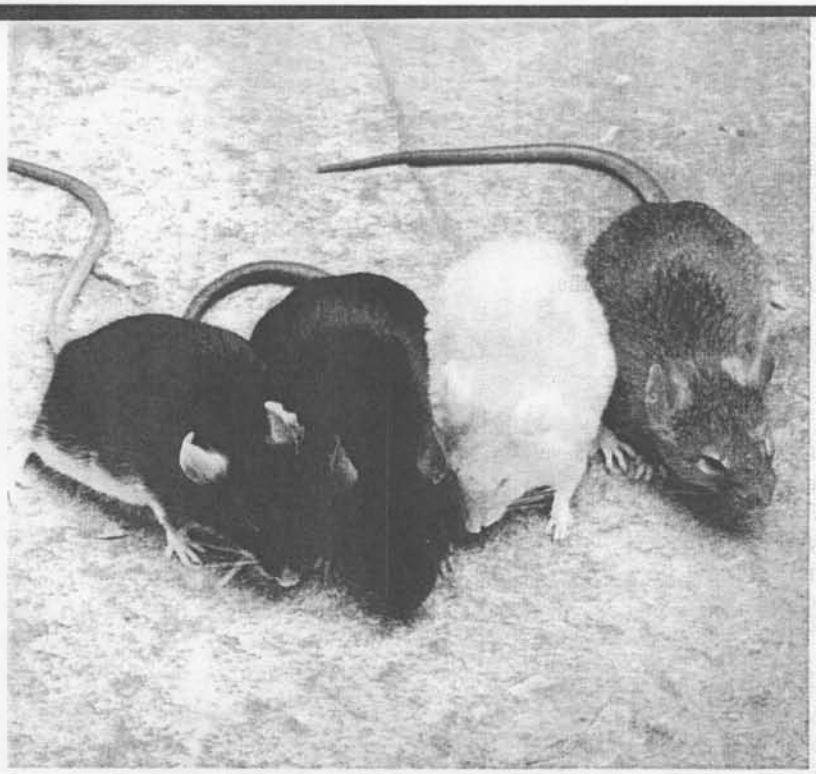

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Concepts of Genetics

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Charles Darwin and Evolution

With the preceding information as background, we conclude our coverage of the historical context of genetics with a brief discussion of the work of Charles Darwin, who in 1859, published the book-length statement of his evolutionary theory, *On the Origin of Species*. Darwin's many geological, geographical, and biological observations convinced him that existing species arose by descent with modification from other ancestral species. Greatly influenced by his now-famous voyage on the H.M.S. *Beagle* (1831–1836), Darwin's thinking culminated in his formulation of the **theory of natural selection**, a theory that attempts to explain the causes of evolutionary change.

Formulated and proposed at the same time, but independently by Alfred Russel Wallace, natural selection is based on the observation that populations tend to consist of more offspring than the environment can support, leading to a struggle for survival among them. Those organisms with heritable traits that allow them to adapt to their environment are better able to survive and reproduce than those with less-adaptive traits. Over a long period of time, slight, but advantageous variations will accumulate. If a population bearing these inherited variations becomes reproductively isolated, a new species may result.

The primary gap in Darwin's theory was a lack of understanding of the genetic basis of variation and inheritance, a gap that left it open to reasonable criticism well into the 20th century. Aware of this weakness in his theory of evolution, in 1868, Darwin published a second book, *Variations in Animals and Plants under Domestication*, in which he attempted to provide a more definitive explanation of how heritable variation arises gradually over time. Two of his major ideas, pangenesis and the inheritance of acquired characteristics, have their roots in the theories involving "humors," as put forward by Hippocrates and Aristotle.

In his provisional hypothesis of **pangenesis**, Darwin coined the term *gemmules* (rather than humors) to describe the physical units representing each body part that were gathered by the blood into the semen. Darwin felt that these gemmules determined the nature or form of each body part. He further believed that gemmules could respond in an adaptive way to an individual's external environment. Once altered, such changes would be passed onto offspring, allowing for the inheritance of acquired characteristics. Jean-Baptiste Lamarck had previously formalized this idea in his 1809 treatise, *Philosophie Zoologique*. Lamarck's theory, which became known as the **doctrine of use and disuse**, proposed that organisms acquire or lose characteristics that then become heritable. Even though Darwin never understood the basis for inherited variation, his ideas concerning evolution may be the most influential theory ever put forward in the history of biology. He was able to distill his extensive observations and synthesize his ideas into a cohesive hypothesis describing the origin of diversity of organisms populating Earth.

As Darwin's work ensued, Gregor Johann Mendel (Figure 1–4) conducted his experiments between 1856 and 1863 and published his classic paper in 1866. In it, Mendel demonstrated a number of statistical patterns underlying inheritance and developed a theory involving hereditary factors in the germ cells to explain these patterns. His research was virtually ignored until it was partially duplicated and then cited by Carl Correns, Hugo de Vries, and Eric Von Tschermak around 1900, after which it was championed by William Bateson.

FIGURE 1–4 Gregor Johann Mendel, who in 1866 put forward the major postulates of transmission genetics as a result of experiments with the garden pea. (*Archiv/Photo Researchers, Inc.*)

By the early part of the 20th century, chromosomes were discovered and support for the epigenetic interpretation of development had grown considerably. It gradually became clear that heredity and development were dependent on "information" contained in chromosomes, which were contributed by gametes to each individual. The "gap" in Darwin's theory had narrowed considerably.

1.2 Genes and Chromosomes Are the Fundamental Units of Genetics

In ensuing chapters, we will consider in detail the experiments of Gregor Mendel and the subsequent research that led to a clear understanding of transmission genetics. Together, this body of work served as the basis of the **chromosomal theory of inheritance**, which states that inherited traits are controlled by genes that reside in chromosomes, which are faithfully transmitted through gametes to future generations. It is useful here to consider some fundamental

issues underlying this theory. These issues provide a brief overview of the discipline of genetics and of genes and chromosomes. We shall set forth this overview by asking and answering a series of questions. You may wish to write or think through a response before reading our answer to each question. Throughout the text, they will be expanded on as more detailed information is presented.

What does "genetics" mean? **Genetics** is the branch of biology concerned with heredity and variation. This discipline involves the study of cells, individuals, their offspring, and the populations within which organisms live. Geneticists investigate all forms of inherited variation, as well as the molecular basis underlying such characteristics.

