage of each method?
- 34.** Slipper limpets are a species of shellfish. They live together in stacked colonies. If no female limpets are present in the colony, some male limpets will turn into females.
- a)** What genetic process can account for this?
- b)** State a hypothesis about how the absence of a female limpet triggers a change in the male limpet. Then outline an experiment you could conduct to test your hypothesis. Describe the results you would expect if your hypothesis is correct.
- 35.** Ainslie and Josh are expecting a baby. They know there is a chance that their child may have inherited a genetic condition that causes achondroplasia (unusually short stature). The condition is caused by a single gene.
- a)** Identify and describe one prenatal screening technique that might enable Ainslie and Josh to know whether their child has this condition.
- b)** Give an example of a broader ethical or moral question that accompanies this kind of prenatal screening.
- 36.** Will cells from your liver and your brain have the same DNA fingerprint? Explain.

Making Connections

- 37.** Create a flow chart or graphic organizer that describes how smoking can lead to the formation of a cancerous tumour of the lung.
- 38.** Your community is hosting a series of public information meetings about health issues. The objective of the series is to teach people about the science behind healthy lifestyle choices. You are asked to make a 10-minute presentation on the topic "DNA and Mutations."
- a)** Write a one- or two-sentence key message you would want your audience to remember.
- b)** Outline your presentation under five main headings, beginning with "Introduction" and ending with "Conclusion."
- c)** Under each heading list three points you would want to cover, and describe each in a few sentences.

- 39.** A farmer plants a strain of transgenic corn in her fields. The corn carries a recombinant gene that confers resistance to a common herbicide. The next year, a species of weed growing near the corn fields is found to be herbicide-resistant. A study shows that the weed is expressing the recombinant gene. You are a journalist assigned to report on the story.
- What is the significance of the discovery of the herbicide-resistant weed?
 - Write two main points that you would expect to hear from each of the following individuals you interview: the farmer; an official from the genetic engineering corporation that created the transgenic corn; the owner of a nearby organic farm; a consumer organization opposed to the development of genetically modified organisms; a genetics researcher.
- 40.** Mendel conducted ground-breaking genetics research using pea plants. What might have been the impact on the field of genetics if Mendel had instead studied patterns of inheritance in cats? Explain.
- 41.** Many conservation programs use scientific research to help protect endangered animals. Some programs breed animals in captivity, and then release the offspring into the wild. Give two specific examples of ways that a knowledge of genetics could contribute to the success of a conservation program like this.
- 42.**
 - Give three examples of the ways in which the development of technology in fields unrelated to genetics helped to advance genetic research in the period between 1800 and 2000.
 - What new breakthrough in an unrelated field might advance genetic research in this century?
- 43.** Explain how the study of genomics differs from the study of genetics. For each field of research, give one example of how this study can be used to benefit human societies.
- 44.** A team of researchers announces that it has identified a gene associated with high IQ. They then develop a form of gene therapy that can insert this gene into the genome of an infant.

- What do you think might be some of the social effects of this discovery?
- What regulations (if any) do you think should be applied to the use of this gene therapy procedure?
- What are some steps that could be taken now to prepare society for this kind of discovery in the future?

45. Imagine that you are an official in the government of Canada. Your job is to support research that will contribute to human health. You must decide how to allocate \$100 million in research funding among the following three areas: development of transgenic crops; development of techniques for somatic cell gene therapy; research into the molecular processes involved in regulation of the cell cycle. How much funding will you allocate to each area? Justify your decision.

46. Copy the following table into your notebook. Using the example of transgenic pigs that have been engineered for the purpose of serving as donors for organ transplants in humans, fill in the benefits and risks that you foresee.

Using transgenic pigs as organ donors	Benefits	Risks
To individual people		
To society		
To the economy		
To other species		
To the environment		

- 47.** The experiments that enabled scientists to infer and model the structure and function of DNA used a variety of organisms. How can such species diversity demonstrate the same genetic principle?
- 48.** The introduction to Chapter 18 noted that molecular genetics involves confronting difficult questions, including the question of the very definition of life itself. Write a paragraph that summarizes your opinions about how the investigations and applications of molecular genetics leads us to question what life is.