13 RNA and Protein Synthesis

Big idea

Information and Heredity

Q: How does information flow from the cell nucleus to direct the synthesis of proteins in the cytoplasm?

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13.1 RNA

Key Questions

- ***How does RNA differ from DNA?***
- ***How does the cell make RNA?***

Vocabulary

RNA
messenger RNA
ribosomal RNA
transfer RNA
transcription
RNA polymerase
promoter
intron
exon

Taking Notes

Preview Visuals Before you read, look at **Figure 13–3.** Write a prediction of how you think a cell makes RNA based on the figure. Then as you read, take notes on how a cell makes RNA. After you read, compare your notes and your prediction.

THINK ABOUT IT We know that DNA is the genetic material, and we know that the sequence of nucleotide bases in its strands must carry some sort of code. For that code to work, the cell must be able to understand it. What exactly do those bases code for? Where is the cell's decoding system?

The Role of RNA

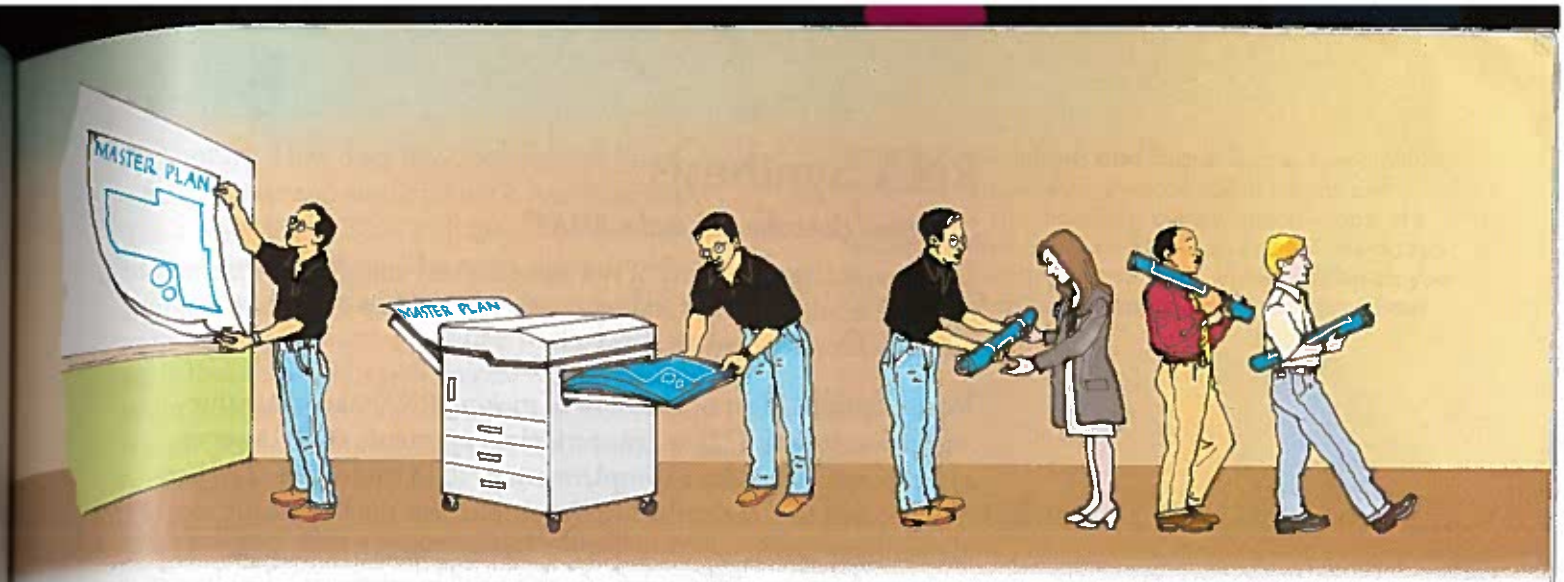
How does RNA differ from DNA?

When Watson and Crick solved the double-helix structure of DNA, they understood right away how DNA could be copied. All a cell had to do was to separate the two strands and then use base pairing to make a new complementary strand for each. But the structure of DNA by itself did not explain how a gene actually works. That question required a great deal more research. The answer came from the discovery that another nucleic acid—ribonucleic acid, or RNA—was involved in putting the genetic code into action. **RNA,** like DNA, is a nucleic acid that consists of a long chain of nucleotides.

In a general way, genes contain coded DNA instructions that tell cells how to build proteins. The first step in decoding these genetic instructions is to copy part of the base sequence from DNA into RNA. RNA then uses these instructions to direct the production of proteins, which help to determine an organisms's characteristics.

Comparing RNA and DNA Remember that each nucleotide in DNA is made up of a 5-carbon sugar, a phosphate group, and a nitrogenous base. This is true for RNA as well. **But there are three important differences between RNA and DNA: (1) the sugar in RNA is ribose instead of deoxyribose, (2) RNA is generally single-stranded and not double-stranded, and (3) RNA contains uracil in placed of thymine.** These chemical differences make it easy for enzymes in the cell to tell DNA and RNA apart.

You can compare the different roles played by DNA and RNA molecules in directing the production of proteins to the two type of plans builders use. A master plan has all the information needed to construct a building. But builders never bring a valuable master plan to the job site, where it might be damaged or lost. Instead, as **Figure 13–1** shows, they work from blueprints, inexpensive, disposable copies of the master plan.



VISUAL ANALOGY

MASTER PLANS AND BLUEPRINTS

FIGURE 13–1 The different roles of DNA and RNA molecules in directing protein synthesis can be compared to the two types of plans used by builders: master plans and blueprints.

Similarly, the cell uses the vital DNA "master plan" to prepare RNA "blueprints." The DNA molecule stays safely in the cell's nucleus, while RNA molecules go to the protein-building sites in the cytoplasm—the ribosomes.

Functions of RNA You can think of an RNA molecule as a disposable copy of a segment of DNA, a working facsimile of a single gene. RNA has many functions, but most RNA molecules are involved in just one job—protein synthesis. RNA controls the assembly of amino acids into proteins. Like workers in a factory, each type of RNA molecule specializes in a different aspect of this job. **Figure 13–2** shows the three main types of RNA: messenger RNA, ribosomal RNA, and transfer RNA.

▶ ***Messenger RNA*** Most genes contain instructions for assembling amino acids into proteins. The RNA molecules that carry copies of these instructions are known as **messenger RNA** (mRNA). They carry information from DNA to other parts of the cell.

▶ ***Ribosomal RNA*** Proteins are assembled on ribosomes, small organelles composed of two subunits. These subunits are made up of several **ribosomal RNA** (rRNA) molecules and as many as 80 different proteins.

▶ ***Transfer RNA*** When a protein is built, a third type of RNA molecule transfers each amino acid to the ribosome as it is specified by the coded messages in mRNA. These molecules are known as **transfer RNA** (tRNA).

FIGURE 13–2 Types of RNA The three main types of RNA are messenger RNA, ribosomal RNA, and transfer RNA.

Messenger RNA
Carries instructions for polypeptide synthesis from nucleus to ribosomes in the cytoplasm.

Ribosome

Ribosomal RNA
Forms an important part of both subunits of the ribosome.

Amino acid

Transfer RNA
Carries amino acids to the ribosome and matches them to the coded mRNA message.

RNA Synthesis

How does the cell make RNA?

Cells invest large amounts of raw material and energy into making RNA molecules. Understanding how cells do this is essential to understanding how genes work.

Transcription Most of the work of making RNA takes place during **transcription.** **In transcription, segments of DNA serve as templates to produce complementary RNA molecules.** The base sequences of the transcribed RNA complement the base sequences of the template DNA.

In prokaryotes, RNA synthesis and protein synthesis take place in the cytoplasm. In eukaryotes, RNA is produced in the cell's nucleus and then moves to the cytoplasm to play a role in the production of protein. Our focus here is on transcription in eukaryotic cells.

Transcription requires an enzyme, known as **RNA polymerase,** that is similar to DNA polymerase. RNA polymerase binds to DNA during transcription and separates the DNA strands. It then uses one strand of DNA as a template from which to assemble nucleotides into a complementary strand of RNA, as shown in **Figure 13–3.** The ability to copy a single DNA sequence into RNA makes it possible for a single gene to produce hundreds or even thousands of RNA molecules.

