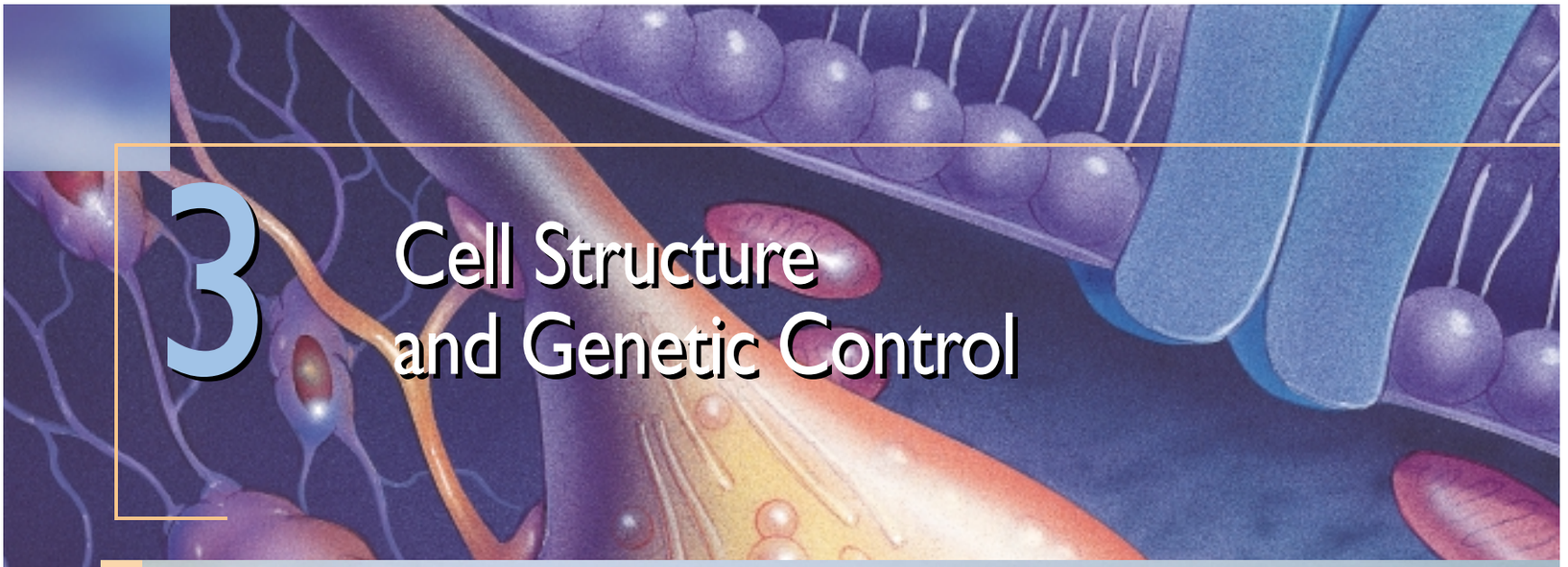
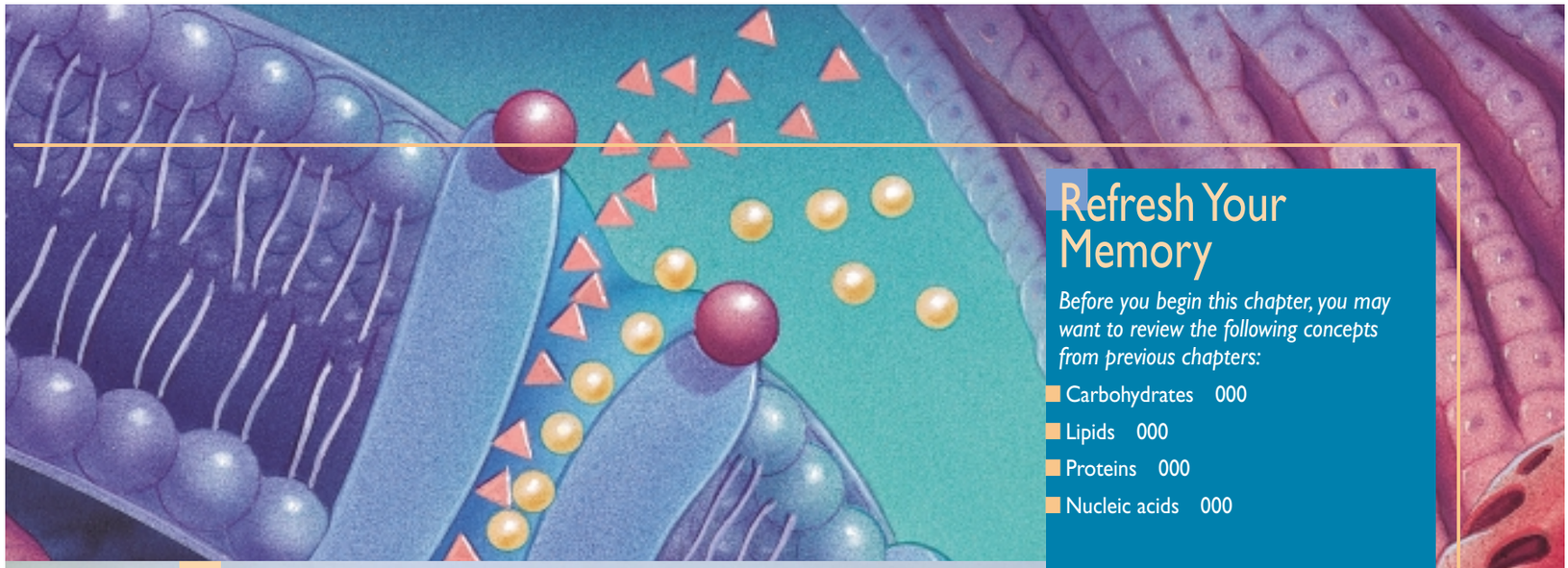


3 Cell Structure and Genetic Control

Objectives

After studying this chapter, you should be able to . . .

1. describe the structure of the plasma membrane and explain its functional significance.
2. state which cells in the human body transport themselves by amoeboid movement and explain how they perform this movement.
3. describe the structure of cilia and flagella, and state some of their functions.
4. describe the processes of phagocytosis, pinocytosis, receptor-mediated endocytosis, and exocytosis.
5. state the functions of the cytoskeleton, lysosomes, mitochondria, and the endoplasmic reticulum.
6. describe the structure of the cell nucleus and explain its significance.
7. explain how RNA is produced according to the genetic information in DNA and distinguish between the different types of RNA.
8. describe how proteins are produced according to the information contained in messenger RNA.
9. describe the structure of the rough endoplasmic reticulum and Golgi complex and explain how they function together in the secretion of proteins.
10. explain what is meant by the semiconservative mechanism of DNA replication.
11. describe the different stages of the cell cycle and list the events that occur in the different phases of mitosis.
12. define the terms *hypertrophy* and *hyperplasia* and explain their physiological importance.
13. describe the events that occur in meiosis, compare them to those that occur in mitosis, and discuss the significance of meiotic cell division in human physiology.



Chapter at a Glance

Refresh Your Memory

Before you begin this chapter, you may want to review the following concepts from previous chapters:

- Carbohydrates 000
- Lipids 000
- Proteins 000
- Nucleic acids 000

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Visit the Online Learning Center for these additional study resources.

- Interactive quizzing
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Clinical Investigation

Timothy is only eighteen years old, but appears to have liver disease. A liver biopsy is performed, and different microscopic techniques are employed for viewing the samples. The biopsy reveals an unusually extensive smooth endoplasmic reticulum. In addition, an abnormally large amount of glycogen granules are found, and many intact glycogen granules are seen within secondary lysosomes.

Upon questioning, Timothy admits that he has a history of drug abuse, but claims that he is now in recovery. Laboratory analysis reveals that he has an abnormally low amount of the enzyme that hydrolyzes glycogen. What is the relationship between these observations?

Plasma Membrane and Associated Structures

The cell is the basic unit of structure and function in the body. Many of the functions of cells are performed by particular subcellular structures known as organelles. The plasma (cell) membrane allows selective communication between the intracellular and extracellular compartments and aids cellular movement.

Cells look so small and simple when viewed with the ordinary (light) microscope that it is difficult to think of each one as a living entity unto itself. Equally amazing is the fact that the physiology of our organs and systems derives from the complex functions of the cells of which they are composed. Complexity of function demands complexity of structure, even at the subcellular level.

As the basic functional unit of the body, each cell is a highly organized molecular factory. Cells come in a wide variety of shapes and sizes. This great diversity, which is also apparent in the subcellular structures within different cells, reflects the diversity of function of different cells in the body. All cells, however, share certain characteristics; for example, they are all surrounded by a plasma membrane, and most of them possess the structures listed in table 3.1. Thus, although no single cell can be considered "typical," the general structure of cells can be indicated by a single illustration (fig. 3.1).

For descriptive purposes, a cell can be divided into three principal parts:

1. **Plasma (cell) membrane.** The selectively permeable plasma membrane surrounds the cell, gives it form, and separates the cell's internal structures from the extracellular environment. The plasma membrane also participates in intercellular communication.

Table 3.1 Cellular Components: Structure and Function

Component	Structure	Function
Plasma (cell) membrane	Membrane composed of double layer of phospholipids in which proteins are embedded	Gives form to cell and controls passage of materials into and out of cell
Cytoplasm	Fluid, jellylike substance between the cell membrane and the nucleus in which organelles are suspended	Serves as matrix substance in which chemical reactions occur
Endoplasmic reticulum	System of interconnected membrane-forming canals and tubules	Agranular (smooth) endoplasmic reticulum metabolizes nonpolar compounds and stores Ca^{2+} in striated muscle cells, granular (rough) endoplasmic reticulum assists in protein synthesis
Ribosomes	Granular particles composed of protein and RNA	Synthesize proteins
Golgi complex	Cluster of flattened membranous sacs	Synthesizes carbohydrates and packages molecules for secretion, secretes lipids and glycoproteins
Mitochondria	Membranous sacs with folded inner partitions	Release energy from food molecules and transform energy into usable ATP
Lysosomes	Membranous sacs	Digest foreign molecules and worn and damaged organelles
Peroxisomes	Spherical membranous vesicles	Contain enzymes that detoxify harmful molecules and break down hydrogen peroxide
Centrosome	Nonmembranous mass of two rodlike centrioles	Helps to organize spindle fibers and distribute chromosomes during mitosis
Vacuoles	Membranous sacs	Store and release various substances within the cytoplasm
Microfilaments and microtubules	Thin, hollow tubes	Support cytoplasm and transport materials within the cytoplasm
Cilia and flagella	Minute cytoplasmic projections that extend from the cell surface	Move particles along cell surface or move the cell
Nuclear envelope	Double-layered membrane that surrounds the nucleus, composed of protein and lipid molecules	Supports nucleus and controls passage of materials between nucleus and cytoplasm
Nucleolus	Dense nonmembranous mass composed of protein and RNA molecules	Produces ribosomal RNA for ribosomes
Chromatin	Fibrous strands composed of protein and DNA	Contains genetic code that determines which proteins (including enzymes) will be manufactured by the cell

2. **Cytoplasm and organelles.** The cytoplasm is the aqueous content of a cell inside the cell membrane but outside the nucleus. Organelles (excluding the nucleus) are subcellular structures within the cytoplasm that perform specific functions. The term **cytosol** is frequently used to describe the fluid portion of the cytoplasm; that is, the part that cannot be removed by centrifugation.
3. **Nucleus.** The nucleus is a large, generally spheroid body within a cell. The largest of the organelles, it contains the DNA, or genetic material, of the cell and thus directs the cell's activities. The nucleus also contains one or more *nucleoli.* Nucleoli are centers for the production of ribosomes, which are the sites of protein synthesis.

Structure of the Plasma Membrane

Because both the intracellular and extracellular environments (or "compartments") are aqueous, a barrier must be present to prevent the loss of enzymes, nucleotides, and other cellular molecules that are water-soluble. Since this barrier surrounding the cell cannot itself be composed of water-soluble molecules, it is instead composed of lipids.

The **plasma membrane** (also called the **cell membrane**), and indeed all of the membranes surrounding organelles within the cell, are composed primarily of phospholipids and proteins. Phospholipids, described in chapter 2, are polar (and hydrophilic) in the region that contains the phosphate group and nonpolar (and hydrophobic) throughout the rest of the molecule. Since the environment on each side of the membrane is aqueous, the hydrophobic parts of the molecules "huddle together" in the center of the membrane, leaving the polar parts exposed to water on both surfaces. This results in the formation of a double layer of phospholipids in the cell membrane.

The hydrophobic middle of the membrane restricts the passage of water and water-soluble molecules and ions. Certain of these polar compounds, however, do pass through the membrane. The specialized functions and selective transport properties of the membrane are believed to be due to its protein content. Membrane proteins are described as peripheral or integral. *Peripheral proteins* are only partially embedded in one face of the membrane, whereas *integral proteins* span the membrane from one side to the other. Since the membrane is not solid—phospholipids and proteins are free to

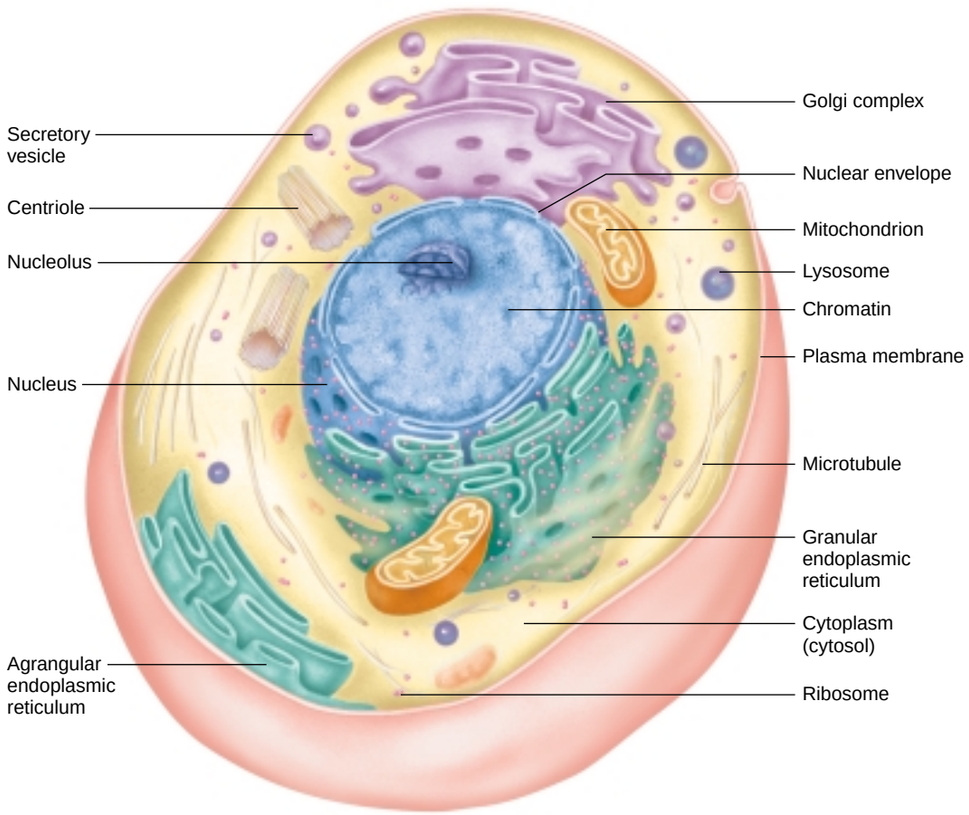


Figure 3.1 **A generalized human cell showing the principal organelles.** Since most cells of the body are highly specialized, they have structures that differ from those shown here.

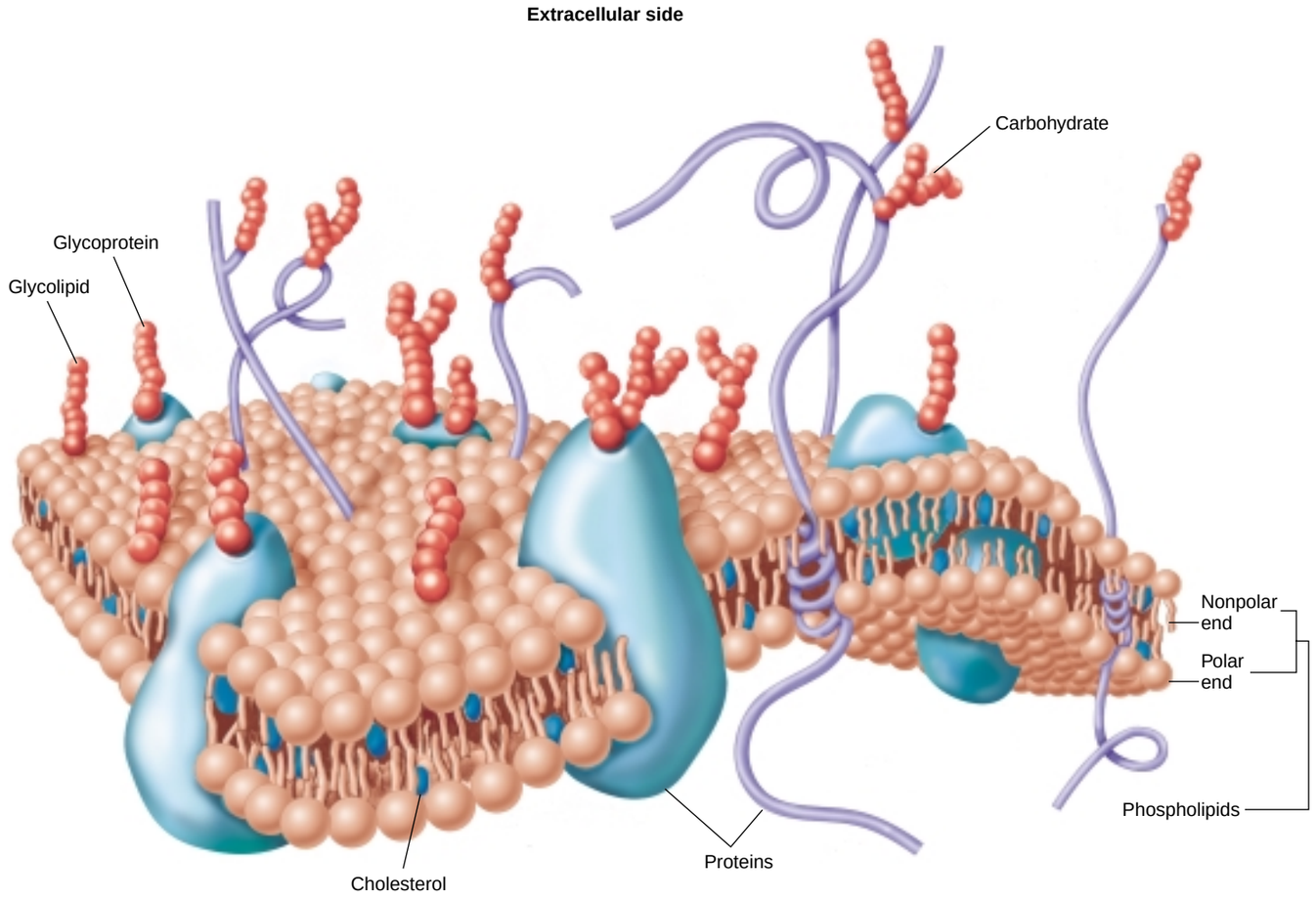


Figure 3.2 **The fluid-mosaic model of the plasma membrane.** The membrane consists of a double layer of phospholipids, with the polar regions (shown by spheres) oriented outward and the nonpolar hydrocarbons (wavy lines) oriented toward the center. Proteins may completely or partially span the membrane. Carbohydrates are attached to the outer surface.

move laterally—the proteins within the phospholipid "sea" are not uniformly distributed. Rather, they present a constantly changing mosaic pattern, an arrangement known as the **fluid-mosaic model** of membrane structure (fig. 3.2).

The proteins found in the plasma membrane serve a variety of functions, including structural support, transport of molecules across the membrane, and enzymatic control of chemical reactions at the cell surface. Some proteins function as receptors for hormones and other regulatory molecules that arrive at the outer surface of the membrane. Receptor proteins are usually specific for one particular messenger much like an enzyme that is specific for a single substrate. Other cellular proteins serve as "markers" (antigens) that identify the blood and tissue type of an individual.

