The Scope of Modern Genetics CHAPTER 1

Genetics plays a central role in modern society. Googling "genetics" on a typical day in the early twenty-first century reveals that during the previous week:

- Scientists discover new genetic link to Alzheimer's disease
- Genetic map points way to a better soybean
- Genetic evidence snares man over unsolved rape

These news stories illustrate the scope of genetics in today's world. Genetics is enabling diseases to be cured or treated so the patient's quality of life is improved. Genetics is the key to improving the nutritional value and productivity of the world's crops. And genetics can even catch criminals. It is no surprise that genetics has been described as the most living of the life sciences.

1.1 WHAT IS GENETICS?

Genetics is the study of **heredity**, the process by which characteristics are passed from parents to offspring so that all organisms, human beings included, resemble their ancestors. The central concept of genetics is that heredity is controlled by a vast number of factors, called **genes**, which are physical particles present inside living cells.

Genes are units of **biological information**. The entire complement of genes in an organism contains the total amount of information needed to construct a living, functioning example of that organism. Some genes are responsible for the visible characteristics of the organism, such as eye color in humans. Other genes are responsible for biochemical activities that are discernible only when the physiology of the organism is examined. Often, we become aware of the function of such genes only when they fail to work properly. An example is the human gene *CFTR*, which contains part of the biological information for transport of chloride ions into and out of cells. If the *CFTR* gene is defective, then chloride transport breaks down, leading to inflammation and mucus accumulation in the lungs. These are the primary symptoms of the disease called cystic fibrosis, and it was through study of the underlying cause of cystic fibrosis that the *CFTR* gene was first discovered. CFTR in fact stands for "cystic fibrosis transmembrane regulator," a term describing the biological information contained in this gene.

Because genes are units of biological information they are also units of **inheritance**. During **sexual reproduction**, genes of the parents are incorporated into the fertilized egg cell. These genes provide the fertilized egg with the full complement of biological information that it needs in order to develop into a new living organism. This new organism therefore inherits physical and biochemical characteristics from both its parents.

An understanding of genetics therefore requires an understanding of genes. The purpose of this book is to help you to acquire that understanding.

Genes are units of biological information

The first topic we will study is the most fundamental of all. How is biological information stored in genes? This problem perplexed early geneticists during the first part of the twentieth century, and it was not until the 1950s that the first step in solving the puzzle was made when it was discovered

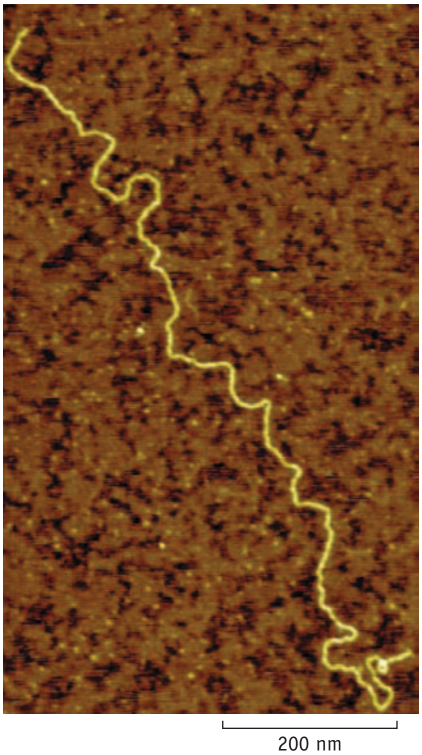

FIGURE 1.1 A molecule of DNA from the yeast *Saccharomyces cerevisiae*, visualized by atomic-force microscopy. (Courtesy of Jim de Yoreo, Lawrence Berkeley National Laboratory. This work was published in R. W. Friddle, J. E. Klare, S. S. Martin et al., *Biophys. J.* 86: 1632–1639, 2004.)

that genes are made of **DNA** (Figure 1.1). Our exploration of genetics must therefore start with DNA. In Chapter 2 we will study the structure of DNA and investigate how this structure enables DNA molecules to contain, in the form of a four-letter language made up of A, C, G, and T, the instructions for making a living organism (Figure 1.2).

