EXPLORATIONS: AN OPEN INVITATION TO BIOLOGICAL ANTHROPOLOGY

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Chapter 3: Molecular Biology and Genetics:

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Learning Objectives

- Define terms useful to molecular biology and genetics.
- Explain and identify the purpose of both DNA replication and the cell cycle.
- Identify key differences between mitosis and meiosis.
- Outline the process of protein synthesis including transcription and translation.
- Use principles of Mendelian inheritance to predict genotypes and phenotypes of future generations.
- Explain complexities surrounding patterns of genetic inheritance and polygenic traits.
- Discuss challenges to and bioethical concerns of genetic testing.

I [Hayley Mann] started my Bachelor's degree in 2003, which was the same year the Human Genome Project released its first draft sequence. I initially declared a genetics major because I thought it sounded cool. However, upon taking an actual class, I discovered that genetics was *challenging*. In addition to my genetics major, I signed up for biological anthropology classes and soon learned that anthropology could bring all those molecular lessons to life. For instance, we are composed of cells, proteins, nucleic acids, carbohydrates, and lipids. Anthropologists often include these molecules in their studies to identify how humans vary; if there are meaningful differences, they propose theories to explain them.

Since the release of the first human genome sequence, the field of *genetics* has grown into *genomics*. Researchers now address these complex questions on a large scale. To process "big data," some scientists have moved to working on a computer full time doing computational biology. As you learned in Chapter 1, molecular anthropologists use genetics to compare ancient and modern populations as well as study nonhuman primates. Molecular anthropologists must also stay current with advancing technology (you will learn about the results of some of this genomic research as it has been applied to fossils in Chapters 11 and 12). If you wish to be part of this dynamic field, then take advantage of available campus laboratory classes and internships and also never stop reading scientific papers.

This chapter provides the basics for understanding human variation and how the evolutionary process works. A few advanced genetics topics are also presented because biotechnology is now commonplace in health and society. Understanding the science behind this remarkable field means you will be able to participate in bioethical and anthropological discussions as well as make more informed decisions regarding genetic testing.
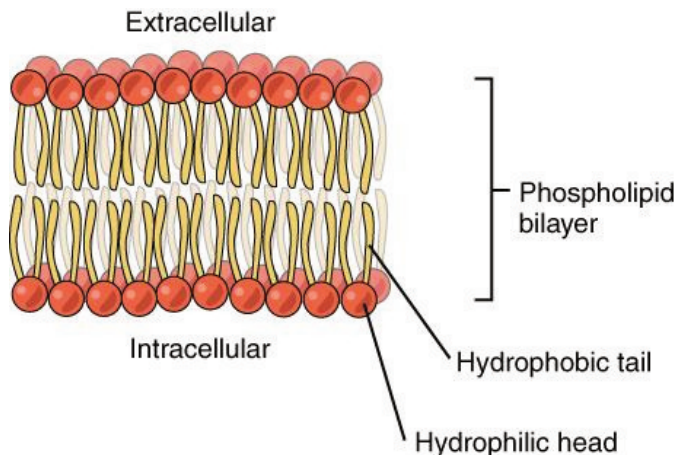
CELLS AND MOLECULES

Molecules of Life

Figure 3.1 Phospholipid molecules forming a bilayer with their hydrophobic tails and hydrophilic heads.

Organisms are composed of four basic types of molecules that are essential for cell structure and function: proteins, lipids, carbohydrates, and nucleic acids. **Proteins** are strings of amino acids that are often folded into complex 3-D shapes. The structure of **lipids** can be described as having a hydrophilic (water-loving) head and a hydrophobic (water-repelling) tail (Figure 3.1). When lipids are chained together, they form more-complex molecules called fats and triglycerides. **Carbohydrates** are composed of carbon and hydrogen atoms that can be broken down to supply energy for an organism. Lastly, **nucleic acids** carry genetic information about a living organism.
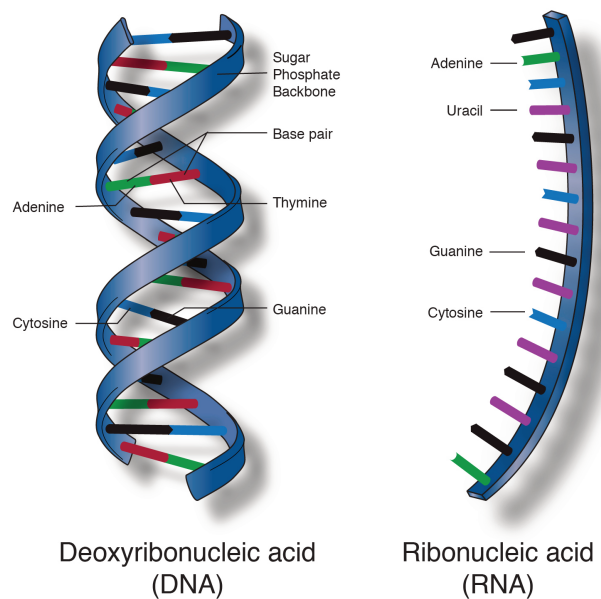
Probably the most familiar nucleic acid is **deoxyribonucleic acid (DNA)**. DNA comprises a **sugar phosphate backbone and nucleotides** (Figure 3.2). (More details on the physical structure of DNA and what information DNA nucleotides provide will be discussed later.) Anthropologists can analyze sequences of DNA nucleotides and determine how different organisms are related to each other, since they all have their own unique DNA *genetic code*. In the case of humans, forensic scientists can identify individuals by analyzing 20 different short **DNA sequences** known as "CODIS Core Loci." Another nucleic acid is called **ribonucleic acid (RNA)**. One type of RNA molecule is responsible for chaining amino acids together in order to build proteins (Figure 3.3 and Figure 3.4). How RNA synthesizes amino acids into proteins will be reviewed further on in the chapter.

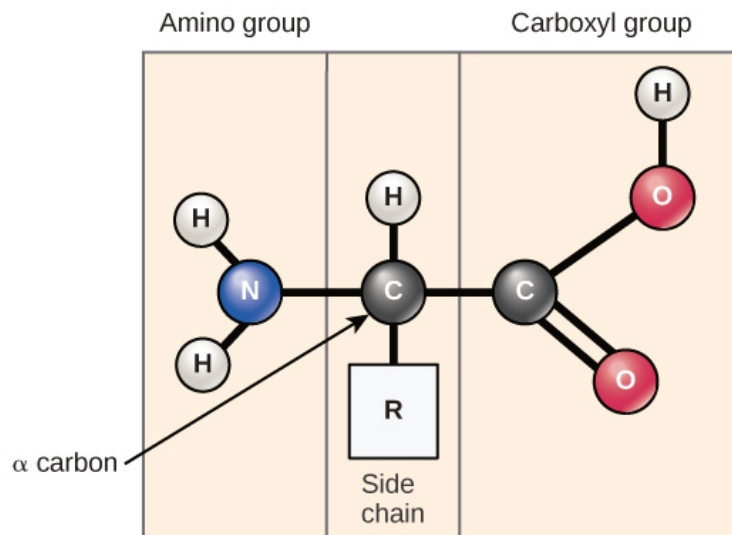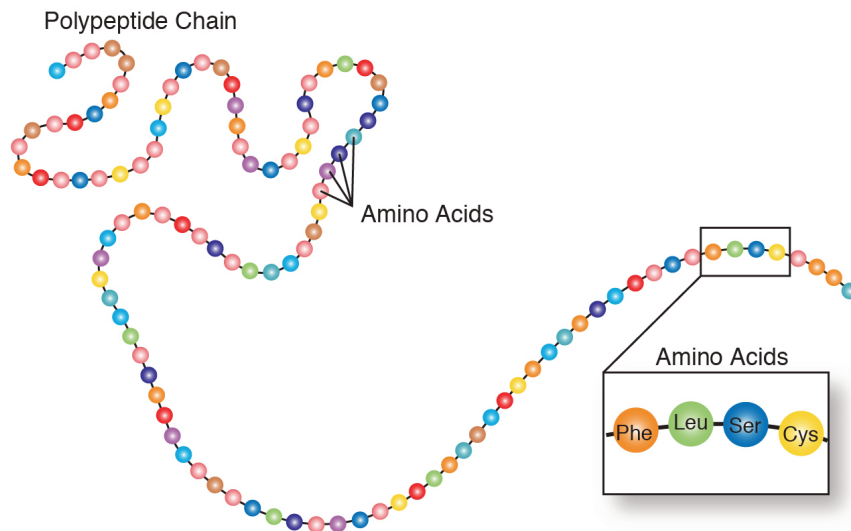*Figure 3.2 Structural components that form double-stranded nucleic acid (DNA) or single-stranded nucleic acid (RNA).*

Figure 3.3 Chemical elements that characterize an amino acid. C: carbon; N: Nitrogen; O: Oxygen; H: Hydrogen.

Amino Acids

Ala: Alanine	Gln: Glutamine	Leu: Leucine	Ser: Serine
Arg: Arginine	Glu: Glutamic acid	Lys: Lysine	Thr: Threonine
Asn: Asparagine	Gly: Glycine	Met: Methionine	Trp: Tryptophane
Asp:Aspartic acid	His: Histidine	Phe: Phenylalanine	Tyr: Tyrosisne
Cys:Cysteine	Ile: Isoleucine	Pro: Proline	Val: Valine

Figure 3.4 Amino acids (20 different types) strung together form a polypeptide chain.

Cells

In 1665, Robert Hooke observed slices of plant cork using a microscope. Hooke noted that the microscopic plant structures he saw resembled *cella*, meaning "a small room" in Latin. Approximately two centuries later, biologists recognized the cell as being the most fundamental unit of life and that all life is composed of cells. Cellular organisms can be characterized as two main cell types: **prokaryotes** and **eukaryotes**.
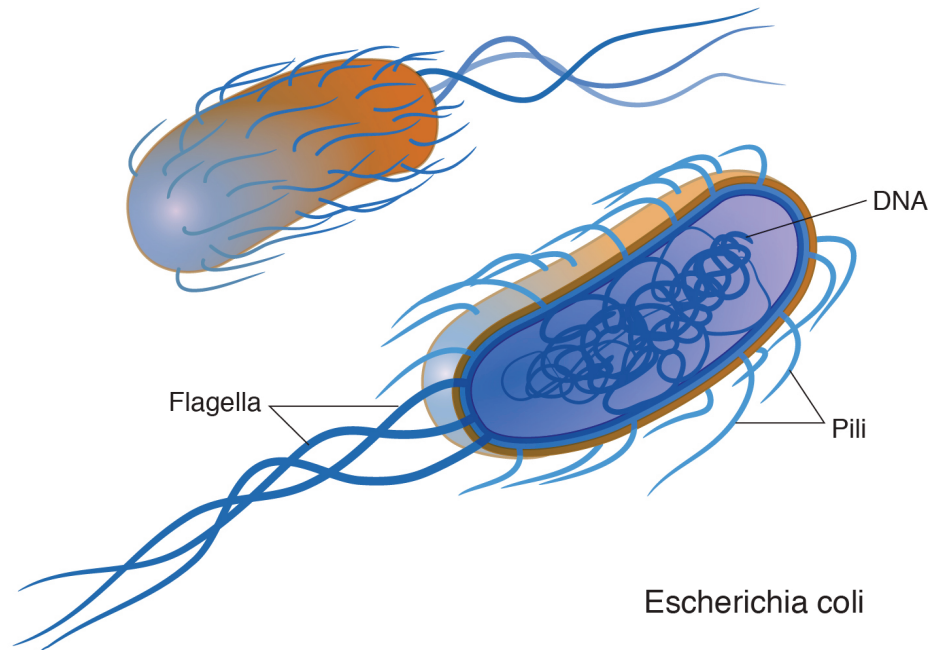

Figure 3.5 A representation of the single-celled body of E. coli bacteria.

Prokaryotes include bacteria and archaea, and they are composed of a single cell. Additionally, their DNA and **organelles** are not surrounded by individual membranes. Thus, no compartments separate their DNA from the rest of the cell (Figure 3.5). It is well known that some bacteria can cause illness in humans. For instance, *Escherichia coli* (*E. coli*) and *Salmonella* contamination can result in food poisoning symptoms. Pneumonia and strep throat are caused by *Streptococcal* bacteria. *Neisseria gonorrhoeae* is a bacterial sexually transmitted disease. Although bacteria are commonly associated with illness, not all bacteria are harmful. For example, researchers are studying the relationship between the **microbiome** and human health. The bacteria that are part of the healthy human microbiome perform beneficial roles, such as food digestion, boosting the immune system, and even making vitamins (e.g., B12 and K).

Archaea, the other type of prokaryotic organism, were once believed to be closely related to bacteria. However, it was determined through genetic analysis that archaea have their own distinct evolutionary lineage so biologists reclassified them into their own taxonomic domain. Archaea were discovered living in extreme environments and are therefore known as "extremophiles." For example, archaea can be found in high temperatures, such as Old Faithful Geyser in Yellowstone National Park.

Eukaryotes can be single-celled or multicelled in their body composition. In contrast to prokaryotes, eukaryotes possess membranes that surround their DNA and organelles. An example of a single-celled eukaryote is the microscopic algae found in ponds (phytoplankton), which can produce oxygen from the sun. Yeasts are also single-celled, and fungi can be single- or multicellular. Plants and animals are all multicellular.
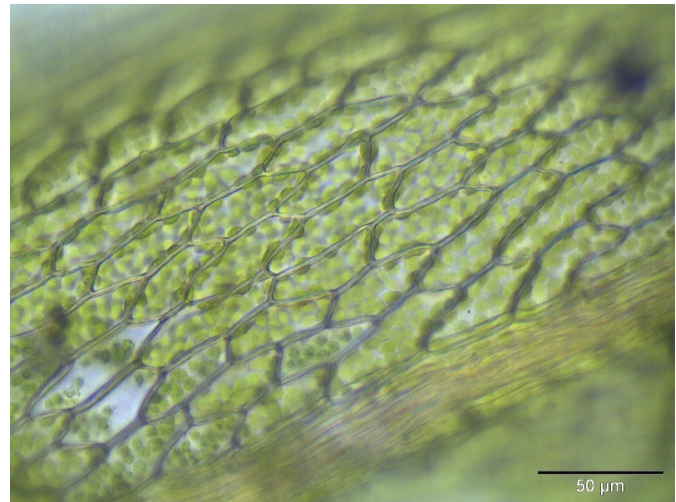

Figure 3.6 A microscopic view of plant cell membranes.