The plasma membranes of all higher organisms contain cholesterol. The cells in the body with the highest content of cholesterol are the Schwann cells, which form insulating layers by wrapping around certain nerve fibers (see chapter 7). Their high cholesterol content is believed to be important in this insulating function. The ratio of cholesterol to phospholipids also helps to determine the flexibility of a plasma membrane. When there is an inherited defect in this ratio, the flexibility of the cell may be reduced. This could result, for example, in the inability of red blood cells to flex at the middle when passing through narrow blood channels, thereby causing occlusion of these small vessels.

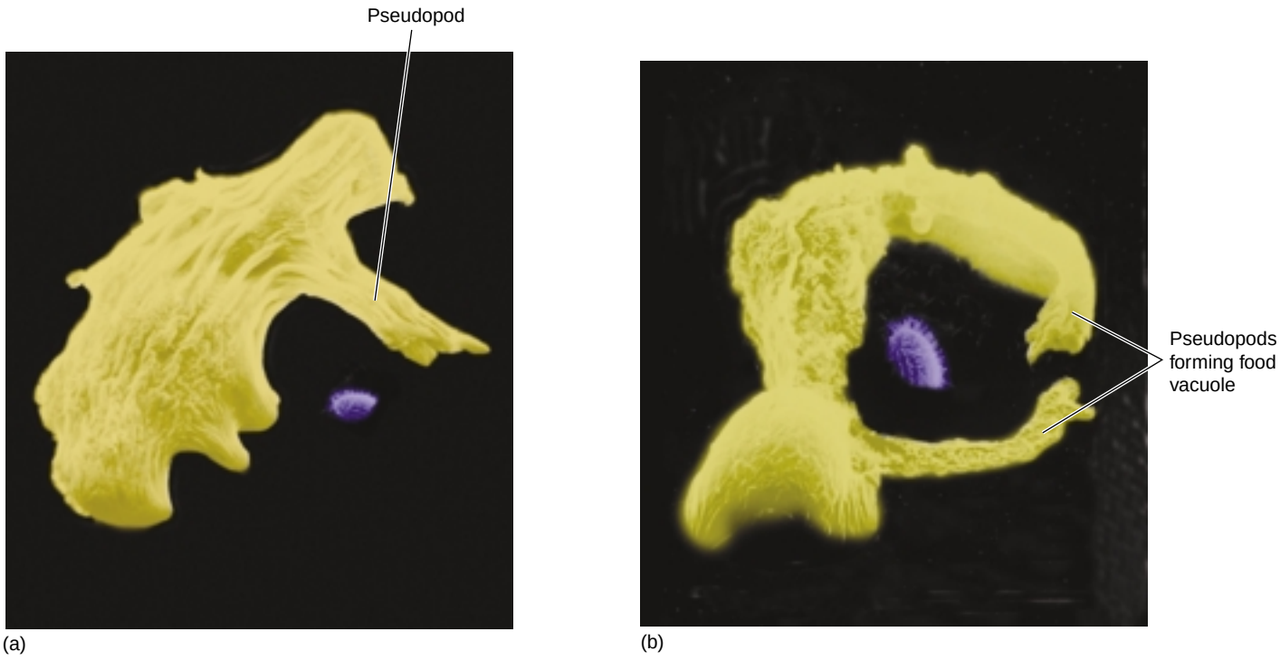


Figure 3.3 **Scanning electron micrographs of phagocytosis.** (*a*) The formation of pseudopods and (*b*) the entrapment of the prey within a food vacuole.

In addition to lipids and proteins, the plasma membrane also contains carbohydrates, which are primarily attached to the outer surface of the membrane as glycoproteins and glycolipids. These surface carbohydrates have numerous negative charges and, as a result, affect the interaction of regulatory molecules with the membrane. The negative charges at the surface also affect interactions between cells—they help keep red blood cells apart, for example. Stripping the carbohydrates from the outer red blood cell surface results in their more rapid destruction by the liver, spleen, and bone marrow.

Phagocytosis

Most of the movement of molecules and ions between the intracellular and extracellular compartments involves passage through the plasma membrane (see chapter 6). However, the plasma membrane also participates in the **bulk transport** of larger portions of the extracellular environment. Bulk transport includes the processes of *phagocytosis* and *endocytosis*.

Some body cells—including certain white blood cells and macrophages in connective tissues—are able to move in the manner of an amoeba (a single-celled organism). They perform this **amoeboid movement** by extending parts of their cytoplasm to form *pseudopods*, which attach to a substrate and pull the cell along. This process depends on the bonding of membrane-spanning proteins called *integrins* with proteins outside the membrane in the *extracellular matrix* (generally, an extracellular gel of proteins and carbohydrates).

Cells that exhibit amoeboid motion—as well as certain liver cells, which are not mobile—use pseudopods to surround and engulf particles of organic matter (such as bacteria). This process is a type of cellular "eating" called **phagocytosis.** It serves to protect the body from invading microorganisms and to remove extracellular debris.

Phagocytic cells surround their victim with pseudopods, which join together and fuse (fig. 3.3). After the inner membrane of the pseudopods has become a continuous membrane surrounding the ingested particle, it pinches off from the plasma membrane. The ingested particle is now contained in an organelle called a *food vacuole* within the cell. The food vacuole will subsequently fuse with an organelle called a lysosome (described later), and the particle will be digested by lysosomal enzymes.

Endocytosis

Endocytosis is a process in which the plasma membrane furrows inward, instead of extending outward with pseudopods. One form of endocytosis, **pinocytosis,** is a nonspecific process performed by many cells. The plasma membrane invaginates to produce a deep, narrow furrow. The membrane near the surface of this furrow then fuses, and a small vesicle containing the extracellular fluid is pinched off and enters the cell. Pinocytosis allows a cell to engulf large molecules such as proteins, as well as any other molecules that may be present in the extracellular fluid.

Another type of endocytosis involves a smaller area of plasma membrane, and it occurs only in response to specific molecules in

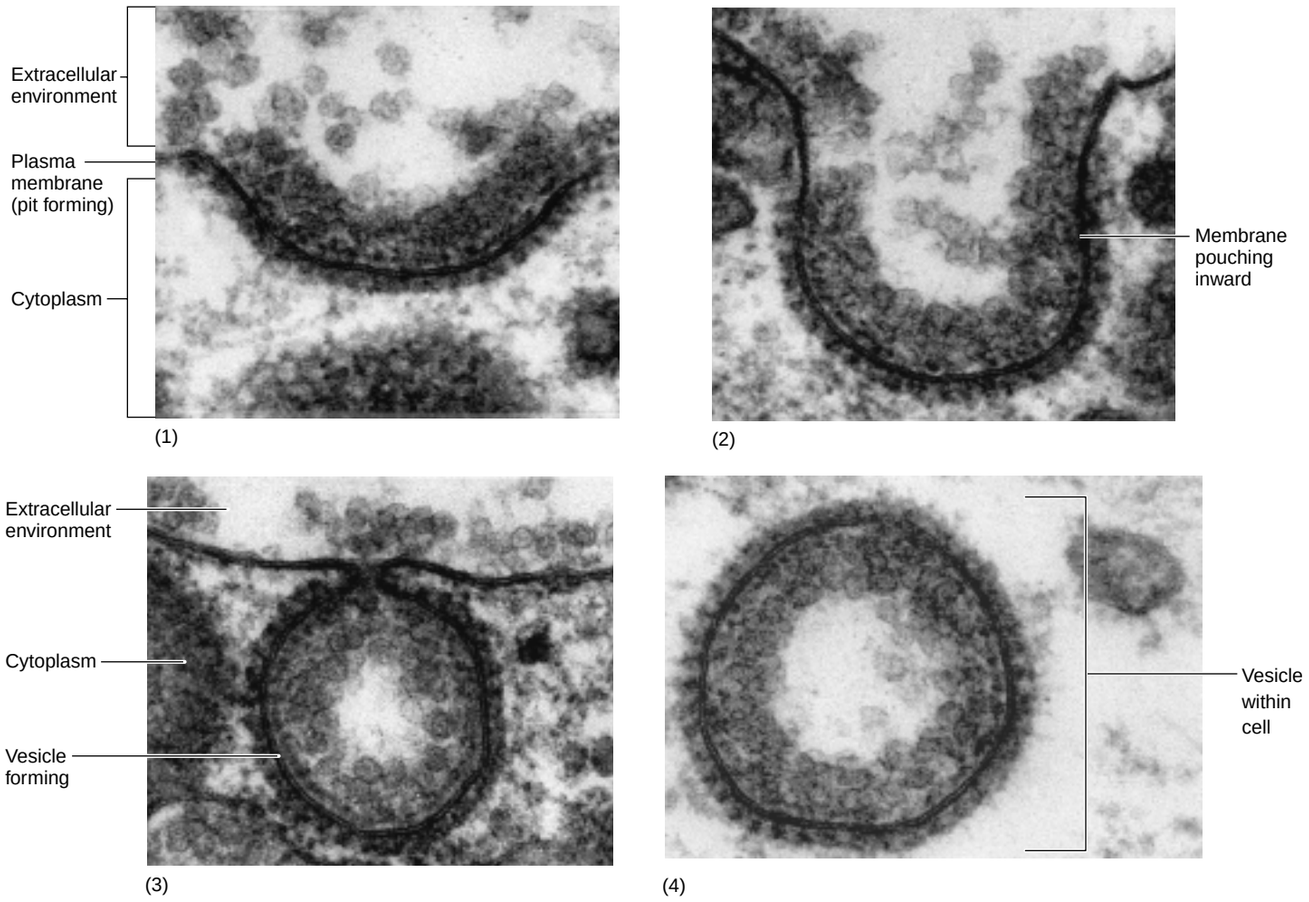


Figure 3.4 **Receptor-mediated endocytosis.** In stages 1 through 4 shown here, specific bonding of extracellular particles with membrane receptor proteins results in the formation of endocytotic vesicles.

the extracellular environment. Since the extracellular molecules must bind to very specific *receptor proteins* in the plasma membrane, this process is known as **receptor-mediated endocytosis.**

In receptor-mediated endocytosis, the interaction of specific molecules in the extracellular fluid with specific membrane receptor proteins causes the membrane to invaginate, fuse, and pinch off to form a vesicle (fig. 3.4). Vesicles formed in this way contain extracellular fluid and molecules that could not have passed by other means into the cell. Cholesterol attached to specific proteins, for example, is taken up into artery cells by receptor-mediated endocytosis. This is in part responsible for atherosclerosis, as described in chapter 13. Hepatitis, polio, and AIDS viruses also exploit the process of receptor-mediated endocytosis to invade cells.

Exocytosis

Exocytosis is a process by which cellular products are secreted into the extracellular environment. Proteins and other molecules produced within the cell that are destined for export (secretion) are packaged within vesicles by an organelle known as the Golgi complex. In the process of exocytosis, these secretory vesicles fuse with the plasma membrane and release their contents into the extracellular environment (see fig. 3.13). Nerve endings, for example, release their chemical neurotransmitters in this manner (see chapter 7).

When the vesicle containing the secretory products of the cell fuses with the plasma membrane during exocytosis, the total surface area of the cell membrane is increased. This process replaces material that was lost from the plasma membrane during endocytosis.

Cilia and Flagella

Cilia are tiny hairlike structures that project from the surface of a cell and, like the coordinated action of rowers in a boat, stroke in unison. Cilia in the human body are found on the apical surface (the surface facing the lumen, or cavity) of stationary epithelial cells in the respiratory and female reproductive tracts. In the respiratory system, the cilia transport strands of mucus to the pharynx (throat), where the mucus can either be swallowed or expectorated. In the female reproductive tract, ciliary movements in the epithelial lining of the uterine tube draw the ovum (egg) into the tube and move it toward the uterus.

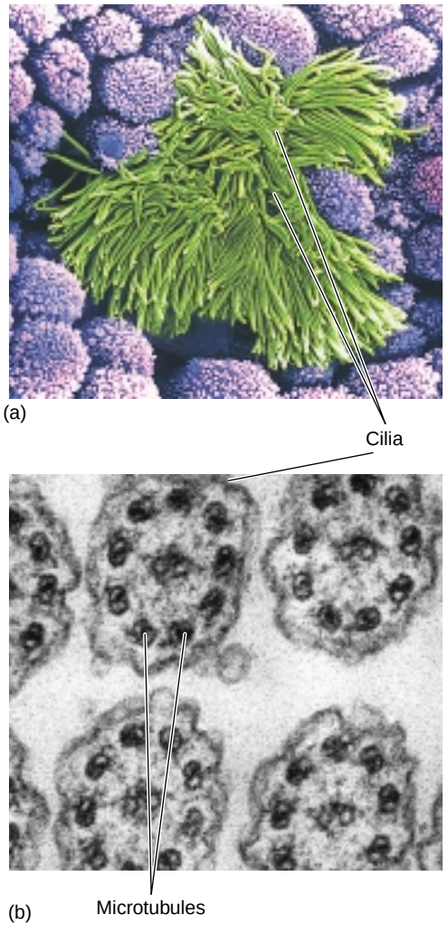


Figure 3.5 **Electron micrographs of cilia.** The cilia can be seen in (*a*) a scanning electron micrograph and (*b*) cross sections in a transmission electron micrograph. Notice the characteristic "9 + 2" arrangement of microtubules in the cross sections.

Sperm cells are the only cells in the human body that have **flagella.** The flagellum is a single whiplike structure that propels the sperm cell through its environment. Both cilia and flagella are composed of *microtubules* (thin cylinders formed from proteins) arranged in a characteristic way. One pair of microtubules in the center of a cilium or flagellum is surrounded by nine other pairs of microtubules, to produce what is often described as a "9 + 2" arrangement (fig. 3.5).

Microvilli

In areas of the body that are specialized for rapid diffusion, the surface area of the cell membranes may be increased by numerous folds called **microvilli.** The rapid passage of the products of digestion across the epithelial membranes in the intestine, for example, is aided by these structural adaptations. The surface

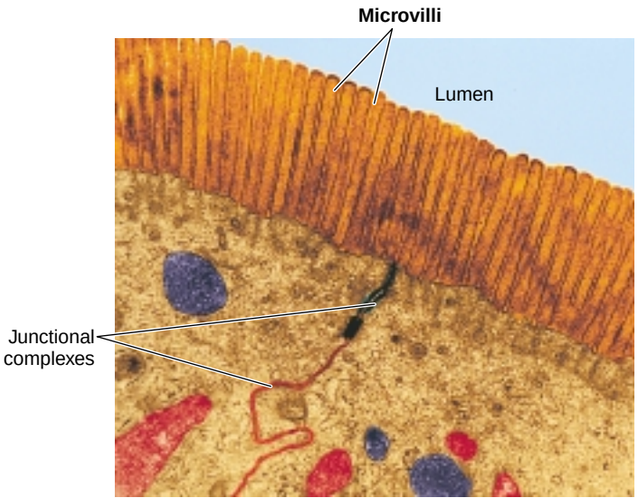


Figure 3.6 **Microvilli in the small intestine.** Microvilli are seen in this colorized electron micrograph, which shows two adjacent cells joined together by junctional complexes.

area of the apical membranes (the part facing the lumen) in the intestine is increased by the numerous tiny fingerlike projections (fig. 3.6). Similar microvilli are found in the epithelium of the kidney tubule, which must reabsorb various molecules that are filtered out of the blood.

Test Yourself Before You Continue

1. Describe the structure of the plasma membrane.
2. Describe the different ways that cells can engulf materials in the extracellular fluid.
3. Explain the process of exocytosis.
4. Describe the structure and function of cilia, flagella, and microvilli.

Cytoplasm and Its Organelles

Many of the functions of a cell that are performed in the cytoplasmic compartment result from the activity of specific structures called organelles. Among these are the lysosomes, which contain digestive enzymes, and the mitochondria, where most of the cellular energy is produced. Other organelles participate in the synthesis and secretion of cellular products.

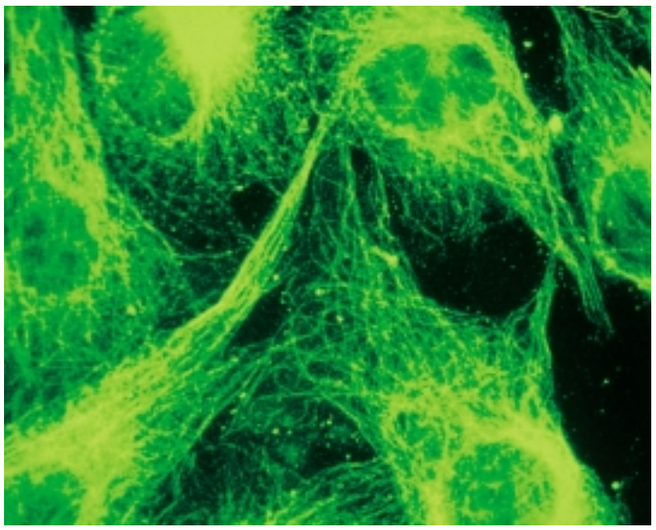


Figure 3.7 An immunofluorescence photograph of microtubules.
The microtubules in this photograph are visualized with the aid of fluorescent antibodies against tubulin, the major protein component of the microtubules.

Cytoplasm and Cytoskeleton

The jellylike matrix within a cell (exclusive of that within the nucleus) is known as **cytoplasm.** Cytoplasm includes structures called **organelles** that are visible under the microscope, and the fluidlike **cytosol** that surrounds the organelles. When viewed in a microscope without special techniques, the cytoplasm appears to be uniform and unstructured. According to modern evidence, however, the cytosol is not a homogenous solution; it is, rather, a highly organized structure in which protein fibers—in the form of *microtubules* and *microfilaments*—are arranged in a complex latticework surrounding the membrane-bound organelles. Using fluorescence microscopy, these structures can be visualized with the aid of antibodies against their protein components (fig. 3.7). The interconnected microfilaments and microtubules are believed to provide structural organization for cytoplasmic enzymes and support for various organelles.

The latticework of microfilaments and microtubules is said to function as a **cytoskeleton** (fig. 3.8). The structure of this "skeleton" is not rigid; it is capable of quite rapid movement and reorganization. Contractile proteins—including actin and myosin, which are responsible for muscle contraction—are microfilaments found in most cells. Such microfilaments aid in amoeboid movement, for example, so that the cytoskeleton is also the cell's "musculature." Microtubules, as another example, form the *spindle apparatus* that pulls chromosomes away from each other in cell division. Microtubules also form the central parts of cilia and flagella and contribute to the structure and movements of these projections from the cells.

The cytoplasm of some cells contains stored chemicals in aggregates called **inclusions.** Examples are *glycogen granules* in the liver, striated muscles, and some other tissues; *melanin granules* in the melanocytes of the skin; and *triglycerides* within adipose cells.

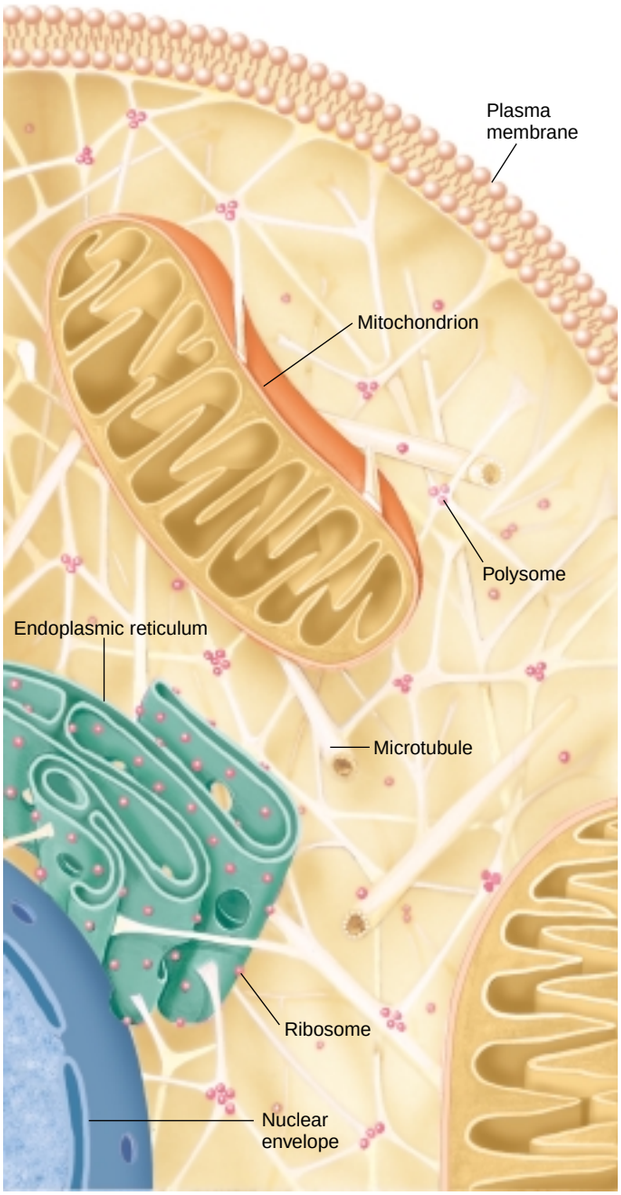


Figure 3.8 The formation of the cytoskeleton by microtubules.
Microtubules are also important in the motility (movement) of the cell, and movement of materials within the cell.