What is the center of heredity in a cell? In eukaryotic organisms, the **nucleus** contains the genetic material in the form of genes present on chromosomes. In prokaryotes, such as bacteria, the genetic material exists in an unenclosed, but recognizable area of the cell called the **nucleoid region** (Figure 1–5). In viruses, which are not true cells, the genetic material is ensheathed in the protein coat, together constituting the viral head or capsid.

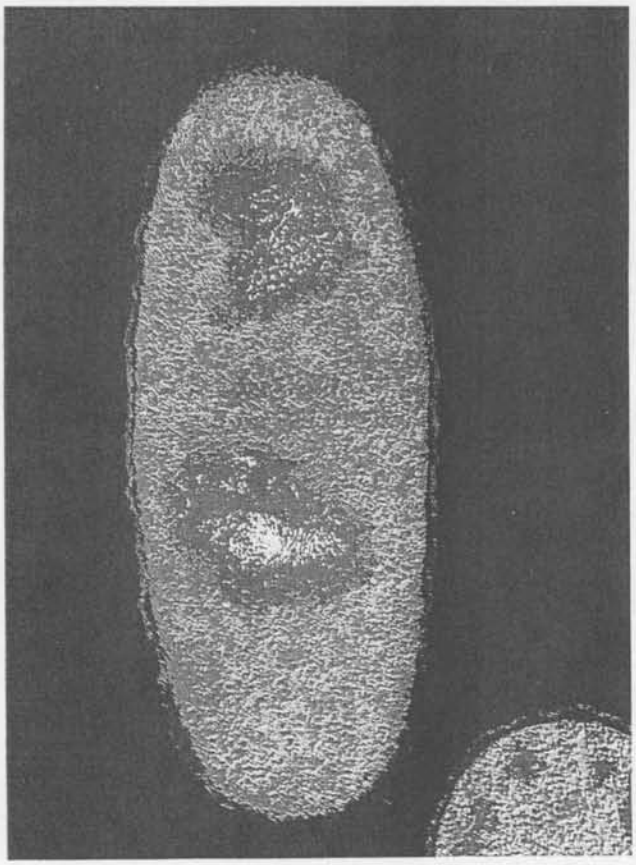

FIGURE 1–5 Enhanced electron micrograph of *Escherichia coli*, demonstrating the nucleoid regions (shown in blue). The bacterium has replicated its DNA and is about to begin cell division.

What is a gene? In simplest terms, the **gene** is the functional unit of heredity residing at a specific point along a chromosome. Conceptually, a gene is an informational storage unit capable of undergoing replication, expression, and mutation. As investigations have progressed, the gene has been found to be a very complex element. Biochemically, a gene is a length of DNA that specifies a product or action.

What is a chromosome? In viruses and bacteria, which have only a single **chromosome**, it is most simply thought of as a long, usually circular DNA molecule organized into genes. Most eukaryotes have many chromosomes (Figure 1–6) that are composed of linear DNA molecules intimately associated with proteins. In addition, eukaryotic chromosomes contain many nongenic regions. It is not yet clear what role, if any, is played by many of these regions. Our knowledge of the chromosome, like that of the gene, is continually expanding.

When and how can chromosomes be visualized? If the chromosomes are released from the viral head or the bacterial cell, they can be visualized under the electron microscope. In eukaryotes, chromosomes are most easily visualized under the light microscope when they are undergoing **mitosis** or **meiosis**. In these division processes, the material constituting chromosomes is tightly coiled and condensed, giving rise to the characteristic image of chromosomes. Following division, this material, called chromatin, uncoils during interphase, where it can be studied under the electron microscope.

How many chromosomes does an organism have? Although there are exceptions, members of most eukaryotic species have a specific number of chromosomes, called the **diploid number (*2n*)**, in each somatic cell. For example, humans have a diploid number of 46 (Figure 1–7). Upon close analysis, these chromosomes are found to occur in pairs, each member of which shares a nearly identical appearance when

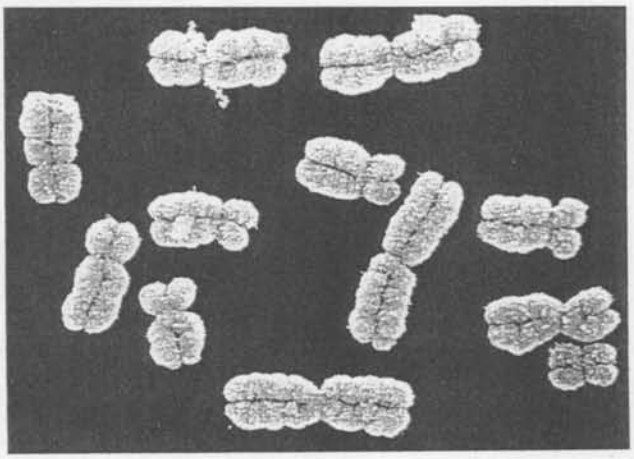

FIGURE 1–6 Human mitotic chromosomes visualized unde the scanning electron microscope.

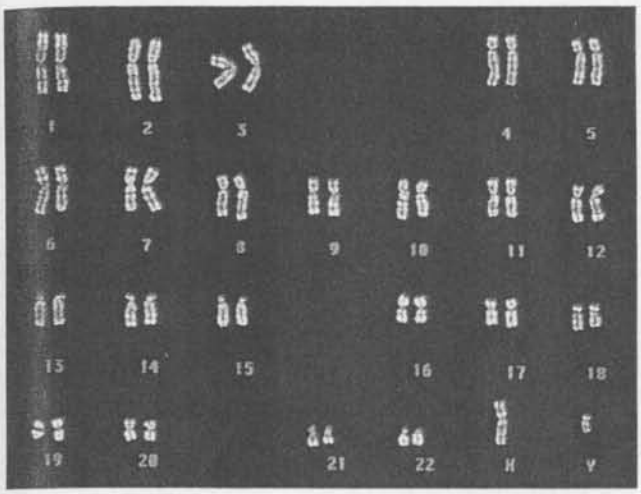

FIGURE 1–7 The human male karyotype. (*Sovereign/Phototake*)

visible during cell division. Called **homologous chromosomes**, the members of each pair are identical in their length and in the location of the **centromere**, the point of spindle-fiber attachment during division. They also contain the same sequence of gene sites, or **loci**, and pair with one another during gamete formation (the process of meiosis).