Understanding the structure of DNA is, however, only the first step in understanding how biological information is contained in genes. When we start to look more closely at the structures of individual genes we realize that DNA contains different types of biological information, with genes specifying characteristics such as eye color and ability to transport chloride ions into and out of cells falling into just one category. There are also regulatory genes, genes that control the activities of other genes. One particular type of regulatory gene was not discovered until the 1990s. There are also genes that contain no biological information. These are thought to be evolutionary relics, genes that were once active but are no longer needed by the organism. Another complication in our study of genes is that in some genes the biological information is split into segments and the segments can be combined in different ways to alter the message being sent to the cell. We will examine all of these aspects of gene structure in Chapter 3.

The biological information in genes is read by the process called gene expression

By studying DNA and genes we will understand what is currently known about the way in which biological information is stored. The next question we must address is how this information is made available to the cell. How, for example, is the biological information in the *CFTR* gene read so that the cell can actually move chloride ions across cell membranes?

The transfer of biological information from gene to cell is called **gene expression** (Figure 1.3). For all genes, the process begins with the transfer of information from a DNA molecule into an **RNA** molecule. In Chapter 4 we will discover that DNA and RNA are very similar types of molecule and that this step of gene expression, called **transcription**, is quite straightforward in chemical terms. We will also learn that the RNA molecules that are made by transcription fall into different groups based on their function. Some RNA molecules are short-lived messengers that direct the second stage of gene expression, in which the gene's biological information, now contained in its RNA molecule, is used to direct the synthesis of a protein. This type of RNA is called **messenger RNA** (**mRNA**), and we will study its structure, and how it is prepared for its role in protein synthesis, in Chapter 5. Other RNA molecules, over 90% of all those that are made by

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TGTTGCAACAGTGCCAGTGATAGTGGCTTTTATTATGTTGAGAGCATATTTCCTCCAAAC
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AAAGGAAACTATATTACAAAGTACACATGGATTTTTTTTCTTAATTAATGACCATGTGAC
TTCATTTTGGTTTTAAAATAGGTATATAGAATCTTACCACAGTTGGTGTACAGGACATTC
ATTTATAATAAACTTATATCAGTCAAATTAAACAAGGATAGTGCTGCTATTACTAAAGGT
TTCTCTGGGTTCCCAAATGATACTTGACCAAATTTGTCCCTTTGGCTTGTTGTCTTCAGA
CACCCTTTCTTCATGTGTTGGAGCTGCCATTTCGTGTGCCCCCAAACTCTACTTGAGCTG
TTAGGGAATCACATTTTGCAGTGACAGCCTTAGTGTGGGTGCATTTTCAGGCAATACTTT
TTCAGTATATTTCTGCTTTGTAGATTATTAGCTAAATCAAGTCACATAAACTTCCTTAAT
TTAGATACTTGAAAAAATTGTCTTAAAAGAAAATTTTTTTAGTAAGAATTAATTTAGAAT
TAGCCAGAAAACTCCCAGTGGTAGCCAAGAAAGAGGAATAAATATTGGTGGTAATTTTTT
AAGTTCCCATCTCTGGTAGCCAAGTAAAAAAAGAGGGTAACTCATTAATAAAATAACAAA
TCATATCTATTCAAAGAATGGCACCAGTGTGAAAAAAAGCTTTTTAACCAATGACATTTG
TGATATGATTATTCTAATTTAGTCTTTTTCAGGTACAAGATATTATGAAATTACATTTTG

FIGURE 1.2 Part of the DNA sequence of the human *CFTR* gene. The biological information contained in DNA is in the form of a language made up of the letters A, T, G, and C. The entire *CFTR* gene contains 4443 letters, of which 1020 are shown here.

transcription, are the end products of gene expression and perform their own functions in the cell. Two important types, **ribosomal RNA** (**rRNA**) and **transfer RNA** (**tRNA**), are involved in converting the information carried by the mRNAs into protein. We will look at the features of rRNA and tRNA in Chapter 6, and then in Chapters 7 and 8 we will examine exactly how these two types of RNA work together to synthesize proteins by **translation** of the mRNAs.

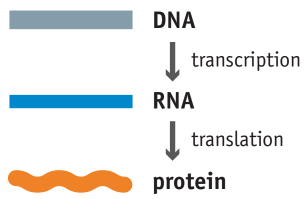

FIGURE 1.3 Gene expression. In its simplest form, gene expression can be looked on as a two-step process. The first step is the transcription of DNA into RNA, and the second step is the translation of some of the RNA molecules into proteins.