Lysosomes

After a phagocytic cell has engulfed the proteins, polysaccharides, and lipids present in a particle of "food" (such as a bacterium), these molecules are still kept isolated from the cytoplasm by the membranes surrounding the food vacuole. The large molecules of proteins, polysaccharides, and lipids must first be digested into their smaller subunits (including amino acids, monosaccharides, and fatty acids) before they can cross the vacuole membrane and enter the cytoplasm.

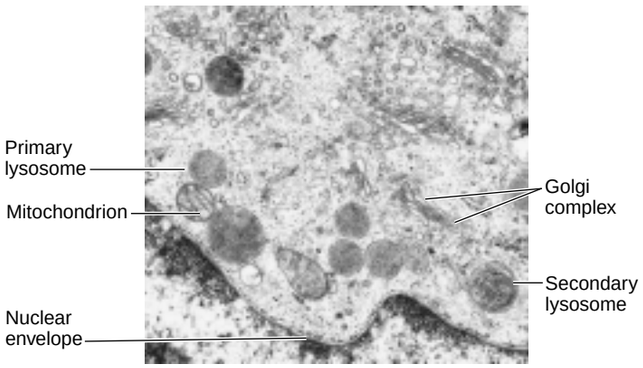


Figure 3.9 An electron micrograph of lysosomes. This photograph shows primary and secondary lysosomes, mitochondria, and the Golgi complex.

The digestive enzymes of a cell are isolated from the cytoplasm and concentrated within membrane-bound organelles called **lysosomes** (fig. 3.9). A *primary lysosome* is one that contains only digestive enzymes (about forty different types) within an environment that is considerably more acidic than the surrounding cytoplasm. A primary lysosome may fuse with a food vacuole (or with another cellular organelle) to form a *secondary lysosome* in which worn-out organelles and the products of phagocytosis can be digested. Thus, a secondary lysosome contains partially digested remnants of other organelles and ingested organic material. A lysosome that contains undigested wastes is called a *residual body.* Residual bodies may eliminate their waste by exocytosis, or the wastes may accumulate within the cell as the cell ages.

Partly digested membranes of various organelles and other cellular debris are often observed within secondary lysosomes. This is a result of **autophagy,** a process that destroys worn-out organelles so that they can be continuously replaced. Lysosomes are thus aptly characterized as the "digestive system" of the cell.

Lysosomes have also been called "suicide bags" because a break in their membranes would release their digestive enzymes and thus destroy the cell. This happens normally in *programmed cell death* (or *apoptosis*), described later in the discussion of the cell cycle. An example is the loss of tissues that must accompany embryonic development, when earlier structures (such as gill pouches) are remodeled or replaced as the embryo matures.

CLINICAL

Most, if not all, molecules in the cell have a limited life span. They are continuously destroyed and must be continuously replaced. Glycogen and some complex lipids in the brain, for example, are normally digested at a particular rate by lysosomes. If a person, because of some genetic defect, does not have the proper amount of these lysosomal enzymes, the resulting abnormal accumulation of glycogen and lipids could destroy the tissues. Examples of such defects include **Tay Sach's disease** and **Gaucher's disease.**

Clinical Investigation Clues

Remember that Timothy has large amounts of glycogen granules, with many intact granules seen within his secondary lysosomes.

Could his apparent liver disease be caused by another disorder?

What condition may Timothy have that would explain the presence of intact glycogen granules in his lysosomes?

Peroxisomes

Peroxisomes are membrane-enclosed organelles containing several specific enzymes that promote oxidative reactions. Although peroxisomes are present in most cells, they are particularly large and active in the liver.

All peroxisomes contain one or more enzymes that promote reactions in which hydrogen is removed from particular organic molecules and transferred to molecular oxygen (O_2), thereby oxidizing the molecule and forming hydrogen peroxide (H_2O_2) in the process. The oxidation of toxic molecules by peroxisomes in this way is an important function of liver and kidney cells. For example, much of the alcohol ingested in alcoholic drinks is oxidized into acetaldehyde by liver peroxisomes.

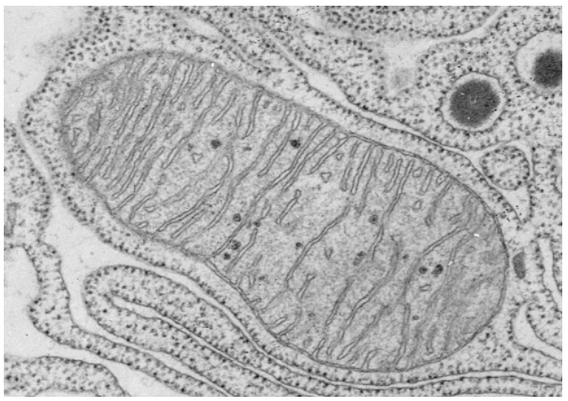
The enzyme *catalase* within the peroxisomes prevents the excessive accumulation of hydrogen peroxide by catalyzing the reaction $2H_2O_2 \rightarrow 2\ H_2O + O_2$. Catalase is one of the fastest acting enzymes known (see chapter 4), and it is this reaction that produces the characteristic fizzing when hydrogen peroxide is poured on a wound.

Mitochondria

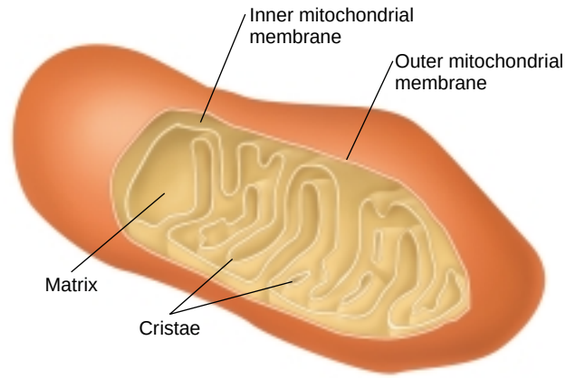
All cells in the body, with the exception of mature red blood cells, have from a hundred to a few thousand organelles called **mitochondria** (singular, **mitochondrion**). Mitochondria serve as sites for the production of most of the energy of cells (see chapter 5).

Mitochondria vary in size and shape, but all have the same basic structure (fig. 3.10). Each mitochondrion is surrounded by an inner and outer membrane, separated by a narrow intermembranous space. The outer mitochondrial membrane is smooth, but the inner membrane is characterized by many folds, called *cristae,* which project like shelves into the central area (or *matrix*) of the mitochondrion. The cristae and the matrix compartmentalize the space within the mitochondrion and have different roles in the generation of cellular energy. The structure and functions of mitochondria will be described in more detail in the context of cellular metabolism in chapter 5.

Mitochondria can migrate through the cytoplasm of a cell and are able to reproduce themselves. Indeed, mitochondria contain their own DNA. This is a more primitive form of DNA (consisting of a circular, relatively small, double-stranded molecule) than that found within the cell nucleus. For this and other reasons, many scientists believe that mitochondria evolved from separate organisms, related to bacteria, that invaded the ancestors of animal cells and remained in a state of symbiosis.



(a)



(b)

Figure 3.10 **The structure of a mitochondrion.** (*a*) An electron micrograph of a mitochondrion. The outer mitochondrial membrane and the infoldings of the inner membrane—the cristae—are clearly seen. The fluid in the center is the matrix. (*b*) A diagram of the structure of a mitochondrion.

An unfertilized ovum (egg cell) contains numerous mitochondria, and upon fertilization, gains few if any mitochondria from the sperm. The mitochondrial DNA replicates itself and the mitochondria subsequently divide by pinching off, so that mitochondria can enter the proliferating cells of the embryo and fetus. Thus, all (or nearly all) of the mitochondria in a person are ultimately inherited from that person's mother. This provides a unique form of inheritance that is passed only from mother to child. A rare cause of blindness known as **Leber's hereditary optic neuropathy,** as well as several other disorders, are inherited only along the maternal lineage and are known to be caused by defective mitochondrial DNA.

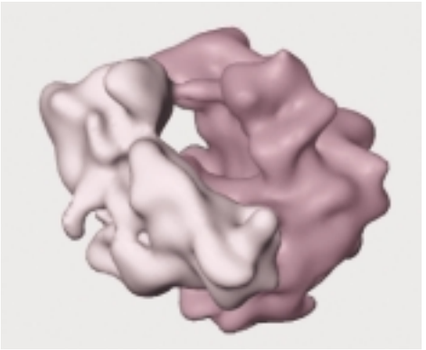


Figure 3.11 **A ribosome is composed of two subunits.** This is a model of the structure of a ribosome, showing the smaller (yellow) and larger (blue) subunits. The space between the two subunits accommodates a molecule of transfer RNA, needed to bring amino acids to the growing polypeptide chain.

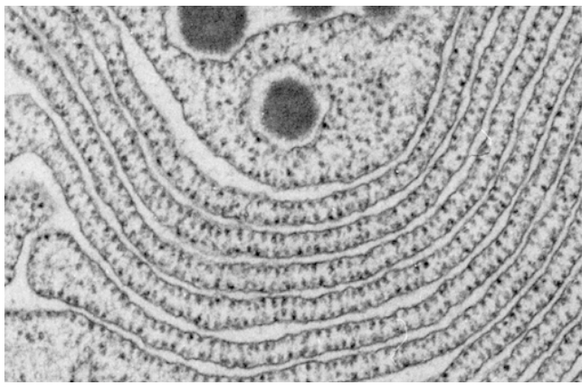
Ribosomes

Ribosomes are often called the "protein factories" of the cell, because it is here that proteins are produced according to the genetic information contained in messenger RNA (discussed in a later section). The ribosomes are quite tiny, about 25 nanometers in size, and can be found both free in the cytoplasm and located on the surface of an organelle called the endoplasmic reticulum (discussed in the next section).

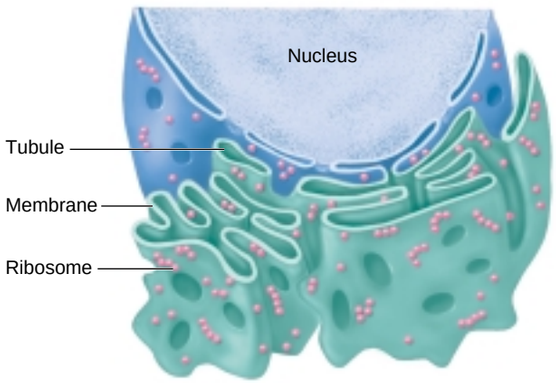
Each ribosome consists of two subunits (fig. 3.11) that are designated 30S and 50S, after their sedimentation rate in a centrifuge (this is measured in Svedberg units, from which the "S" is derived). Each of the subunits is composed of both ribosomal RNA and proteins. Contrary to earlier expectations of most scientists, it now appears that the ribosomal RNA molecules serve as enzymes (called *ribozymes*) for many of the reactions in the ribosomes that are required for protein synthesis. Protein synthesis is covered later in this chapter, and the general subject of enzymes and catalysis is discussed in chapter 4.

Endoplasmic Reticulum

Most cells contain a system of membranes known as the **endoplasmic reticulum,** or **ER.** The ER may be either of two types: (1) a **granular,** or **rough, endoplasmic reticulum** and (2) an **agranular,** or **smooth, endoplasmic reticulum** (fig. 3.12). A granular endoplasmic reticulum bears ribosomes on its surface, whereas an agranular endoplasmic reticulum does not. The agranular endoplasmic reticulum serves a variety of purposes in different cells; it provides a site for enzyme reactions in steroid hormone



(a)



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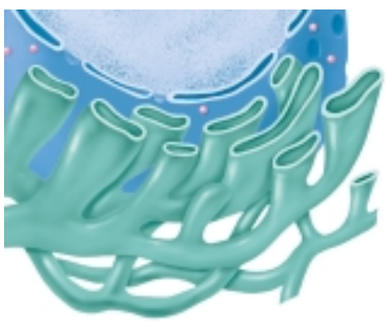


(c)

Figure 3.12 **The endoplasmic reticulum.** (*a*) An electron micrograph of a granular endoplasmic reticulum (about 100,000×). The granular endoplasmic reticulum (*b*) has ribosomes attached to its surface, whereas the agranular endoplasmic reticulum (*c*) lacks ribosomes.

production and inactivation, for example, and a site for the storage of Ca^{2+} in striated muscle cells. The granular endoplasmic reticulum is abundant in cells that are active in protein synthesis and secretion, such as those of many exocrine and endocrine glands.

The agranular endoplasmic reticulum in liver cells contains enzymes used for the inactivation of steroid hormones and many drugs. This inactivation is generally achieved by reactions that convert these compounds to more water-soluble and less active forms, which can be more easily excreted by the kidneys. When people take certain drugs (such as alcohol and phenobarbital) for a long period of time, increasingly large doses of these compounds are required to achieve the effect produced initially. This phenomenon, called **tolerance,** is accompanied by growth of the agranular endoplasmic reticulum, and thus an increase in the amount of enzymes charged with inactivation of these drugs.

Clinical Investigation Clues

Remember that Timothy's liver cells have an unusually extensive smooth endoplasmic reticulum.

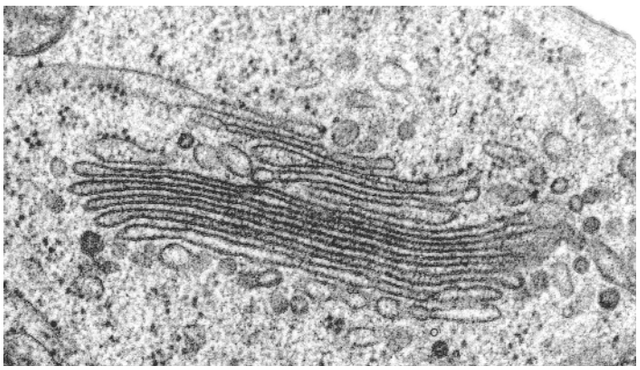
- *Why is his endoplasmic reticulum so well developed, and what beneficial function might this serve?*
- *What could he do to determine if this is the cause of his liver problems?*

Golgi Complex

The **Golgi complex,** also called the **Golgi apparatus,** consists of a stack of several flattened sacs (fig. 3.13). This is something like a stack of pancakes, but the Golgi sac "pancakes" are hollow, with cavities called *cisternae* within each sac. One side of the stack faces the endoplasmic reticulum and serves as a site of entry for vesicles from the endoplasmic reticulum that contain cellular products. These products are passed from one sac to the next, probably by means of vesicles that are budded from one sac and fuse with the next, though other mechanisms may also be involved.

The opposite side of the Golgi stack of sacs faces toward the plasma membrane. As the cellular product passes toward that side it is chemically modified, and then released within vesicles that are budded off the sac. Depending on the nature of the specific product, the vesicles that leave the Golgi complex may become lysosomes, storage granules, secretory vesicles, or additions to the plasma membrane.

(a)



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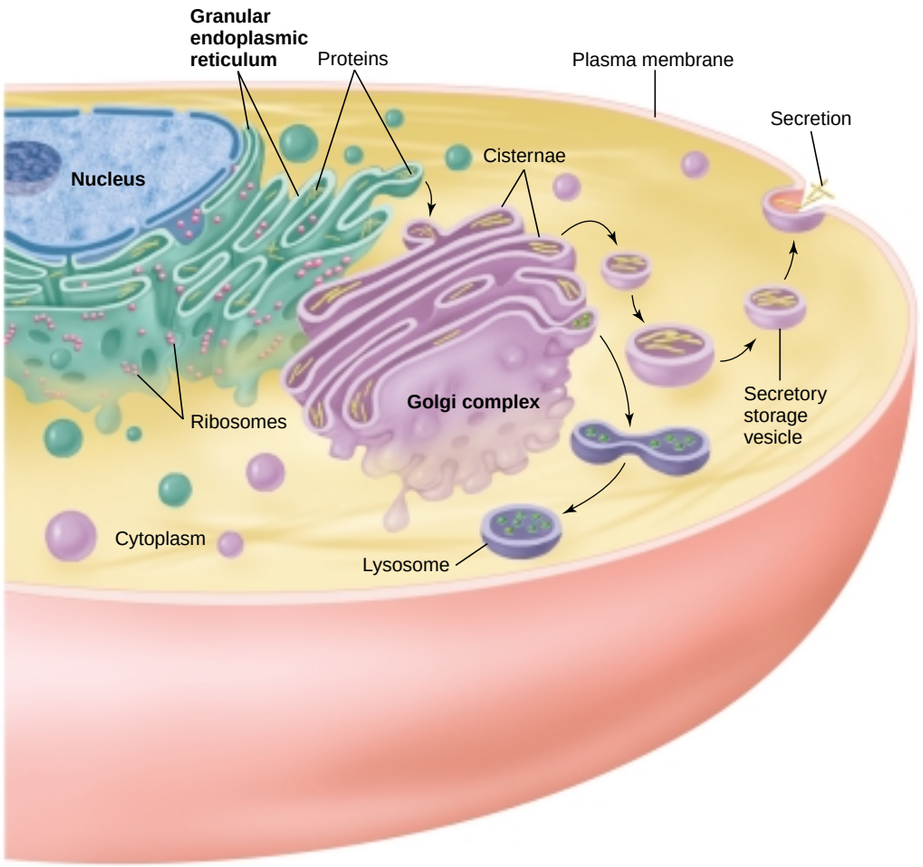


Figure 3.13 **The Golgi complex.** (*a*) An electron micrograph of a Golgi complex. Notice the formation of vesicles at the ends of some of the flattened sacs. (*b*) An illustration of the processing of proteins by the granular endoplasmic reticulum and Golgi complex.

Test Yourself Before You Continue

1. Explain why microtubules and microfilaments can be thought of as the skeleton and musculature of a cell.
2. Describe the functions of lysosomes and peroxisomes.
3. Describe the structure and functions of mitochondria.
4. Explain how mitochondria can provide a genetic inheritance derived only from the mother.
5. Describe the structure and function of ribosomes.
6. Distinguish between a granular and agranular endoplasmic reticulum in terms of their structure and function.

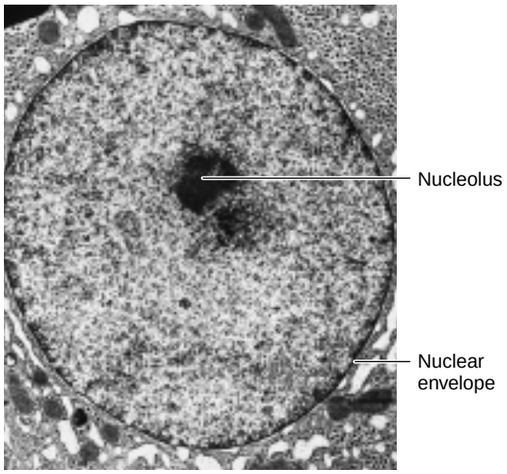


Figure 3.14 **The structure of a nucleus.** The nucleus of a liver cell, with its nuclear envelope and nucleolus, is shown in this electron micrograph.

Cell Nucleus and Gene Expression

The nucleus is the organelle that contains the DNA of a cell. A gene is a length of DNA that codes for the production of a specific polypeptide chain. In order for genes to be expressed, they must first direct the production of complementary RNA molecules. That process is called genetic transcription.

Most cells in the body have a single **nucleus.** Exceptions include skeletal muscle cells, which have two or more nuclei, and mature red blood cells, which have none. The nucleus is enclosed by two membranes—an inner membrane and an outer membrane—that together are called the **nuclear envelope** (fig. 3.14). The outer membrane is continuous with the endoplasmic reticulum in the cytoplasm. At various points, the inner and outer membranes are fused together by structures called *nuclear pore complexes.* These structures function as rivets, holding the two membranes together. Each nuclear pore complex has a central opening, the *nuclear pore* (fig. 3.15), surrounded by interconnected rings and columns of proteins. Small molecules may pass through the complexes by diffusion, but movement of protein and RNA through the nuclear pores is a selective, energy-requiring process.