The number of different *types* of chromosomes in any diploid species is equal to half the diploid number and is called the **haploid number** (***n***). Some organisms, such as yeast, are haploid during most of their life cycle and contain only one "set" of chromosomes. Other organisms, especially many plant species, are sometimes characterized by more than two sets of chromosomes and are said to be **polyploid**.

What is accomplished during the processes of mitosis and meiosis? Mitosis is the process by which the genetic material of eukaryotic cells is duplicated and distributed during cell division. Meiosis is the process whereby cell division produces gametes in animals and spores in most plants, which serve as the basis for transmission of the genetic information between generations. While mitosis occurs in somatic tissue and yields two progeny cells with an amount of genetic material identical to that of the progenitor cell, meiosis creates cells with precisely one-half of the genetic material. Each gamete receives one member of each homologous pair of chromosomes and is haploid. This reduction in chromosome number is essential if the offspring arising from two gametes are to maintain a constant number of chromosomes characteristic of their parents and other members of the species.

What are the sources of genetic variation? Classically, there are two sources of genetic variation, **chromosomal mutations** and **gene mutations**. The former, also called chromosomal aberrations, are the more substantial and include duplication, deletion, or rearrangement of chromosome segments. Gene mutations result from smaller changes in the stored chemical information in DNA, making up a part of the organism's **genotype**. Such a change may include substitution, duplication, or deletion of nucleotides, which compose this chemical information. Alternative forms of the gene, which result from mutation, are called **alleles**. Genetic variation frequently, but not always, results in a change in some characteristic of an organism, referred to as its **phenotype**.

1.3 Nucleic Acids and Proteins Serve as the Molecular Basis of Genetics

It will also be useful as we proceed through the first part of the text, which focuses on transmission genetics, to grasp the most basic tenets that underlie the molecular basis of genetic function. This will provide you with a foundation for a more comprehensive understanding of Mendel's work as well as that which followed it. As you will see, it is indeed remarkable that so much was learned without the knowledge of molecular genetics, which today, we take for granted.

The Trinity of Molecular Genetics

The way in which genes control inherited variation is best understood in terms of three molecules, sometimes referred to as the trinity of molecular genetics: **DNA**, **RNA**, and **protein**. The nucleic acid DNA (deoxyribonucleic acid) serves as the genetic material in all living organisms as well as in most viruses. DNA is organized into genes and stores genetic information. As part of the chromosomes, the information contained in genes can be transmitted faithfully by parents through gametes to their offspring. For the gene's DNA to subsequently influence an inherited trait, the stored genetic information in the DNA in most cases is first transferred to a closely related nucleic acid, RNA (ribonucleic acid). In eukaryotic organisms, RNA most often carries the genetic information out of the nucleus, where chromosomes reside, into the cytoplasm of the cell. There, the information in RNA is translated into proteins, which serve as the end products of most all genes. Ultimately, it is the diverse functions of proteins that determine the biochemical identity of cells and strongly influence the expression of inherited traits. The process of storage and expression of genetic information, upon which life on earth is based, is often summarized as

DNA makes RNA, which makes proteins

The process of transferring information from DNA to RNA is called **transcription**. The subsequent conversion of the genetic information contained in RNA into a protein is called **translation**.

The Structure of Nucleic Acids

Two depictions of the structure and components of DNA are shown in Figure 1–8. The molecule exists in cells as a long, coiled ladderlike structure described as a double helix. Each strand of the helix consists of a linear polymer made up of

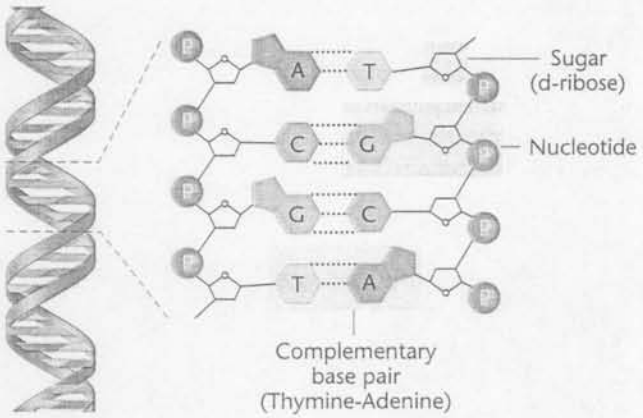

FIGURE 1–8 Summary of the structure of DNA, illustrating on the left, the nature of the double helix and on the right, the chemical components making up both strands.

genetic building blocks called **nucleotides**, of which there are four types. Nucleotides vary, depending upon which of four nitrogenous bases is part of the molecule—A (adenine), G (guanine), T (thymine), or C (cytosine). These comprise the genetic alphabet, which in various combinations, ultimately specify the components of proteins. One of the great discoveries of the 20th century was made in 1953 by James Watson and Francis Crick, who established that the two strands of their proposed double helix are exact complements of one another, such that the rungs of the ladder always consist of either A═T or G≡C base pairs. As we shall see when we pursue molecular genetics in depth later in the text, this **complementarity** between adenine and thymine nitrogenous base pairs and between guanine and cytosine nitrogenous base pairs, attracted to one another by **hydrogen bonds**, is critical to genetic function. Complementarity serves as the basis for both the replication of DNA and for the transcription of DNA into RNA. During both processes, under the direction of the appropriate enzyme, DNA strands serve as templates for the synthesis of the complementary molecule.

RNA is chemically very similar to DNA. However, it demonstrates a small variation in its component sugar (ribose vs. deoxyribose), and it contains the nitrogenous base uracil in place of thymine. Additionally, in contrast to the double helix of DNA, RNA is generally single stranded. Importantly, it can form complementary structures with a strand of DNA. In such cases, uracil base pairs with adenine. As noted earlier, this complementarity is the basis for *transcription* of the chemical information in DNA into RNA, and the process is illustrated at the top of Figure 1–9

The Genetic Code and RNA Triplets

Once an RNA molecule complementary to one strand of a gene's DNA is transcribed, the RNA behaves as a messenger that directs the synthesis of proteins. This is accomplished during the association of this RNA molecule (called messenger RNA, or mRNA, for short) with a complex cellular structure called the **ribosome**. The process by which proteins are synthesized under the direction of mRNA, as mentioned earlier, is called *translation* (Figure 1–9). Ribosomes serve as nonspecific workbenches for protein synthesis.Proteins, as the end product of genes, are linear polymers made up of amino acids, of which there are 20 different types in living organisms. A major question is how information present in mRNA is encoded to direct the insertion of specific amino acids into protein chains as they are synthesized. The answer is now quite clear. The genetic code consists of a linear series of triplet nucleotides present in mRNA molecules. Each triplet reflects, through complementarity, the information stored in DNA and specifies the insertion of a specific amino acid as the mRNA is translated into the growing protein chain. A key discovery in how this is accomplished involved the identification of a series of adapter molecules called **transfer RNA (tRNA)**. Within the ribosome, these adapt the information encoded in the mRNA triplets to the specific amino acid during translation.