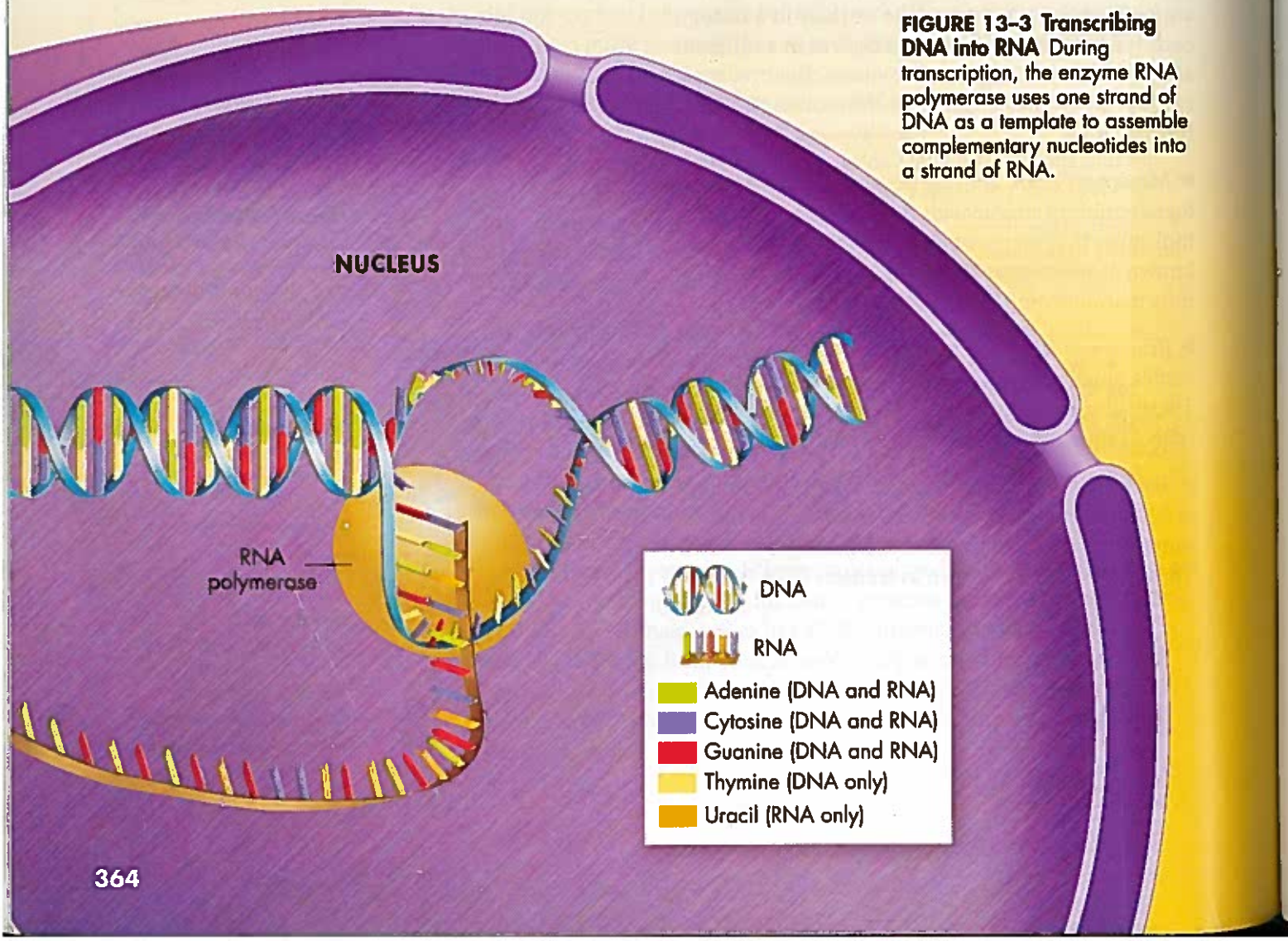


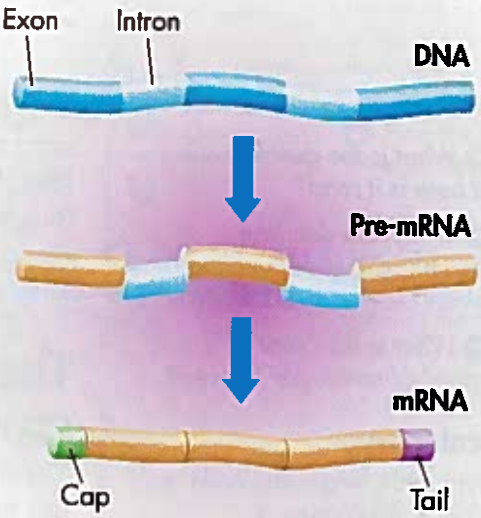
FIGURE 13–3 Transcribing DNA into RNA During transcription, the enzyme RNA polymerase uses one strand of DNA as a template to assemble complementary nucleotides into a strand of RNA.

Promoters How does RNA polymerase know where to start and stop making a strand of RNA? The answer is that RNA polymerase doesn't bind to DNA just anywhere. The enzyme binds only to **promoters,** regions of DNA that have specific base sequences. Promoters are signals in the DNA molecule that show RNA polymerase exactly where to begin making RNA. Similar signals in DNA cause transcription to stop when a new RNA molecule is completed.

RNA Editing Like a writer's first draft, RNA molecules sometimes require a bit of editing before they are ready to be read. These pre-mRNA molecules have bits and pieces cut out of them before they can go into action. The portions that are cut out and discarded are called **introns.** In eukaryotes, introns are taken out of pre-mRNA molecules while they are still in the nucleus. The remaining pieces, known as **exons,** are then spliced back together to form the final mRNA, as shown in **Figure 13–4.**

Why do cells use energy to make a large RNA molecule and then throw parts of that molecule away? That's a good question, and biologists still don't have a complete answer. Some pre-mRNA molecules may be cut and spliced in different ways in different tissues, making it possible for a single gene to produce several different forms of RNA. Introns and exons may also play a role in evolution, making it possible for very small changes in DNA sequences to have dramatic effects on how genes affect cellular function.

FIGURE 13–4 Introns and Exons Before many mRNA molecules can be read, sections called introns are "edited out." The remaining pieces, called exons, are spliced together. Then, an RNA cap and tail are added to form the final mRNA molecule. **Predict** ***What do you think would happen if introns were not removed from pre-mRNA?***



13.1 Assessment

Review Key Concepts

1. a. Review Describe three main differences between RNA and DNA.

b. Explain List the three main types of RNA, and explain what they do.

c. Infer Why is it important for a single gene to be able to produce hundreds or thousands of RNA molecules?

2. a. Review Describe what happens during transcription.

b. Predict What do you think would happen if introns were not removed from pre-mRNA?

WRITE ABOUT SCIENCE

Creative Writing

3. An RNA molecule is looking for a job in a protein synthesis factory. It asks you to write its résumé. This RNA molecule is not yet specialized and could, with some structural changes, function as mRNA, rRNA, or tRNA. Write a résumé for this molecule that reflects the capabilities of each type of RNA.

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13.2 Ribosomes and Protein Synthesis

Key Questions

- ***What is the genetic code, and how is it read?***
- ***What role does the ribosome play in assembling proteins?***
- ***What is the "central dogma" of molecular biology?***

Vocabulary

polypeptide • genetic code • codon • translation • anticodon • gene expression

Taking Notes

Outline Before you read, write down the green headings in this lesson. As you read, keep a list of the main points, and then write a summary for each heading.

THINK ABOUT IT How would you build a system to read the messages that are coded in genes and transcribed into RNA? Would you read the bases one at a time, as if the code were a language with just four words—one word per base? Perhaps you would read them, as we do in English, as individual letters that can be combined to spell longer words.

The Genetic Code

What is the genetic code, and how is it read?

The first step in decoding genetic messages is to transcribe a nucleotide base sequence from DNA to RNA. This transcribed information contains a code for making proteins. You learned in Chapter 2 that proteins are made by joining amino acids together into long chains, called **polypeptides.** As many as 20 different amino acids are commonly found in polypeptides.

The specific amino acids in a polypeptide, and the order in which they are joined, determine the properties of different proteins. The sequence of amino acids influences the shape of the protein, which in turn determines its function. How is the order of bases in DNA and RNA molecules translated into a particular order of amino acids in a polypeptide?

As you know from Lesson 13.1, RNA contains four different bases: adenine, cytosine, guanine, and uracil. In effect, these bases form a "language" with just four "letters": A, C, G, and U. We call this language the **genetic code.** How can a code with just four letters carry instructions for 20 different amino acids? **The genetic code is read three "letters" at a time, so that each "word" is three bases long and corresponds to a single amino acid.** Each three-letter "word" in mRNA is known as a **codon.** As shown in **Figure 13–5,** a codon consists of three consecutive bases that specify a single amino acid to be added to the polypeptide chain.

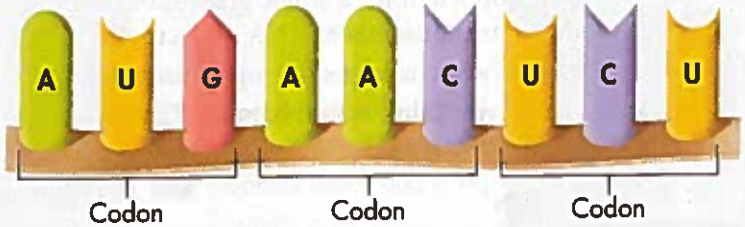
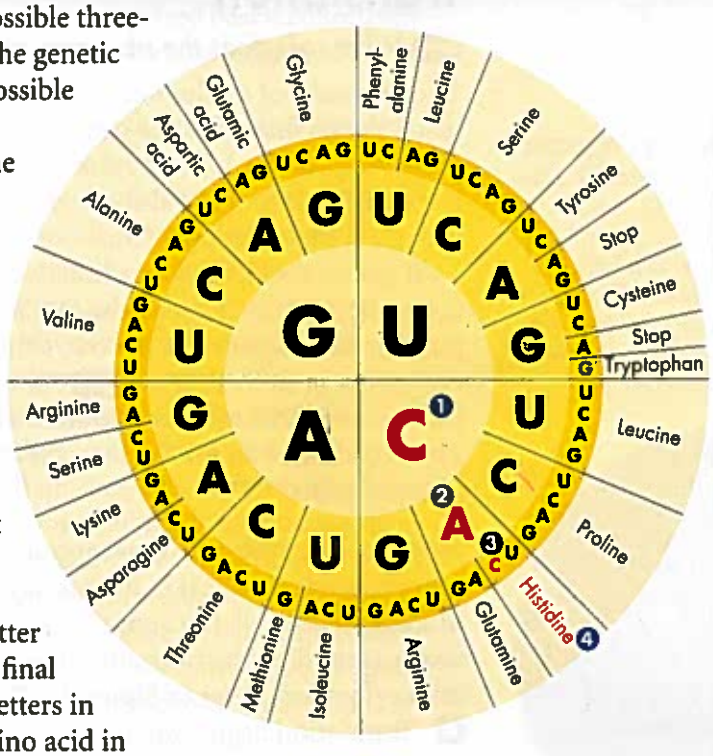


FIGURE 13–5 Codons A codon is a group of three nucleotide bases in messenger RNA that specifies a particular amino acid. **Observe** ***What are the three-letter groups of the codons shown here?***

How to Read Codons Because there are four different bases in RNA, there are 64 possible three-base codons ($4 \times 4 \times 4 = 64$) in the genetic code. **Figure 13–6** shows these possible combinations. Most amino acids can be specified by more than one codon. For example, six different codons—UUA, UUG, CUU, CUC, CUA, and CUG—specify leucine. But only one codon—UGG—specifies the amino acid tryptophan.

Decoding codons is a task made simple by use of a genetic code table. Just start at the middle of the circle with the first letter of the codon, and move outward. Next, move out to the second ring to find the second letter of the codon. Find the third and final letter among the smallest set of letters in the third ring. Then read the amino acid in that sector.



1. To decode the codon CAC, find the first letter in the set of bases at the center of the circle.
2. Find the second letter of the codon A, in the "C" quarter of the next ring.
3. Find the third letter, C, in the next ring, in the "C-A" grouping.
4. Read the name of the amino acid in that sector—in this case histidine.

FIGURE 13–6 Reading Codons This circular table shows the amino acid to which each of the 64 codons corresponds. To read a codon, start at the middle of the circle and move outward.

Start and Stop Codons Any message, whether in a written language or the genetic code, needs punctuation marks. In English, punctuation tells us where to pause, when to sound excited, and where to start and stop a sentence. The genetic code has punctuation marks, too. The methionine codon AUG, for example, also serves as the initiation, or "start," codon for protein synthesis. Following the start codon, mRNA is read, three bases at a time, until it reaches one of three different "stop" codons, which end translation. At that point, the polypeptide is complete.