The expression of individual genes can be switched on and off

The entire complement of genes in a single cell represents a staggering amount of biological information. The information carried in some genes is needed by the cell at all times, but other genes have more specialized roles. Gene expression can therefore be controlled so that only those genes whose units of biological information are needed are active at any particular time.

Even the simplest organisms are able to control the expression of their genes in order to respond to changes in the environment. Many bacteria, for example, deal with sudden increases in temperature by switching on a set of genes whose protein products help to protect the cell from damage (**Figure 1.4**). In multicellular organisms, individual cells change their gene expression patterns in response to hormones, growth factors, and other regulatory molecules. Chemical signals between cells are therefore able to coordinate the activities of groups of cells in a manner that is beneficial to the organism as a whole.

In Chapter 9, we will study the way in which gene expression is controlled. We will learn that gene regulation involves more than simply switching genes on and off. It is also necessary to modulate the rates of expression of those genes that are switched on. We will discover that, in response to these complex requirements, a myriad of different ways of controlling gene expression have evolved, but that the most important of these acts at the very beginning of the gene expression pathway, by controlling whether or not a gene is transcribed into RNA.

Genes are also units of inheritance

In Part II we will study how genes act as units of inheritance. We might think that this simply involves sexual reproduction, but that is only part of the story. The much more frequent type of reproduction is the division of a parent cell into two daughters (**Figure 1.5**). This is the type of reproduction that gives rise to the vast majority of cells in the human body, with

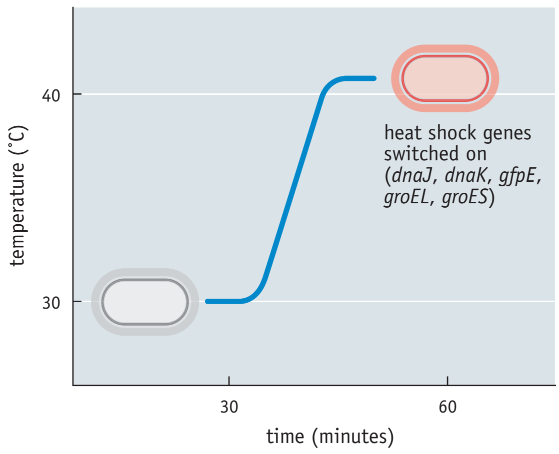

FIGURE 1.4 The heat shock response of a bacterium such as *Escherichia coli*. An increase in temperature from 30°C to 42°C results in the switching on of genes such as *dnaJ* and *dnaK*. The proteins coded by these genes help to protect the cell from damage.

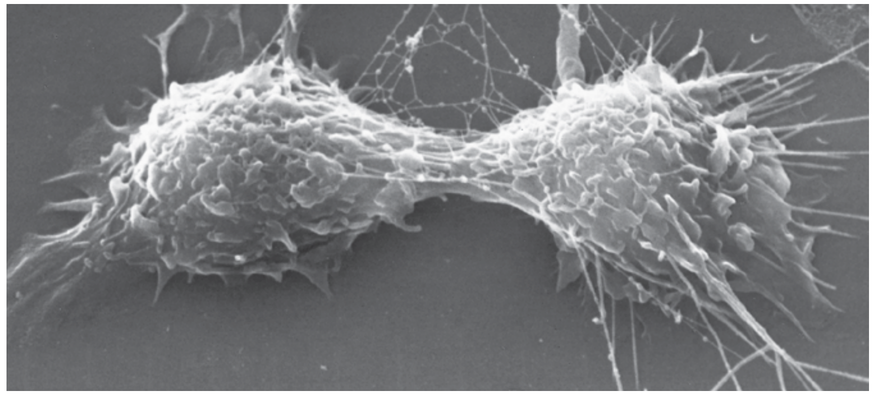

FIGURE 1.5 Cell division. This picture was taken with a scanning electron microscope and shows an animal cell in the final stages of cell division. (Courtesy of Guenter Albrecht-Buehler, Northwestern University.)