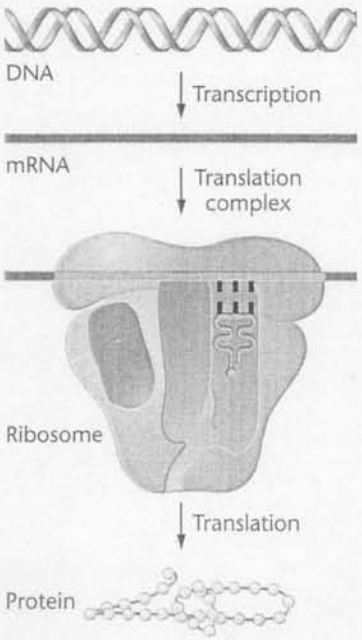

FIGURE 1–9 Depiction of genetic expression involving transcription of DNA into mRNA; and the translation of mRNA on a ribosome into a protein.

As the preceding discussion documents, DNA makes RNA, which most often makes protein. These processes occur with great specificity. Using an alphabet of only four letters (A, T, C, and G), a language exists that directs the synthesis of highly specific proteins that collectively serve as the basis for all biological function.

Proteins and Biological Function

As we have mentioned, proteins are the end products of genetic expression. They are the molecules responsible for imparting the properties that we attribute to the living process. The potential for achieving the diverse nature of biological function rests with the fact that the alphabet used to construct proteins consists of 20 letters (amino acids), which combine to create words that can be thousands of letters long

(Figure 1-10). If we consider a protein chain that is just 100 amino acids in length, and at each position there can be any one of 20 amino acids, then the number of different molecules, each with a unique sequence, is equal to

$$20^{100}$$

Since 20^{10} exceeds 5×10^{12}, or over 5 trillion, imagine how large 20^{100} is! Obviously, evolution has seized on a class of molecules that have the potential for enormous structural diversity as they serve as the mainstay in biological systems.

The main category of proteins is that which includes **enzymes**. These molecules serve as biological catalysts, essentially allowing biochemical reactions to proceed at rates that sustain life under the conditions that exist on earth. For example, by lowering the energy of activation in reactions, metabolism is able to proceed under the direction of enzymes at body temperature (37°C) in humans, where in the absence of enzymes, these chemical reactions would proceed at rates thousands of times more slowly. As a result, enzymes, each under the control of one or more specific genes, are capable of directing both the anabolism (the synthesis) and catabolism (the breakdown) of all organic molecules in the cell, including carbohydrates, lipids, nucleic acids, and proteins themselves.

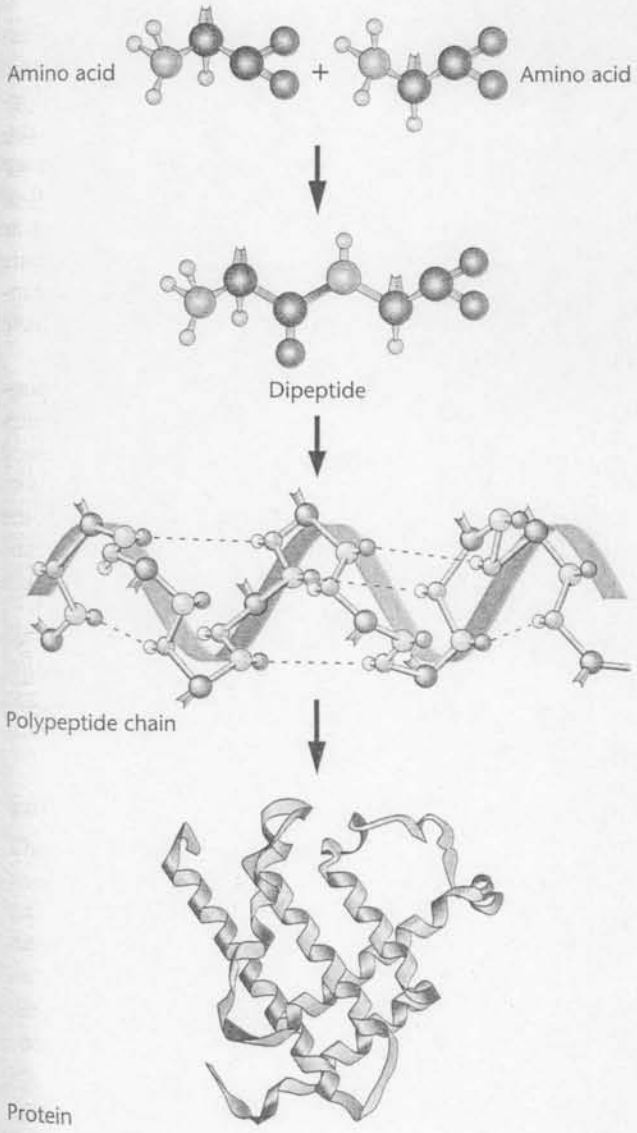

FIGURE 1–10 Depiction of three steps leading to the formation of a protein. Initially, two amino acids are joined to form a dipeptide. As amino acids are added, one by one, a longer polypeptide chain is formed which often coils into a right-handed alpha helical structure. This polypeptide then folds into a three-dimensional conformation specific to the protein's function.

There are countless proteins other than enzymes that are critical components of cells and organisms. These include such diverse examples as **hemoglobin**, the oxygen-binding pigment in red blood cells; **insulin**, the pancreatic hormone; **collagen**, the connective tissue molecule; **keratin**, the structural molecule in hair; **histones**, the proteins integral to chromosome structure in eukaryotes; **actin** and **myosin**, the contractile muscle proteins; and **immunoglobulins**, the antibody molecules of the immune system. Specific proteins are also critical components of all membranes and serve as molecules that regulate genetic expression. The potential for such diverse functions rests with the enormous variation of three-dimensional conformation that may be achieved by proteins. The final conformation of a protein is the direct result of the unique linear sequence of amino acids that constitute the molecule. To come full circle, this sequence is dictated by the stored information in the DNA of a gene that is transferred to RNA, which then directs the synthesis of a protein. DNA makes RNA that then makes protein.