Although plant and animal cells have a surprising number of similarities, there are some key differences. For example, plant cells possess a thick outer cell membrane made of a fibrous carbohydrate called cellulose (Figure 3.6). Animal and plant cells also have different **tissues**. A tissue is an aggregation of cells that are morphologically similar and perform the same task. For most plants, the outermost layer of cells forms a waxy cuticle that helps to protect the cells and to prevent water loss. However, humans have skin, the outermost cell layer of which is mostly composed of a tough protein called keratin. Overall, humans have a diversity of tissue types (e.g., cartilage, brain, and heart).
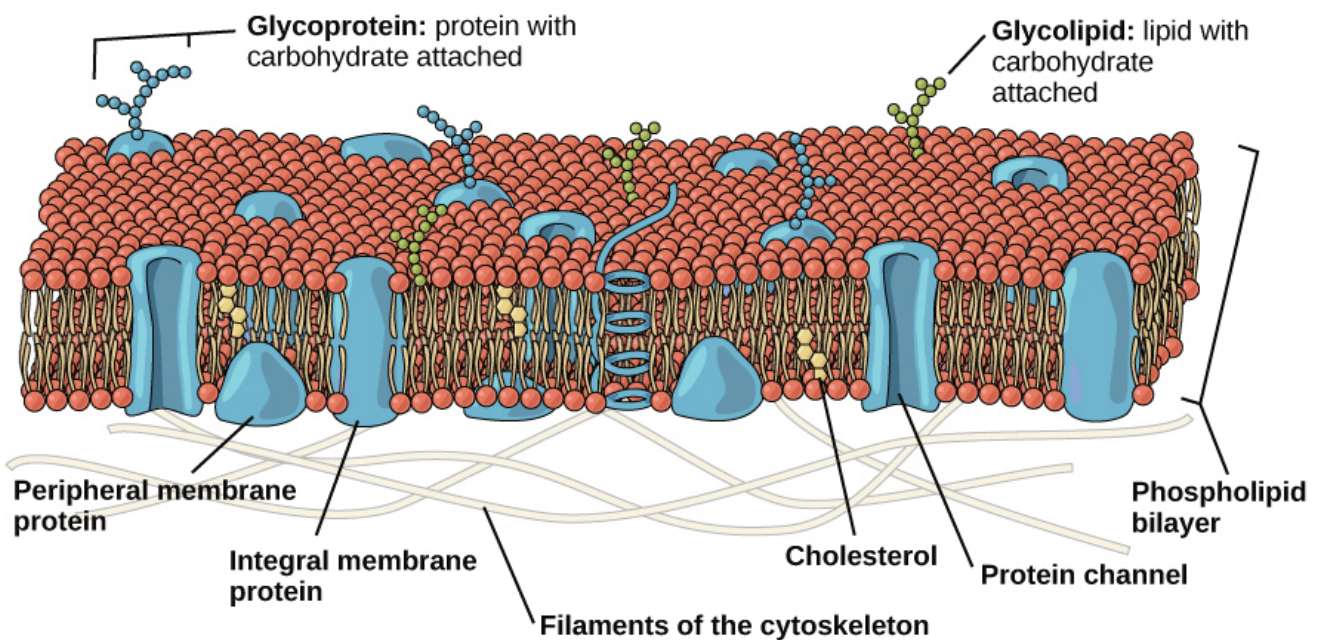
Animal Cell Organelles

Figure 3.7 A phospholipid bilayer with membrane-bound carbohydrates and proteins.

An animal cell is surrounded by a double membrane called the **phospholipid bilayer** (Figure 3.7). A closer look reveals that this protective barrier is made of lipids and proteins that provide structure and function for cellular activities. For example, lipids and proteins embedded in the cell's membrane work together to regulate the passage of molecules and ions (e.g., H_2O and sodium) into and out of the cell. **Cytoplasm** is the jelly-like matrix inside of the cell membrane. Part of the cytoplasm comprises organelles, which perform different specialized tasks for the cell (Figure 3.8). An example of an organelle is the **nucleus**, where the cell's DNA is located (Figure 3.9). The double membrane that encloses the nucleus is known as the **nuclear envelope**; its purpose is to regulate molecules into and out of the nucleus and serve as a barrier to protect DNA integrity.
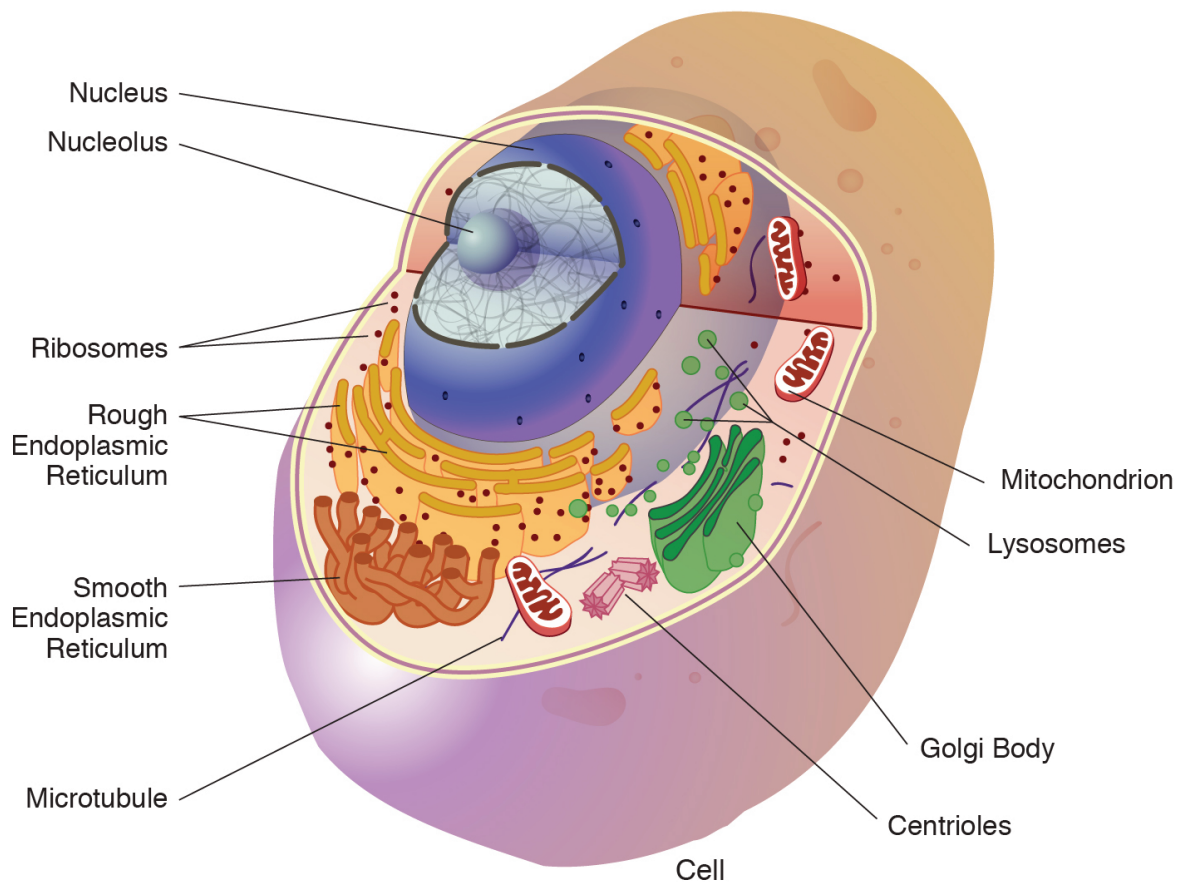

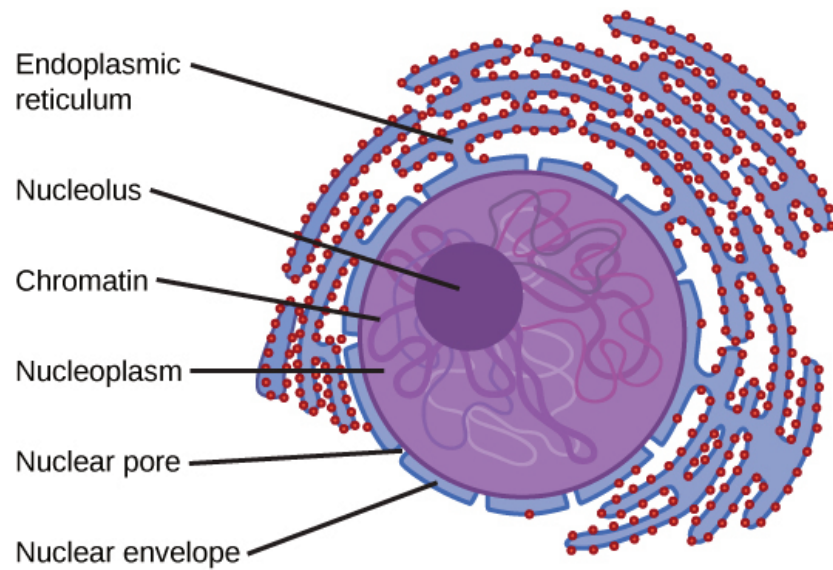*Figure 3.8 An animal cell with membrane-enclosed organelles.*

Figure 3.9 A membrane-enclosed nucleus of an animal cell.

Another important organelle is the **mitochondrion** (Figure 3.10). Mitochondria are often referred to as "powerhouse centers" because they produce energy for the cell in the form of **adenosine triphosphate (ATP)**. Depending on the species and tissue type, multicellular eukaryotes can have hundreds to thousands of mitochondria in each of their cells. Scientists have determined that mitochondria played an important role in the evolution of the eukaryotic cell. Mitochondria were once *symbiotic* prokaryotic organisms (i.e., helpful bacteria) that transformed into cellular organelles over time. Because mitochondria used to be separate organisms, this explains why mitochondria also have their own DNA, called **mitochondrial DNA (mtDNA)**. All organelles have important physiological functions, and when they cannot perform their role optimally, it can result in disease. For example, there are mitochondrial diseases for which cells have abnormally less mitochondria. In humans, this leads to various neurological symptoms and disorders. Figure 3.11 lists other organelles found in the cell and their specialized cellular roles.
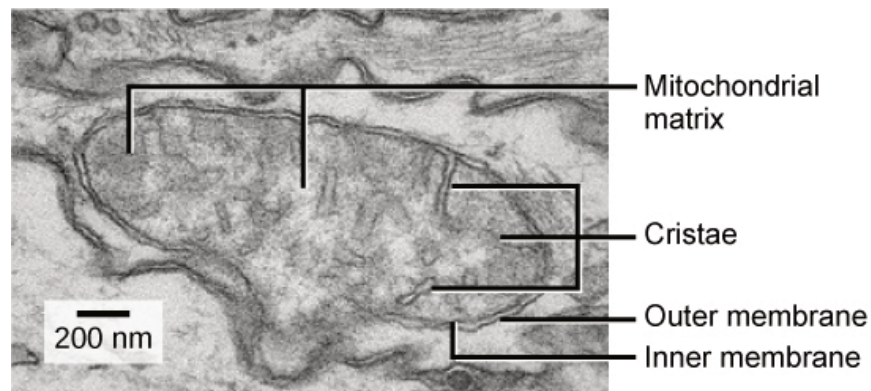

Figure 3.10 Microscopic view of an animal mitochondrion organelle.

Cell structure	Description
Cytoplasm	Fluid substance located inside of cell membrane that contains organelles
Nucleopore	Pores in the nuclear envelope that are selectively permeable
Nucleus	Contains the cell's DNA and is surrounded by the nuclear envelope
Nucleolus	Resides inside of the nucleus and is the site of ribosomal RNA (rRNA) transcription, processing, and assembly
Mitochondrion	Responsible for cellular respiration, where energy is produced by converting nutrients into ATP
Ribosome	Located in the cytoplasm and also the membrane of the rough endoplasmic reticulum. Messenger RNA (mRNA) binds to ribosomes and proteins are synthesized
Endoplasmic reticulum (ER)	Continuous membrane with the nucleus that helps transport, synthesize, modify, and fold proteins. Rough ER has embedded ribosomes, whereas smooth ER lacks ribosomes
Golgi body	Layers of flattened sacs that receive and transmit messages from the ER to secrete and transport proteins within the cell
Lysosome	Located in the cytoplasm and contains enzymes to degrade cellular components
Microtubule	Involved with cellular movement including intracellular transport and cell division
Centrioles	Assist with the organization of mitotic spindles which extend and contract for the purpose of cellular movement during mitosis and meiosis

Figure 3.11 Names of organelles and their cellular functions.

INTRODUCTION TO GENETICS

Genetics is the study of heredity. Parents pass down their genetic traits to their offspring. Although children resemble their parents, traits often vary in appearance or molecular function. For example, two parents with normal color vision can sometimes produce a son with red-green colorblindness. Patterns of genetic inheritance will be discussed in a later section. Molecular geneticists study the biological mechanisms responsible for creating variation between individuals, such as DNA **mutations** (see Chapter 4), cell division, and genetic regulation.

Molecular anthropologists use genetic data to test anthropological questions. Although their interests are diverse, areas of molecular anthropology research include the following: human origins, dispersals, evolution, adaptation, demography, health, disease, behavior, and animal domestication. In addition to conducting research in a laboratory,

molecular anthropologists also work in the field with different communities of people. Some anthropologists also study DNA from individuals who have been deceased for decades−even hundreds or thousands of years. The study of **ancient DNA (aDNA)** has led to the development of specialized laboratory techniques. Over time, the DNA in skeletons of ancient individuals becomes degraded (i.e., less intact), which is why careful methodological considerations must be taken. A recent example of an aDNA study is provided in Special Topic: Native American Immunity and European Diseases, and another will be presented in Chapter 10.

SPECIAL TOPIC: FOCUS ON NATIVE AMERICAN IMMUNITY AND EUROPEAN DISEASES—A STUDY OF ANCIENT DNA

Figure 3.12a Tsimshian Native Americans of the Pacific Northwest Coast.

Beginning in the early 15th century, Native Americans progressively suffered from high mortality rates as the result of colonization from foreign powers. European-borne diseases such as measles, tuberculosis, influenza, and smallpox are largely responsible for the population collapse of indigenous peoples in the Americas. Many Europeans who immigrated to the New World had lived in large sedentary populations, which also included coexisting with domestic animals and pests. Although a few prehistoric Native American populations can be characterized as large agricultural societies (especially in Mesoamerica), their overall culture, community lifestyle, and subsistence practices were markedly different from that of Europeans. Therefore, because they did not share the same urban living environments as Europeans, it is believed that Native Americans were susceptible to old-world diseases.

In 2016, a *Nature* article published by John Lindo and colleagues was the first to investigate whether pre-contact Native Americans possessed a genetic susceptibility to European diseases. Their study included Tsimshians, a First Nation community from British Columbia (Figure 3.12). The DNA from both present-day and ancient individuals (who lived between 500 and 6,000 years ago) was analyzed. The research team discovered that a change occurred in the genetic region HLADQ-1, which is a member of the major histocompatibility complex (MHC) immune system molecules. These molecules are responsible for detecting and triggering an immune response against pathogens. Lindo and colleagues (2016) concluded that HLADQ-1 helped Native Americans adapt to their local environmental ecology. However, when European-borne epidemics occurred in the Northwest during the 1800s, a certain HLADQ-1 DNA sequence associated with ancient Tsimshian immunity was no longer adaptive. As the result of past selective pressures from European diseases, present-day Tsimshians have a different frequency of HLADQ-1 sequences. The precise role that HLADQ-1 plays in immune adaptation still requires further investigation. But overall, this study serves as an example of how studying ancient DNA from the remains of deceased individuals can help provide insight into living human populations and historical events.

Figure 3.12b Tsimshian territory in present-day British Columbia.

DNA Carries Hereditary Information

Surprisingly, the study of inheritance preceded the discovery of DNA. For a period of time, it was believed that proteins carried the hereditary information passed from parents to offspring. Then, in 1944, Oswald Avery, Colin MacLeod, and Maclyn McCarty discovered an association between extracted nucleic acids and the success of their bacterial genetic experiments. Specifically, they demonstrated that DNA was the molecule responsible for the genetic transformation of their pneumonia bacterial strains. Although this was revolutionary work at the time, the field of molecular biology did not fully embrace their findings (it has also been suggested that they were overlooked for a Nobel Prize). It was eventually accepted by the scientific community that DNA is the hereditary material of an organism, especially after the chemical structure of DNA was revealed.

DNA Structure

The 1953 discovery of the molecular structure of DNA was one of the greatest scientific achievements of all time. Using X-ray crystallography, Rosalind Franklin (Figure 3.13) provided the image that clearly showed the double helix shape of DNA. However, due to a great deal of controversy, Franklin's colleague and outside associates received greater publicity for the discovery. In 1962, James Watson, Francis Crick, and Maurice Wilkins received a Nobel Prize for developing a biochemical model of DNA. Unfortunately, Rosalind Franklin had passed away in 1958 from ovarian cancer. In current times, Franklin's important contribution and her reputation as a skilled scientist are widely acknowledged.