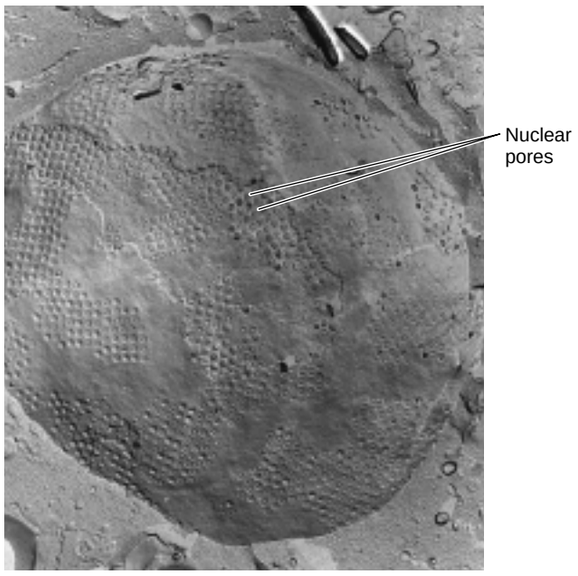
Transport of specific proteins from the cytoplasm into the nucleus through the nuclear pores may serve a variety of functions, including regulation of gene expression by hormones (see chapter 11). Transport of RNA out of the nucleus, where it is formed, is required for gene expression. As described in this section, *genes* are regions of the DNA within the nucleus. Each gene contains the code for the production of a particular type of RNA called messenger RNA (mRNA). As an mRNA molecule is transported through the nuclear pore, it becomes associated with ribosomes that are either free in the cytoplasm or associated with the granular endoplasmic reticulum. The mRNA then provides the code for the production of a specific type of protein.

The primary structure of the protein (its amino acid sequence) is determined by the sequence of bases in mRNA. The base sequence of mRNA has been previously determined by the sequence of bases in the region of the DNA (the gene) that codes for the mRNA. **Genetic expression** therefore occurs in two stages: first **genetic transcription** (synthesis of RNA) and then **genetic translation** (synthesis of protein).

Each nucleus contains one or more dark areas (see fig. 3.14). These regions, which are not surrounded by membranes, are called **nucleoli.** The DNA within the nucleoli contains the genes that code for the production of ribosomal RNA (rRNA).

CLINICAL

The **Human Genome Project** began in 1990 as an international effort to sequence the human genome. In February of 2001, two versions were published: one sponsored by public agencies that was published in the journal *Science,* and one produced by a private company that was published in the journal *Nature.* It soon became apparent that human DNA is 99.9% similar among people; a mere 0.1% is responsible for human genetic variation. It also seems that humans only have about 30,000 to 40,000 genes (segments that code for polypeptide chains), rather than the 100,000 genes that scientists had previously believed.



(a)

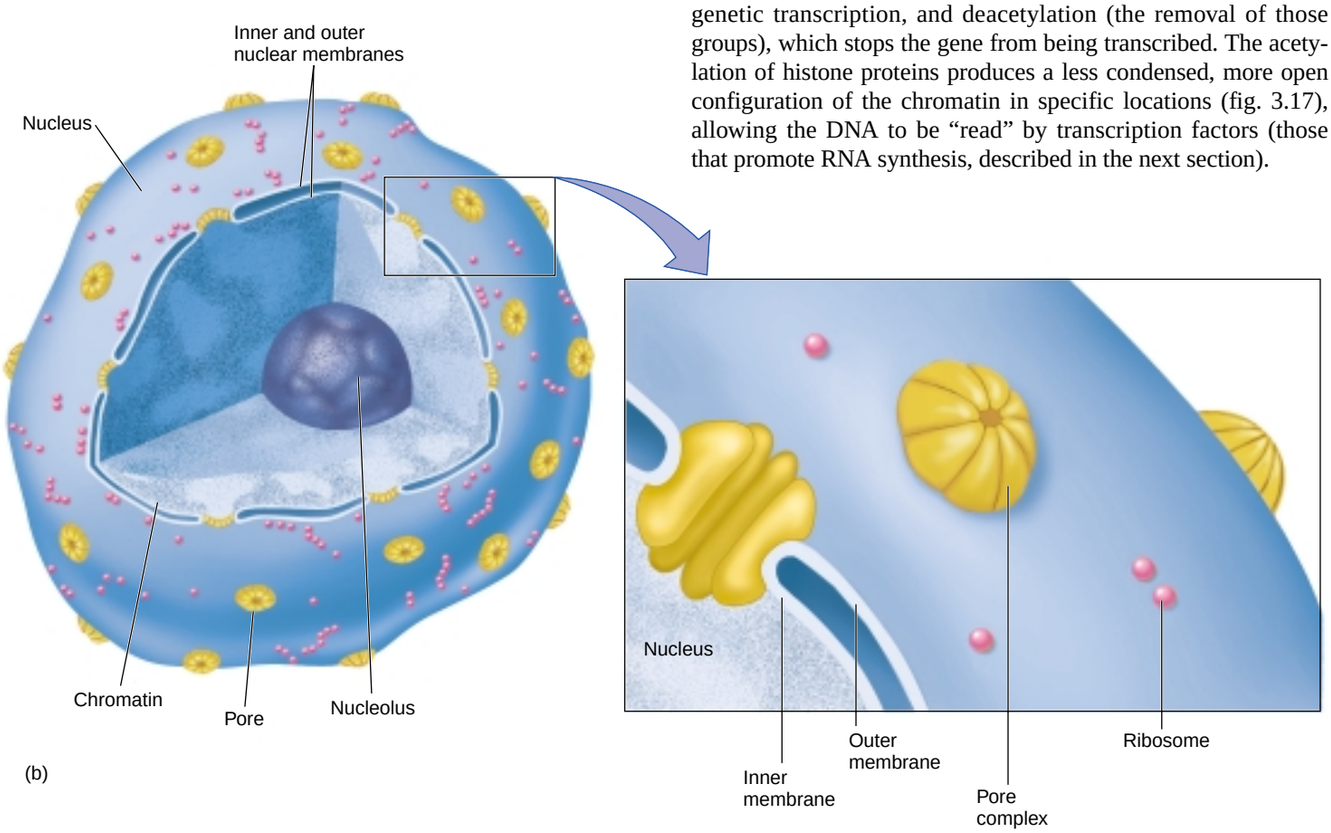
Chromatin

DNA is composed of four different nucleotide subunits that contain the nitrogenous bases adenine, guanine, cytosine, and thymine. These nucleotides form two polynucleotide chains, joined by complementary base pairing and twisted to form a double helix. This structure is discussed in chapter 2 and illustrated in figures 2.30 and 2.31.

The DNA within the cell nucleus is combined with protein to form **chromatin,** the threadlike material that makes up the chromosomes. Much of the protein content of chromatin is of a type known as *histones.* Histone proteins are positively charged and organized to form spools, about which the negatively charged strands of DNA are wound. Each spool consists of two turns of DNA, comprising 146 base pairs, wound around a core of histone proteins. This spooling creates particles known as **nucleosomes** (fig. 3.16).

Chromatin that is active in genetic transcription (RNA synthesis) is in a relatively extended form known as **euchromatin.** Chromatin regions called **heterochromatin,** in contrast, are highly condensed and form blotchy-looking areas in the nucleus. The condensed heterochromatin contains genes that are said to be "silenced," which means that they are permanently inactivated.

In the euchromatin, genes may be activated or repressed at different times. This is believed to be accomplished by chemical changes in the histones. Such changes include acetylation (the addition of two-carbon-long chemical groups), which turns on genetic transcription, and deacetylation (the removal of those groups), which stops the gene from being transcribed. The acetylation of histone proteins produces a less condensed, more open configuration of the chromatin in specific locations (fig. 3.17), allowing the DNA to be "read" by transcription factors (those that promote RNA synthesis, described in the next section).



(b)

Figure 3.15 **The nuclear pores.** (*a*) An electron micrograph of a freeze-fractured nuclear membrane showing the nuclear pores. (*b*) A diagram showing the nuclear pore complexes.

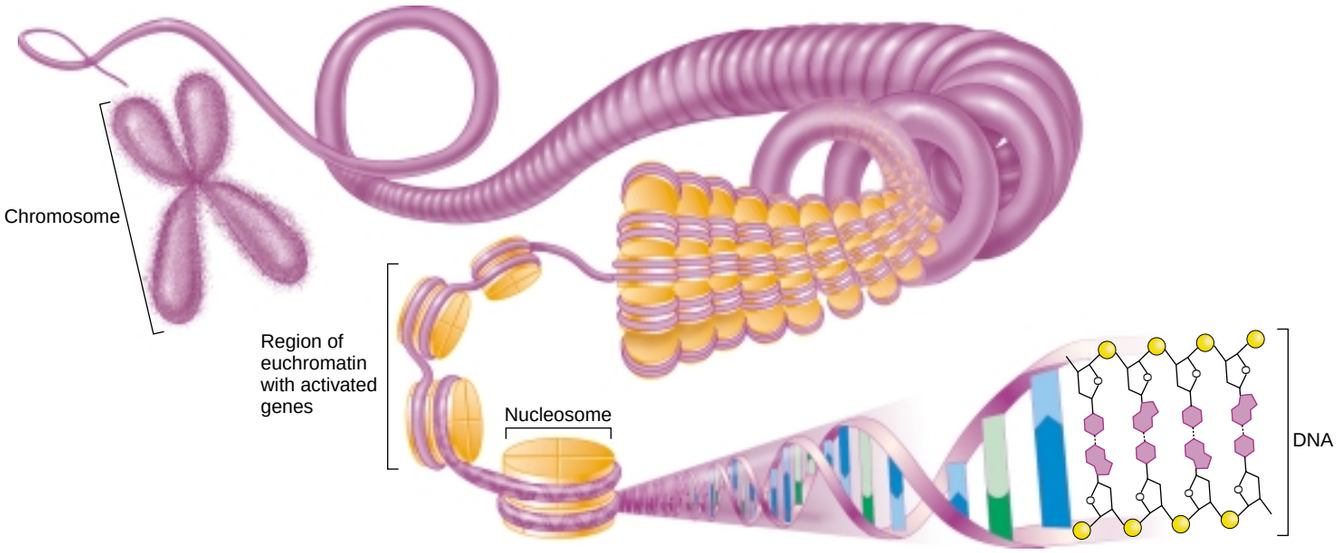


Figure 3.16 **The structure of chromatin.** Part of the DNA is wound around complexes of histone proteins, forming particles known as nucleosomes.

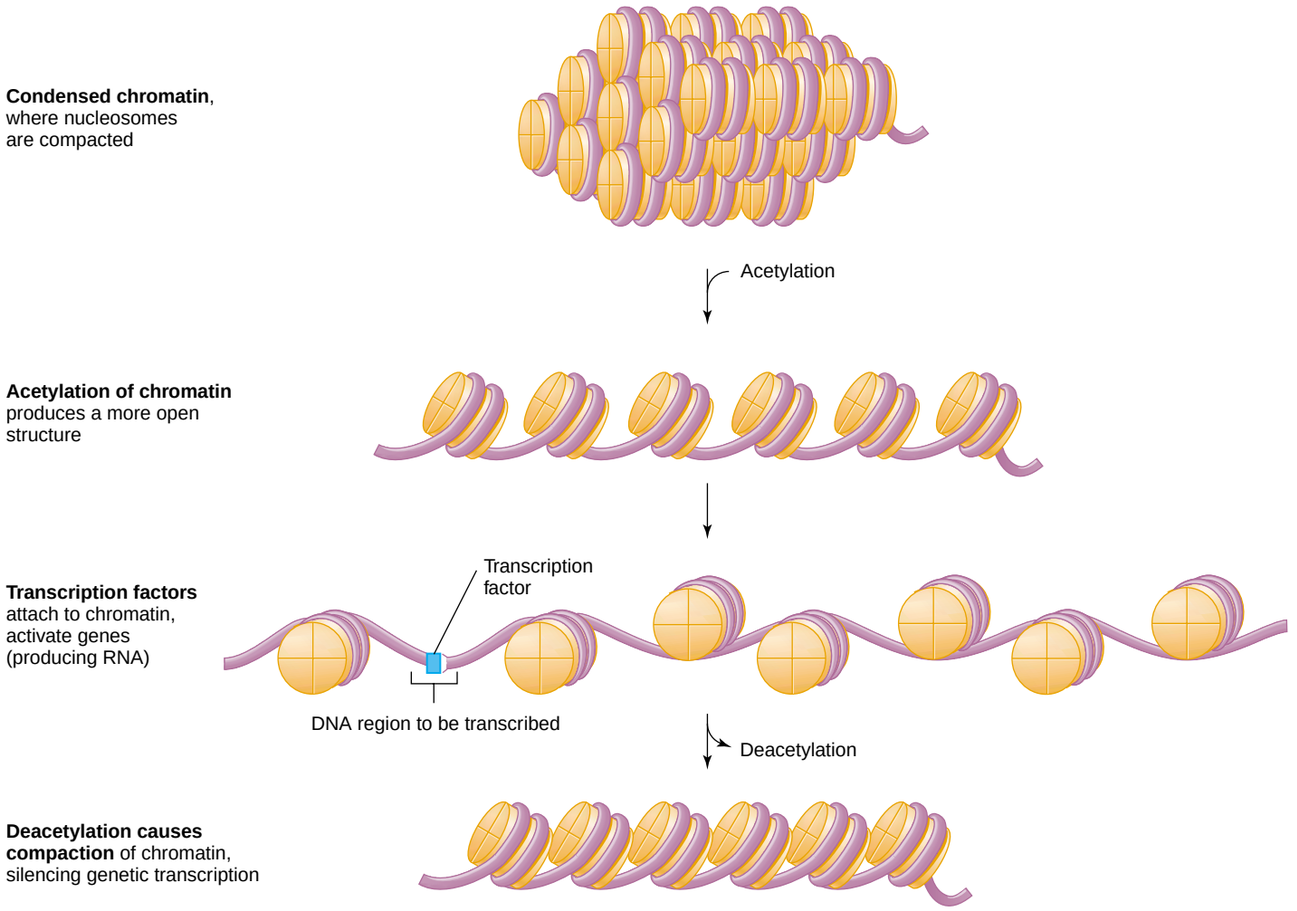


Figure 3.17 **Chromatin structure affects gene expression.** The ability of DNA to be transcribed into messenger RNA is affected by the structure of the chromatin. The genes are silenced when the chromatin is condensed. Acetylation (addition of two-carbon groups) produces a more open chromatin structure that can be activated by transcription factors, producing mRNA. Deacetylation (removal of the acetyl groups) silences genetic transcription.

It is estimated that only about 300 genes out of a total of 30,000 are active in any given cell. This is because each cell becomes specialized for particular functions, in a process called *differentiation.* The differentiated cells of an adult are derived, or "stem from," those of the embryo. Early **embryonic stem cells** can become any cell in the body—they are said to be *totipotent.* As development proceeds, most genes are silenced as cells become more differentiated. *Adult stem cells* can differentiate into a range of specific cell types, but are not normally totipotent. For example, the bone marrow of an adult contains such stem cells (also described in chapter 13, p. 000). These include **hematopoietic stem cells,** which can form the blood cells, and **mesenchymal stem cells,** which can differentiate into osteocytes (bone cells), chondrocytes (cartilage cells), adipocytes (fat cells), and others. **Neural stem cells** (also described in chapter 8, p. 000) have been identified in the adult nervous system. These can migrate to particular locations and differentiate into specific neuron and glial cell types in these locations. Many scientists hope that stem cells grown in tissue culture might someday be used to grow transplantable tissues and organs.

RNA Synthesis

One gene codes for one polypeptide chain. Each gene is a stretch of DNA that is several thousand nucleotide pairs long. The DNA in a human cell contains over 3 billion base pairs—enough to code for at least 3 million proteins. Since the average human cell contains less than this amount (30,000 to 150,000 different proteins), it follows that only a fraction of the DNA in each cell is used to code for proteins. The remainder of the DNA may be inactive or redundant. Also, some segments of DNA serve to regulate those regions that do code for proteins.

In order for the genetic code to be translated into the synthesis of specific proteins, the DNA code first must be copied onto a strand of RNA. This is accomplished by DNA-directed RNA synthesis—the process of **genetic transcription.**

In RNA synthesis, the enzyme **RNA polymerase** breaks the weak hydrogen bonds between paired DNA bases. This does not occur throughout the length of DNA, but only in the regions that are to be transcribed. There are base sequences that code for "start" and "stop," and there are regions of DNA that function as *promoters.* Specific regulatory molecules, such as hormones, act as **transcription factors** by binding to the promoter region of a particular gene and thereby activating the gene. The double-stranded DNA separates in the region to be transcribed, so that the freed bases can pair with the complementary RNA nucleotide bases in the nucleoplasm.

This pairing of bases, like that which occurs in DNA replication (described in a later section), follows the law of complementary base pairing: *guanine bonds with cytosine* (and vice versa), and *adenine bonds with uracil* (because uracil in RNA is equivalent to thymine in DNA). Unlike DNA replication, however, only *one* of the two freed strands of DNA serves as a guide for RNA synthesis (fig. 3.18). Once an RNA molecule has been produced, it detaches from the DNA strand on which it was formed. This process can continue indefinitely, producing many thousands of RNA copies of the DNA strand that is being transcribed. When the gene is no longer to be transcribed, the separated DNA strands can then go back together again.

Types of RNA

There are four types of RNA produced within the nucleus by transcription: (1) **precursor messenger RNA (pre-mRNA),** which is altered within the nucleus to form mRNA; (2) **messenger RNA (mRNA),** which contains the code for the synthesis of specific proteins; (3) **transfer RNA (tRNA),** which is needed for decoding the genetic message contained in mRNA; and (4) **ribosomal RNA (rRNA),** which forms part of the structure of ribosomes. The DNA that codes for rRNA synthesis is located in the part of the nucleus called the nucleolus. The DNA that codes for pre-mRNA and tRNA synthesis is located elsewhere in the nucleus.

In bacteria, where the molecular biology of the gene is best understood, a gene that codes for one type of protein produces an mRNA molecule that begins to direct protein synthesis as soon as it is transcribed. This is not the case in higher organisms, including humans. In higher cells, a pre-mRNA is produced that must be modified within the nucleus before it can enter the cytoplasm as mRNA and direct protein synthesis.

Precursor mRNA is much larger than the mRNA it forms. Surprisingly, this large size of pre-mRNA is not due to excess bases at the ends of the molecule that must be trimmed; rather, the excess bases are located *within* the pre-mRNA. The genetic code for a particular protein, in other words, is split up by stretches of base pairs that do not contribute to the code. These regions of noncoding DNA within a gene are called *introns;* the coding regions are known as *exons.* Consequently, pre-mRNA must be cut and spliced to make mRNA (fig. 3.19). This cutting and splicing can be quite extensive—a single gene may contain up to 50 introns, which must be removed from the pre-mRNA in order to convert it to mRNA.

Introns are cut out of the pre-mRNA, and the ends of the exons spliced, by macromolecules called *snRNPs* (pronounced "snurps"), producing the functional mRNA that leaves the nucleus and enters the cytoplasm. SnRNPs stands for *small nuclear ribonucleoproteins.* These are small, ribosome-like aggregates of RNA and protein that form a body called a *spliceosome* that splices the exons together.

Test Yourself Before You Continue

1. Describe the appearance and composition of chromatin and the structure of nucleosomes. Comment on the significance of histone proteins.
2. Explain how RNA is produced within the nucleus according to the information contained in DNA.
3. Explain how precursor mRNA is modified to produce mRNA.