1.4 Genetics Has Been Investigated Using Many Different Approaches

It will be useful in your study of genetics to know something about the various research approaches that have advanced our knowledge of the field. Investigations have involved viruses, bacteria, and a wide variety of plants and animals and have spanned all levels of biological organization, from molecules to populations. Although some overlap exists, most investigations have used one of four basic approaches.

The most classic investigative approach is the study of **transmission genetics**, in which the patterns of inheritance of traits are examined. Experiments are designed so that the transmission of traits from parents to offspring can be analyzed through several generations. Patterns of inheritance are sought that will provide insights into genetic principles. The first significant experimentation of this kind to have a major impact on the understanding of heredity was performed by Gregor Mendel in the middle of the 19th century. The information derived from his work serves today as the foundation of transmission genetics. In human studies, where designed matings are neither possible nor desirable, **pedigree analysis** is often useful. As illustrated in Figure 1-11, patterns of inheritance are traced through as many generations as possible, leading to inferences concerning the mode of inheritance of the trait under investigation.

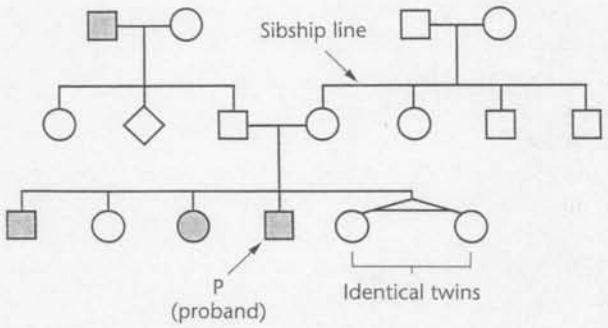

FIGURE 1–11 A representative human pedigree, tracing a genetic characteristic through three generations.

The second approach involves **cytogenetics**—the study of chromosomes. The earliest such studies used light microscopy. The initial discovery of chromosome behavior during mitosis and meiosis, late in the 19th century, was a critical event in the history of genetics, because of the important role these observations played in the rediscovery and acceptance of Mendelian principles. The light microscope continues to be useful in the investigation of chromosome structure and abnormalities and is instrumental in preparing **karyotypes**, which include all of the chromosomes characteristic of any species arranged in a standard sequence. (See the earlier Figure 1–7.) With the advent of electron microscopy, the repertoire of investigative approaches in genetics has grown. In high-resolution microscopy, genetic molecules and their behavior during gene expression can be visualized directly.

The third general approach involves **molecular genetic analysis**, which has had the greatest impact on the recent growth of genetic knowledge. Molecular studies, initiated in the early 1940s, have consistently expanded our knowledge of the role of genetics in life processes. Although experiments initially relied on bacteria and the viruses that infect them, extensive information is now available concerning the nature, expression, replication, and regulation of the genetic information in eukaryotes as well. The precise nucleotide sequence has been determined for many genes cloned in the laboratory. Recombinant DNA studies (Figure 1–12), in which genes from another organism are literally spliced into bacterial or viral DNA and then cloned, serve as the basis of a far-reaching research technology used in molecular genetic investigations. Building on this approach, the new fields of **genomics** and **bioinformatics** now exist whereby the entire genetic makeup of an organism may be cloned, sequenced, and the function of genes explored. Using this new technology, it is now possible to probe gene function in extreme detail. Such molecular and biochemical analysis has created the potential for gene therapy and has profound implications in medicine, agriculture, and bioethics.

One of the most striking achievements in the history of DNA biotechnology occurred in 1996 at the Roslin Institute in Scotland, when the world's most famous lamb, Dolly, was born (Figure 1–13). Representing the first animal ever to be cloned from an adult somatic cell, Dolly was the result of the research of Ian Wilmut, who fused the nucleus of an

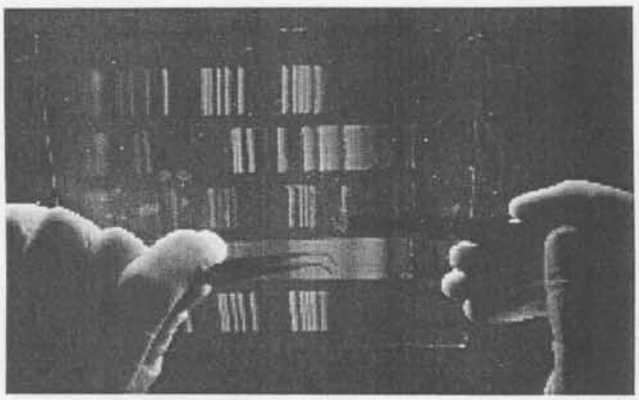

FIGURE 1–12 Visualization of DNA fragments under ultraviolet light. The bands were produced by using recombinant DNA technology. (*Dan McCoy/Rainbow*)

udder cell taken from a six-year-old sheep with an enucleated oocyte of another sheep. Following implantation into a surrogate mother, complete embryonic and fetal development was achieved under the direction of the genetic material of the udder cell. While the implications of this event are profound and raise numerous ethical concerns, the goal of Wilmut's research is to ultimately use cloned animals as models to study human disease and to produce therapeutic drugs beneficial to humans. Since this work, other organisms, including mice and a variety of livestock animals, have been successfully cloned.

The final investigative approach involves the study of **population genetics**. In these investigations, scientists attempt to define how and why certain genetic variation is maintained in populations, while other variation diminishes or is lost with time (Figure 1–14). Such information is critical to the understanding of evolutionary processes. Population genetics also allows us to predict gene frequencies in future generations.