Quick Lab
GUIDED INQUIRY

How Does a Cell Interpret Codons?

1. A certain gene has the following base sequence:

GACAAGTCCACAATC

Write this sequence on a separate sheet of paper.

2. From left to right, write the sequence of the mRNA molecule transcribed from this gene.
3. Using **Figure 13–6**, read the mRNA codons from left to right. Then write the amino acid sequence of the polypeptide.
4. Repeat step 3, reading the codons from right to left.

Analyze and Conclude

1. Apply Concepts Why did steps 3 and 4 produce different polypeptides?

2. Infer Do cells usually decode nucleotides in one direction only or in either direction?

Translation

What role does the ribosome play in assembling proteins?

The sequence of nucleotide bases in an mRNA molecule is a set of instructions that gives the order in which amino acids should be joined to produce a polypeptide. Once the polypeptide is complete, it then folds into its final shape or joins with other polypeptides to become a functional protein.

If you've ever tried to assemble a complex toy, you know that instructions alone don't do the job. You need to read them and then put the parts together. In the cell, a tiny factory—the ribosome—carries out both these tasks. **Ribosomes use the sequence of codons in mRNA to assemble amino acids into polypeptide chains.** The decoding of an mRNA message into a protein is a process known as **translation.**

Steps in Translation Transcription isn't part of the translation process, but it is critical to it. Transcribed mRNA directs that process. In a eukaryotic cell, transcription goes on in the cell's nucleus; translation is carried out by ribosomes after the transcribed mRNA enters the cell's cytoplasm. Refer to **Figure 13–7** as you read about translation.

A Translation begins when a ribosome attaches to an mRNA molecule in the cytoplasm. As each codon passes through the ribosome, tRNAs bring the proper amino acids into the ribosome. One at a time, the ribosome then attaches these amino acids to the growing chain.

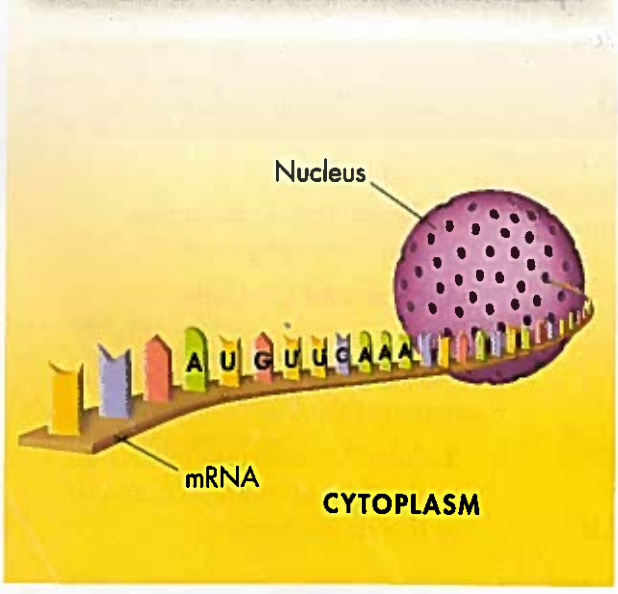
VISUAL SUMMARY

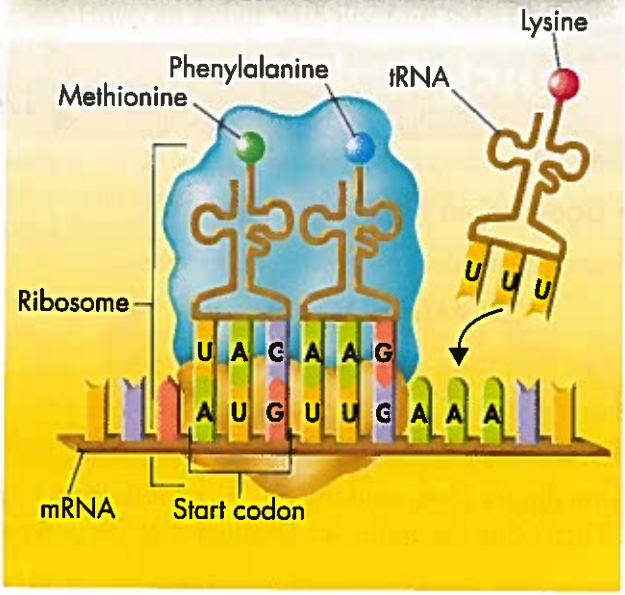
TRANSLATION

FIGURE 13–7 During translation, or protein synthesis, the cell uses information from messenger RNA to produce proteins.

Messenger RNA
Messenger RNA is transcribed in the nucleus and then enters the cytoplasm.

A Transfer RNA
Translation begins at AUG, the start codon. Each transfer RNA has an anticodon whose bases are complementary to the bases of a codon on the mRNA strand. The ribosome positions the start codon to attract its anticodon, which is part of the tRNA that binds methionine. The ribosome also binds the next codon and its anticodon.





Each tRNA molecule carries just one kind of amino acid. In addition, each tRNA molecule has three unpaired bases, collectively called the **anticodon.** Each tRNA anticodon is complementary to one mRNA codon.

In the case of the tRNA molecule for methionine, the anticodon is UAC, which pairs with the methionine codon, AUG. The ribosome has a second binding site for a tRNA molecule for the next codon. If that next codon is UUC, a tRNA molecule with an AAG anticodon fits against the mRNA molecule held in the ribosome. That second tRNA molecule brings the amino acid phenylalanine into the ribosome.

B Like an assembly-line worker who attaches one part to another, the ribosome helps form a peptide bond between the first and second amino acids—methionine and phenylalanine. At the same time, the bond holding the first tRNA molecule to its amino acid is broken. That tRNA then moves into a third binding site, from which it exits the ribosome. The ribosome then moves to the third codon, where tRNA brings it the amino acid specified by the third codon.

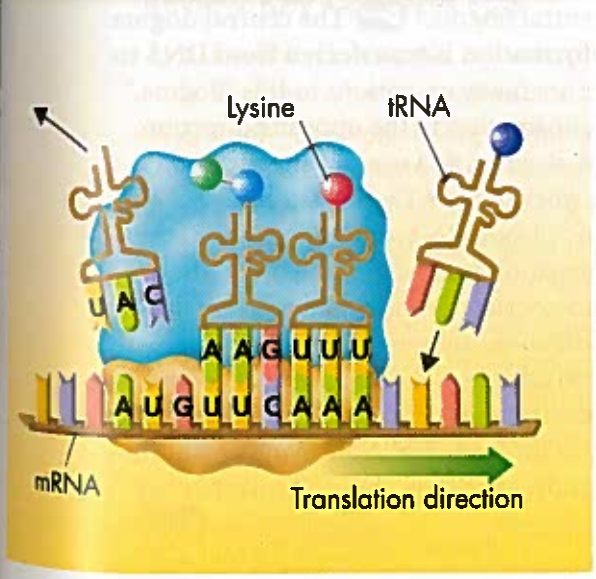
C The polypeptide chain continues to grow until the ribosome reaches a "stop" codon on the mRNA molecule. When the ribosome reaches a stop codon, it releases both the newly formed polypeptide and the mRNA molecule, completing the process of translation.

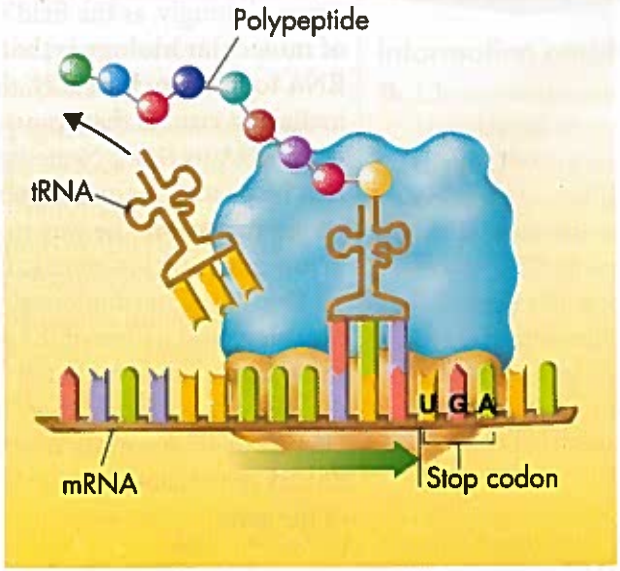
In Your Notebook *Briefly summarize the three steps in translation.*

FIGURE 13–8 Molecular Model of a Ribosome This model shows ribosomal RNA and associated proteins as colored ribbons. The large subunit is blue, green, and purple. The small subunit is shown in yellow and orange. The three solid elements in the center are tRNA molecules.

B The Polypeptide "Assembly Line"
The ribosome joins the two amino acids—methionine and phenylalanine—and breaks the bond between methionine and its tRNA. The tRNA floats away from the ribosome, allowing the ribosome to bind another tRNA. The ribosome moves along the mRNA, from right to left, binding new tRNA molecules and amino acids.

C Completing the Polypeptide
The process continues until the ribosome reaches one of the three stop codons. Once the polypeptide is complete, it and the mRNA are released from the ribosome.





The Roles of tRNA and rRNA in Translation All three major forms of RNA—mRNA, tRNA, and rRNA—come together in the ribosome during translation. The mRNA molecule, of course, carries the coded message that directs the process. The tRNA molecules deliver exactly the right amino acid called for by each codon on the mRNA. The tRNA molecules are, in effect, adaptors that enable the ribosome to "read" the mRNA's message accurately and to get the translation just right.

Ribosomes themselves are composed of roughly 80 proteins and three or four different rRNA molecules. These rRNA molecules help hold ribosomal proteins in place and help locate the beginning of the mRNA message. They may even carry out the chemical reaction that joins amino acids together.

The Molecular Basis of Heredity

What is the "central dogma" of molecular biology?