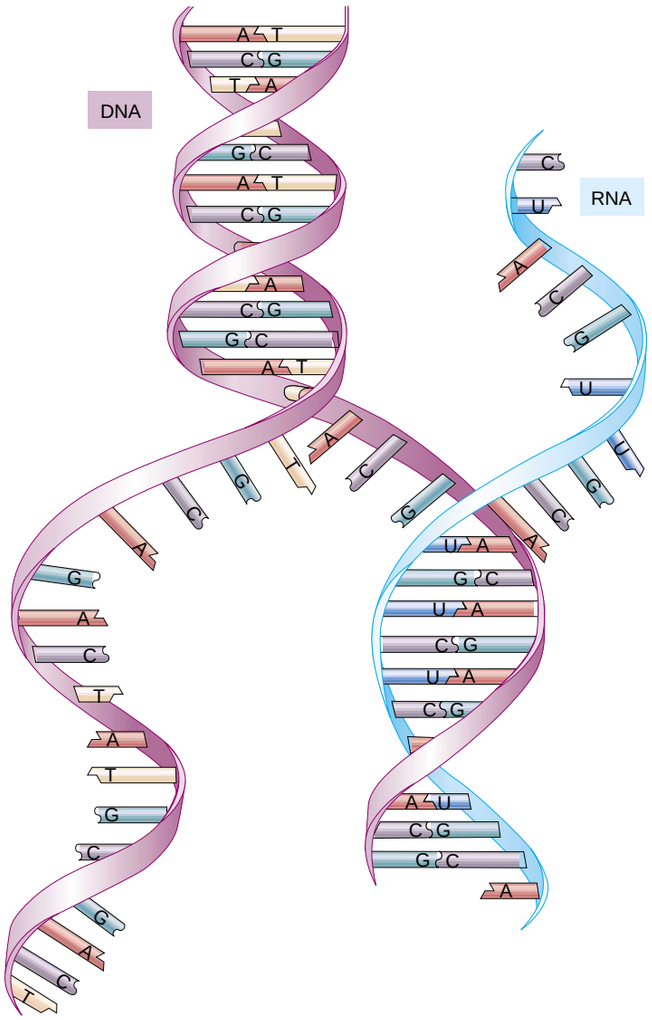


Figure 3.18 **RNA synthesis (transcription).** Notice that only one of the two DNA strands is used to form a single-stranded molecule of RNA.

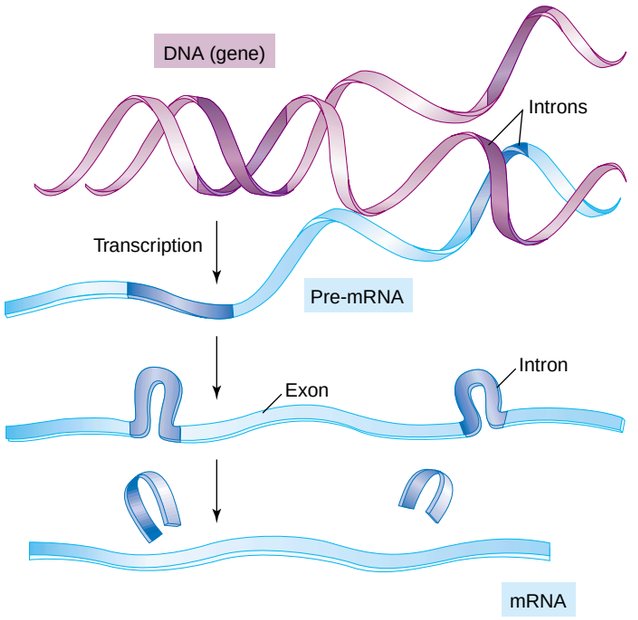


Figure 3.19 **The processing of pre-mRNA into mRNA.** Noncoding regions of the genes, called introns, produce excess bases within the pre-mRNA. These excess bases are removed, and the coding regions of mRNA are spliced together.

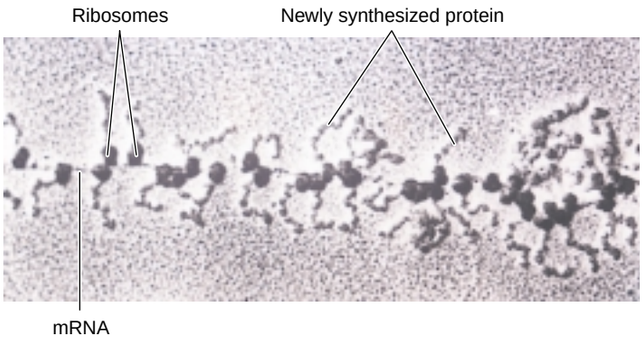


Figure 3.20 **An electron micrograph of a polyribosome.** An RNA strand joins the ribosomes together.

Protein Synthesis and Secretion

In order for a gene to be expressed, it first must be used as a guide, or template, in the production of a complementary strand of messenger RNA. This mRNA is then itself used as a guide to produce a particular type of protein whose sequence of amino acids is determined by the sequence of base triplets (codons) in the mRNA.

When mRNA enters the cytoplasm, it attaches to **ribosomes,** which appear in the electron microscope as numerous small particles. A ribosome is composed of four molecules of ribosomal RNA and eighty-two proteins, arranged to form two subunits of unequal size. The mRNA passes through a number of ribosomes to form a "string-of-pearls" structure called a *polyribosome* (or *polysome,* for short), as shown in figure 3.20. The association of mRNA with ribosomes is needed for the process of **genetic translation**—the production of specific proteins according to the code contained in the mRNA base sequence.

Each mRNA molecule contains several hundred or more nucleotides, arranged in the sequence determined by complementary base pairing with DNA during transcription (RNA synthesis). Every three bases, or *base triplet,* is a code word—called a **codon**—for a specific amino acid. Sample

codons and their amino acid "translations" are listed in table 3.2 and illustrated in figure 3.21. As mRNA moves through the ribosome, the sequence of codons is translated into a sequence of specific amino acids within a growing polypeptide chain.

Table 3.2 Selected DNA Base Triplets and mRNA Codons

DNA Triplet	RNA Codon	Amino Acid
TAC	AUG	"Start" (Methionine)
ATC	UAG	"Stop"
AAA	UUU	Phenylalanine
AGG	UCC	Serine
ACA	UGU	Cysteine
GGG	CCC	Proline
GAA	CUU	Leucine
GCT	CGA	Arginine
TTT	AAA	Lysine
TGC	ACG	Threonine
CCG	GGC	Glycine
CTC	GAG	Glutamic acid

Transfer RNA

Translation of the codons is accomplished by tRNA and particular enzymes. Each tRNA molecule, like mRNA and rRNA, is single-stranded. Although tRNA is single-stranded, it bends in on itself to form a cloverleaf structure (fig. 3.22*a*), which is believed to be further twisted into an upside down "L" shape (fig. 3.22*b*). One end of the "L" contains the **anticodon**—three nucleotides that are complementary to a specific codon in mRNA.

Enzymes in the cell cytoplasm called *aminoacyl-tRNA synthetase enzymes* join specific amino acids to the ends of tRNA, so that a tRNA with a given anticodon can bind to only one specific amino acid. There are twenty different varieties of synthetase enzymes, one for each type of amino acid. Not only must each synthetase recognize its specific amino acid, it also must be able to attach this amino acid to the particular tRNA that has the correct anticodon for that amino acid. The cytoplasm of a cell thus contains tRNA molecules that are each bonded to a specific amino acid, and each of these tRNA molecules is capable of bonding with a specific codon in mRNA via its anticodon base triplet.

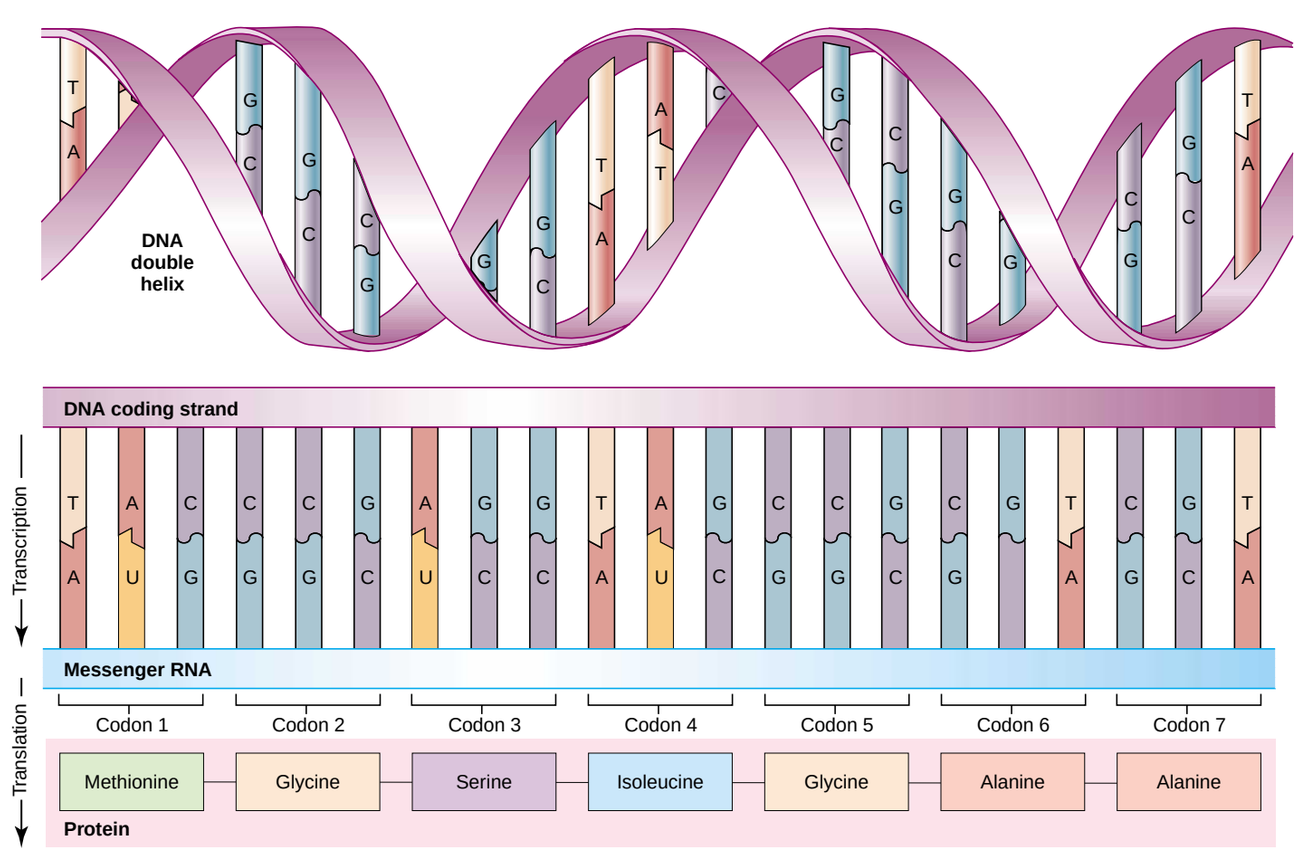


Figure 3.21 **Transcription and translation.** The genetic code is first transcribed into base triplets (codons) in mRNA and then translated into a specific sequence of amino acids in a polypeptide.

Formation of a Polypeptide

The anticodons of tRNA bind to the codons of mRNA as the mRNA moves through the ribosome. Since each tRNA molecule carries a specific amino acid, the joining together of these amino acids by peptide bonds creates a polypeptide whose amino acid sequence has been determined by the sequence of codons in mRNA.

The first and second tRNA bring the first and second amino acids close together. The first amino acid then detaches from its tRNA and is enzymatically transferred to the amino acid on the second tRNA, forming a dipeptide. When the third tRNA binds to the third codon, the amino acid it brings forms a peptide bond with the second amino acid (which detaches from its tRNA). A tripeptide is now attached by the third amino acid to the third tRNA. The polypeptide chain thus grows as new amino acids are added to its growing tip (fig. 3.23). This growing polypeptide chain is always attached by means of only one tRNA to the strand of mRNA, and this tRNA molecule is always the one that has added the latest amino acid to the growing polypeptide.

As the polypeptide chain grows in length, interactions between its amino acids cause the chain to twist into a helix (secondary structure) and to fold and bend upon itself (tertiary structure). At the end of this process, the new protein detaches from the tRNA as the last amino acid is added. Many proteins are further modified after they are formed; these modifications occur in the rough endoplasmic reticulum and Golgi complex.

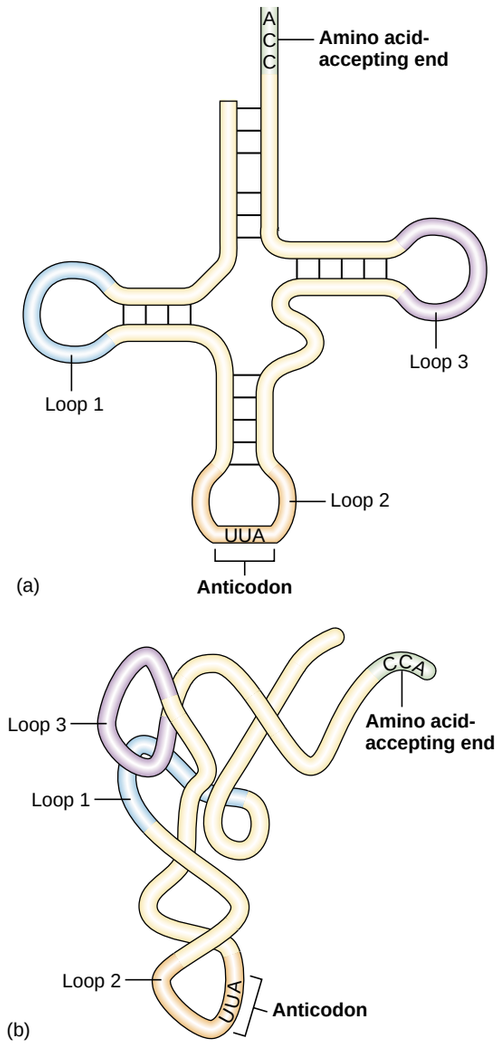


Figure 3.22 The structure of transfer RNA (tRNA). (*a*) A simplified cloverleaf representation and (*b*) the three-dimensional structure of tRNA.

Functions of the Endoplasmic Reticulum and Golgi Complex

Proteins that are to be used within the cell are likely to be produced by polyribosomes that float freely in the cytoplasm, unattached to other organelles. If the protein is to be secreted by the cell, however, it is made by mRNA-ribosome complexes that are located on the granular endoplasmic reticulum. The membranes of this system enclose fluid-filled spaces called *cisternae*, into which the newly formed proteins may enter. Once in the cisternae, the structure of these proteins is modified in specific ways.

When proteins destined for secretion are produced, the first thirty or so amino acids are primarily hydrophobic. This *leader sequence* is attracted to the lipid component of the membranes of the endoplasmic reticulum. As the polypeptide chain elongates, it is "injected" into the cisterna within the endoplasmic reticulum. The leader sequence is, in a sense, an "address" that directs secretory proteins into the endoplasmic reticulum. Once the proteins are in the cisterna, the leader sequence is enzymatically removed so that the protein cannot reenter the cytoplasm (fig. 3.24).

The processing of the hormone insulin can serve as an example of the changes that occur within the endoplasmic reticulum. The original molecule enters the cisterna as a single polypeptide composed of 109 amino acids. This molecule is called *preproinsulin.* The first twenty-three amino acids serve as a leader sequence that allows the molecule to be injected into the cisterna within the endoplasmic reticulum. The leader sequence is then quickly removed, producing a molecule called *proinsulin.* The remaining chain folds within the cisterna so that the first and last amino acids in the polypeptide are brought close together. Enzymatic removal of the central region produces two chains—one of them, twenty-one amino acids long; the other, thirty amino acids long—that are subsequently joined together by disulfide bonds (fig. 3.25). This is the form of insulin that is normally secreted from the cell.

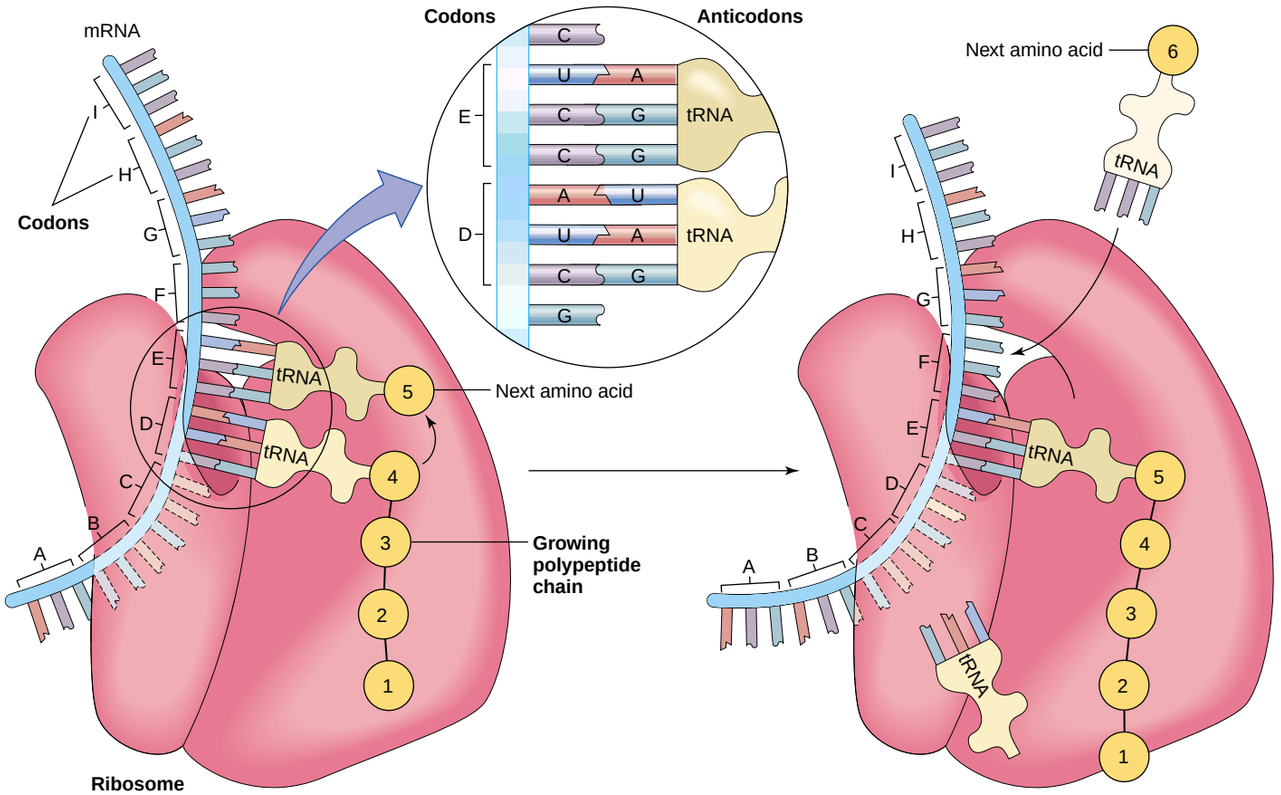


Figure 3.23 **The translation of messenger RNA (mRNA).** As the anticodon of each new aminoacyl-tRNA bonds with a codon on the mRNA, new amino acids are joined to the growing tip of the polypeptide chain.

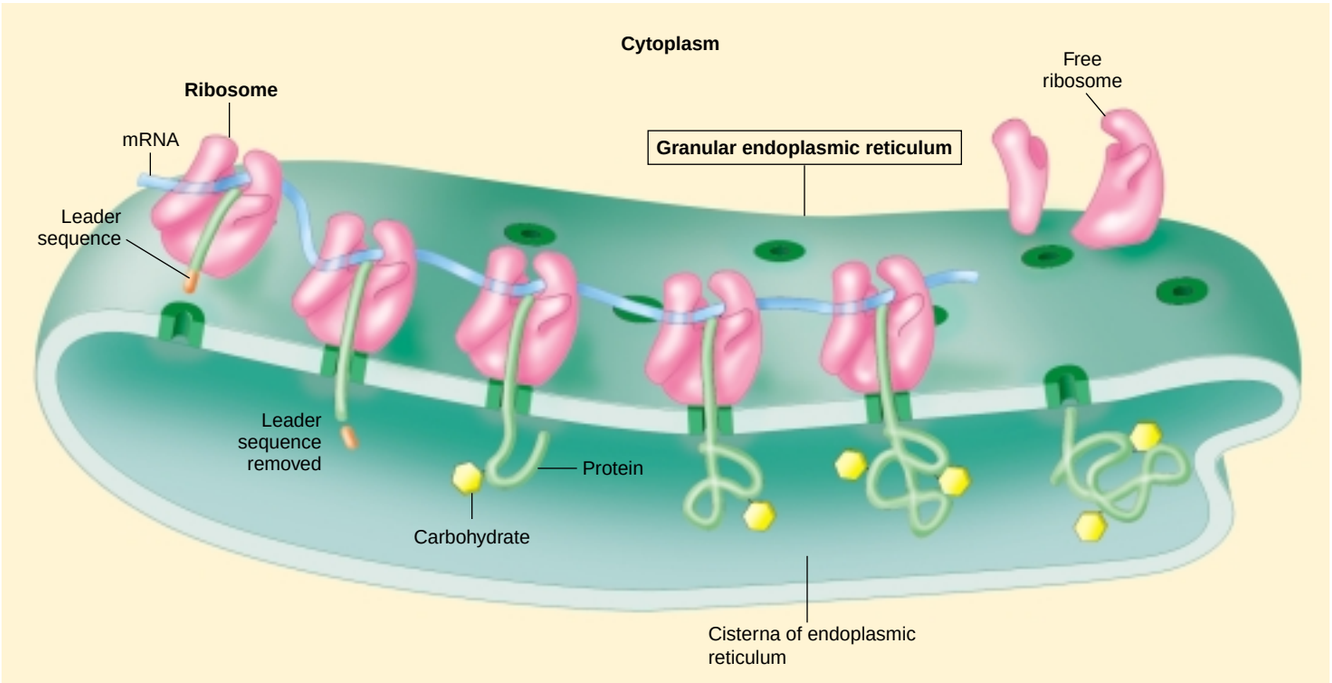


Figure 3.24 **How secretory proteins enter the endoplasmic reticulum.** A protein destined for secretion begins with a leader sequence that enables it to be inserted into the cisterna (cavity) of the endoplasmic reticulum. Once it has been inserted, the leader sequence is removed and carbohydrate is added to the protein.