Together, these varied approaches used in investigative genetics have transformed a subject that was only poorly understood in 1900 into one of the most advanced scientific

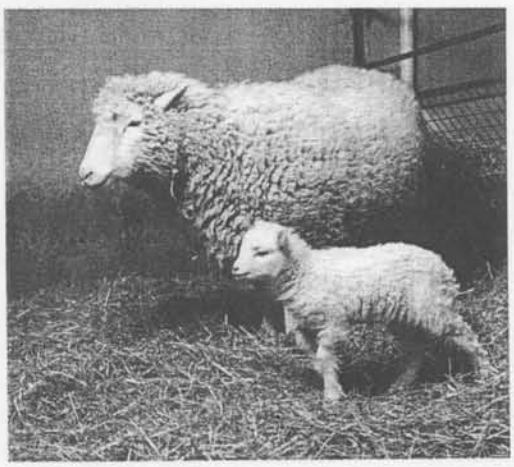

FIGURE 1–13 Dolly, a Finn Dorset sheep cloned from the genetic material of an adult mammary cell, shown next to her first-born lamb, Bonnie. (*Photo courtesy of Roslin Institute*)

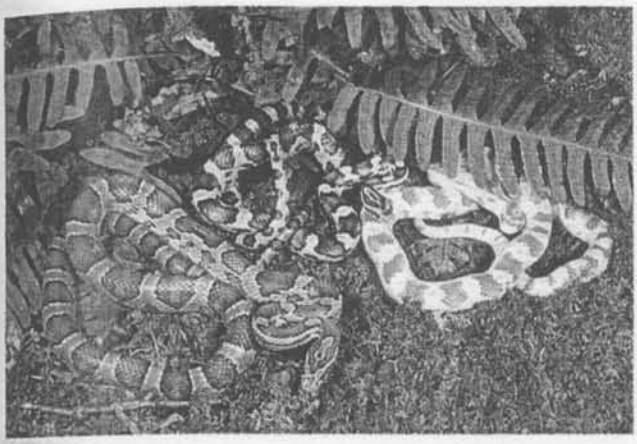

FIGURE 1–14 Genetic variation exhibited in the skin present in populations of corn snakes. The wild type (normal) variety displays orange and black markings. (*Zig Leszczynski/Animals Animals/Earth Scenes*)

disciplines today. As a result, the impact of genetics on society has been, and will continue to be, immense. We shall discuss many examples of the applications of genetics in the following section and throughout the text.

1.5 Genetics Has a Profound Impact on Society

In addition to acquiring information for the sake of extending knowledge in any discipline of science—an experimental approach that is called **basic research**—scientists conduct investigations to solve problems facing society or simply to improve the well-being of members of our society—an approach that is called **applied research**. Together, both types of genetic research have combined to enhance the quality of our existence on this planet and to provide a more thorough understanding of life processes. As we shall see throughout this text, there is very little in our lives that genetics fails to touch.

Eugenics and Euphenics

There is always the danger that scientific findings will be used to formulate policies or actions that are unjust or even tragic. In this section, we review such a case that began near the end of the 19th century. At that time, Darwin's theory of natural selection provided a major influence on some people's thinking concerning the human condition. Our story recounts the initial attempt to apply genetic knowledge directly for the improvement of human existence. Championed in England by Sir Francis Galton, the general approach is called **eugenics**, a term Galton coined in 1883, that is derived from the Greek root meaning "well-born."

Galton, a cousin of Charles Darwin, believed that many human characteristics were inherited and could be subjected to artificial selection if human matings could be controlled. *Positive eugenics* encouraged parents displaying favorable characteristics, (e.g., superior intelligence, intellectual achievement, and artistic talent) to have large families. *Negative eugenics*, on the other hand, attempted to restrict the reproduction of parents displaying unfavorable characteristics (e.g., low intelligence, mental retardation, and criminal behavior).

In the United States, the eugenics movement was a significant social force and led to state and federal laws that required the sterilization of those considered "genetically inferior." Over half of the states passed such laws, commencing in 1907 with Indiana. Sterilization was mandated for "imbeciles, idiots, convicted rapists, and habitual criminals." Not without significant legal controversy, the issue rose to the U.S. Supreme Court, where in the 1927 case of Buck vs. Bell, Justice Oliver Wendel Holmes wrote in favor of upholding these laws:

> It is better for all the world, if instead of waiting to execute degenerate offspring for crime, or to let them starve for their imbecility, society can prevent those who are manifestly unfit from continuing their kind. ... Three generations of imbeciles are enough.*

By 1931, involuntary sterilization also applied to "sexual perverts, drug fiends, drunkards, and epileptics." Often, individuals were just deemed "feeble minded," a phrase applied to countless people displaying a plethora of characteristics or behavior deemed unacceptable. Sterilization programs continued in United States into the 1940s.

Immigration to the United States from certain areas of Europe and from Asia was also restricted to prevent the influx of what were regarded as genetically inferior people. In addition to the violation of individual human rights, such policies were seriously flawed by an inadequate understanding of the genetic basis of various characteristics. The formulation of eugenic policies was premised on the mistaken notions that "superior" and "inferior" traits are totally under genetic control and that genes deemed unfavorable could be removed from a population by selecting against (sterilizing) individuals expressing those traits. The potential impact of the environment and the genetic theory underlying population genetics were largely ignored as eugenic policies were developed.

In Nazi Germany in the 1930s, the concept of achieving a superior, racially pure group was an extension of the eugenics movement. Some historians feel that the Third Reich had modeled their early sterilization program after those that had become common in the United States. Initially applied to individuals considered socially and physically defective, the underlying rationale of negative eugenics was soon applied to entire ethnic groups, including Jews and Gypsies. Fueled by various forms of racial prejudice, Adolf Hitler and the Nazi regime took eugenics to its extreme by instituting policies aimed at the extinction of these "impure" human populations. The deplorable disregard for human life was preceded by incremental policies involving forced sterilization and mercy killings. This movement, based on scientifically invalid premises, culminated in the mass murder of the Holocaust.

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*See *The sterilization of Carrie Buck* by J. D. Smith and K. R. Nelson, in the Selected Readings section.

Even before the Nazi party came to power in 1933, English and American geneticists began separating themselves from the eugenics movement. They were concerned about the validity of the premises underlying the movement and the evidence in support of these premises. Thus, many geneticists chose not to study human genetics for fear of being grouped with those who supported eugenics.

However, since the end of World War II, tremendous strides have been made in human genetics research. Today, a new term, **euphenics**, has replaced eugenics. Euphenics refers to medical or genetic intervention designed to reduce the impact of defective genotypes on individuals. The use of insulin by diabetics and the dietary control of newborn phenylketonurics are longstanding examples. Today, "genetic surgery" to replace defective genes looms clearly on the horizon. Furthermore, social policies now have a solid genetic foundation on which they may be based. Nevertheless, caution is still required to ensure that our expanded knowledge of human genetics does not obscure the role played by the environment in determining an individual's phenotype.