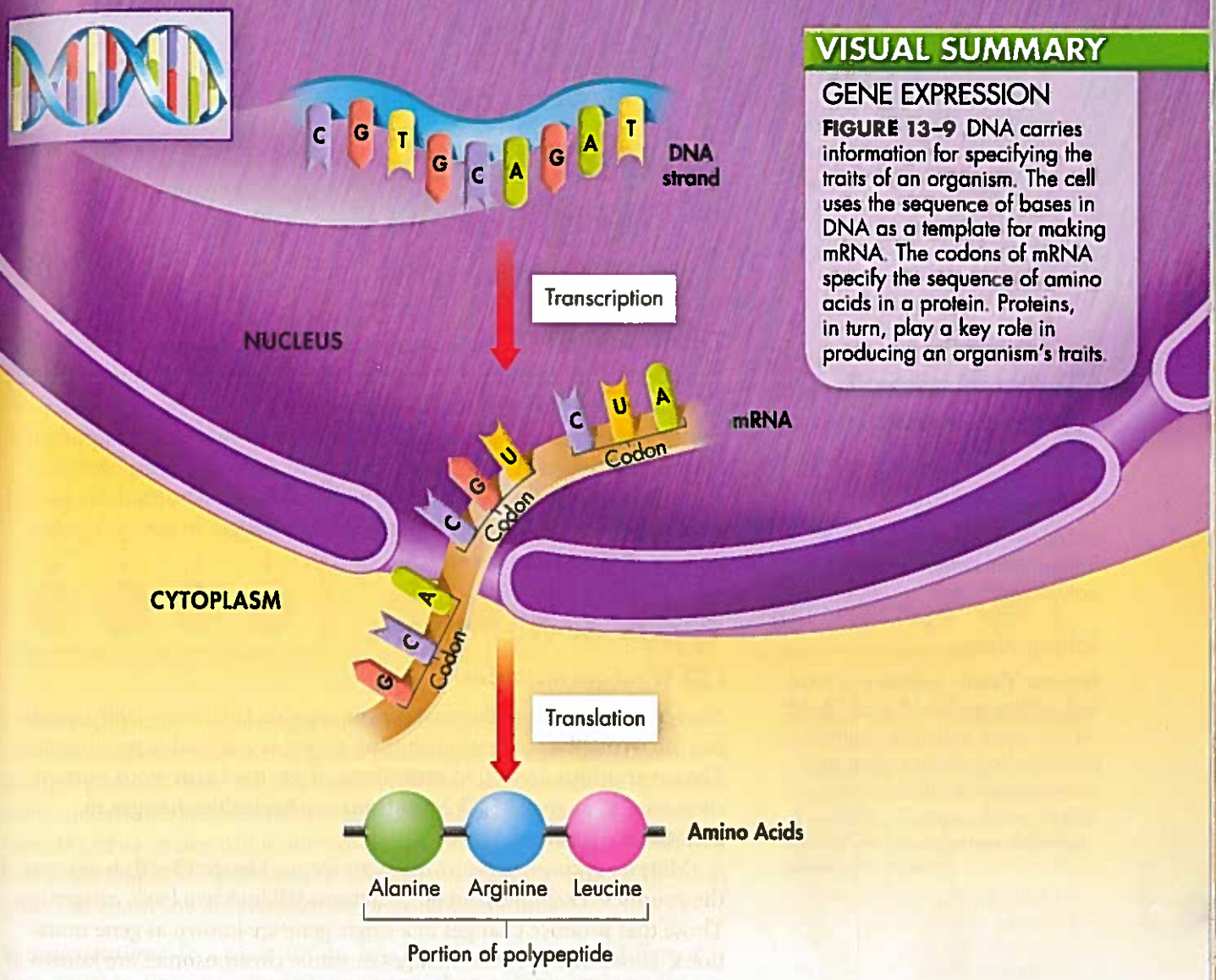
Gregor Mendel might have been surprised to learn that most genes contain nothing more than instructions for assembling proteins. He might have asked what proteins could possibly have to do with the color of a flower, the shape of a leaf, or the sex of a newborn baby. The answer is that proteins have everything to do with these traits. Remember that many proteins are enzymes, which catalyze and regulate chemical reactions. A gene that codes for an enzyme to produce pigment can control the color of a flower. Another gene produces proteins that regulate patterns of tissue growth in a leaf. Yet another may trigger the female or male pattern of development in an embryo. In short, proteins are microscopic tools, each specifically designed to build or operate a component of a living cell.

MYSTERY CLUE

What features of the genetic code make it possible for a mouse's gene to work inside the cells of a fly?

As you've seen, once scientists learned that genes were made of DNA, a series of other discoveries soon followed. Before long, with the genetic code in hand, a new scientific field called molecular biology had been established. Molecular biology seeks to explain living organisms by studying them at the molecular level, using molecules like DNA and RNA. One of the earliest findings came to be known, almost jokingly, as the field's "central dogma." **The central dogma of molecular biology is that information is transferred from DNA to RNA to protein.** In reality, there are many exceptions to this "dogma," including viruses that transfer information in the opposite direction, from RNA to DNA. Nonetheless, it serves as a useful generalization that helps to explain how genes work. **Figure 13–9** illustrates **gene expression,** the way in which DNA, RNA, and proteins are involved in putting genetic information into action in living cells.

One of the most interesting discoveries of molecular biology is the near-universal nature of the genetic code. Although some organisms show slight variations in the amino acids assigned to particular codons, the code is always read three bases at a time and in the same direction. Despite their enormous diversity in form and function, living organisms display remarkable unity at life's most basic level, the molecular biology of the gene.



VISUAL SUMMARY

GENE EXPRESSION

FIGURE 13–9 DNA carries information for specifying the traits of an organism. The cell uses the sequence of bases in DNA as a template for making mRNA. The codons of mRNA specify the sequence of amino acids in a protein. Proteins, in turn, play a key role in producing an organism's traits.

13.2 Assessment

Review Key Concepts

1. a. Review How does a cell interpret the genetic code?

b. Explain What are codons and anticodons?

c. Apply Concepts Using the table in **Figure 13–6,** identify the amino acids specified by codons: UGG, AAG, and UGC.

2. a. Review What happens during translation?

b. Compare and Contrast How is protein synthesis different from DNA replication? (*Hint*: Revisit Lesson 12.3.)

3. a. Review Why is the genetic code considered universal?

b. Explain What does the term *gene expression* mean?

c. Infer In what way does controlling the proteins in an organism control the organism's characteristics?

Apply the Big idea

Information and Heredity

4. Choose one component of translation to consider in depth. For instance, you might choose to consider one form of RNA or one step in the process. Then write a question or a series of questions about that component. Select one question, and use it to form a hypothesis that could be tested in an experiment.

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13.3 Mutations

Key Questions

- ***What are mutations?***
- ***How do mutations affect genes?***

Vocabulary

mutation • point mutation • frameshift mutation • mutagen • polyploidy

Taking Notes

Preview Visuals Before you read, look at **Figures 13–11** and **13–12.** As you read, note the changes produced by various gene and chromosomal mutations.

THINK ABOUT IT The sequence of bases in DNA are like the letters of a coded message, as we've just seen. But what would happen if a few of those letters changed accidentally, altering the message? Could the cell still understand its meaning? Think about what might happen if someone changed at random a few lines of code in a computer program that you rely on. Knowing what you already do about the genetic code, what effects would you predict such changes to have on genes and the polypeptides for which they code?

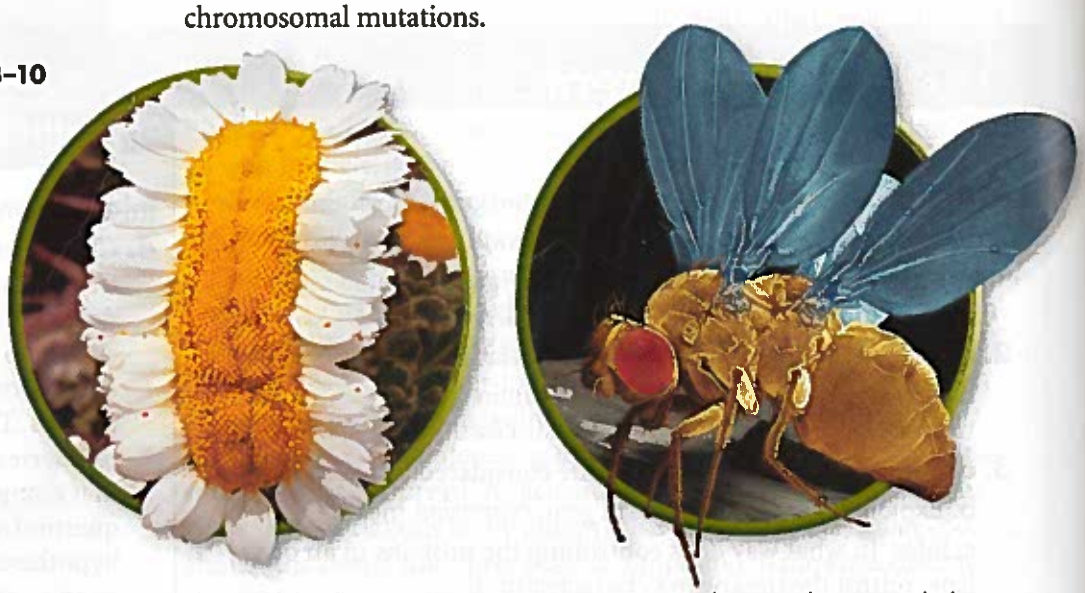
Types of Mutations

What are mutations?

Now and then cells make mistakes in copying their own DNA, inserting the wrong base or even skipping a base as a strand is put together. These variations are called **mutations,** from the Latin word *mutare,* meaning "to change." **Mutations are heritable changes in genetic information.**

Mutations come in many different forms. **Figure 13–10** shows two of the countless examples. But all mutations fall into two basic categories: Those that produce changes in a single gene are known as gene mutations. Those that produce changes in whole chromosomes are known as chromosomal mutations.

FIGURE 13–10 Plant and Animal Mutations



The elongated shape of this flower is caused by a mutation that affects the growing regions of the flower tissue.