The double helix shape of DNA can be described as a twisted ladder (refer back to Figure 3.2). More specifically, DNA is a double-stranded molecule with its two strands oriented in opposite directions (i.e., antiparallel). Each strand is composed of nucleotides with a sugar phosphate backbone. There are four different types of DNA nucleotides: adenine (A), thymine (T), cytosine (C), and guanine (G). The two DNA strands are held together by nucleotide **base pairs**, which have chemical bonding rules. The complementary base-pairing rules are as follows: A and T bond with each other, while C and G form a bond. The chemical

Figure 3.13 Chemist and X-ray crystallographer Rosalind Franklin.

bonds between A–T and C–G are formed by "weak" hydrogen atom interactions, which means the two strands can be easily separated. A DNA sequence is the order of nucleotide bases (A, T, G, C) along only one DNA strand. If one DNA strand has the sequence CATGCT, then the other strand will have a complementary sequence GTACGA. This is an example of a short DNA sequence. In reality, there are approximately three billion DNA base pairs in human cells.
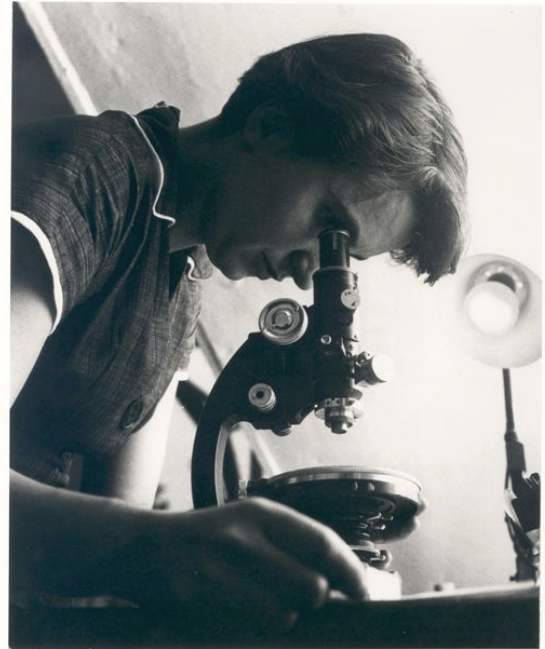
DNA Is Highly Organized Within the Nucleus

If you removed the DNA from a single human cell and stretched it out completely, it would measure approximately two meters (about 6.5 feet). Therefore, DNA molecules must be compactly organized in the nucleus. To achieve this, the double helix configuration of DNA undergoes coiling. An analogy would be twisting a string until coils are formed and then continuing to twist so that secondary coils are formed, and so on. To assist with coiling, DNA is first wrapped around proteins called **histones**. This creates a complex called **chromatin,** which resembles "beads on a string" (Figure 3.14). Next, chromatin is further coiled into a **chromosome**. Another important feature of DNA is that chromosomes can be altered from tightly coiled (chromatin) to loosely coiled (**euchromatin**). Most of the time, chromosomes in the nucleus remain in a euchromatin state so that DNA sequences are accessible for regulatory processes to occur.
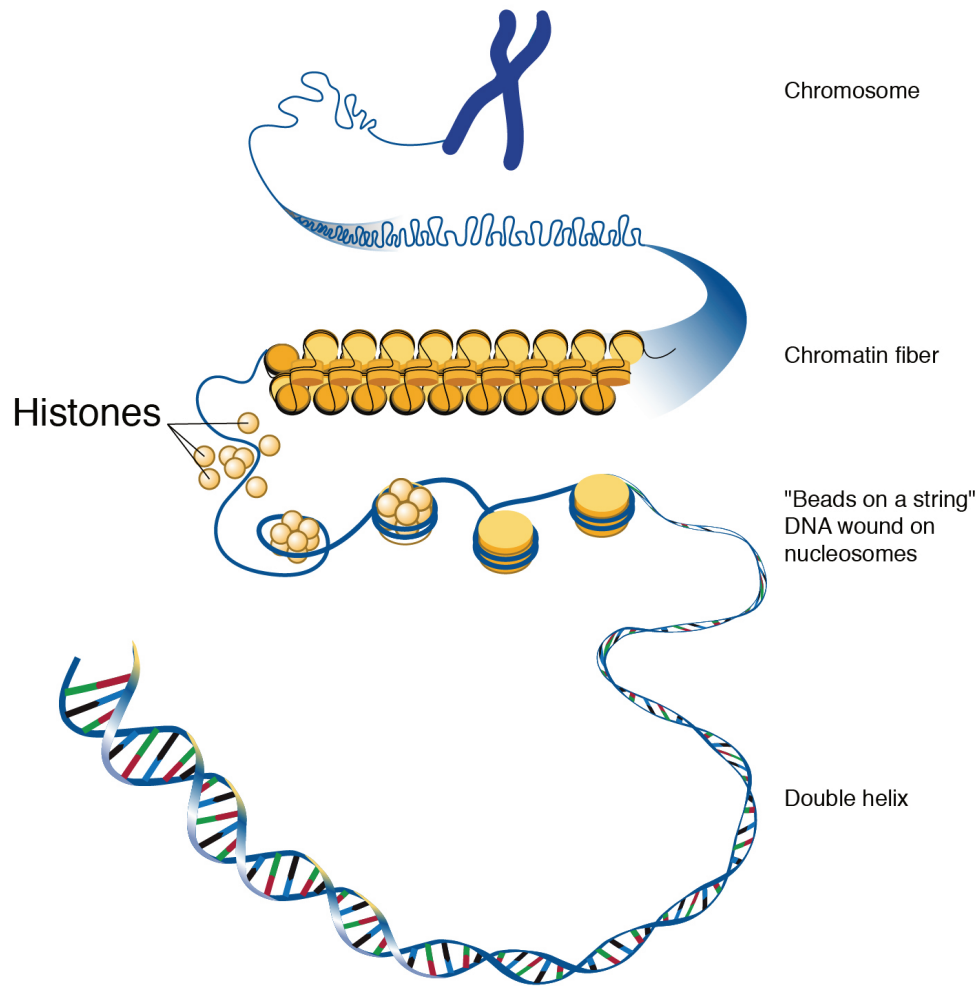
Chromosome

Chromatin fiber

Histones

"Beads on a string"
DNA wound on
nucleosomes

Double helix

Figure 3.14 The hierarchical organization of chromosomes.

Human body cells typically have 23 pairs of chromosomes, for a total of 46 chromosomes in each cell's nucleus (Figure 3.15). An interesting fact is that the number of chromosomes an organism possesses varies, and this figure is not dependent upon the size or complexity of the organism. For instance, chimpanzees have a total of 48 chromosomes, while hermit crabs have 254. Chromosomes also have a distinct physical structure, including **centromeres** (the "centers") and **telomeres** (the ends) (Figure 3.16). Because of centromeres, chromosomes are described as having two different "arms," where one arm is long and the other is shorter. Centromeres play an important role during cell division, which will be discussed in the next section. Telomeres are located at the ends of chromosomes and they help protect the chromosomes from degradation after every round of cell division. However, our telomeres become shorter as we age, and if chromosome telomeres become too short, then the cell will stop dividing. Therefore, the link between the regulation of telomere length and cellular aging is of great interest to researchers.
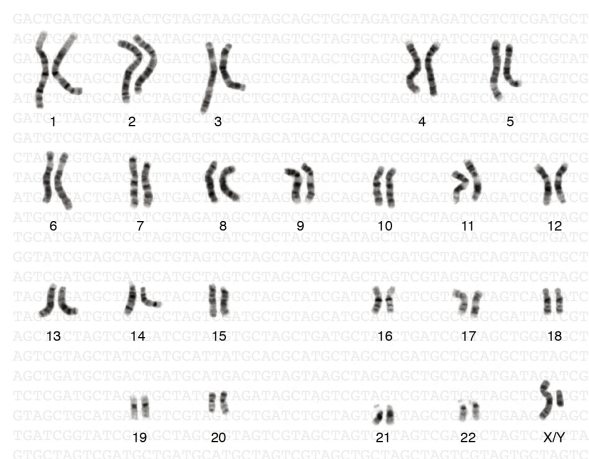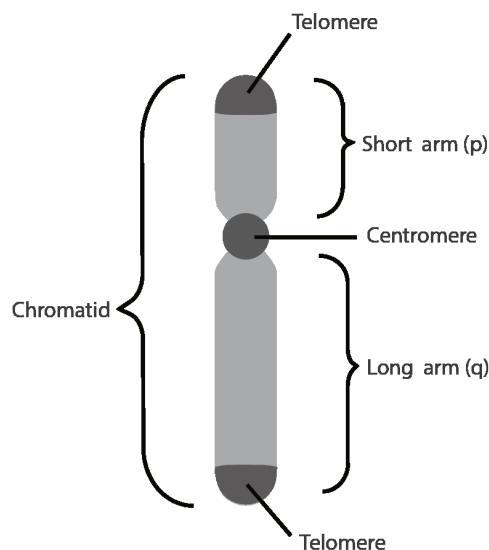
Chromosomes of the Human Genome

Figure 3.15 The 23 human chromosome pairs.

Figure 3.16 The regions of a chromosome.

REPLICATION AND CELL DIVISION

For life to continue and flourish, cells must be able to divide. Tissue growth and cellular damage repair are also necessary to maintain an organism throughout its life. All these rely on the dynamic processes of **DNA replication** and the **cell cycle**. The mechanisms highlighted in this section are tightly regulated and represent only part of the life cycle of a cell.

DNA Replication

DNA replication is the process by which new DNA is copied from an original DNA template. It is one phase of the highly coordinated cell cycle and requires a variety of enzymes with special functions. Specifically, enzymes carry out the structural and high-energy reactions associated with replicating a double helical molecule. The creation of a complementary DNA strand from a template strand is described as **semi-conservative replication**. The result of semi-conservative replication is two separate double-stranded DNA molecules, each of which is composed of an original "parent" template strand and a newly synthesized "daughter" DNA strand.

DNA replication progresses in three steps referred to as **initiation**, **elongation,** and **termination**. Initiation denotes the start of DNA replication by recruiting enzymes to specific sites along the DNA sequence. For example, the double helix of DNA presents structural challenges for replication, so an initiator enzyme, called **helicase**, "unwinds" DNA by breaking the hydrogen bonds between the two parent strands. The unraveling of the helix into two separated strands creates a fork, which is the active site of replication machinery (Figure 3.17). Once both strands are separated, the parent template strands are exposed, meaning they can be read and replicated.
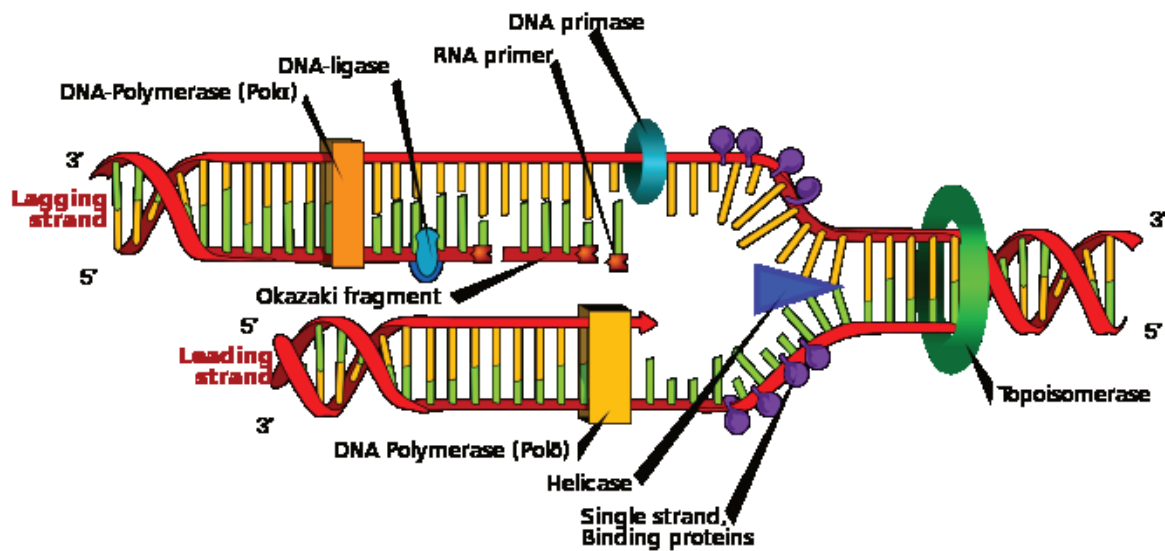
Figure 3.17 The different enzymes associated with DNA replication.

Elongation describes the assembly of new DNA daughter strands from parent strands. The two parent strands can further be classified as **leading strand** or **lagging strand** and are distinguished by the continuous or discontinuous direction of replication, respectively. A short fragment of RNA nucleotides acts as a **primer**, which binds to the parent DNA strand that will be copied. The leading strand receives one primer and the lagging strand receives several. Elongation proceeds with help from enzymes called **DNA polymerases**, which read parent template strands in a specific direction. Complementary nucleotides are added, and the newly formed daughter strand will grow. The direction in which replication proceeds depends on whether it is the leading or lagging strand. On the leading parent strand, a DNA polymerase will create one continuous strand. Because the lagging parent strand requires several primers, disjointed strands (called **Okazaki fragments**) will be generated. Other enzymes will fill in the missing nucleotide gaps between the disconnected lagging strand Okazaki fragments.

Finally, termination refers to the end of DNA replication activity. It is signaled by a stop sequence in the DNA, which is recognized by machinery at the replication fork. The end result of DNA replication is that the number of chromosomes are doubled so that the cell can divide into two.

DNA Mutations

DNA replication should result in the creation of two molecules with identical DNA nucleotide sequences. Although DNA polymerases are quite precise during DNA replication, copying mistakes are estimated to occur every 10^7 DNA nucleotides. Variation from the original DNA sequence is known as a mutation. The different types of mutations will be discussed in greater detail in Chapter 4. Briefly, mutations can result in single nucleotide changes as well as the insertion or deletion of nucleotides and repeated sequences. Depending on where they occur, mutations can be **deleterious** (harmful). For example, mutations may occur in regions that control cell cycle regulation, which can result in cancer (see Special Topic: The Cell Cycle and Immortality of Cancer Cells). Many other mutations, however, are not harmful to an organism.

Regardless of their effect, the cell attempts to reduce the frequency of mutations that occur during DNA replication.

To accomplish this, there are polymerases with proofreading capacities that can identify and correct mismatched nucleotides. These safeguards reduce the frequency of DNA mutations so that they only occur every 10^9 nucleotides.

SPECIAL TOPIC: THE CELL CYCLE AND IMMORTALITY OF CANCER CELLS

DNA replication is part of a series of preparatory phases that a cell undergoes prior to cell division, collectively known as **interphase** (Figure 3.18). During interphase, the cell not only doubles its chromosomes through DNA replication, but it also increases its metabolic capacity to provide energy for growth and division. Transition into each phase of the cell cycle is tightly controlled by proteins that serve as checkpoints. If a cell fails to pass a checkpoint, then DNA replication and/or cell division will not continue. Some of the reasons why a cell may fail at a checkpoint is DNA damage, lack of nutrients to continue the process, or insufficient size. In turn, a cell may undergo **apoptosis**, which is a mechanism for cell death.
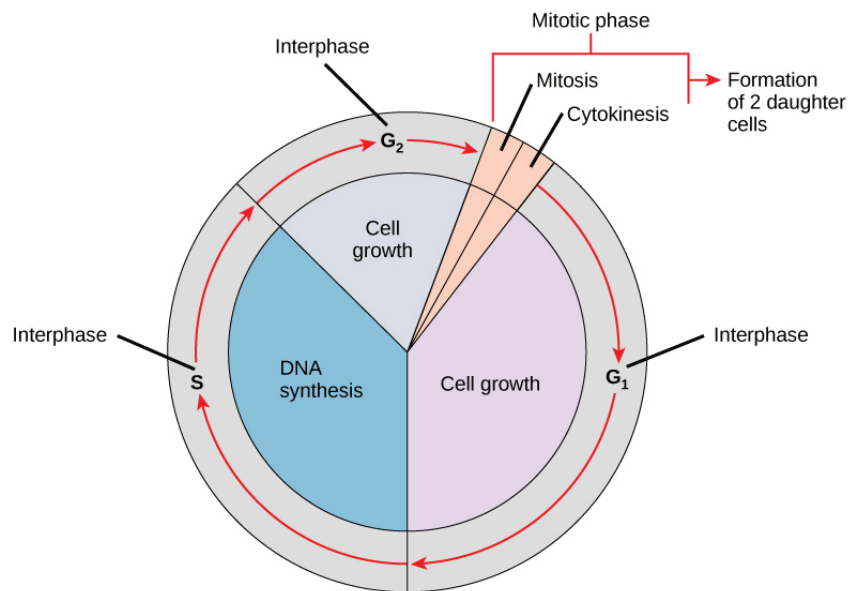

Figure 3.18 The phases and checkpoints of the cell cycle.