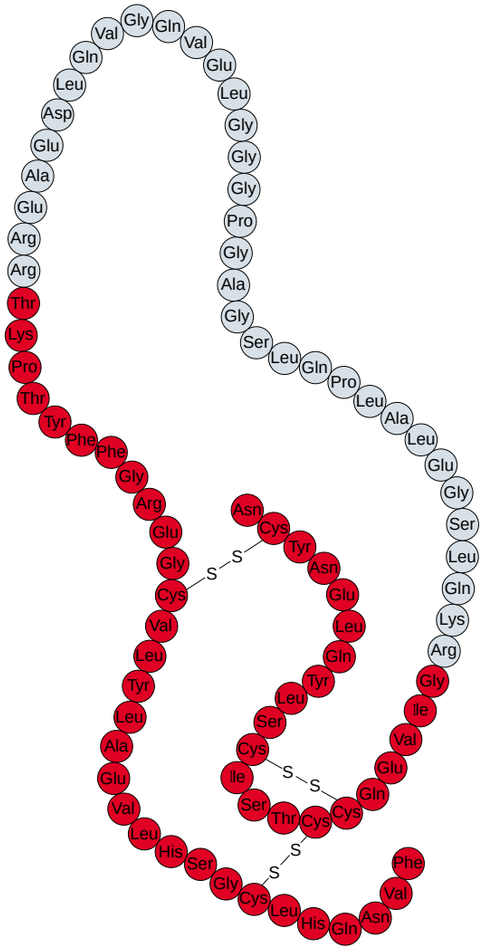


Figure 3.25 **The conversion of proinsulin into insulin.** The long polypeptide chain called proinsulin is converted into the active hormone insulin by enzymatic removal of a length of amino acids (shown in gray). The insulin molecule produced in this way consists of two polypeptide chains (*red circles*) joined by disulfide bonds.

Secretory proteins do not remain trapped within the granular endoplasmic reticulum. Instead, they are transported to another organelle within the cell—the Golgi complex (or Golgi apparatus), as previously described. This organelle serves three interrelated functions:

1. Proteins are further modified (including the addition of carbohydrates to form *glycoproteins*) in the Golgi complex.
2. Different types of proteins are separated according to their function and destination in the Golgi complex.
3. The final products are packaged and shipped in vesicles from the Golgi complex to their destinations (see fig. 3.13).

In the Golgi complex, for example, proteins that are to be secreted are separated from those that will be incorporated into the cell membrane and from those that will be introduced into lysosomes. Each is packaged in different membrane-enclosed vesicles and sent to its proper destination.

Test Yourself Before You Continue

1. Explain how mRNA, rRNA, and tRNA function during the process of protein synthesis.
2. Describe the granular endoplasmic reticulum and explain how the processing of secretory proteins differs from the processing of proteins that remain within the cell.
3. Describe the functions of the Golgi complex.

DNA Synthesis and Cell Division

When a cell is going to divide, each strand of the DNA within its nucleus acts as a template for the formation of a new complementary strand. Organs grow and repair themselves through a type of cell division known as mitosis. The two daughter cells produced by mitosis both contain the same genetic information as the parent cell. Gametes contain only half the number of chromosomes as their parent cell and are formed by a type of cell division called meiosis.

Genetic information is required for the life of the cell and for the ability of the cell to perform its functions in the body. Each cell obtains this genetic information from its parent cell through the process of DNA replication and cell division. DNA is the only type of molecule in the body capable of replicating itself, and mechanisms exist within the dividing cell to ensure that the duplicate copies of DNA will be properly distributed to the daughter cells.

DNA Replication

When a cell is going to divide, each DNA molecule replicates itself, and each of the identical DNA copies thus produced is distributed to the two daughter cells. Replication of DNA requires the action of a complex composed of many enzymes and proteins. As this complex moves along the DNA molecule, certain enzymes (*DNA helicases*) break the weak hydrogen bonds between complementary bases to produce two free strands at a fork in the double-stranded molecule. As a result, the bases of each of the two freed DNA strands can bond with

new complementary bases (which are part of nucleotides) that are available in the surrounding environment.

According to the rules of complementary base pairing, the bases of each original strand will bond with the appropriate free nucleotides; adenine bases pair with thymine-containing nucleotides; guanine bases pair with cytosine-containing nucleotides; and so on. Enzymes called **DNA polymerases** join the nucleotides together to form a second polynucleotide chain in each DNA that is complementary to the first DNA strands. In this way, two new molecules of DNA, each containing two complementary strands, are formed. Thus, two new double-helix DNA molecules are produced that contain the same base sequence as the parent molecule (fig. 3.26).

When DNA replicates, therefore, each copy is composed of one new strand and one strand from the original DNA molecule. Replication is said to be **semiconservative** (half of the original DNA is "conserved" in each of the new DNA molecules). Through this mechanism, the sequence of bases in DNA—the basis of the genetic code—is preserved from one cell generation to the next.

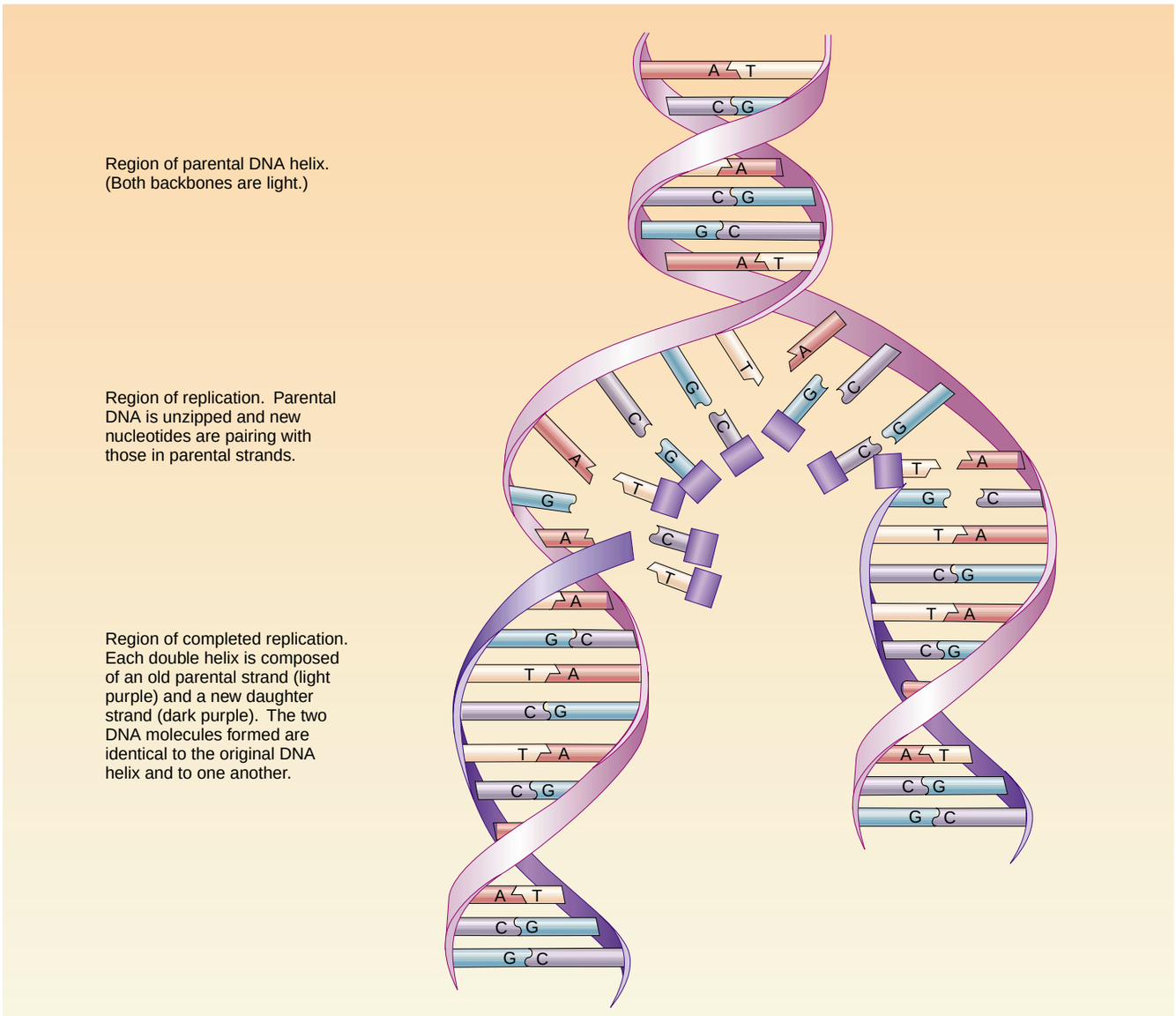


Figure 3.26 **The replication of DNA.** Each new double helix is composed of one old and one new strand. The base sequence of each of the new molecules is identical to that of the parent DNA because of complementary base pairing.

CLINICAL

Advances in the identification of human genes, methods of cloning (replicating) isolated genes, and other technologies have made **gene therapy** a realistic possibility. Although attempts at gene therapy were made as early as 1990, it was not until 2000 that children with the less severe form of *Severe Combined Immunodeficiency,* or *SCID,* were successfully treated by gene therapy. Then, in 2002, two children with the more severe form of SCID were cured of their condition. In this case, the children lack the gene for a specific enzyme, *adenine deaminase,* and this lack prevents the development of a functioning immune system. By inserting genes that code for ADA into the children's blood-forming stem cells, and getting these cells to proliferate in the bone marrow, scientists have apparently restored the immune system of these children. Prior to this new gene therapy, children with SCID had to be kept isolated in sterile environments (the "boy in the bubble"), because even common infections could be fatal.

The Cell Cycle

Unlike the life of an organism, which can be viewed as a linear progression from birth to death, the life of a cell follows a cyclical pattern. Each cell is produced as a part of its "parent" cell; when the daughter cell divides, it in turn becomes two new cells. In a sense, then, each cell is potentially immortal as long as its progeny can continue to divide. Some cells in the body divide frequently; the epidermis of the skin, for example, is renewed approximately every 2 weeks, and the stomach lining is renewed every 2 or 3 days. Other cells, such as striated muscle cells in the adult, do not divide at all. All cells in the body, of course, live only as long as the person lives (some cells live longer than others, but eventually all cells die when vital functions cease).

The nondividing cell is in a part of its life cycle known as interphase (fig. 3.27), which is subdivided into G_1, S, and G_2 phases, as will be described shortly. The chromosomes are in their extended form, and their genes actively direct the synthesis of RNA. Through their direction of RNA synthesis, genes control the metabolism of the cell. The cell may be growing during this time, and this part of interphase is known as the *G_1 phase* (*G* stands for *gap*). Although sometimes described as "resting," cells in the G_1 phase perform the physiological functions characteristic of the tissue in which they are found. The DNA of resting cells in the G_1 phase thus produces mRNA and proteins as previously described.

If a cell is going to divide, it replicates its DNA in a part of interphase known as the S phase (*S* stands for *synthesis*). Once DNA has replicated in the S phase, the chromatin condenses in the *G_2 phase* to form short, thick, structures by the end of G_2. Though condensed, the chromosomes are not yet in their more familiar, visible form in the ordinary (light) microscope; these will first make their appearance at prophase of mitosis (fig. 3.28).

Cyclins and p53

A group of proteins known as the cyclins promote different phases of the cell cycle. During the G_1 phase of the cycle, for example, an increase in the concentration of *cyclin D* proteins within the cell acts to move the cell quickly through this phase. Cyclin D proteins do this by activating a group of otherwise inactive enzymes known as *cyclin-dependant kinases.* Therefore, overactivity of a gene that codes for a cyclin D might be predicted to cause uncontrolled cell division, as occurs in a cancer. Indeed, overexpression of the gene for cyclin D1 has been shown to occur in some cancers, including those of the breast and esophagus. Genes that contribute to cancer are called **oncogenes.** Oncogenes are mutated forms of normal genes, called *proto-oncogenes,* that are functional in normal, healthy cells.

While oncogenes promote cancer, other genes—called **tumor suppressor genes**—inhibit its development. One very important tumor suppressor gene is known as **p53.** This name refers to the protein coded by the gene, which has a molecular weight of 53,000. The normal gene protects against cancer by indirectly blocking the ability of cyclins to stimulate cell division. In part, p53 accomplishes this by inducing the expression of another gene, called *p21,* which produces a protein that binds to and inactivates the cyclin-dependant kinases. The p21 protein thus inhibits cell division as it promotes cell differentiation (specialization).

For these reasons, cancer is likely to develop if the p53 gene becomes mutated and therefore ineffective as a tumor suppressor gene. Indeed, mutated p53 genes are found in over 50% of all cancers. Mice whose p53 genes were "knocked out" all developed tumors. (**Knockout mice** are strains of mice in which a specific

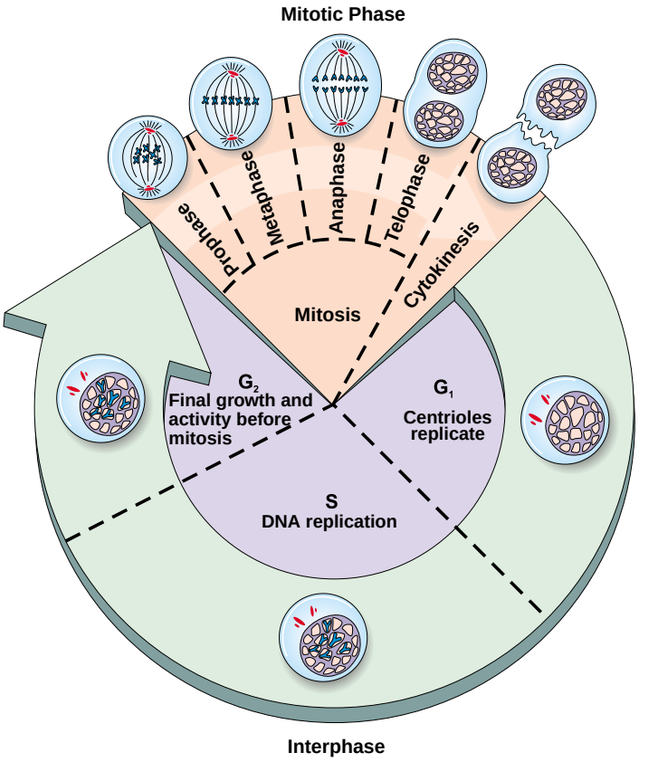


Figure 3.27 **The life cycle of a cell.** The different stages of mitotic division are shown; it should be noted, however, that not all cells undergo mitosis.

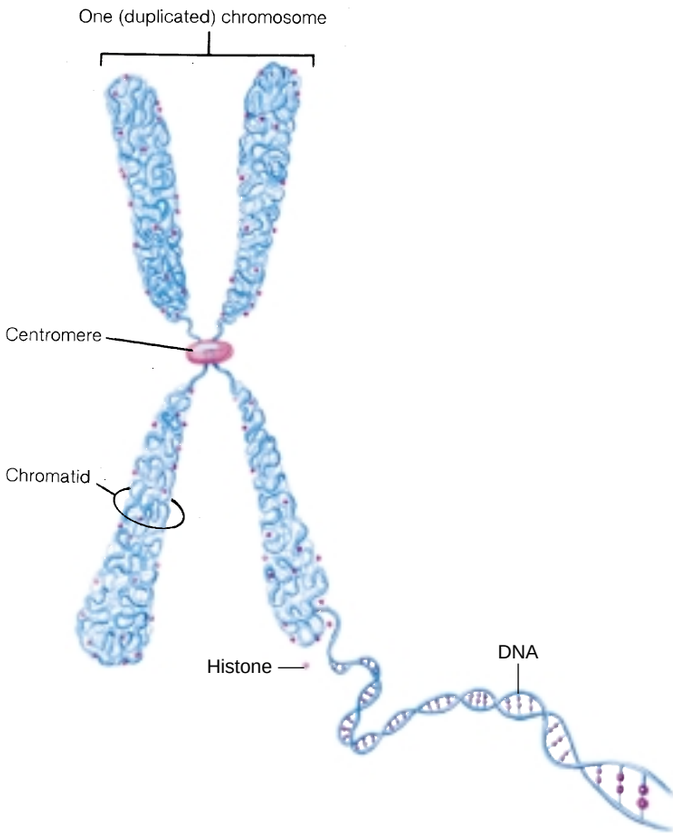


Figure 3.28 The structure of a chromosome after DNA replication. At this stage, a chromosome consists of two identical strands, or chromatids.

targeted gene has been inactivated by developing the mice from embryos injected with specifically mutated cells.) These important discoveries have obvious relevance to cancer diagnosis and treatment.

Cell Death

Cell death occurs both pathologically and naturally. Pathologically, cells deprived of a blood supply may swell, rupture their membranes, and burst. Such cellular death, leading to tissue death, is known as **necrosis.** In certain cases, however, a different pattern is observed. Instead of swelling, the cells shrink. The membranes remain intact but become bubbled, and the nuclei condense. This pattern has been named **apoptosis** (from a Greek term describing the shedding of leaves from a tree).

The machinery of cell death is set in motion by a family of enzymes called *caspases,* which are normally inactive within the cell but become activated during apoptosis. These enzymes have thus been called the "executioners" of the cell. Mitochondria may play an essential role in the activation of caspases and resulting apoptosis. This occurs when certain stimuli cause the outer and inner mitochondrial membranes to become permeable to proteins and other products that do not normally leak into the cell cytoplasm.

Apoptosis has been implicated in many disease processes, but it also occurs normally as part of programmed cell death—a process described previously in the section on lysosomes. Programmed cell death refers to the physiological process responsible for the remodeling of tissues during embryonic development and for tissue turnover in the adult body. As mentioned earlier, the epithelial cells lining the digestive tract are programmed to die 2 to 3 days after they are produced, and epidermal cells of the skin live only for about 2 weeks until they die and become completely cornified. Apoptosis is also important in the functioning of the immune system. A neutrophil (a type of white blood cell), for example, is programmed to die by apoptosis 24 hours after its creation in the bone marrow. A killer T lymphocyte (another type of white blood cell) destroys targeted cells by triggering their apoptosis.

Using mice with their gene for p53 knocked out, scientists have learned that p53 is needed for the apoptosis that occurs when a cell's DNA is damaged. The damaged DNA, if not repaired, activates p53, which in turn causes the cell to be destroyed. If the p53 gene has mutated to an ineffective form, however, the cell will not be destroyed by apoptosis as it should; rather, it will divide to produce daughter cells with damaged DNA. This may be one mechanism responsible for the development of a cancer.

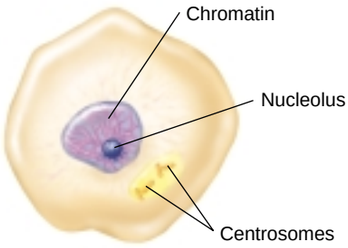
There are three forms of **skin cancer**—squamous cell carcinoma, basal cell carcinoma, and melanoma, depending on the type of epidermal cell involved—all of which are promoted by the damaging effects of the ultraviolet portion of sunlight. Ultraviolet light promotes a characteristic type of DNA mutation in which either of two pyrimidines (cytosine or thymine) is affected. In squamous cell and basal cell carcinoma (but not melanoma), the cancer is believed to involve mutations that affect the p53 gene, among others. Whereas cells with normal p53 genes may die by apoptosis when their DNA is damaged, and are thus prevented from replicating themselves and perpetuating the damaged DNA, those damaged cells with a mutated p53 gene survive and divide to produce the cancer.