A mutation in the gene known as *bithorax* has produced an extra set of wings in this fruit fly. (SEM: 20×)

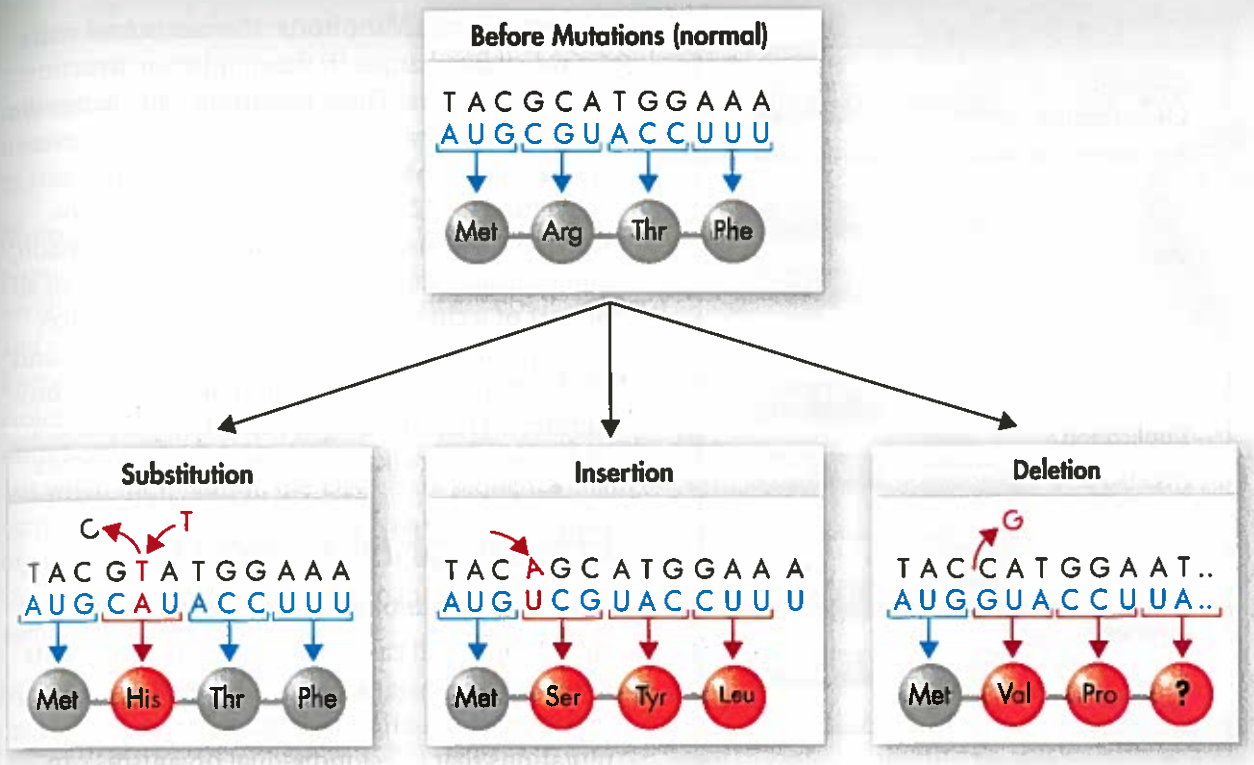


FIGURE 13–11 Point Mutations These diagrams show how changes in a single gene can affect the amino acid sequence of proteins. **Analyze Data** ***Which type of mutation causes the most damage? Why?***

Gene Mutations Gene mutations that involve changes in one or a few nucleotides are known as **point mutations** because they occur at a single point in the DNA sequence. Point mutations include substitutions, insertions, and deletions. They generally occur during replication. If a gene in one cell is altered, the alteration can be passed on to every cell that develops from the original one. Refer to **Figure 13–11** as you read about the different forms of point mutations.

▶ ***Substitutions*** In a substitution, one base is changed to a different base. Substitutions usually affect no more than a single amino acid, and sometimes they have no effect at all. For example, if a mutation changed one codon of mRNA from CCC to CCA, the codon would still specify the amino acid proline. But a change in the first base of the codon—changing CCC to ACC—would replace proline with the amino acid threonine.

▶ ***Insertions and Deletions*** Insertions and deletions are point mutations in which one base is inserted or removed from the DNA sequence. The effects of these changes can be dramatic. Remember that the genetic code is read three bases at a time. If a nucleotide is added or deleted, the bases are still read in groups of three, but now those groupings shift in every codon that follows the mutation.

Insertions and deletions are also called **frameshift mutations** because they shift the "reading frame" of the genetic message. By shifting the reading frame, frameshift mutations can change every amino acid that follows the point of the mutation. They can alter a protein so much that it is unable to perform its normal functions.

In Your Notebook *Use a cause/effect diagram to describe the different types of gene mutations.*

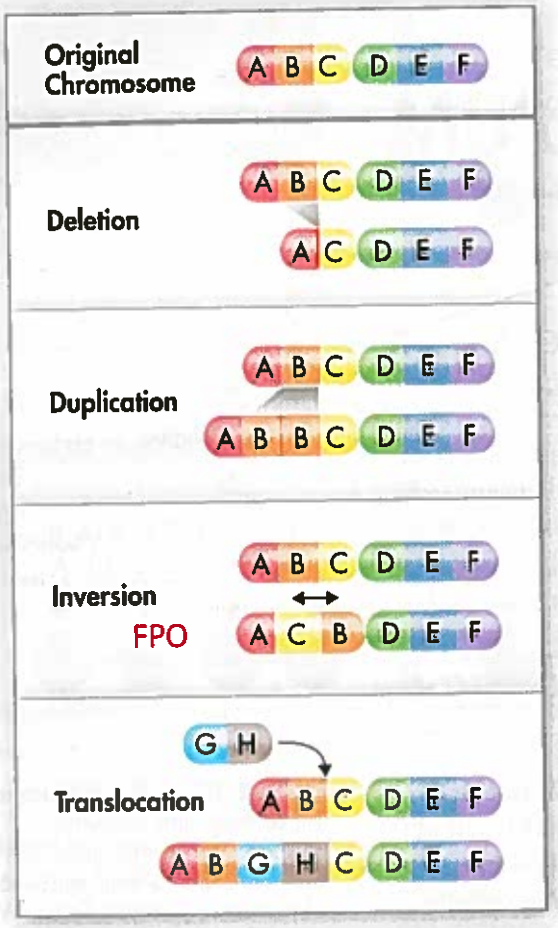


FIGURE 13–12 Chromosomal Mutations Four types of mutations cause changes in whole chromosomes. **Use Diagrams** ***What is the difference between inversion and translocation?***

Chromosomal Mutations Chromosomal mutations involve changes in the number or structure of chromosomes. These mutations can change the location of genes on chromosomes and can even change the number of copies of some genes.

Figure 13–12 shows four types of chromosomal mutations: deletion, duplication, inversion, and translocation. Deletion involves the loss of all or part of a chromosome; duplication produces an extra copy of all or part of a chromosome; and inversion reverses the direction of parts of a chromosome. Translocation occurs when part of one chromosome breaks off and attaches to another.

Effects of Mutations

How do mutations affect genes?

Genetic material can be altered by natural events or by artificial means. The resulting mutations may or may not affect an organism. And some mutations that affect individual organisms can also affect a species or even an entire ecosystem.

Many mutations are produced by errors in genetic processes. For example, some point mutations are caused by errors during DNA replication. The cellular machinery that replicates DNA inserts an incorrect base roughly once in every 10 million bases. But small changes in genes can gradually accumulate over time.

Quick Lab
GUIDED INQUIRY

Modeling Mutations

Small mutations in DNA can cause huge changes in the proteins that are synthesized. Similarly, small changes in a word can dramatically alter its meaning. Look at the following sequence of words:

milk mile wile wise wisp wasp

Notice that each word differs from the previous word by just one letter and that none of the words is meaningless. Think of these changes as "point mutations" that affect word meaning.

Analyze and Conclude

1. Apply Concepts Start with the word *gene*, and change it letter by letter to make new words. Make sure each new word is an actual word but not a proper noun. Write at least four "point mutations" of the word *gene*.

2. Apply Concepts Show how you could use words to model a frameshift mutation. (*Hint*: You can use a sentence.)

3. Use Models Use the words in this sentence to model a substitution mutation.

Stressful environmental conditions may cause some bacteria to increase mutation rates. This can actually be helpful to the organism, since mutations may sometimes give such bacteria new traits, such as the ability to consume a new food source or to resist a poison in the environment.

Mutagens Some mutations arise from **mutagens,** chemical or physical agents in the environment. Chemical mutagens include certain pesticides, a few natural plant alkaloids, tobacco smoke, and environmental pollutants. Physical mutagens include some forms of electromagnetic radiation, such as X-rays and ultraviolet light. If these agents interact with DNA, they can produce mutations at high rates. Cells can sometimes repair the damage; but when they cannot, the DNA base sequence changes permanently. Some compounds interfere with base-pairing, increasing the error rate of DNA replication. Others weaken the DNA strand, causing breaks and inversions that produce chromosomal mutations.

In Your Notebook *Compare and contrast chromosomal mutations and gene mutations.*

Harmful and Helpful Mutations As you've already seen, some mutations don't even change the amino acid specified by a codon, while others may alter a complete protein or even an entire chromosome. **The effects of mutations on genes vary widely. Some have little or no effect; and some produce beneficial variations. Some negatively disrupt gene function.** Many if not most mutations are neutral; they have little or no effect on the expression of genes or the function of the proteins for which they code. Whether a mutation is negative or beneficial depends on how its DNA changes relative to the organism's situation. Mutations are often thought of as negative, since they can disrupt the normal function of genes. However, without mutations, organisms could not evolve, because mutations are the source of genetic variability in a species.

Harmful Effects Some of the most harmful mutations are those that dramatically change protein structure or gene activity. The defective proteins produced by these mutations can disrupt normal biological activities, and result in genetic disorders. Some cancers, for example, are the product of mutations that cause the uncontrolled growth of cells. Sickle cell disease is a disorder associated with changes in the shape of red blood cells. You can see its effects in **Figure 13–13.** It is caused by a point mutation in one of the polypeptides found in hemoglobin, the blood's principal oxygen-carrying protein. Among the symptoms of the disease and anemia, severe pain, frequent infections, and stunted growth.

MYSTERY CLUE

What kind of mutation could cause a fly to develop eyes in unusual places, such as its antennae?

BUILD Vocabulary

WORD ORIGINS The word **mutagen** is a Latin word that means "origin of change." Mutagens change an organism's genetic information.

FIGURE 13–13 Effects of a Point Mutation Sickle cell disease affects the shape of red blood cells. The round cells in this micrograph are normal red blood cells. The crescent and star-shaped cells are sickled cells.