Unchecked cellular growth is a distinguishing hallmark of cancer. In other words, as cancer cells grow and proliferate, they acquire the capacity to avoid death and replicate indefinitely. This uncontrolled and continuous cell division is also known as "immortality." As previously discussed, most cells lose the ability to divide due to shortening of telomeres on the ends of chromosomes over time. One way in which cancer cells retain replicative immortality is that the length of their telomeres is continuously protected. Chemotherapy is often used to treat cancer by targeting cell division, which halts the propagation of genetically abnormal

cells. Another therapeutic approach that continues to be investigated is targeting telomere activity to stop the division of cancer cells.

Researchers have exploited the immortality of cancer cells for molecular research. The oldest immortal cell line is HeLa cells (Figure 3.19), which was harvested from Henrietta Lacks, an African-American woman diagnosed with cervical cancer in 1955. At that time, extracted cells frequently died during experiments, but surprisingly, HeLa cells continued to replicate. Propagation of Lacks's cell line has significantly contributed to medical research, including ongoing cancer research and helping to test the polio vaccine in the 1950s. Unfortunately, Lacks had not given her consent for her tumor biopsy to be used in cell culture research. Moreover, her family was unaware of the extraction and remarkable application of her cells for two decades. The history of HeLa cell origin was

Figure 3.19 A microscopic slide of HeLa cancer cells.

first revealed in 1976. The controversy voiced by the Lacks family was included in an extensive account of HeLa cells published in Rebecca Skloot's 2010 book, *The Immortal Life of Henrietta Lacks*. A film based on the book was also released in 2017.
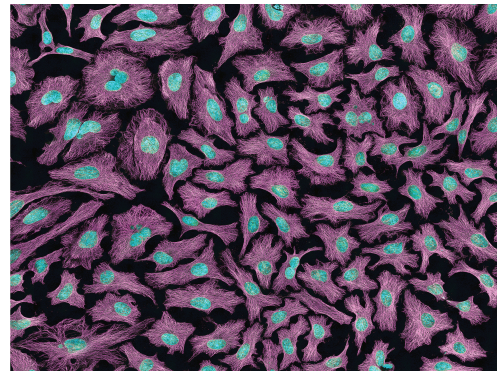
Mitotic Cell Division

The body and its various tissues are comprised of **somatic cells**. Organisms that contain two sets of chromosomes in their somatic cells are called **diploid** organisms. Humans have 46 chromosomes and they are diploid because they inherit one set of chromosomes (n = 23) from each parent. As a result, they have 23 matching pairs of chromosomes, which are known as **homologous chromosomes**. These homologous pairs vary in size and are generally numbered from largest (chromosome 1) to smallest (chromosome 22), as seen in Figure 3.15, with the exception of the 23rd pair, which is made up of the sex chromosomes (X and Y). Typically, the female sex is XX and the male sex is XY. Individuals inherit an X chromosome from their mother and an X or Y from their father.

In order to grow and repair tissues, somatic cells must divide. As discussed previously, a cell must first replicate its genetic material for cell division to occur. During DNA replication, each chromosome produces double the amount of genetic information. The duplicated arms of chromosomes are known as **sister chromatids,** and they are attached at the centromeric region. To elaborate, the number of chromosomes stays the same (n = 46); however, the amount of genetic material is doubled in the cell as the result of replication.

Mitosis is the process of somatic cell division that gives rise to two diploid daughter cells. Figure 3.20 shows a brief overview of mitosis. Once DNA and other organelles in the cell have finished replication, mitotic spindle fibers (microtubules) assist with chromosomal movement by attaching to the centromeric region of each chromosome. Specifically, the spindle fibers physically align each chromosome at the center of the cell. Next, the spindle fibers divide the sister chromatids and move each one to opposite sides of the cell. At this phase, there are 46 chromosomes on each side of the cell. The cell can now divide into two fully separated daughter cells.
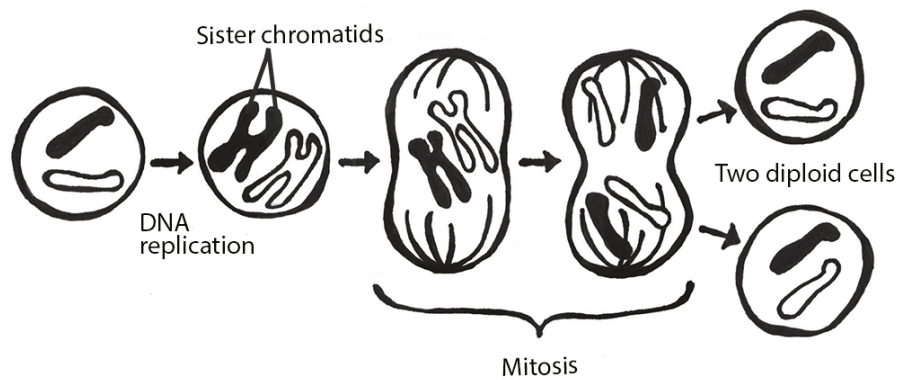
Figure 3.20 Steps of mitotic cell division.

Meiotic Cell Division

Gametogenesis is the production of **gametes** (sperm and egg cells); it involves two rounds of cell division called **meiosis**. Similar to mitosis, the parent cell in meiosis is diploid. However, meiosis has a few key differences, including the number of daughter cells produced (four cells, which require two rounds of cell division to produce) and the number of chromosomes each daughter cell has (Figure 3.21). During the first round of division (known as meiosis I), each chromosome (n = 46) replicates its DNA so that sister chromatids are formed. Next, with the help of spindle fibers, homologous chromosomes align near the center of the cell and sister chromatids physically swap genetic material. In other words, the sister chromatids of matching chromosomes cross over with each other at matching DNA nucleotide positions. The occurrence of homologous chromosomes crossing over, swapping DNA, and then rejoining segments is called **genetic recombination**. The "genetic shuffling" that occurs in gametes increases organismal genetic diversity by creating new combinations of genes on chromosomes that are different from the parent cell. Genetic mutations can also arise during recombination. For example, there may be an unequal swapping of genetic material that occurs between the two sister chromatids, which can result in deletions or duplications of DNA nucleotides. Once genetic recombination is complete, homologous chromosomes are separated and two daughter cells are formed.

The daughter cells after the first round of meiosis are **haploid**, meaning they only have one set of chromosomes (n = 23). During the second round of cell division (known as meiosis II), sister chromatids are separated and two additional haploid daughter cells are formed. Therefore, the four resulting daughter cells have one set of chromosomes (n = 23), and they also have a genetic composition that is not identical to the parent cells nor to each other.
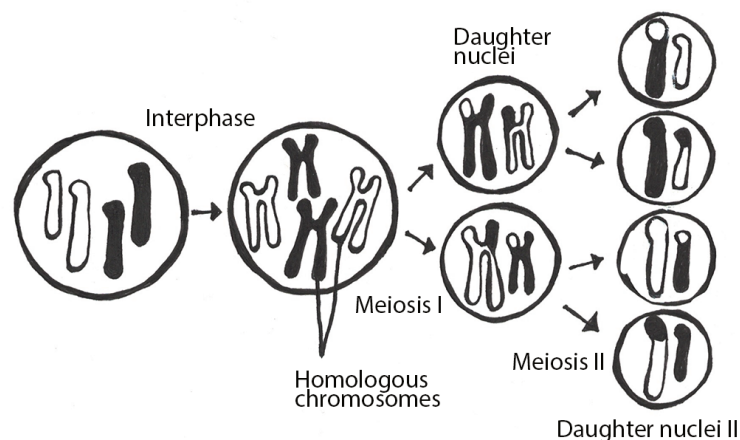

Figure 3.21 Meiotic cell division.

Although both sperm and egg gamete production undergo meiosis, they differ in the final number of viable daughter cells. In the case of spermatogenesis, four mature sperm cells are produced. Although four egg cells are also produced in oogenesis, only one of these egg cells will result in an ovum (mature egg). During fertilization, an egg cell and sperm cell fuse, which creates a diploid cell that develops into an embryo. The ovum also provides the cellular organelles necessary for embryonic cell division. This includes mitochondria, which is why humans, and most other multicellular eukaryotes, have the same mtDNA sequence as their mothers.

Chromosomal Disorders

During mitosis or meiosis, entire deletions or duplications of chromosomes can occur due to error. For example, homologous chromosomes may fail to separate properly, so one daughter cell may end up with an extra chromosome while the other daughter cell has one less. Cells with an unexpected (or abnormal) number of chromosomes are known as **aneuploid**. Adult or embryonic cells can be tested for chromosome number (**karyotyping**). Aneuploid cells are typically detrimental to a dividing cell or developing embryo, which can lead to a loss of pregnancy. However, the occurrence of individuals being born with three copies of the 21st chromosome is relatively common; this genetic condition is known as Down Syndrome. Moreover, human males and females can be born with aneuploid sex chromosome conditions such as XXY, XXX, and XO (referring to only one X chromosome).

PROTEIN SYNTHESIS

At the beginning of the chapter, we defined *proteins* as strings of **amino acids** that fold into complex 3-D shapes. There are 20 standard amino acids that can be strung together in different orders in humans, and the result is that proteins can perform an impressive amount of different functions. For instance, muscle fibers are proteins that help facilitate movement. A special class of proteins (immunoglobulins) help protect the organism by detecting disease-causing pathogens in the body. Protein hormones, such as insulin, help regulate physiological activity. Blood hemoglobin is a protein that transports oxygen throughout the body. **Enzymes** are also proteins, and they are catalysts for biochemical reactions that occur in the cell (e.g., metabolism). Larger-scale protein structures can be visibly seen as physical features of an organism (e.g., hair and nails).

Transcription and Translation

Coding nucleotides in our DNA provide instructions on how to make proteins. Making proteins, also known as **protein synthesis**, can be broken down into two main steps referred to as **transcription** and **translation**. Protein synthesis relies on many molecules in the cell including different types of regulatory proteins and RNAs for each step in the process. Although there are many different types of RNA molecules that have a variety of functions within the cell, we will mainly focus on **messenger RNA (mRNA)**.

A **gene** is a segment of DNA that codes for RNA, and genes can vary in length from a few hundred to as many as two million base pairs in length. The purpose of transcription is to make an RNA copy of that genetic code (Figure 3.22). Unlike double-stranded DNA, RNA molecules are single-stranded nucleotide sequences (refer back to Figure 3.2). Additionally, while DNA contains the nucleotide thymine (T), RNA does not—instead, its fourth nucleotide is uracil (U). Uracil is complementary to (or can pair with) adenine (A), while cytosine (C) and guanine (G) continue to be

complementary to each other. For transcription to proceed, a gene must first be turned "on" by the cell (see Special Topic: Genetic Regulation of the Lactase (*LCT*) Gene for a more detailed discussion of gene regulation). The double-stranded DNA is then separated, and one side of the DNA strand is used as a template where complementary RNA nucleotides are strung together. For example, if a DNA template is TACGGATGC, then the newly constructed mRNA sequence will be AUGCCUACG. Sometimes the end product needed by the cell is that transcribed RNA, but for protein synthesis constructing the RNA (specifically pre-messenger RNA, or pre-mRNA) is just the first step.
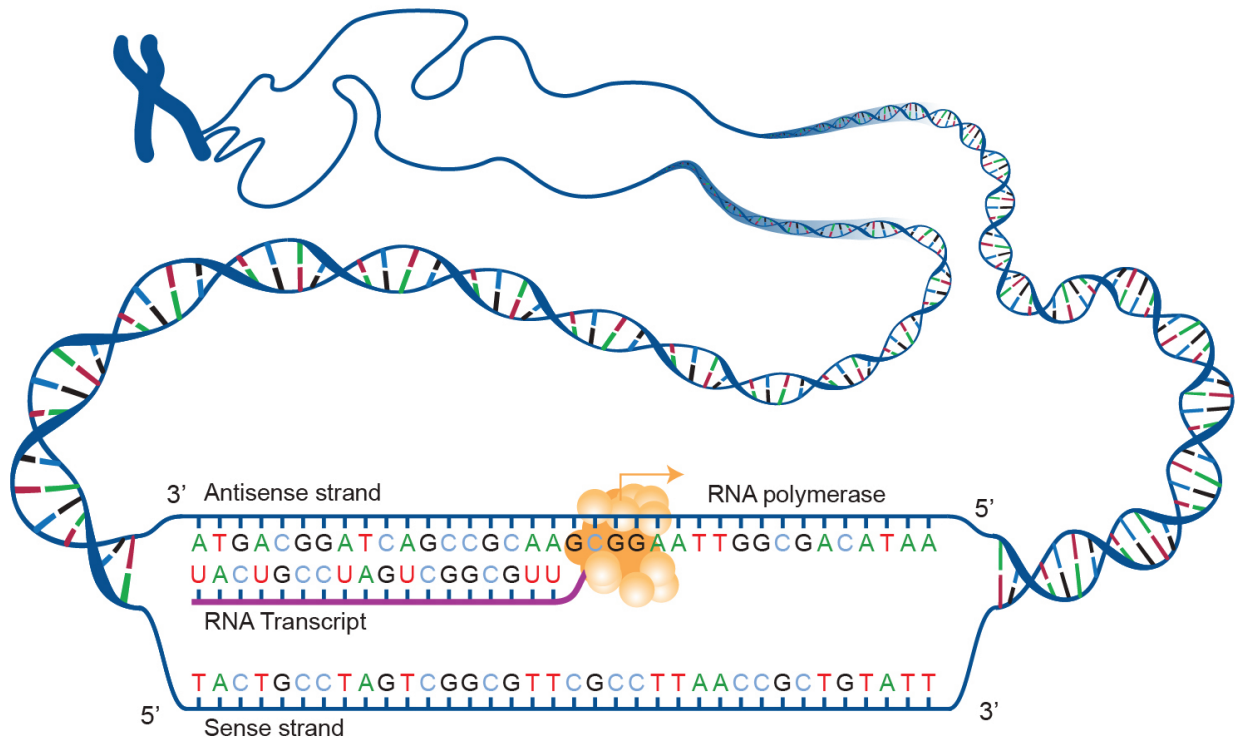

Figure 3.22 RNA polymerase catalyzing DNA transcription.

Genes contain segments called **introns** and **exons**. Exons are considered "coding" while introns are considered "noncoding"—meaning the information they contain will not be needed to construct proteins. When a gene is first transcribed into pre-mRNA, introns and exons are both included (Figure 3.23). However, once transcription is finished, introns are removed in a process called **splicing**. During splicing, a protein/RNA complex attaches itself to the pre-mRNA and removes introns and then connects the remaining exons, thus creating a shorter mature mRNA.
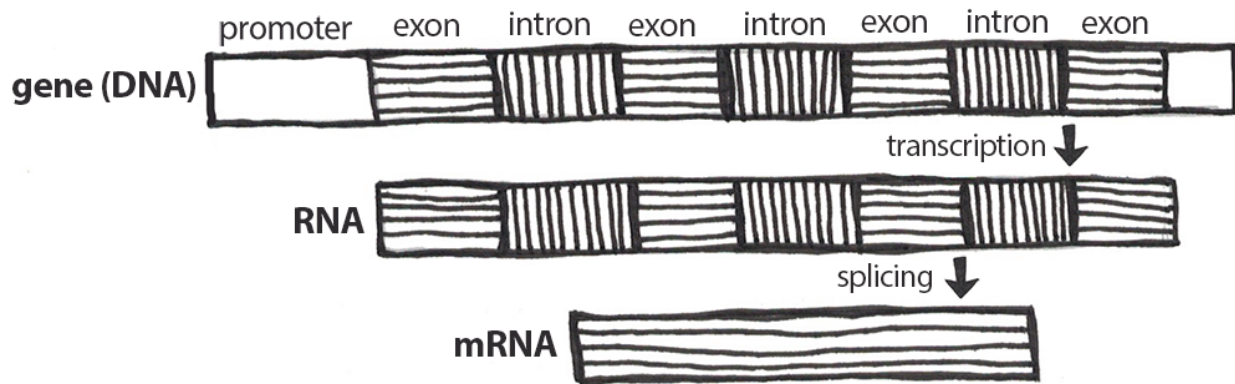
Figure 3.23 RNA processing is the modification of RNA, including the removal of introns, called splicing, between transcription and translation.