Genetic Advances in Agriculture and Medicine

As a result of research in genetics, major benefits have accrued to society in the fields of agriculture and medicine. Although the cultivation of plants and domestication of animals had begun long before, the rediscovery of Mendel's work in the early 20th century spurred scientists to apply genetic principles to these human endeavors. The use of selective breeding and hybridization techniques has had the most significant impact in agriculture.

Plants have been improved in four major ways: (1) enhanced potential for more vigorous growth and increased yields; (2) increased resistance to natural predators and pests, including insects and disease-causing microorganisms; (3) production of hybrids exhibiting a combination of superior traits derived from two different strains (often illustrating the genetic phenomenon of hybrid vigor), or even between two different species (Figure 1–15); and (4) selection of genetic variants with desirable qualities such as increased protein value, increased content of limiting amino acids, which are essential in the human diet, or smaller plant size, reducing vulnerability to adverse weather conditions.

Over the past five decades, these improvements have resulted in a tremendous increase in yield and nutrient value in such crops as barley, beans, corn, oats, rice, rye, and wheat. It is estimated that, in the United States, the use of improved genetic strains has led to a threefold increase in crop yield per acre. In Mexico, where corn is the staple crop, the plant's protein content and yield have increased significantly. A substantial effort has also been made to improve the growth of Mexican wheat. Led by Norman Borlaug, a team of researchers developed varieties of wheat that incorporated favorable genes from other strains found in various parts of the world, revolutionizing wheat production in Mexico and other underdeveloped countries. Because of this effort, which led to the well-publicized "Green Revolution," Borlaug received the Nobel Peace Prize in 1970. There is little question

FIGURE 1–15 *Triticale*, a hybrid grain derived from wheat and rye, produced as a result of applied genetic research breeding experiments. (*Grant Heilman/Grant Heilman Photography, Inc.*)

that this application of genetics, which continues even today, has contributed greatly to the well-being of our own species by improving the quality of nutrition worldwide.

Applied research in genetics has also resulted in the development of superior breeds of livestock (Figure 1–16). Selective breeding has produced chickens that grow faster, yield more high-quality meat per chicken, and lay a greater number of larger eggs. In larger animals, including pigs and cows, the use of artificial insemination has been particularly important. Sperm samples derived from a single male with superior genetic traits can now be used to fertilize thousands

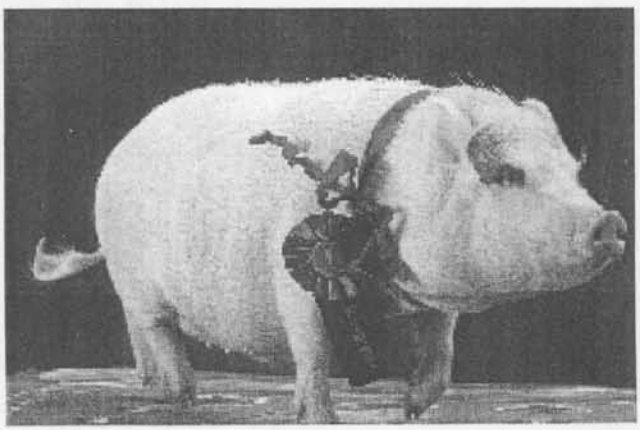

FIGURE 1–16 The effects of breeding and selection, as illustrated by the production of this Vietnamese potbellied pig. (*Renee Lynn/Photo Researchers, Inc.*)

perils of this new technology. GM foods have been developed and marketed so quickly that there has been little time for research on long-term medical or ecological effects of each genetically engineered crops. If this new genetic technology is to deliver benefits as promised, we need time to address the scientific, ethical, and political questions that surround it.

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"Living in a GM World" (a compilation of articles on GM crops and biotechnology). *New Scientist* Web site: http://www.newscientist.com/gm/gm.jsp

of females located in all parts of the world. More recently, at the extreme edge of biotechnological application, champion livestock, such as cows, are being cloned in order to ensure that the specific gene combinations associated with economically superior animals are preserved.

Equivalent strides have been made in medicine as a result of advances in genetics, particularly since 1950. Numerous disorders in humans have been discovered to result from either a single mutation or a specific chromosomal abnormality (Figure 1–17). For example, the genetic basis of disorders such as sickle-cell anemia, erythroblastosis fetalis, cystic fibrosis, hemophilia, muscular dystrophy, Tay–Sachs disease, Down syndrome, and many metabolic disorders is now well documented and often understood at the molecular level. The importance of acquiring knowledge of inherited disorders is underscored by the estimate that more than 10 million children or adults in the United States suffer from some form of genetic affliction and that every childbearing couple stands an approximately 3 percent risk of having a child with some form of genetic anomaly.

Additionally, it is now apparent that all forms of cancer have a genetic basis. Although cancer is not usually an inherited disorder, it is now very clear that *cancer is a genetic disorder at the somatic cell level.* That is, most cancers are derived from somatic cells that have undergone some type of genetic change; malignant tumors are then derived from the genetically altered cell. In some cases, a genetic predisposition to cancer also exists.

The recognition of the molecular basis of human genetic disorders and cancer has provided the impetus for the development of methods for detection and treatment. Based on advances in molecular genetics, particularly in the manipulation and analysis of DNA, prenatal detection of affected fetuses has become routine. Parents can also learn of their status as "carriers" of a large number of inherited disorders. Genetic counseling gives couples objective information on which they can base informed decisions about childbearing. In the case of cancer, recent genetic discoveries have already led to more effective early detection and more efficient treatment.

Applied research in genetics has also provided other medical benefits. Advances in immunogenetics have made possible compatible blood transfusions as well as organ transplants. In conjunction with immunosuppressive drugs, the number of successful transplant operations involving human organs, including the heart, liver, pancreas, and kidney, are increasing annually.

The most recent advances in human genetics have been dependent on the application of DNA biotechnology. First developed in the 1970s, recombinant DNA techniques paved the way for manipulating and cloning a variety of genes, including those that encode many medically important molecules, such as insulin, blood-clotting factors, growth hormone, and interferon. Human genes are isolated and spliced into vectors and transferred to host cells that serve as "production centers" for the synthesis of these proteins.