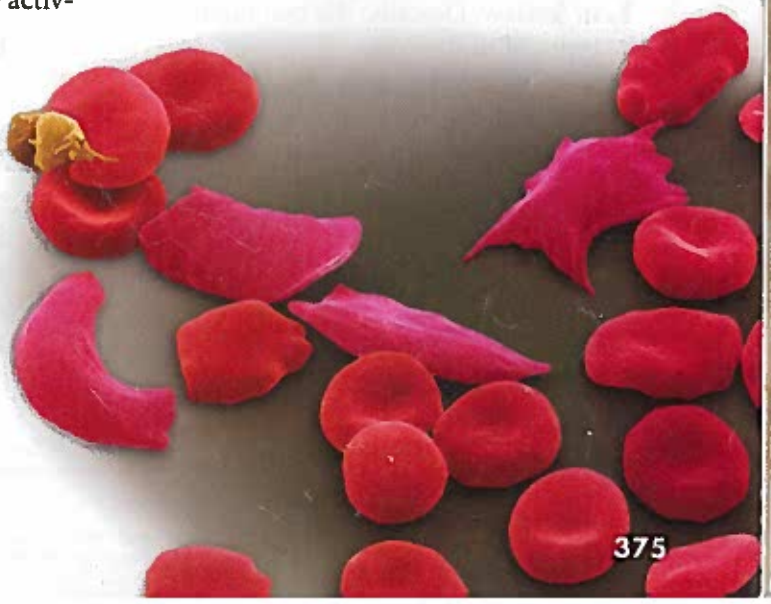


FIGURE 13–14 Polyploid Plants
The fruit of the Tahiti lime is seedless, a result of polyploidy. Changes to the ploidy number of citrus plants can affect the size and strength of the trees as well as the quality and seediness of their fruit.

▶ ***Beneficial Effects*** Some of the variation produced by mutations can be highly advantageous to an organism or species. **Mutations often produce proteins with new or altered functions that can be useful to organisms in different or changing environments.** For example, mutations have helped many insects resist chemical pesticides. And some have enabled microorganisms to adapt to new chemicals in the environment.

Over the past 20 years, mutations in the mosquito genome have made many African mosquitoes resistant to the chemical pesticides once used to control them. This may be bad news for humans, but it is highly beneficial to the insects themselves. Beneficial mutations occur in humans, too, including ones that increase bone strength and density, making fractures less likely, and mutations that increase resistance to HIV, the virus that causes AIDS.

Plant and animal breeders often make use of "good" mutations. For example, when a complete set of chromosomes fails to separate during meiosis, the gametes that result may produce triploid (3N) or tetraploid (4N) organisms. The condition in which an organism has extra sets of chromosomes is called **polyploidy.** Polyploid plants are often larger and stronger than diploid plants. Important crop plants—including bananas and the limes shown in **Figure 13–14**—have been produced this way, polyploidy also occurs naturally in citrus plants, often through spontaneous mutations.

In Your Notebook *List five examples of mutations. Classify each as neutral, harmful, or helpful, and explain your reasoning.*

13.3 Assessment

Review Key Concepts

1. a. Review Describe the two main types of mutations.

b. Explain What is a frameshift mutation? Give an example.

c. Infer The effects of a mutation are not always visible. Choose a species, and explain how a biologist might determine whether a mutation has occurred and, if so, what type of mutation it is.

2. a. Review List four effects mutations can have on genes.

b. Apply Concepts What is the significance of mutations to living things?

VISUAL THINKING

3. Make a compare/contrast table to organize your ideas about gene mutations and chromosomal mutations. Then use your table to write a paragraph comparing and contrasting these two kinds of mutations.

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13.4 Gene Regulation and Expression

THINK ABOUT IT Think of a library filled with how-to books. Would you ever need to use all of those books at the same time? Of course not. If you wanted to know how to fix a leaky faucet, you'd open a book about plumbing but would ignore the one on carpentry. Now picture a tiny bacterium like *E. coli*, which contains more than 4000 genes. Most of its genes code for proteins that do everything from building cell walls to breaking down food. Do you think *E. coli* uses all 4000-plus volumes in its genetic library at the same time?

Prokaryotic Gene Regulation

How are prokaryotic genes regulated?

As it turns out, bacteria and other prokaryotes do not need to transcribe all of their genes at the same time. To conserve energy and resources, prokaryotes regulate their activities, using only those genes necessary for the cell to function. For example, it would be wasteful for a bacterium to produce enzymes that are needed to make a molecule that is readily available from its environment. By regulating gene expression, bacteria can respond to changes in their environment—the presence or absence of nutrients, for example. How? **DNA-binding proteins in prokaryotes regulate genes by controlling transcription.** Some of these regulatory proteins help switch genes on, while others turn genes off.

How does an organism know when to turn a gene on or off? One of the keys to gene transcription in bacteria is the organization of genes into operons. An **operon** is a group of genes that are regulated together. The genes in an operon usually have related functions. *E. coli*, shown in **Figure 13–15**, provides us with a clear example. The 4288 genes that code for proteins in *E. coli* include a cluster of 3 genes that must be turned on together before the bacterium can use the sugar lactose as a food. These three lactose genes in *E. coli* are called the *lac* operon.

Key Questions

- ***How are prokaryotic genes regulated?***
- ***How are genes regulated in eukaryotic cells?***
- ***What controls the development of cells and tissues in multicellular organisms?***

Vocabulary

operon
operator
RNA interference
differentiation
homeotic gene
homeobox gene
Hox gene

Taking Notes

Outline Before you read, use the headings in this lesson to make an outline. As you read, fill in the subtopics and smaller topics. Then add phrases or a sentence after each subtopic that provides key information.

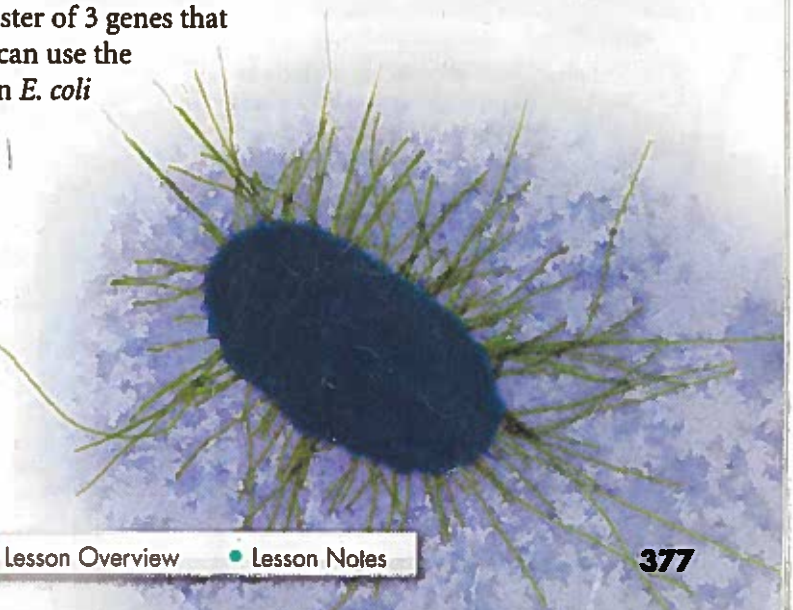


FIGURE 13–15
Small Cell, Many Genes
The common bacterium *E. coli* has more than 4000 genes.

The *Lac* Operon Why must *E. coli* be able to switch the *lac* genes on and off? Lactose is a compound made up of two simple sugars, galactose and glucose. To use lactose for food, the bacterium must transport lactose across its cell membrane and then break the bond between glucose and galactose. These tasks are performed by proteins coded for by the genes of the *lac* operon. This means, of course, that if the bacterium grows in a medium where lactose is the only food source, it must transcribe these genes and produce these proteins. If grown on another food source, such as glucose, it would have no need for these proteins.

Remarkably, the bacterium almost seems to "know" when the products of these genes are needed. When lactose is not present, the *lac* genes are turned off by proteins that bind to DNA and block transcription.

Promoters and Operators On one side of the operon's three genes are two regulatory regions. The first is a promoter (P), which is a site where RNA-polymerase can bind to begin transcription. The other region is called the **operator** (O). The O site is where a DNA-binding protein known as the *lac* repressor can bind to DNA.

▶***The* Lac *Repressor Blocks Transcription*** As **Figure 13–16** shows, when the *lac* repressor binds to the O region, RNA polymerase cannot reach the *lac* genes to begin transcription. In effect, the binding of the repressor protein switches the operon "off" by preventing the transcription of its genes.

▶***Lactose Turns the Operon "On"*** If the repressor protein is always present, how can the *lac* genes ever be switched on? Besides its DNA binding site, the *lac* repressor protein has a binding site for lactose itself. When lactose is added to the medium, it diffuses into the cell and attaches to the *lac* repressor. This changes the shape of the repressor protein in a way that causes it to fall off the operator. Now, with the repressor no longer bound to the O site, RNA polymerase can bind to the promoter and transcribe the genes of the operon. As a result, in the presence of lactose, the operon is automatically switched on.

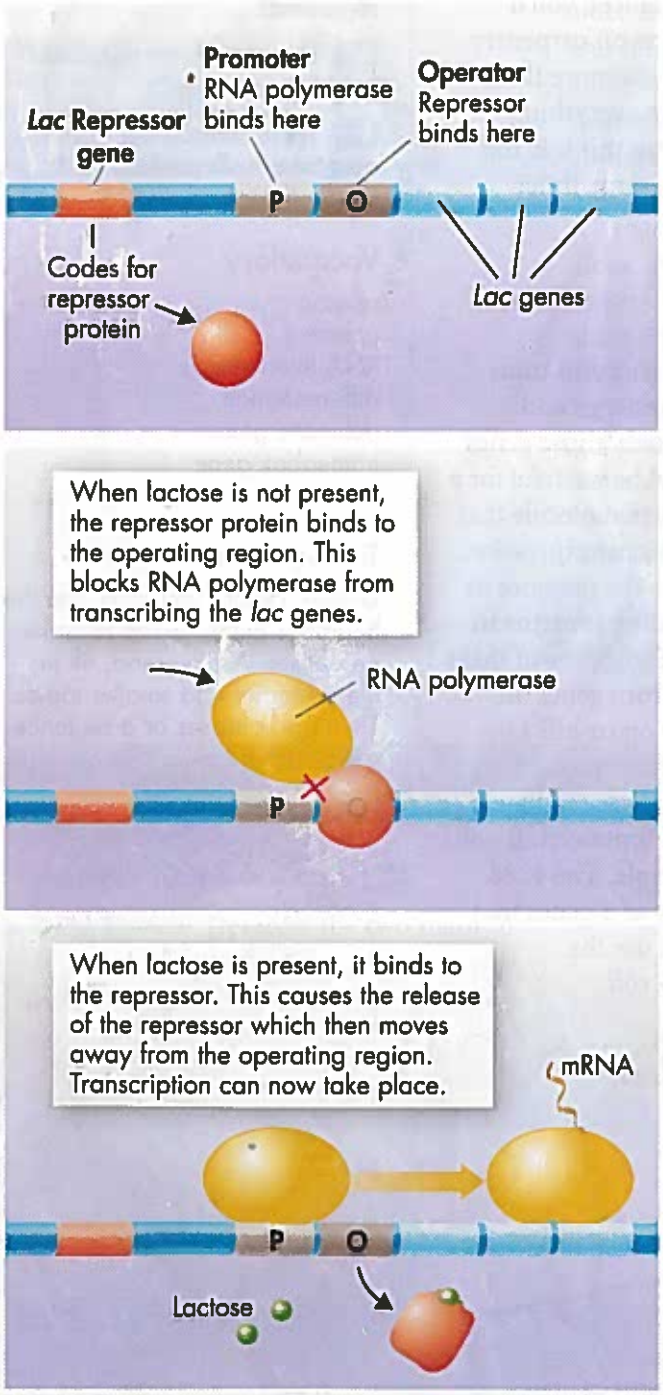


FIGURE 13–16 Gene Expression in Prokaryotes The *lac* genes in *E. coli* are turned off by *lac* repressors and turned on in the presence of lactose. **Use Analogies** ***How is the way lactose turns genes on and off similar to the way cold air signals a furnace to turn on or off?***

Eukaryotic Gene Regulation

How are genes regulated in eukaryotic cells?