The process by which mRNA is "read" and amino acids chained together to form new proteins is called translation. During translation, mature mRNA is transported outside of the nucleus where it is bound to a **ribosome** (Figure 3.24). The nucleotides in the mRNA are read as triplets, which are called **codons**. Each codon corresponds to an amino acid, and this is the basis for building a protein. Continuing with our example from above, the mRNA sequence AUG-CCU-ACG codes for three amino acids. Using a codon table (Figure 3.25), AUG is a codon for methionine (Met), CCU is proline (Pro), and ACG is threonine (Thr). Therefore, the protein sequence is Met-Pro-Thr. Methionine is the most common "start codon" (AUG) for the initiation of protein translation in eukaryotes. As the ribosome moves along the mRNA, the growing amino acid chain exits the ribosome and folds into a protein (Figure 3.26). When the ribosome reaches a "stop" codon (UAA, UAG, or UGA), the ribosome stops adding new amino acids, detaches from the mRNA, and the protein is released. Folded proteins can then be used to complete a structural or functional task.
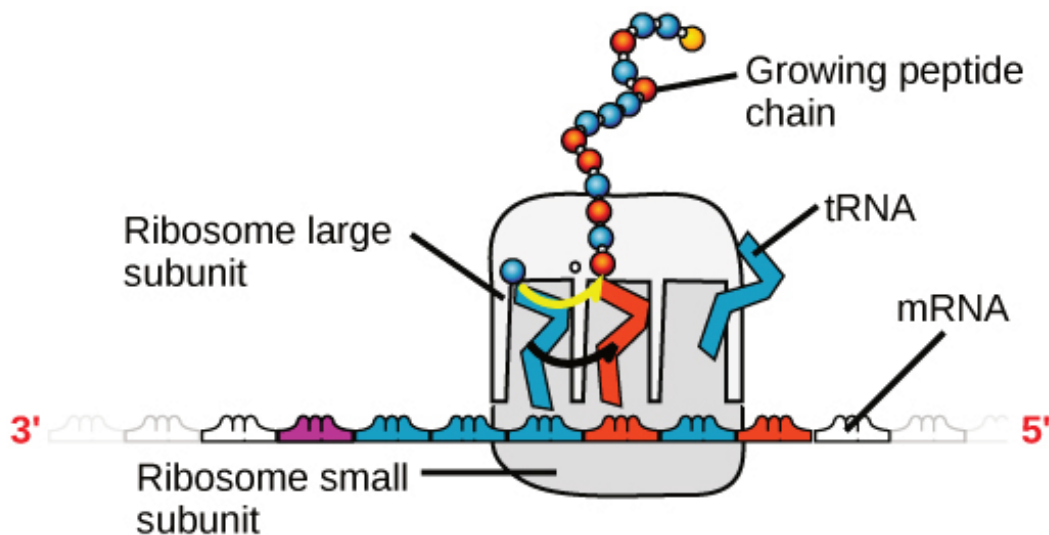

Figure 3.24 Translation of mRNA into an amino acid.

RNA codon table

1st position	2nd position				3rd position
	U	**C**	**A**	**G**	
U	Phe Phe Leu Leu	Ser Ser Ser Ser	Tyr Tyr stop stop	Cys Cys stop Trp	U C A G
C	Leu Leu Leu Leu	Pro Pro Pro Pro	His His Gln Gln	Arg Arg Arg Arg	U C A G
A	Ile Ile Ile Met	Thr Thr Thr Thr	Asn Asn Lys Lys	Ser Ser Arg Arg	U C A G
G	Val Val Val Val	Ala Ala Ala Ala	Asp Asp Glu Glu	Gly Gly Gly Gly	U C A G

Amino Acids

Ala: Alanine
Arg: Arginine
Asn: Asparagine
Asp: Aspartic acid
Cys: Cysteine

Gln: Glutamine
Glu: Glutamic acid
Gly: Glycine
His: Histidine
Ile: Isoleucine

Leu: Leucine
Lys: Lysine
Met: Methionine
Phe: Phenylalanine
Pro: Proline

Ser: Serine
Thr: Threonine
Trp: Tryptophane
Tyr: Tyrosisne
Val: Valine

Figure 3.25 This table can be used to identify which mRNA codons (sequence of three nucleotides) correspond with each of the 20 different amino acids. For example, if the codon is CAU, the first position is "C" and you would look in that corresponding row, the second position is "A" and you would look in that column. "U" is the third position—narrowing the row and indicating that the CAU codon corresponds with the amino acid "histidine" (abbreviated "His"). The table also indicates the most common "start codon" (AUG) that correlates with Methionine, and the three "stop" codons (UAA, UAG, or UGA).
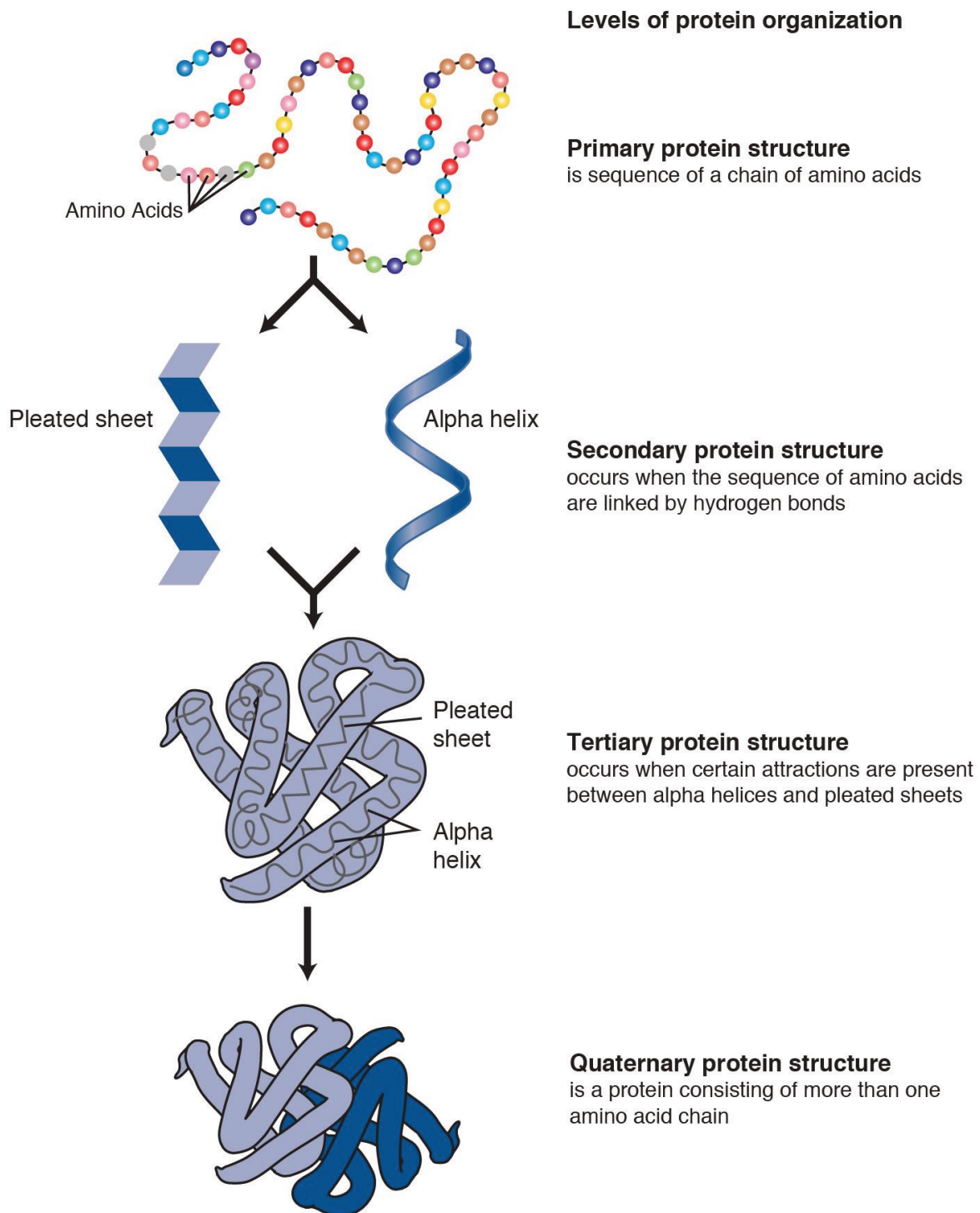
Levels of protein organization

Primary protein structure
is sequence of a chain of amino acids

Amino Acids

Pleated sheet

Alpha helix

Secondary protein structure
occurs when the sequence of amino acids
are linked by hydrogen bonds

Pleated
sheet

Tertiary protein structure
occurs when certain attractions are present
between alpha helices and pleated sheets

Alpha
helix

Quaternary protein structure
is a protein consisting of more than one
amino acid chain

Figure 3.26 Indicates levels of protein organization from the simple amino acid chain that is then folded and organized into more complex protein structures.

SPECIAL TOPIC: GENETIC REGULATION OF THE LACTASE (*LCT*) GENE

The *LCT* gene codes for a protein called lactase, an enzyme produced in the small intestine. It is responsible for breaking down the sugar "lactose" found in milk. Lactose intolerance occurs when not enough lactase enzyme is produced and, in turn, digestive symptoms occur. To avoid this discomfort, individuals may take lactase supplements, drink lactose-free milk, or avoid milk products altogether.

The *LCT* gene is a good example of how cells regulate protein synthesis. The **promoter** region of the *LCT* gene helps regulate whether it is transcribed or not transcribed (i.e., turned "on" or "off," respectively). Lactase production is initiated when a regulatory protein known as a **transcription factor** binds to a site on the *LCT* promoter. **RNA polymerases** are then recruited; they read DNA and string together nucleotides to make RNA molecules (Figure 3.22). An *LCT* pre-mRNA is synthesized (made) in the nucleus, and further chemical modifications flank the ends of the mRNA to ensure the molecule will not be degraded in the cell.

Next, RNA processing occurs. A spliceosome complex removes the introns and connects exons to form the mature mRNA. Once the *LCT* mRNA is transported outside of the nucleus, it is bound to a ribosome, which is a multi-protein complex that includes **ribosomal RNA (rRNA)**. The ribosome of eukaryotes has two main subunits: the smaller bottom subunit that binds to the mRNA and the larger top subunit that contains **transfer RNA (tRNA)** binding sites (see Figure 3.24). Each tRNA has a nucleotide anticodon that recognizes an mRNA codon. When a tRNA binds to an mRNA codon in the ribosome, the tRNA transfers the corresponding amino acid. rRNA ensures the newly added amino acid is linked in the correct order. The growing protein then folds into the lactase enzyme, which can break down lactose.

Most animals lose their ability to digest milk as they mature due to the decreasing transcriptional "silence" of the *LCT* gene over time. However, some humans have the ability to digest lactose into adulthood (also known as "lactase persistence"). This means they have a genetic mutation that leads to continuous transcriptional activity of *LCT*. Lactase persistence mutations are common in populations with a long history of pastoral farming, such as northern European and North African populations. It is believed that lactase persistence evolved because the ability to digest milk was nutritionally beneficial. More information about lactase persistence will be covered in Chapter 14.

MENDELIAN GENETICS AND OTHER PATTERNS OF INHERITANCE

Gregor Johann Mendel (1822–1884) is often described as the "Father of Genetics." Mendel was a monk who conducted pea plant breeding experiments in a monastery located in the present-day Czech Republic (Figure 3.27). After several years of experiments, Mendel presented his work to a local scientific community in 1865 and published his findings the following year. Although his meticulous effort was notable, the importance of his work was not recognized for another 35 years. One reason for this delay in recognition is that his findings did not agree with the predominant scientific viewpoints on inheritance at the time. For example, it was believed that parental physical traits "blended" together and offspring inherited an intermediate form of that trait. In contrast, Mendel showed that certain pea plant physical traits (e.g., flower color) were passed down separately to the next generation in a statistically predictable manner. Mendel also observed that some

Figure 3.27 Statue of Mendel located at the Mendel Museum located at Masaryk University in Brno, Czech Republic.

parental traits disappeared in offspring but then reappeared in later generations. He explained this occurrence by introducing the concept of "dominant" and "recessive" traits. Mendel established a few fundamental laws of inheritance, and this section reviews some of these concepts. Moreover, the study of traits and diseases that are controlled by a single gene is commonly referred to as **Mendelian genetics**.

Mendelian Genetics

Figure 3.28 Various phenotypic characteristics of pea plants resulting from different genotypes.

The physical appearance of a trait is called an organism's **phenotype**. Figure 3.28 shows pea plant (*Pisum sativum*) phenotypes that were studied by Mendel, and in each of these cases the physical traits are controlled by a single gene. In the case of Mendelian genetics, a phenotype is determined by an organism's **genotype**. A genotype consists of two gene copies, wherein one copy was inherited from each parent. Gene copies are also known as **alleles** (Figure 3.29), which means they are found in the same gene location on homologous chromosomes. Alleles have a nonidentical DNA

sequence, which means their phenotypic effect can be different. In other words, although alleles code for the same trait, different phenotypes can be produced depending on which two alleles (i.e., genotypes) an organism possesses. For example, Mendel's pea plants all have flowers, but their flower color can be purple or white. Flower color is therefore dependent upon which two color alleles are present in a genotype.

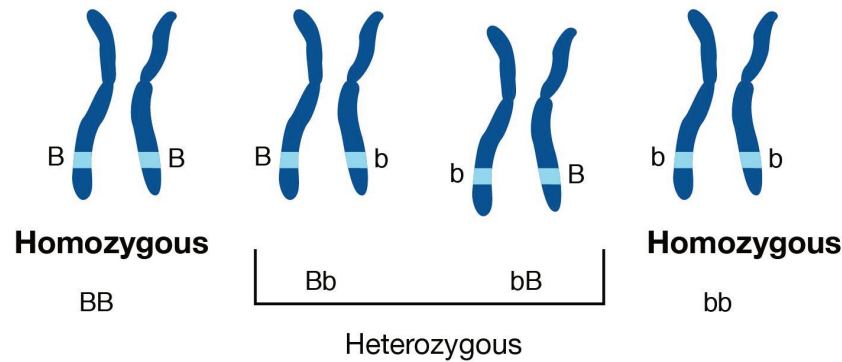*Figure 3.29 Homologous chromosome pairs showing the different homozygous and heterozygous combinations that can exist from two different alleles (B and b).*

A Punnett square is a diagram that can help visualize Mendelian inheritance patterns. For instance, when parents of known genotypes mate, a Punnett square can help predict the ratio of Mendelian genotypes and phenotypes that their offspring would possess. Figure 3.30 is a Punnett square that includes two **heterozygous** parents for flower color (Bb). A heterozygous genotype means there are two different alleles for the same gene. Therefore, a pea plant that is heterozygous for flower color has one purple allele and one white allele. When an organism is **homozygous** for a specific trait, it means their genotype consists of two copies of the same allele. Using the Punnett square example (Figure 3.30), the two heterozygous pea plant parents can produce offspring with two different homozygous genotypes (BB or bb) or offspring that are heterozygous (Bb).

Figure 3.30 Punnett square depicting the possible genetic combinations of offspring from two heterozygous parents.