Recombinant DNA techniques have now been extended considerably. The DNA of any organism of interest can be routinely manipulated in the laboratory. The human genes responsible for inherited disorders, such as cystic fibrosis and Huntington disease, have been identified, isolated, cloned, and studied. It is hoped that such research will pave the way for gene therapy, whereby genetic disorders are treated by inserting normal copies of genes into the cells of afflicted individuals.

Perhaps the most far-reaching use of DNA biotechnology involves the Human Genome Project, in which the DNA sequence of the genome of several species, including our own, has been determined. The genomic sequence of several bacterial species, as well as that of yeast, the fruit fly, the mustard plant (*Arabidopsis*), the round worm (*Caenohabditis elegans*), and our own species is now known.

In later chapters, the applications of DNA biotechnology to agriculture and medicine are discussed in greater detail. Although other scientific disciplines are also expanding in knowledge, none has paralleled the growth of information that is occurring in genetics. As we pointed out at the outset of this chapter, while there never has been a more exciting time to be immersed in the study of genetics, the potential impact of this discipline on society has never been more profound. By the end of this course, we are confident you will agree that the present truly represents the "Age of Genetics."

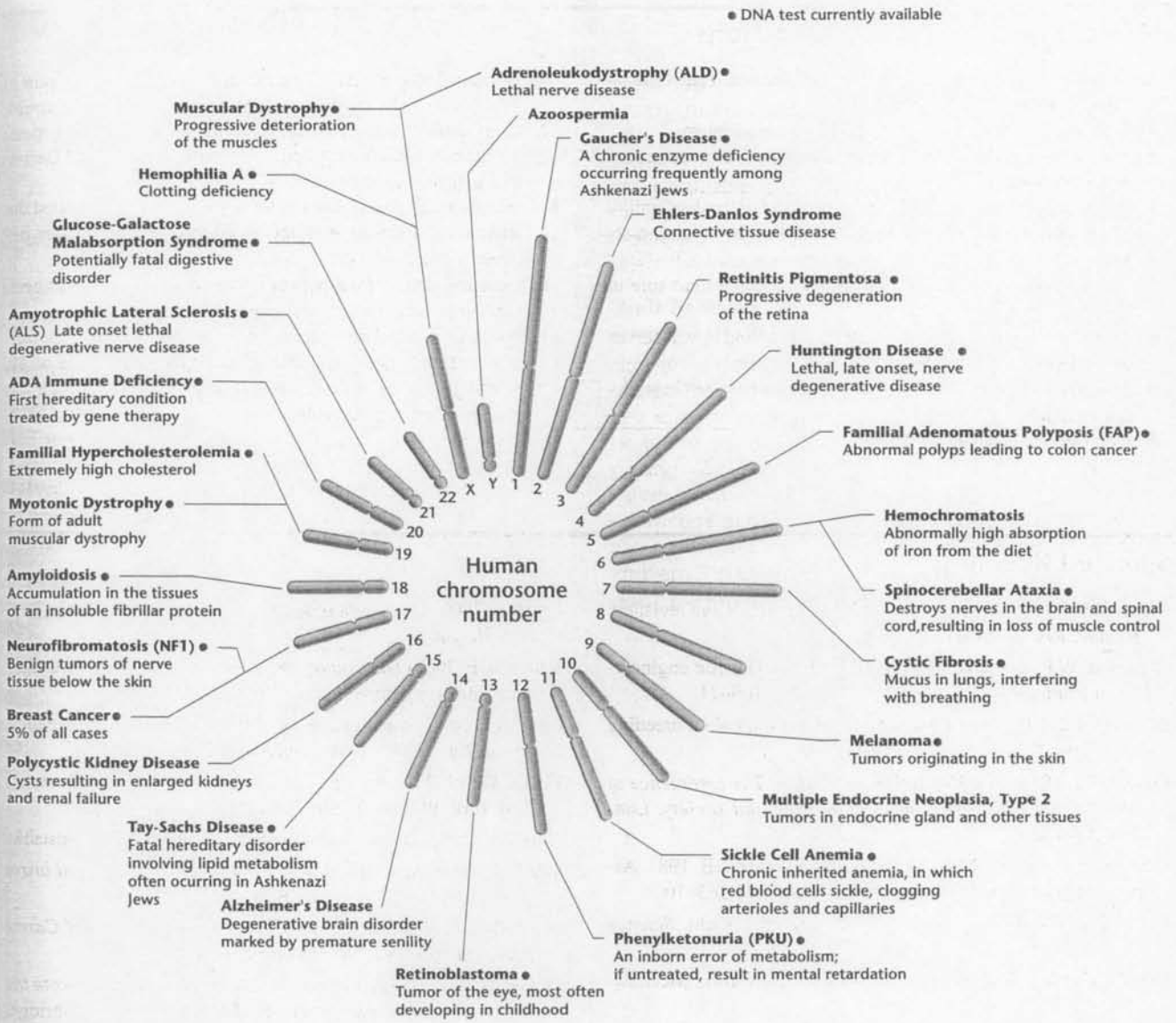

FIGURE 1–17 The chromosomes of a human being, showing the location of genes whose abnormal forms cause some of the better known hereditary diseases. Those inherited conditions that can be diagnosed using DNA analysis are indicated by a (●).

Chapter Summary

1. The history of genetics, which emerged as a fundamental discipline of biology early in the 20th century, dates back to prehistoric times.
2. Genes and chromosomes are the fundamental units in the chromosomal theory of inheritance, which explains the transmission of genetic information controlling phenotypic traits.
3. Molecular genetics, based on the general paradigm that DNA makes RNA which makes protein, serves as the underpinnings of the more classical work referred to as transmission genetics.
4. The four investigative approaches most often used in the study of genetics are (1) transmission genetic studies, (2) cytogenetic analyses, (3) molecular experimentation, and (4) inquiries into the genetic structure of populations.
5. Genetic research can be either basic or applied. Basic genetic research extends our knowledge of the discipline; the objective of applied genetics research is to solve specific problems affecting the quality of our lives and society in general.
6. Eugenics, the application of the knowledge of genetics for the improvement of human existence, has a long and controversial history. Euphenics, genetic intervention designed to ameliorate the impact of genotypes on individuals, represents the modern eugenic approach.
7. Genetic research has had a highly positive impact on many facets of agriculture and medicine.
8. DNA biotechnology is greatly expanding our research capability. It has also had a profound impact on the elucidation of inherited diseases, has made possible the mass production of medically important gene products, and will serve as the foundation on which gene therapy is developed.