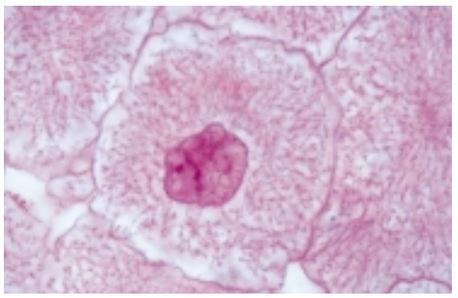
Mitosis

At the end of the G_2 phase of the cell cycle, which is generally shorter than G_1, each chromosome consists of two strands called **chromatids** that are joined together by a *centromere* (see fig. 3.28). The two chromatids within a chromosome contain identical DNA base sequences because each is produced by the semiconservative replication of DNA. Each chromatid, therefore, contains a complete double-helix DNA molecule that is a copy of the single DNA molecule existing prior to replication. Each chromatid will become a separate chromosome once mitotic cell division has been completed.

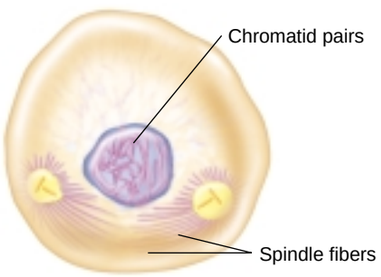
The G_2 phase completes interphase. The cell next proceeds through the various stages of cell division, or **mitosis.** This is the *M phase* of the cell cycle. Mitosis is subdivided into four stages: *prophase, metaphase, anaphase,* and *telophase* (fig. 3.29).

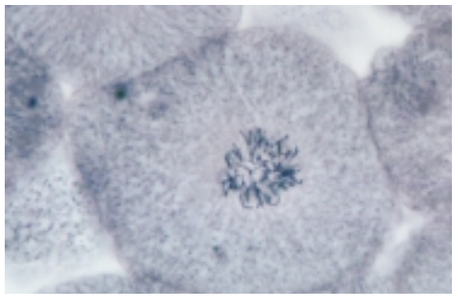
(a) **Interphase**
- The chromosomes are in an extended form and seen as chromatin in the electron microscope.
- The nucleus is visible



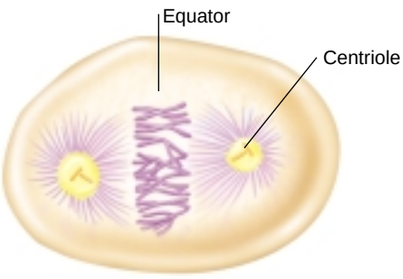


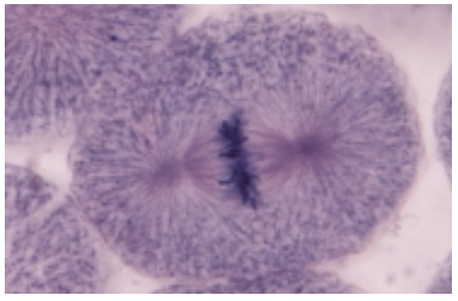
(b) **Prophase**
- The chromosomes are seen to consist of two chromatids joined by a centromere.
- The centrioles move apart toward opposite poles of the cell.
- Spindle fibers are produced and extend from each centrosome.
- The nuclear membrane starts to disappear.
- The nucleolus is no longer visible.



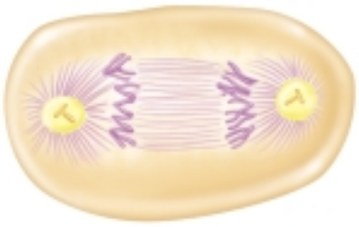


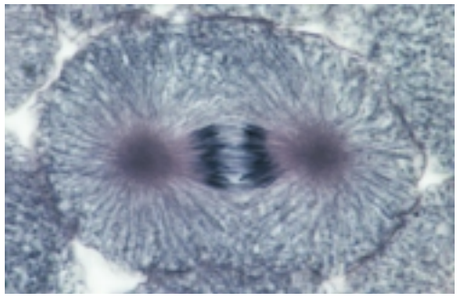
(c) **Metaphase**
- The chromosomes are lined up at the equator of the cell.
- The spindle fibers from each centriole are attached to the centromeres of the chromosomes.
- The nuclear membrane has disappeared.



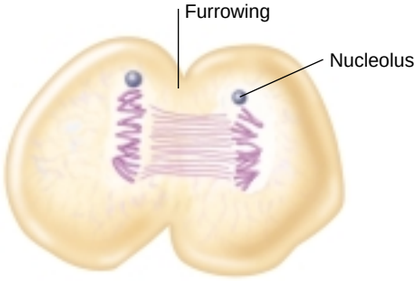


(d) **Anaphase**
- The centromere split, and the sister chromatids separate as each is pulled to an opposite pole.





(e) **Telophase**
- The chromosomes become longer, thinner, and less distinct.
- New nuclear membranes form.
- The nucleolus reappears.
- Cell division is nearly complete.



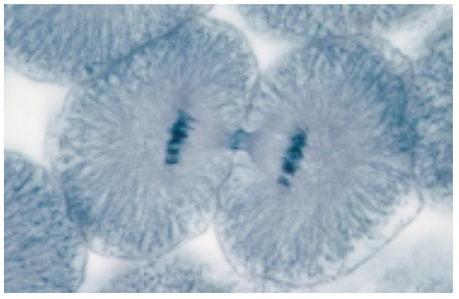


Figure 3.29 **The stages of mitosis.** The events that occur in each stage are indicated in the figure.

In prophase, chromosomes become visible as distinctive structures. In metaphase of mitosis, the chromosomes line up single file along the equator of the cell. This aligning of chromosomes at the equator is believed to result from the action of **spindle fibers,** which are attached to a protein structure called the *kinetochore* at the centromere of each chromosome (fig. 3.29).

Anaphase begins when the centromeres split apart and the spindle fibers shorten, pulling the two chromatids in each chromosome to opposite poles. Each pole therefore gets one copy of each of the forty-six chromosomes. During early telophase, division of the cytoplasm (*cytokinesis*) results in the production of two daughter cells that are genetically identical to each other and to the original parent cell.

Role of the Centrosome

All animal cells have a **centrosome,** located near the nucleus in a nondividing cell. At the center of the centrosome are two **centrioles,** which are positioned at right angles to each other. Each centriole is composed of nine evenly spaced bundles of microtubules, with three microtubules per bundle (fig. 3.30). Surrounding the two centrioles is an amorphous mass of material called the *pericentriolar material.* Microtubules grow out of the pericentriolar material, which is believed to function as the center for the organization of microtubules in the cytoskeleton.

Through a mechanism that is still incompletely understood, the centrosome replicates itself during interphase if a cell is going to divide. The two identical centrosomes then move away from each other during prophase of mitosis and take up positions at opposite poles of the cell by metaphase. At this time, the centrosomes produce new microtubules. These new microtubules are very dynamic, rapidly growing and shrinking as if they were "feeling out" randomly for chromosomes. A microtubule becomes stabilized when it finally binds to the proper region of a chromosome. In this way, the microtubules from both centrosomes form the spindle fibers that are attached to each of the replicated chromosomes at metaphase (fig 3.31).

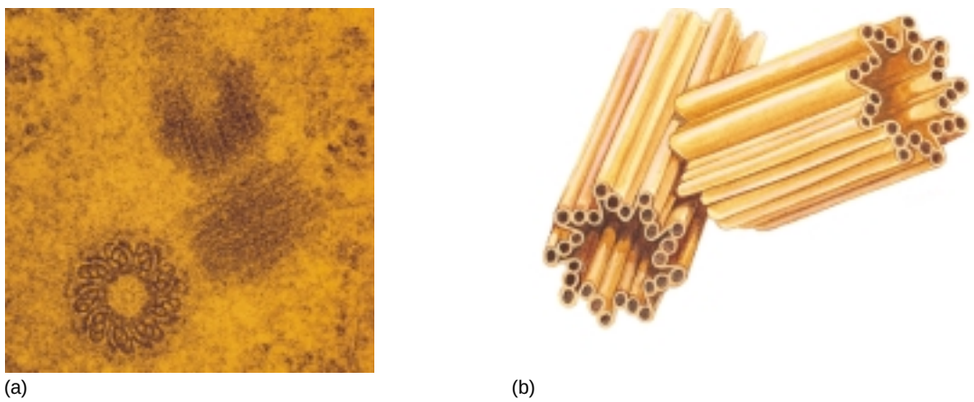
The spindle fibers pull the chromosomes to opposite poles of the cell during anaphase, so that at telophase, when the cell pinches inward, two identical daughter cells will be produced. This also requires the centrosomes, which somehow organize a ring of contractile filaments halfway between the two poles. These filaments are attached to the cell membrane, and when they contract, the cell is pinched in two. The filaments consist of actin and myosin proteins, the same contractile proteins present in muscle.

Telomeres and Cell Division

Certain types of cells can be removed from the body and grown in nutrient solutions (outside the body, or *in vitro*). Under these artificial conditions, the potential longevity of different cell lines can be studied. For unknown reasons, normal connective tissue cells (called fibroblasts) stop dividing in vitro after a certain number of population doublings. Cells from a newborn will divide 80 to 90 times, while those from a 70-year-old will stop after 20 to 30 divisions. The decreased ability to divide is thus an indicator of senescence (aging). Cells that become transformed into cancer, however, apparently do not age and continue dividing indefinitely in culture.

This senescent decrease in the ability of cells to replicate may be related to a loss of DNA sequences at the ends of chromosomes, in regions called **telomeres** (from the Greek *telos* = end). The telomeres serve as caps on the ends of DNA, preventing enzymes from mistaking the normal ends for broken DNA and doing damage by trying to "repair" them.

The DNA polymerase enzyme does not fully copy the DNA at the end-regions. Each time a chromosome replicates, it loses 50 to 100 base pairs in its telomeres. Cell division may ultimately stop when there is too much loss of DNA in the telomeres, and the cell dies because of damage it sustains in the



(a) (b)

Figure 3.30 **The centrioles.** (*a*) A micrograph of the two centrioles in a centrosome. (*b*) A diagram showing that the centrioles are positioned at right angles to each other.

course of aging. Interestingly, Dolly (the famous cloned sheep) had short telomeres, because her DNA was older than she was. For reasons not presently clear, however, cloned cattle seem to have long telomeres, despite the short telomeres of the donors. Will Dolly's life be shorter and the cloned cattle's longer because of this? It is too soon to tell.

Germinal cells that give rise to gametes (sperm cells and ova) can continue to divide indefinitely, perhaps because they produce an enzyme called **telomerase,** which duplicates the telomere DNA. Telomerase is also found in hematopoietic stem cells (those in bone marrow that produce blood cells) and other stem cells that must divide continuously. Similarly, telomerase is produced by most cancer cells, and there is evidence to suggest that telomerase may be responsible for their ability to divide indefinitely.

Hypertrophy and Hyperplasia

The growth of an individual from a fertilized egg into an adult involves an increase in the number of cells and an increase in the size of cells. Growth that is due to an increase in cell number results from an increased rate of mitotic cell division and is termed **hyperplasia.** Growth of a tissue or organ due to an increase in cell size is termed **hypertrophy.**

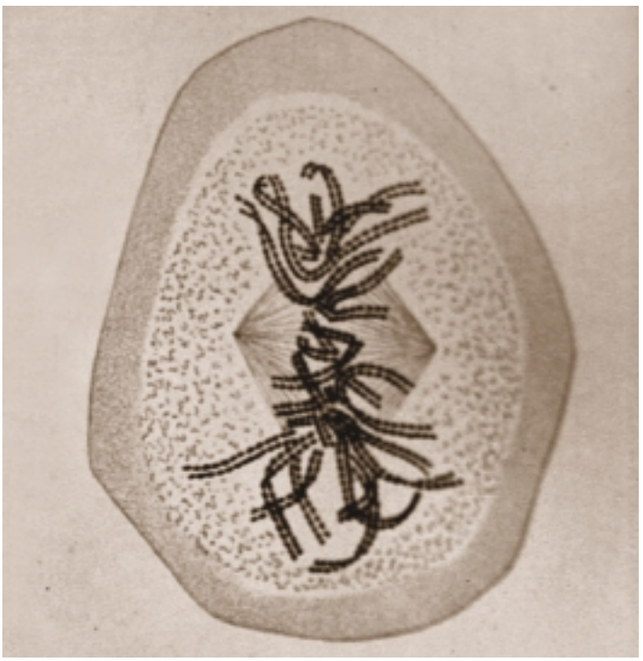
Most growth is due to hyperplasia. A callus on the palm of the hand, for example, involves thickening of the skin by hyperplasia due to frequent abrasion. An increase in skeletal muscle size as a result of exercise, by contrast, is produced by hypertrophy.

Skeletal muscle and cardiac (heart) muscle can grow only by hypertrophy. When growth occurs in skeletal muscles in response to an increased workload—during weight training, for example—it is called **compensatory hypertrophy.** The heart muscle may also demonstrate compensatory hypertrophy when its workload increases because of hypertension (high blood pressure). The opposite of hypertrophy is **atrophy,** the wasting or decrease in size of a cell, tissue, or organ. This may result from the disuse of skeletal muscles, as occurs in prolonged bed rest, various diseases, or advanced age.

Meiosis

When a cell is going to divide, either by mitosis or meiosis, the DNA is replicated (forming chromatids) and the chromosomes become shorter and thicker, as previously described. At this point the cell has forty-six chromosomes, each of which consists of two duplicate chromatids.

The short, thick chromosomes seen at the end of the G_2 phase can be matched as pairs, the members of each pair appearing to be structurally identical. These matched chromosomes are called **homologous chromosomes.** One member of each homologous pair is derived from a chromosome



(a)

(b)

Figure 3.31 **Chromosomes and spindle fibers.** The duplicate chromatids are clearly seen in (*a*), though the spindle fibers are just barely visible. In a technique callled immunofluorescence, the spindle fibers shine in (*b*) due to a reaction with microtubules, the major constituent of the spindles.

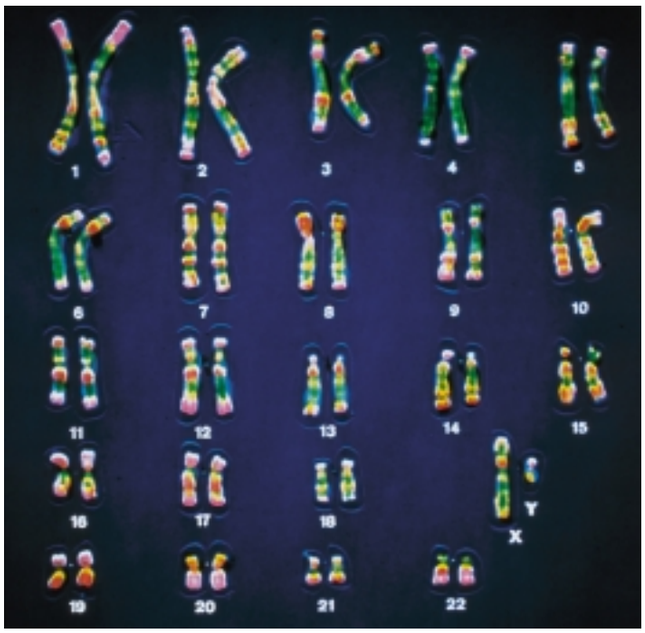


Figure 3.32 **A karyotype, in which chromosomes are arranged in homologous pairs.** A false-color light micrograph of chromosomes from a male arranged in numbered homologous pairs, from the largest to the smallest.

Table 3.3 Stages of Meiosis

Stage	Events
First Meiotic Division	
Prophase I	Chromosomes appear double-stranded.
	Each strand, called a chromatid, contains duplicate DNA joined together by a structure known as a centromere.
	Homologous chromosomes pair up side by side.
Metaphase I	Homologous chromosome pairs line up at equator.
	Spindle apparatus is complete.
Anaphase I	Homologous chromosomes separate; the two members of a homologous pair move to opposite poles.
Telophase I	Cytoplasm divides to produce two haploid cells.
Second Meiotic Division	
Prophase II	Chromosomes appear, each containing two chromatids.
Metaphase II	Chromosomes line up single file along equator as spindle formation is completed.
Anaphase II	Centromeres split and chromatids move to opposite poles.
Telophase II	Cytoplasm divides to produce two haploid cells from each of the haploid cells formed at telophase I.

inherited from the father, and the other member is a copy of one of the chromosomes inherited from the mother. Homologous chromosomes do not have identical DNA base sequences; one member of the pair may code for blue eyes, for example, and the other for brown eyes. There are twenty-two homologous pairs of *autosomal chromosomes* and one pair of *sex chromosomes,* described as X and Y. Females have two X chromosomes, whereas males have one X and one Y chromosome (fig. 3.32).

Meiosis, which has two divisional sequences, is a special type of cell division that occurs only in the gonads (testes and ovaries), where it is used only in the production of gametes—sperm cells and ova. (Gamete production is described in detail in chapter 20.) In the first division of meiosis, the homologous chromosomes line up side by side, rather than single file, along the equator of the cell. The spindle fibers then pull one member of a homologous pair to one pole of the cell, and the other member of the pair to the other pole. Each of the two daughter cells thus acquires only one chromosome from each of the twenty-three homologous pairs contained in the parent. The daughter cells, in other words, contain twenty-three rather than forty-six chromosomes. For this reason, meiosis (from the Greek *meion* = less) is also known as **reduction division.**

At the end of this cell division, each daughter cell contains twenty-three chromosomes—but *each of these consists of two chromatids.* (Since the two chromatids per chromosome are identical, this does not make forty-six chromosomes; there are still only twenty-three *different* chromosomes per cell at this point.) The chromatids are separated by a second meiotic division. Each of the daughter cells from the first cell division itself divides, with the duplicate chromatids going to each of two new daughter cells. A grand total of four daughter cells can thus be produced from the meiotic cell division of one parent cell. This occurs in the testes, where one parent cell produces four sperm cells. In the ovaries, one parent cell also produces four daughter cells, but three of these die and only one progresses to become a mature egg cell (as will be described in chapter 20).

The stages of meiosis are subdivided according to whether they occur in the first or the second meiotic cell division. These stages are designated as prophase I, metaphase I, anaphase I, telophase I; and then prophase II, metaphase II, anaphase II, and telophase II (table 3.3 and fig. 3.33).