A pea plant with purple flowers could be heterozygous (Bb) or homozygous (BB). This is because the purple color allele (B) is **dominant** to the white color allele (b), and therefore it only needs one copy of that allele to phenotypically express purple flowers. Because the white flower allele is **recessive**, a pea plant must be homozygous for the recessive allele in order to have a white color phenotype (bb). As seen by the Punnett square example (Figure 3.30), three of four offspring will have purple flowers and the other one will have white flowers.

The *Law of Segregation* was introduced by Mendel to explain why we can predict the ratio of genotypes and phenotypes in offspring. As discussed previously, a parent will have two alleles for a certain gene (with each copy on a different homologous chromosome). The Law of Segregation states that the two copies will be segregated from each other and will each be distributed to their own gamete. We now know that the process where that occurs is meiosis.

Offspring are the products of two gametes combining, which means the offspring inherits one allele from each gamete

for most genes. When multiple offspring are produced (like with pea plant breeding), the predicted phenotype ratios are more clearly observed. The pea plants Mendel studied provide a simplistic model to understand single-gene genetics. While many traits anthropologists are interested in have a more complicated inheritance (e.g., are informed by many genes), there are a few known Mendelian traits in humans. Additionally, some human diseases also follow a Mendelian pattern of inheritance (Figure 3.31). Because humans do not have as many offspring as other organisms, we may not recognize Mendelian patterns as easily. However, understanding these principles and being able to calculate the probability that an offspring will have a Mendelian phenotype is still important.

Mendelian disorder	Gene	Mendelian disorder	Gene
Alpha Thalassemia	HBA1	Maple Syrup Urine Disease: Type 1A	BCKDHA
Androgen Insensitivity Syndrome	AR	Mitochondrial DNA Depletion Syndrome	TYMP
Bloom Syndrome	BLM	MTHFR Deficiency	MTHFR
Canavan Disease	ASPA	Oculocutaneous Albinism: Type 1	TYR
Cartilage-Hair Hypoplasia	RMRP	Oculocutaneous Albinism: Type 3	TYRP1
Cystic Fibrosis	CFTR	Persistent Mullerian Duct Syndrome: Type I	AMH
Familial Chloride Diarrhea	SLC26A3	Polycystic Kidney Disease	PKHD1
Fragile X Syndrome	FMR1	Sickle-cell anemia	HBB
Glucose-6-Phosphate Dehydrogenase Deficiency	G6PD	Spermatogenic failure	USP9Y
Hemophilia A	F8	Spinal Muscular Atrophy: SMN1 Linked	SMN1
Huntington disease	HTT	Tay-Sachs Disease	HEXA
Hurler Syndrome	IDUA	Wilson Disease	ATP7B

Figure 3.31 Human diseases that follow a Mendelian pattern of inheritance.

Example of Mendelian Inheritance: The ABO Blood Group System

In 1901, Karl Landsteiner at the University of Vienna published his discovery of ABO blood groups. This was a result of conducting blood immunology experiments in which he combined the blood of individuals who possess different blood cell types and observed an agglutination (clotting) reaction. The presence of agglutination implies there is an incompatible immunological reaction, whereas no agglutination will occur in individuals with the same blood type. This work was clearly important because it resulted in a higher survival rate of patients who received blood transfusions.

Blood transfusions from someone with a different type of blood causes agglutinations, and the resulting coagulated blood can not easily pass through blood vessels, resulting in death. Accordingly, Landsteiner received the Nobel Prize (1930) for explaining the ABO blood group system.

Blood **cell surface antigens** are proteins that coat the surface of red blood cells, and **antibodies** are specifically "against" or "anti" to the antigens from other blood types. Thus, antibodies are responsible for causing agglutination between incompatible blood types. Understanding the interaction of antigens and antibodies helps to determine ABO compatibility amongst blood donors and recipients. In order to better understand blood phenotypes and ABO compatibility, blood cell antigens and plasma antibodies are presented in Figure 3.32. Individuals that are blood type A have A antigens on the red blood cell surface, and anti-B antibodies, which will bind with B antigens should they come in contact. Alternatively, individuals with blood type B have B antigens and anti-A antibodies. Individuals with blood type AB have both A and B antigens but do not produce antibodies for the ABO system. This does not mean type AB does not have any antibodies, just that anti-A or anti-B antibodies are not produced. Individuals who are blood type O have nonspecific antigens but produce both anti-A and anti-B antibodies.

	Group A	Group B	Group AB	Group O
Red blood cell type	A	B	AB	O
Antibodies in Plasma	Anti-B	Anti-A	None	Anti-A and Anti-B
Antigens in Red Blood Cell	A antigen	B antigen	A and B antigens	None

Figure 3.32 The different ABO blood types with their associated antibodies and antigens.

Figure 3.33 shows a table of the ABO allele system, which has a Mendelian pattern of inheritance. Both the A and B alleles function as dominant alleles, so the A allele always codes for the A antigen, and the B allele codes for the B antigen. The O allele differs from A and B, because it codes for a nonfunctional antigen protein, which means there is no antigen present on the cell surface of O blood cells. To have blood type O, two copies of the O allele must be inherited, one from each parent, thus the O allele is considered recessive. Therefore, someone who is a heterozygous AO genotype is phenotypically blood type A and a genotype of BO is blood type B. The ABO blood system

	A	B	O
A	AA	AB	AO
B	AB	BB	BO
O	AO	BO	OO

Figure 3.33 The different combinations of ABO blood alleles (A, B, and O) to form ABO blood genotypes.

also provides an example of **codominance**, which is when the effect of both alleles is observed in the phenotype. This is true for blood type AB: when an individual inherits both the A and B alleles, then both A and B antigens will be present on the cell surface.

Also found on the surface of red blood cells is the rhesus group antigen, known as "Rh factor." In reality, there are several antigens on red blood cells independent from the ABO blood system, however, the Rh factor is the second most important antigen to consider when determining blood donor and recipient compatibility. Rh antigens must also be considered when a pregnant mother and her baby have incompatible Rh factors. In such cases, a doctor can administer necessary treatment steps to prevent pregnancy complications and hemolytic disease, which is when the mother's antibodies break down the newborn's red blood cells.

An individual can possess the Rh antigen (be Rh positive) or lack the Rh antigen (be Rh negative). The Rh factor is controlled by a single gene and is inherited independently of the ABO alleles. Therefore, all blood types can either be positive (O+, A+, B+, AB+) or negative (O-, A-, B-, AB-).

Individuals with O+ red blood cells can donate blood to A+, B+, AB+, and O+ blood type recipients. Because O- individuals do not have AB or Rh antigens, they are compatible with all blood cell types and are referred to as "universal donors." Individuals that are AB+ are considered to be "universal recipients" because they do not possess antibodies against other blood types.

Mendelian Patterns of Inheritance and Pedigrees

A pedigree can be used to investigate a family's medical history by determining if a health issue is inheritable and will possibly require medical intervention. A pedigree can also help determine if it is a Mendelian recessive or dominant genetic condition. Figure 3.34 is a pedigree example of a family with Huntington's disease, which has a Mendelian dominant pattern of inheritance. In a standard pedigree, males are represented by a square and females are represented by a circle. When an individual is affected with a certain condition, the square or circle is filled in as a solid color. With a dominant condition, at least one of the parents will have the disease and an offspring will have a 50% chance of inheriting the affected chromosome. Therefore, dominant genetic conditions tend to be present in every generation. In the case of Huntington's, some individuals may not be diagnosed until later in adulthood, so parents may unknowingly pass this dominantly inherited disease to their children.

Figure 3.34 A three-generation pedigree depicting an example of dominant Mendelian inheritance like Huntington's.

Because the probability of inheriting a disease-causing recessive allele is more rare, recessive medical conditions can skip generations. Figure 3.35 is an example of a family that carries a recessive cystic fibrosis mutation. A parent that is heterozygous for the cystic fibrosis allele has a 50% chance of passing down their affected chromosome to the next generation. If a child has a recessive disease, then it means both of their parents are **carriers** (heterozygous) for that condition. In most cases, carriers for recessive conditions show no serious medical symptoms. Individuals whose family have a known medical history for certain conditions sometimes seek family planning services (see the Genetic Testing section).

Figure 3.35 A three-generation pedigree depicting an example of recessive Mendelian inheritance like cystic fibrosis.

Pedigrees can also help distinguish if a health issue has an **autosomal** or **X-linked** pattern of inheritance. As previously discussed, there are 23 pairs of chromosomes and 22 of these pairs are known as **autosomes**. The provided pedigree examples (Figure 3.34–35) are autosomally linked genetic diseases. This means the genes that cause the disease are located on one of the chromosomes numbered 1 to 22. Disease causing genes can also be X-linked, which means they are located on the X chromosome.

Figure 3.36 depicts a family in which the mother is a carrier for the X-linked recessive disease Duchenne Muscular Dystrophy (*DMD*). The mother is a carrier for *DMD*, so daughters and sons will have a 50% chance of inheriting the pathogenic *DMD* allele. Because females have two X chromosomes, females will not have the disease (although in rare cases, female carriers may show some symptoms of the disease). On the other hand, males who inherit a copy of an X-linked pathogenic *DMD* allele will typically be affected with the condition. Males are more susceptible to X-linked conditions because they only have one X chromosome. Therefore, when evaluating a pedigree, if a higher proportion of males are affected with the disease, this could suggest the disease is X-linked recessive. Finally, Y-linked traits are very rare because compared to other chromosomes, the Y chromosome is smaller and only has a few active (transcribed) genes.

Figure 3.36 A three-generation pedigree depicting an example of X-linked Mendelian inheritance like Duchenne Muscular Dystrophy (DMD).

Complexity Surrounding Mendelian Inheritance

Figure 3.37 Snap dragons with different genotypes resulting in different flower color phenotypes.

Pea plant trait genetics are relatively simple compared to what we know about genetic inheritance today. The vast majority of genetically controlled traits are not strictly dominant or recessive, so the relationship among alleles and predicting phenotype is often more complicated. For example, a heterozygous genotype that exhibits an intermediate phenotype of both alleles is known as incomplete dominance. In snapdragon flowers, the red flower color (R) is dominant and white is recessive (r). Therefore, the homozygous dominant RR is red and homozygous recessive rr is white. However, because the R allele is not completely dominant, the heterozygote Rr is a blend of red and white, which results in a pink flower (Figure 3.37).

An example of incomplete dominance in humans is the enzyme β-hexosaminidase A (Hex A), which is encoded by the gene *HEXA*. Patients with two dysfunctional *HEXA* alleles are unable to metabolize a specific lipid-sugar molecule (GM2 ganglioside); because of this, the molecule builds up and causes damage to nerve cells in the brain and spinal cord. This condition is known as Tay-Sachs disease, and it usually appears in infants who are three to six months old. Most children with Tay-Sachs do not live past early childhood. Individuals who are heterozygous for the functional type *HEXA* allele and one dysfunctional allele have reduced Hex A activity. However, the amount of enzyme activity is still sufficient, so carriers do not exhibit any neurological phenotypes and appear healthy.

Some genes and alleles can also have higher **penetrance** than others. Penetrance can be defined as the proportion of individuals who have a certain allele and also express an expected phenotype. If a genotype always produces an expected phenotype, then those alleles are said to be fully penetrant. However, in the case of incomplete (or reduced) penetrance,

an expected phenotype may not occur even if an individual possesses the alleles that are known to control a trait or cause a disease.

A well-studied example of genetic penetrance is the cancer-related genes *BRCA1* and *BRCA2*. Mutations in these genes can affect crucial processes such as DNA repair, which can lead to breast and ovarian cancers. Although *BRCA1* and *BRCA2* mutations have an autosomal dominant pattern of inheritance, it does not mean an individual will develop cancer if they inherit a pathogenic allele. Several lifestyle and environmental factors can also influence the risk for developing cancer. Regardless, if a family has a history of certain types of cancers, then it is often recommended that genetic testing be performed for individuals who are at risk. Moreover, publically available genetic testing companies are now offering health reports that include BRCA1/2 allele testing (see the Genetic Testing section).

POLYGENIC TRAITS

While Mendelian traits tend to be influenced by a single gene, the vast majority of human phenotypes are **polygenic traits**. The term *polygenic* means "many genes." Therefore, a polygenic trait is influenced by many genes that work together to produce the phenotype. Human phenotypes such as hair color, eye color, height, and weight are examples of polygenic traits. **Complex diseases** (e.g., cardiovascular diseases, Alzheimer's, and Schizophrenia) also have a polygenic basis.

Human hair color is an example of a polygenic trait. Hair color is largely determined by the type and quantity of a pigment called melanin, which is produced by a specialized cell type within the skin called melanocytes. The quantity and ratio of melanin pigments determine black, brown, blond, and red hair colors. *MC1R* is a well-studied gene that encodes a protein expressed on the surface of melanocytes that is involved in the production of eumelanin pigment. Typically, people with two functional copies of *MC1R* have brown hair. People with reduced functioning *MC1R* allele copies tend to produce pheomelanin, which results in blond or red hair. However, *MC1R* alleles have variable penetrance, and studies are continually identifying new genes (e.g., *TYR*, *TYRP1*, *SLC24A5*, and *KITLG*) that also influence hair color. Individuals with two non-functioning copies of the gene *TYR* have a condition called oculocuteaneous albinism–their melanocytes are unable to produce melanin so these individuals have white hair, light eyes, and pale skin.

In comparison to Mendelian disease, complex diseases tend to be more prevalent in humans. Complex diseases can also run in families, but they often do not have a clear pattern of inheritance. Geneticists may not know all of the genes involved with a given complex disease. In addition to different gene combinations, complex diseases are also influenced by environment and lifestyle factors. Moreover, how much each of these determinants contribute to a disease phenotype can be difficult to decipher. Therefore, predicting medical risk is often a significant challenge. For instance, cardiovascular diseases (CVDs) continue to be one of the leading causes of death around the world. Development of CVDs has been linked to malnutrition during fetal development, high fat and sedentary lifestyles, smoking/drug usage, adverse socioeconomic conditions, and various genes. Human environments are diverse, and public health research including the field of Human Biology can help identify risk factors and behaviors associated with chronic diseases. Large-scale genetic studies can also help elucidate some of these complex relationships.

GENOMICS AND EPIGENETICS

The **genome** is all of the genetic material for an organism. In the case of humans, this includes 46 chromosomes and mtDNA. The human genome contains approximately three billion base pairs of DNA and has regions that are both

noncoding and coding. Scientists now estimate that the human genome contains 20,000–25,000 protein-coding genes, with each chromosome containing a few hundred to a few thousand genes. As our knowledge of heredity increases, researchers have begun to realize the importance of **epigenetics**, or changes in gene expression that do not result in a change of the underlying DNA sequence. Epigenetics research is also crucial for unraveling gene regulation, which involves complex interactions between DNA, RNA, proteins, and the environment.

Genomics

The vast majority of the human genome is noncoding, meaning there are no instructions to make a protein or RNA product in these regions. Historically, noncoding DNA was referred to as "junk DNA" because these vast segments of the genome were thought to be irrelevant and non-functional. However, continual improvement of DNA **sequencing** technology along with world-wide scientific collaborations and consortia have contributed to our increased understanding of how the genome functions. Through these technological advances and collaborations, we have since discovered that many of these noncoding DNA regions are involved in dynamic genetic regulatory processes.

Genomics is a diverse field of molecular biology that focuses on genomic evolution, structure and function; gene mapping; and **genotyping** (determining the alleles present). Evolutionary genomics determined that humans and chimpanzees share a significant portion of shared DNA sequence (about 98.8%). Given the phenotypic differences between humans and chimpanzees, having a DNA sequence difference of 1.2% seems surprising. However, a lot of genomics research is also focused on understanding how noncoding genomic regions influence how individual genes are turned "on" and "off" (i.e., regulated). Therefore, although DNA sequences are identical, regulatory differences in noncoding genetic regions (e.g., promoters) are believed to be largely responsible for the physical differences between humans and chimpanzees.