The general principles of gene regulation in prokaryotes also apply to eukaryotes, although there are differences. Most eukaryotic genes are controlled individually and have more complex regulatory sequences than those of the *lac* repressor system.

Figure 13–17 shows several features of a typical eukaryotic gene. One of the most interesting is the TATA box, a short region of DNA, about 30 base pairs long, containing the sequence TATATA or TATAAA. This region is usually found just before a gene. The TATA box binds a protein that helps position RNA polymerase by marking a point just before the beginning of a gene.

Transcription Factors Gene expression in eukaryotic cells can be regulated at a number of levels. One of the most critical is the level of transcription, by means of DNA-binding proteins known as transcription factors. **By binding DNA sequences in the regulatory regions of eukaryotic genes, transcription factors control the expression of those genes.** Some transcription factors enhance transcription by opening up tightly packed chromatin. Others help attract RNA polymerase. Still others block access to certain genes, much like prokaryotic repressor proteins. In most cases, multiple transcription factors must bind before RNA polymerase is able to attach to the promoter region and start transcription.

Promoters have multiple binding sites for transcription factors, each of which can influence transcription. Certain factors activate scores of genes at once, dramatically changing patterns of gene expression in the cell. Other factors form only in response to chemical signals. Steroid hormones, for example, are chemical messengers that enter cells and bind to receptor proteins. These "receptor complexes" then act as transcription factors that bind to DNA, allowing a single chemical signal to activate multiple genes. Eukaryotic gene expression can also be regulated by many other factors, including the exit of mRNA molecules from the nucleus, the stability of mRNA, and even the breakdown of a gene's protein products.

In Your Notebook *Compare gene regulation in single-cell organisms and multicellular organisms.*

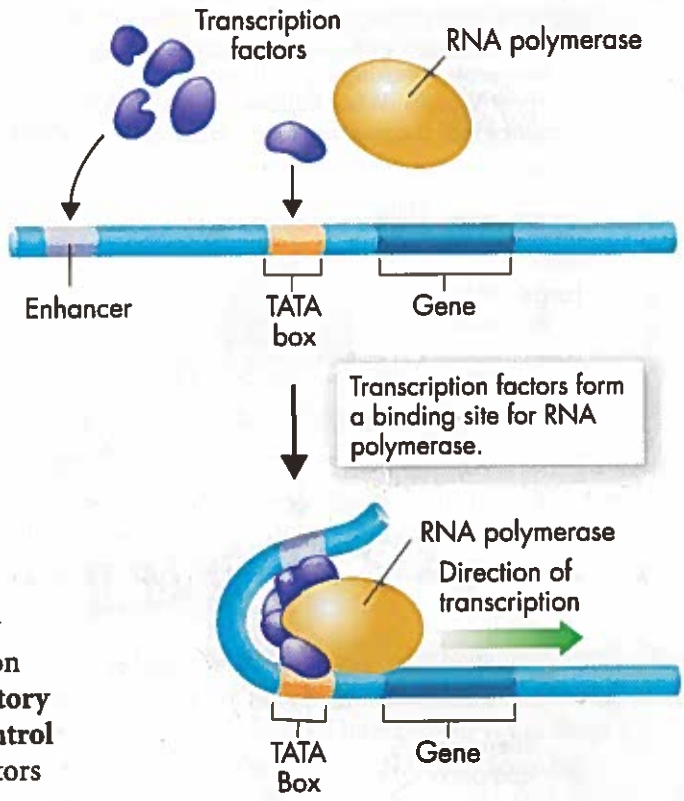
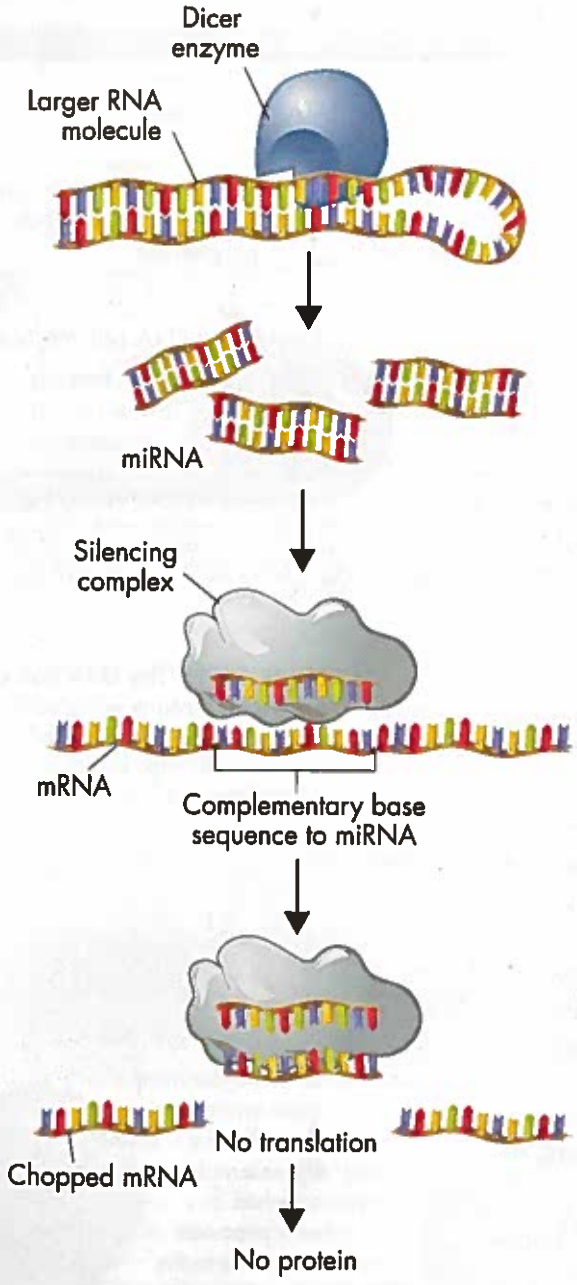


FIGURE 13–17 The TATA Box and Transcription Many eukaryotic genes include a region called the TATA box that helps position RNA polymerase.

MYSTERY CLUE

To make the mouse gene work inside the cells of a fly, researchers attached a new promoter sequence to the gene. Why do you think they did that?

FIGURE 13–18 Blocking Gene Expression Like tiny pieces of sticky tape, microRNAs attach to certain mRNA molecules and stop them from passing on their protein-making instructions.
Interpret Visuals ***What happens to the mRNA sequence that is complementary to the bound miRNA?***



Cell Specialization Why is gene regulation in eukaryotes more complex than in prokaryotes? Think for a moment about the way in which genes are expressed in a multicellular organism. The genes that code for liver enzymes, for example, are not expressed in nerve cells. Keratin, an important protein in skin cells, is not produced in blood cells. Cell specialization requires genetic specialization, yet all of the cells in a multicellular organism carry the same genetic code in their nucleus. Complex gene regulation in eukaryotes is what makes specialization possible.

RNA Interference For years biologists wondered why cells contain lots of small RNA molecules, only a few dozen bases long, that don't belong to any of the major groups of RNA (mRNA, tRNA, or rRNA). In the last decade, a series of important discoveries has shown that these small RNA molecules play a powerful role in regulating gene expression. And they do so by interfering with mRNA.

As **Figure 13–18** shows, after they are produced by transcription, the small interfering RNA molecules fold into double-stranded hairpin loops. An enzyme called the "Dicer" enzyme cuts, or dices, these double-stranded loops into microRNA (miRNA), each about 20 base pairs in length. The two strands of the loops then separate. Next, one of the miRNA pieces attaches to a cluster of proteins to form what is known as a silencing complex. The silencing complex binds to and destroys any mRNA containing a sequence that is complementary to the miRNA. In effect, miRNA sticks to certain mRNA molecules and stops them from passing on their protein-making instructions.

The silencing complex effectively shuts down the expression of the gene whose mRNA it destroys. Blocking gene expression by means of an miRNA silencing complex is known as **RNA interference.** At first, RNA interference (RNAi) seemed to be a rare event, found only in a few plants and other species. It's now clear that RNA interference is found throughout the living world and that it even plays a role in human growth and development.

Analyzing Data

The Discovery of RNA Interference

In 1998, Andrew Fire and Craig Mello carried out an experiment that helped explain the mechanism of RNA interference. They used RNA from a large gene called unc-22, which codes for a protein found in muscle cells. They prepared short mRNA fragments corresponding to two exon regions of the gene and injected them into egg cells of the worm *C. elegans*. Some of their results are shown in the table.

Injections of mRNA into *C. elegans* Eggs

Portion of Gene Used to Produce mRNA	Strand Injected	Result in Adult Worm
Unc-22 (exon 21–22)	Sense	Normal
	Antisense	Normal
	Sense + Antisense	Twitching
Unc-22 (exon 27)	Sense	Normal
	Antisense	Normal
	Sense + Antisense	Twitching

1. Draw Conclusions How did the adult worms' responses differ to injections of single-stranded mRNA (the "sense" strand), its complementary strand ("antisense"), and double-stranded RNA ("sense + antisense")?

2. Form a Hypothesis Twitching results from the failure of muscle cells to control their contractions. What does this suggest about the unc-22 protein in some of the worms? How would you test your hypothesis?