10^{17} divisions needed to produce all the cells needed by a human being during its lifetime. It is also the way that, for example, bacteria reproduce. During each of these cell divisions, a complete set of genes must be passed from the parent to both of the two daughter cells. Any error would be disastrous, as it would give rise to a lineage of cells that possessed an incomplete or altered complement of the organism's biological information. We must therefore begin our study of genes as units of inheritance by investigating how genes are inherited during cell division.

Our first task will be to understand how genes are replicated. If one cell divides into two, then clearly a copy has to be made of every gene. Because genes are made of DNA, the key to making copies of genes lies with the replication of DNA molecules. When we examine DNA in Chapter 2 we will see that the structure of a DNA molecule provides an obvious means for its replication, and that recognition of this fact was the "eureka" moment that convinced geneticists that genes are made of DNA. In Chapter 10, we will study the replication process in more detail. First, we will look at the overall pattern of replication and ask how a single DNA molecule can give rise to two identical daughter molecules. Then we will study the biochemistry and enzymology of DNA replication. What proteins are involved and how are the new DNA molecules synthesized?

By studying replication of DNA we do not, however, fully explain how genes are inherited by daughter cells during cell division. We must also understand how a full set of the replicated DNA molecules is passed to the daughter cells. This requires that we study how DNA molecules are organized inside the cells of different types of organism, and how replication of the DNA is coordinated with division of the cell. In Chapter 11 we will do this for the inheritance of genes during cell division in humans and other higher life forms, and in Chapter 12 we will look at the equivalent, but very different, processes that underlie inheritance of genes by bacteria. We must also, in Chapter 13, explore the extremely different mechanisms by which viruses pass their genes on to their progeny during their infection cycles.

Children inherit genes from their parents

Once we have a firm grasp of the events occurring during cell division, we can move with confidence to the complexities posed by the inheritance of genes during sexual reproduction.

Sexual reproduction is preceded by a specialized type of cell division that produces the male and female sex cells. One male and one female cell then fuse to give a fertilized egg, which then develops into a new version of the organism (Figure 1.6). To understand this process, we must answer two

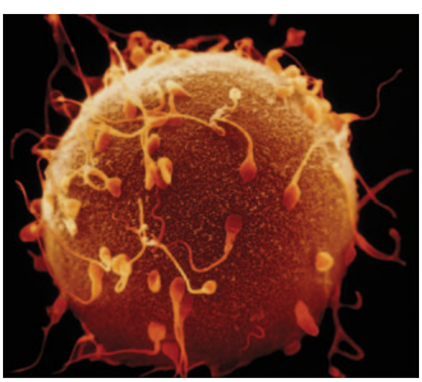

FIGURE 1.6 Fertilization of a female human egg cell. This scanning electron micrograph shows that many sperm cells attach to the outer surface of an egg, but only one will actually fertilize it. (Courtesy of D. Phillips/Science Photo Library.)

questions. First, how are DNA molecules inherited during sexual reproduction? In Chapter 14 we will follow through the steps in sexual reproduction and understand what happens to the DNA molecules at each stage. We will discover that, unlike the type of cell division that occurs during asexual reproduction, the formation of sex cells does not involve simply the replication of DNA molecules and the passage of the daughter molecules into the new cells that are formed when the parent cell divides. Sexual reproduction is more complicated because it also provides an opportunity for DNA molecules to exchange segments by **recombination** (Figure 1.7). We will study how recombination occurs and investigate the effects that it has on the structures of the DNA molecules inherited by the offspring that result from sexual reproduction.

The second question we must answer concerns the inheritance of genes rather than DNA molecules. A child is not an exact image of its mother or father, but instead a composite of the two parents—"she has her mother's eyes". This means that brothers and sisters are not identical, but they share a family resemblance (Figure 1.8). The same is true for all organisms that reproduce sexually. In all of these species the offspring inherit features from both of the two parents. In Chapter 15 we will investigate the ways in which the genes inherited from the two parents interact in the offspring, and how these interactions give rise to the particular set of characteristics displayed by an individual that results from sexual reproduction.