Further understanding of genomic regulatory elements can lead to new therapies and personalized treatments for a broad range of diseases. For example, targeting the regulatory region of a pathogenic gene to "turn off" its expression can prevent its otherwise harmful effects. Such molecular targeting approaches can be personalized based on an individual's genetic makeup. Genome-wide association studies (GWAS) seek to determine genes that are linked to complex traits and diseases and typically require significant computational efforts. This is because millions of DNA sequences must be analyzed and GWAS sometimes include thousands of participants. During the beginning of the genomics field, most of the large-scale genomics studies only included North American, European, and East Asian participants and patients. Researchers are now focusing on increasing ethnic diversity in genomic studies and databases. In turn, accuracy of individual disease risk across all human populations will be improved and more rare-disease-causing alleles will be identified.

Epigenetics

All cells within your body have the same copy of DNA. For example, a brain neuron has the same DNA blueprint as does a skin cell on your arm. Although these cells have the same genetic information, they are considered specialized. The reason all cells within the body have the same DNA but different morphologies and functions is that different subsets of genes are turned "on" and "off" within the different cell types. A more precise explanation is that there is differential expression of genes among different cell types. In the case of neuronal cells, a unique subset of genes are active that allow them to grow axons to send and receive messages. This subset of genes will be inactive in non-neuronal cell types such as skin cells. Epigenetics is a branch of genetics that studies how these genes are regulated through mechanisms

that do not change the underlying DNA sequence. Special Topics: Epigenetics and X Chromosome Inactivation details a well-known example of epigenetic regulation.

The prefix *epi* means "on, above, or near," and epigenetic mechanisms such as **DNA methylation** and histone modifications occur on, above, or near DNA. The addition of a methyl group ($-CH_3$) to DNA is known as DNA methylation (Figure 3.38). DNA methylation and other modifications made to the histones around which DNA are wrapped are thought to make chromatin more compact. This DNA is inaccessible to transcription factors and RNA polymerases, thus preventing genes from being turned on (i.e., transcribed). Other histone modifications have the opposite effect by loosening chromatin, which makes genes accessible to transcription factors.

It is important to note that environmental factors can alter DNA methylation and histone modifications and also that these changes can be passed from generation to generation. For example, someone's **epigenetic profile** can be altered during a stressful time (e.g., natural disasters, famine, etc.), and those regulatory changes can be inherited by the next generation. Moreover, our epigenetic expression profile changes as we age. For example, certain places in our genome become "hyper" or "hypo" methylated over time. Identical twins also have epigenetic profiles that become more different as they age. Researchers are only beginning to understand what all of these genome-wide epigenetic changes mean. Scientists have also discovered that changes in epigenetic modifications can alter gene expression in ways that contribute to diseases. It is also important to note that, unlike DNA mutations (which permanently change the nucleotide sequence), epigenetic changes can be easily reversed. A lot of research now focuses on how drugs can alter or modulate changes in DNA methylation and histone modifications to treat diseases such as cancer.
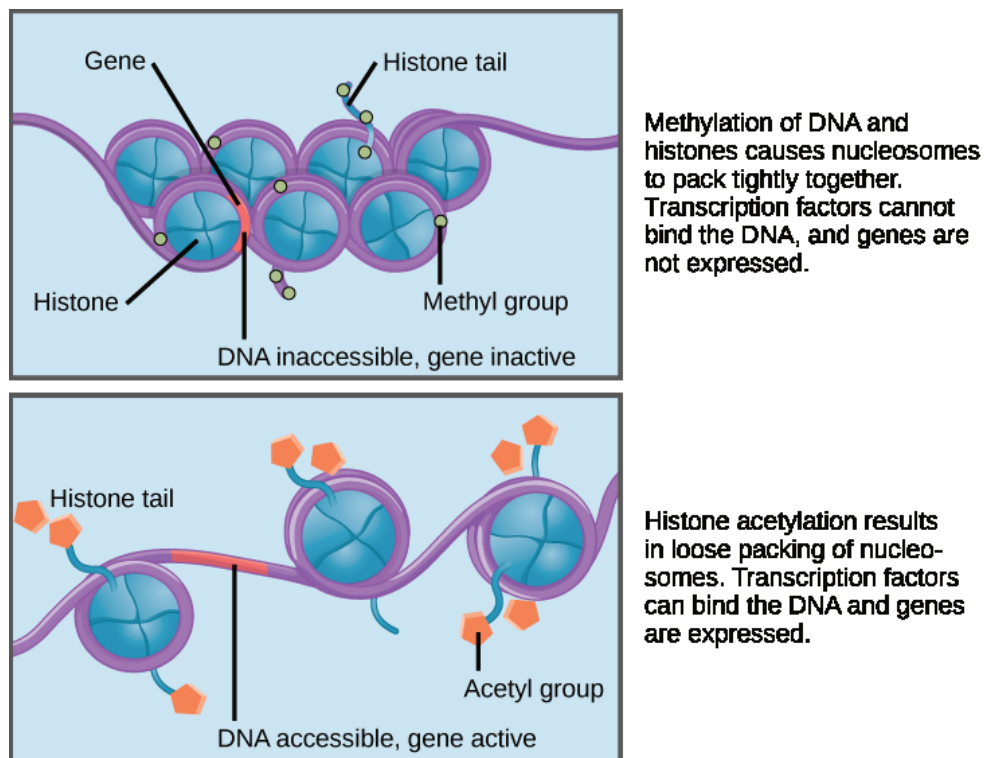

Figure 3.38 Different types of epigenetic histone tail modifications that can tighten (top) and loosen (bottom) the chromatin of DNA.

SPECIAL TOPIC: EPIGENETICS AND X CHROMOSOME INACTIVATION

Mary Lyon was a British geneticist that presented a hypothesis for X chromosome inactivation (called the *Lyon hypothesis*) based on her work and other studies of the day. Females inherit two X chromosomes, one from each parent. Males have one functional X chromosome; however, this does not mean females have more active genes than males. During the genetic embryonic development of many female mammals, one of the X chromosomes is inactivated at random, so females have one functional X chromosome. The process of X chromosome inactivation in females occurs through epigenetic mechanisms, such as DNA methylation and histone modifications. Recent studies have analyzed the role of a long noncoding RNA called X-inactive specific transcript (XIST), which is largely responsible for the random silencing of one of the X chromosomes. The presence of two X chromosomes is the signal for XIST RNA to be expressed so that one X chromosome can be inactivated. However, some cells may have an

Figure 3.39 A multicolored coat pattern as the result of X chromosome inactivation during development.

active paternal X chromosome while other cells may have an active maternal X chromosome. This phenomenon is easily seen in calico and tortoiseshell cats (Figure 3.39). In cats, the gene that controls coat color is found on the X chromosome. During early embryo development, random inactivation of X chromosomes gives rise to populations of cells that express black or orange, which results in the unique coat patterning. Therefore, calico cats are typically always female.

GENETIC TESTING

In order to assist with public health efforts, newborn screening for genetic diseases have been available in the United States for over 50 years. One of the first available genetic tests was to confirm a phenylketonuria (*PKU*) diagnosis in infants, which is easily treatable with a dietary change. Currently, each state decides what genes are included on newborn screening panels and some states even have programs to help with infant medical follow-ups.

There are now hundreds of laboratories that provide testing for a few thousand different genes that can inform medical decisions for infants and adults. What has made this industry possible are the advancements in technology and decreased cost to patients. Moreover, genetic testing has been made available publicly to anyone without the assistance of medical professionals.

Polymerase Chain Reaction (PCR) and Sanger Sequencing

One of the most important inventions in the genetics field was **polymerase chain reaction (PCR)**. In order for researchers to visualize and therefore analyze DNA, the concentration must meet certain thresholds. In 1985, Kary Mullis developed PCR, which can amplify millions of copies of DNA from a very small amount of template DNA (Figure 3.40). For example, a trace amount of DNA at a crime scene can be amplified and tested for a DNA match. Also, aDNA is typically degraded, so a few remaining molecules of DNA can be amplified to reconstruct ancient genomes. The PCR assay uses similar biochemical reactions to our own cells during DNA replication.

Figure 3.40 Gel electrophoresis used to visualize DNA after PCR amplification.

In **Sanger sequencing**, PCR sequences can be analyzed at the nucleotide level with the help of fluorescent labeling. Several different types of alleles and genetic changes can be detected in DNA by using this analysis. Figure 3.41 shows someone who is heterozygous for a single nucleotide allele. These methods continue to be used extensively alongside larger-scale genome technologies.

Figure 3.41 Sanger sequencing results showing a heterozygous DNA nucleotide.

Genetic Biotechnology and Clinical Testing

Figure 3.42 Microarray chip with fluorescent labeled probes that hybridize with DNA to detect homozygous and heterozygous nucleotides throughout the genome.

Genetic innovations are transforming the healthcare industry. However, the different types of technology and the results of these tests often include a learning curve for patients, the public, and medical practitioners. **Microarray technology**, when DNA samples are genotyped (or "screened") for specific alleles, has been available for quite some time (Figure 3.42). Presently, microarray chips can include hundreds of alleles that are known to be associated with various diseases. The microarray chip only binds with a DNA sample if it is "positive" for that particular allele and a fluorescent signal is emitted, which can be further analyzed.

If a patient is suspected of having a rare genetic condition that cannot be easily diagnosed or the diagnosis is entirely unknown, whole genome sequencing may be recommended by a doctor. **Next-generation sequencing (NGS)** is a newer technology that can screen the entire genome by analyzing millions of sequences within a single machine run (Figure 3.43). However, sequencing the entire genome yields a significant amount of data and information. Therefore, clinical NGS genetic testing typically only includes a small subset of the genome known to have pathogenic disease-causing mutations.

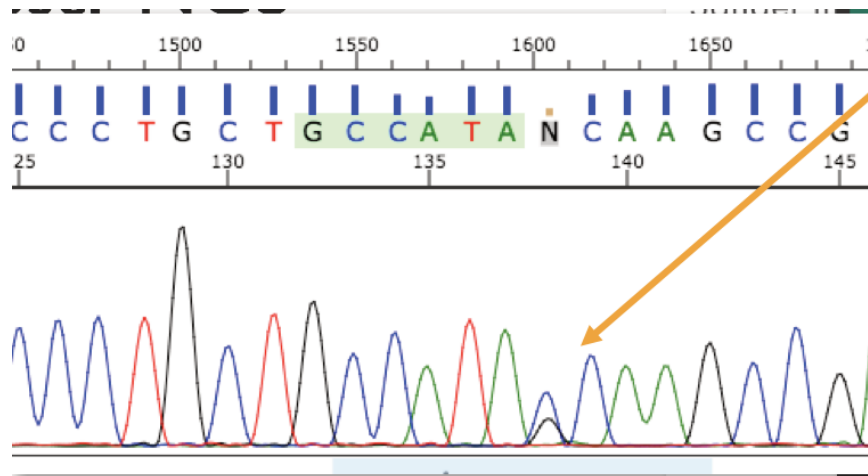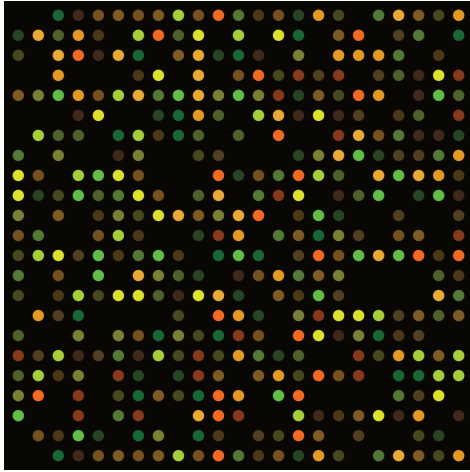*Figure 3.43 Next-generation sequencing machines.*

There is a diversity of clinical genetics tests available to assist patients with making medically informed decisions about family planning and health, including assistance with *in vitro* fertilization (IVF) procedures and embryo genetic screening. To ensure accuracy, it is highly important that all clinical laboratories are continually regulated. The Clinical Laboratory Improvement Amendments (CLIA) are United States federal standards that all human laboratory testing clinics must follow. A major benefit provided by some clinical genetic testing companies is access to genetic counselors, who have specialized education and training in medical genetics and counseling. Both partners are usually tested to see if there is a risk for passing on a disease to a child. Counselors use their skillset to aid patients and doctors with risk assessment for genetic diseases and interpretation of genetic testing results. Genetic counselors also guide and support patients when making impactful medical decisions.

Direct-to-Consumer (DTC) Genetic Testing

People with this result have a slightly increased risk of developing celiac disease. Lifestyle and other factors can also affect your risk.
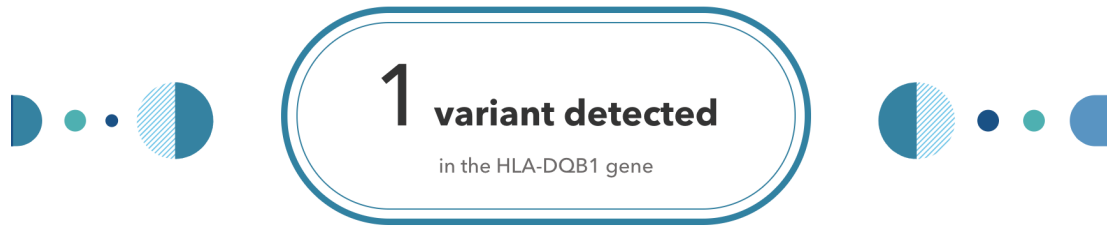

1 variant detected

in the HLA-DQB1 gene

Figure 3.44 A positive result for a genetic allele associated with an increased risk for celiac disease.

Genetic testing that is performed without the guidance of medical professionals is called direct-to-consumer (DTC) genetic testing. Companies that sell affordable genome sequencing products to the public continue to increase in number and popularity. These companies have marketing campaigns typically based on the notion of "personal empowerment," which can be achieved by "knowing more about your DNA." For example, if you are identified as having a slightly increased risk for developing celiac disease (Figure 3.44), then you may be motivated to modify your dietary consumption by removing gluten from your diet. Another scenario is that you could test positive for a known pathogenic *BRCA1* or *BRCA2* allele. In this case, you may want to follow up with additional testing from a medical facility, which could lead to life-altering decisions. DNA sequencing products for entertainment purposes are also available. For example, by having your "Vinome" analyzed, you can discover if you are more predisposed to liking Pinots as your favorite wine. Additionally, an individual and their partner can be genotyped to predict what physical characteristics their baby might inherit.

DTC testing typically lacks genetic counselor services and regulations are not as strict. This has led to some controversies including company genetic products that provide health information. The company 23andMe was the first on the market to offer DTC health testing, and in 2013, the U.S. Food and Drug Administration (FDA) intervened. 23andMe worked toward complying with FDA regulations and then gained approval to offer testing on a few medically related genes. In 2017, 23andMe offered a "Late-Onset Alzheimer's Disease" genetic risk report. Such offerings have been criticized because customers could receive results they may not fully be able to interpret. In turn, this could increase the stress of participants (sometimes called the "burden of knowing") and could also lead to unnecessary medical intervention. In order to address this issue, 23andMe now provides disclaimers and also interactive learning modules that customers must complete if they wish to view certain genotyping results. However, individuals who tested positive for a disease-causing allele have also been able to successfully seek medical help. The potential for harm and the proposed benefits of DTC testing continue to be a topic of debate and investigation.

Ancestry percentage tests are also widely popular (Figure 3.45). Customers are genotyped and their alleles are assigned to different groups from around the world (Chapter 4 will discuss human biological variation in further detail). However, the scientific significance and potential harm of ancestry percentage tests have been called into question. For example, most alleles tested are not exclusive to one population, and populations may be defined differently depending on the testing companies. If an allele is assigned to the "Irish" population, there is a good chance that the allele may have evolved in a different cultural group or region that pre-dates the formation of the country Ireland. In other words, genetic variation often pre-dates the origins the population and geographical names of the region used by genetic testing companies. Another critique is that someone's identity need not include biological relationships. Individuals also have the option to find and connect online with individuals with whom they share portions of their genome, which has resulted in both positive and negative outcomes. Another interesting consideration is that law enforcement is currently developing forensic techniques that involve mining DTC genomic databases for the purpose of identifying suspects linked to crimes. Regardless of these various considerations, there are now millions of individuals worldwide who have "unlocked the secrets" of their DNA, and the multi-billion dollar genomics market only continues to grow.