3. Infer The injected fragments came from two different places in the gene and were only a few hundred bases long. The unc-22 mRNA is thousands of bases long. What does this suggest about the mechanism of RNA interference?

The Promise of RNAi Technology The discovery of RNAi has made it possible for researchers to switch genes on and off at will, simply by inserting double-stranded RNA into cells. The Dicer enzyme then cuts this RNA into miRNA, which activates silencing complexes. These complexes block the expression of genes producing mRNA complementary to the miRNA. Naturally this technology is a powerful way to study gene expression in the laboratory. However, RNAi technology also holds the promise of allowing medical scientists to turn off the expression of genes from viruses and cancer cells, and it may provide new ways to treat and perhaps even cure diseases.

Genetic Control of Development

What controls the development of cells and tissues in multicellular organisms?

Regulating gene expression is especially important in shaping the way a multicellular organism, like the mouse embryo in **Figure 13–19**, develops. Each of the specialized cell types found in the adult originates from the same fertilized egg cell. Cells don't just grow and divide during embryonic development. As the embryo develops, different sets of genes are regulated by transcription factors and repressors. Gene regulation helps cells undergo **differentiation**, becoming specialized in structure and function. The study of genes that control development and differentiation is one of the most exciting areas in biology today.

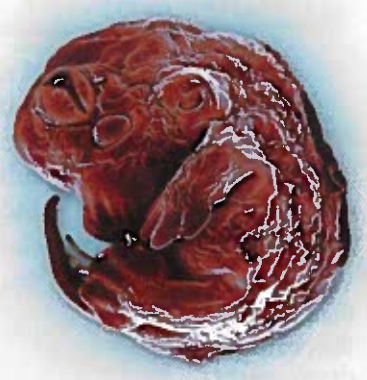


FIGURE 13–19 Differentiation This scanning electron micrograph shows a mouse embryo undergoing cell differentiation 13.5 days after conception.

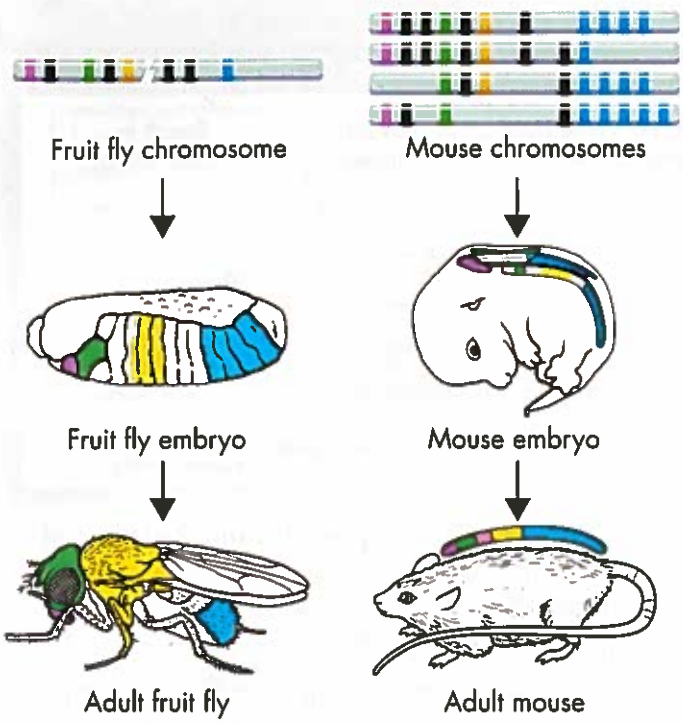


FIGURE 13–20 Hox Genes and Body Development In fruit flies, a series of Hox genes along a chromosome determines the basic body structure. Mice have similar genes on four different chromosomes. The colored areas on the fly and mouse show the approximate body areas affected by genes of the corresponding colors. **Interpret Visuals** ***What section of the bodies of flies and mice is coded by the genes shown in blue?***

Homeotic Genes The American biologist Edward B. Lewis was the first to show that a specific group of genes controls the identities of body parts in the embryo of the common fruit fly. Lewis found that a mutation in one of these genes actually resulted in a fly with a leg growing out of its head in place of an antenna! From Lewis's work it became clear that a set of master control genes, known as **homeotic genes,** regulates organs that develop in specific parts of the body.

Homeobox and Hox Genes Molecular studies of homeotic genes show that they share a very similar 130-base DNA sequence, which was given the name homeobox. **Homeobox genes** code for transcription factors that activate other genes that are important in cell development and differentiation. Homeobox genes are expressed in certain regions of the body, and they determine factors like the presence of wings or legs.

In flies, a group of homeobox genes known as **Hox genes** are located side by side in a single cluster, as shown in **Figure 13–20.** Hox genes determine the identities of each segment of a fly's body. They are arranged in the exact order in which they are expressed, from anterior to posterior. A mutation in one of these genes can completely change the organs that develop in specific parts of the body.

Remarkably, clusters of Hox genes exist in the DNA of other animals, including humans. These genes are arranged in the same way—from head to tail. The function of Hox genes in humans seems to be almost the same as it is in fruit flies: They tell the cells of the body how to differentiate as the body grows. What this means, of course, is that nearly all animals, from flies to mammals, share the same basic tools for building the different parts of the body.

The striking similarity of master control genes—genes that control development—has a simple scientific explanation. Common patterns of genetic control exist because all these genes have descended from the genes of common ancestors. **Master control genes are like switches that trigger particular patterns of development and differentiation in cells and tissues.** The details can vary from one organism to another, but the switches are nearly identical. Recent studies have shown that the very same Hox gene that triggers the development of hands and feet is also active in the fins of certain fish.

MYSTERY CLUE

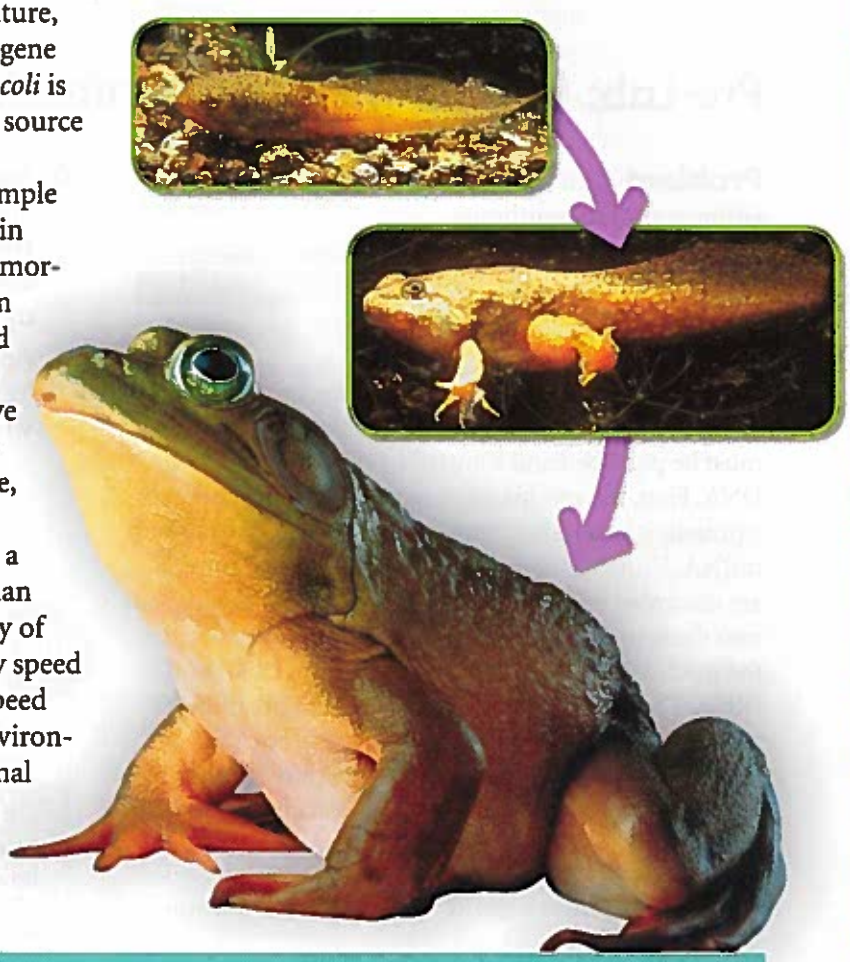
What do you think controls the growth and development of eyes in flies and mice?

Environmental Influences You've seen how cell differentiation is controlled at least in part by the regulation of gene expression. Conditions in an organism's environment play a role too. In prokaryotes and eukaryotes, environmental factors like temperature, salinity, and nutrient availability can influence gene expression. One example: The *lac* operon in *E. coli* is switched on only when lactose is the only food source in the bacteria's environment.

Metamorphosis is another well-studied example of how organisms can modify gene expression in response to change in their environment. Metamorphosis involves a series of transformations from one life stage to another. It is typically regulated by a number of external (environmental) and internal (hormonal) factors. As organisms move from larval to adult stages, their body cells differentiate to form new organs. At the same time, old organs are lost through cell death.

Consider the metamorphosis of a tadpole into a bullfrog, as shown in **Figure 13–21.** Under less than ideal conditions—a drying pond, a high density of predators, low amounts of food—tadpoles may speed up their metamorphosis. In other words, the speed of metamorphosis is determined by various environmental changes that are translated into hormonal changes, with the hormones functioning at the molecular level. Other environmental influences include temperature and population size.

FIGURE 13–21 Metamorphosis Environmental factors can affect gene regulation. If the bullfrog's environment changes for the worse, its genes will direct the production of hormones to speed the transformation of the tadpole (top photo) to the adult bullfrog (bottom photo).



13.4 Assessment

Review Key Concepts

1. a. Review How is the *lac* operon regulated?

b. Explain What is a promoter?

c. Use Analogies Write an analogy that demonstrates how the *lac* repressor functions.

2. a. Review Describe how most eukaryotic genes are controlled.

b. Compare and Contrast How is gene regulation in prokaryotes and eukaryotes similar? How is it different?

3. a. Review What genes control cell differentiation during development?

b. Compare and Contrast How is the way Hox genes are expressed in mice similar to the way they are expressed in fruit flies? How is it different?

PRACTICE PROBLEM

4. A hormone is a chemical that is produced in one part of the body, travels through the blood, and affects cells in other parts of the body. Many hormones are proteins. How might the production of a hormone affect the expression of genes in a eukaryotic cell? Write a hypothesis that could be tested to answer this question. (*Hint*: Include promoters in your hypothesis.)

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