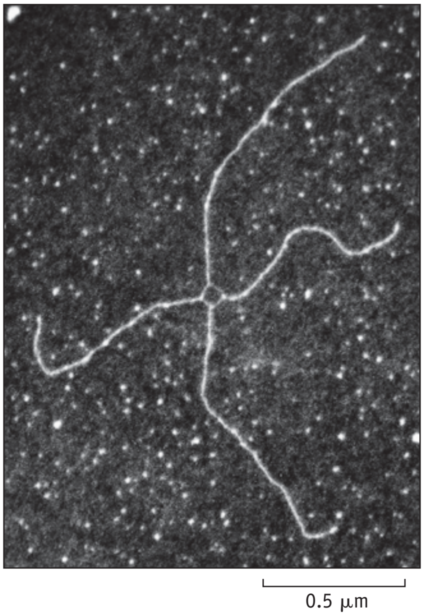

FIGURE 1.7 Two DNA molecules that have attached to one another in order to exchange segments by recombination. (Courtesy of Huntington Potter, University of South Florida, and David Dressler.)

The inheritance of genes underlies evolution

There remains one final topic that we must investigate to complete our study of genes as units of inheritance. How do genes change over time? We know that DNA molecules can undergo structural alterations, called **mutations**. These may be caused by various chemicals present in the environment, or may be brought about, for example, by physical agents such as ultraviolet radiation from the sun. Many mutations are repaired by the cell soon after they occur, but a few slip through, which means that the DNA molecules that are passed to the offspring are not always precise copies of the parental molecules. Sometimes a mutation occurs within a gene, possibly causing a subtle change to the biological information contained in that gene (Figure 1.9).

In Chapter 16 we will investigate the various ways in which mutations can occur, and the mechanisms that cells have for correcting them. We will also look at the effects that a mutation can have on a gene, and in Chapter 17

FIGURE 1.8 Members of a single family share biological characteristics and so look similar to one another. The Corrs are an Irish folk-rock band made up of three sisters—Andrea, Sharon, and Caroline—and their brother Jim. Their family resemblance is clear. (Photo by Dave Hogan/Getty Images.)

FIGURE 1.9 A mutation can change the biological information contained in a gene. On the left is a wild ear of wheat and on the right is an ear of domesticated wheat. The difference between the two is that the wild ear shatters when it becomes mature, so the seeds break away and fall to the ground. In domestic wheat, the ear does not shatter, so the seeds stay attached to the plant, making it easier to collect them. The nonshattering ear is caused by a single mutation in a gene whose biological information specifies the rigidity of the structure that attaches the seed to the ear. (Courtesy of George Willcox, Université de Lyon II. From K. Tanno and G. Willcox *Science* 311: 1886, 2006. With permission from AAAS.)

we will examine the possible fate of the new versions of genes that arise in this way. To do this we will have to investigate how genes are inherited not by individuals but by populations. We will discover that the genetic features of a population can change over time, and that the cumulative effect of these changes, called **microevolution**, underlies the processes by which new species arise.

1.2 GENETICS IN OUR MODERN WORLD

We began this chapter with three headlines illustrating the importance of genetics in today's society. In Part III we will explore some of the areas of research that are responsible for the high profile that genetics has in our modern world.

The first topic that we will study is the role of genes in development. How do genes control the pathway that begins with a fertilized egg cell and ends with an adult organism? Finding the answer to this question is one of the biggest challenges in all of genetics. In Chapter 18 we will learn that advances in understanding developmental processes in humans have been made by studying **model organisms** such as the fruit fly, *Drosophila melanogaster* (**Figure 1.10**). Although the developmental pathway for a fruit fly is much simpler than that of a human, the important genes that control development are very similar in both types of organism. Through use of model organisms, and the combined endeavors of geneticists, cell biologists, physiologists, and biochemists, our knowledge of development has made great leaps forward in recent years.

FIGURE 1.10 The fruit fly *Drosophila melanogaster*. The fruit fly is an important model organism for research in many areas of biology, including genetics. (Courtesy of Nicolas Gompel, Institut de Biologie du Développement de Marseille-Luminy.)

Most of us share the opinion that our own species is the most important on the planet. Chapters 19 through 21 are therefore devoted to the genetics of *Homo sapiens*. In Chapter 19 we will study the human **genome** (**Figure 1.11**). This is the entire complement of DNA molecules in a human cell, containing all our genes and therefore all the biological information needed to make a human being. What genes do we possess, how are they arranged, and how do they make us special when compared, for example, with a chimpanzee?