The reduction of the chromosome number from forty-six to twenty-three is obviously necessary for sexual reproduction, where the sex cells join and add their content of chromosomes together to produce a new individual. The significance of meiosis, however, goes beyond the reduction of chromosome number. At metaphase I, the pairs of homologous chromosomes can line up with either member facing a given pole of the cell. (Recall that each member of a homologous pair came from a different parent.) Maternal and paternal members of homologous pairs are thus randomly shuffled. Hence, when the first meiotic

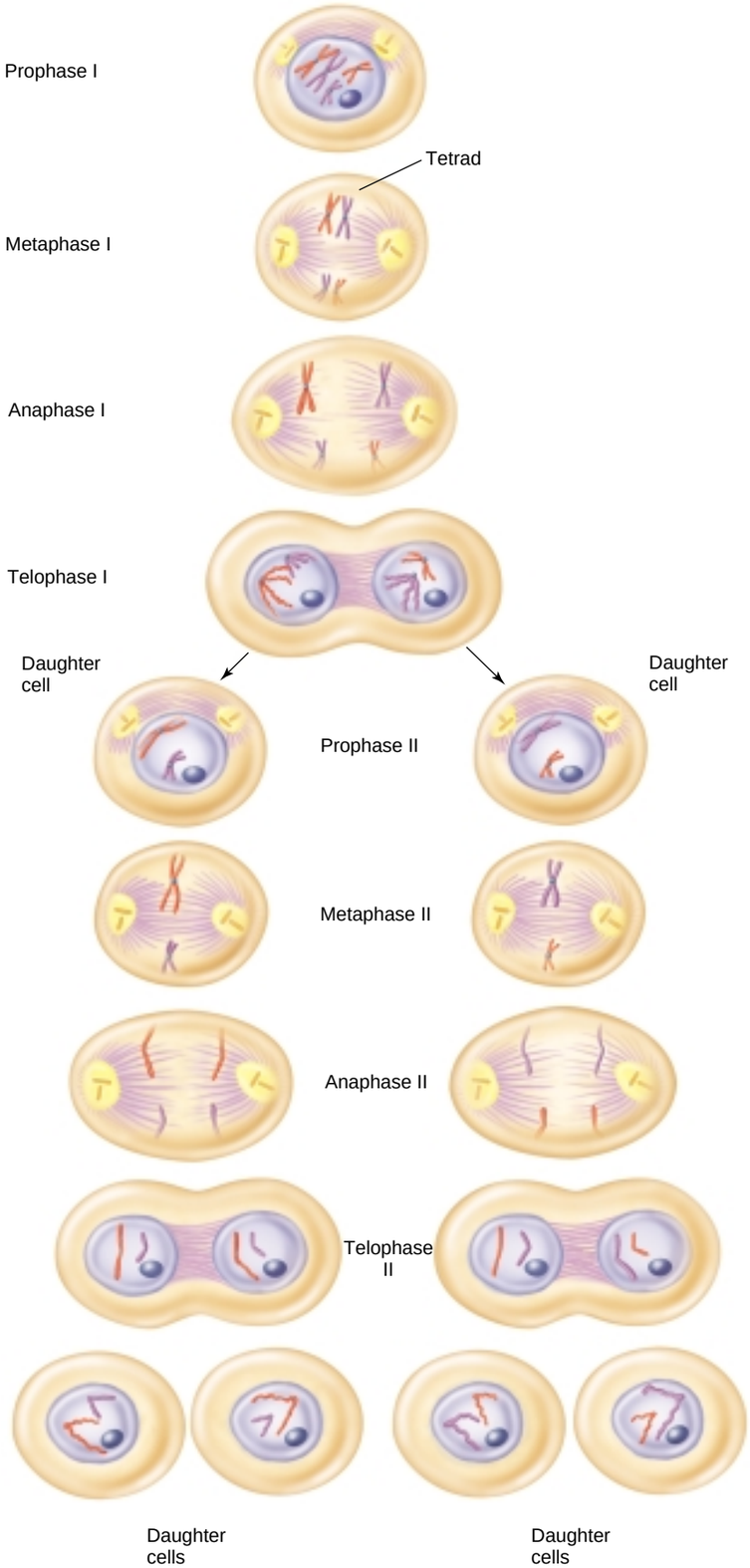


Figure 3.33 **Meiosis, or reduction division.** In the first meiotic division, the homologous chromosomes of a diploid parent cell are separated into two haploid daughter cells. Each of these chromosomes contains duplicate strands, or chromatids. In the second meiotic division, these chromosomes are distributed to two new haploid daughter cells.

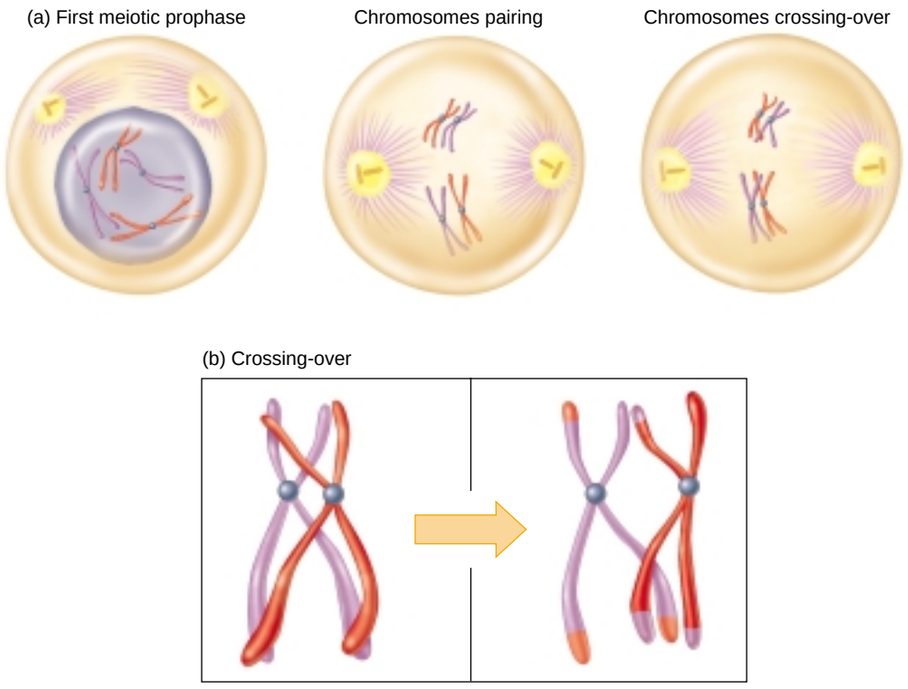


Figure 3.34 **Crossing-over.** (*a*) Genetic variation results from the crossing-over of tetrads, which occurs during the first meiotic prophose. (*b*) A diagram depicting the recombination of chromosomes that occurs as a result of crossing-over.

division occurs, each daughter cell will obtain a complement of twenty-three chromosomes that are randomly derived from the maternal or paternal contribution to the homologous pairs of chromosomes of the parent cell.

In addition to this "shuffling of the deck" of chromosomes, exchanges of parts of homologous chromosomes can occur at prophase I. That is, pieces of one chromosome of a homologous pair can be exchanged with the other homologous chromosome in a process called *crossing-over* (fig. 3.34). These events together result in **genetic recombination** and ensure that the gametes produced by meiosis are genetically unique. This provides additional genetic diversity for organisms that reproduce sexually, and genetic diversity is needed to promote survival of species over evolutionary time.

Test Yourself Before You Continue

1. Draw a simple diagram of the semiconservative replication of DNA using stick figures and two colors.
2. Describe the cell cycle using the proper symbols to indicate the different stages of the cycle.
3. List the phases of mitosis and briefly describe the events that occur in each phase.
4. Distinguish between mitosis and meiosis in terms of their final result and their functional significance.
5. Summarize the events that occur during the two meiotic cell divisions and explain the mechanisms by which genetic recombination occurs during meiosis.

HPer Links of Basic Cell Concepts to the Body Systems

Nervous System

- Regeneration of neurons is regulated by several different chemicals . . . . . .**(p. 000)**
- Different forms (alleles) of a gene produce different forms of receptors for particular neurotransmitter chemicals . . . . . .**(p. 000)**
- Microglia, located in the brain and spinal cord, are cells that transport themselves by amoeboid movement . . . . . .**(p. 000)**
- The insulating material around nerve fibers, called a myelin sheath, is derived from the cell membrane of certain cells in the nervous system . . . . . .**(p. 000)**

Endocrine System

- Many hormones act on their target cells by regulating gene expression . . . . . .**(p. 000)**
- Other hormones bind to receptor proteins located on the outer surface of the cell membrane of the target cells . . . . .**(p. 000)**
- The endoplasmic reticulum of some cells stores Ca^{2+}, which is released in response to hormone action . . . . . .**(p. 000)**
- Chemical regulators called prostaglandins are derived from a type of lipid associated with the cell membrane . . . . . .**(p. 000)**
- Liver and adipose cells store glycogen and triglycerides, respectively, which can be mobilized for energy needs by the action of particular hormones . . . . . .**(p. 000)**
- The sex of an individual is determined by the presence of a particular region of DNA in the Y chromosome . . . . . .**(p. 000)**

Muscular System

- Muscle cells have cytoplasmic proteins called actin and myosin that are needed for contraction . . . . . .**(p. 000)**
- The endoplasmic reticulum of skeletal muscle fibers stores Ca^{2+}, which is needed for muscle contraction . . . . . .**(p. 000)**

Circulatory System

- Blood cells are formed in the bone marrow . . . . . .**(p. 000)**
- Mature red blood cells lack nuclei and mitochondria . . . . . .**(p. 000)**
- The different white blood cells are distinguished by the shape of their nuclei and the presence of cytoplasmic granules . . . . . .**(p. 000)**

Immune System

- The carbohydrates outside the cell membrane of many bacteria help to target these cells for immune attack . . . .**(p. 000)**
- Some white blood cells and tissue macrophages destroy bacteria by phagocytosis . . . . . .**(p. 000)**
- When a B lymphocyte is stimulated by a foreign molecule (antigen), its endoplasmic reticulum becomes more developed and produces more antibody proteins **(p. 000)**
- Apoptosis is responsible for the destruction of T lymphocytes after an infection has been cleared . . . . . .**(p. 000)**

Respiratory System

- The air sacs (alveoli) of the lungs are composed of cells that are very thin, minimizing the separation between air and blood . . . . . .**(p. 000)**
- The epithelial cells lining the airways of the conducting zone have cilia that move mucus . . . . . .**(p. 000)**

Urinary System

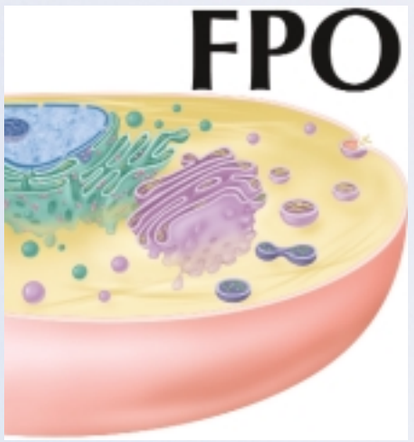
- Parts of the renal tubules have microvilli that increase the rate of reabsorption . .**(p. 000)**
- Some regions of the renal tubules have water channels; these are produced by the Golgi complex and inserted by means of vesicles into the cell membrane . . .**(p.000)**

Digestive System

- The mucosa of the digestive tract has unicellular glands called goblet cells that secrete mucus . . . . . .**(p. 000)**
- The cells of the small intestine have microvilli that increase the rate of absorption . . . . . .**(p. 000)**
- The liver contains phagocytic cells . .**(p. 000)**

Reproductive System

- Males have an X and a Y chromosome, whereas females have two X chromosomes per diploid cell . .**(p. 000)**
- Gametes are produced by meiotic cell division . . . . . .**(p. 000)**
- Follicles degenerate (undergo atresia) in the ovaries by means of apoptosis **(p. 000)**
- Sperm cells are motile through the action of flagella . . . . . .**(p. 000)**
- The uterine tubes are lined with cilia that help to move the ovulated egg toward the uterus . . . . . .**(p. 000)**



Summary

Plasma Membrane and Associated Structures 000

I. The structure of the cell (plasma) membrane is described by a fluid-mosaic model.
- **A.** The membrane is composed predominately of a double layer of phospholipids.
- **B.** The membrane also contains proteins, most of which span its entire width.

II. Some cells move by extending pseudopods; cilia and flagella protrude from the cell membrane of some specialized cells.

III. In the process of endocytosis, invaginations of the plasma membrane allow the cells to take up molecules from the external environment.
- **A.** In phagocytosis, the cell extends pseudopods that eventually fuse together to create a food vacuole; pinocytosis involves the formation of a narrow furrow in the membrane, which eventually fuses.
- **B.** Receptor-mediated endocytosis requires the interaction of a specific molecule in the extracellular environment with a specific receptor protein in the cell membrane.
- **C.** Exocytosis, the reverse of endocytosis, is a process that allows the cell to secrete its products.

Cytoplasm and Its Organelles 000

I. Microfilaments and microtubules produce a cytoskeleton that aids movements of organelles within a cell.

II. Lysosomes contain digestive enzymes and are responsible for the elimination of structures and molecules within the cell and for digestion of the contents of phagocytic food vacuoles.

III. Mitochondria serve as the major sites for energy production within the cell. They have an outer membrane with a smooth contour and an inner membrane with infoldings called cristae.

IV. Ribosomes are small protein factories composed of ribosomal RNA and protein arranged into two subunits.

V. The endoplasmic reticulum is a system of membranous tubules in the cell.
- **A.** The granular endoplasmic reticulum is covered with ribosomes and is involved in protein synthesis.
- **B.** The agranular endoplasmic reticulum provides a site for many enzymatic reactions and, in skeletal muscles, serves to store Ca^{2+}.

VI. The Golgi complex is a series of membranous sacs that receive products from the endoplasmic reticulum, modify those products, and release the products within vesicles.

Cell Nucleus and Gene Expression 000

I. The cell nucleus is surrounded by a double-layered nuclear envelope. At some points, the two layers are fused by nuclear pore complexes that allow for the passage of molecules.

II. Genetic expression occurs in two stages: transcription (RNA synthesis) and translation (protein synthesis).
- **A.** The DNA in the nucleus is combined with proteins to form the threadlike material known as chromatin.
- **B.** In chromatin, DNA is wound around regulatory proteins known as histones to form particles called nucleosomes.
- **C.** Chromatin that is active in directing RNA synthesis is euchromatin; the highly condensed, inactive chromatin is heterochromatin.

III. RNA is single-stranded. Four types are produced within the nucleus: ribosomal RNA, transfer RNA, precursor messenger RNA, and messenger RNA.

IV. Active euchromatin directs the synthesis of RNA in a process called transcription.
- **A.** The enzyme RNA polymerase causes separation of the two strands of DNA along the region of the DNA that constitutes a gene.
- **B.** One of the two separated strands of DNA serves as a template for the production of RNA. This occurs by complementary base pairing between the DNA bases and ribonucleotide bases.

Protein Synthesis and Secretion 000

I. Messenger RNA leaves the nucleus and attaches to the ribosomes.

II. Each transfer RNA, with a specific base triplet in its anticodon, binds to a specific amino acid.
- **A.** As the mRNA moves through the ribosomes, complementary base pairing between tRNA anticodons and mRNA codons occurs.
- **B.** As each successive tRNA molecule binds to its complementary codon, the amino acid it carries is added to the end of a growing polypeptide chain.

III. Proteins destined for secretion are produced in ribosomes located on the granular endoplasmic reticulum and enter the cisternae of this organelle.

IV. Secretory proteins move from the granular endoplasmic reticulum to the Golgi complex.
- **A.** The Golgi complex modifies the proteins it contains, separates different proteins, and packages them in vesicles.
- **B.** Secretory vesicles from the Golgi complex fuse with the plasma membrane and release their products by exocytosis.

DNA Synthesis and Cell Division 000

I. Replication of DNA is semiconservative; each DNA strand serves as a template for the production of a new strand.
- **A.** The strands of the original DNA molecule gradually separate along their entire length and, through complementary base pairing, form a new complementary strand.
- **B.** In this way, each DNA molecule consists of one old and one new strand.

II. During the G_1 phase of the cell cycle, the DNA directs the synthesis of RNA, and hence that of proteins.

III. During the S phase of the cycle, DNA directs the synthesis of new DNA and replicates itself.

IV. After a brief time gap (G_2), the cell begins mitosis (the M stage of the cycle).
- **A.** Mitosis consists of the following phases: interphase, prophase, metaphase, anaphase, and telophase.
- **B.** In mitosis, the homologous chromosomes line up single file and are pulled by spindle fibers to opposite poles.
- **C.** This results in the production of two daughter cells, each containing forty-six chromosomes, just like the parent cell.

V. Meiosis is a special type of cell division that results in the production of gametes in the gonads.
- **A.** The homologous chromosomes line up side by side, so that only one of each pair is pulled to each pole.
- **B.** This results in the production of two daughter cells, each containing only twenty-three chromosomes, which are duplicated.
- **C.** The duplicate chromatids are separated into two new daughter cells during the second meiotic cell division.

Review Activities

Test Your Knowledge of Terms and Facts

1. According to the fluid-mosaic model of the plasma membrane
- **a.** protein and phospholipids form a regular, repeating structure.
- **b.** the membrane is a rigid structure.
- **c.** phospholipids form a double layer, with the polar parts facing each other.
- **d.** proteins are free to move within a double layer of phospholipids.

2. After the DNA molecule has replicated itself, the duplicate strands are called
- **a.** homologous chromosomes.
- **b.** chromatids.
- **c.** centromeres.
- **d.** spindle fibers.

3. Nerve and skeletal muscle cells in the adult, which do not divide, remain in the
- **a.** G_1 phase.
- **b.** S phase.
- **c.** G_2 phase.
- **d.** M phase.

4. The phase of mitosis in which the chromosomes line up at the equator of the cell is called
- **a.** interphase.
- **b.** prophase.
- **c.** metaphase.
- **d.** anaphase.
- **e.** telophase.

5. The phase of mitosis in which the chromatids separate is called
- **a.** interphase.
- **b.** prophase.
- **c.** metaphase.
- **d.** anaphase.
- **e.** telophase.

6. Chemical modifications of histone proteins are believed to directly influence
- **a.** genetic transcription.
- **b.** genetic translation.
- **c.** both transcription and translation.
- **d.** posttranslational changes in the newly synthesized proteins.

7. Which of these statements about RNA is *true?*
- **a.** It is made in the nucleus.
- **b.** It is double-stranded.
- **c.** It contains the sugar deoxyribose.
- **d.** It is a complementary copy of the entire DNA molecule.

8. Which of these statements about mRNA is *false?*
- **a.** It is produced as a larger pre-mRNA.
- **b.** It forms associations with ribosomes.
- **c.** Its base triplets are called anticodons.
- **d.** It codes for the synthesis of specific proteins.

9. The organelle that combines proteins with carbohydrates and packages them within vesicles for secretion is
- **a.** the Golgi complex.
- **b.** the granular endoplasmic reticulum.
- **c.** the agranular endoplasmic reticulum.
- **d.** the ribosome.

10. The organelle that contains digestive enzymes is
- **a.** the mitochondrion.
- **b.** the lysosome.
- **c.** the endoplasmic reticulum.
- **d.** the Golgi complex.

11. Which of these descriptions of rRNA is *true?*
- **a.** It is single-stranded.
- **b.** It catalyzes steps in protein synthesis.
- **c.** It forms part of the structure of both subunits of a ribosome.
- **d.** It is produced in the nucleolus.
- **e.** All of these are true.

12. Which of these statements about tRNA is *true?*
- **a.** It is made in the nucleus.
- **b.** It is looped back on itself.
- **c.** It contains the anticodon.
- **d.** There are over twenty different types.
- **e.** All of these are true.

13. The step in protein synthesis during which tRNA, rRNA, and mRNA are all active is known as
- **a.** transcription.
- **b.** translation.
- **c.** replication.
- **d.** RNA polymerization.

14. The anticodons are located in
- **a.** tRNA.
- **b.** rRNA.
- **c.** mRNA.
- **d.** ribosomes.
- **e.** endoplasmic reticulum.

Test Your Understanding of Concepts and Principles

1. Give some specific examples that illustrate the dynamic nature of the plasma membrane.[1]
2. Describe the structure of nucleosomes, and explain the role of histone proteins in chromatin structure and function.
3. What is the genetic code, and how does it affect the structure and function of the body?
4. Why may tRNA be considered the "interpreter" of the genetic code?
5. Compare the processing of cellular proteins with that of proteins secreted by a cell.
6. Explain the interrelationship between the endoplasmic reticulum and the Golgi complex. What becomes of vesicles released from the Golgi complex?
7. Explain the functions of centrioles in nondividing and dividing cells.
8. Describe the phases of the cell cycle and explain how this cycle may be regulated.
9. Distinguish between oncogenes and tumor suppressor genes and give examples of how such genes may function.
10. Define *apoptosis* and explain the physiological significance of this process.

Test Your Ability to Analyze and Apply Your Knowledge

1. Discuss the role of chromatin proteins in regulating gene expression. How does the three-dimensional structure of the chromatin affect genetic regulation? How do hormones influence genetic regulation?
2. Explain how p53 functions as a tumor suppressor gene. How can mutations in p53 lead to cancer, and how might gene therapy or other drug interventions inhibit the growth of a tumor?
3. Release of lysosomal enzymes from white blood cells during a local immune attack can contribute to the symptoms of inflammation. Suppose, to alleviate inflammation, you develop a drug that destroys all lysosomes. Would this drug have negative side effects? Explain.
4. Antibiotics can have different mechanisms of action. An antibiotic called puromycin blocks genetic translation. One called actinomycin D blocks genetic transcription. These drugs can be used to determine how regulatory molecules, such as hormones, work. For example, if a hormone's effects on a tissue were blocked immediately by puromycin but not by actinomycin D, what would that tell you about the mechanism of action of the hormone?

Related Websites

Check out the Links Library at www.mhhe.com/fox8 for links to sites containing resources related to cell structure and genetic control. These links are monitored to ensure current URLs.

[1]*Note:* This question is answered in the chapter 3 Study Guide found on the Online Learning Center at www.mhhe.com/fox8.