As you have seen in this chapter, DNA provides instructions to our cells, which results in the creation and regulation of proteins. Understanding these fundamental mechanisms is important to being able to understand how the evolutionary process works (see Chapter 4) and how humans vary from one another (see Chapters 13 and 14). It is also the advancement in genetic technologies—including ancient DNA studies, genomics, and epigenetics—that has led to new anthropological understandings about our biological relationships to other living (extant) and extinct primates. Many of these genetic discoveries will be covered in the chapters to come.

European	91.6%
● British & Irish	32.9%
United Kingdom	
● Scandinavian	5.9%
● Iberian	4.3%
● French & German	1.6%
Netherlands	
● Ashkenazi Jewish	0.5%
● Broadly Northwestern European	34.6%
● Broadly Southern European	6.0%
● Broadly European	5.8%
East Asian & Native American	**7.8%**
● Native American	6.4%
Mexico	
We predict you had ancestors that lived in Mexico within the last 200 years.	
● Broadly East Asian	0.1%
● Broadly East Asian & Native American	1.4%
South Asian	**0.2%**
● Broadly South Asian	0.2%
Sub-Saharan African	**0.1%**
● West African	0.1%
Unassigned	**0.4%**

Figure 3.45 An example of ancestry percentage results provided to customers.

Review Questions

- What is the purpose of DNA replication? Explain in a few sentences what happens during DNA replication. When do DNA mutations happen? And how does this create phenotypic variation (i.e., different phenotypes of the same physical trait)?
- Using your own words, what are homologous chromosomes and sister chromatids? What are the key differences between mitosis and meiosis?
- Determine if the pedigree diagram below represents an autosomal dominant, autosomal recessive, or X-linked recessive pattern of inheritance. You should write the genotype (i.e., AA, Aa, or aa) above each square to help you (note: there may sometimes be two possible answers for a square's genotype). Please also explain why you concluded that particular pattern of inheritance.

Figure 3.46

- Use base pairing rules to transcribe the following DNA template sequence into mRNA: **GTAAAGGTGCTGGCCATC**. Next, use the protein codon table (Figure 3.25) to translate the sequence. In regard to transcription, explain what the significance is of the first and last codon/protein in the sequence.
- In your opinion, what do you think the benefits are of direct-to-consumer (DTC) genetic testing? What are the drawbacks and/or greater ethical concerns? Do you think benefits outweigh concerns?
- Imagine that you submit your DNA sample to a genetic testing company and among the various diseases for which they test, there is an allele that is associated with late-onset Alzheimer's disease. You have the option to view your Alzheimer's result or to not view your result. What do you do and why?

Key Terms

Adenosine triphosphate (ATP): A high-energy compound produced by mitochondria that powers cellular processes.

Allele: A non-identical DNA sequence found in the same gene location on a homologous chromosome, or gene copy, that codes for the same trait but produces a different phenotype.

Amino acids: Organic molecules that are the building blocks of protein. Each of the 20 different amino acids have their own unique chemical property. Amino acids are also chained together to form proteins.

Ancient (aDNA): DNA that is isolated from organic remains often dating from hundreds to thousands of years ago. Also, aDNA is typically degraded (i.e., damaged) due to exposure to the elements such as heat, acidity, and humidity.

Aneuploid: A cell with an unexpected amount of chromosomes. The loss or gain of chromosomes can occur during mitotic or meiotic division.

Antibodies: Immune-related proteins that can detect and bind to foreign substances in the blood such as pathogens.

Apoptosis: A series of molecular steps that is activated leading to cell death. Apoptosis can be activated when a cell fails checkpoints during the cell cycle; however, cancer cells have the ability to avoid apoptosis.

Autosomal: Refers to a pattern of inheritance where an allele is located on an autosome.

Base pairs: Chemical bonding between nucleotides, like adenine (A) and thymine (T) or cytosine (C) and guanine (G) in DNA; or (A) and uracil (U) in RNA

Carbohydrate: Molecules composed of carbon and hydrogen atoms that can be broken down to supply energy.

Carrier: An individual who has a heterozygous genotype that is typically associated with a disease.

Cell cycle: A cycle the cell undergoes with checkpoints between phases to ensure that DNA replication and cell division occur properly.

Cell surface antigen: A protein that is found on a red blood cell's surface.

Centromere: A structural feature that is defined as the "center" of a chromosome and which creates two different arm lengths. Term also refers to the region of attachment for microtubules during mitosis and meiosis.

Chromatin: DNA wrapped around histone complexes. During cell division, chromatin becomes a condensed chromosome.

Chromosome: DNA molecule that is wrapped around protein complexes, including histones.

Codominance: The effects of both alleles in a genotype can be seen in the phenotype.

Codons: A sequence that comprises three DNA nucleotides that together code for a protein.

Complex diseases: A category of diseases that are polygenic and are also influenced by environment and lifestyle factors.

Cytoplasm: The "jelly-like" matrix inside of the cell that contains many organelles and other cellular molecules.

Deleterious: A mutation that increases an organism's susceptibility to disease.

Deoxyribonucleic acid (DNA): A molecule that carries the hereditary information passed down from parents to offspring.

DNA can be described as a "double helix'" shape. It includes two chains of nucleotides held together by hydrogen bonds with a sugar-phosphate backbone.

Diploid: Refers to an organism or cell with two sets of chromosomes.

DNA methylation: Methyl groups bind DNA, which modifies the transcriptional activity of a gene by turning it "on" or "off."

DNA polymerase: Enzyme that adds nucleotides to existing nucleic acid strands during DNA replication. These enzymes can be distinguished by their processivity (e.g., DNA replication).

DNA replication: Cellular process in which DNA is copied and doubled.

DNA sequence: The order of nucleotide bases. A DNA sequence can be short, long, or representative of entire chromosomes or organismal genomes.

Dominant: Refers to an allele for which one copy is sufficient to be visible in the phenotype.

Elongation: The assembly of new DNA from template strands with the help of DNA polymerases.

Enzymes: Proteins responsible for catalyzing (accelerating) various biochemical reactions in cells.

Epigenetic profile: The methylation pattern throughout a genome—that is, which genes (and other genomic sites) are methylated and unmethylated.

Epigenetics: Changes in gene expression that do not result in a change of the underlying DNA sequence. These changes typically involve DNA methylation and histone modifications. These changes are reversible and can also be inherited by the next generation.

Euchromatin: Loosely coiled chromosomes found within the nucleus that is accessible for regulatory processing of DNA.

Eukaryote: Single-celled or multicelled organism characterized by a distinct nucleus, with each organelle surrounded by its own membrane.

Exon: Protein-coding segment of a gene.

Gametes: Haploid cells referred to as an egg and sperm that will fuse together during sexual reproduction to form a diploid organism.

Gene: Segment of DNA that contains protein-coding information and various regulatory (e.g., promoter) and noncoding (e.g., introns) regions.

Genetic recombination: A cellular process that occurs during meiosis I in which homologous chromosomes pair up and sister chromatids on different chromosomes physically swap genetic information.

Genome: All the genetic information of an organism.

Genotype: The combination of two alleles that code for or are associated with the same gene.

Genotyping: A molecular procedure that is performed to test for the presence of certain alleles or to discover new ones.

Haploid: Cell or organism with one set of chromosomes (n = 23).

Helicase: A protein that breaks the hydrogen bonds that hold double-stranded DNA together.

Heterozygous: Genotype that consists of two different alleles.

Histones: Protein that DNA wraps around to assist with DNA organization within the nucleus.

Homologous chromosomes: A matching pair of chromosomes wherein one chromosome is maternally inherited and the other is paternally inherited.

Homozygous: Genotype that consists of two identical alleles.

Incomplete dominance: Heterozygous genotype that produces a phenotype that is a blend of both alleles.

Initiation: The recruitment of proteins to separate DNA strands and begin DNA replication.

Interphase: Preparatory period of the cell cycle when increased metabolic demand allows for DNA replication and doubling of the cell prior to cell division.

Introns: Segment of DNA that does not code for proteins.

Karyotyping: The microscopic procedure where the number of chromosomes in a cell is determined.

Lagging strand: DNA template strand that is opposite to the leading strand. Therefore, DNA replication proceeds discontinuously, generating Okazaki fragments.

Leading strand: DNA template strand in which replication proceeds continuously.

Lipids: Fatty acid molecules that serves various purposes in the cell, including energy storage, cell signaling, and structure.

Meiosis: The process that gametes undergo to divide. The end of meiosis results in four haploid daughter cells.

Mendelian genetics: A classification given to phenotypic traits that are controlled by a single gene.

Messenger RNA (mRNA): RNA molecule that is transcribed from DNA. Its tri-nucleotide codons are "read" by a ribosome to build a protein.

Microarray technology: A genotyping procedure that utilizes a microarray chip, which is a collection of thousands of short nucleotide sequences attached to a solid surface that can probe genomic DNA.

Microbiome: The collective genomes of the community of microorganisms that humans have living inside of their body.

Mitochondrial DNA (mtDNA): Circular DNA segment found in mitochondria that is inherited maternally.

Mitochondrion: Specialized cellular organelle that is the site for energy production. It also has its own genome (mtDNA).

Mitosis: The process that somatic cells undergo to divide. The end of mitosis results in two diploid daughter cells.

Mutation: A nucleotide sequence variation from the template DNA strand that can occur during replication. Mutations can also happen during recombination.

Next-generation sequencing: A genotyping technology that involves producing millions of nucleotide sequences (from a single DNA sample) that are then read with a sequencing machine. It can be used for analyzing entire genomes or specific regions and requires extensive program-based applications.

Nuclear envelope: A double-layered membrane that encircles the nucleus.

Nucleic acid: A complex structure (like DNA or RNA) that carries genetic information about a living organism.

Nucleotide: The basic structural component of nucleic acids, which includes DNA (A, T, C, and G) and RNA (A, U, C, and G).

Nucleus: Double-membrane cellular organelle that helps protect DNA and regulation of nuclear activities.

Okazaki fragment: Short DNA strands derived from DNA replication on the lagging strand. They were discovered by Reiji and Tsuneko Okazaki in the 1960s.

Organelle: A structure within a cell that performs specialized tasks that are essential for the cell. There are different types of organelles with their own function.

Pathogenic: A genetic mutation (i.e., allele) that has a harmful phenotypic disease-causing effect.

Penetrance: The proportion of how often the possession of an allele results in an expected phenotype. Some alleles are more penetrant than others.

Phenotype: The physical appearance of a given trait.

Phospholipid bilayer: Two layers of lipids that form a barrier due to the properties of a hydrophilic (water-loving) head and a hydrophobic (water-repelling) tail.

Polygenic trait: A phenotype that is controlled by two or more genes.

Polymerase chain reaction (PCR): A molecular biology procedure that can make copies of genomic DNA segments. A small amount of DNA is used as a starting template and is then used to make millions of copies.

Primer: A primer is a small sequence of nucleotides that bind DNA to start the process of DNA replication or PCR.

Prokaryote: A single-celled organism characterized by lack of a nucleus and membrane-enclosed organelles.

Promoter: The region of a gene that initiates transcription. Transcription factors can bind and DNA methylation may occur at a promoter site, which can modify the transcriptional activities of a gene.

Protein: Chain of amino acids that fold into a three dimensional structure that allow a cell to function in a variety of ways.

Protein synthesis: A multi-step process by which amino acids are strung together by RNA machinery read from a DNA template.

Recessive: Refers to an allele whose effect is not normally seen unless two copies are present in an individual's genotype.

Ribonucleic acid (RNA): Single-stranded nucleic acid molecule.There are different RNAs found within cells and they perform a variety of functions, such as cell signaling and involvement in protein synthesis.

Ribosomal RNA (rRNA): A ribosome-bound molecule that is used to correctly assemble amino acids into proteins.

Ribosome: An organelle in the cell found in the cytoplasm or endoplasmic reticulum. It is responsible for reading mRNA and protein assemblage.

RNA polymerase: An enzyme that catalyzes the process of making RNA from a DNA template.

Sanger-sequencing: A process that involves the usage of fluorescently labeled nucleotides to visualize DNA (PCR fragments) at the nucleotide level.

Semi-conservative replication: DNA replication in which new DNA is replicated from an existing DNA template strand.

Sequencing: A molecular laboratory procedure that produces the order of nucleotide bases (i.e., sequences).

Sister chromatids: During DNA replication, sister chromatids are produced on the chromosome. In cell division, sister chromatids are pulled apart so that two cells can be formed. In meiosis, sister chromatids are also the sites of genetic recombination.

Somatic cells: Diploid cells that comprise body tissues and undergo mitosis for maintenance and repair of tissues.

Splicing: The process by which mature mRNAs are produced. Introns are removed (spliced) and exons are joined together.

Sugar phosphate backbone: A biochemical structural component of DNA. The "backbone" consists of deoxyribose sugars and phosphate molecules.

Telomere: A compound structure located at the ends of chromosomes to help protect the chromosomes from degradation after every round of cell division.

Termination: The halt of DNA replication activity that occurs when a DNA sequence "stop" codon is encountered.

Tissue: A cluster of cells that are morphologically similar and perform the same task.

Transcription: The process by which DNA nucleotides (within a gene) are copied, which results in a messenger RNA molecule.

Transcription factors: Proteins that bind to regulatory regions of genes (e.g., promoter) and increase or decrease the amount of transcriptional activity of a gene, including turning them "on" or "off."

Transfer RNA (tRNA): RNA molecule involved in translation. Transfer RNA transports amino acids from the cell's cytoplasm to a ribosome.

Translation: The process by which messenger RNA codons are read and amino acids are "chained together" to form proteins.

X-linked: Refers to a pattern of inheritance where the allele is located on the X or Y chromosome.

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Hayley Mann received her bachelor's degree in Genetics from the University of California, Davis, and continued her graduate studies in Biological and Molecular Anthropology at the California State University, Sacramento. She is currently a Ph.D. candidate at Binghamton University, where her dissertation focus is on studying genetic variation of Pacific Islanders (Republic of Vanuatu) and also changes in health as the result of colonization. Hayley also works in clinical genomics and specializes in various DNA-sequencing methodologies.

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Xazmin Lowman received her bachelor's degree in Physiology from the University of Arizona. She pursued her doctorate in cancer biology at the University of Minnesota, where she studied how blood cancers evade cell death. Currently, her scientific interests have led to a postdoctoral fellowship at the University of California, Irvine, where she studies how solid tumors adapt to metabolic stress. Beyond figuring out the mechanisms that drive cancer, she enjoys traveling to learn of other cultures and share her own upbringing on the Navajo reservation.

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Malaina Gaddis studied biology at Brigham Young University in Utah and then earned a Ph.D. in genetics and molecular and cellular biology at the University of Southern California. During her Ph.D. studies, she investigated small molecule inhibitors that alter epigenetic modifications and gene expression in cancer cells. Following her Ph.D., she focused on the business side of the biotech industry by completing a master's degree in bioscience management at the Keck Graduate Institute. Malaina is especially interested in using genomics to further genetic testing and personalized treatment and currently works as a genome variation scientist.

Malaina Gaddis

For Further Exploration

Websites

National Human Genome Research Institute https://www.genome.gov/

Genetics Home Reference https://ghr.nlm.nih.gov/

Genetics Generation http://knowgenetics.org/

yourgenome https://www.yourgenome.org/

Cardiovascular Disease: Genes are Important, but Health-Related Behaviors and Lifestyle Choices Can Make or Break Your Health http://ehrweb.aaas.org/ehr/books/3_howard.html

Gene Sequencing Speeds Diagnosis of Deadly Newborn Diseases http://www.pbs.org/wgbh/nova/next/body/newborn-gene-sequencing/

Carl Zimmer's Game of Genomes https://www.statnews.com/feature/game-of-genomes/season-one/

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