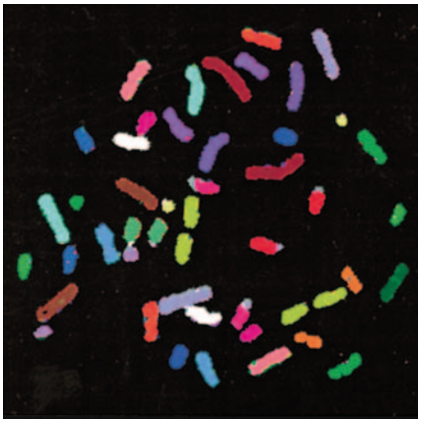

FIGURE 1.11 The human genome. The DNA molecules that make up our genome are contained in a set of chromosomes, which are shown here. Each chromosome has been "painted" a different color so the individual ones can be identified when observed with the light microscope. The painting is carried out with fluorescent dyes designed so that a different dye binds to each chromosome. (From E. Schröck, S. du Manoir, T. Veldman et al., *Science* 273: 494–497, 1996. With permission from AAAS.)

Probably the most important way that genetics is used to benefit humankind is in medical research. Over 6000 **inherited diseases** are known, diseases that are caused by defects in the genome and which, like other genetic features, can be passed from parents to offspring. Approximately 1 in every 200 children who are born suffer from one or another of these disorders. Other diseases, including many cancers, also result from malfunctioning of one or more genes. In Chapter 20 we will look at the progress that geneticists are making in understanding these diseases and devising ways of treating them.

How is genetics used to catch criminals? In Chapter 21 we will examine how genetic profiles are obtained and why these have become so important in forensic biology. We will also learn how similar techniques enable geneticists to study human evolution and to trace the routes taken by early humans as they migrated out of Africa and colonized the globe.

Genetics also has applications in industry and agriculture. Important proteins that are needed to treat diseases, or which have other industrial applications, can be synthesized in large amounts by transferring the gene that codes for the protein into a bacterium or other type of microorganism. Insulin, the protein that is used to treat diabetes, is a good example. The human insulin gene has been transferred to *Escherichia coli*, and these genetically engineered bacteria are now used as a cheap means of producing insulin for use by diabetics (**Figure 1.12**). Genetic engineering is also being used to create improved crops, ones that give higher yields or have higher nutritional values (**Figure 1.13**). These industrial and agricultural applications of genetics are covered in Chapter 22.

FIGURE 1.12 Part of an industrial plant for the production of human insulin from genetically engineered *Escherichia coli* bacteria. (Photo by Felix Denis. With permission from Sanofi-Aventis.)

FIGURE 1.13 Golden rice, on the right, compared with white rice. Golden rice has been genetically modified to synthesize increased amounts of β-carotene, a precursor of vitamin A. Golden rice is designed for consumption in parts of the world where people suffer from vitamin A deficiency. (Courtesy of Golden Rice Humanitarian Board [www.goldenrice.org].)

Each of these applications of genetics raises ethical issues that we must not ignore. It might be possible one day to eradicate inherited diseases by **gene therapy**, in which the defective gene is taken out of the patient's genome and replaced by the correct, functioning gene. But the same technology might be used to replace genes that are not defective with "better" ones, to produce "designer" babies. Genetic profiles are a powerful means of catching criminals, but does that mean that everybody's genetic profile should be stored on an international database? Genetically modified crops might have higher yields and better nutritional qualities, but could they be harmful to the environment? We will attempt to tackle these ethical issues in Chapter 23.

KEY CONCEPTS

- Genetics is the study of heredity. Heredity is the process by which characteristics are passed from parents to offspring so that all organisms resemble their ancestors.
- Heredity is controlled by genes. Genes are physical particles present inside living cells.
- Genes are units of biological information. The entire complement of genes in an organism contains the total amount of information needed to construct a living, functioning example of that organism.
- Genes are also units of inheritance. The transmission of genes from parents to offspring ensures that those offspring inherit the biological characteristics of their parents.
- Genetics is having a huge impact in our modern world. It has important applications in medicine, industry, forensics, and agriculture.
- As students of genetics, we must be aware of the ethical issues raised by some of the ways in which genetics is being applied in today's world.